One-Pot Synthesis of (Z)-β-Halovinyl Ketones via the Cascade of Sonogashira Coupling and Hydrohalogenation

Fa-Jie Chen1✉, Zhenguo Hua1✉, Jianhui Chen1, Jiajia Chen1, Daesung Lee2✉ and Yuanzhi Xia1✉

1 College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou, China, 2 Department of Chemistry, University of Illinois at Chicago, Chicago, IL, United States

Herein, we report an efficient method for the synthesis of (Z)-β-halovinyl ketones through a one-pot Sonogashira coupling and hydrohalogenation reaction promoted by palladium-copper catalyst and Brønsted acid. The ynone intermediates are generated in situ from readily available acid chlorides and terminal alkynes at room temperature, which are directly converted to (Z)-β-halovinyl ketones by treating with triflic acid. This method avoids the use of an external halogen source and features broad substrate scope, high yield, and good to excellent stereoselectivity.

Keywords: Sonogashira coupling, one-pot synthesis, β-halovinyl ketone, hydrohalogenation, ynones

INTRODUCTION

The palladium and copper-catalyzed cross-coupling reaction of terminal alkynes with aryl or vinyl halides, also known as Sonogashira reaction, has emerged as a powerful method for the synthesis of substituted ynones in recent decades (Sonogashira et al., 1975; Sonogashira, 2002). The scope of this reaction has been extended to acid halides, which reacts with terminal alkynes smoothly at room temperature to provide ynones in good yield (Tohda et al., 1977; Eckhardt and Fu, 2003). The electron-deficient ynones are good Michael acceptors and react with various nucleophiles to form vinyl ketones (such as enamino and β-ketoenolether) and heterocycles (such as pyrimidine) (Karpov and Müller, 2003a,b). Ynones are also used as useful precursors for the synthesis of β-halovinyl ketones (Pohland and Benson, 1966; Goossen et al., 2009).

β-Halovinyl ketones are important building blocks in organic synthesis and biochemical processes, and they have been widely used for the constructions of heterocycles such as chromenones, furans, pyrazole, and pyridines (Kim et al., 2012, 2017; Kim and Oh, 2014, 2015, 2017, 2020; Koo et al., 2019a). The methods to form β-halovinyl ketones from ynones generally involve regioselective hydrohalogenation of electron-deficient carbon-carbon triple bond. In these cases, a variety of halogen sources have been employed, including HCl, SnCl4, AlBr3, TMSCl, and LiBr (Scheme 1A) (Kundu and Chaudhuri, 1991; Shchukin and Vasilyev, 2008; Yang et al., 2011; Semenova et al., 2013; Yan et al., 2015; Zeng et al., 2017). However, those methods suffer from relatively low stereoselectivity, which limits their synthetic applications. Recently, Xu and co-workers reported an atom-economical method for the regio- and stereoselective hydrohalogenation of ynone and ynamides using DMPU/HX (X = Br or Cl) reagents. Paixão and co-workers reported the regioselective synthesis of (Z)-β-halo α,β-unsaturated carbonyl systems via combination of halotrimethylsilane and tetrafluoroboric acid (da Silva et al., 2019).
Yrones used in these hydrohalogenation methods are usually not commercially available. One of the common ways to prepare the precursor yrones is the Sonogashira cross-coupling reaction as mentioned above (Kokubo et al., 1996; Hua et al., 2005; Kashiwabara et al., 2005, 2008; Iwai et al., 2009, 2012; Kashiwabara and Tanaka, 2011). This hydrohalogenation strategy for β-halovinyl ketone synthesis requires a multi-step synthetic procedure (Scheme 1A). Moreover, in the starting material preparation step, at least one equivalent of chemical waste hydrohalide salt (for example, triethylamine hydrochloride) will be generated, which is commonly removed in the workup procedure. From the viewpoint of atom-economy and green chemistry, we envisioned that the chemical waste hydrohalide salt can be reused as the halogen source for the sequential hydrohalogenation to form β-halovinyl ketones by the one-pot treatment of strong Brønsted acid, thus avoiding the use of an external halogen source. Compared to the stepwise methods, this strategy is more step- and atom-economical and environmentally friendly.

Similar strategies have been developing relying on transition-metal (rhodium and iridium catalyst) (Kokubo et al., 1996; Hua et al., 2005; Kashiwabara et al., 2005, 2008; Goossen et al., 2009; Iwai et al., 2009, 2012; Kashiwabara and Tanaka, 2011), or Lewis acid (Price and Pappalardo, 1950; Benson and Pohland, 1964; Martens et al., 1975; Zhou et al., 2006; Wang et al., 2010; Hosseini-Sarvari and Mardanesh, 2011; Gandeepan et al., 2012; Koo et al., 2019b). However, these developed methods usually require relatively harsh reaction conditions, such as elevated temperature, long reaction time, use of expensive ligands or catalysts. To the best of our knowledge, the efficient synthesis of β-halovinyl ketones at room temperature through the cascade of the Sonogashira coupling and hydrohalogenation has not been reported.

Herein, we developed a one-pot synthesis of (Z)-β-halovinyl ketone via a Sonogashira coupling and hydrohalogenation sequence at room temperature (Scheme 1B). The ynone intermediates are generated in situ from the palladium and copper catalyzed cross coupling of acid halides and terminal alkynes, which are hydrohalogenated to afford (Z)-β-halovinyl ketone using side product hydrohalide salt as a halogen source. This method shows good stereoselectivity, high yield, and broad substrate scope.

**RESULTS AND DISCUSSION**

We commenced our study with the synthesis of β-chlorovinyl ketone 3a through a cross-coupling reaction of phenylacetylene 1 with benzoyl chloride 2 under the catalysis of PdCl₂(PPh₃)₂ and CuI followed by Bronsted acid treatment (Table 1). After systematic optimization of the reaction conditions, we found that the best reaction conditions: 1.0 equivalent of phenylacetylene reacts with 1.3 equivalent of benzoyl chloride in the presence of 2 mol% of PdCl₂(PPh₃)₂, 4 mol% of CuI, and 1.2 equivalent of triethylamine in 1,2-dichloroethane (0.4 M) at room temperature for 10 min, then treat the reaction mixture with 1.5 equivalent of triflic acid for 4 h at room temperature. The stereoselectivity for this transformation is up to 91/9 (Z/E) and (Z)-β-chlorovinyl ketone 3a was obtained in 87% yield (Table 1, entry 14). When triflic acid was replaced with weaker Bronsted acids, such as trifluoroacetic acid (entry 4), acetic acid (entry 5), and benzoic acid (entry 6), chlorovinyl ketone 3a was not generated. This result indicates the crucial role of triflic acid to react with triethylamine hydrochloride to release hydrochloric acid, which acts as the chloride source for the following hydrochlorination.

**Table 1** Optimization of reaction conditionsa,b.

| Entry | x | Solvent | Acid | Cosolvent | Yield of 3a (%) | Z/E |
|-------|---|---------|------|-----------|---------------|-----|
| 1     | 1.1| THF     | HOTf | -         | 0             | -   |
| 2     | 1.1| THF     | HOTf | EtOH      | 91            | 75/25 |
| 3     | 1.1| THF     | HOTf | MeOH      | 83            | 63/37 |
| 4     | 1.1| THF     | CF₃COOH | EtOH | 0             | -   |
| 5     | 1.1| THF     | CH₃COOH | EtOH | 0             | -   |
| 6     | 1.1| THF     | PhCOOH | EtOH | 0             | -   |
| 7a    | 1.1| THF     | EtOH | -         | trace         | -   |
| 8b    | 1.1| THF     | HOTf | -         | 92            | 76/24 |
| 9     | 1.1| EtOH    | -     | -         | 89            | 11/9 |
| 10    | 1.1| CH₃CN   | HOTf | -         | trace         | -   |
| 11    | 1.1| DCE     | HOTf | -         | 66            | 89/11 |
| 12    | 1.3| DCE     | HOTf | -         | 81            | 91/9 |
| 13    | 1.5| DCE     | HOTf | -         | 81            | 90/10 |
| 14b   | 1.3| DCE     | HOTf | -         | 87            | 91/9 |
| 15b   | 1.3| DCE     | HOTf | -         | 76            | 89/11 |
| 16b   | 1.3| DCE     | HOTf | -         | 65            | 86/14 |

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a Reaction conditions: 1 (0.2 mmol), 2 (x equiv), PdCl₂(PPh₃)₂ (2 mol%), CuI (4 mol%), Et₃N (1.2 equiv) in solvent (1.0 mL) at rt under N₂ for 10 min, then acid (1.5 equiv) in cosolvent at rt for 4 h unless otherwise noted. bIsolated yield. c0.5 equiv of HOTf. d2 equiv of HOTf. e0.5 mL of DCE. f1.5 mL of DCE. gThe reaction time of the first step is 2 min.
TABLE 2 | Substrate scope of alkynes\textsuperscript{a,b}.\textsuperscript{1}

| \(R^1\) | \(R^2\) | \(R^3\) | \(\text{Yield (Z/E)}\) |
| --- | --- | --- | --- |
| Cl | Cl | Ph | 3b, 85% (Z/E = 85/15) |
| Br | Cl | Ph | 3c, 86% (Z/E = 91/9) |
| F | Ph | Cl | 3d, 76% (Z/E = 89/11) |
| Me | Me | Ph | 3e, 84% (Z/E = 87/13) |
| F | Me | Ph | 3f, 81% (Z/E = 93/7) |
| OMe | Me | Ph | 3g, 57% (Z/E = 89/11) |
| OH | Cl | Ph | 3h, 39% (Z/E > 99/1) |
| S | Cl | Ph | 3i, 75% (Z/E = 92/8) |
| HO | Cl | Ph | 3j, 49% (Z/E > 99/1) |
| Bu | Cl | Cl | 3k, 63% (Z/E = 41/59) |
| Me | Cl | Cl | 3l, 75% (Z/E > 99/1) |
| SiMe\textsubscript{3} | Cl | Cl | 3m, 63% (Z/E = 89/11) |

\textsuperscript{1}Reaction conditions: alkyne (0.2 mmol), acyl chloride (0.26 mmol), \(\text{PdCl}_2(\text{PPh}_3)_2\) (2 mol%), CuI (4 mol%), \(\text{Et}_3\text{N}\) (1.2 equiv) in DCE (0.5 mL) at rt under \(\text{N}_2\) for 10 min, then HOTf (1.5 equiv) at rt for 4 h. \textsuperscript{2}Isolated yield.

step. Other solvents such as ethanol (entry 9) and acetonitrile (entry 10) are not effective for this transformation. Extra co-solvent for the hydrohalogenation step is not necessary. Shorten the reaction time of Sonogashira coupling step to 2 min results in a decrement of the yield (65%) and stereoselectivity (86/14, Z/E).

With the optimized reaction conditions in hand, we started to explore the substrate scope of this protocol. As showed in Table 2, a wide range of terminal alkynes were suitable in this transformation. Both electron-withdrawing groups, such as Br (3e), Cl (3b, 3c), F (3d) and electron-donating groups, such as Me (3f), OMe (3g) on the aromatic rings are well-tolerated, giving the (Z)-\(\beta\)-chlorovinyl ketone in good to high yield as well as good stereoselectivity. An alkyne bearing a thiophene moiety is also a good coupling partner, giving \(\beta\)-heterocycle-substituted unsaturated ketone 3i in 75% yield with a 92/8 ratio of Z/E isomers. The Z/E ratio of the product can be further increased up to 99/1 when sterically hindered alkynes were used (3l). The low yields were obtained for hydroxyl group-containing products (3h and 3j). It is likely because the hydroxyl group is acid sensitive. Replacement with a less sterically hindered linear 1-hexyne results in a dramatic decrease of the stereoselectivity of the ketone 3k to 41/59 (Z/E), indicating a bulky substituent at the alkyne moiety is important for high stereoselectivity. Trimethylsilyl-containing chlorovinyl ketone 3m was obtained in 63% yield and 89/11 (Z/E) stereoselectivity.

Encouraged by the broad substrate scope of alkynes, we further examined the generality of the acyl chloride counterpart under standard reaction conditions (Table 3). A variety of benzoic acid chlorides substituted with either electron-donating groups (such as Me, OMe) or electron-withdrawing groups (such as F, Cl, Br) react with phenylacetylene and 1-hexyne smoothly, giving \(\beta\)-chlorovinyl ketone in good to excellent yield and high stereoselectivity. Inclusion of a strong electron-withdrawing CN group results in only 27% yield, while the 4m could be formed in 60% yield when this was replaced by CF\textsubscript{3}. The Z/E ratio of the product is up to 99/1 in most cases. Ketone 4n was obtained in 82% yield from the reaction of aliphatic acid chloride. Thiophene containing product 4o was also obtained in 77% yield and excellent Z/E selectivity (>99/1).

To demonstrate the application of this method in organic synthesis, a gram scale experiment was carried out (Scheme 2A). We were delighted to find that the reaction of tert-butylacetylene 5 (10 mmol) with benzoic acid chloride 2 gave ketone 3l in gram-scale with high yield and stereoselectivity. As acid chlorides have been proved to be efficient for this transformation, we then turned our attention to the reactivity of acyl bromide with benzoic acid bromide (Scheme 2B), which gave rise to the \(\beta\)-bromovinyl ketone 6 in satisfactory yield (70%) with excellent Z/E ratio (99/1). However, reaction of 5 with benzoic acid iodide resulted a complex mixture.

Based on the experimental results and precedents (Chinchilla and Nájera, 2007), a plausible mechanism for this sequential Sonogashira reaction/hydrohalogenation reaction was proposed (Scheme 3). Firstly, palladium precatalyst \(\text{PdCl}_2(\text{PPh}_3)_2\) forms...
a reactive Pd(0) species (Amatore and Jutand, 2000), which undergoes oxidative addition with acyl chloride to produce intermediate A. Secondly, the transmetallation of intermediate A with copper acetylide C, which is formed from terminal alkyne via complexation and deprotonation, gives intermediate D. Sequentially, reductive elimination of D affords ynene and regenerated Pd(0) species. For the hydrohalogenation step, halogen source HX (such as HCl) is generated from the reaction of triflic acid with triethylammonium chloride formed in Sonogashira coupling step. The Michael addition of the halide source to the ynene E generates an allenyl intermediate G, which tautomerizes to the final product β-halovinyl ketone 3.

**CONCLUSION**

We have developed an efficient method for the synthesis of (Z)-β-halovinyl ketones from readily available terminal alkynes and acid chlorides through sequential Sonogashira coupling/hydrohalogenation reaction. This method features simple operations, high yield, and excellent stereoselectivity in most cases. It can be easily scaled up to a gram scale. The broad substrate scopes of both alkyne and acyl chloride show its potential application in organic synthesis.

**EXPERIMENTAL SECTION**

**General Information**

Unless otherwise noted, all chemicals were purchased from J&K, Energy-Chemical or Tansoole, and used as received. All reactions were carried out using oven-dried glassware and magnetic stirring under N₂. The product was monitored and tracked by TLC (iodine, potassium permanganate, and other color reagents will be used if necessary). The product was extracted and filtered with 100–200 mesh silica gel and separated and purified with chromatography silica gel column or chromatography silica gel plate (specification of silica gel is 300–400 mesh silica gel). ¹H NMR spectrum and ¹³C NMR spectrum were determined by Bruker-400 instrument or Bruker-500 instrument with TMS as internal standard and deuterium chloroform as solvent. ¹H NMR chemical shifts were referenced to tetramethylsilane signal (0 ppm), ¹³C NMR chemical shifts were referenced to the solvent resonance (77.00 ppm, CDCl₃). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, q = quadruplet. The melting point of solid compounds was determined by X-5 micro melting point tester.

**Synthesis of β-Halovinyl Ketones**

PdCl₂(PPh₃)₂ (2.8 mg, 0.02 equiv.), CuI (1.5 mg, 0.04 equiv.), Et₃N (33.3 µL, 1.2 equiv.), alkynes (0.2 mmol), acid halides (0.26 mmol), and DCE (0.5 mL) were added sequentially under N₂, and then the resulting mixture was stirred at room temperature for 10 min. HOTf (26.5 µL, 1.5 equiv.) was added to the reaction, which was stirred at room temperature for 4 h. The mixture was filtered through silica gel and the filtrate was concentrated. The residue was purified by flash column chromatography to afford the desired product.

**Gram-Scale Synthesis of β-Chlorovinyl Ketone 3l**

To a round bottom flask (100 mL), equipped with a magnetic stir bar, was added PdCl₂(PPh₃)₂ (140.4 mg, 0.02 equiv.), CuI (76.2 mg, 0.04 equiv.), Et₃N (17.3 mL, 1.2 equiv.), 3,3-dimethyl-1-butene (12 mL, 10 mmol), benzoyl chloride (15.1 mL, 13 mmol), and 25 mL of DCE sequentially under N₂ and then the resulting mixture was stirred at room temperature for 10 min. HOTf (3.1 mL, 1.5 equiv.) was added to the reaction, which was stirred at room temperature for 4 h. The mixture was filtered through silica gel and the filtrate was concentrated. EtOAc (30 mL) was added and
the reaction mixture was washed with NaHCO₃ (10 mL), water (2 × 10 mL), brine (10 mL) to remove excess acid. The organic layer was dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 20/1) to afford the desired product 3l as a pale yellow oil (1.66 g, 74%).

**Characterization Data**

(Z)-3-Chloro-1,3-diphenylprop-2-en-1-one (3a): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 41.8 mg (87% yield) of 3a (Z/E = 91/9) as a pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, J = 8.0 Hz, 2H), 7.77–7.75 (m, 2H), 7.61–7.58 (m, 1H), 7.53–7.42 (m, 5H), 7.36 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 189.9, 143.3, 137.8, 137.3, 133.3, 130.5, 128.7, 128.7, 127.2, 121.5.

(Z)-3-Chloro-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (3b): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 44.2 mg (86% yield) of 3b (Z/E = 85/15) as a pale yellow solid; m.p. 84–86 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.98 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.61–7.59 (m, 1H), 7.51–7.48 (m, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.33 (s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 189.7, 141.8, 137.5, 136.7, 135.7, 133.4, 128.9, 128.7, 128.6, 128.4, 121.8.

(Z)-3-Chloro-3-(3-chlorophenyl)-1-phenylprop-2-en-1-one (3c): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 45.7 mg (85% yield) of 3c (Z/E = 91/9) as a pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, J = 7.5 Hz, 2H), 7.74 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 7.0 Hz, 1H), 7.52–7.49 (m, 2H), 7.44 (d, J = 8.0 Hz, 1H), 7.41–7.37 (m, 1H), 7.33 (s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 189.7, 141.2, 139.0, 137.4, 134.8, 133.5, 130.5, 129.9, 128.8, 128.7, 127.3, 125.3, 122.6. HRMS (ESI): m/z calc'd for C₁₃H₁₁ClO₂ [M + Na]⁺ 299.0001, found 299.0002.

(Z)-3-Chloro-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (3d): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 39.5 mg (76% yield) of 3d (Z/E = 92/8) as a pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, J = 7.2 Hz, 2H), 7.58–7.54 (m, 1H), 7.51–7.47 (m, 2H), 7.43–7.41 (m, 1H), 7.41–7.39 (m, 1H), 7.37 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 207.0, 183.4, 132.6, 129.2, 128.8, 127.1, 98.6, 89.0, 23.1. HRMS (ESI): m/z calc'd for C₁₃H₁₁ClO₂ [M + Na]⁺ 270.0677, found 270.0657.

(Z)-3-Chloro-1-phenyl-3-(thiophen-3-yl)prop-2-en-1-one (3l): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 28.4 mg (63% yield) of 3l as a pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, J = 7.2 Hz, 1H), 7.58–7.54 (m, 1H), 7.51–7.47 (m, 2H), 7.49–7.41 (m, 1H), 7.41–7.39 (m, 1H), 7.37 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 206.9, 183.4, 132.5, 129.3, 128.8, 127.1, 125.0, 119.3. HRMS (ESI): m/z calc'd for C₁₃H₁₁ClO₂ [M + Na]⁺ 270.9955, found 270.9939.

(Z)-3-Chloro-3-(1-hydroxycyclohexyl)-1-phenylprop-2-en-1-one (3m): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 26.0 mg (49% yield) of 3m (Z/E = 99/1) as a pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 7.2 Hz, 2H), 7.58–7.54 (m, 1H), 7.51–7.46 (m, 2H), 7.59 (s, 1H), 1.97–1.52 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 206.9, 183.4, 132.5, 129.3, 128.8, 127.1, 99.2, 90.8, 31.9, 24.5, 21.9. HRMS (ESI): m/z calc'd for C₁₃H₁₂ClO₂ [M + Na]⁺ 265.0990, found 265.1009.

(Z)-3-Chloro-1-phenylethene-2-1-one (3k): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 28.4 mg (63% yield) of 3k as a pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, J = 7.0 Hz, 2H), 7.59–7.55 (m, 1H), 7.49–7.45 (m, 2H), 6.82 (s, 1H), 2.55 (t, J = 8.0 Hz, 2H), 1.72–1.65 (m, 2H), 1.47–1.37 (m, 2H), 0.97 (t, J = 8.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 188.6, 157.8, 138.1, 133.0, 128.7, 128.3, 123.3, 36.2, 29.9, 22.1, 13.8.
(Z)-3-Chloro-4,4-dimethyl-1-phenylpent-2-en-1-one (31): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 20/1 as the eluent to give 33.0 mg (75% yield) of 31 (Z/E > 99/1) as a pale yellow oil; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.91 (d, \(J = 8.8\) Hz, 2H), 7.57–7.49 (m, 2H), 6.72 (s, 1H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 190.6, 163.7, 153.2, 131.3, 130.2, 119.9, 113.8, 55.3, 39.7, 28.7. HRMS (ESI): m/z calc. for C\(_{12}\)H\(_9\)ClO\(_3\) [M + Na]\(^+\) 275.0809, found 275.0805.

(3)-Chloro-4,4-dimethyl-1-(o-toly)pent-2-en-1-one (4f): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 30/1 as the eluent to give 41.4 mg (89% yield) of 4f (Z/E > 99/1) as a pale yellow oil; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.57 (d, \(J = 7.2\) Hz, 1H), 7.40–7.36 (m, 1H), 7.27–7.24 (m, 2H), 6.61 (s, 1H), 2.53 (s, 3H), 1.29 (s, 9H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 194.6, 154.8, 138.4, 138.1, 131.7, 131.4, 129.5, 126.1, 121.8, 39.9, 28.6, 20.9. HRMS (ESI): m/z calc. for C\(_{16}\)H\(_{16}\)ClO \([M + Na]^+\) 259.0860, found 259.0858.

(2)-Chloro-1-(4-fluorophenyl)-4,4-dimethylpent-2-en-1-one (4g): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 20/1 as the eluent to give 42.4 mg (88% yield) of 4g (Z/E > 99/1) as a pale yellow solid; m.p. 54–55°C; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97–7.93 (m, 2H), 7.17–7.12 (m, 2H), 6.65 (s, 1H), 1.31 (s, 9H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 190.2, 165.9, 164.6, 154.7, 133.7, 130.2, 129.4, 128.6, 126.6, 121.8, 21.7.

(Z)-Chloro-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (4a): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 100/1 as the eluent to give 46.6 mg (87% yield) of 4a (Z/E = 95/7) as a colorless oil; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.00 (d, \(J = 8.8\) Hz, 2H), 7.76–7.74 (m, 2H), 7.45–7.43 (m, 3H), 5.33 (s, 1H), 2.97 (d, \(J = 8.0\) Hz, 2H), 2.43 (s, 3H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 189.7, 163.8, 141.9, 137.3, 131.1, 130.5, 130.3, 128.6, 127.0, 122.0, 113.9, 55.5.

(Z)-Chloro-4,4-dimethyl-1-(o-toly)pent-2-en-1-one (4c): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 50/1 as the eluent to give 40.7 mg (92% yield) of 4c (Z/E > 99/1) as a pale yellow oil; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.83 (d, \(J = 8.4\) Hz, 2H), 7.29–7.26 (m, 4H), 6.68 (s, 1H), 2.42 (s, 3H), 1.32 (s, 6H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 190.2, 167.1, 164.6, 154.7, 144.2, 134.8, 129.3, 129.0, 119.7, 39.8, 28.7, 21.7. HRMS (ESI): m/z calc. for C\(_{16}\)H\(_{16}\)ClO \([M + H]^+\) 279.0314, found 279.0327.

(Z)-Chloro-1-(4-bromophenyl)-3-chloro-4,4-dimethylpent-2-en-1-one (4i): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 20/1 as the eluent to give 41 mg (68% yield) of 4i (Z/E > 99/1) as a pale yellow solid; m.p. 68–69°C; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.77 (d, \(J = 8.4\) Hz, 2H), 7.60 (d, \(J = 8.4\) Hz, 2H), 6.65 (s, 1H), 1.31 (s, 9H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 190.6, 155.3, 136.1, 131.9, 130.3, 128.4, 119.0, 40.0, 28.6. HRMS (ESI): m/z calc. for C\(_{16}\)H\(_{16}\)BrClO \([M + Na]^+\) 322.9809, found 322.9795.

(Z)-Chloro-1-(3-chlorophenyl)-4,4-dimethylpent-2-en-1-one (4j): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EA = 20/1 as the eluent to give 42.4 mg (82% yield) of 4j (Z/E > 99/1) as a pale yellow oil; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.88–7.87 (m, 1H), 7.77 (d, \(J = 8.0\) Hz, 2H), 7.55–7.53 (m, 2H), 7.43–7.39 (m, 1H), 6.68 (s, 1H), 1.31 (s, 9H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 190.2, 167.1, 164.6, 154.7, 131.5, 131.4, 119.3, 115.9, 115.6, 39.9, 28.6. HRMS (ESI): m/z calc. for C\(_{16}\)H\(_{16}\)ClO \([M + Na]^+\) 279.0314, found 279.0323.
(Z)-1-(2-Bromophenyl)-3-chloro-4,4-dimethylpent-2-en-1-one (4k): Prepared according to the general procedure. The crude reaction mixture was purified by flash column chromatography using PE/EtOAc = 20/1 as the eluent to give 35.9 mg (82% yield) of 4k (Z/E > 99/1) as a colorless oil; 1H NMR (400 MHz, CDCl3) δ 6.53–6.47 (m, 2H), 2.56–2.50 (m, 1H), 1.83–1.79 (m, 6H), 1.37–1.33 (m, 9H); 13C NMR (100 MHz, CDCl3) δ 203.2, 154.6, 120.3, 51.3, 40.0, 28.7, 28.3, 25.8, 25.6. HRMS (ESI): m/z calcd. for C13H21ClO [M + Na]+ 251.1173, found 251.1174.

(Z)-3-Chloro-3-phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (4m): Prepared according to the general procedure. The crude reaction mixture was purified by prep-TLC using PE/EtOAc = 10/1 as the eluent to give 39.2 mg (70% yield) of 4m (Z/E > 99/1) as a colorless oil; 1H NMR (400 MHz, CDCl3) δ 7.72–7.58 (m, 2H), 7.15–7.13 (m, 1H), 6.76 (s, 1H), 1.30 (s, 9H); 13C NMR (100 MHz, CDCl3) δ 182.1, 156.0, 145.0, 134.1, 132.4, 128.1, 118.4, 40.1, 28.6. HRMS (ESI): m/z calcd. for C19H14ClNO [M + Na]+ 322.9809, found 322.9804.

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DATA AVAILABILITY STATEMENT
The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS
YX designed the research. F-JC and ZH carried out the experiments. All authors contributed to the manuscript.

FUNDING
Financial support was provided by NSFC (Nos. 21801191, 21572163, and 21873074) and the Wenzhou Science & Technology Bureau (G20180016).

SUPPLEMENTARY MATERIAL
The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fchem.2020.621545/full#supplementary-material
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