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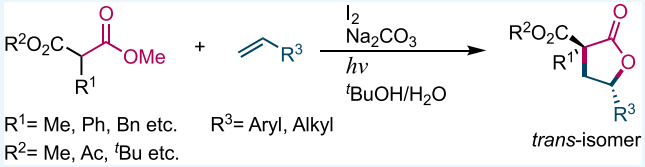
# *trans*-Diastereoselective Syntheses of γ-Lactones by Visible Light-Iodine-Mediated Carboesterification of Alkenes

Saki Maejima, Eiji Yamaguchi,* and Akichika Itoh*

Gifu Pharmaceutical University, 1-25-4, Daigaku-nishi, Gifu 501-1196, Japan

Supporting Information

**ABSTRACT:** This study aims to develop an intermolecular lactonization reaction of alkenes with carbonyls mediated by visible light and molecular iodine. The one-step reaction involved the carboesterification of alkenes to produce the corresponding lactones in moderate to good yield. It was also revealed that it is possible to control the diastereoselectivity of the reaction by altering the base used and the reaction conditions. When water was added as a solvent, the reaction resulted in the formation of lactones with trans-selectivity. A mechanistic investigation was undertaken and it was found that the reaction requires the generation of an iodine radical from molecular iodine, driven by visible light irradiation, and proceeds via the formation of an iodine radical alkene adduct. The proposed reaction is an example of a rare-metal free intermolecular addition cyclization reaction, which is an environment-friendly chemical process that only uses molecular iodine. In addition, since diastereoselectivity was observed without the use of any specific reagents, the developed methodology is an example of a novel stereoselective transformation using only cost-effective reagents.




## INTRODUCTION

Oxygen-containing 5-membered ring systems such as γ-lactones are found in naturally occurring products and pharmaceuticals and are commonly used as building blocks in various fields of chemistry.[1,2] Traditionally, the lactone skeleton is constructed through the intramolecular condensation reaction of a hydroxycarboxylic acid under Brønsted/Lewis acidic and thermal conditions (Scheme 1, top).[3−6] However, this methodology is not suitable for the synthesis of some derivatives. Toward this aim, the intermolecular diversity-oriented synthesis of lactones has been developed.[7] For example, a [3 + 1] type intermolecular cycloaddition reaction based on the generation of carbon radicals using a strong single-electron reductant such as $SmI_2$ was reported by Fukuzawa and Procter (Scheme 1, middle).[8] Furthermore, various intermolecular [2 + 2] type reactions such as the C−C/C−O bond formation of an alkene with an acetyl unit have also been investigated. Among them is a common and powerful method based on the generation of carbon radicals in a one-electron oxidation process using heavy metals (Scheme 1, bottom).[9,10] Recently, a methodology using photo-redox catalysts has also been developed.[11] However, in intermolecular reactions, it is difficult to control the diastereoselectivity by changing only the reaction conditions, and only a few examples of this have been reported in the literature.[12]

Previously, we developed the iodine/visible light-mediated carboesterification of styrene using carbonyls that led to the formation of *cis*-lactones through the photoinduced generation of an iodine radical as the key active species (Scheme 2; previous work).[13,14] Over the course of this study, it was found that the opposite diastereomer could be formed without the use of any specific reagent by simply controlling the reaction conditions. In particular, it was effective for priory to trans-selectivity when water was added as a solvent. Herein, the trans-selective synthesis of γ-lactones is described via visible light/iodine-mediated intermolecular carboesterification of styrenes with carbonyls (Scheme 2; this work). A mechanistic investigation using stereochemical models is also described.

## RESULTS AND DISCUSSION

Previous studies have shown that using $Ca(OH)_2$ as a base in combination with molecular iodine in the presence of alkenes and malonates always affords products with *cis*-diastereoselectivity as a result of an addition/cyclization process (Table 1, entry 1).[15] Therefore, to develop a stereoselective iodine/visible light-mediated alkene carboesterification reaction that can be applied to carbonyls, various inorganic bases were explored. Upon screening of alkaline earth metal-based inorganic bases in the reaction of styrene **1a** with malonate **2a** in the presence of molecular iodine, the formation of *cis*-diastereomer **3aa**-*cis* preferentially occurred when $Ba(OH)_2$ was used (entry 3). Unfortunately, the reaction significantly decreased the yield of the product when the reaction employed other alkaline earth metal bases (entries 2, 4−6). On the other hand, upon the evaluation of alkaline metal-based inorganic bases, such as $NaHCO_3$, $Na_2CO_3$, $K_2CO_3$, $Cs_2CO_3$, and $K_3PO_4$, a slight preference for the formation of *trans*-

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**Scheme 1. Reported Methodology for Lactone Synthesis**

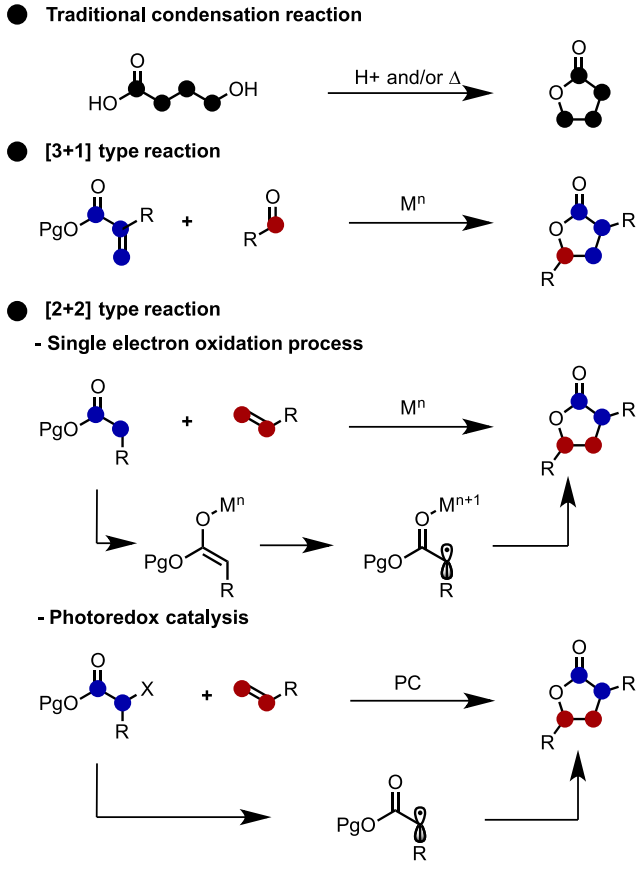
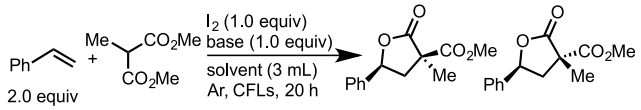



**Table 1. Optimization of the Intermolecular Lactonization of Styrene 1a with Malonate (2a)**[a]




| entry | base | solvent | 3 (%) | dr (cis:trans)[b] |
|---|---|---|---|---|
| 1 | $Ca(OH)_2$ | $^t$BuOH | 83 | 79:21 |
| 2 | $Mg(OH)_2$ | $^t$BuOH | trace | |
| 3 | $Ba(OH)_2$ | $^t$BuOH | 74 | 67:33 |
| 4 | $Sr(OH)_2$ | $^t$BuOH | 33 | 50:50 |
| 5 | $BaCO_3$ | $^t$BuOH | trace | |
| 6 | $SrCO_3$ | $^t$BuOH | trace | |
| 7 | $NaHCO_3$ | $^t$BuOH | 32 | 50:50 |
| 8 | $Na_2CO_3$ | $^t$BuOH | 77 | 45:55 |
| 9 | $K_2CO_3$ | $^t$BuOH | 53 | 40:60 |
| 10 | $Cs_2CO_3$ | $^t$BuOH | 49 | 37:63 |
| 11 | KOH | $^t$BuOH | 36 | 33:67 |
| 12 | $K_3PO_4$ | $^t$BuOH | 26 | 30:70 |
| 13 | $Na_2CO_3$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 69 | 25:75 |
| 14 | $Ca(OH)_2$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 61 | 40:60 |
| 15 | $Ba(OH)_2$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 7 | 29:71 |
| 16 | $Sr(OH)_2$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 29 | 42:58 |
| 17 | $K_2CO_3$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 60 | 26:74 |
| 18 | $Cs_2CO_3$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 56 | 28:72 |
| 19 | KOH | $^t$BuOH/$H_2O$ (2 mL/1 mL) | trace | |
| 20 | $K_3PO_4$ | $^t$BuOH/$H_2O$ (2 mL/1 mL) | 41 | 27:73 |

[a]Reaction conditions: **1a** (2 equiv), **2a** (0.3 mmol), $I_2$ (0.3 mmol), and base (0.3 mmol) in solvent (3 mL) were stirred at ambient temperature irradiated with four of compact fluorescent lamps (CFLs) for 20 h. [b]Diasteromeric ratios (dr) were determined by $^1$H NMR analysis of the crude reaction mixture.

diastereomer **3aa**-*trans* was observed (entries 7−12). The basicity of the base used was found to have a strong effect on the yield of product **3aa**. For instance, the intermolecular addition reaction of styrene with malonate resulted in a significant decrease in the yield of the product in the presence of a weak base, such as $NaHCO_3$ (entry 7). In contrast, the desired lactonization and hydrolysis of the ester proceeded competitively in the presence of strong bases, such as KOH and $K_3PO_4$ (entries 11 and 12). Gratifyingly, when using $Na_2CO_3$, a further variation in the reaction conditions resulted in **3aa**-*trans* being generated in 69% yield with 25:75 diastereoselectivity (entry 13). Under the optimal conditions, further base screening was performed. Interestingly, the reaction in $^t$BuOH with water resulted in an increase in *trans*-diastereoselectivity (entries 13−17), and even more interestingly, inverse diastereoselectivity was observed using

**Scheme 2. Schematic Overview of the *trans*-Diastereoselective Synthesis of Lactones in This Work**

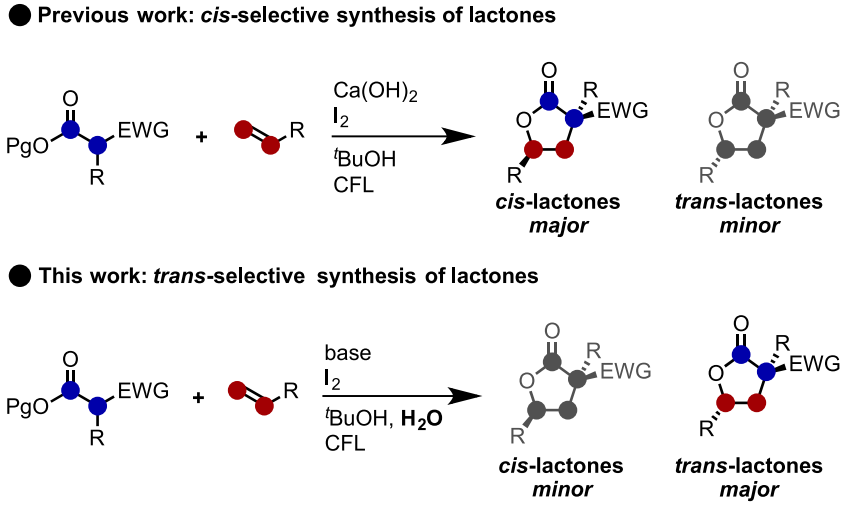





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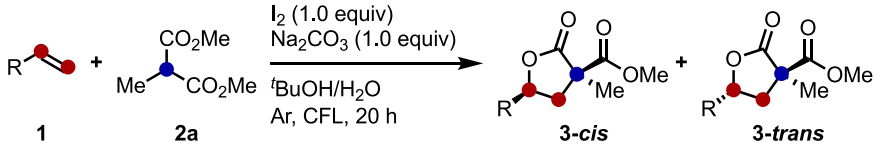
**Table 2. *trans*-Diastereoselective Synthesis of Lactones, 3, from Various Alkenes Using Malonate 2a**




| entry | R | 3 | yield (%) | dr[a] (cis:trans) |
|---|---|---|---|---|
| 1 | Ph (**1a**) | **3aa** | 69 | 25:75 |
| 2 | 4-$^t$Bu-$C_6H_4$ (**1b**) | **3ba** | 65 | 33:67 |
| 3 | 4-Me-$C_6H_4$ (**1c**) | **3ca** | 61 | 33:67 |
| 4 | 3-Me-$C_6H_4$ (**1d**) | **3da** | 72 | 33:67 |
| 5 | 2-Me-$C_6H_4$ (**1e**) | **3ea** | 66 | 26:74 |
| 6 | 4-F-$C_6H_4$ (**1f**) | **3fa** | 28 | 20:80 |
| 7 | 4-Cl-$C_6H_4$ (**1g**) | **3ga** | 60 | 29:71 |
| 8 | 4-Br-$C_6H_4$ (**1h**) | **3ha** | 75 | 26:74 |
| 9 | 4-$MeO_2C$-$C_6H_4$ (**1i**) | **3ia** | nd | |
| 10 | 4-MeO-$C_6H_4$ (**1j**) | **3ja** | trace | |
| 11 | 4-Ph-$C_6H_4$ (**1k**) | **3ka** | 38 | 33:67 |
| 12 | 2-naph (**1l**) | **3la** | 75 | 28:72 |
| 13 | 2-pyridyl (**1m**) | **3ma** | 50 | 37:63 |
| 14 | $C_{10}H_{21}$ (**1n**) | **3na** | 50 | 33:67 |

[a]Diasteromeric ratios (dr) were determined by $^1$H NMR analysis of the crude reaction mixture.

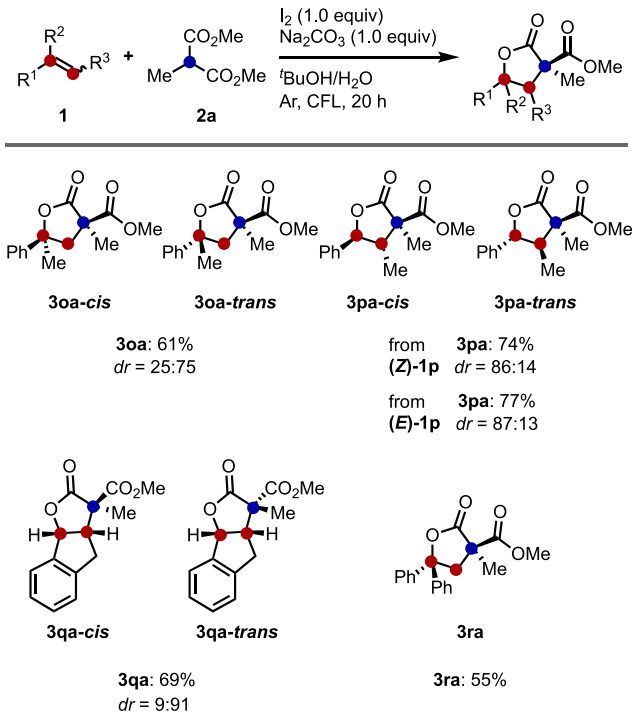
bases such as $Ca(OH)_2$, $Ba(OH)_2$, and $Sr(OH)_2$ under the same conditions (entry 1,3,4 vs 14−16).

After the optimization study, the scope of the *trans*-diastereoselective synthesis of lactones was investigated by making 2-methyl dimethyl malonate **2a** to react with a series of alkenes, **1** (Table 2). Generally, the controllable carboesterification reactions furnished *trans*-butyrolactones with good diastereoselectivities in the presence of water as a co-solvent. At first, trans-selective lactonization was investigated using $Na_2CO_3$ as a base under the optimized reaction conditions (Table 1, entry 13). Most of the reactions proceeded smoothly using the developed system to afford the corresponding butyrolactones **3** in good yield and *trans*-diastereoselectivity. As shown in Table 2, styrenes with various substituents, such as *tert*-butyl, 4-methyl, 3-methyl, and 2-methylstyrene (**1b**−**1e**), gave products in 61−72% isolated yield with moderate to good *trans*-diastereoselectivity. In addition, styrenes bearing halogen substituents (**1f**−**1h**) also furnished the desired products. The stereochemical assignments were corroborated using single-crystal X-ray diffraction analysis of the obtained *trans*-**3ha** adduct.[16] Unfortunately, methyl-4-vinylbenzoate, **1i**, did not work under the present conditions, even though good conversion could be achieved using a set of previous cis-selective conditions.[13] This is probably due to the instability of the ester under these conditions. Electron-rich substrates such as **1j** also did not react with malonate due to the rapid polymerization of styrene.[17]

The biphenyl **1k**, 2-naphthyl **1l**, and 2-pyridyl **1m** derivatives were also found to be good substrates, resulting in the formation of *trans*-**3ka**, *trans*-**3la**, and *trans*-**3ma** in moderate to good yield with good diastereomeric ratios. Finally, the reaction of aliphatic substrates, such as undecene **1n** with malonate **2a**, proceeded to give product **3na** in moderate yield. The diastereoselectivity did not decrease compared with other aromatic alkenes, gave *trans*-**3na** with good dr.

These reaction conditions for the iodine/visible light-mediated carboesterification of alkenes were then applied to the reaction of malonate **2a** with disubstituted styrenes (**1o**−**1r**) (Scheme 3). The combination of $\alpha$-methylstyrenes, **1o**, with malonate **2a** resulted in the formation of products in 61% yield with moderate diastereoselectivity. When *cis* (*Z*)-**1p** and *trans*-$\beta$-methylstyrene (*E*)-**1p** were used, the products **3pa** were synthesized with the same diastereoselectivity regardless of the styrene isomer.[18] Indene **1q** afforded polycyclic lactone *trans*-**3qa** with excellent diastereoselectivity by 9:91. Also, the use of 1,1-diphenylethylene resulted in the formation of product **3ra** in moderate yield.

**Scheme 3. *trans*-Diastereoselective Synthesis of Lactones, 3, via the Reaction of Disubstituted Alkenes with Malonate 2a[a]**




[a]Diasteromeric ratios (dr) were determined by $^1$H NMR analysis of the crude reaction mixture.



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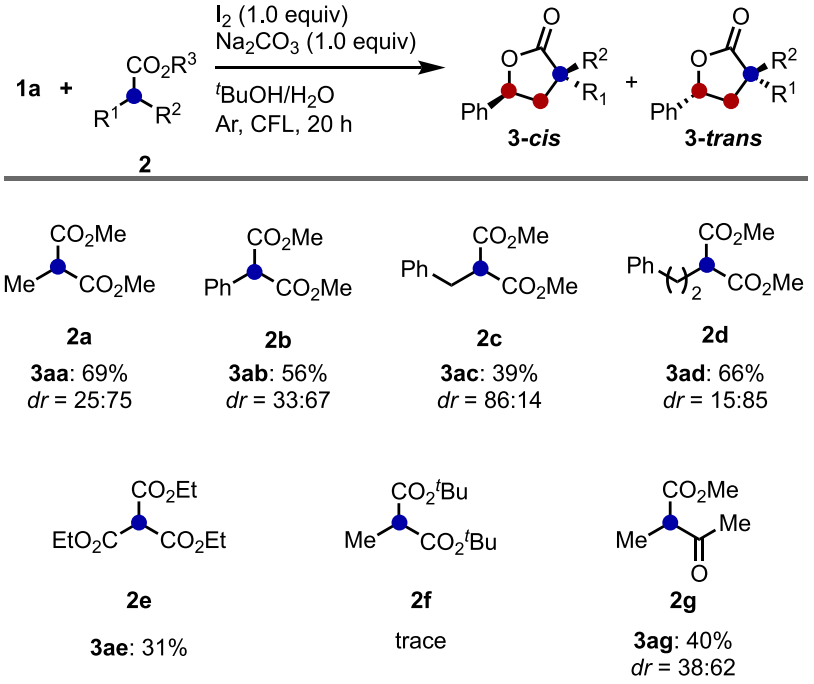
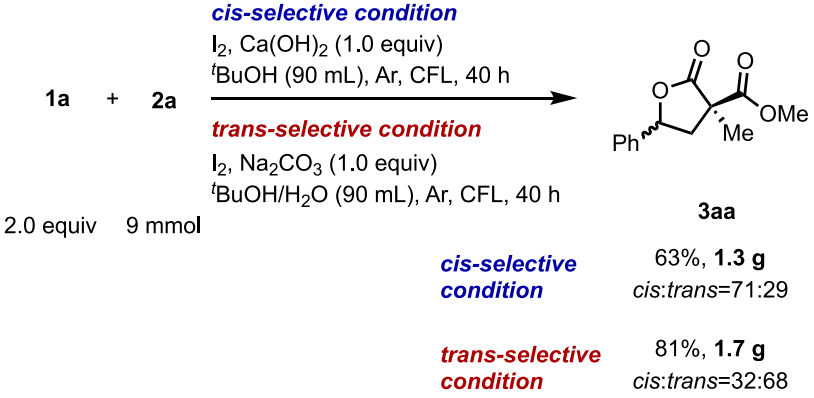
**Scheme 4. *trans*-Diastereoselective Synthesis of Lactones, 3, from Styrene 1a with Various Carbonyls, 2[a]**




[a]Diasteromeric ratios (dr) were determined by $^1$H NMR analysis of the crude reaction mixture.

**Scheme 5. Scale-up of the Intermolecular Lactonization Reactions**




To further evaluate the reaction scope, the optimal conditions for the *trans*-diastereoselective synthesis of lactones were used in the reaction of styrene **1a** with various carbonyls **2** (Scheme 4). The desired *trans*-lactones **3aa**, **3ab**, **3ac**, and **3ad** were obtained in moderate to good yield with diastereoselectivities ranging between ca. 2:1 and 5:1. Interestingly, carbonyl bearing benzyl group **2c** gave *cis*-**3ac** lactone preferentially. The formation of *trans*-**3ac** was suppressed due to the steric repulsion between the phenyl group of styrene and benzyl group (see the cyclization mechanism details, Scheme 10). In addition, when the reaction used triester **2e**, it resulted in the formation of lactone **3ae** albeit in low yield. To probe other substituents, the ester substituent group was changed. Expectedly, the reaction using *tert*-butoxy ester **2f**, it is possible to interfere with nucleophilic attack because of bulky ester could not be obtained the lactone **3af**. When acetyl derivative **2g** was used as a substrate, the desired product **3ag** was obtained in moderate yield.

To test the scalability of the reactions, gram-scale reactions using malonate **2a** and styrene **1a** were performed under both sets of cis-[13] and trans-selective conditions (Scheme 5). When scaled up in size by 30 times to 9 mmol, the reactions under both sets of conditions proceeded as expected to afford 63 and 81% isolated yields, respectively.

**Mechanistic Investigations.** To gain mechanistic insight into the reactions, several control experiments were carried out. Initially, the role of visible light in the reaction was investigated (Scheme 6). As previously reported, we hypothesized that the iodine radical was formed by irradiating molecular iodine with visible light.[19] Indeed, the yield of **3aa** was found to greatly decrease to 24% under dark conditions shielded with aluminum foil sheets. Also, since the reaction could be significantly suppressed in the dark at room temperature, the heat from compact fluorescent light (CFL) bulbs did not affect the reaction. In addition, **3aa** was obtained in a significantly lower yield under heating conditions at 70°. These results indicate that iodine was not thermally activated and that visible light activation of molecular iodine is necessary for the reaction to proceed.



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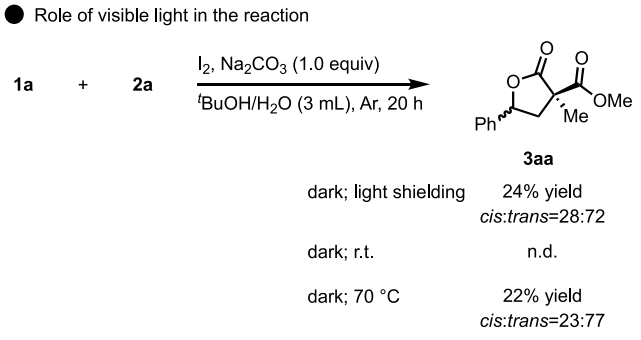
**Scheme 6. Investigation into the Role of Visible Light in the Reaction**




The iodonium cation is one of the reactive species that can be generated by the reaction of molecular iodine or cationic iodine with alkenes without being irradiated with visible light.[19,20] This means that the reaction may proceed via an iodonium intermediate, whereby an alkene is electrophilically activated by cationic iodine.[21] Therefore, we investigated the role of iodine in the reaction (Scheme 7). When reactions were carried out using a cationic iodine source, such as NIS or $(lutidine)_2I^+BF_4^-$, instead of molecular iodine under standard reaction conditions,[22] a significant decrease in the yield of **3aa** was observed. Interestingly, the formation of the iodoalkoxylation product **4a** was observed in some cases. This product is thought to be generated through the solvolysis of an iodonium cation intermediate.[23] However, 2 equiv of NIS produced a similar yield of the product. These observations revealed that alkene was not predominantly activated by a cationic form of iodine to form an iodonium intermediate.

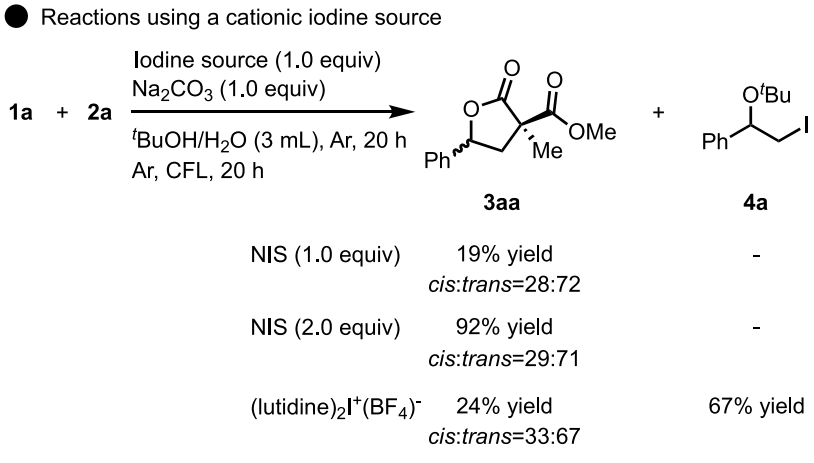
To determine the key intermediate, the reaction was conducted under an oxygen atmosphere (Scheme 8, eq 1). Acetophenone **5a** was formed by dehalogenation of phenacyl iodide,[19a,24] which was generated by the photooxidation of styrene via sequential addition of the iodine radical and triplet oxygen to styrene.[25] To further investigate, we then attempted radical clock experiments (Scheme 8, eq 2). As a result, using 1-cyclopropyl-1-phenylethylene as a radical clock instead of styrene **1a** under general conditions, the ring-opened products **I** and **II** were obtained significantly under visible light irradiation from CFL bulbs. In addition, it is indicated that the iodinated compound **I** was almost entirely consumed to form the nucleophilic substitution product **II** under visible light irradiation. Thus, these observations indicate that an iodine radical intermediate was generated and this radical sequentially reacted with an alkene to form a diiodide intermediate.

To confirm the formation of the above-mentioned diiodo intermediate, reactions employing *cis*- or *trans*-stilbene (*Z*)-**1s** and (*E*)-**1s** were conducted (Table 3). Under a set of cis-selective conditions, the reaction employing both stilbenes gave four possible diastereomers in moderate yield with diastereomeric ratios of approximately 50:10:20:20, respectively (entries 1 and 2).[26] Furthermore, a similar diastereomeric ratio was observed under a set of trans-selective conditions (entries 3 and 4). For both sets of conditions, it was revealed that lactones **3-A**–**D** were produced with similar diastereoselectivity without any influence from the structure of the stilbene itself. Therefore, it was observed that the reaction proceeded via a common intermediate, which could be the diiodo intermediate, as hypothesized previously.[13]

On the basis of the results of these investigations, a tentative mechanism is proposed in Scheme 9. Molecular iodine and the iodine radical are in equilibrium under visible light irradiation and the generated radical is sequentially added to styrene to yield **II**. *vic*-Diiodoalkanes, **II**, when generated in situ, are generally unstable and tend to revert back to iodine and the original alkene.[27] In the absence of water, compound **II** reacts with malonate **2a** to afford the corresponding product **III** and produces lactone **3** by the subsequent cyclization reaction. In the presence of water, compound **III** reacts with water to afford the corresponding product **IV**. Finally, cyclization of compound **III** or **IV** produces the desired lactone, **3**.

As previously described, we were able to successfully determine the reaction conditions that allowed the control of diastereoselectivity (in the absence of water and using $Ca(OH)_2$ as base resulted in the formation of cis-isomers, and in the presence of water and using $Na_2CO_3$ as the base produced the opposite isomer). We then elucidated the stereo determining step. Two types of cyclization mechanisms can be considered, as shown in Scheme 10; route I: cyclization by the nucleophilic substitution reaction from a lone pair on the carbonyl oxygen of the malonate ($S_N1$ or $S_N2$) and route II: cyclization from the hydroxy group, which is generated as a result of the hydrolysis of the iodinated intermediate. A reaction employing $^{18}O$-labeled $H_2{}^{18}O$ was conducted to

**Scheme 7. Reactions Using a Cationic Iodine Source**



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**Scheme 8. Controlled Experiments to Elucidate the Nature of the Radical Intermediate**

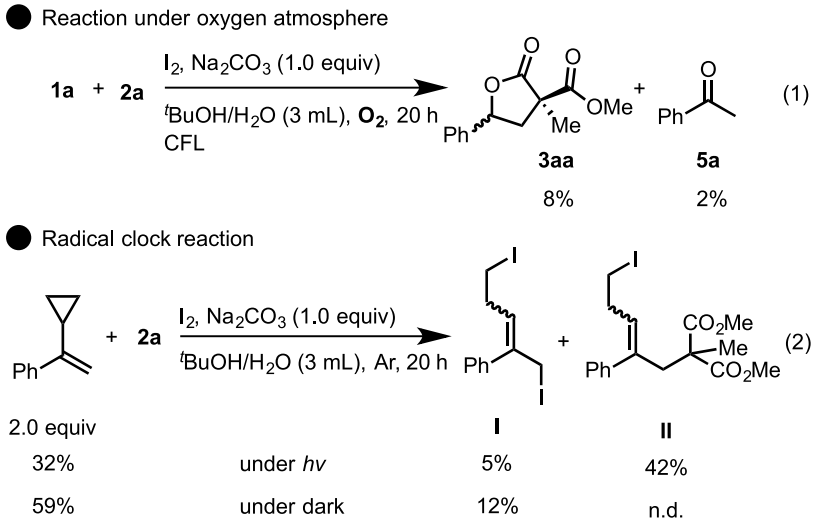
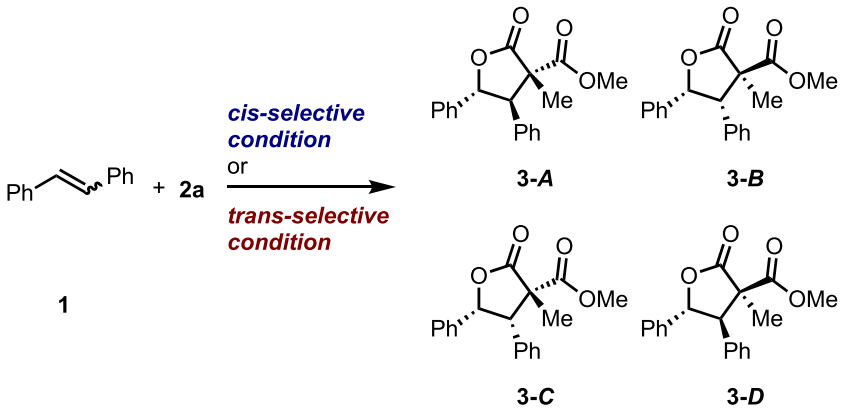



**Table 3. Lactonization Reaction Using *cis*- or *trans*-Stilbene**[a,b]




| | | | | diastereomer | | | |
|---|---|---|---|---|---|---|---|
| entry | conditions | 1s | 3 (%) | A | B | C | D |
| 1 | cis-selective conditions | *Z* | 49 | 52 | 9 | 22 | 17 |
| 2 | | *E* | 70 | 43 | 24 | 21 | 12 |
| 3 | trans-selective conditions | *Z* | 41 | 52 | 31 | 0 | 17 |
| 4 | | *E* | 73 | 53 | 35 | 0 | 18 |

[a]Reaction conditions: cis-selective conditions: **1** (2 equiv), **2a** (0.3 mmol), $I_2$ (0.3 mmol), and $Ca(OH)_2$ (0.3 mmol) in $^t$BuOH (3 mL) were stirred at ambient temperature and irradiated with a compact fluorescent lamp (CFL) for 20 h. trans-Selective conditions: **1** (2 equiv), **2a** (0.3 mmol), $I_2$ (0.3 mmol), and $Na_2CO_3$ (0.3 mmol) in $^t$BuOH (2 mL) and $H_2O$ (1 mL) were stirred at ambient temperature and irradiated with compact fluorescent lamps (CFLs) for 20 h. [b]Diasteromeric ratios (dr) were determined by $^1$H NMR analysis of the crude reaction mixture.

evaluate the preferred route (Scheme 10, eqs 3 and 4). As a result, $^{18}$O-labeled **3aa′** was mainly generated in good yield with moderate trans-selectivity in both cases.[28] Therefore, this indicates that the cyclization reaction mainly proceeds via the route II mechanism in the presence of water.

On the basis of these investigations, the plausible cyclization mechanism and stereo determination are proposed in Scheme 11. Since cyclization is mainly through route I, the product gives the cis-isomer. This is because the less sterically hindered carbonyl oxygen $O^1$ attacks the anti-bonding orbital of the C−I bond or carbocation to avoid steric repulsion of the phenyl group (or substituent R) between the ester. Furthermore, the cis-selectivity appears remarkably when $Ca(OH)_2$ is used[13] (Table 1, entry 1), it is conceivable that the metal cation forms chelate with two esters and contributes to the improvement of cis-selectivity by controlling the free rotation of esters.[29]

On the other hand, it is considered that cyclization in trans-selective conditions, using water as a co-solvent, proceeds mainly according to route II. Thus, a *trans*-diastereomer was obtained when cyclization proceeds through the hydroxy group to carbonyl $C^1$ having a small interference with the phenyl (or substituent R) and another ester.

## CONCLUSIONS

In this study, we have reported the visible light-iodine-mediated *trans*-diastereoselective synthesis of γ-lactones using a broad range of alkenes and carbonyls. The molecular iodine used in the reaction is cost-effective, easy to handle, and can be easily removed from the reaction mixture. The selective



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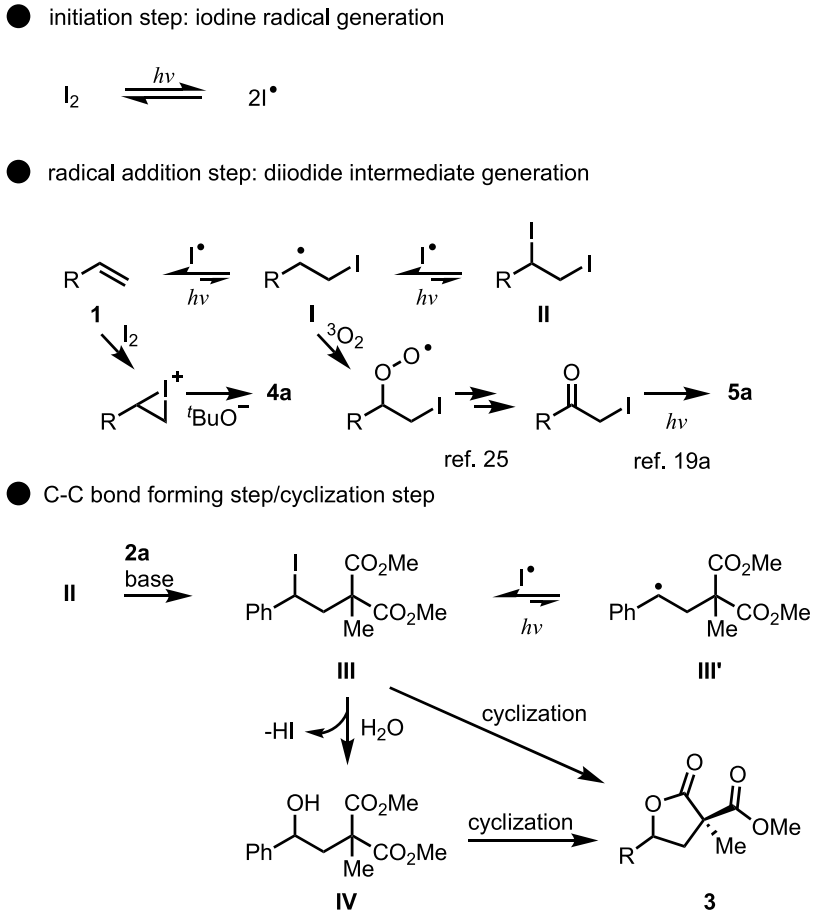
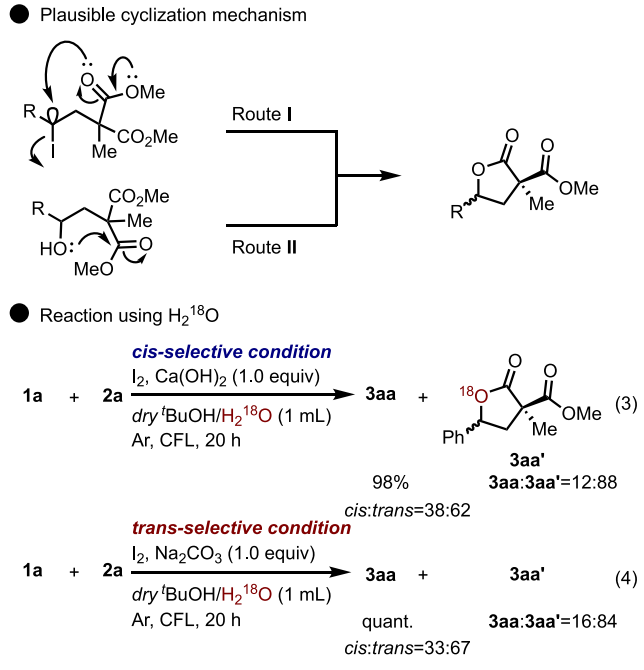
**Scheme 9. Plausible Mechanism of the Intermolecular Lactonization**




**Scheme 10. Experiments of the Mechanism of Cyclization with $H_2{}^{18}O$**




synthesis of trans-isomer was controlled using water as the co-solvent. Furthermore, the selective formation routes of cis- and trans-isomers are identified. Notably, this method does not require any co-catalyst/reagent. 16 terminal alkenes and 5 internal alkenes were converted to the corresponding lactones under visible light irradiation from CFL bulbs in yields of up to 77% with moderate to good diastereoselectivity. Additionally, 7 lactones were prepared from various carbonyls with moderate to good diastereoselectivity.

## EXPERIMENTAL SECTION

**General Information.** Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. Malonate **2a**,[30] **2b**,[31] **2c**,[32] **2d**,[33] **2f**,[3h] styrene **1i**,[34] **1k**,[35] **1l**,[36] and 1-cyclopropyl-1-phenylethyrene[37] were prepared according to the procedure reported.

The fluorescent lamp was ERF25ED/22-SP-F from Panasonic. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Merck silica gel 60 $F_{254}$). Flash column chromatography was performed with Kanto silica gel 60N (Spherical, Neutral, 40−50 mm). Visualization of the developed chromatogram was performed by a UV lamp (254 nm) and *p*-anisaldehyde or basic potassium permanganate stain. NMR spectra were recorded on a JEOL ECA 500 spectrometer (500 MHz for $^1$H NMR, 125 MHz for $^{13}$C NMR, and 470 MHz for $^{19}$F NMR), and are internally referenced to residual protio solvent signals or tetramethylsilane (TMS) (note: $CDCl_3$ referenced at $\delta$ 7.26 and 77.0 ppm respectively, TMS referenced at $\delta$ 0 and 0 ppm respectively). Data for $^1$ H NMR are reported as follows: chemical shift ($\delta$ ppm), multiplicity (s = singlet, d = doublet, t



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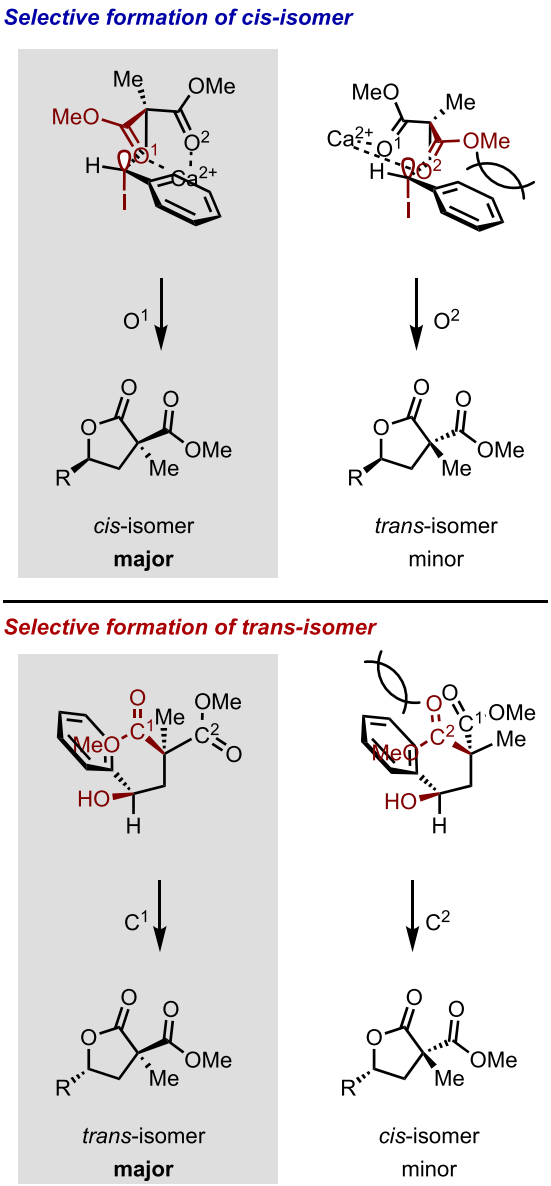
**Scheme 11. Plausible Cyclization Mechanism and Base Effect**




= triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, ddd = doublet of doublet of doublets, dq = doublet of quartets, and td = triplet of doublets), coupling constant (Hz), integration, and assignment. Data for $^{13}C$ NMR are reported in terms of chemical shifts ($\delta$ ppm). IR spectra were recorded on a PerkinElmer Spectrum 100 FTIR spectrometer and are reported in terms of frequency of absorption ($cm^{-1}$). High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100TD or JEOL. The AccuTOF GC JMS-T100GC are reported as $m/z$ (M + $H^+$, relative intensity) or $m/z$ (M, relative intensity). Melting points were measured on a Yanagimoto micro melting point apparatus without correlation. The ultraviolet-visible absorption spectra were recorded with SHIMADZU UV-3600 and are reported in terms of frequency of absorption.

*General Procedure for Iodine-Mediated Lactonization.* A Pyrex test tube (16.5 cm × 1.5 cm) containing a mixture of malonate **2** (1.0 equiv, 0.30 mmol), $I_2$ (76 mg, 1.0 equiv, 0.30 mmol), calcium hydroxide (22 mg, 1.0 equiv, 0.30 mmol), and alkenes **1** (2.0 equiv, 0.60 mmol) in $^t$Butyl alcohol (2.0 mL) and $H_2O$ (1.0 mL) was degassed three times via freeze−pump−thaw (FPT) cycling and backfilled with Ar. The resulting solution was stirred at ambient temperature for 20 h. The reaction was quenched with sat. aq $Na_2S_2O_3$ and extracted with $Et_2O$ (10 mL × 3). The combined organic layers were washed with brine, dried over $Mg_2SO_4$, filtered and concentrated in vacuo. The resulting mixture was purified by flash column chromatography on silica gel ($^n$hexane/EtOAc) to give the desired product **3**.

*Synthesis of Methyl-2-carboxy-2-methyl-4-phenyl-4-butanolide (3aa).*[13] 48 mg (0.21 mmol) of **3aa** as a white solid (69% yield: dr = 25:75). **3aa**-*cis*: TLC ($SiO_2$): $R_f$ = 0.56 ($^n$hexane/ethyl acetate = 4:1); $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43−7.36 (m, 5H), 5.52 (dd, $J$ = 6.9 Hz, 9.1 Hz, 1H), 3.74 (s, 3H), 2.85 (dd, $J$ = 9.1 Hz, 13.1 Hz, 1H), 2.56 (dd, $J$ = 6.9 Hz, 13.1 Hz, 1H), 1.65 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.3, 170.9, 138.3, 128.7, 125.5, 78.7, 53.0, 51.4, 42.8, 19.6. **3aa**-*trans*: TLC ($SiO_2$): $R_f$ = 0.63 ($^n$hexane/ethyl acetate = 4:1); mp: 74.1−74.8 °C; $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43−7.34 (m, 5H), 5.59 (dd, $J$ = 6.3 Hz, 10.4 Hz, 1H), 3.84 (s, 3H), 3.11 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.12 (dd, $J$ = 10.4 Hz, 13.5 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.7, 170.6, 138.4, 128.7, 128.6, 125.3, 78.8, 53.2, 51.9, 43.6, 20.8.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-tert-butylphenyl)-4-butanolide (**3ba**).*[13] 57 mg (0.20 mmol) of **3ba** as a colorless oil (65% yield: dr = 33:67). **3ba**-*cis*: TLC ($SiO_2$): $R_f$ = 0.42 ($^n$hexane/ethyl acetate = 4:1); mp: 71.9−74.1 °C; $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43 (d, $J$ = 8.0 Hz, 2H), 7.32 (d, $J$ = 8.0 Hz, 2H), 5.50 (dd, $J$ = 6.9 Hz, 9.2 Hz, 1H), 3.74 (s, 3H), 2.86 (dd, $J$ = 9.2 Hz, 13.2 Hz, 1H), 2.53 (dd, $J$ = 6.9 Hz, 13.2 Hz, 1H), 1.64 (s, 3H), 1.32 (s, 9H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.4, 171.1, 152.0, 135.2, 125.7, 125.5, 78.8, 53.0, 51.5, 42.8, 34.6, 31.2, 19.5. **3ba**-*trans*: TLC ($SiO_2$): $R_f$ = 0.45 ($^n$hexane/ethyl acetate = 4:1); $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.42 (d, $J$ = 8.5 Hz, 2H), 7.28 (d, $J$ = 8.5 Hz, 2H), 5.56 (dd, $J$ = 6.3 Hz, 10.1 Hz, 1H), 3.84 (s, 3H), 3.08 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.13 (dd, $J$ = 10.1 Hz, 13.5 Hz, 1H), 1.59 (s, 3H), 1.32 (s, 9H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.0, 170.9, 152.0, 135.4, 125.8, 125.3, 79.0, 53.3, 52.0, 43.7, 34.6, 31.2, 20.9.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-methylbutyl-phenyl)-4-butanolide (3ca).*[13] 45 mg of **3ca** as a colorless oil (61% yield: dr = 33:67). **3ca**-*cis*: TLC ($SiO_2$): $R_f$ = 0.33 ($^n$hexane/ethyl acetate = 4:1); mp: 78.6−79.8 °C; $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.26 (d, $J$ = 7.5 Hz, 2H), 7.21 (dd, $J$ = 8.0 Hz, 2H), 5.49 (dd, $J$ = 6.8 Hz, 9.2 Hz, 1H), 3.75 (s, 3H), 2.83 (dd, $J$ = 9.2 Hz, 13.6 Hz, 1H), 2.53 (dd, $J$ = 6.8 Hz, 13.6 Hz, 1H), 2.37 (s, 3H), 1.64 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.4, 171.1, 138.8, 135.3, 129.5, 125.7, 78.8, 53.1, 51.5, 42.9, 21.1, 19.6. **3ca**-*trans*: TLC ($SiO_2$): $R_f$ = 0.36 ($^n$hexane/ethyl acetate = 4:1); $^1H$ NMR: (500 MHz, $CDCl_3$): $\delta$ 7.26 (d, $J$ = 8.6 Hz, 2H), 7.22 (d, $J$ = 8.6 Hz, 2H), 5.55 (dd, $J$ = 6.3 Hz, 10.3 Hz, 1H), 3.84 (s, 3H), 3.07 (dd, $J$ = 6.3 Hz, 13.6 Hz, 1H), 2.37 (s, 3H) 2.11 (dd, $J$ = 10.3 Hz, 13.5 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.0, 170.9, 138.7, 135.5, 129.5, 125.6, 79.0, 53.3, 52.1, 43.8, 21.1, 20.9.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(3-methylphenyl)-4-butanolide (3da).*[13] 53 mg (0.22 mmol) of **3da** as a yellow solid (72% yield: dr = 33:67). **3da**-*cis*: TLC ($SiO_2$): $R_f$ = 0.29 ($^n$hexane/ethyl acetate = 4:1); $^1H$ NMR: (500 MHz,



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$CDCl_3$): δ 7.28 (dd, J = 7.3 Hz, 11.5 Hz, 1H), 7.19−7.15 (m, 3H), 5.48 (dd, J = 6.3 Hz, 9.2 Hz, 1H), 3.75 (s, 3H), 2.83 (dd, J = 9.2 Hz, 13.2 Hz, 1H), 2.53 (dd, J = 6.3 Hz, 13.2 Hz, 1H), 2.38 (s, 3H), 1.64 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.4, 171.0, 138.6, 138.3, 129.5, 128.7, 126.2, 122.7, 78.8, 53.0, 51.5, 42.9, 21.3, 19.6. **3da**-*trans*: TLC ($SiO_2$): $R_f$ = 0.38 ($^n$hexane/ethyl acetate = 4:1); mp: 58.8−60.2 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.28 (dd, J = 7.6 Hz, 10.9 Hz, 1H), 7.17−7.12 (m, 3H), 5.55 (dd, J = 6.3 Hz, 10.3 Hz, 1H), 3.84 (s, 3H), 3.08 (dd, J = 6.3 Hz, 13.4 Hz, 1H), 2.37 (s, 3H), 2.11 (dd, J = 10.3 Hz, 13.4 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$-NMR: (125 MHz, $CDCl_3$): δ 175.0, 170.9, 138.7, 138.5, 129.5, 128.8, 126.1, 122.5, 79.0, 53.3, 52.0, 43.8, 21.3, 20.9.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(2-methylphenyl)-4-butanolide (3ea).*[13] 49 mg of **3ea** as a colorless oil (66% yield: dr = 26:74). **3ea**-*cis*: TLC ($SiO_2$): $R_f$ = 0.29 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.43 (dd, J = 3.8 Hz, 5.3 Hz, 1H), 7.27−7.25 (m, 2H), 7.19 (dd, J = 3.0 Hz, 3.8 Hz, 1H), 5.71 (dd, J = 6.8 Hz, 9.2 Hz, 1H), 3.76 (s, 3H), 2.77 (dd, J = 9.2 Hz, 13.0 Hz, 1H), 2.56 (dd, J = 6.8 Hz, 13.0 Hz, 1H), 2.35 (s, 3H), 1.66 (s, 3H); $^{13}C\{^1H\}$-NMR: (125 MHz, $CDCl_3$): δ 171.1, 169.7, 136.6, 134.3, 130.8, 128.5, 126.5, 124.8, 76.4, 53.1, 51.3, 41.7, 19.9, 19.0. **3ea**-*trans*: TLC ($SiO_2$): $R_f$ = 0.38 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.39 (dd, J = 2.9 Hz, 4.4 Hz, 1H), 7.27−7.24 (m, 2H), 7.18 (dd, J = 3.9 Hz, 4.4 Hz, 1H), 5.77 (dd, J = 6.3 Hz, 10.1 Hz, 1H), 3.85 (s, 3H), 3.14 (dd, J = 6.3 Hz, 13.3 Hz, 1H), 2.35 (s, 3H), 2.03 (dd, J = 10.1 Hz, 13.3 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.0, 170.9, 136.8, 134.5, 130.8, 128.4, 126.6, 124.3, 76.8, 53.3, 51.9, 42.5, 21.0, 19.0.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-fluorophenyl)-4-butanolide (3fa).*[13] 21 mg of **3fa** as a yellow oil (28% yield: dr = 20:80). **3fa**-*cis*: TLC ($SiO_2$): $R_f$ = 0.28 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.36 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 5.50 (dd, J = 6.7 Hz, 9.1 Hz, 1H), 3.76 (s, 3H), 2.83 (dd, J = 9.1 Hz, 13.0 Hz, 1H), 2.55 (dd, J = 6.7 Hz, 13.0 Hz, 1H), 1.64 (s, 3H); $^{13}C\{^1H\}$-NMR: (125 MHz, $CDCl_3$): δ 175.2, 170.9, 163.0 (d, J = 274.4 Hz), 134.1, 127.6 (d, J = 8.2 Hz), 115.8 (d, J = 21.3 Hz), 78.1, 53.2, 51.4, 42.9, 19.6; $^{19}$F NMR: (470 MHz, $CDCl_3$): δ −112.67. **3fa**-*trans*: TLC ($SiO_2$): $R_f$ = 0.31 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.34 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 5.56 (dd, J = 5.9 Hz, 10.3 Hz, 1H), 3.84 (s, 3H), 3.09 (dd, J = 5.9 Hz, 13.2 Hz, 1H), 2.08 (dd, J = 10.3 Hz, 13.2 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$-NMR: (125 MHz, $CDCl_3$): δ 174.7, 170.7, 162.9 (d, J = 274.4 Hz), 134.2, 127.4 (d, J = 8.2 Hz), 115.9 (d, J = 21.3 Hz), 78.4, 53.3, 52.0, 43.8, 20.9; $^{19}$F NMR: (470 MHz, $CDCl_3$): δ −112.70.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-chlorophenyl)-4-butanolide (3ga).*[13] 49 mg of **3ga** as a white solid (60% yield: dr = 29:71). **3ga**-*cis*: TLC ($SiO_2$): $R_f$ = 0.30 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.38 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 8.5 Hz, 2H), 5.49 (dd, J = 6.8 Hz, 9.2 Hz, 1H), 3.74 (s, 3H), 2.80 (dd, J = 9.2 Hz, 13.0 Hz, 1H), 2.56 (dd, J = 6.8 Hz, 13.0 Hz, 1H), 1.64 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.1, 170.8, 137.0, 134.6, 129.0, 127.0, 77.9, 53.1, 51.3, 42.7, 19.6. **3ga**-*trans*: TLC ($SiO_2$): $R_f$ = 0.36 ($^n$hexane/ethyl acetate = 4:1); mp: 66.6−72.7 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.38 (d, J = 8.6, 2H), 7.29 (d, J = 8.6 Hz, 2H), 5.55 (dd, J = 6.3 Hz, 10.3 Hz, 1H), 3.84 (s, 3H), 3.10 (dd, J = 6.3 Hz, 13.2 Hz, 1H), 2.06 (dd, J = 10.3 Hz, 13.2 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 174.6, 170.7, 137.1, 134.6, 129.1, 126.8, 78.2, 77.3, 76.7, 53.4, 52.0, 43.7, 20.9.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-bromophenyl)-4-butanolide (3ha).*[13] 70 mg of **3ha** as a crystalline solid (75% yield: dr = 26:74). **3ha**-*cis*: TLC ($SiO_2$): $R_f$ = 0.30 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.54 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 5.47 (dd, J = 6.8 Hz, 9.1 Hz, 1H), 3.74 (s, 3H), 2.80 (dd, J = 9.2 Hz, 13.0 Hz, 1H), 2.56 (dd, J = 6.8 Hz, 13.0 Hz, 1H), 1.64 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.1, 170.8, 137.5, 132.0, 127.2, 122.7, 77.9, 53.1, 51.3, 42.7, 19.6. **3ha**-*trans*: TLC ($SiO_2$): $R_f$ = 0.28 ($^n$hexane/ethyl acetate = 4:1); mp: 76.8−80.0 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.54 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 5.54 (d, J = 6.3 Hz, 10.2 Hz, 1H), 3.84 (s, 3H), 3.11 (dd, J = 6.3 Hz, 13.2 Hz, 1H), 2.05 (dd, J = 10.2 Hz, 13.2 Hz, 1H), 1.68 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 174.6, 170.6, 137.6, 132.1, 127.1, 122.7, 78.2, 53.3, 51.9, 43.6, 20.8.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-methylcarboxyphenyl)-4-butanolide (3ia).*[13] No product was obtained. **3ia**-*cis*: TLC ($SiO_2$): $R_f$ = 0.15 ($^n$hexane/ethyl acetate = 4:1); mp: 86.1−88.6 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 8.08 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 5.58 (dd, J = 6.8 Hz, 8.5 Hz, 1H), 3.93 (s, 3H), 3.72 (s, 3H), 2.82 (dd, J = 8.5 Hz, 13.5 Hz, 1H), 2.61 (dd, J = 6.8 Hz, 13.5 Hz, 1H), 1.65 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.0, 170.7, 166.6, 143.5, 130.5, 130.1, 125.3, 77.8, 53.1, 52.2, 51.1, 42.6, 19.7. **3ia**-*trans*: TLC ($SiO_2$): $R_f$ = 0.18 ($^n$hexane/ethyl acetate = 4:1); mp: 61.2−87.5 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 8.08 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 5.63 (dd, J = 6.1 Hz, 10.1 Hz, 1H), 3.93 (s, 3H), 3.85 (s, 3H), 3.16 (dd, J = 6.1 Hz, 13.3 Hz, 1H), 2.07 (dd, J = 10.1 Hz, 13.3 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 174.6, 170.6, 166.6, 143.6, 130.5, 130.2, 125.2, 78.2, 53.4, 52.2, 51.9, 43.6, 20.8.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(4-phenyl-phenyl)-4-butanolide (3ka).*[13] 34 mg (0.12 mmol) of **3ka** as a white solid (38% yield: dr = 33:67). **3ka**-*cis*: TLC ($SiO_2$): $R_f$ = 0.34 ($^n$hexane/ethyl acetate = 4:1); mp: 38.8−39.8 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.64−7.58 (m, 4H), 7.48−7.44 (m, 4H), 7.38 (t, J = 6.8 Hz, 1H), 5.56 (dd, J = 6.8 Hz, 9.1 Hz, 1H), 3.76 (s, 3H), 2.89 (dd, J = 9.1 Hz, 13.0 Hz, 1H), 2.58 (dd, J = 6.8 Hz, 13.0 Hz, 1H), 1.66 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.3, 171.0, 141.8, 140.4, 137.3, 128.9, 127.7, 127.5, 127.1, 126.1, 78.5, 53.1, 51.5, 42.8, 19.6. **3ka**-*trans*: TLC ($SiO_2$): $R_f$ = 0.33 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.64−7.58 (m, 4H), 7.48−7.37 (m, 5H), 5.63 (dd, J = 6.3 Hz, 10.1 Hz, 1H), 3.85 (s, 3H), 3.14 (dd, J = 6.3 Hz, 13.0 Hz, 1H), 2.16 (dd, J = 10.1 Hz, 13.0 Hz, 1H), 1.61 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 174.9, 170.8, 141.8, 140.4, 137.4, 128.9, 127.8, 127.6, 127.1, 126.0, 78.8, 53.3, 52.0, 43.8, 20.9.

*Synthesis of Methyl-2-carboxy-2-methyl-4-(2-naphtyl)-4-butanolide (3la).*[13] 64 mg (0.22 mmol) of **3la** as a white solid (75% yield: dr = 28:72). **3la**-*cis*: TLC ($SiO_2$): $R_f$ = 0.24 ($^n$hexane/ethyl acetate = 4:1); mp: 93.3−95.8 °C; $^1$H NMR: (500 MHz, $CDCl_3$): δ 7.90 (d, J = 8.6 Hz, 1H), 7.86−7.84 (m, 3H), 7.53−7.51 (m, 2H), 7.46 (dd, J = 1.7 Hz, 8.6 Hz, 1H), 5.68 (dd, J = 6.9 Hz, 9.3 Hz, 1H), 3.73 (s, 3H), 2.94 (dd, J = 9.3 Hz, 13.2 Hz, 1H), 2.62 (dd, J = 6.9 Hz, 13.2 Hz, 1H), 1.68 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): δ 175.4, 171.0, 135.6, 133.3, 133.0, 129.0, 128.1, 127.8, 126.7, 126.6, 124.9,



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122.9, 78.8, 53.1, 51.4, 42.8, 19.7. **3la**-*trans*: TLC ($SiO_2$): $R_f$ = 0.33 ($^n$hexane/ethyl acetate = 4:1); mp: 58.6−62.5 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.91−7.85 (m, 4H), 7.55−7.51 (m, 2H), 7.42 (d, $J$ = 8.2 Hz, 1H), 5.76 (dd, $J$ = 6.4 Hz, 10.2 Hz, 1H), 3.87 (s, 3H), 3.18 (dd, $J$ = 6.4 Hz, 13.8 Hz, 1H), 2.20 (dd, $J$ = 10.2 Hz, 13.8 Hz, 1H), 1.63 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.0, 170.9, 135.8, 133.3, 133.1, 129.0, 128.1, 127.8, 126.7, 126.6, 124.7, 122.7, 79.1, 53.3, 52.0, 43.7, 20.9.

*Synthesis of Ethyl-2-carboxy-2-methyl-4-(2-pyridyl)-4-butanolide (3ma).*[13] 35 mg (0.15 mmol) of **3ma** as a brown solid (50% yield: dr = 37:63). **3ma**-*cis*: TLC ($SiO_2$): $R_f$ = 0.09 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 8.58 (d, $J$ = 4.3 Hz, 1H), 7.78−7.74 (m, 1H), 7.48 (d, $J$ = 7.7 Hz, 1H), 7.31−7.27 (m, 1H), 5.60 (dd, $J$ = 7.2 Hz, 7.5 Hz, 1H), 3.65 (s, 3H), 3.03 (dd, $J$ = 7.2 Hz, 13.0 Hz, 1H), 2.68 (dd, $J$ = 7.5 Hz, 13.0 Hz, 1H), 1.64 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.3, 169.6, 158.0, 149.3, 137.0, 123.2, 120.1, 78.4, 52.9, 50.6, 40.7, 20.2. **3ma**-*trans*: TLC ($SiO_2$): $R_f$ = 0.09 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 8.61 (dd, $J$ = 4.3 Hz, 1H), 7.78−7.74 (m, 1H), 7.51 (d, $J$ = 7.7 Hz, 1H), 7.31−7.27 (m, 1H), 5.66 (dd, $J$ = 6.8 Hz, 9.7 Hz, 1H), 3.83 (s, 3H), 3.18 (dd, $J$ = 6.8 Hz, 13.5 Hz, 1H), 2.38 (dd, $J$ = 9.7 Hz, 13.5 Hz, 1H), 1.57 (s, 3H); $^{13}$C{$^1$H}-NMR: (125 MHz, $CDCl_3$): $\delta$ 175.0, 170.8, 157.6, 149.6, 137.2, 123.5, 120.6, 78.8, 53.2, 51.5, 41.3, 20.7.

*Synthesis of Methyl-2-carboxy-2-methyl-4-decyl-4-butanolide (3na).*[13] 45 mg (0.15 mmol) of **3na** as a yellow oil (50% yield: dr = 33:67).

**3na**-*cis*: TLC ($SiO_2$): $R_f$ = 0.26 ($^n$hexane/ethyl acetate = 10:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 4.53−4.45 (m, 1H), 3.79 (s, 3H), 2.49 (dd, $J$ = 9.2 Hz, 13.0 Hz, 1H), 2.22 (dd, $J$ = 6.8 Hz, 13.0 Hz, 1H), 1.80−1.27 (m, 18H), 1.54 (s, 3H), 0.88 (t, $J$ = 6.8 Hz, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.6, 171.4, 79.3, 53.0, 51.2, 40.3, 35.3, 31.8, 29.5, 29.43, 29.37, 29.2, 25.21, 22.6, 21.0, 20.0, 14.0. **3na**-*trans*: TLC ($SiO_2$): $R_f$ = 0.38 ($^n$hexane/ethyl acetate = 10:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 4.53−4.45 (m, 1H), 3.78 (s, 3H), 2.78 (dd, $J$ = 9.2 HZ, 13.0 Hz, 1H), 1.80−1.27 (m, 19H), 1.53 (s, 3H), 0.88 (t, $J$ = 6.8 Hz, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.2, 171.2, 78.5, 53.1, 51.7, 41.4, 35.4, 31.8, 29.5, 29.43, 29.37, 29.2, 25.18, 22.6, 21.0, 20.0, 14.0.

*Synthesis of Methyl-2-carboxy-2-methyl-4,4-methyl-phenyl-4-butanolide (3oa).* 42 mg (0.18 mmol) of **3oa** as a white solid (61% yield: dr = 25:75). **3oa**-*cis*: TLC ($SiO_2$): $R_f$ = 0.35 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.36−7.27 (m, 5H), 3.26 (d, $J$ = 13.2 Hz, 1H), 3.24 (s, 3H), 2.32 (d, $J$ = 13.2 Hz, 1H), 1.73 (s, 3H), 1.57 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 174.8, 171.3, 143.4, 128.4, 127.8, 124.4, 84.5, 52.5, 51.5, 48.4, 31.2, 21.9 (one carbon atom was overlapped); HRMS: $m/z$ (DART) calcd for $C_{14}H_{16}O_4$ (M + H)$^+$ 249.1121, found 249.1130 (mixture of diastereomers); Fourier transform infrared (FTIR): (neat): 2981, 2953, 1776, 1736, 1496, 1447, 1378, 1318, 1296, 1242, 1194, 1170, 1152, 1132, 1118, 1082, 1053, 856, 843, 767, 747, 701 cm$^{-1}$ (mixture of diastereomers). **3oa**-*trans*: TLC ($SiO_2$): $R_f$ = 0.38 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.39−7.27 (m, 5H), 3.83 (s, 3H), 3.10 (d, $J$ = 13.0 Hz, 1H), 2.50 (d, $J$ = 13.0 Hz, 1H), 1.74 (s, 3H), 1.35 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.0, 171.7, 145.3, 128.8, 127.7, 123.8, 84.7, 53.3, 52.0, 47.8, 30.6, 21.7 (one carbon atom was overlapped); HRMS: $m/z$ (DART) calcd for $C_{14}H_{16}O_4$ (M + H)$^+$ 249.1121, found 249.1132 (mixture of diastereomers); FTIR: (neat): 2984, 1774, 1740, 1496, 1447, 1380, 1297, 1269, 1236, 1203, 1136, 1116, 1084, 1064, 1029, 857, 767, 702 cm$^{-1}$ (mixture of diastereomers).

*Synthesis of Methyl-2-carboxy-2-methyl-3-methyl-4-phenyl-4-butanolide (3pa).* Using (*Z*)-**1p**: 55 mg (0.22 mmol) of **3pa** as a colorless oil (74% yield: dr = 86:14). using (*E*)-**1p**: 58 mg (0.23 mmol) of **3pa** as a colorless oil (77% yield: dr = 87:13). **3pa**-*cis*: TLC ($SiO_2$): $R_f$ = 0.47 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.44−7.36 (m, 5H), 4.92 (d, $J$ = 10.3 Hz, 1H), 3.80 (s, 3H), 2.97 (dq, $J$ = 10.3 Hz, 6.8 Hz, 1H), 1.50 (s, 3H), 1.01 (d, $J$ = 6.8 Hz, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.1, 170.7, 136.5, 128.9, 128.6, 126.2, 85.2, 54.7, 52.9, 47.1, 13.6, 9.8 (one carbon atom was overlapped); HRMS: $m/z$ (DART) calcd for $C_{14}H_{16}O_4$ (M + H)$^+$ 249.1121, found 249.1115; FTIR: (neat): 3036, 2955, 2850, 1773, 1732, 1496, 1456, 1435, 1389, 1332, 1295, 1285, 1250, 1224, 1188, 1132, 1123, 1097, 1074, 997, 936, 916, 891, 836, 794, 777, 757, 726, 698 cm$^{-1}$. **3pa**-*trans*: TLC ($SiO_2$): $R_f$ = 0.54 ($^n$hexane/ethyl acetate = 4:1); mp: 85.5−86.7 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.41−7.33 (m, 5H), 5.15 (d, $J$ = 10.2 Hz, 1H), 3.84 (s, 3H), 2.26 (dq, $J$ = 10.2 Hz, 6.8 Hz, 1H), 1.53 (s, 3H), 1.01 (d, $J$ = 6.8 Hz, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.2, 169.3, 136.9, 129.0, 128.8, 126.2, 85.3, 55.8, 52.7, 51.1, 19.1, 10.8 (one carbon atom was overlapped); HRMS: $m/z$ (DART) calcd for $C_{14}H_{16}O_4$ (M + H)$^+$ 249.1121, found 249.1110; FTIR: (neat): 3036, 2957, 2937, 2850, 1774, 1741, 1720, 1498, 1455, 1435, 1381, 1345, 1331, 1298, 1282, 1261, 1209, 1174, 1148, 1125, 1105, 1076, 1031, 999, 936, 919, 882, 843, 801, 781, 753, 734, 699 cm$^{-1}$.

*Synthesis of Methyl-2-carboxy-2-methyl-3,4-2H-indeno-4-butanolide (**3qa**).* 51 mg (0.21 mmol) of **3qa** as a yellow oil (69% yield: dr = 9:91). **3qa**-*trans*: TLC ($SiO_2$): $R_f$ = 0.30 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.53−7.27 (m, 4H), 5.86 (d, $J$ = 6.5 Hz, 1H), 3.83 (s, 3H), 3.59 (dt, $J$ = 6.5 Hz, 8.9 Hz, 16.3 Hz, 1H), 3.09 (ddd, $J$ = 8.9 Hz, 16.3 Hz, 2H), 1.51 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.2, 171.6, 143.4, 138.0, 130.4, 127.6, 126.5, 124.9, 85.6, 54.4, 53.3, 47.4, 32.2, 17.0; HRMS: $m/z$ (DART) calcd for $C_{14}H_{14}O_4$ (M + H)$^+$ 247.0965, found 247.0963; FTIR: (neat): 3475, 2953, 2923, 2852, 1770, 1736, 1480, 1460, 1435, 1381, 1346, 1327, 1250, 1224, 1212, 1179, 1150, 1135, 1099, 1036, 967, 893, 878, 749, 708 cm$^{-1}$.

*Synthesis of Methyl-2-carboxy-2-methyl-3,4-2H-indeno-4-butanolide (**3ra**).* 51 mg (0.16 mmol) of **3ra** as a white solid (55% yield). TLC ($SiO_2$): $R_f$ = 0.43 ($^n$hexane/ethyl acetate = 4:1); mp: 94.1−95.0 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.45−7.25 (m, 10H), 3.67 (d, $J$ = 13.4 Hz, 1H), 3.35 (s, 3H), 2.83 (d, $J$ = 13.4 Hz, 1H), 1.47 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 174.3, 171.1, 143.6, 142.3, 128.6, 128.4, 127.9, 127.8, 125.4, 124.9, 87.1, 52.7, 51.7, 47.6, 21.3 (two carbon atoms were overlapped).; HRMS: $m/z$ (DART) calcd for $C_{19}H_{19}O_4$ (M + H)$^+$ 311.1278, found 311.1285; FTIR: (neat): 3062, 3034, 2953, 1779, 1737, 1599, 1493, 1450, 1379, 1259, 1229, 1210, 1153, 1111, 1083, 1042, 978, 951, 918, 889, 748, 697, 667 cm$^{-1}$.

*Synthesis of Methyl-2-carboxy-2-methyl-4,3-diphenyl-4-butanolide (3A−D).* cis-Selective conditions (using (*Z*)-**1s**); 46 mg (0.15 mmol) mixture of **3A−D** as a white solid (49% yield: dr = 52:9:22:17). trans-Selective conditions (using (*Z*)-**1s**): 38 mg (0.12 mmol) mixture of **3A−D** as a white solid (41% yield: dr = 52:31:0:17). cis-Selective conditions (using (*E*)-**1s**): 65 mg (0.21 mmol) mixture of **3A−D** as a white solid



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(70% yield: dr = 43:24:21:12). trans-Selective conditions (using (*E*)-**1s**): 68 mg (0.22 mmol) mixture of **3A**−**D** as a white solid (73% yield: dr = 53:35:0:18). **3-A**: TLC ($SiO_2$): $R_f$ = 0.60 ($^n$hexane/ethyl acetate = 4:1); mp: 105.3−106.2 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.35−6.89 (m, 10H), 5.81 (d, $J$ = 9.8 Hz, 1H), 4.37 (d, $J$ = 9.8 Hz, 1H), 3.81 (s, 3H), 1.30 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.3, 170.5, 136.7, 133.1, 128.9, 128.6, 128.3, 126.1, 81.6, 57.1, 56.2, 53.2, 15.7 (three carbon atoms were overlapped); HRMS: $m/z$ (DART) calcd for $C_{19}H_{19}O_4$ $(M + H)^+$ 311.1278, found 311.1276; FTIR: (neat): 3035, 2954, 2920, 2850, 1775, 1741, 1728, 1604, 1585, 1499, 1454, 1435, 1383, 1301, 1277, 1242, 1218, 1187, 1153, 1110, 1077, 1049, 1031, 997, 942, 913, 860, 809, 794, 756, 697, 661 $cm^{-1}$. **3-B**: TLC ($SiO_2$): $R_f$ = 0.57 ($^n$hexane/ethyl acetate = 4:1); mp: 90.1−91.0 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.17−6.89 (m, 10H), 5.99 (d, $J$ = 5.6 Hz, 1H), 4.31 (d, $J$ = 5.6 Hz, 1H), 3.90 (s, 3H), 1.21 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.9, 171.5, 135.4, 133.8, 129.5, 128.3, 128.0, 127.6, 127.3, 125.2, 81.8, 57.5, 55.7, 53.7, 17.5 (two carbon atoms were overlapped); HRMS: $m/z$ (DART) calcd for $C_{19}H_{19}O_4$ $(M + H)^+$ 311.1278, found 311.1275; FTIR: (neat): 3064, 3034, 2955, 2921, 2850, 1780, 1735, 1605, 1499, 1452, 1434, 1378, 1336, 1248, 1219, 1157, 1129, 1106, 1078, 1035, 1020, 1001, 959, 919, 898, 863, 788, 748, 710, 673 $cm^{-1}$. **3-C**: TLC ($SiO_2$): $R_f$ = 0.57 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.13−6.85 (m, 10H), 6.03 (d, $J$ = 6.3 Hz, 1H), 3.89 (d, $J$ = 6.3 Hz, 1H), 3.24 (s, 3H), 1.90 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.5, 169.2, 135.3, 134.5, 129.3, 128.0, 127.8, 127.5, 127.4, 125.5, 80.5, 58.1, 57.1, 52.1, 21.7. **3-D**: TLC ($SiO_2$): $R_f$ = 0.42 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.39−7.18 (m, 10H), 6.09 (d, $J$ = 10.6 Hz, 1H), 3.63 (s, 3H), 3.43 (d, $J$ = 10.6 Hz, 1H), 1.59 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.2, 168.7, 137.1, 133.0, 129.0, 128.6, 128.1, 125.8, 81.6, 61.9, 58.2, 52.6, 19.3 (three carbon atoms were overlapped); HRMS: $m/z$ (DART) calcd for $C_{19}H_{19}O_4$ $(M + H)^+$ 311.1278, found 311.1282; FTIR: (neat): 2956, 2920, 2850, 1781, 1747, 1719, 1500, 1455, 1379, 1311, 1276, 1251, 1218, 1136, 1110, 1002, 940, 920, 899, 865, 820, 797, 749, 700 $cm^{-1}$.

*Synthesis of Methyl-2-carboxy-2-phenyl-4-phenyl-4-butanolide (3ab).*[13] 50 mg (0.17 mmol) of **3ab** as a colorless oil (56% yield: dr = 33:67). **3ab**-*cis*: TLC ($SiO_2$): $R_f$ = 0.48 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.57−7.34 (m, 10H), 5.27 (dd, $J$ = 5.3 Hz, 10.2 Hz, 1H), 3.74 (s, 3H), 3.24 (dd, $J$ = 10.2 Hz, 13.2 Hz, 1H), 3.09 (dd, $J$ = 5.3 Hz, 13.2 Hz, 1H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 172.4, 169.6, 137.6, 134.6, 129.2, 128.9, 128.8, 128.3, 127.2, 125.8, 78.6, 61.2, 53.5, 43.4. **3ab**-*trans*: TLC ($SiO_2$): $R_f$ = 0.51 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.57−7.34 (m, 10H) 5.55 (dd, $J$ = 5.3 Hz, 10.6 Hz, 1H), 3.84 (s, 3H), 3.61 (dd, $J$ = 5.3 Hz, 13.0 Hz, 1H), 2.58 (dd, $J$ = 10.6 Hz, 13.0 Hz, 1H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 172.0, 169.1, 138.0, 128.9, 128.7, 128.5, 126.9, 125.6, 78.7, 60.4, 53.9, 43.6 (two carbon atoms were overlapped).

*Synthesis of Methyl-2-carboxy-2-benzyl-4-phenyl-4-butanolide (3ac).*[13] 36 mg (0.12 mmol) of **3ac** as a colorless oil (39% yield: dr = 86:14). **3ac**-*cis*: TLC ($SiO_2$): $R_f$ = 0.51 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.33−7.25 (m, 6H), 7.20−7.17, (m, 2H), 6.96−6.94 (m, 2H), 5.45 (dd, $J$ = 6.3 Hz, 10.1 Hz, 1H), 3.87 (s, 3H), 3.43 (d, $J$ = 13.5 Hz, 2H), 3.34 (d, $J$ = 13.5 Hz, 1H), 2.90 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.20 (dd, $J$ = 10.1 Hz, 13.5 Hz, 1H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 173.8, 169.8, 138.5, 135.4, 130.3, 128.8, 128.7, 127.5, 125.8, 79.7, 57.8, 53.4, 39.2, 39.1 (one carbon atom was overlapped).

*Synthesis of Methyl-2-carboxy-2-benzyl-4-phenyl-4-butanolide (3ad).*[13] 64 mg (0.20 mmol) of **3ad** as a colorless oil (66% yield: dr = 12:88). **3ad**-*cis*: TLC ($SiO_2$): $R_f$ = 0.51 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43−7.17 (m, 10H), 5.52 (dd, $J$ = 7.3 Hz, 10.5 Hz, 1H), 3.72 (s, 3H), 2.88 (dd, $J$ = 8.2 HZ, 13.5 Hz, 1H), 2.87−2.69 (m, 3H), 2.41−2.25 (m, 2H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 174.2, 170.2, 140.5, 138.7, 128.9, 128.8, 128.7, 128.6, 128.4, 126.4, 125.5, 78.5, 77.3, 76.7, 55.2, 53.1, 40.3, 35.6, 31.1. **3ad**-*trans*: TLC ($SiO_2$): $R_f$ = 0.54 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.44−7.22 (m, 10H), 5.56 (dd, $J$ = 5.8 Hz, 10.4 Hz, 1H), 3.82 (s, 3H), 3.18 (dd, $J$ = 5.8 Hz, 13.2 Hz, 1H), 2.71 (dd, $J$ = 10.4 Hz, 13.2 Hz, 1H), 2.63−2.48 (m, 2H), 2.20−2.13 (m, 2H); $^{13}C\{^1H\}$-NMR: (125 MHz, $CDCl_3$): $\delta$ 173.7, 169.7, 140.3, 138.6, 128.9, 128.8, 128.6, 128.4, 126.4, 125.5, 79.3, 56.4, 53.3, 40.9, 36.4, 31.2.

*Synthesis of Ethyl-2-dicarboxy-4-phenyl-4-butanolide (3ae).* 29 mg (0.09 mmol) of **3ae** as a colorless oil (31% yield). **3ae**: TLC ($SiO_2$): $R_f$ = 0.48 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.44−7.35 (m, 5H), 5.49 (dd, $J$ = 6.3 Hz, 9.7 Hz, 1H), 4.38 (q, $J$ = 7.2 Hz, 14.0 Hz, 2H), 4.27 (q, $J$ = 7.3 Hz, 14.5 Hz, 2H), 3.27 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.91 (dd, $J$ = 9.7 Hz, 13.5 Hz, 1H), 1.36 (t, $J$ = 7.2 Hz, 14.0 Hz, 3H), 1.29 (t, $J$ = 7.3 Hz, 14.5 Hz, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 168.1, 165.4, 137.5, 129.0, 128.9, 125.7, 79.1, 63.4, 63.1, 39.9, 13.9, 13.8 (two carbon atoms were overlapped); HRMS: $m/z$ (DART) calcd for $C_{16}H_{18}O_6$ $(M + H)^+$ 307.1176, found 307.1186; FTIR: (neat): 2923, 2853, 1788, 1731, 1452, 1368, 1254, 1215, 1193, 1164, 1117, 1092, 1072, 1048, 1020, 999, 860, 763, 698 $cm^{-1}$.

*Synthesis of tert-Butyl-2-carboxy-2-methyl-4-phenyl-4-butanolide (**3af**).*[13] No reaction. **3af**-*cis*: TLC ($SiO_2$): $R_f$ = 0.61 ($^n$hexane/ethyl acetate = 4:1); mp: 57.5−58.7 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.41−7.33 (m, 5H), 5.56 (dd, $J$ = 6.3 Hz, 10.1 Hz, 1H), 3.04 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.08 (dd, $J$ = 10.1 Hz, 13.5 Hz, 1H), 1.52 (s, 9H), 1.48 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 175.4, 169.4, 138.9, 128.8, 128.6, 125.4, 83.2, 78.9, 52.8, 44.0, 29.6, 27.8, 20.7; HRMS: $m/z$ (DART) calcd for $C_{16}H_{21}O_4$ $(M + H)^+$ 277.1434, found 277.1425; FTIR: (neat): 2980, 2936, 1775, 1734, 1498, 1456, 1394, 1369, 1330, 1270, 1259, 1211, 1150, 1101, 1076, 1022, 1001, 940, 893, 845, 760, 698 $cm^{-1}$.

*Synthesis of 2-Acetyl-2-methyl-4-phenyl-4-butanolide (3ag).*[13] 26 mg (0.12 mmol) of **3ag** as a colorless oil (40% yield: dr = 38:62). **3ag**-*cis*: TLC ($SiO_2$): $R_f$ = 0.37 ($^n$hexane/ethyl acetate = 4:1); mp: 63.3−66.7 °C; $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.42−7.33 (m, 5H), 5.38 (dd, $J$ = 6.3 Hz, 10.4 Hz, 1H), 3.32 (dd, $J$ = 6.3 Hz, 13.0 Hz, 1H), 2.38 (s, 3H), 1.95 (dd, J = 10.4 Hz, 13.0 Hz, 1H), 1.60 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 203.2, 175.5, 138.8, 128.8, 128.7, 125.4, 79.2, 77.3, 76.7, 59.2, 41.2, 25.5, 21.4. **3ag**-*trans*: TLC ($SiO_2$): $R_f$ = 0.46 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.42−7.33 (m, 5H), 5.52 (dd, $J$ = 6.6 Hz, 9.2 Hz, 1H), 2.86 (dd, $J$ = 9.2 Hz, 13.5 Hz, 1H), 2.41 (dd, $J$ = 6.6 Hz, 13.5 Hz, 1H), 2.38 (s, 3H), 1.63 (s, 3H); $^{13}C\{^1H\}$NMR: (125 MHz, $CDCl_3$): $\delta$ 203.5, 176.1, 138.4, 128.8, 128.7, 125.4, 78.3, 77.3, 76.7, 57.2, 40.2, 25.9, 20.5.

*Radical Clock Experiments.* A Pyrex test tube (16.5 cm × 1.5 cm) containing a mixture of dimethyl 2-methylmalonate **2a**



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(44 mg, 0.30 mmol), $I_2$ (76 mg, 1.0 equiv, 0.30 mmol), sodium carbonate (32 mg, 1.0 equiv, 0.30 mmol) and 1-cyclopropyl-1-phenylethyrene (86 mg, 2.0 equiv, 0.60 mmol) in $^t$Butyl alcohol (2.0 mL) and $H_2O$ (1.0 mL) was degassed three times via FPT cycling and backfilled with Ar. The resulting solution was stirred at ambient temperature for 2 h. The reaction was quenched with sat. aq $Na_2S_2O_3$ and extracted with $Et_2O$ (10 mL × 3). The combined organic layers were washed with brine, dried over $Mg_2SO_4$, filtered and concentrated in vacuo. The resulting mixture was purified by flash column chromatography on silica gel ($^n$hexane/EtOAc = 100:0−20:1) to give **I** as a colorless oil (5% yield) and **II** as a yellow oil (42% yield). **I**[13]: TLC ($SiO_2$): $R_f$ = 0.35 ($^n$hexane); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ major 7.45−7.31 (m, 5H), 5.84 (t, $J$ = 6.9 Hz, 1H), 4.25 (s, 2H), 3.31 (t, $J$ = 7.5 Hz, 2H), 2.82 (dd, $J$ = 6.9 Hz, 7.5 Hz, 2H). minor 7.45−7.31 (m, 3H), 7.10 (d, $J$ = 6.9 Hz, 2H), 5.89 (t, $J$ = 7.5 Hz, 1H), 4.20 (s, 2H), 3.08 (t, $J$ = 6.9 Hz, 2H), 2.50 (q, $J$ = 6.9 Hz, 2H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ major 139.9, 139.2, 130.9, 128.5, 127.9, 126.1, 32.7, 2.8, 1.9. minor 140.9, 137.7, 129.9, 128.5, 128.4, 127.8, 33.0, 13.2, 4.2. **II**[13]: TLC ($SiO_2$): $R_f$ = 0.10 ($^n$hexane/ethyl acetate = 20:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ major 7.30−7.11 (m, 5H), 5.56 (t, $J$ = 6.9 Hz, 1H), 3.38 (s, 6H), 3.19 (s, 2H), 3.17 (t, $J$ = 6.9 Hz, 2H), 2.78 (q, $J$ = 6.9 Hz, 2H), 1.27 (s, 1H). $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ minor 7.30−7.11 (m, 3H), 7.10 (d, $J$ = 6.9 Hz, 2H), 5.48 (t, $J$ = 6.9 Hz, 1H), 3.73 (s, 6H), 3.07 (t, $J$ = 6.9 Hz, 2H), 3.04 (s, 2H), 2.48 (q, $J$ = 6.9 Hz, 2H), 1.31 (s, 1H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ major 172.1, 142.7, 137.9, 132.8, 127.9, 127. 2, 127.1, 53.1, 52.2, 34.9, 33.0, 19.8, 4.4. $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ minor 170.5, 139.1, 138.0, 131.1, 128.7, 127.9, 127.1, 53.1, 52.2, 45.8, 44.3, 32.5, 5.4.

*Reaction Using $H_2{}^{18}O$ Condition A.* **3aa′** as a yellow oil (98% yield: dr = 38:62, **3aa**: **3aa′** = 12:88). **3aa′** as a yellow oil (quant.: dr = 33:67, **3aa**: **3aa′** = 16:84). **3aa′**-*cis*: TLC ($SiO_2$): $R_f$ = 0.35 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43−7.36 (m, 5H), 5.52 (dd, $J$ = 6.9 Hz, 9.1 Hz, 1H), 3.74 (s, 3H), 2.85 (dd, $J$ = 9.1 Hz, 13.1 Hz, 1H), 2.56 (dd, $J$ = 6.9 Hz, 13.1 Hz, 1H), 1.64 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 175.3, 170.9, 138.3, 128.8, 125.6, 78.7, 53.1, 51.5, 42.9, 19.7; HRMS: $m/z$ (GC-MS) calcd for $C_{13}H_{14}O_3{}^{18}O$ (M) 236.0935, found 236.0924. **3aa′**-*trans*: TLC ($SiO_2$): $R_f$ = 0.41 ($^n$hexane/ethyl acetate = 4:1); $^1$H NMR: (500 MHz, $CDCl_3$): $\delta$ 7.43−7.34 (m, 5H), 5.59 (dd, $J$ = 6.3 Hz, 10.4 Hz, 1H), 3.84 (s, 3H), 3.11 (dd, $J$ = 6.3 Hz, 13.5 Hz, 1H), 2.12 (dd, $J$ = 10.4 Hz, 13.5 Hz, 1H), 1.59 (s, 3H); $^{13}$C{$^1$H}NMR: (125 MHz, $CDCl_3$): $\delta$ 174.8, 170.8, 138.5, 128.8, 128.7, 125.4, 78.9, 53.3, 52.0, 43.8, 20.9; HRMS: $m/z$ (GC-MS) calcd for $C_{13}H_{14}O_3{}^{18}O$ (M) 236.0935, found 236.0926.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.9b00333.

Experimental procedures, optimization studies, NMR spectra for novel compounds; general reaction set up (Figure S1); wave length and spectral irradiance of fluorescent lamp (Figure S2); optimization of reaction conditions (Table S1); reaction with radical scavenger (Scheme S1) (PDF)

X-ray data for **3ha** (CIF)

## ■ AUTHOR INFORMATION


### Corresponding Authors

*E-mail: yamaguchi@gifu-pu.ac.jp (E.Y.).
*E-mail: itoha@gifu-pu.ac.jp (A.I.).

### ORCID

Eiji Yamaguchi: 0000-0002-1167-8832
Akichika Itoh: 0000-0003-3769-7406



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The authors declare no competing financial interest.


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