A Platinum Open Access Journal for Organic Chemistry

Paper

Free to Authors and Readers | DOAJ Seal | *Arkivoc* **2024** (8) 202412318

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

Yongjun Zang and Fucheng Zhu*

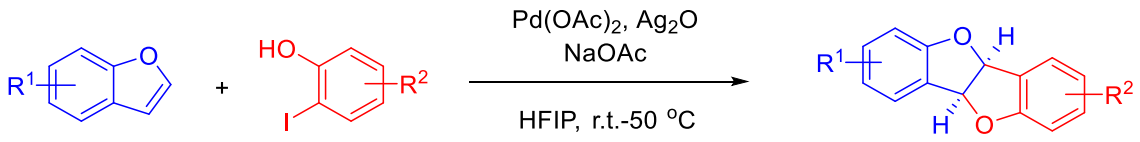
Department of Biological and Pharmaceutical Engineering, West Anhui University, Lu'an, Anhui 237012, P.R. China

E-mail: fucheng323@163.com

Received 11-04-2024 **Accepted Manuscript** 01-19-2025 **Published on line** 02-09-2025

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 Ag_2O 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
- Readily available substrate
- moderate to excellent yields
- Dearomative cyclization

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

Introduction

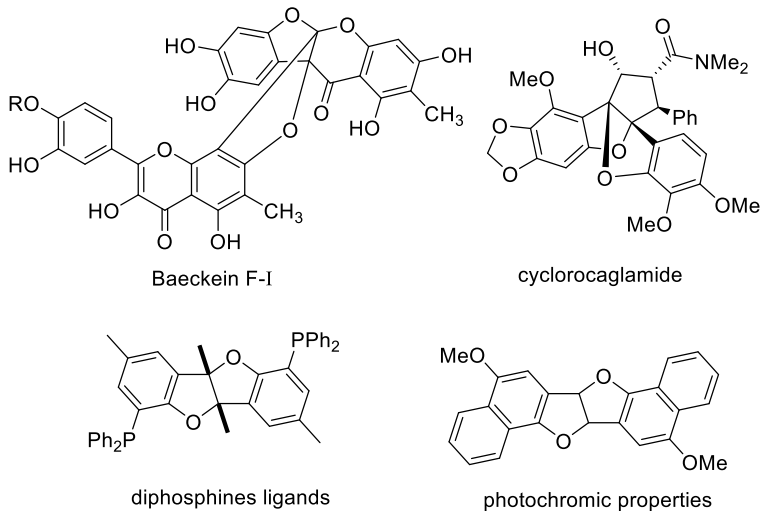
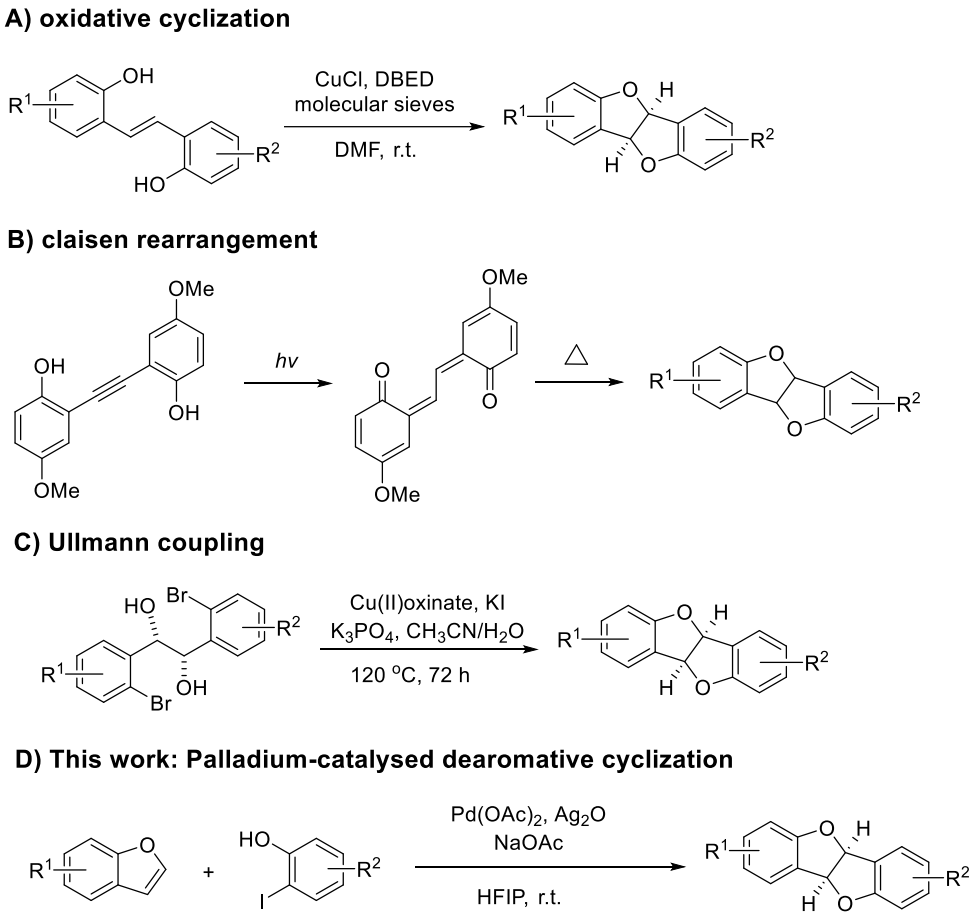


Figure 1. Selected functional products with the core structure of benzofuro[3,2-*b*] benzofurans.

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-butynes 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.



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).

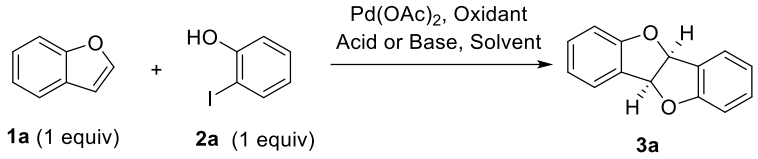
Results and Discussion

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 Ag_2O 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 Ag_2O (entries 7 and 8). The yield of the **3a** was not improved by increasing the among of Pd (data not shown). Control experiments confirmed that no reaction occurred in the absence of Ag_2O, 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 Ag_2O 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]



Entry	Solvent	[Pd] cat.	Acid or Base (eq)	Oxidant (eq)	Yield (%)[b]
1	HFIP	$Pd(OAc)_2$	2-nitrobenzoic acid (1.5)	Ag_2O (0.75)	78
2	DMF	$Pd(OAc)_2$	2-nitrobenzoic acid (1.5)	Ag_2O (0.75)	32
3	HFIP	$Pd_2(dba)_3{\cdot}CHCl_3$	/	Ag_2CO_3 (0.75)	0
4	HFIP	$Pd(OAc)_2$	NaOAc (0.5)	Ag_2O (0.75)	82
5	HFIP	$Pd(OAc)_2$	NaOAc (0.5)	Ag_2O (1.0)	90
6	HFIP	$Pd(OAc)_2$	NaOAc (1.0)	Ag_2O (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_2O (1.0)	0
11	HFIP	/	NaOAc (0.5)	Ag_2O (1.0)	0

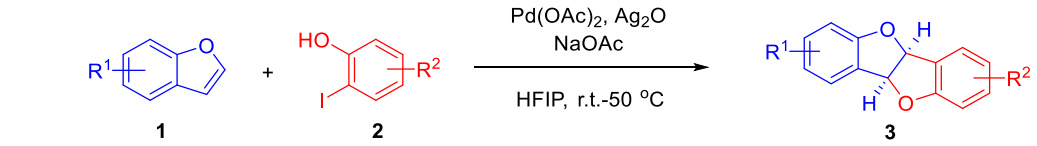
[a] Pd (1.0 mol %), benzofuran (1.0 mmol), and 2-iodophenol (1.0 mmol) in solvent (2 mL), the reaction mixture stirred at r.t. for 24 h. [b] Isolated yield.

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 (-OCH_3, **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-

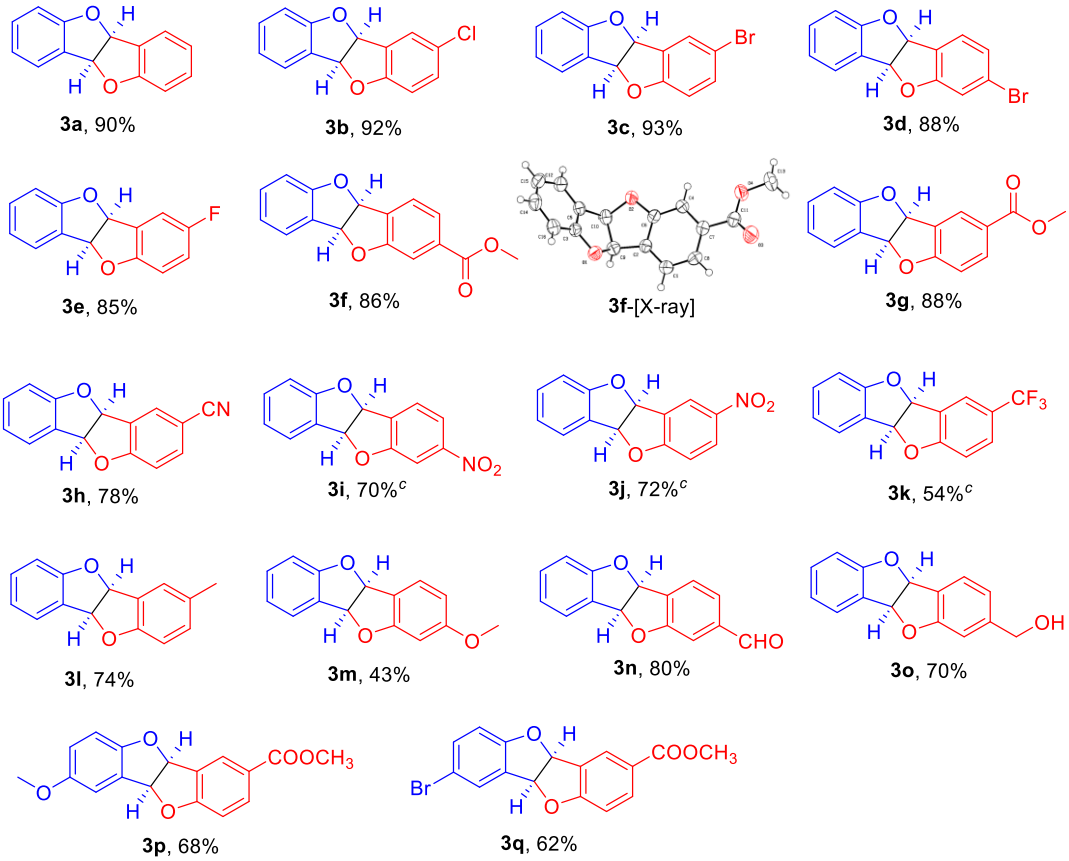
iodophenols were incompatible with the reaction conditions (data not shown), likely due to the steric hindrance.

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]



1 + **2** → **3**

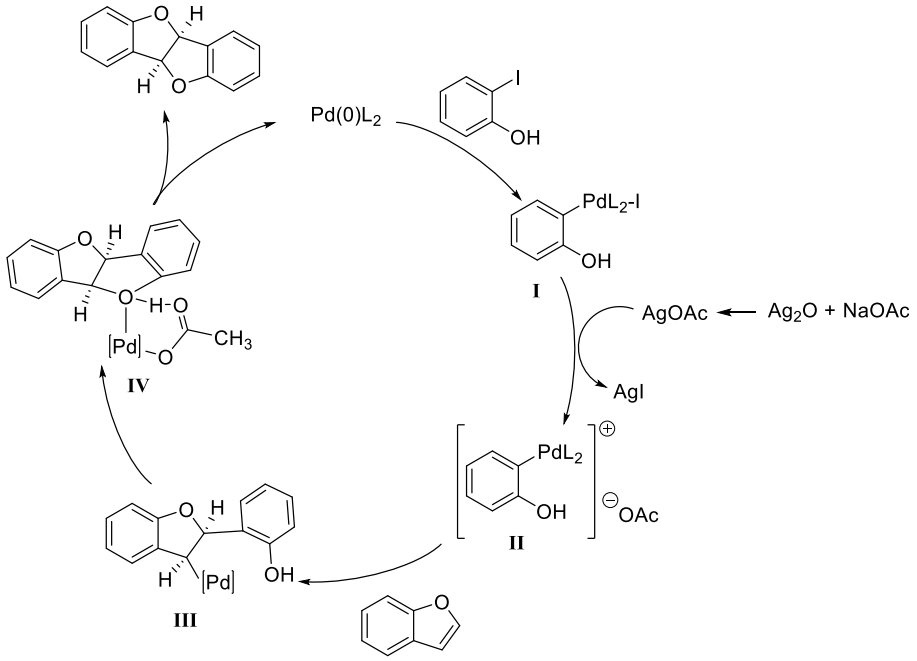


[a] Reaction conditions: a benzo[*b*]furan **1** (1.0 mmol), 2-iodophenol **2** (1.0 mmol), Ag_2O (1.0 mmol), NaOAc (0.5 mmol), 1 mol % $Pd(OAc)_2$, HFIP (2 mL), r.t. 24 h.

[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 $Pd(0)L_2$ 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}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 600 MHz and 151 MHz spectrometers, respectively. Chemical shifts are reported in ppm relativeto solvent signals, ^{1}H NMR (7.26 ppm), and ^{13}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, $Pd(OAc)_2$ (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}H NMR and ^{13}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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1, 131.4, 126.6, 124.4, 121.2, 110.8, 86.5. HRMS (ESI) calcd for $C_{14}H_{11}O_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}ClO_2$: $[M + H]^+$ 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}BrO_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}BrO_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}FO_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{16}H_{13}O_4$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{16}H_{13}O_4$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{10}NO_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}NO_4$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{14}H_{10}NO_4$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{10}F_3O_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{13}O_2$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{13}O_3$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{11}O_3$: $[M + H]^+$ = 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%). ^{1}H NMR (600

MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{15}H_{13}O_3$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{17}H_{15}O_5$: $[M + H]^+$ = 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%). ^{1}H NMR (600 MHz, $CDCl_3$) 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). ^{13}C NMR (151 MHz, $CDCl_3$) 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 $C_{16}H_{12}BrO_4$: $[M + H]^+$ = 346.9913, found *m/z* 346.9914.

Acknowledgements

This research was funded by the Anhui University Scientific Research Project Outstanding Youth Project (2023AH030109). Anhui Scientific Research and Innovation Team of Quality Evaluation and Improvement of Traditional Chinese Medicine (2022AH010090), and the High-Level Talent Project of West Anhui University (WGKQ2022079).

Supplementary Material

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

References

1. Jia, B.-X.; Zeng, X. L.; Ren, F. X.; Jia, L.; Chen, X. Q.; Yang, J.; Liu, H. M.; Wang, Q., *Food Chem.* **2014**, *155*, 31-37. https://10.1016/j.foodchem.2014.01.022
2. Bringmann, G.; Mühlbacher, J.; Messer, K.; Dreyer, M.; Ebel, R.; Nugroho, B. W.; Wray, V.; Proksch, P., *J. Nat. Prod.* **2002,** *66*, 80-85. https://10.1021/np020291k
3. González-Gálvez, D.; Nolis, P.; Philippot, K.; Chaudret, B.; van Leeuwen, P. W. N. M., *ACS Catalysis* **2012,** *2*, 317-321. https://10.1021/cs200633k

4. López-Valbuena, J. M.; Escudero-Adan, E. C.; Benet-Buchholz, J.; Freixa, Z.; van Leeuwen, P. W. N. M., *Dalton Trans.* **2010,** *39*. https://10.1039/c0dt00011f
5. Tschan, M. J. L.; López-Valbuena, J.-M.; Freixa, Z.; Launay, H.; Hagen, H.; Benet-Buchholz, J.; van Leeuwen, P. W. N. M., *Organometallics* **2011,** *30*, 792-799. https://10.1021/om100980m
6. Schmidt, A. J.; Laatsch, H.; Noltemeyer, M., *Angew. Chem.* **1991,** *103*, 858-860. https://10.1002/ange.19911030724
7. Fujita, M.; Qi, G.; Verkerk, U. H.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M., *Org. Lett.* **2004,** *6* , 2653-2656. https://10.1021/ol0491639
8. Wang, Z.; Pan, C.; Yu, J.; Zhou, Y.; Zhou, M. M., *Synlett* **2006,** *2006*, 1657-1662. https://10.1055/s-2006-944204
9. Zhang, Z.-J.; Zhou, X.; Li, D.; Chen, Y.; Xiao, W.-W.; Li, R.-T.; Shao, L.-D., *J. Org. Chem.* **2021,** *86*, 7609-7624. https://10.1021/acs.joc.1c00656
10. Bates, D. K.; Jones, M. C. *J. Org. Chem.* **2002,** *43*, 3856-3861. https://10.1021/jo00414a015
11. Kiehlmann, E.; Li, E. P. M.; Millar, J. G., *Can. J. Chem.* **1986,** *64*, 1989-1997. https://10.1139/v86-329
12. Thyagarajan, B. S.; Balasubramanian, K. K.; Bhima Rao, R., *Tetrahedron* **1965,** *21*, 2289-2295. https://10.1016/s0040-4020(01)93883-9
13. Imrich, H.-G.; Conrad, J.; Beifuss, U., *Eur. J. Org. Chem.* **2015,** *2015*, 7718-7734. https://10.1002/ejoc.201501132
14. Cheng, Q.; Zhang, H. J.; Yue, W.-J.; You, S. L., *Chem.* **2017**, *3*, 428-436. https://10.1016/j.chempr.2017.06.015
15. Laviós, A.; Sanz-Marco, A.; Vila, C.; Muñoz, M. C.; Pedro, J. R.; Blay, G. *Org. Lett.* **2022,** *24*, 2149-2154. https://10.1021/acs.orglett.2c00427
16. Wang, K. K.; Xie, Y. X.; Li, Y. L.; Chen, R.; Wang, Z.-Y., *RSC Adv.* **2020,** *10*, 28720-28724. https://10.1039/d0ra05687a
17. Lebrasseur, N.; Larrosa, I., *J. Am. Chem. Soc.* **2008,** *130*, 2926-7. https://10.1021/ja710731a
18. Kori, S.; Bhujbal, Y.; Vadagaonkar, K.; Kapdi, A. R.; Kommyreddy, S. P.; Gharpure, S. J., *Chem. Commun.* **2022**, *58*, 847-850. https://10.1039/d1cc06063e
19. Colletto, C.; Islam, S.; Julia-Hernandez, F.; Larrosa, I., *J. Am. Chem. Soc.* **2016,** *138*, 1677-83. https://10.1021/jacs.5b12242
20. Colletto, C.; Panigrahi, A.; Fernandez-Casado, J.; Larrosa, I., *J. Am. Chem. Soc.* **2018,** *140*, 9638-9643. https://10.1021/jacs.8b05361
21. Mayhugh, A. L.; Luscombe, C. K., *Org. Lett.* **2021,** *23*, 7079-7082. https://10.1021/acs.orglett.1c02397