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Synthesis of α -hydroxy ketones by copper(I)-catalyzed hydration of propargylic alcohols: CO₂ as a cocatalyst under atmospheric pressure

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ABSTRACT

Inexpensive and efficient Cu(I) catalysis is reported for the synthesis of α -hydroxy ketones from propargylic alcohols, CO₂, and water via tandem carboxylative cyclization and nucleophilic addition reaction. Notably, hydration of propargylic alcohols can be carried out smoothly under atmospheric CO₂ pressure, generating a series of α -hydroxy ketones efficiently and selectively. This strategy shows great potential for the preparation of valuable α -hydroxy ketones by using CO₂ as a crucial cocatalyst under mild conditions.

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1. Introduction

The regioselective addition of water to alkynes presents a straightforward and atom-economic method to obtain versatile carbonyl compounds [1–3]. Since the seminal work on Hg(II)-catalyzed hydration of alkynes by Kutscheroff [4–6], many efforts have been devoted to developing transition metals, especially Au [7–9], Ag [10,11], and Co [12,13], as efficient catalysts that promote this reaction. Among the hydration of multifarious alkynes, propargylic alcohols with hydroxyl groups in alkynes are generally not appropriate substrates, except for Hg catalysis, presumably owing to their low activity and/or the formation of byproducts resulting from the Mey-

er-Schuster or Rupe rearrangements (Scheme 1a) [14–16]. In fact, α -hydroxy ketones obtained from the hydration of propargylic alcohols are important structures because of their existence in various drugs and natural products [17,18]. Therefore, developing a facile and efficient method for preparing α -hydroxy ketones is of great significance and highly desirable in fine chemical synthesis.

α -Alkylidene cyclic carbonates are a kind of functionalized cyclic carbonates that are widely used as versatile intermediates in organic synthesis [19]. Derivatization of α -alkylidene cyclic carbonates is achievable by utilizing their ester groups and/or exocyclic C=C bonds. For example, water as a nucleophile reacts with α -alkylidene cyclic carbonate to produce

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Scheme 1. Hydration of propargylic alcohols without/with CO₂.

α -hydroxy ketone through the ring-opening of α -alkylidene cyclic carbonate followed by decarboxylation and tautomerization [20,21]. In view of the fact that α -alkylidene cyclic carbonates can be easily and efficiently prepared from the commercially available propargylic alcohols and CO₂ [22–30], the development of efficient methods to obtain α -hydroxy ketones from the hydration of propargylic alcohols in the presence of CO₂ will be attractive [20,21]. As shown in Scheme 1b, propargylic alcohol is first converted into α -alkylidene cyclic carbonate by fixation of CO₂, and α -hydroxy ketone is formed through the addition of water to α -alkylidene cyclic carbonate, which is accompanied by the regeneration of CO₂. In the whole process, CO₂ is not consumed, but acts as a cocatalyst [31,32].

Recently, the hydration of propargylic alcohols with CO₂ as a cocatalyst has been investigated by using Ag or ionic liquids (ILs) as catalysts (Scheme 2a) [20,21]. In this regard, silver acetate is found to catalyze this reaction in the presence of 2 MPa CO₂ [20]. This protocol shows good applicability to pyridinyl-substituted internal propargylic alcohols with high reactivity. Subsequently, an excess amount of the IL, [Bu₄P][Im], results in good performance of the various terminal and phenyl-substituted propargylic alcohols [21], even though pressurized CO₂ (1 or 2 MPa) is required to carry out the reaction efficiently in most cases.

Herein, efficient and inexpensive Cu catalysis involving CO₂ as a cocatalyst for the hydration of propargylic alcohols is reported for the preparation of α -hydroxy ketones (Scheme 2b).

(a) Previous work

(b) This work

Scheme 2. Strategies for the hydration of propargylic alcohols with CO₂ as a cocatalyst.

The high efficiency of Cu catalysts ensures that these reactions proceed smoothly under atmospheric CO₂ pressure even in a gram-scale experiment. This protocol is compatible with various terminal propargylic alcohols, affording the corresponding α -hydroxy ketones in high yields.

2. Experimental

2.1. General information

CO₂ of purity 99.99% was supplied by Liquefied Air (Tianjin) Co., Ltd. All reagents were purchased from Aladdin or J&K Scientific Ltd. and used as-received. The solvents were dried before use. NMR spectra were recorded on a Bruker 400 MHz spectrometer operating at 400 MHz (¹H) or 101 MHz (¹³C) with CDCl₃ or DMSO-*d*₆ as the solvent. The chemical shifts were reported relative to CDCl₃ (7.26 ppm) (or DMSO-*d*₆, 2.50 ppm) for ¹H NMR and CDCl₃ (77.0 ppm) (or DMSO-*d*₆, 39.52 ppm) for ¹³C NMR. GC-MS spectra were measured at an ionization voltage of 70 eV on a Shimadzu GCMS-QP2010 equipped with a RTX-5MS capillary column.

2.2. General procedure for CO₂ as a cocatalyst for the hydration of propargylic alcohols

In a 15 mL Schlenk tube, Cu₂O (0.2 mmol, 28.6 mg), cyclohexyldiphenylphosphine (**L1**, 0.2 mmol, 53.6 mg), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.5 mmol, 76.1 mg), propargylic alcohol (1 mmol, 84.1 mg), water, and CH₃CN (1 mL) were added sequentially. Then, the Schlenk tube was sealed and attached to a CO₂ balloon (about 1 L capacity). Finally, the reaction mixture was stirred at 60 °C for 24 h. After completion of the experiment, the CO₂ balloon was taken off and the reaction system cooled to room temperature. Then, 1,3,5-trimethoxybenzene (50 mg) as an internal standard was added for ¹H NMR analysis to determine the yields of the products. The crude reaction mixture was purified by column chromatography on silica gel (200–300 mesh) with *n*-hexane/ethyl acetate (20:1–5:1) as the eluent to yield the desired α -hydroxy ketones, which were further characterized by ¹H and ¹³C NMR as well as GC-MS or HRMS (ESI).

2.3. Typical procedure for one-pot two-step experiment

In a 15 mL Schlenk tube, Cu₂O (0.2 mmol, 28.6 mg), cyclohexyldiphenylphosphine (**L1**, 0.2 mmol, 53.6 mg), DBU (0.5 mmol, 76.1 mg), 2-methylbut-3-yn-2-ol (**1a**, 1 mmol, 84.1 mg), and CH₃CN (1 mL) were added sequentially. Then, the Schlenk tube was sealed and attached to a CO₂ balloon (about 1 L capacity). Finally, the reaction mixture was stirred at room temperature. After 24 h, DBU (0.5 mmol, 76.1 mg) and water (1 mmol, 18.0 mg) were added, and the resulting solution was stirred at 60 °C for another 24 h. Finally, the reaction system was cooled to room temperature. Then, biphenyl (20 mg) as an internal standard was added to determine the yield of 3-hydroxy-3-methylbutan-2-one (**2a**) by GC analysis.

2.4. Characterization data of the products

3-Hydroxy-3-methylbutan-2-one (**2a**). Colorless oil. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 5.23 (s, 1H), 2.15 (s, 3H), 1.17 (s, 6H) ppm. ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 213.83, 75.74, 26.18, 24.23 ppm. GC-MS (EI, 70 eV) m/z (%) 87 (100), 60 (92), 69 (62), 102 (9).

3-Hydroxy-3-methylpentan-2-one (**2b**). Yellow oil. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 5.04 (s, 1H), 2.13 (s, 3H), 1.60 (dq, J = 14.9, 7.5 Hz, 1H), 1.46 (dq, J = 14.8, 7.5 Hz, 1H), 1.12 (s, 3H), 0.74 (t, J = 7.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 214.19, 78.55, 31.77, 25.10, 24.14, 7.88 ppm. GC-MS (EI, 70 eV) m/z (%) 43 (100), 73 (25), 87 (21), 45 (19), 57 (12), 101 (10).

3-Hydroxy-3-methylnonan-2-one (**2c**). Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 3.88 (s, 1H), 2.13 (s, 3H), 1.69–1.51 (m, 2H), 1.38–1.30 (m, 1H), 1.26 (s, 3H), 1.20 (dd, J = 15.9, 5.9 Hz, 6H), 0.94 (tt, J = 15.9, 8.0 Hz, 1H), 0.79 (t, J = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 212.04, 78.43, 39.09, 31.24, 29.08, 24.93, 23.30, 22.92, 22.12, 13.57 ppm. GC-MS (EI, 70 eV) m/z (%) 69 (100), 129 (94), 59 (89), 43 (82), 55 (36), 41 (34), 84 (20), 45 (19), 111 (18), 28 (16), 85 (14).

3-Hydroxy-3,5-dimethylhexan-2-one (**2d**). Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 3.83 (s, 1H), 2.18 (s, 3H), 1.69–1.57 (m, 3H), 1.29 (s, 3H), 0.89 (d, J = 6.4 Hz, 3H), 0.79 (t, J = 6.1 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 212.71, 78.96, 47.71, 26.56, 24.19, 23.76, 23.41 ppm. GC-MS (EI, 70 eV) m/z (%) 81 (100), 99 (96), 43 (29), 55 (21), 79 (19), 57 (10).

1-(1-Hydroxycyclohexyl)ethan-1-one (**2e**). Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 2.24 (s, 3H), 1.75–1.64 (m, 6H), 1.49 (d, J = 6.5 Hz, 2H), 1.28 (dd, J = 15.1, 10.3 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 212.74, 77.97, 33.82, 25.28, 23.69, 21.07 ppm. GC-MS (EI, 70 eV) m/z (%) 81 (100), 99 (71), 79 (21).

3-Hydroxy-3-phenylbutan-2-one (**2f**). Brown oil. ^1H NMR (400 MHz, CDCl_3) δ 7.48–7.42 (m, 2H), 7.38 (t, J = 7.6 Hz, 2H), 7.32 (dd, J = 10.5, 3.8 Hz, 1H), 2.09 (s, 3H), 1.79 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 209.62, 141.37, 128.68, 128.05, 125.96, 79.84, 23.99, 23.43 ppm. GC-MS (EI, 70 eV) m/z (%) 121 (100), 77 (31), 105 (19).

3-Hydroxy-3-methylpent-4-en-2-one (**2g**). Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 5.91 (dd, J = 17.1, 10.5 Hz, 1H), 5.44 (dd, J = 17.1, 0.9 Hz, 1H), 5.22 (dd, J = 10.6, 0.8 Hz, 1H), 3.93 (s, 1H), 2.20 (s, 3H), 1.43 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 209.38, 138.76, 116.23, 79.31, 24.25, 23.60 ppm. GC-MS (EI, 70 eV) m/z (%) 55 (100), 83 (83), 43 (68), 99 (37), 101 (36), 41 (31), 45 (30), 71 (24), 29 (15), 57 (13), 100 (10), 74 (10), 27 (10).

17-Hydroxy-17 β Hpregn-4-ene-3,20-dione (**2h**). White solid, m.p. 192–193 °C. ^1H NMR (400 MHz, CDCl_3) δ 5.72 (s, 1H), 2.92 (d, J = 30.2 Hz, 1H), 2.38–2.23 (m, 8H), 2.03–1.95 (m, 1H), 1.91–1.84 (m, 1H), 1.72–1.40 (m, 10H), 1.18 (s, 3H), 1.10–1.04 (m, 1H), 0.98 (s, 3H), 0.92 (dd, J = 9.8, 5.9 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 214.22, 199.43, 171.01, 123.82, 90.65, 53.18, 49.06, 38.47, 36.08, 35.55, 34.95, 33.81, 32.95, 32.68, 31.49, 28.19, 24.18, 20.66, 17.27, 14.07 ppm. HRMS (ESI): $\text{C}_{21}\text{H}_{31}\text{O}_3$ for $[\text{M} + \text{H}]^+$ calcd 331.2268, found 331.2274.

3. Results and discussion

The reactions were initially investigated with 2-methylbut-3-yn-2-ol (**1a**) as the model substrate that was reacted with water under atmospheric CO_2 pressure to obtain 3-hydroxy-3-methylbutan-2-one (**2a**), as described in Table 1. Obviously, **1a** could not be effectively converted into **2a** without a catalyst or when DBU was used alone (entries 1 and 2). When employing AgOAc, which was the optimal catalyst in previous work [20], to promote the hydration, the yield of **2a** was only 10%, with the remaining being mostly **1a** (entry 3), indicating the low efficiency of Ag catalysis under ambient CO_2 pressure. Mechanically, a tandem process involving the cyclization of propargylic alcohol with CO_2 and the following addition of water to the *in-situ* generated α -alkylidene cyclic carbonate is involved in the hydration of propargylic alcohol with CO_2 as a cocatalyst to prepare α -hydroxy ketone [20,21]. In particular, efficient cyclization is crucial to the whole process. Therefore, several Cu compounds were screened for converting **1a** to **2a**, owing to their excellent performances in the rate-determining cyclization [33–35] (entries 4–10). Excitingly, CuCl as the catalyst allowed the reaction to proceed smoothly, affording 31% of **2a** (entry 4). By changing the Cu source to CuI, the yield of **2a** was increased to 46% (entry 6). Moreover, a significant increase in the yield of **2a** was observed when employing Cu_2O as the catalyst (entry 7). Comparatively, Cu(II) showed a lower catalytic activity than Cu(I) (entries 7–9). The poor activity of CuOAc should be ascribed to its moisture sensitivity (entry 10). Notably, an increase in the amount of water could obviously decrease the rate of hydration (entries 11 and 12), and no **2a** was observed when five equivalents of water was supplied

Table 1

Investigation on Cu catalysis for the hydration of propargylic alcohol with CO_2 as a cocatalyst^a.

Entry	Catalyst	Additive	Yield of 2a ^b (%)
1 ^c	—	—	0
2	—	—	4
3	AgOAc	—	10
4	CuCl	—	31
5	CuBr	—	30
6	CuI	—	46
7	Cu_2O	—	76
8	CuO	—	54
9	CuSO_4	—	7
10	CuOAc	—	13
11 ^d	Cu_2O	—	12
12 ^e	Cu_2O	—	0
13	Cu_2O	PPh_3	73
14	Cu_2O	L1	97
15	Cu_2O	L2	79
16	Cu_2O	L3	71
17	Cu_2O	L4	55

^a Reaction conditions: **1a** (1 mmol, 84.1 mg), H_2O (1 mmol, 18.0 mg), catalyst (20 mol%), additive (20 mol%), DBU (0.5 mmol, 76.1 mg), CO_2 balloon, CH_3CN (1 mL), 60 °C, 24 h. ^b Determined by GC analysis with biphenyl (20 mg) as the internal standard. ^c Without DBU. ^d H_2O .

^e H_2O (5 mmol, 90.0 mg).

Table 2Substrate scope of propargylic alcohols^a.

$ \begin{array}{c} \text{OH} \\ \\ \text{H}-\text{C}\equiv\text{C}-\text{C}-\text{R}^1 \\ \\ \text{R}^2 \end{array} + \text{H}_2\text{O} \xrightarrow[\text{CH}_3\text{CN}, 60^\circ\text{C}, 24\text{ h}]{\text{Cu}_2\text{O}, \text{L1}, \text{DBU}, \text{CO}_2 (\text{balloon})} \begin{array}{c} \text{O} \\ \\ \text{Me}-\text{C}-\text{C}-\text{R}^1 \\ \\ \text{OH} \\ \\ \text{R}^2 \end{array} $			
Entry	Substrate	Product	Yield ^b (%)
1			97
2			93
3			94
4			84
5			87 (67 ^c)
6			79 (70 ^c)
7			70

^a Reaction conditions: **1** (1 mmol), water (1 mmol, 18.0 mg), Cu₂O (0.2 mmol, 28.6 mg), **L1** (0.2 mmol, 53.6 mg), DBU (0.5 mmol, 76.1 mg), and CH₃CN (1 mL), 60 °C, 24 h, atmospheric CO₂ pressure. ^b Determined by ¹H NMR with 1,3,5-trimethoxybenzene as the internal standard. ^c Isolated yield.

(entry 12).

The effect of other reaction parameters on the reaction outcome was further investigated to enhance the yield of **2a** (Table S1, in the Supporting Information). Obviously, a temperature lower than 60 °C is deleterious to the hydration and therefore to the yield of **2a**, which decreased sharply when the hydration was carried out at 40 °C; this can probably be ascribed to the inefficiency of cyclization of **1a** with CO₂. In addition, after increasing the reaction temperature to 80 °C, a slight reduction in the yield of **2a** was detected. Therefore, the optimal reaction temperature was determined as 60 °C. The effect of solvents with different polarities was also studied, and the yield of **2a** decreased in the order of CH₃CN > DMSO > 1,4-dioxane. Therefore, solvents with large polarities favor the hydration.

Then, phosphines as additives were examined (Table 1, entries 13–17). To our delight, cyclohexyldiphenylphosphine (**L1**), with moderate electron-donating capability and proper steric resistance, could largely improve the yield of **2a** to 97% (entry 14). Relatively, monophosphines such as PPh₃ and tricyclohexylphosphine (**L2**) and bisphosphines including

1,2-bis(diphenylphosphino)ethane (**L3**) and 1,4-bis(diphenylphosphino)butane (**L4**) showed poorer performances than **L1** (entries 13, 15–17 vs. entry 14).

The activity of Cu catalysis was subsequently tested with a series of propargylic alcohols, as described in Table 2. In general, this protocol worked well for the hydration of various propargylic alcohols with 70%–97% yields of the corresponding α-hydroxy ketones **2a–g**. This system exhibited good activities for substrates with different lengths of substituted alkyl chains such as methyl, ethyl, and hexyl (entries 1–3). However, a slightly reduced yield was observed for **1d** (entry 4), which might attributed to the increased steric hindrance that leads to unfavorable activation of the hydroxyl group and CO₂ insertion. In addition, the cyclohexyl-substituted propargylic alcohol **1e** is also a suitable substrate, affording **2e** in 87% yield (entry 5). Compared with the alkyl chains, substituents with unsaturated bonds such as phenyl and vinyl result in poorer reactivities of propargylic alcohols (entries 6 and 7), indicating that the interaction of unsaturated bonds with Cu may hinder the activation of the C≡C bond and the intramolecular cyclization of the key alkylcarbonate intermediates.

To broaden the application of this catalysis protocol, a large-scale experiment was performed, as shown in Scheme 3a. By increasing the amount of **1a** to the gram scale, 70% yield of **2a** was successfully obtained, indicating the scalability of this strategy. Moreover, this method can also be applied to the derivatization of oral progesterone ethisterone [36] (Scheme 3b), highlighting its potential and wide applicability.

In order to clarify the reaction pathway, the role of CO₂ was investigated first (Scheme 4a). The hydration of **1a** cannot take place without CO₂, demonstrating the crucial role of CO₂ in this reaction. The tandem process including the carboxylative cyclization and the subsequent reaction of water with α-alkylidene cyclic carbonate involving Cu catalysis was further demonstrated by a two-step reaction (Scheme 4b). Obviously, 66% of **3a** could be obtained from **1a** and CO₂ through Cu catalysis, which could then be smoothly converted into **2a**, which also accounts for high efficiency of Cu catalysis under atmospheric CO₂ pressure.

Insights into the possible interaction between DBU and

(a) Gram-scale experiment

(b) Derivatization of ethisterone

Scheme 3. Gram-scale experiment and synthetic application.

Scheme 4. Control experiments.

propargylic alcohol were obtained by using ¹H NMR technique. As shown in Fig. 1, the O–H signal of **1a** became broad and showed a downfield shift from 5.32 to 5.36 ppm, indicating the activation of propargylic alcohol by DBU through the formation of hydrogen bonding.

A possible mechanism was proposed, as depicted in Scheme 5, based on our investigation and previous work [20,21,33,37]. Initially, the activated propargylic alcohol in the form of intermediate **I** is generated in the presence of Cu(I) catalyst and DBU. After CO₂ insertion, the key intermediate **II** is obtained. Then, intramolecular cyclization of intermediate **II** yields the vinylcopper intermediate **III**. Followed by proto-demetalation, the carboxylative cyclization of propargylic alcohol with CO₂ (Cycle I) is completed, and α-alkylidene cyclic carbonate is afforded. With the aid of DBU, water as the nucleophile reacts with the carbonyl of α-alkylidene cyclic carbonate to form the intermediate **IV** by ring-opening. Finally, α-hydroxy ketone is produced after the decarboxylation and tautomerization of intermediate **IV** (Cycle II). In addition, the interaction between CO₂ and DBU in the entire process cannot be excluded.

Scheme 5. Proposed mechanism.

Fig. 1. ¹H NMR investigation. (a) **1a** (8 mg), DBU (8 mg) in 0.5 mL DMSO-*d*₆; (b) **1a** (8 mg) in 0.5 mL DMSO-*d*₆.

4. Conclusions

Cu catalysis for the hydration of propargylic alcohols with CO₂ as a cocatalyst to synthesize α-hydroxy ketones was achieved. Notably, the reaction can be carried out successfully under atmospheric CO₂ pressure [38,39]. This methodology is highly efficient, showing good performance toward the synthesis of a series of α-hydroxy ketones in good to excellent yields. In addition, this method is scalable and can be applied for the derivatization of complicated bioactive molecules, indicating its practicability and versatility for the preparation of α-hydroxy ketone with CO₂ as a cocatalyst.

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Graphical Abstract

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Liang-Nian He*
Nankai UniversityEfficient and inexpensive copper(I) catalysis was realized for the synthesis of α -hydroxy ketones via the hydration of propargylic alcohols by using CO₂ as a cocatalyst under atmospheric pressure.

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常压CO₂促进的铜催化炔丙醇水解制 α -羟基酮周智华^a, 张 啸^a, 黄永富^a, 陈凯宏^{a,*}, 何良年^{a,b,#}^a南开大学化学学院元素有机化学国家重点实验室, 天津 300071^b天津化学化工协同创新中心, 南开大学, 天津 300071

摘要: α -羟基酮是一类非常有用的结构, 广泛存在于各种具有生物活性的合成药物和天然产物中. 水对炔丙醇的区域选择性加成为合成 α -羟基酮提供了一种简单并且直接的方法. 然而, 目前已经报道的多种用于炔烃水解的方法对于炔丙醇的适用性较差, 这是由于羟基的引入降低了炔烃的活性以及炔丙醇易发生Meyer-Schuster重排和Rupe重排等副反应. 另一方面, CO₂可以作为助催化剂促进炔丙醇水解生成 α -羟基酮. 具体来讲, 炔丙醇与CO₂可以发生羧化环化反应得到 α -亚烷基环状

碳酸酯, 亲核性的水与原位产生的 α -亚烷基环状碳酸酯反应使其开环, 经历脱羧、异构化过程, 最终得到 α -羟基酮。与炔丙醇的直接水解相比, 以 CO_2 为促进剂可以更加高效、高选择性地得到 α -羟基酮。然而, 目前发展的用于 CO_2 促进的炔丙醇水解合成 α -羟基酮的反应中, 高压的 CO_2 和过量的碱是不可缺少的。

本文发展了廉价且高效的铜催化体系用于 CO_2 助催化的炔丙醇水解生成 α -羟基酮的反应。该催化体系可以在不需要过量碱的存在下使得炔丙醇的水解反应在常压 CO_2 条件下顺利进行。控制实验结果表明, 铜催化炔丙醇和 CO_2 的羧化环化反应可以在常压 CO_2 条件下进行, 而有机碱可以有效促进 α -亚烷基环状碳酸酯与水反应生成 α -羟基酮, 这解释了我们发展的铜催化体系在常压 CO_2 条件下高效进行的原因。相同条件下, 本文发展的铜催化体系的催化活性明显高于之前报道的银催化剂, 凸显了该催化体系的高效性。在最优反应条件下, 一系列具有不同烷基或芳基取代基的炔丙醇都表现出良好的反应活性, 能以70%–97%的收率转化为相应的 α -羟基酮。在合成应用方面, 该方法可应用于克级规模实验, 反应能以70%的收率得到相应的 α -羟基酮产物; 而且, 该方法也可以应用于口服药物炔孕酮的进一步衍生化。通过逻辑实验以及对核磁谱图的分析, 我们还对该反应提出了一个可能的反应机理。

总之, 我们使用廉价的过渡金属铜催化剂, 成功实现了炔丙醇在常压 CO_2 为助催化剂条件下发生水解反应合成 α -羟基酮。该催化体系反应条件温和, 底物适用性良好, 催化效率高, 为合成 α -羟基酮提供了一种简单、高效的新方法。

关键词: 铜催化剂; 炔丙醇; 水解; α -羟基酮; 二氧化碳; 助催化剂

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