Synthesis of enantiopure fused bisthiazolidines and thiazolidinyloxazolidines.

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**INTRODUCTION**

Among the different possible methods leading to nitrogen-containing heterocycles, iminium ion cyclization is a widely used process. Cyclic iminium ions of general structure 1 (Figure 1), bearing a nucleophilic tether with a suitable located oxygen, sulfur or nitrogen, are important building blocks for the preparation of synthetically and biologically relevant condensed heterocycles.

Figure 1. Cyclic iminium ion 1, compounds 2 and 3.

1 \[ \begin{array}{c}
\text{X} = \text{O, S, N, C} \\
\text{Y} = \text{O, S, N} \\
\text{R} = \text{alkyl, aryl}
\end{array} \]

The present work describes our findings in the synthesis of enantioenriched new fused thiazolidinyloxazolidines (2) and bisthiazolidines (3) via the generation of cyclic iminium ions (Figure 1).

**RESULTS AND DISCUSSION**

The thiazolidinyloxazolidines 2 were prepared by a 2-step sequence using a modified protocol published previously.\(^{2}\) Syn-bicycles 2a-d, were obtained in good yields and high enantiomeric excess, see Table 1.

Table 1. Synthesis of thiazolidinyloxazolidines 2a-d

<table>
<thead>
<tr>
<th>Compound</th>
<th>R (^{1})</th>
<th>Yield (%)</th>
<th>de % (^{1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>syn-2a</td>
<td>Ph</td>
<td>89</td>
<td>99</td>
</tr>
<tr>
<td>syn-2b</td>
<td>p-CIPh</td>
<td>86</td>
<td>98</td>
</tr>
<tr>
<td>syn-2c</td>
<td>p-NO(_2)Ph</td>
<td>89</td>
<td>99</td>
</tr>
<tr>
<td>syn-2d</td>
<td>CO(_2)Et</td>
<td>60</td>
<td>98</td>
</tr>
</tbody>
</table>

\(^{1}\) de: diastereomeric excess, determined by \(^{1}\)H NMR.

Compounds 3 were obtained by heating 4a or 4b in the presence of the dimeric aldehyde 5, in acidic media, see Figure 2. Smooth decomposition of dithiane 5 led to the formation of 2-mercaptoacetaldehyde. The reaction of two molecules of aldehyde in the presence of aminothiol 4a,b, led to the formation of fused bisthiazolidines 3a,c. Interestingly when we use 4b as starting material, the diastereomeric excess was higher than when we use ester 4a, see Figure 2.

The double cyclization process led to bicycle 3 via iminium ion formation. Further studies in the serie 2 are being carried out in order to study the scope and limitations of this methodology.

Figure 2. Synthesis of fused bisthiazolidines 3

\[ \begin{align*}
4a: & \text{R} = \text{CO}_2\text{H} \\
4b: & \text{R} = \text{CO}_2\text{Et} \\
3a: & \text{R} = \text{CO}_2\text{H}, \text{X} = \text{S}, 60\%, \text{de} 80\% \\
3b: & \text{R} = \text{CO}_2\text{Et}, \text{X} = \text{S}, 45\%, \text{de} 30\%
\end{align*} \]

**CONCLUSION**

The results presented herein provide evidence for the versatility of N acyliminium ions for the synthesis of new bicyclic compounds not easily accessed by other routes. This structure represents new enantiomerically pure scaffolds; and we can envision their application in organocatalysis, new materials or medicinal chemistry.

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**REFERENCES**