

Ethoxide-Mediated Condensation of γ -*tert*-Butylallenoate and Aldehydes: Facile Stereoselective Synthesis of Conjugated Dienes and Enynes

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Received: 12.03.2014; Accepted after revision: 18.03.2014

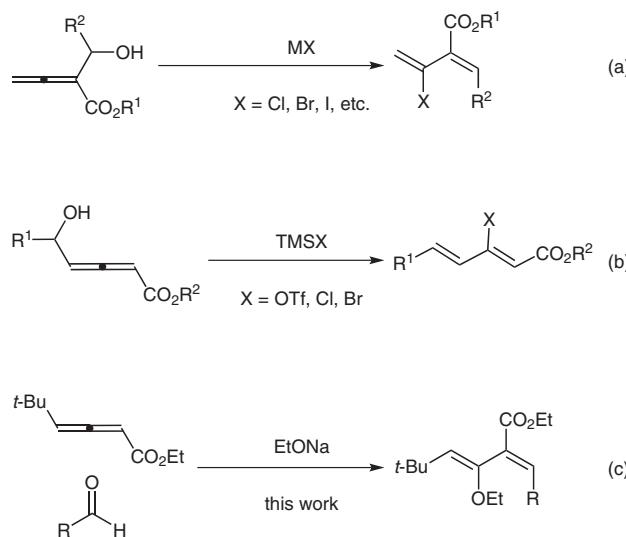
Abstract: The condensation reaction of a γ -*tert*-butylallenoate, ethyl 5,5-dimethylhexa-2,3-dienoate, and aldehydes in the presence of sodium ethoxide is described. A range of aldehydes readily reacts with γ -*tert*-butylallenoate and ethoxide providing a straightforward synthesis of 1,2,3,4-tetrasubstituted conjugated dienes in moderate to good yields and exclusive *E,E* selectivity. For some aldehydes, the condensation chemoselectively delivers conjugated enynes in good yields and exclusive *E* selectivity.

Key words: conjugated diene, enyne, allenoate, condensation, tandem reaction

Conjugated dienes (1,3-dienes) are important organic compounds since they are embedded as key backbones in many biologically active molecules² and serve as intermediates for many important chemical transformations,³ especially the Diels–Alder reaction.^{3d} Due to the great utility of 1,3-dienes, many methods have been developed for their synthesis, these include: elimination reactions,⁴ P-, S-, and Si-based carbonyl olefinations,⁵ and transition-metal-mediated diene formations,⁶ and others.⁷ Despite the effectiveness of these processes, developing new, efficient, and stereoselective syntheses of 1,3-dienes, especially polysubstituted examples, remains an important objective.⁸

Allenoates (α -allenic esters)⁹ are a class of readily available and highly versatile intermediates in organic synthesis. Over the past two decades, a number of new reactivity patterns of allenoates have been disclosed and utilized in the assembly of a range of molecular scaffolds of high diversity and complexity.¹⁰ In this context, allenoates have also emerged as attractive precursors for building conjugated dienes.¹¹ In our investigations on the new reactivity of allenoates toward aldehydes,^{11i–m} we have reported several olefination reactions between allenoates and aldehydes under the mediation of stoichiometric phosphines, which provide an efficient synthetic method for polysubstituted 1,3-dienes. Recently, Ma and co-workers¹² developed an elegant strategy involving a S_N2' -type addition/elimination of α -carbinol-substituted allenoates with halide nucleophiles, which provides an easy synthesis of 2-halo-1,3-dienes [Scheme 1 (a)]. Similar S_N2' reac-

tions of acetylated α -carbinol-substituted allenoates with isatin-derived oximes are documented by Shi and co-workers.¹³ Very recently, Lee and co-workers¹⁴ employed γ -carbinol-substituted allenoates in reactions with trimethylsilyl triflate or chlorotrimethylsilane for the facile generation of (*E,E*)-1,3-dien-2-yl triflates and halides, respectively [Scheme 1 (b)]. As part of our continued interest in exploring the new reactivity of allenoates toward various electrophiles,^{11i–m,15} we herein disclose a new condensation reaction of a γ -*tert*-butylallenoate, ethyl 5,5-dimethylhexa-2,3-dienoate, with aldehydes in the presence of sodium ethoxide, which provides a straightforward and highly stereoselective synthesis of 1,2,3,4-tetrasubstituted conjugated dienes [Scheme 1 (c)]. In a substrate-dependent manner, the condensation can also chemoselectively deliver conjugated enynes from some aldehydes.



Scheme 1 Synthesis of conjugated dienes from allenoates

Originally, we were in the process of exploring possible annulation reactions of γ -*tert*-butylallenoate **1a** with 2-chlorobenzaldehyde (**2a**) under Lewis base catalysis.^{15a} Unexpectedly, in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), the reaction of **1a** with **2a** in ethanol at room temperature afforded 1,3-diene **3a** in 39% yield as a single *E,E*-stereoisomer (Table 1, entry 1). The structure of **3a** was confirmed by ¹H and ¹³C NMR, HRMS, and X-ray crystallographic analysis (Figure 1).

Apparently, the diene **3a** was generated via a base-mediated three-component condensation between allenolate **1a**, aldehyde **2a**, and ethanol with loss of one molecule of water. To our knowledge, this reaction unveils a new reactivity pattern of allenotes with aldehydes, and also provides a straightforward synthesis of functionalized conjugated dienes.

Table 1 Optimization of Reaction Conditions^a

Entry	Base	Time (h)	Yield ^b (%)
1	DBU	24	39
2	DMAP	24	40
3	DABCO	24	0
4	Et ₃ N	24	0
5	HMT	24	0
6	Ph ₃ P	24	trace
7	Bu ₃ P	24	trace
8	K ₂ CO ₃	24	61
9	KOH	24	87
10	Et ₄ NOH ^c	24	77
11	EtONa	1	81
12 ^d	EtONa	0.5	93
13 ^{d,e}	EtONa	0.5	93

^a Reaction conditions: allenolate **1a** (0.75 mmol), 2-chlorobenzaldehyde (0.5 mmol), base (0.5 mmol), EtOH (2 mL), r.t., stirring, N₂ atmosphere.

^b Isolated yield.

^c As an aqueous 25% solution.

^d EtONa (1.5 equiv) was used.

^e The reaction was conducted under an air atmosphere.

A screening of base promoters was carried out using the reaction of γ -*tert*-butylallenolate **1a** with 2-chlorobenzaldehyde (**2a**) to optimize conditions (Table 1). It was found that 4-(dimethylamino)pyridine could also promote the reaction to give **3a** in 40% yield, while 1,4-diazabicyclo[2.2.2]octane, triethylamine, and hexamethylenetetramine (HMT) were ineffective (entries 2–5). Phosphorus-containing Lewis bases such as triphenylphosphine and tributylphosphine were also unsuitable, only giving trace amounts of the product (entries 6 and 7). However, inorganic bases, such as potassium carbonate, potassium hydroxide, tetraethylammonium hydroxide, are more effective providing **3a** in 61%, 87%, and 77% yields, re-

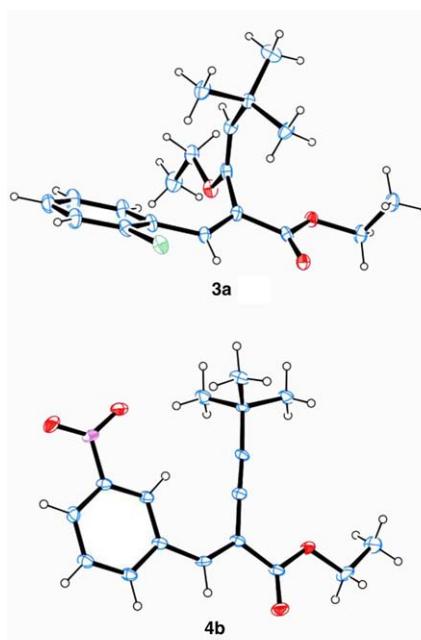


Figure 1 ORTEP drawings for diene **3a** and enyne **4b**

spectively (entries 8–10). As conceivably the ethoxide anion generated *in situ* from base and ethanol could initiate the reaction, we directly employed 1.0 equivalents of sodium ethoxide as the mediator.¹⁶ The model reaction proceeded much faster giving an 81% yield of **3a** (entry 11). The reaction was complete in 30 minutes when the amount of sodium ethoxide was increased to 1.5 equivalents and the product **3a** was obtained in 93% yield (entry 12). The sodium ethoxide mediated reaction was conducted under an air atmosphere without loss of efficiency (entry 13). It is noteworthy that employing other solvents (e.g. CH₂Cl₂, THF, and toluene) instead of ethanol is detrimental, giving lower yields.

Under the optimized conditions, the scope of the condensation reaction was investigated. Some typical results are summarized in Table 2. Halobenzaldehydes worked well giving the corresponding dienes **3a–d** in 33–93% yields (entries 1–4). Electron-poor aldehydes such as nitro- or trifluoromethyl-substituted benzaldehydes as well as pyridinecarbaldehydes were also effective delivering dienes **3e–i** in moderate yields (34–81%) (entries 5–9). For relatively electron-rich aromatic or alkyl aldehydes, the reactions gave low to moderate yields only of the corresponding dienes (entries 10–13). The lowered yields are mainly due to the competitive Michael reaction of ethanol with the allenolate **1a** generating the alkene **5** (Figure 2).

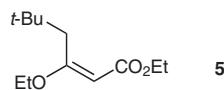


Figure 2 Structure of **5**

Table 2 Substrate Scope of the Condensation Reaction^a

1a $\xrightarrow[\text{R}^2\text{OH}]{\text{R}^1\text{CHO (2)}, \text{R}^2\text{ONa (1.5 equiv)}} \text{3} + \text{4}$

Entry	R ¹ CHO	R ¹	R ²	Yield ^b (%)		
				3	4	5 ^c
1	2a	2-ClC ₆ H ₄	Et	3a , 93	—	n.d.
2	2b	4-ClC ₆ H ₄	Et	3b , 73	—	n.d.
3	2c	4-BrC ₆ H ₄	Et	3c , 43	—	20
4	2d	3-FC ₆ H ₄	Et	3d , 33	—	33
5	2e	4-O ₂ NC ₆ H ₄	Et	3e , 54	4a , 9	n.d.
6	2f	2-O ₂ NC ₆ H ₄	Et	3f , 81	trace	n.d.
7	2g	4-F ₃ CC ₆ H ₄	Et	3g , 63	—	n.d.
8	2h	2-pyridyl	Et	3h , 53	—	n.d.
9	2i	4-pyridyl	Et	3i , 34	—	n.d.
10	2j	Ph	Et	3j , 32	—	28
11	2k	1-naphthyl	Et	3k , 48	—	10
12	2l	4-MeC ₆ H ₄	Et	3l , 16	—	41
13	2m	Pr	Et	3m , 19	—	18
14	2a	2-ClC ₆ H ₄	Me	3n , 40	—	n.d.
15	2n	3-O ₂ NC ₆ H ₄	Et	—	4b , 98	n.d.
16	2o	2-furyl	Et	—	4c , 71	n.d.
17	2p	2-thienyl	Et	—	4d , 68	n.d.
18	2q	(E)-PhCH=CH	Et	—	4e , 67	n.d.

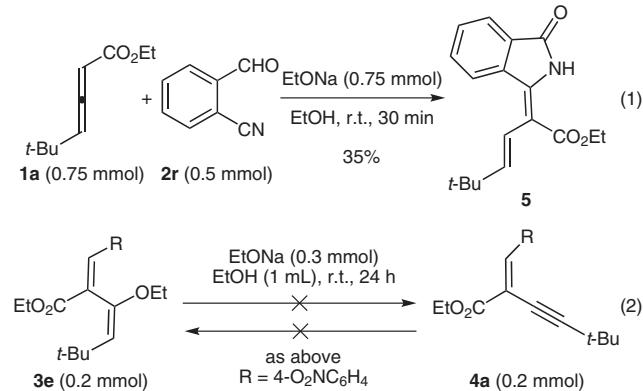
^a Reaction conditions: allenate **1a** (0.75 mmol), aldehyde (0.5 mmol), R²ONa (0.75 mmol), R²OH (2 mL), r.t., air atmosphere, 30 min.

^b Isolated yields based on aldehydes **2**.

^c For the structure of **5** see Figure 2. Isolated yields based on allenate **1a**; n.d. = not determined.

Interestingly, some aldehydes favor the formation of conjugated enyne products **4**¹⁷ under the given conditions. For example, while 2- and 4-nitrobenzaldehydes predominantly produced the diene products **3f** and **3e**, respectively (entries 5 and 6), 3-nitrobenzaldehyde gave exclusively enyne **4b** in an excellent 98% yield (entry 15), whose structure was unequivocally determined by X-ray crystallographic analysis (Figure 1). Furan-2-carbaldehyde, thiophene-2-carbaldehyde, and cinnamaldehyde also favor the formation of enynes **4c–e** (entries 16–18). Another unexpected reaction was observed from 2-cyanobenzaldehyde (**2r**) and allenate **1a** under standard conditions, which produced isoindolinone **6** in 35% yield [Scheme 2 (1)].¹⁸ In contrast to aldehydes, ketones such as acetone,

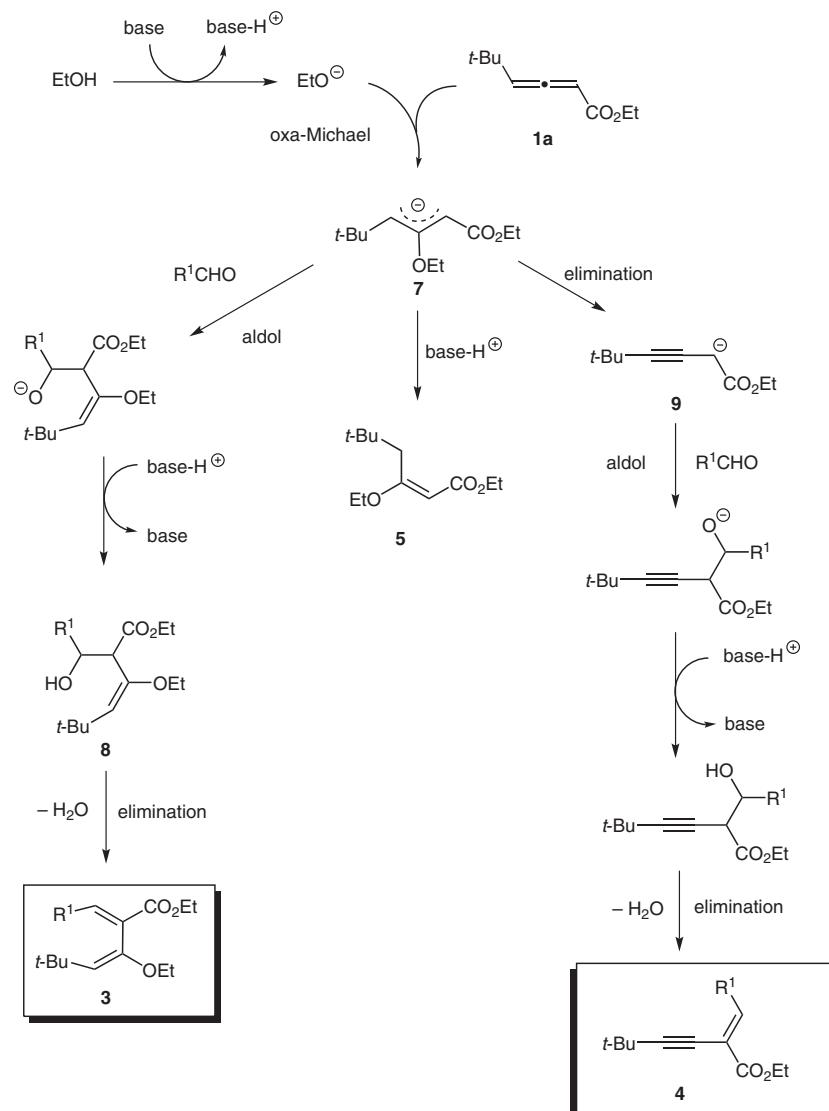
acetophenone, and 2,2,2-trifluoro-1-phenylethanone were unreactive under standard conditions. In these cases, the generation of the byproduct **5** from ethanol and allenate **1a** dominated.

**Scheme 2**

Variation of the alcohols and allenates was investigated. Using methanol and sodium methoxide as the mediator, the corresponding methoxy-substituted diene **3n** with a methyl ester group was generated in 40% yield from allenate **1a** and 2-chlorobenzaldehyde (**2a**) (Table 2, entry 14). However, structurally similar allenates including γ -methyl-, γ -ethyl-, γ -isopropyl-, and γ -phenylallenates as well as the unsubstituted parent all failed to produce the expected dienes and instead afforded complex mixtures, presumably due to their high susceptibility under the strong basic conditions. The result clearly implies the special role of the bulky γ -*tert*-butyl group of the allenate in the condensation.

It is noteworthy that the above ethoxide-mediated condensations are clean and fast, and manifest exclusive regio- and stereoselectivity. Condensation of the aldehydes occurred regioselectively at the α -carbon of the allenate. All dienes and enynes listed in Table 2 were also obtained as single *E,E* and *E* stereoisomers, respectively. Their structures were identified by ¹H, ¹³C NMR, IR, MS, and HRMS, and the stereochemistry was confirmed by X-ray crystallographic analysis for representative products **3a** and **4b**¹⁹ (Figure 1).

To verify possible interconversion relationship between the diene and the enyne products, we treated diene **3e** and enyne **4a** under standard conditions in the absence of the allenate and aldehydes [Scheme 2 (2)]. Interconversion between **3e** and **4a** was not observed. This result indicates that neither the diene nor the enyne serves as an intermediate en route in the reactions.²⁰ On the basis of the current observation and related literatures,^{17,21} a plausible mechanism for the condensation reactions is depicted in Scheme 3. A tandem oxa-Michael/aldol/elimination process is postulated for the formation of **3**. Initially, ethoxide anion (generated in situ from the base and ethanol) undertakes oxa-Michael addition to the allenate **1a**. Subsequently, the resulting anionic intermediate **7** undergoes an aldol



Scheme 3 A plausible mechanism for the formations of **3** and **4**

condensation at the α carbon with aldehydes to give intermediate **8**. Finally, elimination of water under basic conditions produces dienes **3**. Previously, electron-deficient olefins were employed as Michael acceptors in a similar tandem process to deliver trisubstituted alkenes.^{21b-d}

Accordingly, the byproduct **5** in those condensations of less reactive aldehydes or ketones may be generated by a competitive protonation of the intermediate **7**. For the formation of **4**,^{17a} it can be rationalized that the enolate intermediate **7** preferentially undertakes an elimination reaction to give propargyl anion **9**,²² which undergoes a sequential aldol reaction with aldehydes and elimination of water to produce the enynes **4**. Nevertheless, the chemoselectivity between the formation of dienes **3** and enynes **4** from different aldehydes shown in Table 2 could not be well understood in terms of the steric and electron

properties of aldehydes at this moment; more efforts are needed to reach a precise mechanism.²³

In conclusion, we present a new reactivity of allenoates toward aldehydes under base mediation. In the presence of sodium ethoxide, a three-component condensation reaction of γ -*tert*-butylallenoate and aldehydes readily provides 1,2,3,4-tetrasubstituted conjugated dienes **3** in moderate to good yields and excellent *E,E* selectivity. The reaction is believed to proceed in an oxa-Michael–aldol–elimination sequence, which represents a new and straightforward synthesis of polysubstituted 1,3-dienes starting from allenoates. In a substrate-dependent manner, the condensation reaction also chemoselectively delivers trisubstituted 1,3-enynes **4** in good yields and *E* selectivity with several aldehydes. Further efforts in our laboratory will focus on tuning this novel reactivity of allenoates into a useful synthetic method.

Alenoate **1a** was prepared according to a reported procedure.²⁴ EtONa and MeONa were prepared with Na and abs EtOH or MeOH. All other reagents were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Bruker AV 400 or AV 300 spectrometer in CDCl₃ with TMS as the internal standard. IR spectra were recorded on a Nicolet 380 FT-IR spectroscopy (KBr). Low-resolution MS spectra (EI, 70 eV) were measured by a Thermo Finnigan Polaris-Q mass spectrometer. HRMS data were obtained on an IonSpec QFT-ESI instrument. Column chromatography was performed on silica gel (200–300 mesh) using petroleum ether–Et₂O.

Ethoxide-Mediated Condensation of γ -tert-Butylalenoate **1a** and Aldehydes; General Procedure

A 1 M EtONa in EtOH soln (0.75 mL, 0.75 mmol) was added to a mixture of γ -tert-butylalenoate **1a** (126 mg, 0.75 mmol) and aldehyde (0.5 mmol) in EtOH (1.25 mL) at r.t. under an air atmosphere. The mixture was stirred for 30 min, and then neutralized with aq 1 M NH₄Cl soln (5 mL) and extracted with CH₂Cl₂ (3 × 5 mL). The combined organic phases were dried and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, gradient petroleum ether–Et₂O, 50:1 to 10:1) to give the corresponding product.

Ethyl (2E,3E)-2-(2-Chlorobenzylidene)-3-ethoxy-5,5-dimethylhex-3-enoate (**3a**)

Colorless sheet crystal; yield: 156 mg (93%); mp 56–58 °C.

IR (KBr): 2957, 2904, 1716, 1618, 1470, 1245, 1202, 1140, 1068, 751 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 8.06 (s, 1 H), 7.72 (m, 1 H), 7.38 (d, *J* = 7.5 Hz, 1 H), 7.22 (m, 2 H), 4.66 (s, 1 H), 4.30 (q, *J* = 6.8 Hz, 2 H), 3.79 (q, *J* = 6.8 Hz, 2 H), 1.32 (m, 6 H), 0.81 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.6, 145.8, 138.4, 134.8, 133.2, 131.0, 130.5, 130.2, 129.2, 126.3, 114.5, 63.0, 60.9, 30.8, 29.7, 14.7, 14.1.

MS (EI, 70 eV): *m/z* (%) = 169.1 (51), 197.1 (80), 237.1 (74), 247.0 (100), 337.1 (11) [M + H]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅ClNaO₃: 359.1384; found: 359.1390.

Ethyl (2E,3E)-2-(4-Chlorobenzylidene)-3-ethoxy-5,5-dimethylhex-3-enoate (**3b**)

Colorless oil; yield: 123 mg (73%).

IR (KBr): 2956, 2904, 1712, 1662, 1491, 1249, 1199, 1145, 1092, 825 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.66 (s, 1 H), 7.56 (d, *J* = 8.6 Hz, 2 H), 7.31 (d, *J* = 8.6 Hz, 2 H), 4.77 (s, 1 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 3.80 (q, *J* = 7.0 Hz, 2 H), 1.30 (m, 6 H), 0.89 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.9, 145.9, 140.5, 135.6, 133.0, 131.6, 129.2, 128.5, 114.4, 63.0, 61.0, 31.1, 30.8, 14.7, 14.2.

MS (EI, 70 eV): *m/z* (%) = 83.1 (57), 169.1 (68), 237.1 (100), 247.1 (83), 336.0 (17) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅ClNaO₃: 359.1384; found: 359.1387.

Ethyl (2E,3E)-2-(4-Bromobenzylidene)-3-ethoxy-5,5-dimethylhex-3-enoate (**3c**)

Colorless oil; yield: 82 mg (43%).

IR (KBr): 2956, 2921, 2864, 1712, 1656, 1483, 1253, 1069, 746 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.64 (s, 1 H), 7.48 (s, 4 H), 4.76 (s, 1 H), 4.28 (qd, *J* = 7.1, 4.0 Hz, 2 H), 3.79 (q, *J* = 7.0 Hz, 2 H), 1.31 (m, 6 H), 0.88 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ = 167.0, 145.9, 140.6, 133.5, 131.9, 131.6, 129.3, 124.1, 114.3, 63.0, 61.1, 31.2, 30.9, 14.7, 14.2.

MS (EI, 70 eV): *m/z* (%) = 83.1 (62), 197.1 (68), 213.0 (72), 281.0 (100), 291.0 (56), 380.0 (10) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅BrNaO₃: 403.0879; found: 403.0875.

Ethyl (2E,3E)-3-Ethoxy-2-(3-fluorobenzylidene)-5,5-dimethylhex-3-enoate (**3d**)

Colorless oil; yield: 53 mg (33%).

IR (KBr): 2957, 2911, 1712, 1654, 1486, 1251, 1109, 1086, 807 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.67 (s, 1 H), 7.33 (m, 3 H), 7.02 (m, 1 H), 4.76 (s, 1 H), 4.28 (qd, *J* = 7.1, 4.7 Hz, 2 H), 3.81 (m, 2 H), 1.31 (m, 6 H), 0.88 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.9, 162.6 (d, *J*_{CF} = 245.0 Hz), 145.8, 140.6, 136.8 (d, *J*_{CF} = 8.1 Hz), 130.1, 129.7 (d, *J*_{CF} = 8.1 Hz), 126.5, 116.6, 116.3 (d, *J*_{CF} = 4.0 Hz), 114.3, 63.0, 61.1, 31.1, 30.9, 14.7, 14.2.

MS (EI, 70 eV): *m/z* (%) = 83.1 (67), 197.1 (75), 221.1 (100), 320.1 (14) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅FNaO₃: 343.1680; found: 343.1686.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(4-nitrobenzylidene)hex-3-enoate (**3e**)

Yellow oil; yield: 94 mg (54%).

IR (KBr): 2959, 2903, 2870, 1716, 1595, 1522, 1345, 1250, 1200, 1146, 1069, 854 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.21 (d, *J* = 8.8 Hz, 2 H), 7.76 (d, *J* = 8.8 Hz, 2 H), 7.73 (s, 1 H), 4.79 (s, 1 H), 4.31 (m, 2 H), 3.83 (m, 2 H), 1.33 (m, 6 H), 0.86 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.4, 147.8, 145.3, 140.9, 138.9, 132.7, 130.7, 123.4, 114.7, 63.2, 61.3, 31.1, 30.8, 14.6, 14.1.

MS (EI, 70 eV): *m/z* (%) = 197.1 (52), 248.1 (98), 258.0 (100), 347.0 (13) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅NNaO₅: 370.1625; found: 370.1621.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(2-nitrobenzylidene)hex-3-enoate (**3f**)

Yellow oil; yield: 141 mg (81%).

IR (KBr): 2958, 2900, 1717, 1525, 1344, 1246, 1201, 1143, 1069, 810 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.10 (m, 2 H), 7.79 (d, *J* = 7.5 Hz, 1 H), 7.54 (m, 2 H), 4.65 (s, 1 H), 4.31 (q, *J* = 7.1 Hz, 2 H), 3.75 (q, *J* = 6.9 Hz, 2 H), 1.42–1.26 (m, 6 H), 1.22 (s, 2 H), 0.81 (s, 7 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.1, 148.0, 145.2, 139.5, 137.7, 132.9, 132.0, 131.2, 129.4, 124.3, 115.6, 63.1, 61.1, 30.7, 30.2, 14.7, 14.1.

MS (EI, 70 eV): *m/z* (%) = 83.2 (64), 134.2 (80), 174.2 (65), 188.2 (100), 217.1 (65), 258.2 (62), 347.1 (10) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₅NNaO₅: 370.1625; found: 370.1628.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-[4-(trifluoromethyl)benzylidene]hex-3-enoate (**3g**)

Colorless oil; yield: 117 mg (63%).

IR (KBr): 2958, 2901, 2855, 1716, 1324, 1249, 1130, 1067 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.71 (m, 3 H), 7.59 (d, *J* = 8.3 Hz, 2 H), 4.76 (s, 1 H), 4.29 (m, 2 H), 3.80 (q, *J* = 6.7 Hz, 2 H), 1.30 (m, 6 H), 0.86 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.8, 145.7, 140.1, 138.1, 131.2, 130.4, 129.6 (q, *J*_{CF} = 32.8 Hz), 125.2 (q, *J* = 3.7 Hz), 123.9 (q, *J*_{CF} = 272.0 Hz), 114.6, 63.2, 61.2, 31.2, 30.9, 14.7, 14.2.

MS (EI, 70 eV): m/z (%) = 197.1 (51), 271.1 (90), 281.0 (100), 370.1 (13) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₂₀H₂₅F₃NaO₃: 393.1648; found: 393.1647.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(pyridin-2-ylmethylenehex-3-enoate (3h)

Slightly blue oil; yield: 80 mg (53%).

IR (KBr): 2975, 2954, 1709, 1492, 1367, 1211, 1163, 1080, 769 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.65 (d, J = 4.8 Hz, 1 H), 7.85 (s, 1 H), 7.81 (d, J = 8.0 Hz, 1 H), 7.67 (dd, J = 8.0, 4.8 Hz, 1 H), 7.22 (m, 1 H), 4.78 (s, 1 H), 4.29 (q, J = 7.1 Hz, 2 H), 3.83 (q, J = 6.9 Hz, 2 H), 1.36 (m, 6 H), 0.86 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.6, 153.9, 149.4, 145.7, 142.0, 135.9, 131.8, 124.5, 123.3, 114.6, 63.1, 61.0, 31.0, 30.8, 14.7, 14.1.

MS (EI, 70 eV): m/z (%) = 172.3 (51), 246.2 (100), 302.9 (2) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₁₈H₂₅NNaO₃: 326.1727; found: 326.1724.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(pyridin-4-ylmethylenehex-3-enoate (3i)

Yellow oil; yield: 52 mg (34%).

IR (KBr): 2974, 2949, 1710, 1486, 1377, 1208, 1179, 1080, 761 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 8.61 (d, J = 6.0 Hz, 2 H), 7.64 (s, 1 H), 7.45 (d, J = 6.0 Hz, 2 H), 4.77 (s, 1 H), 4.31 (m, 2 H), 3.82 (d, J = 6.8 Hz, 2 H), 1.30 (m, 6 H), 0.87 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.3, 150.0, 145.2, 141.9, 138.9, 133.4, 123.8, 114.6, 63.2, 61.3, 30.9, 30.4, 14.6, 14.1.

MS (EI, 70 eV): m/z (%) = 83.1 (57), 172.1 (51), 246.1 (100), 304.1 (8) [M + 1]⁺.

HRMS: m/z [M + H]⁺ calcd for C₁₈H₂₆NO₃: 304.1907; found: 304.1902.

Ethyl (2E,3E)-2-Benzylidene-3-ethoxy-5,5-dimethylhex-3-enoate (3j)

Colorless oil; yield: 48 mg (32%).

IR (KBr): 2956, 2902, 2864, 1713, 1616, 1248, 1199, 1143, 1067 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.72 (s, 1 H), 7.61 (m, 2 H), 7.34 (m, 3 H), 4.76 (s, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 3.81 (q, J = 7.0 Hz, 2 H), 1.31 (m, 6 H), 0.88 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 167.3, 146.3, 142.2, 134.6, 130.5, 129.7, 128.7, 128.3, 114.3, 63.0, 61.0, 30.9, 30.8, 14.8, 14.2.

MS (EI, 70 eV): m/z (%) = 83.1 (51), 145.1 (62), 203.1 (100), 213.1 (98), 273.1 (50), 302.1 (19) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₁₉H₂₆NaO₃: 325.1774; found: 325.1776.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(naphthalen-1-ylmethylenehex-3-enoate (3k)

Yellow oil; yield: 85 mg (48%).

IR (KBr): 2956, 2903, 1712, 1616, 1469, 1233, 1138, 1090, 1064, 801 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 8.52 (s, 1 H), 8.10 (d, J = 8.2 Hz, 1 H), 7.83 (m, 3 H), 7.48 (m, 3 H), 4.63 (s, 1 H), 4.34 (q, J = 7.0 Hz, 2 H), 3.80 (q, J = 7.1 Hz, 2 H), 1.37 (t, J = 7.1 Hz, 3 H), 1.31 (t, J = 7.0 Hz, 3 H), 0.73 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ = 167.1, 146.4, 139.8, 133.3, 131.9, 131.6, 130.8, 129.7, 128.7, 127.4, 126.6, 125.8, 125.2, 123.7, 114.0, 63.0, 61.0, 31.0, 30.8, 14.8, 14.3.

MS (EI, 70 eV): m/z (%) = 207.1 (100), 296.1 (65), 352.1 (20) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₂₃H₂₈NaO₃: 375.1931; found: 375.1933.

Ethyl (2E,3E)-3-Ethoxy-5,5-dimethyl-2-(4-methylbenzylidene)hex-3-enoate (3l)

Colorless oil; yield: 25 mg (16%).

IR (KBr): 3552, 3406, 2954, 2859, 1710, 1611, 1387, 1249, 1144, 1076, 801 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.69 (s, 1 H), 7.52 (d, J = 8.2 Hz, 2 H), 7.14 (d, J = 8.0 Hz, 2 H), 4.77 (s, 1 H), 4.28 (m, 2 H), 3.79 (q, J = 7.0 Hz, 2 H), 2.35 (s, 3 H), 1.30 (m, 6 H), 0.89 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 167.4, 162.3, 146.5, 142.2, 140.1, 131.8, 130.6, 129.1, 127.4, 114.3, 62.9, 60.9, 31.2, 30.9, 21.4, 14.8, 14.3.

MS (EI, 70 eV): m/z (%) = 159.3 (66), 217.1 (100), 227.1 (75), 316.0 (18) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₂₀H₂₈NaO₃: 339.1931; found: 339.1935.

Ethyl (E)-2-[(E)-1-Ethoxy-3,3-dimethylbut-1-enyl]hex-2-enoate (3m)

Colorless oil; yield: 25 mg (19%).

IR (KBr): 2956, 2863, 1712, 1617, 1461, 1366, 1259, 1132, 1056, 810 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 6.95 (t, J = 7.6 Hz, 1 H), 4.76 (s, 1 H), 4.21 (q, J = 7.0 Hz, 2 H), 3.70 (q, J = 6.9 Hz, 2 H), 2.18 (m, 2 H), 1.50 (m, 2 H), 1.27 (m, 6 H), 0.99 (s, 9 H), 0.95 (t, J = 7.4 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 166.6, 147.6, 146.0, 131.0, 114.7, 62.8, 60.5, 32.2, 31.2, 30.1, 21.5, 14.7, 14.2, 14.0.

MS (EI, 70 eV): m/z (%) = 137.1 (60), 193.1 (100), 267.1 (38) [M - 1]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₁₆H₂₈NaO₃: 291.1931; found: 291.1931.

Methyl (2E,3E)-2-(2-Chlorobenzylidene)-3-methoxy-5,5-dimethylhex-3-enoate (3n)

Slightly yellow oil; yield: 62 mg (40%).

IR (KBr): 2961, 2913, 1720, 1599, 1470, 1243, 1204, 1096, 1065, 774 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.08 (s, 1 H), 7.65 (dd, J = 7.7, 1.6 Hz, 1 H), 7.39 (dd, J = 7.7, 1.2 Hz, 1 H), 7.22 (m, 2 H), 4.65 (s, 1 H), 3.84 (s, 3 H), 3.60 (s, 3 H), 0.81 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ = 167.0, 146.4, 139.1, 134.8, 133.0, 130.9, 130.44, 130.37, 130.3, 129.3, 126.5, 113.5, 54.6, 52.3, 30.8, 30.0.

HRMS: m/z [M + Na]⁺ calcd for C₁₇H₂₁ClNaO₃: 331.1071; found: 331.1073.

Ethyl (E)-5,5-Dimethyl-2-(4-nitrobenzylidene)hex-3-ynoate (4a)

Yellow oil; yield: 14 mg (9%).

IR (KBr): 2969, 2930, 2851, 1721, 1593, 1463, 1292, 1246, 1187, 723 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.25 (d, J = 8.9 Hz, 2 H), 8.18 (d, J = 8.9 Hz, 2 H), 7.81 (s, 1 H), 4.32 (q, J = 7.1 Hz, 2 H), 1.38 (t, J = 7.1 Hz, 3 H), 1.41 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ = 165.1, 147.8, 140.8, 140.2, 130.5, 123.4, 117.9, 110.2, 74.8, 62.0, 30.4, 28.7, 14.0.

MS (EI, 70 eV): m/z (%) = 286.0 (100), 301.0 (36) [M]⁺.

HRMS: m/z [M + Na]⁺ calcd for C₁₇H₁₉NNaO₄: 324.1206; found: 324.1208.

Ethyl (*E*)-5,5-Dimethyl-2-(3-nitrobenzylidene)hex-3-ynoate (4b)

Yellow solid; yield: 148 mg (98%); mp 96–99 °C.

IR (KBr): 2968, 2917, 2863, 1717, 1587, 1427, 1320, 1264, 1193, 725 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 9.29 (t, *J* = 1.8 Hz, 1 H), 8.24 (m, 1 H), 8.02 (d, *J* = 7.7 Hz, 1 H), 7.81 (s, 1 H), 7.57 (t, *J* = 8.0 Hz, 1 H), 4.31 (q, *J* = 7.1 Hz, 2 H), 1.40 (s, 9 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 165.2, 148.3, 140.0, 136.34, 136.28, 129.2, 124.3, 123.4, 117.0, 110.7, 74.4, 61.8, 30.5, 28.7, 14.0.

MS (EI, 70 eV): *m/z* (%) = 286.1 (100), 301.1 (55) [M]⁺, 302.0 (56) [M + 1]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₇H₁₉NNaO₄: 324.1206; found: 324.1207.

Ethyl (*E*)-2-(Furan-2-ylmethylen)-5,5-dimethylhex-3-ynoate (4c)

Colorless oil; yield: 87 mg (71%).

IR (KBr): 2971, 2929, 1717, 1596, 1472, 1269, 1245, 1181, 1023, 749 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.72 (s, 1 H), 7.53 (d, *J* = 1.6 Hz, 1 H), 7.41 (d, *J* = 3.4 Hz, 1 H), 6.54 (dd, *J* = 3.4, 1.6 Hz, 1 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.38 (s, 9 H), 1.34 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 165.5, 151.7, 144.2, 130.9, 114.6, 112.4, 110.6, 109.1, 75.2, 61.2, 30.7, 28.5, 14.0.

MS (EI, 70 eV): *m/z* (%) = 246.0 (100) [M]⁺, 247.0 (47) [M + H]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₅H₁₈NaO₃: 269.1148; found: 269.1155.

Ethyl (*E*)-5,5-Dimethyl-2-(thiophen-2-ylmethylen)hex-3-ynoate (4d)

Colorless oil; yield: 89 mg (68%).

IR (KBr): 2966, 2918, 2864, 1711, 1585, 1368, 1264, 1200, 725 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.02 (s, 1 H), 7.50 (d, *J* = 5.0 Hz, 1 H), 7.46 (d, *J* = 3.8 Hz, 1 H), 7.10 (dd, *J* = 5.0, 3.8 Hz, 1 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.41 (s, 9 H), 1.35 (t, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 165.8, 139.3, 137.0, 133.4, 130.0, 126.8, 110.9, 110.7, 75.3, 61.3, 30.5, 28.7, 14.1.

MS (EI, 70 eV): *m/z* (%) = 219.1 (50), 247.1 (100), 261.9 (41) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₅H₁₈NaO₂S: 285.0920; found: 285.0926.

Ethyl (*E*)-5,5-Dimethyl-2-[(*E*)-3-phenylprop-2-enylidene]hex-3-ynoate (4e)

Colorless oil; yield: 95 mg (67%).

IR (KBr): 2965, 2901, 2865, 1705, 1577, 1368, 1278, 1239, 987, 752 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.59 (d, *J* = 11.3 Hz, 1 H), 7.49 (d, *J* = 7.3 Hz, 2 H), 7.36 (m, 2 H), 7.31 (m, 2 H), 6.98 (d, *J* = 15.7 Hz, 1 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 1.37 (s, 9 H), 1.33 (d, *J* = 7.1 Hz, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 165.6, 145.0, 140.8, 136.4, 129.1, 128.8, 127.4, 125.8, 115.8, 108.0, 73.6, 61.2, 31.0, 28.5, 14.2.

MS (EI, 70 eV): *m/z* (%) = 178.3 (60), 179.3 (67), 193.3 (100), 267.0 (80), 282.0 (38) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₉H₂₂NaO₂: 305.1512; found: 305.1513.

Ethyl (2*E*,3*E*)-5,5-Dimethyl-2-(3-oxoisooindolin-1-ylidene)hex-3-enoate (6)

Yellow solid; yield: 52 mg (35%); mp 91–93 °C.

IR (KBr): 3443, 3298, 2953, 2857, 1719, 1688, 1607, 1465, 1322, 1256, 1102, 773 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 10.20 (br s, 1 H), 8.20 (m, 1 H), 7.96 (m, 1 H), 7.62 (m, 2 H), 6.06 (d, *J* = 12.2 Hz, 1 H), 5.82 (d, *J* = 12.2 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 1.34 (t, *J* = 7.1 Hz, 3 H), 0.99 (s, 9 H).

¹³C NMR (75 MHz, CDCl₃): δ = 168.0, 167.8, 146.9, 142.3, 136.7, 132.1, 130.6, 130.5, 126.2, 123.8, 117.9, 106.3, 61.1, 34.9, 29.8, 14.2.

MS (EI, 70 eV): *m/z* (%) = 210.1 (56), 226.1 (100), 238.1 (58), 253.1 (52), 299.0 (30) [M]⁺.

HRMS: *m/z* [M + Na]⁺ calcd for C₁₈H₂₁NNaO₃: 322.1414; found: 322.1407.

Ethyl (*E*)-3-Ethoxy-5,5-dimethylhex-2-enoate (5)

As a byproduct in the condensation reactions; as a colorless oil.

IR (KBr): 2955, 2928, 1712, 1617, 1372, 1132, 1057 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 5.02 (s, 1 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 3.81 (q, *J* = 7.0 Hz, 2 H), 2.74 (s, 2 H), 1.34 (t, *J* = 7.0 Hz, 3 H), 1.26 (t, *J* = 7.1 Hz, 3 H), 0.97 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ = 174.1, 167.9, 92.5, 63.3, 59.2, 43.3, 32.1, 30.0, 14.4, 14.3.

MS (EI, 70 eV): *m/z* (%) = 153.1 (100), 158.0 (50), 169.1 (53), 215.1 (56) [M + H]⁺.

HRMS: *m/z* [M + H]⁺ calcd for C₁₂H₂₃O₃: 215.1647; found: 215.1646.

Acknowledgment

Financial support from National Natural Science Foundation of China (21072100; 21121002), Research Fund for the Doctoral Program of Higher Education of China (20110031110012), and the Fundamental Research Funds for the Central Universities (08143076), are gratefully acknowledged.

Supporting Information for this article is available online at <http://www.thieme-connect.com/ejournals/toc/synthesis>.

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