New method for the acylation of benzofurans toward the synthesis of 6H-indeno[2,1-b]benzofuran-6-ones and 2,2'-bibenzofurans

Xuebing Zheng, Chuanjun Song, and Yonggang Meng*

College of Chemistry, and Green Catalysis Center, Zhengzhou University, Zhengzhou 450001, China
E-mail: 202011151030123@gs.zzu.edu.cn

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Abstract

We have developed a TFAA-mediated acylation of benzofurans using carboxylic acids as acylating agents. The reaction does not require the aid of Lewis acid catalysts, and lead to the regioselective formation of 2-acyl benzofurans. Among these, 2-bromophenylacetyl benzofurans and 2-[(2-bromophenyl)acetyl benzofurans could be converted into 6H-indeno[2, 1-b]benzofuran-6-ones and 2, 2'-bibenzofurans, respectively.

Keywords: TFAA, 2-acyl benzofurans, 6H-indeno[2, 1-b]benzofuran-6-ones, 2, 2'-bibenzofurans
Introduction

2-Substituted benzofurans have shown unique anti-fungal, anti-viral, anti-diabetic, anti-tumor, anti-osteoporosis and anti-Alzheimer's disease activities. Besides, many medical products such as amiodarone hydrochloride are also derived from 2-substituted benzofurans. A number of strategies for the synthesis of 2-substituted benzofurans have been developed. The base-catalyzed intermolecular or intramolecular condensation reactions to construct a fused furan ring to form 2-substituted benzofuran derivatives is the most common synthetic method (Scheme 1a).

2-Acylbenzofurans can also be obtained by Lewis acid catalyzed acylation of benzofurans using acid anhydrides or acyl chlorides as acylating agents (Scheme 1b). The trifluoroacetic anhydride (TFAA)-mediated acylation using carboxylic acids as the acylating agent have been applied to arenes and heteroarenes including thiophenes, benzothiophenes, pyrroles, and carbazoles. However, to the best of our knowledge, this protocol has never been used with benzofurans, although a single literature precedent with furans as substrates has been reported. Herein, we report the TFAA-mediated acylation of benzofurans using carboxylic acids as the acylating agent. The reaction does not require the aid of Lewis acid catalysts, and leads to the regioselective formation of 2-acyl benzofurans (Scheme 1c).

![Scheme 1. Synthetic routes toward 2-substituted benzofuran derivatives.](image)

Results and Discussion

Our optimization of reaction conditions commenced with acetic acid as the acylating agent. The reaction was complete in different solvents such as N,N-dimethylformamide (DMF), dichloromethane (DCM) and 1,2-dichloroethane (DCE) under appropriate temperature conditions in the presence of 5 equivalent of TFAA. It was found that the optimum yield was 88% when the solvent was DCE and acylation reaction system of benzofuran with acetic acid reacted at 70 °C under TFAA-mediated conditions. Next, the substrate scope was examined and the results were shown in Table 1. Acylation with a variety of aliphatic carboxylic acids provided the corresponding 2-acylbenzofurans 3a-e in good to excellent isolated yields. While acylation with 2-(2-
bromophenyl)acetic acid gave 3f in 66% isolated yield, reaction of 2-(2-bromophenyl)proponic acid was less satisfactory and resulted in the formation of 3g in 36% yield only. Under the reaction conditions, acylation with aromatic acids proceeded as expected to provide 3h-j in good isolated yields. Finally, acylation of representative substituted benzofurans were examined, which resulted in the formation of 3k-m in moderate to excellent isolated yields.

Table 1. Substrate scope of acylation reaction

<table>
<thead>
<tr>
<th>R²</th>
<th>R²</th>
<th>TFAA</th>
<th>DCE, 70 °C</th>
<th>R²</th>
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<tr>
<td>O&lt;sub&gt;H&lt;/sub&gt;</td>
<td>O&lt;sub&gt;H&lt;/sub&gt;</td>
<td>O&lt;sub&gt;H&lt;/sub&gt;</td>
<td>O&lt;sub&gt;H&lt;/sub&gt;</td>
<td>O&lt;sub&gt;H&lt;/sub&gt;</td>
</tr>
<tr>
<td>3a, 68%</td>
<td>3b, 90%</td>
<td>3c, 60%</td>
<td>3d, 75%</td>
<td>3e, 67%</td>
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<tr>
<td>3f, 66%</td>
<td>3g, 36%</td>
<td>3h, 68%</td>
<td>3i, 76%</td>
<td>3j, 80%</td>
</tr>
<tr>
<td>3k, 53%</td>
<td>3l, 48%</td>
<td>3m, 86%</td>
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<td></td>
</tr>
</tbody>
</table>

Based on the results obtained above and literature reports, a plausible mechanism is depicted in Scheme 2. Mixed anhydride formation from acid 1 and TFAA provided A and trifluoroacetic acid (TFA). Because of the strong electron-withdrawing nature of the trifluoromethyl group, protonation of the alternative carbonyl group by TFA generated the acylating agent B, which reacted with benzofuran 2 to provide 3 via intermediate C. The fact that no trifluoroacylation product was observed could be attributed to the inability for TFAA to be protonated.

Scheme 2. Proposed mechanism.

Having established the method, we then turned our attention to the transformation of the products into other useful molecules. First, palladium-catalyzed C-H activation of 3j, 3l provided fluorenones 4 and 5 in
80% and 98% isolated yields, respectively (Scheme 3). Second, under the joint action of FeCl₃ and 2,2,6,6-tetramethyl-3,5-heptanediene (TMHD), 3f, 3g could be converted into 2, 2'-bibenzofurans 6 and 7, respectively, in moderate isolated yields (Scheme 4). The pharmacological activities of 2,2'-bibenzofurans have attracted much attention. Literature methods for the synthesis of 2, 2'-bibenzofurans include homogeneous coupling of benzofurans²⁶,²⁷ or 2-(2,2-dibromovinyl)phenols,²⁸ and condensation of 2-acetylbenzofurans with benzoquinones.²⁹ However, these either suffered from limited substrate scope or could only be applied to the synthesis of symmetrical 2, 2'-bibenzofurans. The method reported herein provided a new entry to access unsymmetrically substituted 2, 2'-bibenzofurans.


Scheme 4. Synthesis of 2,2'-bibenzofurans 6 and 7.

Conclusions

We have developed a TFₐA-mediated approach for the acylation of benzofurans using carboxylic acid as the acylating agent. A series of 2-acyl benzofuran derivatives have been synthesized. Among these, 3j, 3l and 3f, 3g could be further converted into 6H-indeno[2,1-b]benzofuran-6-ones 4, 5 and 2,2'-bibenzofurans 6, 7, respectively.

Experimental Section

General. Melting points were determined on a XT4A hot-stage apparatus and are uncorrected. IR spectra were obtained using a PerkinElmer FT/IR spectrometer. ¹H and ¹³C NMR spectra were obtained on a Agilent AV400 instrument. High-resolution mass spectra were recorded on a Micromass Q-TOF mass spectrometer.

General procedure for the preparation of 3a-m. TFₐA (5.0 mmol) was added to a solution of benzofurans 1a-m (1.0 mmol) and acids 2a-m (1.2 mmol) in DCE (25 mL). The resulting mixture was heated at 70 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), neutralized with saturated aqueous NaHCO₃ (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and then evaporated in vacuo. The residue was purified by column chromatograph on silica gel to afford 3a-m.
1-(Benzofuran-2-yl)ethan-1-one (3a). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), acetic acid (69 μL, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3a (141 mg, 88%) as a colorless solid: mp 61–62 °C; IR (neat, cm⁻¹): ν_max 3120, 1673, 1555, 1295, 928; ¹H NMR (400 MHz, CDCl₃): δ 7.71 (d, J 7.8 Hz, 1H), 7.58 (d, J 8.4 Hz, 1H), 7.51 (s, 1H), 7.48 (t, J 7.8 Hz, 1H), 7.32 (tt, J 7.6 Hz, 1H), 2.62 (t, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 188.7, 155.7, 152.6, 128.3, 127.1, 123.9, 123.3, 113.1, 112.5, 26.5 ppm; HRMS (ESI): m/z calcd for C₁₀H₉O₂ [M+H]+ 161.0597; found 161.0596.

1-(Benzofuran-2-yl)butan-1-one (3b). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), butyric acid (106 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3b (169 mg, 90%) as a colorless solid: mp 56–57 °C; IR (neat, cm⁻¹): ν_max 3253, 2965, 1682, 1561, 1158, 743; ¹H NMR (400 MHz, CDCl₃): δ 7.70 (d, J 7.9 Hz, 1H), 7.57 (d, J 8.4 Hz, 1H), 7.49 (s, 1H), 7.46 – 7.44 (m, 1H), 7.30 (t, J 7.4 Hz, 1H), 2.93 (t, J 7.4 Hz, 2H), 1.81 (m, 2H), 1.02 (t, J 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 191.7, 155.7, 152.8, 128.2, 127.2, 123.9, 123.4, 112.7, 112.6, 40.9, 17.9, 14.0 ppm; HRMS (ESI): m/z calcd for C₁₂H₁₃O₂ [M+H]+ 189.0910; found 189.0912.

1-(Benzofuran-2-yl)-2-methylpropan-1-one (3c). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), isobutyric acid (106 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3c (113 mg, 60%) as a light brown oil: IR (neat, cm⁻¹): ν_max 3423, 2972, 1680, 1553, 1003; ¹H NMR (400 MHz, CDCl₃): δ 7.69 (d, J 7.9 Hz, 1H), 7.56 (d, J 8.4 Hz, 1H), 7.50 (s, 1H), 7.45 (t, J 7.8 Hz, 1H), 7.29 (t, J 7.5 Hz, 1H), 3.50 – 3.45 (m, 1H), 1.26 (d, J 6.9 Hz, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 195.6, 155.6, 152.1, 128.1, 127.1, 123.9, 123.3, 112.9, 112.5, 36.7, 18.9 ppm; HRMS (ESI): m/z calcd for C₁₂H₁₃O₂ [M+H]+ 189.0910; found 189.0909.

1-(Benzofuran-2-yl)-2,2-dimethylpropan-1-one (3d). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), pivalic acid (122 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound 3d (151 mg, 75%) as a bright yellow oil: IR (neat, cm⁻¹): ν_max 3429, 2971, 1671, 1546, 1132; ¹H NMR (400 MHz, CDCl₃): δ 7.70 (d, J 7.9 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.54 (d, J 1.0 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.32 – 7.28 (m, 1H), 1.43 (s, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 196.9, 155.2, 152.8, 127.8, 126.9, 123.8, 123.2, 113.8, 112.4, 43.6, 26.9 ppm; HRMS (ESI): m/z calcd for C₁₅H₁₅O₂ [M+H]+ 203.1067; found 203.1065.

Benzo[b]fur-an-2-yl(cyclohexyl)methanone (3e). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), cyclohexanecarboxylic acid (153 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3e (152 mg, 67%) as a colorless solid: mp 61–62 °C; IR (neat, cm⁻¹): ν_max 3114, 2940, 2858, 1666, 987; ¹H NMR (400 MHz, CDCl₃): δ 7.69 (d, J 7.9 Hz, 1H), 7.58 (d, J 8.4 Hz, 1H), 7.52 – 7.50 (m, 1H), 7.49 – 7.43 (m, 1H), 7.32 – 7.28 (m, 1H), 3.24 – 3.17 (m, 1H), 2.00 – 1.91 (m, 2H), 1.89 – 1.83 (m, 2H), 1.77 – 1.72 (m, 1H), 1.61 – 1.51 (m, 2H), 1.46 – 1.35 (m, 2H), 1.34 – 1.25 (m, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 194.9, 155.7, 152.3; 128.1, 127.2, 123.9, 123.3, 112.9, 112.6, 46.8, 29.9, 25.9, 25.9 ppm; HRMS (ESI): m/z calcd for C₁₅H₁₅O₂ [M+H]+ 229.1223; found 229.1225.

1-(Benzofuran-2-yl)-2-(2-bromophenylethan-1-one (3f). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), 2-(2-bromophenyl)acetic acid (257 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified
by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3f (207 mg, 66%) as a colorless solid: mp 126–127 ºC; IR (neat, cm⁻¹): νmax 3424, 1678, 1159, 1138, 1020; ¹H NMR (400 MHz, CDC13): δ 8.11 (s, 1H), 7.89 (d, J 7.9 Hz, 1H), 7.77 (d, J 8.4 Hz, 1H), 7.65 (d, J 7.9 Hz, 1H), 7.58 – 7.37 (m, 1H), 7.46 (dd, J 7.6, 1.8 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.27 (td, J 7.8, 1.7 Hz, 1H), 4.57 (s, 2H) ppm; ¹³C NMR (100 MHz, CDC13): δ 187.3, 155.8, 152.3, 134.2, 133.0, 131.9, 129.1, 128.5, 127.7, 127.2, 125.2, 124.1, 123.5, 113.5, 112.6, 46.0 ppm; HRMS (ESI): m/z calcd for C₁₆H₁₂⁷⁹BrO₂ [M+H]^+ 315.0015; found 315.0017.

1-(Benzofuran-2-yl)-2-(2-bromophenyl)propan-1-one (3g). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), 2-(2-bromophenyl)propanoic acid (273 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3g (118 mg, 36%) as a light yellow solid: mp 105–106 ºC; IR (neat, cm⁻¹): νmax 2927, 1673, 1547, 1160, 755; ¹H NMR (400 MHz, CDC13): δ 7.65 (d, J 7.9 Hz, 1H), 7.61 (dd, J 8.0, 1.0 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.51 (s, 1H), 7.46 – 7.40 (m, 1H), 7.29 – 7.21 (m, 3H), 7.08 (ddd, J 7.9, 7.2, 1.9 Hz, 1H), 5.10 (q, J 6.9 Hz, 1H), 1.54 (d, J 6.9 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDC13): δ 190.6, 155.7, 151.8, 140.4, 133.3, 128.8, 128.6, 128.4, 128.2, 127.0, 124.2, 123.9, 123.4, 114.0, 112.6, 47.5, 17.6 ppm; HRMS (ESI): m/z calcd for C₁₇H₁₄⁷⁹BrO₂ [M+H]^+; 329.0172; found 329.0174.

Benzofuran-2-yl(phenyl)methanone (3h). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), benzoic acid (146 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3h (150 mg, 68%) as a yellow solid: mp 83–84 ºC; IR (neat, cm⁻¹): νmax 2958, 2925, 2853, 1689, 1291; ¹H NMR (400 MHz, CDC13): δ 8.06 – 8.03 (m, 2H), 7.73 (d, J 7.9 Hz, 1H), 7.64 (t, J 7.4 Hz, 2H), 7.57 – 7.48 (m, 4H), 7.34 (t, J 7.4 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDC13): δ 184.6, 156.1, 152.3, 137.3, 133.0, 129.6, 128.7, 128.5, 127.1, 124.1, 123.5, 116.7, 112.7 ppm; HRMS (ESI): m/z calcd for C₁₅H₁₁O₂ [M+H]^+ 223.0754; found 223.0757.

Benzofuran-2-yl(p-tolyl)methanone (3i). The title compound was prepared according to the general procedure by stirring a mixture of benzo furan (110 μL, 1.0 mmol), 4-methylbenzoic acid (283 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3i (179 mg, 76%) as a colorless solid: mp 74–75 ºC; IR (neat, cm⁻¹): νmax 1755, 1610, 1575, 1545; ¹H NMR (400 MHz, CDC13): δ 7.97 (d, J 8.1 Hz, 2H), 7.72 (d, J 7.8 Hz, 1H), 7.64 (d, J 8.4 Hz, 1H), 7.52 (s, 1H), 7.51 (t, J 7.8 Hz, 1H), 7.35 – 7.31 (m, 3H), 2.46 (s, 3H) ppm; ¹³C NMR (100MHz, CDC13): δ 184.2, 156.0, 152.5, 143.9, 134.7, 129.7, 129.4, 128.3, 127.2, 124.0, 123.4, 116.2, 112.6, 21.8 ppm; HRMS (ESI): m/z calcd for C₁₆H₁₃O₂ [M+H]^+ 237.0910; found 237.0912.

Benzofuran-2-yl(2-bromophenyl)methanone (3j). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 μL, 1.0 mmol), 2-bromobenzoic acid (240 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound 3j (240 mg, 80%) as a bright yellow oil: IR (neat, cm⁻¹): νmax 3425, 2937, 1665, 1548, 972; ¹H NMR (400 MHz, CDC13): δ 7.71 – 7.67 (m, 2H), 7.64 – 7.60 (m, 1H), 7.54 – 7.49 (m, 2H), 7.48 – 7.37 (m, 2H), 7.35 – 7.30 (m, 2H) ppm; ¹³C NMR (100 MHz, CDC13): δ 184.8, 156.6, 151.7, 139.5, 133.6, 131.9, 129.4, 129.1, 127.3, 127.1, 124.3; 123.7, 120.1, 118.1, 112.9 ppm; HRMS (ESI): m/z calcd for C₁₅H₁₀⁷⁹BrO₂ [M+H]^+ 300.9859; found 300.9856.

1-(5-Methylbenzofuran-2-yl)ethan-1-one (3k). The title compound was prepared according to the general procedure by stirring a mixture of 5-methylbenzofuran (132 mg, 1.0 mmol), glacial acetic acid (69 μL, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.2% EtOAc in petroleum ether) to afford compound 3k (92 mg, 53%) as
a colorless solid: mp 74–75 °C; IR (neat, cm\(^{-1}\)): \(\nu_{\text{max}}\) 3101, 2919, 1668, 1551, 818; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.47 – 7.43 (m, 2H), 7.41 (d, J 0.9 Hz, 1H), 7.28 (dd, J 8.6, 1.7 Hz, 1H), 2.58 (s, 3H), 2.44 (s, 3H) ppm; \(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta\) 188.8, 154.3, 152.9, 133.6, 130.0, 127.3, 122.8, 113.0, 112.1, 26.5, 21.4 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{11}\)H\(_{12}\)O\(_2\) [M+H\(^{+}\)]: 175.0754; found 175.0753.

**(2-Bromophenyl)(5-methylbenzofuran-2-yl)methanone (3I).** The title compound was prepared according to the general procedure by stirring a mixture of 5-methylbenzofuran (132 mg, 1.0 mmol), 2-bromobenzoic acid (240 mg, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound 3I (150 mg, 48%) as a bright yellow oil: IR (neat, cm\(^{-1}\)): \(\nu_{\text{max}}\) 2915, 1651, 1429, 1205, 977; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.69 – 7.67 (m, 1H), 7.51 – 7.48 (m, 2H), 7.46 – 7.36 (m, 3H), 7.33 – 7.30 (m, 1H), 7.23 (d, J 0.9 Hz, 1H), 2.45 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 184.7, 155.1, 151.9, 139.6, 133.9, 133.6, 131.9, 130.8, 129.4, 127.3, 127.2, 123.0, 120.1, 117.9, 112.4, 21.4 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{12}\)BrO\(_2\) [M+H\(^{+}\)]: 315.0017; found 315.0017.

**(1-(7-Methoxybenzofuran-2-yl)ethan-1-one (3m).** The title compound was prepared according to the general procedure by stirring a mixture of 7-methoxybenzofuran (148 mg, 1.0 mmol), glacial acetic acid (69 μL, 1.2 mmol) and TFAA (705 μL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound 3m (163 mg, 86%) as a colorless solid: mp 92–93 °C; IR (neat, cm\(^{-1}\)): \(\nu_{\text{max}}\) 3136, 2965, 1655, 1402, 1273; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.79 (dd, J 8.4, 1.7 Hz, 1H), 7.73 (d, J 2.1 Hz, 1H), 7.56 (dd, J 2.1, 0.8 Hz, 1H), 6.79 (dd, J 8.4, 1.5 Hz, 1H), 4.07 (s, 3H), 2.63 (s, 3H) ppm; \(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta\) 197.3, 149.4, 147.1, 144.4, 128.8, 127.9, 123.7, 108.7, 105.3, 56.4, 27.3 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{12}\)O\(_2\) [M+H\(^{+}\)]: 221.0596; found 221.0597.

The preparation of compounds 4-7.

**6H-Indeno[2, 1-b]benzofuran-6-one (4).** PPh\(_3\) (26.0 mg, 0.1 mmol), K\(_2\)CO\(_3\) (276.0 mg, 0.1 mmol) and Pd(OAc)\(_2\) (22.5 mg, 0.1 mmol) was added to a solution of 3j (300.0 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 110 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated in vacuo. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford 4 (176 mg, 80%) as a red solid: mp 97–98 °C; IR (neat, cm\(^{-1}\)): \(\nu_{\text{max}}\) 1705, 1610, 1399, 1141, 1021; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.77 (d, J 7.8 Hz, 1H), 7.57 (d, J 8.4 Hz, 1H), 7.48 (t, J 7.8 Hz, 1H), 7.43 – 7.32 (m, 3H), 7.24 (d, J 7.1Hz, 1H), 7.18 (t, J 7.5 Hz, 1H) ppm; \(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta\) 180.8, 161.7, 154.8, 148.2, 141.5, 136.2, 135.1, 134.0, 128.8, 128.8, 125.0, 124.3, 122.1, 120.4, 114.0 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{15}\)H\(_{12}\)O\(_2\) [M+H\(^{+}\)]: 221.0597; found 221.0596.

**2-Methyl-6H-indeno[2, 1-b]benzofuran-6-one (5).** PPh\(_3\) (26.0 mg, 0.1 mmol), K\(_2\)CO\(_3\) (276.0 mg, 0.1 mmol) and Pd(OAc)\(_2\) (22.5 mg, 0.1 mmol) was added to a solution of 3j (314 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 110 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated in vacuo. The crude product was purified by column chromatography on silica gel (10% EtOAc in petroleum ether) to afford 5 (229 mg, 98%) as an orange solid: mp 129–130 °C; IR (neat, cm\(^{-1}\)): \(\nu_{\text{max}}\) 1705, 1610, 1550, 1260, 1096; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.45 (s, 1H), 7.39 – 7.34 (m, 2H), 7.32 – 7.27 (m, 1H), 7.25 – 7.21 (m, 1H), 7.16 – 7.10 (m, 2H), 2.46 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 180.7, 160.2, 154.7, 141.2, 136., 135.1, 134.6, 133.9, 130.3, 128.5, 124.0, 122.0, 121.6, 120.2, 113.3, 21.5 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{12}\)O\(_2\) [M+H\(^{+}\)]: 235.0754; found 235.0755.
2,2'-Bibenzofuran (6).\(^3\)\(^4\) Fe\(_3\) (16.2 mg, 0.1 mmol), TMHD (36.9 mg, 0.2 mmol) was added to a solution of 3f (314 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 120 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated in vacuo. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford 6 (89 mg, 38%) as a colorless solid: mp 196–197 °C; IR (neat, cm\(^{-1}\)): \(\nu_{max}\) 1468, 1299, 1217, 1211; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.77 – 7.63 (m, 2H), 7.58 – 7.54 (m, 2H), 7.36 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.17 (s, 2H) ppm; \(^{13}\)C NMR (100 MHz, DMSO): \(\delta\) 154.5, 146.8, 128.1, 125.6, 123.8, 121.8, 111.3, 104.3 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{10}\)O\(_2\)Na [M+Na]\(^+\): 257.0573; found 257.0569.

3-Methyl-2,2'-bibenzofuran (7). Fe\(_3\) (16.2 mg, 0.1 mmol), TMHD (36.9 mg, 0.2 mmol) was added to a solution of 3g (328 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 120 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated in vacuo. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford 7 (94 mg, 38%) as a colorless solid: mp 123–124 °C; IR (neat, cm\(^{-1}\)): \(\nu_{max}\) 1442, 1311, 1269, 1221, 1165; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.66 – 7.65 (m, 1H), 7.60 – 7.56 (m, 2H), 7.53 (d, \(J\) 8.0 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 2H), 7.11 (s, 1H), 2.62 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 155.0, 154.5, 148.8, 143.1, 130.5, 128.5, 125.3, 124.8, 123.4, 122.9, 121.3, 119.7, 114.4, 111.4, 111.3, 104.0, 8.9 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{17}\)H\(_{13}\)O\(_2\) [M+H]\(^+\): 249.0910; found 249.0909.

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Supplementary Material

Copies of the \(^1\)H and \(^{13}\)C-NMR spectra are provided in the supplementary material file.

References

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