Synthesis and pesticidal activities of some bis – [2-(substituted phenyl)-thiazolidin-4- one-3-yl] thioureas/ bis-[(2-methyl-2-2 substituted phenyl) thiazolidin -4- one -3- yl]thioureas

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ABSTRACT
Several bis- [2- (substituted phenyl)–thiazolidin -4- one -3-yl] thioureas/ bis – [(2-methyl -2- substituted phenyl) thiazolidin - 4- one -3-yl] thioureas have been synthesized by refluxing a mixture of dihydrazinium thiocarbazinate and substituted araldehyde in methanol with two drops of gl. AcOH for 2-3 hours forms bis – (substituted araldehyde hydrazono) – thiocarbazinate on condensation with thioglycollic acid in benzene/ by refluxing a mixture of dihydrazinium thiocarbazinate with substituted acetophenone in methanol for 2-3 hours. The synthon thus obtained was further treated with thioglycollic acid in benzene to get the titled compounds.

Keywords: Substituted phenyl, 4-thiazolidinone, thiourea, pesticidal activity.

INTRODUCTION
Derivatives of 4- thiazolidinone have been demonstrated to possess antibacterial[1], antifungal[2], anticonvulsant[3], anti cancer[4], anti tuberculosis[5] and antihuman immune deficiency virus type 1 (HIV-1)[6] and other activities[7,8]. The literature survey revealed that many different protocols have been developed in a way that allows the synthesis of 4-thiazolidinone skeletons[9]. In continuation of our work on the synthesis and biological activity of heterocycles including 4-thiazolidinones[10-12], we report herein a simple and one pot route to the synthesis of hitherto unknown bis-[2-(substituted phenyl)-thiazolidine- 4- one- 3-yl] thioureas / bis –[(2-methy -2- substituted phenyl) thiazolidin -4- one -3-yl] thioureas derivatives in order to evaluate their pesticidal activity.

MATERIALS AND METHODS
Herbicidal Activity: All the compounds were subjected to primary post and pre-emergent herbicidal[13] evaluation at a rate of 8.0, 4.0, 1.0 and 0.5 kg ha⁻¹. The test species are Echinochloa oryzicola, Echinochloa crusgalli, oryza sativa and glycine max, using the following scores: 5, (100%); 4, (44-75%); 3, (74-35%); 2, (34-5%) and 1, (4-0%). The most active compound was found to be 3a, 3c, 3d, 3f, 5a and 5c.
**Fungicidal Activity:** The title compounds 3a-g and 5a-e were screened for their antifungal activity against *Pyricularia oryzae, Pseudoperonospora cubensis, Sphaerotheca fuliginea* and *Phytophthora infestans* in DMSO by disc diffusion and broth dilution methods[14]. The results were compared with that of commercial fungicide.

**Experimental:** All melting points are uncorrected. IR spectra were recorded in KBr on a Perkin – Elmer – 881 spectrophotometer and 1H NMR spectra on a Perkin-Elmer R-32 spectrometer at 60MHz.

**Dihydrazinium thiocarbazinate:** It was prepared by the known method[15]. A mixture of carbon disulphide and hydrazine hydrate in cold methanol was dissolved in 150ml of an aq. solution having sufficient hydrazine hydrate. (100CC water, 50CC hydrazine hydrate). The reaction mixture was refluxed on steam bath for 1 hour. The precipitated mass was collected, washed with 95% ethanol and recrystallized from water having 1 drop of methanol. m.p. 169°C, Literature [15] reports m.p. 171°C.

**Sym-(substituted benzilidemino) thioureas (2a.) Ar = 2, 4-Cl₂C₆H₄:** A mixture of dihydrazinium thiocarbazinate (1.06 g, 0.01 M) and 2,4- dichlorobenzaldehyde (3.76 g, 0.02 M) was dissolved in methanol (30 ml) with two drops of gl. AcOH. The reaction mixture was refluxed for 2 h and then poured over crushed ice. The solid mass thus obtained was filtered, washed with excess water and then recrystallized from aq. ethanol m.p. 216°C yield 88% IR (KBr): 3200 (<C=O), 1710 (<C = N), 1370-CH₃ sym-bending, 1510 aromatic ring and 1170 cm⁻¹ (>C=S) stretching; 1H NMR (DMSO-d₆) δ 3.9(s, 6H, OCH₃); 4.8 (s, 2H, -N=CH); 7.2 (d, 8H, aromatic); 7.9 (d, 2H, NH).

**Bis- (2- (Substituted phenyl) – thiazolidin-4- one -3yl) thioureas. (3a) Ar= 2, 4-Cl₂C₆H₄:** This compound was prepared by condensing sym- (2, 4-dichlorobenzilidemino)– thioureas (4.2g) and thioglycollic acid (2.02CC) in benzene (50ml) for 3 hours. Excess of benzene was removed and then poured in to water; the solid mass thus obtained was washed in the sodium bicarbonate solution. It was filtered, washed with excess water and recrystallized with aq. ethanol m.p. 197°C yield 72%. IR (KBr): 3400 (<NH), 1710 (>C= O), 1580, 1510 aromatic ring and 1460 cm⁻¹ –CH₂ bending; 1H NMR (DMSO-d₆) δ 3.3 (d, 4H, CH2); 4.8 (s, 2H, CH); 7.7 (s, 6H, aromatic) 8.5-9.0 (m, 2H, NH).

**Bis – (substituted acetophenone hydrazono) thiocarbazinate (4a) Ar=4-OCH₃ C₆H₄:** It was prepared by taking a mixture of dihydrazinium thiocarbazinate (1.06g) and 4-methoxy acetophenone (3.0g) in methanol (30ml) with two drops of gl. AcOH and refluxed for 2 hours It was poured into crushed ice. The compound thus obtained was filtered, washed, dried and recrystallized from aq. ethanol m.p. 175°C yield 67% IR (KBr): 3240 (-NH), 1630 (>C = N), 1350 (>c=s), 1170 –C=N, 1250 –C-O-C, 1600, 1500 and 1450 cm⁻¹ aromatic rings. 1H NMR (DMSO-d₆) δ 2.0 (m, 1H, NH), 3.73 (s, 3H, OCH₃), 4.8 (s, 1H, N=C), 7.2 (d, 8H, aromatic).

**Bis – [(2-methyl-2- substituted phenyl) – thiazolidine-4-one -3yl) thioureas. (5a), Ar = 4-OCH₃C₆H₄ :** This compound was prepared by condensing bis – (4- methoxy acetophenone hydrazono) – thiocarbazinate (3.7g) with thioglycollic acid (2.02ml) in benzene (30ml) was refluxed for 3h. It was poured into crushed ice. The compound thus obtained was filtered, washed, dried and recrystallized from aq. ethanol m.p. 173°C yield 72% IR (KBr): 3400 (-NH), 1720 (>c=o), 1600 (>C=N), 1580, 1500, 1450 aromatic ring and 1170 cm⁻¹ >C=S. 1H NMR (DMSO-d₆); δ 3.6 (d, 4H, CH₂), 4.8 (s, 2H, CH), 3.7 (s, 3H, OCH₃), 6.8-7.3 (m, 7H, Ar-H).

Other such compounds were also prepared in a similar way and their characterization data are given in table 1.
### TABLE 1. Characterization data of compounds 3a-g and 5a-e

<table>
<thead>
<tr>
<th>Compounds</th>
<th>M.P. (°C)</th>
<th>Yield (%)</th>
<th>Mol. Formula</th>
<th>Found (%) (Calcd.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>197</td>
<td>72</td>
<td>C₁₀H₁₄N₂S₂O₂Cl₂</td>
<td>40.00 (40.14) 2.35 (2.46) 9.72 (9.85)</td>
</tr>
<tr>
<td>3b</td>
<td>252</td>
<td>69</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>52.90 (53.02) 4.07 (4.18) 12.89 (13.00)</td>
</tr>
<tr>
<td>3c</td>
<td>26</td>
<td>68</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>45.62 (45.09) 3.11 (3.20) 11.08 (11.22)</td>
</tr>
<tr>
<td>3d</td>
<td>170</td>
<td>64</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>55.00 (55.02) 4.80 (4.80) 12.14 (12.22)</td>
</tr>
<tr>
<td>3e</td>
<td>135</td>
<td>71</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>53.26 (53.48) 5.31 (5.42) 16.09 (16.27)</td>
</tr>
<tr>
<td>3f</td>
<td>166</td>
<td>69</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>51.34 (51.42) 4.07 (4.18) 9.72 (9.85)</td>
</tr>
<tr>
<td>3g</td>
<td>163</td>
<td>70</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>53.36 (53.20) 4.07 (4.18) 9.72 (9.85)</td>
</tr>
<tr>
<td>3h</td>
<td>173</td>
<td>72</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>54.96 (55.02) 4.80 (4.80) 12.14 (12.22)</td>
</tr>
<tr>
<td>3i</td>
<td>179</td>
<td>68</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>51.44 (51.63) 4.07 (4.18) 9.72 (9.85)</td>
</tr>
<tr>
<td>3j</td>
<td>240</td>
<td>66</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>47.59 (47.81) 3.70 (3.79) 10.51 (10.62)</td>
</tr>
<tr>
<td>3k</td>
<td>292</td>
<td>69</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>51.44 (51.63) 4.78 (4.91) 17.09 (17.21)</td>
</tr>
<tr>
<td>3l</td>
<td>180</td>
<td>70</td>
<td>C₁₀H₁₄N₂S₂O₂</td>
<td>51.27 (51.42) 4.31 (4.48) 11.36 (11.42)</td>
</tr>
</tbody>
</table>

### RESULTS AND DISCUSSION

Compounds 3a-g and 5a-e were screened for their herbicidal activity against *Echinochloa oryzicola*, *Echinochloa crusgalli*, *Oryza sativa* and *Glycine max* as well as fungicidal activity against *Pyricularia oryzae*, *Pseudoperonospora cubensis*, *Sphaerotheca fuliginea* and *phytophthora infestans*. The results were compared with commercial herbicides as well as fungicides under similar conditions. Amongst these the most active compounds are 3a, 3c, 3d, 3f, 5a, 5c and 5e as shown in table 2.

### TABLE 2: Fungicidal activity of compounds 3a-g and 5a-e (zone of inhibition in mm)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Pyricularia oryzae</th>
<th>Pseudoperonospora cubensis</th>
<th>Sphaerotheca fuliginea</th>
<th>Phytophthora infestans</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>3b</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>3c</td>
<td>10</td>
<td>9</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>3d</td>
<td>13</td>
<td>14</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>3e</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>3f</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>3g</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>5a</td>
<td>12</td>
<td>13</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>5b</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>5c</td>
<td>11</td>
<td>10</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>5d</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>5e</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Carbendiazim</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

### APPLICATIONS

We have synthesized bis-[2-(substituted phenyl) -thiazolidin -4- one -3- yl] thioureas/ bis –[(2-methyl -2-substituted phenyl) thiazolidin -4- one -3- yl] thioureas. All these compounds have been assayed for their pesticidal activities. Some of them have shown excellent pesticidal activity.
CS₂ + 2 N₂H₄ • H₂O \[\text{In Cold Reflux} \rightarrow \] H₂N•NH \[\overset{1}{\text{C}}\text{—OH} \rightarrow \] H₂N•NH \[\overset{2}{\text{C}}\text{—CH₃} \rightarrow \]

\[
\begin{align*}
1. & \quad \text{2. } \text{Ar} \quad \text{C—O} \\
2. & \quad \text{MeOH/} \\
& \quad \text{Reflux 3 h}
\end{align*}
\]

\[
\begin{align*}
\text{S} \quad \text{C—N} \quad \text{N} \\
\text{H} \quad \text{C—N} \quad \text{N} \\
\text{H} \quad \text{C—Ar} \\
\end{align*}
\]

\[
\begin{align*}
\text{2HSCH₂COOH} \\
\text{BENZENE/} \\
\text{REFLUX} \\
\text{BENZENE/} \\
\text{REFLUX}
\end{align*}
\]

\[
\begin{align*}
\text{S} \quad \text{C—N} \quad \text{N} \\
\text{H} \quad \text{C—N} \quad \text{N} \\
\text{CH₃} \quad \text{O} \\
\text{S} \quad \text{C—Ar} \\
\end{align*}
\]

\[
\begin{align*}
\text{S} \quad \text{C—N} \quad \text{N} \\
\text{H} \quad \text{C—N} \quad \text{N} \\
\text{CH₃} \quad \text{O} \\
\text{S} \quad \text{C—Ar} \\
\end{align*}
\]

3a. Ar = 2,4 Cl₂C₆H₃
3b. Ar = C₆H₅
3c. Ar = 4-Cl C₆H₄
3d. Ar = 4-CH₃ C₆H₄
3e. Ar = C₆H₄ N(CH₃)₂
3f. Ar = 4-OCH₃ C₆H₄
3g. Ar =

5a. Ar = 4-OCH₃C₆H₄
5b. Ar = C₆H₅
5c. Ar = 4-Cl C₆H₄
5d. Ar = 4-NH₂ C₆H₄
5e. Ar = 4-OHC₆H₄

Scheme

REFERENCES


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