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Tandem Blaise/retro-Blaise Reaction for the Nitrile-Mediated Regioselective Intermolecular Addition of Unstabilized Zinc Ester Enolates (Reformatsky Reagents) to 1-Alkynes and 1,3-Enynes

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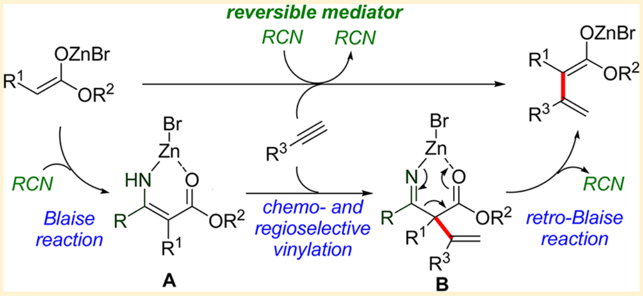
Ⓢ *Supporting Information*

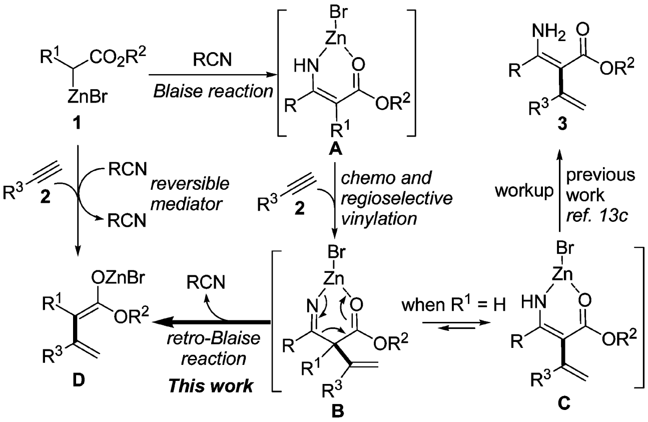
ABSTRACT: We report the novel use of a nitrile as a mediator to achieve the regioselective intermolecular addition of unstabilized zinc ester enolates (Reformatsky reagents) to 1-alkynes and 1,3-enynes. This reaction is made possible by a reversible addition of enolates to a nitrile (Blaise reaction), generating a zinc aza-enolate that, unlike zinc ester enolates, can add intermolecularly to 1-alkynes and 1,3-enynes. Subsequent removal of the nitrile through a retro-Blaise reaction generates the targeted addition product. This method is combined with a Diels–Alder reaction and subsequent oxidative aromatization, providing a tandem one-pot de novo construction of α-arylated alkanoates from Reformatsky reagents.



INTRODUCTION

The addition of enolate nucleophiles to nonactivated carbon–carbon multiple bonds is a synthetically highly challenging and important reaction for carbon–carbon bond formations. During recent decades, significant advances have been made in the addition of metal enolates to unactivated alkenes and alkynes.[1] However, the intermolecular addition of the unstabilized enolates to 1-alkynes is inherently difficult to achieve because the enolate anion is basic enough to deprotonate the acidic terminal C_{sp}–H (for example, $C\underline{H}_3CO_2Et$ pK_a = 29.5[2a] and $PhCC\underline{H}$ pK_a = 28.8 in DMSO).[2b] All reported intermolecular additions of enolates to 1-alkynes to date have been restricted to stabilized enolates formed in situ from a metal catalyst or mediator (i.e., Zn,[3] In,[4] Mn,[5] Re,[6] and Ir[7]) with 1,3-dicarbonyl derivatives. Alternative methods to address this limitation were developed, including the addition to nonactivated 1-alkynes of silyl enol ethers of ketones, promoted by stoichiometric or excess amounts of $GaCl_3$[8] or $SnCl_4$,[9] or of ketene silyl acetals using one equiv of $InCl_3$.[10] However, these approaches required not only the preparation and isolation of silyl enolates as a separate step but also expensive or harmful metallic Lewis acids as mediators. The strategy described in this article is the use of an organic nitrile as a reversible mediator to accomplish the regioselective intermolecular addition of unstabilized zinc ester enolates (Reformatsky reagents) to 1-alkynes (Scheme 1).

Scheme 1. Tandem Blaise/Vinylation/retro-Blaise Reactions for the Nitrile-Mediated Intermolecular Addition of Unstabilized Zinc Ester Enolates to 1-Alkynes



The addition of a Reformatsky reagent to a nitrile, known as the Blaise reaction,[11] proceeds via the zinc bromide complex of β-enaminoester intermediate **A**, which affords a β-ketoester or β-enaminoester after hydrolytic workup under acidic or basic conditions, respectively.[12] However, there is no report on the tandem use of the intermediate **A** as a functionalized organozinc reagent to date. Recently, we recognized the unique features of Blaise reaction intermediate **A** that combines an ambivalent C-/N-nucleophilic enamine moiety with an electrophilic ester group, permitting possible tandem reaction with electrophiles, nucleophiles, or both. During the course of our studies on the use of the intermediate **A** in tandem schemes,[13] we envisioned that **A** could be considered as an isoelectronic variant of the zinc complexes of β-ketoesters that enable intermolecular addition to 1-alkynes **2**.[3] In a previous communication, we have reported that the α-unsubstituted intermediate **A** (R^1 = H) has a propensity to be a C-nucleophile and to react with 1-alkynes

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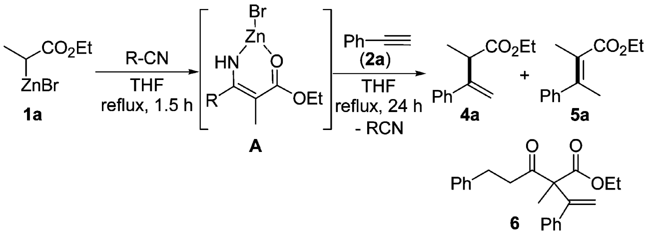
chemoselectively at the α-carbon to afford α-vinylated β-enaminoesters **3** in high yield.[13c] A mechanistic study suggested the formation of zinc complex **B** as a second intermediate, which may rapidly tautomerize to more stable conjugated enamine complex **C**, affording enaminoester **3** after hydrolytic workup. On the basis of these observations, we anticipated that intermediate **B** could also possibly undergo a retro-Blaise fragmentation, excising a nitrile moiety to generate the zinc dienolate **D**. In this tandem Blaise/vinylation/retro-Blaise reaction sequence, the nitrile plays the role of a reversible mediator[14] for the Reformatsky reagent **1**, making possible an intermolecular addition to 1-alkynes that is impossible to conduct directly with **1**.[15] Herein, we report the successful development of the nitrile-mediated tandem intermolecular addition of unstabilized zinc ester enolates (Reformatsky reagents) to 1-alkynes and 1,3-enynes through a Blaise/vinylation/retro-Blaise reaction sequence. To the best of our knowledge, this represents the first example of retro-Blaise reaction.

■ RESULTS AND DISCUSSION

Our previous studies on the chemoselective electrophilic trapping of the Blaise reaction intermediate **A** with various electrophiles suggested that the C-/N-chemoselectivity of **A** is largely determined by the α-subtituent R^1. The α-unsubstituted **A** (R^1 = H) generally showed propensity to be a C-nucleophile,[13a−h] whereas the α-substituted **A** ($R^1 \neq H$) showed N-nucleophilic nature,[13i,l,m] for example, reacting with nitrile electrophiles at the nitrogen atom to afford pyrimidin-2-ones.[13l] Therefore, the success of the nitrile-mediated strategy shown in Scheme 1 would largely be determined by the C-/N-chemoselectivity of the α-substituted intermediate **A** ($R^1 \neq H$) toward 1-alkynes. To determine this outcome, we first investigated the reactivity and C-/N-chemoselectivity of the α-methyl-substituted intermediate **A** (R^1 = Me) toward 1-alkynes (Table 1). The Reformatsky reagent **1a**, generated in situ from ethyl α-bromopropionate and zinc, was reacted with benzonitrile to form the α-methyl-substituted intermediate **A** (R = Ph and R^1 = Me). Tandem reaction of **A** (R = Ph and R^1 = Me) with 1.3 equiv of phenylacetylene (**2a**) in refluxing THF for 24 h resulted in an 89:11 mixture of **4a** and (*E*)-**5a**[16] in 56% yield (entry 1, Table 1). This result clearly indicated that, in sharp contrast to the reaction with nitriles,[13l] the α-substituted intermediate **A** could act as a carbon nucleophile toward 1-alkynes and that the expected retro-Blaise reaction occurred under the reaction conditions, possibly as the result of the steric interactions between R and R^1 in intermediate **B**. After screening different nitriles (entries 2−4, Table 1), we chose 3-phenylpropionitrile as a standard nitrile, which affords a mixture of **4a** and **5a** in 71% yield (entry 4, Table 1). Careful monitoring of the reactions by TLC and GC indicated that the vinylation reaction of **A** to form intermediate **B** and the retro-Blaise reaction proceeded at comparable rates and thus that the generated zinc dienolate **D** could deprotonate alkyne **2a**, affording **4a** and **5a** prior to workup (see Scheme 4 for a detailed mechanism). Gratifyingly, when the same tandem reaction was carried out with 2.1 equiv of phenylacetylene **2a**, the yield increased to 88% while conserving a **4a**/**5a** ratio of 89:11 (entry 5, Table 1). The reaction is quite clean, allowing for an easy separation of the reaction products from the regenerated nitrile by simple silica column chromatography. However, at room temperature, neither the vinylation reaction nor the retro-Blaise reaction proceed efficiently; after 3 days, the ethyl 2-methyl-3-oxo-5-phenyl-2-(1-phenylethenyl)pentanoate (**6**) can be isolated in only 26% yield (entry 6, Table 1), supporting the formation of intermediate **B**.

Table 1. Optimization of the Reaction Conditions[a]

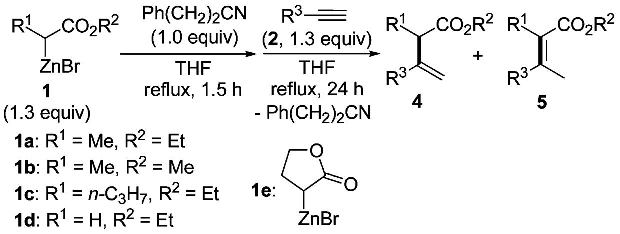


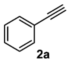
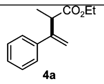
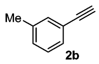
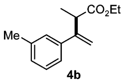
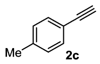
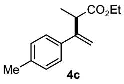
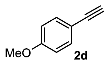
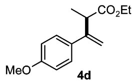
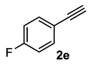
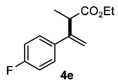
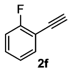
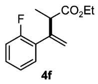
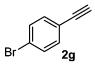
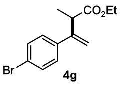
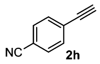
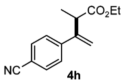
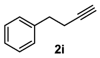
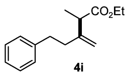
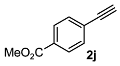
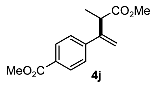
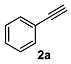
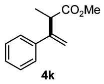
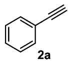
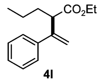
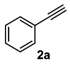
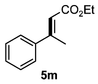
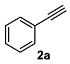
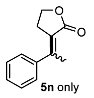
entry	RCN	2a (equiv)	yield (%)[b]	4a/5a[c]
1	PhCN	1.3	56	89/11
2	$PhCH_2CN$	1.3	66	89/11
3	$(CH_3)_2CHCN$	1.3	53	88/12
4	$PhCH_2CH_2CN$	1.3	71	89/11
5	$PhCH_2CH_2CN$	2.1	88	89/11
6[d]	$PhCH_2CH_2CN$	2.1	26	**6**

[a] The reaction conditions are as follows. The Reformatsky reagent **1a**, generated in situ from ethyl α-bromopropionate (2.6 mmol) and zinc (4.0 mmol), was reacted with RCN (2.0 mmol) in THF (0.6 mL). A solution of **2a** in THF (0.6 mL) was added after full conversion of the nitrile to intermediate **A** (>95% by GC). [b] Isolated yield (**4a** + **5a**) (the nitrile was used as a limiting reagent to maximize the formation of **A**, and the yield was calculated on the basis of the limiting reagent). [c] Determined by ^1H NMR analysis. [d] The reaction was carried out at room temperature for 3 days.

We next investigated the generality of this nitrile-mediated intermolecular addition of Reformatsky reagents to 1-alkynes. As shown in Table 2, the established reaction conditions proved to be generally effective for phenylalkynes bearing electron-donating methyl (**2b** and **2c**) and methoxy substituents (**2d**) and afforded the corresponding **4b−d** as major isomers in good yields (entries 2−4, Table 2). The reactions with halogenated phenylacetylenes (**2e−g**) also proceeded efficiently to afford **4e−g** in good yields (entries 5−7, Table 2). The nitrile (**2h**) and ester groups (**2j**) were tolerated under these reaction conditions and resulted in the α-vinylated **4h** (entry 8, Table 2) and **4j** (entry 10, Table 2) with high selectivities, albeit at the expense of slightly decreased yields. The aliphatic alkyne **2i** was less reactive toward the intermediate **A**, and required higher reaction temperatures (100 °C in 1,4-dioxane) for a successful vinylation, but the retro-Blaise reaction occurred rapidly to afford the corresponding addition products **4i** and **5i** (**4i**/**5i** = 83:17) in moderate yields (entry 9, Table 2). Unactivated internal alkynes, such as 1-phenylprop-1-yne, do not participate in the vinylation reaction. Reformatsky reagents bearing a methyl ester (**1b**) or *n*-propyl group at R^1 (**1c**) did not significantly diminish the reaction efficiency and resulted in the corresponding **4k** and **4l** as major isomers in good yields (entries 11 and 12, Table 2). As we observed previously,[13c] the α-unsubstituted intermediate **A** formed from Reformatsky reagent (R^1 = H) (**1d**) undergoes vinylation with phenylacetylene **2a** efficiently in refluxing THF. However, the retro-Blaise reaction did not occur at this temperature, which could be ascribed to the tautomerization of **B** (Scheme 1) to the more thermodynamically stable enamine complex **C**. The complete sequence requires higher temperatures (120 °C in DMF) to afford a mixture of **4m** and **5m** in 57% yield (entry 13, Table 2). In this case, the thermodynamically more stable **5m** was formed as the predominant product with

Table 2. Nitrile-Mediated Intermolecular Addition of Reformatsky Reagent to 1-Alkynes[a]



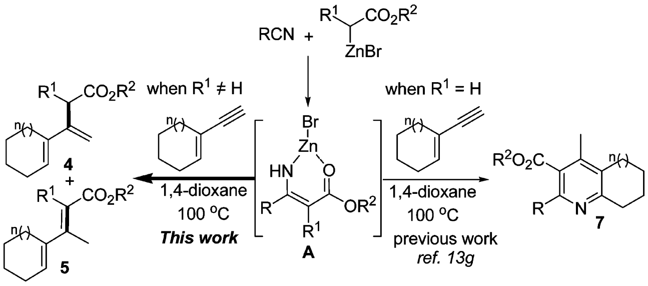
entry	1	2	Major product	4/5 ratio[b]	Yield (%)[c]
1	**1a**	 **2a**	 **4a**	**4a/5a** (89/11)	88
2	**1a**	 **2b**	 **4b**	**4b/5b** (90/10)	85
3	**1a**	 **2c**	 **4c**	**4c/5c** (91/9)	89
4	**1a**	 **2d**	 **4d**	**4d/5d** (88/12)	89
5	**1a**	 **2e**	 **4e**	**4e/5e** (91/9)	82
6	**1a**	 **2f**	 **4f**	**4f/5f** (84/16)	70
7	**1a**	 **2g**	 **4g**	**4g/5g** (87/13)	89
8	**1a**	 **2h**	 **4h**	**4h/5h** (95/5)	60
9[d]	**1a**	 **2i**	 **4i**	**4i/5i** (83/17)	63
10	**1b**	 **2j**	 **4j**	**4j/5j** (94/6)	66
11	**1b**	 **2a**	 **4k**	**4k/5k** (90/10)	80
12	**1c**	 **2a**	 **4l**	**4l/5l** (86/14)	78
13[e]	**1d**	 **2a**	 **5m**	**4m/5m** (5/95)	57
14[d]	**1e**	 **2a**	 **5n** only	**5n** (E/Z = 1/1)	72

[a] The reaction conditions were as follows. The Reformatsky reagent **1**, generated in situ from alkyl bromoalkanoate (2.6 mmol) and Zn (4.0 mmol), was reacted with 3-phenylpropionitrile (2.0 mmol) in THF (0.6 mL). A solution of **2** (4.2 mmol) in THF (0.6 mL) was added after full conversion of the nitrile to intermediate **A** (>95% by GC). [b] The ratio of **4**/**5** was determined either by ^{1}H NMR analysis of crude product or from the isolated yields of **4** and **5**. [c] Isolated yields (**4** + **5**) (the nitrile was used as a limiting reagent to maximize the formation of **A**, and the yield was calculated based on the limiting reagent). [d] The reaction was carried out at 100 °C in 1,4-dioxane. [e] The reaction was carried out at 120 °C in DMF.

ratio of **4m**/**5m** = 5:95. It is interesting to note that all γ-protonated products (E)-**5** were formed stereoselectively with the R^3 and ester groups in trans position, implying stereoselective γ-protonation of zinc dienolate **D**. By contrast, the tandem reaction of intermediate **A**, formed with the Reformatsky reagent **1e**, generated in situ from α-bromo-γ-lactone, with **2a** resulted in a 1:1 mixture of (E/Z)-α-alkenylidenated γ-lactone **5n** in 72% yield.

This nitrile-mediated tandem addition reaction can be extended to 1,3-enynes, where the reaction pathways can be determined by the α-substituents. Previously, we observed that the tandem reaction of α-unsubstituted Blaise reaction intermediate **A** (R^1 = H) with acyclic and cyclic 1,3-enynes in 1,4-dioxane at 100 °C afforded the corresponding pyridine derivatives **7** in high yields (Scheme 2).[13g] In contrast, the tandem reaction with α-substituted intermediate **A** ($R^1 \neq$ H) afforded a mixture of α-dienylated alkanoates **4** and **5**, implying that the retro-Blaise reaction occurred under these reaction conditions (Scheme 2). Thus, the tandem reaction of α-methyl-substituted intermediate **A**, formed by reaction of Reformatsky reagent **1a** with 3-phenylpropionitrile, with cyclohexenyne **2k** at 100 °C for 24 h in 1,4-dioxane afforded an 80:20 mixture of α-dienylated **4o** and **5o** in 73% yield (entry 1, Table 3). There was no sign of the formation of the corresponding pyridine derivative **7**, which was instead obtained in our previous work. The reaction scope with respect to the Reformatsky reagent extends to the synthesis of the methyl ester-(**4p**) and pentanoate-functionalized diene **4q** in good yields with **4**/**5** = 81:19 ratio (entries 2 and 3, Table 3). Under the same reaction conditions, the seven- (**2l**) and eight-membered carbocyclic enynes (**2m**) gave the corresponding α-dienylated alkanoates **4r** (entry 4, Table 3) and **4s** (entry 5, Table 3), respectively, in good yields. In contrast, the *cis*-diphenyl-substituted acyclic 1,3-enyne **2n** afforded the fully conjugated *trans*-**5t** as a major product (entry 6, Table 3).

Scheme 2. Effects of α-Substituent (R^1) on the Reaction Pathway of Intermediate A with 1,3-Enynes

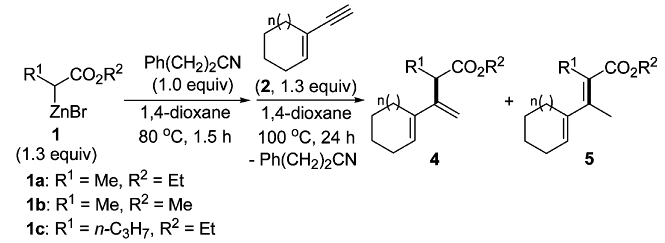


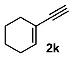
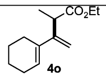
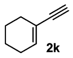
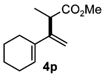
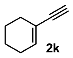
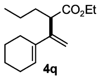
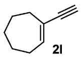
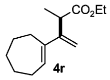
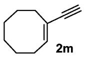
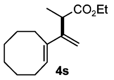
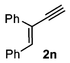
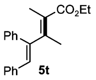
To gain a better understanding of the reaction mechanism, we carried out deuterium-labeling experiments. As shown in Scheme 3a, no deuterium was incorporated into **4a** and **5a** upon quenching the reaction with ND_4Cl in D_2O. This result clearly indicates that the generated zinc dienolate **D** shown in Scheme 1 is protonated to produce **4a** and **5a** prior to workup. In addition, the tandem reaction with deuterium-labeled **2a**-*d* produced 50% deuterium-labeled **4a**-*d* and **5a**-*d*, determined by comparison of the signal intensities of the vinyl protons at 5.40 and 5.24 ppm with methine proton at 3.70 ppm for **4a** and the β-methyl protons at 2.23 ppm for **5a** in ^{1}H NMR spectra (see the Supporting Information) (Scheme 3b). The scrambling of the proton and deuterium atoms at the methine and vinyl and of the methyl groups in **4a** and **5a**, respectively, is consistent with the generation of unlabeled **2a** during the reaction.

On the basis of these deuterium-labeling experiments and our previous results on the formation of α-vinylated β-enaminoesters **3**[13c] and pyridine derivatives **7**,[13g] the plausible reaction pathways of the tandem reactions of **A** with 1-alkynes and 1,3-enynes are summarized in Scheme 4. The Blaise reaction intermediate **A** acts as a C-nucleophile and reacted with alkyne **2** regioselectively to form vinylzinc bromide **E**, which abstracted the proton from the second alkyne **2**, resulting in zinc acetylide **2**-ZnBr and **F**. The inter- and/or intramolecular deprotonation of the N−H proton by **2**-ZnBr could afford the vinylated zinc bromide complex **B**, regenerating starting alkyne **2**. In this manner, even a reaction with deuterium-labeled **2**-*d* can generate the unlabeled **2**-H, which is involved in the reaction cycles explaining the observed proton and deuterium scrambling from the reaction shown in Scheme 3b. The reaction pathways of intermediate **B** are largely determined by the α-substituent R^1. When R^1 = H, **B** is in equilibrium with its fully conjugated tautomeric forms **C** or **C′**. Whereas **C** affords the α-vinylated β-enaminoester **3** after workup,[13c] at high reaction temperature the minor tautomer **B** (R^1 = H) underwent the retro-Blaise reaction to afford **D**, producing **5m** (entry 13, Table 2). The intermediate **C′** could irreversibly isomerize to the N-zincated 1-azatriene **G**, which undergoes a 6π−electrocyclization and/or cycloaddition to form the pyridine ring after elimination of HZnBr.[13g] In contrast, for the intermediate **B** ($R^1 \neq$ H), formed by reaction of α-substituted intermediate **A** ($R^1 \neq$ H), tautomerization is not feasible. Instead, the retro-Blaise reaction pathway dominates, driven by the relaxation of the steric strain imposed by the interactions between R, R^1, and R^3. The α-vinylated zinc enolate **D** thus generated may be in equilibrium with the α-C-bound ZnBr **D-1** and γ-C-bound ZnBr **D-2**, which upon protonation by starting alkyne **2** leads to **4** and *trans*-**5**, respectively, and the zincated alkyne **2**-ZnBr. The formation of **2**-ZnBr at this stage constitutes an unproductive sink for the alkyne, justifying the need for an excess of this reagent to achieve full conversion to **4** and **5**.

Finally, the success of the nitrile-assisted α-dienylation provides, in combination with Diels−Alder and oxidative aromatization, a new tandem one-pot route for the de novo construction of α-arylated alkanoates from Reformatsky reagents (Scheme 5).[17] The α-dienylated product **4o** is more reactive than the pentasubstituted diene **5o**. Consequently, diene **4o** can be selectively reacted with a dienophile in the presence of the less reactive diene **5o**, precluding the need for a separation of **4o** and **5o**. Thus, the Diels−Alder reaction of the nitrile-mediated α-dienylated mixture of **4o** and **5o** (**4o**/**5o** = 80:20) with but-2-ynedioic acid diethyl ester as a model dienophile in 1,4-dioxane at 100 °C for 5 h afforded the Diels−Alder adduct **8** in 92% yield (based on diene **4o**), and the less reactive diene **5o** can be recovered almost quantitatively (Scheme 5a). The oxidative aromatization of **8** using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[18] afforded the α-arylated propionate **9a** in 84% yield. These two reactions could also be telescoped in a single pot without isolation of the Diels−Alder adduct **8**, producing **9** in 77% overall yield. With these results in hand, we next finally attempted the tandem one-pot Blaise/vinylation/Diels−Alder/oxidative aromatization reaction sequence starting from Reformatsky reagent **1a** to afford α-arylated propionate **9a** in 40% overall yield (calculated on the basis of limiting reagent nitrile) (Scheme 5b). Although the nitrile mediator remained in the reaction mixture after the retro-Blaise reaction, it did not interfere with the subsequent Diels−Alder reaction. However,

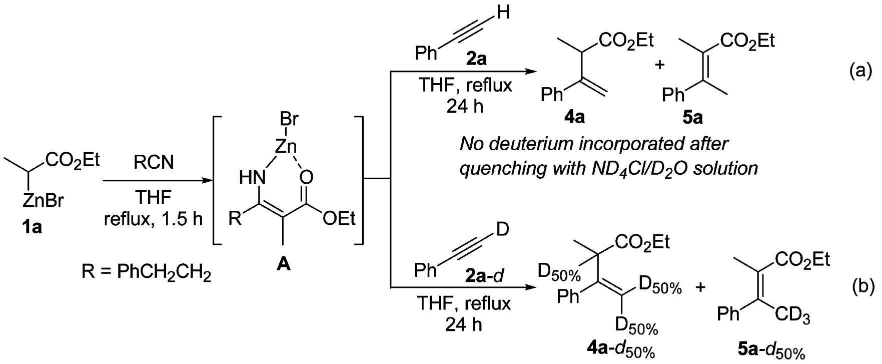
Table 3. Nitrile-Mediated Intermolecular Addition of Reformatsky Reagents to 1,3-Enynes[a]



entry	1	2	Major product	4/5 ratio[b]	Yield (%)[c]
1	**1a**	 **2k**	 **4o**	**4o/5o** (80/20)	73
2	**1b**	 **2k**	 **4p**	**4p/5p** (81/19)	83
3	**1c**	 **2k**	 **4q**	**4q/5q** (81/19)	70
4	**1a**	 **2l**	 **4r**	**4r/5r** (69/31)	76
5	**1a**	 **2m**	 **4s**	**4s/5s** (84/16)	88
6	**1a**	 **2n**	 **5t**	**4t/5t** (38/62)	74

[a] The reaction conditions were as follows. The Reformatsky reagent **1**, generated in situ from alkyl bromoalkanoate (2.6 mmol) and Zn (4.0 mmol), was reacted with 3-phenylpropionitrile (2.0 mmol) in 1,4-dioxane (0.6 mL). A solution of **2** (4.2 mmol) in 1,4-dioxane (0.6 mL) was added after full conversion of the nitrile to intermediate **A** (>95% by GC). [b] The ratio of **4**/**5** was determined either by ^{1}H NMR analysis of the crude product and/or by the isolated yields of **4** and **5**. [c] Isolated yields (**4** + **5**) (the nitrile was used as a limiting reagent to maximize the formation of **A**, and the yield was calculated on the basis of the limiting reagent).

Scheme 3. Deuterium-Labeling Experiments

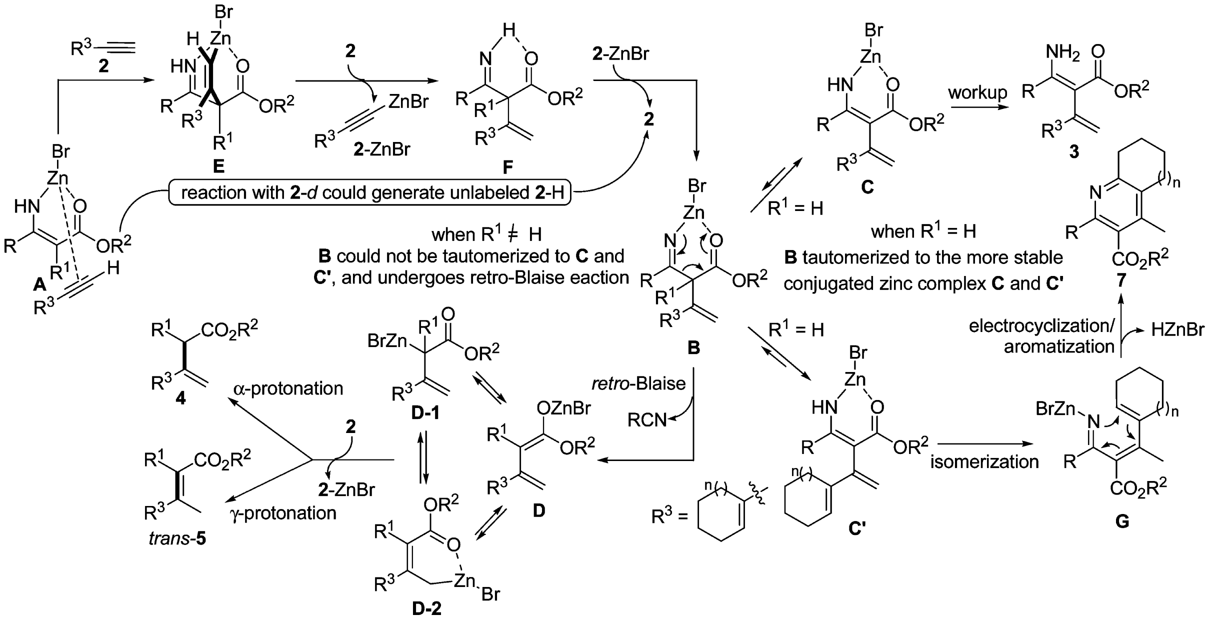


excess amounts of DDQ (3.0 equiv) are necessary to complete the oxidative aromatization reaction in this tandem sequence. Under the same reaction conditions, the α-arylated alkanoates **9b−d** could also be successfully synthesized in good yields.

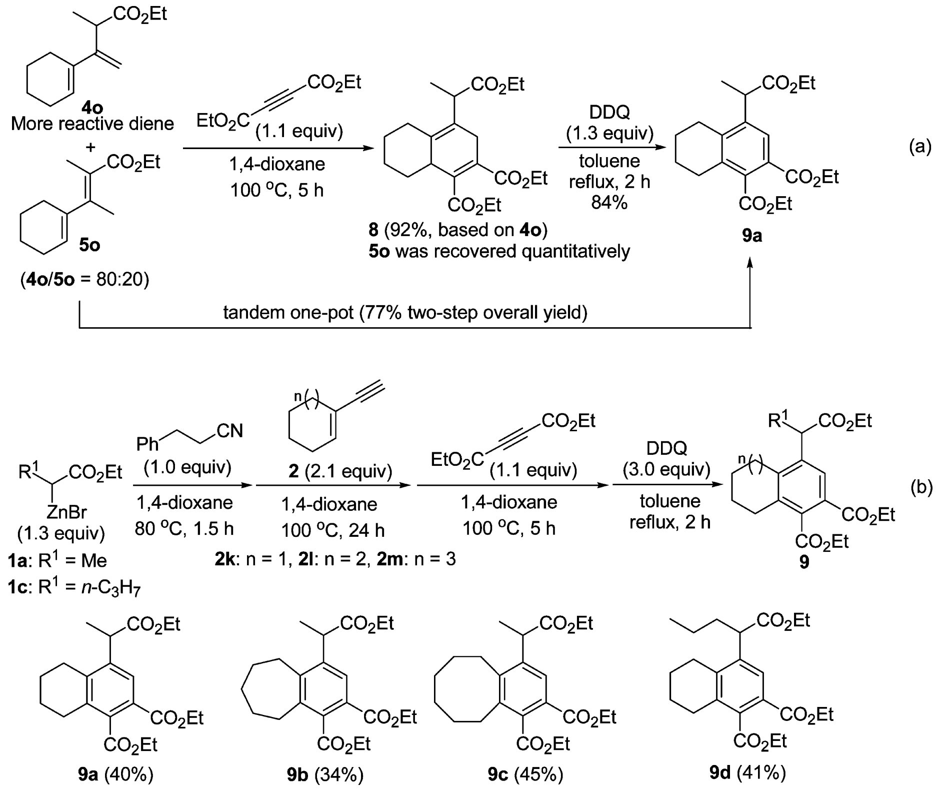
■ CONCLUSIONS

We have developed a new nitrile-mediated tandem regioselective addition of unstabilized zinc enolates (Reformatsky reagent) to 1-alkynes and 1,3-enynes. This reaction is made possible by a reversible addition of enolates to a nitrile, generating a zinc aza-enolate (Blaise reaction intermediate) that unlike zinc ester enolates can add intermolecularly to 1-alkynes and 1,3-enynes. The resulting vinylated intermediates are then directed through bifurcating reaction pathways as a function of the presence of an α-substituent. Although α-unsubstituted vinylated intermediates afford vinylated enaminoesters or pyridines, α-substituted vinylated intermediates undergo a retro-Blaise reaction to generate zinc dienolate. Deuterium-labeling experiments suggest that the zinc dienolates are protonated by acidic acetyletic protons prior to workup to give the targeted α-vinylated and α-dienylated alkanoates. When combined with a Diels−Alder reaction and oxidative aromatization, our approach provides a tandem one-pot method for the de novo synthesis of α-arylated alkanoates. The retro-Blaise reaction is therefore established as a

Scheme 4. Summary of Plausible Reaction Pathways for Tandem Reaction of the Blaise Reaction Intermediate A with 1-Alkynes and 1,3-Enynes



Scheme 5. (a) Stepwise and (b) Tandem De Novo Construction of α-Arylated Alkanoates Based on the Nitrile-Mediated α-Dienylation of Reformatsky Reagents with 1,3-Enynes



highly promising method to access the functionalized surrogates of unstabilized enolates in carbon−carbon-bond-forming reactions.

■ EXPERIMENTAL SECTION

General Methods. All reactions were performed in a nitrogen atmosphere using standard Schlenk techniques. Reaction flasks were flame-dried under a stream of nitrogen. THF and 1,4-dioxane were distilled from sodium benzophenone ketyl, and toluene was distilled from CaH_2. Anhydrous solvent was transferred with an oven-dried syringe. All purchased reagents were used without further purification. The 1,3-enynes **2l**, **2m**, and **2n** were synthesized according to reported procedures.[19] The NMR spectra were recorded at 300 or 400 MHz for ^{1}H and at 75 or 100 MHz for ^{13}C. HRMS data were obtained by electron ionization with a magnetic sector−electronic sector double-focusing mass analyzer.

General Procedure for Tandem Addition of Reformatsky Reagents to 1-Alkynes and 1,3-Enynes. To a stirred suspension of commercial zinc dust (10 μm, 270 mg, 4.0 mmol) in THF (0.6 mL) under reflux was added a solution of methanesulfonic acid in THF (1.0 M, 0.15 mL). After 5 min of stirring, 3-phenylpropionitrile (0.27 mL, 2.0 mmol) was added all at once. While maintaining reflux, alkyl bromoalkanoate (2.6 mmol) was added over 1 h using a syringe pump, and the reaction mixture was further stirred for 30 min. To this reaction mixture was added a solution of 1-alkyne 2 (4.2 mmol) in THF (0.6 mL). After 24 h of reflux, the reaction mixture was cooled to room temperature, quenched with a saturated aqueous NH_4Cl solution, and extracted with ethyl acetate (20 mL x 3). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the corresponding **4** and **5**. For the compounds **4i**/**5i**, **5n**, **4o**/**5o**, **4p**/**5p**, **4q**/**5q**, **4r**/**5r**, **4s**/**5s**, and **4t**/**5t**, the Blaise reactions were carried out at 80 °C in 1,4-dioxane instead of THF, and the vinylation/retro-Blaise reaction was accomplished at 100 °C for 24 h. In the case of **4m**/**5m**, the Blaise reaction/vinylation reactions were carried out in THF, and then, for the retro-Blaise reaction, the reaction mixture was diluted with DMF (3.0 mL) and heated at 120 °C for 24 h. The ratios of **4** and **5** were determined either by analysis of the crude ^{1}H NMR analysis after short filtration through a short plug of silica or by the isolated yield after silica gel column chromatographic purification. The compound pairs **4l**/**5l**, **4q**/**5q**, and **4r**/**5r** were not separable by silica gel chromatography. Consequently, their NMR characterizations were performed by NMR spectra analysis of the mixture of **4** and **5**. The pure form of **5q** and **5r** could be isolated after Diels–Alder reactions of the corresponding mixture of **4** and **5** with but-2-ynedoic acid diethyl ester.

*Ethyl 2-Methyl-3-phenylbut-3-enoate (**4a**) [CAS: 25289-62-7].* Yield: 78% (320 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (t, J = 7.1 Hz, 3H), 1.42 (d, J = 7.1 Hz, 3H), 3.71 (q, J = 7.0 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 5.26 (s, 1H), 5.42 (s, 1H), 7.30–7.43 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 17.1, 44.6, 60.7, 114.0, 126.6, 127.7, 128.4, 141.2, 148.1, 174.5 ppm.

*Ethyl (2E)-2-Methyl-3-phenylbut-2-enoate (**5a**) [CAS: 52094-27-6].* Yield: 10% (40 mg). Pale-yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 1.75 (d, J = 1.5 Hz, 3H), 2.25 (d, J = 1.5 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 7.13–7.16 (m, 2H), 7.27–7.30 (m, 1H), 7.33–7.39 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 17.5, 23.3, 60.5, 125.0, 127.1, 127.4, 128.4, 143.6, 145.5, 170.2 ppm.

*Ethyl 2-Methyl-3-(3-methylphenyl)but-3-enoate (**4b**).* Yield: 77% (334 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, J = 7.1 Hz, 3H), 1.38 (d, J = 7.1 Hz, 3H), 2.35 (s, 3H), 3.66 (q, J = 7.1 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 5.20 (s, 1H), 5.36 (s, 1H), 7.07–7.10 (m, 1H), 7.17–7.24 (m, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 17.2, 21.6, 44.6, 60.7, 113.7, 123.7, 127.3, 128.3, 128.4, 137.9, 141.2, 148.3, 174.6 ppm. HRMS calcd m/z for $C_{14}H_{18}O_2$ [M]$^+$, 218.1307; found; 218.1305.

*Ethyl (2E)-2-Methyl-3-(3-methylphenyl)but-2-enoate (**5b**).* Yield: 8% (37 mg). Pale-yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 1.75 (d, J = 1.4 Hz, 3H), 2.24 (d, J = 1.4 Hz, 3H), 2.36 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 6.93–6.96 (m, 2H), 7.07–7.10 (m, 1H), 7.22–7.27 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 17.6, 21.6, 23.3, 60.5, 124.4, 124.8, 127.9, 128.0, 128.3, 138.1, 143.6, 145.7, 170.2 ppm. HRMS calcd m/z for $C_{14}H_{18}O_2$ [M]$^+$, 218.1307; found; 218.1306.

*Ethyl 2-Methyl-3-(4-methylphenyl)but-3-enoate (**4c**) [CAS: 253663-98-8].* Yield: 81% (354 mg). Eluent: *n*-hexane/EtOAc = 20:1 to 10:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.38 (d, J = 7.1 Hz, 3H), 2.33 (s, 3H), 3.66 (q, J = 7.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 5.18 (s, 1H), 5.36 (s, 1H), 7.12 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 17.1, 21.2, 44.6, 60.7, 113.2, 126.4, 129.1, 137.4, 138.2, 147.9, 174.6 ppm.

*Ethyl (2E)-2-Methyl-3-(4-methylphenyl)but-2-enoate (**5c**) [CAS: 61712-12-7].* Yield: 8% (35 mg). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 1.77 (d, J = 1.5 Hz, 3H), 2.24 (d, J = 1.5 Hz, 3H), 2.36 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 17.6, 21.3, 23.3, 60.5, 124.8, 127.4, 129.1, 136.8, 140.6, 145.5, 170.3 ppm.

*Ethyl 3-(4-Methoxyphenyl)-2-methylbut-3-enoate (**4d**) [CAS: 119139-90-1].* Yield: 78% (367 mg). Eluent: *n*-hexane/EtOAc = 20:1 to 10:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.38 (d, J = 7.1 Hz, 3H), 3.65 (q, J = 7.0 Hz, 1H), 3.79 (s, 3H), 4.10 (q, J = 7.1 Hz, 2H), 5.14 (s, 1H), 5.32 (s, 1H), 6.85 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 17.0, 44.6, 55.3, 60.7, 112.5, 113.7, 127.6, 133.4, 147.4, 159.2, 174.6 ppm.

*Ethyl (2E)-3-(4-Methoxyphenyl)-2-methylbut-2-enoate (**5d**) [CAS: 61712-13-8].* Yield: 11% (50 mg). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 1.78 (d, J = 1.5 Hz, 3H), 2.24 (d, J = 1.5 Hz, 3H), 3.82 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 17.6, 23.3, 55.3, 60.4, 113.7, 124.8, 128.8, 135.7, 145.1, 158.7, 170.3 ppm.

*Ethyl 3-(4-Fluorophenyl)-2-methylbut-3-enoate (**4e**).* Yield: 75% (332 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.38 (d, J = 7.1 Hz, 3H), 3.63 (q, J = 7.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 5.22 (s, 1H), 5.34 (s, 1H), 6.98–7.03 (m, 2H), 7.33–7.37 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 16.9, 44.8, 60.8, 114.2, 115.1, 115.4, 128.3 (d, J = 8.3 Hz), 137.2 (d, J = 3.0 Hz), 147.1, 162.5 (d, J = 246.9 Hz), 174.4 ppm. HRMS calcd m/z for $C_{13}H_{15}FO_2$ [M]$^+$, 222.1056; found; 222.1054.

*Ethyl (2E)-3-(4-Fluorophenyl)-2-methylbut-2-enoate (**5e**) [CAS: 61712-09-2].* Yield: 7% (16 mg). Pale-yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 1.75 (d, J = 1.5 Hz, 3H), 2.23 (d, J = 1.5 Hz, 3H), 4.26 (q, J = 7.1 Hz, 2H), 7.02–7.14 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 17.5, 23.3, 60.6, 115.2, 115.5, 125.6, 129.1 (d, J = 8.3 Hz), 139.3 (d, J = 3.8 Hz), 144.2, 161.9 (d, J = 246.1 Hz), 170.0 ppm.

*Ethyl 3-(2-Fluorophenyl)-2-methylbut-3-enoate (**4f**).* Yield: 59% (261 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, J = 7.1 Hz, 3H), 1.37 (d, J = 7.1 Hz, 3H), 3.62 (q, J = 7.1 Hz, 1H) 4.07 (q, J = 7.1 Hz, 2H), 5.29 (s, 1H), 5.40 (s, 1H), 7.00–7.11 (m, 2H), 7.20–7.28 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.5, 45.3 (d, J = 2.3 Hz), 60.7, 115.7 (d, J = 22.7 Hz), 117.3 (d, J = 1.5 Hz), 124.0 (d, J = 3.0 Hz), 129.2 (d, J = 8.3 Hz), 129.6 (d, J = 15.1 Hz), 130.6 (d, J = 3.8 Hz), 143.8, 159.8 (d, J = 246.9 Hz), 174.2 ppm. HRMS calcd m/z for $C_{13}H_{15}FO_2$ [M]$^+$, 222.1056; found; 222.1058.

*Ethyl (2E)-3-(2-Fluorophenyl)-2-methylbut-2-enoate (**5f**).* Yield: 11% (50 mg). Eluent: *n*-hexane/EtOAc = 20:1. Yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 1.72 (d, J = 1.2 Hz, 3H), 2.25 (d, J = 1.2 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 7.05–7.17 (m, 3H), 7.23–7.30 (m, 1H) ppm. ^{13}C NMR (75 MHz, DMSO) δ 14.1, 17.1, 22.0 60.3, 115.8 (d, J = 21.9 Hz), 124.7 (d, J = 3.8 Hz), 126.7, 129.5 (d, J = 3.8 Hz), 129.7 (d, J = 7.6 Hz), 138.5, 157.9 (d, J = 243.9 Hz), 168.3 ppm. HRMS calcd m/z for $C_{13}H_{15}FO_2$ [M]$^+$, 222.1056; found; 222.1057.

*Ethyl 3-(4-Bromophenyl)-2-methylbut-3-enoate (**4g**).* Yield: 77% (439 mg). Eluent: *n*-hexane/EtOAc = 20:1. Yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, J = 7.1 Hz, 3H), 1.39 (d, J = 7.1 Hz, 3H), 3.63 (q, J = 7.1 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 5.26 (s, 1H), 5.39 (s, 1H), 7.26 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.9, 44.5, 60.8, 114.6, 121.7, 128.2, 131.4, 140.0, 147.0, 174.2 ppm. HRMS calcd m/z for $C_{13}H_{15}BrO_2$ [M]$^+$, 282.0255; found; 282.0255.

*Ethyl (2E)-3-(4-Bromophenyl)-2-methylbut-2-enoate (**5g**) [CAS: 61712-11-6].* Yield: 12% (33 mg). Yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (t, J = 7.1 Hz, 3H), 1.76 (d, J = 1.4 Hz, 3H), 2.23 (d, J = 1.4 Hz, 3H), 4.28 (q, J = 7.1 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 17.5, 23.1, 60.6, 121.1, 12.7, 129.2, 131.7, 142.3, 143.9, 169.9 ppm.

*Ethyl 3-(4-Cyanophenyl)-2-methylbut-3-enoate (**4h**).* Yield: 57% (261 mg). Eluent: *n*-hexane/EtOAc = 10:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.41 (d, J = 7.1 Hz, 3H), 3.67 (q, J = 7.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 5.39 (s, 1H), 5.49 (s, 1H), 7.50 (d, J = 8.6 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 16.8, 44.1, 60.9, 111.2, 116.7, 118.8, 127.2, 132.1, 145.7, 146.6, 173.7 ppm. HRMS calcd m/z for $C_{14}H_{15}NO_2$ [M]$^+$, 229.1103; found; 229.1099.

*Ethyl (2E)-2-Methyl-3-(4-cyanophenyl)but-2-enoate (**5h**) [CAS: 160425-18-3].* Yield: 3% (14 mg). Colorless liquid. ^{1}H NMR (300

MHz, CDCl$_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 1.73 (d, J = 1.4 Hz, 3H), 2.23 (d, J = 1.4 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.4, 17.5, 22.8, 60.8, 111.1, 118.9, 126.6, 128.4, 132.5, 143.0, 148.3, 169.5 ppm.

*Ethyl 2-Methyl-3-methylidene-5-phenylpentanoate (**4i**).* Yield: 45% (209 mg). Eluent: *n*-hexane/EtOAc = 10:1. Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.27 (t, J = 7.1 Hz, 3H), 1.32 (d, J = 7.1 Hz, 3H), 2.30−2.48 (m, 2H), 2.76−2.83 (m, 2H), 3.19 (q, J = 7.1 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 4.97 (s, 1H), 5.01 (s, 1H), 7.21−7.23 (m, 3H), 7.28−7.35 (m, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.3, 16.4, 34.4, 36.5, 46.0, 60.7, 111.4, 126.0, 128.5, 142.0, 147.8, 174.6 ppm. HRMS calcd m/z for C$_{15}$H$_{20}$O$_2$ [M]$^+$, 232.1463; found; 232.1461.

*Ethyl (2E)-2,3-Dimethyl-5-phenylpent-2-enoate (**5i**).* Yield: 10% (46 mg). Yellowish liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.30 (t, J = 7.1 Hz, 3H), 1.81 (s, 3H), 2.02 (s, 3H), 2.39−2.45 (m, 2H), 2.69−2.74 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 7.18−7.24 (m, 3H), 7.26−7.31 (m, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.4, 15.3, 21.1, 33.7, 38.3, 60.2, 123.6, 126.2, 128.5, 128.6, 141.7, 145.2, 170.1 ppm. HRMS calcd m/z for C$_{14}$H$_{16}$O$_4$ [M]$^+$, 232.1463; found; 232.1462.

*Methyl 4-(4-Methoxy-3-methyl-4-oxobut-1-en-2-yl)benzoate (**4j**).* Yield: 62% (273 mg). Eluent: *n*-hexane/EtOAc = 10:1 to 7:1. Pale-yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.40 (d, J = 7.1 Hz, 3H), 3.65 (s, 3H), 3.67−3.74 (m, 1H), 3.92 (s, 3H), 5.33 (s, 1H), 5.48 (s, 1H), 7.45 (d, J = 8.3 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.1, 44.3, 52.2 (52.18), 52.2 (52.21), 115.9, 126.5, 129.4, 129.8, 145.6, 147.2, 166.9, 174.7 ppm. HRMS calcd m/z for C$_{14}$H$_{16}$O$_4$ [M]$^+$, 248.1049; found; 248.1046.

*Methyl 4-[(2E)-4-Methoxy-3-methyl-4-oxobut-2-en-2-yl]benzoate (**5j**).* Yield: 4% (10 mg). Eluent: *n*-hexane/EtOAc = 10:1 to 7:1. Yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.74 (d, J = 1.3 Hz, 3H), 2.26 (d, J = 1.3 Hz, 3H), 3.81 (s, 3H), 3.93 (s, 3H), 7.22 (d, J = 8.2 Hz, 2H), 8.04 (d, J = 8.2 Hz, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.5, 23.0, 51.8, 52.3, 125.5, 127.5, 129.1, 129.9, 145.1, 148.3, 167.0, 170.1 ppm. HRMS calcd m/z for C$_{14}$H$_{16}$O$_4$ [M]$^+$, 248.1049; found; 248.1045.

*Methyl 2-Methyl-3-phenylbut-3-enoate (**4k**) [CAS: 75072-22-9].* Yield: 72% (274 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.38 (d, J = 7.1 Hz, 3H), 3.64 (s, 3H), 3.68−3.71 (m, 1H), 5.22 (s, 1H), 5.39 (s, 1H), 7.24−7.39 (m, 5H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.1, 44.4, 52.0, 114.1, 126.4, 127.7, 128.4, 140.9, 147.9, 175.0 ppm.

*Methyl (2E)-2-Methyl-3-phenylbut-2-enoate (**5k**) [CAS: 14367-28-3].* Yield: 8% (30 mg). Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.75 (d, J = 1.5 Hz, 3H), 2.26 (d, J = 1.5 Hz, 3H), 3.80 (s, 3H), 7.12−7.15 (m, 2H), 7.26−7.29 (m, 1H), 7.33−7.39 (m, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.5, 23.4, 51.6, 124.7, 127.2, 127.3, 128.5, 143.6, 146.3, 170.4 ppm.

*Mixture of Ethyl 2-(1-Phenylethenyl)pentanoate and Ethyl (2E)-2-(1-Phenylethylidene)pentanoate (**4l**/**5l** = 86:14).* Yield: 78% (362 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.77 (t, J = 7.3 Hz, 0.14 × 3H), 0.89 (t, J = 7.3 Hz, 0.86 × 3H), 1.19 (t, J = 7.1 Hz, 0.86 × 3H), 1.27−1.40 (m, 0.86 × 2H + 0.14 × 5H), 1.59−1.71 (m, 0.86 × 1H), 1.84−1.94 (m, 0.86 × 1H), 2.08−2.14 (m, 0.14 × 2H), 2.16 (s, 0.14 × 3H), 3.52 (dd, J = 8.4, 6.4 Hz, 0.86 × 1H), 4.13 (q, J = 7.1 Hz, 0.86 × 2H), 4.27 (q, J = 7.1 Hz, 0.14 × 2H), 5.27 (s, 0.86 × 1H), 5.38 (s, 0.86 × 1H), 7.12−7.14 (m, 0.14 × 2H), 7.24−7.41 (m, 0.86 × 5H + 0.14 × 3H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.0 (13.96), 14.0 (14.02), 14.2, 14.4, 21.1, 21.2, 22.4, 23.4, 33.1, 34.4, 50.4, 60.4, 60.7, 113.8, 114.5, 126.5, 126.6, 127.0, 127.3, 127.6, 128.4, 129.1, 130.9, 141.6, 143.2 (143.16), 143.2 (143.24), 147.2, 170.3, 174.1 ppm. HRMS calcd m/z for C$_{15}$H$_{20}$O$_2$ [M + Na]$^+$, 255.1361; found; 255.1360.

*Ethyl 3-Phenylbut-3-enoate (**4m**) [CAS: 5633-64-7].* Yield: 3% (5 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.18 (t, J = 7.1 Hz, 3H), 3.51 (s, 2H), 4.11 (q, J = 7.1 Hz, 2H), 5.23 (s, 1H), 5.54 (s, 1H), 7.25−7.36 (m, 3H), 7.42−7.45 (m, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.2, 41.5, 60.9, 116.3, 125.9, 127.9, 128.5, 140.0, 141.1, 171.5 ppm.

*Ethyl (2E)-3-Phenylbut-2-enoate (**5m**) [CAS: 1504-72-9].* Yield: 54% (206 mg). Pale-yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.31 (t, J = 7.1 Hz, 3H), 2.58 (d, J = 1.2 Hz, 3H), 4.21 (q, J = 7.1 Hz, 2H), 6.13 (d, J = 1.2 Hz, 2H), 7.34−7.37 (m, 3H), 7.45−7.48 (m, 2H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.4, 18.0, 59.9, 117.2, 126.4, 128.6, 129.0, 142.3, 155.6, 166.9 ppm.

*(3E)-3-(1-Phenylethylidene)dihydrofuran-2(3H)-one (E-**5n**) [CAS: 67404-97-1].* Yield: 38% (143 mg). Eluents: *n*-hexane/EtOAc = 5:1 to 2:1. Yellow solid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.57 (t, J = 2.2 Hz, 3H), 2.84−2.89 (m, 2H), 4.22 (t, J = 7.2 Hz, 2H), 7.24−7.28 (m, 2H), 7.33−7.43 (m, 3H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 19.6, 29.6, 64.7, 120.7, 126.7, 128.3, 128.5, 142.5, 151.1, 171.0 ppm.

*(3Z)-3-(1-phenylethylidene)dihydrofuran-2(3H)-one (Z-**5n**) [CAS: 157494-86-5].* Yield: 35% (128 mg). Brown solid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.14 (t, J = 1.7 Hz, 3H), 2.96−3.01 (m, 2H), 4.30 (t, J = 7.4 Hz, 2H), 7.19−7.22 (m, 2H), 7.29−7.37 (m, 3H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 25.1, 28.3, 64.0, 120.1, 127.4, 127.8, 127.9, 139.9, 150.4, 168.7 ppm.

*Ethyl 3-(Cyclohex-1-en-1-yl)-2-methylbut-3-enoate (**4o**).* Yield: 58% (243 mg). Eluent: *n*-hexane/EtOAc = 20:1. Pale-yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.23 (t, J = 7.1 Hz, 3H), 1.33 (d, J = 7.1 Hz, 3H), 1.55−1.61 (m, 2H), 1.63−1.70 (m, 2H), 2.12−2.18 (m, 4H), 3.51 (q, J = 7.1 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.95 (s, 1H), 5.13 (s, 1H), 5.88−5.92 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.3, 17.4, 22.2, 23.0, 25.9, 26.6, 42.3, 60.6, 109.8, 124.7, 135.7, 148.2, 175.3 ppm. HRMS calcd m/z for C$_{13}$H$_{20}$O$_2$ [M]$^+$, 208.1463; found; 208.1461.

*Ethyl (2E)-3-(Cyclohex-1-en-1-yl)-2-methylbut-2-enoate (**5o**).* Yield: 15% (61 mg). Yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.31 (t, J = 7.1 Hz, 3H), 1.58−1.69 (m, 4H), 1.83 (d, J = 1.4 Hz, 3H), 1.95−2.00 (m, 2H), 2.01 (d, J = 1.4 Hz, 3H), 2.05−2.09 (m, 2H), 4.20 (q, J = 7.1 Hz, 2H), 5.34−5.40 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.5, 16.9, 20.8, 22.2, 22.9, 25.0, 26.9, 60.2, 122.5, 123.2, 140.2, 149.1, 170.3 ppm. HRMS calcd m/z for C$_{13}$H$_{20}$O$_2$ [M]$^+$, 208.1463; found; 208.1464.

*Methyl 3-(Cyclohex-1-en-1-yl)-2-methylbut-3-enoate (**4p**).* Yield: 67% (261 mg). Eluents: *n*-hexane/EtOAc = 20:1 to 10:1. Pale-yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.31 (d, J = 7.1 Hz, 3H), 1.52−1.59 (m, 2H), 1.61−1.69 (m, 2H), 2.08−2.19 (m, 4H), 3.51 (q, J = 7.1 Hz, 1H), 3.64 (s, 3H), 4.93 (s, 1H), 5.11 (s, 1H), 5.86−5.88 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.4, 22.1, 22.9, 25.9, 26.4, 42.0, 51.9, 109.8, 124.6, 135.4, 148.0, 175.7 ppm. HRMS calcd m/z for C$_{12}$H$_{18}$O$_2$ [M]$^+$, 194.1307; found; 194.1307.

*Methyl (2E)-3-(Cyclohex-1-en-1-yl)-2-methylbut-2-enoate (**5p**).* Yield: 16% (62 mg). Yellow liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.58−1.72 (m, 4H), 1.84 (d, J = 1.4 Hz, 3H), 1.96−2.10 (m, 4H), 2.03 (d, J = 1.4 Hz, 3H), 3.74 (s, 3H), 5.36−5.39 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 16.9, 20.9, 22.2, 22.8, 25.0, 26.9, 51.4, 122.2, 123.2, 140.2, 149.9, 170.5 ppm. HRMS calcd m/z for C$_{12}$H$_{18}$O$_2$ [M]$^+$, 194.1307; found; 194.1309.

*Mixture of Ethyl 2-[1-(Cyclohex-1-en-1-yl)ethenyl]pentanoate (**4q**) and Ethyl (2E)-2-[1-(Cyclohex-1-en-1-yl)ethylidene]pentanoate (**5q**) (**4q**/**5q** = 81:19).* Yield: 70% (331 mg). Eluent: *n*-hexane/EtOAc = 20:1. Colorless liquid. For the major compound **4q**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.91 (t, J = 7.3 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.27−1.38 (m, 2H), 1.52−1.70 (m, 6H), 2.10−2.20 (m, 4H), 3.37 (dd, J = 8.9, 5.7 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.99 (s, 1H), 5.12 (s, 1H), 6.92−6.94 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.1, 14.3, 21.3, 22.2, 22.9, 23.0, 25.9, 26.6, 34.6, 47.8, 60.5, 110.1, 124.6, 135.9, 147.2, 174.7 ppm. HRMS calcd m/z for C$_{15}$H$_{24}$O$_2$ [M]$^+$, 236.1776; found; 236.1775.

*Ethyl (2E)-2-[1-(Cyclohex-1-en-1-yl)ethylidene]pentanoate (**5q**).* Isolated after the Diels−Alder reaction of a mixture of **4q** and **5q** with but-2-ynedioic acid diethyl ester. Colorless liquid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.86 (t, J = 7.3 Hz, 3H), 1.25−1.38 (m, 5H), 1.54−1.70 (m, 4H), 1.93 (s, 3H), 1.96−2.02 (m, 2H), 2.04−2.11 (m, 2H), 2.21−2.26 (m, 2H), 4.21 (q, J = 7.1 Hz, 2H), 5.37−5.39 (m, 1H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.3, 14.5, 20.7, 22.2, 22.9, 25.0, 27.5, 33.0, 60.2, 122.9, 128.5, 139.7, 146.8, 170.5 ppm.

*Mixture of Ethyl 3-(Cyclohept-1-en-1-yl)-2-methylbut-3-enoate (**4r**) and Ethyl (2E)-3-(Cyclohept-1-en-1-yl)-2-methylbut-2-enoate (**5r**) (**4r**/**5r** = 69:31).* Yield: 76% (338 mg). Eluent: *n*-hexane/EtOAc = 20:1. Pale-yellow liquid. For the major compound **4r**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.23 (t, J = 7.1 Hz, 3H), 1.31 (d, J = 7.1 Hz, 3H), 3.41 (q, J = 7.1 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.91 (s, 1H), 5.07 (s, 1H), 5.93

(t, J = 6.8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 17.1, 26.5, 26.7, 28.5, 30.9, 32.6, 43.0, 60.5, 110.1, 129.2, 144.7, 150.4, 175.1 ppm. HRMS calcd m/z for $C_{14}H_{22}O_2$ $[M]^+$, 222.1620; found; 222. 1618.

*Ethyl (2E)-3-(Cyclohept-1-en-1-yl)-2-methylbut-2-enoate (**5r**).* Isolated after the Diels–Alder reaction of a mixture of **4r** and **5r** with but-2-ynedioic acid diethyl ester. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, J = 7.1 Hz, 3H), 1.51–1.62 (m, 4H), 1.74–1.82 (m, 2H), 1.87 (d, J = 1.4 Hz, 3H), 2.01 (d, J = 1.4 Hz, 3H), 2.15–2.22 (m, 4H), 4.21 (q, J = 7.1 Hz, 2H), 5.56 (t, J = 6.4 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 17.3, 20.7, 27.2, 27.3, 28.7, 32.3, 32.6, 60.2, 121.5, 128.9, 146.0, 150.6, 170.4 ppm.

*Ethyl 3-(Cyclooct-1-en-1-yl)-2-methylbut-3-enoate (**4s**).* Yield: 74% (349 mg). Eluent: n-hexane/EtOAc = 20:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, J = 7.1 Hz, 3H), 1.34 (d, J = 7.1 Hz, 3H), 1.41–1.56 (m, 8H), 2.18–2.25 (m, 2H), 2.42–2.46 (m, 2H), 3.51 (q, J = 7.1 Hz, 1H), 4.13 (qd, J = 7.1, 2.0 Hz, 2H), 5.01 (s, 1H), 5.20 (s, 1H), 5.84 (t, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 17.3, 26.0, 26.2, 27.1, 27.5, 28.9, 30.3, 42.4, 60.5, 110.9, 127.6, 139.3, 147.5, 175.2 ppm. HRMS calcd m/z for $C_{15}H_{24}O_2$ $[M]^+$, 236.1776; found; 236.1774.

*Ethyl (2E)-3-(Cyclooct-1-en-1-yl)-2-methylbut-2-enoate (**5s**).* Yield: 14% (67 mg). Pale-yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, J = 7.1 Hz, 3H), 1.52–1.57 (m, 8H), 1.88 (d, J = 1.3 Hz, 3H), 2.06 (d, J = 1.3 Hz, 3H), 2.17–2.20 (m, 2H), 2.22–2.32 (m, 2H), 4.22 (q, J = 7.1 Hz, 2H), 5.40 (t, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 17.3, 21.8, 26.4, 26.5, 29.1, 29.5 (29.47), 29.5 (29.53), 60.2, 122.5, 126.9, 142.7, 149.5, 170.5 ppm. HRMS calcd m/z for $C_{15}H_{24}O_2$ $[M]^+$, 236.1776; found; 236.1774.

*Ethyl (4Z)-2-Methyl-3-methylidene-4,5-diphenylpent-4-enoate (**4t**).* Yield: 28% (172 mg). Eluents: n-hexane/EtOAc = 40:1 to 20:1. Yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.32 (d, J = 7.1 Hz, 3H), 3.24 (q, J = 7.1 Hz, 1H), 3.90–4.07 (m, 2H), 5.34 (s, 1H), 5.49 (s, 1H), 6.75 (s, 1H), 7.19–7.25 (m, 1H), 7.29–7.40 (m, 5H), 7.46–7.51 (m, 2H), 7.51–7.58 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 16.2, 44.4, 60.7, 118.8, 127.3, 127.5, 127.8, 128.3, 128.4, 129.1, 129.2, 137.3, 142.1, 143.1, 145.5, 174.2 ppm. HRMS calcd m/z for $C_{21}H_{22}O_2$ $[M]^+$, 306.1620; found; 306.1617.

*Ethyl (2E,4E)-2,3-Dimethyl-4,5-diphenylpenta-2,4-dienoate (**5t**).* Yield: 46% (281 mg). Yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, J = 7.1 Hz, 3H), 1.76 (d, J = 1.3 Hz, 3H), 2.22 (d, J = 1.3 Hz, 3H), 4.31 (q, J = 7.1 Hz, 2H), 6.87 (s, 1H), 7.25–7.30 (m, 1H), 7.32–7.44 (m, 5H), 7.47–7.53 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 16.9, 21.0, 60.4, 126.2, 126.7, 126.8, 127.5, 127.9, 128.6 (128.56), 128.6 (128.60), 128.8, 137.0, 139.6, 142.3, 144.2, 169.3 ppm. HRMS calcd m/z for $C_{21}H_{22}O_2$ $[M]^+$, 306.1620; found; 306.1617.

*Ethyl 2-Methyl-3-oxo-5-phenyl-2-(1-phenylethenyl)pentanoate (**6**).* Yield: 26% (201 mg). Eluent: n-hexane/EtOAc = 10:1. Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) 1.18 (t, J = 7.1 Hz, 3H), 1.50 (s, 3H), 2.80–2.98 (m, 4H), 4.14 (q, J = 7.1 Hz, 2H), 5.19 (s, 1H), 5.39 (s, 1H), 7.12–7.18 (m, 5H), 7.23–7.27 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 21.3, 30.5, 41.5, 61.7, 65.7, 118.9, 126.2, 127.7, 127.9, 128.2, 128.5 (128.50), 128.5 (128.53), 140.4, 141.1, 148.0, 172.0, 206.6 ppm. HRMS calcd m/z for $C_{22}H_{24}O_3$ $[M + Na]^+$, 359.1623; found; 359.1625.

*Procedures for Stepwise and Tandem Synthesis of **9a** from the Isolated Mixture of **4o** and **5o** with an 80:20 Ratio.* To a stirred solution of a mixture of **4o** and **5o** (208 mg, 1 mmol, **4o**/**5o** = 80:20) in 1,4-dioxane (2.0 mL) was added but-2-ynedioic acid diethyl ester (0.18 mL, 1.1 mmol) at room temperature. The reaction mixture was stirred at 100 °C for 5 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford the stereoisomeric mixture **8** (d.r. ≃ 6:4) as a colorless liquid (279 mg, 92% yield, based on **4o**). The less reactive diene **5o** (41 mg) was recovered quantitatively. For the oxidative aromatization of **8**, a solution of **8** (265 mg, 0.70 mmol) in toluene (1.0 mL) was added to a stirred solution of 2,3-dichloro-5,6,-dicyano-1,4-benzoquinone (DDQ, 207 mg, 0.91 mmol) in toluene (1.0 mL). The reaction mixture was stirred for 2 h at reflux. After cooling to room temperature, the reaction mixture was filtered through a short plug of silica gel with the aid of three 10 mL portions of ethyl acetate and concentrated under reduced pressure. The residue was purified by silica chromatography to afford **9a** in 84% (233 mg) yield. To conduct these two reaction steps in one pot without isolation of **8**, the 1,4-dioxane solvent was evaporated after the Diels–Alder reaction, and toluene and DDQ were added to the residue. The resulting mixture was stirred for 2 h at toluene refluxing to afford **9a** in 77% (232 mg) yield.

General Procedure for Tandem De Novo Construction of α-Arylated Alkanotates from Reformatsky Reagents. To a stirred suspension of commercial zinc dust (10 μm, 270 mg, 4.0 mmol) in 1,4-dioxane (0.5 mL) was added a solution of methanesulfonic acid in 1,4-dioxane (1.0 M, 0.15 mL) at 80 °C bath temperature. After 5 min of stirring, 3-phenylpropionitrile (0.27 mL, 2.0 mmol) was added all at once. While maintaining the same temperature, alkyl bromoalkanoate (3.0 mmol) was added over 1 h using a syringe pump, and the reaction mixture was further stirred for 30 min. The reaction mixture was heated at 100 °C, and then cyclic 1,3-enyne **2** (4.2 mmol) was added. After 24 h of stirring at the same temperature, a solution of but-2-ynedioic acid diethyl ester (0.4 mL, 2.4 mmol) in 1,4-dioxane (3.0 mL) was added, and the reaction mixture was stirred at the same temperature for an additional 5 h. The reaction mixture was cooled to room temperature, filtered through Celite, and washed with ethyl acetate (15 mL × 3), and then the filtrate was concentrated under reduced pressure. The resulting mixture was diluted with toluene (6.0 mL) and added to a stirred solution of 2,3-dichloro-5,6,-dicyano-1,4-benzoquinone (DDQ, 1.36 g, 6.0 mmol) in toluene (4.0 mL) at room temperature. The reaction mixture was stirred for 2 h under refluxing toluene. After cooling to room temperature, the reaction mixture was filtered through a plug of silica gel with the aid of three 30 mL portions of ethyl acetate, and the filtrate was concentrated under reduced pressure. The residue was purified by silica chromatography to afford the corresponding α-arylated alkanoates **9a**–**d**.

*Diethyl 4-(1-Ethoxy-1-oxopropan-2-yl)-3,5,6,7,8,8a-hexahydronaphthalene-1,2-dicarboxylate (**8**).* (Mixture of diastereomers, d.r. ≃ 6:4 by ^{1}H NMR). Eluent: n-hexane/EtOAc = 5:1. Colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07–1.29 (m, 14H), 1.35–1.48 (m, 1H), 1.54–1.68 (m, 1H), 1.68–1.80 (m, 2H), 1.84–1.94 (m, 1H), 2.60–2.78 (m, 1H + 0.6 × 1H), 2.81–2.88 (m, 1H), 2.89- 3.06 (m, 1H + 0.4 × 1H), 3.58 (q, J = 7.1 Hz, 0.6 × 1H), 3.60 (q, J = 7.1 Hz, 0.4 × 1H), 3.98–4.07 (m, 2H), 4.07–4.23 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 14.8, 15.3, 26.5, 26.6, 27.3, 27.6, 27.8, 27.9, 29.8, 33.9, 34.0, 40.4, 40.5, 42.2, 42.3, 60.5, 60.9, 121.8, 121.9, 128.9 (128.88), 128.9 (129.92), 133.0, 137.8, 137.9, 167.1, 168.5 (168.46), 168.5 (168.50), 174.1 (174.06), 174.1 (174.11) ppm.

*Diethyl 4-(1-Ethoxy-1-oxopropan-2-yl)-5,6,7,8-tetrahydronaphthalene-1,2-dicarboxylate (**9a**).* Yield: 301 mg (40%, calculated on the basis of the limiting reagent nitrile). Eluent: n-hexane/diethyl ether = 6:1. Colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.44 (d, J = 7.1 Hz, 3H), 1.71–1.83 (m, 4H), 2.67–2.76 (m, 3H), 2.82–2.89 (m, 1H), 3.94 (q, J = 7.1 Hz, 1H), 4.10 (m, 2H), 4.30 (q, J = 7.1 Hz, 2H), 4.38 (q, J = 7.2 Hz, 2H), 7.72 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.3, 17.8, 22.0, 22.5, 26.9, 27.0, 40.7, 61.0, 61.3, 61.4, 125.3, 125.7, 134.6, 134.9, 140.6, 140.7, 165.8, 169.7, 174.2 ppm. HRMS calcd m/z for $C_{21}H_{28}O_6$ $[M]^+$, 376.1886; found; 376.1885.

*Diethyl 4-(1-Ethoxy-1-oxopropan-2-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-1,2-dicarboxylate (**9b**).* Yield: 264 mg (34%, calculated on the basis of the limiting reagent nitrile). Eluent: n-hexane/diethyl ether = 6:1. Pale-yellow viscous liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, J = 7.1 Hz, 3H), 1.29–1.36 (m, 6H), 1.44 (d, J = 7.1 Hz, 3H), 1.52–1.68 (m, 4H), 1.70–1.80 (m, 2H), 2.73–2.76 (m, 2H), 2.85–2.90 (m, 2H), 3.97 (q, J = 7.1 Hz, 1H), 4.09 (qd, J = 7.1, 1.1 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 7.72 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 14.2, 18.1, 26.6, 26.8, 29.3, 31.2, 31.7, 42.5, 60.9, 61.2, 61.3, 125.2, 127.2, 133.8, 139.1, 141.0, 147.3, 165.6, 169.9, 174.2 ppm. HRMS calcd m/z for $C_{22}H_{30}O_6$ $[M]^+$, 390.2042; found; 390.2041.

*Diethyl 4-(1-Ethoxy-1-oxopropan-2-yl)-5,6,7,8,9,10-hexahydrobenzo[8]annulene-1,2-carboxylate (**9c**).* Yield: 367 mg (45%, calculated on the basis of the limiting reagent nitrile). Eluent: n-hexane/diethyl ether = 4:1. Colorless viscous liquid. ^{1}H NMR (300

MHz, $CDCl_3$) δ 1.18 (t, J = 7.1 Hz, 3H), 1.34−1.45 (m, 10H), 1.48 (d, J = 7.1 Hz, 3H), 1.60−1.88 (m, 4H), 2.80−2.85 (m, 2H), 2.86−2.92 (m, 1H), 2.96−3.05 (m, 1H), 4.02−4.17 (m, 3H), 4.33 (q, J = 7.1 Hz, 2H), 4.42 (q, J = 7.1 Hz, 2H), 7.83 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (14.15), 14.2 (14.20), 14.3, 19.0, 25.8, 26.6, 27.3, 30.0, 30.5, 31.4, 41.0, 61.0, 61.4, 61.5, 126.0, 126.7, 134.4, 139.1, 140.3, 144.5, 165.8, 170.1, 174.3 ppm. HRMS calcd m/z for $C_{23}H_{32}O_6$ $[M]^+$, 404.2199; found; 404.2196.

*Diethyl 4-(1-Ethoxy-1-oxopentan-2-yl)-5,6,7,8-tetrahydronaphtahalene-1,2-carboxylate (**9d**).* Yield: 347 mg (41%, calculated on the basis of the limiting reagent nitrile and the ratio of reactive diene **4q** shown in Table 3). Eluents: *n*-hexane/diethyl ether = 6:1 to 4:1. Colorless viscous liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, J = 7.3 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 1.20−1.38 (m, 8H), 1.60−1.81 (m, 5H), 2.02−2.15 (m, 1H), 2.67−2.77 (m, 3H), 2.87−2.95 (m, 1H), 3.85 (t, J = 7.5 Hz, 1H), 4.02−4.15 (m, 2H), 4.31 (q, J = 7.1 Hz, 2H), 4.39 (q, J = 7.1 Hz, 2H), 7.80 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.1 (14.09), 14.1 (14.13), 14.2, 20.9, 22.0, 22.5, 26.9, 27.1, 35.1, 45.8, 60.8, 61.2, 61.4, 125.2, 125.8, 134.5, 134.8, 139.3, 140.9, 165.8, 169.7, 173.6 ppm. HRMS calcd m/z for $C_{23}H_{32}O_6$ $[M]^+$, 404.2199; found; 404.2198.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra of **4a**-$d_{50\%}$, **5a**-$d_{50\%}$, **4a−t**, **5a−t**, **6**, **8**, and **9a−d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This paper is dedicated to Professor Teruaki Mukaiyama in celebration of the 40th anniversary of the Mukaiyama aldol reaction.

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