Supporting Information

Catalytic Asymmetric Michael Reaction of β -Keto Esters: Effects of the Linker Heteroatom in Linked-BINOL

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General: All reactions were carried out under an argon atmosphere with dry solvents, unless otherwise stated. Reagents were purified by the usual methods. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm Merck silica gel plates (60F-254). Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^1H NMR and 125.65 MHz for ^{13}C NMR and calibrated using residual undeuterated solvent as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI mass spectra were measured on a Waters micromass ZQ with Waters 2695 Separation Module (for LC-MS). Experiments were performed in positive ion mode. HR-MS spectra were measured on a JEOL JMS-700D MStation, using Kanto Chemical PEG 400 or PEG 600 matrix as the internal standard. The enantiomeric excess (ee) was determined by GC analysis. GC was performed on Shimadzu GC-14A with Varian Chirasil DEX CB column (0.25 mm x 25 m), carrier gas, nitrogen (4 kPa).

1. The Usefulness of the Michael Adducts

Scheme 1. More Efficient Route of (–)-Strychnine Using the Catalytic Asymmetric Michael Reaction of β -Keto Ester

We recently achieved enantioselective total synthesis of (–)-strychnine using the catalytic asymmetric Michael reaction promoted by (*R*)-ALB complex.^{6d} But in this synthesis, C–C bond cleavage (decarboxylation) and re-construction (aldol reaction) were necessary. If the catalytic asymmetric

Michael reaction of β -keto ester instead of that of malonate can be utilized, it is possible to synthesize the intermediate more efficiently. While the conversion of the Michael adduct to the intermediate is promising, the catalytic asymmetric Michael reaction gave the suitable Michael adduct for the synthesis in exceptionally low yield and enantiomeric excess even using (*R,R*)-La–NMe-linked-BINOL complex or La–NH-linked-BINOL complex. Further investigations are currently ongoing.

2. Procedure for the Preparation of (*S,S*)-La–NMe-linked-BINOL Complex

To a stirred solution of (*S,S*)-NMe-linked-BINOL (**2**) (212.9 mg, including 11.6 w/w % solvent (THF and hexane), 0.30 mmol) in THF (1.95 mL) at $-78\text{ }^{\circ}\text{C}$ was added a solution of $\text{La}(\text{O-}i\text{-Pr})_3$ (1.5 mL, 0.30 mmol, 0.2 M in THF, freshly prepared from the powder of $\text{La}(\text{O-}i\text{-Pr})_3$ and dry THF, $\text{La}(\text{O-}i\text{-Pr})_3$ was purchased from Kojundo Chemical Laboratory CO., LTD., 5-1-28, Chiyoda, Sakado-shi, Saitama 350-0214, Japan (fax, ++(81)-492-84-1351)). The solution was stirred for 2.5 h at room temperature, and then the solvent was evaporated under reduced pressure. The resulting residue was dried for 2 h under reduced pressure (ca. 4 mmHg) to afford yellow powdered (*S,S*)-La–NMe-linked-BINOL complex (254.0 mg, 0.30 mmol). This powdered catalyst can be stored for at least 6 weeks under air at room temperature (See next section).

3. Catalyst Stability under Ar or Air

The (*S,S*)-La–NMe-linked-BINOL complex is very stable even under air and can be stored without any care at ambient temperature for at least 6 weeks. As shown in Table S1, slight loss of catalytic activity, in terms of both chemical yield and enantiomeric excess, was observed using stock catalyst both under Ar and air after 1 week storage (entry 1 and 2). The difference of stability under Ar or air was not observed at all. After 6 weeks storage under air, **5ba** was obtained in 75% yield and 90% ee (entry 4). This result was same as the result after 1 week (entry 2).

Table S1. Catalytic Asymmetric Michael Reaction Using Stored (S,S)-La–NMe-linked-BINOL Complex^a

O=C1C=CCCC1 (1.0 eq) **7b** + CC(=O)CC(=O)OC (1.0 eq) **8a** $\xrightarrow[\text{THF/DME (9/1, 1.0 M), rt, 48 h}]{\text{Stored-(S,S)-La-2 (10 mol \%)}}$ CC(=O)C1C(C(=O)OC)CCCC1 **9ba**

entry	stored period (week)	under Ar		under air	
		yield (%) ^b	ee (%) ^c	yield (%) ^b	ee (%) ^c
1	0	78	92	78	92
2	1	75	90	77	91
3	4	74	90	78	89
4	6	76	89	75	90

^aProduct was obtained as a 1:1 mixture of diastereomers. ^bIsolated yield.

^cEnantiomeric excess was determined by GC analysis after conversion to the appropriate derivatives.

4. Computational Optimization and Calculation of Atomic Charges

Based on the structure of Ga–Li–linked-BINOL complex,^{SI-1} computational optimization of the La–O-linked-BINOL complex was made as a monomeric structure. The initial structure of the La–O-linked-BINOL was obtained by substitutions of center metal (from Ga to La) and counter cation of phenolic oxygen (from Li to H) in the Ga–Li–linked-BINOL complex. The lowest energy conformation of the La–O-linked-BINOL was obtained by molecular mechanics minimization (UNIVERSAL forcefield^{SI-2} (v. 1.0.2) calculation performed on Cerius² (Accelrys Inc.)) followed by *ab initio* calculation (HF/LanL2DZ^{SI-3} level with Gaussian 98^{SI-4} (Gaussian Inc.)) and the B3LYP¹⁶ hybrid density functional method using a LanL2DZ basis set with Gaussian 98.^{SI-5} Because further examination of natural bond orbital analysis (Pop=NPA) and more desirable calculations using the MP2 method for the calculation of atomic charges was not possible due to the existence of lanthanum atoms in the molecule, atomic charges (Mulliken charges) of La–O-linked-BINOL was calculated by the B3LYP¹⁶ hybrid density functional method using a LanL2DZ basis set with Gaussian 98.^{SI-4} Computational optimization and calculation of atomic charges of La–NH-linked-BINOL complex and La–NMe-linked-BINOL complex was performed in a similar way. The pdb data of all three complexes were attached in the last section of this Supporting Information.

Figure S1. Calculation of Atomic Charges of La-O-linked-BINOL and La-NR-linked-BINOL

5. Synthesis of Ligand 1, 2, 3 and 4

Scheme S2. Synthesis of Ligand 1, 2, 3, and 4

(a) $\text{NH}_2\text{R}\cdot\text{HCl}$, $i\text{Pr}_2\text{NEt}$, TBAI, CH_2Cl_2 , CH_3CN (b) $\text{TsOH}\cdot\text{H}_2\text{O}$, CH_2Cl_2 , MeOH (c) aq HCl , Zn dust

Synthesis of (*S,S*)-3-bromomethyl-2,2'-bis(methoxymethoxy)-1,1'-binaphthalene (**20**) was reported in our previous manuscript. See, ref. SI-1.

5-1. General Procedure for the Coupling Reaction

(*S,S*)-3,3'-[Methyliminobis(methylene)]bis[2,2'-bis(methoxymethoxy)-1,1'-binaphthalene] (21**):** To a solution of methylamine hydrochloride (169.3 mg, 2.5 mmol) and $i\text{Pr}_2\text{NEt}$ (2.6 mL, 10 mmol) in the mixture of CH_2Cl_2 (10 mL) and MeCN (20 mL), tetrabutylammonium iodide (367.9 mg, 1.0 mmol) and 3-bromomethyl-2,2'-bis(methoxymethoxy)-1,1'-binaphthalene (**20**) (2.34 g, 5.0 mmol) were added. The reaction mixture was stirred at room temperature for 65 h, then diluted with ethyl acetate and quenched with H_2O . The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic extract was washed with H_2O , brine, and dried over MgSO_4 . After evaporation of the solvent, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate, 10/1) to give **21** (1.86 g, 93%) as a white power: $[\alpha]_D^{24} -54.8$ (c 0.20, CHCl_3); FT-IR (KBr) 3057, 2931, 2825, 1593, 1507, 1240, 1152, 1013, 815, 751; ^1H NMR (500 MHz, CDCl_3) 2.51 (s, 3H), 2.80 (s, 6H), 3.15 (s,

6H), 4.03 (d, $J = 14.5$ Hz, 2H), 4.07 (d, $J = 14.5$ Hz, 2H), 4.61 (d, $J = 5.0$ Hz, 2H), 4.68 (d, $J = 5.0$ Hz, 2H), 5.02 (d, $J = 7.0$ Hz, 2H), 5.11 (d, $J = 7.0$ Hz, 2H), 7.17-7.26 (m, 8H), 7.33-7.40 (m, 4H), 7.58 (d, $J = 9.0$ Hz, 2H), 7.88 (dd, $J = 8.0, 16.3$ Hz, 4H), 7.96 (d, $J = 9.0$ Hz, 2H), 8.23 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) 42.8, 55.9, 56.5, 56.9, 94.9, 99.2, 112.6, 112.9, 116.6, 121.1, 124.1, 124.8, 125.3, 125.7, 126.6, 127.8, 127.9, 129.5, 129.7, 129.7, 131.0, 132.6, 133.1, 134.1, 152.7, 152.9; MS (ESI (+)) m/z 804 ($\text{M}+\text{H}^+$); Anal. Calcd. for $\text{C}_{51}\text{H}_{49}\text{NO}_8$: C, 76.19; H, 6.14; N, 1.74. Found: C, 75.95; H, 6.29; N, 1.70.

(*S,S*)-3,3'-[Hydroxyiminobis(methylene)]bis[2,2'-bis(methoxymethoxy)-1,1'-binaphthalene] (22): **22** was obtained in 99% yield as a white power: $[\alpha]_{\text{D}}^{25} -75.0$ (c 0.57, CHCl_3); FT-IR (KBr) 3057, 2926, 2825, 1623, 1593, 1508, 1469, 1240, 1151, 1013, 811, 750; ^1H NMR (500 MHz, CDCl_3) 2.76 (s, 6H), 3.17 (s, 6H), 4.43 (s, 4H), 4.61 (d, $J = 5.0$ Hz, 2H), 4.68 (d, $J = 5.0$ Hz, 2H), 5.02 (d, $J = 7.0$ Hz, 2H), 5.12 (d, $J = 7.0$ Hz, 2H), 7.16-7.24 (m, 8H), 7.33-7.39 (m, 4H), 7.58 (d, $J = 9.5$ Hz, 2H), 7.87 (t, $J = 8.0$ Hz, 4H), 7.96 (d, $J = 9.0$ Hz, 2H), 8.16 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) 55.9, 56.5, 59.6, 94.8, 99.4, 116.4, 120.8, 124.1, 124.9, 125.6, 125.6, 125.7, 126.0, 126.6, 127.8, 127.9, 129.6, 129.7, 130.5, 130.8, 131.1, 133.4, 134.0, 152.7, 152.9; MS (ESI (+)) m/z 828 ($\text{M}+\text{Na}^+$); Anal. Calcd. for $\text{C}_{50}\text{H}_{47}\text{NO}_9$: C, 74.52; H, 5.88; N, 1.74. Found: C, 74.58; H, 6.12; N, 1.69.

(*S,S*)-3,3'-[Ethyliminobis(methylene)]bis[2,2'-bis(methoxymethoxy)-1,1'-binaphthalene] (23): **23** was obtained in 83% yield as a white power: $[\alpha]_{\text{D}}^{23} -49.3$ (c 0.32, CHCl_3); FT-IR (KBr) 3057, 2931, 2829, 1622, 1593, 1508, 1240, 1150, 1012, 811, 750; ^1H NMR (500 MHz, CDCl_3) 1.27 (t, $J = 7.0$ Hz, 3H), 2.80-2.86 (m, 2H), 2.82 (s, 6H), 3.15 (s, 6H), 4.10 (d, $J = 15.3$ Hz, 2H), 4.12 (d, $J = 15.6$ Hz, 2H), 4.59 (d, $J = 5.2$ Hz, 2H), 4.66 (d, $J = 5.2$ Hz, 2H), 5.01 (d, $J = 7.0$ Hz, 2H), 5.11 (d, $J = 7.0$ Hz, 2H), 7.17-7.24 (m, 8H), 7.34-7.39 (m, 4H), 7.59 (d, $J = 8.9$ Hz, 2H), 7.88 (dd, $J = 8.0, 17.6$ Hz, 4H), 7.96 (d, $J = 9.2$ Hz, 2H), 8.33 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) 12.4, 48.4, 53.3, 55.9, 56.5, 94.9, 99.1, 116.6, 121.1, 124.1, 124.8, 125.1, 125.6, 125.7, 126.6, 127.8, 127.9, 129.1, 129.7, 129.7, 131.0, 133.0, 133.4, 134.1, 152.6, 152.9; MS (ESI (+)) m/z 818 ($\text{M}+\text{H}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{52}\text{H}_{52}\text{NO}_8^+$ ($\text{M}+\text{H}^+$): 818.3693; found 818.3674.

(*S,S*)-3,3'-[2,2,2-Trifluoroethyliminobis(methylene)]bis[2,2'-bis(methoxymethoxy)-1,1'-binaphthalene] (24): **24** was obtained in 11% yield as a white power: $[\alpha]_{\text{D}}^{23} -56.0$ (c 0.22, CHCl_3); FT-IR (KBr) 3059, 2928, 2825, 1593, 1508, 1241, 1150, 1013, 811, 751; ^1H NMR (500 MHz, CDCl_3) 2.86 (s, 6H), 3.17 (s, 6H), 3.48 (m, 2H), 4.34 (s, 4H), 4.53 (d, $J = 5.5$ Hz, 2H), 4.60 (d, $J = 5.5$ Hz, 2H), 5.07 (d, $J = 7.1$ Hz, 2H), 5.12 (d, $J = 6.8$ Hz, 2H), 7.17-7.24 (m, 8H), 7.34-7.41 (m, 4H), 7.60 (d, $J = 8.9$ Hz, 2H),

7.89 (dd, $J = 7.9, 16.5$ Hz, 4H), 7.97 (d, $J = 9.2$ Hz, 2H), 8.27 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) 20.9, 48.9, 53.8, 55.9, 56.6, 94.8, 99.2, 116.4, 120.7, 124.1, 124.9, 125.4, 125.5, 125.7, 125.9, 126.7, 127.9, 128.0, 129.5, 129.6, 129.8, 130.9, 131.6, 133.3, 134.0, 152.7, 152.9; MS (ESI (+)) m/z 894 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{52}\text{H}_{52}\text{NO}_8\text{F}_3^+$ ($\text{M}+\text{H}^+$): 872.3410; found 872.3414.

5-2. General Procedure for MOM Deprotection

(*S,S*)-3,3'-[Methyliminobis(methylene)]bis(1,1'-binaphthalene-2,2'-diol) (2): To a solution of **21** (1.78 g, 2.2 mmol) in MeOH (10 mL) and CH_2Cl_2 (10 mL), was added *p*-toluene sulfonic acid monohydrate (2.05 g, 11.0 mmol). The reaction mixture was stirred for 9 h at 40 °C, and neutralized by addition of 1.0 N NaOH. The organic layer was separated and the aqueous layer extracted with ethyl acetate. The combined organic extracts were washed with H_2O , brine, and dried over MgSO_4 . After the solvent was evaporated under reduced pressure, the residue was purified by flash column chromatography (SiO_2 , hexane/ether, 1/2) to give **2** (1.41 g, 11.6 w/w % of residual solvents were included based on ^1H NMR, 93%) as a yellow powder: $[\alpha]_D^{24} -54.4$ (c 0.84, CHCl_3); FT-IR (KBr) 3501, 3056, 2953, 2923, 2852, 1620, 1597, 1507, 1467, 1198, 816, 749; ^1H NMR (500 MHz, CDCl_3) 2.44 (s, 3H), 4.03 (d, $J = 13.0$ Hz, 2H), 4.09 (d, $J = 13.5$ Hz, 2H), 7.07-7.12 (m, 4H), 7.17 (t, $J = 7.5$ Hz, 2H), 7.23-7.34 (m, 8H), 7.82 (dd, $J = 8.0, 18.0$ Hz, 4H), 7.82 (s, 2H), 7.91 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) 41.5, 59.0, 112.3, 113.0, 117.7, 123.6, 123.9, 124.4, 124.5, 125.2, 127.0, 127.1, 128.0, 128.2, 128.7, 129.3, 130.5, 130.7, 133.4, 133.5, 152.0, 153.3; MS (ESI (+)) m/z 628 ($\text{M}+\text{H}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{43}\text{H}_{33}\text{NO}_4^+$ ($\text{M}+\text{H}^+$): 628.2482; found 628.2487.

(*S,S*)-3,3'-[Hydroxyiminobis(methylene)]bis(1,1'-binaphthalene-2,2'-diol) (25): **25** was obtained in 74% yield as a white power: $[\alpha]_D^{25} -23.7$ (c 1.2, CHCl_3); FT-IR (KBr) 3510, 3396, 3054, 2925, 1620, 1596, 1505, 1434, 1211, 815, 744; ^1H NMR (500 MHz, CDCl_3) 4.29 (br-s, 4H), 7.03-7.07 (m, 4H), 7.14 (t, $J = 7.5$ Hz, 4H), 7.20 (t, $J = 7.5$ Hz, 2H), 7.24-7.27 (m, 4H), 7.74-7.82 (m, 8H); ^{13}C NMR (125 MHz, CDCl_3) 61.5, 112.9, 113.1, 117.7, 123.6, 124.0, 124.1, 124.4, 124.6, 126.9, 127.2, 128.1, 128.2, 128.7, 129.3, 130.5, 131.3, 133.4, 133.6, 151.8, 152.4; MS (ESI (+)) m/z 652 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{42}\text{H}_{31}\text{NO}_5^+$ ($\text{M}+\text{H}^+$): 630.2275; found 630.2273.

(*S,S*)-3,3'-[Ethyliminobis(methylene)]bis(1,1'-binaphthalene-2,2'-diol) (3): **3** was obtained in 66% yield as a white power: $[\alpha]_D^{23} -60.4$ (c 0.7, CHCl_3); FT-IR (KBr) 3511, 3056, 2969, 2927, 2844, 1620, 1597, 1508, 1431, 1344, 1196, 816, 749; ^1H NMR (500 MHz, CDCl_3) 1.19 (t, $J = 7.0$ Hz, 3H), 2.76-2.85 (m, 2H), 4.06 (d, $J = 13.5$ Hz, 2 H), 4.13 (d, $J = 13.5$ Hz, 2H), 7.06-7.13 (m, 6H), 7.23-7.32 (m, 8H),

7.81 (dd, $J = 8.2, 22.3$ Hz, 4H), 7.82 (s, 2H), 7.90 (d, $J = 8.9$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) 10.9, 47.4, 55.3, 112.4, 113.0, 117.8, 123.5, 123.9, 124.4, 124.6, 125.5, 126.9, 127.1, 128.0, 128.2, 128.7, 129.3, 130.5, 130.8, 133.5, 133.5, 152.0, 153.4; MS (ESI (+)) m/z 642 ($\text{M}+\text{H}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{44}\text{H}_{36}\text{NO}_4^+$ ($\text{M}+\text{H}^+$): 642.2644; found 642.2637.

(*S,S*)-3,3'-[2,2,2-Trifluoroethyliminobis(methylene)]bis(1,1'-binaphthalene-2,2'-diol) (4): **4** was obtained in 27% yield as a white powder: $[\alpha]_D^{24} -57.9$ (c 0.45, CHCl_3); FT-IR (KBr) 3510, 3389, 3202, 3057, 2955, 2923, 1621, 1597, 1506, 1433, 1147, 816, 749; ^1H NMR (500 MHz, CDCl_3) 3.29-3.43 (m, 2H), 4.20 (d, $J = 13.1$ Hz, 2H), 4.34 (d, $J = 13.1$ Hz, 2H), 7.05 (d, $J = 8.3$ Hz, 2H), 7.10-7.12 (m, 4H), 7.21-7.31 (m, 8H), 7.80 (dd, $J = 4.0, 8.3$ Hz, 4H), 7.82 (s, 2H), 7.85 (d, $J = 8.9$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) 52.6, 52.8, 56.4, 56.5, 56.7, 112.6, 113.1, 117.7, 123.6, 124.2, 124.4, 127.0, 127.5, 128.0, 128.1, 128.7, 129.2, 130.7, 131.5, 131.6, 133.3, 133.8, 152.0, 152.7; MS (ESI (+)) m/z 718 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{44}\text{H}_{33}\text{NO}_4\text{F}_3^+$ ($\text{M}+\text{H}^+$): 696.2362; found 696.2349.

(*S,S*)-3,3'-[Iminobis(methylene)]bis(1,1'-binaphthalene-2,2'-diol) (1): To a solution of **25** (2.1 g, 3.3 mmol) in THF (25 mL) were added 10% aqueous HCl (10 mL) and Zn dust (783.4 mg, 12.0 mmol). The resulting suspension was stirred for 17 h at room temperature, then neutralized by addition of 5.0 N NaOH. Precipitate was filtered and the filtrate was extracted with CH_2Cl_2 . Combined organic extracts were washed with H_2O , brine, and dried over Na_2SO_4 . After the solvent was evaporated under reduced pressure, the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate, 2/1) to give **1** (1.63 g, 90.9 w/w %, residual solvents were included based on ^1H NMR, 73%) as a yellow powder: $[\alpha]_D^{26} -19.3$ (c 0.76, CHCl_3); FT-IR (KBr) 3501, 3055, 2925, 1620, 1596, 1507, 1432, 1210, 816, 748; ^1H NMR (500 MHz, CDCl_3) 4.23 (br-s, 4H), 7.15 (d, $J = 8.5$ Hz, 4H), 7.25-7.29 (m, 4H), 7.32-7.37 (m, 6H), 7.77 (br-s, 2H), 7.82 (d, $J = 8.0$ Hz, 2H), 7.87 (d, $J = 8.0$ Hz, 2H), 7.92-7.94 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) 50.4, 101.4, 112.3, 112.8, 117.7, 123.6, 124.1, 124.4, 124.5, 125.6, 127.0, 127.2, 128.0, 128.3, 128.7, 129.4, 130.2, 130.7, 133.5, 152.1, 153.3; MS (ESI (+)) m/z 614 ($\text{M}+\text{H}^+$); HRMS (FAB(+)) calcd for $\text{C}_{42}\text{H}_{31}\text{NO}_4^+$ ($\text{M}+\text{H}^+$): 614.2326; found 614.2321.

6. Synthesis of Substrates

Substrates **7a-c**, **8a-d** are commercially available and used after distillation under reduced pressure. **8e-g** were synthesized according to the literature procedure from corresponding carboxylic acid via Weinreb amide formation and nucleophilic addition of lithium enolate of methyl acetate.^{SI-6}

7. Catalytic Asymmetric Michael Reaction of β -Keto Esters

7-1. General Procedure for the Catalytic Asymmetric Michael Reaction Promoted by (*S,S*)-La-NMe-linked-BINOL Complex: THF (9.0 mL) and DME (1.0 mL) were added to the (*S,S*)-La-NMe-linked-BINOL complex (687 mg, 1.0 mmol, prepared by the procedure mentioned above) in a flask at $-78\text{ }^{\circ}\text{C}$, and the mixture was stirred for 5 min at the same temperature. Then, 2-cyclohexen-1-one (**7b**) (0.97 mL, 10 mmol) and methyl acetoacetate (**8a**) (1.08 mL, 10 mmol) were added. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 5 min, then the dry-ice acetone bath was removed and the reaction mixture was stirred at room temperature. After 24 h, the reaction mixture was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl , and dried over Na_2SO_4 . After the solvent was evaporated under reduced pressure, the residue was purified by flash column chromatography (SiO_2 , hexane/acetone, 9/1) to give (*S*)-**9ba** (1.62 g, 7.63 mmol, 76%) in 92% ee. The enantiomeric excess was determined by GC analysis after the derivatization shown below.

7-2. General Procedure for the Catalytic Asymmetric Michael Reaction Promoted by (*S,S*)-La-NH-linked-BINOL Complex: Preparation of the (*S,S*)-La-NH-linked-BINOL complex is same as the preparation of (*S,S*)-La-NMe-linked-BINOL complex. THF (0.95 mL) and HFIP (0.05 mL) were added to the (*S,S*)-La-NH-linked-BINOL complex (15.0 mg, 0.02 mmol) in a test tube at $-78\text{ }^{\circ}\text{C}$, and the mixture was stirred for 5 min at the same temperature. Then, 2-cyclohepten-1-one (**7c**) (22.3 μL , 0.2 mmol) and methyl propionylacetate (**8c**) (25.0 μL , 0.2 mmol) were added. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 5 min, then the dry-ice acetone bath was removed and the reaction mixture was stirred at room temperature. After 24 h, the reaction mixture was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl , and dried over Na_2SO_4 . After the solvent was evaporated under reduced pressure, the residue was purified by flash column chromatography (SiO_2 , hexane/acetone, 9/1) to give (*S*)-**9cc** (44.5 mg, 0.175 mmol, 91%) in 90% ee. The enantiomeric excess was determined by GC analysis after the derivatization shown below.

7-3 Determination of the Enantiomeric Excess

Enantiomeric excess was determined by GC analysis after appropriate derivatization shown below (Scheme S3). Varian Chirasil DEX CB column (0.25 mm x 25 m), isothermal, injection temperature $250\text{ }^{\circ}\text{C}$, detection temperature $250\text{ }^{\circ}\text{C}$.

These Michael adducts were obtained as a 1:1 mixture of diastereomers, thus derivatization was needed for determining enantiomeric excess (Scheme 3). For **9ba-bd**, **9bg**, **9ca-cd**, and **9cg**, by conversion to **27xx**, separable peaks were obtained on chiral GC analysis. For **9be**, **9bf**, **9ce**, and **9cf**,

these products having carbon-carbon multiple bond didn't give separable peaks on chiral GC analysis after conversion to **27xx**. In this case, conversion to **28xx** gave separable peaks. For **9aa**, **9ac**, and **9ad**, conversion to **27xx** didn't also give separable peaks, so that deprotection of ketal after decarboxylation (conversion to **29ax**) was needed. For **9ae**, conversion to **28ae** and deprotection of ketal (conversion to **29ae**) were needed.

Scheme S3. Derivatization for the Determination of the Enantiomeric Excess

The detailed experimental procedure is described at latter part of this Supporting Information.

(S)-3-Oxo-2-(3-oxo-cyclopentyl)butyric acid methyl ester (9aa):

colorless oil: $[\alpha]_D^{24} -52.7$ (c 0.83, $CHCl_3$) (73% ee); FT-IR (neat) 3465, 2957, 1742, 1710, 1436, 1361, 1203, 1158, 1083; For a 1:1 mixture of diastereomers, 1H NMR (500 MHz, $CDCl_3$) 1.50-1.63 (m, 2H), 1.81 (dd, $J = 11.0, 18.3$ Hz, 1H), 1.94 (dd, $J = 11.0, 18.3$ Hz, 1H), 2.14-2.35 (m, 6H), 2.23 (s, 3H), 2.26 (s, 3H), 2.44 (t, $J = 7.4$ Hz, 1H), 2.48 (t, $J = 7.4$ Hz, 1H), 2.83-2.89 (m, 2H), 3.43 (d, $J = 9.5$ Hz, 1H), 3.45 (d, $J = 8.6$ Hz, 1H), 3.73 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 27.4, 27.5, 29.3, 29.5, 35.8, 35.9, 38.0, 38.1, 42.7, 42.9, 52.6, 64.3, 64.5, 168.8, 168.8, 201.3, 201.5, 216.9, 216.9; MS (ESI (+)) m/z 221 ($M+Na^+$); HRMS (FAB(+)) calcd. for $C_{10}H_{15}O_4^+$ ($M+H^+$): 199.0970; found 199.0973; After conversion to **29aa**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 90 °C, isothermal, t_R (minor) = 110.7 min, t_R (major) = 111.9 min; Absolute configuration was *S*. Determination of the absolute configuration of **9aa** is described later.

(S)-3-Oxo-2-(3-oxo-cyclopentyl)pentanoic acid methyl ester (9ac):

colorless oil: $[\alpha]_D^{24} -64.9$ (c 0.81, $CHCl_3$) (80% ee); FT-IR (neat) 2956, 1742, 1714, 1436, 1405, 1201,

1157, 1103; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.05 (t, $J = 7.3$ Hz, 3H), 1.07 (t, $J = 7.3$ Hz, 3H), 1.45-1.62 (m, 2H), 1.79 (dd, $J = 11.0, 18.3$ Hz, 1H), 1.92 (dd, $J = 11.0, 18.3$ Hz, 1H), 2.12-2.24 (m, 4H), 2.27-2.33 (m, 2H), 2.40-2.51 (m, 4H), 2.58-2.67 (m, 2H), 2.85-2.93 (m, 2H), 3.45 (d, $J = 9.5$ Hz, 1H), 3.47 (d, $J = 9.5$ Hz, 1H), 3.72 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 7.5, 7.5, 27.4, 27.6, 35.8, 35.9, 36.0, 36.2, 38.0, 38.2, 42.8, 42.9, 52.5, 63.3, 63.5, 168.8, 168.9, 204.1, 204.3, 217.0, 217.0; MS (ESI (+)) m/z 235 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{11}\text{H}_{17}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 213.1127; found 213.1124; After conversion to **29ac**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 113 °C, isothermal, t_R (minor) = 49.9 min, t_R (major) = 50.8 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ac** is described later.

(S)-3-Oxo-2-(3-oxo-cyclopentyl)pentanoic acid methyl ester (9ad):

colorless oil: $[\alpha]_D^{24} -48.8$ (c 0.76, CHCl_3) (60% ee); FT-IR (neat) 3463, 2963, 1742, 1714, 1436, 1404, 1366, 1203, 1156; For a 1:1 mixtures of diastereomers, ^1H NMR (500 MHz, CDCl_3) 0.89 (t, $J = 7.4$ Hz, 3H), 0.91 (t, $J = 7.4$ Hz, 3H), 1.45-1.54 (m, 2H), 1.56-1.65 (m, 4H), 1.79 (dd, $J = 11.0, 17.9$ Hz, 1H), 1.92 (dd, $J = 11.0, 17.9$ Hz, 1H), 2.13-2.24 (m, 4H), 2.27-2.33 (m, 2H), 2.41-2.57 (m, 6H), 2.85-2.92 (m, 2H), 3.44 (d, $J = 9.8$ Hz, 1H), 3.46 (d, $J = 9.8$ Hz, 1H), 3.72 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 13.4, 13.5, 16.8, 16.8, 27.5, 27.6, 35.8, 36.0, 38.0, 38.2, 42.7, 42.9, 44.3, 44.6, 52.5, 63.6, 63.9, 168.7, 168.8, 203.5, 203.7, 217.0, 217.1; MS (ESI (+)) m/z 249 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{12}\text{H}_{19}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 227.1283; found 227.1284; After conversion to **29ad**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 105 °C, isothermal, t_R (major) = 127.2 min, t_R (minor) = 129.6 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ad** is described later.

(S)-3-Oxo-2-(3-oxo-cyclopentyl)hept-6-enoic acid methyl ester (9ae):

colorless oil: $[\alpha]_D^{24} -43.1$ (c 0.85, CHCl_3) (72% ee); FT-IR (neat) 3464, 3080, 2955, 1742, 1714, 1436, 1403, 1264, 1199, 1158, 998, 918; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.44-1.61 (m, 2H), 1.78 (dd, $J = 11.0, 18.3$ Hz, 1H), 1.91 (dd, $J = 11.0, 18.3$ Hz, 1H), 2.13-2.21 (m, 4H), 2.25-2.35 (m, 6H), 2.43 (t, $J = 19.6$ Hz, 1H), 2.44 (t, $J = 19.6$ Hz, 1H), 2.52-2.60 (m, 2H), 2.63-2.72 (m, 2H), 2.85-2.93 (m, 2H), 3.45 (d, $J = 9.8$ Hz, 1H), 3.47 (d, $J = 10.1$ Hz, 1H), 3.71 (s, 3H), 3.74 (s, 3H), 4.96-5.04 (m, 4H), 5.72-5.79 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) 27.2, 27.3, 27.4, 27.5, 35.8, 35.9, 37.9, 38.1, 41.4, 41.8, 42.7, 42.8, 52.5, 63.6, 63.8, 115.7, 115.7, 136.3, 136.3, 168.6, 168.7, 202.7, 202.9, 216.9, 217.0; MS (ESI (+)) m/z 261 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 239.1283; found 239.1283; After conversion to **29ae**, ee was determined by chiral GC. Separation conditions:

Chirasil DEX CB, 120 °C, isothermal, t_R (major) = 90.5 min, t_R (minor) = 92.4 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ae** is described later.

(S)-3-Oxo-2-(3-oxo-cycloheptyl)butyric acid methyl ester (9ba):

colorless oil: $[\alpha]_D^{25}$ -2.30 (*c* 0.75, CHCl₃) (92% ee); FT-IR (neat) 3437, 2953, 2867, 1747, 1713, 1640, 1435, 1269, 1254, 1223, 1158; For a 1:1 mixture of diastereomers, ¹H NMR (500 MHz, CDCl₃) 1.36-1.49 (m, 2H), 1.63-1.74 (m, 2H), 1.85 (d, *J* = 16.5 Hz, 1H), 1.88 (d, *J* = 16.5 Hz, 1H), 2.02-2.07 (m, 2H), 2.10-2.28 (m, 4H), 2.21 (s, 3H), 2.23 (s, 3H), 2.34-2.40 (m, 4H), 2.53-2.62 (m, 2H), 3.39 (d, *J* = 9.2 Hz, 1H), 3.41 (d, *J* = 9.5 Hz, 1H), 3.73 (s, 3H), 3.74 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 24.5, 24.5, 28.6, 29.0, 29.6, 29.6, 37.8, 41.0, 41.0, 45.0, 45.3, 52.5, 52.5, 64.5, 64.9, 168.5, 168.7, 201.4, 201.5, 209.4, 209.4; MS (ESI (+)) *m/z* 235 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₁H₁₇O₄⁺ (M+H⁺): 213.1127; found 213.1124; After conversion to **27ba**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 140 °C, isothermal, t_R (major) = 20.8 min, t_R (minor) = 22.7 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ba** is described later.

(S)-3-Oxo-2-(3-oxo-cyclohexyl)pentanoic acid ethyl ester (9bb):

colorless oil: $[\alpha]_D^{24}$ -10.2 (*c* 0.67, CHCl₃) (88% ee); FT-IR (neat) 3626, 3413, 2940, 2867, 1740, 1712, 1422, 1154, 951; For a 1:1 mixture of diastereomers, ¹H NMR (500 MHz, CDCl₃) 1.27 (t, *J* = 7.0 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.37-1.50 (m, 2H), 1.63-1.73 (m, 2H), 1.85 (d, *J* = 13.4 Hz, 1H), 1.90 (d, *J* = 13.4 Hz, 1H), 2.02-2.06 (m, 2H), 2.11-2.28 (m, 4H), 2.21 (s, 3H), 2.23 (s, 3H), 2.33-2.41 (m, 4H), 2.54-2.61 (m, 2H), 3.36 (d, *J* = 9.2 Hz, 1H), 3.38 (d, *J* = 9.2 Hz, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.20 (q, *J* = 7.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) 14.1, 14.1, 24.5, 28.5, 29.0, 29.5, 37.7, 41.0, 41.1, 45.0, 45.4, 61.6, 61.6, 64.7, 65.2, 168.0, 168.2, 201.5, 201.6, 209.4, 209.5; MS (ESI (+)) *m/z* 249 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₂H₁₉O₄⁺ (M+H⁺): 227.1283; found, 227.1278; After conversion to **27bb**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 140 °C, isothermal, t_R (major) = 20.8 min, t_R (minor) = 22.7 min; Absolute configuration was *S*. Determination of the absolute configuration of **9bb** is described later.

(S)-3-Oxo-2-(3-oxo-cyclohexyl)pentanoic acid methyl ester (9bc):

colorless oil: $[\alpha]_D^{24}$ -11.9 (*c* 0.72, CHCl₃) (91% ee); FT-IR (neat) 3415, 2952, 1740, 1713, 1435, 1342, 1229, 1162, 918, 740; For a 1:1 mixture of diastereomers, ¹H NMR (500 MHz, CDCl₃) 1.04 (t, *J* = 7.0 Hz, 3H), 1.06 (t, *J* = 7.0 Hz, 3H), 1.34-1.49 (m, 2H), 1.63-1.73 (m, 2H), 1.81 (d, *J* = 13.1 Hz, 1H), 1.89 (d, *J* = 13.1 Hz, 1H), 2.01-2.05 (m, 2H), 2.08-2.18 (m, 2H), 2.20-2.49 (m, 8H), 2.55-2.62 (m, 4H), 3.43

(d, $J = 6.7$ Hz, 1H), 3.44 (d, $J = 6.7$ Hz, 1H), 3.71 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 7.4, 7.5, 24.4, 24.5, 28.6, 29.0, 36.2, 37.9, 41.0, 41.0, 45.1, 45.3, 52.5, 52.5, 63.4, 63.9, 168.5, 168.7, 204.2, 204.3, 209.4, 209.5; MS (ESI (+)) m/z 249 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{12}\text{H}_{19}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 227.1283; found 227.1284; After conversion to **27bc**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 15.7 min, t_R (minor) = 16.7 min; Absolute configuration was *S*. Determination of the absolute configuration of **9bc** is described later.

(S)-3-Oxo-2-(3-oxo-cyclohexyl)hexanoic acid methyl ester (9bd):

colorless oil: $[\alpha]_D^{24} -11.6$ (c 0.85, CHCl_3) (87% ee); FT-IR (neat) 3412, 2959, 2876, 1742, 1713, 1435, 1228, 1162, 1120; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 0.89 (t, $J = 7.3$ Hz, 3H), 0.90 (t, $J = 7.3$ Hz, 3H), 1.33-1.48 (m, 2H), 1.58 (q, $J = 7.3$ Hz, 2H), 1.60 (q, $J = 7.3$ Hz, 2H), 1.63-1.73 (m, 2H), 1.82 (d, $J = 13.1$ Hz, 1H), 1.88 (d, $J = 13.2$ Hz, 1H), 2.02-2.04 (m, 2H), 2.07-2.17 (m, 2H), 2.21-2.27 (m, 2H), 2.32-2.62 (m, 10H), 3.41 (d, $J = 8.0$ Hz, 1H), 3.43 (d, $J = 8.9$ Hz, 1H), 3.71 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 13.4, 13.5, 16.7, 16.8, 24.4, 24.5, 28.6, 29.0, 37.8, 37.8, 41.0, 41.1, 44.7, 45.1, 45.3, 52.4, 52.5, 63.8, 64.3, 168.4, 168.7, 203.5, 203.6, 209.5, 209.5; MS (ESI (+)) m/z 263 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{13}\text{H}_{21}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 241.1440; found 241.1434; After conversion to **27bd**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 15.8 min, t_R (minor) = 16.9 min; Absolute configuration was *S*. Determination of the absolute configuration of **9bd** is described later.

(S)-3-Oxo-2-(3-oxo-cyclohexyl)hept-6-enoic acid methyl ester (9be):

colorless oil: $[\alpha]_D^{25} -9.2$ (c 1.78, CHCl_3) (80% ee); FT-IR (neat) 3412, 2952, 2865, 1749, 1714, 1641, 1435, 1232, 1161, 997, 917, 756; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.33-1.47 (m, 2H), 1.61-1.72 (m, 2H), 1.80 (d, $J = 13.1$ Hz, 1H), 1.87 (d, $J = 12.2$ Hz, 1H), 1.99-2.05 (m, 2H), 2.07-2.16 (m, 2H), 2.20-2.38 (m, 10H), 2.48-2.66 (m, 6H), 3.42 (d, $J = 8.6$ Hz, 1H), 3.43 (d, $J = 9.2$ Hz, 1H), 3.70 (s, 3H), 3.71 (s, 3H), 4.96-5.02 (m, 4H), 5.71-5.78 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) 24.4, 24.5, 27.2, 27.2, 28.6, 29.0, 37.8, 41.0, 41.0, 41.9, 45.0, 45.3, 52.4, 52.5, 63.7, 64.2, 115.6, 136.3, 168.3, 168.5, 202.7, 202.8, 209.4, 209.4; MS (ESI (+)) m/z 275 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{14}\text{H}_{21}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 253.1440; found 253.1444; After conversion to **28be**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 24.7 min, t_R (minor) = 26.6 min; Absolute configuration was *S*. Determination of the absolute configuration of **9be** is described later.

(S)-3-Oxo-2-(3-oxo-cyclohexyl)hept-6-ynoic acid methyl ester (9bf):

colorless oil: $[\alpha]_D^{24}$ -6.9 (c 0.53, CHCl_3) (73% ee); FT-IR (neat) 3285, 2953, 1739, 1712, 1434, 1224, 1160, 1069; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.36-1.49 (m, 2H), 1.64-1.72 (m, 2H), 1.83 (d, $J = 13.1$ Hz, 1H), 1.88 (d, $J = 12.5$ Hz, 1H), 1.94 (s, 2H), 2.01-2.04 (m, 2H), 2.10-2.27 (m, 4H), 2.33-2.46 (m, 8H), 2.59-2.61 (m, 2H), 2.64-2.73 (m, 2H), 2.77-2.84 (m, 2H), 3.43 (d, $J = 8.6$ Hz, 1H), 3.45 (d, $J = 8.9$ Hz, 1H), 3.71 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 12.7, 24.4, 24.5, 28.6, 28.9, 37.8, 37.8, 41.0, 41.0, 41.3, 41.4, 45.0, 45.2, 52.5, 52.6, 63.6, 64.1, 69.0, 69.1, 82.3, 82.4, 168.1, 168.4, 201.5, 201.5, 209.3, 209.3; MS (ESI (+)) m/z 273 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{14}\text{H}_{19}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 251.1283; found 251.1288; After conversion to **28bf**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 24.7 min, t_R (minor) = 26.6 min; Absolute configuration was *S*. Determination of the absolute configuration of **5bf** is described later.

(S)-4-Cyclohexyl-3-oxo-2-(3-oxo-cyclohexyl)butyric acid methyl ester (9bg):

white solid: $[\alpha]_D^{24}$ -6.4 (c 1.91, CHCl_3) (61% ee); FT-IR (neat) 3413, 2925, 2852, 1749, 1711, 1448, 1227, 1160, 952, 756; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 0.87 (m, 4H), 1.11 (m, 2H), 1.23 (m, 4H), 1.36 (q, $J = 11.9$ Hz, 1H), 1.43 (q, $J = 11.0$ Hz, 1H), 1.63 (m, 12H), 1.84 (m, 4H), 2.00 (br, 2H), 2.06-2.16 (m, 2H), 2.22-2.26 (m, 2H), 2.29-2.39 (m, 8H), 2.58 (m, 2H), 3.39 (d, $J = 8.5$ Hz, 1H), 3.40 (d, $J = 8.5$ Hz, 1H), 3.69 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) 24.4, 24.5, 25.9, 25.9, 26.1, 28.6, 29.0, 32.8, 33.0, 33.0, 33.2, 33.2, 37.6, 37.7, 41.0, 41.0, 45.0, 45.3, 50.4, 52.4, 52.4, 64.2, 64.7, 168.3, 168.6, 203.0, 203.1, 209.5, 209.5; MS (ESI (+)) m/z 317 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{17}\text{H}_{27}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 295.1909; found 295.1918; After conversion to **27bg**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 180 °C, isothermal, t_R (major) = 47.1 min, t_R (minor) = 49.0 min; Absolute configuration was *S*. Determination of the absolute configuration of **9bg** is described later.

(S)-3-Oxo-2-(3-oxo-cycloheptyl)butyric acid methyl ester (9ca):

colorless oil: $[\alpha]_D^{25}$ -33.0 (c 0.67, CHCl_3) (92% ee); FT-IR (neat) 3444, 2932, 2859, 1743, 1703, 1436, 1359, 1258, 1202, 1158; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.26-1.37 (m, 2H), 1.46-1.61 (m, 4H), 1.69-1.78 (m, 2H), 1.83-1.89 (m, 4H), 2.21 (s, 3H), 2.21 (s, 3H), 2.40-2.47 (m, 6H), 2.50-2.56 (m, 4H), 3.40 (d, $J = 8.9$ Hz, 1H), 3.40 (d, $J = 8.9$ Hz, 1H), 3.71 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) 24.2, 24.3, 28.1, 28.5, 29.7, 29.9, 33.8, 34.3, 35.1, 35.2, 43.5, 43.5, 46.9, 47.0, 52.5, 64.6, 65.0, 168.8, 168.9, 201.9, 202.0, 212.5, 212.6; MS (ESI (+)) m/z 249 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd.

for $C_{12}H_{19}O_4^+$ ($M+H^+$): 227.1283; found 227.1278; After conversion to **27ca**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 150 °C, isothermal, t_R (major) = 18.2 min, t_R (minor) = 19.0 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ca** is described later.

(S)-3-Oxo-2-(3-oxo-cycloheptyl)butyric acid ethyl ester (9cb):

colorless oil: $[\alpha]_D^{24}$ -29.4 (*c* 0.70, $CHCl_3$) (88% ee); FT-IR (neat) 3629, 2931, 1702, 1448, 1158, 1034; For a 1:1 mixture of diastereomers, 1H NMR (500 MHz, $CDCl_3$) 1.27 (t, J = 7.0 Hz, 6H), 1.29-1.37 (m, 2H), 1.48-1.61 (m, 4H), 1.68-1.82 (m, 2H), 1.86-1.91 (m, 4H), 2.23 (s, 3H), 2.24 (s, 3H), 2.43-2.49 (m, 6H), 2.54-2.60 (m, 4H), 3.39 (d, J = 8.6 Hz, 1H), 3.40 (d, J = 8.6 Hz, 1H), 4.19 (q, J = 7.1 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) 14.1, 14.1, 24.4, 24.4, 28.3, 28.6, 29.7, 29.9, 33.9, 34.3, 35.1, 35.3, 43.5, 43.6, 47.0, 47.1, 61.6, 61.6, 64.9, 65.3, 168.4, 168.4, 202.0, 202.1, 212.6, 212.7; MS (ESI (+)) m/z 263 ($M+Na^+$); HRMS (FAB(+)) calcd. for $C_{13}H_{21}O_4^+$ ($M+H^+$): 241.1440; found 241.1434; After conversion to **27cb**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 150 °C, isothermal, t_R (major) = 18.2 min, t_R (minor) = 19.0 min; Absolute configuration was *S*. Determination of the absolute configuration of **9cb** is described later.

(S)-3-Oxo-2-(3-oxo-cycloheptyl)pentanoic acid methyl ester (9cc):

colorless oil: $[\alpha]_D^{25}$ -29.4 (*c* 0.91, $CHCl_3$) (88% ee); FT-IR (neat) 3439, 2936, 1747, 1702, 1437, 1348, 1254, 1199, 1164, 1102, 967; For a 1:1 mixture of diastereomers, 1H NMR (500 MHz, $CDCl_3$) 1.05 (t, J = 7.0 Hz, 3H), 1.05 (t, J = 7.0 Hz, 3H), 1.24-1.37 (m, 2H), 1.45-1.62 (m, 4H), 1.69 (d, J = 14.1 Hz, 1H), 1.78 (d, J = 14.1 Hz, 1H), 1.83-1.91 (m, 4H), 2.39-2.62 (m, 14H), 3.44 (d, J = 8.9 Hz, 2H), 3.72 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) 7.5, 24.4, 24.4, 28.2, 28.6, 33.9, 34.3, 35.1, 35.3, 36.3, 36.4, 43.5, 43.6, 47.1, 52.5, 63.7, 64.1, 168.9, 169.0, 204.7, 204.8, 212.6, 212.7; MS (ESI (+)) m/z 263 ($M+Na^+$); HRMS (FAB(+)) calcd. for $C_{13}H_{21}O_4^+$ ($M+H^+$): 241.1440; found 241.1436; After conversion to **27cc**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 150 °C, isothermal, t_R (major) = 25.9 min, t_R (minor) = 27.4 min; Absolute configuration was *S*. Determination of the absolute configuration of **9cc** is described later.

(S)-3-Oxo-2-(3-oxo-cycloheptyl)hexanoic acid methyl ester (9cd):

colorless oil: $[\alpha]_D^{24}$ -24.2 (*c* 0.83, $CHCl_3$) (79% ee); FT-IR (neat) 2933, 2876, 1747, 1704, 1436, 1254, 1164, 917, 733; For a 1:1 mixture of diastereomers, 1H NMR (500 MHz, $CDCl_3$) 0.89 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H), 1.24-1.37 (m, 2H), 1.48-1.62 (m, 4H), 1.59 (q, J = 7.4 Hz, 2H), 1.59 (q, J = 7.4

Hz, 2H), 1.70 (d, $J = 16.5$ Hz, 1H), 1.77 (d, $J = 14.1$ Hz, 1H), 1.84-1.91 (m, 4H), 2.36-2.64 (m, 14H), 3.42 (d, $J = 8.9$ Hz, 1H), 3.43 (d, $J = 8.9$ Hz, 1H), 3.72 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) 13.4, 13.5, 16.7, 16.8, 24.4, 24.4, 28.3, 28.6, 33.9, 34.3, 35.0, 35.2, 43.5, 43.6, 44.8, 45.0, 47.1, 47.1, 52.4, 52.5, 64.0, 64.4, 168.8, 168.9, 204.0, 204.1, 212.6, 212.8; MS (ESI (+)) m/z 277 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{14}\text{H}_{23}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 255.1596; found 255.1593; After conversion to **27cd**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 24.1 min, t_R (minor) = 25.1 min; Absolute configuration was *S*. Determination of the absolute configuration of **9cd** is described later.

(*S*)-3-Oxo-2-(3-oxo-cycloheptyl)hept-6-enoic acid methyl ester (9ce):

colorless oil: $[\alpha]_D^{25} -28.5$ (c 1.25, CHCl_3) (83% ee); FT-IR (neat) 2932, 2859, 1744, 1703, 1641, 1436, 1260, 1200, 1163, 1074, 1000, 916, 756; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.22-1.36 (m, 2H), 1.47-1.58 (m, 4H), 1.68 (d, $J = 14.1$ Hz, 1H), 1.76 (d, $J = 14.1$ Hz, 1H), 1.79-1.92 (m, 4H), 2.29 (d, $J = 6.4$ Hz, 2H), 2.32 (d, $J = 6.4$ Hz, 2H), 2.38-2.47 (m, 6H), 2.51-2.68 (m, 8H), 3.42 (d, $J = 8.9$ Hz, 1H), 3.43 (d, $J = 8.9$ Hz, 1H), 3.70 (s, 6H), 4.95-5.02 (m, 4H), 5.71-5.79 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) 24.3, 27.2, 27.2, 28.2, 28.6, 33.9, 34.3, 35.0, 35.2, 41.9, 42.1, 43.5, 43.5, 47.0, 47.0, 52.4, 52.5, 63.9, 64.4, 115.5, 115.6, 136.4, 136.4, 168.7, 168.8, 203.2, 203.3, 212.6, 212.7; MS (ESI (+)) m/z 289 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{15}\text{H}_{23}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 267.1596; found 267.1594; After conversion to **28ce**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 36.3 min, t_R (minor) = 37.8 min; Absolute configuration was *S*. Determination of the absolute configuration of **9ce** is described later.

(*S*)-3-Oxo-2-(3-oxo-cycloheptyl)hept-6-ynoic acid methyl ester (9cf):

colorless oil: $[\alpha]_D^{25} -24.0$ (c 1.03, CHCl_3) (73% ee); FT-IR (neat) 3283, 2932, 2860, 1749, 1714, 1435, 1362, 1255, 1196, 1164, 1080, 939, 756; For a 1:1 mixture of diastereomers, ^1H NMR (500 MHz, CDCl_3) 1.30-1.37 (m, 2H), 1.47-1.59 (m, 4H), 1.71 (d, $J = 14.7$ Hz, 1H), 1.77 (d, $J = 13.8$ Hz, 1H), 1.81-1.89 (m, 4H), 1.92 (s, 1H), 1.93 (s, 1H), 2.41-2.47 (m, 10H), 2.50-2.61 (m, 4H), 2.65-2.84 (m, 4H), 3.44 (d, $J = 8.6$ Hz, 1H), 3.44 (d, $J = 8.9$ Hz, 1H), 3.71 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) 12.7, 24.3, 28.1, 28.5, 33.8, 34.2, 35.0, 35.3, 41.4, 41.6, 43.5, 43.5, 46.9, 47.0, 52.5, 52.5, 63.7, 64.2, 68.9, 69.0, 82.4, 82.4, 168.5, 168.6, 201.9, 202.0, 212.4, 212.6; MS (ESI (+)) m/z 287 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{15}\text{H}_{21}\text{O}_4^+$ ($\text{M}+\text{H}^+$): 265.1440; found 265.1443; After conversion to **28cf**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 160 °C, isothermal, t_R (major) = 36.3 min, t_R (minor) = 37.8 min; Absolute configuration was *S*. Determination of the absolute configuration of **9cf** is

described later.

(S)-4-Cyclohexyl-3-oxo-2-(3-oxo-cycloheptyl)butyric acid methyl ester (9cg):

white solid: $[\alpha]_D^{25} -18.0$ (*c* 2.5, CHCl₃) (60% ee); FT-IR (neat) 3441, 2925, 2852, 1749, 1704, 1448, 1344, 1260, 1196, 1164, 1097; For a 1:1 mixture of diastereomers, ¹H NMR (500 MHz, CDCl₃) 0.82-0.91 (m, 4H), 1.08-1.13 (m, 2H), 1.23-1.35 (m, 6H), 1.47-1.85 (m, 22H), 2.23-2.45 (m, 10H), 2.52-2.59 (m, 4H), 3.39 (d, *J* = 9.2 Hz, 2H), 3.70 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) 24.4, 24.4, 25.9, 25.9, 26.1, 28.3, 28.6, 32.8, 32.8, 33.0, 33.0, 33.1, 33.1, 33.8, 34.3, 34.9, 35.1, 43.5, 43.5, 47.1, 47.1, 50.4, 50.5, 52.4, 52.4, 64.5, 64.9, 168.7, 168.8, 203.5, 203.6, 212.6, 212.7; MS (ESI (+)) *m/z* 331 (*M*+Na⁺); HRMS (FAB(+)) calcd. for C₁₈H₂₉O₄⁺ (*M*+H⁺): 309.2066; found 309.2071; After conversion to **27cg**, ee was determined by chiral GC. Separation conditions: Chirasil DEX CB, 180 °C, isothermal, *t_R* (major) = 66.9 min, *t_R* (minor) = 68.6 min; Absolute configuration was *S*. Determination of the absolute configuration of **9cg** is described later.

8. Determination of the Enantiomeric Excess

Scheme S3. Derivatization for the Determination of the Enantiomeric Excess

8-1. General Procedure for the Derivatization of Michael Adduct: To **9ba** (24.4 mg, 0.12 mmol) were added catalytic amount of *p*-TsOH·H₂O and 2-ethyl-2-methyl-1,3-dioxolane (0.43 mL, 3.45 mmol) and the mixture was stirred at room temperature. After 24 h, the mixture was diluted with ethyl acetate, quenched with saturated aqueous NaHCO₃, and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was dried under vacuum. To the residue were added DABCO (129 mg, 1.15 mmol) and xylene (0.4 mL), and the mixture was stirred at 140 °C. After stirring for 24 h at the

same temperature, the mixture was diluted with diethyl ether, quenched with 1 N HCl, and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (SiO₂, hexane/acetone, 9/1) to give **27ba** (13.1 mg, 57% yield). colorless oil: FT-IR (neat) 3508, 2934, 2885, 1714, 1447, 1431, 1356, 1281, 1167, 1150, 1099, 1069, 919; ¹H NMR (500 MHz, CDCl₃) 0.85-0.94 (m, 1H), 1.18 (t, *J* = 12.5 Hz, 1H), 1.38-1.44 (m, 1H), 1.51-1.59 (m, 1H), 1.66-1.75 (m, 4H), 2.09-2.18 (m, 1H), 2.12 (s, 3H), 2.23-2.37 (m, 2H), 3.90-3.95 (m, 4H); ¹³C NMR (125 MHz, CDCl₃) 22.9, 30.3, 31.5, 31.7, 34.6, 41.2, 50.6, 64.2, 64.0, 108.8, 208.2; MS (ESI (+)) *m/z* 221 (M+Na⁺).

8-2. General Procedure for the Reduction of C-C Multiple Bond: For the compounds which have C-C multiple bond, general derivatization didn't give separable peaks on chiral GC analysis and determination of the enantiomeric excess was impossible. Thus reduction of C-C multiple bond was needed. To the **27be** (19.1 mg, 0.076 mmol) was added MeOH (0.38 mL) and replaced by three cycles of vacuum/argon at room temperature. To the mixture was added 10% Pd/C (4 mg, 5 mol %) and the mixture was stirred under hydrogen atmosphere at room temperature. After 2 to 3 h, the reaction mixture was filtrated over Celite pad and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO₂, hexane/acetone 9/1) to give **28be** (9.9 mg, 0.04 mmol). colorless oil: ¹H NMR (500 MHz, CDCl₃) 0.89 (t, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 12.5 Hz, 1H), 1.25-1.32 (m, 2H), 1.41-1.44 (m, 1H), 1.50-1.73 (m, 4H), 1.66-1.75 (m, 4H), 2.13-2.16 (m, 1H), 2.30-2.32 (m, 2H), 2.37 (t, *J* = 7.0 Hz, 2H), 3.91-3.95 (m, 4H); ¹³C NMR (125 MHz, CDCl₃) 14.1, 22.6, 23.2, 26.1, 31.9, 31.9, 35.0, 41.4, 43.2, 49.9, 64.4, 64.5, 109.1, 210.7.

9. Determination of the Absolute Configuration

The absolute configurations of **9aa**, **9ba**, and **9bb** were determined to be *S* by the comparison of the optical rotation with the reported value after conversion to the corresponding 3-acetyl-cycloalkanone, **29aa**, **29ba** (**29ba** and **29bb** is same compound). The procedure is shown in Scheme S4. The absolute configurations of **9bc-bg**, **9ca**, **9cc-cg** were determined to be *S* by the comparison of the optical rotation with the authentic samples prepared from known Michael adducts of malonates. The procedure is shown in Scheme S5. For **9cb**, after conversion to **29ca** (**29cb** and **29ca** is same compound), the absolute configuration was determined by the comparison of the optical rotation with the authentic sample prepared from **9ca**.

Scheme S4. Determination of the Absolute Configuration of the Michael Adducts (**9aa**, **9ba**, and **9bb**)

Scheme S5. Determination of the Absolute Configuration of the Michael Adducts (**9bc-9bg**, **9ca**, **9cc-9cg**)

9-1. General Procedure of Deprotection of Ketal: 27ba (92% ee) (21.5 mg, 0.11 mmol) was dissolved in acetone/H₂O = 9/1 (0.3 mL), and catalytic amount of PPTS was added. After stirring for 1 h at reflux temperature, the reaction mixture was diluted with ethyl acetate, quenched with saturated aqueous NaHCO₃ and dried over Na₂SO₄. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (SiO₂, hexane/acetone, 9/1) to give **29ba** (12.8 mg, 0.084 mmol, 78%). **29ba**: This product was found to be identical with the reported compound by comparison with ¹H NMR. **29ba**: [α]_D²⁴ -11.3 (*c* 0.33, C₆H₆) (90% ee) [lit^{SI-8}: [α]_D²² +3.9 (*c* 3.1, C₆H₆) (26% ee, *S* enantiomer)], **29ba** was *R* enantiomer, thus **9ba** is *S* enantiomer.

For **9aa**, same derivatization gave **29aa**: [α]_D²⁴ -56.9 (*c* 0.30, C₆H₆) (73% ee) [lit^{SI-7}: [α]_D²⁵ -59.8 (C₆H₆) (78% ee, *R* enantiomer)], **29aa** was *R* enantiomer, thus **9aa** was *S* enantiomer.

For **9bb**, same derivatization gave **29bb**: [α]_D²⁵ -5.0 (*c* 0.1, C₆H₆) (88% ee) [lit^{SI-8}: [α]_D²² +3.9 (*c* 3.1, C₆H₆) (26% ee, *S* enantiomer)], **29bb** was *R* enantiomer, thus **9bb** is *S* enantiomer.

9-2. General Procedure for the Conversion of the Michael Adduct of Malonates to That of β -Keto Esters

Michael adduct of malonates **31a-c** were synthesized by using (*S,S*)-La-O-linked-BINOL or (*R,R*)-La-O-linked-BINOL. The procedure is reported in our previous report.^{4d}

2-(1,4-Dioxa-spiro[4.5]dec-7-yl)-3-oxo-butyric acid methyl ester (26bd): To a solution of

diisopropylamine (0.27 mL, 1.95 mmol) in THF (2.25 mL) was added *n*-BuLi (1.54 M in *n*-hexane, 1.17 mL, 1.8 mmol) at $-78\text{ }^{\circ}\text{C}$ and the solution was stirred for 1 h at the same temperature. Then **32b** (1.0 M in THF, 1.5 mL, 1.5 mmol) was added, and the solution was stirred for 1 h at the same temperature again. In another test tube, to a solution of *n*-butyric acid (46 μL , 0.5 ml) in THF (0.5 mL) was added *N*-methylmorpholine (58 μL , 0.53 mmol) at $-15\text{ }^{\circ}\text{C}$, and then isopropyl chlorocarbonate (57 μL , 0.5 mmol) was added gradually not to raise the temperature. After the solution was stirred for 30 min at the same temperature, the solution of Li-enolate of **32b** prepared above was added via a cannula. The solution was stirred at $-15\text{ }^{\circ}\text{C}$, and after the reaction stopped on TLC (while **32b** still remained), it was quenched by saturated aqueous NH_4Cl at the same temperature, extracted with ethyl acetate, and dried over Na_2SO_4 . The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (SiO_2 , hexane/acetone, 19/1) to give **26bd** (90.9 mg, 0.32 mmol, 64%).

(*S*)-**31a**, (*R*)-**31b**, and (*S*)-**31c** were used as a starting material of the transformation in Scheme S5.

9ac: $[\alpha]_{\text{D}}^{25} -79.0$ (*c* 3.70, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{24} -64.9$ (*c* 0.81, CHCl_3) (80% ee)], thus **9ac** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9ad: $[\alpha]_{\text{D}}^{23} -58.4$ (*c* 0.34, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{24} -48.8$ (*c* 0.76, CHCl_3) (60% ee)], thus **9ad** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9ae: $[\alpha]_{\text{D}}^{24} -55.0$ (*c* 0.27, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25} -43.1$ (*c* 0.85, CHCl_3) (72% ee)], thus **9ae** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9bc: $[\alpha]_{\text{D}}^{23} +13.3$ (*c* 2.50, CHCl_3) (> 99% ee) (*R*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{24} -11.9$ (*c* 0.72, CHCl_3) (91% ee)], thus **9bc** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9bd: $[\alpha]_{\text{D}}^{23} +17.9$ (*c* 1.77, CHCl_3) (> 99% ee) (*R*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{24} -11.6$ (*c* 0.85, CHCl_3) (87% ee)], thus **9bd** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9be: $[\alpha]_{\text{D}}^{23} +5.31$ (*c* 4.29, CHCl_3) (> 99% ee) (*R*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25} -9.2$ (*c* 1.78, CHCl_3) (80% ee)], thus **9be** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9bf: $[\alpha]_{\text{D}}^{25} +10.1$ (*c* 1.50, CHCl_3) (> 99% ee) *R*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25} -6.9$ (*c* 0.53, CHCl_3) (73% ee)], thus **9bf** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9bg: $[\alpha]_{\text{D}}^{25} +7.04$ (*c* 1.07, CHCl_3) (> 99% ee) (*R*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25} -6.4$ (*c* 1.91, CHCl_3) (61% ee)], thus **9bg** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9ca: $[\alpha]_{\text{D}}^{25} -36.3$ (*c* 0.70, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{24} -33.0$ (*c* 0.67, CHCl_3) (92% ee)], thus **9ca** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9cc: $[\alpha]_{\text{D}}^{23} -38.4$ (*c* 3.36, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25} -29.4$ (*c* 0.91, CHCl_3) (88% ee)], thus **9cc** from Michael reaction of β -keto ester was (*S*)-enantiomer.

9cd: $[\alpha]_{\text{D}}^{22} -37.7$ (*c* 0.66, CHCl_3) (> 99% ee) (*S*-enantiomer) [Michael adduct of β -keto ester: $[\alpha]_{\text{D}}^{25}$

–24.2 (*c* 0.83, CHCl₃) (79% ee)], thus **9be** from Michael reaction of β-keto ester was (*S*)-enantiomer.

9ce: [α]²³_D –34.9 (*c* 0.51, CHCl₃) (> 99% ee) (*S*-enantiomer) [Michael adduct of β-keto ester: [α]²⁵_D –28.5 (*c* 1.25, CHCl₃) (83% ee)], thus **9ce** from Michael reaction of β-keto ester was (*S*)-enantiomer.

9cf: [α]²²_D –31.6 (*c* 3.09, CHCl₃) (> 99% ee) (*S*-enantiomer) [Michael adduct of β-keto ester: [α]²⁵_D –24.0 (*c* 1.03, CHCl₃) (73% ee)], thus **9cf** from Michael reaction of β-keto ester was (*S*)-enantiomer.

9cg: [α]²²_D –27.6 (*c* 0.49, CHCl₃) (> 99% ee) (*S*-enantiomer) [Michael adduct of β-keto ester: [α]²⁵_D –18.0 (*c* 0.45, CHCl₃) (60% ee)], thus **9cg** from Michael reaction of β-keto ester was (*S*)-enantiomer.

For **9cb**,

29ca: [α]²²_D –31.4 (*c* 0.16, CHCl₃) (88% ee) (*R*-enantiomer) [**29ca** converted from **9ca**: [α]²⁵_D –37.2 (*c* 0.45, CHCl₃) (90% ee)], **29cb** was *R* enantiomer, thus **9cb** from Michael reaction of β-keto ester was (*S*)-enantiomer.

For all the Michael adducts of β-keto esters using (*S,S*)-La–NR-linked-BINOL complex, absolute configuration was *S*.

10. Application to the Synthesis of the Key Intermediate of (–)-Tubifolidine and (–)-19,20-Dihydroakuammicine

2-(3-Oxo-cyclohexyl)but-2-enoic acid methyl ester (10): To a solution of anhydrous RuCl₃ (10.4 mg, 0.05 mmol) and DPPB (20.6 mg, 0.05 mmol) in MeOH (2.2 mL) was added (*R*)-**9ba** (212.2 mg, 1.0 mmol). After placed in stainless steel autoclave, the argon atmosphere was replaced with hydrogen by three cycles of pressurizing. The reaction was performed under 30 atm of hydrogen pressure for 24 h at 50 °C. Then hydrogen was replaced by argon by three cycles of vacuum/argon at room temperature, and the reaction mixture was filtered over a Celite pad. The filtrate was evaporated under reduced pressure and the residue was diluted with ethyl acetate, quenched with 1N HCl, washed with brine, and dried over Na₂SO₄. After evaporation to remove the solvent, the residue was purified by flash column chromatography (SiO₂, hexane/acetone, 9/1) to give β-hydroxy ester (180.1 mg, 84%). colorless oil: [α]²²_D +6.15 (*c* 2.55, CHCl₃); FT-IR (neat) 3436, 2952, 2871, 1698, 1436, 1379, 1348, 1251, 1165, 1131, 1098, 993; For a mixture of 4 diastereomers, ¹H NMR (500 MHz, CDCl₃) 1.16-1.21 (m, 12H), 1.33-1.42 (m, 4H), 1.60-1.87 (m, 8H), 2.04-2.34 (m, 28H), 2.72 (br, 4H), 3.64-3.71 (m, 12H), 3.98 (d, *J* = 23.5 Hz, 4H); For a mixture of major 2 diastereomers, ¹³C NMR (125 MHz, CDCl₃) 21.9, 22.0, 24.6, 24.7, 28.9, 29.0, 37.8, 37.9, 41.0, 41.2, 45.4, 45.6, 51.5, 51.6, 56.8, 57.1, 65.3, 65.4, 174.4, 174.5, 210.2, 210.2; MS (ESI (+)) *m/z* 237 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₁H₁₉O₄⁺ (M+H⁺): 215.1283; found

215.1281. To a solution of β -hydroxy ester (104 mg, 0.49 mmol) in benzene (0.5 mL) were added CuCl (62.4 mg, 0.63 mmol) and DCC (121.5 mg, 0.59 mmol) and the mixture was stirred for 18 h at reflux temperature. After cooling down to room temperature, the reaction mixture was filtered over a Celite pad and the filtrate was diluted with benzene, washed with brine, and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (SiO₂, hexane/ethyl acetate, 15/1) to give **10** as an *E/Z* mixture (77.8 mg, 81%, *E* isomer was major). colorless oil: $[\alpha]_D^{23} +33.0$ (*c* 1.76, CHCl₃); FT-IR (neat) 3406, 2952, 2871, 1710, 1640, 1435, 1281, 1256, 1193, 1134, 1071, 946, 754; For an *E* isomer, ¹H NMR (500 MHz, CDCl₃) 1.65-1.68 (m, 2H), 1.80 (d, *J* = 7.5 Hz, 3H), 2.09-2.12 (m, 1H), 2.21-2.26 (m, 2H), 2.33-2.39 (m, 2H), 2.92-2.98 (m, 1H), 3.03 (t, *J* = 13.1 Hz, 1H), 3.73 (s, 3H), 6.81(q, *J* = 7.5 Hz, 1H); For an *E/Z* mixture, ¹³C NMR (125 MHz, CDCl₃) 13.9, 15.6, 24.8, 25.7, 28.7, 30.5, 37.8, 41.1, 41.1, 41.9, 45.4, 46.9, 51.3, 51.3, 133.7, 134.4, 135.9, 138.0, 167.2, 168.2, 210.8, 211.3; MS (ESI (+)) *m/z* 219 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₁H₁₇O₃⁺ (M+H⁺): 197.1178; found 197.1180.

2-(2,3,4,9-Tetrahydro-1*H*-carbazol-2-yl)but-2-en-1-ol (11): To a solution of **10** (921 mg, 4.69 mmol) in AcOH (7.8 mL) was added phenylhydrazine hydrochloride (746 mg, 5.16 mmol). After stirring for 2 h at 80 °C, the solvent was evaporated under reduced pressure and diluted with ethyl acetate, washed with saturated aqueous NaHCO₃, and extracted with ethyl acetate. Combined organic extracts were washed with saturated aqueous NaHCO₃, brine, and dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was roughly purified through short pad silica gel column (hexane/ethyl acetate, 15/1) to remove polar reagents. Because of the instability of this indole, it was immediately used to the next reaction. yellow oil: $[\alpha]_D^{23} +1.00$ (*c* 0.82, CHCl₃); FT-IR (neat) 3400, 3048, 2930, 2844, 1708, 1465, 1434, 1256, 1129, 742; MS (ESI (+)) *m/z* 292 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₇H₂₀NO₂⁺ (M+H⁺): 270.1494; found, 270.1492. To a solution of indole (87 mg, 0.32 mmol) in toluene (3.7 mL) was added DIBAL-H (1.1 mL, 1.01 M in toluene) at -78 °C. After stirring for 3 h at -78 °C, the reaction mixture was poured into a vigorously stirred mixture of saturated aqueous potassium sodium tartrate and Et₂O via a cannula at 0 °C. The whole mixture was stirred vigorously for 30 min at room temperature. Then, organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated. The residue was then purified by flash column chromatography (SiO₂, hexane/ethyl acetate, 4/1) to give **11** (56.4 mg, 72% for 2 steps). Pale red oil: $[\alpha]_D^{23} +39.4$ (*c* 0.76, CHCl₃); FT-IR (neat) 3400, 3053, 2921, 2844, 1467, 1300, 995, 742; For an *E* isomer, ¹H NMR (500 MHz, CDCl₃) 1.31 (s, 1H), 1.76 (d, *J* = 6.7 Hz, 3H), 1.88-1.97 (m, 2H), 2.62-2.92 (m, 4H), 3.10 (m, 1H), 4.20 (dd, *J* = 12.8, 26.6 Hz, 2H), 5.68 (q, *J* = 6.7 Hz, 1H),

7.15 (m, 2H), 7.27 (d, $J = 7.7$ Hz, 1H), 7.51 (d, $J = 7.3$ Hz, 1H), 7.81 (s, 1H); For an *E/Z* mixture, ^{13}C NMR (125 MHz, CDCl_3) 12.7, 13.2, 20.9, 21.2, 27.7, 28.2, 29.0, 29.2, 30.9, 31.7, 35.2, 40.1, 53.7, 59.2, 65.1, 109.4, 110.4, 110.5, 117.6, 119.0, 119.0, 120.8, 120.9, 122.7, 122.7, 127.4, 133.9, 134.0, 135.8, 135.9, 142.4, 142.8; MS (ESI (+)) m/z 264 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{16}\text{H}_{20}\text{NO}_1^+$ ($\text{M}+\text{H}^+$): 242.1545; found, 242.1546.

Dimethoxymethyl-[2-(2,3,4,4',9,9'-hexahydro-1*H*-carbazol-2-yl)but-2-enyl]-amine (12): To a solution of **11** (56.4 mg, 0.23 mmol) in CH_2Cl_2 (1.2 mL) were added diisopropyl ethyl amine (90 μL , 0.70 mmol) and methanesulfonic anhydride (174 mg, 0.46 mmol) at -20°C . The mixture was stirred and warmed up to 4°C for 2 h and aminoacetaldehyde dimethyl acetal (125 μL , 1.15 mmol) was added. The reaction mixture was stirred for 24 h at room temperature, Then, diluted with CH_2Cl_2 , quenched with saturated aqueous NaHCO_3 , and dried over Na_2SO_4 . The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (SiO_2 , hexane/ethyl acetate/ Et_3N , 2/1/0.05) to give **12** (45 mg, 60%) as a yellow oil: $[\alpha]_D^{23} +21.5$ (c 0.72, CHCl_3); FT-IR (neat) 3403, 3340, 2923, 2836, 1467, 1299, 1193, 1132, 1063, 741; For an *E* isomer, ^1H NMR (500 MHz, CDCl_3) 1.70 (d, $J = 6.8$ Hz, 3H), 1.85-1.93 (m, 2H), 2.60-2.91 (m, 4H), 2.76 (d, $J = 5.5$ Hz, 2H), 3.05 (m, 1H), 3.28 (s, 2H), 3.40 (s, 6H), 4.51 (t, $J = 5.5$ Hz, 1H), 5.52 (q, $J = 6.8$ Hz, 1H), 7.07-7.14 (m, 2H), 7.28 (d, $J = 7.9$ Hz, 1H), 7.47 (d, $J = 7.9$ Hz, 1H), 7.81 (br-s, 1H); For an *E/Z* mixture, ^{13}C NMR (125 MHz, CDCl_3) 12.9, 13.4, 21.0, 21.4, 27.5, 28.1, 29.2, 29.4, 35.7, 40.0, 47.5, 50.7, 50.7, 52.3, 53.9, 54.0, 54.0, 54.1, 103.8, 104.0, 109.7, 110.4, 117.7, 119.0, 119.1, 120.8, 120.9, 121.0, 121.3, 127.5, 134.0, 134.1, 135.8, 135.9, 140.6, 141.8; MS (ESI (+)) m/z 351 ($\text{M}+\text{Na}^+$); HRMS (FAB(+)) calcd. for $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_2^+$ ($\text{M}+\text{H}^+$): 329.2229; found, 329.2231.

11. Chemoselective Allylation at the α -Position of β -Keto Ester Moiety

2-Acetyl-2-(3-oxo-cyclohexyl)pent-4-enoic acid methyl ester (17): In a test tube, to a solution of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (34.8 mg, 0.034 mmol, 5 mol %) in THF (1.3 mL) was added PCy_3 (0.35 mL, 25% in toluene, 0.27 mmol, 40 mol %) and the solution was stirred for 15 min at room temperature under Ar. In another flask, a solution of Michael adduct **9ba** (143 mg, 0.67 mmol) and allyl ethyl carbonate (110 μL , 0.81 mmol) in THF (0.67 mL) was prepared and added to the catalyst solution at 4°C . The flask was rinsed with THF (0.67 mL) and the washing was also added to the solution. The mixture was stirred for 1 h at 4°C and filtered through Florisil. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (SiO_2 , hexane/acetone, 19/1) to give **17** (167 mg, 0.66 mmol, y. 99%, dr = 2:1). Diastereomeric ratio was determined by ^1H NMR analysis. colorless oil:

For the major diastereomer, $[\alpha]_D^{23} +3.9$ (*c* 2.51, CHCl₃); FT-IR (neat) 2294, 1710, 1434, 1356, 1218, 994; ¹H NMR (500 MHz, CDCl₃) 1.28 (dd, *J* = 13.0, 27.0 Hz, 1H), 1.60 (dd, *J* = 13.0, 27.0 Hz, 1H), 1.93 (d, *J* = 13.0 Hz, 1H), 2.01-2.20 (m, 3H), 2.14 (s, 3H), 2.36-2.46 (m, 3H), 2.54 (dd, *J* = 7.0, 15.0 Hz, 1H), 2.67 (dd, *J* = 7.0, 15.0 Hz, 1H), 3.77 (s, 3H), 5.06-5.12 (m, 2H), 5.55 (dt, *J* = 7.4, 17.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) 24.8, 27.7, 28.7, 36.1, 40.2, 41.2, 43.1, 52.1, 66.0, 119.4, 131.6, 171.3, 203.8, 210.0; MS (ESI (+)) *m/z* 275 (M+Na⁺); HRMS (FAB(+)) calcd. for C₁₄H₂₁O₄⁺ (M+H⁺): 253.1440; found, 253.1443.

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The pdb data for La–O-linked-BINOL complex

HEADER	Title	Card	Required				
REMARK	1	C	1	.000	.000	.000	C
HETATM	2	C	1	.000	.000	1.445	C
HETATM	3	C	1	1.254	.000	2.154	C
HETATM	4	C	1	2.467	-.014	1.439	C
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HETATM	6	C	1	1.246	-.081	-.692	C
HETATM	7	C	1	.864	.956	4.522	C
HETATM	8	C	1	.899	.774	5.953	C
HETATM	9	C	1	1.402	-.449	6.495	C
HETATM	10	C	1	1.876	-1.444	5.656	C
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HETATM	76	H		1	5.091	-10.747	3.745	H
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CONNECT	3	1	6	7				
CONNECT	4	1	9	10				
CONNECT	5	2	11	12				
CONNECT	6	3	11	13				
CONNECT	7	3						
CONNECT	8	2	14	15				
CONNECT	9	4	14	16				
CONNECT	10	4						
CONNECT	11	5	6	20	23			
CONNECT	12	5	17	18				
CONNECT	13	6	19	21	22			
CONNECT	14	8	9	24				
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CONNECT	17	12	25	32				
CONNECT	18	12	26	29				
CONNECT	19	13	23	28	33			
CONNECT	20	11	23					
CONNECT	21	13						
CONNECT	22	13						
CONNECT	23	11	19	20	27			
CONNECT	23	29	30	31				
CONNECT	24	14						
CONNECT	25	17	34	43				
CONNECT	26	18	34	38				
CONNECT	27	23	30	35	36			
CONNECT	28	19	36	39	40			
CONNECT	29	18	23	41				
CONNECT	30	23	27					
CONNECT	31	23	37					
CONNECT	32	17	42	44				
CONNECT	33	19						
CONNECT	34	25	26	49				
CONNECT	35	27	45	48				
CONNECT	36	27	28	46				
CONNECT	37	21	47	48				
CONNECT	38	26						
CONNECT	39	28						
CONNECT	40	28						
CONNECT	41	29						
CONNECT	42	32	50	51				
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CONNECT	44	32						
CONNECT	45	35	53	58				
CONNECT	46	36	53	56				
CONNECT	47	37	55	57				
CONNECT	48	35	37	54				
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CONNECT	58	45	63	64				
CONNECT	59	50						
CONNECT	60	54	55	70				
CONNECT	61	55						
CONNECT	62	53	66	67				
CONNECT	63	58	67	68				
CONNECT	64	58						
CONNECT	65	54	69	71				
CONNECT	66	62						
CONNECT	67	62	63	72				
CONNECT	68	63						
CONNECT	69	65	73	74				
CONNECT	70	60	74	75				
CONNECT	71	65						
CONNECT	72	67						
CONNECT	73	69						
CONNECT	74	69	70	76				
CONNECT	75	70						
CONNECT	76	74						
END								

The pdb data for La-NMe-linked-BINOL complex
HEADER

REMARK	Title	Card	Required				
HE	TATM	1	C	1	.000	.000	.000
HE	TATM	2	C	1	.000	.000	1.444
HE	TATM	3	C	1	1.250	.000	-.691
HE	TATM	4	C	1	-1.238	-.054	-.710
HE	TATM	5	C	1	1.253	.069	2.149
HE	TATM	6	C	1	2.456	.030	-.012
HE	TATM	7	H	1	1.242	-.053	-1.779
HE	TATM	8	C	1	-1.267	-.095	2.111
HE	TATM	9	C	1	-2.448	-.126	-.033
HE	TATM	10	H	1	-1.217	-.048	-1.799
HE	TATM	11	C	1	2.468	.126	1.435
HE	TATM	12	C	1	1.310	-.022	3.643
HE	TATM	13	C	1	3.782	-.053	-.734
HE	TATM	14	C	1	-2.455	-.156	1.393
HE	TATM	15	H	1	-1.295	-.120	3.195
HE	TATM	16	H	1	-3.387	-.170	-.580
HE	TATM	17	C	1	.848	1.036	4.509
HE	TATM	18	C	1	1.832	-1.161	4.253
HE	TATM	19	N	1	4.515	-1.376	-.530
HE	TATM	20	O	1	3.671	.193	2.074
HE	TATM	21	H	1	4.452	.727	-.355
HE	TATM	22	H	1	3.639	.105	-1.816
HE	TATM	23	La	1	4.607	-1.998	2.135
HE	TATM	24	H	1	-3.402	-.227	1.922
HE	TATM	25	C	1	.895	.869	5.942
HE	TATM	26	C	1	1.898	-1.340	5.660
HE	TATM	27	C	1	4.311	-4.387	.395
HE	TATM	28	C	1	3.796	-2.517	-1.247
HE	TATM	29	O	1	2.432	-2.193	3.448
HE	TATM	30	H	1	3.419	-3.747	1.241
HE	TATM	31	O	1	5.984	-3.672	2.962
HE	TATM	32	C	1	.359	2.275	3.984
HE	TATM	33	C	1	1.420	-.341	6.493
HE	TATM	34	C	1	5.112	-5.459	.831
HE	TATM	35	C	1	4.446	-3.851	-.942
HE	TATM	36	C	1	5.655	-4.973	3.249
HE	TATM	37	C	1	2.321	-2.261	6.053
HE	TATM	38	H	1	2.761	-2.500	-.897
HE	TATM	39	H	1	3.811	-2.318	-2.332
HE	TATM	40	H	1	1.837	-2.919	3.162
HE	TATM	41	C	1	-.077	3.286	4.829
HE	TATM	42	C	1	.430	1.926	6.787
HE	TATM	43	H	1	.343	2.417	2.908
HE	TATM	44	C	1	5.983	-6.105	-.126
HE	TATM	45	C	1	5.239	-4.510	-1.867
HE	TATM	46	C	1	5.821	-5.416	4.605
HE	TATM	47	C	1	5.134	-5.862	2.277
HE	TATM	48	H	1	1.454	-.463	7.572
HE	TATM	49	C	1	-.049	3.110	6.245
HE	TATM	50	H	1	-.441	4.223	4.413
HE	TATM	51	H	1	.465	1.787	7.865
HE	TATM	52	C	1	6.000	-5.660	-1.500
HE	TATM	53	C	1	4.667	-7.161	2.698
HE	TATM	54	C	1	5.422	-6.678	5.004
HE	TATM	55	H	1	5.324	-4.127	-2.884
HE	TATM	56	H	1	6.273	-4.715	5.302
HE	TATM	57	C	1	6.864	-7.176	.237
HE	TATM	58	H	1	-.398	3.909	6.895
HE	TATM	59	C	1	4.815	-7.577	4.072
HE	TATM	60	H	1	5.556	-6.996	6.036
HE	TATM	61	C	1	6.834	-6.325	-2.452
HE	TATM	62	C	1	7.673	-7.796	-.707
HE	TATM	63	H	1	6.895	-7.503	1.270
HE	TATM	64	C	1	4.023	-8.070	1.794
HE	TATM	65	H	1	6.825	-5.981	-3.485
HE	TATM	66	C	1	7.653	-7.379	-2.071
HE	TATM	67	H	1	8.330	-8.608	-.404
HE	TATM	68	C	1	3.571	-9.313	2.218
HE	TATM	69	C	1	4.349	-8.865	4.478
HE	TATM	70	H	1	3.877	-7.768	.761
HE	TATM	71	H	1	8.285	-7.879	-2.800
HE	TATM	72	H	1	3.081	-9.979	1.512
HE	TATM	73	C	1	3.740	-9.725	3.574
HE	TATM	74	H	1	4.476	-9.161	5.519
HE	TATM	75	H	1	3.386	-10.703	3.891
HE	TATM	76	C	1	5.919	-1.226	-1.032
HE	TATM	77	H	1	6.472	-2.160	-.898
HE	TATM	78	H	1	5.941	-.968	-2.104
HE	TATM	79	H	1	6.422	-.420	-.482
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CONNECT	1	5	8				
CONNECT	3	6	7				
CONNECT	4	9					
CONNECT	5	2	10				
CONNECT	6	11	12				
CONNECT	6	3	13				

[illegible]

CONNECT	7	3			
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CONNECT	14	8	9	24	
CONNECT	15	8			
CONNECT	16	9			
CONNECT	17	12	25	32	
CONNECT	18	12	26	29	
CONNECT	19	13	23	28	76
CONNECT	20	11	23		
CONNECT	21	13			
CONNECT	22	13			
CONNECT	23	11	19	20	27
CONNECT	23	29	30	31	
CONNECT	24	14			
CONNECT	25	17	33	42	
CONNECT	26	18	33	37	
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CONNECT	28	19	35	38	39
CONNECT	29	18	23	40	
CONNECT	30	23	27		
CONNECT	31	23	36		
CONNECT	32	17	41	43	
CONNECT	33	25	26	48	
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CONNECT	62	57	66	67	
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CONNECT	64	53	68	70	
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CONNECT	66	61	62	71	
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CONNECT	71	66			
CONNECT	72	68			
CONNECT	73	68	69	75	
CONNECT	74	69			
CONNECT	75	73			
CONNECT	76	19	77	78	79
CONNECT	77	76			
CONNECT	78	76			
CONNECT	79	76			
END					