Palladium-Catalyzed Cross-Coupling Reactions of 1,2-Diiodoalkenes with Terminal Alkynes: Selective Synthesis of Unsymmetrical Buta-1,3-diynes and 2-Ethynylbenzofurans

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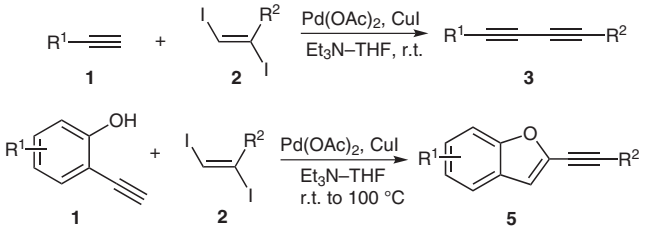
Abstract: (*E*)-1,2-Diiodoalkenes were found to be effective building blocks for the preparation of unsymmetrical buta-1,3-diynes and 2-ethynylbenzofurans. In the presence of palladium(II) acetate and copper(I) iodide, unsymmetrical buta-1,3-diynes were selectively obtained in moderate to good yields. Moreover, 2-ethynylbenzofurans were obtained in one pot from the reaction of 2-ethynylphenol with (*E*)-1,2-diiodoalkenes, palladium(II) acetate, and copper(I) iodide by simple heating.

Key words: palladium(II) acetate, copper(I) iodide, (*E*)-1,2-diiodoalkene, terminal alkyne, buta-1,3-diyne, 2-ethynylbenzofuran

Buta-1,3-diynes are an important structural motif frequently found in a wide range of natural products, bioactive molecules, and functional materials; they are also extremely valuable intermediates in organic synthesis.[1] Accordingly, considerable efforts have been devoted to the development of efficient methods for their preparation.[1–8] The Glaser coupling reaction represents one of the most reported transformations using a copper complex as the catalyst.[2] However, this technique is often unsatisfactory for the synthesis of unsymmetrical buta-1,3-diynes.[3] In 1955, the reaction of terminal alkynes with bromoacetylenes, copper(I) salts, and amines was reported by Chodliewicz and Cadiot,[4] which provided a particularly useful route for the preparation of unsymmetrical buta-1,3-diynes.[1,4,5] Subsequently, the use of palladium as a co-catalyst to improve the copper(I)-catalyzed reaction has been developed.[6] Although 1-haloalk-1-ynes are usually synthesized under highly basic conditions and are quite often unstable, little attention has been given to use other reagents as haloacetylene precursors for the reaction. Recently, 1,1-dibromoalk-1-enes instead of 1-bromoalk-1-ynes were successfully employed for the preparation of unsymmetrical buta-1,3-diynes.[7] Herein, we wish to report that the application of easily available (*E*)-1,2-diiodoalkenes,[9] as iodoacetylene precursors, reacted with terminal alkynes for the highly selective synthesis of unsymmetrical buta-1,3-diynes in the presence of palladium(II) acetate and copper(I) iodide. Furthermore, the standard conditions were extended to construct 2-ethynylbenzofurans in one pot (Scheme 1).[10]

Initially, we examined the reaction of phenylacetylene (**1a**) with (*E*)-2,3-diiodoprop-2-en-1-ol (**2a**) to explore the standard conditions (Table 1). The results showed that unsymmetrical buta-1,3-diyne **3aa** could be obtained using either copper(I) iodide or palladium(II) acetate as the catalyst, but both yield and rate were enhanced by using copper(I) iodide and palladium(II) acetate co-catalyst (entries 1–3). Without palladium(II) acetate, treatment of alkyne **1a** with **2a** and copper(I) iodide in triethylamine–tetrahydrofuran for 20 hours afforded the target product **3aa** in a 53% yield together with a homocoupling product **4aa** in a 48% yield (entry 1), whereas the addition of 1 mol% of palladium(II) acetate increased the yield of **3aa** to 68% in two hours (entry 3). This prompted us to further test other copper salts, including copper(I) bromide and copper(I) chloride, but they were less effective than copper(I) iodide (entries 4 and 5). Subsequently, a series of other palladium catalysts were also evaluated; they all were inferior to palladium(II) acetate to some extent (entries 6–9). Finally, the effects of both solvent and base were screened (entries 3 and 10–13). It turned out that a mixture of triethylamine and tetrahydrofuran (1:4) provided the best results.



Scheme 1

Subsequently, the scope of both alkynes and 1,2-diiodoalkenes was investigated under the standard reaction conditions (Table 2). We were happy to find that a large range of functional groups were tolerated well at various positions on the both alkyne and 1,2-diiodoalkene. Reaction of phenylacetylene (**1a**) with ethyl (*E*)-2,3-diiodoacrylate (**2b**), palladium(II) acetate, and copper(I) iodide provided the target product **3ab** in 81% yield (entry 1). Unsymmetrical buta-1,3-diynes **3ba**, **3cc**, **3dc**, **3dd**,

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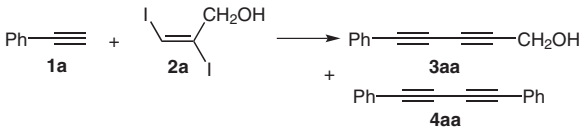
and **3ec** were also obtained in moderate yields from the corresponding alkynes **1b–e** bearing an ester, hydroxy, or amino group (entries 2–6). Substrate **1c** bearing a hydroxy group, for instance, was treated with (*E*)-(1,2-diiodovinyl)benzene (**2c**) for 18 hours to afford smoothly the corresponding product **3cc** in 58% yield (entry 3). Aliphatic alkynes including dec-1-yne (**1f**) and bulky 3,3-dimethylbut-1-yne (**1g**) underwent reaction with 1,2-diiodoalkenes **2a**, **2c**, or **2e** successfully in good yields using palladium(II) acetate and copper(I) iodide as the co-catalyst and triethylamine as the base (entries 7–9). Interestingly, unprotected and protected alkynols **1h–j** were all suitable substrates for coupling with (*E*)-1,2-diiodoalkenes **2c–e** in moderate to excellent yields (entries 10–13). 2-Ethynylcyclohexanol (**1i**), for instance, underwent a smooth reaction with 1,2-diiodoalkene **2d**, palladium(II) acetate, and copper(I) iodide to give the target product **3fe** in quantitative yield (entry 11).

Based on the observation of entry 3 in Table 2, we decided to explore the preparation of 2-ethynylbenzofurans in one step. To our delight, 2-ethynylbenzofurans could be obtained by heating in the presence of palladium(II) acetate and copper(I) iodide (Table 3). We found that the reaction of 2-ethynylphenol (**1c**) with (*E*)-1,2-diiodoalkenes **2b–d** and **2f** at room temperature for 18 hours and then at 100 °C for 10–18 hours gave the desired 2-ethynylbenzofurans **5** in moderate yields (entries 1–4). Other 2-ethynylphenols **1k–m**, bearing either electron-withdrawing or/and electron-donating substituents, also underwent the reaction with (*E*)-1,2-diiodoalkenes **2c** or **2d** in moderate to good yields (entries 5–8). 2-Ethynyl-4-nitrophenol (**1k**), for example, reacted successfully with (*E*)-1,2-di-

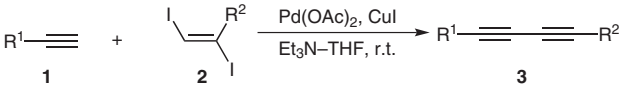
Table 1 Screening Conditions[a]



Entry	[Pd]	[Cu]	Time (h)	Isolated yield[b] (%)	
				3aa	**4aa**
1	–	CuI	20	53	48
2	$Pd(OAc)_2$	–	20	35	24
3	$Pd(OAc)_2$	CuI	2	68	45
4	$Pd(OAc)_2$	CuBr	2	56	49
5	$Pd(OAc)_2$	CuCl	2	58	50
6[c]	$Pd(OAc)_2/Ph_3P$	CuI	4	49	45
7	$PdCl_2(MeCN)_2$	CuI	2	62	44
8	$PdCl_2(PPh_3)_2$	CuI	2	44	66
9	$Pd(dba)_2$	CuI	12	50	56
10[d]	$Pd(OAc)_2$	CuI	2	60	62
11[e]	$Pd(OAc)_2$	CuI	15	33	37
12[f]	$Pd(OAc)_2$	CuI	14	38	42
13[g]	$Pd(OAc)_2$	CuI	2	56	63

[a] Reaction conditions: **1a** (1 mmol), **2a** (0.5 mmol), [Pd] (1 mol%), [Cu] (5 mol%), Et_3N–THF (1:4, 5 mL), r.t., under argon atmosphere.
[b] Isolated yield of **3aa** based on the amount of **2a** and yield of **4aa** base on the amount of **1a**.
[c] Ph_3P (2 mol%).
[d] Et_3N–THF (1:1, 5 mL).
[e] Et_3N (3 equiv) in THF (5 mL).
[f] Cs_2CO_3 (3 equiv) in THF (5 mL).
[g] Et_3N (5 mL).

Table 2 Palladium(II) Acetate/Copper(I) Iodide-Catalyzed Cross-Coupling Reaction of Terminal Alkynes **1** with (*E*)-2,3-Diiodoalkenes **2**[a]

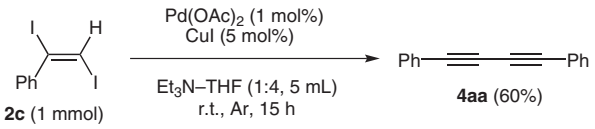


Entry	Imidazole				Time (h)	Yield[b] (%)
1	**1a**	Ph	**2b**	I, CO_2Et, I	16	81 (**3ab**)
2	**1b**	CO_2Me	**2a**	I, CH_2OH, I	7	75 (**3ba**)
3	**1c**	OH	**2c**	I, Ph, I	18	58 (**3cc**)
4	**1d**	NH_2	**2c**		16	51 (**3dc**)
5	**1d**		**2d**	I, $^nC_8H_{17}$, I	17	46 (**3dd**)
6	**1e**	NHAc	**2c**		16	57 (**3ec**)
7	**1f**	$^nC_8H_{17}$	**2c**		12	89 (**3fc**)
8	**1f**		**2e**	OH, I, I	9	76 (**3fe**)
9	**1g**	^tBu	**2a**		6	81 (**3ga**)
10	**1h**	CH_2OH	**2c**		18	81 (**3aa**)
11	**1i**	OH	**2d**		8	99 (**3fe**)
12	**1j**	CH_2OAc	**2c**		15	88 (**3jc**)
13	**1j**		**2e**		15	70 (**3je**)

[a] Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (1 mol%), CuI (5 mol%), Et_3N–THF (1:4, 5 mL), r.t., under argon atmosphere.
[b] Isolated yield based on the amount of **2**.

iodoalkenes **2c** or **2d**, palladium(II) acetate, and copper(I) iodide in high yields (entries 5 and 6). Substrate **1l**, bearing both a methoxy group and a formyl group, still provided the desired product **5lc** in 36% yield under the same conditions (entry 7). It is worth noting that no target products **5**, but only the corresponding buta-1,3-diyne products **3dc** and **3ec** are isolated from the reaction of 2-ethynylanilines **1d** or **1e** with **2c** even at 100 °C.

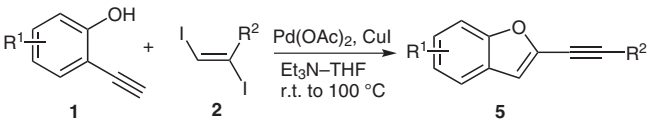
A controlled reaction was conducted as outlined in Scheme 2 to elucidate the mechanism. 1-[(*E*)-1,2-Diiodovinyl]benzene (**2c**) was treated with palladium(II) acetate and copper(I) iodide in triethylamine–tetrahydrofuran to give 1,4-diphenylbuta-1,3-diyne (**4aa**) in 60% yield.



Scheme 2

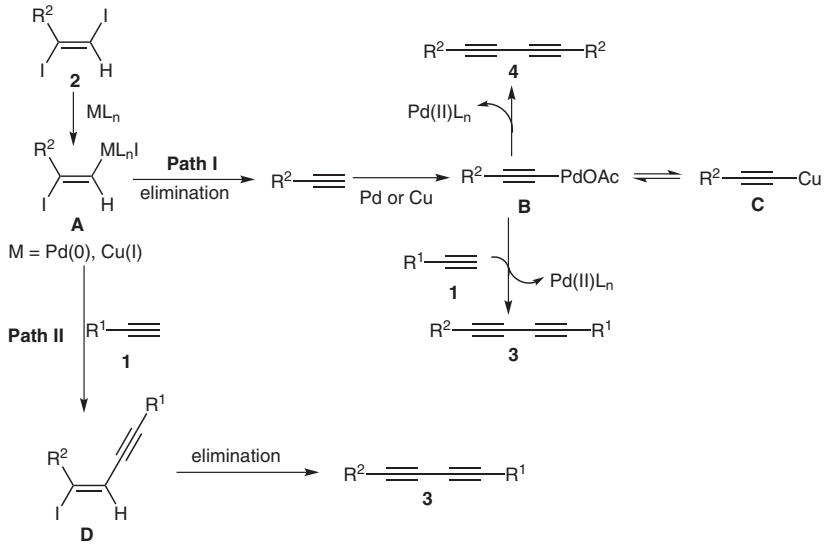
Two working mechanisms, as shown in Scheme 3, are proposed on the basis of the previously reported mechanism[1–8] and the present results. Insertion of M (Cu or Pd) into the C–I bond of 1,2-diiodoalkene **2** occurs readily to form intermediate **A**. Intermediate **A** may proceed by two pathways: (1) Elimination of I–I and then H^+ from intermediate **A** affords intermediate **B** and/or **C** with the aid of base.[6a] Intermediate **B** and/or **C** can selectively undergo the homocoupling reaction and/or the cross-coupling reaction. In the presence of an excess amount of alkyne **1**, selectivity toward the cross-coupling reaction of intermediate **B** with **1** takes place to yield the unsymmetrical buta-1,3-diyne **3**. It is well-known that alkyne **1** undergoes the homocoupling reaction easily to afford **4** in the presence of both palladium(0) and copper(I) iodide.[1g,8] (2) Intermediate **A** reacted with terminal alkyne **1** via the Sonogashira mechanism[1] to give intermediate **D**, followed by elimination of H–I from intermediate **D** in situ to generate unsymmetrical buta-1,3-diyne **3**.[4–6] Further exploration of the true mechanism is in progress.

Table 3 One-Pot Synthesis of 2-Ethynylbenzofurans **5**[a]



Entry	Imidazole	Aryl halide	Time (h)	Yield[b] (%)
1	**1c**	**2b**	29	33 (**5cb**)
2	**1c**	**2c**	36	63 (**5cc**)
3	**1c**	**2d**	28	32 (**5cd**)
4	**1c**	**2f**	30	58 (**5cf**)
5	**1k**	**2c**	18	91 (**5kc**)
6	**1k**	**2d**	18	81 (**5kd**)
7	**1l**	**2c**	32	36 (**5lc**)
8	**1m**	**2d**	36	57 (**5md**)

[a] Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (1 mol%), CuI (5 mol%), Et_3N–THF (1:4, 5 mL), r.t. for 18 h, and then 100 °C for the remaining time, under argon atmosphere.
[b] Isolated yield based on the amount of **2**.



Scheme 3 Two possible mechanisms

In summary, we have developed a new approach for the highly selective synthesis of unsymmetrical buta-1,3-diynes using (*E*)-1,2-diiodoalk-1-enes as an attractive alternative to 1-iodoalk-1-ynes. Furthermore, 2-ethynylbenzofurans were also prepared successfully by simple heating, where a C–C bond and a C–O bond are formed in one pot. We are currently exploring the application of this methodology in organic synthesis.

NMR spectroscopy was performed on an Inova-400 (Varian) spectrometer operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). TMS was used an internal standard and $CDCl_3$ was used as the solvent. Mass spectrometric analysis was performed by GC-MS analysis (Shimadzu GCMS-QP2010). (*E*)-1,2-Diiodoalkenes were prepared from the reaction of the corresponding alkynes with I_2 by known procedures.[9] All solvents are dried according to standard procedures and the other reagents are used directly from commercial sources. All melting points are uncorrected.

Buta-1,3-diynes 3; General Procedure

A mixture of alkyne **1** (1.0 mmol), (*E*)-1,2-diiodoalkene **2**, $Pd(OAc)_2$ (1 mol%), CuI (5 mol%), Et_3N (1 mL), and THF (4 mL) was stirred under an argon atmosphere at r.t. for the indicated time (Table 2) until complete consumption of the starting material (TLC and GC-MS). Then the mixture was filtered and evaporated and the residue was purified by flash column chromatography to afford **3** (hexane or hexane–EtOAc).

2-Ethynylbenzofurans 5; Typical Procedure

A mixture of alkyne **1** (1.0 mmol), (*E*)-1,2-diiodoalkene **2**, $Pd(OAc)_2$ (1 mol%), CuI (5 mol%), Et_3N (1 mL), and THF (4 mL) was stirred under an argon atmosphere at r.t. for 18 h, and then at 100 °C for the remaining time until complete consumption of the starting material (TLC and GC-MS). The mixture was filtered and evaporated and the residue was purified by flash column chromatography to afford **5** (hexane or hexane–EtOAc).

5-Phenylpenta-2,4-diyn-1-ol (3aa)[5f]

Brown oil.

^{1}H NMR (400 MHz): δ = 7.47 (d, *J* = 8.4 Hz, 2 H), 7.35–7.28 (m, 3 H), 4.40 (s, 2 H), 2.20 (br s, 1 H).

^{13}C NMR (100 MHz): δ = 132.6, 129.3, 128.4, 121.4, 80.6, 78.5, 73.2, 70.3, 51.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 156 (M^+, 27), 147 (16), 139 (14), 128 (40), 102 (49), 69 (53), 57 (31), 44 (100).

Ethyl 5-Phenylpenta-2,4-diynoate (3ab)[11]

Yellow oil.

^{1}H NMR (400 MHz): δ = 7.49 (d, *J* = 6.8 Hz, 2 H), 7.37–7.32 (m, 3 H), 4.81 (s, 2 H), 2.12 (s, 3 H).

^{13}C NMR (100 MHz): δ = 170.0, 132.6, 129.4, 128.4, 121.1, 78.7, 76.1, 73.0, 71.1, 52.5, 20.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 198 (M^+, 3), 181 (5), 169 (66), 147 (34), 119 (29), 113 (25), 97 (48), 85 (31), 69 (100).

Methyl 2-(5-Hydroxypenta-1,3-diynyl)benzoate (3ba)

Yellow solid; mp 74.4–74.8 °C.

^{1}H NMR (400 MHz): δ = 7.97 (d, *J* = 8.8 Hz, 1 H), 7.61 (d, *J* = 8.8 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H), 4.45 (s, 2 H), 3.95 (s, 3 H), 2.40 (br s, 1 H).

^{13}C NMR (100 MHz): δ = 166.1, 135.2, 132.7, 131.8, 130.5, 128.8, 122.1, 82.3, 78.0, 76.6, 70.3, 52.4, 51.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 214 (M^+, 84), 199 (17), 185 (26), 169 (31), 143 (38), 128 (35), 115 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{10}O_3$: 214.0630; found: 214.0628.

2-(4-Phenylbuta-1,3-diynyl)phenol (3cc)

Light yellow solid; mp 78.6–79.7 °C.

^{1}H NMR (400 MHz): δ = 7.54 (d, *J* = 8.0 Hz, 2 H), 7.42–7.34 (m, 4 H), 7.29 (t, *J* = 8.4 Hz, 1 H), 6.96 (d, *J* = 8.4 Hz, 1 H), 6.89 (t, *J* = 7.6 Hz, 1 H), 5.80 (s, 1 H).

^{13}C NMR (100 MHz): δ = 158.1, 132.7, 132.5, 131.3, 129.5, 128.5, 121.3, 120.6, 115.1, 108.2, 83.4, 80.5, 75.6, 73.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 218 (M^+, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{10}O$: 218.0732; found: 218.0732.

2-(4-Phenylbuta-1,3-diynyl)aniline (3dc)

Brown oil.

^{1}H NMR (400 MHz): δ = 7.53 (d, *J* = 8.0 Hz, 2 H), 7.37–7.31 (m, 4 H), 7.15 (t, *J* = 8.0 Hz, 1 H), 6.69 (d, *J* = 8.0 Hz, 2 H), 4.32 (br s, 2 H).

^{13}C NMR (100 MHz): δ = 149.5, 133.0, 132.3, 130.6, 129.1, 128.4, 121.8, 117.9, 114.4, 106.0, 82.6, 79.0, 78.6, 73.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 217 (M^+, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{11}O$: 217.0892; found: 217.0891.

2-(Dodeca-1,3-diynyl)aniline (3dd)[12]
Brown oil.

^{1}H NMR (400 MHz): δ = 7.29 (d, *J* = 7.6 Hz, 1 H), 7.12 (t, *J* = 7.2 Hz, 1 H), 6.67–6.63 (m, 2 H), 4.26 (br s, 2 H), 2.37 (t, *J* = 7.2 Hz, 2 H), 1.59–1.53 (m, 2 H), 1.43–1.39 (m, 2 H), 1.29–1.24 (m, 8 H), 0.89 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 149.4, 133.1, 130.1, 117.8, 114.2, 106.5, 85.9, 79.5, 71.6, 65.0, 31.8, 29.1, 29.0, 28.9, 28.2, 22.6, 19.6, 14.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 253 (M^+, 18), 238 (48), 181 (53), 167 (51), 139 (60), 69 (100).

***N*-[2-(4-Phenylbuta-1,3-diynyl)phenyl]acetamide (3ec)**
Light yellow solid; mp 112.8 °C.

^{1}H NMR (400 MHz): δ = 8.40 (d, *J* = 8.0 Hz, 1 H), 7.86 (br s, 1 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.49 (d, *J* = 8.8 Hz, 1 H), 7.41–7.34 (m, 4 H), 7.05 (t, *J* = 7.6 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz): δ = 168.4, 140.3, 132.9, 132.5, 130.6, 129.6, 128.5, 123.5, 121.2, 119.6, 110.4, 83.8, 80.5, 76.4, 73.1, 25.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 259 (M^+, 55), 217 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{13}NO$: 259.0997; found: 259.0997.

(Dodeca-1,3-diynyl)benzene (3fc)[13]
Yellow oil.

^{1}H NMR (400 MHz): δ = 7.47 (d, *J* = 9.6 Hz, 2 H), 7.31–7.29 (m, 3 H), 2.35 (t, *J* = 6.8 Hz, 2 H), 1.59–1.55 (m, 2 H), 1.41–1.28 (m, 10 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 132.5, 128.7, 128.3, 122.1, 84.9, 74.7, 74.4, 65.0, 31.8, 29.1 (d), 28.9, 28.2, 22.6, 19.6, 14.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 238 (M^+, 43), 181 (51), 169 (45), 167 (52), 139 (54), 115 (37), 91 (58), 79 (46), 69 (100).

1-(Dodeca-1,3-diynyl)cyclohexanol (3fe)
Yellow oil.

^{1}H NMR (400 MHz): δ = 2.28 (t, *J* = 7.2 Hz, 2 H), 2.12 (br s, 1 H), 1.93–1.89 (m, 2 H), 1.71–1.67 (m, 2 H), 1.62–1.49 (m, 7 H), 1.42–1.35 (m, 2 H), 1.32–1.27 (m, 9 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 81.6, 79.1, 69.2, 64.4, 39.7 (d), 31.8, 29.1, 29.0, 28.8, 28.1, 25.0, 23.1, 22.6, 19.3, 14.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 260 (M^+, 3), 245 (2), 231 (9), 217 (30), 203 (16), 175 (58), 149 (40), 119 (34), 91 (86), 81 (44), 79 (54), 69 (26), 55 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{28}O$: 260.2140; found: 260.2139.

6,6-Dimethylhepta-2,4-diyn-1-ol (3ga)[14]
Light yellow oil.

^{1}H NMR (400 MHz): δ = 4.25 (s, 2 H), 2.21 (br s, 1 H), 1.18 (s, 9 H).

^{13}C NMR (100 MHz): δ = 89.2, 74.8, 70.5, 63.0, 51.3, 30.3, 27.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 136 (M^+, 68), 119 (100).

5-Phenylpenta-2,4-diynyl Acetate (3jc)[15]
Yellow oil.

^{1}H NMR (400 MHz): δ = 7.49 (d, *J* = 6.8 Hz, 2 H), 7.38–7.32 (m, 3 H), 4.82 (s, 2 H), 2.12 (s, 3 H).

^{13}C NMR (100 MHz): δ = 170.1, 132.6, 129.5, 128.4, 121.2, 78.8, 76.1, 73.0, 71.1, 52.5, 29.7.

LRMS (EI, 70 eV): *m*/*z* (%) = 198 (M^+, 58), 139 (100).

5-(1-Hydroxycyclohexyl)penta-2,4-diynyl Acetate (3je)
Yellow oil.

^{1}H NMR (400 MHz): δ = 4.75 (s, 2 H), 2.11 (s, 3 H), 1.93–1.90 (m, 2 H), 1.72–1.69 (m, 2 H), 1.63–1.51 (m, 5 H), 1.27–1.25 (m, 1 H).

^{13}C NMR (100 MHz): δ = 170.1, 83.5, 73.0, 70.6, 69.1, 68.0, 52.4, 39.5, 24.9, 23.0, 20.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 220 (M^+, 59), 178 (65), 160 (52), 135 (55), 132 (59), 121 (42), 118 (65), 117 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{16}O_3$: 220.1099; found: 220.1097.

Ethyl 3-(Benzofuran-2-yl)propynoate (5cb)
Brown yellow oil.

^{1}H NMR (400 MHz): δ = 7.53 (d, *J* = 7.6 Hz, 1 H), 7.42 (d, *J* = 8.8 Hz, 1 H), 7.31 (t, *J* = 8.4 Hz, 1 H), 7.22 (t, *J* = 8.0 Hz, 1 H), 6.96 (s, 1 H), 4.93 (s, 2 H), 2.11 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.0, 156.7, 139.4, 129.0, 127.7, 125.1, 123.2, 114.5, 113.1, 97.0, 78.7, 54.2, 22.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 214 (M^+, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{10}O_3$: 214.0630; found: 214.0630.

2-(2-Phenylethynyl)benzofuran (5cc)[16]
White solid; mp 69.2–70.1 °C.

^{1}H NMR (400 MHz): δ = 7.59–7.57 (m, 3 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 7.39–7.31 (m, 4 H), 7.26–7.23 (m, 1 H), 7.00 (s, 1 H).

^{13}C NMR (100 MHz): δ = 154.9, 138.7, 131.6, 129.1, 128.4, 127.7, 125.6, 123.3, 121.8, 121.2, 111.5, 110.2, 95.0, 79.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 218 (M^+, 100).

2-(Dec-1-ynyl)benzofuran (5cd)
Light yellow oil.

^{1}H NMR (400 MHz): δ = 7.52 (d, *J* = 7.6 Hz, 1 H), 7.42 (d, *J* = 8.8 Hz, 1 H), 7.29 (t, *J* = 8.4 Hz, 1 H), 7.21 (t, *J* = 7.6 Hz, 1 H), 6.82 (s, 1 H), 2.48 (t, *J* = 7.2 Hz, 2 H), 1.64–1.62 (m, 2 H), 1.32–1.27 (m, 10 H), 0.88 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 154.5, 139.3, 127.8, 125.0, 123.0, 120.9, 111.0, 110.0, 97.1, 77.6, 31.8, 29.1, 29.0, 28.9, 28.8, 28.2, 22.6, 19.6, 14.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 254 (M^+, 8), 219 (5), 154 (4), 40 (35), 28 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{22}O$: 254.1671; found: 254.1670.

4-(Benzofuran-2-yl)but-3-yn-1-ol (5cf)
Brown yellow oil.

^{1}H NMR (400 MHz): δ = 7.53 (d, *J* = 7.6 Hz, 1 H), 7.43 (d, *J* = 8.8 Hz, 1 H), 7.31 (t, *J* = 8.4 Hz, 1 H), 7.23 (t, *J* = 8.0 Hz, 1 H), 6.88 (s, 1 H), 3.87 (t, *J* = 6.0 Hz, 2 H), 2.78 (t, *J* = 6.4 Hz, 2 H), 2.00 (br s, 1 H).

^{13}C NMR (100 MHz): δ = 154.5, 138.6, 127.5, 125.3, 123.2, 121.1, 111.1, 110.8, 93.2, 72.9, 60.7, 30.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 186 (M^+, 28), 169 (26), 141 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{10}O_2$: 186.0681; found: 186.0680.

5-Nitro-2-(2-phenylethynyl)benzofuran (5kc)
Yellow solid; mp 131.4–135.2 °C.

^{1}H NMR (400 MHz): δ = 8.51 (s, 1 H), 8.26 (d, *J* = 11.6 Hz, 1 H), 7.61–7.58 (m, 2 H), 7.55 (d, *J* = 8.8 Hz, 1 H), 7.43–7.40 (m, 3 H), 7.11 (s, 1 H).

^{13}C NMR (100 MHz): δ = 157.4, 148.0, 144.5, 142.0, 131.8, 129.7, 128.6, 128.2, 121.2, 121.0, 117.6, 111.5, 96.7, 78.3.

LRMS (EI, 70 eV): *m*/*z* (%) = 263 (M^+, 63), 217 (24), 189 (15), 163 (11), 32 (28), 28 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_9NO_3$: 263.0582; found: 263.0582.

2-(Dec-1-ynyl)-5-nitrobenzofuran (5kd)
Red brown oil.

^{1}H NMR (400 MHz): δ = 8.47 (s, 1 H), 8.23 (d, *J* = 11.6 Hz, 1 H), 7.50 (d, *J* = 9.2 Hz, 1 H), 6.93 (s, 1 H), 2.51 (t, *J* = 7.2 Hz, 2 H), 1.67–1.64 (m, 2 H), 1.31–1.23 (m, 10 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 157.1, 144.3, 142.5, 128.3, 120.8, 117.4, 111.3, 110.3, 99.3, 70.2, 31.8, 29.1, 29.0, 28.9, 28.0, 22.6, 19.6, 14.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 299 (M^+, 7), 243 (4), 202 (6), 154 (4), 40 (31), 28 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{21}NO_3$: 299.1521; found: 299.1521.

7-Methoxy-2-(2-phenylethynyl)benzofuran-5-carbaldehyde (5lc)
Yellow solid; mp 90.1–93.2 °C.

^{1}H NMR (400 MHz): δ = 10.00 (s, 1 H), 7.70 (s, 1 H), 7.57 (d, *J* = 7.6 Hz, 2 H), 7.40–7.38 (m, 4 H), 7.08 (s, 1 H), 4.07 (s, 3 H).

^{13}C NMR (100 MHz): δ = 191.5, 147.7, 145.8, 140.7, 133.7, 131.6, 129.4, 129.2, 128.5, 121.4, 119.5, 111.7, 105.0, 95.9, 78.7, 56.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{12}O_3$: 276.0786; found: 276.0786.

5,7-Dichloro-2-(dec-1-ynyl)benzofuran (5md)
Light yellow oil.

^{1}H NMR (400 MHz): δ = 7.39 (s, 1 H), 7.29 (s, 1 H), 6.76 (s, 1 H), 2.48 (t, *J* = 7.2 Hz, 2 H), 1.66–1.62 (m, 2 H), 1.46–1.27 (m, 10 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz): δ = 148.8, 141.5, 130.1, 128.9, 125.0, 119.0, 117.0, 109.9, 98.9, 70.3, 31.8, 29.1, 29.0, 28.8, 28.1, 22.6, 19.6, 14.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 324 ([M^+ + 2], 11), 323 ([M^+ + 1], 12), 322 (M^+, 65), 289 (10), 287 (M^+ – Cl, 31), 267 (8), 252 (M^+ – 2 Cl, 25), 40 (56), 28 (100).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{20}{}^{35}Cl_2O$: 322.0891; found: 322.0890.

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