

Direct synthesis of benzofuro[3,2-*b*]benzofurans via a palladium-catalyzed dearomative cyclization

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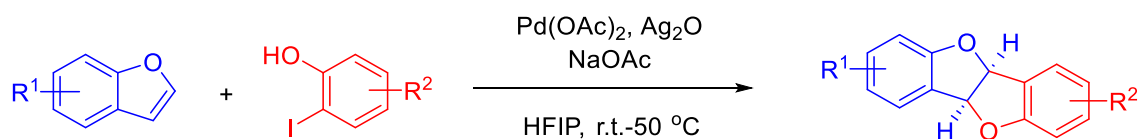
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Abstract

A palladium-catalyzed dearomative [3+2] cycloaddition of benzofurans with 2-iodophenols to produce benzofuro[3,2-*b*]benzofurans is described. This approach employs Pd(OAc)₂ as the catalyst and Ag₂O as the oxidant in HFIP as the solvent with NaOAc as the base. This straightforward and highly atom-economical method affords moderate to excellent yields and tolerates a range of functional groups. A plausible mechanism involving a Pd(0/II) catalytic cycle is proposed.



- Mild, one-step reaction conditions
- Ready available substrate
- moderate to excellent yields
- Dearomative cyclization

Keywords: Benzofuro[3,2-*b*]benzofurans, palladium, dearomative, cyclization, oxygen heterocycles

Introduction

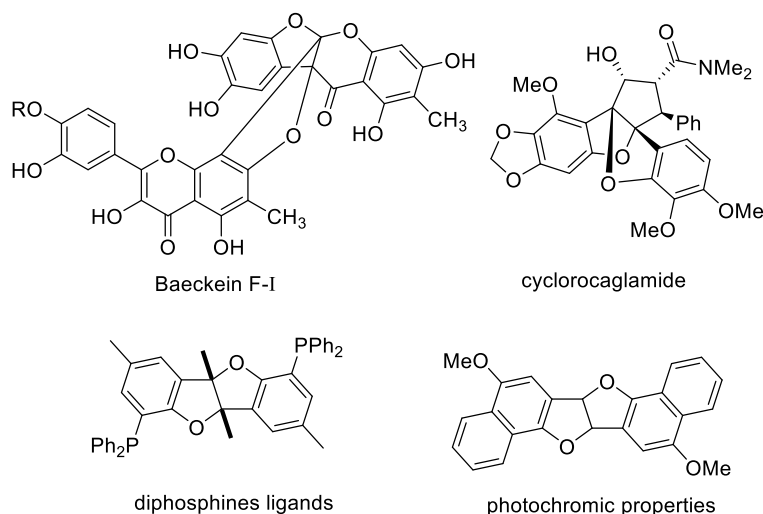
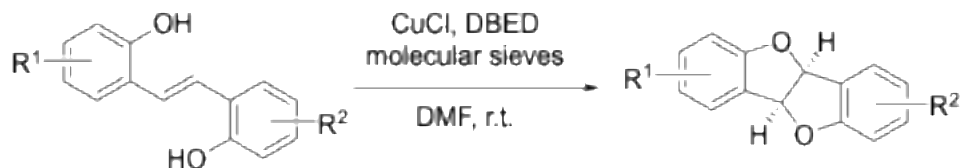
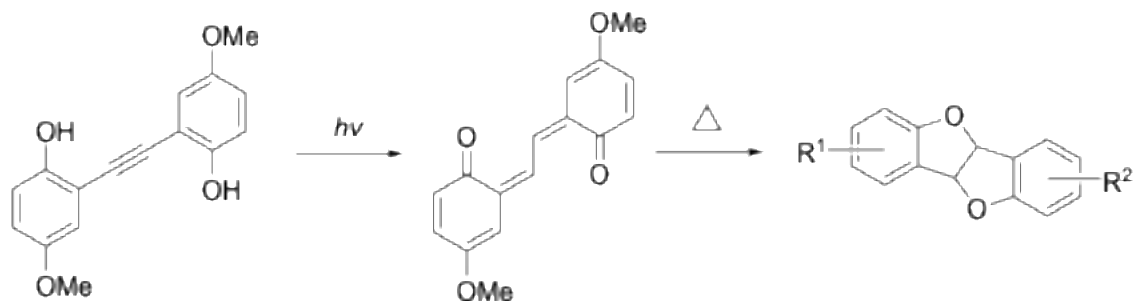
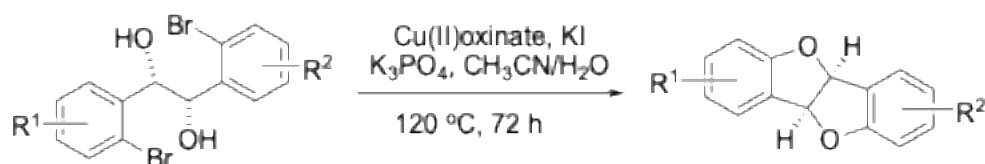
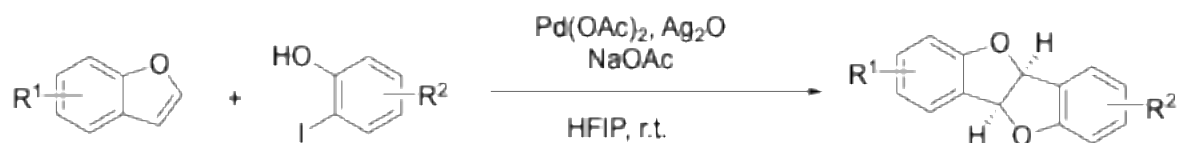


Figure 1. Selected functional products with the core structure of benzofuro[3,2-*b*]benzofurans

Benzofuro[3,2-*b*]benzofurans are interesting structural motifs found in a variety of natural products, encompassing a broad range of biological activities (Figure 1).^{1,2} In addition, some synthetic derivatives of these compounds can serve as ligands in catalysis,³⁻⁵ or have been shown to have remarkable photochromic properties.⁶ Owing to the functional importance of benzofuro[3,2-*b*]benzofurans, the development of sustainable and efficient synthetic protocols becomes a necessity. The traditional synthetic strategy allowing access to such skeletons relies on the oxidative cyclization of 2,2-dihydroxystilbenes.^{7,8} For example, Gilbertson et al. prepared benzofuro[3,2-*b*]benzofurans via an aerobic copper-catalyzed oxidative [4+4] cyclization from the corresponding 2,2'-disubstituted stilbenes (Scheme 1 A).⁹ The Claisen rearrangement of 1,4-bis(aryloxy)-2-butyne is another common synthetic option for preparation of benzofuro[3,2-*b*]benzofurans (Scheme 1 B).¹⁰⁻¹² In addition, in 2015, a copper-catalyzed double intramolecular Ullmann coupling was successfully applied to prepare benzofuro[3,2-*b*]benzofurans (Scheme 1 C).¹³

Despite advances made thus far, most methods to access these structures often require drastic conditions, and lengthy synthetic sequences, which limit both their scope and functional group tolerance. Therefore, a convenient, one-step, and milder methodology for constructing benzofuro[3,2-*b*]benzofurans is desirable.

A) oxidative cyclization**B) Claisen rearrangement****C) Ullmann coupling****D) This work: Palladium-catalysed dearomative cyclization****Scheme 1.** Methods for construction of benzofuro[3,2-*b*]benzofurans

In recent years, catalytic dearomative cycloadditions have emerged as promising strategies to construct polycyclic carbocycles and heterocycles from arenes and heteroarenes.¹⁴⁻¹⁶ Here, we report a convenient one-step palladium-catalyzed dearomative [3 + 2] cycloaddition of benzo[*b*]furans with 2-iodophenols to construct benzofuro[3,2-*b*]benzofurans (Scheme 1 D).

Results and Discussion

Our preliminary investigations were guided by previous work on the palladium-catalyzed room temperature arylation of heteroarenes.¹⁷⁻²¹ Interestingly, when 2-iodophenol was reacted with benzo[*b*]furan, the product obtained was dihydrobenzofuro[3,2-*b*]benzofuran, instead of the expected arylation product.²¹ To initiate our study, benzo[*b*]furan (**1a**) and 2-iodophenol (**2a**) were chosen as model substrates (Table 1). Using the same conditions previously applied to the arylation of benzo[*b*]furan,²¹ a 78% yield of the dihydrobenzofuro[3,2-*b*]benzofuran (**3a**) was obtained after 24 h (Table 1, entry 1). Changing the solvent from hexafluoro-2-propanol (HFIP) to DMF, which had been used in the arylation of indoles, dramatically reduced the yield to 32% (entry

2).¹⁷ The reaction did not occur under the catalytic system used for β -arylation of benzo[*b*]thiophenes and thiophenes (entry 3).¹⁹ When room temperature α -arylation conditions for benzo[*b*]thiophenes were applied, the yield of **3a** increased to 82% (entry 4).²⁰ Increasing the Ag₂O to 1.0 eq further improved the yield to 90% (entry 5). However, increasing the NaOAc loading was detrimental, producing only a 78% yield (entry 6), consistent with the previous reports.¹⁸ Other oxidants, such as AgOAc and Cu(OAc)₂, performed poorly compared to Ag₂O (entries 7 and 8). The yield of the **3a** was not improved by increasing the amount of Pd (data not shown). Control experiments confirmed that no reaction occurred in the absence of Ag₂O, NaOAc, or Pd(OAc)₂ (entries 9–11).

After evaluating various parameters, we found that using 1 mol% Pd(OAc)₂ as the catalyst, 1.0 eq of Ag₂O as the oxidant, along with 0.5 eq of NaOAc as the base, and HFIP as the solvent, provided benzofuro[3,2-*b*]benzofuran (**3a**) in a 90% yield.

Table 1. Optimization of the reaction conditions ^a

c1ccc2c(c1)occc2 (1a, 1 equiv) + Oc1ccc(I)cc1 (2a, 1 equiv) $\xrightarrow{\text{Pd(OAc)}_2, \text{Oxidant, Acid or Base, Solvent}}$ Oc1ccc2c(c1)oc3ccccc23 (3a)

| Entry | Solvent | [Pd] cat. | Acid or Base (eq) | Oxidant (eq) | Yield (%) ^b |
|-------|---------|---|---------------------------|--|------------------------|
| 1 | HFIP | Pd(OAc) ₂ | 2-nitrobenzoic acid (1.5) | Ag ₂ O (0.75) | 78 |
| 2 | DMF | Pd(OAc) ₂ | 2-nitrobenzoic acid (1.5) | Ag ₂ O (0.75) | 32 |
| 3 | HFIP | Pd ₂ (dba) ₃ ·CHCl ₃ | / | Ag ₂ CO ₃ (0.75) | 0 |
| 4 | HFIP | Pd(OAc) ₂ | NaOAc (0.5) | Ag ₂ O (0.75) | 82 |
| 5 | HFIP | Pd(OAc) ₂ | NaOAc (0.5) | Ag ₂ O (1.0) | 90 |
| 6 | HFIP | Pd(OAc) ₂ | NaOAc (1.0) | Ag ₂ O (1.0) | 78 |
| 7 | HFIP | Pd(OAc) ₂ | NaOAc (0.5) | Cu(OAc) ₂ (1.0) | 58 |
| 8 | HFIP | Pd(OAc) ₂ | NaOAc (0.5) | AgOAc(1.0) | 47 |
| 9 | HFIP | Pd(OAc) ₂ | NaOAc (0.5) | / | 0 |
| 10 | HFIP | Pd(OAc) ₂ | / | Ag ₂ O (1.0) | 0 |
| 11 | HFIP | / | NaOAc (0.5) | Ag ₂ O (1.0) | 0 |

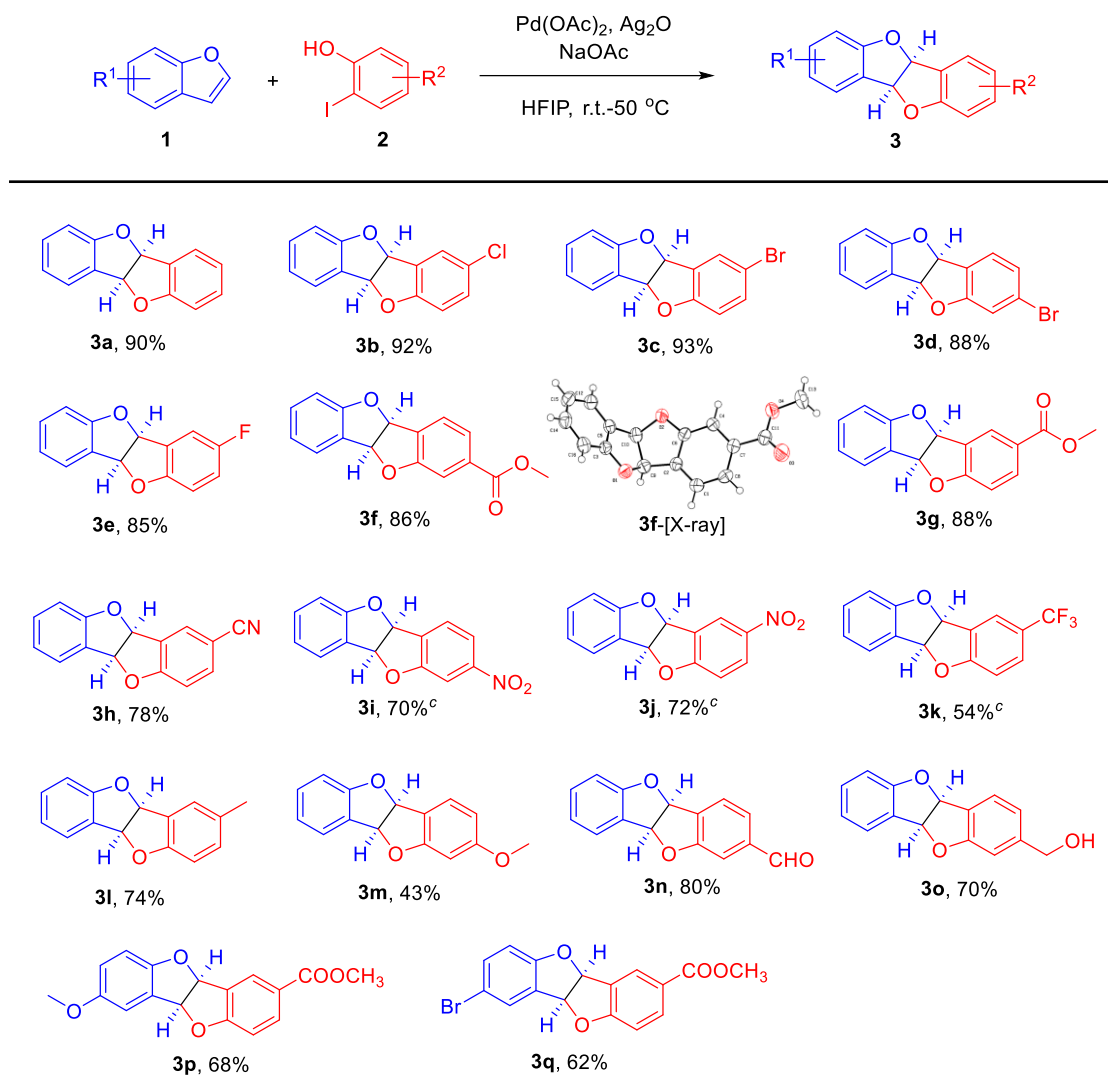
^a Pd (1.0 mol%), benzofuran (1.0 mmol), and 2-iodophenol (1.0 mmol) in solvent (2 mL), the reaction mixture stirred at r.t. for 24 h. ^b Isolated yield.

Having determined the optimal conditions, the scope of the 2-iodophenol component was investigated, and the results are summarized in **Table 2**. 2-iodophenol with various halogen-substituents underwent dearomative cyclization to provide the corresponding products (**3b–3e**) in good to excellent yields (85–93%), which allows further functionalization through traditional cross-coupling methods. In addition to the halogens, 2-iodophenols-bearing an electron-withdrawing substituents demonstrated moderate to good reactivity (**3f–3k**). For example, substrates bearing ester group or CN provided the expected benzofuro[3,2-*b*]benzofuran products (**3f–3h**) in good yields (78–88%). In addition, the structure of **3f** was confirmed by X-ray single-crystal diffraction. Highly electron-withdrawing substituents, such as nitro and trifluoromethyl (**3i–3k**), proceeded in moderate yield, although an elevated temperature (50 °C) was required. Moderately electron-donating substituents in 2-iodophenol such as methyl were compatible with the reaction (**3l**), but lower yields were observed with strongly electron-donating substituents (-OCH₃, **3m**). Notably, the mild reaction

conditions were compatible with unprotected aldehyde (**3n**) and alcohol (**3o**) substituents, which often present chemoselectivity issues under harsh conditions. In contrast, the more hindered *ortho*-substituted 2-iodophenols were incompatible with the reaction conditions (data not shown), likely due to the steric hindrance.

Furthermore, benzofurans bearing various substituents at different positions were also tested. Remarkably, only those with substituents at the C-6 position were converted successfully in moderate yields (**3p** and **3q**). Attempts to use furfuran instead of benzofuran were unsuccessful.

Table 2. Substrate scope of dihydrobenzofuro[3,2-*b*]benzofurans ^{a,b}



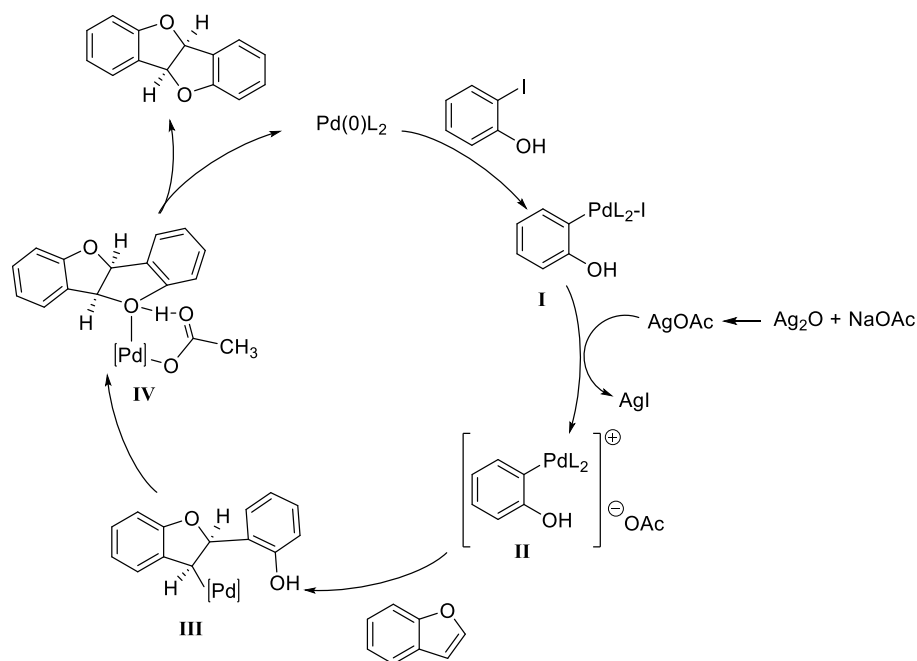
^a Reaction conditions: a benzo[*b*]furan **1** (1.0 mmol), 2-iodophenol **2** (1.0 mmol), Ag₂O (1.0 mmol), NaOAc (0.5 mmol), 1 mol % Pd(OAc)₂, HFIP (2 mL), r.t. 24 h.

^b Isolated yields are shown.

^c Reaction at 50 °C.

A plausible mechanistic pathway involving a Pd[0/II] catalytic cycle is outlined in Scheme 2. The reaction would start with the oxidative addition of 2-iodophenol to Pd(0)L₂ forming palladium complex **I**. An Ag salt assists in the abstraction of the iodide from **I** generating a more reactive palladium center **II**, which would then undergo the C-H arylation step on the benzo[*b*]furan, forming complex **III**. The *o*-hydroxyl group

replaces the palladium substituent on the benzo[*b*]furan to generate intermediate **IV** and which then produces the benzofuro[3,2-*b*]benzofuran final product.



Scheme 2. Proposed mechanism for synthesis of Benzofuro[3,2-*b*]benzofurans

Conclusions

In conclusion, a method for synthesizing benzofuro[3,2-*b*]benzofurans was developed via a palladium-catalyzed dearomatization [3+2] cycloaddition of benzo[*b*]furans with 2-iodophenols. This powerful approach eliminates the need for prefunctionalization, thus leading to a short synthetic route.

Experimental Section

General. All the reagents and solvents were obtained from commercial sources and used without further purification. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 plates (Qingdao Ocean Chemical Company, China). Column chromatography was performed using silica gel (200-300 mesh, Qingdao Ocean Chemical Company, China). $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were recorded on Bruker 600 MHz and 151 MHz spectrometers, respectively. Chemical shifts are reported in ppm relative to solvent signals, $^1\text{H NMR}$ (7.26 ppm), and $^{13}\text{C NMR}$ (77.00 ppm). Data are reported in chemical shifts, integration, multiplicity (*s* = singlet, *d* = doublet, *t* = triplet, *m* = multiplet, *dd* = doublet of doublet), and coupling constants (*J*) in Hertz.

Typical procedures. To a dry round-bottom flask was added a benzo[*b*]furan (1 equiv, 1 mmol), iodophenol (1 equiv, 1 mmol), and the reactants were dissolved by adding hexafluoro-2-propanol (2 mL). Subsequently, $\text{Pd}(\text{OAc})_2$ (1 mol%, 0.01 mmol, 2.3 mg) was added, followed by Ag_2O (1 equiv, 1 mmol, 231.7 mg), NaOAc (0.5 equiv, 0.5 mmol, 41.0 mg). The flask was evacuated and backfilled with N_2 three times. The reaction mixture was stirred at rt for 24 h and monitored by TLC. The mixture was then filtered through a silica plug with EtOAc to transfer and subsequently concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether/ EtOAc , 50:1 to 5:1 to obtain the desired products. The $^1\text{H NMR}$ and $^{13}\text{C NMR}$ spectra of the isolated products were recorded in CDCl_3 .

4b,9b-Dihydrobenzofuro[3,2-*b*]benzofuran (3a). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (188.8 mg, 90%). ¹H NMR (600 MHz, CDCl₃) δ 7.53 (d, *J* 7.5 Hz, 2H), 7.27 (t, *J* 7.2 Hz, 2H), 6.97 (t, *J* 7.4 Hz, 2H), 6.86 (d, *J* 8.2 Hz, 2H), 6.28 (s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 160.1, 131.4, 126.6, 124.4, 121.2, 110.8, 86.5. HRMS (ESI) calcd for C₁₄H₁₁O₂: [M + H]⁺ = 211.0754, found *m/z* = 211.0750.

3-Chloro-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran (3b). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (224.6 mg, 92%). ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J* 7.5 Hz, 1H), 7.49 (d, *J* 2.2 Hz, 1H), 7.29 (t, *J* 7.8 Hz, 1H), 7.22 (dd, *J* 8.6, 2.2 Hz, 1H), 6.98 (t, *J* 7.4 Hz, 1H), 6.87 (d, *J* 8.2 Hz, 1H), 6.78 (d, *J* 8.6 Hz, 1H), 6.32 (d, *J* 7.3 Hz, 1H), 6.23 (d, *J* 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 159.9, 158.7, 131.6, 131.3, 126.5, 126.5, 126.2, 125.8, 124.0, 121.4, 111.9, 110.9, 87.3, 85.8. HRMS (ESI) calcd for C₁₄H₁₀ClO₂: [M + H]⁺ 245.0364, found *m/z* = 245.0367.

3-Bromo-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran (3c). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (267.8 mg, 93%). ¹H NMR (600 MHz, CDCl₃) δ 7.63 (d, *J* 2.1 Hz, 1H), 7.52 (d, 7.5 Hz, 1H), 7.36 (dd, *J* 8.6, 2.1 Hz, 1H), 7.29 (t, *J* 7.2 Hz, 1H), 6.98 (t, *J* 7.5 Hz, 1H), 6.87 (d, *J* 8.2 Hz, 1H), 6.74 (d, *J* 8.6 Hz, 1H), 6.32 (d, *J* 7.3 Hz, 1H), 6.24 (d, *J* 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 159.9, 159.2, 134.2, 131.6, 129.5, 126.8, 126.5, 123.9, 121.4, 112.8, 112.5, 110.9, 87.3, 85.7. HRMS (ESI) calcd for C₁₄H₁₀BrO₂: [M + H]⁺ = 288.9859, found *m/z* 288.9864.

2-Bromo-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran (3d). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (253.5 mg, 88%). ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J* 7.5 Hz, 1H), 7.38 (d, *J* 8.0 Hz, 1H), 7.29 (t, *J* 7.7 Hz, 1H), 7.10 (d, *J* 8.0 Hz, 1H), 6.98 (t, *J* 7.5 Hz, 1H), 6.86 (d, *J* 8.2 Hz, 1H), 6.32 (d, *J* 7.2 Hz, 1H), 6.22 (d, *J* 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 160.9, 159.9, 131.6, 127.5, 126.6, 124.8, 124.4, 123.9, 123.8, 121.4, 114.5, 110.9, 87.5, 85.6. HRMS (ESI) calcd for C₁₄H₁₀BrO₂: [M + H]⁺ = 288.9859, found *m/z* 288.9864.

3-Fluoro-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran (3e). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (193.7 mg, 85%). ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J* 7.5 Hz, 1H), 7.29 (t, *J* 7.8 Hz, 1H), 7.22 (dd, *J* 7.6, 2.7 Hz, 1H), 7.02 – 6.94 (m, 2H), 6.88 (d, *J* 8.2 Hz, 1H), 6.78 (dd, *J* 8.8, 4.0 Hz, 1H), 6.32 (d, *J* 7.4 Hz, 1H), 6.25 (d, 7.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 159.1 (d, *J* 231.4 Hz), 156.7, 155.9, 131.5, 126.5, 125.4 (d, *J* 8.7 Hz), 124.2, 121.4, 118.1 (d, *J* 24.2 Hz), 113.1 (d, *J* 24.5 Hz), 111.3 (d, *J* 8.1 Hz), 110.8, 87.2, 86.2. HRMS (ESI) calcd for C₁₄H₁₀FO₂: [M + H]⁺ = 229.0659, found *m/z* 229.0661.

Methyl 4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran-2-carboxylate (3f). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (230.4 mg, 86%). ¹H NMR (600 MHz, CDCl₃) δ 8.25 (s, 1H), 8.01 (d, *J* 8.5 Hz, 1H), 7.54 (d, *J* 7.3 Hz, 1H), 7.30 (t, *J* 7.8 Hz, 1H), 6.99 (t, 7.4 Hz, 1H), 6.88 (dd, *J* 8.3, 2.5 Hz, 2H), 6.39 (d, *J* 7.3 Hz, 1H), 6.28 (d, *J* 7.3 Hz, 1H), 3.89 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.3, 163.6, 159.1, 134.5, 133.9, 129.5, 128.8, 126.0, 124.6, 123.8, 113.0, 112.6, 110.7, 87.2, 86.2, 51.9. HRMS (ESI) calcd for C₁₆H₁₃O₄: [M + H]⁺ = 269.0808, found *m/z* 269.0799.

Methyl 4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran-3-carboxylate (3g). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (235.8 mg, 88%). ¹H NMR (600 MHz, CDCl₃) δ 7.68 (d, *J* 7.9 Hz, 1H), 7.58 (d, *J* 7.9 Hz, 1H), 7.54 (d, *J* 7.5 Hz, 1H), 7.50 (s, 1H), 7.29 (t, *J* 7.2 Hz, 1H), 6.99 (t, *J* 7.4 Hz, 1H), 6.87 (d, *J* 8.2 Hz, 1H), 6.36 (d, *J* 7.4 Hz, 1H), 6.29 (d, *J* 7.4 Hz, 1H), 3.89 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.5, 160.1, 159.9, 133.3, 131.5, 129.3, 126.6, 126.4, 124.1, 122.8, 121.4, 111, 110.9, 87.1, 85.7, 52.3. HRMS (ESI) calcd for C₁₆H₁₃O₄: [M + H]⁺ = 269.0808, found *m/z* 269.0800.

4b,9b-Dihydrobenzofuro[3,2-b]benzofuran-3-carbonitrile (3h). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (183.3 mg, 78%). ¹H NMR (600 MHz, CDCl₃) δ 7.62 (d, *J* 7.7 Hz, 1H), 7.53 (d, *J* 7.5 Hz, 1H), 7.31 (t, *J* 7.7 Hz, 1H), 7.26 (d, *J* 8.2 Hz, 1H), 7.11 (s, 1H), 7.01 (t, *J* 7.5 Hz, 1H), 6.88 (d, *J* 8.2 Hz, 1H), 6.39 (d, *J* 7.4 Hz, 1H), 6.28 (d, *J* 7.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 160.0, 159.8, 131.8, 129.8, 127.5, 126.6, 125.3, 123.4, 121.7, 118.4, 114.7, 114.4, 110.9, 87.6, 85.2. HRMS (ESI) calcd for C₁₅H₁₀NO₂: [M + H]⁺ = 236.0706, found *m/z* 236.0705.

2-Nitro-4b,9b-dihydrobenzofuro[3,2-b]benzofuran (3i). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (178.5 mg, 70%). ¹H NMR (600 MHz, CDCl₃) δ 7.89 (d, *J* 8.2 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.58 (d, *J* 7.6 Hz, 1H), 7.34 (t, *J* 7.8 Hz, 1H), 7.04 (t, *J* 7.4 Hz, 1H), 6.91 (d, *J* 8.2 Hz, 1H), 6.48 (d, *J* 7.4 Hz, 1H), 6.33 (d, *J* 7.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 160.6, 159.7, 150.6, 131.8, 131.4, 127.0, 126.6, 123.4, 121.7, 116.7, 110.9, 106.4, 88.3, 84.8. HRMS (ESI) calcd for C₁₄H₁₀NO₄: [M + H]⁺ = 256.0604, found *m/z* 256.0610.

3-Nitro-4b,9b-dihydrobenzofuro[3,2-b]benzofuran (3j). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (183.6 mg, 72%). ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* 2.2 Hz, 1H), 8.22 (d, *J* 2.3 Hz, 1H), 7.55 (d, *J* 7.5 Hz, 1H), 7.33 (t, *J* 7.7 Hz, 1H), 7.02 (t, *J* 7.5 Hz, 1H), 6.91 (dd, *J* 13.6, 8.6 Hz, 2H), 6.49 (d, *J* 7.3 Hz, 1H), 6.30 (d, *J* 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 165.1, 159.9, 142.4, 132.1, 128.2, 126.6, 126.1, 123.4, 123.0, 121.7, 111.1, 111.0, 89.2, 84.6. HRMS (ESI) calcd for C₁₄H₁₀NO₄: [M + H]⁺ = 256.0604, found *m/z* 256.0609.

3-(Trifluoromethyl)-4b,9b-dihydrobenzofuro[3,2-b]benzofuran (3k). The product was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 50:1, v/v) as a white solid (150.1 mg, 54%). ¹H NMR (600 MHz, CDCl₃) δ 7.81 (s, 1H), 7.57 – 7.52 (m, 2H), 7.00 (t, *J* 7.1 Hz, 1H), 6.93 (d, *J* 8.5 Hz, 1H), 6.89 (d, *J* 8.2 Hz, 1H), 6.39 (d, *J* 7.3 Hz, 1H), 6.29 (d, *J* 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 162.6, 159.9, 131.7, 129.0, 129.0, 126.6, 125.3, 124.3, 123.6, 121.5, 111.1, 110.9, 87.8, 85.4. HRMS (ESI) calcd for C₁₅H₁₀F₃O₂: [M + H]⁺ = 279.0627, found *m/z* 279.0631.

3-Methyl-4b,9b-dihydrobenzofuro[3,2-b]benzofuran (3l). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 50:1, v/v) as a white solid (165.8 mg, 74%). ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J* 7.5 Hz, 1H), 7.33 (s, 1H), 7.30 – 7.25 (m, 1H), 7.07 (d, *J* 8.1 Hz, 1H), 6.96 (t, *J* 7.4 Hz, 1H), 6.86 (d, *J* 8.1 Hz, 1H), 6.75 (d, *J* 8.2 Hz, 1H), 6.31 – 6.20 (m, 2H), 2.32 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 160.0, 157.9, 132.0, 131.3, 126.7, 126.5, 124.6, 124.3, 121.1, 110.8, 110.4, 86.6, 86.5, 20.0. HRMS (ESI) calcd for C₁₅H₁₃O₂: [M + H]⁺ = 225.0910, found *m/z* 225.0909.

3-Methoxy-4b,9b-dihydrobenzofuro[3,2-b]benzofuran (3m). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 20:1, v/v) as a white solid (103.2 mg, 43%). ¹H NMR (600 MHz, CDCl₃) δ 7.52 (d, *J* 7.5 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.08 (d, *J* 2.7 Hz, 1H), 6.97 (t, *J* 7.4 Hz, 1H), 6.89 – 6.83 (m, 2H), 6.77 (d, *J* 8.8 Hz, 1H), 6.30 – 6.24 (m, 2H), 3.79 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 159.9, 154.5, 154.0, 131.3, 126.5, 124.8, 124.6, 121.2, 118.0, 111.1, 110.9, 110.8, 86.9, 86.7, 56.1. HRMS (ESI) calcd for C₁₅H₁₃O₃: [M + H]⁺ = 241.0859, found *m/z* 241.0857.

4b,9b-Dihydrobenzofuro[3,2-b]benzofuran-2-carbaldehyde (3n). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (190.4 mg, 80%). ¹H NMR (600 MHz, CDCl₃) δ 9.95 (s, 1H), 7.69 (d, *J* 7.6 Hz, 1H), 7.55 (d, *J* 7.0 Hz, 1H), 7.50 (d, *J* 8.9 Hz, 1H), 7.34 (s, 1H), 7.30 (t, *J* 7.8 Hz, 1H), 7.00 (t, *J* 7.8 Hz, 1H), 6.88 (d, *J* 8.2 Hz, 1H), 6.39 (d, *J* 7.4 Hz, 1H), 6.30 (d, *J* 7.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 191.5, 160.7, 159.8, 139.4, 131.6, 131.0, 127.2, 126.6, 123.9, 123.7, 121.6, 110.9, 110.8, 87.3, 85.8. HRMS (ESI) calcd for C₁₅H₁₁O₃: [M + H]⁺ = 239.0703, found *m/z* 239.0704.

(4b,9b-Dihydrobenzofuro[3,2-b]benzofuran-2-yl)methanol (3o). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 5:1, v/v) as a white solid (168.0 mg, 70%). ¹H NMR (600

MHz, CDCl₃) δ 7.53 (d, *J* 7.5 Hz, 1H), 7.51 (d, *J* 7.7 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.97 (t, *J* 7.5 Hz, 2H), 6.89 (s, 1H), 6.86 (d, *J* 8.1 Hz, 1H), 6.31 (d, *J* 7.3 Hz, 1H), 6.27 (d, *J* 7.3 Hz, 1H), 4.65 (s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 160.5, 160.0, 144.9, 131.4, 126.6, 124.4, 123.9, 121.2, 119.7, 110.8, 109.1, 86.9, 86.2, 65.1. HRMS (ESI) calcd for C₁₅H₁₃O₃: [M + H]⁺ = 241.0859, found *m/z* 241.0857.

Methyl 8-methoxy-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran-3-carboxylate (3p). The product was obtained by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1, v/v) as a white solid (202.6 mg, 68%). ¹H NMR (600 MHz, CDCl₃) δ 7.67 (dd, *J* 7.9, 1.3 Hz, 1H), 7.56 (d, *J* 7.8 Hz, 1H), 7.50 (s, 1H), 7.07 (d, *J* 2.7 Hz, 1H), 6.86 (dd, *J* 8.8, 2.7 Hz, 1H), 6.78 (d, *J* 8.8 Hz, 1H), 6.32 (d, *J* 7.4 Hz, 1H), 6.27 (d, *J* 7.4 Hz, 1H), 3.89 (s, 3H), 3.79 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.5, 160.0, 154.7, 153.8, 133.3, 129.5, 126.3, 124.4, 122.8, 118.2, 111.9, 111.2, 110.8, 87.5, 85.9, 56.1, 52.3. HRMS (ESI) calcd for C₁₇H₁₅O₅: [M + H]⁺ = 299.0914, found *m/z* 299.0907.

Methyl 8-bromo-4b,9b-dihydrobenzofuro[3,2-*b*]benzofuran-3-carboxylate (3q). The product was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 10:1, v/v) as a white solid (214.5 mg, 62%). ¹H NMR (600 MHz, CDCl₃) δ 7.68 (dd, *J* 7.9, 1.3 Hz, 1H), 7.64 (d, *J* 2.1 Hz, 1H), 7.57 (d, *J* 7.9 Hz, 1H), 7.51 (s, 1H), 7.37 (dd, *J* 8.6, 2.1 Hz, 1H), 6.75 (d, *J* 8.6 Hz, 1H), 6.31 (s, 1H), 6.31 (s, 1H), 3.90 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.4, 159.9, 159.0, 134.3, 133.5, 129.5, 128.7, 126.4, 123.0, 113.1, 112.5, 112.0, 86.5, 52.4. HRMS (ESI) calcd for C₁₆H₁₂BrO₄: [M + H]⁺ = 346.9913, found *m/z* 346.9914.

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Supplementary Material

Characterization data including copies of ¹H and ¹³C NMR spectra associated with this paper and X-ray crystallography data for compound **3f** can be found in the online version

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