Synthesis and reactions of 4-(aminoaryl)-methylene-2-aryl-2-imidazolin-5-ones

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Benzimidic acid methyl esters on heating with glycine ester in toluene in presence of sodium acetate yield 4-(aminoaryl)-methylene-2-aryl-2-imidazolin-5-ones. They undergo acetylation and benzoylation on reaction with acetic anhydride and benzoyl chloride, respectively. The 13C assignment of some of the carbon atoms of one of the acetyl derivatives has been done by HMOC and HMBC experiments.

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Formation of 2-phenyl-2-imidazolin-5-one 1 by the reaction between benzimidic acid ester and glycine ester is well known.1 During this reaction some red compounds also are formed. Attempts by Wieland and Biener2 to identify these compounds were in vain. In the present study one of the orange red compounds formed in this reaction has been isolated and characterized.

The title compounds were synthesized by the multicomponent reaction as follows: Glycine ester was heated in toluene under reflux with more than two equivalents of benzimidic acid methyl ester or toluimidic acid methyl ester in presence of anhydrous sodium acetate. The imidic acid ester first reacts with glycine ester to form 2-aryl-2-imidazolin-5-one 1 which reacts in presence of the base sodium acetate, with another molecule of imidic acid ester to give 4-(amino aryl) methylene-2-aryl-2-imidazoline-5-one 2 (Scheme I).

The structure of 2 was elucidated as follows (for Ar = Ph). The mass spectrum gave M+ ion at m/z 263 corresponding to the proposed structure. The 1H NMR spectrum showed absorptions for 11 protons (multiplet) in the region δ 7.3-8.05. This corresponds to the ten aromatic protons and one of the protons in the amino group. The other proton in the amino group and hydrogen bonded to the carbonyl oxygen absorbed at δ 9.04. The –NH– proton of the imidazolinone ring absorbed at δ 11.75. All these three protons vanished...
after deuterium wash. In the region $\delta$ 7.3-8.05 the integration for 11 protons reduced to 10 protons. The IR spectrum showed a sharp carbonyl absorption at 1667 cm$^{-1}$. The reduction in absorption frequency of the carbonyl group is attributed to intramolecular hydrogen bonding (the carbonyl absorption frequency of 2-phenyl-4-benzylidine-2-imidazolin-5-one, 'H' instead of $-\text{NH}_2$ in 2, is 1698 cm$^{-1}$).$^3$

Acetylation of the amino compounds were effected by stirring with acetic anhydride in pyridine (Scheme II). Their structures were also ascertained from spectral data (Table I) and elemental analysis. 4-(Acetylamino phenyl)methylene-2-phenyl-2-imidazolin-5-one gave M$^+$ at m/z 305 in its mass spectrum corresponding to the expected structure. Its $^1$H NMR spectrum has absorptions in the region $\delta$ 7.4-8 (10H, aromatic protons). A singlet (3H) at $\delta$ 2.14 corresponds to the acetyl group. The proton on the acetylated nitrogen which is also hydrogen bonded to the oxygen of the imidazolinone ring gave a singlet at $\delta$ 10.47 and the proton on the nitrogen of the heterocyclic ring absorbed at 12.18.

Similarly benzylation was brought about by stirring the amino compounds with freshly distilled benzyl chloride in pyridine at room temp. (Scheme II). The structures of the benzyl derivatives were assigned from spectral data and elemental analysis. The mass spectrum of 4-(benzylamino phenyl)methylene-2-phenyl-2-imidazolin-5-one gave M$^+$ peak at m/z 367. The $^1$H NMR spectrum also supported the proposed structure with peaks at $\delta$ 11.41 (1H, N-H proton of the benzylamino group) and another at 12.3 (1H, N-H of the imidazoline ring). The aromatic protons (15H) absorbed in the region $\delta$ 7.4-8.

The $^{13}$C NMR spectrum of 4-(acetylamino phenyl)methylene-2-phenyl-2-imidazolin-5-one showed absorptions at $\delta$ 196.68 and 171.18 along with other absorptions. The HMQC (Heteronuclear Multiple Quantum Coherence) spectrum of this compound gave cross peak between the protons absorbing at $\delta$ 2.14 and the carbon at 24.36 corresponding to the acetyl $-\text{CH}_3$ group. The same set of protons gave cross peak with the carbon at $\delta$ 169.68 in the HMBC (Heteronuclear Multiple Bond Coherence) proving its identity as the acetyl carbonyl carbon. This observation automatically assigns $\delta$ 171.18 to the carbonyl carbon of the imidazolinone ring.

### Experimental Section

Melting points recorded using open capillary are uncorrected. All the $^1$H NMR spectra were recorded on a Bruker AM 360 spectroscope and $^{13}$C on a Bruker AC 250 spectroscope using TMS as reference. Standard chemical shifts are recorded in $\delta$ values. The mass spectra were recorded on a Finnigan MAT 8200 spectrometer. IR spectrum was recorded as KBr pellet using Shimadzu 8101 A FT IR equipment.

**Synthesis of starting materials.** Glycine ethyl ester, benzimidic acid methyl ester hydrochloride, m-toluimidic acid methyl ester hydrochloride, p-toluimidic acid methyl ester hydrochloride and their free esters were prepared according to the method of Kidwai and Devasia.$^4$

### Table I — Physical data of 4-(aminoaryl)methylene-2-aryl-2-imidazolin-5-ones 2 and their acetyl 3a and benzoyl 3b derivatives

<table>
<thead>
<tr>
<th>Ar</th>
<th>m.p. °C</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenyl (2a)</td>
<td>199</td>
<td>64</td>
</tr>
<tr>
<td>p-Tolyl (2b)</td>
<td>259</td>
<td>63</td>
</tr>
<tr>
<td>m-Tolyl (2c)</td>
<td>258</td>
<td>72</td>
</tr>
<tr>
<td>Acetyl derivatives (3a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenyl</td>
<td>275</td>
<td>72</td>
</tr>
<tr>
<td>p-Tolyl</td>
<td>276</td>
<td>65</td>
</tr>
<tr>
<td>m-Tolyl</td>
<td>273</td>
<td>75</td>
</tr>
<tr>
<td>Benzoyl derivatives (3b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenyl</td>
<td>234</td>
<td>75</td>
</tr>
<tr>
<td>p-Tolyl</td>
<td>221</td>
<td>65</td>
</tr>
<tr>
<td>m-Tolyl</td>
<td>217</td>
<td>63</td>
</tr>
</tbody>
</table>
10 mL of ether and dried in the oven at 90°C for one hr. The orange yellow crystals of 2 were recrystallised from toluene.

4-(Aminophenyl)methylene-2-phenyl-2-imidazolin-5-one 2a: Yield 64%, m.p. 199°C. Anal. Calcd for C16H13N3O: C, 73.0; H, 4.94; N, 15.92. Found: C, 72.8; H, 4.5; N, 16.1%; IR: 1666.7 cm⁻¹ (νC = O); ¹H NMR δ 7.3-8.05 (m, 11H, Ar-H and one H of NH₂), 9.04 (s, 1H, hydrogen bonded –NH–), 11.75 (s, 1H, –NH– of ring); MS: m/z 263 (M⁺), 188 (base peak).


4-(Aminophenyl)methylene-2-phenyl-2-imidazolin-5-one 2c: 4-(Aminophenyl)methylene-2-phenyl-2-imidazolin-5-one, 2c: Yield 72%, m.p. 215°C. Anal. Calcd for C18H17N3O: C, 74.22; H, 5.84; N, 14.43. Found: C, 73.95; H, 6.18; N, 14.37%.

4-(Acetylaminoaryl)methylene-2-aryl-2-imidazolin-5-one 3a. General. Compound 2 (0.0076 mole) was taken in a 100 mL conical flask. To this pyridine (10 mL) and acetic anhydride (2 mL) were added and stirred using a magnetic stirrer for 6 hr and then poured into ice-cold water and kept in the refrigerator for 4 hr. The product formed was filtered, washed thrice with 10 mL portions of water and dried. The yellow crystals of 3a were recrystallised from ethanol.


4-(Acetylamino-p-tolyl)methylene-2-(m-tolyl)-2-imidazolin-5-one 2e: 4-(Acetylamino-p-tolyl)methylene-2-(m-tolyl)-2-imidazolin-5-one, 2e: Yield 75%, m.p. 234°C. Anal. Calcd for C23H17N3O2: C, 75.20; H, 4.63; N, 11.44. Found: C, 75.18; H, 4.61; N, 11.45%; ¹H NMR δ 7.4-8 (m, 15 ArH), 11.41 (NH proton in benzoylamino gp); 12.32 (N-H proton in heterocyclic ring) MS: (m/z) 367 (M⁺), 105 (base peak).

4-(Benzoylaminoaryl)methylene-2-aryl-2-imidazolin-5-one 3b. General. Compound 2 (0.0076 mole) was dissolved in 10 mL pyridine. To this freshly distilled benzoyl chloride (0.0076 mole) in 5 mL pyridine was added and stirred for 5 hr. It was then poured into cold water, filtered, washed with cold water and dried. The yellow crystals of 3b were recrystallised from ethanol.

4-(Benzoylaminoaryl)methylene-2-phenyl-2-imidazolin-5-one 2f: 4-(Benzoylaminoaryl)methylene-2-phenyl-2-imidazolin-5-one, 2f: Yield 75%, m.p. 275°C. Anal. Calcd for C23H17N3O2: C, 75.08; H, 4.90; N, 14.0%; ¹H NMR δ 7.4-8 (m, 15 ArH), 11.41 (NH proton in benzoylamino gp); 12.32 (N-H proton in heterocyclic ring) MS: (m/z) 367 (M⁺), 105 (base peak).


4-(Benzoylamino-m-tolyl)methylene-2-(m-tolyl)-2-imidazolin-5-one 2h: 4-(Benzoylamino-m-tolyl)methylene-2-(m-tolyl)-2-imidazolin-5-one, 2h: Yield 63%, m.p. 217°C. Anal. Calcd for C25H21N3O2: C, 75.94; H, 5.31; N, 10.63. Found: C, 75.96; H, 5.32; N, 10.62%.

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References