# Asymmetric Total Synthesis of (-)-Clovan-2,9-dione Using Rh(I)-Catalyzed [3+2+1] Cycloaddition of 1-Yne-vinylcyclopropane and CO 

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## Experimental Procedures

General Information. Air- and moisture-sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry argon. Reactions were stirred using Teflon coated magnetic stir bars. Elevated temperatures were maintained using thermostat-controlled silicone oil baths. Organic solutions were concentrated using a rotary evaporator with a desktop vacuum pump. Tetrahydrofuran (THF) and toluene were distilled from sodium and benzophenone prior to use. Dichloromethane (DCM) was distilled from $\mathrm{CaH}_{2}$ prior to use. $N, N$-dimethylformamide (DMF) and methanol were dried by molecular sieves prior to use. Synthetic reagents were purchased and used without further purification unless otherwise indicated. Analytical TLC was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with phosphomolybdic acid stain followed by gentle heating or iodine/silica-gel followed by water washing. Purification of products was accomplished by flash chromatography on silica gel, and the purified compounds showed a single spot by analytical TLC if not special instructions. The diastereomeric ratio was determined by ${ }^{1} \mathrm{H}$ NMR of crude reaction mixtures. NMR spectra were recorded at 400 MHz for ${ }^{1} \mathrm{H}$ and 100 MHz for ${ }^{13} \mathrm{C}$ using $\mathrm{CDCl}_{3}\left({ }^{1} \mathrm{H}, 7.26\right.$ ppm; $\left.{ }^{13} \mathrm{C}, 77.0 \mathrm{ppm}\right)$ or $\mathrm{CD}_{2} \mathrm{Cl}_{2}\left({ }^{1} \mathrm{H}, 5.30 \mathrm{ppm} ;{ }^{13} \mathrm{C}, 53.52 \mathrm{ppm}\right)$ as internal standard. The following abbreviations were used to explain the multiplicities: $\mathrm{s}=$ singlet, brs $=$ broad singlet, $\mathrm{d}=$ doublet, $\mathrm{t}=$ triplet, $\mathrm{q}=$ quartet, $\mathrm{dd}=$ doublet of doublets, ddd $=$ doublet of doublet of doublets, $m=$ multiplet, coupling constant $(\mathrm{Hz})$, and integration. HRMS were recorded on Bruker Apex IV FTMS mass spectrometer (ESI) or Micromass U.K. GCT GC-MS mass spectrometer (EI). Optical rotations were measured on a Perkin-Elmer 341 LC spectrometer. Enantiomer excess (ee) values were determined by analytical liquid chromatography (HPLC) analysis on a Shimadzu chromatograph (Daicel chiral columns Chiralpak IA, IC, and ID $(4.6 \times 250 \mathrm{~mm})$ ). PE refers to petroleum ether and EA refers to ethyl acetate.

| Abbreviations: |  |
| :--- | :--- |
| ${ }^{t} \mathrm{BuLi}=$ tert-butyllithium; | $\mathrm{TEMPO}=2,2,6,6$-tetramethyl-1-piperidinyloxy; |
| TBAC $=$ tetra- $n$-butylammonium chloride | $\mathrm{NCS}=N$-chlorosuccinimide |
| DIBAL $=$ diisobutylaluminum hydride | $\mathrm{TBSCl}=$ tert-butyldimethylsilyl chloride |
| PDC $=$ pyridinium dichromate | $\mathrm{BnBr}=$ benzyl bromide |
| TBAI $=$ tetra- $n$-butylammonium iodide | $\mathrm{LDA}=$ lithium diisopropylamide |
| HMPA $=$ hexamethylphosphoramide | $\mathrm{PCC}=$ pyridium chlorochromate |
| TsNHNH ${ }_{2}=4$-methylbenzenesulfonohydrazide | ${ }^{n} \mathrm{BuLi}=n$-butyllithium |

DMF = N,N-dimethylformamide
DCM $=$ dichloromethane
DMAP $=N, N$-4-dimethylaminopyridine
CBS $=$ Corey-Bakshi-Shibata reagent

THF = tetrahydrofuran
$\mathrm{PhMe}=$ toluene
TBSOTf $=$ tert -butyldimethylsilyl trifluoromethanesulfonate

We have achieved both racemic (Scheme S1) and asymmetric (Scheme S2) total syntheses of clovan-2,9-dione. In the experimental part, we present synthesis details of both routes.

Scheme S1: Racemic total synthesis of ( $\pm$ )-clovan-2,9-dione




Scheme S2: Asymmetric total synthesis of (-)-clovan-2,9-dione


## Detailed synthesis procedures



Preparation of ( $\pm$ )-7. To a solution of 2,6-di-tert-butyl-4-methylphenyl cyclopropanecarboxylate $\mathbf{6}^{\mathbf{1}}$ (7.90 g, 27.4 $\mathrm{mmol})$ in THF ( 40 mL ) was added ${ }^{t} \mathrm{BuLi}\left(21.0 \mathrm{~mL}, 1.3 \mathrm{M}\right.$ in pentane, 27.3 mmol ) dropwise at $-78{ }^{\circ} \mathrm{C}$ under an argon atmosphere. After stirred for 30 min , a solution of 3, 3-dimethylpent-4-ynal $\mathbf{5}^{\mathbf{2}}(2.51 \mathrm{~g}, 22.8 \mathrm{mmol})$ in THF ( 10 mL ) was added dropwise at $-78{ }^{\circ} \mathrm{C}$. The reaction mixture was stirred for 1.5 h at the same temperature, and then $\mathrm{LiAlH}_{4}$ $(2.60 \mathrm{~g}, 68.4 \mathrm{mmol})$ was added at $0{ }^{\circ} \mathrm{C}$ portionwise. After refluxing at $60^{\circ} \mathrm{C}$ for 3 h , the reaction mixture was transferred dropwise to a 250 mL conical flask containing saturated aqueous ammonium chloride solution ( 50 mL ) and saturated potassium sodium tartrate tetrahydrate solution $(50 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ and stirred, then diethyl ether $(50 \mathrm{~mL})$ was added. The mixture was stirred overnight and extracted with diethyl ether $(3 \times 30 \mathrm{~mL})$. The combined organic layer was washed with water $(50 \mathrm{~mL})$ and brine $(50 \mathrm{~mL})$, dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE, then PE/EA 2:1, 1:1) to give $( \pm)-7(2.74 \mathrm{~g}, 66 \%$ yield $)$ as a white solid. $\mathrm{Mp}=60-62{ }^{\circ} \mathrm{C} . \mathrm{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 2: 1)=0.20 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 4.04(\mathrm{dd}, J=11.5,1.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.33(\mathrm{~d}$, $J=9.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.00(\mathrm{dd}, J=11.5,0.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.76(\mathrm{brs}, 2 \mathrm{H}), 2.24(\mathrm{~s}, 1 \mathrm{H}), 1.92(\mathrm{dd}, J=14.4,9.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.66(\mathrm{dd}$, $J=14.2,1.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.27(\mathrm{~s}, 3 \mathrm{H}), 1.22(\mathrm{~s}, 3 \mathrm{H}), 0.68-0.58(\mathrm{~m}, 2 \mathrm{H}), 0.34(\mathrm{dd}, J=8.4,6.4 \mathrm{~Hz}, 2 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (100 $\mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 91.8,76.9,69.5,67.5,47.8,30.1,29.8,29.0,27.2,11.4,7.7$. HRMS (ESI): calcd for $\mathrm{C}_{11} \mathrm{H}_{18} \mathrm{NaO}_{2}$ $\left([\mathrm{M}+\mathrm{Na}]^{+}\right)$205.1199, found 205.1200 .


Preparation of ( $\pm$ )-8. To a solution of $( \pm)-7(958.9 \mathrm{mg}, 5.26 \mathrm{mmol})$, NCS $(1.05 \mathrm{~g}, 7.88 \mathrm{mmol})$, TBAC $(146.6 \mathrm{mg}$, 0.528 mmol ) and TEMPO ( $411.8 \mathrm{mg}, 2.63 \mathrm{mmol}$ ) in DCM ( 17.5 mL ) was added buffer ( $17.5 \mathrm{~mL}, 0.5 \mathrm{M}$ $\mathrm{NaHCO}_{3} / 0.05 \mathrm{M} \mathrm{K}_{2} \mathrm{CO}_{3}$ ). After stirred for 3 h at room temperature, the reaction mixture was extracted with diethyl ether $(3 \times 30 \mathrm{~mL})$. The combined organic layer was washed with water ( 50 mL ) and brine ( 50 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 20:1, then PE/EA
$5: 1)$ to give $( \pm) \mathbf{8}(830.7 \mathrm{mg}, 88 \%$ yield $)$ as a light yellow oil. TLC $\mathrm{R}_{f}($ PE/EA $5: 1)=0.27 .{ }^{1} \mathrm{H} \mathrm{NMR}(400 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right): \delta 8.82(\mathrm{~s}, 1 \mathrm{H}), 3.93(\mathrm{dd}, J=9.4,1.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.92(\mathrm{brs}, 1 \mathrm{H}), 2.21(\mathrm{~s}, 1 \mathrm{H}), 1.86(\mathrm{dd}, J=14.3,9.4 \mathrm{~Hz}, 1 \mathrm{H})$, $1.70(\mathrm{dd}, J=14.3,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.31(\mathrm{~s}, 3 \mathrm{H}), 1.30(\mathrm{~s}, 3 \mathrm{H}), 1.26-1.16(\mathrm{~m}, 3 \mathrm{H}), 1.16-1.11(\mathrm{~m}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 100 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 201.6,91.8,69.6,69.5,48.2,37.6,30.2,30.0,29.1,12.0,10.7$. HRMS (ESI): calcd for $\mathrm{C}_{11} \mathrm{H}_{16} \mathrm{NaO}_{2}([\mathrm{M}+$ $\mathrm{Na}]^{+}$) 203.1043, found 203.1041.


Preparation of ( $\mathbf{\pm})$-9. To a solution of $\mathrm{NaH}(860.7 \mathrm{mg}, 60 \%$ weight in mineral oil, 21.5 mmol$)$ in THF ( 40 mL ) was added ethyl 2-(diethoxyphosphoryl)acetate ( $2.84 \mathrm{~mL}, 14.3 \mathrm{mmol}$ ) dropwise at $0{ }^{\circ} \mathrm{C}$ under an argon atmosphere. A solution of $( \pm)-8(1.29 \mathrm{~g}$, in 20 mL THF, 7.15 mmol$)$ was added dropwise at $0^{\circ} \mathrm{C}$. After stirred for 40 min at $0^{\circ} \mathrm{C}$, the reaction was quenched by saturated aqueous ammonium chloride solution ( 20 mL ) and water ( 20 mL ). The reaction mixture was extracted with diethyl ether $(2 \times 30 \mathrm{~mL})$. The combined organic layer was washed with water ( 50 mL ) and brine ( 50 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 5:1) to give ( $\pm$ )-9 $(1.61 \mathrm{~g}, 90 \%$ yield) as a yellow oil. The double bond in $( \pm)-9$ was assigned as a trans configuration judged by the NMR coupling constant of the hydrogen atoms in the alkene moiety. TLC $\mathrm{R}_{f}$ (PE/EA 5:1) $=0.31 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 7.08(\mathrm{~d}, J=15.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.75(\mathrm{~d}, J=15.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.17(\mathrm{q}, J=$ $7.2 \mathrm{~Hz}, 2 \mathrm{H}), 3.52(\mathrm{dd}, J=9.6,1.2 \mathrm{~Hz}, 1 \mathrm{H}), 2.62(\mathrm{brs}, 1 \mathrm{H}), 2.32(\mathrm{~s}, 1 \mathrm{H}), 1.82(\mathrm{dd}, J=14.4,9.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.65(\mathrm{dd}, J=$ $14.4,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.21-1.34(\mathrm{~m}, 9 \mathrm{H}), 1.07-0.97(\mathrm{~m}, 1 \mathrm{H}), 0.93-0.76(\mathrm{~m}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 166.8$, $151.0,118.1,91.6,73.9,69.8,60.2,48.0,30.4,29.8,29.0,28.3,15.9,14.3,13.3$. HRMS (ESI): calcd for $\mathrm{C}_{15} \mathrm{H}_{26} \mathrm{NO}_{3}$ $\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right)$268.1907, found 268.1911.


Preparation of $( \pm) \mathbf{- 1 0}$. To a solution of $( \pm)-\mathbf{9}(434.3 \mathrm{mg}, 1.74 \mathrm{mmol})$ in DCM $(17 \mathrm{~mL})$ was added DIBAL $(6.9 \mathrm{~mL}$, 1.0 M in hexanes, 6.90 mmol ) at $-78^{\circ} \mathrm{C}$ under an argon atmosphere. After stirred for 1.5 h at the same temperature, the reaction was quenched by saturated aqueous ammonium chloride solution ( 20 mL ) and saturated potassium sodium tartrate tetrahydrate solution ( 20 mL ). It was extracted with diethyl ether $(3 \times 20 \mathrm{~mL})$. The combined organic layer was washed with water $(20 \mathrm{~mL})$ and brine $(20 \mathrm{~mL})$, dried over anhydrous sodium sulphate, filtered, concentrated to give the crude alcohol product, which was directly used in the next step without further purification.

To a solution of above alcohol in dry DCM ( 17 mL ) was added $\operatorname{TBSCl}(288.7 \mathrm{mg}, 1.92 \mathrm{mmol})$ and imidazole ( 260.1 $\mathrm{mg}, 3.82 \mathrm{mmol}$ ) at room temperature. The reaction mixture was stirred for 1 h , then quenched by water ( 20 mL ) and extracted with diethyl ether $(3 \times 20 \mathrm{~mL})$. The combined organic layer was washed with water ( 20 mL ) and brine ( 20 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 20:1) to give $( \pm)-\mathbf{1 0}(514.2 \mathrm{mg}, 92 \%$ yield over 2 steps $)$ as a colorless oil. $\mathrm{TLC} \mathrm{R}_{f}\left(\right.$ PE/EA 20:1) $=0.17 .{ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 5.92(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 5.50(\mathrm{dt}, J=15.6,5.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.15(\mathrm{dd}, J=5.2,1.6 \mathrm{~Hz}, 2 \mathrm{H}), 3.35(\mathrm{dd}, J=$ 8.6, 2.4 Hz, 1H), $2.39(\mathrm{brs}, 1 \mathrm{H}), 2.19(\mathrm{~s}, 1 \mathrm{H}), 1.78-1.65(\mathrm{~m}, 2 \mathrm{H}), 1.28(\mathrm{~s}, 3 \mathrm{H}), 1.25(\mathrm{~s}, 3 \mathrm{H}), 0.90(\mathrm{~s}, 9 \mathrm{H}), 0.80-0.69(\mathrm{~m}$, $1 \mathrm{H}), 0.69-0.55(\mathrm{~m}, 3 \mathrm{H}), 0.06(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 130.7,128.6,91.9,75.3,69.4,64.0,48.1,30.3$, 29.8, 29.2, 27.8, 26.0, 18.4, 13.3, 10.7, -5.1. HRMS (ESI): calcd for $\mathrm{C}_{19} \mathrm{H}_{34} \mathrm{NaO}_{2} \mathrm{Si}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 345.2220$, found 345.2217.


Preparation of 11. To a solution of $( \pm)-\mathbf{1 0}(214.2 \mathrm{mg}, 0.664 \mathrm{mmol})$ in $\mathrm{DCM}(13 \mathrm{~mL})$ was added $4 \AA \mathrm{MS}(2.25 \mathrm{~g})$ and PDC ( $749.8 \mathrm{mg}, 1.99 \mathrm{mmol}$ ). After stirred for 2 h at room temperature, the reaction mixture was filtered through silica-gel by washing with eluent (PE/EA 40:1), concentrated and purified by column chromatography (PE/EA 30:1) to give the product ( $172.1 \mathrm{mg}, 81 \%$ yield) as a colorless oil. TLC $\mathrm{R}_{f}(\operatorname{PE} / \mathrm{EA} 20: 1)=0.36 .{ }^{1} \mathrm{H}$ NMR $(400 \mathrm{MHz}$,
$\left.\mathrm{CDCl}_{3}\right): \delta 6.28(\mathrm{~d}, J=15.2 \mathrm{~Hz}, 1 \mathrm{H}), 5.58(\mathrm{dt}, J=15.2,4.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.19(\mathrm{dd}, J=4.8,1.6 \mathrm{~Hz}, 2 \mathrm{H}), 2.72(\mathrm{~s}, 2 \mathrm{H}), 2.10$ $(\mathrm{s}, 1 \mathrm{H}), 1.39(\mathrm{dd}, J=6.8,3.6 \mathrm{~Hz}, 2 \mathrm{H}), 1.32(\mathrm{~s}, 6 \mathrm{H}), 0.97(\mathrm{dd}, J=6.8,3.6 \mathrm{~Hz}, 2 \mathrm{H}), 0.92(\mathrm{~s}, 9 \mathrm{H}), 0.08(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (100 MHz, $\mathrm{CDCl}_{3}$ ): $\delta 206.9,131.1,128.4,91.0,67.7,63.3,51.5,33.4,29.3,29.2,25.9,18.9,18.4,-5.2$. HRMS (ESI): calcd for $\mathrm{C}_{19} \mathrm{H}_{36} \mathrm{NO}_{2} \mathrm{Si}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{\dagger}\right) 338.2510$, found 338.2510 .


Preparation of $(+)$-10. To a solution of $\mathbf{1 1}(135.8 \mathrm{mg}, 0.42 \mathrm{mmol})$ in toluene $(10.6 \mathrm{~mL})$ was added ( $S$ )-CBS $(0.42 \mathrm{~mL}$, 1 M in toluene, 0.42 mmol ). The solution was cooled to $-30^{\circ} \mathrm{C}$, and then boron methyl sulfide complex ( $0.85 \mathrm{~mL}, 2 \mathrm{M}$ in THF, 1.70 mmol ) was added. The reaction mixture was stirred for 4 h . It was quenched by 2 mL methanol at $-30^{\circ} \mathrm{C}$ The mixture was warmed to room temperature and then saturated aqueous ammonium chloride solution ( 10 mL ) and water ( 10 mL ) was added. It was extracted with diethyl ether $(3 \times 20 \mathrm{~mL})$. The combined organic layer was washed with water ( 20 mL ) and brine ( 20 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 20:1) to give (+)-10 (119.2 mg, $87 \%$ yield) as a colorless oil. $\mathrm{ee}=96 \%$, (Chiralpak IC, hexanes: $\mathrm{DCM}=199: 1,205 \mathrm{~nm}$; retention times of major stereoisomer, 5.367 min ; minor stereoisomer, 6.205 min ). $\operatorname{TLC~R}_{f}(\operatorname{PE} / \mathrm{EA} 20: 1)=0.17 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 5.92(\mathrm{~d}, J=15.4 \mathrm{~Hz}, 1 \mathrm{H}), 5.50(\mathrm{dt}, J=15.4,5.4 \mathrm{~Hz}, 1 \mathrm{H})$, $4.15(\mathrm{dd}, J=5.4,1.4 \mathrm{~Hz}, 2 \mathrm{H}), 3.35(\mathrm{dd}, J=8.8,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.20(\mathrm{~s}, 1 \mathrm{H}), 1.78-1.65(\mathrm{M}, 2 \mathrm{H}), 1.28(\mathrm{~s}, 3 \mathrm{H}), 1.25(\mathrm{~s}$, $3 \mathrm{H}), 0.90(\mathrm{~s}, 9 \mathrm{H}), 0.78-0.71(\mathrm{~m}, 1 \mathrm{H}), 0.69-0.56(\mathrm{~m}, 3 \mathrm{H}), 0.06(\mathrm{~s}, 6 \mathrm{H}) .[\alpha]_{\mathrm{D}}{ }^{20}:+17.1^{\circ}\left(c 2.59, \mathrm{CHCl}_{3}\right)$.


Preparation of (+)-12. To a solution of (+)-10 $(585.4 \mathrm{mg}, 1.81 \mathrm{mmol})$ in DMF $(18 \mathrm{~mL})$ was added TBAI $(133.9 \mathrm{mg}$, $0.362 \mathrm{mmol})$ and $\mathrm{NaH}(290.7 \mathrm{mg}, 60 \%$ weight in mineral oil, 7.27 mmol$)$ at $0^{\circ} \mathrm{C}$. After stirred for $20 \mathrm{~min}, \mathrm{BnBr}(0.65$
$\mathrm{mL}, 5.42 \mathrm{mmol}$ ) was added. The reaction mixture was stirred for 6 h at ${ }^{\circ} \mathrm{C}$ under an argon atmosphere and another $\mathrm{NaH}(232.4 \mathrm{mg}, 60 \%$ weight in mineral oil, 5.81 mmol ) was added. It was stirred for another 13 h and then quenched by saturated aqueous ammonium chloride solution ( 20 mL ) and water ( 20 mL ), extracted with diethyl ether ( $3 \times 30$ $\mathrm{mL})$. The combined organic layer was washed with water $(3 \times 40 \mathrm{~mL})$ and brine ( 30 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 100:1) to give a mixture $(908.6 \mathrm{mg})$ consisting of desired product and ether $\mathrm{Bn}_{2} \mathrm{O}$. Ratio of the product to $\mathrm{Bn}_{2} \mathrm{O}$ was $1.2: 1$ by ${ }^{1} \mathrm{H}$ NMR analysis and they could not be separated by column chromatography. The calculated mass of desired product was 647.9 mg ( $87 \%$ yield) as a colorless oil. A small portion of the material was purified further by big TLC and separate pure product to characterize it. $\operatorname{TLC~R}_{f}(\operatorname{PE} / E A 20: 1)=0.58 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 7.40-7.26(\mathrm{~m}, 4 \mathrm{H}), 7.26-7.19(\mathrm{~m}, 1 \mathrm{H})$, $5.90(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 5.54(\mathrm{dt}, J=15.6,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 4.80(\mathrm{~d}, J=11.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.36(\mathrm{~d}, J=11.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.11$ (dd, $J=5.4,1.4 \mathrm{~Hz}, 2 \mathrm{H}), 3.09(\mathrm{dd}, J=6.4,4.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.11(\mathrm{~s}, 1 \mathrm{H}), 1.80-1.74(\mathrm{~m}, 2 \mathrm{H}), 1.24(\mathrm{~s}, 3 \mathrm{H}), 1.21(\mathrm{~s}, 3 \mathrm{H})$, $0.95-0.89(\mathrm{~m}, 1 \mathrm{H}), 0.87(\mathrm{~s}, 9 \mathrm{H}), 0.89-0.81(\mathrm{~m}, 1 \mathrm{H}), 0.62(\mathrm{ddd}, J=9.2,6.0,4.4 \mathrm{~Hz}, 1 \mathrm{H}), 0.47(\mathrm{ddd}, J=9.6,6.0,4.6 \mathrm{~Hz}$, $1 \mathrm{H}), 0.03(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta$ 139.3, 131.0, 128.2, 128.0, 127.8, 127.3, 92.2, 83.8, 70.8, 68.0, 64.1, 47.5, 31.0, 30.8, 28.6, 25.8, 24.3, 18.3, 17.1, 9.2, -5.3. HRMS (ESI): calcd for $\mathrm{C}_{26} \mathrm{H}_{40} \mathrm{NaO}_{2} \mathrm{Si}\left(\left[M+\mathrm{Na}^{+}\right)\right.$ 435,2690 , found $435.2686 .[\alpha]_{\mathrm{D}}^{20}:+70.1^{\circ}\left(c 0.03, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1 2}$. With $( \pm)-\mathbf{1 0}(1.9 \mathrm{~g}, 5.89 \mathrm{mmol}), \mathrm{BnBr}(2.1 \mathrm{~mL}, 17.7 \mathrm{mmol})$, TBAI $(435.8 \mathrm{mg}, 1.18 \mathrm{mmol})$, $\mathrm{NaH}(945.4 \mathrm{mg}+755.7 \mathrm{mg}, 42.5 \mathrm{mmol})$ and DMF $(59 \mathrm{~mL})$ as starting materials, $( \pm) \mathbf{- 1 2}$ was prepared by using the same procedure. Reaction time was $6 \mathrm{~h}+13 \mathrm{~h}$. Total mass was 2.79 g consisting of desired product ( $\pm$ )- $\mathbf{1 2}$ and ether $\mathrm{Bn}_{2} \mathrm{O}$. Ratio of the product to $\mathrm{Bn}_{2} \mathrm{O}$ was $2.1: 1$ by ${ }^{1} \mathrm{H}$ NMR analysis and they could not be separated by column chromatography. The calculated mass of desired product was 2.27 g ( $93 \%$ yield) as a colorless oil.


Preparation of (-)-13. A solution in 250 mL round bottomed flask of the compound $( \pm) \mathbf{- 1 2}(908.6 \mathrm{mg}$, ratio of substrate to $\mathrm{Bn}_{2} \mathrm{O}$ was 1.2:1, real mass of substrate $\left.647.9 \mathrm{mg}, 1.57 \mathrm{mmol}\right)$ and $\left[\mathrm{Rh}(\mathrm{CO})_{2} \mathrm{Cl}\right]_{2}(30.7 \mathrm{mg}, 0.079 \mathrm{mmol})$ in anhydrous toluene ( 31 mL ) was bubbled by $\mathrm{CO}(0.2 \mathrm{~atm})$ for 10 min . The reaction mixture was stirred at $100{ }^{\circ} \mathrm{C}$
under balloon pressure gas of $\mathrm{CO}(0.2 \mathrm{~atm})$ for 1 h . The reaction mixture was cooled to room temperature and concentrated in vacuo. Purification of the residue through column chromatography on silica gel (PE/EA 10:1) afforded the product $\mathbf{1 3}$ as a brown oil ( $574.2 \mathrm{mg}, 83 \%$ combined yield). The diastereoselectivity of ( - )-trans- $\mathbf{- 1 3}$ and (-)-cis-13 was determined by the ${ }^{1} \mathrm{H}$ NMR of the final product as 3:1. The two diastereomers were columned again on silica gel (PE/EA 10:1) to separate them carefully ((-)-trans-13, 412.4 mg ; (-)-cis-13, 102.9 mg ).
(-)-trans-13. Brown oil. TLC $\mathrm{R}_{f}(\operatorname{PE} / \mathrm{EA} 10: 1)=0.30 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.37-7.27(\mathrm{~m}, 4 \mathrm{H}), 7.27-7.20$ $(\mathrm{m}, 1 \mathrm{H}), 5.94(\mathrm{~s}, 1 \mathrm{H}), 5.61-5.48(\mathrm{~m}, 2 \mathrm{H}), 4.60(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.38(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.20-4.06(\mathrm{~m}, 2 \mathrm{H}), 3.82$ (d, $J=3.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.55(\mathrm{ddd}, J=13.9,12.9,4.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.38(\mathrm{ddd}, J=17.2,14.2,5.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.20(\mathrm{ddd}, J=17.4$, $4.6,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.95(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.80(\mathrm{dd}, J=14.2,3.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.71(\mathrm{ddd}, J=12.7,5.1,2.1 \mathrm{~Hz}, 1 \mathrm{H}), 1.26$ (s, 3H), $1.19(\mathrm{~s}, 3 \mathrm{H}), 0.87(\mathrm{~s}, 9 \mathrm{H}), 0.03(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta$ 199.7, 180.9, 138.8, 132.5, 129.9, $128.3,127.5,127.4,123.4,86.0,70.8,63.0,56.2,42.4,41.8,33.0,31.3,29.8,27.8,25.7,18.3,-5.5$. HRMS (ESI): calcd for $\mathrm{C}_{27} \mathrm{H}_{40} \mathrm{NaO}_{3} \mathrm{Si}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 463.2639$, found 463.2632. $[\alpha]_{\mathrm{D}}{ }^{20}:-13.4^{\circ}\left(c 1.14, \mathrm{CHCl}_{3}\right)$.
(-)-cis-13. Brown oil. TLC $\mathrm{R}_{f}(\operatorname{PE} / \mathrm{EA} 10: 1)=0.20 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.40-7.29(\mathrm{~m}, 4 \mathrm{H}), 7.29-7.21(\mathrm{~m}$, $1 \mathrm{H}), 5.98(\mathrm{dt}, J=15.6,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.93(\mathrm{~s}, 1 \mathrm{H}), 5.49(\mathrm{dt}, J=16.0,4.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.61(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.55(\mathrm{~d}, J$ $=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.23-4.11(\mathrm{~m}, 2 \mathrm{H}), 3.73(\mathrm{dd}, J=11.2,6.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.36(\mathrm{ddd}, J=18.2,14.0,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.21-2.12$ $(\mathrm{m}, 2 \mathrm{H}), 1.92-1.82(\mathrm{~m}, 2 \mathrm{H}), 1.68(\mathrm{dd}, J=11.6,11.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.21(\mathrm{~s}, 3 \mathrm{H}), 1.10(\mathrm{~s}, 3 \mathrm{H}), 0.86(\mathrm{~s}, 9 \mathrm{H}), 0.03(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 200.4,179.0,138.5,132.9,128.3,127.6,127.3,126.3,123.7,85.2,72.1,63.3,53.2,43.3$, 38.5, 33.7, 32.9, 30.8, 29.6, 25.8, 18.3, -5.2, -5.3. HRMS (ESI): calcd for $\mathrm{C}_{27} \mathrm{H}_{40} \mathrm{NaO}_{3} \mathrm{Si}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 463.2639$, found 463.2644. $[\alpha]_{\mathrm{D}}{ }^{20}:-8.98^{\circ}\left(c 2.28, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1 3}$. With $( \pm)$ - $\mathbf{1 2}\left(1.23 \mathrm{~g}\right.$, ratio of substrate to $\mathrm{Bn}_{2} \mathrm{O}$ was $2.1: 1$, real mass of substrate $1.0 \mathrm{~g}, 2.42$ $\mathrm{mmol}),\left[\mathrm{Rh}(\mathrm{CO})_{2} \mathrm{Cl}\right]_{2}(47.8 \mathrm{mg}, 0.123 \mathrm{mmol})$ and $\mathrm{PhMe}(48 \mathrm{~mL})$ as starting materials, $( \pm)-\mathbf{1 3}(848.9 \mathrm{mg}, 80 \%$ yield $)$ as a brown oil was prepared by using the same procedure. Reaction time was 1 h . The two diastereomers were columned again on silica gel (PE/EA 10:1) to separate them carefully ( $( \pm)$-trans-13, 602.5 mg ; ( $\pm$ )-cis-13, 224.4 mg ).


Preparation of (-)-14. To a solution of diisopropylamine ( $0.92 \mathrm{~mL}, 6.53 \mathrm{mmol}$ ) in anhydrous THF ( 10 mL ) at $-78{ }^{\circ} \mathrm{C}$ under an argon atmosphere was added ${ }^{n} \mathrm{BuLi}(4.1 \mathrm{~mL}, 1.6 \mathrm{M}$ in hexanes, 6.56 mmol$)$ and the solution was stirred at $0^{\circ} \mathrm{C}$ for 30 min . Then the freshly prepared LDA was cooled to $-78^{\circ} \mathrm{C}$ and a solution of (-)-trans $-13(412.4 \mathrm{mg}, 0.936$ $\mathrm{mmol})$ in anhydrous THF ( 13 mL ) was added. After stirred for 1 h , HMPA ( 1.2 mL ) was added and stirred for another 40 min at $-78{ }^{\circ} \mathrm{C}$. Then MeI ( $0.82 \mathrm{~mL}, 13.2 \mathrm{mmol}$ ) was added to the reaction mixture. The mixture was warmed up naturally and stirred for 4 h . The reaction was quenched by saturated aqueous ammonium chloride solution ( 20 mL ) and water ( 20 mL ), extracted with diethyl ether $(3 \times 30 \mathrm{~mL})$. The combined organic layer was washed with water ( 30 mL ) and brine ( 30 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 10:1) to give the product ( $403.2 \mathrm{mg}, 95 \%$ yield) as a yellow oil. The diastereoselectivity of $(-)-\mathbf{1 4 - 1}$ and (-)-14-2 was determined by the crude ${ }^{1} \mathrm{H}$ NMR as 1.3:1. A small portion of the material was purified further and separate diastereomers to characterize them respectively.
$(-)$-14-1. Yellow oil. $\mathrm{TLC}_{f}(\mathrm{PE} / \mathrm{EA} 10: 1)=0.43 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.50-7.28(\mathrm{~m}, 4 \mathrm{H}), 7.28-7.20(\mathrm{~m}$, $1 \mathrm{H}), 5.93(\mathrm{~s}, 1 \mathrm{H}), 5.72-5.40(\mathrm{~m}, 2 \mathrm{H}), 4.60(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.39(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.21-4.02(\mathrm{~m}, 2 \mathrm{H}), 3.80(\mathrm{~d}$, $J=3.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.53-2.37(\mathrm{~m}, 1 \mathrm{H}), 2.30(\mathrm{dd}, J=13.0,13.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.93(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.88-1.68(\mathrm{~m}, 2 \mathrm{H})$, $1.25(\mathrm{~s}, 3 \mathrm{H}), 1.20(\mathrm{~s}, 3 \mathrm{H}), 1.06(\mathrm{~d}, J=6.4 \mathrm{~Hz}, 3 \mathrm{H}), 0.88(\mathrm{~s}, 9 \mathrm{H}), 0.03(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 201.9$, $180.0,138.7,132.3,130.4,128.4,127.47,127.42,123.1,86.1,70.8,63.0,56.7,42.3,41.7,36.8,36.3,31.5,29.7,25.7$, 18.3, 15.4, -5.5. HRMS (ESI): calcd for $\mathrm{C}_{28} \mathrm{H}_{43} \mathrm{O}_{3} \mathrm{Si}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 455.2976$, found 455.2975. $[\alpha]_{\mathrm{D}}{ }^{20}:-6.87^{\circ}(c 1.35$, $\mathrm{CHCl}_{3}$ ).
(-)-14-2. Yellow oil. TLC $\mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 10: 1)=0.36 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.39-7.27(\mathrm{~m}, 4 \mathrm{H}), 7.27-7.21(\mathrm{~m}$, $1 \mathrm{H}), 5.98(\mathrm{~s}, 1 \mathrm{H}), 5.71(\mathrm{dt}, J=15.6,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 5.43(\mathrm{dt}, J=15.6,4.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.59(\mathrm{~d}, J=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.37(\mathrm{~d}, J$ $=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.15-4.02(\mathrm{~m}, 2 \mathrm{H}), 3.76(\mathrm{~d}, J=3.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.75(\mathrm{dd}, J=13.6,8.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.43(\mathrm{qd}, J=7.8,7.6 \mathrm{~Hz}$, $1 \mathrm{H}), 1.90(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.81(\mathrm{dd}, J=14.0,4.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.71(\mathrm{dd}, J=13.6,0.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.27(\mathrm{~s}, 3 \mathrm{H}), 1.23(\mathrm{~s}$, $3 \mathrm{H}), 1.16(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 3 \mathrm{H}), 0.86(\mathrm{~s}, 9 \mathrm{H}), 0.02(\mathrm{~s}, 6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta$ 202.7, 180.4, 138.7, 135.1,
$131.7,128.3,127.5,127.4,122.8,86.1,70.9,63.1,55.2,41.92,41.88,38.1,33.9,31.5,29.5,25.7,20.2,18.3,-5.6$. HRMS (ESI): calcd for $\mathrm{C}_{28} \mathrm{H}_{43} \mathrm{O}_{3} \mathrm{Si}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$455.2976, found 455.2975. $[\alpha]_{\mathrm{D}}{ }^{20}:-33.9^{\circ}\left(c\right.$ 1.28, $\left.\mathrm{CHCl}_{3}\right)$.

Preparation of ( $\mathbf{\pm}$ )-14. With $( \pm)$-trans- $\mathbf{1 3}(602.5 \mathrm{mg}, 1.37 \mathrm{mmol})$, diisopropylamine $(1.35 \mathrm{~mL}, 9.57 \mathrm{mmol}),{ }^{n} \mathrm{BuLi}$ ( $6.0 \mathrm{~mL}, 1.6 \mathrm{M}$ in hexanes, 9.57 mmol ), HMPA ( 1.8 mL ), MeI ( $1.2 \mathrm{~mL}, 19.1 \mathrm{mmol}$ ) and THF (total 34 mL ) as starting materials, $( \pm) \mathbf{- 1 4}(553.6 \mathrm{mg}, 89 \%$ yield) as a yellow oil was prepared by using the same procedure. Reaction time was $30 \mathrm{~min}, 40 \mathrm{~min}$ and 4 h .


Preparation of 15. To a solution of diastereomers (-)-14-1 and (-)-14-2 (107.5 mg, 0.236 mmol ) in anhydrous toluene ( 2.4 mL ) was added $\mathrm{Pd}(\mathrm{OH})_{2} / \mathrm{C}(164.2 \mathrm{mg}, 20 \%$ on dry basis, 0.234 mmol$)$ and bubbled by $\mathrm{H}_{2}(1.0 \mathrm{~atm})$ for 20 min . Then $\mathrm{MeOH}(2.4 \mathrm{~mL})$ was added and the reaction mixture was bubbled by $\mathrm{H}_{2}(1.0 \mathrm{~atm})$ for another 10 min . The reaction mixture was stirred at $50^{\circ} \mathrm{C}$ under balloon pressure gas of $\mathrm{H}_{2}(1.0 \mathrm{~atm})$ for 4 d . The mixture was filtered through celite by washing with EA and followed by removal of solvent. The crude product was dissolved in THF (4.7 $\mathrm{mL})$, and then $\mathrm{HCl}(4.7 \mathrm{~mL}, 1 \mathrm{M})$ was added. The reaction mixture was stirred for 6 h at room temperature and quenched by saturated aqueous sodium bicarbonate solution ( 2 mL ) and water ( 10 mL ), extracted with diethyl ether (3 $\times 20 \mathrm{~mL})$. The combined organic layer was washed with water $(20 \mathrm{~mL})$ and brine $(20 \mathrm{~mL})$, dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 2:1) to give $\mathbf{1 5}$ ( $68.5 \mathrm{mg}, 84 \%$ yield) as a colorless oil. A small portion of the material was purified further and separated a pure diastereomer to characterize it.
(-)-15 (one single diastereomer spererated from its diastereomers). Colorless oil. $\mathrm{TLC} \mathrm{R}_{f}(\operatorname{PE} / \mathrm{EA} 2: 1)=0.22 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 7.36-7.27(\mathrm{~m}, 4 \mathrm{H}), 7.27-7.21(\mathrm{~m}, 1 \mathrm{H}), 4.57(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.38(\mathrm{~d}, J=11.8 \mathrm{~Hz}$, $1 \mathrm{H}), 3.81(\mathrm{dd}, J=6.2,6.2 \mathrm{~Hz}, 1 \mathrm{H}), 3.56(\mathrm{t}, J=6.4 \mathrm{~Hz}, 2 \mathrm{H}), 2.67-2.53(\mathrm{~m}, 1 \mathrm{H}), 2.37-2.31(\mathrm{~m}, 2 \mathrm{H}), 2.22(\mathrm{dd}, J=14.0$, $5.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.85-1.74(\mathrm{~m}, 2 \mathrm{H}), 1.66-1.52(\mathrm{~m}, 3 \mathrm{H}), 1.51-1.45(\mathrm{~m}, 2 \mathrm{H}), 1.44(\mathrm{brs}, 1 \mathrm{H}), 1.36(\mathrm{dd}, J=14.0,12.0 \mathrm{~Hz}, 1 \mathrm{H})$, $1.02(\mathrm{~s}, 3 \mathrm{H}), 1.01(\mathrm{~d}, J=6.8 \mathrm{~Hz}, 3 \mathrm{H}), 0.91(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 217.4,139.3,128.3,127.33$,
127.26, 87.2, 71.6, 63.3, 54.2, 47.4, 45.2, 41.8, 41.1, 40.3, 39.5, 35.5, 32.2, 28.3, 24.9, 16.6. HRMS (ESI): calcd for $\mathrm{C}_{22} \mathrm{H}_{36} \mathrm{NO}_{3}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right) 362.2690$, found 362.2683. $[\alpha]_{\mathrm{D}}{ }^{20}:-53.6^{\circ}\left(c 1.14, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1 5}$. With $( \pm) \mathbf{- 1 4}(313.2 \mathrm{mg}, 0.689 \mathrm{mmol}), \mathrm{Pd}(\mathrm{OH})_{2} / \mathrm{C}(482.2 \mathrm{mg}, 20 \%$ on dry basis, 0.689 mmol$)$ and $\mathrm{PhMe}(6.9 \mathrm{~mL}), \mathrm{MeOH}(6.9 \mathrm{~mL}), \mathrm{HCl}(13.8 \mathrm{~mL}, 1 \mathrm{M})$ and THF $(13.8 \mathrm{~mL})$ as starting materials, $( \pm)-\mathbf{1 5}(202.0 \mathrm{mg}$, $85 \%$ yield) as a colorless oil was prepared by using the same procedure. Reaction time was 4 d and 6 h .


Preparation of (-)-16. To a solution of $\mathbf{1 5}(136.5 \mathrm{mg}, 0.396 \mathrm{mmol})$ from the asymmetric route (Scheme 1) in DCM $(8.0 \mathrm{~mL})$ was added silica-gel ( 769.0 mg ) and PCC ( $256.5 \mathrm{mg}, 1.19 \mathrm{mmol}$ ). After stirred for 5 h at room temperature, the reaction mixture was filtered through silica-gel by washing with eluent (PE/EA 5:1) and followed by removal of solvent. The crude product was dissolved in $\mathrm{MeOH}(8.0 \mathrm{~mL})$, and then $\mathrm{KOH}(137.6 \mathrm{mg}, 2.45 \mathrm{mmol})$ was added. The reaction mixture was stirred for 6 h at $30^{\circ} \mathrm{C}$, and then concentrated in vacuo. Purification of the residue through column chromatography on silica gel (PE/EA 5:1) afforded the product (-)-16-1 and (-)-16-2 (83.5 mg, 62\% combined yield) and ( - )-16-3 (12.2 mg, $9 \%$ yield). The two diastereomers were columned again on silica gel (PE/EA 20:1) to separate them ((-)-16-1 $(58.6 \mathrm{mg})$ and $(-)-\mathbf{1 6 - 2}(17.1 \mathrm{mg}))$.
(-)-16-1. White solid. $\mathrm{Mp}=67-69^{\circ} \mathrm{C} . \operatorname{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 3: 1)=0.41 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.43-7.28(\mathrm{~m}, 4 \mathrm{H})$, 7.28-7.21(m, 1H), $4.55(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.39(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.71(\mathrm{dd}, J=6.4,6.4 \mathrm{~Hz}, 1 \mathrm{H}), 3.23(\mathrm{dd}, J=$ $12.0,4.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.06(\mathrm{brs}, 1 \mathrm{H}), 2.41(\mathrm{dd}, J=13.4,13.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.16(\mathrm{dd}, J=13.6,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.10(\mathrm{dd}, J=14.4$, $3.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.91-1.81(\mathrm{~m}, 1 \mathrm{H}), 1.80-1.72(\mathrm{~m}, 2 \mathrm{H}), 1.69(\mathrm{dd}, J=13.2,4.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.59(\mathrm{dd}, J=13.0,5.8 \mathrm{~Hz}, 1 \mathrm{H})$, $1.46-1.39(\mathrm{~m}, 1 \mathrm{H}), 1.37(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.14(\mathrm{~s}, 3 \mathrm{H}), 1.12-1.04(\mathrm{~m}, 1 \mathrm{H}), 1.01(\mathrm{~s}, 3 \mathrm{H}), 1.00(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (100 MHz, $\mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 223.4,139.3,128.3,127.4,87.2,77.5,72.0,49.6,48.0,45.9,43.2,40.9,39.4,39.0,37.8,31.6$, 31.2, 24.9, 21.7. HRMS (ESI): calcd for $\mathrm{C}_{22} \mathrm{H}_{30} \mathrm{KO}_{3}\left([\mathrm{M}+\mathrm{K}]^{+}\right) 381.1827$, found 381.1824. $[\alpha]_{\mathrm{D}}{ }^{20}:-122.7^{\circ}(c 3.0$, $\mathrm{CHCl}_{3}$ ).
$(-)-\mathbf{1 6 - 2}$. Colorless oil. $\mathrm{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 3: 1)=0.29 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.44-7.29(\mathrm{~m}, 4 \mathrm{H}), 7.29-7.20(\mathrm{~m}$, $1 \mathrm{H}), 4.55(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.42(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.75-3.63(\mathrm{~m}, 2 \mathrm{H}), 2.45(\mathrm{dd}, J=13.4,13.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.17$ (dd, $J=14.0,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.91(\mathrm{ddd}, J=13.4,13.4,4.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.85-1.73(\mathrm{~m}, 3 \mathrm{H}), 1.73-1.67(\mathrm{~m}, 2 \mathrm{H}), 1.67-1.61(\mathrm{~m}$, $1 \mathrm{H}), 1.58(\mathrm{dd}, J=13.2,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.48-1.35(\mathrm{~m}, 1 \mathrm{H}), 1.26-1.15(\mathrm{~m}, 1 \mathrm{H}), 1.00(\mathrm{~s}, 9 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 100 MHz , $\mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 218.8,139.4,128.3,127.44,127.35,87.9,72.0,71.7,49.2,49.0,46.2,43.3,40.7,39.7,34.3,31.3,31.0$, 28.8, 24.8, 21.7. HRMS (ESI): calcd for $\mathrm{C}_{22} \mathrm{H}_{34} \mathrm{NO}_{3}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right) 360.2533$, found 360.2532 . $[\alpha]_{\mathrm{D}}{ }^{20}:-125.6^{\circ}(c 1.43$, $\mathrm{CHCl}_{3}$ ).
$(-)-16-3$. Colorless oil. $\mathrm{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 3: 1)=0.12 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.40-7.28(\mathrm{~m}, 4 \mathrm{H}), 7.28-7.22(\mathrm{~m}$, $1 \mathrm{H}), 4.50(\mathrm{~d}, J=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.46(\mathrm{~d}, J=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.94(\mathrm{ddd}, J=11.2,5.8,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.56(\mathrm{dd}, J=9.2,8.4$ $\mathrm{Hz}, 1 \mathrm{H}), 2.75(\mathrm{dd}, J=5.4,1.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.49-2.33(\mathrm{~m}, 1 \mathrm{H}), 2.18(\mathrm{dd}, J=13.4,6.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.13-1.96(\mathrm{~m}, 4 \mathrm{H}), 1.82-$ $1.75(\mathrm{~m}, 1 \mathrm{H}), 1.75-1.64(\mathrm{~m}, 2 \mathrm{H}), 1.54-1.43(\mathrm{~m}, 2 \mathrm{H}), 1.10(\mathrm{~d}, J=6.4 \mathrm{~Hz}, 3 \mathrm{H}), 0.97(\mathrm{~s}, 3 \mathrm{H}), 0.80(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (100 MHz, $\mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 214.3,139.2,128.3,127.5,127.4,86.7,72.4,71.9,57.3,54.7,45.7,43.8,43.0,38.0,35.7,35.6$, 33.0, 30.2, 28.5, 16.7. HRMS (EI): calcd for $\mathrm{C}_{22} \mathrm{H}_{30} \mathrm{O}_{3}\left(\mathrm{M}^{+}\right) 342.2190$, found 342.2187. $[\alpha]_{\mathrm{D}}{ }^{20}:-79.3^{\circ}\left(c 1.02, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1 6}$. With $( \pm)-\mathbf{1 5}(227.6 \mathrm{mg}, 0.661 \mathrm{mmol})$, silica-gel $(1.28 \mathrm{~g})$, PCC $(427.8 \mathrm{mg}, 1.98 \mathrm{mmol})$, DCM $(13.2 \mathrm{~mL}), \mathrm{KOH}(222.0 \mathrm{mg}, 3.96 \mathrm{mmol})$ and $\mathrm{MeOH}(13.2 \mathrm{~mL})$ as starting materials, $( \pm)-\mathbf{1 6 - 1}$ and $( \pm) \mathbf{- 1 6 - 2}(152.9 \mathrm{mg}$, $68 \%$ yield) and ( $\pm$ )-16-3 ( $21.5 \mathrm{mg}, 10 \%$ yield) as a colorless oil were prepared by using the same procedure. Reaction time was 5 h and 6 h . The two diastereomers were columned again on silica gel (PE/EA 20:1) to separate them ( $\pm$ )-16-1 $(122.3 \mathrm{mg})$ and $( \pm)-\mathbf{1 6 - 2}(29.9 \mathrm{mg}))$. The relative configurations of these two compounds were assigned based on the X-ray structure of $( \pm)-\mathbf{2 0}$, the derivative of $( \pm) \mathbf{- 1 6 - 2}$, which is given below.


Preparation of $( \pm)$-20. To a solution of the compound $( \pm) \mathbf{- 1 6 - 2}(31.8 \mathrm{mg}, 0.0928 \mathrm{mmol})$ in $\mathrm{DCM}(3.1 \mathrm{~mL})$ was added DMAP $(4.7 \mathrm{mg}, 0.0385 \mathrm{mmol})$ and $\mathrm{Et}_{3} \mathrm{~N}(41.0 \mathrm{mg}, 0.405 \mathrm{mmol})$ at room temperature under an argon atmosphere. Then 4-bromobenzoyl chloride ( $63.6 \mathrm{mg}, 0.29 \mathrm{mmol}$ ) was added. The reaction mixture was stirred for 36 h and then diethyl ether ( 10 mL ) was added. It was concentrated and purified by column chromatography (PE/EA 40:1, then 20:1)
to give ( $\pm$ )-20 ( $38.2 \mathrm{mg}, \mathbf{7 8 \%}$ yield) as a white solid. The relative configuration was determined by X-ray analysis. Mp $=105-107{ }^{\circ} \mathrm{C} . \mathrm{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 3: 1)=0.72 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 7.91(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.59(\mathrm{~d}, J=8.4$ $\mathrm{Hz}, 2 \mathrm{H}), 7.41-7.28(\mathrm{~m}, 5 \mathrm{H}), 5.23(\mathrm{~s}, 1 \mathrm{H}), 4.67(\mathrm{~d}, J=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.49(\mathrm{~d}, J=12.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.75(\mathrm{dd}, J=6.0,6.0$ $\mathrm{Hz}, 1 \mathrm{H}), 2.54(\mathrm{dd}, J=13.6,13.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.30(\mathrm{dd}, J=13.8,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.05(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.00-1.87(\mathrm{~m}$, $3 \mathrm{H}), 1.85(\mathrm{dd}, J=12.8,7.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.76(\mathrm{dd}, J=12.8,5.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.64(\mathrm{dd}, J=13.0,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.59-1.47(\mathrm{~m}$, $1 \mathrm{H}), 1.33-1.23(\mathrm{~m}, 1 \mathrm{H}), 1.06(\mathrm{~s}, 6 \mathrm{H}), 1.05(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 217.3,164.9,139.0,131.8,131.0$, $129.4,128.3,128.1,127.5,127.1,87.4,74.7,71.9,49.2,48.1,45.9,43.1,40.5,39.6,34.7,32.4,31.6,26.0,25.0,21.8$. HRMS (ESI): calcd for $\mathrm{C}_{29} \mathrm{H}_{34} \mathrm{BrO}_{4}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$525.1635, found 525.1636.


Preparation of $(+) \mathbf{- 1 7}$. To a solution of $(-) \mathbf{- 1 6 - 1}(58.6 \mathrm{mg}, 0.171 \mathrm{mmol})$ in $\mathrm{MeOH}(3.4 \mathrm{~mL})$ was added $\mathrm{TsNHNH}_{2}$ $(95.9 \mathrm{mg}, 0.515 \mathrm{mmol})$ and a drop of concentrated HCl . The reaction mixture was refluxed at $67^{\circ} \mathrm{C}$ for 24 h and then concentrated. Purification of the residue through column chromatography on silica gel (PE/EA 3:1) afforded the product $(+)-17(54.2 \mathrm{mg}, 62 \%$ yield $)$ as a white solid. $\mathrm{Mp}=77-79^{\circ} \mathrm{C}$. $\mathrm{TLC}_{f}\left(\right.$ PE/EA 2:1) $=0.43 .{ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.77(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}), 7.33(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}), 7.31-7.18(\mathrm{~m}, 5 \mathrm{H}), 4.50(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.36$ $(\mathrm{d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.64(\mathrm{dd}, J=7.4,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.17(\mathrm{dd}, J=11.8,4.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.54(\mathrm{dd}, J=14.2,5.8 \mathrm{~Hz}, 1 \mathrm{H})$, $2.41(\mathrm{~s}, 3 \mathrm{H}), 1.88-1.54(\mathrm{~m}, 6 \mathrm{H}), 1.40-1.28(\mathrm{~m}, 2 \mathrm{H}), 1.23(\mathrm{~d}, J=14.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.05(\mathrm{~s}, 3 \mathrm{H}), 0.99(\mathrm{~s}, 3 \mathrm{H}), 0.98(\mathrm{~s}, 3 \mathrm{H})$, 1.03-0.90 (m, 1H). ${ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 170.3,144.6,139.2,135.1,129.8,128.3,128.1,127.40,127.39$ 87.0, 77.6, 72.0, 49.2, 45.4, 43.1, 42.5, 39.2, 38.9, 37.4, 31.2, 31.0, 25.5, 25.2, 24.8, 21.4. HRMS (ESI): calcd for $\mathrm{C}_{29} \mathrm{H}_{38} \mathrm{~N}_{2} \mathrm{NaO}_{4} \mathrm{~S}\left([\mathrm{M}+\mathrm{Na}]^{+}\right) 533.2444$, found 533.2439. $[\alpha]_{\mathrm{D}}^{20}:+10.3^{\circ}\left(c 1.63, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1 7}$. With $( \pm)$ - $\mathbf{1 6 - 1}(83.9 \mathrm{mg}, 0.245 \mathrm{mmol}), \mathrm{TsNHNH}_{2}(137.3 \mathrm{mg}, 0.737 \mathrm{mmol}), \mathrm{HCl}(2$ drop) and $\mathrm{MeOH}(4.9 \mathrm{~mL})$ as starting materials, $( \pm) \mathbf{- 1 7}(90.4 \mathrm{mg}, 72 \%$ yield) as a white solid was prepared by using the same procedure. Reaction time was 12 h .


Preparation of (-)-18. To a solution of (+)-17 (54.2 $\mathrm{mg}, 0.106 \mathrm{mmol})$ in anhydrous THF $(4.2 \mathrm{~mL})$ at $70{ }^{\circ} \mathrm{C}$ under an argon atmosphere was added ${ }^{n} \mathrm{BuLi}(0.39 \mathrm{~mL}, 1.6 \mathrm{M}$ in hexanes, 0.62 mmol$)$ dropwise. The reaction mixture was stirred at $70{ }^{\circ} \mathrm{C}$ for 10 min and then quenched by saturated aqueous ammonium chloride solution ( 5 mL ) and water ( 5 $\mathrm{mL})$ at room temperature. It was extracted with diethyl ether $(3 \times 15 \mathrm{~mL})$. The combined organic layer was washed with water ( 10 mL ) and brine ( 10 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 10:1) to give (-) $\mathbf{- 1 8}(18.0 \mathrm{mg}, 52 \%$ yield $)$ as a colorless oil. TLC $\mathrm{R}_{f}($ PE/EA 3:1 $)=$ 0.47. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 7.35-7.28(\mathrm{~m}, 4 \mathrm{H}), 7.28-7.21(\mathrm{~m}, 1 \mathrm{H}), 5.86(\mathrm{dd}, J=9.8,4.0 \mathrm{~Hz}, 1 \mathrm{H}), 5.49(\mathrm{~d}, J$ $=9.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.52(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 4.37(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.50(\mathrm{dd}, J=8.8,6.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.25(\mathrm{dd}, J=10.6$, $4.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.81(\mathrm{dd}, J=12.8,6.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.77-1.65(\mathrm{~m}, 3 \mathrm{H}), 1.64(\mathrm{dd}, J=12.6,9.0 \mathrm{~Hz}, 1 \mathrm{H}), 1.44-1.34(\mathrm{~m}, 2 \mathrm{H})$, $1.33-1.23(\mathrm{~m}, 3 \mathrm{H}), 1.09(\mathrm{~s}, 3 \mathrm{H}), 1.05(\mathrm{~s}, 3 \mathrm{H}), 0.92(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 139.5,131.8,130.9,128.2$, $127.4,127.3,84.8,77.3,72.0,54.5,45.9,44.8,37.9,37.8,37.2,36.0,32.7,30.3,27.5,25.4$. HRMS (ESI): calcd for $\mathrm{C}_{22} \mathrm{H}_{34} \mathrm{NO}_{2}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right) 344.2584$, found 344.2583. $[\alpha]_{\mathrm{D}}{ }^{20}:-93.5^{\circ}\left(c 1.50, \mathrm{CHCl}_{3}\right)$.

Preparation of ( $\mathbf{\pm}) \mathbf{- 1 8}$. With $( \pm) \mathbf{- 1 7}(42.8 \mathrm{mg}, 0.084 \mathrm{mmol}),{ }^{n} \mathrm{BuLi}(0.3 \mathrm{~mL}, 1.6 \mathrm{M}$ in hexanes, 0.48 mmol$)$ and THF $(3.3 \mathrm{~mL})$ as starting materials, $( \pm)-\mathbf{1 8}(19.5 \mathrm{mg}, 71 \%$ yield) as a colorless oil was prepared by using the same procedure. Reaction time was 10 min .


Preparation of (-)-19. To a solution of (-)-18(15.3 mg, 0.0469 mmol$)$ in $\mathrm{MeOH}(3.1 \mathrm{~mL})$ was added $\mathrm{Pd} / \mathrm{C}(49.9 \mathrm{mg}$, $10 \%$ on dry basis, 0.0469 mmol$)$ and bubbled by $\mathrm{H}_{2}(1.0 \mathrm{~atm})$ for 10 min . The reaction mixture was stirred at $60^{\circ} \mathrm{C}$ under balloon pressure gas of $\mathrm{H}_{2}(1.0 \mathrm{~atm})$ for 24 h . The mixture was filtered through celite by washing with EA and followed by removal of eluent. The crude product mixture was dissolved in $\mathrm{MeOH}(3.1 \mathrm{~mL})$, and $\mathrm{Pd} / \mathrm{C}(99.9 \mathrm{mg}, 10 \%$
on dry basis, 0.0939 mmol ) was added. The reaction mixture was stirred for 3 d at $60^{\circ} \mathrm{C}$ and then filtered through celite by washing with EA, concentrated and purified by column chromatography (PE/EA 2:1) to give the product (8.7 $\mathrm{mg}, 79 \%$ yield $)$ as a white solid. $\mathrm{Mp}=145-146{ }^{\circ} \mathrm{C} . \operatorname{TLC} \mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 2: 1)=0.26 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 3.87$ $(\mathrm{dd}, J=9.8,6.2 \mathrm{~Hz}, 1 \mathrm{H}), 3.26(\mathrm{dd}, J=10.6,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 1.82-1.75(\mathrm{~m}, 1 \mathrm{H}), 1.71(\mathrm{dd}, J=12.2,6.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.67-$ $1.48(\mathrm{~m}, 5 \mathrm{H}), 1.46-1.37(\mathrm{~m}, 2 \mathrm{H}), 1.36-1.23(\mathrm{~m}, 4 \mathrm{H}), 1.22-1.14(\mathrm{~m}, 1 \mathrm{H}), 1.02(\mathrm{~s}, 3 \mathrm{H}), 0.98(\mathrm{~s}, 6 \mathrm{H}), 0.82(\mathrm{~d}, J=12.8 \mathrm{~Hz}$, 1H). ${ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 79.7,77.9,51.2,46.8,44.6,37.8,37.7,35.1,34.0,32.2,29.5,29.2,27.3,25.7$, 21.9. HRMS (ESI): calcd for $\mathrm{C}_{15} \mathrm{H}_{30} \mathrm{NO}_{2}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right)$256.2277, found 256.2271. $[\alpha]_{\mathrm{D}}{ }^{20}:-18.5^{\circ}(c 0.73, \mathrm{MeOH})$.

Preparation of $( \pm) \mathbf{- 1 9}$. With $( \pm)-\mathbf{1 8}(7.8 \mathrm{mg}, 0.024 \mathrm{mmol}), \mathrm{Pd} / \mathrm{C}(25.1+50.8 \mathrm{mg}, 10 \%$ on dry basis, 0.0713 mmol$)$ and $\mathrm{MeOH}(1.6+2.0 \mathrm{~mL})$ as starting materials, $( \pm) \mathbf{- 1 9}(5.2 \mathrm{mg}, 91 \%$ yield $)$ as a white solid was prepared by using the same procedure. Reaction time was $20 \mathrm{~h}+3 \mathrm{~d}$.


Preparation of (-)-1. To a solution of (-)-19 ( $8.7 \mathrm{mg}, 0.037 \mathrm{mmol})$ in $\mathrm{DCM}(1.8 \mathrm{~mL})$ was added silica-gel $(141.7 \mathrm{mg})$ and PCC ( $47.5 \mathrm{mg}, 0.22 \mathrm{mmol}$ ). After stirred for 3 h at room temperature, the reaction mixture was filtered through silica-gel by washing with eluent (PE/EA 5:1), concentrated and purified by column chromatography (PE/EA 5:1) to give the product ( $7.5 \mathrm{mg}, 88 \%$ yield) as a light yellow oil. $\mathrm{TLC}_{f}(\mathrm{PE} / \mathrm{EA} 5: 1)=0.27 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta$ 2.56-2.46 (m, 2H), $2.39(\mathrm{~d}, J=17.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.22(\mathrm{~d}, J=17.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.21-2.11(\mathrm{~m}, 1 \mathrm{H}), 1.96(\mathrm{dd}, J=6.8,6.8 \mathrm{~Hz}$, $1 \mathrm{H}), 1.80-1.70(\mathrm{~m}, 2 \mathrm{H}), 1.68-1.57(\mathrm{~m}, 4 \mathrm{H}), 1.47(\mathrm{ddd}, J=14.3,7.3,7.3 \mathrm{~Hz}, 1 \mathrm{H}), 1.15(\mathrm{~s}, 3 \mathrm{H}), 1.09(\mathrm{~s}, 3 \mathrm{H}), 1.04(\mathrm{~s}$, $3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 220.6,214.4,52.3,49.8,48.8,43.9,39.0,37.0,36.2,35.1,34.4,30.6,24.8,24.7$, 20.0. HRMS (EI): calcd for $\mathrm{C}_{15} \mathrm{H}_{22} \mathrm{O}_{2}\left([\mathrm{M}]^{+}\right)$234.1614, found 234.1612. $[\alpha]_{\mathrm{D}}{ }^{20}:-100.5^{\circ}\left(c 0.63, \mathrm{CHCl}_{3}\right)$.

Preparation of $( \pm) \mathbf{- 1}$. With $( \pm)-\mathbf{1 9}(4.3 \mathrm{mg}, 0.018 \mathrm{mmol})$, silica-gel $(70.1 \mathrm{mg})$, PCC $(23.3 \mathrm{mg}, 0.108 \mathrm{mmol})$ and DCM $(1 \mathrm{~mL})$ as starting materials, $( \pm) \mathbf{- 1}(3.6 \mathrm{mg}, 85 \%$ yield $)$ as a light yellow oil was prepared by using the same procedure. Reaction time was 3 h .

( $\pm$ )-9
$( \pm)-21$

Preparation of $( \pm)$-21. To a solution of $( \pm)-\mathbf{9}(451.8 \mathrm{mg}, 1.81 \mathrm{mmol})$ in DCM $(20 \mathrm{~mL})$ was added 2,6 -lutidine $(0.42$ $\mathrm{mL}, 3.61 \mathrm{mmol}$ ) at $0{ }^{\circ} \mathrm{C}$ under an argon atmosphere. After 5 min , TBSOTf ( $0.66 \mathrm{~mL}, 2.89 \mathrm{mmol}$ ) was added. The reaction mixture was stirred for 1 h at $0^{\circ} \mathrm{C}$, then quenched with water $(20 \mathrm{~mL})$, extracted with diethyl ether $(3 \times 20$ $\mathrm{mL})$. The combined organic layer was washed with water ( 30 mL ) and brine ( 30 mL ), dried over anhydrous sodium sulphate, filtered, concentrated and purified by column chromatography (PE/EA 20:1) to give the product ( 642.1 mg , $98 \%$ yield $)$ as a white solid. $\mathrm{Mp}=66-68{ }^{\circ} \mathrm{C} . \operatorname{TLC} \mathrm{R}_{f}($ PE/EA 5:1 $)=0.81 .{ }^{1} \mathrm{H} \mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 7.01(\mathrm{~d}, J=$ $16.0 \mathrm{~Hz}, 1 \mathrm{H}), 5.84(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.25-4.06(\mathrm{~m}, 2 \mathrm{H}), 3.33(\mathrm{dd}, J=5.6,4.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.08(\mathrm{~s}, 1 \mathrm{H}), 1.88-1.74(\mathrm{~m}$, $2 \mathrm{H}), 1.27(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}), 1.24(\mathrm{~s}, 3 \mathrm{H}), 1.21(\mathrm{~s}, 3 \mathrm{H}), 1.06-0.98(\mathrm{~m}, 1 \mathrm{H}), 0.93-0.84(\mathrm{~m}, 3 \mathrm{H}), 0.88(\mathrm{~s}, 9 \mathrm{H}), 0.08(\mathrm{~s}$, $3 \mathrm{H}), 0.06(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta 166.8,151.4,118.1,91.8,77.3,68.6,60.0,49.9,30.93,30.86,29.1$, 29.0, 25.9, 20.7, 18.2, 14.8, 14.2, -3.3, -5.0. HRMS (ESI): calcd for $\mathrm{C}_{21} \mathrm{H}_{40} \mathrm{NO}_{3} \mathrm{Si}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right) 382.2772$, found 382.2769 .


Preparation of 22 and 23. A solution of the compound $( \pm)-21(45.3 \mathrm{mg}, 0.124 \mathrm{mmol})$ and $\left[\mathrm{Rh}(\mathrm{CO})_{2} \mathrm{Cl}\right]_{2}(4.7 \mathrm{mg}$, $0.0121 \mathrm{mmol})$ in anhydrous toluene ( 2.5 mL ) was bubbled by $\mathrm{CO}(0.2 \mathrm{~atm})$ for 5 min . The reaction mixture was stirred at $100{ }^{\circ} \mathrm{C}$ under balloon pressure gas of $\mathrm{CO}(0.2 \mathrm{~atm})$ for 3 h . The reaction mixture was cooled to room temperature and concentrated in vacuo. Purification of the residue through column chromatography on silica gel (PE/EA 100:1, then PE/EA 5:1) afforded the inseparable diastereomers 22 ( $32.0 \mathrm{mg}, 71 \%$ yield) as a yellow oil and inseparable diastereomers $\mathbf{2 3}$ ( $8.3 \mathrm{mg}, \mathbf{1 7 \%}$ yield) as a yellow oil.
22. Yellow oil. TLC $\mathrm{R}_{f}(\mathrm{PE} / \mathrm{EA} 5: 1)=0.84 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 7.39(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.00(\mathrm{~d}, J=$ $15.6 \mathrm{~Hz}, 1.2 \mathrm{H}), 5.86(\mathrm{~d}, J=11.6 \mathrm{~Hz}, 2.2 \mathrm{H}), 5.82(\mathrm{~d}, J=11.2 \mathrm{~Hz}, 2.2 \mathrm{H}), 5.49-5.43(\mathrm{~m}, 2.3 \mathrm{H}), 4.17(\mathrm{q}, J=7.2 \mathrm{~Hz}$, $4.6 \mathrm{H}), 3.97(\mathrm{~d}, J=4.0 \mathrm{~Hz}, 1.2 \mathrm{H}), 3.93(\mathrm{dd}, J=10.4,6.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.63-2.52(\mathrm{~m}, 2.3 \mathrm{H}), 2.47-2.36(\mathrm{~m}, 2.2 \mathrm{H}), 2.36-2.27$ $(\mathrm{m}, 1 \mathrm{H}), 2.05(\mathrm{dd}, J=13.6,4.4 \mathrm{~Hz}, 1.3 \mathrm{H}), 1.92-1.70(\mathrm{~m}, 5.7 \mathrm{H}), 1.48(\mathrm{dd}, J=11.8,5.8 \mathrm{~Hz}, 1.2 \mathrm{H}), 1.29(\mathrm{t}, J=7.2 \mathrm{~Hz}$, $7.3 \mathrm{H}), 1.18(\mathrm{~s}, 3.6 \mathrm{H}), 1.13(\mathrm{~s}, 3 \mathrm{H}), 1.09(\mathrm{~s}, 3 \mathrm{H}), 1.08(\mathrm{~s}, 3.7 \mathrm{H}), 0.89(\mathrm{~s}, 9 \mathrm{H}), 0.88(\mathrm{~s}, 11 \mathrm{H}), 0.08-0.02(\mathrm{~m}, 14.4 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (100 MHz, $\mathrm{CDCl}_{3}$ ): $\delta 167.13,167.07,161.1,159.8,151.9,149.2,121.5,120.5,119.9,119.1,78.6,74.7,68.1$, $65.6,60.3,60.1,53.6,53.0,39.1,35.6,34.9,34.7,34.6,32.2,31.5,31.2,30.3,30.0,25.9,25.8,18.2,18.1,14.3,14.2$, 1.0, -4.6, -4.65, -4.74, -5.0. HRMS (ESI): calcd for $\mathrm{C}_{21} \mathrm{H}_{40} \mathrm{NO}_{3} \mathrm{Si}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right)$382.2772, found 382.2770 .
23. Yellow oil. TLC $\mathrm{R}_{f}\left(\right.$ PE/EA 5:1) $=0.42 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}\right): \delta 7.19(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1 \mathrm{H}), 6.83(\mathrm{~d}, J=$ $16.0 \mathrm{~Hz}, 1.7 \mathrm{H}), 5.99(\mathrm{~s}, 1.5 \mathrm{H}), 5.98(\mathrm{~s}, 1 \mathrm{H}), 5.75(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1.7 \mathrm{H}), 5.70(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.21-4.07(\mathrm{~m}$, $7.3 \mathrm{H}), 3.96(\mathrm{dd}, J=11.2,6.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.51-2.39(\mathrm{~m}, 1.7 \mathrm{H}), 2.31-2.20(\mathrm{~m}, 5.3 \mathrm{H}), 2.18-2.12(\mathrm{~m}, 1 \mathrm{H}), 1.83(\mathrm{dd}, J=13.8$, $3.8 \mathrm{~Hz}, 2.2 \mathrm{H}), 1.78-1.64(\mathrm{~m}, 4.7 \mathrm{H}), 1.62-1.53(\mathrm{~m}, 2 \mathrm{H}), 1.29(\mathrm{~s}, 5.2 \mathrm{H}), 1.24(\mathrm{t}, J=7.2 \mathrm{~Hz}, 9.6 \mathrm{H}), 1.20(\mathrm{~s}, 3 \mathrm{H}), 1.17(\mathrm{~s}$, $4.8 \mathrm{H}), 1.12(\mathrm{~s}, 3 \mathrm{H}), 0.92(\mathrm{~s}, 9 \mathrm{H}), 0.87(\mathrm{~s}, 16.8 \mathrm{H}), 0.10(\mathrm{~s}, 3 \mathrm{H}), 0.07(\mathrm{~s}, 13.6 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CD}_{2} \mathrm{Cl}_{2}$ ): $\delta$ $198.98,198.96,179.4,176.9,165.8,165.7,148.3,145.9,124.5,124.3,124.1,123.8,78.9,78.7,60.6,60.4,57.5,47.5$, $47.1,41.9,38.5,32.9,32.8,32.6,31.7,30.6,29.8,29.4,27.9,25.64,25.58,18.1,18.0,14.1,14.0,-4.7,-4.9,-5.1,-5.2$. HRMS (ESI): calcd for $\mathrm{C}_{22} \mathrm{H}_{40} \mathrm{NO}_{4} \mathrm{Si}\left(\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}\right)$410.2721, found 410.2715.

## References

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${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra


( $\pm$ )-7







$( \pm)-9$



$( \pm)-9$




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| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 20 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | $\begin{gathered} 90 \\ \mathrm{fl}(\mathrm{ppm}) \end{gathered}$ | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 |  |



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(-)-cis-13






S40









S46



$(-)-16-3$










|  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 10 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 |

(-)-19



## 








-220.55
-214.43









| $\begin{aligned} & n \\ & 0 \\ & \hline 1 \end{aligned}$ |  | $\stackrel{\circ}{\stackrel{\infty}{\infty}}$ | $\stackrel{0}{\square}$ | $\stackrel{\text { ® }}{\substack{1}}$ | 6\% <br> 8 | 8 8 8 | $\stackrel{\otimes}{\text { ¢ }}$ |  | ले\% |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |



|  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 30 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | $\begin{gathered} 90 \\ \mathrm{fl}(\mathrm{ppm}) \end{gathered}$ | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 | -1 |




22







HPLC spectra


50
:
50


| Peak | RetTime | Area | Height | Concentration |
| :--- | :--- | :--- | :--- | :--- |
| $\mathbf{1}$ | 5.299 | 2977031 | 449497 | 49.649 |
| $\mathbf{2}$ | 6.064 | 30.19135 | 391212 | 50.351 |

=

2


| Peak | RetTime | Area | Height | Concentration |
| :--- | :--- | :--- | :--- | :--- |
| $\mathbf{1}$ | 5.367 | 1229682 | 177549 | 98.146 |
| $\mathbf{2}$ | 6.205 | 23231 | 2915 | 1.854 |

## X-ray data of ( $\pm$ )-20




Ellipsoids are drawn at $30 \%$ probability

Table 1 Crystal data and structure refinement for exp_8114.
Identification code
Empirical formula
Formula weight
Temperature/K
Crystal system
Space group
a/Å
b/Å
c/Å
$\alpha{ }^{\circ}$
$\beta /{ }^{\circ} \quad 80.759(8)$
$\gamma^{\circ} \quad 83.195(9)$
Volume $/$ A $^{3}$
Z
$\rho_{\text {calc }} \mathrm{g} / \mathrm{cm}^{3}$
$\mu / \mathrm{mm}^{-1}$
F(000)
Crystal size $/ \mathrm{mm}^{3}$
Radiation
$2 \Theta$ range for data collection $/{ }^{\circ} 6.23$ to 52.026
Index ranges
$-8 \leq \mathrm{h} \leq 12,-12 \leq \mathrm{k} \leq 12,-14 \leq 1 \leq 17$
Reflections collected
7667
Independent reflections $\quad 4975\left[\mathrm{R}_{\text {int }}=0.0503, \mathrm{R}_{\text {sigma }}=0.1214\right]$
Data/restraints/parameters 4975/0/310
Goodness-of-fit on $\mathrm{F}^{2} \quad 1.036$
Final $R$ indexes $[I>=2 \sigma(\mathrm{I})] \quad \mathrm{R}_{1}=0.0841, \mathrm{wR}_{2}=0.1968$
Final R indexes [all data] $\quad \mathrm{R}_{1}=0.1742, \mathrm{wR}_{2}=0.2466$
Largest diff. peak/hole /e $\AA^{-3} 0.91 /-0.52$

