A NOVEL ONE-STEP SYNTHESIS OF 3-SUBSTITUTED-5,6-DIHYDROTHIAZOLO[2,3-c]-1,2,4-
TRIAZoles AND -6,7-DIHYDRO-5H-1,2,4-TRIAZOlO[3,4-b][1,3]THIAZines

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Abstract - 3-Substituted-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazenes and -6,7-
dihydro-5H-1,2,4-triazolo[3,4-b][1,3]thiazines have been synthesized in one
step by reaction of the acid hydrazides with haloalkyl isothiocyanates.

The availability and chemical versatility of haloalkyl isothiocyanates have made them useful
starting materials for preparative heterocyclic chemistry. We have recently described a new one-
step synthesis of 2,3-dihydro-5H-thiazolo[2,3-b]quinazolin-5-one and 3,4-dihydro-2H,6H-[1,3]-
thiazolo[2,3-b]quinazolin-6-one by the reaction of methyl anthranilate with chloroalkyl isothio-
cyanates. In this communication we report the discovery of a novel general method for the synthesis of 3-
substituted-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazenes and -6,7-dihydro-5H-1,2,4-triazolo[3,4-b]-
[1,3]thiazines.

Reaction of 2-furoic acid hydrazide with 2-chloroethyl isothiocyanate in refluxing xylene fol-
lowed by addition of triethylamine gave 3-(2-furanyl)-5,6-dihydrothiazolo[2,3-c]-1,2,4-triazole
\[1\] in 59% yield as white leaflets, m.p. 142-143°C; \(\text{ir} \ \nu_{\text{max}} \ \text{(Nujol)}: 1620 \ \text{cm}^{-1}
\]
\((C=N) \text{ and } 1520 \ \text{cm}^{-1} \ (C-C)) ; \text{\[1\]nmr (CDCl}_3\): \(\delta \text{ (ppm)} 4.15 \text{ (t, } 2H, \text{ CH}_2S), 4.50 \text{ (t, } 2H, \text{ CH}_2N), 6.55 \text{ (q, } H, \text{ FurH}_4), 6.95 \text{ (d, } 1H, \text{ FurH}_3) \); \text{ ms (electron impact, 70 eV): } m/e 193 \ (M^+, \text{ base}). The
reaction involves the intermediate formation of a thiazoline and the elimination of water to give
\[1\] via an intramolecular ring closure.

Similarly, we found that the reaction of 2-furoic acid hydrazide with 3-chloropropyl isothio-
cyanate and triethylamine, yielded 3-(2-furanyl)-6,7-dihydro-5H-1,2,4-triazolo[3,4-b][1,3]-
thiazine 2 (80%), m.p. 211-212°C; \(\text{ir} \ \nu_{\text{max}} \ \text{(Nujol)}: 1615 \ \text{cm}^{-1} \ (C=C)) ; \text{\[1\]nmr (DMSO-
d6): \(\delta \text{ (ppm)} 2.45 \text{ (m, } 2H, \text{ C-CH}_2-C), 3.30 \text{ (t, } 2H, \text{ CH}_2S), 4.43 \text{ (t, } 2H, \text{ CH}_2N), 6.63 \text{ (q, } 1H, \text{ FurH}_4), 7.25 \text{ (d, } 1H, \text{ FurH}_3) \); ms (electron impact, 70 eV): } m/e 207 \ (M^+, \text{ base}).
The physical and spectral properties of some representative examples are summarized in Table 1. The reaction is generally effective for a wide range of aliphatic, aromatic and heterocyclic acid hydrazides.

### TABLE 1

Physical and Spectral Properties of Selected 3-Substituted-5,6-Dihydrothiazolo[2,3-c]-1,2,4-triazoles and 6,7-Dihydro-5H-1,2,4-triazolo[3,4-b][1,3]thiazines.

<table>
<thead>
<tr>
<th>R</th>
<th>n</th>
<th>m.p. °C. (Solvent)</th>
<th>Yield, %</th>
<th>Spectral Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>2</td>
<td>228.5-230 (Ethanol)</td>
<td>55</td>
<td>ir v max (Nujol): 1600, 1520 cm⁻¹; ¹Hnmr (DMSO- d₆ + TFA): 4.15 (t, 2H, CH₂S), 4.70 (t, 2H, CH₂N), 7.80 (q, 4H, ArH); ms: m/e 237.</td>
</tr>
<tr>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>2</td>
<td>192-193 (Ethanol)</td>
<td>42</td>
<td>ir v max (Nujol): 1640, 1585 cm⁻¹; ¹Hnmr (DMSO- d₆): 4.15 (t, 2H, CH₂S), 4.55 (t, 2H, CH₂N), 7.52 (t, 1H, ArH), 8.20 (d, 1H, ArH), 8.70 (d, 1H, ArH), 9.00 (s, 1H, ArH); ms: m/e 204.</td>
</tr>
<tr>
<td>R</td>
<td>n</td>
<td>m.p. °C. (Solvent)</td>
<td>Yield, %</td>
<td>Spectral Data</td>
</tr>
<tr>
<td>------------</td>
<td>----</td>
<td>-------------------</td>
<td>----------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>-CH₂</td>
<td>2</td>
<td>225.5-227</td>
<td>55</td>
<td>ir vmax (Nujol): 1630, 1615, 1540 cm⁻¹; ¹Hnmr (DMSO-d₆): 2.45 (s, 3H, CH₃), 4.15 (t, 2H, CH₂S), 4.73 (t, 2H, CH₂N), 7.60 (q, 4H, ArH); ms: m/e 217.</td>
</tr>
<tr>
<td>0</td>
<td>3</td>
<td>154-156</td>
<td>25</td>
<td>ir vmax (Nujol): 1530 cm⁻¹; ¹Hnmr (CDCl₃): 2.2-2.6 (m, 2H, CH₂C), 2.40 (s, 3H, CH₃), 3.20 (t, 2H, CH₂S), 4.00 (t, 2H, CH₂N); ms: m/e 155.</td>
</tr>
<tr>
<td>-CH₂CH₂CH₃</td>
<td>3</td>
<td>57-58</td>
<td>67</td>
<td>ir vmax (Nujol): 1525 cm⁻¹; ¹Hnmr (DMSO-d₆): 1.10 (t, 3H, CH₂CH₂CH₃), 1.75 (m, 2H, -SCH₂CH₂CH₂N-), 2.70 (t, 2H, CH₂CH₂CH₃), 3.25 (t, 2H, CH₂S), 4.05 (t, 2H, CH₂N), ms: m/e 183.</td>
</tr>
<tr>
<td>Cl</td>
<td>3</td>
<td>186-187</td>
<td>62</td>
<td>ir vmax (Nujol): 1600, 1615, 1530 cm⁻¹; ¹Hnmr (DMSO-d₆): 2.20 (m, 2H, C-CH₂-C), 3.23 (t, 2H, CH₂S), 4.15 (t, 2H, CH₂N), 7.70 (q, 4H, ArH); ms: m/e 251.</td>
</tr>
<tr>
<td>-CH₃</td>
<td>3</td>
<td>163-164</td>
<td>63</td>
<td>ir vmax (Nujol): 1630, 1615, 1530 cm⁻¹; ¹Hnmr (DMSO-d₆): 2.25 (m, CH₂C), 2.45 (s, 3H, CH₃), 3.28 (t, 2H, CH₂S), 4.15 (t, 2H, CH₂N), 7.45 (q, 4H, ArH); ms: m/e 231.</td>
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<tr>
<td>0</td>
<td>3</td>
<td>244-245</td>
<td>69</td>
<td>ir vmax (Nujol): 3150, 1620; 1530 cm⁻¹; ¹Hnmr (DMSO-d₆): 2.20 (m, 2H, -SCH₂CH₂CH₂N-), 3.10 (t, 2H, CH₂S), 3.90 (t, 2H, CH₂N), 4.05 (s, 2H, CH₂S), 6.90 (s, 1H, C=CH), 7.20 (m, 4H, ArH), 7.50 (s, 1H, NH); ms: m/e 270.</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENT

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REFERENCES AND NOTES

Satisfactory analytical data have been obtained for all crystalline compounds described in this communication.


2. The only previously known member of this series, 3-phenyl-6,7-dihydro-5H-1,2,4-triazolo-[3,4-b][1,3]thiazine was prepared from 2-benzoylhydrazino-5,6-dihydro-4H-1,3-thiazine by K. S. Dhaka, J. Mohan, V. K. Chadha and H. K. Pujari, Indian J. Chem., 1974, 12, 485.


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