Synthesis and reactions of *p*-hydroxythiobenzamides

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Abstract
Ethoxycarbonyl isothiocyanate reacted with phenols in a nitromethane solution of aluminum chloride to yield the appropriate 4-hydroxy-*N*-ethoxycarbonylthiobenzamides. In the reaction with dinucleophiles they gave heterocyclic compounds which were subsequently functionalized on the hydroxy group. The reaction of *p*-hydroxythiobenzamides with carbamoyl chloride, chlorides of α,β-unsaturated carboxylic acids, and isocyanates yielded the corresponding *O*-acylated products.

Keywords: Ethoxycarbonylisothiocyanate, 4-hydroxythiobenzamides, Friedel-Crafts thiocarbamoylation, heterocyclization

Introduction

Thioamides have been known for more than one hundred years but owing to their high practical utility and synthetic versatility they still attract the attention of researchers. In particular, many interesting articles on the functionalization of thioamides and their synthetic importance in the regio- and stereoselective heterocyclization reactions have been published in the last decades. The recent advances in thioamide chemistry were detailed in a comprehensive review a few years ago.[1]

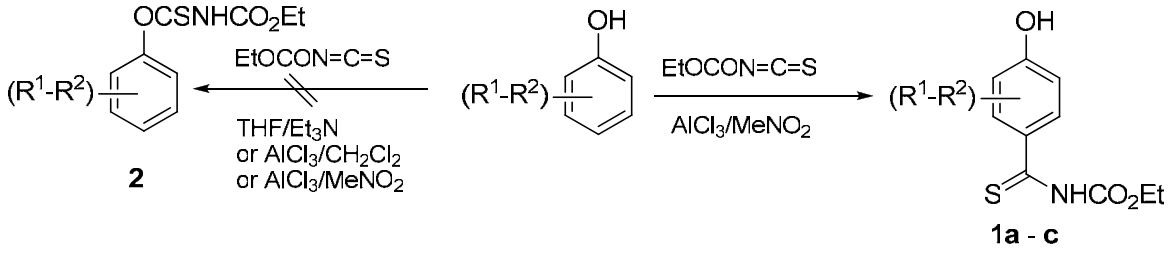
Most methods for the preparation of thioamides make use of the reaction of amide thionation with the aid of phosphorus pentasulfide or the Lawesson's reagent [2,3]. Although this synthetic route appears to be rather easy, it is often limited by low availability of the appropriate amide. In order to overcome this difficulty we have developed a very simple synthetic approach to thioamides in a direct reaction of isothiocyanates with aromatic [4,5] and heteroaromatic compounds [6,7] in the presence of Lewis acids, that means in a modification of the Friedel-Crafts reaction. The preparative value of this method prompted us to make an attempt at elucidating its mechanism, in particular to explain the increased activity of isothiocyanates in the presence of Lewis acids.[6] Since some heteroaromatic substrates showed poor stability in a strong acid medium we have also developed an alternative method depending on the reaction of their metallo-organic derivatives with isothiocyanates.[8-10] In the present research we used the readily

available *p*-hydroxythiobenzamides as the starting compounds in the reactions leading to functionalization of the *p*-hydroxyphenyl and thioamide groups.

Results and Discussion

Depending on the reaction conditions and on the structure of the phenol substrate different products may be formed in the reaction with ethoxycarbonyl isothiocyanate. As it is known, in the case of sodium phenolate this reagent caused only ethoxycarbonylation of the hydroxy group; the expected formation of a thiourethan **2** was not observed.[11] When the procedure developed by Papadopoulos[12] for the reactions of ethoxycarbonyl isothiocyanate with aromatic hydrocarbons was adapted under the conditions of heterogeneous catalysis (aluminum chloride, dichloromethane), only traces of **1a** could be found in the products of the reaction of ethoxycarbonyl isothiocyanate with phenol. However, **1a-c** were obtained in the homogeneous catalysis reaction (aluminum chloride, nitromethane) analogous to that we have reported earlier for aromatic compounds[4,5] and thiophene derivatives.[6,7] There was no side-formation of the thiourethans **2**.

In our earlier investigations we have also found that phenols having an aliphatic *p*-substituent as well as the hydroquinone-derived compounds reacted with ethoxycarbonyl isothiocyanate in the *ortho* position but the initially formed *o*-hydroxy-*N*-ethoxycarbonylthiobenzamide spontaneously cyclized intramolecularly to yield a 4-thioxo-3,4-dihydrobenzo[e][1,3]oxazin-2-one derivative.[5] Moreover, it has been evidenced that boron trifluoride-acetic acid complex was a similarly effective catalyst in the reactions between isothiocyanates and phenols provided that the latter had an additional activating group. Although these reactions were slower, the yields of readily isolable high purity *N*-ethoxycarbonylthioamides were fairly high. However, not all phenols were capable of reacting in that way.



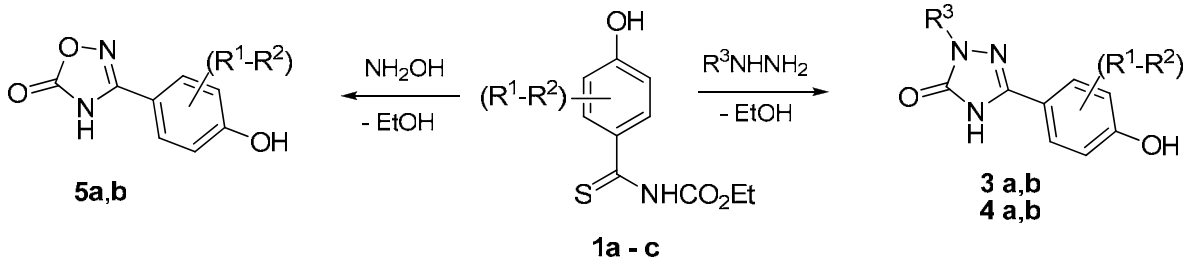
Scheme 1

Table 1. Physical data of compounds **1a-c**

Compound	Substituents		Yield [%]
	R^1	R^2	
1a	H	H	81
1b	2-CH_3	H	87
1c	3-CH_3	5-CH_3	84

N-Ethoxycarbonylthioamides are known as highly versatile starting compounds in the synthesis of heterocyclic systems.[5, 14-16] They react with dinucleophiles having a primary amine group to yield five-, six- and seven-membered heterocycles with the intermediate formation of *N*-ethoxycarbonylamidines.[14-16] Heterocyclization of the latter takes place as a result of the attack of the other nucleophilic group (NH_2, OH or SH) on the carbonyl or imine carbon atom with concomitant elimination of ethanol or urethan.

N-Ethoxycarbonylthiobenzamides **1a-c** were found to react in a similar way. When heated in ethanol with hydrazine, phenylhydrazine or hydroxylamine they yielded the 2-(4-hydroxyphenyl) derivatives of triazolones **3a**,**b** and **4a**,**b** and oxadiazolones **5a**,**b** (Scheme 2). Elimination of ethanol served as the evidence that the heterocyclization occured *via* the carbonyl carbon atom of the ester function.

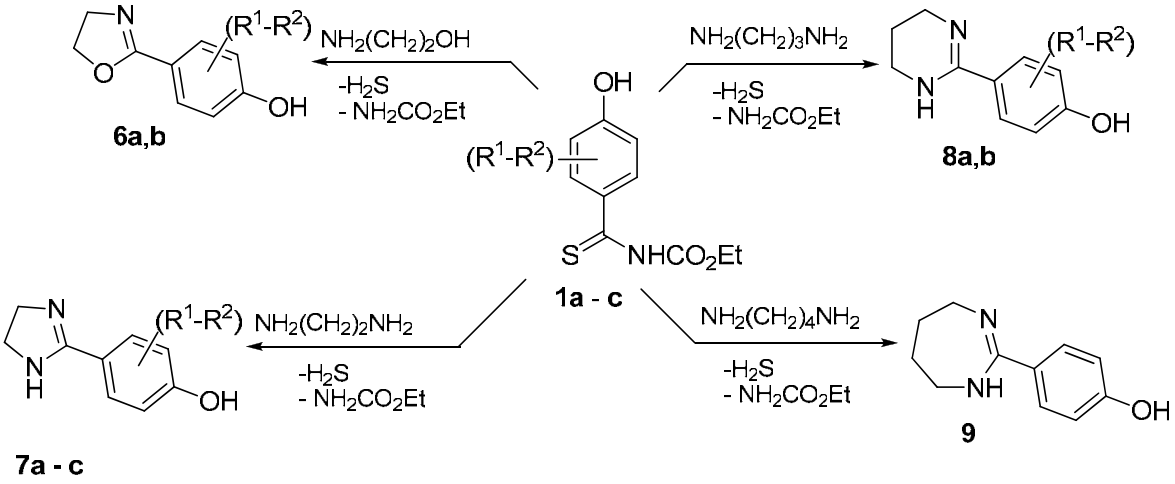


Scheme 2

Table 2. Physical data of compounds **3a-5b**

Compound	Substituents			Yield [%]
	R^1	R^2	R^3	
3a	H	H	H	98
3b	3-CH_3	5-CH_3	H	90
4a	H	H	Ph	94
4b	2-CH_3	H	Ph	97
5a	2-CH_3	H	-	95
5b	3-CH_3	5-CH_3	-	98

1,2-, 1,3-, And 1,4-dinucleophiles reacted with thiobenzamides **1a-c** in a much different way. Their heterocyclizations were accompanied by elimination of an urethan molecule and the reaction rate was rather low. The carbon atom of the thiocarbonyl group was here the single target of both nucleophilic centers. Thus, the reactions of 4-hydroxy-*N*-ethoxycarbonyl-thioamides **1a-c** with ethanolamine, ethylenediamine, 1,3-diaminopropane, and 1,4-diaminobutane gave, respectively, the derivatives of 4,5-dihydrooxazoles **6a**,**b**, 4,5-dihydroimidazoles **7a-c**, 1,4,5,6-tetrahydropyrimidines **8a**,**b**, and 4,5,6,7-tetrahydro-1*H*-[1,3]diazepine **9** (Scheme 3).

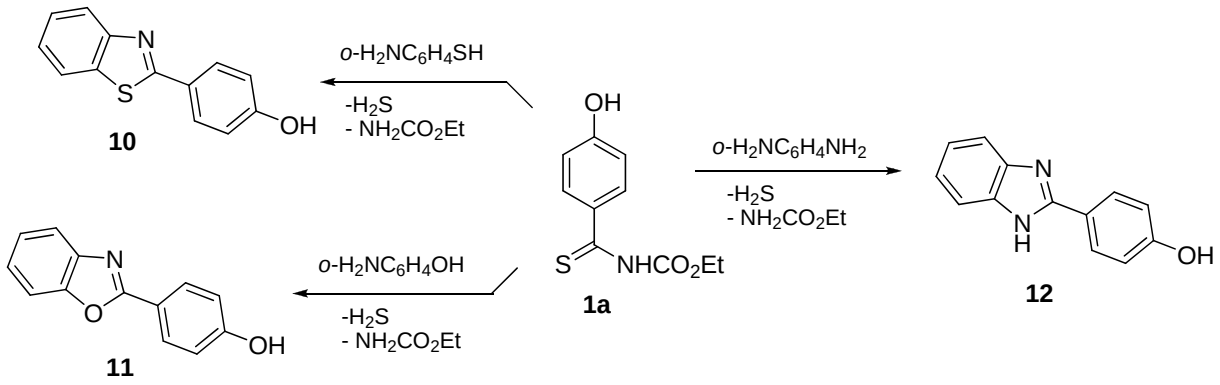


Scheme 3

Table 3. Physical data of compounds **6a-8a**

Compound	Substituents		Yield [%]
	R^1	R^2	
6a	H	H	95
6b	3-CH_3	5-CH_3	98
7a	H	H	85
7b	2-CH_3	H	68
7c	3-CH_3	5-CH_3	77
8a	H	H	65
8b	2-CH_3	H	50
9	H	H	46

The reactions with *o*-aminothiophenol, *o*-aminophenol, and *o*-phenylenediamine required more drastic conditions. An approximately 20-h refluxing in ethanol had to be used to convert them into the 4-hydroxyphenyl-substituted derivatives of, respectively, benzothiazole **10**, benzoxazole **11**, and benzimidazole **12** (Scheme 4).



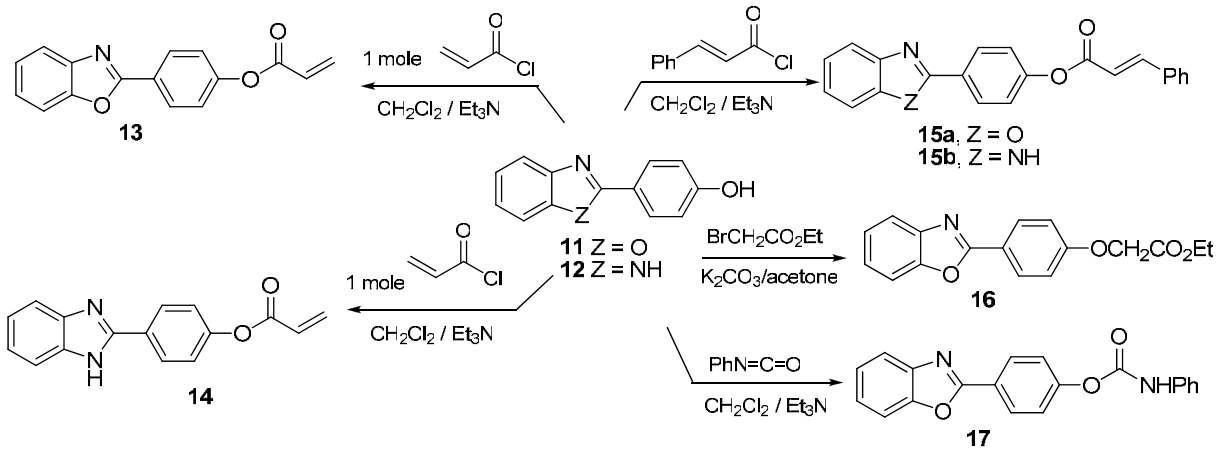
Scheme 4

Table 4. Physical data of compounds **10-12**

Compound	Substituents		Yield [%]
	R^1	R^2	
10	H	H	67
11	H	H	68
12	H	H	72

All heterocyclic compounds **3-12** have a *p*-hydroxyphenyl substituent capable of further functionalization. When the introduction of an ester or a carbamate function is considered a previous conversion of the thioamide **1** into a heterocycle seems to be a prerequisite. If these groups were present in the starting **1**, they would split off in the reactions with dinucleophiles. Some examples of the functionalization reactions are shown in Scheme 5. Thus, benzimidazole **12** was acylated by the highly reactive acryloyl chloride on the oxygen atom to yield the *O*-acryloyl derivative **14**. In an analogous reaction benzoxazole **11** yielded the *O*-acylated derivative **13**. Both **11** and **12** in the reaction with cinnamoyl chloride underwent acylation only on the phenol hydroxy group to yield **15a,b** irrespective of the amount of the acylating agent.

When benzoxazole **11** was made to react with ethyl bromoacetate in acetone in the presence of potassium carbonate only *O*-alkylation of the phenol hydroxy function took place to yield the ester **16**. In another reaction, the anionic form of **11** treated with phenyl isocyanate gave the corresponding phenylcarbamate **17** (Scheme 5).



Scheme 5

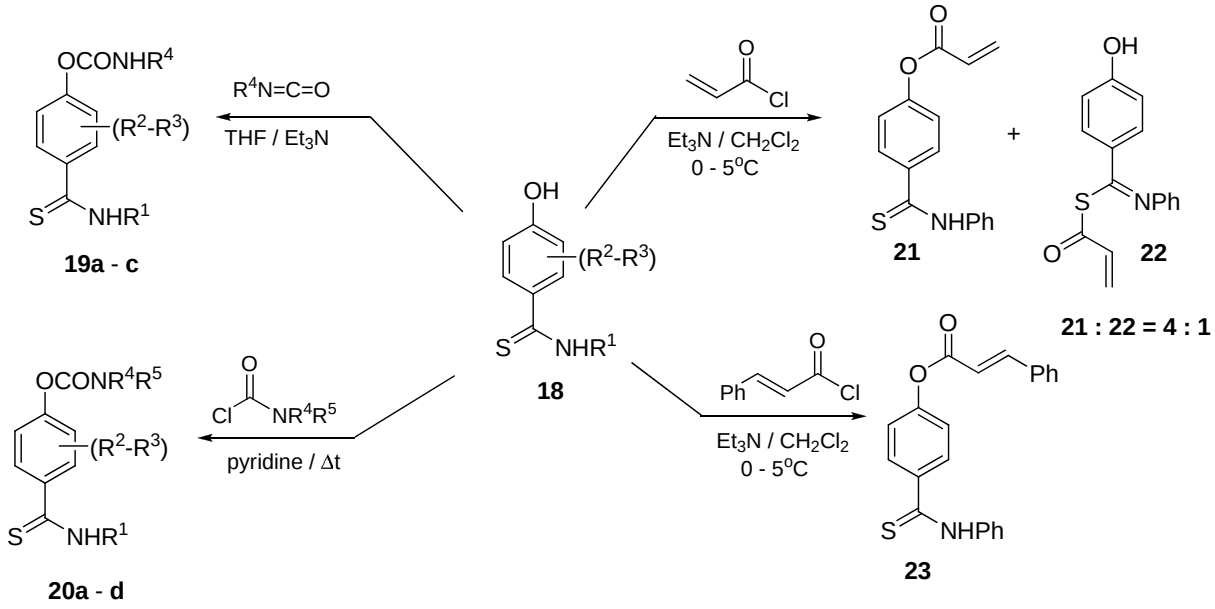
Table 5. Physical data of compounds **13-15**

Compound	Heteroatom Z	Yield [%]
13	O	87
14	N	77.3
15a	O	89
15b	N	93.5
16	O	78.7
17	O	98

A similar procedure may be used for modification of 4-hydroxythiobenzamides **18** which can be obtained in the simple and highly efficient reaction of isothiocyanates with phenols in the presence of anhydrous aluminum chloride.[4] The compounds **18** readily reacted with isocyanates in the presence of triethylamine to yield carbamates **19a-c**. Triethylamine was used in this reaction to produce the phenolate anion which was indispensable for the reaction. The *N*,*N*-disubstituted carbamates **20a-d** were easily obtained by acylation of thioamides **18** with carbamoyl chlorides in pyridine; although elevated temperature (approximately 70°C) was required to make the reaction proceed, regioselectivity of the phenol group esterification was preserved (Scheme 6).

Acylation of **18** with acryloyl chloride was not selective since the reagent attacked both the hydroxy group and the thioamide sulfur atom. The products (**21** and **22**) were formed in the ratio of 4:1, respectively, as determined by the GC/MS and ^{1}H-NMR methods. Rather qualitative experiments with other thioamides revealed that depending on the amounts of acryloyl chloride and triethylamine used and on the structure of the thioamide the products were mixtures consisting of *O*- and *S*-monoacylated.

Under analogous reaction conditions cinnamoyl chloride selectively, presumably owing to its lower reactivity, acylated only the hydroxy group of **18** to yield **23** (Scheme 6). The reactions, like those with chlorides of other α,β–unsaturated carboxylic acids, were carried out at 0-5°C in dichloromethane in the presence of triethylamine.



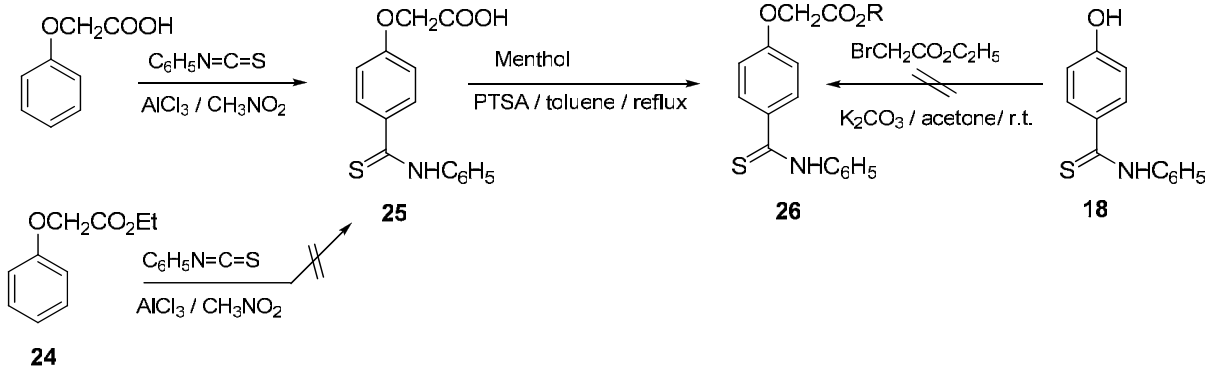
Scheme 6

Table 6. Physical data of compounds **19-20**

Compound	Substituents					Yield [%]
	R^1	R^2	R^3	R^4	R^5	
19a	4-BrPh	H	H	CH_3	-	98
19b	4-BrPh	H	H	4-ClPh	-	98
19c	Ph	2-CH_3	3-CH_3	CH_3	-	98
20a	Ph	H	H	CH_3	CH_3	84
20b	Ph	H	H	C_2H_5	C_2H_5	62
20c	4-BrPh	H	H	CH_3	CH_3	98
20d	4-BrPh	H	H	C_2H_5	C_2H_5	95

Attempts at alkoxylation of the hydroxy function of 4-hydroxythiobenzamide with ethyl bromoacetate were unsuccessful. The thioamide sulfur atom was found to be the preferred target, in particular when the bromoacetate was used in a small excess. In order to obtain the appropriate phenoxyacetate-derived product **26** we had to develop another procedure. Thus, thioamide **25** was converted into **26** by heating with menthol in toluene. Although the starting **25** was readily prepared in the reaction of phenoxyacetic acid with phenyl isothiocyanate in a nitromethane solution of aluminum chloride, an analogous reaction with the ethyl ester of

phenoxyacetic acid gave a product the structure of which has not been identified to date. Therefore, it seems legitimate to assume that esterification of thioamides **25** is the only available route in the synthesis of 4-phenylthiocarbamoylphenoxy acetates **26** (Scheme 7).



Conclusions

A simple method for substituting the benzene ring of phenols with the thioamide group was developed. It may be helpful as another step intended to widen the field of thioamide applicability in organic synthesis. The reactions investigated and shown in the present research have to be considered as mere examples which still leave much space to investigate the full potential of the synthetic importance of thioamides. It has been shown, however, that any new functional group introduced to the thioamide structure opens some as yet unexplored preparative paths.

Experimental Section

General Procedures. Melting points were determined on a digital apparatus Electrothermal model IA9300 and are uncorrected. NMR spectra were recorded on a Bruker DPX apparatus (400 MHz) spectrometer in deuteriochloroform and deuteriodimethyl sulfoxide with tetramethysilane as internal standard. In some cases trifluoroacetic acid (TFFA) was added to the solvent. The IR spectra were taken with Specord M80 instruments in potassium bromide pellets, nujol or hexachlorobutadiene. Purity and molecular mass determinations were carried out by gas chromatography-mass spectrometry (GC/MS) on a Hewlett-Packard instrument model HP 6890 equipped with a mass detector HP 5973. The analytical procedure was developed for a 30m long capillary column, 0.2 mm in diameter, with methylsiloxane modified with phenyl groups (5% Ph, Me siloxane) in the 0.25 cm thick active phase layer. Elemental analyses were performed on EuroEA 3000 series, Euro Vector CHNS-O Elemental Analyzer. All compounds gave satisfactory elemental analysis (C, H, N, S).

General procedure for the preparation of 4-hydroxy-*N*-ethoxycarbonylthiobenzamides 1a-d

Ethoxycarbonyl isothiocyanate (2.62g, 20 mmol) was added at 0-5^{o}C to a stirred solution of 5.5 g (40 mmol) of anhydrous aluminum chloride in dry nitromethane (30 mL). The appropriate phenol (22 mmol) was then added portionwise at the same temperature. The mixture was stirred at 0-5^{o}C for 1 h, then left overnight in a refrigerator and finally hydrolyzed by pouring onto crushed ice. If the product precipitated in quantity, it was collected and washed with cold water. In case of incomplete precipitation, the mixture was extracted with ethyl acetate and the extract washed with water, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. The residue was dissolved in ethyl acetate and filtered through a layer (10x2 cm) of aluminum oxide (Brockmann II, neutral, standard) using ethyl acetate as the eluent. Reduced pressure helped to make this operation less time-consuming. The filtrate was again evaporated under reduced pressure and the crude product recrystallized from a suitable solvent.

4-Hydroxy-*N*-ethoxycarbonylthiobenzamide (1a). M.p.: 174-177˚C (aq. ethanol); IR (nujol) νmax: 3320, 3376 (NH, OH), 1742 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 1.23 (t, J= 7.01 Hz, 3H, CH_3), 4.16 (q, J= 6.92 Hz, 2H, CH_2), 6.73 (d, J= 8.50 Hz, 2H, Ph), 7.62 (d, J=8.47 Hz, 2H, Ph), 10.27 (br.s., 1H, OH), 11.72 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 14.61, 62.00, 114.93, 131.15, 133.61, 162.02, 152.82, 202.77; Anal. calcd. for $C_{10}H_{11}NO_3S$: C 53.32, H 4.92, N 6.23, S 14.23 %. Found C 53.66, H 5.11, N 6.28, S 14.44%.

4-Hydroxy-2-methyl-*N*-ethoxycarbonylthiobenzamide (1b). M.p.: 139-141˚C (aq. ethanol); IR (nujol) νmax: 3340, 3192 (NH, OH), 1732 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 1.17 (t, J= 7.03 Hz, 3H, $C\underline{H}_3CH_2$), 2.15 (s, 3H, CH_3), 4.09 (dd, J= 14.02, 6.95 Hz, 2H, CH_2), 6.53 (s, 1H, Ph), 6.56 (d, J= 8.38 Hz, 1H, Ph), 7.07 (d, J= 8.27 Hz, 1H, Ph), 9.74 (br.s., 1H, OH), 12.11 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 14.46, 19.84, 62.20, 112.70, 116.74, 129.95, 134.62, 136.10, 151.47, 158.64, 208.22; Anal. calcd. for $C_{11}H_{13}NO_3S$: C 55.21, H 5.48, N 5.87, S 13.40 %. Found C 55.54, H 5.87, N 5.85, S 13.73%.

4-Hydroxy-3,5-dimethyl-*N*-ethoxycarbonylthiobenzamide (1c). M.p.: 154-155˚C (nitro-methane); IR (nujol) νmax: 3424, 3156 (NH, OH), 1744 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 1.24 (t, J= 7.00 Hz, 3H, CH_3), 2.18 (s, 6H, $2CH_3$), 4.17 (q, J= 6.92 Hz, 2H, CH_2), 7.40 (s, 2H, Ph), 9.11 (br.s., 1H, OH), 11.64 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 14.62, 17.00, 61.93, 123.67, 129.61, 133.46, 152.87, 158.14, 202.67; Anal. Calcd. for $C_{12}H_{15}NO_3S$: C 56.90, H 5.97, N 5.53, S 12.66 %. Found C 57.21, H 6.02, N 5.50, S12.54%.

General procedure for preparation of heterocycles 3-12

A solution of 0.005 mol of *N*-ethoxycarbonylthiobenzamide (**1a**, **b**) and 0.006 mol of the dinucleophilic reagent in 15 mL of ethanol (20 mL for compounds **10 -12**) was refluxed until the evolution of hydrogen sulfide ceased (lead acetate paper) and for additional 1-2 h (or overnight for compounds **10-12**), then cooled and poured into water. Any solid product was collected by filtration. The filtrate was concentrated to a small volume and new precipitate was combined

with the first one. The crude product was recrystallized from an appropriate solvent. The reaction progress can be monitored by TLC as well (silica gel, benzene/EtOAc 3:1 or $CHCl_3$).

5-(4-Hydroxyphenyl)-2,4-[dihydro-[1,2,4]triazol-3-one (3a). M.p.: 354-256˚C (aq. ethanol); IR (nujol) νmax: 3360-2800 (br., NH, OH), 1745 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.80 (d, J= 8.61 Hz, 2H, Ph), 7.57 (d, J= 8.63 Hz, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 116.13, 118.33, 126.89, 145.97, 157.02, 159.70.Anal.Calcd. for $C_8H_7N_3O_2$: C 54.24, H 3.98, N 23.72%. Found: C 54.44, H 4.10, N 23.48%.

5-(4-Hydroxy-3,5-dimethyl-phenyl)-2,4-[dihydro-[1,2,4]triazol-3-one (3b). M.p.: >350˚C (aq. ethanol); IR (nujol) νmax: 3320, 3070 (br, NH, OH), 1676 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.15 (s, 6H, $2CH_3$), 7.34 (s, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 17.21, 118.30, 125.12, 125.53, 146.63, 155.88, 157.53; Anal.Calcd. for $C_{10}H_{11}N_3O_2$: C 58.53, H 5.40, N 20,48%. Found: C 58.22, H 5.77, N 20.40%

5-(4-Hydroxy-phenyl)-2-phenyl-2,4-dihydro[1,2,4]triazol-3-one (4a). M.p.: 245-246˚C (aq. ethanol); IR (nujol) νmax: 3428, 3000 (br., NH, OH), 1710 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.85-6.94 (m, 2H, Ph), 7.18 (t, J= 7.37 Hz, 1H, Ph), 7.38-7.48 (m, 2H, Ph), 7.70-7.81 (m, 2H, Ph), 7.98 (d, J= 7.68 Hz, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 116.26, 117.42, 118.29, 125.07, 127.56, 129.40, 138.42, 145.52, 153.40, 160.11; Anal. Calcd. for $C_{14}H_{11}N_3O_2$: C 66.40, H 4.38, N 16.59%. Found: C 66.54, H 4.53, N 16.32%.

5-(4-Hydroxy-3-methyl-phenyl)-2-phenyl-2,4-dihydro[1,2,4]triazol-3-one (4b). M.p.: 248-250˚C (aq. ethanol); IR (nujol) νmax: 3460, 3140 (br., NH, OH), 1690 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.52 (s, 3H, CH_3), 6.74 (d, J= 8.42 Hz, 1H, Ph), 6.77 (s, 1H, Ph), 7.20 (t, J= 7.20 Hz, 1H, Ph), 7.46 (dd, J= 14.67, 8.25 Hz, 3H, Ph), 7.97 (d, J= 7.83 Hz, 2H, Ph), 9.94 (br.s., 1H, OH), 12.20 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 21.89, 113.46, 116.71, 118.20, 118.65, 125.05, 129.44, 130.37, 138.45, 139.28, 146.15, 153.06, 159.31; Anal. Calcd. for $C_{15}H_{13}N_3O_2$: C 67.40, H 4.90, N 15.72%. Found: C 67.22, H 5.05, N 15.36%.

3-(4-Hydroxy-2-methyl-phenyl)-4*H*-[1,2,4]oxadiazol-5-one (5a). M.p.: 184-186˚C (aq. ethanol); IR (hexachlorobutadiene) νmax: 3328-2984 (br., NH, OH), 1748 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.38 (s, 3H, CH_3), 6.67-6.80 (m, 2H, Ph), 7.40 (d, J= 8.32 Hz, 1H, Ph), 10.14 (s, 1H, OH), 12.47 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 21.46, 113.62, 113.76, 118.60, 131.06, 139.83, 158.43, 160.18, 160.43; Anal. calcd. for $C_9H_8N_2O_3$: C 56.25, H 4.20, N 14.58%. Found: C 56.44, H 4.40, N 14.26%.

3-(4-Hydroxy-3,5-dimethyl-phenyl)-4*H*-[1,2,4]oxadiazol-5-one (5b). M.p.: 223-224˚C (aq. ethanol); IR (nujol) νmax: 3400, 3240 (NH, OH), 1974 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.21 (s, 6H, $2CH_3$), 7.40 (s, 2H, Ph), 9.14 (s, 1H, OH), 12.63 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 17.05, 114.06, 125.46, 126.75, 157.33, 157.76, 160.47; Anal. Calcd. for $C_{10}H_{10}N_2O_3$: C 58.25, H 4.89, N 13.59%. Found: C 58.44, H 4.95, N 13.26%.

2-(4-Hydroxy-2-methyl-phenyl)-4,5-dihydro-oxazole (6a). M.p.: 221-223˚C (aq. ethanol); IR (nujol) νmax: 3340 (OH), 1738 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 3.99 (t, J= 6.02 Hz, 2H, CH_2), 4.19-4.32 (m, 2H, CH_2), 6.85 (d, J=7.60 Hz, 2H, Ph), 7.71 (d, J= 7.63 Hz, 2H, Ph), 8.91 (br.s., 1H, OH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 62.68, 68.36, 113.90,

129.88, 134.00, 150.88, 162.88; Anal. Calcd. for $C_9H_9NO_2$: C 66.25, H 5.56, N 8.58%. Found: C 66.19, H 5.57, N 8.60%.

2-(4-Hydroxy-3,5-dimethyl-phenyl)-4,5-dihydro-oxazole (6b). M.p.: 223-224˚C (aq. ethanol); IR (nujol) νmax: 3400 (OH), 1794 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.17 (s, 6H, $2CH_3$), 3.86 (t, J= 9.39 Hz, 2H, CH_2), 4.30 (t, J= 9.38 Hz, 2H, CH_2), 7.43 (s, 2H, Ph), 8.83 (br.s., 1H, OH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 17.01, 54.72, 67.34, 118.74, 124.50, 128.58, 156.58, 163.52; Anal. Calcd. for $C_{11}H_{13}NO_2$: C 69.09, H 6.85, N 7.32%. Found: C 69.38, H 7.05, N 7.22%

2-(4-Hydroxy-phenyl)-4,5-dihydro-1*H*-imidazole (7a). M.p. 297-299˚C (water); M.p. Lit.[17] 208˚C; IR (nujol) νmax: 3200 (br., NH), 1614, 1590 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ (ppm): 3.91 (s, 4H, $2CH_2$), 6.95 (d, J= 8.80 Hz, 2H, Ph), 7.80 (d, J= 8.81 Hz, 2H, Ph), 10. 32 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 44.52, 112.63, 116.48, 131.21, 163.77, 164.94; Anal. Calcd. for $C_9H_{10}N_2O$: C 66.65, H 6.21, N 17.27%. Found: C 66.46, H 6.51, N 17.17%.

2-(4-Hydroxy-2-methyl-phenyl)-4,5-dihydro-1*H*-imidazole (7b). M.p.: 221-223˚C (aq. ethanol); IR (nujol) νmax: 3000 (br.), 1586 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ (ppm): 2.36 (s, 3H, CH_3), 3.95 (s, 4H, 2 CH_2), 6.78 (d, J= 7.33 Hz, 2H, Ph), 7.39 (d, J= 8.02 Hz, 1H, Ph), 10.07 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 19.95, 44.70, 113.67, 113.90, 118.43, 131.72, 140.01, 161.98, 167.13; Anal. Calcd. for $C_{10}H_{12}N_2O$: C 68.16, H 6.86, N 15.90%. Found: C 68.54, H 6.98, N 16.22%.

2-(4-Hydroxy-3,5-dimethyl-phenyl)-4,5-dihydro-1*H*-imidazole (7c). M.p.: >310˚C (aq. ethanol); IR (hexachlorobutadiene) νmax: 3320 (NH), 1596, 1584 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ (ppm): 2.21 (s, 6H, $2CH_3$), 3.92 (s, 4H, $2CH_2$), 7.92 (s, 2H, Ph), 10.36 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 16.91, 44.49, 112.41, 125.51, 129.51, 159.77, 165.05; Anal. Calcd. for $C_{11}H_{14}N_2O$: C 69.45, H 7.42, N 14.73%. Found: C 69.78, H 7.73, N 15.03%.

2-(4-Hydroxy-phenyl)-1,4,5,6-tetrahydro-pyrimidine (8a). M.p. 285-287˚C (water); M.p. Lit.[18] 290-292˚C; IR (nujol) νmax: 2900 (CH_2), 1610, 1584 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ (ppm): 1.91 (s, 2H, CH_2), 3.42 (s, 4H, $2CH_2$), 6.93 (d, J= 8.52 Hz, 2H, Ph), 7.56 (d, J= 8.54 Hz, 2H, Ph), 9.71 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 18.32, 116.11, 119.02, 129.76, 159.73, 162.51; Anal. calcd. for $C_{10}H_{12}N_2O$: C 68.16, H 6.86, N 15.90%. Found: C 68.00, H 7.03, N 16.14%.

2-(4-Hydroxy-2-methyl-phenyl)-1,4,5,6-tetrahydro-pyrimidin (8b). M.p.: 277-279˚C (water); IR (nujol) νmax: 2880, 2670 (CH_2), 1630, 1580 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ (ppm): 1.94 (t, J= 4.98 Hz, 2H, CH_2), 2.25 (s, 3H, CH_3), 3.42 (s, 4H, $2CH_2$), 6.72 (d, J= 8.08 Hz, 2H, Ph), 7.22 (d, J= 7.99 Hz, 1H, Ph), 9.64 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 113.33, 114.08, 117.74, 130.56, 138.32, 160.66, 160.78; Anal. calcd. for $C_{11}H_{14}N_2O$: C 69.45, H 7.42, N 14.73%. Found: C 69.19, H 7.77, N 14.94%.

2-(4-Hydroxy-phenyl)-4,5,6,7-tetrahydro-1*H*-[1,3]diazepine (9). M.p.: 298-300˚C (water); IR (nujol) νmax: 3160, 2840 (br.), 1570 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/TFAA) δ

(ppm): 1.89 (s, 4H, $2CH_2$), 3.59 (s, 4H, $2CH_2$), 6.92 (d, J= 8.05 Hz, 2H, Ph), 7.56 (d, J= 7.84 Hz, 2H, Ph), 9.45 (s, 2H, NH, OH); ^{13}C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 25.90, 44.05, 116.04, 120.17, 131.54, 163.15, 165.06; Anal. calcd. for $C_{11}H_{14}N_2O$: C 69.45, H 7.42, N 14.73%. Found: C 69.67, H 7.62, N 14.84%.

2-(4-Hydroxy-phenyl)-benzothiazole (10). M.p.: 229-230˚C (aq. ethanol); M.p. Lit.[19] 220-221˚C; IR (hexachlorobutadiene) νmax: 3300 (OH), 1608-1578 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.87-6.97 (m, 2H, Ph), 7.33-7.41 (m, 1H, Ph), 7.44-7.54 (m, 1H, Ph), 7.87-7.93 (m, 2H, Ph), 7.96 (d, J= 7.69, 1H, Ph), 8.03-8.11 (m, 1H, Ph), 10.25 (br.s., 1H, OH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 116.55, 122.58, 122.76, 124.49, 125.36, 126.89, 129.51, 134.57, 154.19, 161.00, 167.92; MS *m/z*: 227 (M^+, 100%) Anal. calcd. for $C_{13}H_9NOS$: C 68.70, H 3.99, N 6.17, S 14.11%. Found: C 68.58, H 4.28, N 6.20, S 14.44%.

2-(4-Hydroxy-phenyl)-benzoxazol (11). M.p.: 258-259˚C (ethanol); M.p. Lit.[20] 257-260˚C; IR (nujol) νmax: 3300-2900 (OH), 1620-1608 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.96 (d, J= 6.98 Hz, 2H, Ph), 7.31-7.39 (m, 2H, Ph), 7.67-7.75 (m, 2H, Ph), 8.03 (d, J= 6.96 Hz, 2H, Ph), 10.33 (s, 1H, OH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 111.05, 116.57, 117.63, 119.72, 125.05, 125.18, 129.78, 142.25, 150.51, 161.43, 163,23; MS *m/z*: 211 (M^+, 100%); Anal.calcd. for $C_{13}H_9NO_2$: C 73.92, H 4.29, N 6.63%. Found: C 74.14, H 4.45, N 6.93%.

2-(4-Hydroxyphenyl)-benzoimidazol (12). M.p.: 286-287˚C (aq. ethanol); M.p. Lit.[21] 255.1-256.6˚C; IR (nujol) νmax: 3500-3200 (NH, OH), 1610 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.94 (d, J= 8.69 Hz, 2H, Ph), 7.10-7.22 (m, 2H, Ph), 7.55 (br.s., 2H, Ph), 8.03 (d, J= 8.68 Hz, 2H, Ph), 10.10 (br.s., 1H, OH), 12.71 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 116.19, 118.57, 121.52, 122.09, 128.64, 144.25, 152.26, 159.61; MS *m/z:* 210 (M^+, 100%); Anal. calcd. for $C_{13}H_{10}N_2O_3$: C 74.27, H 4.79, N 13.33%. Found: C 74.46, H 4.98, N 13.11%.

General procedure for the synthesis of acrylic and cinnamic esters (13-15) and (21-23)

To a solution of the heterocycle **3-12** or 4-hydroxythiobenzamide **18** (1.0 mmol) and triethylamine (1.5 mmol) in dry methylene chloride (15 mL) acryloyl or cinnamoyl chloride (1.0 mol) was added dropwise under nitrogen at approximately 0˚C. The resultant mixture was allowed to warm to the room temperature, stirred for 3 h, and finally was passed through a 10-cm column packed with neutral aluminum oxide, activity II. Evaporation of methylene chloride left the crude product, which was purified by recrystallization from an appropriate solvent (toluene or toluene/ethyl acetate) or chromatography in a silica gel – packed column using the n-hexane/ethyl acetate (3:2) mixture as the eluent, to give the esters **13**,**14**,**15** and **21, 22**, **23** respectively.

Acrylic acid 4-Benzoxazol-2-yl-phenylester (13). M.p.: 126-128˚C (toluene/ethyl acetate); IR (KBr) νmax: 1742 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.11 (d, J= 10.18 Hz, 1H, CHH), 6.37 (dd, J= 17.05, 10.35 Hz, 1H, CHH), 6.53 (d, J= 17.26 Hz, 1H, CH=), 7.21-7.48 (m, 4H, Ph), 7.72 (dd, J= 22.18, 6.93 Hz, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 111.17, 120.16, 123.06, 124.93, 125.78, 127.73, 129.10, 134.08, 141.96, 153.34, 157.75, 162.06, 164.15;

MS *m/z*: 265 (M^+, 33.7%), 211 (100%); Anal. calcd. for $C_{16}H_{11}NO_3$: C 72.45, H 4.18, N 5.28%. Found: C 72.40, H 4.13, N 5.23%.

Acrylic acid 4-(1*H*-benzoimidazol-2-yl) phenyl ester (14). Oil; IR (KBr) νmax: 1722 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 5.89 (dd, J= 10.17, 1.97 Hz, 1H, CHH), 6.16 (d, J= 11.15 Hz, 1H, CH), 6.25 (d, J= 1.97 Hz, 1H, CHH), 7.14-7.27 (m, 2H, Ph), 7.69-7.84 (m, 4H, Ph), 8.17-8.32 (m, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 116.94, 121.33, 122.00, 126.88, 128.63, 130.45, 130.62, 151.76, 159.78, 162.00, 172.05; MS *m/z*: 264 (M^+, 26.22%), 210 (100%).

Cinnamic acid 4-benzoxazol-2-yl-phenyl ester (15a). M.p.: 169-171˚C (toluene); IR (KBr) νmax: 1722 (C=O), 1632-1626 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 6.59 (d, J= 15.98 Hz, 1H, COCH=), 7.27 (t, J=2.9 Hz, 3H, Ph), 7.30 (d, J= 2.16 Hz, 1H, Ph), 7.32-7.40 (m, 3H, Ph), 7.42-7.56 (m, 3H, Ph), 7.68-7.72 (m, 1H, Ph), 7.85 (d, J= 16.01, 1H, =CH Ph), 8.25 (d, J= 8.67 Hz, 2H, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 110.63, 116.85, 120.05, 122.31, 124.67, 124.74, 125.18, 128.41, 129.02, 129.07, 130.94, 134.03, 142.13, 147.26, 150.82, 153.40, 162.39, 164.93; MS *m/z*: 341 (M^+, 40.5%), 131 (100%); Anal. calcd. for $C_{22}H_{15}NO_3$: C 77.41, H 4.43, N 4.10%. Found: C 77.18, H 4.53, N 3.93%.

Cinnamic acid 4-(1*H*-benzimidazol-2-yl) phenyl ester (15b). M.p.: 218-221˚C (toluene/ methanol); IR (KBr) νmax: 3484 (NH), 1714 (C=O), 1632 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.92 (d, J= 16.05 Hz, 1H, CH=), 7.21-7.25 (m, 2H, Ph), 7.37-7.44 (m, 2H, Ph), 7.45-7.53 (m, 3H, Ph), 7.61 (s, 2H, Ph), 7.79-7.87 (m, 2H, Ph), 7.90 (d, J= 16.05 Hz, 1H, =CH), 8.21-8.27 (m, 2H, Ph), 12.94 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 117.48, 122.61, 122.96, 128.20, 128.33, 129.19, 129.49, 131.45, 134.29, 147.24, 151.05, 152.10, 165.27; MS *m/z*: 340 (M^+, 6.7%), 131 (100%); Anal. calcd. for $C_{22}H_{16}N_2O_2$: C 77.63, H 4.74, N 8.23%. Found: C 77.46, H 4.62, N 8.01%.

(4-Benzooxazol-2-yl-phenoxy)-acetic acid ethyl ester (16). Was prepared according to the method reported erlier.[22] Oil; IR (neat) νmax: 2960 (CH), 1740 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO/$CDCl_3$) δ (ppm):1.25 (t, J= 7.13Hz, 3H, CH_3), 4.02-4.23 (m, 2H, CH_2), 4.62-4.73 (m, 2H, CH_2), 7.77-7.86 (m, 1H, Ph), 7.88-7.95 (m, 2H, Ph), 8.03 (dd, J= 10.45, 3.51Hz, 3H, Ph), 8.29 (s, 2H, Ph); ^{13}C-NMR (100 MHz, DMSO/$CDCl_3$) δ (ppm): 13.21 (CH_3), 60.61 (CH_2), 64.07 (CH_2), 113.14, 113.42, 121.40, 121.73, 128.41, 130.72, 131.15, 160.78, 164.45, 167.26, 167.67, 169.09; MS *m/z*: 297 (M^+, 100%).

Acrylic acid 4-phenylthiocarbamoyl-phenyl ester (21). Yield 80 %; m.p. 92-95˚C (hexane/ ethyl acetate); IR (KBr) νmax: 3300 (NH), 1726 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 5.98 (d, J= 10.46 Hz, 1H, =CH_2), 6.24 (dd, J= 17.27, 10.43 Hz, 1H, CH=), 6.55 (d, J= 17.31 Hz, 1H, =CH_2), 7.01 (t, J= 7.30 Hz, 1H, Ph), 7.14 (d, J= 8.60 Hz, 2H, Ph), 7.17-7.28 (m, 2H, Ph), 7.44 (d, J= 7.98 Hz, 2H, Ph), 7.68 (s, 1H, NH), 7.91 (d, J=8.61 Hz, 2H, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 118.91, 120.85, 123.37, 126.40, 127.81, 127.95, 132.49, 133.29, 136.69, 153.61, 162.87, 190.12; MS *m/z*: 283 (M^+, 71.4 %), 137 (100%).

(4-Hydroxyphenyl-phenylimino-methyl)-prop-2-enethioate (22). Yield 20%; oil, IR (neat) ν_{max}: 3200 (OH), 1724 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 6.07 (d, J= 11.57 Hz,

1H, CHH), 6.33 (dd, J= 18.09 Hz, 10.73 Hz, 1H, CHH), 6.64 (d, J= 16.13 Hz, 1H, CH), 6.97-7.07 (m, 1H, Ph), 7.12-7.20 (m, 1H, Ph), 7.21-7.36 (m, 3H, Ph), 7.56 (d, J= 8.0Hz, 2H, Ph), 8.01 (d, J= 8.77 Hz, 2H, Ph); MS *m/z*: 283 (M^+, 78.8 %), 137 (100%).

3-Phenyl-acrylic acid 4-phenylthiocarbamoyl-phenyl ester (23). Yield: 76%; m.p.: 168-170˚C (toluene); IR (KBr) νmax: 1726 (C=O), 1668, 1660 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$/DMSO (95:5)) δ (ppm): 6.62 (dd, J= 16.0, 2.64 Hz, 1H, OCH=), 7.13-7.31 (m, 3H, Ph), 7.37-7.52 (m, 5H, Ph), 7.59 (d, J= 3.67 Hz, 2H, Ph), 7.79-7.92 (m, 3H, =CHPh, Ph), 7.94 (d, J= 7.22 Hz, 2H, Ph), 10.43 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$/DMSO (95:5)) δ (ppm): 116.77, 121.52, 123.91, 126.68, 128.22, 128.38, 128.73, 128.83, 129.07, 130.96, 133.94, 140.80, 147.21, 153.50, 165.12, 197.28; MS *m/z*: 359 (M^+, 29.0 %), 131 (100%); Anal. calcd. for $C_{22}H_{17}NO_2S$: C 73.51, H 4.77, N 3.90, S 8.92%. Found: C 73.15, H 4.87, N 4.00, S 8.95%.

General procedure for preparation of *N*-alkyl(aryl)carbamates (17, 19a-c)

4-Hydroxythiobenzamides **18** were prepared as reported earlier.[4] The appropriate isocyanate (0.027 mol) was added to a solution of **18** or benzoxazole **11** (0.025 mol) and triethylamine (1 mL) in 30 mL of dry THF or methylene chloride. After standing 24h at room temperature the solvent was evaporated in vacuo. The solid residue was recrystallized from a suitable solvent.

Phenylamino-acetic acid 4-benzoxazol-2-yl-phenyl ester (17). M.p.: 224-226˚C (toluene); IR (KBr) νmax: 3324 (NH), 1716 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 6.90-7.04 (m, 2H, Ph), 7.28 (t, J= 7.31 Hz, 2H, Ph), 7.32-7.40 (m, 1H, Ph), 7.43-7.62 (m, 5H, Ph), 8.27 (d, J= 8.02 Hz, 1H, Ph), 8.67 (s, 2H, Ph), 10.40 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 114.32, 116.58, 118.64, 119.73, 120.29, 122.26, 123.33, 129.24, 129.78, 140.17, 149.07, 150.76, 152.99, 163.24; Anal. calcd. for $C_{20}H_{14}N_2O_3$: C 72.72, H 4.27, N 8.48%. Found: C 72.69, H 4.13, N 8.45%.

Methyl-carbamic acid 4-(4-bromo-phenylthiocarbamoyl]-phenyl ester (19a). M.p.: 185-187˚C (toluene); IR (nujol) νmax: 3432, 3308 (NH), 1724 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.67 (s, 3H, CH_3), 7.19 (d, J= 8.18 Hz, 2H, Ph), 7.62 (d, J= 8.28 Hz, 2H, Ph), 7.74 (br.s., 1H, NHCH$_3$), 7.78-7.89 (m, 4H, Ph), 11.80 (br.s., 1H, NHPh); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 27.59, 118.75, 121.67, 126.50, 129.24, 131.85, 139.58, 139.81, 153.70, 154.87, 197.26; Anal. calcd. for $C_{15}H_{13}BrN_2O_2S$: C 49.33, H 3.59, N 7.67, S 8.78%. Found: C 49.21, H 3.75, N 7.81, S 8.62%.

(4-Chlorophenyl)- carbamic acid 4-(4-bromo-phenylthiocarbamoyl]-phenyl ester (19b). M.p.: 191-193˚C (nitromethane); IR (nujol) νmax: 3388, 3340 (NH), 1737 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 7.33 (d, J= 8.67 Hz, 2H, Ph), 7.37-7.43 (m, 2H, Ph), 7.49-7.56 (m, 2H, Ph), 7.60-7.68 (m, 2H, Ph), 7.84 (d, J= 8.78 Hz, 2H, Ph), 7.88 (d, J= 8.62 Hz, 2H, Ph),10.50 (s, 1H, NH), 11.84 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 118.79, 120.47, 121.94, 126.47, 129.10, 129.33, 129.38, 131.88, 137.94, 139.78, 140.27, 151.71, 152.85, 197.19; Anal. calcd. for $C_{20}H_{14}BrClN_2O_2S$: C 52.02, H 3.06, N 6.07, S 6.94%. Found: C 51.89, H 3.27, N 7.91, S 7.14%.

Methyl-carbamic acid 2,3-dimethyl-4-phenylthiocarbamoyl-phenyl ester (19c). M.p.: 208-210˚C (toluene); IR (nujol) νmax: 3282, 3200 (NH), 1722 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz,

$CDCl_3$) δ (ppm): 2.09 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.68 (s, 3H, NCH_3), 6.87-7.01 (m, 1H, Ph), 7.07-7.35 (m, 2H, Ph), 7.42 (s, 2H, Ph), 7.69 (s, 1H, NH), 7.95 (d. J= 6.98 Hz, 2H, Ph), 11.93 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 12.87, 16.83, 27.66, 120.22, 123.56, 125.22, 126.72, 129.03, 130.01, 132.99, 139.99, 143.00, 149.58, 155.28, 199.55; Anal. calcd. for $C_{17}H_{18}N_2O_2S$: C 64.94, H 5.77, N 8.91, S 10.20%. Found: C 64.49, H 5.86, N 8.81, S 10.44%.

General procedure for preparation of *N,N*-dialkylcarbamates 20a-d

4-Hydroxythiobenzamides **18** were prepared as reported earlier.[4] To a stirred solution of **18** (0.03 mol) in 25 mL of anhydrous pyridine the appropriate *N,N*-dialkylcarbamoyl chloride (0.045 mol) was slowly added. The solution was stirred at 70°C for 6 h and then poured onto ice water. The precipitate was filtered and washed with water. The crude product was dissolved in ethyl acetate and passed under reduced pressure through a short column (10x2cm) packed with aluminum oxide (Brockmann II, neutral, standard) using ethyl acetate as the eluent. Upon evaporation of the solvent, the residue was recrystallized from a suitable solvent.

Dimethyl-carbamic acid 4-phenylthiocarbamoyl-phenyl ester (20a). M.p.: 146-148˚C (toluene); IR (nujol) νmax: 1700 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 2.89 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 6.98 (d, J= 7.90 Hz, 2H, Ph), 7.15-7.36 (m, 3H, Ph), 7.64 (d, J= 6.53 Hz, 2H, Ph), 7.71 (d, J= 7.35 Hz, 2H, Ph), 9.39 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 35.51, 35.70, 120.52, 122.80, 125.78, 127.23, 127.82, 138.23, 152.67, 153.39, 196.09; MS *m/z*: 300 (M^+, 55.1%), 72 (100%); Anal. calcd. for $C_{16}H_{16}N_2O_2S$: C 63.98, H 5.37, N 9.33, S 10.67%. Found: C 63.47, H 5.53, N 9.23, S 10.47%.

Diethyl-carbamic acid 4-phenylthiocarbamoyl-phenyl ester (20b). M.p.: 111-112˚C (toluene); IR (nujol) νmax: 1700 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 1.13 (dt, J= 26.21, 7.02 Hz, 6H, $2CH_3$), 3.19-3.42 (m, 4H, $2CH_2$), 6.98 (d, J= 7.95 Hz, 2H, Ph), 7.12-7.24 (m, 1H, Ph), 7.32 (t, J= 7.29 Hz, 2H, Ph), 7.64 (d, J= 7.26 Hz, 2H, Ph), 7.72 (d, J= 7.86 Hz, 2H, Ph), 9.40 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 13.36, 14.24, 42.02, 42.34, 121.53, 123.91, 126.82, 128.28, 128.88, 139.31, 139.56, 153.65, 153.78, 197.17; MS *m/z*: 328 (M^+, 64.2%), 100 (100%); Anal. calcd. for $C_{18}H_{20}N_2O_2S$: C 65.83, H 6.14, N 8.53, S 9.76%. Found: C 65.98, H 6.28, N 8.61, S 9.70%.

Dimethyl-carbamic acid 4-(4-bromo-phenylthiocarbamoyl)-phenyl ester (20c). M.p.: 216-218˚C (toluene); IR (nujol) νmax: 3268 (NH), 1700 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 2.91 (s, 3H, CH_3), 3.04 (s, 3H, CH_3), 7.20 (d, J= 8.68 Hz, 2H, Ph), 7.62 (d, J= 8.77 H z, 2H, Ph), 7.81 (d, J= 8.78 Hz, 2H, Ph), 7.85 (d, J= 8.67 Hz, 2H, Ph), 11.80 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, DMSO) δ (ppm): 36.64, 38.82, 118.78, 121.87, 126.57, 129.21, 131.86, 139.71, 139.80, 153.89, 154.08, 197.23; MS *m/z*: 379 (M^+, 16.7 %), 72 (100%); Anal. calcd. for $C_{16}H_{15}BrN_2O_2S$: C 50.67, H 3.99, N 7.39, S 8.45%. Found: C 50.91, H 4.11, N 7.51, S 8.24%.

Diethyl-carbamic acid 4-(4-bromo-phenylthiocarbamoyl)-phenyl ester (20d). M.p.: 129-131˚C (toluene/hexane); IR (nujol) νmax: 3280 (NH), 1700 (C=O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 1.12 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 3.30 (d, J= 5.35 Hz, 2H, CH_2), 3.40 (d, J=

4.37 Hz, 2H, CH_2), 7.21 (d, J= 7.60 Hz, 2H, Ph), 7.61 (d, J= 7.70 Hz, 2H, Ph), 7.71-7.95 (m, 4H, Ph), 11.72 (br.s., 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 13.74, 14.67, 42.04, 42,28, 118.76, 121.79, 126.57, 129.24, 131.83, 139.66, 139.85, 153.37, 153.88, 197.20; MS *m/z*: 407 (M^+, 5.8 %), 100 (100%);

(4-Phenylthiocarbamoyl-phenoxy)-acetic acid (25)

Phenyl isothiocyanate (5.95g, 5.3 mL, 44 mmol) was added at room temperature to a stirred solution of anhydrous aluminum chloride (11.0g, 80 mmol) in dry nitromethane (50 mL). The mixture was cooled with ice-water and phenoxyacetic acid (6.1g, 40 mmol) was added in a single portion. An isothermal effect was observed. The mixture was then stirred for 1 h at room temperature, left standing overnight, and finally poured onto crushed ice to decompose the aluminium complex; rapid crystallization of **26** occurred. The precipitate was filtered, washed with water, dried and recrystallized from nitromethane. Yield 78%, pale yellow crystals m.p. 203-206˚C (aq. ethanol). IR (KBr) νmax: 3400-2900 (br., NH, OH), 1746 (C=O), 1602, 1504 (C=C), 1442, 1418 (C-O) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO) δ (ppm): 4.79 (s, 2H, CH_2), 6.98 (s, 2H, Ph), 7.15-7.51 (m, 3H, Ph), 7.77 (s, 1H, Ph), 7.85 (s, 1H, Ph), 11.57 (s, 1H, NH), 13.10 (s, 1H, OH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 65.00, 114.17, 124.86, 126.56, 128.91, 129.86, 135.66, 140.68, 160.54, 170.37, 196.93; Anal. calcd. for $C_{15}H_{13}NO_3S$: C 62.64, H 4.52, N 4.87, S 11.14%. Found: C 62.02, H 4.59, N 4.93, S 11.07%.

Menthyl (4-phenylthiocarbamoyl-phenoxy)-acetate (**26**)

A mixture of thioanilide phenoxyacetic acid (**25**, 1.16 g, 4 mmol), menthol (1.6 g, 10 mmol) and *p*-toluenesulfonic acid (0.2 g) in toluene (60 mL) was refluxed 10 h with azeotropic removal of water. The reaction progress was monitored by TLC (silica gel, benzene/ethyl acetate 3:1). Upon cooling to room temperature the mixture was washed with a saturated aqueous solution of sodium hydrogen carbonate, next with water and finally dried over magnesium sulfate. The solvent was then removed and the residue was purified by column chromatography (silica gel, hexane/ethyl acetate 3:2, to give **26** as pale yellow needles. Yield: 81%, m.p. 97-100˚C (hexane/ethyl acetate). IR (KBr) νmax: 3296 (NH), 1738 (C=O), 1598 (C=C) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 0.65-0.78 (m, 3H, CH_3), 0.81-0.94 (m, 6H, $2CH_3$), 1.02 (q, J=11.57Hz, 2H, CH_2), 1.32-1.56 (m, 2H, CH_2), 1.60-1.85 (m, 3H, CH, CH_2), 2.00 (s, 1H, CH), 2.10-2.19 (m, 1H, CH), 4.63 (d, J=10.58Hz, 2H, OCH_2), 4.72-4.92 (m, 1H, OCH), 6.88 (s, 2H, Ph), 7.17-7.50 (m, 3H, Ph), 7.72 (s, 2H, Ph), 7.83 (s, 2H, Ph), 9.04 (br.s, 1H, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 16.26, 20.74, 21.99, 23.34, 26.28, 31.40, 34.09, 46.92, 65.38, 75.88, 114.33, 123.89, 126.84, 128.70, 129.04, 136.34, 139.19, 160.40, 168.01, 196.52; MS *m/z*: 425 (M^+, 68.3 %), 195 (100%).

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