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Synthesis of β-Allylbutenolides via One-Pot Copper-Catalyzed Hydroallylation/Cyclization of γ-Hydroxybutynoate Derivatives

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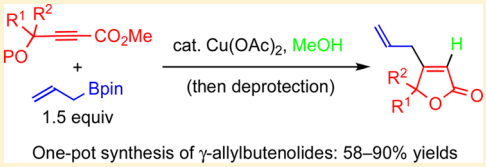
Supporting Information

ABSTRACT: One-pot copper-catalyzed hydroallylation/lactone cyclization of γ-hydroxybutynoate derivatives was developed to afford β-allylbutenolides.



INTRODUCTION

Furan-2(5*H*)-one or $\Delta^{\alpha,\beta}$-butenolide has attracted considerable attention because this privileged heterocyclic motif has been found in numerous natural products with interesting biological activities.[1] Therefore, various synthetic procedures have been devised to construct the furan-2(5*H*)-one framework.[2] Among these, the one-pot catalytic hydroarylation/lactone cyclization of readily available γ-hydroxybutynoates is one of the most powerful strategies for assembling arylated butenolides.[3,4] Aryl iodides have been employed as the arylating reagents in a pioneering study by Cacchi and co-workers.[3] Later, arylboron reagents were utilized as less toxic and stable alternatives.[4] Although these methods enabled the synthesis of butenolides with an aryl group at the α or β positions, a related method to introduce a functionalizable substituent has been underdeveloped. In a seminal study, the Cacchi group has also investigated the palladium-catalyzed hydrovinylation/lactone cyclization using alkenyl halides and triflates to afford α- or β-alkenylbutenolides.[5] However, no further development has been made in this field.

Our group has independently developed the copper-catalyzed hydroarylation of electron-deficient alkynes.[6] Our method has several advantages over previous hydroarylations: (1) Inexpensive copper(I) or copper(II) acetate is employed as the catalyst, and no extra ligand is required. (2) Readily available and easy-to-handle arylboronic acids are used as the arylating reagents. (3) The reaction proceeds under mild conditions. (4) Diverse functional groups are tolerated. (5) Trisubstituted alkene products are obtained regio- and stereoselectively. Taking advantage of these features of the copper-catalyzed hydroarylation, we have successfully synthesized biologically interesting compounds such as 4-arylcoumarins,[7a] 3,3-diarylacrylonitriles including the potential anticancer agent CC-5079,[7b] and 3-arylindole-2-carboxylates.[7c] As an extension of these studies, we recently investigated the copper-catalyzed hydroallylation of electron-deficient alkynes using a commercially available allylboronic acid pinacol ester.[8] The hydroallylation regio- and stereoselectively proceeds under mild reaction conditions to afford the desired skipped diene (1,4-diene) products. The introduced allylic substituent enabled further derivatization; the allyl group was successfully utilized in hydroboration/oxidation, hydroboration/Suzuki–Miyaura cross-coupling, ring-closing metathesis (RCM), and cross metathesis (CM). To further demonstrate the synthetic potential of the copper-catalyzed hydroallylation, we investigated the one-pot hydroallylation/lactone cyclization of γ-hydroxybutynoate derivatives to afford β-allylbutenolides.

Although various synthetic methods for β-allylbutenolides have been developed because of their synthetic utility, they essentially rely on the transformation of substrates bearing a pre-introduced allylic moiety or the allylation of preformed butenolides.[9] To the best of our knowledge, only a few examples are reported on the synthesis of β-allylated butenolides via combined catalytic allylation and lactone-ring formation. For example, Trost and co-workers reported the one-pot ruthenium-catalyzed allylation of γ-hydroxybutynoates/lactone cyclization.[10] However, this method afforded regioisomeric products depending on the substrate structure. Ma and Yu developed the palladium-catalyzed allylative cyclization of 2,3-allenoic acids with allylic halides.[11a] Later, Chen and Ma also reported a similar synthesis of β-allylbutenolides from 2,3-allenoates and allylic bromides using the Pd/Fe combined catalytic system.[11b] Furthermore, Blum and co-workers designed an interesting Au/Pd bimetallic catalyst system, which used allyl 2,3-allenoates as the substrates bearing a latent allylating agent; β-allylbutenolides were produced via the gold-catalyzed lactone cyclization of the allenoates and subsequent allylation with the resultant π-allylpalladium species.[12] Although these methods are regioselective with wide substrate scope, precious metal catalysts and an excess amount of toxic allylic halides are required to obtain the desired products. Therefore, a new protocol for synthesizing β-allylbutenolides should be developed using an inexpensive catalyst and a less toxic allylating agent. Herein, we report the

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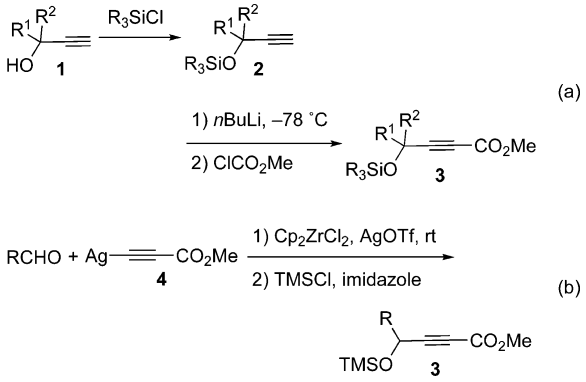
development of copper-catalyzed one-pot hydroallylation/lactone cyclization.

RESULTS AND DISCUSON

1. Preparation of Butynoate Substrates. The required butynoate substrates were prepared from readily available propargylic alcohol derivatives **1** as outlined in Scheme 1a.

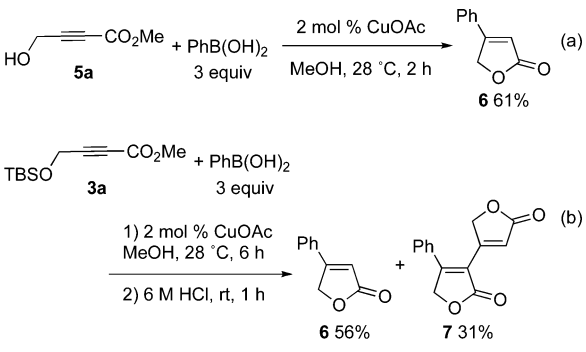
Scheme 1. Preparation of Substrates



Alkyne **1** can be obtained from commercial suppliers or prepared by the ethynylation of the corresponding carbonyl compounds. After protecting the γ-hydroxyl group with an appropriate silyl group, the alkyne terminal of **1** was methoxycarbonylated according to the reported procedure.[13] Thus, obtained silylated substrates **3** were used for this study without deprotection. However, desilylation was performed using tetrabutylammonium fluoride (TBAF) if required (*vide infra*). Other alkyne substrates with a methoxymethyl (MOM) protecting group were also obtained from **1** and methoxymethyl chloride using the standard procedures. Alternatively, γ-hydroxybutynoates were directly prepared by the addition of silver acetylide **4**, derived from methyl propiolate, to aldehydes using the procedure reported by Shahi and Koide (Scheme 1b).[14] The subsequent silylation of the obtained γ-hydroxybutynoates with trimethylsilyl (TMS) chloride afforded secondary propargylic alcohol derivatives **3**.

2. One-Pot Hydroallylation/Lactone Cyclization. Previously, we attempted the one-pot hydroarylation/lactone cyclization of γ-hydroxybutynoate **5a** with phenylboronic acid under the optimal copper-catalyzed hydroarylation conditions (Scheme 2a).[6] However, the desired β-phenylbutenolide **6** was isolated in 61% yield, even though substrate **5a** was completely

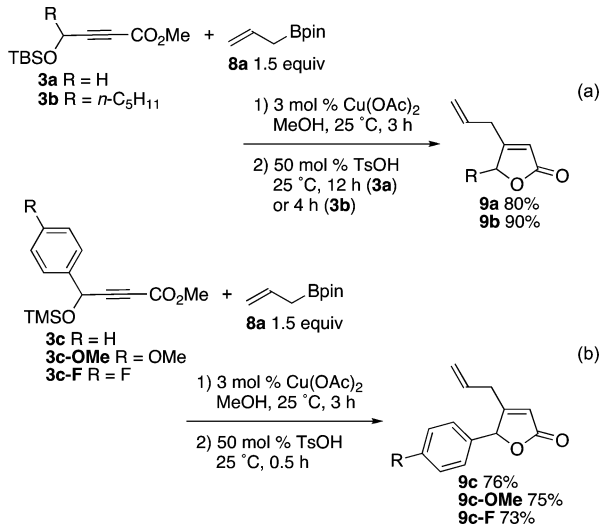
Scheme 2. One-Pot Hydroarylation/Cyclization of Alkynoates 5a and 3a with Phenylboronic Acid



consumed within 2 h. Next, we examined the effect of the protecting group of the γ-hydroxyl group (Scheme 2b). When *tert*-butyldimethylsilyl (TBS)-protected γ-hydroxybutynoate **3a** was subjected to the same reaction for 6 h followed by the acidic desilylation, the same butenolide **6** was obtained along with unexpected bisbutenolide **7**.[15] The isolated yields of **6** and **7** were 56% and 31%, respectively. This is in striking contrast to the reactions of a higher homologue, i.e., the TBS-ether of δ-hydroxypentynoate afforded the corresponding β-phenylpentenolide as the sole product in a high yield.[14] We also repeated the reaction of **3a** using 1 equiv of phenylboronic acid pinacol ester. In this case, a longer reaction time of 24 h was required for the hydroarylation, and bisbutenolide **7** was obtained as the major product along with **6** after the one-pot deprotection.

With these previous results in mind, we examined the selectivity of the one-pot hydroallylation/lactone cyclization of **3a** as the substrate (Scheme 3a). Under the previously

Scheme 3. One-Pot Hydroallylation/Cyclization of Alkynoates 3a–c with Allylboronate 8a



optimized reaction conditions for hydroallylation, **3a** and allylboronate **8a** (1.5 equiv) were treated with 3 mol % $Cu(OAc)_2$ for 3 h, and the resultant reaction mixture was then treated with 50 mol % TsOH at room temperature for 12 h in the same pot. The latter procedure effectively removed the silyl group under mild conditions to afford the desired β-allylbutenolide **9a** in 80% yield. To our delight, the anticipated bisbutenolide byproduct was not formed in this case. The formation of **9a** was confirmed as follows: In the ^{1}H NMR spectra of **9a**, the singlet peaks corresponding to the methoxy and TBS groups of **3a** were not observed. Instead, the signals of the newly introduced allyl group appeared at δ ppm 3.17 (d, J = 6.8 Hz, 2 H), 5.22 (dd, J = 16.8, 2.4, 1.2 Hz, 1 H), 5.24 (dd, J = 10.0, 1.2 Hz, 1 H), and 5.85 (ddt, J = 16.8, 10.0, 6.8 Hz, 1 H) along with the vinylic proton at the α position to the lactone carbonyl group at δ ppm 5.88 (t, J = 1.2 Hz, 1 H). The ^{13}C NMR spectra of **9a** also showed two peaks for the sp^3 carbons at δ ppm 32.5 and 72.6 and five peaks for the sp^2 carbons at δ ppm 115.6, 118.8, 131.4, 168.4, and 173.6. The high-resolution mass spectroscopy (HRMS) measurement also supported the formation of **9a**.

After achieving the selective one-pot hydroallylation/lactone cyclization for simple γ-silyloxybutynoate **3a**, the effect of the

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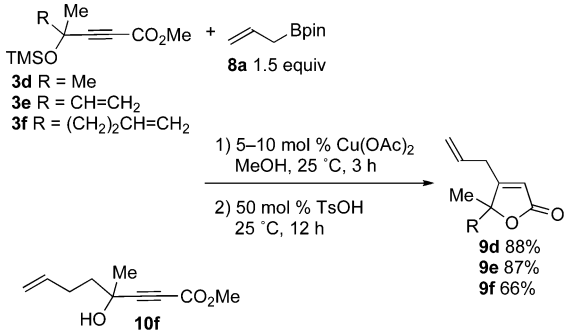
propargylic substituents of alkynoate substrates was examined. The use of alkynoate **3b** bearing *n*-pentyl and *tert*-butyldimethylsilyloxy substituents at the propargylic position was subjected to the same reaction conditions with **3a** to afford the corresponding *β*-allylbutenolide **9b** in 90% yield (Scheme 3a). Although a *γ*-hydroxybutynoate substrate having a phenyl group at the *γ* position (**10c**, Scheme 9) was directly obtained from the addition of a silver acetylide of methyl propiolate to benzaldehyde, the copper-catalyzed hydroallylation of this unprotected substrate resulted in a lower conversion. Moreover, an increased catalyst loading (10 mol %) afforded the desired butenolide **9c** in a moderate yield. Therefore, TMS-protected substrate **3c** was subjected to the hydroallylation to afford **9c** in 76% yield (Scheme 3b). The use of a TBS protecting group instead of the TMS group in this case resulted in a lower conversion. In addition, similar substrates **3c**-OMe and **3c**-F with an electron-donating methoxy group or an electron-withdrawing fluorine substituent at the *para* positions of the propargylic phenyl ring were subjected to the one-pot reaction, affording the corresponding butenolide products **9c**-OMe and **9c**-F in comparable yields. Therefore, these *para* substituents on the propargylic phenyl rings have virtually no effect on the efficiency of the present one-pot hydroallylation/lactone cyclization.

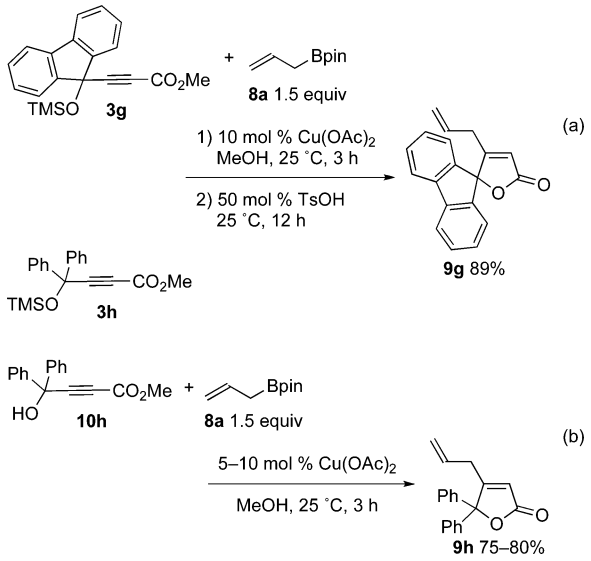
Next, alkynoate substrates bearing two propargylic substituents were investigated because the steric hindrance at the propargylic position would cause negative effects on both the hydroallylation and subsequent lactone cyclization. The reaction of dimethyl-substituted alkynoate **3d** with allylboronate **8a** in the presence of 5 mol % of $Cu(OAc)_2$ for 3 h, followed by the same deprotection procedure, afforded the desired *β*-allylbutenolide **9d** in 88% yield (Scheme 4). In the same manner, vinyl-substituted pentynoate **3e** was converted into the corresponding *β*-allylbutenolide **9e** in 87% yield. In contrast, the hydroallylation of pentynoate **3f** with a homoallyl substituent was sluggish under the similar reaction conditions using 10 mol % $Cu(OAc)_2$, resulting in an incomplete reaction. Consequently, **9f** was obtained in 66% yield along with the deprotected alkynoate (**10f**, 31%).

Scheme 4. One-Pot Hydroallylation/Cyclization of Alkynoayes 3d−f with Allylboronate 8a



Interesting spirocyclic *β*-allylbutenolide **9g** was also obtained without difficulty in 89% yield when this one-pot procedure was applied to fluorenone-derived alkynoate **3g** (Scheme 5a). However, the transformation of a similar alkynoate **3h** bearing two phenyl substituents in place of a fluorenyl group failed (Scheme 5b). This is probably because of the higher conformational flexibility of the two phenyl rings compared with that of the rigid fluorenyl moiety. Therefore, to reduce the steric crowding, the effect of the protecting group was examined. As expected, an alkynoate with a smaller protecting group, i.e., MOM group, showed an improved reactivity. Although the hydroallylation did not complete, the desired product was detected, albeit in a low yield after acidic deprotection. Thus, we attempted to use an unprotected substrate. The hydroallylation of *γ*-hydroxybutynoate **10h** with allylboronate **8a** was performed under the standard conditions. Consequently, *β*-allylbutenolide **9h** was obtained in 80% yield without the deprotection procedure. The decreased catalyst loading of 5 mol % afforded **9h** in a still good yield (75%).

Scheme 5. One-Pot Hydroallylation/Cyclization of Alkynoates 3g and 10h with Allylboronate 8a



The protection-free procedure was further applied to the synthesis of several spirocyclic *β*-allylbutenolides as shown in Figure 1. Spirocyclic butenolide **9i** containing a bulky dibenzocycloheptyl moiety was obtained in 76% yield from *γ*-hydroxybutynoate **10i**, which was derived from dibenzosuberone. Although the hydroallylation of less sterically demanding cyclohexanone-derived *γ*-siloxybutynoate **3j** failed, the corresponding unprotected butynoate **10j** successfully afforded spirocyclic butenolide **9j** in 79% yield. Similarly, tetrahydropyran derivative **9k** was obtained in a comparable yield when the hydroallylation/cyclization was performed for 1 h. In contrast,

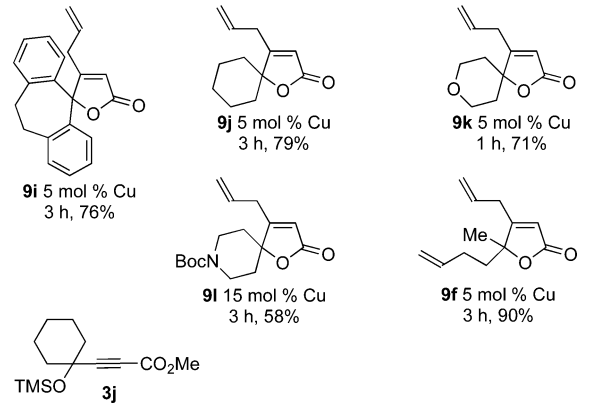


Figure 1. Results of one-pot hydroallylation/cyclization of alkynoates **10f** and **10i−k** with allylboronate **8a**.

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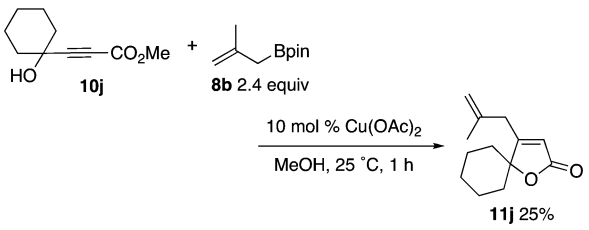
N-Boc piperidine analogue **9l** was obtained in 58%, albeit with increased loadings of the catalyst (15 mol %) and allylboronate **8a** (2.5 equiv). Moreover, butenolide **9f** bearing both allyl and homoallyl substituents was obtained in 90% yield (Figure 1) when the corresponding protection-free pentynoate **10f** was used in place of **3f** with the TMS protecting group (Scheme 4).

To examine the scope of the allylboronate, the reaction of **10j** with methallylboronate **8b** was performed as shown in Scheme 6. In our previous study on the copper-catalyzed

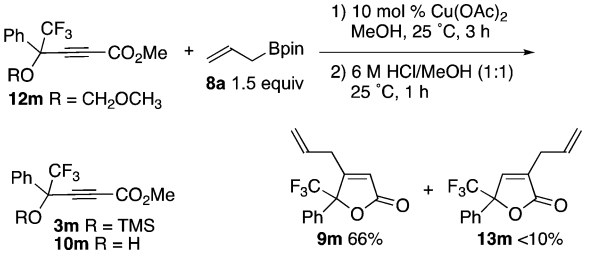
Scheme 6. One-Pot Hydroallylation/Cyclization of Alkynoates 10j with Methallylboronate 8b



hydroallylation of electron-deficient alkynes, methallylboronate **8b** was found to be less reactive than parent allylboronate **8a**.[8] Therefore, the reaction was conducted using an increased loading of $Cu(OAc)_2$ (10 mol %) and **8b** (2.4 equiv). However, the reaction was very sluggish, and ca. 30% conversion of **10j** was observed after 1 h, even though the ^1H NMR analysis of the crude reaction mixture showed that **8b** was completely consumed. The desired product, **11j**, was obtained in 25% yield, and **10j** was recovered (71%).

We then turned to the synthesis of a trifluoromethyl-substituted β-allylbutenolide because CF_3-substituted compounds have been extensively used as pharmaceuticals and agrochemicals.[16] To this aim, CF_3-substituted γ-silyloxyalkynoate **3m**, which was prepared from commercially available trifluoroacetophenone, was subjected to the one-pot hydroallylation/lactone cyclization (Scheme 7). However, a complex

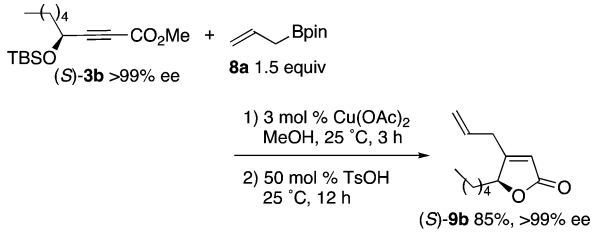
Scheme 7. One-Pot Hydroallylation/cyclization of Alkynoate 12m with Allylboronate 8a



mixture containing a small amount of desired **9m** was obtained along with deprotected substrate **10m**. We suspected that the bulkiness of the CF_3 group caused a detrimental effect on the allylation. Therefore, deprotected alkynoate **10m** was then subjected to the hydroallylation conditions; however, the yield of **9m** only moderately improved. Although the reason for the unsuccessful reaction of **10m** was not clear, probably the protonation of allylcopper species with the hydroxyl group was enhanced by the inductive effect of the CF_3 substituent. Finally, MOM-protected substrate **12m** was prepared, with the expectation that the small MOM group would make this substrate amenable to the copper-catalyzed hydroallylation. In fact, the reaction of **12m** with **8a** in the presence of 10 mol % $Cu(OAc)_2$ followed by the removal of the MOM group by treatment with 6 M HCl at 25 °C for 1 h successfully afforded the desired **9m** in 66% yield. In this case, a small amount of regioisomer **13m** was also isolated. The formation of **13m** can probably be attributed to the directing effect of the MOM group.

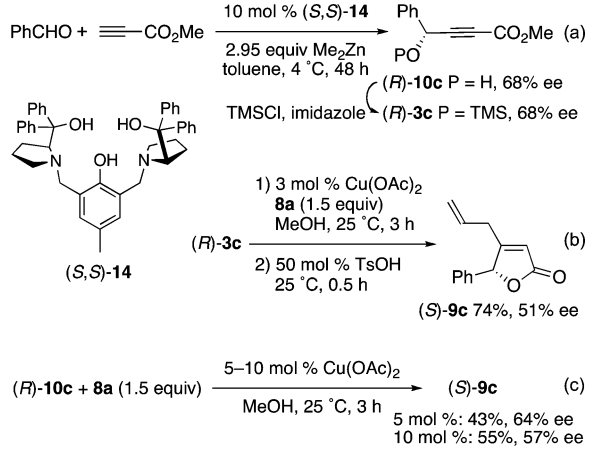
3. Synthesis of Nonracemic β-Allylbutenolides. As shown in Scheme 3, the racemic γ-monosubstituted 4-silyloxy-2-butynoate, **3b**, underwent smooth hydroallylation to afford the desired butenolide, **9b**, in a good yield after the acidic deprotection. We then revisited this reaction using optically pure substrate (*S*)-**3b**, which was prepared from commercially available (*S*)-oct-1-yn-3-ol. The γ chiral center of butenolides is prone to undergo epimerization under basic conditions.[17] In our hand, the desired **9b** was obtained in 85% yield with no significant decrease in the optical purity when the reaction was performed in the same manner as the racemic substrate (Scheme 8). Thus, the acidic deprotection procedure was compatible to the synthesis of nonracemic γ-alkyl-substituted butenolides.

Scheme 8. Synthesis of Nonracemic β-Allylbutenolide (*S*)-9b



Then, (*R*)-**10c** bearing a phenyl substituent at the propargylic position was prepared with 68% enantiomeric excess (ee) by the asymmetric addition of methyl propiolate to benzaldehyde using a chiral ligand, i.e., ProPhenol (*S,S*)-**14**, according to the procedure reported by Trost and co-workers (Scheme 9a).[18] After the silylation of the hydroxyl group, the obtained (*R*)-**3c** (68% ee) was subjected to one-pot hydroallylation/deprotection to afford (*S*)-**9c** in 74% yield (Scheme 9b). However, in contrast to the case of (*S*)-**9b**, the ee decreased to 51%. This is clearly attributed to the phenyl substituent that makes the γ proton more labile. Thus,

Scheme 9. Synthesis of Nonracemic β-Allylbutenolide (*S*)-9c



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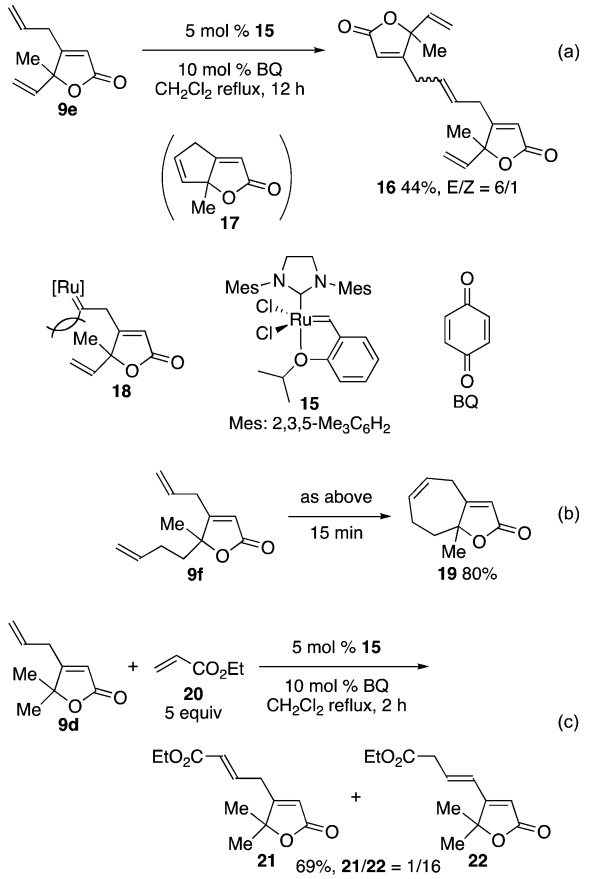
butenolide (*S*)-**9c** probably underwent epimerization under acidic deprotection conditions. In contrast, deprotection using 1.1 equiv of TBAF or CsF was sluggish, and the increased loading of CsF (3 equiv) resulted in the formation of complex mixture. Therefore, we attempted the hydroallylation of protection-free (*R*)-**10c**, which directly produces (*S*)-**9c** without the acidic deprotection (Scheme 9c). Consequently, the reaction of (*R*)-**10c** with allylboronate **8a** in the presence of 5 mol % $Cu(OAc)_2$ afforded (*S*)-**9c** in 43% yield with the improved ee of 64%, even though the reaction did not complete (76% conversion). Furthermore, the catalyst loading was increased to 10 mol % to reach complete conversion of (*R*)-**10c**. However, the ee of obtained (*S*)-**9c** was lowered to 57%. This is presumably attributed to copper salts acting as Lewis acids.

4. Derivatization of *β*-Allylbutenolides. As discussed above, we successfully developed a synthetic method for butenolides with a skipped diene moiety via the regio- and stereoselective hydroallylation and subsequent lactone cyclization. The introduced allyl group is very useful because it can be used as a synthetic handle for further derivatization of the products. In our previous study, similar skipped dienes, which were obtained by the hydroallylation of activated alkynes, were subjected to several functionalization reactions such as hydroboration/oxidation, hydroboration/Suzuki–Miyaura cross-coupling, and ring-closing diene metathesis.[8] Although these reactions were effective for the selective functionalization of the terminal alkene moiety of the introduced allyl group, the CM of the skipped diene product with methyl acrylate was problematic, resulting in the isomerizations of the skipped diene moiety. In the *β*-allylbutenolides prepared in this study, the skipped diene moiety was combined with the 2(5*H*)-furanone framework; thus, this situation demands further investigation of the selective functionalization of the *β*-allylbutenolide products.

With the above considerations in mind, we first investigated the RCM of butenolide **9e** as shown in Scheme 10a.[19] However, the treatment of **9e** with the Hoveyda–Grubbs catalyst, **15**,[20] in refluxing dichloromethane resulted in an undesirable isomerization of the allyl substituent to an internal alkene.[21] Therefore, we repeated the same reaction by adding 10 mol % 1,4-benzoquinone (BQ) to suppress the alkene isomerization according to the report by Grubbs and co-workers.[22] Consequently, the alkene isomerization was effectively suppressed, affording new product **16** along with intact **9e** (17%). The ^{1}H NMR analysis of **16** showed that the vinyl moiety, *α* to the lactone oxygen, is intact. A new peak for an internal alkene appeared at *δ* ppm 5.65 instead of the absorption of the terminal alkene moiety of the allyl substituent. The ^{13}C NMR spectrum of **16** showed nine peaks (one peak less than those presents in parent **9e**). These facts indicate that **16** is a homometathesis product rather than the expected RCM product **17**. This was also corroborated by the HRMS measurement.

The failure of the RCM of **9e** can be attributed to the inaccessibility of the ruthenium alkylidene moiety to the hindered alkene moiety adjacent to the fully substituted carbon, thus preventing the RCM of **18**. This was also confirmed by the fact that the RCM of butenolide **9f** with the homoallyl substituent was much more amenable (Scheme 10b). When **9f** was subjected to the same reaction conditions, the reaction completed within 15 min to afford the expected cycloheptene-fused product, **19**, in 80% yield.

Scheme 10. Derivatization of *β*-Allylbutenolides 9d–f Using Alkene Metathesis



We also attempted the CM of butenolide **9d** with ethyl acrylate **20** (Scheme 10c).[23] In our previous study, extensive isomerization of activated alkene moiety was observed in the CM of a skipped diene product bearing a sulfonyl group with methyl acrylate. Therefore, BQ was used in this study to suppress the alkene isomerization. In the presence of 5 mol % **15** and 10 mol % BQ, **9d** and 5 equiv of **20** were refluxed in dichloromethane for 2 h. The analysis of the crude material by ^{1}H NMR showed that the expected CM product **21** was obtained selectively. However, the purification by silica gel column chromatography afforded alkene isomerization product **22** along with a trace of **21** in 69% yield.

■ CONCLUSION

In conclusion, we developed the one-pot copper-catalyzed hydroallylation/lactone cyclization of *γ*-hydroxyalkynoate derivatives to afford *β*-allylbutenolides in good yields. The efficiency of the hydroallylation step was found to be dependent on the environment around the (protected) alcohol moiety at the *γ* position. For instance, sterically demanding tertiary alcohol substrates were used without protection, even though silyl protecting groups were effective for most substrates. As an exception, a trifluoromethyl-substituted derivative required a MOM protecting group to complete the reaction. As a synthetic application of the *β*-allylbutenolide products, we also demonstrated the feasibility of the RCM and CM reactions involving the introduced allyl moiety by using the Hoveyda–Grubbs catalyst. In these reactions, a BQ additive

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was necessary to inhibit the undesired isomerization of the allyl moiety.

EXPERIMENTAL SECTION

General Considerations. Column chromatography was performed on silica gel (Cica silica gel 60N) with solvents specified below. ^{1}H, ^{13}C, and ^{19}F NMR spectra were obtained for samples in $CDCl_3$ solutions at 25 °C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the singlet at 7.26 ppm for chloroform. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in hertz. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the singlet at −63.7 ppm for CF_3Ph as an external standard. High-resolution mass spectra were acquired on a TOF mass spectrometer using ESI or DART methods. $Cu(OAc)_2$, allylboronate **8a**, and dry solvents were purchased and used directly as received.

Synthesis of γ-Hydroxybutynoate Derivatives. General Procedure A. Synthesis of Methyl 4-(*tert*-Butyldimethylsilyloxy)non-2-ynoate (3b). To a solution of 3-(*tert*-butyldimethylsilyloxy)oct-1-yne (481 mg, 2.0 mmol) in dry THF (10 mL) was added dropwise *n*-BuLi (1.6 M hexane solution, 1.9 mL, 3.0 mmol) at −78 °C, and the solution was stirred at 0 °C for 30 min. To the resultant solution was then added methyl chloroformate (386 μL, 5.0 mmol) at −78 °C, and the solution was stirred at 0 °C for 1 h. The reaction was quenched with sat. NH_4Cl (10 mL). The aqueous layer was extracted with AcOEt (10 mL × 2). The combined organic layer was washed with brine (10 mL × 2) and dried over $MgSO_4$. The organic layer was concentrated in vacuo. The obtained crude product was purified with column chromatography on silica gel (elution with hexane/AcOEt = 300:1) to give **3b** (535 mg, 90% yield) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.11 (s, 3 H), 0.14 (s, 3 H), 0.89 (t, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 1.27−1.34 (m, 4 H), 1.35−1.46 (m, 2 H), 1.67−1.72 (m, 2 H), 3.00 (s, 3 H), 4.44 (t, J = 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ −5.2, −4.6, 13.9, 18.1, 22.5, 24.6, 25.7, 31.3, 37.7, 52.6, 62.6, 89.2, 154.0; IR (neat) 2236 (C≡C), 1721 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{30}O_3Si{\cdot}Na$ 321.1862, found 321.1876 $[M + Na]^+$.

Other alkynoates were also prepared in a similar manner, and desilylation was performed by the treatment with TBAF or CsF (1.1 equiv) in THF at 0 °C. Alkynoates **3a**,[24a] **10c**,[14] **10h**,[24b] and **10j**[5b] were known compounds.

Methyl 4-(*tert*-Butyldimethylsilyloxy)but-2-ynoate (3a). Colorless oil (388 mg, 57% yield); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.13 (s, 6 H), 0.91 (s, 9 H), 3.78 (s, 3 H), 4.43 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ −5.3, 18.2, 25.6, 51.3, 52.6, 76.3, 86.1, 153.7.

Methyl 4-Methyl-4-(trimethylsilyloxy)pent-2-ynoate (3d). Colorless oil (133 mg, 59%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.21 (s, 9 H), 1.53 (s, 6 H), 3.78 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 1.7, 32.1, 52.6, 66.2, 74.7, 92.0, 154.0; IR (neat) 2234 (C≡C), 1720 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{10}H_{18}O_3Si{\cdot}NH_4$ 232.1369, found 232.1386 $[M + NH_4]^+$.

Methyl 4-Methyl-4-(trimethylsilyloxy)hex-5-en-2-ynoate (3e). Colorless oil (591 mg, 85%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.20 (s, 9 H), 1.57 (s, 3 H), 3.79 (s, 3 H), 5.13 (d, J = 10.0 Hz, 1 H), 5.45 (d, J = 16.8 Hz, 1 H), 5.89 (dd, J = 16.8, 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 1.7, 31.5, 52.7, 69.4, 89.2, 113.9, 141.3, 153.8; IR (neat) 2237 (C≡C), 1722 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{11}H_{18}O_3Si{\cdot}NH_4$ 244.1369, found 244.1355 $[M + NH_4]^+$.

Methyl 4-Methyl-4-(trimethylsilyloxy)oct-7-en-2-ynoate (3f). Colorless oil (1.2 g, 74%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.21 (s, 9 H), 1.51 (s, 3 H), 1.69−1.83 (m, 2 H), 2.14−2.32 (m, 2 H), 3.78 (s, 3 H), 4.96 (ddd, J = 10.0, 2.8, 1.6 Hz, 1 H), 5.04 (ddd, J = 16.8, 3.2, 1.2 Hz, 1 H), 5.83 (ddt, J = 16.8, 10.0, 6.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 1.6, 28.7, 30.3, 43.5, 52.6, 68.9, 76.1, 91.0, 114.6, 137.9, 153.8; IR (neat) 2234 (C≡C), 1721 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{13}H_{22}O_3Si{\cdot}NH_4$ 272.1682, found 272.1668 $[M + NH_4]^+$.

Methyl 3-(9-(Trimethylsilyloxy)-9*H*-fluoren-9-yl)propiolate (3g). Colorless solids, mp 115.0−116.0 °C (685 mg, 47%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ −0.13 (s, 9 H), 3.72 (s, 3 H), 7.34 (t, J = 7.2 Hz, 2 H), 7.41 (t, J = 7.6 Hz, 2 H), 7.62 (d, J = 7.2 Hz, 2 H), 7.66 (d, J = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 1.5, 52.6, 73.1, 76.0, 88.8, 120.2, 125.2, 128.4, 129.9, 139.2, 145.9, 153.7; IR (neat) 2224 (C≡C), 1711 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{20}O_3Si{\cdot}Na$ 359.1079, found 359.1092 $[M + Na]^+$.

Methyl 4-Hydroxy-4-methyloct-7-en-2-ynoate (10f). Colorless oil (292 mg, 59%, 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.55 (s, 3 H), 1.79−1.85 (m, 2 H), 2.21−2.39 (m, 2 H), 3.79 (s, 3 H), 5.01 (ddd, J = 10.0, 2.8, 1.6 Hz, 1 H), 5.10 (ddd, J = 16.8, 3.2, 1.2 Hz, 1 H), 5.86 (ddt, J = 16.8, 10.0, 6.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 28.8, 29.0, 41.7, 52.7, 67.8, 75.0, 90.5, 115.2, 137.6, 153.9; IR (neat) 3415 (OH), 2235 (C≡C), 1719 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{10}H_{14}O_3{\cdot}NH_4$ 200.1287, found 200.1276 $[M + NH_4]^+$.

Methyl 4-Hydroxy-4,4-diphenylbut-2-ynoate (10h). Colorless solids, mp 103.2−105.0 °C, lit.[3] mp 90−92 °C (86 mg, 67%, 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.93 (s, 1 H), 3.81 (s, 3 H), 7.28−7.37 (m, 6 H), 7.55−7.58 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 52.9, 74.3, 78.2, 88.8, 126.0, 128.3, 128.5, 143.0, 153.8.

Methyl 10,11-Dihydro-5-hydroxy-5*H*-dibenzo[*a*,*d*]cycloheptene-5-propiolate (10i). Brown solids, mp 79.7−81.0 °C (31 mg, 59%, 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.13 (s, 1 H), 3.24−3.34 (m, 2 H), 3.52−3.62 (m, 2 H), 3.79 (s, 3 H), 7.14−7.24 (m, 6 H), 7.90−7.93 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.3, 52.9, 72.6, 78.5, 88.8, 124.9, 126.2, 128.7, 131.0, 138.3, 139.5, 153.8; IR (neat) 3463 (OH), 2231 (C≡C), 1714 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{16}O_3{\cdot}Na$ 315.0997, found 315.0991 $[M + Na]^+$.

Methyl 3-(1-Hydroxycyclohexyl)propiolate (10j). Colorless solids, mp 56.5−58.2 °C, lit.[3] mp 55−57 °C (254 mg, 56%, 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.25−1.34 (m, 1 H), 1.50−1.74 (m, 8 H), 1.94−2.00 (m, 2 H), 3.78 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 22.8, 24.8, 39.0, 52.8, 68.5, 75.7, 90.7, 154.0.

Methyl 3-(4-Hydroxytetrahydro-2*H*-pyran-4-yl)propiolate (10k). Colorless oil (515 mg, 75%, 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.85 (ddd, J = 12.0, 8.8, 3.6 Hz, 2 H), 1.97−2.05 (m, 2 H), 3.80 (s, 3 H), 3.66 (ddd, J = 12.8, 8.8, 3.6 Hz, 2 H), 3.90 (ddd, J = 11.6, 5.6, 4.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 38.7, 52.8, 64.0, 65.1, 75.8, 89.4, 153.7; IR (neat) 3368 (OH), 2233 (C≡C), 1716 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_9H_{12}O_4{\cdot}NH_4$ 202.1079, found 202.1076 $[M + NH_4]^+$.

***tert*-Butyl 4-Hydroxy-4-(3-methoxy-3-oxoprop-1-ynyl)-piperidine-1-carboxylate (10l).** Colorless oil (540 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.46 (s, 9 H), 1.76 (ddd, J = 12.8, 8.8, 4.0 Hz, 2 H), 1.91−1.99 (m, 2 H), 3.34 (ddd, J = 13.2, 8.8, 4.0 Hz, 2 H), 3.67−3.76 (m, 2 H), 3.79 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 28.3, 37.9, 40.0 (broad), 52.8, 66.2, 75.9, 80.0, 89.3, 153.7, 154.6; IR (neat) 3384 (OH), 2234 (C≡C), 1719 (C═O), 1697 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{21}NO_5{\cdot}Na$ 306.1317, found 306.1327 $[M + Na]^+$.

Methyl 5,5,5-Trifluoro-4-(methoxymethoxy)-4-phenylpent-2-ynoate (12m). Pale-yellow oil (195 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.45 (s, 3 H), 3.86 (s, 3 H), 4.92 (d, J = 6.4 Hz, 1 H), 4.98 (d, J = 6.4 Hz, 1 H), 7.43−7.45 (m, 3 H), 7.69−7.72 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 53.1, 56.7, 77.8 (q, J = 32.0 Hz), 78.7, 81.2, 94.2, 122.4 (q, J = 284.1 Hz), 127.8, 128.5, 130.1, 132.5, 152.6; ^{19}F NMR (370 MHz, $CDCl_3$, 25 °C) δ −72.9; IR (neat) 2248 (C≡C), 1724 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{14}H_{13}F_3O_4{\cdot}H$ 303.0844, found 303.0842 $[M + H]^+$.

Synthesis of Methyl 4-Phenyl-4-(trimethylsilyloxy)but-2-ynoate (3c). To a solution of methyl 4-hydroxy-4-phenylbut-2-ynoate (**10c**, 288 mg, 1.51 mmol) and imidazole (370 mg, 5.44 mmol) in dry

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THF (5 mL) was added Me_3SiCl (3.84 μL, 3.62 mmol) at room temperature, and the solution was stirred for 2 h. After filtration through a pad of Celite, the filtrate was concentrated in vacuo. The obtained crude product was purified with column chromatography on silica gel (elution with hexane/AcOEt = 100:1−50:1) to give **3c** (328 mg, 83% yield) as pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.20 (s, 9 H), 3.77 (s, 3 H), 5.56 (s, 1 H), 7.32−7.40 (m, 3 H), 7.45−7.48 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 0.05, 52.7, 64.3, 87.4, 126.4, 128.4, 128.6, 139.4, 153.7; IR (neat) 2237 (C≡C), 1719 (C═O) cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{18}O_3Si{\cdot}NH_4$ 280.1369, found 280.1384 $[M + NH_4]^+$.

Methyl 4-(4-Methoxyphenyl)-4-(trimethylsilyloxy)but-2-ynoate (3c-OMe). Pale-yellow oil (105.7 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.18 (s, 9 H), 3.77 (s, 3 H), 3.81 (s, 3 H), 5.50 (s, 1 H), 6.89 (d, *J* = 8.4 Hz, 2 H), 7.38 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 0.07, 52.7, 55.3, 64.0, 76.8, 87.6, 113.9, 127.8, 131.6, 153.8, 159.7; IR (neat) 2236 (C≡C), 1718 (C═O) cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{20}O_4Si{\cdot}Na$ 315.1029, found 315.1036 $[M + Na]^+$.

Methyl 4-(4-Fluorophenyl)-4-(trimethylsilyloxy)but-2-ynoate (3c-F). Pale-yellow oil (90.4 mg, 79%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.20 (s, 9 H), 3.78 (s, 3 H), 5.53 (s, 1 H), 7.05 (t, *J* = 8.4 Hz, 2 H), 7.43 (dd, *J* = 8.4, 5.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 0.00, 52.7, 63.7, 77.1, 87.0, 115.5 (d, *J* = 21.9 Hz), 128.1 (d, *J* = 8.6 Hz), 135.3 (d, *J* = 3.8 Hz), 153.6, 162.6 (d, *J* = 245.0 Hz); ^{19}F NMR (370 MHz, $CDCl_3$, 25 °C) δ −113.5; IR (neat) 2238 (C≡C), 1719 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{14}H_{17}FO_3Si{\cdot}NH_4$ 298.1275, found 298.1281 $[M + NH_4]^+$.

Synthesis of β-Allylbutenolides. General Procedure A. Cyclization of γ-Siloxybutynoate 3a. A solution of butynoate **3a** (114 mg, 0.50 mmol), allylboronate **8a** (141 μL, 0.75 mmol), and $Cu(OAc)_2$ (2.72 mg, 0.015 mmol) in dry degassed MeOH (1.0 mL) was stirred under an argon atmosphere at 25 °C for 3 h. The reaction progress was traced by TLC analysis. After addition of $TsOH{\cdot}H_2O$ (47.6 mg, 0.25 mmol), the reaction mixture was further stirred for 12 h at 25 °C. The resultant mixture was diluted with diethyl ether (10 mL) and filtered through a pad of neutral alumina. The filtrate was concentrated in vacuo, and the crude material was purified with silica gel column chromatography (hexane/toluene = 5:1) to give β-allylbutenolide **9a** (49.5 mg, 80% yield) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.17 (d, *J* = 6.8 Hz, 2 H), 4.75 (s, 2 H), 5.22 (ddd, *J* = 16.8, 2.4, 1.2 Hz, 1 H), 5.24 (dd, *J* = 10.0, 1.2 Hz, 1 H), 5.85 (ddt, *J* = 16.8, 10.0, 6.8 Hz, 1 H), 5.88 (t, *J* = 1.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.5, 72.6, 115.6, 118.8, 131.4, 168.4, 173.6; IR (neat) 1748 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_7H_8O_2{\cdot}NH_4$ 142.0868, found 142.0874 $[M + NH_4]^+$.

4-Allyl-5-pentylfuran-2(5*H*)-one (9b). Colorless oil (87 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 0.89 (t, *J* = 6.8 Hz, 3 H), 1.24−1.59 (m, 8 H), 1.85−1.94 (m, 1 H), 3.00 (dd, *J* = 17.2, 6.4 Hz, 1 H), 3.13 (ddd, *J* = 17.2, 6.4, 1.6 Hz, 1 H), 4.87−4.91 (m, 1 H), 5.18−5.25 (m, 2 H), 5.81 (d, *J* = 1.2 Hz, 1 H), 5.83 (ddt, *J* = 17.2, 10.4, 6.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 13.9, 22.4, 24.0, 31.4, 32.0, 32.5, 83.7, 116.5, 119.1, 131.6, 170.9, 173.0; IR (neat) 1756 (C═O) cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{12}H_{18}O_2{\cdot}NH_4$ 212.1651, found 212.1651 $[M + NH_4]^+$.

4-Allyl-5-phenylfuran-2(5*H*)-one (9c). Pale-yellow oil (26 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.86 (dd *J* = 17.6, 6.4 Hz, 1 H), 2.92 (ddd, *J* = 17.6, 6.4, 1.6 Hz, 1 H), 5.10 (dd, *J* = 17.2, 1.2 Hz, 1 H), 5.18 (dd, *J* = 10.0, 1.2 Hz, 1 H), 5.77 (ddt, *J* = 17.2, 10.0, 6.8 Hz, 1 H), 5.77 (s, 1 H), 5.95 (q, *J* = 1.6 Hz, 1 H), 7.21−7.24 (m, 2 H), 7.37−7.42 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.4, 85.5, 115.8, 119.1, 126.8, 129.0, 129.5, 131.5, 134.1, 170.8, 173.0; IR (neat) 1758 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{13}H_{12}O_2{\cdot}NH_4$ 218.1181, found 218.1197 $[M + NH_4]^+$.

4-Allyl-5-(4-methoxyphenyl)furan-2(5*H*)-one (9c-OMe). Colorless oil (62 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.85 (dd *J* = 17.2, 7.2 Hz, 1 H), 2.92 (dd, *J* = 17.2, 6.4 Hz, 1 H), 3.82 (s, 3 H), 5.10 (d, *J* = 16.4 Hz, 1 H), 5.18 (d, *J* = 10.0 Hz, 1 H), 5.73 (s, 1 H), 5.77 (ddt, *J* = 17.2, 10.0, 6.8 Hz, 1 H), 5.94 (d, *J* = 1.2 Hz, 1 H), 6.92 (d, *J* = 8.6 Hz, 2 H), 7.14 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.4, 55.2, 85.3, 114.3, 115.8, 119.0, 125.8, 128.3, 131.5, 160.4, 170.8, 173.0; IR (neat) 1757 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{14}H_{14}O_3{\cdot}NH_4$ 248.1287, found 248.1288 $[M + NH_4]^+$.

4-Allyl-5-(4-fluorophenyl)furan-2(5*H*)-one (9c-F). Pale-red oil (40 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.85 (dd *J* = 17.2, 7.2 Hz, 1 H), 2.91 (ddd, *J* = 17.2, 6.4, 1.2 Hz, 1 H), 5.10 (dd, *J* = 17.2, 1.2 Hz, 1 H), 5.19 (dd, *J* = 10.0, 1.2 Hz, 1 H), 5.76 (ddt, *J* = 17.2, 10.0, 7.0 Hz, 1 H), 5,76 (s, 1 H), 5.96 (q, *J* = 1.6 Hz, 1 H), 7.10 (t, *J* = 8.4 Hz, 2 H), 7.21 (dd, *J* = 8.4, 5.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.5, 84.7, 116.1, 116.2 (d, *J* = 21.9 Hz), 119.3, 128.8 (d, *J* = 8.6 Hz), 130.0 (d, *J* = 2.9 Hz), 131.3, 163.3 (d, *J* = 247.9 Hz), 170.5, 172.7; ^{19}F NMR (370 MHz, $CDCl_3$, 25 °C) δ −111.3; IR (neat) 1758 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{13}H_{11}FO_2{\cdot}NH_4$ 236.1087, found 236.1068 $[M + NH_4]^+$.

4-Allyl-5,5-dimethylfuran-2(5*H*)-one (9d). Colorless oil (67 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.46 (s, 6 H), 3.01 (ddd, *J* = 6.8, 2.6, 1.4 Hz, 2 H), 5.23 (ddd, *J* = 17.0, 2.6, 1.6 Hz, 1 H), 5.25 (ddd, *J* = 10.2, 2.6, 1.0 Hz, 1 H), 5.71 (t, *J* = 1.4 Hz, 1 H), 5.86 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 24.8, 31.4, 87.1, 115.0, 119.0, 131.7, 171.8, 175.4; IR (neat) 1751 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_9H_{12}O_2{\cdot}H$ 153.0916, found 153.0926 $[M + H]^+$.

4-Allyl-5-methyl-5-vinylfuran-2(5*H*)-one (9e). Colorless oil (72 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.56 (s, 3 H), 2.98 (d, *J* = 6.8 Hz, 2 H), 5.21 (ddd, *J* = 17.0, 3.0, 1.4 Hz, 1 H), 5.23 (ddd, *J* = 10.0, 2.4, 1.0 Hz, 1 H), 5.29 (d, *J* = 10.8 Hz, 1 H), 5.41 (d, *J* = 17.2 Hz, 1 H), 5.75 (t, *J* = 1.6 Hz, 1 H), 5.77 (dd, *J* = 17.2, 10.8 Hz, 1 H), 5.83 (ddt, *J* = 17.0, 10.0, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 22.0, 31.3, 88.5, 115.2, 117.1, 119.1, 131.6, 136.3, 171.9, 173.9; IR (neat) 1747 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{10}H_{12}O_2{\cdot}NH_4$ 182.1181, found 182.1197 $[M + NH_4]^+$.

3′-Allyl-5′*H*-spiro[fluorene-9,2′-furan]-5′-one (9g). Orange solids, mp 77.0−77.5 °C (122 mg, 89%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.46 (ddd, *J* = 6.8, 2.8, 1.6 Hz, 2 H), 4.91 (ddd, *J* = 17.0, 2.8, 1.2 Hz, 1 H), 5.03 (dq, *J* = 10.0, 1.2 Hz, 1 H), 5.60 (ddt, *J* = 17.0, 10.0, 6.8 Hz, 1 H), 6.14 (dd, *J* = 2.0, 1.2 Hz, 1 H), 7.22 (dd, *J* = 7.6, 1.2 Hz, 2 H), 7.31 (dt, *J* = 7.6, 1.2 Hz, 2 H), 7.45 (dt, *J* = 7.6, 1.2 Hz, 2 H), 7.69 (dd, *J* = 7.6, 1.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 30.9, 94.3, 116.3, 118.7, 120.6, 123.7, 128.4, 130.5, 131.3, 140.1, 141.0, 171.7, 172.9; IR (neat) 1765 (C═O) cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{14}O_2{\cdot}Na$ 297.0891, found 297.0905 $[M + Na]^+$.

General Procedure B. Cyclization of γ-Hydroxybutynoate 10h. A solution of butynoate **10h** (66.5 mg, 0.25 mmol), allylboronate **8a** (70 μL, 0.38 mmol), and $Cu(OAc)_2$ (2.28 mg, 0.0125 mmol) in dry degassed MeOH (0.5 mL) was stirred under an argon atmosphere at 25 °C for 3 h. The reaction progress was traced by TLC analysis. The resultant mixture was diluted with diethyl ether (10 mL) and filtered through a pad of neutral alumina. The filtrate was concentrated in vacuo, and the crude material was purified with silica gel column chromatography (hexane/toluene = 5:1) to give β-allylbutenolide **9h** (51.8 mg, 75% yield) as colorless solids (mp 65.0−66.7 °C): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.04 (ddd, *J* = 7.0, 2.8, 1.2 Hz, 2 H), 5.13 (ddd, *J* = 16.8, 2.8, 1.2 Hz, 1 H), 5.19 (dd, *J* = 10.4, 7.0 Hz, 1 H), 5.79 (ddt, *J* = 16.8, 10.4, 1.2 Hz, 1 H), 5.98 (t, *J* = 1.6 Hz, 1 H), 7.24−7.29 (m, 4 H), 7.35−7.40 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 33.0, 93.8, 116.7, 119.1, 127.5, 128.5, 128.8, 131.5, 138.3, 171.8, 173.6; IR (neat) 1763 (C═O) cm^{-1}; HRMS (DART) *m*/*z* calcd for $C_{19}H_{16}O_2{\cdot}H$ 277.1229, found 277.1225 $[M + H]^+$.

4-Allyl-5-(but-3-enyl)-5-methylfuran-2(5*H*)-one (9f). Colorless oil (257 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.46 (s, 3 H), 1.71 (ddd, *J* = 13.2, 11.2, 4.4 Hz, 1 H), 1.80−1.91 (m, 1 H), 1.97 (ddd, *J* = 13.2, 11.2, 4.4 Hz, 1 H), 2.00−2.11 (m, 1 H), 2.94 (ddq, *J* = 18.0, 6.8, 1.2 Hz, 1 H), 3.00 (ddq, *J* = 18.0, 6.8, 1.2 Hz, 1 H), 4.97 (dq, *J* = 10.0, 1.6 Hz, 1 H), 5.01 (dq, *J* = 17.2, 1.6 Hz, 1 H), 5.23 (dq, *J* = 17.2, 1.6 Hz, 1 H), 5.25 (dq, *J* = 10.0, 1.6 Hz, 1 H), 5.75 (ddt, *J* = 17.2, 10.0, 6.8 Hz, 1 H), 5.76 (t, *J* = 2.0 Hz, 1 H), 5.86 (ddt, *J* = 17.2, 10.0, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 23.7, 27.0, 31.3, 35.8, 88.6, 115.0, 115.8, 118.9, 131.3, 136.7, 171.5, 174.0; IR (neat)

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1756 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{12}H_{16}O_2{\cdot}NH_4$ 210.1494, found 210.1504 $[M + NH_4]^+$.

3′-Allyl-5′*H*-spiro[10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5,2′-furan]-5′-one (9i). Colorless solids, mp 93.2−93.5 °C (53 mg, 76%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 2.87 (dd, J = 6.8, 1.6 Hz, 2 H), 3.08−3.24 (m, 4 H), 5.05 (dd, J = 16.8, 1.2 Hz, 1 H), 5.15 (d, J = 10.0 Hz, 1 H), 5.73 (ddt, J = 16.8, 10.0, 6.8 Hz, 1 H), 5.95 (t, J = 1.6 Hz, 1 H), 7.17−7.32 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 33.1, 36.2, 94.6, 114.6, 119.3, 126.8, 128.6, 128.8, 130.5, 131.4, 134.1, 142.8, 173.2, 178.3; IR (neat) 1759 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{18}O_2{\cdot}Na$ 325.1204, found 325.1194 $[M + Na]^+$.

4-Allyl-1-oxaspiro[4.5]dec-3-en-2-one (9j). Colorless solids, mp 54.8−56.5 °C (76 mg, 79%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.15−1.30 (m, 1 H), 1.55−1.80 (m, 9 H), 3.00 (ddd, J = 7.0, 2.8, 1.6 Hz, 2 H), 5.21 (ddd, J = 17.0, 2.8, 1.6 Hz, 1 H), 5.23 (ddd, J = 10.0, 2.4, 1.6 Hz, 1 H), 5.70 (t, J = 1.6 Hz, 1 H), 5.84 (ddt, J = 17.0, 10.0, 7.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 21.8, 24.5, 31.5, 33.6, 88.8, 115.1, 118.9, 131.8, 172.1, 175.6; IR (neat) 1750 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{12}H_{16}O_2{\cdot}H$ 193.1229, found 193.1221 $[M + H]^+$.

4-Allyl-1,8-dioxaspiro[4.5]dec-3-en-2-one (9k). Pale-yellow oil (69 mg, 71%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.42 (d, J = 13.0 Hz, 2 H), 2.08 (dt, J = 13.0, 5.6 Hz, 2 H), 3.03 (dq, J = 6.8, 1.4 Hz, 2 H), 3.86 (dt, J = 12.0, 2.0 Hz, 2 H), 3.97 (dd, J = 12.0, 5.6 Hz, 2 H), 5.23 (ddd, J = 17.0, 2.8, 1.6 Hz, 1 H), 5.26 (ddd, J = 10.0, 2.4, 0.8 Hz, 1 H), 5.79 (t, J = 1.6 Hz, 1 H), 5.84 (ddt, J = 17.0, 10.0, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 31.4, 33.4, 63.7, 85.8, 116.1, 119.2, 131.4, 171.3, 173.8; IR (neat) 1751 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{11}H_{14}O_3{\cdot}NH_4$ 212.1287, found 212.1295 $[M + NH_4]^+$.

***tert*-Butyl 4-Allyl-2-oxo-1-oxa-8-azaspiro[4.5]dec-3-ene-8-carboxylate (9l).** Colorless solids, mp 134.5−135.8 °C (96 mg, 58%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.48 (s, 9 H), 1.45−1.49 (m, 2 H), 1.85−1.93 (m, 2 H), 2.99 (ddd, J = 6.8, 2.8, 1.2 Hz, 2 H), 3.16 (br s, 2 H), 4.16 (br s, 2 H), 5.22 (ddd, J = 17.0, 2.8, 1.6 Hz, 1 H), 5.25 (ddd, J = 10.0, 2.0, 1.2 Hz, 1 H), 5.79 (t, J = 1.2 Hz, 1 H), 5.83 (ddt, J = 17.0, 10.0, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 28.3, 31.4, 33.1, 39.6 (broad), 79.9, 86.5, 116.1, 119.3, 131.3, 154.4, 171.3, 174.0; IR (neat) 1755 (C═O), 1692 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{23}NO_4{\cdot}Na$ 316.1525, found 316.1544 $[M + Na]^+$.

4-(2-Methylallyl)-1-oxaspiro[4.5]dec-3-en-2-one (11j). Colorless solids, mp 69.2−71.5 °C (25 mg, 25%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.15−1.29 (m, 1 H), 1.55 (br t, J = 14.0 Hz, 2 H), 1.64−1.80 (m, 7 H), 1.73 (s, 3 H), 2.96 (s, 2 H), 4.86 (s, 1 H), 4.97 (t, J = 2.0 Hz, 1 H), 5.70 (t, J = 1.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 21.9, 22.0, 24.5, 33.5, 36.0, 89.0, 114.9, 115.8, 139.8, 172.2, 175.0; IR (neat) 1736 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{13}H_{18}O_2{\cdot}H$ 207.1385, found 207.1390 $[M + H]^+$.

Cyclization of MOM-Protected γ-Hydroxybutynoate 12m. The deprotection step was carried out using 6 M HCl/MeOH (1:1) instead of $TsOH{\cdot}H_2O$ in the general procedure B.

4-Allyl-5-phenyl-5-(trifluoromethyl)furan-2(5*H*)-one (9m). Colorless oil (88 mg, 66%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.00 (dd, J = 18.8, 6.8 Hz, 1 H), 3.23 (dd, J = 18.8, 6.8 Hz, 1 H), 5.16 (dd, J = 17.0, 1.2 Hz, 1 H), 5.23 (dd, J = 10.0, 1.2 Hz, 1 H), 5.74 (ddt, J = 17.0, 10.0, 6.8 Hz, 1 H), 6.06 (s, 1 H), 7.43−7.48 (m, 3 H), 7.49−7.55 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 32.1, 88.4 (q, J = 30.5 Hz), 119.1, 120.0, 122.9 (q, J = 284.1 Hz), 125.8, 126.2, 130.0, 130.6, 130.8, 168.1, 169.9; ^{19}F NMR (370 MHz, $CDCl_3$, 25 °C) δ −78.0; IR (neat) 1785 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{14}H_{11}F_3O_2{\cdot}NH_4$ 286.1055, found 286.1057 $[M + NH_4]^+$.

3-Allyl-5-phenyl-5-(trifluoromethyl)furan-2(5*H*)-one (13m). Colorless oil (14 mg, 10%); ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 3.07 (dd, J = 17.6, 6.8 Hz, 1 H), 3.14 (dd, J = 17.6, 6.8 Hz, 1 H), 5.20 (dd, J = 16.8, 1.2 Hz, 1 H), 5.21 (dd, J = 10.0, 1.2 Hz, 1 H), 5.88 (ddt, J = 16.8, 10.0, 6.8 Hz, 1 H), 7.38 (t, J = 1.6 Hz, 1 H), 7.43−7.48 (m, 3 H), 7.53−7.58 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 29.6, 85.6 (q, J = 32.4 Hz), 118.9, 122.6 (q, J = 282.2 Hz), 126.6, 128.9, 130.0, 131.5, 131.7, 136.3, 143.3, 170.3; ^{19}F NMR (370 MHz, $CDCl_3$, 25 °C) δ −77.0; IR (neat) 1789 (C═O) cm^{-1}; HRMS (DART) m/z calcd for $C_{14}H_{11}F_3O_2{\cdot}NH_4$ 286.1055, found 286.1064 $[M + NH_4]^+$.

Derivatization of β-Allylbutenolides Using Alkene Metathesis. Ring-Closing Metathesis of Butenolide 9f. A degassed solution of butenolide **9g** (96.1 mg, 0.50 mmol), Hoveyda−Grubbs catalyst **15** (15.7 mg, 0.025 mmol), and 1,4-benzoquinone (5.4 mg, 0.050 mmol) in dry CH_2Cl_2 (25 mL) was stirred at 40 °C under an argon atmosphere for 15 min. The reaction mixture was concentrated in vacuo, and the residue was purified with chromatography on silica gel (hexane/AcOEt = 10:1−5:1) to afford RCM product **19** (65.7 mg, 80% yield) as colorless oil: ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.54 (s, 3 H), 1.74−1.81 (m, 1 H), 2.00−2.25 (m, 3 H), 3.03 (dsext, J = 16.4, 2.0 Hz, 1 H), 3.29 (dd, J = 16.4, 7.2 Hz, 1 H), 5.62−5.68 (m, 1 H), 5.68 (d, J = 1.6 Hz, 1 H), 5.82 (ddt, J = 11.4, 6.0, 2.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 22.4, 22.9, 28.0, 36.6, 89.9, 114.9, 124.4, 131.7, 172.3, 172.7; IR (neat) 1755 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{10}H_{12}O_2{\cdot}NH_4$ 182.1181, found 182.1167 $[M + NH_4]^+$.

The reaction of butenolide **9e** (49.3 mg, 0.30 mmol) was also carried out using **15** (9.4 mg, 0.015 mmol) and 1,4-benzoquinone (3.2 mg, 0.030 mmol) in dry CH_2Cl_2 (15 mL) at 40 °C for 12 h. Purification with chromatography on silica gel (hexane/AcOEt = 5:1−3:1) afforded homo metathesis product **16** (19.6 mg, 44% yield) as brown solids (mp 63.5 °C decomp) along with unreacted **9e** (8.4 mg, 17%).

4,4′-(But-2-ene-1,4-diyl)bis(5-methyl-5-vinylfuran-2(5*H*)-one) (16). ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.55 (s, 6 H), 2.98−3.01 (m, 24/7 H) [2.91−2.94 (m, 4/7 H) for the minor isomer], 5.29 (d, J = 10.0 Hz, 12/7 H) [5.30 (d, J = 10.0 Hz, 2/7 H) for the minor isomer], 5.40 (d, J = 17.2 Hz, 2 H), 5.65 (ddd, J = 5.4, 3.6, 1.8 Hz, 12/7 H) [the corresponding peak for the minor isomer obscurely appeared at δ 5.77], 5.69 (t, J = 1.2 Hz, 1 H), 5.75 (dd, J = 17.2, 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): For major isomer: δ 21.9, 30.0, 88.3, 115.2, 117.2, 128.0, 136.1, 171.6, 173.6; IR (neat) 1749 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{20}O_4{\cdot}Na$ 323.1259, found 323.1274 $[M + Na]^+$.

Cross Metathesis of Butenolide 9d with Ethyl Acrylate (20). A degassed solution of butenolide **9d** (45.7 mg, 0.30 mmol), acrylate **20** (163 μL, 1.5 mmol), Hoveyda−Grubbs catalyst **15** (9.4 mg, 0.015 mmol), and 1,4-benzoquinone (3.2 mg, 0.030 mmol) in dry CH_2Cl_2 (1.2 mL) was stirred at 40 °C under an argon atmosphere for 2 h. The reaction mixture was concentrated in vacuo. The ^1H NMR analysis of the crude product showed that CM product **21** is the major product: ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.31 (t, J = 7.2 Hz, 3 H), 1.48 (s, 6 H), 3.16 (dt, J = 7.6, 1.6 Hz, 2 H), 4.23 (q, J = 7.2 Hz, 2 H), 5.16 (s, 1 H), 5.99 (dt, J = 15.4, 1.6 Hz, 1 H), 6.95 (dt, J = 15.4, 7.6 Hz, 1 H).

Purification with chromatography on silica gel (hexane/AcOEt = 10:1−5:1) ultimately afforded a mixture of **21** and **22** (1/16, 46.8 mg, 69% yield) as a yellow oil.

(*E*)-Ethyl 4-(2,2-dimethyl-5-oxo-2,5-dihydrofuran-3-yl)but-3-enoate (22). ^1H NMR (400 MHz, $CDCl_3$, 25 °C) δ 1.29 (t, J = 7.2 Hz, 3 H), 1.54 (s, 6 H), 3.28 (dd, J = 7.0, 1.2 Hz, 2 H), 4.19 (q, J = 7.2 Hz, 2 H), 5.90 (s, 1 H), 6.20 (d, J = 16.0 Hz, 1 H), 6.42 (dt, J = 16.0, 7.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 14.1, 25.6, 38.5, 61.2, 86.2, 114.1, 122.8, 133.5, 168.9, 170.0, 171.7; IR (neat) 1745 (C═O) cm^{-1}; HRMS (ESI) m/z calcd for $C_{12}H_{16}O_4{\cdot}NH_4$ 242.1392, found 242.1401 $[M + NH_4]^+$.

Analysis of Nonracemic γ-Allylbutenolides. (*S*)-**9b** ($[\alpha]^{25}_D$ = −35.4° (*c* 1.02, $CHCl_3$)) was obtained in 85% yield from (*S*)-**3b** ($[\alpha]^{25}_D$ = +16.4° (*c* 0.99, $CHCl_3$)) according to the general procedure A. The optical purities of (*S*)-**3b** and (*S*)-**9b** were determined as >99% ee by HPLC analysis with DAICEL CHIRALCEL OD-H (hexane, 1.0 mL/min, λ = 215 nm, t_R = 5.7/6.1 min) or CHIRALPAC AD-H (hexane/^{i}PrOH = 100:1−95:5 per 30 min, 1.0 mL/min, λ = 215 nm, t_R = 22.4/23.4 min), respectively (Supplemental Figures S1 and S2).

(*S*)-**9c** ($[\alpha]^{25}_D$ = −140.4° (*c* 0.80, $CHCl_3$)) was obtained in 43% yield with 64% ee from (*R*)-**10c** ($[\alpha]^{25}_D$ = +2.7° (*c* 0.97, $CHCl_3$)) according to the general procedure A. The optical purities of (*R*)-**3c**,

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(*S*)-**9c**, and (*R*)-**10c** were determined as 68% ee by HPLC analysis with DAICEL CHIRALCEL OD-H (hexane, 1.0 mL/min, λ = 220 nm, t_R = 22.6/32.0 min), as 51% ee by CHIRALPAC AD-H (hexane/*i*PrOH = 90:1, 1.0 mL/min, λ = 220 nm, t_R = 11.0/12.0 min), and 68% ee by HPLC analysis with CHIRALCEL OD-H (hexane/*i*PrOH = 90:10, 1.0 mL/min, λ = 220 nm, t_R = 13.2/16.7 min), respectively (Supplementary Figures S3−S5).

■ ASSOCIATED CONTENT

Supporting Information

HPLC and NMR charts. 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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