bacterial strains were more susceptible to the extracts when compared to gram negative bacteria. This may be attributed to the fact that these two groups differ in their structure of the cell wall components[14]. The ability of tannin compounds to cause the bacterial colonies to disintegrate, probably results from their interference with the bacterial cell wall; thereby inhibiting the microbial growth[15,16]. The results of the present study support the traditional use of the *Lantana indica* as an ethnomedicine. It also suggests that the tannins isolated from the *Lantana indica* possess remarkable antimicrobial activity against microbial pathogens.

**ACKNOWLEDGEMENTS**

Authors are grateful to Dr. T. K. Ravi, Principal, Ramakrishna College of Pharmacy, Coimbatore for providing gifts of the drugs and chemicals of I.P. grades necessary for the above studies.

**REFERENCES**


**New Benzofuran Derivatives as an Antioxidant Agent**

S. S. RINDHE*, M. A. RODE, AND B. K. KARALE

Department of Chemistry, New Arts Commerce and Science College, Ahmednagar- 414 001, 1Department of Chemistry, Radhabai Kale Mahila Mahavidyalaya, Ahmednagar-414 001, India

Rindhe, et al.: New Benzofuran Antioxidants

A series of substituted benzofuran derivatives were synthesized and characterized by spectral data. Some of the synthesized compounds were tested for *in vitro* antioxidant activity. Some of them have shown very good antioxidant

*Address for correspondence*

E-mail: rindhe_ss@yahoo.com
Various natural and synthetic benzofuran derivatives are found to possess diverse applications in the field of medicine. A crystalline antioxidant extracted from yeast was shown to protect in vitro the erythrocytes of vitamin E deficient rats from hemolysis. The structure of this compound was determined as benzofuran derivative\(^1\). It is well known that Vitamin E having chroman skeleton have a very good antioxidant activity. It has been reported that the activity is increased by the transformation of skeleton from chroman to benzofuran\(^2\). The antioxidant activity of a novel water soluble antioxidant of the benzofuran family (5-hydroxy-4,6,7-trimethyl-2,3-dihydrobenzofuran-2-acetic acid, BFA) is reported to possess better antioxidant activity than that of congener compound Trolox C\(^3\).

Benzofuran in conjunction with cyclic β-amino hydroxamic acid scaffolds have found to possess very potent and selective tumor necrosis factor-α converting enzyme (TACE) inhibitory activity. Similarly some of the benzofuran derivatives have shown very good antimicrobial activity and β-amylloid aggregation inhibitory activity\(^4-6\). Owing to the biological importance of benzofurans, we herein, report the synthesis and biological testing of some benzofurans.

In the present work, substituted phenacyl bromide (1) was treated with 2'-hydroxy-5'-nitro acetophenone (2) in presence of K\(_2\)CO\(_3\) in DMF to get aryl-3-methyl-5-nitro-1-benzofuran-2-ylmethanone (3), which was further reduced to aryl-5-amino-3-methyl-1-benzofuran-2-ylmethanone (4). Compound 4 was further treated with 5-chloronicotinoyl chloride to get N-(2-aroyl)-3-methyl-1-benzofuran-5-yl)-6-chloronicotinamide (5). Compound 5 was treated with various substituted amines in pyridine to get benzofuran derivatives 6(a-r), respectively.

All recorded melting points were determined in open capillary tubes and were uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. \(^1\)H NMR spectra were recorded on 400 MHz spectrophotometer in DMSO-d\(_6\) as a solvent and TMS as an internal standard. Peak values are shown in δ ppm. Mass spectra were obtained by Waters mass spectrometer.

General procedure employed for the preparation of aryl-3-methyl-5-nitro-1-benzofuran-2-ylmethanone (3) was equimolar mixture of substituted (0.1 mol) phenacyl bromide 1 and (0.1 mol) 2'-hydroxy-5'-nitro-acetophenone 2 with (0.3 mol) K\(_2\)CO\(_3\) in DMF was heated at 80\(^\circ\)C for 5 h. The reaction mixture was cooled to room temperature and then poured into ice cooled water. The solid product was separated by filtration and crystallized from DCM-hexane.

The procedure for the preparation of aryl-5-amino-3-methyl-1-benzofuran-2-yl phenyl methanone (4) involved adding to a suspension of (0.1 mol) nitro derivative (3) in methanol (50 ml) 5 equivalents of SnCl\(_2\).2H\(_2\)O and heating the reaction mixture at 60\(^\circ\)C for 4 h. The reaction mixture was cooled to room temperature. It was poured into liquid NH\(_3\) and filtered through hyflow. Filtrate was extracted by EtOAc. EtOAc layer separated, dried over Na\(_2\)SO\(_4\) and concentrated under vacuum. The product was crystallized from ethanol.

N-(2-aroyl)-3-methyl-1-benzofuran-5-yl)-6-chloronicotinamide (5) was prepared by stirring an equimolar mixture of (0.1 mol) amino compound (4) and (0.1 mol) 6-chloro nicotinoyl chloride in THF with (0.3 mol) K\(_2\)CO\(_3\) for 6 h at room temperature. The reaction mixture was concentrated under vacuum and then poured into water. The solid product was separated by filtration and recrystallized from ethanol.

General procedure for the preparation of (6 a-r) involved adding a suspension of (0.1 mol) chloro compound 5 in pyridine to (0.12 mol) substituted amine. The suspension was heated for 12 h at 110\(^\circ\)C. The reaction mixture was then cooled to room temperature and poured into water. The solid product was separated by filtration and crystallized from DCM-Hexane. The compounds synthesized by the above procedure are listed in Table 1 and their structural data, spectral data and physical constant values are given in Tables 1 and 2.
A series of 18 new compounds were synthesized. The structural data of all benzofuran derivatives is shown in Table 1. Scheme 1 illustrates the preparation of target compounds. The structure of the synthesized compounds was elucidated by IR, ¹H NMR, mass spectral data and elemental analysis.

In the ¹H NMR spectra of the compounds, NH proton of the benzofuran ring was seen as singlet at about 10.20-10.70 δ ppm. Signal due CH₃ of benzofuran appeared at 2.55-2.58 δ ppm as a singlet. All other aromatic and aliphatic protons were observed in the expected regions. Mass spectra of all compounds showed M⁺ peaks in agreement with their molecular formula. In the IR spectra of all compounds C=O stretching bands were observed at 1635-1644 cm⁻¹ and stretching band of CH₃ of benzofuran ring observed at 2914-2932 cm⁻¹.

The benzofuran derivatives were evaluated for their in vitro antimicrobial activity. MICs were recorded as the minimum concentration of compound, which inhibit the growth of tested microorganisms. Antimicrobial activities of the compounds were tested using Mueller-Hinton broth (Hi Media M 391) medium. Microbial strains used for testing included, *Staphylococcus aureus* (NCIM 5021) and *Salmonella typhimurium* (NCIM 2501). All test compounds were found to be inactive against above bacterial strains.

**TABLE 1: STRUCTURAL AND ANALYTICAL DATA OF THE SYNTHESIZED BENZOFURAN DERIVATIVES**

<table>
<thead>
<tr>
<th>Compds.</th>
<th>R1</th>
<th>R</th>
<th>M.P. (°)</th>
<th>Yield (%)</th>
<th>Elemental analysis Calcd % (Found %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>6a</td>
<td>morpholine</td>
<td>Br</td>
<td>109-11</td>
<td>92</td>
<td>60.01 (60.00)</td>
</tr>
<tr>
<td>6b</td>
<td>OCH₃</td>
<td></td>
<td>140-2</td>
<td>95</td>
<td>68.78 (68.77)</td>
</tr>
<tr>
<td>6c</td>
<td>N-methyl piperazine</td>
<td>Br</td>
<td>129-31</td>
<td>89</td>
<td>60.80 (60.79)</td>
</tr>
<tr>
<td>6d</td>
<td>OCH₃</td>
<td></td>
<td>196-18</td>
<td>88</td>
<td>69.41 (69.40)</td>
</tr>
<tr>
<td>6e</td>
<td>N-benzyl piperazine</td>
<td>Br</td>
<td>118-20</td>
<td>95</td>
<td>65.03 (65.02)</td>
</tr>
<tr>
<td>6f</td>
<td>thiomorpholine</td>
<td>OCH₃</td>
<td>119-21</td>
<td>90</td>
<td>72.84 (72.83)</td>
</tr>
<tr>
<td>6g</td>
<td>pyrrolidine</td>
<td>OCH₃</td>
<td>147-9</td>
<td>59</td>
<td>58.21 (58.20)</td>
</tr>
<tr>
<td>6h</td>
<td>pyrrolidine</td>
<td></td>
<td>135-7</td>
<td>55</td>
<td>66.51 (66.50)</td>
</tr>
<tr>
<td>6i</td>
<td>tetrahydroisoquinoline</td>
<td>Br</td>
<td>128-30</td>
<td>69</td>
<td>61.91 (61.90)</td>
</tr>
<tr>
<td>6j</td>
<td>tetrahydroisoquinoline</td>
<td>OCH₃</td>
<td>126-8</td>
<td>67</td>
<td>71.19 (71.20)</td>
</tr>
<tr>
<td>6k</td>
<td>piperidine</td>
<td>Br</td>
<td>119-21</td>
<td>75</td>
<td>62.56 (62.55)</td>
</tr>
<tr>
<td>6l</td>
<td>piperidine</td>
<td>OCH₃</td>
<td>107-9</td>
<td>78</td>
<td>71.63 (71.62)</td>
</tr>
<tr>
<td>6m</td>
<td>tetrahydroisoquinoline</td>
<td>Br</td>
<td>131-3</td>
<td>88</td>
<td>65.73 (65.72)</td>
</tr>
<tr>
<td>6n</td>
<td>tetrahydroisoquinoline</td>
<td>OCH₃</td>
<td>139-41</td>
<td>80</td>
<td>74.26 (74.25)</td>
</tr>
<tr>
<td>6o</td>
<td>1-pyridyl-2-ylpiperazine</td>
<td>Br</td>
<td>218-20</td>
<td>76</td>
<td>62.42 (64.41)</td>
</tr>
<tr>
<td>6p</td>
<td>1,4-dioxo-8-azaspiro[4,5] decane</td>
<td>Br</td>
<td>174-6</td>
<td>66</td>
<td>70.19 (70.18)</td>
</tr>
<tr>
<td>6q</td>
<td>2-piperzin-1-yethanol</td>
<td>OCH₃</td>
<td>102-4</td>
<td>55</td>
<td>67.69 (67.68)</td>
</tr>
</tbody>
</table>
The in vitro antioxidant activity of the test compounds was determined by DPPH method using L-ascorbic acid (an antioxidant agent) as a positive control. The compounds were tested for antioxidant activity at 200, 100 and 50 µg/ml concentration. Amongst the compounds screened for antioxidant activity, 6a, 6b, 6d, 6h, 6o, 6p and 6r showed very good antioxidant activity as shown in Table 3.

The compounds with morpholine, 1-pyridyl-2-yl piperazine at R1 and with Br and OMe at R showed very significant antioxidant activity. While the compounds with thiomorpholine and piperzin-1-yl ethanol at R1 and OMe at R also showed good antioxidant activity. Compounds with pyrrolidine, piperidine and N-benzylpiperazine at R1 do not show any antioxidant activity.

**REFERENCES**


