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Palladium-Catalyzed Asymmetric Formal [3+2] Cycloaddition of Vinyl Cyclopropanes and β,γ-Unsaturated α-Keto Esters: An Effective Route to Highly Functionalized Cyclopentanes

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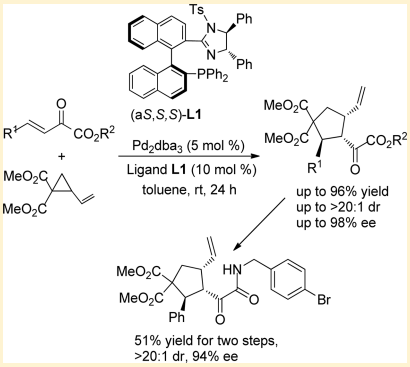
Supporting Information

ABSTRACT: Palladium-catalyzed asymmetric formal [3+2] cycloaddition of vinyl cyclopropanes and β,γ-unsaturated α-keto esters proceeded smoothly in the presence of chiral imidazoline−phosphine ligands to give the corresponding highly functionalized cyclopentanes in good yields along with high diastereo- and enantioselectivities under mild conditions.

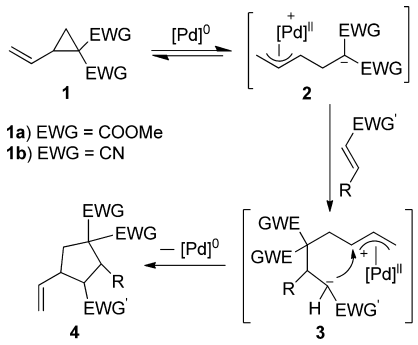


INTRODUCTION

Cyclopentanes containing multiple stereocenters have been widely used as important building blocks in pharmaceuticals, agrochemicals, and materials.[1] The development of asymmetric synthetic methodologies for producing highly functionalized cyclopentanes is highly desirable. An effective method used to synthesize this interesting scaffold would be a metal-catalyzed asymmetric formal [3+2] cycloaddition between 1,3-dipolar species and an electron-deficient olefin.

Recently, as a new family of "three-carbon-atom" precursors for asymmetric cycloadditions, vinyl cyclopropanes bearing electron-withdrawing groups have attracted much attention.[2] By generating 1,3-dipolar equivalents in the presence of Pd(0) catalysts and subsequent trapping with a dipolarophile such as olefins,[2e] isocyanates,[3,4] carbodiimides,[5] aldehydes,[6] and azlactone,[2g] vinyl cyclopropanes can provide direct routes to different substituted five-membered rings. The pioneering work on this topic has been explored by Tsuji and co-workers (Scheme 1).[2e] The cycloaddition reaction proceeded via zwitterionic (π-allyl) palladium intermediate **2**, generated by ring-opening of vinylcyclopropane **1** in the presence of Pd(0) catalyst, followed by the reaction with the electron-deficient olefin to give intermediate **3**, which undergoes intramolecular nucleophilic attack, producing the five-membered product **4**. Later, in a related process, Johnson and co-workers showed Pd(0)-catalyzed [3+2] cycloaddition of vinylcyclopropane **1** with aldehydes to afford 2,5-*cis*-disubstituted tetrahydrofuran derivatives in high yields and diastereoselectivities.[6a] Afterward,

Scheme 1. Palladium-Catalyzed Cycloaddition of Vinyl Cyclopropanes 1 with Electron-Deficient Olefins[a]



[a]EWG = electron-withdrawing groups.

Stoltz et al. reported a palladium-catalyzed addition of vinylcyclopropane **1** with a β-nitrostyrene to rapidly assemble the cyclopentane core of *Melodinus* alkaloids.[7] At the same time, Trost et al. introduced palladium-catalyzed [3+2] cycloaddition of vinyl cyclopropanes with alkylidene azlactones to afford the corresponding cyclopentanes bearing three stereogenic centers in good yields and good enantio- and diastereoselectivities.[2g] All these findings aroused our interest in

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exploring Pd(0)-catalyzed [3+2] cycloaddition of vinylcyclopropanes **1** with other types of activated olefins.

We previously reported the development of novel chiral imidazoline−phosphines **L1**−**L5** with a 1,1′-binaphthalene framework as new types of N,P ligands in both palladium-catalyzed asymmetric allylic alkylation[8a] and zinc(II)-catalyzed Mannich-type difluorination of hydrazones with difluoroenoxysilanes,[8b] affording the corresponding products with good results (Figure 1). Since these chiral imidazoline−-phosphine--

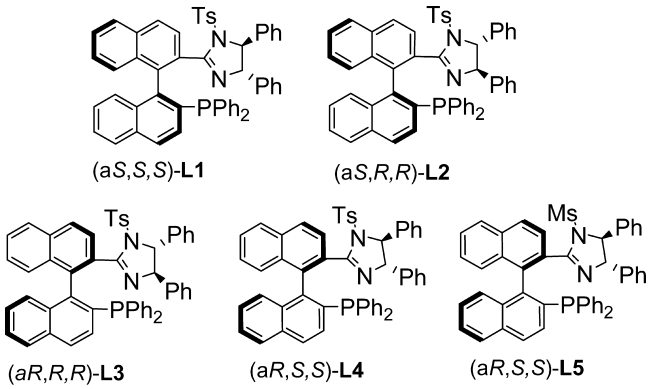


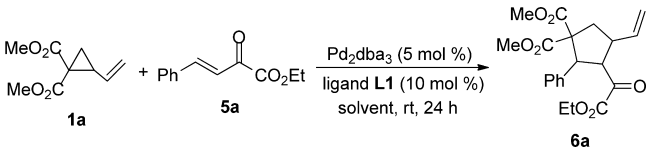
Figure 1. Novel chiral imidazoline−phosphine-type ligands.

palladium(II) complexes are efficient catalysts for asymmetric allylic alkylation reactions, we envisaged using these new chiral ligands in Pd(0)-catalyzed ring-opening of **1** and the subsequent cycloaddition with β,γ-unsaturated α-keto esters.

RESULTS AND DISCUSSION

Initial examinations using dimethyl 2-vinylcyclopropane-1,1-dicarboxylate (**1a**) and (*E*)-ethyl 2-oxo-4-phenylbut-3-enoate (**5a**) as the model substrates in the presence of chiral imidazoline−phosphine-type ligand (a*S*,*S*,*S*)-**L1** and $Pd_2(dba)_3$ were aimed at screening the optimal conditions, and the results of these experiments are summarized in Table 1. Delightfully,

Table 1. Screening of Solvents and Concentration for Pel-Catalyzed [3+2] Cycloaddition



entry[a]	solvent	yield [%][b]	dr[c]	ee [%][d]
1a	toluene	67	13:1	92
2	THF	72	11:1	90
3	CH_3CN	64	4:1	68
4	DCM	49	5:1	51
5	DMF	70	3:1	80
6	DMSO	88	2:1	74
7	Et_2O	75	3:1	80
8[e]	toluene	93	19:1	92

[a]The reaction was conducted with **1a** (0.1 mmol) and **5a** (0.15 mmol) in solvent (1.0 mL). [b]Isolated yield. [c]The diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [d]The ee values were determined by chiral HPLC on Chiralcel IC. [e]The reaction was conducted with **1a** (0.1 mmol) and **5a** (0.15 mmol) in solvent (0.5 mL).

dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate (**6a**) was obtained in 67% yield, with 13:1 dr and 92% ee in toluene (Table 1, entry 1). The examination of solvent effects revealed that the reaction in toluene provided a higher diastereoselectivity and better enantiomeric excess than those in tetrahydrofuran (THF), acetonitrile (CH_3CN), dichloromethane (DCM), *N*,*N*-dimethyl formamide (DMF), dimethyl sulfoxide (DMSO), or diethyl ether (Et_2O), albeit in a slightly lower yield (Table 1, entry 1 vs 2−7). Raising the concentration of reaction mixtures from 0.1 to 0.2 M in toluene at room temperature afforded the corresponding product **6a** in 93% yield, along with 19:1 dr and 92% ee (Table 1, entry 8).

Using toluene as solvent, other chiral ligands were screened, and the results are shown in Table 2. Ligands (a*S*,*R*,*R*)-**L2** and (a*R*,*S*,*S*)-**L4** provided the product **6a** in 26% and 31% yields along with 77% and −78% ee values as well as 2:1 dr, respectively (Table 2, entries 1 and 3). Ligand (a*R*,*R*,*R*)-**L3** afforded the product **6a** in 90% yield along with 90% ee and 10:1 dr as well as opposite absolute configuration (Table 2, entry 2). Meanwhile, ligand (a*R*,*S*,*S*)-**L5** afforded the product **6a** in 23% yield, along with −69% ee and 2:1 dr (Table 2, entry 4). For comparison, we also examined the chiral phosphine−oxazoline ligands **L6** and **L7** in this reaction under identical conditions.[9] The use of chiral phosphine−oxazoline ligand (a*R*,*S*)-**L6** resulted in a low yield and poor diastereoselectivity and enantioselectivity (Table 2, entry 5), while ligand (a*S*,*S*)-**L7** afforded **6a** in 93% yield with poor dr and low ee value, suggesting that axially chiral imidazoline−phosphine ligand **L1** was the best ligand for this reaction (Table 2, entry 6). As compared with the opposite ee values using (a*S*,*S*,*S*)-**L1**, (a*S*,*R*,*R*)-**L2**, and (a*S*,*S*)-**L7** with (a*R*,*R*,*R*)-**L3**, (a*R*,*S*,*S*)-**L4**, (a*R*,*S*,*S*)-**L5**, and (a*R*,*S*)-**L6**, we found that the absolute configuration of product **6a** is determined by the axial chirality of the ligands.

The substrate scope was next investigated under the optimized conditions, and the results are shown in Table 3. When R^1 is an electron-rich aromatic ring, the reactions proceeded smoothly to give the corresponding cyclopentanes **6b**, **6c**, and **6g**−**6k** in good yields with excellent diastereoselectivities and 90−98% ee values, respectively (Table 3, entries 1, 2, and 6−10). However, when R^1 is an electron-deficient aromatic ring, the corresponding adducts **6d** and **6e** were obtained in moderate yields along with relatively lower ee values, although the diastereoselectivities were excellent (Table 3, entries 3 and 4). Moreover, when R^1 is a strongly electron-deficient aromatic ring such as *para*-$NO_2C_6H_4$, no desired product was observed, presumably due to the electronic effect. Upon changing R^1 to heteroaromatic groups (R^1 = 2-furan, 2-thiophene) or a sterically bulky 2-naphthalene moiety, the reactions also proceeded efficiently to afford the corresponding products **6l**−**6n** in 87−90% yields with good diastereoselectivities and 90% ee values (Table 3, entries 11−13). Replacing the aromatic group with a cyclopropyl group provided the corresponding product **6o** in 83% yield along with >20:1 dr and 96% ee value (Table 3, entry 14). The other β,γ-unsaturated α-keto esters such as isopropyl, *tert*-butyl, or benzyl esters are also suitable substrates for this asymmetric [3+2] cycloaddition, giving the corresponding products **6p**−**6r** in 71−87% yields along with 13:1 to >20:1 dr and 87−94% ee values (Table 3, entries 15−17).

To illustrate the generality of the Pd(0)/**L1** catalytic system, the other activated olefin **7** and vinyl cyclopropane **1b** were

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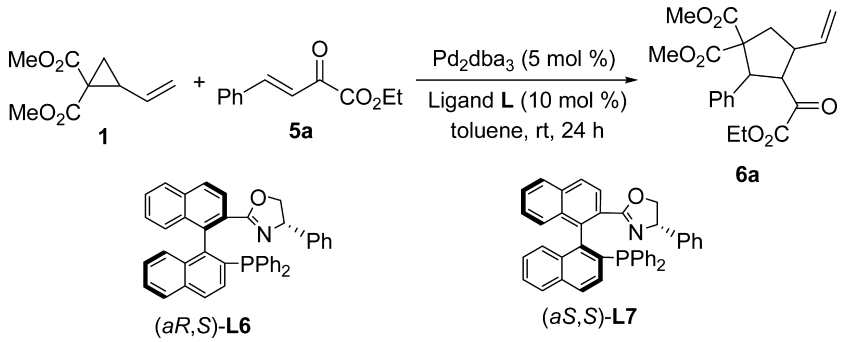
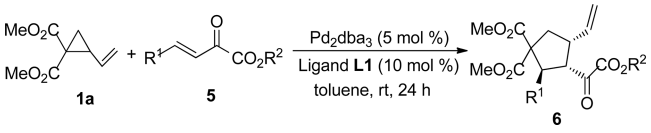
Table 2. Optimization of Ligand for Pd-Catalyzed Asymmetric Formal [3+2] Cycloaddition



entry[a]	ligand	yield [%][b]	dr[c]	ee [%][d]
1	**L2**	26	2:1	77
2	**L3**	77	10:1	−90
3	**L4**	31	2:1	−78
4	**L5**	23	2:1	−69
5	**L6**	34	1:1	−50
6	**L7**	93	2:1	7

[a]The reaction was conducted with **1a** (0.1 mmol) and **5a** (0.15 mmol) in solvent (0.5 mL). [b]Isolated yield. [c]The diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [d]The ee values were determined by chiral HPLC on Chiralcel IC.

Table 3. Substrate Scope for Pd/L1-Catalyzed Asymmetric Formal [3+2] Cycloaddition



entry[a]	R^1	R^2	yield [%][b]	dr[c]	ee [%][d]
1	4-MeC_6H_4, **5b**	Et	**6b**, 95	>20:1	94
2	4-$MeOC_6H_4$, **5c**	Et	**6c**, 96	>20:1	94
3	4-BrC_6H_4, **5d**	Et	**6d**, 52	16:1	88
4	4-ClC_6H_4, **5e**	Et	**6e**, 61	>20:1	82
5	4-$NO_2C_6H_4$, **5f**	Et	**6f**, 0	n.d.	n.d.
6	2-$MeOC_6H_4$, **5g**	Et	**6g**, 96	>20:1	98
7	3-$MeOC_6H_4$, **5h**	Et	**6h**, 86	17:1	92
8	3-MeC_6H_4, **5i**	Et	**6i**, 97	>20:1	90
9	2,5-$(MeO)_2C_6H_3$, **5j**	Et	**6j**, 90	>20:1	98
10	3,4,5-$(MeO)_3C_6H_2$, **5k**	Et	**6k**, 88	14:1	90
11	2-thiophene, **5l**	Et	**6l**,90	>20:1	90
12	2-furyl, **5m**	Et	**6m**, 90	10:1	90
13	2-naphthyl, **5n**	Et	**6n**, 87	>20:1	90
14	cyclopropyl, **5o**	Et	**6o**, 83	>20:1	96
15	C_6H_5, **5p**	*i*Pr	**6p**, 87	17:1	87
16	C_6H_5, **5q**	*t*Bu	**6q**, 86	>20:1	94
17	C_6H_5, **5r**	Bn	**6r**, 71	13:1	92

[a]The reaction was conducted with **1a** (0.1 mmol) and **5** (0.15 mmol) in solvent (0.5 mL). [b]Isolated yield. [c]The diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [d]The ee values were determined by chiral HPLC on Chiralcel IC.

used as the substrates and examined under the standard conditions, respectively (Scheme 2). Notably, the desired products **8a** and **8b** were also obtained in 72% and 94% yields, 16:1 and >20:1 dr values, and 97% and 82% ee values. Moreover, the absolute configurations of **8a** and **8b** have been assigned by their X-ray diffraction as 2*S*, 3*S*, 4*R*. The ORTEP drawings of **8a** and **8b** together with their CIF data are summarized in the Supporting Information.[10]

The product **6q** could be easily converted into compound **9** through hydrolysis and condensation with 4-bromobenzylamine in 51% yield after two steps along with a 94% ee value as well as >20:1 dr value (Scheme 3). X-ray diffraction analysis of compound **9** showed that its absolute configuration is 2*S*, 3*S*, 4*R*, which is consistent with **8a** and **8b**. Accordingly, the product **6q** has the 2*S*, 3*S*, 4*R* absolute configuration. With the same sign of the optical rotation of products **6a**−**6p** and **6r** as that of **6q**, we concluded that products **6a**−**6r** also have the 2*S*, 3*S*, 4*R* absolute configuration. However, since the minor diastereoisomer of **6** cannot be separated by silica gel column chromatography, its absolute configuration is unable to be determined at the present stage. The ORTEP drawings of **9** together with the CIF data are summarized in the Supporting Information.[10]

To explain the observed stereoselectivity, we tentatively propose a mechanistic model in Scheme 4 based on the previous mechanistic studies by Tsuji[2e] and Trost.[2g] First, an activated zwitterionic (π-allyl) palladium intermediate, **10**, is initially associated through ring-opening of vinylcyclopropane **1** in the presence of a chiral imidazoline−phosphine (**L1**)−palladium(II) complex during the reaction. Then, attack of malonate anion onto the β,γ-unsaturated α-keto ester provides another (π-allyl) palladium complex, **11**. Finally, the observed major diastereomer **6a** was obtained by the attack of the carbon anion of the α-keto ester to the backside of the in situ generated (π-allyl) palladium complex **11**.

In summary, an efficient palladium-catalyzed diastereo- and enantioselective formal [3+2] cycloaddition reaction of vinyl cyclopropanes with β,γ-unsaturated α-keto esters has been developed, affording functionalized cyclopentanes containing multiple stereocenters in good to excellent yields with good to excellent diastereo- and enantioselectivities under mild conditions in the presence of chiral imidazoline−phosphine ligand (a*S*,*S*,*S*)-**L1**. This newly developed chiral ligand is crucial for this reaction. A reversal of enantioselectivity was also observed in this reaction when ligand (a*R*,*R*,*R*)-**L3** was used instead of **L1**. Further investigations on the substrate scope as well as the applications of the protocol are in progress.

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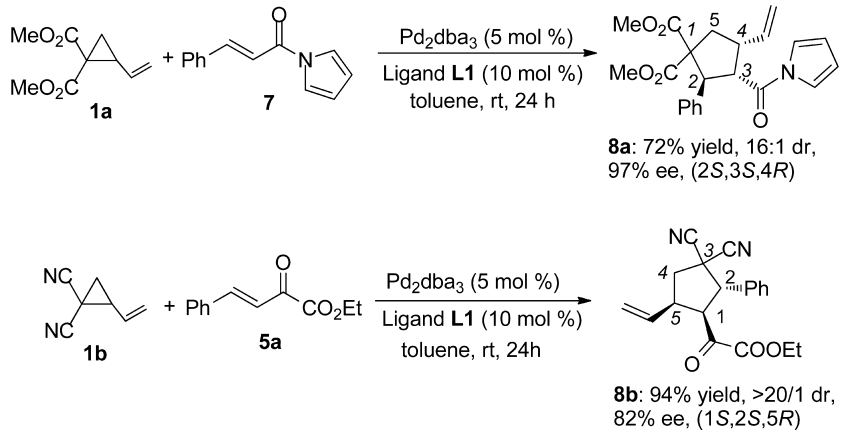
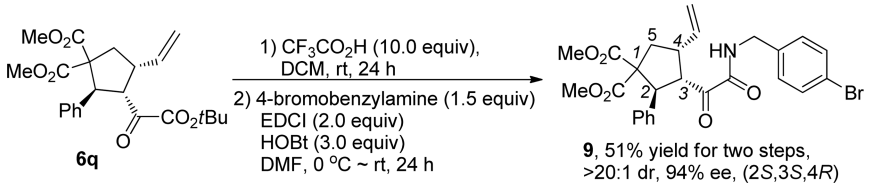
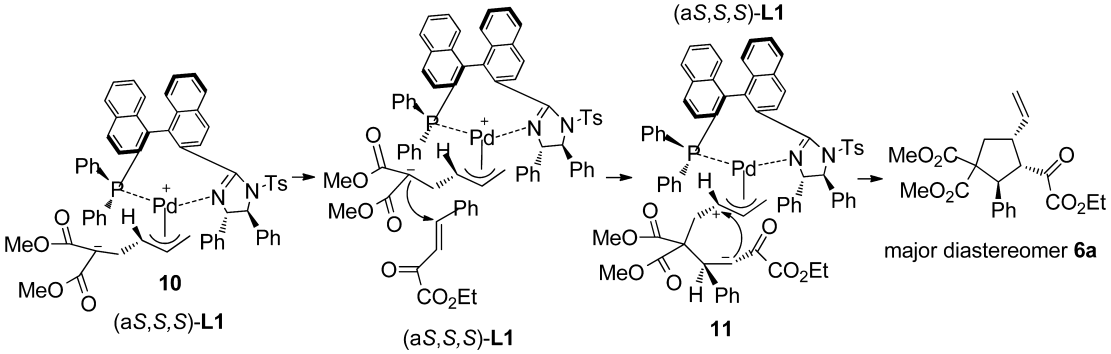
Scheme 2. Pd/L1-Catalyzed Asymmetric [3+2] Cycloaddition of ther Vinyl Cyclopropanes and Electron-Deficient Olefins



Scheme 3. Transformation of the Cycloadduct for X-ray Crystallographic Analysis



Scheme 4. Proposed Mechanistic Model



EXPERIMENTAL SECTION

General Remarks. Melting point was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Optical rotations were determined in a solution of $CHCl_3$ or CH_2Cl_2 at 20 °C by using a Perkin-Elmer-241 MC polarimeter; $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were measured on a spectrometer. ^1H NMR spectra were recorded for a solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; ^{31}P NMR spectra were recorded for a solution in $CDCl_3$ with 85% H_3PO_4 as the external reference. *J* values are in Hz. Mass spectra were recorded with a HP-5989 instrument, and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300−400 mesh silica gel at increased pressure. All reactions were performed under argon using standard Schlenk techniques. The optical purities of products were determined by HPLC analysis using a Shimadzu SPD-10A *vp* series with chiral columns (Chiralpak AD-H, OD-H, and IC-H columns 4.6 × 250 mm, Daicel Chemical Ind., Ltd.), and the absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation.

Ligands **L1**−**L5**[8a] and **L6**/**L7**[9b] were prepared according to the previously reported procedures.

Vinyl cyclopropanes **1a**[6a] and **1b**[2h] were prepared according to the previously reported procedures.

β,γ-Unsaturated *α*-keto esters **5a**−**5e**,[11] **5f**,[12] **5h**,[13] **5l**,[14] **5m**,[12] **5n**,[13] **5p**,[15] and **5r**[16] were prepared according to the previously reported procedures.

General Procedure for the Synthesis of *β,γ*-Unsaturated *α*-Keto Esters 5. To the appropriate aldehyde (1.0 equiv) solution in methanol was added pyruvic acid (1.0 equiv), and the mixture was cooled to 10 °C under an atmosphere of nitrogen. To this was added a solution of KOH (1.5 equiv) in methanol dropwise at 15−20 °C. After the addition of two-thirds of the alkali, the rest of the alkali was added in one part before precipitation of potassium pyruvate could occur. Then the ice bath was removed, and the temperature of the reaction mixture increased from 20 °C to 35−40 °C. The reaction mixture was stirred at this temperature for 3 h and then maintained at 10 °C for 10 h. The precipitate was filtered on a Buchner funnel under suction and washed with chilled methanol followed by diethyl ether to afford potassium 4-aryl-2-oxobut-3-enoate (4-cyclopropyl-2-oxobut-3-enoate) as a yellow solid.

Acetyl chloride (10 mL) was added dropwise to the corresponding alcohol (70 mL) cooled in an ice bath to produce dry hydrochloric acid. Potassium 4-aryl-2-oxobut-3-enoate (4-cyclopropyl-2-oxobut-3-enoate) (10 mmol) was added at 0 °C. The reaction was warmed to

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room temperature, stirred for 2 h, and then refluxed for 6 h. The solvent was removed by evaporation. Water (15 mL) was added to the crude product, which was then extracted with CH_2Cl_2 (18 mL × 2). The combined organic phase was washed with $NaHCO_3$ (10 mL × 2) and then with water (10 mL). After the organic layer was separated and dried over Na_2SO_4.The crude product was purified by flash silica gel chromatography to afford products **5g**, **5i**−**5k**, **5o**, and **5q**.

(*E*)-Ethyl 4-(2-methoxyphenyl)-2-oxobut-3-enoate, 5g: 10.0 mmol scale, yellow oil, 66% yield (1.54 g). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.42 (t, J = 7.2 Hz, 3H, CH_3), 3.91 (s, 3H, CH_3), 4.40 (q, J = 7.2 Hz, 2H, CH_2), 6.92−7.02 (m, 2H, ArH), 7.38−7.45 (m, 2H, ArH, =CH), 7.63 (d, J = 7.8 Hz, 1H, ArH), 8.20 (d, J = 16.5 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 14.0, 55.5, 62.3, 111.2, 120.8, 120.9, 122.9, 129.4, 133.0, 143.9, 159.2, 162.6, 183.5. IR (CH_2Cl_2) ν 2955, 2933, 1725, 1688, 1660, 1594, 1570, 1488, 1465, 1244, 1143, 1107, 1077, 1049, 1022, 857, 801, 752 cm^{-1}. MS (EI) m/z (%): 63 (4.16), 77 (9.65), 89 (6.43), 105 (14.07), 118 (12.09), 161 (100.00), 162 (11.24), 234 (6.56). HRMS (EI): calcd for $C_{13}H_{14}O_4$ requires 234.0892, found 234.0889.

(*E*)-Ethyl 2-oxo-4-*m*-tolylbut-3-enoate, 5i: 10.0 mmol scale, yellow oil, 72% yield (1.56 g). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.42 (t, J = 7.2 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.40 (q, J = 7.2 Hz, 2H, CH_2), 7.28−7.38 (m, 3H, ArH, =CH), 7.44 (d, J = 7.2 Hz, 2H, ArH), 7.84 (d, J = 16.4 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 14.0, 21.1, 62.3, 120.2, 126.2, 128.9, 129.5, 132.4, 133.9, 138.7, 148.5, 162.2, 182.8. IR (CH_2Cl_2) ν 2960, 2927, 1723, 1693, 1664, 1560, 1582, 1447, 1370, 1263, 1140, 1107, 1075, 1015, 986, 857, 768, 700 cm^{-1}. MS (EI) m/z (%): 145 (100.00), 115 (30.02), 149 (23.10), 117 (19.58), 91 (12.01), 146 (11.57), 218 (10.80), 116 (6.39). HRMS (EI): calcd for $C_{13}H_{14}O_3$ requires 218.0943, found 218.0941.

(*E*)-eEthyl 4-(2,5-dimethoxyphenyl)-2-oxobut-3-enoate, 5j: 10.0 mmol scale, yellow oil, 62% yield (1.64 g). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.42 (t, J = 7.5 Hz, 3H, CH_3), 3.81 (s, 3H, CH_3), 3.87 (s, 3H, CH_3), 4.40 (q, J = 7.5 Hz, 2H, CH_2), 6.87 (d, J = 9.3 Hz, 1H, ArH), 6.99 (dd, J = 3.3 Hz, 9.3 Hz, 1H, ArH), 7.13 (d, J = 3.3 Hz, 1H, ArH), 7.37 (d, J = 16.2 Hz, 1H, =CH), 8.19 (d, J = 16.2 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 14.0, 55.7, 56.0, 62.3, 112.5, 113.0, 119.1, 120.9, 123.3, 143.6, 153.4, 153.7, 162.5, 183.3. IR (CH_2Cl_2): ν 2955, 2925, 1726, 1687, 1659, 1593, 1494, 1465, 1429, 1281, 1221, 1141, 1076, 1042, 1019, 848, 808, 740, 700 cm^{-1}. MS (EI) m/z (%): 191 (100.00), 176 (46.02), 264 (19.23), 192 (13.07), 148 (10.91), 161 (9.96), 133 (8.26), 77 (6.51). HRMS (EI): calcd for $C_{14}H_{16}O_5$ requires 264.0998, found 264.1002.

(*E*)-Ethyl 2-oxo-4-(3,4,5-trimethoxyphenyl)but-3-enoate, 5k: 10.0 mmol scale, yellow oil, 56% yield (1.65 g). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.43 (t, J = 7.2 Hz, 3H, CH_3), 3.91 (s, 9H, CH_3), 4.41 (q, J = 7.2 Hz, 2H, CH_2), 6.87 (s, 2H, ArH), 7.29 (d, J = 16.2 Hz, 1H, =CH), 7.81 (d, J = 16.2 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 14.0, 56.1, 60.9, 62.5, 106.2, 119.5, 129.3, 141.3, 148.4, 153.4, 162.3, 182.4. IR (CH_2Cl_2): ν 2954, 2924, 1722, 1689, 1588, 1498, 1460, 1421, 1328, 1241, 1124, 1069, 1008, 840, 807, 781, 738 cm^{-1}. MS (EI) m/z (%): 221 (100.00), 294 (20.81), 190 (14.40), 191 (14.32), 222 (13.87), 163 (7.92), 193 (7.30), 161 (6.70). HRMS (EI): calcd for $C_{15}H_{18}O_6$ requires 294.1103, found 294.1101.

(*E*)-Ethyl 4-cyclopropyl-2-oxobut-3-enoate, 5o: 10.0 mmol scale, yellow oil, 56% yield (940 mg). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.77−0.83 (m, 2H, CH_2), 1.07−1.14 (m, 2H, CH_2), 1.38 (t, J = 7.5 Hz, 3H, CH_3), 1.63−1.76 (m, 1H, CH), 4.34 (q, J = 7.5 Hz, 2H, CH_2), 6.66 (dd, J = 10.2 Hz, 15.3 Hz, 1H, =CH), 6.81 (d, J = 15.3 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 10.2, 14.0, 16.0, 62.2, 121.9, 160.4, 162.4, 182.0. IR (CH_2Cl_2) ν 3021, 2985, 2934, 1727, 1691, 1665, 1606, 1455, 1368, 1311, 1247, 1178, 1138, 1080, 1012, 981, 939, 896, 853, 778, 736 cm^{-1}. MS (EI) m/z (%): 95 (100.00), 67 (63.00), 41 (20.00), 65 (12.37), 96 (7.14), 66 (5.31), 140 (4.12), 68 (3.96). HRMS (EI): calcd for $C_9H_{12}O_3$ requires 168.0786, found 168.0790.

(*E*)-*tert*-Butyl 2-oxo-4-phenylbut-3-enoate, 5q: 10.0 mmol scale, yellow oil, 42% yield (974 mg). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.60 (s, 9H, CH_3), 7.28 (d, J = 16.5 Hz, 1H, =CH), 7.39−7.44 (m, 3H, ArH), 7.59−7.63 (m, 2H, ArH), 7.79 (d, J = 16.5 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 27.8, 84.0, 120.7, 128.9, 129.0, 131.4, 134.0, 147.9, 161.7, 184.0. IR (CH_2Cl_2): ν 2981, 2932, 1721, 1693, 1666, 1605, 1578, 1479, 1450, 1370, 1259, 1135, 1078, 982, 941, 839, 776, 742, 689 cm^{-1}. MS (ESI) m/z (%): 255.1 (100) [M$^+$+Na]. HRMS (ESI): calcd for $C_{14}H_{16}O_3$ requires 232.1099, found 232.1090.

General Procedure for Palladium-Catalyzed Asymmetric Formal [3+2] Cycloaddition of Vinylcyclopropane with the Electron-Deficient Olefins in the Presence of Pd_2dba_3 and Chiral Imidazoline−Phosphine Ligand L1. A solution of enantiomerically pure ligand **L1** (0.01 mmol, 10 mol %) and palladium dibenzylideneacetone Pd_2dba_3 (0.005 mmol, 5 mol %) in toluene (0.25 mL) was stirred at room temperature under an argon atmosphere for 30 min. To the solution was added a solution of dimethyl 2-vinylcyclopropane-1,1-dicarboxylate (**1a**; 0.1 mmol, 1 equiv) and (*E*)-ethyl 2-oxo-4-phenylbut-3-enoate (**5a**, 0.15 mmol, 1.5 equiv) in toluene (0.25 mL), and the reaction was stirred at room temperature for 24 h. The mixture was concentrated in vacuo to yield the crude product, which was purified by flash chromatography on silica gel (eluent: PE/EtOAc, 10:1to 20:1) to furnish the desired cyclopentane **6a** as a colorless oil.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate, 6a: colorless oil, 93% yield (36 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 0.7 mL/min, 214 nm). Main product: t_{major} = 54.3 min, t_{minor} = 44.7 min. $[\alpha]^{20}_D$ = −22.8 (*c* 0.50, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.31 (t, J = 6.9 Hz, 3H, CH_3), 2.07 (dd, J = 4.8 Hz, 14.1 Hz, 1H, CH_2), 3.05 (dd, J = 7.5 Hz, 14.1 Hz, 1H, CH_2), 3.22 (s, 3H, CH_3), 3.62−3.71 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.25 (q, J = 6.9 Hz, 2H, CH_2), 4.47 (dd, J = 8.7 Hz, 11.1 Hz, 1H, CH), 4.62 (d, J = 11.1 Hz, 1H, CH), 5.01 (d, J = 9.6 Hz, 1H, =CH_2), 5.05 (d, J = 16.8 Hz, 1H, =CH_2), 5.54−5.67 (m, 1H, =CH), 7.18−7.30 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 40.9, 44.7, 49.9, 52.1, 52.7, 55.9, 62.4, 64.3, 117.5, 127.3, 128.0, 128.4, 136.9, 137.6, 160.4, 171.0, 171.9, 192.5. IR (CH_2Cl_2): ν 2953, 2911, 1721, 1496, 1434, 1253, 1211, 1171, 1092, 1070, 922, 811, 750, 700, 667 cm^{-1}. MS (ESI) m/z (%): 411.3 (100) [M$^+$ + Na]. HRMS (MALDI): calcd for $C_{21}H_{24}O_7Na^+$ (M$^+$ + Na) requires 411.1424, found 411.1414.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-*p*-tolyl-4-vinylcyclopentane-1,1-dicarboxylate, 6b: colorless oil, 95% yield (38 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 1.0 mL/min, 214 nm). Main product: t_{major} = 58.9 min, t_{minor} = 28.0 min. $[\alpha]^{20}_D$ = −16.9 (*c* 1.35, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.30 (t, J = 6.9 Hz, 3H, CH_3), 2.04 (dd, J = 4.8 Hz, 14.1 Hz, 1H, CH_2), 2.27 (s, 3H, CH_3), 3.02 (dd, J = 7.8 Hz, 14.1 Hz, 1H, CH_2), 3.27 (s, 3H, CH_3), 3.61−3.70 (m, 1H, CH), 3.73 (s, 3H, CH_3), 4.24 (q, J = 6.9 Hz, 2H, CH_2), 4.46 (dd, J = 8.1 Hz, 11.7 Hz, 1H, CH), 4.56 (d, J = 11.7 Hz, 1H, CH), 5.00 (d, J = 10.2 Hz, 1H, =CH_2), 5.05 (d, J = 17.4 Hz, 1H, =CH_2), 5.52−5.65 (m, 1H, =CH), 7.05 (d, J = 7.8 Hz, 2H, ArH), 7.16 (d, J = 7.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 20.9, 40.9, 44.6, 49.7, 52.1, 52.6, 55.8, 62.3, 64.2, 117.4, 128.3, 128.7, 134.4, 136.8, 137.1, 160.4, 171.1, 171.9, 192.6. IR (CH_2Cl_2): ν 3081, 2976, 2914, 2953, 1517, 1435, 1254, 1212, 1176, 1092, 1070, 925, 839, 716 cm^{-1}. MS (ESI) m/z (%): 425.2 (100) [M$^+$ + Na]. HRMS (MALDI): calcd for $C_{22}H_{26}O_7Na^+$ (M$^+$ + Na) requires 425.1578, found 425.1571.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(4-methoxyphenyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6c: colorless oil, 96% yield (40 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 0.5 mL/min, 214 nm). Main product: t_{major} = 81.7 min, t_{minor} = 49.8 min. $[\alpha]^{20}_D$ = −23.1 (*c* 2.05, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.30 (t, J = 7.2 Hz, 3H, CH_3), 2.05 (dd, J = 5.2 Hz, 14.0 Hz, 1H, CH_2), 3.02 (dd, J = 7.6 Hz, 14.0 Hz, 1H, CH_2), 3.28 (s, 3H, CH_3), 3.61−3.70 (m, 1H, CH), 3.73 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 4.25 (q, J = 7.2 Hz, 2H, CH_2), 4.43 (dd, J = 8.8 Hz, 11.6 Hz, 1H, CH), 4.55 (d, J = 11.6 Hz, 1H, CH), 5.00 (d, J = 10.4 Hz, 1H, =CH_2), 5.04 (d, J = 17.2 Hz, 1H,

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=CH_2), 5.54−5.64 (m, 1H, =CH), 6.78 (d, J = 8.4 Hz, 2H, ArH), 7.20 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 13.9, 40.9, 44.6, 49.4, 52.2, 52.7, 55.1, 55.9, 62.4, 64.2, 113.4, 117.5, 129.5, 137.1, 158.7, 160.5, 171.2, 172.0, 192.7. IR (CH_2Cl_2): ν 3081, 2988, 2954, 2915, 2841, 1725, 1612, 1514, 1435, 1251, 1213, 1181, 1070, 925, 843, 732 cm^{-1}. MS (ESI) m/z (%): 419.1 (100) [M^+ + 1]. HRMS (ESI): calcd for $C_{22}H_{26}O_8Na^+$ (M^+ + Na) requires 441.1520, found 441.1529.

(2*S*,3*S*,4*R*)-Dimethyl 2-(4-bromophenyl)-3-(2-ethoxy-2-oxoacetyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6d: colorless oil, 52% yield (24 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 97:3, 0.5 mL/min, 214 nm). Main product: t_{major} = 54.2 min, t_{minor} = 42.0 min. $[\alpha]^{20}_D$ = −20.2 (*c* 1.30, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.31 (t, J = 7.2 Hz, 3H, CH_3), 2.05 (dd, J = 4.8 Hz, 14.1 Hz, 1H, CH_2), 3.03 (dd, J = 7.8 Hz, 14.1 Hz, 1H, CH_2), 3.30 (s, 3H, CH_3), 3.61−3.70 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.25 (q, J = 7.2 Hz, 2H, CH_2), 4.42 (dd, J = 8.7 Hz, 11.4 Hz, 1H, CH), 4.53 (d, J = 11.4 Hz, 1H, CH), 5.01 (d, J = 9.6 Hz, 1H, =CH_2), 5.05 (d, J = 15.6 Hz, 1H, =CH_2), 5.50−5.63 (m, 1H, =CH), 7.17 (d, J = 8.4 Hz, 2H, ArH), 7.37 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 40.9, 44.5, 49.4, 52.3, 52.8, 55.7, 62.5, 64.0, 117.8, 121.3, 130.2, 131.1, 136.6, 136.8, 160.4, 170.9, 171.7, 192.4. IR (CH_2Cl_2) ν 2987, 2952, 2917, 1723, 1610, 1516, 1434, 1248, 1208, 1176, 1092, 1069, 924, 899, 828 cm^{-1}. MS (ESI) m/z (%): 469.0 (100) [M^+ + 1]. HRMS (ESI) calcd for $C_{21}H_{23}Br_1O_7Na^+$ (M^+ + Na) requires 489.0519, found 489.0537.

(2*S*,3*S*,4*R*)-Dimethyl 2-(4-chlorophenyl)-3-(2-ethoxy-2-oxoacetyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6e: colorless oil, 61% yield (26 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 0.7 mL/min, 214 nm). Main product: t_{major} = 23.9 min, t_{minor} = 18.9 min. $[\alpha]^{20}_D$ = −19.9 (*c* 1.10, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.31 (t, J = 6.9 Hz, 3H, CH_3), 2.05 (dd, J = 4.8 Hz, 14.1 Hz, 1H, CH_2), 3.03 (dd, J = 7.5 Hz, 14.1 Hz, 1H, CH_2), 3.30 (s, 3H, CH_3), 3.62−3.71 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.26 (q, J = 6.9 Hz, 2H, CH_2), 4.43 (dd, J = 8.7 Hz, 11.7 Hz, 1H, CH), 4.55 (d, J = 11.7 Hz, 1H, CH), 5.01 (d, J = 8.7 Hz, 1H, =CH_2), 5.05 (d, J = 15.9 Hz, 1H, =CH_2), 5.50−5.63 (m, 1H, =CH), 7.23 (br, 4H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.9, 40.9, 44.5, 49.3, 52.3, 52.8, 55.8, 62.5, 64.1, 117.8, 128.2, 129.9, 133.2, 136.0, 136.8, 160.4, 170.9, 171.8, 192.4. IR (CH_2Cl_2): ν 2976, 2953, 2917, 2848, 1725, 1493, 1435, 1250, 1366, 1209, 1175, 1090, 1070, 1015, 925, 843, 819, 746, 717 cm^{-1}. MS (ESI) m/z (%): 423.0 (100) [M^+ + 1]. HRMS (ESI): calcd for $C_{21}H_{23}Cl_1O_7Na^+$ (M^+ + Na) requires 445.1025, found 445.1022.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(2-methoxyphenyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6g: colorless oil, 96% yield (40 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK AD-H, hexane/*i*PrOH, 90:10, 1.0 mL/min, 214 nm). Main product: t_{major} = 22.0 min, t_{minor} = 23.6 min. $[\alpha]_D^{20}$ = −43.2 (*c* 1.90, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.29 (t, J = 6.9 Hz, 3H, CH_3), 2.11 (dd, J = 6.3 Hz, 13.8 Hz, 1H, CH_2), 2.97 (dd, J = 7.8 Hz, 13.8 Hz, 1H, CH_2), 3.32 (s, 3H, CH_3), 3.58−3.67 (m, 1H, CH), 3.70 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 4.23 (q, J = 6.9 Hz, 2H, CH_2), 4.66 (dd, J = 9.3 Hz, 10.8 Hz, 1H, CH), 4.87 (d, J = 10.8 Hz, 1H, CH), 4.99 (d, J = 10.2 Hz, 1H, =CH_2), 5.07 (d, J = 14.1 Hz, 1H, =CH_2), 5.59−5.72 (m, 1H, =CH), 6.79 (d, J = 7.5 Hz, 1H, ArH), 6.86 (t, J = 7.5 Hz, 1H, ArH), 7.17 (dt, J = 1.5 Hz, 7.5 Hz, 1H, ArH), 7.29 (d, J = 7.5 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 41.1, 45.3, 46.3, 51.9, 52.6, 55.2, 55.4, 62.2, 63.4, 110.5, 117.4, 120.3, 126.4, 128.4, 130.7, 137.1, 158.0, 160.1, 170.7, 171.8, 193.4. IR (CH_2Cl_2) ν 2987, 2952, 2921, 2833, 1726, 1601, 1495, 1461, 1434, 1245, 1174, 1071, 1027, 927, 858, 755 cm^{-1}. MS (ESI) m/z (%): 419.2 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{22}H_{26}O_8Na^+$ (M^+ + Na) requires 441.1524, found 441.1520.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(3-methoxyphenyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6h: colorless oil, 86% yield (36 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK PC-2, hexane/*i*PrOH, 90:10, 0.5 mL/min, 230 nm). Main product: t_{major} = 39.1 min, t_{minor} = 48.3 min. $[\alpha]^{20}_D$ = −48.5 (*c* 1.65, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.31 (t, J = 7.2 Hz, 3H, CH_3), 2.05 (dd, J = 5.1 Hz, 14.1 Hz, 1H, CH_2), 3.05 (dd, J = 8.1 Hz, 14.1 Hz, 1H, CH_2), 3.26 (s, 3H, CH_3), 3.61−3.70 (m, 1H, CH), 3.74 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 4.25 (q, J = 7.2 Hz, 2H, CH_2), 4.45 (dd, J = 8.7 Hz, 11.7 Hz, 1H, CH), 4.58 (d, J = 11.7 Hz, 1H, CH), 5.00 (d, J = 9.6 Hz, 1H, =CH_2), 5.05 (d, J = 16.2 Hz, 1H, =CH_2), 5.53−5.66 (m, 1H, =CH), 6.73 (dd, J = 1.8 Hz, 7.8 Hz, 1H, ArH), 6.83 (d, J = 7.8 Hz, 1H, ArH), 6.88 (s, 1H, ArH), 7.15 (t, J = 7.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 41.0, 44.7, 49.9, 52.2, 52.7, 55.1, 55.9, 62.4, 64.3, 112.8, 114.6, 117.5, 120.4, 128.9, 137.0, 139.2, 159.2, 160.4, 171.0, 171.9, 192.5. IR (CH_2Cl_2) ν 2953, 2917, 2829, 1724, 1601, 1585, 1489, 1435, 1369, 1250, 1209, 1172, 1068, 927, 861, 781, 699 cm^{-1}. MS (ESI) m/z (%): 419.2 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{22}H_{26}O_8Na^+$ (M^+ + Na) requires 441.1531, found 441.1520.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-*m*-tolyl-4-vinylcyclopentane-1,1-dicarboxylate, 6i: colorless oil, 97% yield (39 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 97:3, 0.7 mL/min, 214 nm). Main product: t_{major} = 85.7 min, t_{minor} = 58.1 min. $[\alpha]^{20}_D$ = −51.8 (*c* 2.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.30 (t, J = 6.9 Hz, 3H, CH_3), 2.05 (dd, J = 5.1 Hz, 13.8 Hz, 1H, CH_2), 2.30 (s, 3H, CH_3), 3.04 (dd, J = 7.5 Hz, 13.8 Hz, 1H, CH_2), 3.24 (s, 3H, CH_3), 3.62−3.71 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.24 (q, J = 6.9 Hz, 2H, CH_2), 4.44 (dd, J = 8.4 Hz, 11.1 Hz, 1H, CH), 4.57 (d, J = 11.1 Hz, 1H, CH), 5.00 (d, J = 10.5 Hz, 1H, =CH_2), 5.06 (d, J = 17.1 Hz, 1H, =CH_2), 5.53−5.66 (m, 1H, =CH), 6.99 (d, J = 6.9 Hz, 1H, ArH), 7.03−7.15 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 21.4, 41.0, 44.8, 49.9, 52.1, 52.7, 56.0, 62.4, 64.3, 117.5, 125.3, 127.9, 128.1, 129.3, 137.1, 137.48, 137.53, 160.5, 171.1, 171.9, 192.6. IR (CH_2Cl_2): ν 3024, 2980, 2952, 2914, 2837, 1725, 1608, 1434, 1254, 1210, 1175, 1070, 928, 859, 812, 782, 703 cm^{-1}. MS (ESI) m/z (%): 403.1 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{22}H_{26}O_7Na^+$ (M^+ + Na) requires 425.1569, found 425.1571.

(2*S*,3*S*,4*R*)-Dimethyl 2-(2,5-dimethoxyphenyl)-3-(2-ethoxy-2-oxoacetyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6j: colorless oil, 90% yield (40 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK AD-H, hexane/*i*PrOH, 90:10, 1.0 mL/min, 214 nm). Main product: t_{major} = 25.6 min, t_{minor} = 21.1 min. $[\alpha]^{20}_D$ = −46.6 (*c* 1.20, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.30 (t, J = 6.9 Hz, 3H, CH_3), 2.10 (dd, J = 6.6 Hz, 13.8 Hz, 1H, CH_2), 2.96 (dd, J = 7.5 Hz, 13.8 Hz, 1H, CH_2), 3.37 (s, 3H, CH_3), 3.57−3.66 (m, 1H, CH), 3.70 (s, 3H, CH_3), 3.74 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 4.23 (q, J = 6.9 Hz, 2H, CH_2), 4.64 (dd, J = 9.0 Hz, 10.5 Hz, 1H, CH), 4.80 (d, J = 10.5 Hz, 1H, CH), 4.99 (d, J = 9.9 Hz, 1H, =CH_2), 5.07 (d, J = 16.8 Hz, 1H, =CH_2), 5.57−5.70 (m, 1H, =CH), 6.67−6.75 (m, 2H, ArH), 6.89 (d, J = 1.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 41.1, 44.9, 46.4, 52.0, 52.6, 55.3, 55.6, 56.0, 62.3, 63.4, 111.6, 112.8, 116.8, 117.4, 127.5, 137.1, 152.3, 153.1, 160.6, 170.6, 171.7, 193.4. IR (CH_2Cl_2): ν 3090, 2983, 2952, 2837, 1726, 1590, 1502, 1432, 1368, 1225, 1176, 1094, 1071, 1050, 1024, 927, 860, 804, 734 cm^{-1}. MS (MALDI) m/z (%): 471.1 (100) [M^+ + Na]. HRMS (MALDI): calcd for $C_{23}H_{28}O_9Na^+$ (M^+ + Na) requires 471.1633, found 471.1626.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(3,4,5-trimethoxyphenyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6k: colorless oil, 88% yield (42 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK AD-H, hexane/*i*PrOH, 90:10, 0.7 mL/min, 230 nm). Main product: t_{major} = 52.2 min, t_{minor} = 33.8 min. $[\alpha]^{20}_D$ = −41.3 (*c* 2.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.32 (t, J = 6.9 Hz, 3H, CH_3), 2.07 (dd, J = 4.2 Hz, 14.1 Hz, 1H, CH_2), 3.07 (dd, J = 7.5 Hz, 14.1 Hz, 1H, CH_2), 3.30 (s, 3H, CH_3), 3.59−3.68 (m, 1H, CH), 3.75 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.84 (s, 6H, CH_3), 4.27 (q, J = 6.9 Hz, 2H, CH_2), 4.43 (dd, J = 8.1 Hz, 11.7 Hz, 1H, CH), 4.55 (d, J = 11.7 Hz, 1H, CH), 5.01 (d, J = 5.4 Hz, 1H, =CH_2), 5.05 (d, J = 11.7 Hz, 1H, =CH_2), 5.53−5.66 (m, 1H, =CH), 6.53 (d, J = 5.7 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 40.9, 44.6, 50.2, 52.3, 52.7, 55.99, 56.01, 60.7, 62.5, 64.1, 105.5, 117.5, 133.2, 136.9, 137.1, 152.6, 160.6, 171.1, 172.0, 192.5. IR (CH_2Cl_2): ν 2955, 2924, 2853, 1725, 1589, 1509, 1461, 1244, 1208, 1125, 1094, 1071, 924, 848, 803, 701 cm^{-1}. MS (ESI) m/z (%): 479.1 (100) [M^+ + 1].

HRMS (MALDI): calcd for $C_{24}H_{30}O_{10}Na^+$ (M^+ + Na) requires 501.1718, found 501.1731.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(thiophen-2-yl)-4-vinylcyclopentane-1,1-dicarboxylate, 6l: colorless oil, 90% yield (35 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK AD-H, hexane/*i*PrOH, 80:20, 0.5 mL/min, 230 nm). Main product: t_{major} = 28.1 min, t_{minor} = 42.6 min. $[\alpha]^{20}_D$ = −41.5 (*c* 1.60, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.33 (t, *J* = 7.2 Hz, 3H, CH_3), 2.03 (dd, *J* = 5.7 Hz, 14.1 Hz, 1H, CH_2), 2.99 (dd, *J* = 7.8 Hz, 14.1 Hz, 1H, CH_2), 3.38 (s, 3H, CH_3), 3.63−3.69 (m, 1H, CH), 3.78 (s, 3H, CH_3), 4.28 (q, *J* = 7.2 Hz, 2H, CH_2), 4.49 (dd, *J* = 9.0 Hz, 11.7 Hz, 1H, CH), 4.79 (d, *J* = 11.7 Hz, 1H, CH), 5.01 (d, *J* = 9.6 Hz, 1H, =CH_2), 5.05 (d, *J* = 16.2 Hz, 1H, =CH_2), 5.48−5.60 (m, 1H, =CH), 6.87 (dd, *J* = 3.3 Hz, 4.8 Hz, 1H, ArH), 6.93 (d, *J* = 3.3 Hz, 1H, ArH), 7.12 (dd, *J* = 1.2 Hz, 4.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.8, 40.6, 44.0, 45.5, 52.4, 52.7, 56.7, 62.5, 64.2, 117.6, 124.3, 125.8, 126.4, 136.9, 140.2, 160.2, 170.8, 171.4, 192.1. IR (CH_2Cl_2): ν 2980, 2953, 2914, 1723, 1640, 1434, 1253, 1205, 1177, 1092, 1067, 924, 856, 700 cm^{-1}. MS (ESI) *m*/*z* (%): 395.0 (100) [M^+ + 1]. HRMS (ESI): calcd for $C_{19}H_{22}S_1O_7Na^+$ (M^+ + Na) requires 417.0978, found 417.0987.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(furan-2-yl)-4-vinylcyclopentane-1,1-dicarboxylate, 6m: colorless oil, 90% yield (34 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 1.0 mL/min, 214 nm). Main product: t_{major} = 64.8 min, t_{minor} = 73.6 min. $[\alpha]^{20}_D$ = −7.5 (*c* 1.25, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.33 (t, *J* = 6.9 Hz, 3H, CH_3), 1.95 (dd, *J* = 6.0 Hz, 13.8 Hz, 1H, CH_2), 2.95 (dd, *J* = 7.5 Hz, 13.8 Hz, 1H, CH_2), 3.47 (s, 3H, CH_3), 3.61−3.73 (m, 1H, CH), 3.76 (s, 3H, CH_3), 4.28 (q, *J* = 6.9 Hz, 2H, CH_2), 4.46 (dd, *J* = 9.6 Hz, 11.4 Hz, 1H, CH), 4.63 (d, *J* = 11.4 Hz, 1H, CH), 5.00 (d, *J* = 10.2 Hz, 1H, =CH_2), 5.06 (d, *J* = 17.1 Hz, 1H, =CH_2), 5.46−5.59 (m, 1H, =CH), 6.25 (d, *J* = 2.1 Hz, 2H, ArH), 7.25 (br, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 13.9, 40.4, 44.2, 44.3, 52.8, 53.4, 53.9, 62.5, 62.9, 108.2, 110.5, 117.8, 136.9, 141.6, 151.1, 160.3, 170.7, 171.2, 192.4. IR (CH_2Cl_2): ν 3141, 2983, 2954, 2910, 1727, 1504, 1435, 1256, 1206, 1176, 1072, 1013, 926, 831, 741 cm^{-1}. MS (ESI) *m*/*z* (%): 379.0 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{19}H_{22}O_8Na^+$ (M^+ + Na) requires 401.1218, found 401.1207.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-ethoxy-2-oxoacetyl)-2-(naphthalen-2-yl)-4-vinylcyclopentane-1,1-dicarboxylate, 6n: colorless oil, 87% yield (38 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 1.0 mL/min, 214 nm). Main product: t_{major} = 60.7 min, t_{minor} = 26.3 min. $[\alpha]^{20}_D$ = −27.3 (*c* 0.50, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.29 (t, *J* = 7.2 Hz, 3H, CH_3), 2.10 (dd, *J* = 4.8 Hz, 14.4 Hz, 1H, CH_2), 3.10 (dd, *J* = 8.0 Hz, 14.4 Hz, 1H, CH_2), 3.13 (s, 3H, CH_3), 3.70−3.78 (m, 4H, CH_3, CH), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 4.61 (dd, *J* = 8.8 Hz, 11.6 Hz, 1H, CH), 4.76 (d, *J* = 11.6 Hz, 1H, CH), 5.03 (d, *J* = 10.0 Hz, 1H, =CH_2), 5.08 (d, *J* = 17.6 Hz, 1H, =CH_2), 5.59−5.68 (m, 1H, =CH), 7.40−7.45 (m, 3H, ArH), 7.71−7.79 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 13.9, 41.1, 44.8, 50.2, 52.2, 52.8, 56.1, 62.5, 64.4, 117.7, 125.8, 125.9, 126.9, 127.2, 127.4, 127.6, 127.9, 132.7, 133.0, 135.2, 137.1, 160.5, 171.1, 172.0, 192.6. IR (CH_2Cl_2): ν 3053, 2980, 2951, 2840, 1723, 1601, 1508, 1434, 1250, 1206, 1176, 1069, 925, 859, 746, 700, 655 cm^{-1}. MS (ESI) *m*/*z* (%): 439.1 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{25}H_{26}O_7Na^+$ (M^++Na) requires 461.1580, found 461.1571.

(2*S*,3*S*,4*R*)-Dimethyl 2-cyclopropyl-3-(2-ethoxy-2-oxoacetyl)-4-vinylcyclopentane-1,1-dicarboxylate, 6o: colorless oil, 83% yield (29 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 97:3, 1.0 mL/min, 214 nm). Main product: t_{major} = 25.8 min, t_{minor} = 32.0 min. $[\alpha]^{20}_D$ = −10.7 (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.25−0.29 (m, 1H, CH_2), 0.34−0.42 (m, 3H, CH_2), 0.64−0.72 (m, 1H, CH), 1.35 (t, *J* = 6.9 Hz, 3H, CH_3), 2.07 (dd, *J* = 7.5 Hz, 13.2 Hz, 1H, CH_2), 2.64−2.75 (m, 2H, CH, CH_2), 3.36−3.48 (m, 1H, CH), 3.75 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 3.98 (dd, *J* = 8.7 Hz, 9.3 Hz, 1H, CH), 4.29 (q, *J* = 6.9 Hz, 2H, CH_2), 4.96 (d, *J* = 9.9 Hz, 1H, =CH_2), 5.02 (d, *J* = 16.8 Hz, 1H, =CH_2), 5.42−5.55 (m, 1H, =CH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 4.0, 4.2, 12.4, 13.9, 41.1, 45.2, 50.7, 52.3, 52.6, 56.3, 62.4, 63.0, 117.3, 136.7, 160.8, 171.6, 172.1, 194.1. IR (CH_2Cl_2): ν 2991, 2954, 2859, 1724, 1640, 1434, 1251, 1178, 1072, 1023, 924, 859, 804, 726 cm^{-1}. MS (ESI) *m*/*z* (%): 353.2 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{18}H_{24}O_7Na^+$ (M^+ + Na) requires 375.1422, found 375.1414.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-isopropoxy-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate, 6p: colorless oil, 87% yield (35 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 97:3, 0.7 mL/min, 214 nm). Main product: t_{major} = 57.8 min, t_{minor} = 45.8 min. $[\alpha]^{20}_D$ = −44.6 (*c* 1.65, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.27 (d, *J* = 1.5 Hz, 3H, CH_3), 1.29 (d, *J* = 1.5 Hz, 3H, CH_3), 2.06 (dd, *J* = 5.1 Hz, 14.1 Hz, 1H, CH_2), 3.05 (dd, *J* = 7.8 Hz, 14.1 Hz, 1H, CH_2), 3.22 (s, 3H, CH_3), 3.62−3.70 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.47 (dd, *J* = 8.7 Hz, 11.7 Hz, 1H, CH), 4.62 (d, *J* = 11.7 Hz, 1H, CH), 4.99−5.11 (m, 3H, =CH_2, CH), 5.54−5.67 (m, 1H, =CH), 7.17−7.31 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 21.37, 21.40, 40.9, 44.8, 49.9, 52.1, 52.7, 55.9, 64.4, 70.5, 117.5, 127.2, 128.0, 128.5, 137.0, 137.7, 160.1, 171.0, 171.9, 192.8. IR (CH_2Cl_2): ν 3082, 3024, 2983, 2953, 1724, 1455, 1435, 1254, 1210, 1177, 1093, 1068, 927, 837, 700 cm^{-1}. MS (ESI) *m*/*z* (%): 425.1 (100) [M^+ + Na]. HRMS (ESI): calcd for $C_{22}H_{26}O_7Na^+$ (M^+ + Na) requires 425.1571, found 425.1556.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-*tert*-butoxy-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate, 6q: colorless oil, 86% yield (36 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 95:5, 0.7 mL/min, 214 nm). Main product: t_{major} = 33.0 min, t_{minor} = 27.3 min. $[\alpha]^{20}_D$ = −41.9 (*c* 1.70, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.48 (s, 9H, CH_3), 2.05 (dd, *J* = 4.8 Hz, 14.1 Hz, 1H, CH_2), 3.03 (dd, *J* = 7.5 Hz, 14.1 Hz, 1H, CH_2), 3.21 (s, 3H, CH_3), 3.60−3.69 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.43 (dd, *J* = 8.7 Hz, 11.1 Hz, 1H, CH), 4.60 (d, *J* = 11.1 Hz, 1H, CH), 5.02 (d, *J* = 11.4 Hz, 1H, =CH_2), 5.07 (d, *J* = 18.0 Hz, 1H, =CH_2), 5.55−5.68 (m, 1H, =CH), 7.18−7.30 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 27.6, 40.9, 44.8, 50.0, 52.0, 52.7, 55.8, 64.4, 83.7, 117.3, 127.2, 128.0, 128.5, 137.1, 137.8, 159.8, 171.0, 171.9, 193.4. IR (CH_2Cl_2): ν 2981, 2952, 1724, 1456, 1434, 1250, 1208, 1161, 1092, 1067, 922, 838, 746, 699 cm^{-1}. MS (ESI) *m*/*z* (%): 439.0 (100) [M^+ + Na]. HRMS (ESI): calcd for $C_{23}H_{28}O_7Na^+$ (M^+ + Na) requires 439.1727, found 439.1715.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-(benzyloxy)-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate, 6r: colorless oil, 71% yield (32 mg). The ee was determined by chiral HPLC (Daicel CHIRALPACK AD-H, hexane/*i*PrOH, 80:20, 0.5 mL/min, 230 nm). Main product: t_{major} = 36.7 min, t_{minor} = 43.8 min. $[\alpha]^{20}_D$ = −36.8 (*c* 1.40, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 2.04 (dd, *J* = 5.2 Hz, 14.0 Hz, 1H, CH_2), 3.02 (dd, *J* = 7.6 Hz, 14.0 Hz, 1H, CH_2), 3.20 (s, 3H, CH_3), 3.58−3.67 (m, 1H, CH), 3.73 (s, 3H, CH_3), 4.46 (dd, *J* = 8.4 Hz, 11.6 Hz, 1H, CH), 4.61 (d, *J* = 11.6 Hz, 1H, CH), 4.87 (d, *J* = 9.6 Hz, 1H, =CH_2), 4.90 (d, *J* = 6.0 Hz, 1H, =CH_2), 5.205 (s, 1H, CH_2), 5.208 (s, 1H, CH_2), 5.49−5.60 (m, 1H, =CH), 7.15−7.29 (m, 5H, ArH), 7.35 (br, 5H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 40.9, 44.8, 49.9, 52.1, 52.7, 56.1, 64.4, 67.9, 117.6, 127.3, 128.1, 128.5, 128.57, 128.64, 128.7, 134.4, 136.8, 137.6, 160.3, 171.0, 171.9, 192.2. IR (CH_2Cl_2): ν 2952, 2924, 2853, 1725, 1497, 1455, 1434, 1252, 1210, 1175, 1093, 1067, 926, 810, 749, 698 cm^{-1}. MS (MALDI) *m*/*z* (%): 473.0 (100) [M^+ + 1]. HRMS (MALDI): calcd for $C_{26}H_{26}O_7Na^+$ (M^+ + Na) requires 473.1584, found 473.1571.

(2*S*,3*S*,4*R*)-Dimethyl 2-phenyl-3-(1*H*-pyrrole-1-carbonyl)-4-vinylcyclopentane-1,1-dicarboxylate, 8a: colorless solid, 63% yield (24 mg), mp 92−95 °C. The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 90:10, 0.5 mL/min, 230 nm). Main product: t_{major} = 50.4 min, t_{minor} = 19.5 min. $[\alpha]^{20}_D$ = −9.9 (*c* 0.6, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.19 (dd, *J* = 5.1 Hz, 14.1 Hz, 1H, CH_2), 3.04 (dd, *J* = 7.2 Hz, 14.1 Hz, 1H, CH_2), 3.25 (s, 3H, CH_3), 3.45−3.57 (m, 1H, CH), 3.75 (s, 3H, CH_3), 4.21 (dd, *J* = 9.0 Hz, 10.8 Hz, 1H, CH), 4.77 (d, *J* = 10.8 Hz, 1H, CH), 4.91 (d, *J* = 17.1 Hz, 1H, =CH_2), 4.93 (d, *J* = 9.6 Hz, 1H, =CH_2), 5.64−5.76 (m, 1H, =CH), 6.25 (br, 2H, ArH), 7.16−7.33 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 40.8, 45.3, 51.3,

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52.2, 52.5, 52.7, 64.2, 113.1, 117.2, 118.9, 127.4, 128.2, 128.3, 136.5, 137.4, 168.6, 171.5, 171.7. IR (CH_2Cl_2): ν 3156, 3079, 2951, 2914, 1724, 1603, 1468, 1434, 1266, 1210, 1178, 1105, 1075, 921, 891, 744, 700, 663^{-1}. MS (ESI) m/z (%): 382.1 (100) [M^+ + 1]. HRMS (ESI): calcd for $C_{22}H_{23}N_1O_5Na^+$ (M^+ + Na) requires 404.1468, found 404.1465.

Ethyl 2-((1*S*,2*S*,5*R*)-3,3-dicyano-2-phenyl-5-vinylcyclopentyl)-2-oxoacetate, 8b: white solid, 94% yield (30 mg), mp 110−112 °C. The ee was determined by chiral HPLC (Daicel CHIRALPACK IC-H, hexane/*i*PrOH, 98:2, 0.6 mL/min, 214 nm). Main product: t_{major} = 66.7 min, t_{minor} = 73.9 min. $[\alpha]^{20}_D$ = −20.6 (*c* 1.30, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.32 (t, *J* = 7.2 Hz, 3H, CH_3), 2.39 (dd, *J* = 9.6 Hz, 14.0 Hz, 1H, CH_2), 2.93 (dd, *J* = 7.6 Hz, 14.0 Hz, 1H, CH_2), 3.69−3.79 (m, 1H, CH), 4.16 (d, *J* = 11.2 Hz, 1H, CH), 4.28 (q, *J* = 7.2 Hz, 2H, CH_2), 4.69 (dd, *J* = 11.2 Hz, 11.2 Hz, 1H, CH), 5.17 (dd, *J* = 0.8 Hz, 9.6 Hz, 1H, =CH_2), 5.23 (d, *J* = 16.8 Hz, 1H, =CH_2), 5.48−5.58 (m, 1H, =CH), 7.39−7.48 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 13.8, 41.5, 43.2, 43.8, 51.7, 54.9, 63.0, 113.9, 114.4, 120.3, 128.0, 129.2, 129.5, 132.4, 134.1, 159.9, 191.1. IR (CH_2Cl_2): ν 2965, 2923, 1726, 1443, 1370, 1296, 1260, 1210, 1094, 1063, 1043, 933, 856, 740, 700 cm^{-1}. MS (ESI) m/z (%): 323.0 (100) [M^+ + H]. HRMS (ESI): calcd for $C_{19}H_{18}N_2O_3Na^+$ (M^+ + Na) requires 345.1210, found 345.1225.

General Procedure for the Synthesis of 9. To a solution of (2*S*,3*S*,4*R*)- dimethyl 3-(2-*tert*-butoxy-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate (**6q**; 1.0 equiv) in DCM (0.1 M) was added CF_3COOH (10 equiv) slowly at room temperature, and the reaction was stirred at room temperature for 24 h. The mixture was concentrated in vacuo to yield the crude product, which was purified by flash chromatography on silica gel (eluent: PE/EtOAc, 2:1) to furnish the desired acid as a colorless oil.

A solution of the desired acid (1.0 equiv) in DMF (0.02 M) with 1-ethyl-3-(3-dimethyllaminopropyl)carbodiimide hydrochloride (EDCI) (2.0 equiv) and 1-hydroxybenzotriazole (HOBt) (3.0 equiv) was stirred at 0 °C for 15 min; then a solution of 4-bromobenzylamine (1.5 equiv) in DMF (0.02 M) was added into the solution by syringe at 0 °C. The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was diluted by the addition of EtOAc, then washed with H_2O and brine and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by silica gel column chromatography (PE/EA = 10:1) to give the desired product **9** as a white solid.

(2*S*,3*S*,4*R*)-Dimethyl 3-(2-(4-bromobenzylamino)-2-oxoacetyl)-2-phenyl-4-vinylcyclopentane-1,1-dicarboxylate, 9: white solid, 51% yield (24 mg), mp 102−105 °C. The ee was determined by chiral HPLC (Daicel CHIRALPACK OJ-H, hexane/*i*PrOH, 70:30, 0.5 mL/min, 230 nm). Main product: t_{major} = 23.8 min, t_{minor} = 32.9 min. $[\alpha]^{20}_D$ = −8.5 (*c* 0.8, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 2.09 (dd, *J* = 4.4 Hz, 14.0 Hz, 1H, CH_2), 3.13 (dd, *J* = 7.6 Hz, 14.0 Hz, 1H, CH_2), 3.18 (s, 3H, CH_3), 3.69−3.735 (m, 1H, CH), 3.74 (s, 3H, CH_3), 4.29 (dd, *J* = 6.4 Hz, 14.8 Hz, 1H, CH_2), 4.42 (dd, *J* = 6.4 Hz, 14.8 Hz, 1H, CH_2), 4.62 (d, *J* = 11.6 Hz, 1H, CH), 4.70 (dd, *J* = 8.4 Hz, 11.6 Hz, 1H, CH), 4.94 (d, *J* = 10.0 Hz, 1H, =CH_2), 5.01 (d, *J* = 16.8 Hz, 1H, =CH_2), 5.54−5.63 (m, 1H, =CH), 7.07 (d, *J* = 8.4 Hz, 2H, ArH), 7.18−7.30 (m, 5H, ArH), 7.42 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 40.9, 42.6, 45.2, 49.9, 52.2, 52.8, 54.0, 64.4, 117.1, 121.7, 127.3, 128.1, 128.5, 129.4, 131.8, 135.9, 137.3, 137.8, 159.7, 170.8, 172.3, 197.1. IR (CH_2Cl_2): ν 3349, 2952, 2925, 2853, 1726, 1678, 1522, 1488, 1456, 1434, 1254, 1209, 1175, 1103, 1071, 1011, 923, 795, 736, 700 cm^{-1}. MS (ESI) m/z (%): 528.1 (100) [M^+ + 1]. HRMS (ESI): calcd for $C_{26}H_{27}BrNO_6^+$ (M^+ + H) requires 527.0944, found 527.0932.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data and chiral HPLC traces of the compounds shown in Tables 1−3 and Schemes 2 and 3, detailed descriptions of experimental procedures, and the crystal structure of **8a** (CCDC 872181), **8b** (CCDC 883008), and **9** (CCDC 895309). 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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■ REFERENCES

(1) For leading references and examples, see: (a) Hartley, R. C.; Caldwell, S. T. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 477−501. (b) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66−72. (c) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C. *Chem. Rev.* **1989**, *89*, 165−198. (d) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151−1196. (e) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321−347. (f) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27−31. (g) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597−2632. (h) Paquette, L. A. *Chem. Rev.* **1986**, *86*, 733−750. (i) Reissig, H. U. *Top. Curr. Chem.* **1988**, *144*, 73−135. (j) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117−3179. (k) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (l) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467−1486. (m) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293−1316. (n) Helmchen, G.; Ernst, M.; Paradies, G. *Pure Appl. Chem.* **2004**, *76*, 495−506. (o) Little, R. D. In *Comprehensive Organic Synthesis, Vol. 5*; Trost, B. M.; Fleming, I., Eds.; Pergamon: New York, 1991; pp 239−270.

(2) (a) Goldschmidt, Z.; Crammer, B. *Chem. Soc. Rev.* **1988**, *17*, 229−267. (b) Hudlicky, T.; Kutchan, T. M.; Naqvi, S. M. *Org. React.* **1985**, *33*, 247−335. (c) Burgess, K. *J. Org. Chem.* **1987**, *52*, 2046−2051. (d) Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 2871−2874. (e) Shimizu, I.; Ohashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 3825−3828. (f) Hiroi, K.; Yamada, A. *Tetrahedron: Asymmetry* **2000**, *11*, 1835−1841. (g) Trost, B. M.; Morris, P. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 6167−6170. (h) Dieskau, A. P.; Holzwarth, M. S.; Plietker, B. *J. Am. Chem. Soc.* **2012**, *134*, 5048−5051.

(3) Shimizu, I.; Ohashi, Y.; Tsuji, J. *Chem. Lett.* **1987**, *6*, 1157−1158.

(4) Trost, B. M.; Fandrick, D. R. *J. Am. Chem. Soc.* **2003**, *125*, 11836−11837.

(5) Larksarp, C.; Alper, H. *J. Org. Chem.* **1998**, *63*, 6229−6233.

(6) (a) Parsons, A. T.; Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2008**, *10*, 2541−2544. (b) For chiral Lewis acid catalyzed [3+2] cycloaddition of cyclopropanes with aldehydes and imines, see: Parsons, A. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 3122−3123. (c) See also: Parsons, A. T.; Smith, A. G.; Neel, A. J.; Johnson, J. S. *J. Am. Chem. Soc.* **2010**, *132*, 9688−9692.

(7) Goldberg, A. F. G.; Stoltz, B. M. *Org. Lett.* **2011**, *13*, 4474−4476.

(8) (a) Mei, L.-Y.; Yuan, Z.-L.; Shi, M. *Organometallics* **2011**, *30*, 6466−6475. (b) Yuan, Z.-L.; Mei, L.-Y.; Wei, Y.; Shi, M.; Kattamuri, P. V.; McDowell, P.; Li, G.-G. *Org. Biomol. Chem.* **2012**, *10*, 2509−2513.

(9) (a) Ogasawara, M.; Yoshida, K.; Kamei, H.; Kato, K.; Uozumi, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1779−1787. (b) Deng, H.-P.; Wei, Y.; Shi, M. *Adv. Synth. Catal.* **2009**, *351*, 2897−2902.

(10) (a) Flack, H. D. *Acta Crystallogr. A* **1983**, *39*, 876−881. (b) Hooft, R. W. W.; Straver, L. H.; Spek, A. L. *J. Appl. Crystallogr.* **2008**, *41*, 96−103.

(11) Meng, Q.-H.; Zhu, L.-F.; Zhang, Z.-G. *J. Org. Chem.* **2008**, *73*, 7209−7212.

(12) Palacios, F.; Vicario, J.; Aparicio, D. *Eur. J. Org. Chem.* **2006**, 2843−2850.
(13) Larios, E. S.; Thai, K.; Bilodeau, F.; Gravel, M. *Org. Lett.* **2011**, *13*, 4942−4945.
(14) Srivastava, B. K.; Joharapurkar, A.; Raval, S.; Patel, J. Z.; Soni, R.; Raval, P.; Gite, A.; Goswami, A.; Sadhwani, N.; Gandhi, N.; Patel, H.; Mishra, B.; Solanki, M.; Pandey, B.; Jain, M. R.; Patel, P. R. *J. Med. Chem.* **2007**, *50*, 5951−5966.
(15) Belmessieri, D.; Morrill, L. C.; Simal, C.; Slawin, A. M. Z.; Smith, A. D. *J. Am. Chem. Soc.* **2011**, *133*, 2714−2720.
(16) Duan, H.-F.; Xie, J.-H.; Qiao, X.-C.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4351−4353.