Cu-Catalyzed solvent-free, pot-economic synthesis of 1,3-dynes from 1,1-dibromoalkenes in the presence of DBU•H₂O

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Abstract

An efficient synthesis of 1,3-dynes directly from 1,1-dibromoalkenes has been achieved by utilizing hydrated 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU.H₂O) as a sole reagent and a catalyst CuI. In general, 1,3-dynes were synthesized from corresponding terminal alkynes, which in turn were obtained from 1,1-dibromoalkenes. The DBU.H₂O allowed the synthesis of 1,3-dynes not only in a pot-efficient manner but also under solvent-free conditions at ambient temperature. A plausible mechanism is proposed via 1-bromoalkynes intermediate instead of terminal alkynes.

Keywords: 1,1-dibromoalkenes, Solvent-free, Bicyclic amidine, 1,3-Dynes, DBU, Pot-economic

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Symmetric and unsymmetric 1,3-Diynes are versatile structural motifs present in many natural products. Some important natural products containing a 1,3-diynes system are Norcapillene, Neocapillene, Dihydro-PHT, Atractylodin, Eneriyn, Triynol, Triynol acetate, Repandiol, Montiporyne, and Cicutoxin. In particular, aryl conjugated 1,3-diynes and their derivatives exhibit a broad spectrum of biological activity, which has made them essential synthons in the synthesis of naturally occurring biologically active complex molecules and pharmaceuticals. Besides, they have found numerous applications in supramolecular materials and electronic applications due to their unique electronic and thermal stability properties. They are also useful in the preparation of π-conjugated acetylenic oligomers and anticancer drug delivery micelles.

In view of their pharmacology and material science applications, the synthesis of aryl 1,3-diynes has received much attention in the recent development of organic chemistry. Many methods have been developed to synthesize aryl 1,3-diynes involving oxidative homocoupling of terminal alkynes, first reported by Glaser in 1869 (Scheme 1). In 1956, Eglinton and Galbraith developed base mediated Cu(OAc)\(_2\) catalyzed oxidative coupling of terminal alkynes. Later, Hay et al. reported ligand assisted CuCl catalyzed synthesis of aryl 1,3-diynes. Starting material terminal acetylenes in these reactions, in turn, are usually synthesized from 1,1-dibromoalkenes using Corey-Fuchs reaction. Recently, a few domino synthetic protocols are also available to access aryl 1,3-diynes directly from 1,1-dibromoalkenes. Satyanarayana et al. synthesized symmetrical 1,3-diynes using Cu-catalyzed homocoupling of 1,1-dibromoalkenes. Few metal-catalyzed syntheses of symmetrical 1,3-diynes from 1,1-dibromoalkenes also have been reported in the recent literature.

However, all these methods result in unsatisfactory yields or costly reagents, or harsh reaction conditions. Therefore, the development of new, improved methods for synthesizing aryl 1,3-diynes has gained much importance to current research. In our ongoing research on the development of improved methods for the synthesis of terminal acetylenes, we first explored nucleophilic reagent bicyclic imidine DBU in our laboratory to synthesize terminal acetylenes from 1,1-dibromoalkenes. Very recently, we have revealed that 1-bromoalkynes can be synthesized using two molar equivalents of non-nucleophilic reagent DBU.H\(_2\)O under solvent-free conditions at room temperature. However, Chunxiang et al. reported the ligand-free copper-catalyzed synthesis of symmetrical diynes from 1,1-dibromoalkenes using DBU in DMSO as a solvent. One of DMSO's main disadvantages in organic reactions is its removal after a reaction, and the substance dissolved in DMSO is quickly absorbed by the skin. Herein, we demonstrated the domino synthesis of aryl 1,3-diynes from 1,1-dibromoalkenes using DBU and its hydrate DBU.H\(_2\)O under solvent-free conditions at room
temperature. This effort resulted in an eco-friendly and environmentally benign solvent-free synthesis of 1,3-diynes from 1,1-dibromoalkenes.

### Results and Discussion

We commenced our investigation by examining the reaction of 5-(2,2-dibromovinyl)-1,2,3-trimethoxybenzene 1a employing DBU as base and CuI as catalyst under solvent-free conditions. We have observed very low yields of product 2a (Entry 1, Table 1); this result is attributed to the observed exothermic reaction in the absence of solvent. Our attention then turned to milder base hydrated DBU (DBU.H₂O) as a base instead of a strong base dry DBU, which was previously employed for the controlled solvent-free synthesis of 1-bromoalkynes from 1,1-dibromoalkenes. Subsequently, 1,1-dibromolakene 1a was subjected to reaction with DBU.H₂O (2 mmol) and a catalytic amount of CuI (0.1 mmol) under solvent-free conditions at room temperature. To our delight, the reaction proceeded smoothly within 2 hours without forming any by-products and produced the only product 2a with a 96 % yield (Entry 2, Table 1). Inspired by this result, we screened this organic transformation to test the efficiency of mild base DBU.H₂O and catalyst CuI with respect to time. When the reaction time was decreased to 1 hour and conducted the reaction by utilizing DBU.H₂O (2 mmol) and a catalytic amount of CuI (0.1 mmol), we observed a reduced yield of product 2a (Entry 3, Table 1). Next, it was proved when this reaction was tested by reducing the Cu catalyst loading to 0.05 mmol gave further diminishing the yield of product 2a (Entry 4, Table 1). Additionally, we also conducted the reaction by reducing the loading of DBU.H₂O to 1 mmol, gave the low yield of product 2a (Entry 5, Table 1). Finally, the optimization reaction conditions revealed that using 2 mmol of DBU.H₂O and a catalytic amount of CuI (0.1 mmol) under the solvent-free condition at room temperature is a suitable condition to afford the desired product 2a in excellent yields (Entry 2, Table 1).

**Table 1. Optimization of the reaction conditions**

| Entry | Base (equiv.)         | Cul (equiv.) | Time [h] | Yieldb |
|-------|-----------------------|--------------|----------|--------|
| 1     | Dry DBU (2)           | 0.1          | 2        | 12     |
| 2     | **DBU.H₂O (2)**       | **0.1**      | **2**    | **96** |
| 3     | DBU.H₂O (2)           | 0.1          | 1        | 87     |
| 4     | DBU.H₂O (2)           | 0.05         | 2        | 71     |
| 5     | DBU.H₂O (1)           | 0.1          | 2        | 56     |

a Reaction conditions: all reactions were carried out with 1a and Cul in the presence of DBU.H₂O at RT;
b Yields of the isolated product.
Table 2. Substrate Scope 2

| Reaction conditions: all reactions were carried out at room temperature, 1a (2 mmol) and CuI (0.1 mmol) in the presence of DBU.H₂O; Yields are for isolated products. |

In order to evaluate the substrate scope, various 1,1-dibromoalkenes 1a-q were treated with DBU.H₂O and a catalytic amount of CuI using developed solvent-free conditions. All the reactions proceeded smoothly afforded the desired products 2a-q in good to excellent yields (Table 2). The reactions with substituted 1,1-dibromoalkenes 1a-f having electron-donating group gave the desired products 2a-f in very good yields. Importantly, substrates bearing polyaromatic groups like naphthalene 1g and anthracene 1h also compatible with the conditions and gave the products 2g and 2h in 89% and 91% yields. The substrates containing electron-withdrawing groups substitution 1i-n were also well-tolerated and provided the corresponding products 2i-q in good to excellent yields. |
products 2i-n in good yields. Heteroaromatic substituted substrates 1o, and 1p underwent this reaction smoothly and gave the desired products 2o and 2p in 91% and 96% yields, respectively. Significantly, the substrate, which has aryl-vinyl substitution 1q, afforded the desired product 2q in 84% yield without affecting the reaction rate. Further, we examined this organic transformation's scope to synthesize unsymmetrical diynes 2r and 2s (Scheme 2). Experiments were conducted by utilizing substrates containing two different substituted dibromides like 1m (1 mmol) and 1a (1 mmol) reacted to give the corresponding unsymmetrical diyne 2r in 54% yield. Due to the formation of some amounts of the corresponding homo coupled by-products 21% of 2m & 13% of 2a along with unsymmetrical diyne 54 % of 2r, chromatography was necessitated to separate the products. A similar reaction was carried out with substrates like enyne 1f with 1a, giving unsymmetrical enediyne product 2s in 42% and homocoupled products 2f and 2a in 25% and 11%, respectively.

Scheme 2. Synthesis of unsymmetrical diynes 2r & 2s.

On the other hand, we also conducted experiments on a gram scale to confirm the present protocol's efficiency and robustness. Treatment of 1a and 1f under the optimized conditions gave the desired products 2a and 2f in excellent yields (Scheme 3).

Scheme 3. Gram scale synthesis of representative 1,3-diynes 2a & 2f.
It is well known from literature\textsuperscript{37} that 1,3-diynes can be straightforwardly obtained by treating terminal alkynes 3 using the Glaser-Hay coupling reaction. Further, based on the above results, our interest turned on to confirm the possible intermediate terminal alkyne or 1-bromoalkyne involved in the reaction (Scheme 4). The developed solvent-free and pot-economic reaction was performed with 1,1-bromoalkyne 1a and base DBU.H\textsubscript{2}O alone without using copper catalyst at ambient temperature. Interestingly, only corresponding 1-bromoalkyne 4a formed in good yield and there was neither 1,3-diyne 2a nor expected terminal alkyne 3a formed. These results indicated that the reaction proceeds via alkynyl bromide 2a intermediate and not through terminal alkyne intermediate 3a.

**Scheme 4.** Mechanistic investigations.

Based on the above experimental results and previous reports, a plausible catalytic mechanism can be proposed for this organic transformation (Scheme 5). We assume this reaction proceeds through the formation of 1-bromoalkyne 4 instead of terminal acetylene 3. Initially, the DBU.H\textsubscript{2}O acts as a base and eliminates HBr from dibromoalkene 1 would form bromoalkyne 4, which would further convert to complex A with Cu(I). Then, complex A added by another molecule of bromoalkyne 4 to generate dialkyne iodo complex B with Cu(III) and subsequently undergo reductive elimination to produce 1,3-diyne 2 and release the copper catalyst Cu(I).

**Scheme 5.** A plausible reaction mechanism through 1-bromoalkyne intermediate.
Conclusions

In conclusion, we have developed a green and straightforward synthetic method to access 1,3-diynes at ambient temperature. The products can be obtained in pure form without chromatography purification technique leads to save time and solvents. The usage of hydrated DBU as the sole reagent can be evidenced as a better reagent than dry DBU. This method avoids the costly palladium catalysts, harsh reaction conditions, and usage of phosphine reagents/ligands. This method proves to be an efficient synthetic approach than the existing methods in the literature.

Experimental Section

General. All reactions were carried out in oven-dried reaction flasks under nitrogen atmosphere, and dry solvents and reagents were transferred by oven-dried syringes to ambient temperature. TLC was performed on Merck silica gel aluminium sheets, and solvents were removed under reduced pressure. Columns were packed as slurry of silica gel in hexane and ethyl acetate solvent mixture. The elution was assisted by applying pressure with an air pump. $^{13}$C NMR spectra were recorded on 101 MHz spectrometers. $^1$H NMR spectra were recorded on 400 and 500 MHz spectrometers in appropriate solvents using TMS as an internal standard. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. All reactions were performed at room temperature. Reagents were obtained from Aldrich, Alfa Aesar, and TCI used without further purification. All compounds data are recorded on 400 and 500 MHz spectrometers in appropriate solvents using TMS as internal standard. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. All reactions were performed at room temperature. Reagents were obtained from Aldrich, Alfa Aesar, and TCI used without further purification. All compounds data are in consistent with the given literature report.

Typical procedure for the preparation of 1,3-Diynes. Synthesis of 1,4-bis(3,4,5-trimethoxyphenyl)buta-1,3-diyne (2a). To a 5 mL screw cap vial containing dibromoalkene 1a (0.34 g, 0.1 mmol) and CuI (19 mg, 0.2 mmol), freshly prepared DBU.H$_2$O (0.334 mL, 2.0 mmol) was added dropwise over a period of 1 min against the walls of vial at ambient temperature (25-30 °C) and stirred for 2h. The reaction mixture was quenched by the addition of water (10 mL) and extracted with EtOAc (2 x 10 mL). Organic layers were washed with 5N aqueous HCl (10 mL), water (10 mL), dried (Na$_2$SO$_4$), and evaporated to afford pure 2,5-dihydrofurane derivative 2a (0.36 g, 96%) as colorless solid. Similar experimental procedure was adopted for the preparation of 1,3-diynes 2b-q.

1,4-Bis(3,4,5-trimethoxyphenyl)buta-1,3-diyne (2a). Mp 187–189 °C, Yield 96%. $^1$H NMR (400 MHz, CDCl$_3$, 298K): δ 6.76 (4H, s, C$_6$H$_2$), 3.87 (6H, s, OCH$_3$), 3.86 (12H, s, OCH$_3$). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): δ 153.14, 139.92, 116.61, 109.72, 81.72, 73.06, 61.04, 56.21. MS (ESI, 70 eV) m/z 383 (M+H$^+$, 100%).

1,4-Di-p-tolylbuta-1,3-diyne (2b). Mp 184–187 °C, Yield 94%. $^1$H NMR (400 MHz, CDCl$_3$, 298K): δ 7.44 – 7.40 (d, 4H), 7.14 (d, J 7.9 Hz, 4H), 2.36 (6H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): δ 139.52, 132.41, 129.24, 118.82, 81.57, 73.48, 21.66. MS (ESI, 70 eV) m/z 231 (M+H$^+$, 100%).

1,4-Bis(4-methoxynaphthalen)buta-1,3-diyne (2c). Mp 130–133 °C, Yield 91%. $^1$H NMR (500 MHz, CDCl$_3$, 298K): δ 7.48 – 7.44 (d, 4H), 6.87 – 6.84 (d, 4H), 3.82 (6H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): δ 160.26, 134.07, 114.16, 113.97, 81.27, 72.99, 55.37. MS (ESI, 70 eV) m/z 263 (M+H$^+$,100%).

1,4-Bis(2,4-dimethoxyphenyl)buta-1,3-diyne (2d). Mp 186–189 °C, Yield 94%. $^1$H NMR (400 MHz, CDCl$_3$, 298K): δ 7.40 (m, 2H), 6.46 – 6.42 (m, 4H), 3.87 (s, 6H), 3.82 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): δ 162.61,
1,4-Bis(4-ethylphenyl)buta-1,3-diyne (2e). Mp 115–118 °C, Yield 86%. 1H NMR (500 MHz, CDCl₃, 298K): δ 7.39 (d, J 8.1 Hz, 4H), 7.13 (d, J 8.0 Hz, 4H), 2.64 (q, J 7.6 Hz, 4H), 0.91 (t, J 7.0 Hz, 6H). 13C NMR (101 MHz, CDCl₃, 298K): δ 145.37, 132.52, 127.94, 119.25, 84.51, 73.74, 31.06, 22.20. HRMS (El) m/z calculated for C₂₀H₁₈O₄ (M⁺) 322.121, found 322.121.

1,4-Bis(4-(benzoxyl)phenyl)buta-1,3-diyne (2f). Mp 184–186 °C, Yield 96%; 1H NMR (400 MHz, CDCl₃, 298K): δ 7.43 – 7.31 (m, 14H), 6.92 – 6.88 (m, 4H), 5.06 (s, 4H). 13C NMR (101 MHz, CDCl₃, 298K): δ 159.08, 136.52, 133.50, 128.63, 128.16, 127.50, 115.11, 114.90, 79.93, 70.07, 48.02. HRMS (El) m/z calculated for C₃₀H₂₂O₂ (M⁺) 414.162, found 414.162.

1,4-Di(naphthalen-2-yl)buta-1,3-diyne (2g). Mp 172–174 °C, Yield 89%; 1H NMR (500 MHz, CDCl₃, 298K): δ 8.43 (d, J 8.2 Hz, 2H), 7.89 (dd, J 8.2, 4.5 Hz, 4H), 7.83 (dd, J 7.2, 1.0 Hz, 2H), 7.65 – 7.62 (m, 2H), 7.56 (ddd, J 8.1, 6.9, 1.2 Hz, 2H), 7.47 (dd, J 8.2, 7.2 Hz, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 133.95, 133.16, 132.10, 129.81, 128.49, 127.28, 126.75, 126.19, 125.28, 119.57, 80.81, 78.75. MS (ESI, 70 eV) m/z 303 (M²⁺, 100%)

1,4-Di(anthracen-9-yl)buta-1,3-diyne (2h). Mp 187–189 °C, Yield 91%. 1H NMR (500 MHz, CDCl₃, 298K): δ 8.71 (d, J 8.7 Hz, 4H), 8.51 (s, 2H), 8.06 (d, J 8.5 Hz, 4H), 7.70 – 7.66 (m, 4H), 7.58 – 7.54 (m, 4H). 13C NMR (101 MHz, CDCl₃, 298K): δ 134.07, 131.17, 128.94, 127.32, 126.72, 125.98, 115.84, 85.12, 81.71. HRMS (El) m/z calculated for C₃₂H₁₈ (M⁺) 402.141, found 402.141.

1,4-Bis(4-fluorophenyl)buta-1,3-diyne (2i). Mp 86–89 °C, Yield 89%. 1H NMR (500 MHz, CDCl₃, 298K): δ 7.55 – 7.36 (m, 4H), 7.09 – 6.93 (m, 4H). 13C NMR (101 MHz, CDCl₃, 298K): δ 164.19, 161.79, 134.69, 115.95, 115.76, 89.34, 74.48. HRMS (El) m/z calculated for C₁₆H₈F₂ (M⁺) 238.059, found 238.059.

1,4-Bis(3-fluorophenyl)buta-1,3-diyne (2j). Mp 130–133 °C, Yield 91%. 1H NMR (400 MHz, CDCl₃, 298K): δ 7.34 – 7.29 (m, 4H), 7.24 – 7.19 (m, 2H), 7.13 – 7.05 (m, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 163.52, 161.06, 130.22, 130.13, 128.51, 128.49, 123.45, 123.36, 119.36, 119.13, 117.05, 116.84, 80.68, 80.65, 74.45. HRMS (El) m/z calculated for C₁₄H₁₈ (M⁺) 238.059, found 238.059.

1,4-Bis(4-(trifluoromethyl)phenyl)buta-1,3-diyne (2k). Mp 163–166 °C, Yield 86%. 1H NMR (400 MHz, CDCl₃, 298K): δ 77.67 – 7.60 (m, 8H). 13C NMR (101 MHz, CDCl₃, 298K): δ 132.83, 133.25, 130.56, 125.50, 125.46, 125.28, 125.06, 122.35, 82.58, 75.65. HRMS (El) m/z calculated for C₁₆H₁₈F₂O (M⁺) 338.053, found 338.053.

1,4-Bis(2,6-dichlorophenyl)buta-1,3-diyne (2l). Mp 192–195 °C, Yield 90%. 1H NMR (400 MHz, CDCl₃, 298K): δ 7.38 – 7.32 (m, 4H), 7.25 – 7.20 (m, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 138.61, 130.12, 127.81, 122.04, 83.02, 77.81. HRMS (El) m/z calculated for C₁₄H₁₈Cl₂ (M⁺) 337.922, found 337.922.

1,4-Bis(2,4-dichlorophenyl)buta-1,3-diyne (2m). Mp 185–187 °C, Yield 90%. 1H NMR (500 MHz, CDCl₃, 298K): δ 7.49 (d, J 8.4 Hz, 2H), 7.45 (d, J 2.0 Hz, 2H), 7.25 – 7.23 (m, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 137.83, 135.98, 134.92, 129.59, 127.22, 120.31, 79.06, 78.90. HRMS (El) m/z calculated for C₁₆H₁₂Cl₄ (M⁺) 337.922, found 337.922.

3,3’-(Buta-1,3-diyne-1,4-diyldibenzonitrile (2n). Mp 229–231 °C, Yield 89%. 1H NMR (500 MHz, CDCl₃, 298K): δ 7.81 (q, J 1.1 Hz, 2H), 7.76 – 7.74 (m, 2H), 7.67 (dt, J 7.8, 1.4 Hz, 2H), 7.51 – 7.48 (m, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 136.50, 135.83, 132.65, 129.55, 123.07, 117.65, 113.28, 79.97, 75.54. HRMS (El) m/z calculated for C₁₆H₁₂N₂ (M⁺) 252.069, found 252.069.

1,4-Di(thiophen-2-yl)buta-1,3-diyne (2o). Mp 98–100 °C, Yield 91%. 1H NMR (400 MHz, CDCl₃, 298K): δ 7.38 – 7.32 (m, 4H), 7.25 – 7.20 (m, 2H). 13C NMR (101 MHz, CDCl₃, 298K): δ 134.43, 128.94, 127.24, 121.96, 77.80, 76.67. MS (ESI, 70 eV) m/z 214 (M+H⁺, 100%).
1,4-Bis(3-methylthiophen-2-yl)buta-1,3-diyn (2p). Mp 88–89 °C, Yield 96%. $^1$H NMR (400 MHz, CDCl$_3$, 298K): $\delta$ 7.19 (d, $J$ 5.1 Hz, 2H), 6.85 (d, $J$ 5.1 Hz, 2H), 2.37 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): $\delta$ 167.37, 145.73, 129.36, 127.53, 117.63, 80.02, 15.23. HRMS (EI) m/z calculated for C$_{14}$H$_{10}$S$_2$ (M) $^+$ 242.359, found 242.359.

(1E, 7E)-1,8-Diphenylocta-1,7-dien-3,5-diyn (2q). Mp 130–132 °C, Yield 84%. $^1$H NMR (500 MHz, CDCl$_3$, 298K): $\delta$ 7.41 – 7.39 (m, 4H), 7.36 – 7.31 (m, 6H), 7.10 (d, $J$ 16.1 Hz, 2H), 6.29 – 6.24 (d, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): $\delta$ 144.45, 135.82, 129.27, 128.83, 126.48, 106.89, 82.08, 76.41. HRMS (EI) m/z calculated for C$_{20}$H$_{14}$ (M) $^+$ 254.110, found 254.110.

Typical procedure for the preparation of unsymmetrical diynes. Synthesis of 5-((2,6-dichlorophenyl)buta-1,3-diyn-1-yl)-1,2,3-trimethoxybenzene (2r). To a 5 mL screw cap vial containing dibromoalkenes 1m (0.32 g, 1 mmol), 1a (0.34 g, 1 mmol) and CuI (38 mg, 0.2 mmol), freshly prepared DBU.H$_2$O (0.668 mL, 4.0 mmol) was added dropwise over a period of 1 min against the walls of vial at ambient temperature (25–30 °C) and stirred for 3 h. The reaction mixture was quenched by the addition of water (10 mL) and extracted with EtOAc (2 x 10 mL). Organic layers were washed with 5N aqueous HCl (10 mL), water (10 mL), dried (Na$_2$SO$_4$), evaporated, and purified by column chromatography (60 – 120 mesh silica gel, 2% ethyl acetate in pet ether) to afford the diyne 2r (0.19 g, 54%) as a colorless solid. Similar experimental procedure was adopted for the synthesis of 2s.

5-((2,6-Dichlorophenyl)buta-1,3-diyn-1-yl)-1,2,3-trimethoxybenzene (2r). Mp 196–198 °C, Yield 54%. $^1$H NMR (500 MHz, CDCl$_3$, 298K): $\delta$ 7.34 (d, $J$ 8.2 Hz, 2H), 7.23 – 7.19 (m, 1H), 6.81 (s, 2H), 3.88 (s, 3H), 3.86 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$, 298K): $\delta$ 153.14, 140.19, 138.40, 129.72, 127.65, 122.33, 116.17, 109.85, 84.87, 83.72, 76.61, 74.90, 72.72, 61.04, 56.22. HRMS (EI) m/z calculated for C$_{19}$H$_{14}$Cl$_2$O$_3$ (M) $^+$ 361.218, found 361.218.

(E)-1,2,3-Trimethoxy-5-(6-phenylhexa-5-en-1,3-diyn-1-yl)benzene (2s). Mp 84–86 oC, Yield 42%. 1H NMR (500 MHz, CDCl$_3$, 298K): $\delta$ 7.42 – 7.31 (m, 5H), 7.12 (d, $J$ 16.3 Hz, 1H), 6.75 (s, 2H), 6.27 (d, $J$ 16.2 Hz, 1H), 3.87 (d, $J$ 1.6 Hz, 3H), 3.86 (d, J 2.2 Hz, 6H). 13C NMR (101 MHz, CDCl$_3$, 298K): $\delta$ 153.12, 144.59, 139.87, 135.76, 129.32, 128.84, 126.48, 116.74, 109.69, 106.75, 82.34, 81.40, 76.50, 73.41, 61.04, 56.20. HRMS (EI) m/z calculated for C$_{21}$H$_{18}$O$_3$ (M) $^+$ 318.365, found 318.365.

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Supplementary Material

$^1$H and $^{13}$C NMR Spectra for compounds 2a-s can be found using the link “Supplementary Material” in the journal issue contents page.

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