Palladium-Catalyzed Esterification-Hydroarylation Reactions of 2-Alkynylbenzaldehydes with Aryl Iodides in Methanol

Li-Lan Wei,[b,c] Li-Mei Wei,[b] Wen-Bin Pan,[b] Ming-Jung Wu*[a]

[a] Faculty of Medicinal and Applied Chemistry, Kaohsiung Medicial University, 807 Kaohsiung, Taiwan
E-mail: mijuwu@cc.kmu.edu.tw

[b] Fooyin University, 831 Kaohsiung county, Taiwan

[c] Graduate Institute of Pharmaceutical Science, Kaohsiung Medicial University, 807 Kaohsiung, Taiwan

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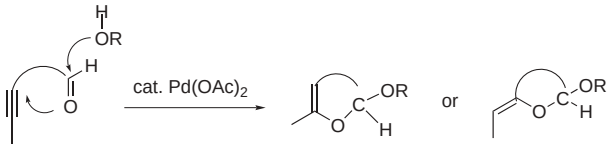
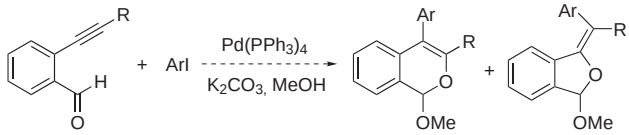
Abstract: The reaction of 2-alkynylbenzaldehydes with aryl iodides in the presence of $Pd(PPh_3)_4$ and K_2CO_3 in refluxing methanol for 24 hours gave the dehydrogenation-addition products, methyl 2-(2,2-disubstituted-vinyl)benzoates in modest yields; together with the cyclization products, 3-methoxy-1-monosubstituted-methylene-3-hydroisobenzofurans in 3–18% yields.

Key words: palladium, coupling, esterification-hydroarylation, 2-alkynylbenzaldehydes

The palladium-catalyzed sequential cyclization and coupling reactions of acetylenic molecules containing a heteronucleophile with organic halides or triflates are a well established strategy that has led to the successful synthesis of a variety of heterocycles.[1] For example, the palladium-induced intermolecular cyclization of acetylenic alcohols has been shown to be an efficient route to exocyclic enol ethers.[2] In the same manner, *o*-ethynylphenols have been converted to 2-substituted benzo[*b*]furans.[3] This methodology has also been applied to molecules bearing amino-,[4] carboxyl-,[5] and carbo-nucleophiles.[6] Recently we reported an analogous palladium-promoted coupling of 2-alkynylbenzonitriles with aryl iodides for the synthesis of 3,4-disubstituted isoquinolines and diarylmethylideneisoindoles in one step.[7] More recently, we also have established a novel route to synthesize 2-(diarylmethylene)-3-benzofuranones by palladium-catalyzed cyclization of 3-aryl-1-(2-*tert*-butyldimethylsilyoxy)phenyl-2-propyn-1-ones in moderate to good yields.[8] Yamamoto et al. have reported that the Pd(II) catalyst can act both as a Lewis acid and catalyst; whereby alkynyl aldehydes and ROH in the presence of $Pd(OAc)_2$ were found to afford the alkenyl cyclic ethers in good to high yields (Equation 1).[9] Our continuing interest in the successive annulation/coupling reaction of 2-alkynylbenzaldehydes **1** with aryl iodides **2** to give the coupling products encouraged us to further examine the palladium-catalyzed addition/coupling sequences of acetylenic aldehydes (Equation 2).



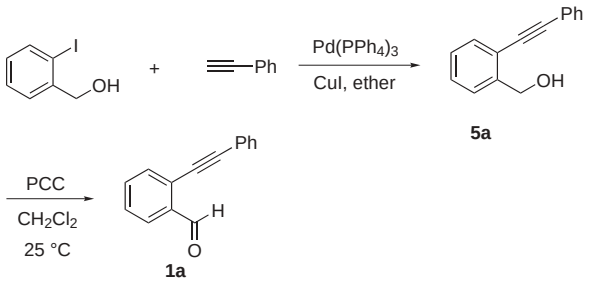
Equation 1



1 **2**

Equation 2

The synthesis of starting material 2-(2-phenylethynyl)benzaldehyde (**1a**)[10] is summarized in Scheme 1. However, the first attempt for the generation of our proposed annulation/coupling products, methylene-3-methoxy-3-hydroisobenzofuran derivatives, was carried out by treatment of 2-(2-phenylethynyl)benzaldehyde (**1a**) and 4-iodotoluene (**2a**) in the presence of catalytic amount of $Pd(PPh_3)_4$ and K_2CO_3 as a base in refluxing MeOH for 24 hours to give the addition-oxidation product 2-[(1*Z*)-2,2-diphenylvinyl]benzoate **3aa** in 50% yield together with the monosubstituted methylene-3-methoxy-3-hydroisobenzofuran **4a** in 16% yield (Equation 3). The structure of **3aa** was unambiguously determined by X-ray crystallographic analysis (Figure 1).[11] Herein, we describe our results on the tandem addition-oxidation of 2-alkynylbenzaldehydes with aryl iodides in MeOH leading to regio- and stereoselective products, methyl 2-(2,2-disubstituted-vinyl)benzoates.



Scheme 1

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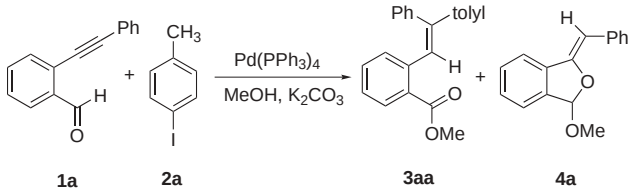


1a 2a 3aa 4a

Equation 3

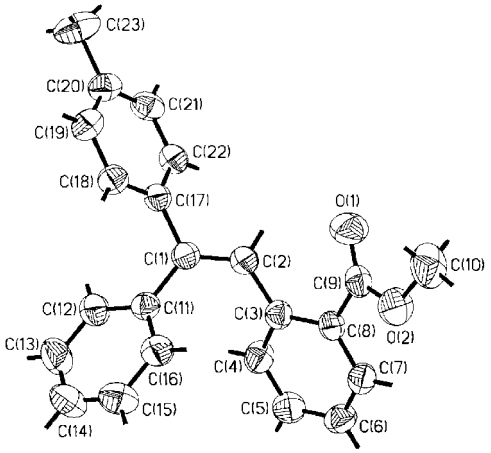


Figure 1 X-ray spectrum of compound **3aa**

Thus, various aryl iodides bearing electron-donating or electron-withdrawing groups on the phenyl ring were reacted with aryl acetylenic benzaldehyde **1** using $Pd(PPh_3)_4$ as a catalyst and K_2CO_3 as the base in MeOH to give the oxidation products **3** in 35–74% yields, along with only the cyclization products **4** in 3–18% yields. The results are summarized in Table 1. Iodobenzene (**2b**) afforded the ester **3ab** in 44% yield and uncoupled product **4a** was obtained in 18% yield (entry 2). The reaction of 4-methoxyiodobenzene (**2c**) produced **3ac** and **4a** in 53% and 5% yields, respectively (Table 1, entry 3). 2-Methoxyiodobenzene (**2d**) gave **3ad** in 35% yield and simultaneously afforded **4a** in 17% yield (entry 4), indicating that steric hindrance may reduce the rate of the addition reaction. In a further exploration of the substituent effect on the alkyne terminus on compound **1**, 2-alkynylbenzaldehydes derivatives **1b**–**d** were prepared according to the procedure described above. The reaction of 2-[2-(*p*-methoxyphenyl)ethynyl]benzaldehyde (**1b**) with 4-iodotoluene (**2a**) under the optimal reaction conditions gave the methyl benzoate **3ba** in 67% yield together with a small amount of the adduct **4b** in 5% yield (entry 5). Figure 2 shows the crystal structure of **4b**.[12] Similar results were obtained by employing other aryl iodides. Phenyl iodide (**2b**) afforded **3bb** in 50% yield along with the product **4b** in 11% yield, and *p*-methoxyphenyl iodide (**2c**) gave **3bc** in 74% yield together with the minor product **4b** in 3% yield (entries 6 and 7). Aryl iodides with an electron withdrawing group, such as 4-trifluorophenyl iodide (**2e**) and 2-iodopyridine (**2f**) produced the cyclization product **4b** in 40% and 88% yields based on recovered yields of **2**, respectively (entries 8 and 9). However, the reaction of 2-(hexynyl)benzaldehyde (**1c**) with iodobenzene (**2b**) afforded compound **3cb** in 63% yield as the only product (entry 10). Moreover, 2-[2-(4-trifluoromethylphenyl)ethynyl]benzaldehyde (**1d**) has also been examined and this gave cyclization product **4d** in 100% based on recovered yield of **2** (entry 11). The above profile suggested that the phenyl ring on the alkyne terminus carried an electron-withdrawing group, deactivating the formation of the complex between an aryl palladium and an acetylene. At the same time, it accelerated the rate of the cyclization reaction to form the uncoupled product **4d**.

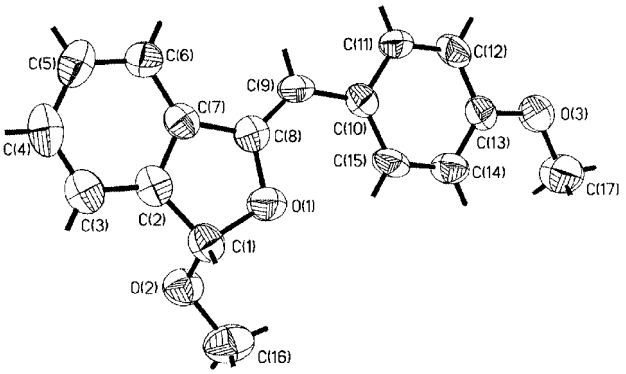
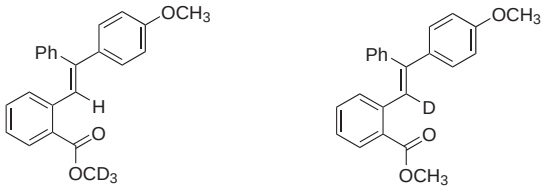


Figure 2 X-ray spectrum of compound **4b**

To investigate the mechanism of this tandem oxidation-reduction reaction, two reactions were carried out. Treatment of 4-iodoanisole with 2-(2-phenylethynyl)benzaldehyde under the optimal conditions using CD_3OD as the solvent gave the product **3ac′** in 48% yield. No deuterium incorporation was found in the vinylic position of the product. However, the reaction of deuterium-labeled **1a** (-CDO) with 4-iodoanisole in CH_3OH produced the deutero adduct **3ac″** in 56% yield.

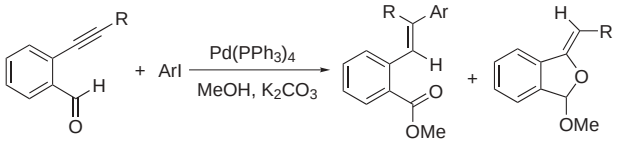


3ac' 3ac''

Figure 3

According to the above results and our previous work,[13–15] we proposed a mechanism for this esterification/addition process as shown in Scheme 2. This reaction pathway involves: (a) the oxidative addition of aryl iodide to Pd(0) to give an arylpalladium intermediate, (b) arylpalladium coordination of the carbon-carbon triple bond of **1** and subsequent regio- and stereoselective insertion of the 2-alkynylbenzaldehydes to produce a vinylpalladium intermediate **5**, (c) addition of methoxide ion to the carbonyl group to produce a cyclic oxypalladium complex **6**, which gives the palladium hydride species **7** by β-hydrogen elimination, and (d) reductive elimination of **7** to afford

Table 1 Palladium-Catalyzed Addition-Oxidation Reactions of 2-Alkynylbenzaldehydes with Aryl Iodides



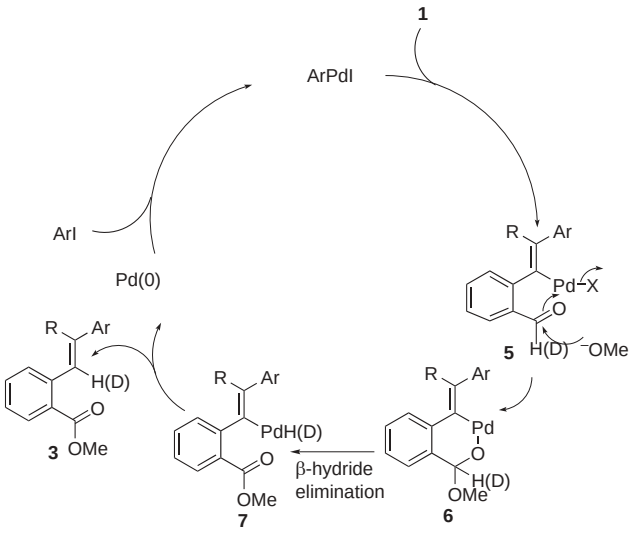
1 **2** **3** **4**

Entry	2-Alkynylbenzaldehydes	Aryl iodides	Products (Yield, %)[a]	
1	**1a** (R = C_6H_5)	**2a** (Ar = 4-tolyl)	**3aa** (50%)	**4a** (16%)
2	**1a**	**2b** (Ar = phenyl)	**3ab** (44%)	**4a** (18%)
3	**1a**	**2c** (Ar = 4-methoxyphenyl)	**3ac** (53%)	**4a** (5%)
4	**1a**	**2d** (Ar = 2-methoxyphenyl)	**3ad** (35%)	**4a** (17%)
5	**1b** (R = 4-$CH_3OC_6H_4$)	**2a**	**3ba** (67%)	**4b** (5%)
6	**1b**	**2b**	**3bb** (50%)	**4b** (11%)
7	**1b**	**2c**	**3bc** (74%)	**4b** (3%)
8	**1b**	**2e** (Ar = 4-trifluoromethylphenyl)		**4b** (40%[b])
9	**1b**	**2f** (Ar = 2-pyridinyl)		**4b** (88%[b])
10	**1c** (R = *n*-C_4H_9)	**2b**	**3cb** (63%)	
11	**1d** (R = 4-$CF_3C_6H_4$)	**2b**		**4d** (100%[b])

[a] Yields refer to isolated yields. All of the compounds gave satisfactory ^1H, ^{13}C NMR and MS spectra data.
[b] Based on recovered starting material.

the stereoisomer **3**. The fact that no cyclization/coupling products were observed suggests that β-hydrogen elimination of **6** is much faster than reductive elimination of a C–O bond. Addition of hemiacetal anion to a palladacycle also explains the fact that the aryl group coming from the aryl iodide always ends up *trans* to the methyl benzoate group. Meanwhile the isotope study supported the proposed mechanism, which implied that the hydrogen source for the reduction of an alkyne to an alkene comes from formyl hydrogen of the aldehyde substituent of the substrate. The other plausible reaction pathway involving oxidation insertion into the aldehyde C–H bond to form a palladium(IV) intermediate have been reported by several research groups[16] in the similar reactions. We feel that further experiments are needed to prove the exact reaction pathway.

In conclusion, the novel palladium(0)-catalyzed cascade addition/oxidation reaction of 2-alkynylbenzaldehydes with aryl iodides in MeOH affords one-step synthesis of stereoisomerical methyl 2-(2,2-disubstituted-vinyl)benzoates. These products are formed regio- and stereoselectively in modest yields. This tandem process simultaneously couples the oxidation of an aldehyde to an ester with the hydroarylation of an alkyne to an alkene. Currently, the optimization of the selectivity of the tandem transformations of 2-alkynylbenzaldehydes with aryl iodides to 2-vinylbenzoate derivatives is under investigation.



Scheme 2

Addition-Oxidation Reaction of 2-(2-Phenylethynyl)benzaldehydes with Aryl Iodides; Typical Procedure

A slurry of the 2-(2-phenylethynyl)benzaldehyde **1a** (0.3 mmol), aryl iodides **2** (0.6 mmol), $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 (1.5 mmol) in refluxing MeOH (8 mL) was stirred for 24 h. The reaction mixture was filtered through a short pad of silica gel to remove precipitated inorganic salts. The silica gel pad was washed three times with a small amount of EtOAc and the combined solution was

evaporated to dryness under reduced pressure. The residue was chromatographed on silica gel using *n*-hexane–EtOAc (v/v, 40:1) as eluent to give the products **3** and **4**.

Methyl 2-[(1*E*)-2-(4-Methylphenyl)-2-phenylvinyl]benzoate (3aa)
Compound **3aa** was obtained in 50% yield as a white solid; mp 75–76 °C.

^{1}H NMR (200 MHz, C_6D_6): δ = 7.96–7.92 (m, 1 H), 7.76 (s, 1 H), 7.37 (dt, *J* = 8.2, 2.0 Hz, 2 H), 7.24–7.19 (m, 2 H), 7.07–6.93 (m, 6 H), 6.83–6.78 (m, 2 H), 3.45 (s, 3 H), 2.11 (s, 3 H).

^{13}C NMR (50 MHz, C_6D_6): δ = 168.2, 144.1, 141.6, 141.5, 141.0, 138.1, 132.7, 132.1, 132.0, 131.4, 131.2, 130.0, 129.1, 129.0, 128.5, 128.0, 127.2, 52.2, 21.7.

Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.11; H, 6.14. Found: C, 84.09; H, 6.13.

Methyl 2-(2,2-Diphenylvinyl)benzoate (3ab)
Compound **3ab** was obtained in 44% yield as a white solid; mp 98–100 °C.

^{1}H NMR (200 MHz, C_6D_6): δ = 7.91–7.86 (m, 1 H), 7.69 (s, 1 H), 7.40–7.35 (m, 2 H), 7.15–7.00 (m, 6 H), 6.99–6.90 (m, 3 H), 6.79–6.73 (m, 2 H), 3.40 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.2, 144.3, 144.2, 141.3, 140.9, 132.6, 132.1, 131.4, 131.2, 129.2, 129.1, 128.1, 127.3, 52.2.

Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.04; H, 5.78. Found: C, 83.78; H, 5.87.

Methyl 2-[(1*E*)-2-(4-Methoxyphenyl)-2-phenylvinyl]benzoate (3ac)
Compound **3ac** was obtained in 53% yield as a white solid; mp 90–92 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 7.95–7.92 (m, 1 H), 7.73 (s, 1 H), 7.35 (dt, *J* = 8.8, 2.8 Hz, 2 H), 7.24–7.21 (m, 2 H), 7.06–6.97 (m, 4 H), 6.86–6.78 (m, 2 H), 6.73 (dt, *J* = 6.4, 3.2 Hz, 2 H), 3.47 (s, 3 H), 3.30 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.3, 160.6, 143.9, 141.6, 141.1, 136.9, 132.7, 132.1, 132.0, 131.4, 131.2, 130.4, 129.1, 128.1, 127.6, 127.1, 114.7, 55.5, 52.2.

Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.20; H, 5.86. Found: C, 80.27; H, 5.87.

Methyl 2-[(1*E*)-2-(2-Methylphenyl)-2-phenylvinyl]benzoate (3ad)
Compound **3ad** was obtained in 35% yield as a white solid; mp 121–122 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 7.94–7.92 (m, 1 H), 7.60 (s, 1 H), 7.42 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.26 (dt, *J* = 6.4, 2.0 Hz, 2 H), 7.15–7.10 (m, 1 H), 6.98–6.82 (m, 7 H), 6.56 (dd, *J* = 8.4, 1.2 Hz, 1 H), 3.41 (s, 3 H), 3.14 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.1, 158.7, 142.2, 141.5, 141.1, 132.9, 132.6, 132.1, 131.5, 131.2, 131.1, 131.0, 129.7, 128.8, 127.9, 127.5, 127.3, 121.6, 112.7, 55.9, 52.2.

Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.20; H, 5.86. Found: C, 80.06; H, 5.83.

Methyl 2-[(1Z)-2-(4-Methoxyphenyl)-2-(4-methylphenylvinyl)]benzoate (3ba)
Compound **3ba** was obtained in 67% yield.

^{1}H NMR (400 MHz, C_6D_6): δ = 8.07–8.05 (m, 1 H), 7.81 (s, 1 H), 7.51 (dt, *J* = 8.0, 2.0 Hz, 2 H), 7.26–7.22 (m, 3 H), 7.10–7.08 (m, 2 H), 6.96–6.93 (m, 2 H), 6.70 (dt, *J* = 8.8, 2.4 Hz, 2 H), 3.56 (s, 3 H), 3.29 (s, 3 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.4, 160.1, 143.9, 142.1, 141.4, 138.1, 133.5, 133.3, 132.7, 132.1, 131.5, 131.3, 129.9, 129.3, 127.8, 127.1, 114.7, 55.2, 52.2, 21.8.

MS (EI): *m*/*z* = 358 (100) [M$^+$], 299 (14), 269 (15).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{22}O_3$: 358.1569; found: 358.1537.

Methyl 2-[(1Z)-2-(4-Methoxyphenyl)-2-(phenylvinyl)]benzoate (3bb)
Compound **3bb** was obtained in 50% yield as a yellow solid; mp 84–86 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 7.96–7.94 (m, 1 H), 7.70 (s, 1 H), 7.47 (dt, *J* = 6.8, 1.6 Hz, 2 H), 7.15–7.09 (m, 6 H), 6.86–6.83 (m, 2 H), 6.59 (td, *J* = 8.8, 2.4 Hz, 2 H), 3.45 (s, 3 H), 3.19 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.3, 160.1, 144.8, 144.0, 141.3, 133.3, 133.3, 132.7, 132.1, 131.5, 131.2, 129.4, 129.2, 128.6, 128.5, 127.2, 114.7, 55.2, 52.2.

Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.20; H, 5.86. Found: C, 80.20; H, 5.98.

Methyl 2-[2-(4-Methoxyphenyl)-2-(4-methoxyphenylvinyl)]benzoate (3bc)
Compound **3bc** was obtained in 74% yield.

^{1}H NMR (400 MHz, C_6D_6): δ = 7.98–7.95 (m, 1 H), 7.69 (s, 1 H), 7.41 (dt, *J* = 9.2, 2.4 Hz, 2 H), 7.18–7.13 (m, 3 H), 6.87–6.83 (m, 2 H), 6.77 (dt, *J* = 9.2, 2.4 Hz, 2 H), 6.62 (dt, *J* = 8.8, 2.0 Hz, 2 H), 3.48 (s, 3 H), 3.31 (s, 3 H), 3.20 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 168.3, 160.7, 160.1, 143.7, 141.5, 137.3, 133.6, 133.4, 132.7, 132.1, 131.5, 131.3, 130.6, 127.0, 126.9, 114.7, 114.7, 55.5, 55.3, 52.2.

MS (EI): *m*/*z* = 374 (100) [M$^+$], 314 (10).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{22}O_4$: 374.1518; found: 374.1534.

Methyl 2-[(1*E*)-2-Phenylhex-1-enyl]]benzoate (3cb)
Compound **3cb** was obtained in 63% yield.

^{1}H NMR (400 MHz, C_6D_6): δ = 8.03 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.62 (dt, *J* = 7.6, 1.2 Hz, 2 H), 7.40 (s, 1 H), 7.29–7.11 (m, 5 H), 7.03–6.99 (m, 1 H), 3.46 (s, 3 H), 2.57 (t, *J* = 7.6 Hz, 2 H), 1.33–1.29 (m, 2 H), 1.13–1.08 (m, 2 H), 0.63 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 167.9, 143.9, 142.3, 141.4, 132.4, 131.7, 131.6, 131.0, 129.7, 129.4, 128.0, 127.9, 127.5, 52.1, 31.5, 30.5, 23.2, 14.5.

MS (EI): *m*/*z* = 294 (73) [M$^+$], 236 (38), 219 (100).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{22}O_2$: 294.1620; found: 294.1621.

3-Methoxy-1-(phenylmethylene)-3-hydroisobenzofuran (4a)
Compound **4a** was obtained in 5–18% yield.

^{1}H NMR (200 MHz, C_6D_6): δ = 7.99 (d, *J* = 7.4 Hz, 2 H), 7.34 (t, *J* = 7.6 Hz, 2 H), 7.17–7.05 (m, 3 H), 7.02–6.96 (m, 2 H), 6.25 (s, 1 H), 6.00 (s, 1 H), 3.15 (s, 3 H).

^{13}C NMR (50 MHz, C_6D_6): δ = 154.2, 138.3, 137.3, 136.8, 130.5, 129.6, 129.5, 129.5, 127.0, 124.0, 120.7, 108.5, 99.5, 54.4.

MS (EI): *m*/*z* = 238 (55) [M$^+$], 206 (30), 178 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}O_2$: 238.0994; found: 238.1003.

3-Methoxy-1-[(4-methoxyphenyl)methylene]-3-hydroisobenzofuran (4b)
Compound **4b** was obtained in 3–88% yield as a white solid; mp 97–99 °C.

^{1}H NMR (200 MHz, C_6D_6): δ = 7.94 (d, *J* = 8.8 Hz, 2 H), 7.21–6.93 (m, 6 H), 6.31 (s, 1 H), 6.01 (s, 1 H), 3.36 (s, 3 H), 3.19 (s, 3 H).

^{13}C NMR (50 MHz, C_6D_6): δ = 159.3, 152.7, 138.0, 137.1, 134.3, 130.9, 130.5, 130.0, 124.0, 120.4, 115.1, 108.3, 99.4, 55.5, 54.2.

Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.09; H, 6.01. Found: C, 75.79; H, 6.31.

3-Methoxy-1-[(4-trifluoromethylphenyl)methylene]-3-hydroisobenzofuran (4d)
Compound **4d** was obtained in 100% yield as a yellow solid; mp 55–57 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 7.76 (d, *J* = 8.0 Hz, 2 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 7.15–7.10 (m, 2 H), 7.03 (td, *J* = 7.2, 1.6 Hz, 1 H), 6.99 (td, *J* = 7.2, 1.2 Hz, 1 H), 6.16 (s, 1 H), 5.81 (s, 1 H), 3.15 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 156.0, 140.8, 138.6, 136.2, 130.6, 130.2, 129.4, 128.1, 126.3, 126.3, 124.1, 120.9, 108.8, 97.9, 54.7.

MS (EI): *m*/*z* = 306 (100) [M^+], 275 (53), 274 (40).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{13}O_2F_3$: 306.0862; found: 306.0867.

2-(2-Phenylethynyl)benzaldehyde (1a)
Compound **1a** was obtained in 88% yield.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 10.66 (s, 1 H), 7.96 (dd, *J* = 7.6, 1.5 Hz, 1 H), 7.69–7.53 (m, 4 H), 7.51–7.37 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 191.7, 135.9, 133.8, 133.2, 131.7, 129.1, 128.6, 128.5, 127.3, 126.9, 122.3, 96.3, 84.9.

MS (EI): *m*/*z* = 206 (100) [M^+], 205 (31), 178 (35), 176 (36).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}O$: 206.0732; found: 206.0730.

2-[2-(4-Methoxyphenyl)ethynyl]benzaldehyde (1b)
Compound **1b** was obtained in 92% yield as a yellow solid; mp 46–47 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 10.82 (s, 1 H), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.38–7.33 (m, 3 H), 6.93 (td, *J* = 7.6, 1.6 Hz, 1 H), 6.84 (t, *J* = 8.0 Hz, 1 H), 6.62 (dt, *J* = 9.2, 2.4 Hz, 2 H), 3.19 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 191.3, 161.3, 137.1, 134.3, 134.1, 133.7, 129.0, 128.2, 128.0, 115.6, 115.2, 97.8, 85.2, 55.5.

MS (EI): *m*/*z* = 236 (93) [M^+], 221 (70), 165 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}O_2$: 236.0832 found: 236.0834.

2-Hex-1-ynylbenzaldehyde (1c)
Compound **1c** was obtained in 90% yield.

^{1}H NMR (400 MHz, C_6D_6): δ = 10.80 (s, 1 H), 7.90 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.30 (dd, *J* = 7.6, 1.2 Hz, 1 H), 6.92 (td, *J* = 7.6, 1.6 Hz, 1 H), 6.83 (t, *J* = 7.6 Hz, 1 H), 2.11 (t, *J* = 6.8 Hz, 2 H), 1.36–1.23 (m, 4 H), 0.77 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 191.6, 137.5, 134.1, 134.0, 134.0, 127.9, 127.9, 98.8, 77.7, 31.4, 22.9, 20.0, 14.3.

MS (EI): *m*/*z* = 186 (13) [M^+], 157 (29), 144 (96), 115 (100).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{14}O$: 186.1039; found: 186.1042.

2-[2-(4-Trifluoromethylphenyl)ethynyl]benzaldehyde (1d)
Compound **1d** was obtained in 96% yield as a white solid; mp 57–58 °C.

^{1}H NMR (400 MHz, C_6D_6): δ = 10.62 (s, 1 H), 7.84 (ddd, *J* = 8.0, 1.6, 0.4 Hz, 1 H), 7.29 (ddd, *J* = 7.6, 1.2, 0.4 Hz, 1 H), 7.19–7.11 (m, 4 H), 6.91 (td, *J* = 7.6, 1.6 Hz, 1 H), 6.86 (td, *J* = 7.6, 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 190.7, 137.4, 134.1, 133.9, 132.8, 129.9, 128.6, 126.3, 126.3, 126.2, 126.2, 126.2, 95.4, 88.4.

MS (EI): *m*/*z* = 274 (100) [M^+], 205 (79), 176 (83).

HRMS (EI): *m*/*z* calcd for $C_{16}H_9OF_3$: 274.0600; found: 274.0602.

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(10) Treatment of 2-iodobenzyl alcohol with phenylacetylene in the presence of catalytic amount of $Pd(PPh_3)_4$ and CuI, *n*-$BuNH_2$ as a base in Et_2O for 5 h gave compound **5a** in 82% yield. The 2-alkynylbenzaldehyde **1a** was obtained by oxidation of **5a** with PCC in 91% yield.

(11) Crystal data for **3aa**: $C_{23}H_{20}O_2$; M = 328.39 g/mol, crystal size: 0.50 × 0.50 × 0.50 mm, monoclinic, space group $P2_1/n$, λ = 0.71073 Å, a = 9.7557 (6) Å, b = 11.9347 (7) Å, c = 15.7626 (9) Å, α = 90°, β = 99.370 (1)°, γ = 90°, V = 1810.77 (19) Å^3, Z = 4, D = 1.205 Mg/m^3. μ = 0.076 mm^{-1}, T = 295 (2) K, θ range: 2.15–27.50°, reflections collected: 17775, independent reflections: 4167 (R_{int} = 0.0303), refinement method: full-matrix least-squares on F^2, final R values[I> 2σ(I)]: *R*1 = 0.0499, *wR*2 = 0.1234. Diffractometer: BRUKER SMART APEXCCD. Crystallographic data (excluding structure factors) for this structure have been deposited at the Cambridge Crystallographic Data centre as supplementary publication no. CCDC-223977, and may be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1ED, UK [fax: +44 (1223)336033; e-mail deposit@ccdc.cam.ac.uk].

(12) Crystal data for **4b**: $C_{17}H_{16}O_3$; M = 268.30 g/mol, crystal size: 0.27 × 0.23 × 0.02 mm, orthorhombic, space group $Pca2_1$, λ = 0.71073 Å, a = 20.9353 (13) Å, b = 8.6773 (5) Å, c = 7.7543 (5) Å, α = 90°, β = 90°, γ = 90°, V = 1408.66 (15) $Å^3$, Z = 4, D = 1.265 Mg/m^3. μ = 0.086 mm^{-1}, T = 295 (2) K, θ range: 1.95–27.50°, reflections collected: 13064, independent reflections: 3220 (R_{int} = 0.0619), refinement method: full-matrix least-squares on F^2, final R values[I > 2σ(I)]: *R*1 = 0.0902, *wR*2 = 0.1693. Diffractometer: BRUKER SMART APEXCCD. Crystallographic data (excluding structure factors) for this structure have been deposited at the Cambridge Crystallographic Data center as supplementary publication no. CCDC-231702.

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