
A V Karnik* & S P Upadhyay
Department of Chemistry, University of Mumbai,
Vidyannagar, Kalina, Mumbai 400 098, India
E-mail: avkarnik@chem.mun.ac.in

Received 19 March 2003; accepted (revised) 23 September 2003

Successful preparation of novel penta-heterocyclic compounds, 12H-benzo[e]indolo[3,2-b]benzofurans, in good yields is reported. The synthesized compounds with planar geometry and extended conjugation exhibit excellent fluorescence properties.

IPC: Int.CI. C07 D 307/78

Fluorescent organic compounds have been the focus of considerable interest because of their potential applications to a variety of fields, including their use as fluorescent probes and optoelectronics. As a result, the development of a new series of fluorophores has been actively pursued. Besides the intrinsic structural features such as extended π-conjugation, rigidity of π framework, nature of substituent(s) (electron donor and acceptor) the presence of hetero atoms and heavy atoms etc.; are known to influence emission wavelength and intensity of fluorescence band. Indole derivatives have been found to be useful as a tool for qualitative and quantitative analysis of inorganic ions, for detection as fast response potentiometric sensors and for monitoring direct oxidation and reduction of biomolecules.

In addition to the usefulness as fluorescent probes, the indole moiety is widely distributed in nature and exhibits important bioactivities. Presence of naphthofurans/benzofurans in natural products and their useful bioactivities has always attracted the unabated attention of synthetic chemists. Considering the above factors the present work was envisaged in the synthesis of compounds incorporating indole and furan moieties in the same molecule. A search of the literature revealed that there are only a few reports for the preparation of benzofuro[3,2-b]indole.

Results and Discussion

Though the synthesis of benzofuro[3,2-b]indoles are reported, their fluorometric studies were not investigated. The benzofuro[3,2-b]indole and its derivatives with extended conjugation were expected to enhance the fluorescence activity.

Retrosynthetic analysis revealed that the title compound could be obtained from naphtho[2,1-b]furan-1(2H)-ones 2a,b which in turn could be obtained from β-naphthol 1a,b as a starting material. Preparation of 2 was achieved by slight modification of reported procedure, by using CS₂ as solvent instead of PhNO₂. As a result, the yield was increased from 60% to 70% and the total reaction time was significantly reduced from 24 to 8 hours.

Fischer indole procedure was employed for the synthesis of 12H-benzo[e]indolo[3,2-b]benzofuran 3a (Scheme I) in good yield. Strikingly in 1H NMR
spectrum of 3a, the signal for N-H was deshielded and appeared at δ 10.99. The signal at δ 8.44 (d, J=8Hz) due to proton at C-1 is also slightly deshielded. These signals suggest that these protons also experience additional deshielding due to the proximity with ring E and nitrogen respectively. Similar additional deshielding is also seen for the N-alkyl substituents. N-CH₂ group giving signal between δ 4.32 to δ 6.01 for compounds 4a-f, which are obtained by N-alkylation of 3a-b using alkyl halides in presence of K₂CO₃ in DMF (Scheme I). Energy minimized structures using ACD labs. (Chemsketch) showed planar structures for the compounds 3a-b and 4a-f. The planar, rigid, polycyclic structures with extended conjugation are supposed to exhibit good fluorescence properties and hence our compounds, 3a-b and 4a-f with the said required structural features were best suited to exhibit good fluorescence activity. We are happy to report that as expected the newly synthesized compounds, 3a-b and 4a-f exhibited excellent fluorescence properties. The results are presented in the Table I.

Conclusion
The newer heterocycles, namely, 12H-benzo[e]-indolo[3,2-b]benzofurans 3a,b and their N-alkylated derivatives 4a-f were successfully prepared in good yields. Excellent fluorescence properties of our compounds were noticed (stokes values between 60-70 nm). Modification of the core for tailor made physical properties is possible on R₁ and R₂. Therefore, our molecules hold a potential as good analytical tool as sensors along with some other useful applications. The extended conjugation and the planar nature of the pentacyclic ring structure containing heteroatoms are most probably responsible for excellent fluorescence properties shown by our compounds.

Experimental Section
Reagents were of LR grade and were used without further purification. Column chromatography was carried out using silica gel (S. D. Fine Chemicals, India) 60-120 mesh. Melting points reported are uncorrected. IR spectra were recorded on a Shimadzu FTIR-4200 spectrometer and 'H NMR spectra recorded on a Varian VR (500 MHz) spectrometers using TMS as an internal standard. Mass spectrum was recorded on GC-MSQP-1000. UV spectra were recorded on a Shimadzu UV-visible spectrophotometer UV-2100. Fluorescence spectra were recorded on a Shimadzu RF-5501 PC spectrofluorophotometer.

**Table I**—Characterisation data of compounds 3a,b and 4a-f

<table>
<thead>
<tr>
<th>Compd</th>
<th>R₁</th>
<th>R₂</th>
<th>m.p. °C</th>
<th>Yield (%)</th>
<th>λmax (nm)</th>
<th>log ε</th>
<th>λem (nm)</th>
<th>Stokes shifts (Å²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td></td>
<td>144</td>
<td>92</td>
<td>355</td>
<td>4.42</td>
<td>417</td>
<td>62</td>
</tr>
<tr>
<td>3b</td>
<td>Br</td>
<td></td>
<td>180</td>
<td>65</td>
<td>360</td>
<td>4.26</td>
<td>421</td>
<td>61</td>
</tr>
<tr>
<td>4a</td>
<td>H</td>
<td>CH₃</td>
<td>147</td>
<td>96</td>
<td>350</td>
<td>4.45</td>
<td>419</td>
<td>69</td>
</tr>
<tr>
<td>4b</td>
<td>CH₃</td>
<td></td>
<td>113</td>
<td>94</td>
<td>351</td>
<td>4.47</td>
<td>418</td>
<td>67</td>
</tr>
<tr>
<td>4c</td>
<td>H</td>
<td>CH₂Ph</td>
<td>166</td>
<td>95</td>
<td>350</td>
<td>4.52</td>
<td>415</td>
<td>65</td>
</tr>
<tr>
<td>4d</td>
<td>Br</td>
<td>CH₃</td>
<td>206</td>
<td>97</td>
<td>358</td>
<td>4.15</td>
<td>422</td>
<td>64</td>
</tr>
<tr>
<td>4e</td>
<td>Br</td>
<td>C₆H₅</td>
<td>163</td>
<td>96</td>
<td>359</td>
<td>4.43</td>
<td>422</td>
<td>63</td>
</tr>
<tr>
<td>4f</td>
<td>Br</td>
<td>C₆H₅</td>
<td>201</td>
<td>94</td>
<td>358</td>
<td>4.41</td>
<td>421</td>
<td>63</td>
</tr>
</tbody>
</table>

Solvents used for UV and fluorescence studies were of spectral grade. Elemental analyses were carried on Carlo Erba EA-1108 elemental analyser.

**Naphtho[2,1-b]furan-1(2H)-one 2a.** To a stirred solution of β-naphthol 1a (10.0 g, 69.4 mmole) in dryCS₂ (250 mL) under moisture free condition was added chloroacetyl chloride (6.5 mL, 69.0 mmole). The reaction mixture was stirred at r.t. for 1 hr. Then powdered anhy. AlCl₃ (14 g, 105.0 mmole) was introduced slowly in 4 hr. After complete addition of anhy. AlCl₃ the reaction mixture was stirred for further 2 hr. Then it was refluxed for 2 hr (till the evolution of hydrogen chloride gas stopped). CS₂ was separated by distillation and the reaction mixture was allowed to cool to r.t. To this mixture approx. 150 mL of mixture of ice cold water and HCl (1:1) was added at 0-5°C (approx). The separated solid residue was filtered and was washed with dil. HCl and then with cold water to remove the traces of aq. HCl and was dried in an electric oven maintained at 50°C. This crude mass was then purified by column chromatography using 80:20 (pet.ether:chloroform) as an eluent to furnish 2a (8.94 g, 70%), m.p. 133°C (lit.19, m.p. 133°C).

**7-Bromonaphtho[2,1-b]furan-1(2H)-one 2b.** Compound 2b was prepared from 6-Bromo-2-naphthol 1b1 (10.0 g, 44.8 mmole) following the similar procedure as described for 2a. Product obtained was purified by column chromatography using 60:40 (petroleum-ether:chloroform) as an eluent to afford pure 2b (7.10 g, 60%), m.p. 201°C; IR (KBr): 1700, 1630, 1580 cm⁻¹. 'H NMR (CDCl₃): δ 8.63 (d, 1H, C₅-Ar, J = 8.75Hz), 7.99 (s, 1H, C₆-Ar), 7.97 (d, 1H, Ar), 7.30 (d, 1H, Ar) and 4.77 (s, 2H, CH₂). Anal. Calcd for C₁₃H₁₀BrO₂: C, 54.75; H, 2.66; Br, 30.42; Found: C, 54.60; H, 2.64; Br, 30.53%.

**12H-Benz[e]indolo[3,2-b]benzofuran 3a.** To a solution of 2a (1.0 g, 5.43 mmole) in glacial acetic acid (10 mL) were added phenyl hydrazine (0.55 g,
5.09 mmole) and a catalytic amount (0.2 mL) of BBr₃-etherate and the reaction mixture was kept on water bath (100°C) for 2 hr. After completion of the reaction (monitored by TLC), the mixture was removed and was allowed to cool to r.t. This mixture was then poured onto ice cold water. The solid separated out was then filtered and washed with water till the smell of aqueous acetic acid disappeared. The solid was dried and then purified by column chromatography using 70:30 (pet-ether:chloroform) as an eluent to furnish 3a (1.22 g, 92%), m.p.144°C. IR (KBr): 3420, 3100, 1570, 1510, 1460 cm⁻¹. ¹H NMR (CDCl₃): δ 10.90 (s, 1H, NH), 8.44 (d, 1H, C₁⁻Ar, J=8 Hz) and 7.85-7.07 (m, 9H, Ar). Anal. Calc'd for C₁₉H₁₆NO: C, 83.66; H, 4.49; N, 5.71. Found: C, 83.00; H, 4.32; N, 5.55%.

3-Bromo-12H-benzo[e]indolo[3,2-b]benzofuran 3b: Compound 3b was prepared from 2b (1.0 g, 3.8 mmole) by following the similar procedure as given for 3a. The crude solid obtained was purified by column chromatography using 70:30 (pet-ether: chloroform) as an eluent to yield pure 3b (0.8 g, 65%), m.p.180°C. IR (KBr): 3440, 3110, 1570, 1520, 1450 cm⁻¹. ¹H NMR (CDCl₃): δ 8.30 (s, 1H, NH), 8.16 (s, 1H, C₁⁻Ar), 8.09 (d, 1H, C₁⁻Ar, J=8Hz) and 7.90-7.27 (m, 7H, Ar). Anal. Calc'd for C₁₉H₁₅NO: C, 83.26; H, 4.49; N, 5.71. Found: C, 83.00; H, 4.32; Br, 4.49; N, 5.55%.

N-alkylation of 3a-b: Preparation of 4a-f: Typical procedure. A mixture of 3a-b (4 mmole), alkyl halide (MeI, C₂H₅I, PhCH₂Cl) (4.0 mmole) and K₂CO₃ (200 mg) in dry DMF (20 mL) was stirred at 5°C for 6 hr and monitored by TLC. After completion of the reaction, the mixture was poured onto ice water. The solid was separated and purified by column chromatography using pet-ether as an eluent to yield 4a-f.

N-Methyl-12H-benzo[e]indolo[3,2-b]benzofuran 4a: m.p.147°C, IR(KBr): 3150, 2910, 1500, 1460 cm⁻¹; ¹H NMR (CDCl₃): δ 8.63 (d, 1H, C₁⁻Ar, J=8Hz), 8.02-7.24 (m, 9H, Ar), 4.41 (s, 3H, N-CH₃); M⁺(m/z) 271. Anal. Calc'd for C₁₉H₁₅NO: C, 84.13; H, 4.80; N, 5.05. Found: C, 84.00; H, 4.60; N, 5.05%.

N-Ethyl-12H-benzo[e]indolo[3,2-b]benzofuran 4b: m.p.113°C, IR(KBr): 3110, 2950, 1560, 1500, 1450 cm⁻¹; ¹H NMR (CDCl₃): δ 8.46 (d, 1H, C₁⁻Ar, J=8Hz), 8.03-7.24 (m, 9H, Ar), 4.84 (q, 2H, CH₂, J=7Hz), 1.63 (t, 3H, CH₃, J=7Hz). Anal. Calc'd for C₁₉H₁₇NO: C, 84.21; H, 5.26; N, 4.91. Found: C, 84.00; H, 5.10; N, 4.75%.

N-Benzyl-12H-benzo[e]indolo[3,2-b]benzofuran 4c: m.p.166°C. IR (KBr): 3150, 2990, 1500, 1460 cm⁻¹; ¹H NMR (CDCl₃): δ 8.24 (d, 1H, C₁⁻Ar, J=8 Hz), 7.96-7.22 (m, 14H, Ar). 6.01 (s, 2H, CH₂). Anal. Calc'd for C₂₆H₂₃NO: C, 86.45; H, 4.90; N, 4.03. Found: C, 86.20; H, 4.72; N, 3.85%.

3-Bromo-N-methyl-12H-benzo[e]indolo[3,2-b]benzofuran 4d: m.p.206°C IR(KBr): 3150, 2950, 1620, 1560, 1500, 1470, 740 cm⁻¹; ¹H NMR (CDCl₃): δ 8.42 (d, 1H, C₁⁻Ar, J=8Hz), 8.40 (s, 1H, C₆⁻Ar), 7.86-7.23 (m, 7H, Ar), 4.32 (s, 3H, N-CH₃). Anal. Calc'd for C₁₉H₁₅NO: C, 85.14; H, 3.43; Br, 22.86; N, 4.00. Found: C, 85.60; H, 3.30; Br, 23.05; N, 3.86%.

3-Bromo-N-ethyl-12H-benzo[e]indolo[3,2-b]benzofuran 4f: m.p.163°C. IR (KBr): 3110, 2900, 1570, 1500, 1460 cm⁻¹; ¹H NMR (CDCl₃): δ 8.28 (d, 1H, C₁⁻Ar, J=8Hz), 8.14 (s, 1H, C₆⁻Ar), 7.88-7.23 (m, 7H, Ar), 4.76 (q, 2H, CH₂, J=7Hz). 1.59 (t, 3H, CH₃, J=7Hz). Anal. Calc'd for C₂₃H₂₂BrNO: C, 69.93; H, 3.85; Br, 21.98; N, 3.85. Found: C, 65.80; H, 3.70; Br, 22.15; N, 3.68%.

Acknowledgement
One of the author (SPU) wishes to thank G. D. Gokhale Trust for awarding fellowship.

References
19 (a) Fries K & Finek G, Ber, 34, 1921, 715.