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Asymmetric Allylation of 2-Oxocycloalkanecarboxylates

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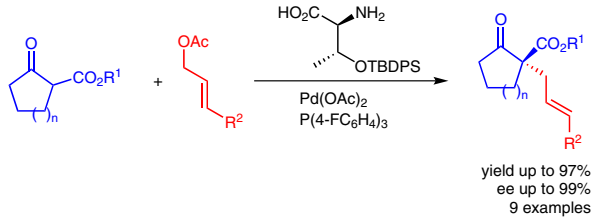

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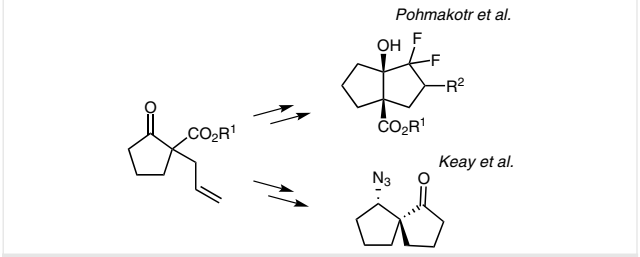
Abstract In this study, the highly enantioselective α-allylation of α-substituted β-ketoesters, particularly 2-oxocycloalkanecarboxylates, is achieved by synergistic catalysis with an achiral palladium complex and a chiral primary amino acid. Various α-allylated β-ketoesters containing a quaternary carbon stereogenic center are synthesized in high yields (up to 97%) with excellent enantioselectivity (up to 99% ee).

Key words allylation, amino acids, asymmetric catalysis, ketones, palladium

The stereoselective construction of quaternary carbon stereogenic centers is frequently required in the total synthesis of complex organic molecules, such as natural organic compounds; nevertheless, it remains one of the challenging topics in organic synthesis.[1,2] Furthermore, for accurately synthesizing a target molecule, it is imperative to introduce functional groups into synthetic intermediates, as well as for additional carbon–carbon bond formation reactions. For furnishing synthetic intermediates with a quaternary carbon stereogenic center and functional groups, the α-allylation of α-substituted β-ketoesters is attractive as both a quaternary carbon stereogenic center and multiple functional groups, such as carbonyl, alkoxycarbonyl, and allyl, are simultaneously obtained.[3] By employing 2-oxocycloalkanecarboxylates as β-ketoester substrates for allylation, synthetically useful 1-(prop-2-enyl)-2-oxocycloalkanecarboxylates, which can be converted into various complex cyclic compounds, such as fused-ring and spiro compounds, are obtained. For example, the groups of Pohmakotr[4] and Keay[5] have successfully synthesized bicyclo[3,3,0]octane and spiro[4.4]nonane, respectively, from 1-(prop-2-enyl)-2-oxocyclopentanecarboxylate (Scheme 1).[6] Hanessian et al. have reported the total synthesis of a calyciphylline B type alkaloid, isodaphlongamine H, using 1-(prop-2-enyl)-2-oxocyclopentanecarboxylate.[7] Thus, α-allylated β-ketoesters, particularly 1-(prop-2-enyl)-2-oxocycloalkanecarboxylates, are potentially attractive as synthetic intermediates. Although the asymmetric α-allylation of 2-oxocycloalkanecarboxylates is straightforward for obtaining 1-(prop-2-enyl)-2-oxocycloalkanecarboxylates in a stereoselective manner, it is still challenging to achieve allylation with high enantioselectivity by asymmetric catalysis.[8] Indeed, enantiopure 1-(prop-2-enyl)-2-oxocyclopentanecarboxylate is generally prepared by kinetic reduction of the racemate with baker's yeast.[6,7,9] Recently, we reported that synergistic catalysis using an achiral palladium complex and a chiral primary amino acid was effective for the asymmetric α-allylation of α-branched aldehydes, and a quaternary carbon stereogenic center possessing four substituents (allyl, alkyl, aryl, and formyl groups) was constructed with high enantioselectivity.[10–12] In this study, the α-allylation of α-substituted β-ketoesters, particularly 2-oxocycloalkanecarboxylates, via synergistic catalysis using an achiral palladium complex and a chiral primary amino acid is described.

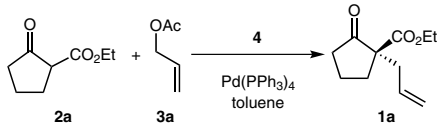


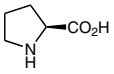
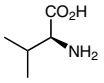
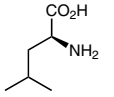
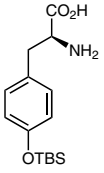
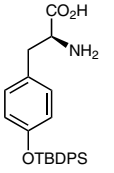
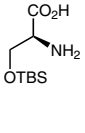
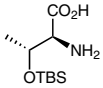
Scheme 1 Transformation of 1-(prop-2-enyl)-2-oxocyclopentanecarboxylate into bicyclo[3,3,0]octane and spiro[4.4]nonane

For optimizing the reaction conditions for the allylation, ethyl 2-oxocyclopentanecarboxylate (**2a**) and allyl acetate (**3a**) were chosen as model substrates. The screening of catalysts with amino acids **4** was performed in the presence of tetrakis(triphenylphosphine)palladium(0) [$Pd(PPh_3)_4$] in toluene at 25 °C, and Table 1 summarizes the results obtained. The reaction time was maintained constant at 16 hours for evaluating the activity of the amino acid catalysts. Allylation in the presence of a catalytic amount of naturally occurring amino acids, such as proline (**4a**), alanine (**4b**), valine (**4c**), leucine (**4d**), and phenylalanine (**4e**), afforded ethyl 1-(prop-2-enyl)-2-oxocyclopentanecarboxylate (**1a**) in 32–46% yields, albeit with very low enantioselectivity (0–5% ee). As allylation in the absence of an amino acid catalyst gave a similar result (46%, 0% ee), amino acids **4a–e** were not found to be effective as catalysts for allylation. The results with low enantioselectivity can be explained by the low solubility of amino acids **4a–e** in an organic solvent, as white solids due to the amino acids were observed in the reaction vessel at the end of each experiment. As expected, lipophilic primary amino acids **4f–k**, which contain a siloxy group in the side chain, afforded allylated product **1a** in moderate-to-good enantioselectivity.[13] Finally, the use of *O*-*tert*-butyldiphenylsilyl L-threonine (**4k**) as the catalyst afforded a better enantioselectivity compared with those observed for the other amino acids.

Next, the reaction conditions were optimized with respect to the amount of allyl acetate (**3a**), the reaction temperature, and the concentration of **2a** in toluene; Table 2 shows the results obtained. By decreasing the amount of **3a**, the enantioselectivity of the allylation was improved to 90% ee, although the reaction was slow (Table 2, entries 1 and 2). The concentration of the substrates in the solvent also affected the reaction rate, with the allylation proceeding at a more rapid rate in a reduced amount of the solvent (Table 2, entries 3 and 4). When the allylation was conducted at 40 °C, the reaction rate was improved without significant loss of the enantioselectivity, although the reaction terminated in a short time at 60 °C (Table 2, entries 5–7). Hence, further investigation of the allylation was conducted using **2a** (0.5 mmol) in toluene (0.6 mL) at 40 °C (Table 2, entry 6).

Table 1 Screening of Amino Acid Catalysts **4** for the Allylation of Ethyl 2-Oxocyclopentanecarboxylate (**2a**) with Allyl Acetate (**3a**) in the Presence of $Pd(PPh_3)_4$[a]



Amino acid catalyst **4**, yield of **1a**,[b] ee[c]		
none		
46%, 0% ee	**4a**, 32%, 2% ee	**4b**, 44%, 2% ee
		
4c, 44%, 2% ee	**4d**, 46%, 0% ee	**4e**, 46%, 5% ee
		
4f, 76%, 48% ee	**4g**, 72%, 60% ee	**4h**, 36%, 41% ee
		
4i, 54%, 52% ee	**4j**, 78%, 61% ee	**4k**, 66%, 64% ee

[a] The reaction was carried out with **2a** (0.5 mmol), **3a** (1.25 mmol), **4** (0.1 mmol), and $Pd(PPh_3)_4$ (0.025 mmol) in toluene (1 mL) at 25 °C for 16 h.
[b] Yield of isolated product **1a**.
[c] Determined by chiral HPLC analysis.

Table 2 Optimization of the Reaction Conditions Relative to the Amount of Allyl Acetate (**3a**), Reaction Temperature, and Concentration of Ketoester **2a** in Toluene[a]

Entry	Temp (°C)	Concn (M)[b]	Yield (%)[c]	ee (%)[d]
1[e]	25	0.50	66	64
2	25	0.50	41	90
3	25	0.83	86	78
4	25	1.30	84	76
5	40	0.50	52	85
6	40	0.83	91	87
7	60	0.83	23[f]	31

[a] Unless otherwise mentioned, the reaction was carried out with **2a** (0.5 mmol), **3a** (1.0 mmol), **4k** (0.1 mmol), and $Pd(PPh_3)_4$ (0.025 mmol) in toluene for 16 h.
[b] Concentration of **2a** in toluene. The amount of toluene used was 1.0 mL (0.50 M), 0.60 mL (0.83 M), and 0.40 mL (1.30 M).
[c] Yield of isolated product **1a**.
[d] Determined by chiral HPLC analysis.
[e] An increased amount of **3a** (1.25 mmol) was used.
[f] A large amount of unreacted **2a** remained.

Next, the screening of ligands on the palladium catalysts was conducted using palladium(II) acetate [$Pd(OAc)_2$] and various organophosphines; Table 3 shows the results obtained. The use of triphenylphosphine (PPh_3) with $Pd(OAc)_2$ furnished results similar to those obtained with $Pd(PPh_3)_4$, and the use of two equivalents of PPh_3 relative to $Pd(OAc)_2$ was found to be optimum (Table 3, entries 1–6). Although tris(*o*-tolyl)phosphine [$P(2\text{-}CH_3C_6H_4)_3$] and tris(pentafluorophenyl)phosphine [$P(C_6F_5)_3$] were not effective for allylation, tris(4-fluorophenyl)phosphine [$P(4\text{-}FC_6H_4)_3$] afforded

1a in 90% yield and 95% ee (Table 3, entries 7–9). Bidentate ligands such as 1,2-bis(diphenylphosphino)ethane (dppe), 1,3-bis(diphenylphosphino)propane (dppp), 1,4-bis(diphenylphosphino)butane (dppb), 1,1′-bis(diphenylphosphino)ferrocene (dppf), and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) furnished results that were worse than those obtained with the use of PPh_3 and $P(4\text{-}FC_6H_4)_3$ (Table 3, entries 10–14). As both racemic and chiral forms of BINAP furnished the same enantiomer with similar enantiomeric excess, the stereocontrol for the current allylation significantly depends on the chirality of the amino acid catalyst used (Table 3, entries 14–16). Thus, $P(4\text{-}FC_6H_4)_3$ was chosen as the ligand on the palladium catalyst for the allylation reactions.

Table 3 Screening of Ligands on the Palladium Catalyst for the Allylation of Ketoester **2a** with Allyl Acetate (**3a**) in the Presence of Amino Acid Catalyst **4k**[a]

Entry	Ligand (mol%)	Yield (%)[b]	ee (%)[c]
1[d]	none	91	87
2	none	nr	nd
3	PPh_3 (5)	trace	nd
4	PPh_3 (10)	94	86
5	PPh_3 (15)	92	87
6	PPh_3 (20)	81	88
7	$P(2\text{-}MeC_6H_4)_3$ (10)	nr	nd
8	$P(C_6F_5)_3$ (10)	nr	nd
9	$P(4\text{-}FC_6H_4)_3$ (10)	90	95
10	dppe[e] (5)	nr	nd
11	dppp[f] (5)	trace	nd
12	dppb[g] (5)	8	84
13	dppf[h] (5)	72	84
14	(±)-BINAP[i] (5)	44	57
15	(*R*)-BINAP (5)	60	66
16	(*S*)-BINAP (5)	44	60

[a] Unless otherwise mentioned, the reaction was carried out with **2a** (0.5 mmol), **3a** (1.0 mmol), **4k** (0.1 mmol), and $Pd(OAc)_2$ (0.025 mmol) in toluene (0.6 mL) at 40 °C for 16 h.
[b] Yield of isolated product **1a**. nr = no reaction.
[c] Determined by chiral HPLC analysis. nd = not determined.
[d] $Pd(PPh_3)_4$ was used instead of $Pd(OAc)_2$.
[e] 1,2-Bis(diphenylphosphino)ethane.
[f] 1,3-Bis(diphenylphosphino)propane.
[g] 1,4-Bis(diphenylphosphino)butane.
[h] 1,1′-Bis(diphenylphosphino)ferrocene.
[i] 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl.

Finally, the substrate scope of the present allylation was investigated; Table 4 shows the results obtained. By decreasing the reaction temperature from 40 °C to 25 °C, higher enantioselectivity was observed, albeit the reaction took a longer time for completion, and the allylation of **2a** with **3a** afforded **1a** in 92% yield and with 98% ee (Table 4, entries 1 and 2). The effect of the alkoxycarbonyl group of 2-oxocyclopentanecarboxylates **2a–c** on the allylation was investigated, and the results indicated that the bulkiness of the alkoxycarbonyl group did not significantly affect the yields and enantiomeric excesses of the allylated products **1a–c** (Table 4, entries 2–4). On the other hand, the structures of the β-ketoesters **2** significantly affected their reactivity. For example, cyclohexanonecarboxylate **2d**, which has a ring size greater than that of cyclopentanone, required a reaction time longer than that required by **2a** (Table 4, entry 5). By increasing the catalyst loading of the Pd complex, the reaction time was considerably reduced (Table 4, entry 6),[14] and cycloheptanonecarboxylate **2e** also afforded allylated product **1e** in high yield and with excellent enantioselectivity (Table 4, entry 7). The allylation of an acyclic β-ketoester, ethyl 2-methyl-3-oxobutanoate (**2f**), was very sluggish, affording allylated product **1f** in 42% yield, with a significant amount of unreacted substrates even when the reaction was conducted for 120 hours with an increased catalyst loading of the Pd complex (Table 4, entry 8). Next, the effect of the α-substituents of β-ketoesters **2f–h** on the allylation was investigated, and the results indicated that the allylation was sensitive to steric hindrance at the α-carbon atom (Table 4, entries 8–10). Although the allylation of 2-ethoxycarbonyl-1-indanone (**2i**) using **3a** afforded allylated product **1i** in 87% yield, no enantioselectivity was observed (Table 4, entry 11). The reaction between aromatic ketones and the amino acid catalyst probably afforded insufficient enamine, which is a possible intermediate in the allylation.[15] The current allylation of **2a** can be applied to the reaction with *trans*-cinnamyl acetate (**3b**), affording the corresponding allylated product **1j** in high yield and with excellent enantioselectivity (Table 4, entry 12).

By comparing the spectroscopic data with those reported previously, both cyclic product **1a** and acyclic product **1f** were found to be *R*-enantiomers.[16] With these results, a plausible mechanism was proposed for the stereocontrol of the allylation (Scheme 2). By the formation of an intramolecular hydrogen bond between NH and CO, enamine **Im-1**, generated from β-ketoester **2** and amino acid **4k**, possibly adopts *Z*-geometry. Next, the acetate ion of a π-allylpalladium complex, generated from $Pd(OAc)_2$, $P(4\text{-}FC_6H_4)_3$, and allyl acetate **3a**, is exchanged with the carboxyl group of **Im-1**, affording **Im-2**.[10,17] As the *Re*-face of the α-carbon atom of the enamine comes closer to the π-allylpalladium moiety as compared to the *Si*-face, allylation predominantly occurs at the *Re*-face, furnishing an *R*-enantiomer.

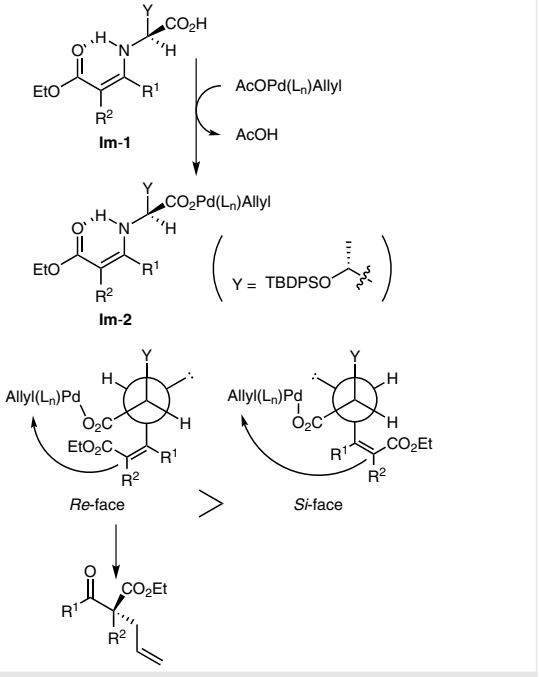
In conclusion, a primary amino acid, *O*-TBDPS L-threonine (**4k**), is an effective asymmetric catalyst for the α-allylation of α-substituted β-ketoesters, particularly 2-oxocycloalkanecarboxylates. Allylation proceeds under mild reaction conditions, furnishing various α-allylated β-ketoesters possessing a quaternary carbon stereogenic center in high yields and with excellent enantioselectivities.

Table 4 Substrate Scope[a]

2 3 1

Entry	Ketoester	Allyl acetate	Time (h)	Product	Yield (%)[b]	ee (%)[c]
1[d]	**2a** [R^1–R^2 = $(CH_2)_3$, R^3 = Et]	**3a** (R^4 = H)	16	**1a**	90	95
2	**2a** [R^1–R^2 = $(CH_2)_3$, R^3 = Et]	**3a** (R^4 = H)	24	**1a**	92	98
3	**2b** [R^1–R^2 = $(CH_2)_3$, R^3 = Me]	**3a** (R^4 = H)	24	**1b**	96	98
4	**2c** [R^1–R^2 = $(CH_2)_3$, R^3 = Bn]	**3a** (R^4 = H)	24	**1c**	97	98
5	**2d** [R^1–R^2 = $(CH_2)_4$, R^3 = Et]	**3a** (R^4 = H)	120	**1d**	87	96
6[e]	**2d** [R^1–R^2 = $(CH_2)_4$, R^3 = Et]	**3a** (R^4 = H)	72	**1d**	91	96
7[e]	**2e** [R^1–R^2 = $(CH_2)_5$, R^3 = Et]	**3a** (R^4 = H)	120	**1e**	86	99
8[e]	**2f** (R^1 = R^2 = Me, R^3 = Et)	**3a** (R^4 = H)	120	**1f**	42	94
9	**2g** (R^1 = Me, R^2 = Ph, R^3 = Et)	**3a** (R^4 = H)	72	**1g**	nr	nd
10	**2h** (R^1 = Me, R^2 = H, R^3 = Et)	**3a** (R^4 = H)	72	**1h**	73	nd
11[e]	**2i** (2-CO_2Et-1-indanone)	**3a** (R^4 = H)	240	**1i**	87	0
12[e]	**2a** [R^1–R^2 = $(CH_2)_3$, R^3 = Et]	**3b** (R^4 = Ph)	144	**1j**	84	98

[a] Unless otherwise mentioned, the reaction was carried out with **2** (0.5 mmol), **3** (1.0 mmol), **4k** (0.1 mmol), $Pd(OAc)_2$ (0.025 mmol), and $P(4\text{-}FC_6H_4)_3$ (0.05 mmol) in toluene (0.6 mL) at 25 °C.
[b] Yield of isolated product **1**. nr = no reaction.
[c] Determined by chiral HPLC analysis. nd = not determined.
[d] The reaction was carried out at 40 °C.
[e] Increased amounts of $Pd(OAc)_2$ (0.05 mmol) and $P(4\text{-}FC_6H_4)_3$ (0.10 mmol) were used.



Scheme 2 A plausible mechanism for the stereocontrol

Ketoesters **2a**,**b**,**d**,**f**,**h** were purchased and used after distillation; ketoesters **2c**,[18a] **2e**,[18b] **2g**,[18c] and **2i**[18d] were synthesized according to literature procedures. Allyl acetates **3a**,**b** were purchased and used after distillation. Amino acids **4a**–**e** were purchased and used without purification. *O*-Silylated L-tyrosines **4f**,**g**, L-serines **4h**,**i**, and L-threonines **4j**,**k** were synthesized according to the literature.[13] Palladium catalysts and phosphine ligands were purchased and used without purification. Purification of the products was accomplished by column chromatography on Kanto Chemical Co., Inc. Silicagel 60N (spherical, neutral; 63–210 μm). Specific rotations were measured using a HORIBA SEPA-500 polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JNM-ECS400 FT NMR spectrometer. Chemical shifts (δ) are referenced with respect to TMS as an internal standard. HPLC was carried out using a JASCO PU-2089 Plus intelligent pump and a UV-2075 Plus UV detector.

Ethyl (*R*)-1-(Prop-2-enyl)-2-oxocyclopentanecarboxylate (1a); Typical Procedure

To a 7 mL vial were added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $P(4\text{-}FC_6H_4)_3$ (15.6 mg, 0.05 mmol), *O*-TBDPS L-threonine (**4k**) (35.7 mg, 0.1 mmol) and toluene (0.6 mL). After the mixture became homogeneous, allyl acetate (**3a**) (100 mg, 1 mmol) and ethyl 2-oxocyclopentanecarboxylate (**2a**) (78 mg, 0.5 mmol) were added and the mixture was stirred for 24 h at 25 °C. The resulting mixture was filtered through a small plug of silica gel, eluted with Et_2O (4 × 1 mL) and concentrated under reduced pressure. Ethyl (*R*)-1-(prop-2-enyl)-2-oxocyclopentanecarboxylate (**1a**) was isolated by column chromatography (silica gel, hexane–Et_2O, 9:1). The enantioselectivity was determined by chi-

ral HPLC analysis. The absolute configuration was determined by comparison of the specific rotation with that reported in the literature.[6a] Spectroscopic data are in agreement with the published data.[4]

Yield: 90.2 mg (92%); colorless oil; $[\alpha]_{589}^{24}$ –38.4 (*c* 1.0, $CHCl_3$); ee = 98%; R_f = 0.43 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 1.83–2.06 (m, 3 H), 2.17–2.26 (m, 1 H), 2.31–2.47 (m, 3 H), 2.62–2.67 (m, 1 H), 4.11–4.17 (m, 2 H), 5.06–5.10 (m, 2 H), 5.61–5.72 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 29.6, 32.2, 37.9, 38.2, 60.0, 61.5, 119.2, 133.1, 171.0, 214.8.

Methyl (*R*)-1-(Prop-2-enyl)-2-oxocyclopentanecarboxylate (1b)

Spectroscopic data are in agreement with the published data.[19a]

Yield: 87.4 mg (96%); colorless oil; $[\alpha]_{589}^{24}$ –51.7 (*c* 1.0, $CHCl_3$); ee = 98%; R_f = 0.46 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85–2.04 (m, 3 H), 2.18–2.27 (m, 1 H), 2.32–2.49 (m, 3 H), 2.62–2.68 (m, 1 H), 3.69 (s, 3 H), 5.06–5.11 (m, 2 H), 5.61–5.71 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6, 32.2, 38.0, 38.2, 52.7, 60.1, 119.3, 133.0, 171.4, 214.7.

Benzyl 1-(Prop-2-enyl)-2-oxocyclopentanecarboxylate (1c)

Spectroscopic data are in agreement with the published data.[19b]

Yield: 125.1 mg (97%); colorless oil; $[\alpha]_{589}^{24}$ –27.0 (*c* 1.0, $CHCl_3$); ee = 98%; R_f = 0.51 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84–2.03 (m, 3 H), 2.18–2.27 (m, 1 H), 2.32–2.49 (m, 3 H), 2.65–2.70 (m, 1 H), 5.04–5.09 (m, 2 H), 5.13 (s, 2 H), 5.60–5.71 (m, 1 H), 7.28–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6, 32.2, 37.9, 38.2, 60.0, 67.2, 119.3, 128.0, 128.4, 128.7, 133.0, 135.7, 170.9, 214.5.

Ethyl (*R*)-1-(Prop-2-enyl)-2-oxocyclohexanecarboxylate (1d)

Spectroscopic data are in agreement with the published data.[8g]

Yield: 95.6 mg (91%); colorless oil; $[\alpha]_{589}^{24}$ +130.3 (*c* 1.0, $CHCl_3$); ee = 96%; R_f = 0.31 (*n*-hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.2 Hz, 3 H), 1.40–1.48 (m, 1 H), 1.55–1.78 (m, 3 H), 1.96–2.03 (m, 1 H), 2.28–2.34 (m, 1 H), 2.42–2.49 (m, 3 H), 2.57–2.62 (m, 1 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 5.00–5.04 (m, 2 H), 5.67–5.78 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.6, 27.6, 35.9, 39.4, 41.2, 60.9, 61.3, 118.4, 133.4, 171.6, 207.7.

Ethyl 1-(Prop-2-enyl)-2-oxocycloheptanecarboxylate (1e)

Spectroscopic data are in agreement with the published data.[19c]

Yield: 96.3 mg (86%); colorless oil; $[\alpha]_{589}^{24}$ +85.1 (*c* 1.0, $CHCl_3$); ee = 99%; R_f = 0.69 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.2 Hz, 3 H), 1.34–1.43 (m, 1 H), 1.58–1.81 (m, 6 H), 2.04–2.12 (m, 1 H), 2.29–2.47 (m, 2 H), 2.61–2.75 (m, 2 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 5.02–5.06 (m, 2 H), 5.65–5.76 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 24.6, 25.6, 30.0, 32.1, 39.7, 42.2, 61.3, 62.9, 118.7, 133.7, 172.1, 209.3.

(*R*)-3-Ethoxycarbonyl-3-methylhex-5-en-2-one (1f)

Spectroscopic data are in agreement with the published data.[3d,e]

Yield: 38.6 mg (42%); colorless oil; $[\alpha]_{589}^{24}$ +23.7 (*c* 1.0, $CHCl_3$); ee = 94%; R_f = 0.37 (*n*-hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 3 H), 1.30 (s, 3 H), 2.13 (s, 3 H), 2.45–2.64 (m, 2 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 5.05–5.10 (m, 2 H), 5.57–5.68 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 19.0, 26.3, 39.4, 59.5, 61.5, 119.1, 132.7, 172.6, 205.2.

3-Ethoxycarbonylhex-5-en-2-one (1h)

Spectroscopic data are in agreement with the published data.[19d]

Yield: 62.1 mg (73%); colorless oil; R_f = 0.23 (*n*-hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.0 Hz, 3 H), 2.24 (3H s), 2.58–2.62 (m, 2 H), 3.53 (t, *J* = 7.6 Hz, 1 H), 4.17 (m, 2 H), 5.03–5.13 (m, 2 H), 5.70–5.80 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 29.2, 32.3, 59.3, 61.5, 117.6, 134.3, 169.3, 202.7.

2-Ethoxycarbonyl-2-(prop-2-enyl)-1-indanone (1i)

Spectroscopic data are in agreement with the published data.[8e]

Yield: 106.1 mg (87%); colorless oil; R_f = 0.51 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.0 Hz, 3 H), 2.58–2.92 (m, 2 H), 3.12–3.67 (m, 2 H), 4.14–4.20 (m, 2 H), 5.03–5.16 (m, 2 H), 5.59–5.70 (m, 1 H), 7.38–7.78 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 36.1, 39.2, 60.1, 61.8, 119.4, 124.8, 126.5, 127.8, 132.9, 135.3, 135.5, 153.2, 170.8, 202.3.

Ethyl 1-(3-Phenylprop-2-enyl)-2-oxocyclopentanecarboxylate (1j)

Spectroscopic data are in agreement with the published data.[4]

Yield: 114.2 mg (84%); colorless oil; $[\alpha]_{589}^{24}$ –60.6 (*c* 1.0, $CHCl_3$); ee = 98%; R_f = 0.54 (*n*-hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.2 Hz, 3 H), 1.86–2.08 (m, 3 H), 2.19–2.29 (m, 1 H), 2.39–2.55 (m, 3 H), 2.78–2.83 (m, 1 H), 4.14–4.20 (m, 2 H), 6.08 (dt, *J* = 7.2, 16.0 Hz, 1 H), 6.44 (d, *J* = 16.0 Hz, 1 H), 7.18–7.33 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 19.7, 32.3, 37.1, 38.2, 60.4, 61.6, 124.6, 126.3, 127.5, 128.6, 134.2, 137.1, 171.1, 214.9.

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Supporting Information

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