LIST OF RESEARCH PUBLICATIONS AND REPRINTS


Guru S. Gadaginamath and Manjunath G. Bhovi,


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4. Chemoselective reaction of benz(g)indole dicarboxylates towards hydrazine hydrate: Bisheterocycles: Synthesis and antimicrobial activity of oxadiazolyl/triazolyl and pyrrolylaminocarbonylmethoxybenz(g)indole derivatives.

Guru S. Gadaginamath, Manjunath G. Bhovi and Veena B. Megadi.


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G. S. Gadaginamath, S. R. Pujar and M. G. Bhovi
37th Annual Convention of Chemists, Hardwar (Org.) AP – 8, November 2000.


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Presented at the National seminar: Pharmaceutical diversity in heterocyclic compounds, NACB (India) Lucknow, June 1st (2001).


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6. 1,3-Dipolar cycloaddition reactions: Synthesis and antimicrobial activity of new 1,2,3-triazolylindole/ benz[g]indole derivatives.

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7. 1,3-Dipolar cycloaddition reaction of 2-azidomethylindole: Synthesis and antimicrobial activity of some new triazolylindole derivatives.

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8. Chemoselective reaction of triazolylindole/ benz(g)indole tricarboxylates towards hydrazine hydrate: Synthesis and antimicrobial activity of novel bioxadiazolyl and bipyrrrolylaminocarbonyltriazolethylindole/ benz(g) indole.

Guru S. Gadaginamath and Manjunath G. Bhovi
CHEMoselectivity of indole dicarboxylate towards hydrazine hydrate: Part V: Synthesis of some new 1-(2-hydroxyethyl)-3-ethoxycarbonyl-5-oxadiazolyl/pyrrolylamino carbonylmethoxy-2-methylindoles

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The exclusive formation of 1-(2-hydroxyethyl)-2-methyl-3-ethoxycarbonylindolyl-5-ylox acetamide hydrazide from 3-ethoxycarbonyl-5-methoxycarbonylmethoxy-2-methylindole revealed the chemoselectivity of the C3-ester over C5-ester towards nucleophilic attack of hydrazine hydrate. This monocarbohydrazide was reacted separately with KOH/CS2 and acetonyl acetone in boiling ethanol to secure the desired 1-(2-hydroxyethyl)-5-(5-mercapto-1,3,4-oxadiazol-2-yl)methoxy-2-methylindole (4) and 5-(2,5-dimethylpyrrol-1-yl)aminocarbonylmethoxy-2-methylindole (5). The structures of all new compounds were confirmed by their analytical and spectral data.

A large number of heterocyclic compounds have displayed valuable properties as chemotherapeutic agents. The 1,3,4-oxadiazoles have shown antitubercular, antiviral and amoebicidal properties. Derivatives of 2,5-dimethylpyrrole have shown antihelical and hypotensive properties. 5-Hydroxytryptamine plays an important role in modulating mood, social behaviour, appetite and pain. Some of indole derivatives reported from our laboratory have exhibited interesting antiserotonin and antibacterial properties. Literature survey has revealed that bisheterocycles display enhanced biological activities. In the light of above reports and also in continuation of our work on bisheterocycles and chemoselectivity of indole dicarboxylate towards hydrazine hydrate, we synthesized title compounds linking oxadiazole and pyrrole to the C5-position of biologically active indole moiety.

The convenient starting material for the synthesis of title compounds was 5-hydroxyindole (1) which was obtained by adopting the Nemtzes reaction. Further this hydroxyindole (1) was reacted with methyl chloroacetate in presence of anhyd K2CO3 & KI in refluxing dry acetone to yield the corresponding indole dicarboxylate (2). When this indole dicarboxylate (2) was heated with hydrazine hydrate in refluxing ethanol it reacted chemoselectively producing only monocarbohydrazide (3) wherein C5-carbethoxy group remained unaffected & this observation is in conformity with our earlier reports. The monocarbohydrazide (3) was further reacted separately with KOH/CS2, acetonyl acetone to afford the desired substituted 5-(5-mercapto-1,3,4-oxadiazol-2-yl)methoxy-2-methylindole (4) & 5-(2,5-dimethylpyrrol-1-yl)aminocarbonylmethoxy-2-methylindole (5). The structures of all these newly synthesized compounds were confirmed by spectral & analytical data.

Experimental

Melting points were determined in open capillary tubes & are uncorrected. IR spectra (cm⁻¹) were recorded on Perkin Elmer 881. ¹H NMR spectra in CDCl3 or DMSO-d6 as solvents on 300 MHz NMR spectrometer (chemical shift in δ ppm). Elemental analysis was carried out on Heraeus CHN rapid analyser.

1-(2-Hydroxyethyl)-3-ethoxycarbonyl-5-hydroxy-2-methylindole (1)

To a solution of p-benzoquinone (0.5 mol) in dichloroethane was added a solution of β-amino crotonate (0.9 mol) in dichloroethane & the mixture was refluxed on a water bath for 2 hr. Solvents were removed, ethanol was added & left overnight. Solid separated was filtered, washed with ethanol and crystallized from ethanol (Table-1).
Table-1
Physical and analytical data of compounds prepared

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<th>Compd</th>
<th>M’P  (°C)</th>
<th>Yield (%)</th>
<th>Mol formula</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>Analysis (%) Found (Calcd)</th>
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<td>50</td>
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<td>(63 86) (6 60) (5 03)</td>
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<td>72</td>
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<td>60 79</td>
<td>8 28</td>
<td>5 15</td>
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<td>62</td>
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<td>5 58</td>
<td>12 13</td>
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<tr>
<td>5</td>
<td>164-5</td>
<td>45</td>
<td>C_{22}H_{22}N_{3}O_{6}</td>
<td>63 86</td>
<td>6 61</td>
<td>10 13</td>
<td></td>
</tr>
</tbody>
</table>

Compound 1
IR (KBr) cm⁻¹ 3427 & 3300 (alcoholic phenolic OH) & 1651 (C₂-ester C=O). ¹H NMR (CDCl₃/TMS) δ 1.42 (t, J=7 1 Hz, 3H, C₆-ester CH₃), 2.75 (s, 3H, C₂-CH₃), 3.80 (q, J=7 1 Hz, CH₂-CH₂-OH), 4.19 (t, J=7 1 Hz, 2H, CH₂-CH₂-OH), 4.33 (q, J=7 1 Hz, 2H, C₂-ester-CH₂). 4.61 (t, J=7 1 Hz, 1H, CH₂-OH vanished on D₂O exchange), 6.73 (dd, J=6 & 3Hz, 1H, C₆-H), 7.16 (d, J=9Hz, 1H, C₇-H), 7.52 (d, J=3Hz, 1H, C₅-H) and 8.47 (s, 1H, C₅-OH, disappeared on D₂O exchange).

1-(2-Hydroxyethyl)-3-ethoxycarbonyl-5-methoxycarbonylmethoxy-2-methylindole (2)

To a solution of (1) (0.015 mol) in dry acetone (100 ml), were added methyl chloroacetate (0.030 mol), and K₂CO₃ (3g) & KI (0.1g). The reaction mixture was refluxed for 50 hr and the hot solvoni was filtered. The solvents were removed under reduced pressure and the residue was crystallized from ethanol (Table-1) IR (KBr) 3413 (alcoholic OH), 1766 (C₂-ester C=O) and 1676 (C₂-ester C=O). ¹H NMR (CDCl₃/TMS) 1.41 (t, J=7 1 Hz, 3H, C₆-ester CH₃), 2.73 (s, 3H, C₂-CH₃), 3.80 (s, 1H, C₂-ester CH₃), 3.91 (q, J=7 1 Hz, 2H, CH₂-CH₂-OH), 4.2-4.35 (m, 5H, CH₂-ester CH₃ and CH₂-CH₂-OH), 4.67 (s, 2H, C₅-OCH₂), 6.89 (dd, J=3Hz, 1H, C₅-C₆-H), 7.20 (d, J=9Hz, 1H, C₇-H) and 7.56 (d, J=3Hz, 1H, C₅-C₆-H).

Compound 3
IR (KBr) 3322 (OH/NH/NH₂) and 1685 (C₂-ester and C₅-amide carbonyls). ¹H NMR (CDCl₃ + DMSO-d₆/TMS) 1.42 (t, J=7 1 Hz, 3H, C₂-ester CH₃), 2.76 (s, 3H, C₂-CH₃), 3.81 (t, J=7 1 Hz, 2H, CH₂-CH₂-OH), 4.59 (s, 2H, C₅-OCH₂), 6.90 (dd, J=9 & 3Hz, 1H, C₅-H), 7.33 (d, J=9Hz, 1H, C₇-H) and 7.69 (s, 1H, C₅-amide NH, disappeared on D₂O exchange).

1-(2-Hydroxyethyl)-3-ethoxycarbonyl-(5-mercapto-1,3,4-oxadiazol-2-yl) methoxy-2-methylindole (4)

A mixture of indole carbodiazide (3) (0.0015 mol) in abs ethanol (20 ml), KOH (0.003 mol) dissolved in water (3 ml) and CS₂ (0.0045 mol) was heated under reflux till the evolution of H₂S ceased. The reaction mixture was cooled to room temp and poured into ice cold water. It was then neutralized with dil hydrochloric acid. The precipitated solid was filtered, washed with water & dried. Product was crystallized from ethanol (Table-1) IR (KBr) 3382 (OH/NH/CH₃). ¹H NMR (CDCl₃ + DMSO-d₆/TMS) 1.49 (t, J=7 1 Hz, 3H, C₂-ester CH₃), 2.79 (s, 3H, C₂-CH₃), 3.86 (t, J=7 1 Hz, 2H, CH₂-CH₂-OH), 4.26 (t, J=7 1 Hz, 2H, CH₂-CH₂-OH), 4.39 (q, J=7 1 Hz, 2H, C₂-ester-CH₂), 5.09 (s, 2H, C₅-OCH₂), 6.91 (dd, J=9 & 3Hz, 1H, C₅-H), 7.30 (d, J=3Hz, 1H, C₇-H) and 7.72 (d, J=3Hz, 1H, C₅-H) and 8.5 (s, 1H, NH, disappeared on D₂O exchange).