$InCl_3$-Catalyzed Propargylation of Indoles and Phenols with Propargylic Acetates: Application to the Syntheses of Benzofurans and Naphthofurans

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Abstract: $InCl_3$-catalyzed propargylation of indoles and phenols was developed. A strategy combining propargylation with intramolecular cyclization was used to easily prepare 2-benzyl-3-arylbenzofurans and -naphthofurans, which are important pharmaceutical intermediates.

Key words: Friedel–Crafts alkylation, propargylation, cyclization, benzofuran, $InCl_3$

Friedel–Crafts alkylation is one of the most versatile and widely used C–C bond-forming reactions, which has attracted great deal of attention in organic chemistry.[1] Among them, the development of Friedel–Crafts allylation[2] and propargylation,[3] is still a challenging task. Although the uses of transition-metal complexes and Lewis acid catalyzed allylation have been widely studied, which provided novel protocols for the functionalization of aromatic compounds, the propargylation of aromatic compounds is relatively less investigated. The features that alkynes can be readily transformed into many pharmaceutically useful key motifs and fused ring systems drove attention of chemists to develop practical and efficient propargylation methods.

Transition-metal complexes have been employed for propargylation of aromatic compounds,[4] but have some drawbacks, for example, requirement of a stoichiometric amount of catalyst,[5] limitation of the substrates,[6] and high cost.[7] The propargylation of aromatic compounds with propargylic alcohols can be also promoted by Lewis acids, such as $Ti(O\text{-}iPr)_4$,[8a] $TiCl_4$,[8b,c] CuCl,[8d] $BF_3{\cdot}EtO_2$,[8e,f] $B(C_6F_5)_3$,[8g] and $AuCl_3$.[8h] However, poor selectivity, narrow scope of the reaction, and handling with metal complexes restricted their practical applications. Very recently, it was reported that by using $FeCl_3$[9] and $Bi(OTf)_3$[10] as catalysts, propargylic alcohols/acetates could react with heteroatom nucleophiles under mild conditions. To our knowledge there are only few examples of the propargylation of heteroaromatic compounds, such as indoles with propargylic acetate/alcohol had been reported.[11]

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Benzofuran and naphthofuran derivatives are common subunits because of their physiological properties[12] and potential applications as fluorescent dyes[13] and probes.[14] Moreover, 3-aryl-2-benzylbenzofurans and -naphthofurans have been found in wide pharmacological applications for drug discovery. For example, benzofuran **A** is a potent inhibitor of PTPases[15] with good oral antihyperglycemic activity, which can be utilized for the treatment of Type II diabetes, and benzofuran **B**, is a promising antiandrogenic agent,[16] which was isolated from the stems of *Dalbergia cochinchinensis* (Figure 1). Many methods have been developed for the synthesis of benzofurans, such as cyclodehydration of aryl ketones, palladium-mediated Heck reactions,[17] and three-component Friedel–Crafts reaction of arylglyoxal monohydrates, phenols, and $TsNH_2$, described by our group.[18] Herein, we report $InCl_3$-catalyzed propargylation of indoles and phenols with propargylic acetates and their application to the synthesis of benzofuran and naphthofuran derivatives.

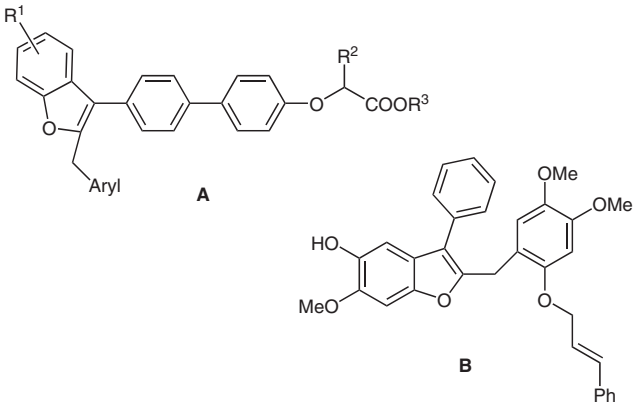
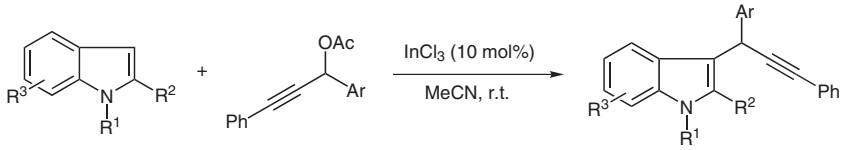


Figure 1

Initially, the reactions of indole (**1a**) with 1,3-diphenylpropargyl acetate (**2a**) in the presence of various Lewis acid catalysts (10 mol%) were carried out in MeCN at room temperature, giving the propargylated product, 3-(3-indolyl)-1,3-diphenylpropargylene (**3a**). It can be seen from Table 1 that indium(III) chloride is the most efficient Lewis acid catalyst for the reaction of indole with propargylic acetate under mild conditions. This protocol (Scheme 1) has a broad substrate scope for both electron-rich and electron-poor indoles **1b–i**. Good to excellent



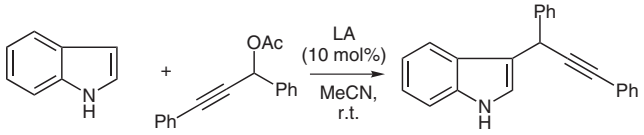
1a–i 2a–d 3a–j

Scheme 1

yields of propargylated products were obtained (Table 2), except for N-substituted indoles **1c**, **1g**, which showed low reactivity (entries 3,7). Various cross-substituted propargylic acetates **2b–d** were prepared and used to examine the regioselectivity of the $InCl_3$-catalyzed propargylation reaction. It is noteworthy that the propargylation only occurred at the benzylic position, while no reaction took place if the aryl group (Ar) of propargylic acetate was replaced by an alkyl group (Me). Furthermore, except for **2d**, the propargylations of *p*-tolyl **2b** and β-naphthyl **2c** acetates with indoles proceeded smoothly to give the propargylation products **3h–i** in reasonable yields (Table 2, entries 8,9).

In addition, $InCl_3$ could also catalyze the propargylation of less reactive aromatic C-nucleophiles such as phenols **4a–e** with propargyl acetate **2a** to afford mono- or bis-C-propargylated products **5a–e** instead of O-propargylated isomers efficiently under mild reaction conditions in 54–95% yields (Scheme 2, Table 3).

Table 1 Lewis Acid Catalyzed Propargylation of **1a** with **2a**



1a **2a** **3a**

Entry	Catalyst	Yield of **3a** (%)[a]
1	AgOTf	n.r.[b]
2	$Sc(OTf)_3$	n.r.
3	$CuCl_2$	8
4	CuBr	n.r.
5	$Cu(OTf)_2$	21
6	$FeCl_3$	trace
7	$InCl_3$	68

[a] Isolated yield.
[b] No reaction.

Table 2 $InCl_3$-Catalyzed Propargylation of Indoles with Propargylic Acetates[a]

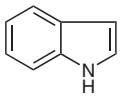
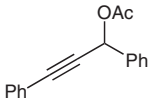
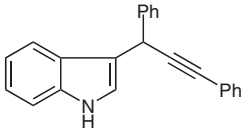
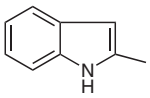
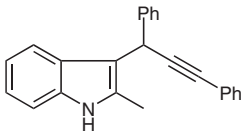
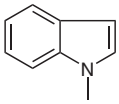
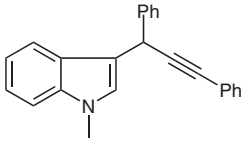
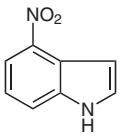
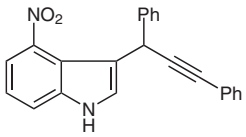
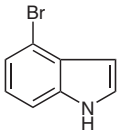
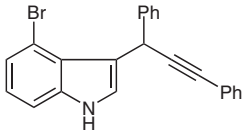
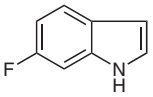
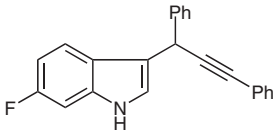
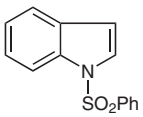
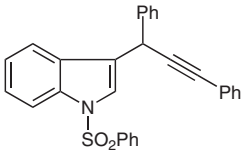
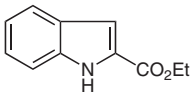
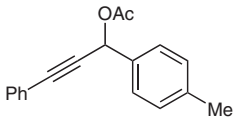
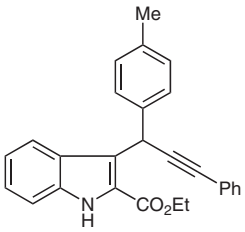
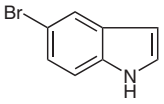
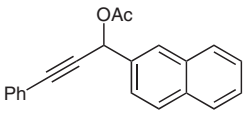
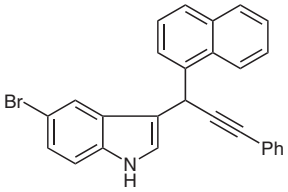
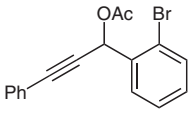
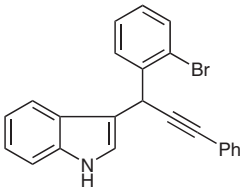
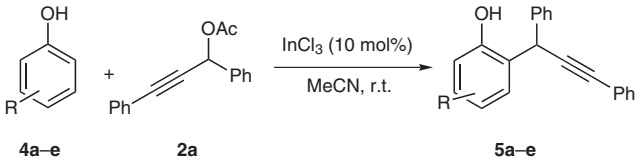
Entry	Indole		Propargyl acetate	Time (h)	Product		Yield (%)[b]
1	**1a**		**2a** 	3	**3a**		68
2	**1b**		**2a**	17	**3b**		73
3	**1c**		**2a**	24	**3c**		47
4	**1d**		**2a**	3	**3d**		99
5	**1e**		**2a**	5	**3e**		86

Table 2 InCl$_3$-Catalyzed Propargylation of Indoles with Propargylic Acetates[a] (continued)

Entry	Indole	Propargyl acetate	Time (h)	Product	Yield (%)[b]
6	**1f** 	**2a**	18	**3f** 	77
7	**1g** 	**2a**	16	**3g** 	48
8	**1h** 	**2b** 	17	**3h** 	82
9	**1i** 	**2c** 	14	**3i** 	97
10	**1a**	**2d** 	24	**3j** 	37

[a] **1/2** = 1:1. Reaction temperature: r.t., catalyst loading = 10 mol%.
[b] Isolated yield.

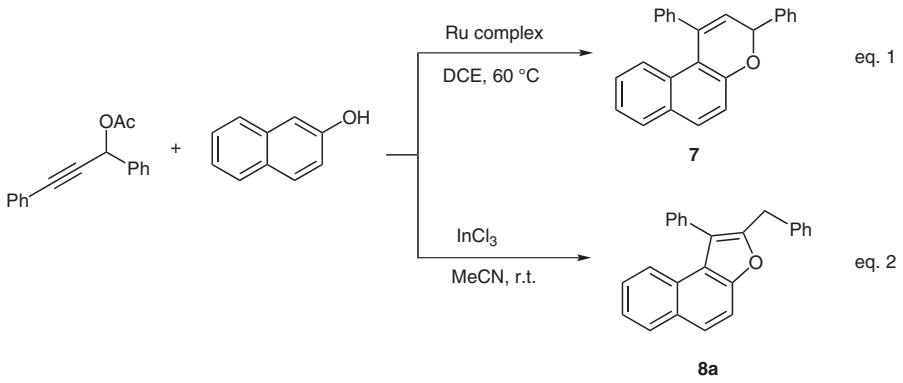


4a–e **2a** **5a–e**

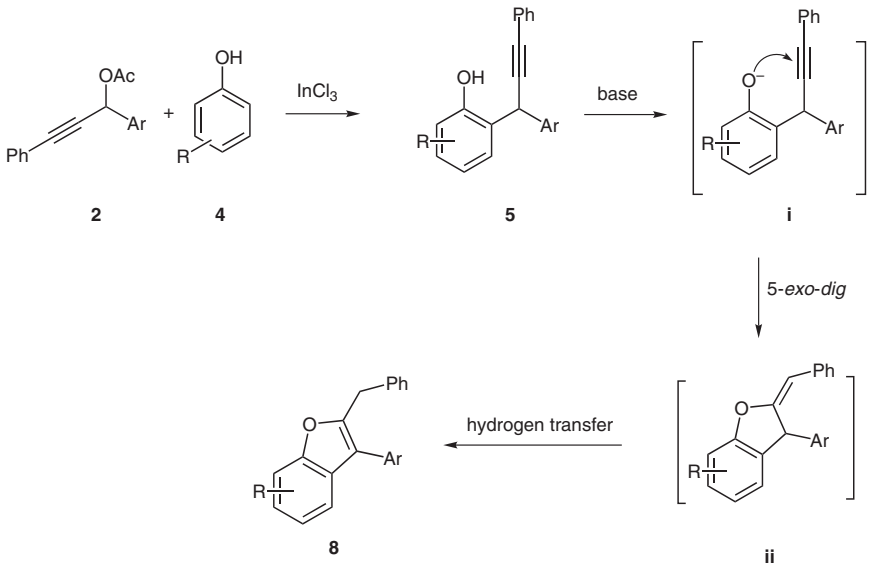
Scheme 2

As reported by Uemura,[19] the reaction of 2-naphthol (**4a**) with propagylic alcohols under the catalysis of ruthenium complex gave propargylation/cyclization product, naphthopyran **7** (Scheme 3, equation 1). However, in contrast to Uemura's result, our investigation indicated that under basic conditions (*t*-BuOK/THF), the propargylation/cyclization product was naphthofuran **8a** in 74% yield (Scheme 3, equation 2). The opposite result was attributed to the use of base, which could trap the proton of propargylated phenols **5**, and facilitate *exo*-attack of the generated oxo-anion (**i**) to triple bond rather than *endo*-attack, thus affording fused five-member ring system (**ii**).[20] Finally, the benzofuran product **8** was obtained by hydrogen transfer. The reaction sequence is presented in the proposed mechanism shown in Scheme 3. Benzofurans can be prepared under basic conditions through two synthetic pathways (Scheme 4). Pathway I starts from propargylated products. With the optimized conditions in hand, substrate scope of the reaction was studied. Several propargylated phenols **5a–c** afforded benzofurans and naphthofurans **8a–c** in good to excellent yields (Table 4). One-pot protocol was also developed to directly synthesize benzofurans from phenols and propargylic acetate without purification of the propargylation product (Scheme 4, pathway II).

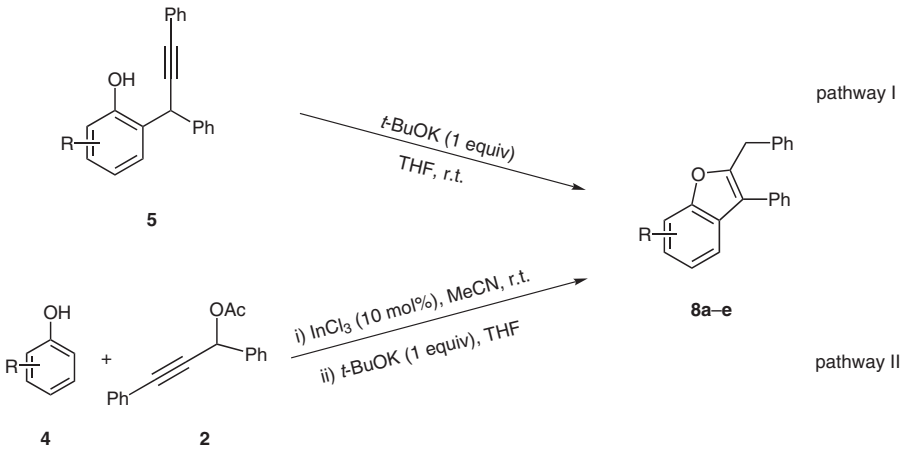
In order to pursue application of the developed protocol in the synthesis of pharmaceutically useful intermediates, 2,4-dimethylphenol (**4c**) was employed to prepare [3-(4′-hydroxybiphenyl-4-yl)benzofuran-2-yl]phenylmethane (**9**), a precursor and an analogue of benzofuran **A**, a potent drug for the treatment of type II diabetes (Scheme 5). After one-pot propargylation/cyclization, the desired product **8e** was obtained in good yield (72%). The following Suzuki coupling reaction provided **9** in excellent yield



Proposed mechanism



Scheme 3

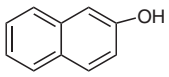
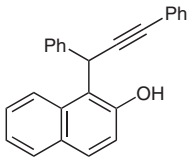
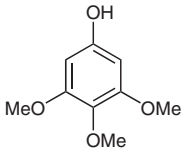
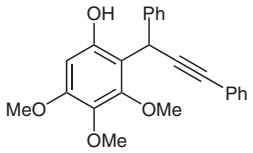
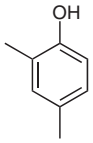
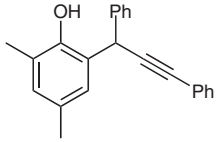
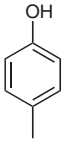
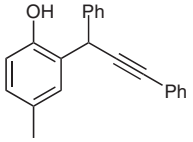
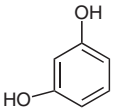
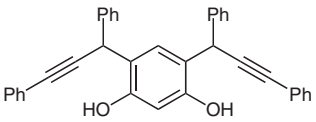


Scheme 4

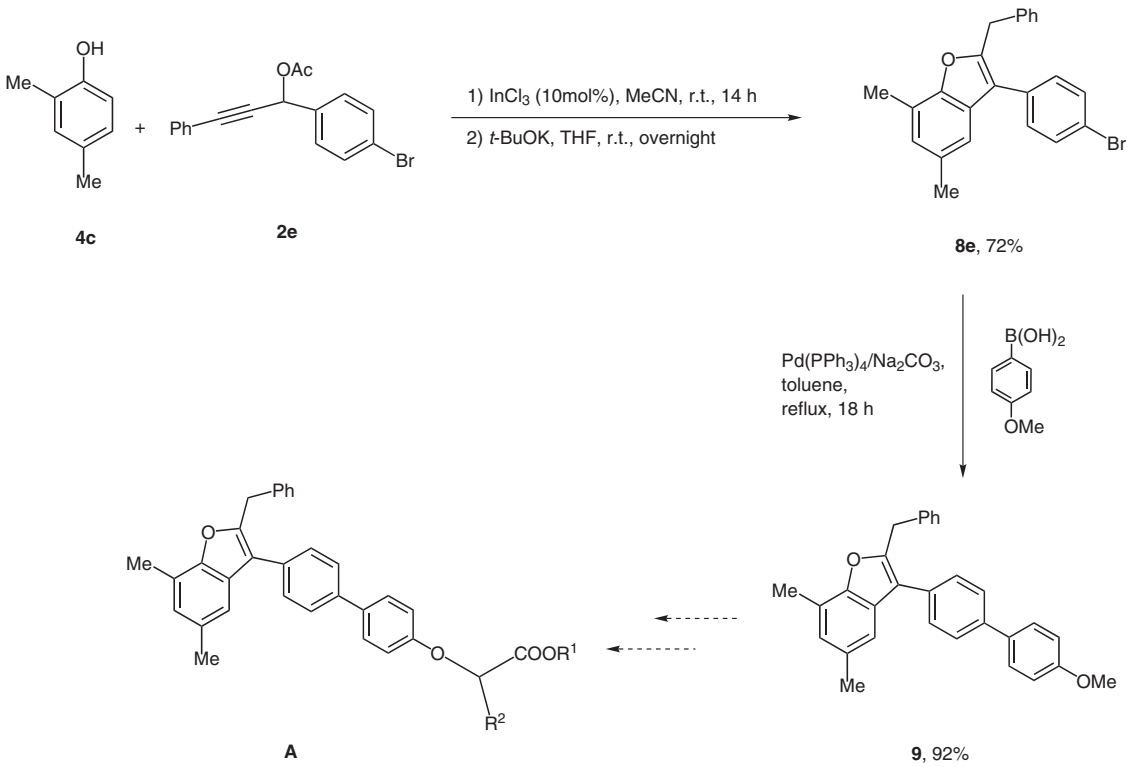
(92%). In contrast to multi-step synthetic transformations,[15] the one-pot strategy provided a mild and efficient protocol to synthesize compound **9** and therefore analogues of **A**, following a sequence of the known transformations (Scheme 5).

In conclusion, a mild, efficient and regioselective propargylation of indoles and phenols catalyzed by $InCl_3$ has been developed, which combined with selective cyclization provides 2-benzyl-3-arylbenzofurans and -naphthofurans. Studies on detailed reaction mechanism and

Table 3 $InCl_3$-Catalyzed Propargylation of Phenols with **2a**[a]

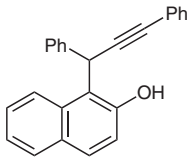
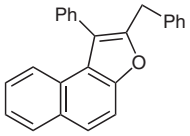
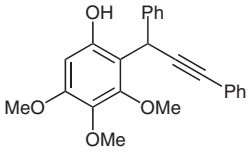
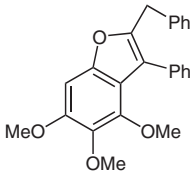
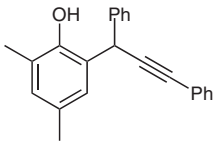
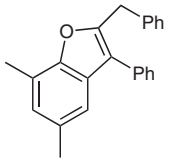
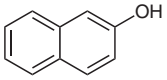
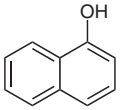
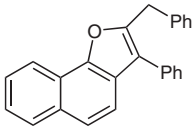
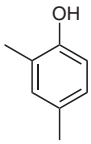
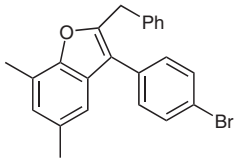
Entry		Phenol	Time (h)	Product	Yield (%)[b]
1	**4a**		10	**5a** 	95
2	**4b**		8	**5b** 	54
3	**4c**		4	**5c** 	82
4	**4d**		5	**5d** 	61[c]
5[d]	**4e**		6	**5e** 	86

[a] **4/2a** = 1: 1, reaction temperature: r.t., catalyst loading: 10 mol%.
[b] Isolated yield.
[c] With disubstituted product **6** (11%).
[d] **4e/2a** = 1:2.



Scheme 5

Table 4 Syntheses of Benzofuran and Naphthofuran

Entry		Substrate	Time (h)	Pathway		Product	Yield (%)[a]
1	**5a**		5	I[b]	**8a**		91
2	**5b**		8	I	**8b**		61
3	**5c**		5	I	**8c**		43
4	**4a**		15	II[c]	**8a**		74
5	**4f**		14	II	**8d**		46[d]
6	**4c**		24	II[e]	**8e**		72

[a] Isolated yield.
[b] Pathway I: THF/*t*-BuOK, r.t.
[c] Pathway II: with **2a** catalyzed by $InCl_3$, then under THF/*t*-BuOK, r.t.
[d] With 38% propargylated 1-naphthol.
[e] Pathway II: with **2e**.

asymmetric propargylation reactions are underway in our laboratory.

^{1}H NMR spectra were recorded on Bruker 300 (300 MHz) spectrometer. Chemical shifts are reported in ppm with TMS as an internal standard. EI and HRMS spectra were recorded on GCT-MS Micromass UK. IR analyses were performed with a Bruker FT-IR spectrophotometer. Melting points were measured with a Beijing-Taike X- 4 apparatus and are uncorrected. Petroleum ether used refers to the fraction boiling in the range 30–60 °C.

Propargylation of Indoles and Phenols; 1-(1,3-Diphenylprop-2-ynyl)-2-naphthol (5a); Typical Procedure

To a solution of 2-naphthol (**4a**; 144 mg, 1.0 mmol) and propargylic acetate (**2a**; 250 mg, 1.0 mmol) in MeCN (10 mL), was added $InCl_3$ (22 mg, 0.1 mmol), followed by stirring at r.t. for 10 h. TLC showed that the starting materials were consumed completely. Then H_2O (10 mL) was added to quench the reaction. The aqueous layer was extracted with Et_2O (3 × 20 mL) and the organic layers were combined and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by flash chromatography on silica gel (eluent: EtOAc–petroleum ether, 1:20) to give the desired product **5a**[9a] in 95% yield.

3-(1,3-Diphenylprop-2-ynyl)-1*H*-indole (3a)

Brown liquid.

IR (film): 3419, 3057, 2924, 1598, 1490, 1455, 744, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.42 (s, 1 H) 6.96–7.59 (m, 15 H), 7.70 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.6, 83.5, 90.7, 111.4, 116.9, 119.7, 122.3, 122.8, 123.8, 126.2, 127.0, 128.0, 128.1, 128.4, 128.6, 131.8, 137.0, 141.4.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{17}N$: 307.1361; found: 307.1359.

3-(1,3-Diphenylprop-2-ynyl)-2-methyl-1*H*-indole (3b)

Green liquid.

IR (film): 3407, 3057, 2923, 1597, 1489, 1458, 753, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 5.51 (s, 1 H), 7.06–7.668 (m, 14 H), 7.70 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2, 33.8, 83.6, 90.2, 110.3, 111.4, 119.0, 119.5, 121.2, 123.8, 126.5, 127.4, 127.5, 127.8, 128.2, 128.4, 131.6, 131.7, 135.2, 141.4.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{19}N$: 321.1517; found: 321.1515.

3-(1,3-Diphenylprop-2-ynyl)-1-methyl-1*H*-indole (3c)
Brown oil.

IR (film): 3056, 3027, 2927, 1597, 1489, 1369, 755, 739, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 3 H), 5.45 (s, 1 H), 6.96–7.63 (m, 15 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 35.4, 83.2, 90.7, 109.3, 115.4, 119.1, 119.7, 131.8, 123.8, 126.5, 126.7, 127.3, 127.8, 127.9, 128.2, 128.5, 131.7, 137.5, 141.5.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{19}N$: 321.1517; found: 321.1520.

3-(1,3-Diphenylprop-2-ynyl)-4-nitro-1*H*-indole (3d)
Red solid; mp 165–167 °C.

IR (KBr): 3358, 3020, 2921, 1562, 1321, 1286, 1225, 752, 730 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.87 (s, 1 H), 7.19–7.78 (m, 14 H), 8.48 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 36.2, 83.8, 90.7, 117.1, 117.4, 117.8, 117.9, 121.1, 123.5, 127.0, 127.8, 127.9, 128.1, 128.3, 128.6, 131.7, 139.2, 141.0, 143.6.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}N_2O_2$: 352.1212; found: 352.1209.

3-(1,3-Diphenylprop-2-ynyl)-4-bromo-1*H*-indole (3e)
Brown liquid.

IR (film): 3424, 3060, 2923, 1599, 1488, 909, 759, 692 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.25 (s, 1 H), 6.95–7.50 (m, 14 H), 8.01 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.5, 83.4, 91.6, 110.7, 114.0, 117.8, 123.1, 123.8, 124.4, 124.6, 125.4, 126.7, 127.8, 128.1, 128.2, 128.4, 131.7, 137.7, 142.3.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}BrN$: 385.0466; found: 385.0471.

3-(1,3-Diphenylprop-2-ynyl)-6-fluoro-1*H*-indole (3f)
Red liquid.

IR (film): 3427, 3063, 2925, 1617, 1494, 1137, 908, 836, 702, 604 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.42 (s, 1 H), 6.83 (t, *J* = 8.9 Hz, 1 H), 7.04 (d, *J* = 7.4 Hz, 1 H), 7.11 (s, 1 H), 7.25–7.53 (m, 11 H), 7.99 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.5, 83.5, 90.2, 97.3, 97.7, 108.3, 108.6, 117.2, 120.4, 120.5, 122.7, 122.8, 122.8, 123.6, 127.0, 127.9, 127.9, 128.2, 128.5, 131.7, 136.63, 136.79, 141.0, 158.5, 161.6.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}FN$: 325.1267; found: 325.1269.

3-(1,3-Diphenylprop-2-ynyl)-1-benzenesulfonylindole (3g)
Red liquid.

IR (film): 3062, 2923, 1597, 1490, 1372, 1178, 749, 687, 585 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.32 (s, 1 H), 7.12–7.98 (m, 20 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.4, 84.3, 88.7, 113.8, 120.4, 123.2, 123.3, 123.6, 124.3, 124.9, 126.8, 127.4, 127.9, 128.2, 128.3, 128.7, 129.3, 129.4, 131.7, 133.8, 135.8, 138.2, 139.5.

HRMS (EI): *m*/*z* calcd for $C_{29}H_{21}NO_2S$: 447.1293; found: 447.1289.

Ethyl 3-[1-(4-Methylphenyl)-3-phenylprop-2-ynyl]-1*H*-indole-2-carboxylate (3h)
Yellow oil.

IR (film): 3334, 3054, 2923, 1689, 1242, 743, 690 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3H), 2.27 (s, 3 H), 4.46 (m, 2 H), 6.52 (s, 1 H), 7.05–8.02 (m, 13 H), 8.95 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 21.1, 33.4, 61.3, 84.0, 90.2, 112.0, 120.4, 122.67, 122.9, 123.0, 123.8, 125.7, 126.5, 127.4, 127.9, 128.3, 129.1, 131.7, 136.2, 136.3, 138.0, 162.3.

HRMS (EI): *m*/*z* calcd for $C_{27}H_{23}NO_2$: 393.1729; found: 393.1726.

3-[1-(2-Naphthyl)-3-phenylprop-2-ynyl]-5-bromo-1*H*-indole (3i)
Black liquid.

IR (film): 3430, 3056, 2923, 1599, 1451, 736, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.52 (s, 1 H), 7.03–7.94 (m, 17 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.5, 84.0, 90.0, 112.8, 113.0, 116.5, 122.2, 123.5, 124.0, 125.2, 125.9, 126.2, 126.3, 127.7, 127.9, 128.0, 128.1, 128.3, 128.5, 131.8, 132.6, 133.5, 135.4, 138.3.

HRMS (EI): *m*/*z* calcd for $C_{27}H_{18}BrN$: 435.0623; found: 435.0618.

3-[1-(2-Bromophenyl)-3-phenylprop-2-ynyl]-1*H*-indole (3j)
Brown liquid.

IR (film): 3419, 3057, 2925, 1489, 1457, 741, 691 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.90 (s, 1 H), 7.05–7.65 (m, 14 H), 7.99 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.4, 83.2, 89.7, 111.3, 115.7, 119.7, 119.7, 122.3, 123.1, 123.5, 123.9, 126.0, 127.9, 128.0, 128.2, 128.6, 130.2, 131.8, 132.9, 136.7, 140.5.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{16}BrN$: 385.0466; found: 385.0464.

2-(1,3-Diphenylprop-2-ynyl)-3,4,5-trimethoxyphenol (5b)
Colorless liquid.

IR (film): 3466, 2925, 1602, 1462, 1200, 1081, 757, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 3.83 (s, 3 H), 3.88 (s, 3 H), 5.83 (s, 1 H), 6.14 (s, 1 H), 6.30 (s, 1 H), 7.23–7.49 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.3, 55.8, 61.0, 61.4, 85.5, 88.4, 97.5, 112.2, 122.5, 127.1, 127.1, 128.4, 128.5, 128.7, 131.8, 136.1, 139.9, 151.1, 153.4.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{22}O_4$: 374.1518; found: 374.1514.

2,4-Dimethyl-6-(1,3-diphenylpropyn-2-yl)phenol (5c)
Orange liquid.

IR (film): 3463, 2923, 1645, 1601, 1488, 757, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 3 H), 2.23 (s, 3 H), 5.24 (s, 1 H), 5.38 (s, 1 H), 6.86 (s, 1 H), 6.99 (s, 1 H), 7.19–7.48 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 20.6, 39.1, 85.6, 89.1, 123.1, 124.9, 126.6, 127.1, 127.7, 127.8, 128.3, 128.7, 129.7, 130.8, 131.8, 140.3, 149.6.

4-Methyl-2-(1,3-diphenylprop-2-ynyl)phenol (5d)
Colorless liquid.

IR (film): 3536, 3058, 2923, 1599, 1497, 1266, 812, 756, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 5.26 (s, 1 H), 5.43 (s, 1 H), 6.68–7.48 (m, 13 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7, 38.5, 85.3, 89.2, 116.6, 123.1, 127.1, 127.2, 127.8, 128.3, 128.4, 128.7, 129.1, 130.1, 130.4, 131.8, 140.4, 151.1.

HRMS (EI): *m*/*z* calcd for $C_{22}H_{18}O$: 298.1358; found: 298.1361.

2,4-Bis(1,3-diphenylprop-2-ynyl)resorcinol (5e)
Red liquid.

IR (film): 3533, 2946, 1602, 1491, 1278, 1195, 836, 757, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.34 (d, *J* = 4.8 Hz, 2 H), 5.49 (s, 2 H), 6.31 (d, *J* = 3.1 Hz, 1 H), 7.22–7.46 (m, 21 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.2, 38.3, 85.5, 85.6, 89.0, 89.1, 105.2, 105.3, 120.0, 122.9, 127.1, 127.6, 127.7, 128.3, 128.7, 130.5, 131.8, 140.4, 140.5, 153.6, 153.7.

HRMS (EI): *m*/*z* calcd for $C_{36}H_{26}O_2$: 490.1933; found: 490.1937.

3-Aryl-2-benzylbenzofurans and 3-Aryl-2-benzylnaphthofurans; 2-Benzyl-1-phenylnaphtho[2,1-*b*]furan (8a); Typical One-Pot Procedure
To a solution of 2,4-dimethylphenol (**4c**; 183 mg, 1.5 mmol) and 1-phenyl-3-(4′-bromophenyl)propargyl-3-ol acetate (**2e**; 493 mg, 1.5 mmol) in MeCN (10 mL), was added $InCl_3$ (33 mg, 0.15 mmol), followed by stirring at r.t. for 14 h. Then the solvent was evaporated and the residue was dissolved in THF (15 mL). *t*-BuOK (179 mg, 1.0 equiv) was added and the resulting mixture was stirred overnight at r.t. Then H_2O (15 mL) was added to quench the reaction and the aqueous media was extracted with Et_2O (2 × 25 mL). The organic layers were combined, and dried (Na_2SO_4). The crude product was purified by flash chromatography on silica gel (EtOAc–petroleum ether, 1:25) to give the product **8e** in 72% overall yield.

Colorless liquid.

IR (film): 3058, 3029, 2924, 1606, 1392, 1277, 1232, 1005, 804, 738, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.06 (s, 2 H), 7.18–7.89 (m, 16 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 112.3, 120.0, 122.2, 123.2, 124.1, 125.0, 125.8, 126.5, 127.9, 128.1, 128.6, 128.8, 128.9, 130.6, 130.8, 133.9, 138.2, 151.7, 152.8.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{18}O$: 334.1358; found: 334.1361.

2-Benzyl-4,5,6-trimethoxy-3-phenylbenzofuran (8b)
Orange liquid.

IR (film): 3060, 3028, 2933, 1615, 1468, 1238, 1000, 810, 765, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.50 (s, 3 H), 3.85 (s, 3 H), 3.88 (s, 3 H), 4.05 (s, 2 H), 6.82 (s, 1 H), 7.20–7.51 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.6, 56.3, 61.3, 61.4, 91.5, 115.0, 117.9, 126.5, 127.1, 127.9, 128.5, 128.5, 130.1, 132.8, 138.2, 138.8, 146.7, 151.1, 151.5, 151.8.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{22}O_4$: 374.1518; found: 374.1520.

2-Benzyl-5,7-dimethyl-3-phenylbenzofuran (8c)
Yellow liquid.

IR (film): 3028, 2922, 1605, 1201, 982, 848, 732, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.46 (s, 3 H), 4.20 (s, 2 H), 6.90–7.48 (m, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, 21.3, 32.9, 117.0, 118.3, 120.8, 126.2, 126.4, 127.1, 128.3, 128.5, 128.6, 128.7, 129.1, 132.2, 133.0, 138.2, 151.8, 152.3.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{20}O$: 312.1514; found: 312.1516.

2-Benzyl-3-phenylnaphtho[1,2-*b*]furan (8d)
Pale yellow solid; mp 95–97 °C.

IR (KBr): 3058, 3029, 2923, 1494, 1392, 1005, 804, 736, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.07 (s, 2 H), 7.02–7.29 (m, 6 H), 7.37 (t, *J* = 7.0 Hz, 1 H), 7.48–7.53 (m, 5 H), 7.60–7.74 (m, 3 H), 7.90 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 112.3, 120.0, 122.2, 123.2, 124.1, 125.0, 125.8, 126.5, 127.8, 128.1, 128.5, 128.7, 128.8, 130.6, 130.8, 133.9, 138.2, 151.7, 152.7.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{18}O$: 334.1358, found: 334.1361.

2-Benzyl-5,7-dimethyl-3-(4-bromophenyl)benzofuran (8e)
Yellow liquid.

IR (film): 3029, 2923, 1605, 1492, 1284, 1201, 983, 848, 729 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.46 (s, 3 H), 4.15 (s, 2 H), 6.90–7.57 (m, 11 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0, 21.3, 33.0, 116.7, 117.3, 120.9, 121.2, 126.5, 126.6, 127.9, 128.4, 128.6, 130.7, 131.9, 132.0, 132.5, 138.0, 151.8, 152.6.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{19}BrO$: 390.0619; found: 390.0622.

2-Benzyl-5,7-dimethyl-3-(4-methoxybiphenyl)benzofuran (9)
White solid; mp 128–130 °C.

IR (KBr): 3030, 2923, 1606, 1498, 1249, 983, 823, 735 cm^{-1}.

^{1}H NMR (300 MHz,$CDCl_3$): δ = 2.39 (s, 3 H), 2.47 (s, 3 H), 3.84 (s, 3 H), 4.23 (s, 2 H), 6.91–7.65 (m, 15 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0, 21.3, 33.0, 55.4, 114.3, 117.1, 118.0, 120.8, 126.3, 126.5, 127.0, 128.1, 128.3, 128.5, 128.6, 129.4, 131.3, 132.3, 133.4, 138.3, 139.6, 151.8, 152.4, 159.3.

HRMS (EI): *m*/*z* calcd for $C_{30}H_{26}O_2$: 418.1933; found: 418.1936.

Acknowledgment

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