USE OF N-BROMOSUCCINIMIDE IN THE SYNTHESIS OF HETEROCYCLIC SYSTEMS

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Abstract

N-Bromosuccinimide has been used in the synthesis of a series of imidazothiazoles. It is both quicker and more convenient to use than other reagents.

The use of α-halo ketones in the synthesis of imidazothiazoles\(^1\)\(^2\) has been reported in the literature. α-Halo ketones have been successfully replaced by halogens and ketones in the syntheses of the above compounds.\(^3\) The latter method avoids the use of α-halo ketones, which are difficult to obtain, yet suffers from the drawback that the procedure is cumbersome and more time consuming. (It requires about 25 hr of refluxing.) These defects have been removed in the present communication by using N-bromosuccinimide (NBS) in the synthesis of imidazothiazoles (2). The NBS method considerably reduces the time period (5–6 hr of refluxing) and at the same time simplifies the workup. The yields of imidazothiazoles, in general, are comparable to those in the previous methods. The NBS method might find general applicability in the syntheses of other condensed thiazoles.

2-Mercapto-2-imidazoline (1a)\(^4\) was made to react with ketones in the presence of NBS in anhydrous benzene; subsequent basification with potassium carbonate yielded imidazothiazole (2a). Similarly, 2-mercapto-4-methyl-2-imidazoline (1b)\(^5\) used in place of (1a) in the above reaction gave (2b). A small amount of benzoyl peroxide was added to the reaction mixture to facilitate the synthesis of (2).

Experimental

3-p-Bromophenyl-5,6-dihydro-4H-imidazo[2,1-b]thiazole (2a; \(R' = p-BrC_6H_4, R^* = H\))

A mixture of 2-mercapto-2-imidazoline (1a) (3·06 g, 0·03 mol), p-bromoacetophenone (5·87 g, 0·03 mol), N-bromosuccinimide (5·34 g, 0·03 mol), and a small amount of benzoyl peroxide in anhydrous benzene (40 ml) was heated, under reflux, for about 6 hr on a steam bath. The solvent

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was distilled off and the hydrobromide thus obtained was purified (charcoal), m.p. 296° (EtOH) (lit. 296-297°), yield 90%. The hydrobromide on neutralization with potassium carbonate gave the free base, m.p. 144-145° (EtOH) (lit. 145-146°). The structure was confirmed by i.r. and n.m.r. spectra and elementary analysis for sulphur.

\[
\begin{align*}
(1a) & \quad R = H \\
(1b) & \quad R = CH_3
\end{align*}
\]

\[
\begin{align*}
(2a) & \quad R = H \\
(2b) & \quad R = CH_3
\end{align*}
\]

3-p-Bromophenyl-6-methyl-5,6-dihydro-4H-imidazo[2,1-b]thiazole (2b; \( R' = p-BrC_6H_4, R'' = H \))

This compound was obtained by heating a mixture of 2-mercapto-4-methyl-2-imidazoline (2.30 g, 0.02 mol), \( p \)-bromacetophenone (3.98 g, 0.02 mol), \( N \)-bromosuccinimide (3.56 g, 0.02 mol), and a small amount of benzoyl peroxide in anhydrous benzene (40 ml) following the above procedure. HBr salt, m.p. 270° (lit. 3 270°), yield 37%. The hydrobromide on neutralization with potassium carbonate gave the free base, m.p. 129° (EtOH) (lit. 3 130°). The structure was confirmed by i.r. and n.m.r. spectra and elementary analysis for sulphur.

Other results are shown in Table 1.

**Table 1**

<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>R''</th>
<th>Yield</th>
<th>HBr salt</th>
<th>Lit. m.p.</th>
<th>Thiazole</th>
<th>Lit. m.p.</th>
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<tbody>
<tr>
<td>H</td>
<td>C_6H_5</td>
<td>H</td>
<td>53%</td>
<td>245°</td>
<td>234-244°</td>
<td>40%</td>
<td>110-111°</td>
</tr>
<tr>
<td>H</td>
<td>p-ClC_6H_4</td>
<td>H</td>
<td>56</td>
<td>272</td>
<td>272-274°</td>
<td>45</td>
<td>116-117</td>
</tr>
<tr>
<td>H</td>
<td>p-O_2NC_6H_4</td>
<td>H</td>
<td>58</td>
<td>285</td>
<td>287-290°</td>
<td>48</td>
<td>215-216</td>
</tr>
<tr>
<td>H</td>
<td>CH_3</td>
<td>C_6H_5</td>
<td>51</td>
<td>246</td>
<td>246-248°</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>H</td>
<td>C_6H_5</td>
<td>CH_3</td>
<td>49</td>
<td>234-236</td>
<td>236-238°</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CH_3</td>
<td>p-ClC_6H_4</td>
<td>H</td>
<td>48</td>
<td>255-256</td>
<td>256°</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CH_3</td>
<td>p-O_2NC_6H_4</td>
<td>H</td>
<td>59</td>
<td>250 (dec.)</td>
<td>248-250°</td>
<td>43</td>
<td>212</td>
</tr>
<tr>
<td>CH_3</td>
<td>C_6H_5</td>
<td>CH_3</td>
<td>66</td>
<td>258-259</td>
<td>258°</td>
<td>—</td>
<td>—</td>
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