Two ways of cyclization of 5-imidazolylthioureas with dimethyl acetylenedicarboxylate

Oleg S. Eltsov,* Maria V. Smirnova, Yuri Yu. Morzherin, Nataliya P. Belskaiya, and Vladimir S. Mokrushin

Department of Technology for Organic Synthesis, The Urals State Technical University
19 Mira str., Ekaterinburg 620002, Russian Federation
E-mail: oleg-eltsov@yandex.ru

Abstract
Two ways of cyclization of imidazolyl derivatives of thiourea with dimethylacetylene dicarboxylate (DMAD) were studied. Reaction of N,N'-disubstituted thioureas with DMAD led to formation of a thiazoline ring whereas transformation of trisubstituted thioureas under the same conditions give the novel imidazo[1,5-c][1,3,5]thiadiazine heterocyclic system.

Keywords: Imidazolylthiourea, DMAD, heterocyclization, imidazo[1,5-c][1,3,5]thiadiazine, thiazolidine

Introduction
Organic dithiocarbamates and thioureas are valuable synthetic intermediates, which are used widely in the synthesis of biologically active compounds. Functionalization of such moieties offers an attractive method for the generation of derivatives which may possess interesting medicinal and biological properties. For these reasons, the transformation of dithiocarbamate and thiourea derivatives with different substituents has become a field of increasing interest in synthetic organic chemistry during the past few years.

We have reported earlier some aspects of the chemistry of imidazolylthioureas. Recently we communicated the reaction of imidazolylalkyl dithiocarbamates 1a,b and thioureas 2a,b with DMAD which are the first examples of the construction of the novel heterocyclic system of imidazo[1,5-c][1,3,5]thiadiazines (Scheme 1). These compositions are close structural analogs of pyrazolo[1,3,5]thiadiazine which are a potent antifungal pro-drugs and inhibitors of photosynthetic electron transport.

Due to our interest to the chemistry of imidazolyl derivatives of alkyl dithiocarbamate and thiourea, now we present the extended studies of reaction of imidazolylthioureas with DMAD. The aim of this work was to determine the scope and limitations of annelation of 1,3,5-thiadiazine ring to imidazoles.
**Results and Discussion**

It is well known that acetylenedicarboxylic acid esters are very reactive dienophiles and may form both cycloaddition products (way A, for example: 1,4-diazines, pyrimidines, etc.)\(^7\) and cyclocondensation products with elimination of one alcohol molecule (way B, for example: thiazolidines, thiazines, etc.).\(^8\) Therefore it was very surprising to find another type of cyclization involving only one carbon atom of acetylene component resulting in formation of 1,3,5-thiadiazines ring (way C) (Scheme 2).
Most reported 1,3,5-thiadiazines contain carbonyl or thiocarbonyl groups in the ring: such compounds were previously synthesized by treatment of heterocyclic primary thioamides with phenoxy carbonyl isocyanate,\(^9\) cyclization of perchloroethyl isocyanate with thioamides;\(^{10}\) reaction of thiobenzoyl isocyanates with arylhydrazones,\(^{11}\) benzaldazines,\(^{12}\) carbodiimides,\(^{13}\) or anils;\(^{14}\) \([4+2]\) cycloaddition of 1-thia-3-azadienes with electron-deficient nitriles;\(^{15}\) dimerization of thiocarbamoyl isothiocyanates\(^{16}\) or dimerization of carbamoyl isothiocyanates\(^{17}\) and 1,3,5-oxathiazines.\(^{15}\) Previously reported condensed azolo[1,3,5]thiadiazines were made by reaction of isothiocarbamoylisothiocyanates with isocyanate,\(^{19}\) by transformation of 2-mercaptopimidazolines,\(^{20}\) or pyrazolylcarbothioamides.\(^{6a,6c,6d}\)

![Crystal structure of 3a.](image)

**Figure 1.** Crystal structure of 3a.

To get more information about the structure of novel heterocyclic system of imidazo[1,5-c][1,3,5]thiadiazine we grew a crystal of compound 3a and performed its X-ray analysis (Figure 1). According to the X-ray data, the imidazo[1,5-c][1,3,5]thiadiazine is non-planar. It is worthwhile to note that the N(3) atom is close to the plane of the imidazole ring whereas the sp\(^3\)-hybrid C(1) atom is situated above the plane (the dihedral angle between the planes is 172.31\(^\circ\)) and S(1) and C(2) atom are located under the plane of the imidazole ring (the dihedral angles between the planes are -167.37\(^\circ\) and -173.40\(^\circ\) respectively).

For expansion of the series of new imidazo[1,5-c][1,3,5]thiadiazines we used the secondary amines 4a,b with a tryptamine core prepared by means of reductive amination of aromatic and heteroaromatic aldehydes (Scheme 3).
Scheme 3

Heating of compounds 5a,b in ethanol with amines 4a,b for a short time afforded thiourea derivatives 6a-d. Reaction with DMAD led to imidazo[1,5-c][1,3,5]thiadiazines 7a-d containing the tryptamine pharmacophoric moiety. Their $^1$H NMR spectra display signals of protons of a tryptamine fragment, imidazole core, both OMe groups (3.75 and 3.70 ppm), and the AB-system of protons of the CH$_2$ group (3.65-3.67 ppm, and 3.52-3.57 ppm, $J$ 12.9-17.3 Hz). In the $^{13}$C NMR spectra, the characteristic signals for a CH$_2$ group (50.5-50.9 ppm, $J$ 134.6-135.4 Hz) and the sp$^3$-hybrid C- atom of the thiadiazine ring (63.3–63.4 ppm, $J$ 4.7-5.2 Hz) were observed. Parent ions in the mass-spectra of compounds 7a-d corresponded to addition products (Scheme 4).

Scheme 4

To determine the influence of substituents on the new transformation of 5-imidazolyl-thioureas we synthesized disubstituted thioureas 9a-e by reacting 5-amino-imidazoles with isothiocyanates (Scheme 5). In this case, reaction of imidazolyl derivatives with DMAD led to a thiazoline ring and formation of compounds 10a-e. The $^1$H NMR spectra of 10a-e show one OMe and a CH singlet on the exocyclic double bond. The $^{13}$C NMR spectrum has characteristic doublets for the CH group (134.3-134.9 ppm, $J$ 157.9-161.2 Hz). Parent ions in mass-spectra confirm the formation of cyclocondensation products resulting from the elimination of one methanol molecule. As a result of conjugation of a carbon-carbon double bond with two heterocycles, all substances 10a-e have a bright yellow color.
Table 1. $^1$H NMR data of compounds 6,7a-d (all $J$ values are in Hz)

<table>
<thead>
<tr>
<th>Cpd</th>
<th>CH</th>
<th>CONHR$^1$</th>
<th>Ar and Indolyl</th>
<th>CH$_2$</th>
<th>CO$_2$ Me</th>
<th>NH (all s, 1xH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>7.53</td>
<td>7.68 (br s, 1H), 6.53 (br s, 1H)</td>
<td>7.38-7.30 (m, 5H), 6.94 (m, 1H), 6.45 (br s, 1H)</td>
<td>5.04 (br s, 2H), 3.90 (br s, 2H), 2.93 (t, 2H, $J = 7.02$)</td>
<td>12.86, 11.32, 11.02</td>
<td></td>
</tr>
<tr>
<td>6b</td>
<td>7.52</td>
<td>8.14 (br s, 1H, NH), 2.80 (br s, 3H, CH$_3$)</td>
<td>7.52-7.30 (m, 6H), 6.90 (m, 1H)</td>
<td>5.15 (br s, 2H), 3.84 (br s, 2H), 3.00 (t, 2H, $J = 7.02$)</td>
<td>12.87, 11.40 (br), 11.02</td>
<td></td>
</tr>
<tr>
<td>6c</td>
<td>7.53</td>
<td>8.24 (br s, 1H), 6.53 (br s, 1H)</td>
<td>7.59-7.30 (m, 6H), 6.90 (m, 1H)</td>
<td>5.10 (br s, 2H), 3.83 (br s, 2H), 3.01 (t, 2H, $J = 7.02$)</td>
<td>12.87, 11.32 (br), 11.04</td>
<td></td>
</tr>
<tr>
<td>6d</td>
<td>7.50</td>
<td>7.43 (br s, 1H, NH), 2.81 (s, 3H, CH$_3$)</td>
<td>7.39-7.29 (m, 7H), 6.89 (m, 1H)</td>
<td>5.06 (br s, 2H), 3.88 (br s, 2H), 3.05 (t, 2H, $J = 7.32$)</td>
<td>12.87, 11.35, 11.01</td>
<td></td>
</tr>
<tr>
<td>7a</td>
<td>7.53</td>
<td>7.15 (br s, 1H), 6.87 (br s, 1H)</td>
<td>7.51 (s, 1H), 7.28 (m, 1H)</td>
<td>4.75 (br s, 2H), 3.80 (br s, 2H), 3.61 (AB, 1H, $J = 16.8$), 3.55 (AB, 1H, $J = 16.8$), 2.98 (t, 2H, $J = 7.6$)</td>
<td>3.76, 3.70, 10.85</td>
<td></td>
</tr>
<tr>
<td>7b</td>
<td>7.52</td>
<td>7.15 (br s, 1H), 2.76 (d, 3H, CH$_3$, $J = 5.0$)</td>
<td>7.31-7.23 (m, 2H, H$_A$), 6.82 (td, 1H, $J = 9.3$), 6.47 (br s, 1H), 6.37 (dd, 1H, $J = 3.0$)</td>
<td>4.75 (br s, 2H): 3.81 (br s, 2H), 3.61 (AB, 1H, $J = 17.3$), 3.55 (AB, 1H, $J = 17.3$), 2.98 (t, 2H, $J = 7.2$)</td>
<td>3.75, 3.70, 10.85</td>
<td></td>
</tr>
<tr>
<td>7c</td>
<td>7.33</td>
<td>7.17-6.78 (br s, 2H, CONH$_2$)</td>
<td>7.31-7.27 (m, 5H), 7.21 (br s, 1H), 7.20 (br d, 1H, $J = 4.5$), 6.81 (td, 1H, $J = 9.0$)</td>
<td>4.79 (br s, 2H), 3.78 (br s, 2H), 3.67 (AB, 1H, $J = 12.9$), 3.57 (AB, 1H, $J = 12.9$), 2.98 (t, 2H, $J = 7.5$)</td>
<td>3.75, 3.70, 10.84</td>
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</tr>
<tr>
<td>7d</td>
<td>7.34</td>
<td>7.17-6.78 (br s, 1H, NH), 2.66 (d, 3H, CH$_3$, $J = 5.0$)</td>
<td>7.32-7.24 (m, 4H), 7.24 (dd, 1H, $J = 9.8$)</td>
<td>4.82 (br s, 2H), 3.82 (br s, 2H), 3.65 (AB, 1H, $J = 17.3$), 3.52 (AB, 1H, $J = 17.3$), 2.98 (br s, 2H)</td>
<td>3.75, 3.70, 10.85</td>
<td></td>
</tr>
</tbody>
</table>
Scheme 5

Table 2. $^1$H NMR data of compounds 9a-c and 10a-e (all $J$ values in Hz).

<table>
<thead>
<tr>
<th>Cpd</th>
<th>CH (s)</th>
<th>CONHR$^1$</th>
<th>R$^2$</th>
<th>CO$_2$Me</th>
<th>NH (all 1xH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a</td>
<td>7.67</td>
<td>7.27 (br s, 2H)</td>
<td>3.10 (d, 3H, $J$ 4.58)</td>
<td>12.47 (br s), 10.29 (d, $J$ 3.97), 9.83 (s, 1H)</td>
<td></td>
</tr>
<tr>
<td>9b</td>
<td>7.64</td>
<td>7.27 (s, 2H)</td>
<td>6.01-5.88 (m, 1H), 5.30-5.12 (d, 2H, $J$ 5.6), 4.26 (d, 2H, $J$ 8.80)</td>
<td>12.47 (t, $J$ 4.60), 10.70 (br s), 9.88 (s)</td>
<td></td>
</tr>
<tr>
<td>9c</td>
<td>7.58</td>
<td>7.25 (s, 2H)</td>
<td>7.37-7.20 (m, 5H), 4.86 (d, 2H, $J$ 4.5)</td>
<td>12.44 (br s), 10.76 (br s), 9.94 (s)</td>
<td></td>
</tr>
<tr>
<td>10a</td>
<td>7.81, 6.75</td>
<td>7.62, (s, 1H), 7.27 (s, 2H)</td>
<td>3.21 (s, 3H)</td>
<td>3.79</td>
<td>13.03 (br s)</td>
</tr>
<tr>
<td>10b</td>
<td>7.65, 6.71</td>
<td>7.41 (s, 1H), 7.14 (s, 1H)</td>
<td>5.91 (m, 1H), 5.24 (t, 2H, $J$ 7.53), 4.54 (d, 2H, $J$ 5.4)</td>
<td>3.83</td>
<td>12.93 (br s)</td>
</tr>
<tr>
<td>10c</td>
<td>7.64, 6.9</td>
<td>7.41 (s, 2H), 7.14 (s, 1H)</td>
<td>7.34-7.25 (m, 5H), 5.11 (s, 2H)</td>
<td>3.79</td>
<td>12.9 (br s), 6.82 (s)</td>
</tr>
<tr>
<td>10d</td>
<td>7.65, 6.76</td>
<td>7.64 (q, 2H, $J$ 6.74), 2.91 (d, 3H, $J$ 4.8)</td>
<td>3.4 (s, 3H)</td>
<td>3.82</td>
<td>12.96 (br s)</td>
</tr>
<tr>
<td>10e</td>
<td>7.64, 6.8</td>
<td>7.01 (br s, 1H), 2.41 (d, 3H, $J$ 4.9)</td>
<td>7.63-7.46 (5H, m)</td>
<td>3.84</td>
<td>12.96 (br s)</td>
</tr>
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</table>
Table 3. Selected chemical shifts of $^{13}$C NMR of compounds 7a-d and 10a-e

<table>
<thead>
<tr>
<th>Comp.</th>
<th>COOMe</th>
<th>$C_{sp}^3$</th>
<th>$CH_2$</th>
<th>$CH=\ $</th>
<th>$C_{sp}^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>168.2, 166.8, 40.3* 39.2*</td>
<td>63.3</td>
<td>50.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7b</td>
<td>168.2, 166.8, 40.5* 39.2*</td>
<td>63.3</td>
<td>50.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7c</td>
<td>168.2, 166.9, 40.5* 38.8*</td>
<td>63.4</td>
<td>50.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7d</td>
<td>168.2, 166.9, 40.5* 39.1*</td>
<td>63.3</td>
<td>50.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10a</td>
<td>161.5, 163.3, 51.7</td>
<td></td>
<td></td>
<td>134.5</td>
<td></td>
</tr>
<tr>
<td>10b</td>
<td>165.6, 163.3, 52.4</td>
<td></td>
<td></td>
<td>134.4</td>
<td></td>
</tr>
<tr>
<td>10c</td>
<td>165.0, 163.5, 51.7</td>
<td></td>
<td></td>
<td>134.5</td>
<td></td>
</tr>
<tr>
<td>10d</td>
<td>165.1, 163.3, 51.7</td>
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<td></td>
<td>134.3</td>
<td></td>
</tr>
<tr>
<td>10e</td>
<td>165.8, 163.2, 52.5</td>
<td></td>
<td></td>
<td>134.9</td>
<td></td>
</tr>
</tbody>
</table>

*Signals are overlapped with signal of solvent.

In summary, contrary to prior art we have found that reactions of DMAD with 5-imidazolylthioureas bearing tert-amino group involves the nitrogen atom of the imidazole ring and the only one carbon atom of the acetylene component leading to formation of novel system of imidazo[1,5-c][1,3,5]thiadiazine.

Experimental Section

General Procedures. $^1$H NMR spectra were recorded on a Bruker WM-250 instrument (250.13 MHz) and Bruker AVANCE II instrument (400 MHz) in DMSO-d$_6$ with Me$_4$Si as the internal
standard. $^{13}$C NMR spectra were recorded on a Varian Mercury-300 (75.5 MHz) in DMSO-d$_6$. The course of the reaction was monitored and the purity of the products was checked by TLC on Sorbfil UV-254 plates in ethyl acetate. Mass spectra (EI, 70 eV) were recorded on a Varian MATT 311A instrument. Melting points are uncorrected. $^1$H NMR data of all compounds are in Tables 1 and 2.

Tryptamine derivatives 4a,b were prepared according to known procedures. Trisubstituted thioureas 6a-d and imidazothiadiazines 7a-d were synthesized by the conditions described in our earlier communication.

5-{3-[2-(5-Fluoro-1$^H$-indol-3-yl)-ethyl]-3-furan-2-yl-methyl)-thioureido]-3$^H$-imidazole-4-carboxylic acid amide (6a). Colorless solid; yield 60%, mp 201-3 °C. Anal. Calcd. for C$_{20}$H$_{19}$FN$_6$O$_2$S (%): C, 56.34; H, 4.49; N, 19.71; S, 7.52. Found (%): C 56.60, H 4.29; N 19.45; S 7.30. m/z 426 (60%) (M$^+$).

5-{3-[2-(5-Fluoro-1$^H$-indol-3-yl)-ethyl]-3-furan-2-yl-methyl)-thioureido}-3$^H$-imidazole-4-carboxylic acid methylamide (6b). Colorless solid; yield 51%, mp 169-170 °C. Anal. Calcd. for C$_{21}$H$_{21}$FN$_6$O$_2$S (%): C, 57.26; H, 4.81; N, 19.08; S 7.28. Found (%): C, 57.49; H, 4.55; N, 19.00; S, 7.01. m/z 440 (52%) (M$^+$).

5-{3-(4-Chlorobenzyl)-3-[2-(5-fluoro-1$^H$-indol-3-yl)-ethyl]-thioureido}-3$^H$-imidazole-4-carboxylic acid amide (6c). Colorless solid; yield 60%, mp 189-190 °C. Anal. Calcd. for C$_{22}$H$_{20}$ClFN$_6$OS (%): C, 56.11; H, 4.28; N, 17.84; S, 6.81. Found (%): C 56.02; H 4.40; N 17.69; S 7.00. MS m/z 470 (44%) (M$^+$).

5-{3-(4-Chlorobenzyl)-3-[2-(5-fluoro-1$^H$-indol-3-yl)-ethyl]-thioureido}-3$^H$-imidazole-4-carboxylic acid methylamide (6d). Colorless solid; yield 51%, mp 200-1 °C. Anal. Calcd. for C$_{23}$H$_{22}$ClFN$_6$OS (%): C, 56.96; H 4.57; N 17.58; S 6.41. m/z 484 (52%) (M$^+$).

Methyl 8-carbamoyl-4-methoxycarbonylmethyl-2-[2-(5-fluoro-1$^H$-indol-3-yl)-ethyl]-furan-2-ylmethylamino}-imidazo[1,5-c][1,3,5]thiadiazine 4-carboxylate (7a). Colorless solid; yield 69%, mp 118-9 °C. Anal. Calcd. for C$_{26}$H$_{25}$FN$_6$O$_6$S (%): C, 54.92; H, 4.43; N, 14.78; S, 5.64. Found (%): C, 54.80; H, 4.50; N, 15.01; S, 5.50. $^{13}$C NMR (75.5 MHz, DMSO-d$_6$) δ 168.2, 166.8, 163.4, 158.3, 155.2, 151.0, 149.9, 142.9, 137.9, 132.8, 129.9, 127.2, 125.4, 121.6, 112.4, 110.6, 109.3, 108.9, 102.9, 63.3, 54.1, 52.4, 50.7, 40.5, *40.3, *39.2, *m/z 568 (41%) (M$^+$).

4-Methoxycarbonylmethyl-8-methylcarbamoyl-2-[2-(5-fluoro-1$^H$-indol-3-yl)-ethyl]-furan-2-ylmethylamino}-imidazo[1,5-c][1,3,5]thiadiazine-4-carboxylic acid methyl ester (7b). Colorless solid; yield 59%, mp 195-7 °C. Anal. Calcd. for C$_{27}$H$_{27}$FN$_6$O$_6$S (%): C 55.66; H 4.67; N 14.42; S 5.50. Found (%): C, 55.49; H, 4.95; N, 14.26; S 5.66. $^{13}$C NMR (75.5 MHz, DMSO-d$_6$) δ 168.2, 166.8, 162.4, 158.2, 155.2, 151.0, 149.9, 142.9, 137.9, 132.8, 129.9, 127.2, 125.4, 121.6, 112.4, 110.6, 109.3, 108.9, 102.9, 63.3, 54.1, 52.3, 50.5, 40.6, *40.5, *39.2, *m/z 582 (50%) (M$^+$).

8-Carbamoyl-4-methoxycarbonylmethyl-2-{[4-chlorobenzyl]-[2-(5-fluoro-1$^H$-indol-3-yl)-ethyl]-amino}-imidazo[1,5-c][1,3,5]thiadiazine-4-carboxylic acid methyl ester (7c). Colorless
solid; yield 65%, mp 122-4 °C. Anal. Calcd. for C_{28}H_{26}ClFNO_{5}S (%): C, 54.86; H, 4.27; N, 13.71; S 5.50. Found (%): C, 55.00; H, 4.04; N, 13.89; S, 5.00. 13C NMR (75.5 MHz, DMSO-d_6) δ 168.2, 166.9, 163.4, 158.3, 155.2, 151.4, 137.9, 135.9, 132.8, 131.9, 128.8, 128.5, 127.2, 125.4, 121.5, 112.4, 110.5, 109.3, 108.9, 102.9, 102.6, 63.4, 54.1, 52.3, 50.9, 40.6, *40.5, *38.8. * MS m/z 611 (47%) (M^+).

4-Methoxycarbonylmethyl-8-methylcarbamoyl-2-{(4-chlorobenzyl)-[2-(5-fluoro-1H-indol-3-yl)-ethyl]-amino}-imidazo[1,5-c][1,3,5]thiadiazine-4-carboxylic acid methyl ester (7d). Colorless solid; yield 69%, m p 203-4 °C. Anal. Calcd. for C_{29}H_{28}ClFN_{6}O_{5}S (%): C, 55.55; H, 4.50; N, 13.40; S, 5.11. Found (%): C, 55.80; H, 4.32; N, 13.66; S, 5.00.

The N,N'-disubstituted thioureas (9a-c) were prepared according to procedures described for 9d,e earlier.3c,21

5-(3-Methylthioureido)-3H-imidazole-4-carboxamide (9a). Colorless solid; yield 80%, mp >250 °C. Anal. Calcd. for C_{6}H_{9}N_{5}O (%): C, 36.17; H, 4.55; N, 35.15; S, 16.09. Found (%): C, 36.33; H, 4.31; N, 35.00; S, 16.20. m/z 199 (55%) (M^+).

5-(3-Allylthioureido)-3H-imidazole-4-carboxamide (9b). Colorless solid; yield 75%, mp >250 °C. Anal. Calcd. for C_{8}H_{11}N_{5}O (%): C, 42.65; H, 4.92; N, 31.09; S, 14.23. Found (%): C, 42.99; H, 5.12; N, 31.40; S, 14.20. m/z 225 (62%) (M^+).

5-(3-Benzylthioureido)-3H-imidazole-4-carboxamide (9c). Colorless solid; yield 86%, mp >250 °C. Anal. Calcd. for C_{17}H_{15}N_{5}O (%): C, 52.70; H, 4.39; N, 25.80; S, 11.31. m/z 275 (40%) (M^+).

General procedure for the synthesis of compounds (10a-e)

A solution of each of the compounds 9a-e (0.69 mmol) and 0.09 ml (0.71 mmol) DMAD in 20 mL of methanol was stirred for 1-4 h. The precipitates of compounds 10a-e were filtered off and recrystallized from methanol.

5-(5-Methoxycarbonylmethylen-4-oxo-3-methylthiazolidin-2-ylidenamino)-3H-imidazole-4-carboxamide (10a). Yellow solid; yield 75%, mp >250 °C. Anal. Calcd. for C_{11}H_{11}N_{5}O_{4}S (%): C, 42.72; H, 3.58; N, 22.64; S, 10.37. Found (%): C, 43.00; H, 3.90; N, 22.40; S, 10.31. m/z 309 (41%) (M^+). 13C NMR (75.5 MHz, DMSO-d_6) δ 161.5, 163.3, 159.9, 151.2, 143.1, 142.8, 134.5, 117.4, 115.0, 51.7, 28.8.

5-(3-Allyl-5-methoxycarbonylmethylen-4-oxo-thiazolidin-2-ylidenamino)-3H-imidazole-4-carboxamide (10b). Yellow solid; yield 71%, mp >250 °C. Anal. Calcd. for C_{13}H_{13}N_{5}O_{4}S (%): C, 46.56; H, 3.91; N, 20.88; S, 9.56. Found (%): C, 46.25; H, 3.95; N, 20.50; S, 9.81. m/z 335 (45%) (M^+). 13C NMR (75.5 MHz, DMSO-d_6) δ 165.6, 163.3, 156.2, 150.6, 143.2, 143.1, 135.2, 134.4, 117.8, 117.1, 115.6, 52.4, 44.8.

5-(3-Benzyl-5-methoxycarbonylmethylen-4-oxo-thiazolidin-2-ylidenamino)-3H-imidazole-4-carboxamide (10c). Yellow solid; yield 68%, mp >250 °C. Anal. Calcd. for C_{17}H_{15}N_{5}O_{4}S (%):
C, 52.98; H, 3.92; N, 18.17; S, 8.32. Found (%): C, 53.32; H, 3.80; N, 18.00; S, 8.00. m/z 385 (49%) (M+). 13C NMR (75.5 MHz, DMSO-d6) δ 165.0, 163.5, 159.6, 150.4, 142.7, 142.4, 135.2, 134.5, 128.1, 127.0, 126.4, 117.5, 115.6, 51.7, 45.6.

5-(5-Methoxycarbonylmethylen-4-oxo-3-methylthiazolidin-2-ylidenamino)-3H-imidazole-4-methylcarboxamide (10d). Yellow solid; yield 69%, mp >250 °C. Anal. Calcd. for C12H13N5O4S (%): C, 44.58; H, 4.05; N, 21.16; S, 9.92. Found (%): C, 44.90; H, 3.80; N, 21.40; S, 10.00. m/z 323 (55%) (M+). 13C NMR (75.5 MHz, DMSO-d6) δ 165.1, 163.3, 159.1, 151.0, 142.8, 142.4, 134.3, 117.4, 115.0, 51.7, 28.9, 24.9.

5-(5-Methoxycarbonylmethylen-4-oxo-3-phenylthiazolidin-2-ylidenamino)-3H-imidazole-4-methylcarboxamide (10e). Yellow solid; yield 77%, mp >250 °C. Anal. Calcd. for C17H15N5O4S (%): C, 52.98; H, 3.92; N, 18.17; S, 8.32. Found (%): C, 53.21; H, 3.81; N, 18.40; S, 8.44. m/z 385 (51%) (M+). 13C NMR (75.5 MHz, DMSO-d6) δ 165.8, 163.2, 159.2, 151.7, 143.5, 142.4, 135.3, 134.9, 129.2, 129.1, 128.4, 117.6, 115.6, 52.5, 24.8.

**Supplementary Materials**

CCDC 694964 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.ac.uk/data_request.cif.

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**References**


