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 \( \alpha,\beta \)-unsaturated carboxylic acids, and isocyanates yielded the corresponding \( O \)-acylated products.

Keywords: Ethoxycarbonylisothiocyanate, 4-hydroxythiobenzamides, Friedel-Crafts thio-carbamoylation, 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 \( \mathbf{2} \) 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 \( \mathbf{1a} \) could be found in the products of the reaction of ethoxycarbonyl isothiocyanate with phenol. However, \( \mathbf{1a-c} \) 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 \( \mathbf{2} \).

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](image)

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Substituents</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>H</td>
<td>H</td>
</tr>
<tr>
<td>1b</td>
<td>2-CH₃</td>
<td>H</td>
</tr>
<tr>
<td>1c</td>
<td>3-CH₃</td>
<td>5-CH₃</td>
</tr>
</tbody>
</table>

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 (NH₂, 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 occurred via the carbonyl carbon atom of the ester function.

Scheme 2

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Substituents</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
</tr>
<tr>
<td>3b</td>
<td>3-CH₃</td>
<td>5-CH₃</td>
</tr>
<tr>
<td>4a</td>
<td>H</td>
<td>H</td>
</tr>
<tr>
<td>4b</td>
<td>2-CH₃</td>
<td>H</td>
</tr>
<tr>
<td>5a</td>
<td>2-CH₃</td>
<td>H</td>
</tr>
<tr>
<td>5b</td>
<td>3-CH₃</td>
<td>5-CH₃</td>
</tr>
</tbody>
</table>
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-1H-[1,3]diazepine 9 (Scheme 3).

![Diagram](https://via.placeholder.com/150)

\[ \text{Scheme 3} \]

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Substituents</th>
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<tbody>
<tr>
<td>6a</td>
<td>H</td>
<td>95</td>
</tr>
<tr>
<td>6b</td>
<td>3-CH(_3)</td>
<td>5-CH(_3)</td>
</tr>
<tr>
<td>7a</td>
<td>H</td>
<td>H</td>
</tr>
<tr>
<td>7b</td>
<td>2-CH(_3)</td>
<td>H</td>
</tr>
<tr>
<td>7c</td>
<td>3-CH(_3)</td>
<td>5-CH(_3)</td>
</tr>
<tr>
<td>8a</td>
<td>H</td>
<td>H</td>
</tr>
<tr>
<td>8b</td>
<td>2-CH(_3)</td>
<td>H</td>
</tr>
<tr>
<td>9</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>

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, benzoaxazole 11, and benzimidazole 12 (Scheme 4).
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).
Table 5. Physical data of compounds 13-15

<table>
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<th>Compound</th>
<th>Heteroatom</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
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<td>13</td>
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<tr>
<td>14</td>
<td>N</td>
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<td>15a</td>
<td>O</td>
<td>89</td>
</tr>
<tr>
<td>15b</td>
<td>N</td>
<td>93.5</td>
</tr>
<tr>
<td>16</td>
<td>O</td>
<td>78.7</td>
</tr>
<tr>
<td>17</td>
<td>O</td>
<td>98</td>
</tr>
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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. 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).

Acetylation 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 1H-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 $\alpha,\beta$-unsaturated carboxylic acids, were carried out at 0-5°C in dichloromethane in the presence of triethylamine.

![Scheme 6](attachment:scheme6.png)

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Substituents</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>19a</td>
<td>4-BrPh</td>
<td>H</td>
</tr>
<tr>
<td>19b</td>
<td>4-BrPh</td>
<td>H</td>
</tr>
<tr>
<td>19c</td>
<td>Ph</td>
<td>2-CH$_3$</td>
</tr>
<tr>
<td>20a</td>
<td>Ph</td>
<td>H</td>
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<tr>
<td>20b</td>
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<tr>
<td>20c</td>
<td>4-BrPh</td>
<td>H</td>
</tr>
<tr>
<td>20d</td>
<td>4-BrPh</td>
<td>H</td>
</tr>
</tbody>
</table>

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°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°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 was 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) \(\nu_{\text{max}}: 3320, 3376 (\text{NH, OH}), 1742 (\text{C=O}) \text{ cm}^{-1}\); \(^1\)H-NMR (400 MHz, DMSO) \(\delta\) (ppm): 1.23 (t, \(J= 7.01 \text{ Hz}, 3\text{H}, \text{CH}_3\)), 4.16 (q, \(J= 6.92 \text{ Hz}, 2\text{H}, \text{CH}_2\)), 6.73 (d, \(J= 8.50 \text{ Hz}, 2\text{H}, \text{Ph}\)), 7.62 (d, \(J=8.47 \text{ Hz}, 2\text{H}, \text{Ph}\)), 10.27 (br.s., 1H, OH), 11.72 (br.s., 1H, NH); \(^{13}\)C-NMR (100 MHz, DMSO) \(\delta\) (ppm): 14.61, 62.00, 114.93, 131.15, 133.61, 162.02, 152.82, 202.77; Anal. calcd. for \(\text{C}_{10}\text{H}_{11}\text{NO}_3\text{S}\): 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) \(\nu_{\text{max}}: 3340, 3192 (\text{NH, OH}), 1732 (\text{C=O}) \text{ cm}^{-1}\); \(^1\)H-NMR (400 MHz, DMSO) \(\delta\) (ppm): 1.17 (t, \(J= 7.03 \text{ Hz}, 3\text{H}, \text{CH}_3\CH}_2\)), 2.15 (s, 3H, \text{CH}_3), 4.09 (dd, \(J= 14.02, 6.95 \text{ Hz}, 2\text{H}, \text{CH}_2\)), 6.53 (s, 1H, Ph), 6.56 (d, \(J= 8.38 \text{ Hz}, 1\text{H}, \text{Ph}\)), 7.07 (d, \(J= 8.27 \text{ Hz}, 1\text{H}, \text{Ph}\)), 9.74 (br.s., 1H, OH), 12.11 (br.s., 1H, NH); \(^{13}\)C-NMR (100 MHz, DMSO) \(\delta\) (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 \(\text{C}_{11}\text{H}_{13}\text{NO}_3\text{S}\): 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 (nitromethane); IR (nujol) \(\nu_{\text{max}}: 3424, 3156 (\text{NH, OH}), 1732 (\text{C=O}) \text{ cm}^{-1}\); \(^1\)H-NMR (400 MHz, DMSO) \(\delta\) (ppm): 1.24 (t, \(J= 7.00 \text{ Hz}, 3\text{H}, \text{CH}_3\)), 2.18 (s, 6H, 2\text{CH}_3), 4.17 (q, \(J= 6.92 \text{ Hz}, 2\text{H}, \text{CH}_2\)), 7.40 (s, 2H, Ph), 9.11 (br.s., 1H, OH), 11.64 (br.s., 1H, NH); \(^{13}\)C-NMR (100 MHz, DMSO) \(\delta\) (ppm): 14.62, 17.00, 61.93, 123.67, 129.61, 133.46, 152.87, 158.14, 202.67; Anal. Calcd. for \(\text{C}_{12}\text{H}_{15}\text{NO}_3\text{S}\): 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 CHCl₃).

5-(4-Hydroxyphenyl)-2,4-[dihydro-[1,2,4]triazol-3-one (3a). M.p.: 354-256°C (aq. ethanol); IR (nujol) vmax: 3360-2800 (br., NH, OH), 1745 (C=O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 6.80 (d, J= 8.61 Hz, 2H, Ph), 7.57 (d, J= 8.63 Hz, 2H, Ph); ¹³C-NMR (100 MHz, DMSO) δ (ppm): 116.13, 118.33, 126.89, 145.97, 157.02, 159.70. Anal. Calcd. for C₈H₇N₃O₂: 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) vmax: 3320, 3070 (br., NH, OH), 1676 (C=O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 2.15 (s, 6H, 2CH₃), 7.34 (s, 2H, Ph); ¹³C-NMR (100 MHz, DMSO) δ (ppm): 17.21, 118.30, 125.12, 125.53, 146.63, 155.88, 157.53; Anal. Calcd. for C₁₀H₁₁N₃O₂: 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) vmax: 3428, 3000 (br., NH, OH), 1710 (C=O) cm⁻¹; ¹H-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); ¹³C-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 C₁₄H₁₁N₃O₂: 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) vmax: 3460, 3140 (br., NH, OH), 1690 (C=O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 2.52 (s, 3H, CH₃), 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); ¹³C-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 C₁₄H₁₁N₃O₂: 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)-4H-[1,2,4]oxadiazo1-5-one (5a). M.p.: 184-186°C (aq. ethanol); IR (hexachlorobutadiene) vmax: 3328-2984 (br., NH, OH), 1748 (C=O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 2.38 (s, 3H, CH₃), 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); ¹³C-NMR (100 MHz, DMSO) δ (ppm): 21.46, 113.62, 113.76, 118.60, 131.06, 139.83, 158.43, 158.43, 160.18, 160.43; Anal. calcd. for C₉H₈N₂O₃: 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)-4H-[1,2,4]oxadiazo1-5-one (5b). M.p.: 223-224°C (aq. ethanol); IR (nujol) vmax: 3400, 3240 (NH, OH), 1974 (C=O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 2.21 (s, 6H, 2CH₃), 7.40 (s, 2H, Ph), 9.14 (s, 1H, OH), 12.63 (br.s., 1H, NH); ¹³C-NMR (100 MHz, DMSO) δ (ppm): 17.05, 114.06, 125.46, 126.75, 157.33, 157.76, 160.47; Anal. Calcd. for C₁₀H₁₀N₂O₃: 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) vmax: 3340 (OH), 1738 (C=O) cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ (ppm): 3.99 (t, J= 6.02 Hz, 2H, CH₂), 4.19-4.32 (m, 2H, CH₂), 6.85 (d, J= 7.60 Hz, 2H, Ph), 7.71 (d, J= 7.63 Hz, 2H, Ph), 8.91 (br.s., 1H, OH); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm): 62.68, 68.36, 113.90,
129.88, 134.00, 150.88, 162.88; Anal. Calcd. for C9H3NO2: 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) vmax: 3400 (OH), 1794 (C=O) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, DMSO/TFAA) 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); \(^1^3\)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-1H-imidazole (7a). M.p. 297-299°C (water); M.p. Lit.\(^1\) 208°C; IR (nujol) vmax: 3200 (br., NH), 1614, 1590 (C=O) 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); \(^1^3\)C-NMR (100 MHz, DMSO/TFAA) δ (ppm): 44.52, 112.63, 116.48, 131.21, 163.77, 164.94; Anal. Calcd. for C\(_{9}\)H\(_{10}\)N\(_2\)O: 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-1H-imidazole (7b). M.p.: 221-223°C (aq. ethanol); IR (nujol) vmax: 3000 (br.), 1586 (C=O) 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); \(^1^3\)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\(_2\)O: 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-1H-imidazole (7c). M.p. >310°C (aq. ethanol); IR (hexachlorobutadiene) vmax: 3320 (NH), 1596, 1584 (C=O) 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); \(^1^3\)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\(_2\)O: 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.\(^1\) 290-292°C; IR (nujol) vmax: 2900 (CH\(_2\)), 1610, 1584 (C=O) 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); \(^1^3\)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\(_2\)O: 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) vmax: 2880, 2670 (CH\(_2\)), 1630, 1580 (C=O) 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); \(^1^3\)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\(_2\)O: 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-1H-[1,3]diazepine (9). M.p.: 298-300°C (water); IR (nujol) vmax: 3160, 2840 (br.), 1570 (C=O) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, DMSO/TFAA) δ
Genera

Genera A

(1) 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_{2}O: 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. 220-221˚C; IR (hexachlorobutadiene) ν max: 3300 (OH), 1608-1578 (C=C) cm^{-1}; ¹H-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); ¹³C-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_{9}NO_{2}: C 73.92, H 4.29, N 6.63%. Found: C 74.14, H 4.45, N 6.93%.

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) vamax: 1742 (C=O) cm^{-1}; ¹H-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); ¹³C-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-(1H-benzoimidazol-2-yl) phenyl ester (14).** Oil; IR (KBr) \( \nu_{\text{max}} \): 1722 (C=O) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, DMSO) \( \delta \) (ppm): 5.89 (dd, \( J = 10.17, 1.97 \) Hz, 1H, CH\(_2\)), 6.16 (d, \( J = 11.15 \) Hz, 1H, CH), 6.25 (d, \( J = 1.97 \) Hz, 1H, CH\(_2\)), 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) \( \delta \) (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) \( \nu_{\text{max}} \): 1722 (C=O), 1632-1626 (C=C) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) (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\(_3\)) \( \delta \) (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-(1H-benzimidazol-2-yl) phenyl ester (15b).** M.p.: 218-221°C (toluene/methanol); IR (KBr) \( \nu_{\text{max}} \): 3484 (NH), 1714 (C=O), 1632 (C=C) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, DMSO) \( \delta \) (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\(_3\)) \( \delta \) (ppm): 117.48, 122.61, 122.96, 128.20, 128.33, 129.19, 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\(_2\)O\(_2\): C 77.63, H 4.74, N 8.23%. Found: C 77.46, H 4.62, N 8.01%.

**Acrlyic acid 4-phenylthiocarbamoyl-phenyl ester (21).** Yield 80%; m.p. 92-95°C (hexane/ethyl acetate); IR (KBr) \( \nu_{\text{max}} \): 3300 (NH), 1740 (C=O) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) (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\(_3\)) \( \delta \) (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) \( \nu_{\text{max}} \): 3200 (OH), 1724 (C=O) cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) (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; 1H-NMR (400 MHz, CDCl₃/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); 13C-NMR (100 MHz, CDCl₃/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 C₂₂H₁₇NO₂S: 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. 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; 1H-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); 13C-NMR (100 MHz, CDCl₃) δ (ppm): 114.32, 116.58, 118.64, 119.73, 120.29, 122.26, 123.33, 129.24, 129.78, 129.84, 140.17, 149.07, 150.76, 152.99, 163.24; Anal. calcd. for C₂₀H₁₄N₂O₃: 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 (KBr) νmax: 3324 (NH), 1716 (C=O) cm⁻¹; 1H-NMR (400 MHz, DMSO) δ (ppm): 2.67 (s, 3H, CH₃), 7.19 (d, J= 8.18 Hz, 2H, Ph), 7.62 (d, J= 8.28 Hz, 2H, Ph), 7.74 (br.s., 1H, NHCH₃). 7.78-7.89 (m, 4H, Ph), 11.80 (br.s., 1H, NHPh); 13C-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 C₁₅H₁₃BrN₂O₂S: C 49.33, H 3.59, S 8.78%.

Methyl-carbamic acid 2,3-dimethyl-4-phenylthiocarbamoyl-phenyl ester (19c). M.p.: 208-210°C (toluene); IR (nujol) νmax: 3388, 3340 (NH), 1737 (C=O) cm⁻¹; 1H-NMR (400 MHz, DMSO) δ (ppm): 3.83 (s, 3H, CH₃); 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); 13C-NMR (100 MHz, DMSO) δ (ppm): 34.90, 40.02, 121.49, 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 C₁₉H₁₃BrClN₂O₂S: C 52.02, H 3.06, S 6.94%. Found: C 51.89, H 3.27, N 7.91, S 7.14%.

(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; 1H-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); 13C-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 C₂₀H₁₄BrClN₂O₂S: C 52.02, H 3.06, S 6.94%. Found: C 51.89, H 3.27, N 7.91, S 7.14%.
CDCl$_3$ $\delta$ (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$_3$) $\delta$ (ppm): 12.87, 16.83, 27.66, 120.22, 123.56, 126.72, 129.03, 130.01, 132.99, 143.00, 149.58, 155.28, 199.55; Anal. calcd. for C$_{17}$H$_{18}$N$_2$O$_2$S: 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. 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) vmax: 1700 (C=O) cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ (ppm): 1.13 (dt, $J=7.02$ Hz, 2H, Ph), 7.15-7.36 (m, 3H, Ph), 7.64 (d, $J=6.53$ Hz, 2H, Ph), 9.39 (br.s., 1H, NH); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ (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$_2$O$_2$S: 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) vmax: 1700 (C=O) cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ (ppm): 1.13 (dd, $J=26.21$, 7.02 Hz, 6H, 2CH$_3$), 3.19-3.42 (m, 4H, 2CH$_2$), 6.98 (d, $J=7.95$ Hz, 2H, Ph), 7.64 (d, $J=7.86$ Hz, 2H, Ph), 9.40 (br.s., 1H, NH); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ (ppm): 36.64, 38.82, 118.78, 121.87, 126.57, 129.21, 131.86, 139.71, 139.80, 153.89, 154.08, 197.17; MS m/z: 328 (M$^+$, 64.2%), 100 (100%); Anal. calcd. for C$_{18}$H$_{20}$N$_2$O$_2$S: 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-bromophenylthiocarbamoyl)-phenyl ester (20c).** M.p.: 216-218°C (toluene); IR (nujol) vmax: 3268 (NH), 1700 (C=O) cm$^{-1}$; $^1$H-NMR (400 MHz, DMSO) $\delta$ (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, $J=8.77$ Hz, 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) $\delta$ (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$_2$O$_2$S: 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-bromophenylthiocarbamoyl)-phenyl ester (20d).** M.p.: 129-131°C (toluene/hexane); IR (nujol) vmax: 3280 (NH), 1700 (C=O) cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ (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, CH₂), 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); ¹³C-NMR (100 MHz, CDCl₃) 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) v max: 3400-2900 (br., NH, OH), 1746 (C=O), 1602, 1504 (C=C), 1442, 1418 (C-O) cm⁻¹; ¹H-NMR (400 MHz, DMSO) δ (ppm): 4.79 (s, 2H, CH₂), 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); ¹³C-NMR (100 MHz, CDCl₃) 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 C₁₅H₁₃NO₃S: 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) v max: 3296 (NH), 1738 (C=O), 1598 (C=C) cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ (ppm): 0.65-0.78 (m, 3H, CH₃), 0.81-0.94 (m, 6H, 2CH₃), 1.02 (q, J=11.57Hz, 2H, CH₂), 1.32-1.56 (m, 2H, CH₂), 1.60-1.85 (m, 3H, CH, CH₂), 2.00 (s, 1H, CH), 2.10-2.19 (m, 1H, CH), 4.63 (d, J=10.58Hz, 2H, OCH₂), 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); ¹³C-NMR (100 MHz, CDCl₃) 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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References