

A Clean Synthesis of Novel 3-Alkoxy-2-(benzofuran-3-yl)benzofurans via a One-pot Pseudo Three-component Reaction using $\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$ as a Catalyst

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Z. Naturforsch. **2012**, *67b*, 165 – 170; received January 2, 2012

$\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$ efficiently catalyzes the one-pot pseudo three-component reaction of benzofuran-3(2*H*)-ones and various alcohols to afford the corresponding bibenzofuran derivatives with various alkoxy groups in 3-position.

Key words: Heteropolyacids, Bisbenzofuran, Synthesis, Three-component Reaction, Catalyst

Introduction

Benzofurans and their analogs are a family of heterocyclic compounds which have a broad range of bioactivity, *e. g.* as antitumor, antifungal [1], cardiovascular [2], antimicrobial [3], anti-HIV [4] and potent inhibitory agents against the Na, K-ATPase enzyme [5].

Moreover, several bibenzofuran derivatives show excellent antitrypanosomal, antiplasmodial and good protein tyrosine phosphatase 1B (PTP-1B) inhibitory activity [6, 7].

In other fields of chemistry, substituted benzofurans have abundant applications *e. g.* as fluorescent sensors [8] and brightening agents [9].

Although several methodologies are available for the synthesis of simple benzofurans [10], only a few reports have been given for the synthesis of 2-(benzofuran-3-yl)benzofuran derivatives. The synthesis of bibenzofurans was first described by K. Fries [11]. He obtained bibenzofurans through the reaction of sodium with benzofuran-3(2*H*)-one. Some alternative catalysts used for this purpose are sodium ethoxide [12a, 12b], sulfuric acid [12b, 12c] or sodium hydroxide [12d]. Royer reported the synthesis of diethylaminoethyl ethers of bis[benzyl-hydroxy]bibenzofurans, either from 2-hydroxy-5-methoxybenzyl alcohol, or from benzofurancarboxylic acids [13]. Unexpectedly, in the preparation of dimethoxy benzofurans, 3,6-dimethoxy-2-(6-methoxybenzofuran-3-yl)benzofuran was separated as a by-product [14]. All

these methods, however, suffer from some drawbacks, such as application of hazardous and corrosive catalysts, time consuming procedure and poor yield of the products.

Heteropolyacids (HPAs) have attracted high interest in the field of catalysis. These green catalysts have several benefits such as low toxicity, flexibility in modifying the acid strength, experimental simplicity, easy work-up procedures, and reduction of cost and waste due to recycling of the catalysts [15]. The acid strength of Keggin HPAs decreases in the following order: $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (PW) > $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ (SiW) > $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ (PMo) > $\text{H}_4\text{SiMo}_{12}\text{O}_{40}$ (SiMo) [16], and HPAs generally exhibit higher catalytic activities than conventional catalysts [17]. Among heteropolyacids, polytungstic acids are the most widely used catalysts because of their stronger acidity, low reducibility, lower oxidation potential compared to molybdenum acids, and higher thermal stability [18].

The significance of the bibenzofuran system and its diverse pharmacological properties [6, 7], has encouraged us to develop a new methodology for the efficient synthesis of this framework. Accordingly, as a part of our continuing studies concerning the synthesis of new heterocyclic compounds [19], herein we report a versatile method for the synthesis of novel bibenzofuran derivatives with various alkoxy groups in 3-position via a one-pot pseudo three-component reaction of benzofuran-3(2*H*)-ones **1** and alcohols **2** in the presence of catalytic amounts of PW (Scheme 1).

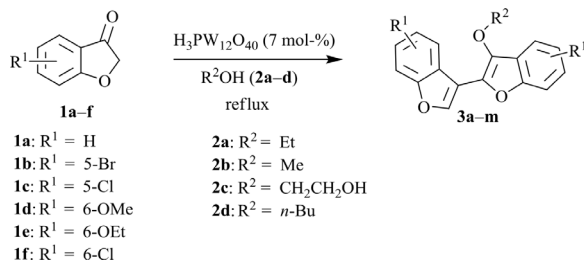
Results and Discussion

Benzofuran-3(2*H*)-one derivatives were synthesized according to the route reported in our previous work [20]. As a model reaction for the catalyst screening, 6-methoxybenzofuran-3(2*H*)-one (**1d**) was treated with *p*-TsOH in EtOH (**2a**) (Scheme 2). Two products **3i** and **4i** were formed under reflux condition.

Since Keggin-type HPAs (*e. g.* PW, SiW and PMo) were previously reported as highly effective solid acid catalysts [21], we examined the performance of such HPAs in our model reaction (Table 1, entries 7–9). As expected [21], tungsten HPAs (PW and SiW) were more effective than other HPAs, and PW was found particularly useful for the synthesis of compound **3i** (Table 1, entry 7).

In the next experiments the required quantity of catalyst, optimum time and reusability of the catalyst for the formation of compound **3i** were studied. The results showed that PW (7 mol-%) is the most efficient catalyst for the synthesis of compound **3i** (3 h in refluxing ethanol). The results also showed that an increase in the acidity of the catalyst increased the dimer to monomer ratio, and replacement of PW with PMo resulted in the formation of only monomer **4i**.

According to the obtained results, different benzofuran-3(2*H*)-ones (**1a–f**) were treated with alcohols **2a–d** in the presence of 7 mol-% PW under reflux conditions (Table 2). As shown in Table 2, both electron-donating and electron-withdrawing substituents on the precursors afforded the correspond-



Scheme 1. Synthesis of 3-alkoxy-2-(benzofuran-3-yl)benzofuran derivatives **3a–m**.

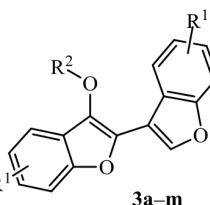
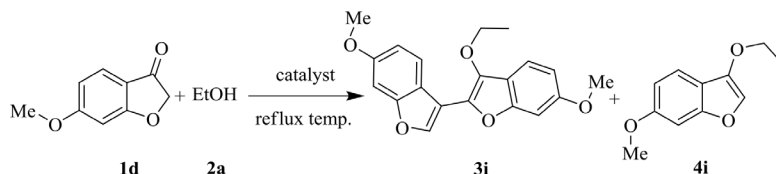


Table 1. Comparison between PW and other conventional acid catalysts for the synthesis of **3i**.

| Entry | Catalyst | Time (h) | Yield of 3i (%) ^a |
|-------|---|----------|-------------------------------------|
| 1 | – | 10 | 0 |
| 2 | H ₂ SO ₄ (1 mmol) | 5 | 40 |
| 3 | SiO ₂ (1 g) | 10 | 0 |
| 4 | <i>p</i> -TsOH (1 mmol) | 5 | 40 |
| 5 | HClO ₄ -SiO ₂ (10 mol-%) ^b | 7 | 20 |
| 6 | SSA (10 mol-%) ^c | 5 | 20 |
| 7 | PW (7 mol-%) | 3 | 75 |
| 8 | PMo (7 mol-%) | 4 | 0 |
| 9 | SiW (7 mol-%) | 8 | 65 |

^a Isolated yield; ^b HClO₄-SiO₂ was prepared as described previously [22]; ^c silica sulfuric acid (SSA) was prepared as described previously [23].

Table 2. Synthesis of 3-alkoxy-2-(benzofuran-3-yl)benzofurans **3a**.

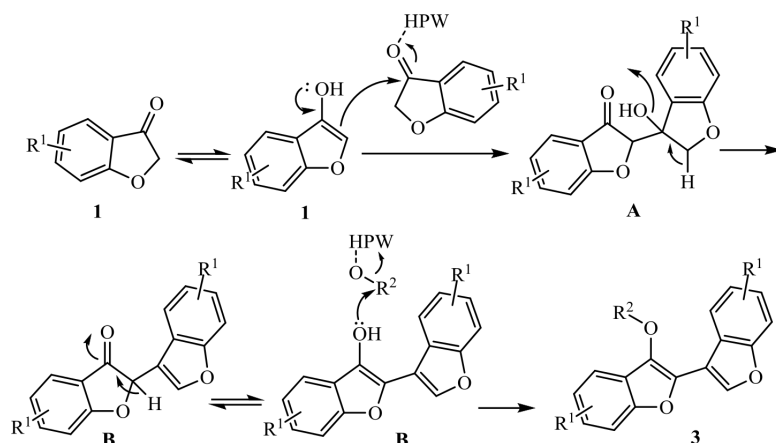
| No. | R ¹ | R ² | Time (h) | Yield ^b (%) |
|-----------|----------------|------------------------------------|----------|------------------------|
| 3a | H | Et | 5 | 70 |
| 3b | 5-Br | Et | 3 | 72 |
| 3c | 5-Br | CH ₂ CH ₂ OH | 3 | 70 |
| 3d | 5-Cl | Me | 4 | 71 |
| 3e | 5-Cl | Et | 4 | 69 |
| 3f | 6-OMe | <i>n</i> -Bu | 4 | 68 |
| 3g | 6-OMe | Me | 4 | 72 |
| 3h | 6-OMe | CH ₂ CH ₂ OH | 4 | 70 |
| 3i | 6-OMe | Et | 4 | 72 |
| 3j | 6-OEt | CH ₂ CH ₂ OH | 4 | 65 |
| 3k | 6-OEt | Et | 4 | 70 |
| 3l | 6-OEt | <i>n</i> -Bu | 4 | 69 |
| 3m | 6-Cl | Et | 5 | 52 |

^a Reaction conditions: benzofuran-3(2*H*)-one, 1 mmol; alcohol, 5 mL; PW, 7 mol-%; reflux; ^b isolated yield.

ing products in good to excellent yields. Spectroscopic data confirmed the structure of the synthesized compounds.

A possible mechanism for the formation of 3-alkoxy-2-(benzofuran-3-yl)benzofurans **3** is illustrated in Scheme 3. It is conceivable that initially the aldol condensation between two molecules of benzofuran-3(2*H*)-ones **1** form intermediate **A** which then pro-

Scheme 2. Model reaction for catalyst screening.



Scheme 3. A possible mechanism for the formation of compound **3**.

vides intermediate **B** via water elimination. In the next step, intermolecular nucleophilic substitution of the hydroxyl group leads to the formation of the target product.

Conclusion

In conclusion, we have developed a general and green protocol for the synthesis of 3-alkoxy-2-(benzofuran-3-yl)benzofurans. This process avoids the use of hazardous organic solvents and catalysts, with the alcohol itself playing the dual role of a solvent and reagent. Furthermore, the procedure offers several advantages including a simple experimental protocol, good to excellent yields and low costs, which makes it a useful and charming strategy in view of economic and environmental advantages.

Experimental Section

All chemicals and reagents were obtained from Merck. The desired benzofuran-3(2H)-ones [20], $\text{HClO}_4\text{-SiO}_2$ [22] and silica sulfuric acid (SSA) [23] were prepared according to the literature. All melting points were determined with a Kofler hot stage apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 500.1 and 125.8 MHz, respectively, on a Bruker DRX-500 AVANCE instrument with CDCl_3 as solvent and TMS as internal standard. Chemical shifts δ are given in ppm. The IR spectra were taken on KBr disks using a Nicolet FT-IR Magna 550 spectrometer. Mass spectra were recorded on a Finnigan MAT TSQ-70 spectrometer operating at an ionization potential of 70 eV. The results of elemental analyses (C, H) were within $\pm 0.4\%$ of the theoretical values for C and H. Column chromatography was performed on Merck silica gel (70–230 mesh).

General experimental procedure for the synthesis of 3-alkoxy-2-(benzofuran-3-yl)benzofurans (**3**)

A mixture of benzofuran-3(2H)-one derivative **1** (1 mmol), alcohol **2** (5 mL) and an appropriate amount of the catalyst was refluxed for the length of time as indicated in Table 2. The progress of the reaction was monitored by TLC. After completion of the reaction, evaporation of the excess of alcohol and dilution of the residue with dichloromethane (10 mL), the catalyst was filtered off and washed with dichloromethane (3×10 mL). Then the solvent was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane-ethyl acetate = 9 : 1) to give the pure product.

2-(Benzofuran-3-yl)-3-ethoxybenzofuran (**3a**)

Yellow oil. Yield 70%. – IR (KBr): $\nu = 1101$ (C=O) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 1.46$ (t, 3H, $J = 7.3$ Hz, OCH_2CH_3), 4.36 (q, 2H, $J = 7.3$ Hz, OCH_2), 7.26 (t, 1H, 5-H, $J = 7.2$ Hz), 7.30 (t, 1H, 5'-H, $J = 7.2$ Hz), 7.38 (m, 2H, 6-H, 6'-H), 7.51 (d, 1H, 7'-H, $J = 7.2$ Hz), 7.55 (d, 1H, 7-H, $J = 7.2$ Hz), 7.64 (d, 1H, 4'-H, $J = 7.2$ Hz), 8.23 (s, 1H, 2'-H), 8.31 (d, 1H, 4-H, $J = 7.2$ Hz). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 15.7$ (OCH_2CH_3), 68.8 (OCH_2), 111.4, 111.8, 112.1, 118.6, 122.5, 122.6, 123.1, 123.6, 124.8, 124.9, 137.6, 137.9, 142.3, 152.9, 155.0. – $\text{C}_{18}\text{H}_{14}\text{O}_3$ (278.3): calcd. C 77.68, H 5.07; found C 77.73, H 5.20.

5-Bromo-2-(5-bromobenzofuran-3-yl)-3-ethoxybenzofuran (**3b**)

Colorless crystals. Yield 72%. M.p.: 113–115 °C. – IR (KBr): $\nu = 1102$ (C=O) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 1.47$ (t, 3H, $J = 6.8$ Hz, OCH_2CH_3), 4.32 (q, 2H, $J = 6.8$ Hz, CH_2), 7.40–7.41 (m, 2H, 6'-H, 7'-H),

7.42 (d, 1H, 7-H, $J = 8.5$ Hz), 7.48 (dd, 1H, 6-H, $J = 8.5$, 2.0 Hz), 7.76 (m, 1H, 4'-H), 8.22 (s, 1H, 2'-H), 8.42 (d, 1H, $J = 2.0$ Hz, 4-H). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 15.7$ (OCH_2CH_3), 69.1 (OCH_2), 111.6, 113.0, 113.4, 115.9, 116.4, 121.3, 125.2, 125.3, 126.5, 127.4, 128.1, 137.2, 138.4, 143.7, 151.7, 153.9. – MS (EI, 70 eV): m/z (%) = 438 ($\text{M}^+ + 4$, 28), 436 ($\text{M}^+ + 2$, 56), 434 (M^+ , 27), 407 (100), 328 (21), 300 (21), 163 (27). – $\text{C}_{18}\text{H}_{12}\text{Br}_2\text{O}_3$ (436.09): calcd. C 49.57, H 2.77; found C 49.49, H 2.85.

5-Bromo-2-(5-bromobenzofuran-3-yl)-3-(2-hydroxyethyl)benzofuran (3c)

Colorless crystals. Yield 70%. M.p.: 134–136 °C. – IR (KBr): $\nu = 1044$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 4.01$ (t, 2H, $J = 7.2$ Hz, CH_2OH), 4.33 (t, 2H, $J = 7.2$ Hz, $\text{OCH}_2\text{CH}_2\text{OH}$), 7.41–7.42 (m, 2H, 6'-H, 7'-H), 7.43 (d, 1H, 7-H, $J = 8.8$ Hz), 7.49 (dd, 1H, 6-H, $J = 8.8$, 2.0 Hz), 7.78 (m, 1H, 4'-H), 8.30 (s, 1H, 2'-H), 8.39 (d, 1H, 4-H, $J = 2.0$ Hz). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 61.8$ (CH_2OH), 74.5 (CH_2O), 111.2, 113.0, 113.4, 116.1, 116.5, 121.1, 124.8, 124.9, 126.4, 127.5, 128.1, 136.8, 138.7, 144.0, 151.6, 153.9. – $\text{C}_{18}\text{H}_{12}\text{Br}_2\text{O}_4$ (452.09): calcd. C 47.82, H 2.68; found C 48.07, H 2.75.

5-Chloro-2-(5-chlorobenzofuran-3-yl)-3-methoxybenzofuran (3d)

Colorless crystals. Yield 71%. M.p.: 124–126 °C. – IR (KBr): $\nu = 1104$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 4.11$ (s, 3H, OCH_3), 7.28 (dd, 1H, 6-H, $J = 8.4$, 2.0 Hz), 7.35 (dd, 1H, 6'-H, $J = 8.4$, 2.0 Hz), 7.44 (d, 1H, 7-H, $J = 8.4$ Hz), 7.46 (d, 1H, 7'-H, $J = 8.4$ Hz), 7.65 (d, 1H, 4'-H, $J = 2.0$ Hz), 8.21 (m, 2H, 2'-H, 4-H). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 69.8$ (OCH_3), 111.3, 112.8, 113.1, 115.9, 116.4, 120.8, 124.6, 125.2, 126.2, 127.9, 128.1, 136.9, 138.4, 143.9, 151.3, 153.8. – $\text{C}_{17}\text{H}_{10}\text{Cl}_2\text{O}_3$ (333.17): calcd. C 61.29, H 3.03; found C 61.38, H 2.91.

5-Chloro-2-(5-chlorobenzofuran-3-yl)-3-ethoxybenzofuran (3e)

Colorless crystals. Yield 69%. M.p.: 108–110 °C. – IR (KBr): $\nu = 1106$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 1.47$ (t, 3H, $J = 7.2$ Hz, OCH_2CH_3), 4.33 (q, 2H, $J = 7.2$ Hz, CH_2), 7.24–7.27 (dd, 1H, 6'-H, $J = 8.0$, 2.0 Hz), 7.32–7.35 (dd, 1H, 6-H, $J = 8.0$, 2.0 Hz), 7.44 (d, 1H, 7'-H, $J = 8.0$ Hz), 7.46 (d, 1H, 7-H, $J = 8.0$ Hz), 7.60 (d, 1H, 4'-H, $J = 2.0$ Hz), 8.22 (s, 1H, 2'-H), 8.25 (d, 1H, 4-H, $J = 2.0$ Hz). – $\text{C}_{18}\text{H}_{12}\text{Cl}_2\text{O}_3$ (347.19): calcd. C 62.27, H 3.48; found C 62.38, H 3.35.

3-Butoxy-5-chloro-2-(5-chlorobenzofuran-3-yl)benzofuran (3f)

Yellow oil. Yield 68%. – IR (KBr): $\nu = 1018$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 0.97$ (t,

3H, $J = 7.2$ Hz, CH_3 , butoxy), 1.52 (m, 2H, CH_2 , butoxy), 1.82 (m, 2H, OCH_2CH_2 , butoxy), 3.88 (s, 3H, OCH_3), 4.26 (t, 2H, $J = 6.8$ Hz, OCH_2), 6.88 (dd, 1H, 5'-H, $J = 8.4$, 2.0 Hz), 6.97 (dd, 1H, 5-H, $J = 8.4$, 2.0 Hz), 7.04 (m, 2H, 7-H, 7'-H), 7.50 (d, 1H, 4'-H, $J = 8.4$ Hz), 8.04 (s, 1H, 2'-H), 8.12 (d, 1H, 4-H, $J = 8.4$ Hz). – $\text{C}_{22}\text{H}_{22}\text{O}_5$ (366.41): calcd. C 62.27, H 3.48; found C 62.38, H 3.35.

3,6-Dimethoxy-2-(6-methoxybenzofuran-3-yl)benzofuran (3g)

Colorless crystals. Yield 72%. M.p.: 106–108 °C. – IR (KBr): $\nu = 1027$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 3.88$ (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 6.89 (dd, 1H, 5'-H, $J = 8.4$, 2.0 Hz), 6.98 (dd, 1H, 5-H, $J = 8.4$, 2.0 Hz), 7.04 (m, 2H, 7-H, 7'-H), 7.53 (d, 1H, 4'-H, $J = 8.4$ Hz), 8.03 (s, 1H, 2'-H), 8.09 (d, 1H, 4-H, $J = 8.4$ Hz). – $\text{C}_{19}\text{H}_{16}\text{O}_5$ (324.33): calcd. C 70.36, H 4.97; found C 70.21, H 5.04.

6-Methoxy-2-(6-methoxybenzofuran-3-yl)-3-(2-hydroxyethyl)benzofuran (3h)

Yellow oil. Yield 70%. – IR (KBr): $\nu = 1172$ ($\text{C}=\text{O}$) and 1092 cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 3.88$ (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.96 (t, 2H, $J = 5.0$ Hz, CH_2OH), 4.34 (t, 2H, $J = 5.0$ Hz, $\text{OCH}_2\text{CH}_2\text{OH}$), 6.88 (dd, 1H, 5'-H, $J = 8.2$, 2.0 Hz), 6.98 (dd, 1H, 5-H, $J = 8.2$, 2.0 Hz), 7.05 (m, 2H, 7-H, 7'-H), 7.50 (d, 1H, 4'-H, $J = 8.2$ Hz), 8.09 (m, 2H, 2'-H, 4-H). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 55.6$ (OCH_3), 55.7 (OCH_3), 61.9 (CH_2OH), 74.2 (CH_2O), 111.9, 112.3, 116.7, 118.1, 118.6, 122.3, 128.7, 130.8, 132.4, 140.9, 153.9, 156.1, 158.2, 158.4. – $\text{C}_{20}\text{H}_{18}\text{O}_6$ (354.35): calcd. C 67.79, H 5.12; found C 67.63, H 5.01.

3-Ethoxy-6-methoxy-2-(6-methoxybenzofuran-3-yl)benzofuran (3i)

Colorless crystals. Yield 72%. M.p.: 110–112 °C. – IR (KBr): $\nu = 1036$ ($\text{C}=\text{O}$) cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 1.44$ (t, 3H, $J = 7.0$ Hz, OCH_2CH_3), 3.88 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.32 (q, 2H, $J = 7.0$ Hz, OCH_2), 6.88 (dd, 1H, 5'-H, $J = 8.2$, 2.0 Hz), 6.97 (dd, 1H, 5-H, $J = 8.2$, 2.0 Hz), 7.04 (m, 2H, 7-H, 7'-H), 7.49 (d, 1H, 4'-H, $J = 8.2$ Hz), 8.06 (s, 1H, 2'-H), 8.13 (d, 1H, 4-H, $J = 8.2$ Hz). – ^{13}C NMR (125.7 MHz, CDCl_3): $\delta = 15.8$ (OCH_2CH_3), 55.6 (OCH_3), 55.7 (OCH_3), 61.9 (OCH_2), 96.3, 96.6, 111.5, 112.3, 116.4, 118.2, 118.7, 122.3, 128.5, 130.8, 132.6, 140.4, 154.1, 157.1, 157.9, 158.6. – $\text{C}_{20}\text{H}_{18}\text{O}_5$ (338.35): calcd. C 70.99, H 5.36; found C 70.73, H 5.42.

6-Ethoxy-2-(6-ethoxybenzofuran-3-yl)-3-(2-hydroxyethyl)benzofuran (3j)

Yellow Oil. Yield 65%. – IR (KBr): $\nu = 1112$ ($\text{C}=\text{O}$) and 1087 cm^{-1} . – ^1H NMR (500 MHz, CDCl_3): $\delta = 1.14$ –1.48

(m, 6H, 2OCH₂CH₃), 3.95 (t, 2H, *J* = 4.5 Hz, CH₂OH), 4.05–4.12 (m, 4H, 2OCH₂CH₃), 4.31 (t, 2H, *J* = 4.5 Hz, OCH₂CH₂OH), 6.89 (d, 1H, 5'-H, *J* = 8.2 Hz), 6.98 (d, 1H, 5-H, *J* = 8.2 Hz), 7.04 (m, 2H, 7-H, 7'-H), 7.49 (d, 1H, 4'-H, *J* = 8.2 Hz), 8.08 (m, 2H, 2'-H, 4-H). – C₂₂H₂₂O₆ (382.41): calcd. C 69.10, H 5.80; found C 69.23, H 5.42.

3,6-Diethoxy-2-(6-ethoxybenzofuran-3-yl)benzofuran (**3k**)

Colorless crystals. Yield 70%. M.p.: 74–76 °C. – IR (KBr): ν = 1017 (C=O) cm⁻¹. – ¹H NMR (500 MHz, CDCl₃): δ = 1.41–1.49 (m, 9H, 3OCH₂CH₃), 4.05–4.12 (m, 4H, 2CH₂), 4.31 (q, 2H, *J* = 7.2 Hz, OCH₂), 6.86 (dd, 1H, 5'-H, *J* = 8.0, 2.0 Hz), 6.96 (dd, 1H, 5-H, *J* = 8.0, 2.0 Hz), 7.02 (m, 2H, 7-H, 7'-H), 7.47 (d, 1H, 4'-H, *J* = 8.2 Hz), 8.04 (s, 1H, 2'-H), 8.11 (d, 1H, 4-H, *J* = 8.2 Hz). – ¹³C NMR (125.7 MHz, CDCl₃): δ = 14.8 (OCH₂CH₃), 14.8 (OCH₂CH₃), 15.7 (OCH₂CH₃), 63.9 (OCH₂CH₃), 63.9 (OCH₂CH₃), 68.7 (OCH₂CH₃), 96.3, 97.0, 112.2, 112.6, 117.0, 118.1, 118.8, 122.6, 136.8, 137.6, 140.5, 140.5, 153.9, 156.1, 157.2, 157.6. – C₂₂H₂₂O₅ (366.41): calcd. C 72.12, H 6.05; found C 72.03, H 5.92.

3-Butoxy-6-ethoxy-2-(6-ethoxybenzofuran-3-yl)benzofuran (**3l**)

Yellow oil. Yield 69%. – IR (KBr): ν = 1020 (C=O) cm⁻¹. – ¹H NMR (500 MHz, CDCl₃): δ = 0.97

(t, 3H, *J* = 7.2 Hz, CH₃, butoxy), 1.45–1.60 (m, 8H, 2OCH₂CH₃ and CH₂CH₃, butoxy), 1.81 (m, 2H, OCH₂CH₂, butoxy), 4.07–4.13 (m, 4H, 2OCH₂CH₃), 4.25 (t, 2H, *J* = 6.8 Hz, OCH₂, butoxy), 6.83 (dd, 1H, 5'-H, *J* = 8.0, 2.0 Hz), 6.96 (dd, 1H, 5-H, *J* = 8.0, 2.0 Hz), 7.02 (m, 2H, 7-H, 7'-H), 7.48 (d, 1H, 4'-H, *J* = 8.2 Hz), 8.03 (s, 1H, 2'-H), 8.10 (d, 1H, 4-H, *J* = 8.2 Hz). – C₂₄H₂₆O₅ (394.46): calcd. C 73.08, H 6.64; found C 73.13, H 6.52.

6-Chloro-2-(6-chlorobenzofuran-3-yl)-3-ethoxybenzofuran (**3m**)

Yellow oil. Yield 52%. – IR (KBr): ν = 1097 (C=O) cm⁻¹. – ¹H NMR (500 MHz, CDCl₃): δ = 1.42 (t, 3H, *J* = 7.3 Hz, OCH₂CH₃), 4.31 (q, 2H, *J* = 7.3 Hz, CH₂), 6.86 (dd, 1H, 5'-H, *J* = 8.2, 2.0 Hz), 7.00 (d, 1H, 7'-H, *J* = 2.0 Hz), 7.19 (dd, 1H, 5-H, *J* = 8.2, 2.0 Hz), 7.21 (s, 1H, 7-H), 7.39 (d, 1H, 4'-H, *J* = 2.0 Hz), 7.51 (d, 1H, 2'-H, *J* = 8.2 Hz), 7.77 (d, 1H, 4-H, *J* = 8.2 Hz). – C₁₈H₁₂Cl₂O₃ (347.19): calcd. C 62.27, H 3.48; found C 62.09, H 3.51.

Acknowledgement

This work was financially supported by grants from the Research Council of Tehran University of Medical Sciences and INSF (Iran National Science Foundation).

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