Supporting Information

Direct Generation of Nucleophilic Chiral Palladium Enolate from 1,3-Dicarbonyl Compounds: Catalytic Enantioselective Michael Reaction with Enones

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General: NMR spectra were recorded on a JEOL JNM-LA400 spectrometer, operating at 400 MHz for ^1H -NMR, 100.4 MHz for ^{13}C -NMR. Chemical shifts were reported downfield from TMS (= 0) for ^1H -NMR. For ^{13}C -NMR, chemical shifts were reported in the scale relative to the solvent used as an internal reference. FAB-MS (low and high resolution) was taken on JEOL JMS GCmate II using *m*-nitrobenzyl alcohol (mNBA) as matrix. ESI-MS experiments were carried out using Bruker Bio-TOF. Optical rotations were measured on a JASCO DIP-370 polarimeter. Column chromatography was performed with silica gel 60 (40-100 μm) purchased from KANTO CHEMICAL Co. The enantiomeric excesses (ee's) were determined by HPLC analysis. HPLC analysis was performed on Shimazu HPLC systems consisting of the followings: pump, LC-10AD; detector, SPD-10A measured at 254 nm or 280 nm; column, DAICEL CHIRALPAK AS, AD, AD-H or DAICEL CHIRALCEL OJ, OD, OD-H; mobile phase, hexane / 2-propanol (IPA). In general, reactions were carried out under a nitrogen atmosphere, unless noted otherwise. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Other reagents were purified by usual methods.

Preparation of Palladium Complexes **1a**, **2a**, and **2b**

$[\{\text{Pd}(\text{R})\text{-tol-binap}\}_2(\mu\text{-OH})_2]^{2+}2\text{TfO}^-$ (**1a**), $[\text{Pd}\{(\text{R})\text{-tol-binap}\}(\text{H}_2\text{O})_2]^{2+}2\text{TfO}^-$ (**2a**), and $[\text{Pd}\{(\text{R})\text{-binap}\}(\text{H}_2\text{O})_2]^{2+}2\text{TfO}^-$ (**2b**) were synthesized according to the representative procedures¹ which have been reported from our laboratory.

(1). Fujii, A.; Hagiwara, E.; Sodeoka, M. *J. Am. Chem. Soc.* **1999**, *121*, 5450-5458.

NMR experiments

The reaction using palladium complex **1a**

Palladium complex **1a** (52 mg, 0.0273 mmol) was placed in NMR tube under nitrogen atmosphere. The complex was dissolved in THF- d_8 (0.6 mL). THF- d_8 was purchased from Merck and used directly as a solvent. Diketone **4a** (10 μL , 0.055 mmol) was added to this solution. The resulting mixture was stirred at room temperature for 2 h. The reaction between **1a** and **4a** was monitored by ^1H -NMR 15 min, 1h, and 2h after the addition of **4a**. By comparing the integration ratio of *t*-Bu groups derived from **4a** (1.0 ppm) and palladium enolate **5a** (0.5 ppm) (**Figure 1**), the yields of **5a** were estimated: about 9%, 58% of **4a** were

Figure 1. Generation of Palladium Enolate **5a** : ^1H -NMR Spectra in THF-d_8 .

(A) **4a**; (B) **1a**; (C) reaction mixture 2 h after the addition of **4a** (1 eq.) to **1a** (0.5 eq.); (D) **2a**; (E) reaction mixture 2 h after the addition of **4a** (1 eq.) to **2a**. (F) **5a** + MVK (2.0 eq.); (G) **5a** + MVK (2.0 eq.) + TfOH (1.0 eq. to **5a**), 1 h; (H) **5a** + MVK (2.0 eq.) + TfOH (1.0 eq. to **5a**), 5 h.

found to be converted to **5a** after 15 min and 1 h, respectively. After 2 h, the starting material **4a** disappeared and the complete generation of **5a** was observed (**Figure 1**, (C)). For references, ^1H -NMR of palladium complex **1a** and dikeotne **4a** were measured in THF-d_8 independently (**Figure 1**, (A), (B)). The singlets (1.0 ppm, blue) corresponding to *t*-Bu of **4a** moved upfield to 0.5 ppm due to the anisotropic effect of the neighboring tolyl group (A, C). The characteristic two singlets (green) of **1a**, at 1.9 and 2.1 ppm, changed to four singlets, 2.05, 2.06, 2.40 and 2.42 ppm, indicating that the four methyl groups on

(*R*)-Tol-BINAP were located in different environments (**B**, **C**). In the aromatic field, the original peaks changed and distinct peaks shown in red appeared (**B**, **C**). Together with the results of ESI mass spectroscopy discussed later, this NMR experiment showed clean formation of palladium enolate **5a**.

To this palladium enolate was added 2 eq. of methyl vinyl ketone **6a**. But, the reaction did not proceed (**Figure 1**, (F))

As discussed in the text, addition of TfOH was effective to promote the reaction. To the reaction mixture was added TfOH (4.5 μ L, 0.051 mmol, 1 eq. to **5a**) at 0 °C. A singlet corresponding to the *t*-Bu group (0.97 ppm) of the Michael product was increased according to the decrease of that of **5a**. As the **Figure 1** (G) shows, about 55% of **5a** was converted to **7a** after 1 h. Further stirring for 4 h led to the completion of the reaction (**Figure 1**, (H)). The reaction was quenched by adding saturated NH₄Cl (2 mL) and aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layers were washed with brine and dried over Na₂SO₄. Further purification was carried out by flash column chromatography (SiO₂, eluent: hexane / ethyl acetate = 9 / 1) to afford **7a** in 96%. The enantiomeric excess was determined to be 97% by HPLC.

The reaction using palladium complex **2a**

2a (61 mg, 0.055 mmol) was placed in NMR tube under nitrogen atmosphere and dissolved in THF-*d*₈ (0.6 mL). First of all, ¹H-NMR of **2a** was taken as a reference (**Figure 1**, (D)). To this solution was added **4a** (10 μ L, 0.055 mmol) at room temperature. It is likely that the reaction reached the equilibrium between **4a** and **5a** quickly (**Figure 1**, (E)). While 70% conversion was observed only after 15 min, about 30 % of **4a** still remained unchanged even after 2 h. Comparing (C) and (E) in **Figure 1**, the same peaks corresponding to the chiral palladium enolate **5a** were observed.

This enolate formation should entail the concomitant generation of TfOH. Thus, the addition of TfOH would be unnecessary when **2a** is used as a catalyst. Indeed, the reaction with **6a** was found to proceed smoothly without any additional TfOH. Thus, 2 eq. of **6a** (9 μ L, 0.11 mmol) was added to this equilibrium mixture at 0 °C. The reaction was monitored by observing the disappearance of *t*-Bu group of **4a** and **5a** as well as the appearance of *t*-Bu of **7a**. After 5 h, the reaction was quenched by adding saturated NH₄Cl (2 mL). The aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layers were washed with brine. Further purification was performed by flash column chromatography (SiO₂, eluent: hexane / ethyl acetate = 9 / 1) to give the desired product **7a** as the colorless oil. Isolated yield was 99% and the ee was 97%.

2-(3,3-dimethyl-butyryl)-2-(3-oxobutyl)-cyclopentanone (**7a**)

¹H-NMR (400 MHz, CDCl₃) δ 1.12 (s, 9H), 1.59-1.66 (m, 1H), 1.77-2.00 (m, 3H), 2.26-2.37 (m, 5H), 2.49-2.58 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 19.3, 27.4, 29.5, 30.0, 31.7, 38.5, 38.6, 49.7, 68.1, 205.8, 207.3, 216.5; FAB-MS (mNBA) *m/z* 253 (M+1)⁺; [α]_D²⁵ +115.4 (c = 0.2, CHCl₃) (96% ee); HPLC (DAICEL CHIRALCEL OJ, hexane / IPA = 95 / 5, 0.44 mL / min, 280 nm) *t*_r(major) = 20.7 min, *t*_r(minor) = 26.5 min; FAB-HRMS (mNBA) Calcd for C₁₅H₂₅O₃ (M+1)⁺ 253.1804. Found 253.1811.

ESI-MS for palladium enolate **5a**

The mass spectrum of the sample prepared by method (I)

The mass spectrum of the sample prepared by method (II)

The palladium enolate complex (**5a**) was prepared in 2 ways as shown below.

(I) According to the similar procedure to the NMR experiments, **1a** and **4a** were mixed in THF.

(II) According to the similar procedure to the NMR experiments, **2a** and **4a** were mixed in THF.

Both samples were diluted with IPA keeping the concentration at 10 pmol / μ L. IPA solution was infused into Bio-TOF at 2 μ L / min using a syringe pump. The capillary was maintained at 4000V, and the heat gas was used at 120 °C.

From both samples the same mass values were obtained.

Sample (I) m/z observed: 965.2901, calcd. for **5a**: 965.2887

Sample (II) m/z observed: 965.2908, calcd. for **5a**: 965.2887

The observed mass values and isotope distribution were matched with calculated ones. These data strongly indicate the generation of the chiral palladium enolate (**5a**) from both palladium complexes **1a** and **2a**.

General procedure for the catalytic enantioselective Michael reaction of 1,3-diketones (GP 1)

The palladium catalyst **2b** (0.02 mmol, 10 mol %) was dissolved in THF (50 μ L) under nitrogen

atmosphere. To this solution was added **4** (0.2 mmol) at $-10\text{ }^{\circ}\text{C}$, followed by the addition of **6a** (33 μL , 0.4 mmol). The reaction mixture was allowed to stir at the same temperature for the time described in the text (30 h for **4a**, 36 h for **4b**). After the completion of the reaction (TLC), saturated NH_4Cl (2 mL) was added to the mixture. Aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 . The removal of solvent under the reduced pressure, followed by flash column chromatography (SiO_2 , eluent: hexane / ethyl acetate = 9 / 1) afforded the desired product as a colorless oil.

3-Acetyl-1-(2-bromophenyl)-3-methyl-heptane-2,6-dione (**7b**)

^1H -NMR (400 MHz, C_6D_6) δ 1.09 (s, 3H), 1.58 (s, 3H), 1.83 (s, 3H), 2.02-2.17 (m, 4H), 3.65 (d, $J = 17.8$ Hz, 1H), 3.69 (d, $J = 17.8$ Hz, 1H), 6.68 (ddd, $J = 1.7, 7.6, 8.8$ Hz, 1H), 6.90 (ddd, $J = 1.2, 7.6, 7.6$ Hz, 1H), 6.97 (dd, $J = 1.7, 7.6$ Hz, 1H), 7.33 (dd, $J = 1.2, 8.8$ Hz, 1H); ^{13}C -NMR (100 MHz, C_6D_6) δ 19.1, 26.4, 28.4, 29.3, 38.3, 45.8, 65.3, 125.6, 127.5, 128.9, 132.3, 132.8, 134.7, 204.8, 205.7, 206.2; FAB-MS (mNBA) m/z 341 ($\text{M}+2+1$)⁺, 339 ($\text{M}+1$)⁺; $[\alpha]_{\text{D}}^{25} -1.3$ ($c = 2.37$, CHCl_3) (90% ee); HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 4 / 1, 0.44 mL / min, 280 nm) t_{r} (minor) = 28.8 min, t_{r} (major) = 35.1 min; FAB-HRMS (mNBA) Calcd for $\text{C}_{16}\text{H}_{20}\text{BrO}_3$ ($\text{M}+1$)⁺ 339.0596. Found 339.0595.

Optimization of the reaction conditions: catalytic enantioselective Michael reaction of β -ketoester **8a**.

We tried various reaction conditions to develop an efficient Michael reaction of β -ketoesters. Representative results are provided in Table 2. First we carried out the reaction using *tert*-butyl 2-oxocyclopentanecarboxylate **8a** with 5 mol % of **2a**. The reaction of **8a** with **6a** in THF (1 M) afforded the desired product **9a** with *R* configuration (87%, 84 h) and the observed enantioselectivity was excellent (94% ee) (entry 1). Higher substrate concentration shortened the reaction time (4 M, 92% after 24 h, 92% ee; neat, quant. After 15 h, 88% ee) (entries 2, 3). Other solvents such as acetone and CH_2Cl_2 gave

Table 2. Optimization of Michael Reaction Using β -Ketoester

	8a, f, g	6a				
entry	ester : R	solvent	time (h)	product	yield (%)	ee (%)
1	<i>t</i> -Bu (8a)	THF	84	9a	87	94
2 ^a	<i>t</i> -Bu (8a)	THF	24	9a	92	92
3	<i>t</i> -Bu (8a)	neat	15	9a	quant.	88
4	<i>t</i> -Bu (8a)	acetone	12	9a	92	90
5	<i>t</i> -Bu (8a)	CH_2Cl_2	36	9a	96	89
6	Et (8f)	CH_2Cl_2	24	9j	90	38
7	Me (8g)	CH_2Cl_2	24	9k	83	25

^a The reaction was conducted with 4 M **8a**.

comparable results (entries 4, 5), and no reaction proceeded in DMF, toluene, or ether. The bulkiness of

the ester group is critical for high asymmetric induction. As the size of the ester group decreased, enantioselectivity dramatically dropped from 89% ee (*t*-Bu ester) to 25% ee (Me ester) (entries 5-7).

General procedure for the catalytic asymmetric Michael reaction of β -ketoesters (GP 2)

The palladium catalyst **2** (0.02 mmol, 5 mol %) was dissolved in THF (0.1 mL) under nitrogen atmosphere. To this solution was added **8** (0.4 mmol) at ambient temperature. After cooling to the temperature shown in **Table 1**, 2 eq. of enone (0.8 mmol) was added. The reaction was monitored by TLC. The reaction mixture was allowed to stir at the same temperature for the time described in **Table 1**. Saturated NH_4Cl (2 mL) was added to the mixture for quenching. Aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 . Removal of solvent under the reduced pressure, followed by flash column chromatography (SiO_2 , eluent: hexane / ethyl acetate = 9 / 1) afforded the desired product.

(*R*)-*tert*-Butyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate (**9a**):

^1H -NMR (400 MHz, CDCl_3) δ 1.39 (s, 9H), 1.76-2.02 (m, 5H), 2.09 (s, 3H), 2.15-2.45 (m, 4H), 2.64-2.27 (m, 1H); ^{13}C -NMR (100 MHz, CDCl_3) δ 19.6, 27.0, 27.8, 29.9, 34.5, 37.9, 38.8, 59.4, 81.9, 170.6, 207.9, 215.2; FAB-MS (mNBA) m/z 255 ($\text{M}+1$)⁺, 199 ($\text{M}+2\text{H}-t\text{-Bu}$)⁺; $[\alpha]_{\text{D}}^{20} +8.7$ ($c = 0.41$, CHCl_3) (92% ee)²; HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 99 / 1, 0.44 mL / min, 280 nm) t_{r} (major) = 54.6 min, t_{r} (minor) = 77.7 min; FAB-HRMS (mNBA) Calcd for $\text{C}_{14}\text{H}_{23}\text{O}_4$ ($\text{M}+1$)⁺ 255.1596. Found 255.1601.

(2). Determination of the absolute configuration of **9a** is described later.

(*R*)- *tert*-Butyl 2-oxo-1-(3-oxobutyl)cyclohexanecarboxylate (**9b**):

^1H -NMR (400 MHz, CDCl_3) δ 1.39 (s, 9H), 1.29-1.77 (m, 5H), 1.90-2.00 (m, 2H), 2.06 (s, 3H), 2.22-2.35 (m, 3H), 2.41-2.56 (m, 2H); ^{13}C -NMR (100 MHz, CDCl_3) δ 22.5, 27.4, 27.8, 28.5, 29.8, 36.7, 38.9, 40.9, 60.4, 82.1, 171.0, 207.7, 208.0; FAB-MS (mNBA) m/z 269 ($\text{M}+1$)⁺, 213 ($\text{M}+2\text{H}-t\text{-Bu}$)⁺; $[\alpha]_{\text{D}}^{13} +92.5$ ($c = 0.29$, CHCl_3) (86% ee)³; HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 9 / 1, 0.44 mL / min, 280 nm) t_{r} (major) = 20.7 min, t_{r} (minor) = 30.9 min; FAB-HRMS (mNBA) Calcd for $\text{C}_{15}\text{H}_{25}\text{O}_4$ ($\text{M}+1$)⁺ 269.1753. Found 269.1757.

(3). Determination of the absolute configuration of **9b** is described later.

tert-Butyl 1-oxo-2-(3-oxobutyl)-2-indanecarboxylate (**9c**):

^1H -NMR (400 MHz, CDCl_3) δ 1.39 (s, 9H), 2.13 (s, 3H), 2.16-2.21 (m, 2H), 2.47-2.68 (m, 2H), 3.00 (d, $J = 17.4$ Hz, 1H), 3.61 (d, $J = 17.4$ Hz, 1H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.47 (d, $J = 7.8$ Hz, 1H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.76 (d, $J = 7.8$ Hz, 1H); ^{13}C -NMR (100 MHz, CDCl_3) δ 27.8, 28.4, 29.9, 37.9, 38.9, 59.9, 82.0, 124.7, 126.3, 127.8, 135.2, 135.3, 152.6, 170.1, 202.7, 207.7; FAB-MS (mNBA) m/z 303 ($\text{M}+1$)⁺, 247 ($\text{M}-t\text{-Bu}$)⁺; $[\alpha]_{\text{D}}^{20} -16.5$ ($c = 1.98$, CHCl_3) (81% ee); HPLC (DAICEL CHIRALCEL OJ, hexane / IPA = 9 / 1, 0.44 mL / min, 280 nm) t_{r} (major) = 26.6 min, t_{r} (minor) = 41.6 min; FAB-HRMS (mNBA) Calcd for $\text{C}_{18}\text{H}_{23}\text{O}_4$ ($\text{M}+1$)⁺ 303.1596. Found 303.1587.

***tert*-Butyl 2-acetyl-2-methyl-5-oxohexanoate (9d):**

¹H-NMR (400 MHz, CDCl₃) δ 1.20 (s, 3H), 1.36 (s, 9H), 1.86-1.94 (m, 1H), 1.97-2.03 (m, 1H), 2.05 (s, 3H), 2.06 (s, 3H), 2.22-2.39 (m, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 19.1, 26.1, 27.8, 28.3, 29.7, 38.6, 59.3, 82.0, 171.7, 205.5, 207.4; FAB-MS (mNBA) m/z 243 (M+1)⁺, 187 (M+2H-*t*-Bu)⁺; [α]_D¹⁴ +13.6 (c = 1.17, CHCl₃) (89% ee); HPLC (DAICEL CHIRALCEL OB-H, hexane / IPA = 200 / 1, 0.44 mL / min, 280 nm) t_r (minor) = 57.5 min, t_r (major) = 62.5 min; FAB-HRMS (mNBA) Calcd for C₁₃H₂₃O₄ (M+1)⁺ 243.1596. Found 243.1597.

***(R)*-Phenyl 2-acetyl-2-methyl-5-oxohexanoate (9e):**

¹H-NMR (400 MHz, CDCl₃) δ 1.50 (s, 3H), 2.14-2.60 (m, 10H), 7.06-7.42 (m, 5H); ¹³C-NMR (100 MHz, CDCl₃) δ 19.5, 26.2, 28.4, 30.0, 38.5, 59.0, 121.1, 126.2, 129.5, 171.3, 204.9, 207.2; FAB-MS (mNBA) m/z 263 (M+1)⁺; [α]_D¹⁸ -2.3 (c = 1.02, CHCl₃) (93% ee)⁴; HPLC (DAICEL CHIRALPAK AD-H, hexane / IPA = 19 / 1, 0.44 mL / min, 280 nm) t_r (minor) = 45.7 min, t_r (major) = 48.9 min; FAB-HRMS (mNBA) Calcd for C₁₅H₁₉O₄ (M+1)⁺ 263.1283. Found 263.1296.

(4) Determination of the absolute configuration of **9e** is described later.

***tert*-Butyl 2-oxo-1-(3-oxopentyl)cyclopentanecarboxylate (9f):**

¹H-NMR (400 MHz, CDCl₃) δ 0.99 (t, *J* = 7.3 Hz, 3H), 1.74-2.03 (m, 5H), 2.16-2.25 (m, 1H), 2.29-2.42 (m, 4H), 2.63 (ddd, *J* = 5.6, 9.8, 17.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 7.74, 19.5, 27.1, 27.8, 34.4, 35.8, 37.5, 37.9, 59.5, 81.9, 170.6, 210.6, 215.1; FAB-MS (mNBA) m/z 269 (M+1)⁺, 213 (M+2H-*t*-Bu)⁺; [α]_D²⁰ +5.5 (c = 1.14, CHCl₃) (88% ee); HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 99 / 1, 0.44 mL / min, 280 nm) t_r (major) = 27.3 min, t_r (minor) = 37.9 min; FAB-HRMS (mNBA) Calcd for C₁₅H₂₅O₄ (M+1)⁺ 269.1753. Found 269.1742.

***tert*-Butyl 2-oxo-1-(3-oxopentyl)cyclohexanecarboxylate (9g):**

¹H-NMR (400 MHz, CDCl₃) δ 1.32-1.41 (m, 1H), 1.41 (s, 9H), 1.49-1.81 (m, 4H), 1.93-2.03 (m, 2H), 2.23-2.55 (m, 7H); ¹³C-NMR (100 MHz, CDCl₃) δ 7.80, 22.6, 27.5, 27.9, 28.6, 35.8, 36.7, 37.3, 41.0, 60.5, 82.1, 171.1, 208.1, 210.6; FAB-MS (mNBA) m/z 283 (M+1)⁺, 227 (M+2H-*t*-Bu)⁺; [α]_D²⁶ +73.5 (c = 2.18, CHCl₃) (86% ee); HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 9 / 1, 0.44 mL / min, 280 nm) t_r (major) = 15.3 min, t_r (minor) = 19.0 min; FAB-HRMS (mNBA) Calcd for C₁₆H₂₇O₄ (M+1)⁺ 283.1909. Found 283.1916.

Diastereo- and enantioselective Michael reaction

The reaction was conducted according to the general procedure (**GP 2**). The determination of the absolute configuration as well as relative configuration of these products is now underway.

***tert*-Butyl 2-oxo-1-(1-phenyl-3-oxobutyl)cyclopentanecarboxylate (9h, major):**

¹H-NMR (400 MHz, CDCl₃) δ 1.42 (s, 9H), 1.68-1.95 (m, 3H), 1.95-2.01 (m, 1H), 2.01 (s, 3H), 2.17-2.26 (m, 1H), 2.34-2.40 (m, 1H), 3.00 (d, *J* = 7.10 Hz, 2H), 3.96 (t, *J* = 7.80 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 19.4, 27.8, 29.9, 30.4, 38.3, 43.5, 45.3, 64.8, 82.3, 127.1, 128.2, 129.8, 138.9, 169.2, 206.8, 213.6; FAB-MS (mNBA) *m/z* 331 (M+1)⁺, 275 (M+2H-*t*-Bu)⁺; [α]_D²⁰ -64.9 (*c* = 1.49, CHCl₃) (97% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 49 / 1, 0.44 mL / min, 280 nm) *t*_r (minor) = 19.1 min, *t*_r (major) = 20.5 min; FAB-HRMS (mNBA) Calcd for C₂₀H₂₇O₄ (M+1)⁺ 331.1922. Found 331.1909.

***tert*-Butyl 2-oxo-1-(1-methyl-3-oxobutyl)cyclopentanecarboxylate (**9i**, major):**

¹H-NMR (400 MHz, CDCl₃) δ 0.87 (d, *J* = 6.8 Hz, 9H), 1.44 (s, 9H), 1.84-2.00 (m, 3H), 2.09-2.23 (m, 4H), 2.36-2.44 (m, 1H), 2.34-2.40 (m, 2H), 2.69-2.77 (m, 1H), 2.84 (dd, *J* = 3.00, 16.4 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 15.6, 19.4, 27.9, 29.6, 29.9, 32.3, 38.5, 46.8, 64.0, 82.0, 169.4, 207.7, 241.6; FAB-MS (mNBA) *m/z* 269 (M+1)⁺, 213 (M+2H-*t*-Bu)⁺; [α]_D²⁰ -28.4 (*c* = 1.01, CHCl₃) (99% ee); HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 99 / 1, 0.44 mL / min, 280 nm) *t*_r (major) = 54.0 min, *t*_r (minor) = 70.0 min; HRMS (mNBA) Calcd for C₁₅H₂₅O₄ (M+1)⁺ 269.1753. Found 269.1759.

Determination of the absolute configuration

We have determined the absolute configuration of three compounds: **9a**, **9b**, and **9e**.

9a: The absolute configuration of **9a** was determined to be *R* by the comparison of the optical rotation with the reported value⁵ after the conversion to the corresponding methyl ester **10**.

Scheme 4. Conversion of **9a** into **10**

The starting material **9a** (92% ee) (45 mg, 0.177 mmol) was dissolved in TFA (0.5 mL) at 0 °C. After stirring for 50 min, the reaction mixture was diluted with ether (5 mL) and water (5 mL) was added. The aqueous layer was extracted with ether (2 x 10 mL) and the combined organic layers were washed with water (2 x 10 mL). The organic layer was dried over Na₂SO₄. Ether was evaporated under reduced pressure below 20 °C. To this crude mixture was added freshly prepared CH₂N₂ in ether until the color of the reaction mixture became yellow. A small amount of acetic acid was added for quenching. The organic layer was washed with saturated NaHCO₃, water, and brine. Further purification was carried out by flash column chromatography (SiO₂, eluent: hexane / acetone = 10 / 1) to give the corresponding methyl ester **10** in 23% (colorless oil).

10: This product was found to be identical with the reported compound by comparison with ¹H-NMR.

[α]_D¹⁵ -12.4 (*c* = 0.44, CHCl₃) [Lit⁵: [α]_D²³ -5.6 (*c* = 9.9, CHCl₃) (31% ee, *R* enantiomer)]

(5) Christoffers, J.; Rößler, U.; Werner, T. *Eur. J. Org. Chem.* **2000**, 701-705. The authors assigned the absolute configuration by analogy to that of other products obtained using their reaction conditions.

9b: The absolute configuration of **9b** was determined to be *R* by comparing the retention times (HPLC) of **11** which was synthesized from either **9b** or ethyl ester **15** with *R* configuration reported by Belfield *et al.*⁶

Scheme 5. Conversion of **9b** into **11** (*t*-Bu)

tert*-Butyl 3, 4, 5, 6, 7, 8-hexahydro-2-oxo-4a(2*H*)-naphthalenecarboxylate: **12*

To a stirred solution (benzene, 3 mL) of **9b** (90% ee) (138 mg, 0.514 mmol) were added pyrrolidine (52 μ L, 0.537 mmol) and acetic acid (35 μ L, 0.537 mmol) at 5 °C. The reaction mixture was stirred at 0–10 °C for 12 h. After the completion of the reaction (TLC), water (3 mL) was added for quenching. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) and the combined organic layers were washed with water and brine. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (SiO₂, eluent: hexane / acetone = 15 : 1). The desired product **12** was obtained in 63% (82 mg) as a yellowish oil. It was found that this conversion was performed without any loss of enantioselectivity (90% ee).

¹H-NMR (400 MHz, CDCl₃) δ 1.25–1.32 (m, 1H), 1.41–1.53 (m, 10H), 1.53–1.75 (m, 2H), 1.77–1.90 (m, 6H), 5.90 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 23.0, 26.4, 27.8, 34.0, 34.6, 34.8, 38.3, 49.4, 81.7, 126.0, 163.7, 172.3, 198.8; HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 99 / 1, 0.44 mL / min, 280 nm) t_r (major) = 27.4 min, t_r (minor) = 32.8 min.

tert*-Butyl 3', 4', 5', 6', 7', 8'-hexahydro-spiro([1,3]-dioxolane-2, 2'-naphthalene)-4'a-carboxylate: **13*

The compound **12** (81.7 mg, 0.039 mmol) was dissolved in dry CH₂Cl₂ (0.25 mL) under nitrogen atmosphere. After cooling to –60 °C, 1,2-bis(trimethylsilyloxy)ethane (100 μ L, 0.408 mmol) and TMSOTf (10 μ L, 0.056 mmol) were added successively. The resulting mixture was allowed to stir at –40 °C for 38 h. The reaction mixture was diluted with ether (5 mL) and saturated NH₄Cl (5 mL) was added. The organic layer was separated and the aqueous layer was extracted with ether (2 x 5 mL). The combined ether was washed with brine and dried over Na₂SO₄. The crude product obtained after evaporation was purified by flash column chromatography (SiO₂, eluent: hexane / ethyl acetate = 12 / 1) to give the desired product **13** in 73% (66.3 mg).

¹H-NMR (400 MHz, CDCl₃) δ 1.34-1.70 (m, 16H), 1.97-2.07 (m, 3H), 2.15-2.23 (m, 2H), 2.56 (ddd, *J* = 3.2, 5.6, 14.2 Hz, 1H), 3.87-3.95 (m, 4H), 5.56 (dd, *J* = 3.6, 5.9 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 19.3, 25.2, 27.9, 32.5, 34.6, 35.4, 43.2, 47.8, 64.2, 64.4, 80.4, 109.1, 125.2, 134.6, 174.9.

(3', 4', 5', 6', 7', 8'-Hexahydro-spiro[[1,3]-dioxolane-2, 2'-naphthalene]-4'a-yl)-methanol: 14

13 (27.6 mg, 0.0938 mmol) was dissolved in THF (1 mL). Lithium aluminum hydride (LAH) (14 mg, 0.37 mmol) was added, and the reaction mixture was stirred at 50 °C for 24 h. Excess LAH was filtered off through celite. The residue was washed with ether several times. The solvent was removed under reduced pressure. The resulting crude product was purified by flash column chromatography (SiO₂, eluent : hexane / acetone = 8 / 1) to afford **14** in 95% (20 mg) as a white solid.

¹H-NMR (400 MHz, CDCl₃) δ 1.17-1.41 (m, 3H), 1.54-1.71 (m, 3H), 1.74-1.85 (m, 2H), 1.91-2.11 (m, 3H), 2.16 (dd, *J* = 2.7, 14.2 Hz, 1H), 2.41 (ddd, *J* = 3.2, 5.3, 14.2 Hz, 1H), 3.62 (d, *J* = 11.2 Hz, 1H), 3.67 (d, *J* = 11.2 Hz, 1H), 3.92-4.00 (m, 4H), 5.61-5.63 (m, 1H).

4a-Hydroxymethyl-4, 4a, 5, 6, 7, 8-hexahydro-(3*H*)-naphthalene-2-one: 11 (*t*-Bu)

To a solution (THF, 2 mL) of **14** (60.7 mg, 0.206 mmol) was added 1N HCl (2 drops). The reaction mixture was stirred at room temperature. After the completion of the reaction (about 24 h) (TCL), saturated NaHCO₃ (1 mL) was added. The aqueous layer was extracted with ether (2 x 10 mL) and the combined organic layers were washed with brine. Further purification was carried out by flash column chromatography (SiO₂, eluent : hexane / ether = 5 / 1) to give **11 (*t*-Bu)** in 62% as a white solid. HPLC analysis revealed the ee of **11 (*t*-Bu)** to be 90%.

¹H-NMR (400 MHz, CDCl₃) δ 1.22 (ddd, *J* = 5.1, 13.0, 13.0 Hz, 1H), 1.38-1.50 (m, 1H), 1.56-1.72 (m, 3H), 1.91-2.04 (m, 3H), 2.18 (ddd, *J* = 3.16, 5.36, 13.7 Hz, 1H), 2.30-2.36 (m, 3H), 2.61 (ddd, *J* = 5.6, 14.4, 19.8 Hz, 1H), 3.77 (d, *J* = 11.2 Hz, 1H), 3.8 (d, *J* = 11.2 Hz, 1H), 5.88 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.7, 26.9, 32.9, 33.2, 34.2, 35.4, 41.3, 63.5, 126.8, 166.9, 200.0; FAB-MS (mNBA) *m/z* 181 (*M*+1)⁺; HPLC (DAICEL CHIRALPAK AD, hexane / IPA = 9 / 1, 0.44 mL / min, 254 nm) *t_r* (minor) = 25.4 min, *t_r* (major) = 26.8 min; FAB-HRMS (mNBA) Calcd for C₁₁H₁₇O₂ (*M*+1)⁺ 181.1229. Found 181.1230.

15 with *R* configuration was prepared according to the procedure reported by Belfield.⁶ The enantiomeric excess was determined to be 70% ee by HPLC (DAICEL CHIRALPAK AS, hexane / IPA = 9 / 1, 0.44 mL / min, 280 nm: *t_r* (major) = 31.3 min, *t_r* (minor) = 40.1 min). According to the procedures for the synthesis of **11 (*t*-Bu)**, the conversion of **15** to **11 (Et)** was achieved. The obtained **11 (Et)** was found to be identical with **11(*t*-Bu)** by comparing NMR data. The enantiomeric excess was determined to be 70% ee by HPLC.

11 (Et): HPLC (DAICEL CHIRALPAK AD, hexane / IPA = 9 / 1, 0.44 mL / min, 254 nm) *t_r* (minor) = 25.4 min, *t_r* (major) = 26.8 min.

(6) Belfield, K. D.; Seo, J. *Synth. Commun.* **1995**, 25, 461-466.

The retention time (major enantiomer) of both compounds **11 (t-Bu)** and **11 (Et)** was revealed to be identical. Therefore, it is concluded that the absolute configuration of **9b** produced by **2a** is *R*.

9e: The absolute configuration of **9e** was determined to be *R* by the comparison of the optical rotation with the reported value⁷ after the conversion to the corresponding ethyl ester **16**.

To a stirred solution (anhydrous EtOH, 1 mL) of **9e** (30 mg, 0.114 mmol, 93% ee) was added Ti(OEt)_4 (5 μL , 0.024 mmol) under nitrogen atmosphere. The reaction mixture was kept at 40 °C. When the reaction completed (TLC), 1N HCl (1 mL) was added. Ethyl acetate (5 mL) was added for extraction. The organic layer was washed with saturated NaHCO_3 (5 mL), water and brine. After the removal of solvent, the residue was carefully purified by flash column chromatography (SiO_2 , eluent: hexane / ethyl acetate = 15 / 1) to afford the corresponding ethyl ester **16** (14 mg, 57%).

16: The product was found to be identical with the compound reported by Shibasaki *et al.*

$[\alpha]_D^{25} +11.3$ ($c = 1.40$, CHCl_3) (93% ee) [Lit.^{7a}: $[\alpha]_D^{23} +7.2$ ($c = 1.01$, CHCl_3) (74% ee, *R* enantiomer)]

(7) a) Sasai, H.; Emori, E.; Arai, T.; Shibasaki, T. *Tetrahedron Lett.* **1996**, 37, 5561-5564.

b) Fráter, G.; Müller, U.; Günther, W. *Tetrahedron* **1984**, 40, 1269-1277.