SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 5-[2(3)]-DIALKYLAMINO ALKOXY] INDOLE 2, 3-DIONES AND 5-[2(3)]-DIALKYLAMINO ALKOXY] INDOLE 2-ONE, 3-SEMIRCARBAZONES

K.SWATHI**, M. SARANGAPANI*

1Medicinal Chemistry Laboratory, U.C.P.S.C., Kakatiya University, Wararagal-506009, A.P., India, Email: kswathi84@yahoo.co.in

ABSTRACT

In the present work, some new, 5-[2(3)]-dialkylamino alkoxy] Indole 2,3-diones and 5-[2(3)]-dialkylamino alkoxy] Indole 2-one,3-semircarbazones were prepared. Hydroxy Isatin was synthesized from p-amino phenol by using Sandmayer method and it react with semicarbazides gives 5-hydroxy isatin 3-semicarbazone. 5-hydroxy isatin 3-semicarbazones were condensed with dialkylamino alkylhalide by using William son synthesis to prepare the 5-[2(3)]-dialkylamino alkoxy] Indole 2, 3-dione and 5-[2(3)]-dialkylamino alkoxy] Indole 2-one, 3-semircarbazone derivatives. The structures of the products were characterized by IR, NMR, and MASS Spectral study. All the compounds were evaluated for Antimicrobial activity. Some of these compounds showed good antibacterial activities compared with standard compounds.

Keywords: Synthesis, 5-[2(3)]-dialkyl amino alkoxy] Indole 2, 3-diones, 5-[2(3)]-dialkyl amino alkoxy] Indole 2-one, 3-semircarbazones, Antimicrobial activity

INTRODUCTION

Surendranath pandya et al. reported the synthesis and anticonvulsant activity of some novel n-methyl/acetylL-5-(un)-substituted isatin-3-semicarbazones. In the last few years, Isatin derivatives have been discovered which show potential hypnotic1, antidepressant2, MAO inhibitory3, antioxidant4 activity.

We are reporting in the present communication the synthesis and characterization of some new compounds: 5-[2(3)]-dialkyl amino alkoxy] Indole2, 3-diones, 5-[2(3)]-dialkyl amino alkoxy] Indole2-one, 3-semircarbazones 5-hydroxy Isatin was synthesized from p-amino phenol by using Sandmayer method. 5-Hydroxyisatin was heated under reflux in methanol containing two or three drops of acetic acid with semicarbazide hydrochloride for half an hour to get 5-Hydroxy isatin Semicarbazone. 5-Hydroxyisatin and 5-Hydroxy isatin semicarbazone condensed with dialkylamino alkyl halide by using William son synthesis to prepare 5-[2(3)]-dialkylamino alkoxy] Indole 2, 3-dione and 5-[2(3)]-dialkylamino alkoxy] Indole 2-one, 3-semircarbazone derivatives. All the compounds of the series have been screened antibacterial activity, the structures of these compounds were identified by IR, NMR and Mass Spectra.

MATERIALS AND METHODS

The compounds were mostly synthesized by conventional methods and described in experimental selection and also by the methods established in our laboratory.

Chemicals

Dialkyl amino alkylhalides purchased from Sigma- Aldrich Chemicals Private Limited, Hyderabad, India. p-amino phenol, hydroxylamine hydrochloride, sodium sulfate were purchased from Merck Chemicals Private Limited, Hyderabad, India.

Chemistry

Solvents were dried or distilled before use. Melting points were obtained on a Thoshniwall melting point apparatus in open capillary tubes and are uncorrected. The purity of the compounds were ascertained by TLC on silica gel –G plates(Merck). Infrared spectra(IR) were recorded with KBr pellet on a Perkin-Elmer BX series, Infrared spectrophotometer. Mass spectra were recorded by the direct inlet method on Thadmammass-quantam API 400H mass spectrophotometer. 41 NMR spectra were recorded on Brucker spectrospin 400 MHz spectrophotometer in DMSO-d6.

5-Hydroxyisatin was synthesized from p-amino phenol by using Sandmayer method. It consists in the reaction of aniline with chloral hydrate and hydroxylamine hydrochloride in aqueous sodium sulfate to form an isonitrosoacetanilide, which after isolation, when treated with concentrated sulfuric acid, furnishes isatin in >75% overall yield.

1 Preparation of 5-Hydroxy Indole 3-semicarbazone 2-one

5-Hydroxyisatin was heated under reflux in methanol containing two or three drops of acetic acid with semicarbazide hydrochloride for half an hour. The product thus separated was filtered and purified by recrystallization from suitable solvent.

2 Preparation of 5-[2(3)]-dialkyl amino alkoxy] Indole 2,3-dione, 5-[2(3)]-dialkyl amino alkoxy] Indole 2-one, 3-semircarbazone derivatives

A mixture of 5-Hydroxyisatin/5-Hydroxyisatin-3-semicarbazone (0.01 moles) and dialkylamino alkylhalide (0.01 moles) placed in 10% alcoholic potassium hydroxide and this mixture was heated under reflux on water bath for 6 hours. The alcohol was reduced to half of its volume and cooled. The product separated was filtered, washed with small portions of cold alcohol repeatedly and dried. It was purified by recrystallization from hydro alcoholic mixtures to get a crystalline solid.

Adopting these procedure 10 compounds of 5-OH-Isatin derivative was prepared. The physical data of the title compounds were presented in Table –I. The compounds were characterized by spectral data.

Similarly other 5-Hydroxy Isatin derivatives were prepared and their melting points were determined in Open capillary tubes using Toshiwall melting point apparatus and are uncorrected. Purity of the compounds was checked by TLC.
Spectral Data

The compounds have been characterized by the spectral data IR, PMR and Mass.

1. 5-Hydroxy indole 2, 3 di one (III). Yield - 90.2%; 1H NMR (DMSO-d6): 13.3 (s, 1H, OH), 10.36(s, 1H,-CONH), 6.65-7.29(m, 3 H; Ar-H); MS (ESI), m/z =263[M+ 1]; IR (KBr); 3421.47 (OH), 1630.08 (C = O), 1548 (Ar, C=C), 1282(C-O-C), 883.85-579.8 (Ar) cm-1.

2. 5-[2(3)-dimethyl amino ethoxy] Indole 2, 3 di one (IIla). Yield - 91%; 1H NMR (DMSO-d6): 10.36(s, 1H,-CONH), 7.01-7.29(m,3 H,Ar-H) 3.2 (T,2H,0-CH2), 2.9 (2,2H-N-CH3), 1.36 [s,6H,N-(CH3)]; MS (ESI), m/z =231 [M+ 1]; IR (KBr); 3274(NH), 1651.96 (C=O), 1569.82 (Ar,C=C), 1276(C-O-C), 807.93(Ar).

3. 5-[2(3)-diethyl amino ethoxy] Indole 2, 3 di one (IIlb). Yield - 86%; 1H NMR (DMSO-d6): 10.25(s, 1H,-CONH), 7.03-7.45(m,3 H,Ar-H) 2.99 (t,2H,0-CH2), 2.72 (t,2H,N-CH3), 1.24 [s,10H,N-(C,H3)]; MS (ESI), m/z =263[M+ 1]; IR (KBr); 3274(NH), 1681.53 (C=O), 1570.21 (Ar, C=C), 1243(C-O-C), 845.51(Ar).

4. 5-[2(3)-dimethyl amino propoxy] Indole 2, 3 di one (IIlc). Yield - 93%; 1H NMR (DMSO-d6): 10.46(s, 1H,-CONH), 7.21-7.49(m,3 H,Ar-H) 2.94 (t,2H,0-CH2), 2.51 (m,2H, CH3), 2.48 (2,2H-N-CH2), 1.25 [s,6H,N-(CH3)]; MS (ESI), m/z =247[M+ 1]; IR (KBr); 3274(NH), 1651.96 (C=O), 1579.72 (Ar, C=C), 1266(C-O-C), 805.91(Ar).

5. 5-[2(3)-dimethyl amino isopropoxy] Indole 2, 3 di one (IIId). Yield - 97%; 1H NMR (DMSO-d6): 10.45(s, 1H,-CONH), 7.21-7.49(m,3 H,Ar-H) 2.94 (t,2H,0-CH2), 2.51 (m,2H, CH3), 2.48 (2,2H-N-CH2), 1.25 [s,6H,N-(CH3)]; MS (ESI), m/z =247[M+ 1]; IR (KBr); 3274(NH), 1651.96 (C=O), 1579.72 (Ar, C=C), 1266(C-O-C), 805.91(Ar).

6. 5-[2(3)-diisopropyl amino ethoxy] Indole 2, 3 di one (IIle). Yield - 81%; 1H NMR (DMSO-d6): 10.26(s, 1H,-CONH), 7.34-7.51(m,3 H,Ar-H) 2.96 (t,2H,0-CH2), 2.82 (2,2H,N-CH2), 1.35 [m, 2H,N-CH], 1.21 (d,4,4H,2-(CH3)); MS (ESI), m/z =291[M+ 1]; IR (KBr); 3274(NH), 1681.53 (C=O), 1570.21 (Ar, C=C), 1243(C-O-C), 845.51(Ar).

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound R</th>
<th>R1</th>
<th>X</th>
<th>M.F</th>
<th>% YIELD</th>
<th>MP</th>
<th>M.Wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IIla</td>
<td>CH3</td>
<td>H</td>
<td>0</td>
<td>91%</td>
<td>320</td>
<td>234</td>
</tr>
<tr>
<td>2</td>
<td>IIib</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>86%</td>
<td>320</td>
<td>262</td>
</tr>
<tr>
<td>3</td>
<td>IIic</td>
<td>CH3</td>
<td>H</td>
<td>2</td>
<td>93%</td>
<td>320</td>
<td>248</td>
</tr>
<tr>
<td>4</td>
<td>IIId</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>85%</td>
<td>320</td>
<td>248</td>
</tr>
<tr>
<td>5</td>
<td>IIle</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>81.8%</td>
<td>320</td>
<td>292</td>
</tr>
<tr>
<td>6</td>
<td>IVa</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>92%</td>
<td>320</td>
<td>291</td>
</tr>
<tr>
<td>7</td>
<td>IVb</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>83%</td>
<td>320</td>
<td>319</td>
</tr>
<tr>
<td>8</td>
<td>IVc</td>
<td>CH3</td>
<td>H</td>
<td>2</td>
<td>92%</td>
<td>320</td>
<td>365</td>
</tr>
<tr>
<td>9</td>
<td>IVd</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>86%</td>
<td>320</td>
<td>365</td>
</tr>
<tr>
<td>10</td>
<td>IVe</td>
<td>CH3</td>
<td>H</td>
<td>1</td>
<td>82%</td>
<td>320</td>
<td>349</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

Table II shows the antibacterial activity data of 5-Hydroxyisatin (III) and 5-Hydroxyisatin 3-semicarbazone (IV) derivatives, which had significant antibacterial activity. Amongst them, compounds IIIa, IIIc, IVa and IVd has been found to be relatively more effective against B. subtilis with a zone of inhibition of 85 mm, 76 mm, 72 mm respectively. Compounds IVe, IVd, IVc, IIIe and IIId relatively more effective against the standard drug. IIIe, IVe and IIId are more effective against S. aureus with a zone of inhibition of 94 mm, 89 mm, 91 mm, and 71 mm respectively.

From the observed data that the compounds IVd, IVe and IIId, IIIe have shown more antibacterial activity. The compound IIIa, IIIc, IVa, IVd and IVc shows moderate antibacterial activity whereas no antibacterial activity was observed against E.coli and B.subtilis.

ACKNOWLEDGEMENTS

The First author would like to thank the CSIR, New Delhi for providing financial support. Authors are thankful to Principal University College of Pharmaceutical Sciences, Kakatiya University for providing facilities.

REFERENCES