Formation and thermal rearrangement of 4,4′-diarylmethyl-2,2′-diaryl-4,4′-biimidazolin-5,5′-diones

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Received 19 November 2012; accepted (revised) 21 August 2014

Recrystallisation of 4-arylmethyl-2-aryl-2-imidazolin-5-ones from ethanol results in the formation of 4,4′-diarylmethyl-2,2′-diaryl-4,4′-biimidazolin-5,5′-diones. These products undergo a McLafferty type rearrangement to give one molecule of 4-arylmethyl-2-aryl-2-imidazolin-5-one and one molecule of 4-arylidene-2-aryl-2-imidazolin-5-one under mass spectrometric conditions. The same rearrangement is also found to occur on heating the compounds just above their melting points.

Keywords: 4-Arylmethyl-2-aryl-2-imidazolin-5-one, dimerisation, mass spectral fragmentation, thermal rearrangement, 4-arylidene-2-aryl-2-imidazolin-5-one, 4,4′-diarylmethyl-2,2′-diaryl-4,4′-biimidazolin-5,5′-diones

4-Arylidene-2-aryl-2-imidazolin-5-ones are an important class of imidazole derivatives because of their marked biological properties like antimicrobial1, immunomodulatory2, potential COX-2 inhibitors3, L-DOPA prodrugs in the treatment of Parkinson’s diseases3 and leishmanicidal5. This class of compounds can also be converted into acylamino acid amides and acylamino acids by reduction and hydrolysis6. Compounds having structure comparable to the reduced imidazolinone are reported to dimerise on dissolving in appropriate solvent7. In the present work, formation of a new derivative is being reported while recrystallising the reduced 4-arylidene-2-aryl-2-imidazolin-5-ones from ethanol. These new compounds under mass spectrometric condition underwent a McLafferty type rearrangement to give saturated and unsaturated imidazolinone derivatives. The same rearrangement was also found to occur under thermal conditions.

Results and Discussion

4-Benzylidene-2-phenyl-2-imidazolin-5-one 1 a deep yellow compound with m.p. 284-85°C (Ref 8) was prepared by three component condensation of benzimidic acid methyl ester hydrochloride, glycine ethyl ester hydrochloride and benzaldehyde in presence of a base8.

4-Benzyl-2-phenyl-2-imidazolin-5-one 2 is the reduction product of 1. Reduction of the compound was carried out using red phosphorous, hydriodic acid and acetic anhydride which resulted in the formation of a pale yellow product with m.p.166-69°C (Ref 6). Recrystallisation of 2 from ethanol gave an unexpected colourless product 4,4′-dibenzyl-2,2′-diphenyl-4,4′-biimidazolin-5,5′-dione 3, a dimer of 2. The structure of this compound was arrived at as follows.

The EI-MS spectrum of 3, dimer of 4-benzyl-2-phenyl-2-imidazolin-5-one, gave M+ peak at m/z 250 and another intense peak at m/z 248. A peak at m/z 91(60%) indicated the presence of benzyl group in the molecule. The CI-MS spectrum has (M+1)+ peak at m/z 499 suggesting a molecular mass 498 for this molecule. A molecule with this mass can be a dimer of the reduced imidazolinone which has undergone dehydrogenation leading to C-C bond formation:

\[
\begin{align*}
\text{HN} & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{O} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{O} \\
\text{C}_6\text{H}_5 & \quad \text{NH} \\
\end{align*}
\]

The 1H NMR spectrum of this dimer showed a singlet at δ 11.1 (2H) corresponding to –NH- protons in the heterocyclic ring, multiplets in the region δ 7 to 7.7 (20H) corresponding to aromatic protons and two doublets at δ 3.98 (J=12Hz) and δ 3.40 (J=12Hz) integrating to two protons each is also observed. These peaks can be attributed to the protons of methylene group that are geminally coupled. These two protons are magnetically non-equivalent due to the presence of the adjacent chiral carbon. The 13C NMR spectrum had 12 peaks which is consistent with the proposed structure. The DEPT 135 spectrum has a negative peak at δ 35.3 which is due to the presence of methylene group.

The products undergo a McLafferty type rearrangement to give one molecule of 4-arylmethyl-2-aryl-2-imidazolin-5-one and one molecule of 4-arylidene-2-aryl-2-imidazolin-5-one under mass spectrometric conditions.
at $\delta$ 3.98 and 3.40 gave cross peaks with the carbon absorbing at 35.4 in HMQC spectrum. Moreover in the HMBC spectrum, these two protons also gave cross peaks with the carbonyl carbon absorbing at $\delta$ 183.7.

During the EI-MS analysis, this compound underwent a McLafferty type rearrangement to yield one molecule of 4-benzyl-2-phenyl-2-imidazolin-5-one 2 and one molecule of 4-benzylidene-2-phenyl-2-imidazolin-5-one 1 with molecular masses 250 and 248 respectively as evident from its mass spectrum (Scheme I).

Many of the rearrangements in mass spectrometry have a close parallelism with rearrangements in the condensed phase in pyrolytic and photochemical reactions\textsuperscript{9,10}. In this context it was decided to investigate the possible rearrangement of the dimers under thermal conditions. Each of the dimers were heated 5-10°C above their melting points and kept at that temperature for 10 min and then allowed to cool. On workup 4-arylidene-2-aryl-2-imidazolin-5-one and 4-arylmethyl-2-aryl-2-imidazolin-5-one could be isolated/ detected proving the rearrangement of the dimer under thermal conditions (mechanism similar to that in Scheme I).

**Experimental Section**

Melting points recorded using open capillary are uncorrected. IR spectra (KBr) were obtained using Shimadzu 8101 FTIR equipment and mass spectra on a Finnigan MAT 8200 spectrometer. NMR spectra were recorded on Brucker AM 360 at 360 MHz for $^1$H and 90.5 MHz for $^{13}$C NMR.

General synthetic procedure is given with specific compound. The same procedure was followed for all the compounds prepared.

**4-Arylidene-2-aryl-2-imidazolin-5-ones, 1.** They were prepared according to an earlier method\textsuperscript{8}, by condensation of corresponding aromatic imidic acid methyl ester hydrochloride (0.027 mol), glycine ethyl ester hydrochloride (0.07 mol) and aromatic aldehyde (0.024 mol) in presence of the base, sodium bicarbonate. The crude deep yellow product was purified by recrystallisation from ethanol and melting point determined and compared\textsuperscript{8,11} (Table I).

**4-Arylmethyl-2-aryl-2-imidazolin-5-ones, 2.** These compounds were prepared by the reduction of 4-arylidene-2-aryl-2-imidazolin-5-one (2 g) using acetic anhydride (12 mL), red phosphorous (1.8 g) and hydriodic acid (7.5 mL). The melting point of the

![Scheme I](image-url)

**Table I — Physical characterization data of 4,4′-diaryl-2,2′-diaryl-4,4′-bimidazolin-5,5′-dione**

<table>
<thead>
<tr>
<th>Compd</th>
<th>Ar$^1$</th>
<th>Ar$^2$</th>
<th>m.p. (°C)</th>
<th>Yield (%)</th>
<th>N (%) Found</th>
<th>Calcd</th>
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<tbody>
<tr>
<td>1</td>
<td>Phenyl</td>
<td>Phenyl</td>
<td>261</td>
<td>40</td>
<td>11.20</td>
<td>11.24</td>
</tr>
<tr>
<td>2</td>
<td>Phenyl</td>
<td>$p$-Methylphenyl</td>
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<td>41</td>
<td>10.60</td>
<td>10.64</td>
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<tr>
<td>3</td>
<td>Phenyl</td>
<td>$p$-Chlorophenyl</td>
<td>252</td>
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<td>10.01</td>
<td>9.89</td>
</tr>
<tr>
<td>4</td>
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<td>Phenyl</td>
<td>236</td>
<td>33</td>
<td>10.61</td>
<td>10.68</td>
</tr>
<tr>
<td>5</td>
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<td>$p$-Chlorophenyl</td>
<td>248</td>
<td>34</td>
<td>9.40</td>
<td>9.45</td>
</tr>
<tr>
<td>6</td>
<td>$p$-Hydroxyphenyl</td>
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<td>248</td>
<td>38</td>
<td>10.52</td>
<td>10.57</td>
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<tr>
<td>7</td>
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<td>$o$-Chlorophenyl</td>
<td>238</td>
<td>29</td>
<td>9.31</td>
<td>9.35</td>
</tr>
<tr>
<td>8</td>
<td>$p$-Hydroxyphenyl</td>
<td>$m$-Methylphenyl</td>
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<tr>
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<td>Phenyl</td>
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<tr>
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<td>$p$-Chlorophenyl</td>
<td>256</td>
<td>24</td>
<td>9.40</td>
<td>9.41</td>
</tr>
</tbody>
</table>
pale yellow crystals of 4-arylmethyl-2-aryl-2-imidazolin-5-one were determined and compared\(^6\) (Table I).

4,4′-Dibenzyl-2,2′-diphenyl-4, 4′-biimidazolin-5,5′-dione, 1(Table I). 4-Benzylidene-2-phenyl-2-imidazolin-5-one (2 g) and red phosphorous (1.8 g) was taken in a 100 mL round bottom flask and acetic anhydride (12 mL) was added. To this mixture hydriodic acid (12 mL) was added. To this mixture was taken in a 100 mL round bottom flask and acetic anhydride (12 mL) was added. To this mixture was taken in a 100 mL round bottom flask and hydriodic acid (7.5 mL) was added in portions slowly and heated under reflux for 2 hr. After cooling it was filtered and the filtrate neutralised with saturated sodium carbonate solution. The precipitate obtained was collected and dissolved in ethanol (50 mL) by heating and filtering. After keeping the solution overnight, white crystals of 4,4′-dibenzyl-2,2′-diphenyl-4, 4′-biimidazolin-5,5′-dione was formed. The product was filtered, washed with 5 mL of ethanol and dried. It melted at 261°C (Table I). IR (KBr): 1724 (C=O), 3400 cm\(^{-1}\) (N-H); \(^1\)H NMR (DMso-d\(_6\)): \(\delta 11.1\) (s, 2H, -NH-, imidazolinone ring), 7.75 (m, 20H, aromatic protons), 3.98-3.4 (d, 2H, methylene group); CI-MS: m/z 499 [M+1]\(^+\); \(^13\)C NMR: \(\delta 35.4\), 76.9, 126.3, 126.4, 127.4, 128.3, 128.4, 130.3, 131.3, 135.3, 160.0, 183.7.

4,4′-Dibenzyldiene-2,2′-di(p-tolyl)-4, 4′-biimidazolin-5,5′-dione, 9 (Table I). 4-Benzylidene-2-(p-tolyl)-2-imidazolin-5-one (2.1 g) was taken in 100 mL round bottomed flask and reduced using red phosphorous (1.8 g), hydriodic acid (12 mL) and acetic anhydride (12 mL). The same procedure as above were used for the preparation of 4,4′-dibenzyldiene-2,2′-di(p-tolyl)-4, 4′-biimidazolin-5,5′-dione. The colourless product obtained was purified by recrystallization from isopropanol (30 mL) and melted at 238°C (Table I). IR (KBr): 1731 (C=O), 3394 cm\(^{-1}\) (N-H); \(^1\)H NMR (DMso-d\(_6\)): \(\delta 11.0\) (s, 2H, -NH-, imidazolinone ring), 10.16 (s, 2H, hydroxyl proton on aromatic ring), 6.76-7.57 (m, 16H, aromatic protons), 3.86-3.43 (d, 2H, methylene group); CI-MS: m/z 599 [M+1]\(^+\).

Thermal rearrangement: 4,4′-dibenzyl-2,2′-diphenyl-4, 4′-biimidazolin-5,5′-dione. 4,4′-Dibenzyl-2,2′-diphenyl-4, 4′-biimidazolin-5,5′-dione (0.5 g, was taken in a clean dry test tube and heated in an oil bath. When the temperature reached 261°C it melted. The temperature was raised to 266°C and maintained for 5 min. The colour of imidazolinone dimer turned to yellow. It was cooled and benzene (5 mL) added, the mass boiled and filtered hot. 4-Benzylidene-2-phenyl-2-imidazolin-5-one formed was filtered and dried. It melted at 284°C (Ref 8). To the filtrate petroleum ether (5 mL) was added. The precipitated 4-benzyl-2-phenyl-2-imidazolin-5-one was filtered and dried. It melted at 167-69°C (The identities of these rearranged products were verified by comparing their melting points with authentic samples and comparing their IR spectra).

References