One pot synthesis of 3-(1H-imidazo[4,5-f]quinolin-2-yl)-chromen-2-one under microwave irradiation

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Rapid and efficient method for the synthesis of imidazoquinolinyl-chromen-2-ones under microwave (MW) irradiation is described. A comparative study of conventional and MW methods is briefly discussed.

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Quinoline derivatives exhibit marked biological activities like, cardiotonic, and anti-psychotic agents. Coumarin derivatives are reported to cure Alzheimer's disease (AD) and to possess other biological activities. Benzimidazole possess a wide range of pharmacological activities.

The use of microwave-induced rate acceleration technology is becoming a powerful tool in organic synthesis because of its milder reaction conditions, reduction of reaction times, enhanced selectivity and associated ease of manipulation. Earlier we reported the synthesis of desyl ethers, benzofurans and benzodifurans under MW irradiation. In the literature there is no report on imidazoquinolinyl chromenes 3a-f. In continuation of our studies on quinolines, we wish to report here the synthesis of 3a-f by conventional and MW methods.

Results and Discussion

Coumarin-3-carboxylic acids on condensation with quinoline-5,6-diamine in polyphosphoric acid (PPA) at 250°C for about 5-8 hr furnished 3a-f. Alternatively when 2a-f with 1, taken in a domestic MW oven at 300 watt-power level are irradiated in an open vessel for 3-4.5min in p-toluene sulphonic acid (PTSA) furnish 3a-f in good yields. The results are tabulated in Table I. The schematic representations of the above two methods are depicted in Scheme I. A comparison between the two methods shows that in the microwave technique the reaction time is drastically reduced, and the yields are comparable. The compounds 3a-f were characterized by IR, H NMR and mass spectral data (Table II).

Scheme I

![Scheme I](image-url)
Table I—Analytical data of title compounds 3a-f

<table>
<thead>
<tr>
<th>Compd</th>
<th>Mol. formula (Mol.Wt)</th>
<th>m.p (°C)</th>
<th>Method A</th>
<th>Method B</th>
<th>Calc (Found) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>C_{10}H_{11}N_{2}O_{2} (313.32)</td>
<td>313</td>
<td>188</td>
<td>84</td>
<td>3.15</td>
</tr>
<tr>
<td>3b</td>
<td>C_{10}H_{11}N_{2}O_{2} (341.37)</td>
<td>341</td>
<td>155</td>
<td>82</td>
<td>3.00</td>
</tr>
<tr>
<td>3c</td>
<td>C_{10}H_{11}N_{2}O_{2} (363.38)</td>
<td>363</td>
<td>275</td>
<td>65</td>
<td>4.50</td>
</tr>
<tr>
<td>3d</td>
<td>C_{11}H_{10}BrN_{2}O_{2} (392.21)</td>
<td>392</td>
<td>215</td>
<td>73</td>
<td>3.50</td>
</tr>
<tr>
<td>3e</td>
<td>C_{10}H_{10}BrN_{2}O_{2} (471.11)</td>
<td>471</td>
<td>178</td>
<td>76</td>
<td>4.00</td>
</tr>
<tr>
<td>3f</td>
<td>C_{10}H_{13}N_{2}O_{2} (343.34)</td>
<td>343</td>
<td>154</td>
<td>63</td>
<td>3.00</td>
</tr>
</tbody>
</table>

Table II—^{1}H NMR spectra of compounds 3a-f

<table>
<thead>
<tr>
<th>Compd</th>
<th>^{1}H NMR data</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>δ7.4-7.6(m, 4H, C-5', C-6', C-7' &amp; C-8'H), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.0-8.2(m, 3H, C-7, C-8, C-9'H), 8.8(s, 1H, C-4'H) 12.2(bs, 1H, NH).</td>
</tr>
<tr>
<td>3b</td>
<td>δ7.5(s, 6H, C-6', C-8', CH_3), 7.4-7.6(m, 2H, C-5', C-7'H), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.2-8.4(m, 3H, C-7, C-8 &amp; C-9'H), 8.8(s, 1H, C-4'H) 12.2(bs, 1H, NH).</td>
</tr>
<tr>
<td>3c</td>
<td>δ7.4-7.6(m, 6H, Ar- H), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.2-8.4(m, 3H, C-7, C-8 &amp; C-9'H), 8.8(s, 1H, C-4'H) 12.2(bs, 1H, NH).</td>
</tr>
<tr>
<td>3d</td>
<td>δ7.4-7.6(m, 3H, C-5', C-7', C-8' &amp; C-9'H), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.2-8.4(m, 3H, C-7, C-8 &amp; C-9'H), 8.8(s, 1H, C-4'H) 12.2(bs, 1H, NH).</td>
</tr>
<tr>
<td>3e</td>
<td>δ7.4-7.6(m, 2H, C-5', C-7' &amp; C-8'H), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.2-8.4(m, 3H, C-7, C-8 &amp; C-9'H), 8.8(s, 1H, C-4'H) 12.2(bs, 1H, NH).</td>
</tr>
<tr>
<td>3f</td>
<td>δ3.8(s, 3H, OCH_3), 7.4-7.6(m, 3H, C-5', C-6', C-8' HII), 7.7(d, 1H, C-5'H), 7.8(d, 1H, C-4'H), 8.2-8.4(m, 3H, C-7, C-8 &amp; C-9'H), 8.8(s, 1H, C-4'H), 12.2(bs, 1H, NH).</td>
</tr>
</tbody>
</table>

Th e IR spectra of the products 3a-f show absorption range at 3326-3340, 1700-1740, 1610-1675, 1570-1580 cm^{-1}, which are characteristic of N-H, C=O, C=N, and C=C stretching respectively.

The ^{1}H NMR spectrum of 3a shows a multiplet at δ 7.4-7.6 for the 5', 6', 7' and 8' of aromatic region of the coumarin protons. Two doublets are obtained at δ 7.7 and 7.8 due to C-5H and C-4H of quinoline. One more multiplet is obtained at δ 8.0 to 8.2 due to three protons of C-6, C-7 and C-8 of quinoline. The sharp singlet at δ 8.8 integrating for one proton is assigned to C-4'H. A noteworthy feature of this signal is its position at a much farther downfield position than that (δ 7.5) of an average C-4H of typical coumarin. Thus C-4' H experienced a strong deshielding effect. The broad signal (D_2O exchangeable) at δ12.2 is assigned to NH. The mass spectrum of 3a shows molecular ion peak at m/z 313 (60%), which is consistent with its molecular formula C_{10}H_{11}N_{2}O_{2}.

Experimental Section

All the melting points were determined in open capillary in liquid paraffin bath and are uncorrected. The purity of the compounds was checked by TLC. IR spectra (KBr) were recorded on Shimadzu FTIR Model 8010 Spectrometer and the ^{1}H NMR spectra in CDCl_3 on Varian C17-20-ZM-390-200 MHz NMR spectrometer using TMS as an internal standard. The C, H and N analysis of the compounds was done on a Carlo Erba Model EA1108 C, H and N elemental analyser.
Synthesis of 3-(1H-imidazo[4,5-f]quinolin-2-yl)chromen-2-one 3a

Method A (microwave irradiation method). The coumarin-3-carboxylic acid 2a (0.01 mole) and quinolin-5,6-diamine 1 were (0.01 mole) mixed with PTSA (0.001 mole, irradiated in domestic microwave oven at 300 watt-power level for 3.15 minutes (Scheme 1). The reaction was monitored over TLC. The mixture was poured into cold water, filtered, dried and the solid product was recrystallised from chloroform as shining needles.

Compounds 3b-f were prepared similarly.

Method B (conventional heating method). An intimate mixture of quinolin-5,6-diamine 1 (0.01 mole) and coumarin-3-carboxylic acid 2a (0.01 mole) was added to PPA (10 times the weight of the reactants). The mixture was refluxed at 250°C for 5 hr, it was cooled and poured into cold water. The slurry was filtered and dried. The crude product was extracted with benzene, on concentration the solid obtained was recrystallised from chloroform as shining needles.

Compounds 3b-f were prepared similarly.

Acknowledgement

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References

    (b) Knowenagel F & Schrote R, Ber, 37, 1904, 4484.