# An efficient heterogeneous palladium(0)-catalysed cross-coupling between 1-bromoalkynes and terminal alkynes leading to unsymmetrical 1,3-diynes

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An efficient heterogeneous palladium(0)-catalysed cross-coupling of 1-bromoalkynes with terminal alkynes was achieved in DMF at room temperature in the presence of 5 mol% of MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] and 2 mol% of CuI with $Et_3N$ as base, yielding a variety of unsymmetrical 1,3-diynes in moderate to good yields. This heterogeneous palladium(0) complex could be easily recovered by a simple filtration of the reaction solution and recycled at least seven times without significant decrease in activity.

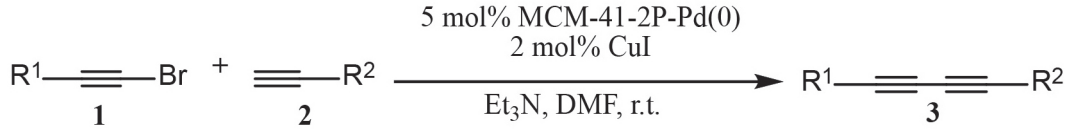
**Keywords:** supported palladium catalyst, cross-coupling, 1,3-diyne, 1-bromoalkyne, heterogeneous catalysis, terminal alkynes

Conjugated diynes and polyynes are attractive compounds since they are frequently found in a variety of biologically active molecules and natural products.[1–3] They have also shown a wide application in organic synthesis, organometallic chemistry and advanced organic materials.[4–7] Therefore, the development of efficient methods for the preparation of conjugated diynes, especially unsymmetrical 1,3-diynes, has attracted much attention.[8,9] The conjugated diyne compounds are prepared mainly by Glaser–Hay coupling[3,10–12] and Cadiot–Chodkiewicz coupling.[13–15] Traditional Glaser–Hay coupling is usually used for the construction of symmetrical 1,3-diynes. Cadiot–Chodkiewicz coupling, developed over five decades ago, utilises a 1-haloalkyne as the electrophile and a terminal alkyne as the nucleophile to synthesise unsymmetrical 1,3-diynes. However, this methodology usually suffers from complex reaction conditions[16] and poor selectivity, and results in a considerable amount of homocoupled byproducts, especially when the electronic nature of the substituents attached to the 1-haloalkynes and the terminal alkynes are similar.[1,7,17] To inhibit homocoupling of 1-haloalkynes, excess of the terminal alkyne is usually utilised.[1] During the past three decades, several palladium-catalysed 1,3-diyne construction methods have been developed. Negishi and co-workers reported an efficient tandem protocol by combining Sonogashira coupling of terminal alkynes with ICH=CHCl with subsequent base-induced elimination to furnish 1,3-diynes.[18–20] Nye,[21] Wityak,[22] and Alami and Ferri[23] reported palladium-catalysed C(sp)–C(sp) cross-coupling reactions for the construction of unsymmetrical 1,3-diynes with improved yields and selectivity in some cases. Lei and co-workers reported an efficient palladium-catalysed C(sp)–C(sp) cross-coupling reaction of terminal alkynes with 1-haloalkynes leading to unsymmetrical 1,3-diynes in good to excellent yields with high selectivity.[24] Recently, gold-catalysed oxidative cross-coupling of terminal alkynes[25] and Cadiot–Chodkiewicz-type cross-coupling of terminal alkynes with alkynyl hypervalent iodine reagents[26] have been reported to be alternative methods for selective synthesis of unsymmetrical 1,3-diynes.

Although these palladium- or gold-catalysed cross-coupling reactions are highly efficient for the construction of unsymmetrical 1,3-diynes, industrial applications of these homogeneous palladium or gold catalysts remain a challenge because they are quite expensive and are difficult to separate from the product mixture. Recycling of homogeneous precious metal catalysts is a task of great economic and environmental importance in the chemical and pharmaceutical industries.[27] Immobilised metal catalysts have attracted growing attention because of the advantages of high catalytic efficiency and easy recycling, which are important for expensive or toxic heavy metal catalysts and flow chemistry processes.[28–30] Recently, mesoporous MCM-41 materials have emerged as smart and promising supports with great industrial potential for immobilisation. This is due to their outstanding advantages such as extremely high surface areas, combined with the large and defined pore sizes of mesoporous materials, compared with other solid supports.[31–33] In our previous work, we reported the first synthesis of an MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] and found that it is a highly efficient catalyst for the heterogeneous Suzuki coupling reaction.[34] In continuing our efforts to develop green synthetic pathways for organic transformations, we report here the first heterogeneous palladium(0)-catalysed cross-coupling of 1-bromoalkynes with terminal alkynes leading to unsymmetrical 1,3-diynes by using the MCM-41-2P-Pd(0) complex as a recyclable catalyst (Scheme 1).

## Results and discussion

The MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] was prepared from commercially readily available reagents according to the procedure[34] summarised in Scheme 2. Firstly, the mesoporous material MCM-41 was treated with 3-aminopropyltriethoxysilane in toluene at 100 °C for 24 h, followed by silylation with $Me_3SiCl$ in toluene at room temperature for 24 h to afford 3-amino-propyl-functionalised MCM-41 (MCM-41-$NH_2$). The latter was subsequently reacted with $Ph_2PCH_2OH$, derived from the




1 2 3

**Scheme 1**

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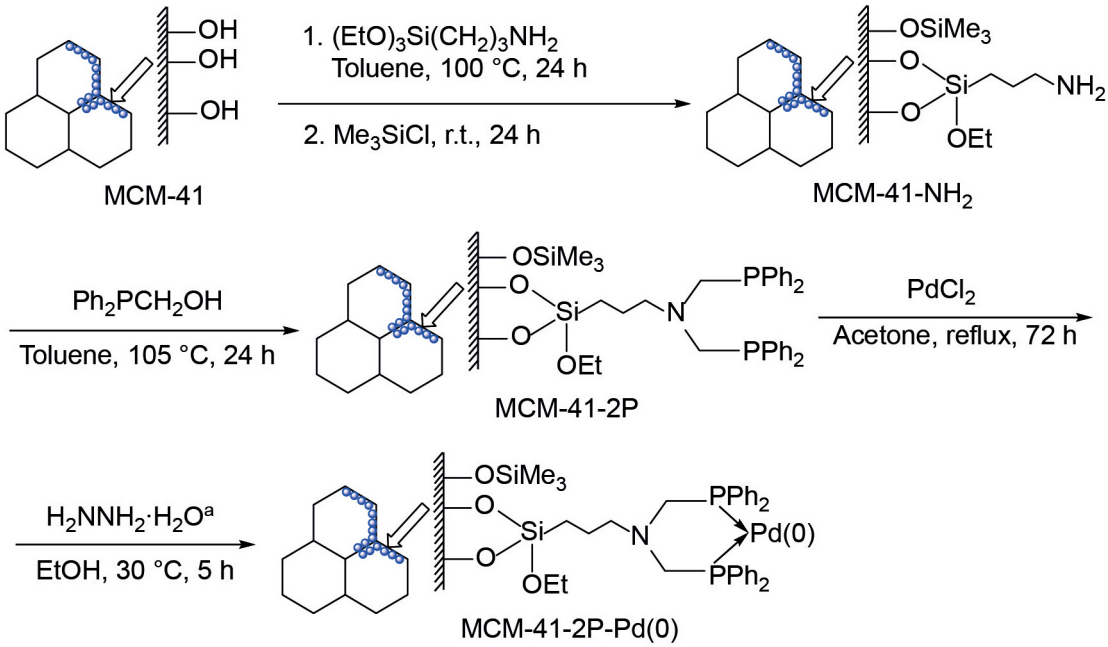



[a]see SAFETY CAUTION in Experimental

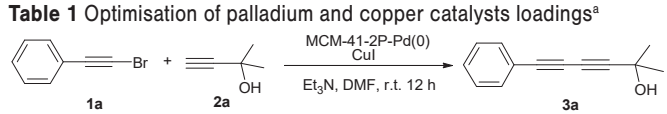
**Scheme 2**

reaction of $Ph_2PH$ with $(CH_2O)_n$, to generate the diphosphino-functionalised MCM-41 (MCM-41-2P). Finally, the reaction of MCM-41-2P with $PdCl_2$ in acetone under reflux for 72 h, followed by reduction with hydrazine hydrate (see SAFETY CAUTION in Experimental) in ethanol at 30 °C for 5 h, gave the MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] as a grey powder. The palladium content was determined to be 0.45 mmol $g^{-1}$ by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis.

The MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] was then used as a catalyst for the cross-coupling reaction of 1-bromoalkynes with terminal alkynes. In our initial screening experiments, the cross-coupling of bromoethynylbenzene (**1a**) with 2-methylbut-3-yn-2-ol (**2a**) in DMF as solvent with $Et_3N$ as base was selected as the model reaction to optimise the catalyst loadings and the results are summarised in Table 1. Palladium was essential under the tested conditions and only 7% of the desired cross-coupling product **3a** was formed after 12 h without the Pd(0) catalyst (Table 1, entry 1). It was found that CuI was also essential in this reaction. In the absence of CuI, only 25% of **3a** was generated and a low selectivity of 69:31 over the homocoupled product from **1a** was observed (Table 1, entry 2). When the ratio of Pd(0) catalyst to CuI was 1:1, 72% of **3a** was produced and the selectivity was 87:13 (Table 1, entry 3). Increasing the loading of CuI to 5 or 10 mol% resulted in a decreased yield and a lower selectivity (Table 1, entries 4 and 5). At the same CuI loading (2 mol%), enhancing the loading of the Pd(0) catalyst was observed to increase the yield and selectivity (Table 1, entry 6), but further increasing loading of the Pd(0) catalyst did not improve the yield and selectivity significantly (Table 1, entry 7). Thus, the optimal catalyst loadings were 5 mol% MCM-41-2P-Pd(0) and 2 mol% CuI (Table 1, entry 6).

With this promising result in hand, we started to examine the scope of this heterogeneous palladium(0)-catalysed cross-coupling reaction by employing various 1-bromoalkynes and terminal alkynes and the results are summarised in Table 2.

**Table 1** Optimisation of palladium and copper catalysts loadings[a]



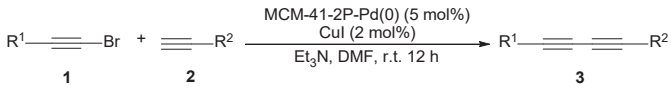

1a 2a 3a

| Entry | Pd(0) (mol%) | CuI (mol%) | Yield (%)[b] | Selectivity[c] |
|---|---|---|---|---|
| 1 | 0 | 2 | 7 | – |
| 2 | 2 | 0 | 25 | 69:31 |
| 3 | 2 | 2 | 72 | 87:13 |
| 4 | 2 | 5 | 61 | 82:18 |
| 5 | 2 | 10 | 49 | 73:27 |
| 6 | 5 | 2 | 76 (65[d]) | 89:11 |
| 7 | 8 | 2 | 77 | 90:10 |

[a]Reaction conditions: **1a** (1 mmol), **2a** (1.5 mmol), $Et_3N$ (2 mmol) in 2 mL of DMF at room temperature under Ar.
[b]Determined by gas chromatography with biphenyl as the internal standard.
[c]Molar ratio of **3a** to 1,4-diphenylbutadiyne.
[d]Isolated yield.

When bromoethynylbenzene (**1a**) was the electrophile, the cross-coupling reactions with terminal alkynes bearing either an alkyl group or an aryl group **2b–f** proceeded smoothly to afford the corresponding unsymmetrical 1,3-diynes **3b–f** in good yields (Table 2, entries 2–6). It was noteworthy that the protocol exhibited excellent tolerance towards a bromophenyl group and the reaction of **1a** with 1-bromo-4- ethynylbenzene (**2e**) gave the desired cross-coupled 1,3-diyne **3e** in 72% isolated yield (Table 2, entry 5). 1-Bromoalkynes bearing either aliphatic or hydroxyl groups were all suitable coupling partners in the reactions with various terminal alkynes (Table 2, entries 7–20). For example, 1-bromooct-1-yne (**1b**) and 1-bromohept-1-yne (**1c**) could undergo the cross-coupling reactions with electron-neutral, electron-rich and electron-deficient aromatic alkynes effectively to give the desired unsymmetrical 1,3-diynes **3f–j** in moderate to good yields (Table 2, entries 7–11). The reaction between **1c** and propargyl acetate (**2j**) afforded the expected product **3k** in 60% yield and the reactive acetate group was well preserved (Table 2, entry 12). Interestingly, the coupling reaction of **1c** with hex-1-yne (**2k**) produced the cross-coupled

**Table 2** Heterogeneous palladium(0)-catalysed cross-coupling of 1-bromoalkynes with terminal alkynes[a]



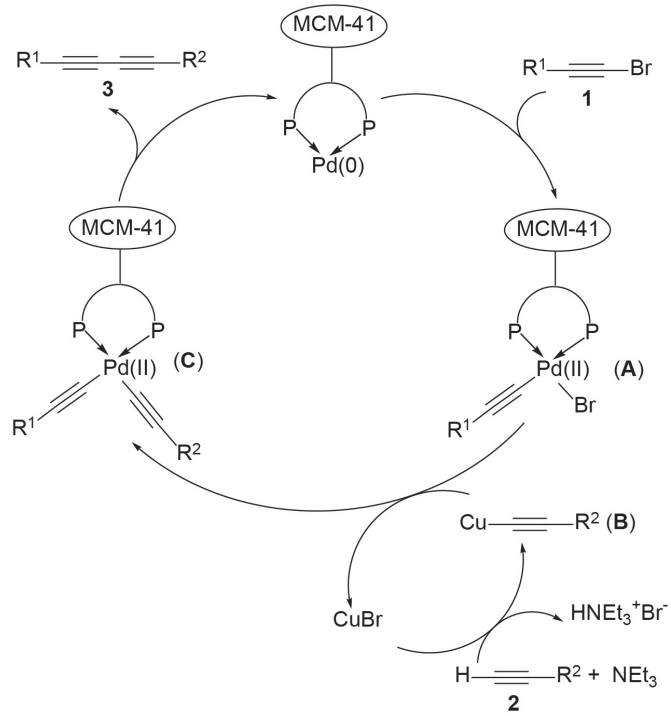

| Entry | $R^1$ | $R^2$ | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | Ph | $HOMe_2C$ | **3a** | 65 |
| 2 | Ph | $HOCH_2CH_2$ | **3b** | 64 |
| 3 | Ph | $MeOCH_2CH_2$ | **3c** | 66 |
| 4 | Ph | 4-$MeOC_6H_4$ | **3d** | 63 |
| 5 | Ph | 4-$BrC_6H_4$ | **3e** | 72 |
| 6 | Ph | *n*-$C_5H_{11}$ | **3f** | 62 |
| 7 | *n*-$C_6H_{13}$ | 4-$EtOC_6H_4$ | **3g** | 59 |
| 8 | *n*-$C_6H_{13}$ | 4-$MeOC_6H_4$ | **3h** | 52 |
| 9 | *n*-$C_6H_{13}$ | 4-$EtC_6H_4$ | **3i** | 49 |
| 10 | *n*-$C_5H_{11}$ | Ph | **3f** | 67 |
| 11 | *n*-$C_5H_{11}$ | 4-$BrC_6H_4$ | **3j** | 58 |
| 12 | *n*-$C_5H_{11}$ | $MeCO_2CH_2$ | **3k** | 60 |
| 13 | *n*-$C_5H_{11}$ | *n*-$C_4H_9$ | **3l** | 51 |
| 14 | $HOMe_2C$ | 4-$EtC_6H_4$ | **3m** | 57 |
| 15 | $HOMe_2C$ | 3-$FC_6H_4$ | **3n** | 46 |
| 16 | $HOMe_2C$ | 4-$EtOC_6H_4$ | **3o** | 71 |
| 17 | $HOMe_2C$ | $Me_3Si$ | **3p** | 52 |
| 18 | $HOCH_2CH_2$ | 4-$EtC_6H_4$ | **3q** | 59 |
| 19 | $HOCH_2CH_2$ | 4-$EtOC_6H_4$ | **3r** | 55 |
| 20 | $HOCH_2CH_2$ | 3-$FC_6H_4$ | **3s** | 48 |

[a]Reaction conditions: **1** (1.0 mmol), **2** (1.5 mmol), $Et_3N$ (2 mmol), MCM-41-2P-Pd(0) (5 mol%), CuI (2 mol%) in 2 mL of DMF at room temperature under Ar for 12 h.
[b]Isolated yield.

product trideca-5,7-diyne (**3l**) in moderate yield (Table 2, entry 13). 4-Bromo-2-methylbut-3-yn-2-ol (**1d**) was coupled with various terminal aromatic alkynes to give the corresponding unsymmetrical 1,3-diynes **3m–o** in 46–71% yields (Table 2, entries 14–16). Notably, the reaction of **1d** with a trimethysilyl-functionalised terminal alkyne gave the desired product **3p** in 52% yield (Table 2, entry 17). The reactions of 4-bromobut-3-yn-1-ol (**1e**) also worked well with different aromatic alkynes to furnish the corresponding cross-coupled products **3q–s** in moderate yields (Table 2, entries 18–20).

To ensure that the activity of the MCM-41-2P-Pd(0) complex arises from the palladium sites on the channel walls and not from the leached palladium species in solution, the heterogeneity of the MCM-41-2P-Pd(0) complex was tested. For this, the cross-coupling reaction of **1a** with **2a** (1.5 equiv.) was carried out until a conversion of 30% of **1a** was reached. Then the catalyst was removed from the solution by filtration and the filtrate was allowed to react further under identical reaction conditions for 8 h. We found that, after removal of the catalyst, no increase in conversion of **1a** was observed. We also determined the palladium content in the filtrate by ICP-AES analysis and no palladium was detected in the clear solution. These results rule out any contribution to the observed catalysis from the leached palladium species, indicating that the catalyst was stable during the reaction and the observed catalysis was intrinsically heterogeneous.

A plausible mechanism for the heterogeneous palladium(0)-catalysed cross-coupling reaction of 1-bromoalkynes **1** with terminal alkynes **2** is illustrated in Scheme 3.[24] First, oxidative addition of 1-bromoalkyne **1** to MCM-41-2P-Pd(0) gives an MCM-41-bound bidentate phosphine $R^1C{\equiv}C–Pd(II)Br$ complex intermediate **A**. Transmetalation between intermediate **A** and alkynylcopper **B** then forms an MCM-41-bound bidentate phosphine $R^1C{\equiv}C–Pd(II)–C{\equiv}CR^2$ complex intermediate **C**. Alkynylcopper **B** is generated from the Cu(I) salt and terminal alkyne **2** with the assistance of $Et_3N$. Finally, reductive




**Scheme 3**

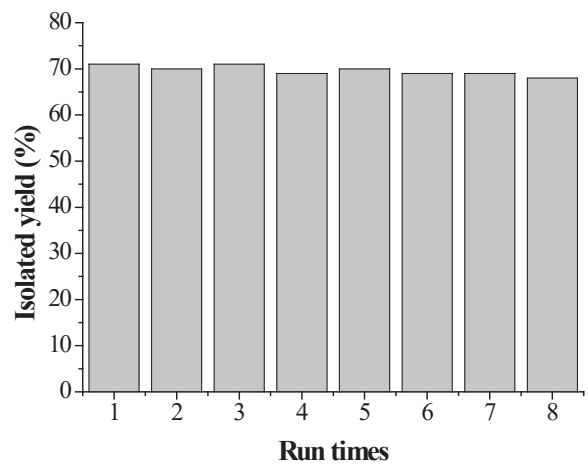



**Fig. 1** Results from recycling of the MCM-41-2P-Pd(0) catalyst.

elimination of intermediate **C** affords the desired 1,3-diyne **3** and regenerates the MCM-41-2P-Pd(0) complex to complete the catalytic cycle.

For the practical application of a supported precious metal catalyst, its ease of separation, recoverability and reusability are important factors. This heterogeneous palladium catalyst can be easily separated and recovered by a simple filtration of the reaction solution. We next examined the recyclability of the catalyst by using the cross-coupling of 4-bromo-2-methylbut-3-yn-2-ol (**1d**) with 4-ethoxyphenylacetylene (**2g**). After completion of the reaction, the catalyst was recovered by a simple filtration of the reaction solution and washed with distilled water and ethanol. After being air-dried, it could be reused directly without further purification. The recovered palladium catalyst was used in the next run and almost consistent activity was observed for eight consecutive cycles (Fig. 1). The satisfactory recyclability of the catalyst is likely attributable to the chelating action of the bidentate phosphine ligand on palladium and the mesoporous structure of the MCM-41 support. The result is important from the standpoint

of green and sustainable chemistry. No copper is retained in the support.

In summary, we have developed a novel, efficient and practical method for the synthesis of unsymmetrical 1,3-diynes through the cross-coupling of 1-bromoalkynes with terminal alkynes by using an MCM-41-immobilised bidentate phosphine palladium(0) complex [MCM-41-2P-Pd(0)] as the catalyst in the presence of CuI as a cocatalyst. The reactions generated a variety of unsymmetrical 1,3-diynes in moderate to good yields under mild conditions and were applicable to various 1-bromoalkynes and terminal alkynes. In addition, this methodology offers the competitiveness of recyclability of the palladium catalyst without significant loss of catalytic activity and the catalyst could be easily recovered and reused at least seven times, thus making this procedure economically and environmentally more acceptable.

## Experimental

All chemicals were obtained from commercial suppliers and used as received, unless otherwise noted. All products were characterised by comparison of their spectra and physical data with the literature where possible. $^1$H NMR spectra were recorded on a Bruker Avance 400 (400 MHz) spectrometer with TMS as an internal standard in $CDCl_3$ as solvent. $^{13}$C NMR spectra were recorded on a Bruker Avance 400 (100 MHz) spectrometer in $CDCl_3$ as solvent. HRMS spectra were recorded on a quadrupole-time–of-flight Bruker MicroTOF-Q II mass spectrometer equipped with an ESI and APCI source. The MCM-41-2P-Pd(0) complex was prepared according to our previous procedure;[34] the palladium content was determined to be 0.45 mmol $g^{-1}$ by ICP-AES. 1-Bromoalkynes were prepared by the reaction of terminal alkynes with NBS in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene according to a literature method.[35]

**CAUTION**: Stringent safety precautions are required in the preparation of MCM-41-2P-Pd(0) when using hydrazine hydrate as it is highly toxic and harmful to health.

*Heterogeneous Pd(0)-catalysed cross-coupling of 1-bromoalkynes with terminal alkynes; general procedure*

A 25 mL round-bottomed flask equipped with a magnetic stirring bar was charged with 1-bromoalkyne **1** (1.0 mmol), terminal alkyne **2** (1.5 mmol), $Et_3N$ (2 mmol), MCM-41-2P-Pd(0) (0.05 mmol), CuI (0.02 mmol) and DMF (2 mL) under Ar. The resulting mixture was stirred at room temperature for 12 h. After completion of the reaction, the mixture was diluted with ethyl acetate (20 mL) and filtered. The catalyst was washed with distilled water (5 mL) and EtOH (2 × 5 mL) and could be reused in the next run. The filtrate was washed with aqueous 25% $NH_3$, which removed any CuI, and brine. It was then dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether (boiling range 60-90 ºC) and EtOAc as eluent.

*2-Methyl-6-phenylhexa-3,5-diyn-2-ol* (**3a**): White solid; m.p. 59–61 °C (lit.[24] 57–59 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (m, 2H), 7.37–7.33 (m, 3H), 2.03 (br, 1H), 1.60 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 132.6, 129.3, 128.5, 121.5, 86.7, 78.8, 73.2, 67.1, 65.8, 31.1.

*6-Phenylhexa-3,5-diyn-1-ol* (**3b**): Colourless oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 6.4 Hz, 2H), 7.38–7.30 (m, 3H), 3.81 (t, *J* = 6.2 Hz, 2H), 2.65 (t, *J* = 6.2 Hz, 2H), 1.82 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 132.6, 129.1, 128.4, 121.7, 81.0, 75.4, 74.0, 66.9, 60.8, 24.0; HRMS calcd for $C_{12}H_{10}O^+$: [$M^+$]: 170.0732; found: 170.0737.

*(6-Methoxyhexa-1,3-diynyl)benzene* (**3c**): Colourless oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.48–7.45 (m, 2H), 7.37–7.27 (m, 3H), 3.56 (t, *J* = 6.8 Hz, 2H), 3.39 (s, 3H), 2.64 (t, *J* = 6.8 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 132.5, 128.9, 128.4, 122.0, 81.1, 75.2, 74.2, 70.2, 66.1, 58.8, 20.9; HRMS calcd for $C_{13}H_{12}O^+$: [$M^+$]: 184.0888; found: 184.0875.

*1-Methoxy-4-(phenylbuta-1,3-diynyl)benzene* (**3d**): White solid; m.p. 85–87 °C (lit.[36] 86–89 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ 7.54–7.50 (m, 2H), 7.48–7.44 (m, 2H), 7.36–7.30 (m, 3H), 6.88–6.84 (m, 2H), 3.82 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 160.4, 134.1, 132.4, 129.0, 128.4, 122.1, 114.2, 113.8, 81.9, 81.0, 74.2, 72.8, 55.3.

*1-Bromo-4-(phenylbuta-1,3-diynyl)benzene* (**3e**): White solid; m.p. 142–144 °C (lit.[36] 143–145 °C); $^1$H NMR (300 MHz, $CDCl_3$): δ 7.54–7.50 (m, 2H), 7.48–7.44 (m, 2H), 7.39–7.31 (m, 5H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 134.1, 132.9, 132.1, 129.6, 128.8, 123.8, 121.9, 121.1, 82.6, 80.7, 75.3, 74.1.

*Nona-1,3-diynylbenzene* (**3f**):[24] Light yellow oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.2 Hz, 2H), 7.36–7.31 (m, 3H), 2.36 (t, *J* = 7.0 Hz, 2H), 1.61–1.57 (m, 2H), 1.43–1.34 (m, 4H), 0.93 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 132.8, 129.2, 128.6, 122.5, 85.3, 75.1, 74.7, 65.4, 31.3, 28.3, 22.5, 19.9, 14.2.

*1-Hexyl-4-(4-ethoxyphenyl)buta-1,3-diyne* (**3g**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.03 (q, *J* = 6.8 Hz, 2H), 2.34 (t, *J* = 7.0 Hz, 2H), 1.59–1.26 (m, 11H), 0.90 (t, *J* = 6.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.4, 134.0, 114.5, 113.9, 84.2, 74.9, 73.1, 65.2, 63.6, 31.3, 28.6, 28.3, 22.5, 19.6, 14.7, 14.1; HRMS calcd for $C_{18}H_{22}O^+$: [$M^+$]: 254.1671; found: 254.1662.

*1-Hexyl-4-(4-methoxyphenyl)buta-1,3-diyne* (**3h**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.2 Hz, 2H), 6.82 (d, *J* = 7.6 Hz, 2H), 3.81 (s, 3H), 2.35 (t, *J* = 6.8 Hz, 2H), 1.59–1.52 (m, 2H), 1.44–1.37 (m, 2H), 1.34–1.20 (m, 4H), 0.90 (t, *J* = 6.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 160.0, 134.1, 114.0, 112.6, 84.3, 74.8, 73.1, 65.2, 55.3, 31.3, 28.6, 28.3, 22.5, 19.6, 14.1; HRMS calcd for $C_{17}H_{20}O^+$: [$M^+$]: 240.1514; found: 240.1508.

*1-Hexyl-4-(4-ethylphenyl)buta-1,3-diyne* (**3i**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 3.81 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.59–1.54 (m, 2H), 1.44–1.39 (m, 2H), 1.36–1.19 (m, 7H), 0.90 (t, *J* = 6.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 145.4, 132.5, 128.0, 119.2, 84.5, 75.0, 73.7, 65.1, 31.3, 28.9, 28.6, 28.3, 22.6, 19.6, 15.3, 14.1; HRMS calcd for $C_{18}H_{22}^+$: [$M^+$]: 238.1722; found: 238.1734.

*1-Bromo-4-(nona-1,3-diynyl)benzene* (**3j**):[24] Light yellow oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.27 (t, *J* = 7.0 Hz, 2H), 1.51–1.47 (m, 2H), 1.32–1.21 (m, 4H), 0.83 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 134.2, 131.8, 123.4, 121.3, 85.8, 75.9, 73.7, 65.3, 31.3, 28.3, 22.5, 19.9, 14.1.

*Deca-2,4-diynyl acetate (**3k**)*:[24] Light yellow oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 4.68 (s, 2H), 2.25–2.21 (m, 2H), 2.05 (s, 3H), 1.52–1.47 (m, 2H), 1.35–1.26 (m, 4H), 0.87–0.84 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 170.2, 82.4, 71.8, 69.4, 64.5, 52.7, 31.2, 28.1, 22.4, 20.9, 19.4, 14.1.

*Trideca-5,7-diyne* (**3l**):[24] Light yellow oil; $^1$H NMR (300 MHz, $CDCl_3$): δ 2.24–2.20 (m, 4H), 1.51–1.44 (m, 4H), 1.37–1.28 (m, 6H), 0.91–0.85 (m, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 77.7, 65.4, 31.3, 30.6, 28.3, 22.5, 22.1, 19.4, 19.1, 14.2, 13.9.

*2-Methyl-6-(4-ethylphenyl)hexa-3,5-diyne-2-ol* (**3m**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 7.0 Hz, 2H), 2.65 (q, *J* = 7.0 Hz, 2H), 2.11 (br, 1H), 1.58 (s, 6H), 1.22 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 145.9, 132.6, 128.1, 118.6, 86.4, 79.2, 72.5, 67.2, 65.8, 31.2, 28.9, 15.3; HRMS calcd for $C_{15}H_{16}O^+$: [$M^+$]: 212.1201; found: 212.1192.

*2-Methyl-6-(3-fluorophenyl)hexa-3,5-diyne-2-ol* (**3n**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.32–7.23 (m, 2H), 7.19–7.14 (m, 1H), 7.10–7.01 (m, 1H), 2.01 (br, 1H), 1.59 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, $^1J_{C-F}$ = 246.0 Hz), 130.1 (d, $^3J_{C-F}$ = 9.0 Hz), 128.4 (d, $^4J_{C-F}$ = 2.0 Hz), 123.4 (d, $^3J_{C-F}$ = 10.0 Hz), 119.2 (d, $^2J_{C-F}$ = 23.0 Hz), 116.8 (d, $^2J_{C-F}$ = 21.0 Hz), 87.3, 77.3, 74.0, 66.8, 65.8, 31.1; HRMS calcd for $C_{13}H_{11}FO^+$: [$M^+$]: 202.0794; found 202.0788.

*2-Methyl-6-(4-ethoxyphenyl)hexa-3,5-diyne-2-ol* (**3o**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 2H), 6.82 (d, *J* = 7.6 Hz, 2H), 4.02 (q, *J* = 6.2 Hz, 2H), 2.22 (br, 1H), 1.57 (s, 6H), 1.41 (t, *J* = 6.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.7, 134.1,

114.6, 113.2, 86.2, 79.1, 72.0, 67.3, 65.7, 63.6, 31.2, 14.7; HRMS calcd for $C_{15}H_{16}O_2^+$: [M+]: 228.1150; found: 228.1153.

*2-Methyl-6-trimethylsilylhexa-3,5-diyne-2-ol* (**3p**):[25] Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 1.98 (br, 1H), 1.53 (s, 6H), 0.20 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 88.3, 87.6, 82.4, 67.7, 66.0, 31.5, 0.0.

*6-(4-Ethylphenyl)hexa-3,5-diyne-1-ol* (**3q**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 3.80 (t, *J* = 6.2 Hz, 2H), 2.68–2.60 (m, 4H), 1.83 (br, 1H), 1.22 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 145.7, 132.6, 128.0, 118.8, 80.6, 75.7, 73.3, 67.0, 60.8, 28.9, 24.0, 15.3; HRMS calcd for $C_{14}H_{14}O^+$: [M+]: 198.1045; found: 198.1033.

*6-(4-Ethoxylphenyl)hexa-3,5-diyne-1-ol* (**3r**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 4.02 (q, *J* = 7.0 Hz, 2H), 3.79 (t, *J* = 6.2 Hz, 2H), 2.64 (t, *J* = 6.2 Hz, 2H), 1.85 (br, 1H), 1.42 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.6, 134.1, 114.6, 113.4, 80.3, 75.7, 72.7, 67.1, 63.6, 60.9, 24.0, 14.7; HRMS calcd for $C_{14}H_{14}O_2^+$: [M+]: 214.0994; found: 214.0997.

*6-(3-Fluorophenyl)hexa-3,5-diyne-1-ol* (**3s**): Light yellow oil; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.32–7.23 (m, 2H), 7.19–7.14 (m, 1H), 7.09–7.03 (m, 1H), 3.81 (t, *J* = 6.2 Hz, 2H), 2.66 (t, *J* = 6.2 Hz, 2H), 1.84 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, $^1J_{C-F}$ = 246.0 Hz), 130.1 (d, $^3J_{C-F}$ = 9.0 Hz), 128.5 (d, $^4J_{C-F}$ = 3.0 Hz), 123.6 (d, $^3J_{C-F}$ = 9.0 Hz), 119.3 (d, $^2J_{C-F}$ = 23.0 Hz), 116.6 (d, $^2J_{C-F}$ = 21.0 Hz), 81.8, 74.8, 73.9 (d, $^4J_{C-F}$ = 3.0 Hz), 66.6, 60.7, 24.0; HRMS calcd for $C_{12}H_9FO^+$: [M+]: 188.0637; found: 188.0635.

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