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A mild CuI-catalyzed Glaser-type homo-coupling reaction using α,α-dibromo-β-dicarbonyl compounds as oxidants

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ABSTRACT

Exploration of α,α-dibromo-β-dicarbonyl compounds as novel organic oxidants for the mild Cu(I)-catalyzed Glaser-type homo-coupling reaction has been achieved, which provides an alternatively efficient pathway for the construction of 1,3-conjugated structures. In addition, the mechanism of this reaction was investigated.

1. Introduction

Oxidative homo-coupling of terminal alkynes provides an easy and efficient access to 1,3-conjugated structures, which are an important class of building blocks with diverse applications in organic chemistry and functional materials,[1] such as for the synthesis of natural products,[2] pharmaceuticals,[3] π-conjugated acetylenic polymers,[4] and carbon-rich materials.[5] The first example of this reaction was reported by Glaser in 1869 via the treatment of terminal alkynes with Cu(I) salt in the presence of aqueous ammonia followed by air oxidation.[6] Almost one century later, two important modifications for Glaser reaction were developed by Eglinton and Hay, respectively.[7] Nowadays, a significant number of catalyst systems have been explored for this reaction, including palladium,[8,9] nickel,[10] copper,[11] cobalt,[12a] and gold[12b] catalyst systems. Among them, the copper-mediated Glaser-type coupling reactions represent the most promising methods for the synthesis of 1,3-diynes due to its economy and environmental friendliness. However, despite many copper-catalytic systems have been developed over the past decades, most of them usually required large amounts of copper salts, excessive oxidants, poisonous ligands, high reaction temperature,[13] special reaction medium,[14] or palladium complexes as co-catalysts. Recent efforts have brought about the development of several improved methods that use air as oxidant and permit the copper-catalyzed homo-coupling reactions undergoing either under mild conditions with the assistance of a ligand and base[15] or at high reaction temperature without additives.[16] In addition, a few efficient solvent-free and heterogeneous copper-catalytic systems have also been developed.[17] Given the importance of the 1,3-diyne derivatives in organic chemistry and functional materials, further exploration of mild and efficient methods for diversely synthesis of these compounds would be valuable.

α,α-Dibromo-β-dicarbonyl compounds are a series of less investigated reagents in organic synthesis that possess a similar structure with NBS.[18] We reasoned that these compounds would be prone to release one bromonium ion or two under Lewis acid or base conditions and could be used as oxidants or brominating agents[19] for the development of novel reaction methods (Eq. 1). Inspired by the pioneering works reported by Rossi and Zhang's groups in which chloroacetone and ethyl bromoacetate combined with Pd complexes were used as efficient catalytic systems for the Glaser-type coupling,[8,20] recently we launched a study to examine the conversion of terminal alkynes to 1,3-conjugated compounds via using a α,α-dibromo-β-dicarbonyl compound as oxidant. We were gratified to find that the high reactivity of these compounds allows the homo-coupling of terminal alkynes to proceed with catalytic amount of CuI in air at room temperature. Furthermore, the preliminary mechanistic study revealed that the α,α-dibromo-

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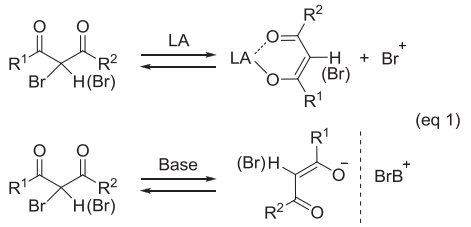
β-dicarbonyl compound most likely serve as both oxidant and ligand in this coupling reaction. Herein, we wish to report our study results on this topic.

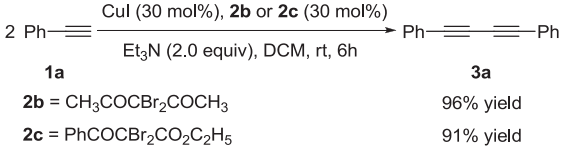


(1)

2. Results and discussion

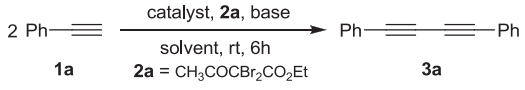
At our starting point for the development of this methodology, phenylacetylene (**1a**, 1.0 equiv) was chosen as the model substrate, CuI (15 mol %), ethyl α,α-dibromoacetoacetate (**2a** 30 mol %), and triethylamine (2.0 equiv) were selected as the catalyst, oxidant, and base, respectively (Table 1, entry 1). To our delight, the desired homo-coupling product **3a** was obtained in 52% yield in dichloromethane at room temperature. Encouraged by this initial result, extensive examination of the catalyst loading, oxidant loading, and base loading were conducted (Table 1, entries 2–7). Gratifyingly, the yield of **3a** could be improved to 95% under the optimized conditions, which employed 30 mol % CuI, 30 mol % **2a**, and 200 mol % triethylamine (Table 1, entry 3). Further investigation of solvent effects under the latter conditions revealed that dichloromethane is the most suitable solvent (Table 1, entries 3 and 8–14). Other copper salts, such as $Cu(OAc)_2 \cdot H_2O$, $Cu(acac)_2$, CuCl, and CuBr were proved to be less effective or ineffective to promote this transformation (Table 1, entries 15–18). Similar yields were obtained when triethylamine was replaced by DBU or piperidine (Table 1, entries 19 and 20). In contrast, employing either NaOAc or Cs_2CO_3 as the base, the reaction proceeded very slowly and low yields were achieved (Table 1, entries 22 and 23). Control experiments indicated that the combination of CuI, ethyl α,α-dibromoacetoacetate (**2a**), and triethylamine were essential for this coupling reaction (Table 1, entries 24–26). Furthermore, the reaction could proceed smoothly under argon atmosphere at longer reaction time (Table 1, entry 27), which suggests that ethyl α,α-dibromoacetoacetate (**2a**) acts as an oxidant and oxygen can accelerate this oxidative coupling reaction.[21]

Subsequently, other activated dibromides, such as α,α-dibromoacetylacetone (**2b**) and ethyl α,α-dibromobenzoylacetate (**2c**), were examined for this coupling reaction (Scheme 1). Expectedly, under the optimal reaction conditions (Table 1, entry 3), either **2b** or **c** can serve as oxidant and gave the corresponding homo-coupling product **3a** in 96% and 91% yields, respectively.



Scheme 1. Other dibromides for homo-coupling of **1a**.

Table 1
Optimization of homo-coupling reaction conditions[a]

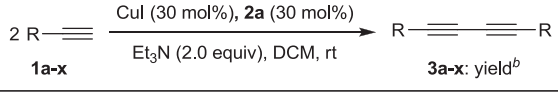


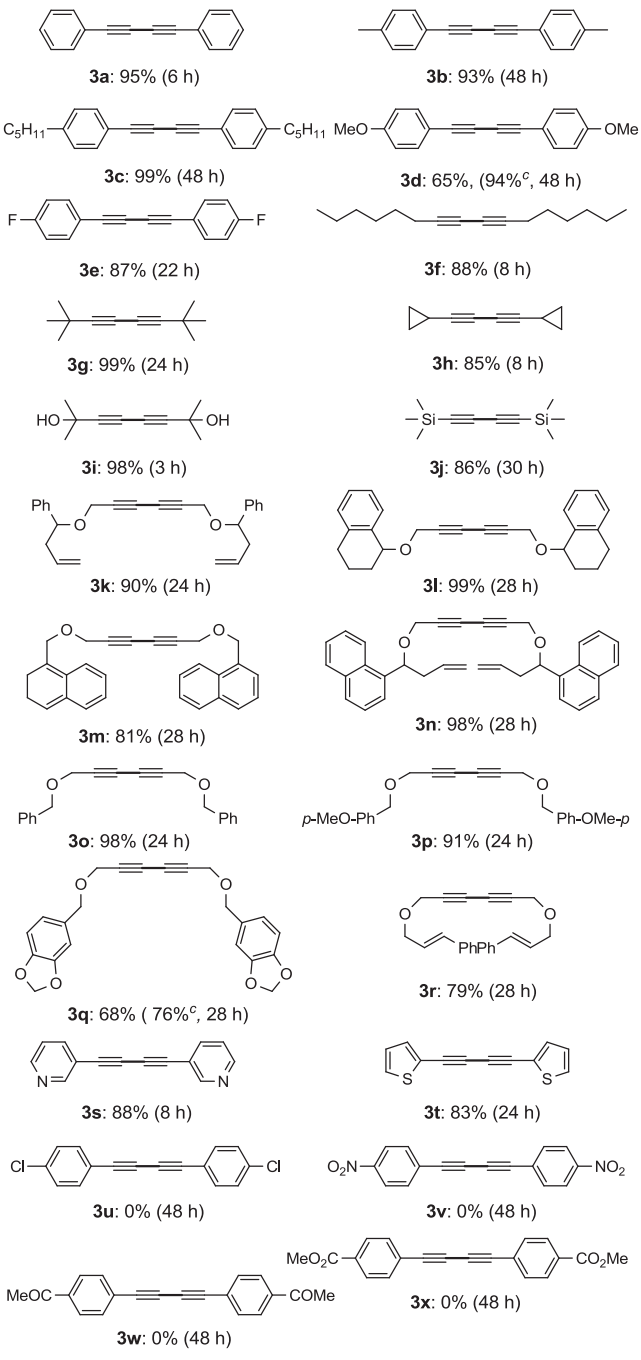
Entry	Catalyst (mol %)	**2a** (mol %)	Base (mol %)	Solvent	Yield (%)[b]
1	CuI (15)	30	Et_3N (200)	DCM	52
2	CuI (25)	30	Et_3N (200)	DCM	87
3	**CuI (30)**	**30**	**Et_3N (200)**	**DCM**	**95**
4	CuI (30)	25	Et_3N (200)	DCM	88
5	CuI (30)	50	Et_3N (200)	DCM	60
6	CuI (30)	30	Et_3N (300)	DCM	75
7	CuI (30)	30	Et_3N (100)	DCM	56
8	CuI (30)	30	Et_3N (200)	Toluene	65
9	CuI (30)	30	Et_3N (200)	DMF	66
10	CuI (30)	30	Et_3N (200)	THF	66
11	CuI (30)	30	Et_3N (200)	DMSO	81
12	CuI (30)	30	Et_3N (200)	CH_3OH	39
13	CuI (30)	30	Et_3N (200)	CH_3CN	64
14	CuI (30)	30	Et_3N (200)	CH_3NO_2	62
15	$Cu(OAc)_2$(30)	30	Et_3N (200)	DCM	78
16	$Cu(acac)_2$ (30)	30	Et_3N (200)	DCM	0
17	CuCl (30)	30	Et_3N (200)	DCM	32
18	CuBr (30)	30	Et_3N (200)	DCM	30
19	CuI (30)	30	DBU (200)	DCM	94
20	CuI (30)	30	piperidine (200)	DCM	92
21	CuI (30)	30	DABCO (200)	DCM	44
22[c]	CuI (30)	30	NaOAc (200)	DCM	29
23[c]	CuI (30)	30	Cs_2CO_3 (200)	DCM	31
24	—	30	Et_3N (200)	DCM	0
25	CuI (30)	—	Et_3N (200)	DCM	5
26	CuI (30)	30	—	DCM	0
27[d]	CuI (30)	30	Et_3N (200)	DCM	89

[a] Reaction conditions: phenylacetylene (0.55 mmol), solvent (2.0 mL), room temperature, 6 h, in air.
[b] Isolated yield.
[c] 48 h.
[d] 26 h, under argon.

With a suitable set of reaction conditions developed, the substrate scope and limitations of this copper-catalyzed oxidative coupling reaction were then investigated (Table 2). Gratifyingly, it was found that the present catalytic system showed good substrate compatibility with various aliphatic and electron-rich aromatic alkynes, providing the corresponding homo-coupling products in good to excellent yields (Table 2, **3a**–**d** and **3f**–**r**). Heteroaromatic terminal alkynes, such as 3-ethynylpyridine (**1s**) and 2-ethynyl thiophene (**1t**), also underwent this Glaser-type dimerization smoothly and afforded the desired products **3s** and **t** in 88% and 83% yields, respectively. Functional groups, including aromatic fluoro or methoxy groups, etheric groups, C=C double bond, hydroxyl, trimethylsilyl, cyclopropyl, and acetal, tolerate the reaction conditions very well (Table 2, **3d**, **e**, and **h**–**r**). Intriguingly, when the electron-poor terminal aromatic alkynes **1e**, **u**, and **v**, which bear a fluorine, chlorine atom or nitryl group at the *para*-position of the phenyl ring, were subjected to the optimized coupling conditions, a quite opposite result was obtained. **1e** was compatible with the optimal reaction conditions and gave the desired 1,3-diyne product **3e** in 87% yield. In contrast, **1u** and **v** were found to be kept intact even under the prolonged reaction time and heating condition.[22] Further employment of 1-(4-ethynyl-phenyl)-ethanone **1w** and 4-ethynyl-benzoic acid methyl ester **1x** as substrates also failed to give the desired homo-coupling products. Although the exact reason for such a dramatic difference in reactivity between **1e**, **u**, **v**, **w**, and **x** is unclear, the electronic properties of these substituents should be responsible for the results being observed. Furthermore, it is worth noting that the present catalyst system is more efficient for homo-coupling of electron-rich terminal alkynes (Table 2, **3f**–**j**) in comparison with the previously reported catalytic systems, in which the terminal aliphatic alkynes are less reactive in the Glaser coupling due to its weak acidity.[7a,17h,23]

Table 2
Homo-coupling of various terminal alkynes[a]

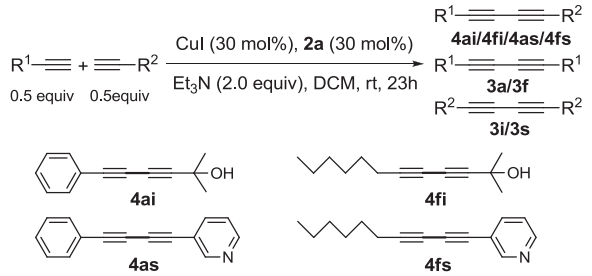




[a] Reaction conditions: Alkyne (0.55 mmol, 1.0 equiv), CuI (30 mol%), **2a** (30 mol%), Et_3N (2.0 equiv), DCM (2.0 mL), room temperature, in air.
[b] Isolated yield.
[c] Using DBU (2.0 equiv) as base.

To further investigation of the utility of this methodology, we subsequently applied our catalyst system to the cross-coupling of two different terminal alkynes.[2a,24] Unsymmetrical diynes are widely present in natural products and functional materials, and generally synthesized by cross-coupling of a 1-haloalkyne with a terminal alkyne.[25] However, this reaction often suffers from some drawbacks, such as advanced preparation of the 1-haloalkyne, formation of considerable amounts of two homocoupled byproducts, and requirement of large excessive terminal alkyne to get good yield. Under our catalyst system, it was found that a moderate yield of cross-coupling product **4ai** were obtained when reaction of equal equivalent of 2-methylbut-3-yn-2-ol (**1i**) with phenylacetylene (**1a**) (Table 3, entry 1). Further varying the ratio of two different terminal alkynes resulted in a lower yield of cross-coupling product. The 1:1 ratio of two different terminal alkynes gave the best result of cross-coupling. Other terminal alkynes including **1f** and **s** were also examined to this cross-coupling reaction, and gave comparable results with that of **4ai** (Table 3, entries 2–4).

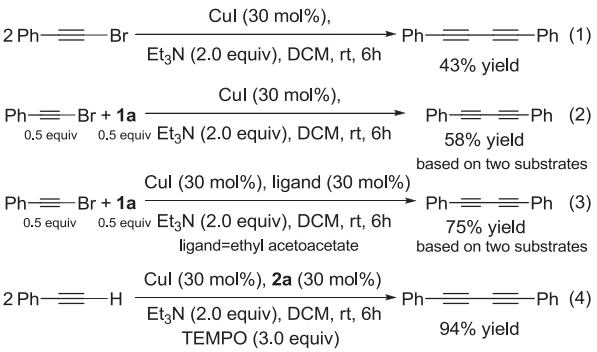
Table 3
Cross-coupling of two different terminal alkynes



Entry	R^1—	—R^2	Yield (%)[a]	Ratio[b]
1	**1a**	**1i**	99%	42/32/26 (**4ai**/**3a**/**3i**)
2	**1f**	**1i**	99%	40/40/20 (**4fi**/**3f**/**3i**)
3	**1a**	**1s**	93%	48/18/34 (**4as**/**3a**/**3s**)
4	**1f**	**1s**	98%	43/19/38 (**4fs**/**3f**/**3s**)

[a] Total isolated yield.
[b] Ratio of isolated yields.

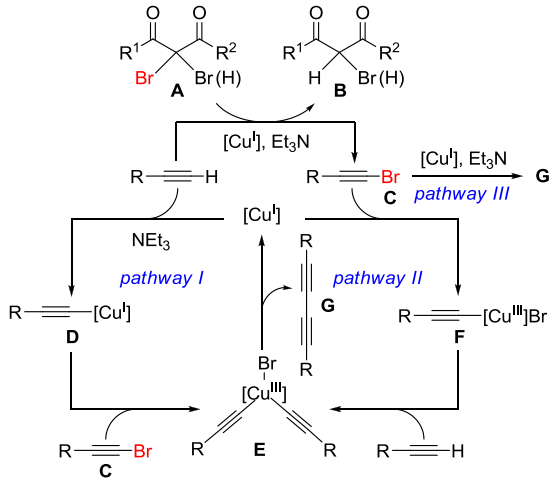
To gain some understanding of the mechanism, preliminary studies were carried out. First, during the homo-coupling of **1a**, dibromide **2a** was found to be converted into ethyl acetoacetate and ethyl α-bromoacetoacetate.[26] This indicated that both α,α-dibromo- and α-monobromo-β-dicarbonyl compounds can act as the oxidant by losing their bromine atom.[27] Second, when the homo-coupling reaction of **1a** was quenched after 2 h, in addition to product **3a**, phenylethynyl bromide can be isolated in 11% yield as a byproduct,[28] suggesting that the bromoalkyne might be a reactive intermediate. Third, a moderate yield of product **3a** can be obtained (Scheme 2, Eq. 1) through homo-coupling of phenylethynyl bromide under the reaction conditions without oxidant **2a**, indicating that part of product **3a** might be generated from direct dimerization of the in situ formed bromoalkyne intermediate. Fourth, the phenylethynyl bromide could react with alkyne **1a** under the reaction conditions without oxidant **2a** to give a moderate yield of product



Scheme 2. Control experiments.

3a, which could be improved by addition of ethyl acetoacetate (Scheme 2, Eqs. 2 and 3). This suggested that Cu(I)-catalyzed cross-coupling between in situ formed phenylethynyl bromide and the terminal alkyne might be the major reaction pathway, and the 1,3-dicarbonyl compounds most likely serve as ligand in this reaction.[29] Fifth, it was found that addition of a radical scavenger, TEMPO, did not inhibit the reaction (Scheme 2, Eq. 4). Therefore, the radical process was unlikely in our reaction.[14b]

Based on the above results, two tentative pathways for this reaction were proposed in Scheme 3. Part of terminal alkyne substrate was first transformed to the corresponding bromoalkyne **C** by the bromodicarbonyl compound **A** in the presence of Cu(I) and Et_3N. Then, cross-coupling between bromoalkyne **C** and the terminal alkyne proceeded through either pathway I or II, in which the generation of dialkynylcopper(III) intermediate **E** and the reductive elimination on this intermediate were the key steps. Besides these two pathways, part of diyne product **G** can be derived from homo-coupling of the bromoalkyne (pathway III). We assumed that the 1,3-dicarbonyl compounds in the reaction system, i.e., ethyl α-monobromoacetoacetate and ethyl acetoacetate, may act as the ligand for the involved copper intermediates.



Scheme 3. Tentative reaction pathways.

3. Conclusions

In summary, we have disclosed a novel copper-based catalytic system for Glaser-type coupling reactions using α,α-dibromo-β-dicarbonyl compounds as oxidants. This catalytic system provides a very mild and efficient method for the construction of various symmetric 1,3-conjugated diynes. Moreover, preliminary study indicates that this versatile catalytic system has a potential for synthesizing of unsymmetrical diynes. Further investigation of this catalytic system in cross-coupling of two different alkynes and the utility of α,α-dibromo-β-dicarbonyl compounds in organic synthesis are underway in our laboratory.

4. Experimental

4.1. General informations

Reactions were monitored by analytical thin-layer chromatography (TLC) using ultraviolet light, phosphomolybdic acid or $KMnO_4$ for visualization. All reagents were purchased as reagent grade and used without further purification. Purification of products was accomplished by flash chromatography on silica gel (200–300 mesh) and the purified compounds show a single spot by analytical TLC. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $CDCl_3$ as the solvent with TMS as internal standard. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (Hertz), respectively. High-resolution mass spectra (HRMS) were performed on a ICP-MS or ITCI-Orbitrap Elite spectrometer. Melting points were measured on a micro melting apparatus and uncorrected.

4.2. General procedure for the synthesis of alkynes 1k–r[30]

To a stirred solution of alcohol (14.5 mmol, 1.0 equiv) in anhydrous DMF (25 mL) was added sodium hydride (60 percent in oil, 1.16 g, 29 mmol, 2.0 equiv) at 0 °C. The mixture was further stirred at 0 °C for 2 h before slowly addition of propargyl bromide (2.59 g, 21.6 mmol, 1.5 equiv). After stirred at room temperature overnight, the reaction was quenched by addition of ice-water and extracted with EtOAc twice. The combined organic phase was washed with brine and dried over $MgSO_4$. Evaporation of solvent provided the crude product as a color residue. The crude product was purified by column chromatography on silica gel with mixture of petroleum ether and ethyl acetate to afford alkynes **1k**–**r**.

4.3. General procedure for the synthesis of α,α-dibromo-β-dicarbonyl compounds[18b]

To a solution of β-dicarbonyl compound (ethyl acetoacetate, acetylacetone or ethyl benzoylacetate) (1.0 equiv) in 20 mL of DCE was added *N*-bromosuccinimide (NBS) (3.42 g, 19.2 mmol, 2.5 equiv), and the mixture was stirred at 60 °C for 7 h. Filtration followed by removal of the solvent and the crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=10:1) to afford the title compound (**2a**, **b** or **c**).

4.4. General procedure for homo-coupling of alkynes

Ethyl α,α-dibromoacetoacetate **2a** (46.1 mg, 0.16 mmol, 30 mol %), alkynes **1a**–**v** (0.55 mmol, 1.0 equiv), CuI (30.5 mg, 0.16 mmol, 30 mol %), and triethylamine (0.15 mL, 1.1 mmol, 2.0 equiv) were added under ambient temperature to 2 mL of CH_2Cl_2 in air. After stirred at room temperature for the appropriate time (monitored by TLC), the reaction was quenched by addition of H_2O (3 mL) and then extracted with ethyl acetate (3×3 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel with mixture of petroleum ether and ethyl acetate as eluent to afford the corresponding products **3a**–**v**.

4.5. General procedure for cross-coupling of two different alkynes

Ethyl α,α-dibromoacetoacetate **2a** (106.5 mg, 0.37 mmol, 30 mol %), phenylacetylene **1a** (63.3 mg, 0.62 mmol, 0.5 equiv) or 1-octyne **1f** (68.3 mg, 0.62 mmol, 0.5 equiv), 2-methyl-3-butyn-2-ol **1i** (52.2 mg, 0.62 mmol, 0.5 equiv) or 3-ethynylpyridine **1s** (64 mg, 0.62 mmol, 0.5 equiv), CuI (70.5 mg, 0.37 mmol, 30 mol %), and triethylamine (0.35 mL, 2.48 mmol, 2.0 equiv) were added under ambient temperature to 2 mL of CH_2Cl_2 in air. After stirred at room temperature for the appropriate time (monitored by TLC), the reaction was quenched by addition of H_2O (3 mL) and then extracted with ethyl acetate (3×3 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel with mixture of petroleum ether and ethyl acetate as eluent. The radio of products: **3a**:**4ai**:**3i**=32:42:26; **3f**:**4fi**:**3i**=40:40:20; **3a**:**4as**:**3s**=18:48:34; **3f**:**4fs**:**3s**=19:43:38.

4.6. Characterization data

*4.6.1. 1,4-Diphenylbuta-1,3-diyne (**3a**).* White solid: 53 mg, 95%; mp 86.8–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, J=8.0, 1.4 Hz, 4H), 7.39–7.28 (m, 6H). This compound was known.[21a]

*4.6.2. 1,4-Dip-tolylbuta-1,3-diyne (**3b**).* White solid: 59 mg, 93%; mp 179–183 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J=7.9 Hz, 4H), 7.14 (d, J=7.8 Hz, 4H), 2.37 (s, 6H). This compound was known.[21a]

*4.6.3. 1,4-Bis(4-pentylphenyl)buta-1,3-diyne (**3c**).* White solid: 93 mg, 99%; mp 87–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J=8.1 Hz, 4H), 7.14 (d, J=8.0 Hz, 4H), 2.62–2.58 (m, 4H), 1.64–1.55 (m, 4H), 1.36–1.25 (m, 8H), 0.89 (t, J=6.8 Hz, 6H). This compound was known.[11b]

*4.6.4. 1,4-Bis(4-methoxyphenyl)buta-1,3-diyne (**3d**).* White solid: 47 mg, 65% or 68 mg, 94% (using DBU as base); mp 138–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J=8.8 Hz, 4H), 6.85 (d, J=8.4 Hz, 4H), 3.82 (s, 6H). This compound was known.[21a]

*4.6.5. 1,4-Bis(4-fluorophenyl)buta-1,3-diyne (**3e**).* White solid: 57 mg, 87%; mp 188–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.47 (m, 4H), 7.04 (t, J=8.6 Hz, 4H). This compound was known.[11a]

*4.6.6. Hexadeca-7,9-diyne (**3f**).* Yellow oil: 53 mg, 88%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (t, J=7.0 Hz, 4H), 1.56–1.47 (m, 4H), 1.42–1.34 (m, 4H), 1.29 (ddd, J=10.2, 8.7, 2.5 Hz, 8H), 0.89 (t, J=6.9 Hz, 6H). This compound was known.[8b]

*4.6.7. 2,2,7,7-Tetramethylocta-3,5-diyne (**3g**).* White solid: 44 mg, 99%; mp 86–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (s, 18H). This compound was known.[21a]

*4.6.8. 1,4-Dicyclopropylbuta-1,3-diyne (**3h**).* Yellow oil: 30 mg, 85%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31–1.25 (m, 2H), 1.08–0.49 (m, 8H). This compound was known.[11a]

*4.6.9. 2,7-Dimethylocta-3,5-diyne-2,7-diol (**3i**).* White solid: 45 mg, 98%; mp 133–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 (s, 2H), 1.35 (s, 12H). This compound was known.[8b]

*4.6.10. 1,4-Bis(trimethylsilyl)buta-1,3-diyne (**3j**).* White solid: 46 mg, 86%; mp 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.19 (s, 18H). This compound was known.[31]

*4.6.11. 1,6-Bis(1-phenylbut-3-enyloxy)hexa-2,4-diyne (**3k**).* Yellow oil: 92 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.26 (m, 10H), 5.76 (ddt, J=14.0, 10.1, 6.9 Hz, 2H), 5.05 (t, J=13.0 Hz, 4H), 4.53 (t, J=6.7 Hz, 2H), 4.19 (d, J=16.3 Hz, 2H), 3.93 (d, J=16.3 Hz, 2H), 2.62 (dt, J=14.3, 7.1 Hz, 2H), 2.52–2.38 (m, 2H). This compound was known.[14a]

*4.6.12. 1,6-Bis(1,2,3,4-tetrahydronaphthalen-1-yloxy)hexa-2,4-diyne (**3l**).* Yellow oil: 101 mg, 99%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.41–7.33 (m, 2H), 7.25–7.14 (m, 4H), 7.13–7.06 (m, 2H), 4.67 (t, J=4.3 Hz, 2H), 4.33 (s, 4H), 2.84 (dt, J=16.8, 5.3 Hz, 2H), 2.76–2.66 (m, 2H), 2.08–1.97 (m, 4H), 1.92 (ddd, J=15.2, 5.9, 3.2 Hz, 2H), 1.79–1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 135.5, 129.6, 129.0, 127.8, 125.7, 76.0, 74.0, 70.2, 55.8, 28.9, 27.7, 18.5; HRMS (EI, m/z) calcd for $C_{26}H_{26}O_2$ $[M]^+$, 370.1933, found 370.1939.

*4.6.13. 1,6-Bis(naphthalen-1-ylmethoxy)hexa-2,4-diyne (**3m**).* Yello w oil: 87 mg, 81%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J=8.3 Hz, 2H), 7.84 (dd, J=13.2, 8.1 Hz, 4H), 7.57–7.47 (m, 6H), 7.46–7.40 (m, 2H), 5.07 (s, 4H), 4.29 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.6, 132.3, 131.7, 129.0, 128.4, 127.1, 126.3, 125.8, 125.0, 123.9, 75.4, 70.7, 70.1, 57.4; HRMS (EI, m/z) calcd for $C_{28}H_{22}O_2$ $[M]^+$, 390.1620, found 390.1619.

*4.6.14. 1,6-Bis(1-(naphthalen-1-yl)but-3-enyloxy)hexa-2,4-diyne (**3n**).* Yellow oil: 127 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.19 (d, J=8.0 Hz, 2H), 7.88 (d, J=7.5 Hz, 2H), 7.80 (d, J=8.0 Hz, 2H), 7.50 (dt, J=15.4, 7.4 Hz, 8H), 5.87 (dd, J=17.1, 10.1 Hz, 2H), 5.30 (t, J=5.5 Hz, 2H), 5.08 (dd, J=17.8, 14.3 Hz, 4H), 4.27 (d, J=16.4 Hz, 2H), 4.00 (d, J=16.4 Hz, 2H), 2.71 (dtd, J=20.6, 14.3, 6.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.9, 134.6, 133.9, 130.9, 128.9, 128.3, 126.1, 125.5, 125.3, 124.6, 123.2, 116.9, 78.5, 75.4, 70.3, 56.3, 41.5; HRMS (EI, m/z) calcd for $C_{34}H_{30}O_2$ $[M]^+$, 470.2246, found 470.2230.

*4.6.15. 1,6-Bis(benzyloxy)hexa-2,4-diyne (**3o**).* Yellow oil: 78 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.26 (m, 10H), 4.61 (s, 4H), 4.25 (s, 4H). This compound was known.[24a]

*4.6.16. 1,6-Bis(4-methoxybenzyloxy)hexa-2,4-diyne (**3p**).* Yellow solid: 88 mg, 91%; mp 63–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J=8.4 Hz, 4H), 6.88 (d, J=8.5 Hz, 4H), 4.53 (s, 4H), 4.21 (s, 4H), 3.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 129.8, 129.1, 113.8, 75.4, 71.4, 70.5, 57.1, 55.2; HRMS (EI, m/z) calcd for $C_{22}H_{22}O_4$ $[M]^+$, 350.1518, found 350.1526.

*4.6.17. 1,6-Bis(benzo[d][1,3]dioxol-5-ylmethoxy)hexa-2,4-diyne (**3q**).* Yellow solid: 71 mg, 68% or 79 mg, 76% (using DBU as base); mp 58–63 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93–6.73 (m, 6H), 5.95 (s, 4H), 4.50 (s, 4H), 4.22 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 147.4, 130.8, 121.9, 108.8, 108.1, 101.0, 75.3, 71.6, 70.5, 57.1; HRMS (EI, m/z) calcd for $C_{22}H_{18}O_6$ $[M]^+$, 378.1103, found 378.1102.

*4.6.18. 1,6-Bis(cinnamyloxy)hexa-2,4-diyne (**3r**).* White solid: 74 mg, 79%; mp 64–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, J=7.6 Hz, 4H), 7.31 (t, J=7.5 Hz, 4H), 7.24 (t, J=7.1 Hz, 2H), 6.64 (d, J=15.9 Hz, 2H), 6.25 (dt, J=15.9, 6.2 Hz, 2H), 4.27 (s, 4H), 4.23 (d, J=6.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 133.6, 128.5, 127.8, 126.5, 124.7, 75.4, 70.4, 57.4; HRMS (EI, m/z) calcd for $C_{24}H_{22}O_2$ $[M]^+$, 342.1620, found 342.1609.

*4.6.19. 1,4-Di(pyridin-3-yl)buta-1,3-diyne (**3s**).* White solid: 49 mg, 88%; mp 156–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (s, 2H), 8.61 (d, J=4.8 Hz, 2H), 7.88–7.79 (m, 2H), 7.31 (dd, J=7.9, 5.0 Hz, 2H). This compound was known.[11b]

*4.6.20. 1,4-Di(thiophen-2-yl)buta-1,3-diyne (**3t**).* White solid: 49 mg, 83%; mp 85–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dd, J=7.5, 4.4 Hz, 2H), 7.04–6.96 (m, 1H). This compound was known.[11a]

*4.6.21. 2-Methyl-6-phenylhexa-3,5-diyn-2-ol (**4ai**).* White solid: 48 mg, 42%; mp 68–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, J=8.0, 1.4 Hz, 2H), 7.38–7.27 (m, 3H), 1.57 (d, J=5.5 Hz, 6H). This compound was known.[24a]

*4.6.22. 2-Methyldodeca-3,5-diyn-2-ol (**4fi**).* Colorless oil: 47 mg, 40%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (t, J=7.0 Hz, 2H), 1.59–1.46 (m, 8H), 1.43–1.25 (m, 6H), 0.89 (t, J=6.9 Hz, 3H). This compound was known.[32]

*4.6.23. 3-(Phenylbuta-1,3-diynyl)pyridine (**4as**).* White solid: 56 mg, 48%; mp 102–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.63–8.55 (m, 1H), 7.85–7.78 (m, 1H), 7.58–7.52 (m, 2H),

7.41–7.33 (m, 3H), 7.29 (dd, *J*=7.7, 5.2 Hz, 1H). This compound was known.[33]

*4.6.24. 3-(Deca-1,3-diynyl)pyridine (**4fs**).* Yellow oil: 55 mg, 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.54 (d, *J*=4.8 Hz, 1H), 7.76 (dd, *J*=7.9, 2.0 Hz, 1H), 7.28–7.23 (m, 1H), 2.38 (t, *J*=7.0 Hz, 2H), 1.65–1.53 (m, 3H), 1.47–1.39 (m, 2H), 1.32–1.28 (m, 3H), 0.90 (t, *J*=6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 143.7, 134.2, 117.8, 81.2, 71.7, 66.0, 59.5, 26.1, 23.4, 22.9, 17.3, 14.4, 8.9; HRMS (ITCI, *m*/*z*) calcd for $C_{15}H_{18}N$ $[M+H]^+$, 212.1434, found 212.1436.

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Supplementary data

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27. Two control experiments were conducted by using ethyl α-bromoacetoacetate as oxidant to homo-coupling of alkyne **1a** under the optimal reaction conditions. **3a** could be isolated in 46% and 78% yields, respectively, when 30 mol % and 60 mol % of ethyl α-bromoacetoacetate were used. This indicated that the α-bromo-β-dicarbonyl compounds also can serve as oxidant.
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