INTRODUCTION

Much attention has been recently paid to the synthesis of some thieno[1,2,4]triazolopyrimidines and thieno[1,2,4]triazolopyrimidinones because of their biological activities.1-4 With this in mind and in continuation of our recent work on the synthesis of 2-phenylthieno[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine derivatives7 we describe here a facile synthesis of 2-phenylthieno[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine derivatives5 that have not been reported hitherto as a new ring system. Previous observations revealed that the thieno[3,2-e][1,2,4]triazolo[4,3-c]pyrimidin-5(6H)-ones6 can isomerizes in the presence of base to the thermodynamically more stable thieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5(6H)-ones.4

The compounds 4 were prepared through a series of reaction starting with 3-aminophenyl-2-carbonitrile (1) according to the modified procedure we have previously reported (Scheme 1).1 The required starting material 1 was obtained by adopting the new synthetic method.6 Reaction of 1 with triethyl orthoformate and the successive hydrazine hydrate gave 4-hydrazinothieno[3,2-d]pyrimidine (2). The hydrazone derivatives 3 were synthesized by condensation of hydrazine compound 2 with the corresponding benzaldehydes in refluxing ethanol in the presence of catalytic amount of piperidine. The oxidative cyclization of the resultant hydrazone derivatives 3 to 4 was achieved using alumina-supported calcium hypochlorite (Ca(OCl)2/Al2O3 = 1:1, grounded mixture) as a new oxidant. For instance, a maximum yield of 73% for 4a in 1 h was achieved with 1:3 molar ratio of hydrazone to calcium hypochlorite. The use of alumina-supported calcium hypochlorite as a heterogeneous oxidant in this reaction has advantage of enhanced reaction rate and yield, simple work-up, low cost, and eco-friendly reagent when compared to other oxidants such as bromine,7 lead tetraacetate,8 iodobenzene diacetate1,9 or copper dichloride.10 When each of 4 was treated with sodium acetate in refluxing ethanol, it underwent a Dimroth-type rearrangement to give compounds 5 through a sequence of ring opening and ring closure reaction. For instance, the reaction of 4a (1 mmol) with sodium acetate (2 mmol) in refluxing ethanol for 5 h afforded only one product, 5a in 68% yield. The structures of all new compounds 5 were identified by elemental analyses and spectral data. The results are summarized in Table 1. It was noticed that the two isomeric 4 and 5 showed no appreciable differences in the fragmentation pattern of MS spectra, however, the 1H NMR spectra of 5 revealed that the most prominent pyrimidine proton showed signal little more downfield than the one of their isomeric 4. These results were in agreement with those reported in earlier report.5 The conversion of 4 into 5 is also analogous to rearrangement of thieno[2,3-e][1,2,4]triazolo[4,3-c]pyrimidin-5(6H)-ones in base to the isomeric thieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5(6H)-ones.4

In conclusion, we report a facile synthesis of 2-phenyl-
Table 1. Preparation of compounds 5 from 4

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Mp (°C)</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>5a</td>
<td>105 - 107</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>4-Cl</td>
<td>5b</td>
<td>250 - 252</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>4-Me</td>
<td>5c</td>
<td>203 - 205</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>4-MeO</td>
<td>5d</td>
<td>201 - 203</td>
<td>62</td>
</tr>
<tr>
<td>5</td>
<td>3-Br</td>
<td>5e</td>
<td>207 - 208</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td>3-Cl</td>
<td>5f</td>
<td>140 - 142</td>
<td>63</td>
</tr>
<tr>
<td>7</td>
<td>3-Me</td>
<td>5g</td>
<td>164 - 166</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>3-BR</td>
<td>5h</td>
<td>134 - 136</td>
<td>65</td>
</tr>
<tr>
<td>9</td>
<td>2-MeO</td>
<td>5i</td>
<td>127 - 129</td>
<td>50</td>
</tr>
</tbody>
</table>

aIsolated yields.

**General procedure for the preparation of 2-phenylthieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidine derivatives (5)**

To a solution of each 3-phenylthieno[2,3-e][1,2,4]triazolo[4,3-c]pyrimidine 4 (1 mmol) in ethanol (30 mL) was added sodium acetate (0.164 g, 2 mmol) and the mixture was refluxed for 5 h and cooled. The precipitated solid was filtered, washed with water, dried and finally crystallized from ethanol to give the respective 2-phenylthieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidine 5.

**EXPERIMENTAL**

All products were characterized by IR, $^1$H NMR, MS and elemental analysis. Melting points were measured by using the capillary tubes on Büchi apparatus and are uncorrected. Each compound of the reactions was checked on thin-layer chromatography of Merck Kieselgel 60F254 and purified by column chromatography using Merck silica gel (70 - 230 mesh). IR spectra were recorded on the FT-IR Bruker Tensor 27. The $^1$H NMR spectra were recorded on Bruker DRX-300 FT-NMR spectrometer (300 MHz) with Me$_4$Si as internal standard and chemical shifts are given in ppm ($\delta$). Electron ionization mass spectra were recorded on a HP 59580 B spectrometer. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.
1370 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 9.30 (s, 1H, H-4), 8.23 (d, 2H, H-2' and H-6'), 7.86 (d, \(J = 5.9\) Hz, 1H, H-6), 7.63 (d, \(J = 5.9\) Hz, 1H, H-6), 7.34 (d, 2H, H-3' and H-5'), 2.44 (s, 3H, Me); MS: (m/z) 266 (M\(^+\), 99), 149 (35), 134 (20). Anal. Calcd. for C\(_{14}\)H\(_{10}\)N\(_4\)S: C, 63.14; H, 3.78; N, 21.04. Found: C, 63.12; H, 3.81; N, 21.11.

2-(3-Chlorophenyl)thieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidine (5f)

Yield 60%; mp 165 - 166 °C; IR (KBr): 3036, 2980, 1625 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 9.28 (s, 1H, H-4), 8.18-8.14 (m, 2H, H-2' and H-6'), 7.87 (d, \(J = 5.9\) Hz, 1H, H-7), 7.64 (d, \(J = 5.9\) Hz, 1H, H-6), 7.42 (t, 1H, H-5'), 7.33 (d, 1H, H-4'), 2.48 (s, 3H, Me); MS: (m/z) 266 (M\(^+\), 100), 149 (10). Anal. Calcd. for C\(_{14}\)H\(_{10}\)N\(_4\)S: C, 63.14; H, 3.78; N, 21.04. Found: C, 63.29; H, 3.65; N, 21.11.

2-(3-Bromophenyl)thieno[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine (5g)

Yield 65%; mp 137 - 139 °C; IR (KBr): 3034, 1622 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 9.29 (s, 1H, H-4), 8.05 (d, 1H, H-6), 7.74 (d, \(J = 5.9\) Hz, 1H, H-7), 7.59 (d, \(J = 5.9\) Hz, 1H, H-6), 7.54 (d, 1H, H-4'), 7.36 (t, 1H, H-5'), 1.90 (s, 3H, OMe); MS: (m/z) 328 (M\(^+\), 98), 149 (14), 134 (22). Anal. Calcd. for C\(_{14}\)H\(_{10}\)N\(_4\)OS: C, 59.56; H, 3.57; N, 19.85. Found: C, 59.44; H, 3.66; N, 19.93.

2-(3-Chlorophenyl)thieno[3,2-e][1,2,4]triazolo[1,5-c]pyrimidine (5i)

Yield 50%; mp 127 - 129 °C; IR (KBr): 3030, 2975, 1620, 1375 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 9.30 (s, 1H, H-4), 8.22 (d, 2H, H-2' and H-6'), 7.88 (d, \(J = 5.9\) Hz, 1H, H-6), 7.69 (d, \(J = 5.9\) Hz, 1H, H-6), 7.65 (d, 2H, H-3' and H-5'); MS: (m/z) 331 (M\(^+\), 100), 149 (11), 134 (20). Anal. Calcd. for C\(_{14}\)H\(_{10}\)BrN\(_4\)S: C, 47.14; H, 2.13; N, 16.92. Found: C, 47.28; H, 2.26; N, 17.11.

2-(2-Methoxyphenyl)thieno[2,3-e][1,2,4]triazolo[1,5-c]pyrimidine (5h)

Yield 65%; mp 134 - 136 °C; IR (KBr): 3034, 1622 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 9.28 (s, 1H, H-4), 8.14-8.10 (m, 2H, H-4' and H-6'), 7.88 (d, \(J = 5.9\) Hz, 1H, H-6), 7.55 (d, \(J = 5.9\) Hz, 1H, H-6), 7.36 (t, 1H, H-5'), 2.47 (s, 3H, OMe); MS: (m/z) 282 (M\(^+\), 100), 149 (14), 134 (18). Anal. Calcd. for C\(_{14}\)H\(_{10}\)N\(_4\)OS: C, 59.56; H, 3.57; N, 19.85. Found: C, 59.69; H, 3.42; N, 19.62.

REFERENCES