Synthesis of some thiazolidinones and N-acetyl amino derivatives from 4-amino sulphamethaoxazole

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Abstract

4-amino sulphamethaoxazole was reacted with chloro acetyl chloride to convert the amino group to 4-chloro acetyl amino sulphamethaoxazole (compound 1). The amide was then allowed to react with potassium thiocyanate to prepare 4-(2-imino-4-oxo-thiazolidinyl) compound (2) which contained thiazolidinone ring. Some aromatic amines were reacted with 4-chloro acetyl amino sulphamethaoxazole compound (1) to prepare 4-substituted anilino acetyl amino sulphamethaoxazole compounds (1A-H). 4-(2-imino-4-oxo-thiazolidinyl) Compound (2) was reacted with different aromatic aldehydes to prepare 4-(5-arylidene-2-imino-4-oxo-thiazolidinyl sulphamethaoxazole) compounds (2A-H). The prepared compounds were identified and for the prepared compounds such as (1D,1H,2,2B,2E) \(^1\)H-n.m.r. spectra was used.

Key word: 4-amino sulphamethaoxazole, thiazolidinone, N-acetyl amino compounds.
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1. Introduction

Thiazolidine ring is of considerable interest as it is a structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities\(^{(1-5)}\). Many compounds of 5-arylidine-2-imino-4-thiazolidinone have been prepared by Ameya and et.al\(^{(6)}\). Glyoxilic acid was reacted with cysteine to prepare thiazolidine-2,4-dicarboxilic acid that used as a ligand with divalent and trivalent metal ion\(^{(7-8)}\). Derivatives of thiazolidinone have been prepared by different methods and chemical reagents\(^{(9-15)}\). Oxazoles which are part of structures of prepared compounds are known to exhibit interesting biological activities\(^{(16-20)}\). Oxazoles have been demonstrated to be very versatile building blocks in organic synthesis\(^{(21-28)}\). So many methods were used to prepare thiazolidinone derivatives\(^{(29-32)}\).

2. Experimental

2.1. Materials

All Materials were from Aldrich and were used further purification.

2.2. Instruments

1- FT-IR Spectrophotometer model Shimadzu 8400, [400-4000 cm\(^{-1}\)].
2- Melting Point Apparatus model Gallenkamp.
3- \(\text{H-n.m.r. 300 MHz Bruker 2003 Jordan in DMSO-d6.}\)

2.3. synthesis of 4-chloro acetyl amino sulphamethaoxazole (compound 1)

To a stirred solution of 4-amino sulphamethaoxazole (0.01 mole, 1.26g) and triethyl amine (0.01 mole, 1.02ml) in dioxine (50ml), mono chloro acetyl chloride (0.01 mole, 1.13ml) was added dropwise. The reaction mixture was refluxed for 12 h. The excess of solvent was evaporated. The solid obtained was washed with water, filtered, dried and crystallized from ethanol\(^{(6)}\).

2.4. synthesis of 4-substituted anilino acetyl amino sulphamethaoxazole (compound 1A-H).

A mixture of [compound1 (0.1 mole, 32.95g)] and the substituted aromatic amine (0.1 mole) in ethanol (30ml) was refluxed for 6h. after cooling the resulting solid was filtered, dried and crystallized from 80% ethanol\(^{(29)}\).

2.5. synthesis of 4-(2-imino-4-oxo-thiazolidinyl) sulphamethaoxazole (compound 2).

A mixture of [compound1(0.01 mole, 3.29g)], potassium thiocyanate (0.02 mole, 1.94g) and acetone (50ml) is refluxed for about 3h. excess of solvent is removed and the residue is stirred
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with water (50 ml). The solid product is filtered washed with water, dried and crystallized from ethanol (6).

2.6. synthesis of 4-(5-arylidene-2-imino-4-oxo-thiazolidinyl sulphamethaoxazole) (compounds 2A-H).

The substituted aromatic aldehyde (0.02 mole) and [compound 2 (0.01 mole, 3.52 g)] are added to a solution of anhydrous sodium acetate (0.02 mole) in acetic acid (30 ml). The mixture is refluxed for 5 h. and cooled to room temperature. The solid product is filtered, washed with water, dried and crystallized from methanol (6).

Scheme 1: Path ways for prepared compounds
Results and Discussion

4-Amino sulphamethoxazole was reacted with chloro acetyl chloride to prepare compound (1) in which amino group converted to amide group. Infrared data showed that disappearing of amino group at 3460 cm$^{-1}$ and appearing of –NH at 3234 cm$^{-1}$, -CONH at 1679 cm$^{-1}$. The chloro atom in compound (1) was replaced by different aromatic amines to prepare compounds (1A-H) infra red data showed that appearing of –CH$_2$NH peak at 2886 cm$^{-1}$ and disappearing of carbone-chlore peak at 750 cm$^{-1}$. Chloro acetyl group in compound (1) was completely converted to thiazolidinone ring system (compound 2) infra red data showed peaks at 1714 cm$^{-1}$ (C=O), 1537 cm$^{-1}$ (C=N-H). Using different aromatic aldehyde, Compound (2) was converted to compounds (2A-H), Infra red data showed that peaks at 1720 cm$^{-1}$, 1714 cm$^{-1}$, (C=O), 1550 cm$^{-1}$ (C=N-H). $^1$H-n.m.r. spectra showed peaks at (10.6-10.7 ppm) for N-H proton, CH$_3$ and CH$_2$ at (2.2-3.4 ppm), protons of Benzene ring were showed at area (7.2-7.9 ppm) as multiple peaks. The figures from (3-7) state the signals of some prepared compounds and table (2).

Fig. (1) IR spectrum of synthesized compound (1)
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Fig. (2) IR spectrum of synthesized compound (2)

Fig. (3) $^1$H-n.m.r. spectrum of synthesized compound (1D)
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Fig. (4) $^1$H-n.m.r. spectrum of synthesized compound (1H)

Fig. (5) $^1$H-n.m.r. spectrum of synthesized compound (2)
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Fig.(6) $^1$H-n.m.r. spectrum of synthesized compound (2B)

Fig.(7) $^1$H-n.m.r. spectrum of synthesized compound (2E)

Scheme 2: Mechanism of reaction for compounds (2) and (2A-H)
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Table 1. Physical properties of the prepared compounds

<table>
<thead>
<tr>
<th>Compound no.</th>
<th>R</th>
<th>M.P</th>
<th>Color</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>195-197</td>
<td>white</td>
<td>83</td>
</tr>
<tr>
<td>1A</td>
<td>p-OCH₃</td>
<td>182-184</td>
<td>White</td>
<td>75</td>
</tr>
<tr>
<td>1B</td>
<td>p-COOH</td>
<td>175-177</td>
<td>White</td>
<td>77</td>
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<tr>
<td>1C</td>
<td>m-NO₂</td>
<td>114-116</td>
<td>Yellow</td>
<td>72</td>
</tr>
<tr>
<td>1D</td>
<td>o-NO₂</td>
<td>186-188</td>
<td>Orange</td>
<td>70</td>
</tr>
<tr>
<td>1E</td>
<td>m-OH</td>
<td>212-214</td>
<td>Brown</td>
<td>76</td>
</tr>
<tr>
<td>1F</td>
<td>p-OH</td>
<td>225-227</td>
<td>Brown</td>
<td>74</td>
</tr>
<tr>
<td>1G</td>
<td>p-Br</td>
<td>206-208</td>
<td>White</td>
<td>72</td>
</tr>
<tr>
<td>1H</td>
<td>o-CH₃,p-NO₂</td>
<td>180-182</td>
<td>Yellow</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>167-169</td>
<td>Yellow</td>
<td>70</td>
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<tr>
<td>2B</td>
<td>p-N(CH₃)₂</td>
<td>247-249</td>
<td>Red</td>
<td>55</td>
</tr>
<tr>
<td>2C</td>
<td>p-OH,m-OCH₃</td>
<td>204-206</td>
<td>Yellow</td>
<td>62</td>
</tr>
<tr>
<td>2D</td>
<td>p-Cl</td>
<td>253-255</td>
<td>White</td>
<td>60</td>
</tr>
<tr>
<td>2E</td>
<td>p-OCH₃</td>
<td>264-266</td>
<td>White</td>
<td>56</td>
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<tr>
<td>2F</td>
<td>m-OH</td>
<td>241-243</td>
<td>Red</td>
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</tr>
<tr>
<td>2G</td>
<td>o-Cl</td>
<td>244-246</td>
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<tr>
<td>2H</td>
<td>O-CH₃</td>
<td>248-250</td>
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<td>53</td>
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</table>

Table 2. ¹H.N.M.R signals in ppm for some prepared compounds

<table>
<thead>
<tr>
<th>Compound no.</th>
<th>(-CH₃) ppm</th>
<th>(-CH₂) ppm</th>
<th>(-CH₃)ₐ ppm</th>
<th>(N-H) ppm</th>
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<tbody>
<tr>
<td>1D</td>
<td>2.29-2.50</td>
<td>3.34-4.29</td>
<td>7.76-7.84</td>
<td>10.70</td>
</tr>
<tr>
<td>1H</td>
<td>2.11-2.72</td>
<td>3.32</td>
<td>7.75-7.86</td>
<td>10.69</td>
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</tbody>
</table>
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<table>
<thead>
<tr>
<th>Compound no.</th>
<th>(C-H)$_\text{aliph}$</th>
<th>(C-H)$_\text{Ar}$</th>
<th>(C=O)$_\text{Ar}$</th>
<th>(C=N)</th>
<th>(C=O)</th>
<th>(N-H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2886</td>
<td>3066</td>
<td>1550</td>
<td>1608</td>
<td>1670</td>
<td>3234</td>
</tr>
<tr>
<td>1A-H</td>
<td>2882-2889</td>
<td>3075-3098</td>
<td>1540-1560</td>
<td>1612-1620</td>
<td>1665-1668</td>
<td>3165-3223</td>
</tr>
<tr>
<td>2</td>
<td>2908</td>
<td>3093</td>
<td>1537</td>
<td>1616</td>
<td>1716-1720</td>
<td>3206</td>
</tr>
<tr>
<td>2A-H</td>
<td>2885-2997</td>
<td>3095-3103</td>
<td>1530-1542</td>
<td>1610-1625</td>
<td>1714-1716</td>
<td>3220-3340</td>
</tr>
</tbody>
</table>

Table 3. Wave numbers in cm$^{-1}$ of I.R spectrum for prepared compounds
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References