A novel synthesis of 1-(1-aza-2-arylviny1)-2-[(1E)-2-arylviny1]-4-(phenyl methylene) -2-imidazolin-5-ones

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A simple and novel procedure for the preparation of the title compounds is described. Treatment of azlactone (4-benzylidene-2-methyloxazolin-5-one) with hydrazine hydrate gives α-acetamido-cinnamhydrazide, which with aromatic aldehydes produces N-(1-aza-2-arylvinyl)-2-(acetamino)-3-phenylprop-2-enamides. This on treatment with Schiff bases in acetic acid yields the title compounds.

Keywords: Imidazolin-5-ones, hydrazine hydrate, α-acetamido-cinnamhydrazide, enamides, Schiff’s bases, acetic acid

IPC: Int.Cl.7 C 07 D

In its various oxidation states, the imidazole nucleus has been proven to be an unusually fertile source of medicinal agents such as nasal decongestants1, anti-histamines2, anti-protozoal agents 3, antiulcers 4, anti-depressants5 and α-adrenergic blocking agents 6. They also have been shown to display exceptional activity against anti-fungal7, anti-cancer 8. In continuation of our synthesis of various heterocyclic compounds with azlactones9-11, we herein report the synthesis of novel unknown title compounds.

Azlactone 1 on treatment with hydrazine hydrate in ethanol at room temperature gave α-acetamido-cinnamhydrazide 2, which with one equivalent of benzaldehyde in ethanol with a few drops of acetic acid at 60°C yielded a colourless crystalline compound, m.p. 160°C (TLC single spot on benzene - ethyl acetate, 2:8); IR (KBr) showed the presence of sharp NH absorptions at 3059 and 3249 cm⁻¹. ¹H NMR (DMSO-d₆) revealed the peaks at δ 2.0 (s, 3H, -CH₃), 6.8 (s, 1H, C₆H₅=CH-), 7.2-7.8 (m, 10H, Ar-H), 8.4 (s, 1H, Ar=CH=N-), 9.6 (br, 1H, NH, D₂O exchangeable), 11.4 (br, 1H, NH, D₂O exchangeable). The spectral data confirmed the assigned structure N-(1-aza-2-phenylvinyl)-2-(acetamino)-3-phenylprop-2-enamide for 3a.

The reaction of 3a with Schiff bases 4b (p-methoxybenzylideneaniline) in 1:1 molar ratio in acetic acid gave an orange red crystalline compound, m.p. 189°C (single spot on TLC, benzene). The mass spectrum showed the molecular ion at m/z 407 corresponding to the molecular formula, C₂₆H₂₁N₃O₂. The IR spectrum (KBr) indicated the absence of absorptions for NH group and presence of strong carbonyl absorption at 1701 cm⁻¹. ¹H NMR (CDCl₃) lacked signals for methyl protons (of acetamido group); instead two trans olefinic protons appeared as doublets at δ 7.3 and δ 8.1 (J = 16 Hz) along with additional signals for aromatic protons.

These data led us to assign the structure 1-(1-aza-2-phenylvinyl)-2-[(1E)-2-p-methoxyphenylvinyl]-4-(phenylmethylene)-2-imidazolin-5-one to 5b. Apparently it is formed by styrylation of the acetamido group of 3, followed by dehydration. The reaction of 3a with anisaldehyde under identical conditions could not lead to the compound 5b.

From the above observations the mechanism of the reaction can be rationalised as follows. Michael type addition of the active methyl group 3 across the carbon-nitrogen double bond of the Schiff base 4 may be expected to be the first rational step. The addition product can lead to the generation of styryl group by the loss of aniline. The resulting unstable intermediate readily undergoes dehydration cyclisation to form stable compound 5 (Scheme I, Table I). The driving force for aniline elimination is formation of stable conjugated cinnamoyl chromophore in compound 5.

Experimental Section

Melting points were taken in sulphuric acid bath and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer 1650 spectrophotometer;¹H NMR spectra on a Bruker DRX-200 spectrometer with TMS as an internal standard (chemical shifts in δ, ppm); and mass spectra on MS PE SCIEX API 3000 instruments.

α-Acetamido-cinnamhydrazide 2. Azlactone¹² 1 (5.6 g, 0.03 mole) was mixed with a solution of hydrazine hydrate (100%, 3 g, 0.06 mole) in ethanol
Scheme I

Table 1 — 1-(1-Aza-2-arylvinyl)-2-[(1E)-2-arylvinyl]-4-(phenylmethylene)-2-imidazolin-5-ones 5

<table>
<thead>
<tr>
<th>Compd</th>
<th>Ar</th>
<th>Ar$^1$</th>
<th>m.p. °C</th>
<th>Yield (%)</th>
<th>Mol. formula</th>
<th>UV (λmax) nm</th>
<th>Calcd % (Found)</th>
</tr>
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<tbody>
<tr>
<td>5a</td>
<td>Ph</td>
<td>Ph</td>
<td>209-10</td>
<td>60</td>
<td>C$<em>2$H$</em>{10}$N$_2$O</td>
<td>298.5, 408</td>
<td>79.57 (79.75)</td>
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<tr>
<td>5b</td>
<td>Ph</td>
<td>p-MeO.C$_6$H$_4$</td>
<td>189-91</td>
<td>58</td>
<td>C$<em>2$H$</em>{10}$N$_2$O$_2$</td>
<td>303.2, 409</td>
<td>76.65 (76.80)</td>
</tr>
<tr>
<td>5c</td>
<td>p-MeO.C$_6$H$_4$</td>
<td>Ph</td>
<td>172-75</td>
<td>63</td>
<td>C$<em>2$H$</em>{10}$N$_2$O$_2$</td>
<td>299, 409.5</td>
<td>76.65 (76.80)</td>
</tr>
<tr>
<td>5d</td>
<td>p-MeO.C$_6$H$_4$</td>
<td>p-MeO.C$_6$H$_4$</td>
<td>188-89</td>
<td>65</td>
<td>C$<em>2$H$</em>{10}$N$_2$O$_3$</td>
<td>302, 410</td>
<td>74.14 (74.00)</td>
</tr>
<tr>
<td>5e</td>
<td>p-MeO.C$_6$H$_4$</td>
<td>p-NO$_2$.C$_6$H$_4$</td>
<td>194-96</td>
<td>69</td>
<td>C$<em>2$H$</em>{10}$N$_2$O$_4$</td>
<td>323.8, 409</td>
<td>69.02 (69.20)</td>
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<td>5f</td>
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<td>p-MeO.C$_6$H$_4$</td>
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<td>59</td>
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<td>299.6, 409</td>
<td>73.41 (73.50)</td>
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<tr>
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<td>Ph</td>
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<td>206-08</td>
<td>57</td>
<td>C$<em>2$H$</em>{10}$N$_2$O</td>
<td>298.4, 409.5</td>
<td>75.94 (75.88)</td>
</tr>
<tr>
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<td>Ph</td>
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<td>60</td>
<td>C$<em>2$H$</em>{10}$N$_2$O</td>
<td>298.4, 409</td>
<td>75.94 (75.80)</td>
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<tr>
<td>5i</td>
<td>p-F.C$_6$H$_5$</td>
<td>p-F.C$_6$H$_5$</td>
<td>218-21</td>
<td>65</td>
<td>C$<em>2$H$</em>{10}$N$_2$O$_2$F</td>
<td>298, 410</td>
<td>76.14 (76.00)</td>
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</table>
(25 mL). The deep yellow colour of the azlactone immediately changed to the light yellow coloured solid, which was filtered, washed and crystallised from methanol, yield 5.5 g (84%); m.p. 160°C (lit.13 m.p. 156°C); IR (KBr): 3228.6, 3163 (NH); 1HNMR (DMSO-d6): δ 1.9 (s, 3H, COCH3), 2.0 (s, 3H, COCH3), 6.7 (s, 1H, C6H5-CH=), 7.2-7.8 (m, 9 H, Ar-H), 8.4 (s, 1H, Ar-C=H=N=), 9.5 (br, 1H, NH, D2O exchangeable), 11.3 (br, 1H, NH, D2O exchangeable); MS (m/z): 325.

N-(1-Aza-2-arylvinyl)-2-(acetylamino)-3-phenylprop-2-enamide 3a: yield 86%, m.p. 160°C; IR (KBr): 3058, 3247 cm−1; 1H NMR (DMSO-d6): δ 2.0 (s, 3H, COCH3), 6.8 (s, 1H, C6H5-CH=), 7.1-7.9 (m, 9 H, Ar-H), 8.4 (s, 1H, Ar-C=H=N=), 9.5 (br, 1H, NH, D2O exchangeable), 11.4 (br, 1H, NH, D2O exchangeable); MS (m/z): 307.

N-(1-Aza-2-phenylvinyl)-2-(acetylamino)-3-phenylprop-2-enamide 3b: yield 85%, m.p. 160°C; IR: 1705 cm−1; 1H NMR (CDCl3): δ 3.8 (s, 3H, OCH3), 7.3 (d, 1H, J = 16 Hz), 7.2-8.4 (m, 14 H, Ar-H), 8.4 (s, 1H, Ar-C=H=N=), 7.1 (s, 1H, C6H5-CH=), 7.2-8.4 (m, 14 H, Ar-H), 9.7 (s, 1H ArCH=)=N-); MS (m/z): 407; UV : 205, 303.2 nm.

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