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 CaH₂ 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 ¹H NMR of crude reaction mixtures. NMR spectra were recorded at 400 MHz for ¹H and 100 MHz for ¹³C using CDCl₃ (¹H, 7.26 ppm; ¹³C, 77.0 ppm) or CD₂Cl₂ (¹H, 5.30 ppm; ¹³C, 53.52 ppm) as internal standard. The following abbreviations were used to explain the multiplicities: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets, m = multiplet, coupling constant (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 × 250 mm)). PE refers to petroleum ether and EA refers to ethyl acetate.

Abbreviations:

| ^t BuLi = <i>tert</i> -butyllithium; | TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxy; |
|--|--|
| TBAC = tetra- <i>n</i> -butylammonium chloride | NCS = <i>N</i> -chlorosuccinimide |
| DIBAL = diisobutylaluminum hydride | TBSCl = <i>tert</i> -butyldimethylsilyl chloride |
| PDC = pyridinium dichromate | BnBr = benzyl bromide |
| TBAI = tetra- <i>n</i> -butylammonium iodide | LDA = lithium diisopropylamide |
| HMPA = hexamethylphosphoramide | PCC = pyridium chlorochromate |
| $TsNHNH_2 = 4$ -methylbenzenesulfonohydrazide | n BuLi = <i>n</i> -butyllithium |

| DMF = N, N-dimethylformamide | THF = tetrahydrofuran |
|-------------------------------------|---|
| DCM = dichloromethane | PhMe = toluene |
| DMAP = N, N-4-dimethylaminopyridine | TBSOTf = tert-butyl dimethyl silyl trifluoromethane sulfonate |
| CBS = Corey-Bakshi-Shibata reagent | |

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 (±)-clovan-2,9-dione



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

Detailed synthesis procedures



Preparation of (±)-7. To a solution of 2,6-di-*tert*-butyl-4-methylphenyl cyclopropanecarboxylate **6**¹ (7.90 g, 27.4 mmol) in THF (40 mL) was added 'BuLi (21.0 mL, 1.3 M in pentane, 27.3 mmol) dropwise at -78 °C under an argon atmosphere. After stirred for 30 min, a solution of 3, 3-dimethylpent-4-ynal **5**² (2.51 g, 22.8 mmol) in THF (10 mL) was added dropwise at -78 °C. The reaction mixture was stirred for 1.5 h at the same temperature, and then LiAlH₄ (2.60 g, 68.4 mmol) was added at 0 °C portionwise. After refluxing at 60 °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 mL) at 0 °C and stirred, then diethyl ether (50 mL) was added. The mixture was stirred overnight and extracted with diethyl ether (3 × 30 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, then PE/EA 2:1, 1:1) to give (±)-7 (2.74 g, 66% yield) as a white solid. Mp = 60–62 °C. TLC R_{*f*} (PE/EA 2:1) = 0.20. ¹H NMR (400 MHz, CD₂Cl₂): δ 4.04 (dd, *J* = 11.5, 1.0 Hz, 1H), 3.33 (d, *J* = 9.6 Hz, 1H), 3.00 (dd, *J* = 11.5, 0.8 Hz, 1H), 2.76 (brs, 2H), 2.24 (s, 1H), 1.92 (dd, *J* = 14.4, 9.6 Hz, 1H), 1.66 (dd, *J* = 14.2, 1.4 Hz, 1H), 1.27 (s, 3H), 1.22 (s, 3H), 0.68-0.58 (m, 2H), 0.34 (dd, *J* = 8.4, 6.4 Hz, 2H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₁₁H₁₈NaO₂ ([M + Na]⁺) 205.1199, found 205.1200.



Preparation of (±)-8. To a solution of (±)-7 (958.9 mg, 5.26 mmol), NCS (1.05 g, 7.88 mmol), TBAC (146.6 mg, 0.528 mmol) and TEMPO (411.8 mg, 2.63 mmol) in DCM (17.5 mL) was added buffer (17.5 mL, 0.5 M NaHCO₃/0.05 M K₂CO₃). After stirred for 3 h at room temperature, the reaction mixture was extracted with diethyl ether (3 × 30 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 (±)-8 (830.7 mg, 88% yield) as a light yellow oil. TLC R_f (PE/EA 5:1) = 0.27. ¹H NMR (400 MHz, CDCl₃): δ 8.82 (s, *I*H), 3.93 (dd, *J* = 9.4, 1.0 Hz, 1H), 2.92 (brs, 1H), 2.21 (s, 1H), 1.86 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.70 (dd, *J* = 14.3, 1.6 Hz, 1H), 1.31 (s, 3H), 1.30 (s, 3H), 1.26-1.16 (m, 3H), 1.16-1.11 (m, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₁H₁₆NaO₂ ([M + Na]⁺) 203.1043, found 203.1041.



Preparation of (±)-9. To a solution of NaH (860.7 mg, 60% weight in mineral oil, 21.5 mmol) in THF (40 mL) was added ethyl 2-(diethoxyphosphoryl)acetate (2.84 mL, 14.3 mmol) dropwise at 0 °C under an argon atmosphere. A solution of (±)-8 (1.29 g, in 20 mL THF, 7.15 mmol) was added dropwise at 0 °C. After stirred for 40 min at 0 °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 × 30 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 (±)-9 (1.61 g, 90% yield) as a yellow oil. The double bond in (±)-9 was assigned as a *trans* configuration judged by the NMR coupling constant of the hydrogen atoms in the alkene moiety. TLC R_f (PE/EA 5:1) = 0.31. ¹H NMR (400 MHz, CDCl₃): δ 7.08 (d, *J* = 15.8 Hz, 1H), 5.75 (d, *J* = 15.8 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.52 (dd, *J* = 9.6, 1.2 Hz, 1H), 2.62 (brs, 1H), 2.32 (s, 1H), 1.82 (dd, *J* = 14.4, 9.2 Hz, 1H), 1.65 (dd, *J* = 14.4, 1.6 Hz, 1H), 1.21-1.34 (m, 9H), 1.07-0.97 (m, 1H), 0.93-0.76 (m, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₅H₂₆NO₃ ([M + NH₄]⁺) 268.1907, found 268.1911.



Preparation of (\pm)-10. To a solution of (\pm)-9 (434.3 mg, 1.74 mmol) in DCM (17 mL) was added DIBAL (6.9 mL, 1.0 M in hexanes, 6.90 mmol) at -78 °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 × 20 mL). The combined organic layer was washed with water (20 mL) and brine (20 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 TBSCl (288.7 mg, 1.92mmol) and imidazole (260.1 mg, 3.82mmol) at room temperature. The reaction mixture was stirred for 1 h, then quenched by water (20 mL) and extracted with diethyl ether (3 × 20 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)-**10** (514.2 mg, 92% yield over 2 steps) as a colorless oil. TLC R_{*f*} (PE/EA 20:1) = 0.17. ¹H NMR (400 MHz, CDCl₃): δ 5.92 (d, *J* = 15.6 Hz, 1H), 5.50 (dt, *J* = 15.6, 5.2 Hz, 1H), 4.15 (dd, *J* = 5.2, 1.6 Hz, 2H), 3.35 (dd, *J* = 8.6, 2.4 Hz, 1H), 2.39 (brs, 1H), 2.19 (s, 1H), 1.78-1.65 (m, 2H), 1.28 (s, 3H), 1.25 (s, 3H), 0.90 (s, 9H), 0.80-0.69 (m, 1H), 0.69-0.55 (m, 3H), 0.06 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₉H₃₄NaO₂Si ([M + Na]⁺) 345.2220, found 345.2217.



Preparation of 11. To a solution of (±)-10 (214.2 mg, 0.664 mmol) in DCM (13 mL) was added 4 Å MS (2.25 g) and PDC (749.8 mg, 1.99 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 mg, 81% yield) as a colorless oil. TLC R_f (PE/EA 20:1) = 0.36. ¹H NMR (400 MHz,

CDCl₃): δ 6.28 (d, J = 15.2 Hz, 1H), 5.58 (dt, J = 15.2, 4.8 Hz, 1H), 4.19 (dd, J = 4.8, 1.6 Hz, 2H), 2.72 (s, 2H), 2.10 (s, 1H), 1.39 (dd, J = 6.8, 3.6 Hz, 2H), 1.32 (s, 6H), 0.97 (dd, J = 6.8, 3.6 Hz, 2H), 0.92 (s, 9H), 0.08 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₉H₃₆NO₂Si ([M + NH₄]⁺) 338.2510, found 338.2510.



Preparation of (+)-**10.** To a solution of **11** (135.8 mg, 0.42 mmol) in toluene (10.6 mL) was added (*S*)-CBS (0.42 mL, 1 M in toluene, 0.42 mmol). The solution was cooled to -30 °C, and then boron methyl sulfide complex (0.85 mL, 2 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 °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 × 20 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. ee = 96%, (Chiralpak IC, hexanes:DCM = 199:1, 205 nm; retention times of major stereoisomer, 5.367 min; minor stereoisomer, 6.205 min). TLC R_f (PE/EA 20:1) = 0.17. ¹H NMR (400 MHz, CDCl₃): δ 5.92 (d, *J* = 15.4 Hz, 1H), 5.50 (dt, *J* = 15.4, 5.4 Hz, 1H), 4.15 (dd, *J* = 5.4, 1.4 Hz, 2H), 3.35 (dd, *J* = 8.8, 2.4 Hz, 1H), 2.20 (s, 1H), 1.78-1.65 (M, 2H), 1.28 (s, 3H), 1.25 (s, 3H), 0.90 (s, 9H), 0.78-0.71 (m, 1H), 0.69-0.56 (m, 3H), 0.06 (s, 6H). [α]_D²⁰: + 17.1° (*c* 2.59, CHCl₃).



Preparation of (+)-**12.** To a solution of (+)-**10** (585.4 mg, 1.81 mmol) in DMF (18 mL) was added TBAI (133.9 mg, 0.362 mmol) and NaH (290.7 mg, 60% weight in mineral oil, 7.27 mmol) at 0 °C. After stirred for 20 min, BnBr (0.65

mL, 5.42 mmol) was added. The reaction mixture was stirred for 6 h at $^{\circ}$ C under an argon atmosphere and another NaH (232.4 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 × 30 mL). The combined organic layer was washed with water (3 × 40 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 mg) consisting of desired product and ether Bn₂O. Ratio of the product to Bn₂O was 1.2:1 by ¹H 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. TLC R_{*f*} (PE/EA 20:1) = 0.58. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.40-7.26 (m, 4H), 7.26-7.19 (m, 1H), 5.90 (d, *J* = 15.6 Hz, 1H), 5.54 (dt, *J* = 15.6, 5.4 Hz, 1H), 4.80 (d, *J* = 11.2 Hz, 1H), 4.36 (d, *J* = 11.2 Hz, 1H), 4.11 (dd, *J* = 5.4, 1.4 Hz, 2H), 3.09 (dd, *J* = 6.4, 4.0 Hz, 1H), 2.11 (s, 1H), 1.80-1.74 (m, 2H), 1.24 (s, 3H), 1.21 (s, 3H), 0.95-0.89 (m, 1H), 0.87 (s, 9H), 0.89-0.81 (m, 1H), 0.62 (ddd, *J* = 9.2, 6.0, 4.4 Hz, 1H), 0.47 (ddd, *J* = 9.6, 6.0, 4.6 Hz, 1H), 0.03 (s, 6H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₀H₄₀NaO₂Si ([M + Na]⁺) 435.2690, found 435.2686. [α]_D²⁰: + 70.1° (c 0.03, CHCl₃).

Preparation of (\pm)-12. With (\pm)-10 (1.9 g, 5.89 mmol), BnBr (2.1 mL, 17.7 mmol), TBAI (435.8 mg, 1.18 mmol), NaH (945.4 mg + 755.7 mg, 42.5 mmol) and DMF (59 mL) as starting materials, (\pm)-12 was prepared by using the same procedure. Reaction time was 6 h + 13 h. Total mass was 2.79 g consisting of desired product (\pm)-12 and ether Bn₂O. Ratio of the product to Bn₂O was 2.1:1 by ¹H 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)-12 (908.6 mg, ratio of substrate to Bn₂O was 1.2:1, real mass of substrate 647.9 mg, 1.57 mmol) and [Rh(CO)₂Cl]₂ (30.7 mg, 0.079 mmol) in anhydrous toluene (31 mL) was bubbled by CO (0.2 atm) for 10 min. The reaction mixture was stirred at 100 °C

under balloon pressure gas of CO (0.2 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 **13** as a brown oil (574.2 mg, 83% combined yield). The diastereoselectivity of (–)-*trans*-**13** and (–)-*cis*-**13** was determined by the ¹H 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 R_f (PE/EA 10:1) = 0.30. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.37-7.27 (m, 4H), 7.27-7.20 (m, 1H), 5.94 (s, 1H), 5.61-5.48 (m, 2H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.38 (d, *J* = 11.8 Hz, 1H), 4.20-4.06 (m, 2H), 3.82 (d, *J* = 3.6 Hz, 1H), 2.55 (ddd, *J* = 13.9, 12.9, 4.4 Hz, 1H), 2.38 (ddd, *J* = 17.2, 14.2, 5.0 Hz, 1H), 2.20 (ddd, *J* = 17.4, 4.6, 1.6 Hz, 1H), 1.95 (d, *J* = 14.0 Hz, 1H), 1.80 (dd, *J* = 14.2, 3.8 Hz, 1H), 1.71 (ddd, *J* = 12.7, 5.1, 2.1 Hz, 1H), 1.26 (s, 3H), 1.19 (s, 3H), 0.87 (s, 9H), 0.03 (s, 6H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₇H₄₀NaO₃Si ([M + Na]⁺) 463.2639, found 463.2632. [α]_D²⁰: - 13.4° (*c* 1.14, CHCl₃).

(-)-*cis*-**13.** Brown oil. TLC R_{*f*} (PE/EA 10:1) = 0.20. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.40-7.29 (m, 4H), 7.29-7.21 (m, 1H), 5.98 (dt, *J* = 15.6, 1.8 Hz, 1H), 5.93 (s, 1H), 5.49 (dt, *J* = 16.0, 4.6 Hz, 1H), 4.61 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.23-4.11 (m, 2H), 3.73 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.36 (ddd, *J* = 18.2, 14.0, 5.8 Hz, 1H), 2.21-2.12 (m, 2H), 1.92-1.82 (m, 2H), 1.68 (dd, *J* = 11.6, 11.6 Hz, 1H), 1.21 (s, 3H), 1.10 (s, 3H), 0.86 (s, 9H), 0.03 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₂₇H₄₀NaO₃Si ([M + Na]⁺) 463.2639, found 463.2644. [α]_D²⁰: - 8.98° (*c* 2.28, CHCl₃).

Preparation of (\pm)-13. With (\pm)-12 (1.23 g, ratio of substrate to Bn₂O was 2.1:1, real mass of substrate 1.0 g, 2.42 mmol), [Rh(CO)₂Cl]₂ (47.8 mg, 0.123 mmol) and PhMe (48 mL) as starting materials, (\pm)-13 (848.9 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 mL, 6.53 mmol) in anhydrous THF (10 mL) at -78 $^{\circ}$ C under an argon atmosphere was added ^{*n*}BuLi (4.1 mL, 1.6 M in hexanes, 6.56 mmol) and the solution was stirred at 0 $^{\circ}$ C for 30 min. Then the freshly prepared LDA was cooled to –78 $^{\circ}$ C and a solution of (–)-*trans*-13 (412.4 mg, 0.936 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 $^{\circ}$ C. Then MeI (0.82 mL, 13.2 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 × 30 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 mg, 95% yield) as a yellow oil. The diastereoselectivity of (–)-14-1 and (–)-14-2 was determined by the crude ¹H 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. TLC R_{*f*} (PE/EA 10:1) = 0.43. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.50-7.28 (m, 4H), 7.28-7.20 (m, 1H), 5.93 (s, 1H), 5.72-5.40 (m, 2H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.21-4.02 (m, 2H), 3.80 (d, *J* = 3.6 Hz, 1H), 2.53-2.37 (m, 1H), 2.30 (dd, *J* = 13.0, 13.0 Hz, 1H), 1.93 (d, *J* = 14.0 Hz, 1 H), 1.88-1.68 (m, 2H), 1.25 (s, 3H), 1.20 (s, 3H), 1.06 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₈H₄₃O₃Si ([M + H]⁺) 455.2976, found 455.2975. [α]_D²⁰: - 6.87° (*c* 1.35, CHCl₃).

(-)-**14-2.** Yellow oil. TLC R_{*f*} (PE/EA 10:1) = 0.36. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.39-7.27 (m, 4H), 7.27-7.21 (m, 1H), 5.98 (s, 1H), 5.71 (dt, *J* = 15.6, 1.6 Hz, 1H), 5.43 (dt, *J* = 15.6, 4.6 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.15-4.02 (m, 2H), 3.76 (d, *J* = 3.6 Hz, 1H), 2.75 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.43 (qd, *J* = 7.8, 7.6 Hz, 1H), 1.90 (d, *J* = 14.0 Hz, 1 H), 1.81 (dd, *J* = 14.0, 4.0 Hz, 1H), 1.71 (dd, *J* = 13.6, 0.8 Hz, 1H), 1.27 (s, 3H), 1.23 (s, 3H), 1.16 (d, *J* = 7.8 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 6H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 $C_{28}H_{43}O_3Si$ ([M + H]⁺) 455.2976, found 455.2975. [α]_D²⁰: – 33.9° (*c* 1.28, CHCl₃).

Preparation of (\pm)-14. With (\pm)-trans-13 (602.5 mg, 1.37 mmol), diisopropylamine (1.35 mL, 9.57 mmol), ⁿBuLi (6.0 mL, 1.6 M in hexanes, 9.57 mmol), HMPA (1.8 mL), MeI (1.2 mL, 19.1 mmol) and THF (total 34 mL) as starting materials, (\pm)-14 (553.6 mg, 89% yield) as a yellow oil was prepared by using the same procedure. Reaction time was 30 min, 40 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 Pd(OH)₂/C (164.2 mg, 20% on dry basis, 0.234 mmol) and bubbled by H₂ (1.0 atm) for 20 min. Then MeOH (2.4 mL) was added and the reaction mixture was bubbled by H₂ (1.0 atm) for another 10 min. The reaction mixture was stirred at 50 °C under balloon pressure gas of H₂ (1.0 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 mL), and then HCl (4.7 mL, 1 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 × 20 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 2:1) to give **15** (68.5 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. TLC R_f (PE/EA 2:1) = 0.22. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.36-7.27 (m, 4H), 7.27-7.21 (m, 1H), 4.57 (d, J = 11.8 Hz, 1H), 4.38 (d, J = 11.8 Hz, 1H), 3.81 (dd, J = 6.2, 6.2 Hz, 1H), 3.56 (t, J = 6.4 Hz, 2H), 2.67-2.53 (m, 1H), 2.37-2.31 (m, 2H), 2.22 (dd, J = 14.0, 5.6 Hz, 1H), 1.85-1.74 (m, 2H), 1.66-1.52 (m, 3H), 1.51-1.45 (m, 2H), 1.44 (brs, 1H), 1.36 (dd, J = 14.0, 12.0 Hz, 1H), 1.02 (s, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.91 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 $C_{22}H_{36}NO_3 ([M + NH_4]^+)$ 362.2690, found 362.2683. $[\alpha]_D^{-20}$: – 53.6° (*c* 1.14, CHCl₃).

Preparation of (±)-15. With (±)-14 (313.2 mg, 0.689 mmol), Pd(OH)₂/C (482.2 mg, 20% on dry basis, 0.689 mmol) and PhMe (6.9 mL), MeOH (6.9 mL), HCl (13.8 mL, 1 M) and THF (13.8 mL) as starting materials, (±)-15 (202.0 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 15 (136.5 mg, 0.396 mmol) from the asymmetric route (Scheme 1) in DCM (8.0 mL) was added silica-gel (769.0 mg) and PCC (256.5 mg, 1.19 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 MeOH (8.0 mL), and then KOH (137.6 mg, 2.45 mmol) was added. The reaction mixture was stirred for 6 h at 30 °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 mg) and (–)-16-2 (17.1 mg)).

(-)-**16-1**. White solid. Mp = 67-69 °C. TLC R_{*f*} (PE/EA 3:1) = 0.41. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.43-7.28 (m, 4H), 7.28-7.21 (m, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 3.71 (dd, *J* = 6.4, 6.4 Hz, 1H), 3.23 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.06 (brs, 1H), 2.41 (dd, *J* = 13.4, 13.4 Hz, 1H), 2.16 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.10 (dd, *J* = 14.4, 3.2 Hz, 1H), 1.91-1.81 (m, 1H), 1.80-1.72 (m, 2H), 1.69 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.59 (dd, *J* = 13.0, 5.8 Hz, 1H), 1.46-1.39 (m, 1H), 1.37 (d, *J* = 14.0 Hz, 1H), 1.14 (s, 3H), 1.12-1.04 (m, 1H), 1.01 (s, 3H), 1.00 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₂H₃₀KO₃ ([M + K]⁺) 381.1827, found 381.1824. [α]_D²⁰: – 122.7° (*c* 3.0, CHCl₃).

(-)-**16-2.** Colorless oil. TLC R_{*f*} (PE/EA 3:1) = 0.29. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.44-7.29 (m, 4H), 7.29-7.20 (m, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 3.75-3.63 (m, 2H), 2.45 (dd, *J* = 13.4, 13.4 Hz, 1H), 2.17 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.91 (ddd, *J* = 13.4, 13.4, 4.4 Hz, 1H), 1.85-1.73 (m, 3H), 1.73-1.67 (m, 2H), 1.67-1.61 (m, 1H), 1.58 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.48-1.35 (m, 1H), 1.26-1.15 (m, 1H), 1.00 (s, 9H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₂H₃₄NO₃ ([M + NH₄]⁺) 360.2533, found 360.2532. [*α*]_D²⁰: – 125.6° (*c* 1.43, CHCl₃).

(-)-**16-3**. Colorless oil. TLC R_{*f*} (PE/EA 3:1) = 0.12. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.40-7.28 (m, 4H), 7.28-7.22 (m, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 3.94 (ddd, *J* = 11.2, 5.8, 5.8 Hz, 1H), 3.56 (dd, *J* = 9.2, 8.4 Hz, 1H), 2.75 (dd, *J* = 5.4, 1.4 Hz, 1H), 2.49-2.33 (m, 1H), 2.18 (dd, *J* = 13.4, 6.2 Hz, 1H), 1.13-1.96 (m, 4H), 1.82-1.75 (m, 1H), 1.75-1.64 (m, 2H), 1.54-1.43 (m, 2H), 1.10 (d, *J* = 6.4 Hz, 3H), 0.97 (s, 3H), 0.80 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₂H₃₀O₃ (M⁺) 342.2190, found 342.2187. [α]_D²⁰: – 79.3° (*c* 1.02, CHCl₃).

Preparation of (\pm)-16. With (\pm)-15 (227.6 mg, 0.661 mmol), silica-gel (1.28 g), PCC (427.8 mg, 1.98 mmol), DCM (13.2 mL), KOH (222.0 mg, 3.96 mmol) and MeOH (13.2 mL) as starting materials, (\pm)-16-1 and (\pm)-16-2 (152.9 mg, 68% yield) and (\pm)-16-3 (21.5 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 mg) and (\pm)-16-2 (29.9 mg)). The relative configurations of these two compounds were assigned based on the X-ray structure of (\pm)-20, the derivative of (\pm)-16-2, which is given below.



Preparation of (\pm)-20. To a solution of the compound (\pm)-16-2 (31.8 mg, 0.0928 mmol) in DCM (3.1 mL) was added DMAP (4.7 mg, 0.0385 mmol) and Et₃N (41.0 mg, 0.405 mmol) at room temperature under an argon atmosphere. Then 4-bromobenzoyl chloride (63.6 mg, 0.29 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 (±)-**20** (38.2 mg, 78% yield) as a white solid. The relative configuration was determined by X-ray analysis. Mp = 105-107 °C. TLC R_f (PE/EA 3:1) = 0.72. ¹H NMR (400 MHz, CDCl₃): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.41-7.28 (m, 5H), 5.23 (s, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 3.75 (dd, *J* = 6.0, 6.0 Hz, 1H), 2.54 (dd, *J* = 13.6, 13.6 Hz, 1H), 2.30 (dd, *J* = 13.8, 5.8 Hz, 1H), 2.05 (d, *J* = 14.0 Hz, 1H), 2.00-1.87 (m, 3H), 1.85 (dd, *J* = 12.8, 7.2 Hz, 1H), 1.76 (dd, *J* = 12.8, 5.6 Hz, 1H), 1.64 (dd, *J* = 13.0, 5.8 Hz, 1H), 1.59-1.47 (m, 1H), 1.33-1.23 (m, 1H), 1.06 (s, 6H), 1.05 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₂₉H₃₄BrO₄ ([M + H]⁺) 525.1635, found 525.1636.



Preparation of (+)-**17.** To a solution of (-)-**16-1** (58.6 mg, 0.171 mmol) in MeOH (3.4 mL) was added TsNHNH₂ (95.9 mg, 0.515 mmol) and a drop of concentrated HCl. The reaction mixture was refluxed at 67 °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 mg, 62% yield) as a white solid. Mp = 77-79 °C. TLC R_{*f*} (PE/EA 2:1) = 0.43. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.31-7.18 (m, 5H), 4.50 (d, *J* = 11.8 Hz, 1H), 4.36 (d, *J* = 11.8 Hz, 1H), 3.64 (dd, *J* = 7.4, 5.8 Hz, 1H), 3.17 (dd, *J* = 11.8, 4.6 Hz, 1H), 2.54 (dd, *J* = 14.2, 5.8 Hz, 1H), 2.41 (s, 3H), 1.88-1.54 (m, 6H), 1.40-1.28 (m, 2H), 1.23 (d, *J* = 14.0 Hz, 1H), 1.05 (s, 3H), 0.99 (s, 3H), 0.98 (s, 3H), 1.03-0.90 (m, 1H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂9H₃₈N₂NaO₄S ([M + Na]⁺) 533.2444, found 533.2439. [α]_D²⁰: +10.3° (*c* 1.63, CHCl₃).

Preparation of (\pm)-17. With (\pm)-16-1 (83.9 mg, 0.245 mmol), TsNHNH₂ (137.3 mg, 0.737 mmol), HCl (2 drop) and MeOH (4.9 mL) as starting materials, (\pm)-17 (90.4 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 mg, 0.106 mmol) in anhydrous THF (4.2 mL) at 70 °C under an argon atmosphere was added ^{*n*}BuLi (0.39 mL, 1.6 M in hexanes, 0.62 mmol) dropwise. The reaction mixture was stirred at 70 °C for 10 min and then quenched by saturated aqueous ammonium chloride solution (5 mL) and water (5 mL) at room temperature. It was extracted with diethyl ether (3 × 15 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 (-)-**18** (18.0 mg, 52% yield) as a colorless oil. TLC R_{*f*} (PE/EA 3:1) = 0.47. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.35-7.28 (m, 4H), 7.28-7.21 (m, 1H), 5.86 (dd, *J* = 9.8, 4.0 Hz, 1H), 5.49 (d, *J* = 9.8 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.37 (d, *J* = 11.6 Hz, 1H), 3.50 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.25 (dd, *J* = 10.6, 4.6 Hz, 1H), 1.81 (dd, *J* = 12.8, 6.8 Hz, 1H), 1.77-1.65 (m, 3H), 1.64 (dd, *J* = 12.6, 9.0 Hz, 1H), 1.44-1.34 (m, 2H), 1.33-1.23 (m, 3H), 1.09 (s, 3H), 1.05 (s, 3H), 0.92 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₂H₃₄NO₂ ([M + NH₄]⁺) 344.2584, found 344.2583. [α]₀²⁰: – 93.5° (*c* 1.50, CHCl₃).

Preparation of (±)-18. With (±)-17 (42.8 mg, 0.084 mmol), ^{*n*}BuLi (0.3 mL, 1.6 M in hexanes, 0.48 mmol) and THF (3.3 mL) as starting materials, (±)-18 (19.5 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 MeOH (3.1 mL) was added Pd/C (49.9 mg, 10% on dry basis, 0.0469 mmol) and bubbled by H_2 (1.0 atm) for 10 min. The reaction mixture was stirred at 60 °C under balloon pressure gas of H_2 (1.0 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 MeOH (3.1 mL), and Pd/C (99.9 mg, 10%

on dry basis, 0.0939 mmol) was added. The reaction mixture was stirred for 3 d at 60 °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 mg, 79% yield) as a white solid. Mp = 145-146 °C. TLC R_f (PE/EA 2:1) = 0.26. ¹H NMR (400 MHz, CDCl₃): δ 3.87 (dd, J = 9.8, 6.2 Hz, 1H), 3.26 (dd, J = 10.6, 5.4 Hz, 1H), 1.82-1.75 (m, 1H), 1.71 (dd, J = 12.2, 6.2 Hz, 1H), 1.67-1.48 (m, 5H), 1.46-1.37 (m, 2H), 1.36-1.23 (m, 4H), 1.22-1.14 (m, 1H), 1.02 (s, 3H), 0.98 (s, 6H), 0.82 (d, J = 12.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₅H₃₀NO₂ ([M + NH₄]⁺) 256.2277, found 256.2271. [α]_D²⁰: – 18.5° (*c* 0.73, MeOH).

Preparation of (\pm)-19. With (\pm)-18 (7.8 mg, 0.024 mmol), Pd/C (25.1 + 50.8 mg, 10% on dry basis, 0.0713 mmol) and MeOH (1.6 + 2.0 mL) as starting materials, (\pm)-19 (5.2 mg, 91% yield) as a white solid was prepared by using the same procedure. Reaction time was 20 h + 3 d.



Preparation of (–)-**1.** To a solution of (–)-**19** (8.7 mg, 0.037 mmol) in DCM (1.8 mL) was added silica-gel (141.7 mg) and PCC (47.5 mg, 0.22 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 mg, 88% yield) as a light yellow oil. TLC R_{*f*} (PE/EA 5:1) = 0.27. ¹H NMR (400 MHz, CDCl₃): δ 2.56-2.46 (m, 2H), 2.39 (d, *J* = 17.6 Hz, 1H), 2.22 (d, *J* = 17.6 Hz, 1H), 2.21-2.11 (m, 1H), 1.96 (dd, *J* = 6.8, 6.8 Hz, 1H), 1.80-1.70 (m, 2H), 1.68-1.57 (m, 4H), 1.47 (ddd, *J* = 14.3, 7.3, 7.3 Hz, 1H), 1.15 (s, 3H), 1.09 (s, 3H), 1.04 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₁₅H₂₂O₂ ([M]⁺) 234.1614, found 234.1612. [α]_D²⁰: – 100.5° (*c* 0.63, CHCl₃).

Preparation of (±)-1. With (±)-19 (4.3 mg, 0.018 mmol), silica-gel (70.1 mg), PCC (23.3 mg, 0.108 mmol) and DCM (1 mL) as starting materials, (±)-1 (3.6 mg, 85% yield) as a light yellow oil was prepared by using the same procedure. Reaction time was 3 h.



Preparation of (±)-**21.** To a solution of (±)-**9** (451.8 mg, 1.81 mmol) in DCM (20 mL) was added 2, 6-lutidine (0.42 mL, 3.61 mmol) at 0 °C under an argon atmosphere. After 5 min, TBSOTf (0.66 mL, 2.89 mmol) was added. The reaction mixture was stirred for 1 h at 0 °C, then quenched with water (20 mL), extracted with diethyl ether (3 × 20 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. Mp = 66-68 °C. TLC R_{*f*} (PE/EA 5:1) = 0.81. ¹H NMR (400 MHz, CDCl₃): δ 7.01 (d, *J* = 16.0 Hz, 1H), 5.84 (d, *J* = 16.0 Hz, 1H), 4.25-4.06 (m, 2H), 3.33 (dd, *J* = 5.6, 4.4 Hz, 1H), 2.08 (s, 1H), 1.88-1.74 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.24 (s, 3H), 1.21 (s, 3H), 1.06-0.98 (m, 1H), 0.93-0.84 (m, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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 C₂₁H₄₀NO₃Si ([M + NH₄]⁺) 382.2772, found 382.2769.



Preparation of 22 and 23. A solution of the compound (\pm)-**21** (45.3 mg, 0.124 mmol) and [Rh(CO)₂Cl]₂ (4.7 mg, 0.0121 mmol) in anhydrous toluene (2.5 mL) was bubbled by CO (0.2 atm) for 5 min. The reaction mixture was stirred at 100 °C under balloon pressure gas of CO (0.2 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 mg, 71% yield) as a yellow oil and inseparable diastereomers **23** (8.3 mg, 17% yield) as a yellow oil.

22. Yellow oil. TLC R_{*f*} (PE/EA 5:1) = 0.84. ¹H NMR (400 MHz, CDCl₃): δ 7.39 (d, *J* = 16.0 Hz, 1H), 7.00 (d, *J* = 15.6 Hz, 1.2H), 5.86 (d, *J* = 11.6 Hz, 2.2H), 5.82 (d, *J* = 11.2 Hz, 2.2H), 5.49-5.43 (m, 2.3H), 4.17 (q, *J* = 7.2 Hz, 4.6H), 3.97 (d, *J* = 4.0 Hz, 1.2H), 3.93 (dd, *J* = 10.4, 6.8 Hz, 1H), 2.63-2.52 (m, 2.3H), 2.47-2.36 (m, 2.2H), 2.36-2.27 (m, 1H), 2.05 (dd, *J* = 13.6, 4.4 Hz, 1.3H), 1.92-1.70 (m, 5.7H), 1.48 (dd, *J* = 11.8, 5.8 Hz, 1.2H), 1.29 (t, *J* = 7.2 Hz, 7.3H), 1.18 (s, 3.6H), 1.13 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3.7H), 0.89 (s, 9H), 0.88 (s, 11H), 0.08-0.02 (m, 14.4H). ¹³C NMR (100 MHz, CDCl₃): δ 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 C₂₁H₄₀NO₃Si ([M + NH₄]⁺) 382.2772, found 382.2770.

23. Yellow oil. TLC R_f (PE/EA 5:1) = 0.42. ¹H NMR (400 MHz, CD_2Cl_2): δ 7.19 (d, J = 16.0 Hz, 1H), 6.83 (d, J = 16.0 Hz, 1.7 H), 5.99 (s, 1.5H), 5.98 (s, 1H), 5.75 (d, J = 16.0 Hz, 1.7H), 5.70 (d, J = 16.0 Hz, 1 H), 4.21-4.07 (m, 7.3H), 3.96 (dd, J = 11.2, 6.4 Hz, 1H), 2.51-2.39 (m, 1.7H), 2.31-2.20 (m, 5.3H), 2.18-2.12 (m, 1H), 1.83 (dd, J = 13.8, 3.8 Hz, 2.2H), 1.78-1.64 (m, 4.7H), 1.62-1.53 (m, 2H), 1.29 (s, 5.2H), 1.24 (t, J = 7.2 Hz, 9.6H), 1.20 (s, 3H), 1.17 (s, 4.8H), 1.12 (s, 3H), 0.92 (s, 9H), 0.87 (s, 16.8H), 0.10 (s, 3H), 0.07 (s, 13.6H). ¹³C NMR (100 MHz, CD₂Cl₂): δ 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, 47.1, 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 C₂₂H₄₀NO₄Si ([M + NH₄]⁺) 410.2721, found 410.2715.

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U. J. Am. Chem. Soc. 1986, 108, 1039. (b) Stevens, R. V.; Christensen, C. G.; Edmonson, W. L.; Kaplan, M.; Reid, E.

B.; Wentland, M. P. J. Am. Chem. Soc. 1971, 93, 6629.













































































50

50 :

| Peak | RetTime | Area | Height | Concentration |
|------|---------|----------|--------|---------------|
| 1 | 5.299 | 2977031 | 449497 | 49.649 |
| 2 | 6.064 | 30.19135 | 391212 | 50.351 |

| Peak | RetTime | Area | Height | Concentration |
|------|---------|---------|--------|---------------|
| 1 | 5.367 | 1229682 | 177549 | 98.146 |
| 2 | 6.205 | 23231 | 2915 | 1.854 |

X-ray data of (±)-20

Ellipsoids are drawn at 30% probability

Table 1 Crystal data and structure refinement for exp_8114.

| Identification code | exp_8114 |
|---|---|
| Empirical formula | $C_{29}H_{33}BrO_4$ |
| Formula weight | 525.46 |
| Temperature/K | 180.00(10) |
| Crystal system | triclinic |
| Space group | P-1 |
| a/Å | 9.8378(11) |
| b/Å | 10.0606(10) |
| c/Å | 14.0335(12) |
| α/° | 70.001(9) |
| β/° | 80.759(8) |
| γ/° | 83.195(9) |
| Volume/Å ³ | 1285.2(2) |
| Z | 2 |
| $\rho_{calc}g/cm^3$ | 1.358 |
| μ/mm^{-1} | 1.631 |
| F(000) | 548.0 |
| Crystal size/mm ³ | 0.15	imes 0.1	imes 0.1 |
| Radiation | MoKa ($\lambda = 0.71073$) |
| 2Θ range for data collection/° | 6.23 to 52.026 |
| Index ranges | $-8 \le h \le 12, -12 \le k \le 12, -14 \le l \le 17$ |
| Reflections collected | 7667 |
| Independent reflections | 4975 [$R_{int} = 0.0503$, $R_{sigma} = 0.1214$] |
| Data/restraints/parameters | 4975/0/310 |
| Goodness-of-fit on F ² | 1.036 |
| Final R indexes [I>= 2σ (I)] | $R_1 = 0.0841$, $wR_2 = 0.1968$ |
| Final R indexes [all data] | $R_1 = 0.1742, wR_2 = 0.2466$ |
| Largest diff. peak/hole / e Å ⁻³ | 0.91/-0.52 |