RESEARCH ARTICLE

Cu-catalyzed, Mn-mediated propargylation and allenylation of aldehydes with propargyl bromides

Rongli Zhang[1*], Yanping Xia[2], Yuchen Yan[1] and Lu Ouyang[2*]

Abstract

A simple, practical, and high chemo-selective method for the synthesis of propargyl alcohol and allenyl alcohols via Cu-catalyzed, Mn-mediated propargylation and allenylation of aldehydes with propargyl bromides has been established. When 3-bromo-1-propyne was conducted under the standard condition, the aldehydes were transformed to the corresponding propargylation products completely, while when 1-bromo-2-pentyne was used, allenic alcohol was the only product. Variety of homopropargyl alcohols and allenyl alcohols were obtained in high yields and the reaction is compatible with broad substrate scopes. In addition, the large-scale reaction could also be proceeded smoothly indicating the potential synthetic applications of this transformation.

Keywords: Propargylation, Allenylation, Mn powder, Cu-catalyzed, Gram scale

Graphical Abstract

- **High yield**
- **Mild reaction condition**
- **Good chemoselectivity**
- **Wide substrates scope**
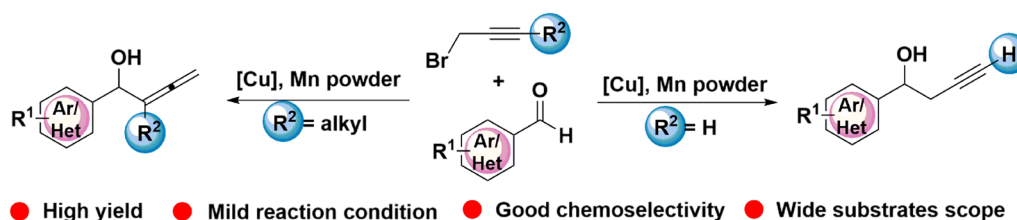
Introduction

Propargyl and allenyl groups are not only valuable building blocks for further manipulations and organic transformations in organic synthesis [1–7], but also sever as active structural moieties in plentiful functional molecules which are important in bioactive molecules, pharmaceuticals agents and natural products [8–13]. Thus, this interesting and promising synthetic method has been attracting a great deal of attentions [14–23]. Numerous methods have been established by using propargyl halides and metals to produce the nucleophilic character of the propargyl metal species [24–26]. When the nucleophilic receptor is an aldehyde, the homopropargyl alcohol can be obtained by the nucleophilic addition of propargyl metal species and aldehyde [27, 28]. Variety of metals, including In [29–31], Sb [32], Pb [33], Ti [34], Cr [35], Ga [36], Sn [37], Zn [38, 39], Mn [40] and Sc [41], have been used for this coupling reaction which could afford the corresponding homopropargyl alcohols. While, the by-product allenyl alcohol is inevitable, which can be owned

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to the rearrangement of the crucial intermediate propargyl metal species to allenyl metal species [42]. Therefore, a mixture of homopropargyl alcohol and allenyl alcohol were generally obtained. Despite the encouraging progress has been made [43–45], long reaction time–cost, moderate yields and low chemo-selectivity has limited the applications. Therefore, there is still demands for the improved method with respect to selectivities for homopropargyl alcohol and allenyl alcohols.

As we known, Cu catalyst, is not only abundant, easy to utilize, and relatively insensitive to water and air, but also has advantageous for the controllable access to Cu(0), Cu(I), Cu(II), and Cu(III) oxidation states [46, 47]; possibly because of its single-electron transfer (SET) and two-electron processes (TEPs) pathway [48, 49]; which make the catalytic system with high catalytic activities and rate. Moreover, Manganese has been widely used in organic reactions by virtue of its environmentally benign and sustainable nature, low cost and versatile reactivity [50, 51]. Up to now, there were only few examples had been reported, but they showed the activity of Mn in the proparylation reaction. So will the combination of Cu-catalyst and Mn powder increase the catalytic efficiency in the proparylation of propargyl bromide with aldehyde?

In this paper, we developed the first example of Cu-catalyzed and Mn-mediated propargylation and allenylation of aldehydes with propargyl bromides under a novel catalytic system, which is covered with advantages of high efficiency, good chemo-selectivity, and wide substrates scopes under mild reaction conditions (Fig. 1).

We initiated our investigation using benzaldehyde (**1a**) and propargyl bromide (**2a**) as model substrates which catalyzed by copper salts and Mn powder (Table 1). Without Mn, only trace amount of desired product was observed which indicated that Mn powder is indispensable (Table 1, entry 1). While in the absence of CuBr$_2$, 16% of **3a** was produced which demonstrated the great importance of Cu catalyst (entry 2). Screening of different solvents illustrated that MeCN is the best reaction medium, giving the desired product **3a** in 47% yield (entry 3). While, only trace amount of product was observed in THF or DCM and 24% in EtOH (entries 4–6). The yield of products dropped sharply when the reaction was carried out in the open system (entry 7). Meanwhile, without the addition of CF$_3$COOH, only 13% yield of **3a** was achieved (entry 8). Subsequently, extensive experiments were conducted to investigate the effects of different copper salts on the reaction. Series of Cu catalysts, including CuSO$_4$, CuCl, CuCl$_2$, CuBr and CuI were tested and CuCl gave the best result (entries 9–13). Adding 5 equiv. Mn powder, a remarkable increase has been presented (entry 14). Simultaneously, a light increase of yield was observed by increasing the amount of catalyst (entry 15). Further studies indicated that extending the reaction time to 24 h, **1a** can be transformed to **3a** completely under the standard conditions (entry 16).
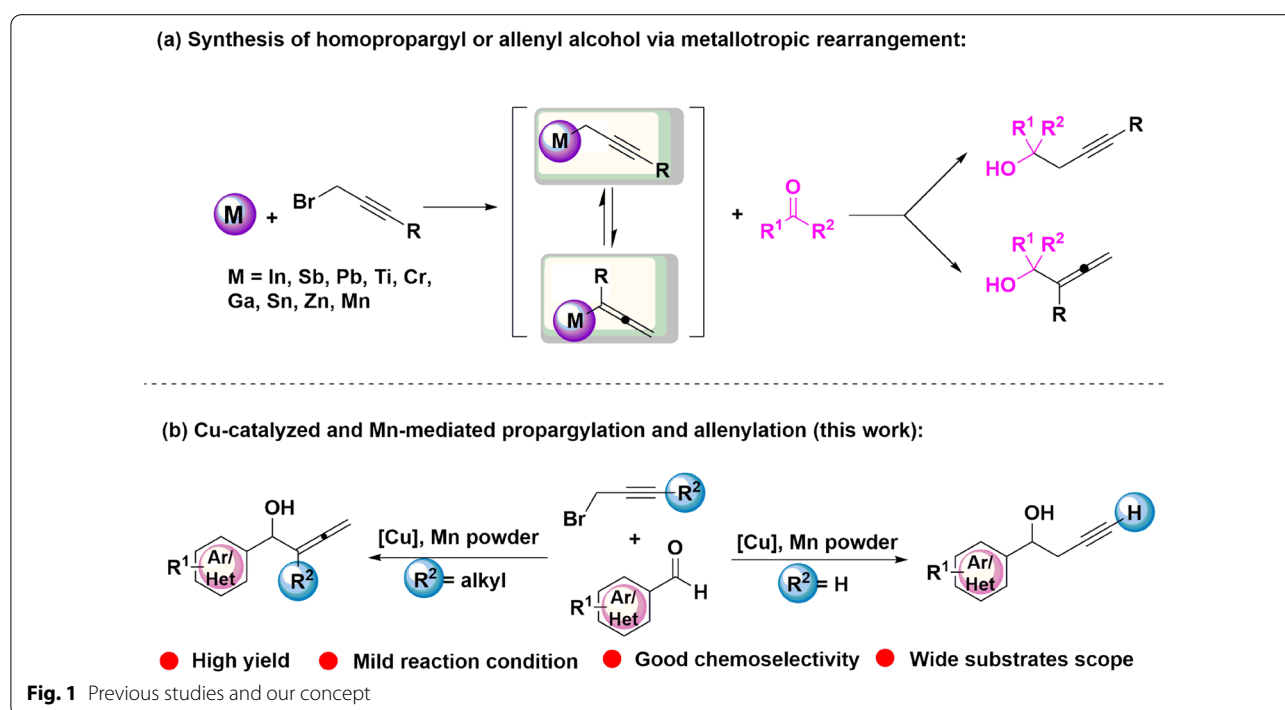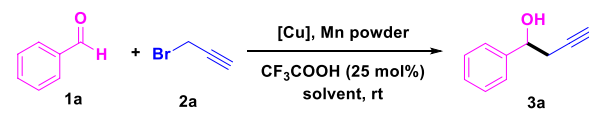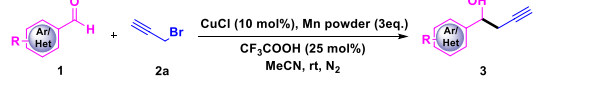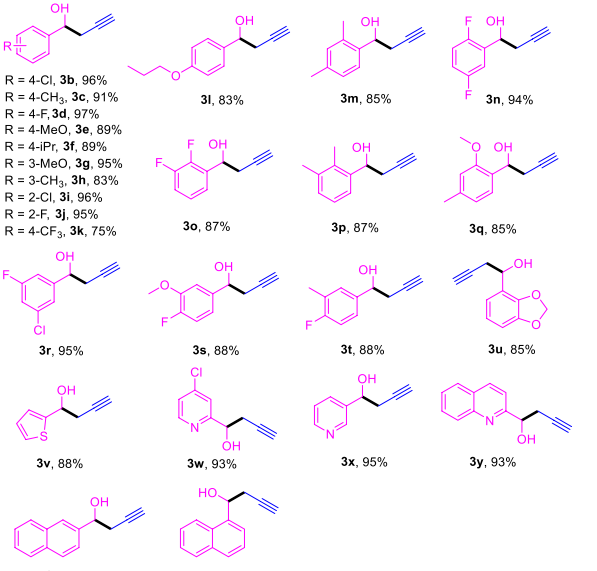

Fig. 1 Previous studies and our concept

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Table 1 The effect of different parameters on the reaction of **1a** and **2a**.[a]

Entry	[Cu]	Solvent	Mn	Time/h	Yield/% of 3a[b]
1	CuBr$_2$	MeCN	–	12	Trace
2	–	MeCN	Mn	12	16
3	CuBr$_2$	MeCN	Mn	12	47
4	CuBr$_2$	THF	Mn	12	Trace
5	CuBr$_2$	DCM	Mn	12	Trace
6	CuBr$_2$	EtOH	Mn	12	24
7[c]	CuBr$_2$	MeCN	Mn	12	24
8[d]	CuBr$_2$	MeCN	Mn	12	13
9	CuSO$_4$	MeCN	Mn	12	59
10	CuCl	MeCN	Mn	12	83
11	CuCl$_2$	MeCN	Mn	12	63
12	CuBr	MeCN	Mn	12	74
13	CuI	MeCN	Mn	12	41
14[e]	CuCl	MeCN	Mn	12	75
15[f]	CuCl	MeCN	Mn	12	33
16	CuCl	MeCN	Mn	24	>99

[a] Reaction conditions: All reactions were performed with **1a** (0.5 mmol), **2a** (1.5 equiv.), copper catalyst (10 mol%), Mn powder (3 equiv.), CF$_3$COOH (25 mol%), solvent (2 mL), at room temperature under N$_2$ atmosphere. [b] Yield was determined by GC with dodecane as internal standard based on **1a**. [c] Reaction in the air. [d] Without CF$_3$COOH. [e] 5.0 equiv. of Mn was added. [f] CuCl (20 mol%) added.

Table 2 Cu-catalyzed and Mn-mediated propargylation of different aldehydes[a]
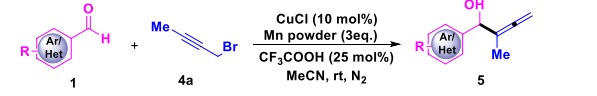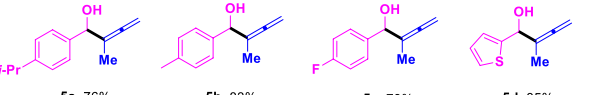
[a] Standard condition: a solution of **1** (0.5 mmol), **2a** (1.5 equiv.), CuCl (10 mol%), Mn powder (3 equiv.) and CF$_3$COOH (0.25 equiv.) in MeCN (2.0 mL) was reacted conducted at room temperature under N$_2$ atmosphere for 24 h

With the optimized setup in hand, we next explored the substrates scope of aldehydes with different functional groups as shown in Table 2. It is pleasing that substrates bearing both electron-donating groups (EDGs) and electron-withdrawing groups (EWGs) can proceed smoothly. For example, substrates **3c**, **3e**, **3f**, **3g**, **3h**, **3i**, **3k** and **3o** with alkyl and alkoxy groups can be transformed to the corresponding products in excellent yield. Substrates containing the halogen (**3b**, **3d**, **3i**, **3j**) can also deliver the corresponding products with excellent yields. In addition, disubstituted benzaldehydes, such as 2,4-dimethyl (**3m**), 2,3-dimethyl (**3p**), 2,5-difluoro (**3n**), 2,3-difluoro (**3o**), 2-methoxy-4-methyl (**3q**) 3-chloro-5-fluoro (**3r**), 3-methoxy-4-fluoro (**3s**) and 3-methyl-4-fluor (**3t**) benzaldehydes were found to be compatible with the reaction in 85%- 95% yields. To further expand the scopes of the present catalytic system, reactions of heteroaromatic aldehydes including thiophenecarboxaldehyde (**3v**), pyridylaldehydes (**3w** and **3x**) and quinolinecarboxaldehyde (**3y**) which contain aromatic heterocycle in the molecules were also explored. Interesting, all of these substrates were compatible with the reaction conditions and

produced the homopropargyl alcohols in excellent yield. Naphthyl compounds is also effective for the transformation converted to **3z** and **3ab** in the yield of 94% and 96% respectively.

When 1-bromo-2-butyne (**4a**) was used instead of propargyl bromide, the rearrangement product allenyl alcohol was achieved with good yield under the same reaction conditions (Table 3). Importantly, the direct propargylation product was not detected in this catalytic system, which indicated that the chemo-selectivity for this reaction is quite good. For example, substrates (**5a–5c**) which substituted by isopropyl-, methyl- and

Table 3 Cu-catalyzed and Mn-mediated allenylation of different aldehydes[a]

[a] Standard condition: a solution of **1** (0.5 mmol), **4a** (1.5 equiv.), CuCl (10 mol%), Mn powder (3 equiv.) and CF$_3$COOH (0.25 equiv.) in MeCN (2.0 mL) was reacted conducted at room temperature under N$_2$ atmosphere for 24 h

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fluoro- groups on the aromatic ring, reacted well and provided the corresponding products in moderate yields. In addition, heteroaromatic aldehyde (**5d**) is also worked for the transformation and an allenyl substituted alcohol (**5e**) was obtained with 85% yield.

To demonstrate the synthetic applications of our protocols, we tried to scale up the reaction of benzaldehyde (**1a**) with 3-bromo-1-propyne (**2a**) or 1-bromo-2-pentyne (**4a**) independently under standard conditions (Fig. 2). The corresponding products **3a** or **5a** was obtained in a gram-scale, which highlightened the potential applicability of this transformation in organic synthesis.

Based on the above results and studies reported in the previous reference, a tentative mechanism for the Cu-Catalyzed, Mn-mediated propargylation and allenylation of aldehydes with propargyl bromides was proposed in Fig. 3 [52–56]. Mn, which is severed as a strong reducing agent, reduced the Cu^I to Cu^0 in an active form in situ. Insertion of Cu^0 to propargyl bromides gives the crucial intermediate progargyl metal species (**Int-I**) and allenyl metal species (**Int-II**). Then, nucleophilic addition of aldehydes conducted smoothly with metal species to deliver the **Int-III** and **Int-IV**. Finally, desired products were obtained in the presence
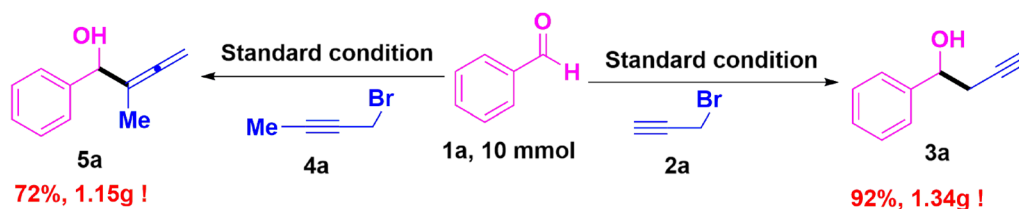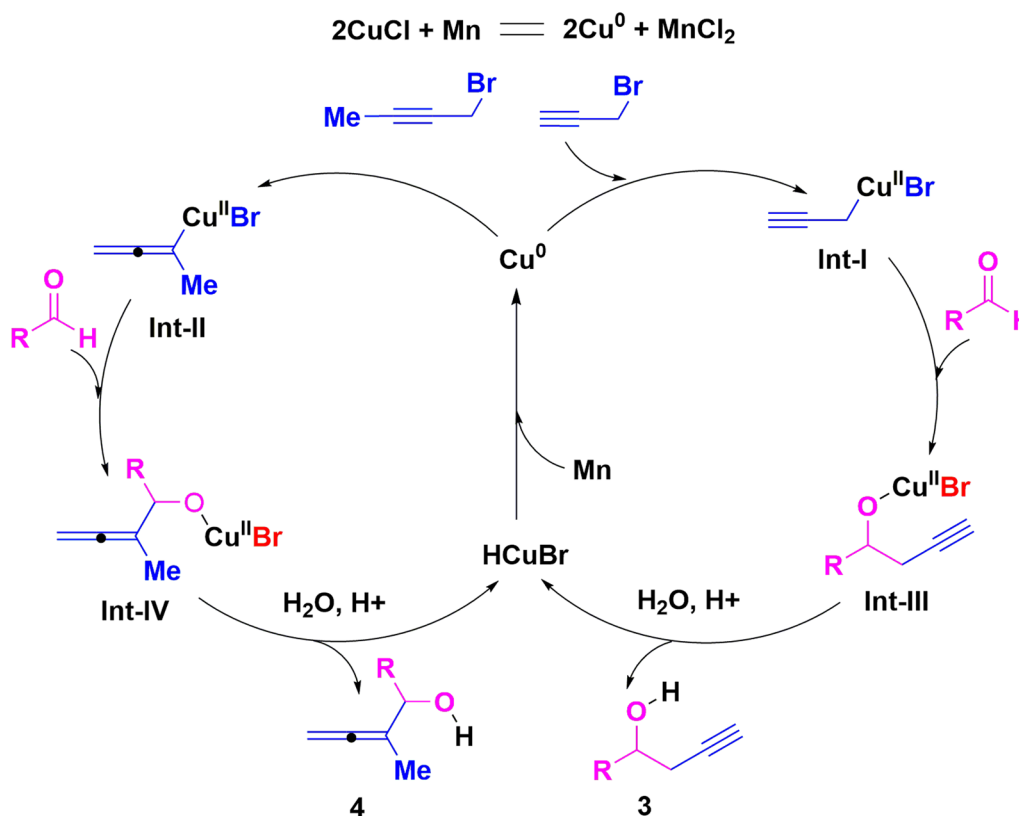
Fig. 2 Gram-scale experiment

Fig. 3 Proposed mechanism

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of CF_3COOH. The Cu^{II} complex was reduced to Cu^0 with Mn powder to continue the next catalytic cycle.

In conclusion, the practical propargylation and allenylation of propargyl bromide has been discovered. The unique combination of the Cu catalyst and Mn powder present a novel and effective catalyst system in the preparation of homopropargylation alcohols and allenyl alcohols. Wide substrates compatibility has been exhibited with a variety of different substituent. This process represents a rare example of propargylation reaction and opens a new area of research. Further mechanistic studies and synthetic applications of this reaction are under progress in our laboratory.

Experiment

Procedure for the synthesis of homopropargyl alcohol
In a 10 mL Schlenk tube, aldehyde (0.5 mmol) was added to a stirred solution of 3-bromo-1-propyne (1.5 eq.), CuCl (10 mol%), Mn powder (3.0 eq.), and CF_3COOH (25 mol%) in MeCN (2 mL) at room temperature under N_2 atmosphere. After 24 h, the mixture was extracted with EtOAc (3×10 mL). The combined EtOAc layer was distilled and the crude product was then purified via column chromatograph.

Procedure for the synthesis of allenyl alchols
In a 10 mL Schlenk tube, aldehyde (0.5 mmol) was added to a stirred solution of 1-bromo-2-pentyne (1.5 eq.) (1.5 eq.), CuCl (10 mol%), Mn powder (3.0 eq.), and CF_3COOH (25 mol%) in MeCN (2 mL) at room temperature under N_2 atmosphere. After 24 h, the mixture was extracted with EtOAc (3×10 mL). The combined EtOAc layer was distilled and the crude product was then purified via column chromatograph.

1-phenylbut-3-yn-1-ol (3a) [57]
98% yield (71.6 mg), colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46–7.34 (m, 4H), 7.30 (ddd, J=8.5, 3.6, 1.6 Hz, 1H), 4.88 (t, J=5.4 Hz, 1H), 2.71–2.56 (m, 2H), 2.45 (s, 1H), 2.19–1.96 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.4, 128.5, 128.0, 125.8, 80.7, 72.3, 71.0, 29.5.

1-(4-chlorophenyl)but-3-yn-1-ol (3b) [57]
96% yield (86.7 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.33–7.25 (m, 4H), 4.80 (t, J=5.1 Hz, 1H), 2.81 (s, 1H), 2.58 (dd, J=6.4, 2.5 Hz, 2H), 2.06 (dd, J=3.4, 1.7 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.9, 133.7, 128.6, 127.2, 80.3, 71.6, 71.4, 29.4.

1-(p-tolyl)but-3-yn-1-ol (3c) [57]
91% yield (72.8 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (d, J=7.7 Hz, 2H), 7.14 (d, J=7.7 Hz, 2H), 4.79 (s, 1H), 2.58 (dd, J=11.1, 8.7 Hz, 3H), 2.33 (s, 3H),

2.03 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.6, 137.7, 129.2, 125.8, 80.9, 72.2, 70.9, 29.3, 21.2.

1-(4-fluorophenyl)but-3-yn-1-ol (3d) [57]
97% yield (79.6 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46–7.32 (m, 2H), 7.05 (t, J=8.7 Hz, 2H), 4.86 (t, J=5.5 Hz, 1H), 2.62 (dd, J=6.3, 2.6 Hz, 2H), 2.49 (d, J=2.5 Hz, 1H), 2.08 (t, J=2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.4 (d, J=245 Hz), 138.2 (d, J=3 Hz), 127.5 d, J=8 Hz), 115.4 (d, J=21 Hz), 80.4, 71.7, 71.2, 29.6.

1-(4-methoxyphenyl)but-3-yn-1-ol (3e) [57]
89% yield (78.4 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (d, J=8.6 Hz, 2H), 6.95–6.80 (m, 2H), 4.80 (t, J=6.4 Hz, 1H), 3.79 (s, 3H), 2.64–2.58 (m, 2H), 2.05 (t, J=2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.3, 134.8, 127.1, 113.9, 80.9, 72.0, 70.9, 55.3, 29.3.

1-(4-isopropylphenyl)but-3-yn-1-ol (3f) [57]
89% yield (83.7 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (d, J=8.1 Hz, 2H), 7.21 (d, J=8.2 Hz, 2H), 4.82 (s, 1H), 2.90 (dt, J=13.8, 6.9 Hz, 1H), 2.62 (dd, J=6.4, 2.6 Hz, 2H), 2.51 (s, 1H), 2.06 (t, J=2.6 Hz, 1H), 1.24 (d, J=6.9 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 148.7, 139.9, 126.6, 125.8, 81.0, 72.3, 70.9, 33.9, 29.3, 24.0.

1-(3-methoxyphenyl)but-3-yn-1-ol (3g) [57]
95% yield (83.6 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.27 (dd, J=10.3, 5.9 Hz, 1H), 6.99–6.93 (m, 2H), 6.84 (ddd, J=8.2, 2.5, 1.0 Hz, 1H), 4.85 (t, J=6.3 Hz, 1H), 3.81 (s, 3H), 2.69–2.59 (m, 2H), 2.51 (s, 1H), 2.08 (t, J=2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.7, 144.2, 129.6, 118.1, 113.5, 111.3, 80.7, 72.3, 71.0, 55.3, 29.4.

1-(m-tolyl)but-3-yn-1-ol (3h) [57]
83% yield (66.5 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24 (t, J=7.5 Hz, 1H), 7.21–7.14 (m, 2H), 7.10 (d, J=7.4 Hz, 1H), 4.82 (t, J=6.4 Hz, 1H), 2.62 (dd, J=6.4, 2.6 Hz, 2H), 2.51 (s, 1H), 2.35 (s, 3H), 2.06 (t, J=2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.5, 138.2, 128.8, 128.4, 126.4, 122.9, 80.9, 72.4, 70.9, 29.4, 21.5.

1-(2-chlorophenyl)but-3-yn-1-ol (3i) [57]
96% yield (86.4 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.62 (dd, J=7.7, 1.4 Hz, 1H), 7.36–7.26 (m, 2H), 7.26–7.20 (m, 1H), 5.28 (dd, J=7.8, 4.0 Hz, 1H), 2.80 (ddd, J=16.9, 3.9, 2.7 Hz, 1H), 2.69 (s, 1H), 2.54 (ddd, J=16.9, 7.8, 2.6 Hz, 1H), 2.10 (t, J=2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.7, 131.7, 129.4, 129.0, 127.1, 127.1, 80.3, 71.2, 68.7, 27.7.

1-(2-fluorophenyl)but-3-yn-1-ol (3j) [57]

95% yield (79.9 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.52 (td, J = 7.5, 1.5 Hz, 1H), 7.26 (ddd, J = 7.1, 4.6, 1.9 Hz, 1H), 7.16 (td, J = 7.5, 0.8 Hz, 1H), 7.02 (ddd, J = 10.4, 8.2, 0.9 Hz, 1H), 5.18 (dd, J = 7.2, 4.9 Hz, 1H), 2.74 (ddd, J = 16.8, 4.7, 2.6 Hz, 1H), 2.62 (ddd, J = 16.8, 7.6, 2.6 Hz, 2H), 2.07 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.0 (d, J = 244 Hz), 129.5, 129.3 (d, J = 8 Hz), 127.2 (d, J = 4 Hz), 124.3 (d, J = 3 Hz), 115.3 (d, J = 22 Hz), 80.3, 71.1, 66.4 (d, J = 2 Hz), 28.2.

1-(4-(trifluoromethyl)phenyl)but-3-yn-1-ol (3ak) [57]

75% yield (80.0 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 8.1 Hz, 2H), 4.90 (t, J = 6.3 Hz, 1H), 2.83 (s, 1H), 2.65 – 2.59 (m, 2H), 2.08 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.3, 130.0 (q, J = 32 Hz), 126.1, 125.4 (q, J = 4 Hz), 123.9 (q, J = 270 Hz), 79.9, 71.6 (d, J = 7 Hz), 29.4.

1-(4-propoxyphenyl)but-3-yn-1-ol (3l) [57]

85% yield (86.8 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 4.83 (t, J = 6.2 Hz, 1H), 3.91 (t, J = 6.6 Hz, 2H), 2.68–2.58 (m, 2H), 2.36 (s, 1H), 2.07 (d, J = 2.3 Hz, 1H), 1.80 (dd, J = 14.1, 7.0 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.9, 134.4, 127.0, 114.4, 80.9, 72.1, 70.8, 69.5, 29.4, 22.6, 10.5.

1-(2,4-dimethylphenyl)but-3-yn-1-ol (3m) [57]

85% yield (74.0 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 (d, J = 7.9 Hz, 1H), 7.03 (d, J = 7.7 Hz, 1H), 6.95 (s, 1H), 5.04 (t, J = 6.4 Hz, 1H), 2.62–2.54 (m, 2H), 2.45 (d, J = 4.8 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 2.05 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.6, 137.4, 134.6, 131.3, 127.0, 125.1, 81.1, 70.7, 68.8, 28.3, 21.0, 19.0.

1-(2,5-difluorophenyl)but-3-yn-1-ol (3n) [57]

94% yield (85.6 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.26 (ddd, J = 8.8, 5.8, 3.0 Hz, 1H), 7.10–6.79 (m, 2H), 5.24–5.07 (m, 1H), 2.83–2.48 (m, 3H), 2.10 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.9 (dd, J = 241, 2 Hz), 155.3 (dd, J = 238, 3 Hz), 131.2 (dd, J = 16, 7 Hz), 116.3 (dd, J = 24, 8 Hz), 115.5 (dd, J = 24, 9 Hz), 113.9 (dd, J = 25, 4 Hz), 79.7, 71.6, 65.9, 28.2 (d, J = 1 Hz).

1-(2,3-difluorophenyl)but-3-yn-1-ol (3o) [57]

87% yield (79.2 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.33–7.23 (m, 1H), 7.18–7.01 (m, 2H), 5.19 (dd, J = 6.9, 5.2 Hz, 1H), 2.82 (s, 1H), 2.74 (ddd, J = 16.8, 4.8, 2.6 Hz, 1H), 2.63 (ddd, J = 16.8, 7.4, 2.5 Hz, 1H), 2.08 (t, J = 2.5 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 150.2 (dd, J = 246, 12 Hz), 147.6 (dd, J = 246, 13), 131.9 (d, J = 10 Hz), 124.2 (dd, J = 7, 5 Hz), 121.8 (t, J = 3 Hz), 116.5 (d, J = 2 Hz), 79.8, 71.4, 66. 0 (t, J = 2 Hz), 28.2.

1-(2,3-dimethylphenyl)but-3-yn-1-ol (3p) [57]

87% yield (75.7 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.36 (d, J = 7.4 Hz, 1H), 7.17–7.04 (m, 2H), 5.15 (dd, J = 7.6, 5.0 Hz, 1H), 2.61–2.51 (m, 2H), 2.28 (s, 3H), 2.22 (s, 3H), 2.07 (d, J = 2.4 Hz, 1H), 1.97 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.4, 137.0, 133.2, 129.4, 125.8, 122.9, 81.2, 70.7, 69.3, 28.3, 20.7, 14.7.

1-(2-methoxy-4-methylphenyl)but-3-yn-1-ol (3q) [57]

85% yield (80.8 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (d, J = 7.6 Hz, 1H), 6.77 (d, J = 7.6 Hz, 1H), 6.68 (s, 1H), 5.09- 4.96 (m, 1H), 3.83 (d, J = 6.7 Hz, 3H), 2.98 (s, 1H), 2.67 (dddd, J = 24.2, 10.1, 6.3, 2.6 Hz, 2H), 2.34 (s, 3H), 2.03 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 156.2, 138.9, 127.4, 126.8, 121.2, 111.4, 81.5, 70.4, 68.9, 55.2, 27.5, 21.6.

1-(3-chloro-5-fluorophenyl)but-3-yn-1-ol (3r) [57]

95% yield (94.1 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19 (s, 1H), 7.07–6.99 (m, 2H), 4.84 (t, J = 4.6 Hz, 1H), 2.65–2.61 (m, 1H), 2.59 (dd, J = 6.5, 3.0 Hz, 1H), 2.11 (t, J = 2.6 Hz, 1H), 1.68 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 163.7 (d, J = 248 Hz), 146.2 (d, J = 7 Hz), 135.1 (d, J = 10 Hz), 121.9 (d, J = 4 Hz), 115.6 (d, J = 25 Hz), 111.4 (d, J = 22 Hz), 79.6, 71.8, 71.2 (d, J = 2 Hz), 29.4.

1-(4-fluoro-3-methoxyphenyl)but-3-yn-1-ol (3s) [57]

88% yield (85.4 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.09–7.01 (m, 2H), 6.88 (ddd, J = 8.3, 4.3, 2.1 Hz, 1H), 4.83 (t, J = 6.3 Hz, 1H), 3.89 (d, J = 5.9 Hz, 3H), 2.62 (dd, J = 6.4, 2.6 Hz, 2H), 2.55 (s, 1H), 2.09 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.914.7 (d, J = 244 Hz), 147.6 (d, J = 11 Hz), 138.8 (d, J = 3 Hz), 118.1 (d, J = 7 Hz), 115.8 (d, J = 19 Hz), 110.9 (d, J = 2 Hz), 80.4, 71.9, 71.3, 56.2, 29.6.

1-(4-fluoro-3-methylphenyl)but-3-yn-1-ol (3t) [57]

88% yield (78.4 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24–7.08 (m, 2H), 6.97 (t, J = 8.9 Hz, 1H), 4.81 (t, J = 6.3 Hz, 1H), 2.61 (dd, J = 6.3, 2.4 Hz, 2H), 2.45 (s, 1H), 2.27 (s, 3H), 2.08 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.9 (d, J = 243 Hz), 137.87, 128.9 (d, J = 2 Hz), 125.0, 124.7(d, J = 8 Hz), 114.9 (d, J = 22 Hz), 80.6, 71.8, 71.1, 29.5, 14.7(d, J = 4 Hz).

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2-(benzo[d][1,3]dioxol-4-yl)but-3-yn-1-ol (3u) [57]

85% yield (80.8 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.95–6.89 (m, 1H), 6.84 (t, J = 7.8 Hz, 1H), 6.78 (dd, J = 7.6, 1.0 Hz, 1H), 5.96 (dd, J = 9.2, 1.1 Hz, 2H), 4.98 (dd, J = 10.2, 6.3 Hz, 1H), 2.84–2.58 (m, 3H), 2.06 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.4, 144.1, 124.1, 121.8, 119.3, 108.2, 101.0, 80.5, 70.9, 68.3, 27.6.

1-(thiophen-2-yl)but-3-yn-1-ol (3v) [57]

88% yield (66.9 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32–7.22 (m, 1H), 6.99 (ddd, J = 11.1, 6.1, 2.5 Hz, 2H), 5.11 (d, J = 3.7 Hz, 1H), 2.79–2.68 (m, 3H), 2.11 (dd, J = 5.2, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.2, 126.7, 125.0, 124.2, 80.1, 71.5, 68.5, 29.5.

1-(4-chloropyridin-2-yl)but-3-yn-1-ol (3w) [57]

93% yield (84.1 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.46 (d, J = 5.3 Hz, 1H), 7.49 (d, J = 1.7 Hz, 1H), 7.26 (dd, J = 5.4, 2.0 Hz, 1H), 4.88 (t, J = 6.0 Hz, 1H), 2.78–2.65 (m, 2H), 2.06 (t, J = 2.6 Hz, 1H), 1.25 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.0, 149.4, 144.9, 123.3, 121.2, 80.0, 71.3, 71.1, 28.2.

1-(pyridin-3-yl)but-3-yn-1-ol (3x) [57]

95% yield (69.9 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.54 (d, J = 2.0 Hz, 1H), 8.47 (dd, J = 4.8, 1.5 Hz, 1H), 7.79 (dt, J = 7.9, 1.8 Hz, 1H), 7.33–7.26 (m, 1H), 4.92 (t, J = 6.4 Hz, 1H), 2.70–2.65 (m, 2H), 2.08 (t, J = 2.6 Hz, 1H), 1.35–1.23 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 148.9, 147.6, 138.3, 133.9, 123.5, 79.9, 71.5, 70.0, 29.3.

1-(quinolin-2-yl)but-3-yn-1-ol (3y) [57]

93% yield (92.0 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.73 (dd, J = 8.4, 1.4 Hz, 1H), 7.59–7.49 (m, 2H), 5.07 (t, J = 5.9 Hz, 1H), 2.80 (ddd, J = 5.9, 2.5, 1.7 Hz, 2H), 2.02 (t, J = 2.7 Hz, 1H), 1.25 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.0, 146.5, 137.0, 129.9, 128.9, 127.8, 127.7, 126.7, 118.5, 80.5, 71.0, 71.0, 28.3.

1-(naphthalen-2-yl)but-3-yn-1-ol (3z) [57]

94% yield (92.5 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87–7.70 (m, 4H), 7.56–7.36 (m, 3H), 4.98 (t, J = 6.3 Hz, 1H), 2.75 (s, 1H), 2.69 (dd, J = 6.4, 2.6 Hz, 2H), 2.05 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.9, 133.2, 133.2, 128.4, 128.1, 127.8, 126.3, 126.1, 124.8, 123.8, 80.8, 72.5, 71.2, 29.4.

1-(naphthalen-1-yl)but-3-yn-1-ol (3ab) [57]

96% yield (94.1 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, J = 8.2 Hz, 1H), 7.89–7.83 (m, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H), 7.54–7.44 (m, 3H), 5.63 (dd, J = 8.2, 4.2 Hz, 1H), 2.87 (ddd, J = 17.0, 4.2, 2.7 Hz, 1H), 2.73 (ddd, J = 17.0, 8.2, 2.6 Hz, 2H), 2.12 (t, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.8, 133.8, 130.2, 129.1, 128.5, 126.3, 125.7, 125.4, 123.0, 122.8, 81.0, 71.3, 69.3, 28.7.

1-(4-isopropylphenyl)-2-methyl-3λ5-buta-2,3-dien-1-ol (5a) [57]

76% yield (76.8 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 5.07 (s, 1H), 4.96–4.85 (m, 2H), 2.90 (dt, J = 13.8, 6.9 Hz, 1H), 2.18 (s, 1H), 1.58 (t, J = 3.0 Hz, 3H), 1.24 (d, J = 7.0 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 204.6, 148.6, 139.2, 126.6, 126.5, 102.7, 77. 9, 74.5, 33.9, 24.0, 14.7.

2-methyl-1-(p-tolyl)-3λ[5]-buta-2,3-dien-1-ol (5b) [57]

83% yield (54.9 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 5.05 (s, 1H), 4.96–4.82 (m, 2H), 2.34 (s, 3H), 2.30 (s, 1H), 1.56 (t, J = 3.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 204.7, 138.9, 137.5, 129.1, 126. 6, 102.7, 77.8, 74.5, 21.2, 14.7.

1-(4-fluorophenyl)-2-methyl-3λ[5]-buta-2,3-dien-1-ol (5c) [57]

73% yield (73 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34 (dd, J = 8.4, 5.6 Hz, 2H), 7.03 (t, J = 8.7 Hz, 2H), 5.08 (s, 1H), 4.93–4.86 (m, 2H), 2.39 (s, 1H), 1.55 (t, J = 3.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.3(d, J = 244 Hz), 137.5 (d, J = 3 Hz), 128.3 (d, J = 8 Hz), 115.2 (d, J = 21 Hz), 102.6, 78.1, 77.4, 74.0, 14.5.

2-methyl-1-(thiophen-2-yl)-3λ[5]-buta-2,3-dien-1-ol (5d) [57]

76% yield (63.1 mg), colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29–7.25 (m, 1H), 7.02 (d, J = 3.1 Hz, 1H), 6.99–6.95 (m, 1H), 5.35 (s, 1H), 4.99–4.86 (m, 2H), 2.34 (d, J = 4.4 Hz, 1H), 1.69 (t, J = 3.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 204.4, 146.1, 126.6, 125.2, 125.0, 102.6, 78.6, 70.7, 14.7.

Conclusions

In conclusion, we have established the first Cu-catalyzed, Mn-mediated propargylation and allenylation of aldehydes with propargyl bromides. The unique combination of the Cu catalyst and Mn powder present a novel and effective catalyst system in the preparation of homopropargylation alcohols and allenyl alcohols. The overall transformation is highly efficient with mild conditions, large substrate scope, and excellent chem-selectivity.

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Supplementary Information

> **Additional file 1.**

Acknowledgements
Not applicable.

Authors' contributions
ZRL contributed to the conception of the study. XY and OL performed the experiment. ZRL and YYC contributed to analysis and manuscript preparation. All authors read and approved the final manuscript.

Funding

Availability of data and materials
All data generated or analyzed during this study are included in this published and its Additional file 1.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

References

1. Alami M, Hamze A, Provot O. Hydrostannation of alkynes. ACS Catal. 2019;9:3437.
2. Parker KDJ, Fryzuk MD. Synthesis, structure, and reactivity of Niobium and Tantalum alkyne complexes. Organometallics. 2015;34:2037.
3. Corpas J, Mauleón P, Gómez Arrayá M, Carretero JC. Transition-metal-catalyzed functionalization of alkynes with organoboron reagents: new trends, mechanistic insights, and applications. ACS Catal. 2021;11:7513.
4. Gilmore K, Alabugin IV. Cyclizations of Alkynes: Revisiting Baldwin's rules for ring closure. Chem Rev. 2011;111:6513.
5. Liu L, Ward RM, Schomaker JM. Mechanistic aspects and synthetic applications of radical additions to allenes. Chem Rev. 2019;119:12422.
6. Blieck R, Taillefer M, Monnier F. Metal-catalyzed intermolecular hydrofunctionalization of allenes: easy access to allylic structures via the selective formation of C-N, C–C, and C–O Bonds. Chem Rev. 2020;120:13545.
7. Zhai R, Xue Y, Liang T, Mi J, Xu Z. Regioselective arene and heteroarene functionalization: N-Alkenoxypyridinium salts as electrophilic alkylating agents for the synthesis of α-aryl/α-heteroaryl ketones. J Org Chem. 2018;83:10051.
8. Baran PS, Shenvi RA. Total synthesis of (±)-Chartelline C. J Am Chem Soc. 2006;128:14028.
9. Farahat AA, Kumar A, Say M, Barghash AEM, Goda FE, Eisa HM, Wenzler T, Brun R, Liu Y, Mickelson L, Wilson WD, Boykin DW. Synthesis, DNA binding, fluorescence measurements and antiparasitic activity of DAPI related diamidines. Bioorg Med Chem. 2010;18:557.
10. Grover HK, Lebold TP, Kerr MA. Tandem Cyclopropane ring-opening/Conia-ene reactions of 2-alkynyl indoles: A [3 + 3] annulative route to tetrahydrocarbazoles. Org Lett. 2011;13:220.
11. Zhang W, Ready JM. A concise total synthesis of dictyodendrins F, H, and I using aryl ynol ethers as key building blocks. J Am Chem Soc. 2016;138:10684.
12. Praveen C, Ananth DB. Design, synthesis and cytotoxicity of pyrano[4,3-b]indol-1(5H)-ones: A hybrid pharmacophore approach via gold catalyzed cyclization. Bioorg Med Chem Lett. 2016;26:2507.
13. Brasholz M, Reissig HU, Zimmer R. Sugars, alkaloids, and heteroaromatics: exploring heterocyclic chemistry with alkoxyallenes. Acc Chem Res. 2009;42:45.
14. Urgoita G, San Martin R, Teresa Herrero M, Domínguez E. Aerobic cleavage of alkenes and alkynes into carbonyl and carboxyl compounds. ACS Catal. 2017;7:3050.
15. Chinchilla R, Nájera C. Chemicals from alkynes with palladium catalysts. Chem Rev. 2014;114:1783.
16. Lin W, Ma S. Enantioselective synthesis of naturally occurring isoquinoline alkaloids: (S)-(−)-trolline and (R)-(+)-oleracein E. Org Chem Front. 2017;4:958.
17. Lu T, Lu Z, Ma ZX, Zhang Y, Hsung RP. Allenamides: A powerful and versatile building block in organic synthesis. Chem Rev. 2013;113:4862.
18. Han Y, Ma S. Rhodium-catalyzed highly diastereoselective intramolecular [4 + 2] cycloaddition of 1,3-disubstituted allene-1,3-dienes. Org Chem Front. 2018;5:2680.
19. Li QH, Jiang X, Wu K, Luo RQ, Liang M, Zhang ZH, Huang ZY. Research progress on the catalytic enantioselective synthesis of axially chiral allenes by chiral organocatalysts. Curr Org Chem. 2020;24:694.
20. Shao XB, Zhang Z, Li QH, Zhao ZG. Synthesis of multi-substituted allenes from organoalane reagents and propargyl esters by using a nickel catalyst. Org Biomol Chem. 2018;16:4797.
21. Shao X, Wen C, Zhang G, Cao K, Wu L, Li QJ. Palladium-catalyzed, ligand-free SN$_2'$ substitution reactions of organoaluminum with propargyl acetates for the synthesis of multi-substituted allenes. Organomet Chem. 2018;870:68.
22. Zhang Z, Shao XB, Zhang G, Li Q, Li X. Highly efficient synthesis of multi-substituted allenes from propargyl acetates and organoaluminum reagents mediated by palladium. Synthesis. 2017;493:643.
23. Zhang Z, Mo S, Zhang G, Shao X, Li Q, Zhong Y. Synthesis of multisubstituted allenes via Palladium-catalyzed cross-coupling reaction of propargyl acetates with an organoaluminum reagent. Synlett. 2017;5:611.
24. Panek JS. Comprehensive organic synthesis. Oxford: Pergamon Press; 1991. p. 595.
25. Yamamoto H. Comprehensive organic synthesis. Oxford: Pergamon Press; 1991. p. 81.
26. Yamaguchi M. Main group metals in organic synthesis. New York: Wiley-VCH. Weinheim; 2004. p. 307.
27. Smith MB, March J. March's advanced organic chemistry: Reactions, mechanisms, and structure, 6th (Ed), Jon Wiley and Sons, Inc.: New York, 2006; 752.
28. Yamamoto H. In Comprehensive organic synthesis. New York: Pergamon Press; 1991. p. 81.
29. Isaac MB, Chan TH. Indium-mediated coupling of aldehydes with prop-2-ynyl bromides in aqueous media. J Chem Soc Chem Commun. 1995;1003:89.
30. Loh TP, Lin MJ, Tan KL. Indium-mediated propargylation of aldehydes: regioselectivity and enantioselectivity studies. Tetrahedron Lett. 2003;44:507.
31. Haddad TD, Hirayama LC, Buckley JJ, Singaram BJ. Indium-mediated asymmetric Barbier-type propargylations: additions to aldehydes and ketones and mechanistic investigation of the organoindium reagents. Org Chem. 2012;77:889.
32. Hojo M, Harada H, Ito H, Hosomi A. A new type of allyl- and prop-2-ynyl-manganese species: generation and reactions with electrophiles. Chem Commun. 1997;21:2077.
33. Zha ZG, Hui AL, Zhou YQ, Miao Q, Wang ZY, Zhang HC. A Recyclable Electrochemical Allylation in Water. Org Lett. 2005;7:1903.
34. López-Martínez JL, Torres-García I, Rodríguez-García I, Muñoz-Dorado M, Álvarez-Corral M. Stereoselective Barbier-Type allylations and propargylations mediated by CpTiCl$_3$. J Org Chem. 2019;84:806.
35. Hojo M, Sakuragi R, Okabe S, Hosomi A. Allyl- and propargylchromium reagents generated by a chromium(III) ate-type reagent as a reductant and their reactions with electrophiles. Chem Commun. 2001;357:8.

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36. Han Y, Chi Z, Huang YZ. Gallium-mediated highly regioselective reaction of allyl-type bromide and propargyl-type bromide with aldehyde. Synth Commun. 1999;29:1287.

37. Zha ZG, Qiao S, Jiang JY, Wang YS, Miao Q, Wang ZY. Barbier-type reaction mediated with tin nano-particles in water. Tetrahedron. 2005;61:2521.

38. Bieber LW, da Silva MF, da Costa RC, Silva LOS. Zinc barbier reaction of propargyl halides in water. Tetrahedron Lett. 1998;39:3655.

39. Fandrick DR, Reeves JT, Bakonyi J, Nyalapatla PR. Zinc catalyzed and mediated asymmetric propargylation of trifluoromethyl ketones with a propargyl boronate. J Org Chem. 2013;78:3592.

40. Iseki K, Kuroki Y, Kobayashi Y. Asymmetric allenylation of aliphatic aldehydes catalyzed by a chiral formamide. Tetrahedron Asymmetry. 1998;9:2889.

41. Evans DA, Sweeney ZK, Rovis T, Tedrow JS. Highly enantioselective syntheses of homopropargylic alcohols and dihydrofurans catalyzed by a bis(oxazolinyl)pyridine—Scandium triflate complex. J Am Chem Soc. 2001;123:12095.

42. Marshall JA, Gung BW, Grachan ML. Synthesis and reactions of allenylmetal compounds. In: Modern Allene Chemistry; (Ed.) Wiley-VCH: Weinheim, 2004; 493.

43. Thaima T, Zamani F, Hyland CJT, Pyne SG. Allenylation and propargylation reactions of ketones, aldehydes, imines, and iminium ions using organoboronates and related derivatives. Synthesis. 2017;49:1461.

44. Denmark SD, Fu J. Catalytic enantioselective addition of allylic organometallic reagents to aldehydes and ketones. Chem Rev. 2003;103:2763.

45. Ma X, Li S, Devaramani S, Zhao G, Xu D. One-pot, regioselective synthesis of homopropargyl alcohols using propargyl bromide and carbonyl compound by the Mg-mediated reaction under solvent-free conditions. Lett Org Chem. 2020;17:438.

46. Wendlandt AE, Suess AM, Stahl SS. Copper-catalyzed aerobic oxidative C-H functionalizations: trends and mechanistic insights. Angew Chem Int Ed. 2011;50:11062.

47. McCann SD, Stahl SS. Copper-catalyzed aerobic oxidations of organic molecules: pathways for two-electron oxidation with a four-electron oxidant and a one-electron redox-active catalyst. Acc Chem Res. 2015;48:1756.

48. Allen SC, Walvoord RR, Padilla-Salinas R, Kozlowski MC. Aerobic copper-catalyzed organic reactions. Chem Rev. 2013;113:6234.

49. Guo XX, Gu DW, Wu Z, Zhang W. Copper-catalyzed C-H functionalization reactions: efficient synthesis of heterocycles. Chem Rev. 2015;115:1622.

50. Crossley SWM, Obradors C, Martinez RM, Shenvi RA. Mn-, Fe-, and Co-catalyzed radical hydrofunctionalizations of olefins. Chem Rev. 2016;116:8912.

51. Irrgang T, Kempe R. 3d-Metal catalyzed N- and C-alkylation reactions via borrowing hydrogen or hydrogen autotransfer. Chem Rev. 2019;119:2524.

52. Durandetti M, Périchon J. A simple practical method for the synthesis of 4,6-dimethoxy-1,3,5-triazin-2(1H)-one using dimethylamine-functionalized solid-phase reagents. Synthesis. 2009;1:542.

53. Chattopadhyay A, Kr DA. A simple and efficient procedure of low valent iron- or copper-mediated reformatsky reaction of aldehydes. J Org Chem. 2007;72:9357.

54. Hojo M, Harada H, Cto H, Hosomi A. Manganese ate complexes as new reducing agents: perfectly regiocontrolled generation and reactions of the manganese enolates with electrophiles. J Am Chem Soc. 1997;119:5459.

55. Suh S, Rieke RD. Synthesis of β-hydroxy esters using highly active manganese. Tetrahedron Lett. 2004;45:1807.

56. Liu XY, Li XR, Zhang R, Chu XQ, Rao W, Loh TP, Shen ZL. Iron(0)-mediated reformatsky reaction for the synthesis of β-hydroxyl carbonyl compounds. Org Lett. 2019;21:5873.

57. Mori-Quiroz LM, Maloba EW, Maleczka RE. Silylcyclopropanes by selective [1,4]-Wittig rearrangement of 4-silyl-5,6-dihydropyrans. Org Lett. 2021;23:5724.

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