Supporting Information
for DOI: 10.1055/s-0028-1083542
© Georg Thieme Verlag KG Stuttgart · New York 2008
Supporting Information

Prolinamide/PPTS Catalyzed Hajos-Parrish Annulation: Efficient Approach to the Tricyclic Core of Cylindricine Type Alkaloids

Xiao-Ming Zhang, Min Wang, Yong-Qiang Tu,* Chun-An Fan, Yi-Jun Jiang, Shu-Yu Zhang
State Key Laboratory of Applied Organic Chemistry & Department of Chemistry, Lanzhou University, Lanzhou 730000, PRC
Fax +86(931)8912582 ; E-mail: tuyq@lzu.edu.cn

Contents

1. Typical Experimental Procedures of the Products 2a to 2j and Spectroscopic and Analytical Data of them.

   Typical Experimental Procedures ............................................................S2
   Spectroscopic and Analytical Data of 2a to 2j ...........................................S2 to S6

2. Experimental Procedures and Spectroscopic and Analytical Data of the Products 8 to 16

   Synthesis of Compound 8..................................................................................S7
   Synthesis of Compound 9..................................................................................S7
   Synthesis of Compound 10.................................................................................S8
   Synthesis of Compound 11.................................................................................S8
   Synthesis of Compound 12.................................................................................S9
   Synthesis of Compound 13.................................................................................S9
   Synthesis of Compound 14.................................................................................S10
   Synthesis of Compound 15...............................................................................S10
   Synthesis of Compound 16...............................................................................S11

3. Copies of $^1$H NMR and $^{13}$C NMR

   Copies of 2a to 2j..............................................................................................S12 to S31
   Copies of 8 to 16..............................................................................................S32 to S49
**General:** $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ solution on Varian Mercury-300 MHz or Bruker Apex II 400 MHz. The MS data were obtained with EI (70 eV), and the relative intensity (%) is given in brackets. High-resolution mass spectral analysis (HRMS) data were measured on the Bruker Apex II by means of the ESI technique. Optical rotations were measured using sodium light (D line 589 nm) on Model 341 Polarimeter. X-ray crystallographic analysis data were measured on the Bruker Apex II. Enantiometric determination was accomplished by Agilent 1100 HPLC.

1. **Typical Experimental Procedures of the Products 2a to 2j and Spectroscopic and Analytical Data of them.**

1.1 — **Typical Experimental Procedure.**

A solution of 1a (80 mg, 0.3 mmol) in CH$_3$CN (1mL) was added L-prolinamide (10mg, 0.09 mmol) and PPTS (23mg, 0.09 mmol) at 50 °C under Ar atmosphere. After stirring for 144 hours, water was added to the reaction mixture and extracted with AcOEt. The organic phase was washed with sat. NH$_4$Cl, sat. NaHCO$_3$, sat. brine and dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure to give a crude oil, which was purified on silica gel to give 2a (49 mg, 65%) as colorless oil.

1.2 — **Spectroscopic and Analytical Data of 2a to 2j.**

![Structure of 2a](image)

$^1$H NMR (400 MHz, CDCl$_3$): δ = 5.87 (s, 1H), 3.61 (d, J = 1.6Hz, 3H), 2.80 (tdd, J = 14.4Hz, 5.6Hz, 2.0Hz, 1H), 2.68 (td, J = 14.8Hz, 2.0Hz, 1H), 2.43-2.50 (m, 2H), 2.35-2.42 (m, 1H), 2.33-2.34 (m, 1H), 2.30-2.32 (m, 2H), 2.12-2.28 (m, 3H), 2.00-2.12 (m, 2H), 1.67 ppm (qt, J = 13.6Hz, 4.0Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 209.9, 197.8, 172.7, 165.0, 126.6, 53.7, 51.9, 38.3, 33.3, 31.7, 29.4, 28.8, 25.4, 23.2 ppm; EI MS (70 eV): m/z (%): 250 (7.1) [M$^+$], 177(11), 121(17), 91(33), 55(46), 43(100); HRMS (ESI): [M+H]$^+$ calcd for C$_{14}$H$_{19}$O$_4$: 251.1278; found: 251.1280 [M+H]$^+$; HPLC: Chiralpcel OD column, hexane/PrOH 90:10 1 mL/min, $t_1$= 30.3 min(major), $t_2$ = 34.1 min(minor) (87% ee)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.88 (s, 1H), 4.10 (q, J = 7.2Hz, 2H), 2.81 (td, J = 14.4Hz, 6.4Hz, 1H), 2.47-2.51 (m, 2H), 2.36-2.43 (m, 2H), 2.27-2.35 (m, 2H), 2.07-2.19 (m, 4H), 1.97-2.07 (m, 2H), 1.69 (qt, J = 13.6Hz, 4.0Hz, 1H), 1.23 ppm (t, J = 7.2Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 209.8, 197.7, 172.2, 165.0, 126.5, 60.8, 53.7, 38.3, 33.3, 31.7, 29.5, 29.0, 25.5, 23.2, 14.1 ppm; EI MS (70 eV): m/z (%): 264 (5.7) [M]$^+$, 219(20), 177(17), 134(39), 91(79), 77(100), 55(55); HRMS (ESI): [M+H] calcd for C$_{15}$H$_{21}$O$_4$: 265.1434; found: 265.1431[M+H]$^+$; HPLC: Chiralcel OD column, hexane/iPrOH 90:10 1 mL/min, $t_1$ = 22.0 min(major), $t_2$ = 24.6 min(minor) (82% ee)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.86 (s, 1H), 4.02 (t, J = 6.4Hz, 2H), 2.79 (tdd, J = 14.0Hz, 5.2Hz, 1.6Hz, 1H), 2.68 (td, J = 14.8Hz, 6.0Hz, 1H), 2.41-2.49 (m, 2H), 2.31-2.38 (m, 2H), 2.21-2.30 (m, 2H), 2.08-2.18 (m, 3H), 1.96-2.06 (m, 2H), 1.66 (qt, J = 13.6Hz, 4.0Hz, 1H), 1.52-1.59 (m, 2H), 1.21-1.37 (m, 2H), 0.89 ppm (t, J = 7.2Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 209.8, 197.7, 172.3, 165.0, 126.4, 64.6, 53.6, 38.2, 33.2, 31.7, 30.4, 29.3, 28.9, 25.3, 23.1, 18.9, 13.5 ppm; EI MS (70 eV): m/z (%): 292 (2.5) [M]$^+$, 219(12), 177(60), 121(50), 91(55), 55(100), 41(89); HRMS (ESI): [M+H] calcd for C$_{17}$H$_{25}$O$_4$: 293.1747; found: 293.1745[M+H]$^+$; HPLC: Chiralcel OD column, hexane/iPrOH 90:10 1 mL/min, $t_1$ = 18.8 min(major), $t_2$ = 22.0 min(minor) (82% ee)
$^1$H NMR (400 MHz, CDCl$_3$): \( \delta = 5.84 \) (s, 1H), 3.62 (d, \( J = 4.8 \text{Hz} \), 3H), 2.80 (d, \( J = 14.4 \text{Hz} \), 1H), 2.64 (d, \( J = 14.4 \text{Hz} \), 1H), 2.38-2.48 (m, 2H), 2.16-2.30 (m, 5H), 2.00-2.10 (m, 2H), 1.88 (td, \( J = 14.4 \text{Hz} \), 4.0Hz, 1H), 1.09 (s, 3H), 1.04 ppm (s, 3H); 13C NMR (100 MHz, CDCl$_3$): \( \delta = 210.1, 197.5, 172.7, 164.3, 127.8, 52.2, 51.8, 51.6, 33.9, 33.1, 30.6, 28.8, 25.9, 25.2 \) ppm; EI MS (70 eV): m/z (%): 278 (31) [M$^+$], 205(56), 161(35), 121(61), 83(100), 55(77); HRMS (ESI): [M+H] calcd for C$_{16}$H$_{23}$O$_4$: 279.1591; found: 295.1589[M+H]$^+$; HPLC: Chiralpak AD column, hexane/iPrOH/CH$_3$CH$_2$OH 90:9:1 1 mL/min, \( t_1 = 14.4 \text{ min} \) (minor), \( t_2 = 15.5 \text{ min} \) (major) (70% ee)

$^1$H NMR (400 MHz, CDCl$_3$): \( \delta = 5.86 \) (s, 1H), 5.53-5.60 (m, 1H), 5.09-5.13 (m, 2H), 2.76 (td, \( J = 13.2 \text{Hz} \), 5.2Hz, 1H), 2.60-2.89 (m, 2H), 2.54 (d, \( J = 7.6 \text{Hz} \), 1H), 2.49-2.52 (m, 1H), 2.46-2.48 (m, 1H), 2.40-2.41 (m, 1H), 2.38 (d, \( J = 4.4 \text{Hz} \), 1H), 2.20 (dt, \( J = 14.4 \text{Hz} \), 6.0Hz, 1H), 2.12-2.17 (m, 1H), 2.01-2.07 (m, 1H), 1.69 ppm (qt, \( J = 13.6 \text{Hz} \), 4.4Hz, 1H); 13C NMR (100 MHz, CDCl$_3$): \( \delta = 209.2, 198.1, 164.9, 131.5, 126.4, 119.4, 54.6, 39.8, 38.4, 33.3, 31.9, 26.1, 23.3 \) ppm; EI MS (70 eV): m/z (%): 204 (32) [M$^+$], 135(36), 106(42), 91(100), 77(74), 55(92), 39(86); HRMS (ESI): [M+H] calcd for C$_{13}$H$_{17}$O$_2$: 205.1223; found: 205.1228[M+H]$^+$; HPLC: Chiralpak AS column, hexane/iPrOH 65:35 1.1 mL/min, \( t_1 = 33.4 \text{ min} \) (major), \( t_2 = 69.5 \text{ min} \) (minor) (85% ee)
$^1$H NMR (400 MHz, CDCl$_3$): δ = 5.89 (d, J = 1.2Hz, 1H), 5.60-5.62 (m, 2H), 3.15 (d, J = 14.8Hz, 1H), 2.98 (d, J = 14.8Hz, 1H), 2.87 (td, J = 13.6Hz, 6.0Hz, 1H), 2.78 (tdd, J = 14.4Hz, 4.8Hz, 1.6Hz, 1H), 2.54-2.60 (m, 1H), 2.48-2.52 (m, 1H), 2.42-2.46 (m, 2H), 2.34 (dt, J = 14.4Hz, 4.0Hz, 1H), 2.10-2.21 (m, 2H), 1.70 ppm (qt, J = 13.6Hz, 4.4Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 208.8, 197.7, 164.0, 127.1, 126.3, 122.3, 54.6, 46.4, 39.0, 33.5, 32.1, 26.0, 23.7 ppm; EI MS (70 eV): m/z (%): 203 (79) [M-79]$^+$, 105(26), 91(49), 77(42), 55(100); HRMS (ESI): [M+H] calcd for C$_{13}$H$_{16}$O$_2$Br: 283.0823; found: 283.0823[M+H]$^+$; HPLC: Chiralpak AD column, hexane/iPrOH/C$_2$H$_5$OH 90:9:1 1.1 mL/min, t$_1$ = 14.4 min(minor), t$_2$ = 15.4 min(major) (83% ee)

$^1$H NMR (400 MHz, CDCl$_3$): δ = 5.93 (s, 1H), 2.76 (tdd, J = 14.4Hz, 5.6Hz, 1.2Hz, 1H), 2.64 (ddd, J = 14.0Hz, 5.6Hz, 2.0Hz, 1H), 2.53-2.60 (m, 2H), 2.48 (dt, J = 17.2Hz, 4.8Hz, 1H), 2.22-2.39 (m, 3H), 2.11-2.20 (m, 4H), 2.06 (m, 1H), 1.73 ppm (qt, J = 13.2Hz, 4.4Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 209.0, 197.0, 163.3, 127.1, 118.4, 53.1, 38.3, 33.0, 31.5, 29.8, 25.1, 22.9, 12.5 ppm; EI MS (70 eV): m/z (%): 217 (12) [M]$^+$, 177(23), 135(43), 91(68), 84(90), 55(100); HRMS (ESI): [M+NH$_4$] calcd for C$_{13}$H$_{19}$N$_2$O$_2$: 235.1441; found: 235.1446[M+NH$_4$]$^+$; HPLC: Chiralcel OD column, hexane/iPrOH/CH$_3$CN 88:10:2 1 mL/min, t$_1$ = 42.5 min(minor), t$_2$ = 49.3 min(major) (88% ee)
**HRMS** (ESI): [M+H] calcd for C_{11}H_{15}O_{2}: 179.1067; found: 179.1070[M+H]^+;

Spectral data are identical to authentic sample and to those previously reported.\(^1\)

![](image)

\(^1\)H **NMR** (400 MHz, CDCl\(_3\)): \(\delta = 5.81\) (d, \(J = 1.6\)Hz, 1H), 2.74 (tdd, \(J = 14.2\)Hz, 4.8Hz, 1.2Hz, 1H), 2.61 (td, \(J = 14.0\)Hz, 6.0Hz, 1H), 2.44-2.46 (m, 1H), 2.43-2.44 (m, 1H), 2.29-2.41 (m, 2H), 2.16 (tt, \(J = 14.4\)Hz, \(J = 4.0\)Hz, 1H), 2.07-2.12 (m, 1H), 1.93-2.01 (m, 2H), 7.74-1.84 (m, 2H), 1.64 (qt, \(J = 13.6\)Hz, 4.4Hz, 1H), 0.80 ppm (t, \(J = 7.2\)Hz, 3H); **C** **NMR** (100 MHz, CDCl\(_3\)): \(\delta = 210.0, 198.2, 166.2, 125.9, 55.0, 38.2, 33.3, 31.7, 28.1, 24.7, 23.3, 8.7\) ppm; **EI MS** (70 eV): m/z (%): 192 (21) [M]^+, 135(100), 107(40), 93(48), 79(62), 55(48); **HRMS** (ESI): [M+H] calcd for C_{12}H_{17}O_{2}: 193.1223; found: 193.1221[M+H]^+; **HPLC**: Chiralpak AD column, hexane/PrOH 95:5 1 mL/min, \(t_1 = 16.4\) min(minor), \(t_2 = 17.8\) min(major) (86% ee)

![](image)

\(^1\)H **NMR** (400 MHz, CDCl\(_3\)): \(\delta = 7.24-7.28\) (m, 3H), 7.01-7.03 (m, 2H), 5.95 (s, 1H), 3.20 (d, \(J = 13.6\)Hz, 1H), 3.13 (d, \(J = 13.6\)Hz, 1H), 2.61-2.75 (m, 2H), 2.40-2.59 (m, 2H), 2.24-2.40 (m, 2H), 2.06-2.16 (m, 2H), 1.98 (td, \(J = 14\)Hz, 6.0Hz, 1H), 1.68 ppm (qt, \(J = 13.2\)Hz, 4.4Hz, 1H); **C** **NMR** (100 MHz, CDCl\(_3\)): \(\delta = 209.9, 198.1, 165.0, 135.5, 129.5, 128.5, 127.5, 126.9, 55.8, 42.6, 39.1, 37.5, 32.6, 27.5, 23.1 ppm; **EI MS** (70 eV): m/z (%): 254 (5.5) [M]^+, 162(1.9), 134(5.4), 105(2.1), 91(100), 77(7.6), 55(13); **HRMS** (ESI): [M+H] calcd for C_{17}H_{19}O_{2}: 255.1338; found: 255.1377[M+H]^+; **HPLC**: Chiralpak AD column, hexane/PrOH/CH\(_3\)CH\(_2\)OH 92:7:1 1 mL/min, \(t_1 = 15.2\) min(minor), \(t_2 = 16.2\) min(major) (86% ee)
2. Experimental Procedures and Spectroscopic and Analytical Data of the Products 8 to 16.

1.1 — Synthesis of Compound 8.

To a dried 250mL flask, (PdCl₂H₅)₂ (422 mg, 1.15 mmol), dppe (1.84 g, 4.6 mmol) and the solvent THF (90 mL) was added under argon atmosphere, then allyl acetate (0.046 mol, 4.99 mL), 1,3-Cyclopentadione (0.046 mol, 4.5 g), BSA (0.046 mol, 11.39 mL), NaOAc (1.38 mmol, 0.11 g) was added. The mixture was heated to reflux for 40 h. The resulting brown solution was cooled to room temperature, quenched by addition of 70 mL CH₃OH, then the solvent was removed in vacuo. Purification of the residue through column chromatography on silica gel (CH₂Cl₂/CH₃OH 50:1) afforded the crude product 2-allylcyclopentane-1,3-dione.

To a solution of the crude 2-allylcyclopentane-1,3-dione in H₂O: AcOH = 100: 1.5 (90 mL) was added MVK (7.8 mL, 0.092 mol). The mixture was heated to reflux for 4 h. The resulting mixture was extracted with EtOAc (150 × 3 mL). The combined extracts were washed with saturated NaHCO₃ (20 × 5 mL) and dried over Na₂SO₄, and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 10:1 to 8:1) afforded 8 (6.21 g, 65% 2 steps).

¹H NMR (400 MHz, CDCl₃): δ = 5.60-5.48 (dtd, 1H, J = 15.2 Hz, 7.6 Hz and 7.6 Hz), 5.10-5.00 (m, 2H), 2.79-2.67 (A part of AA’BB’ system, m, 2H), 2.67-2.55 (B part of AA’BB’ system, m, 2H), 2.42-2.35 (t, J = 7.2 Hz, 2H), 2.31-2.25 (d, J = 7.6 Hz, 2H), 2.08-2.02 (s, 3H), 1.89-1.82 ppm (t, J = 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 215.7, 207.8, 131.0, 120.1, 59.2, 39.4, 37.4, 35.6, 29.9, 26.8 ppm; EI MS (70 eV): m/z (%): 208 (36) [M⁺], 137 (32), 122 (21), 105 (28), 43 (100), 41 (49); HRMS (ESI): m/z calcd for C₁₂H₁₅O₃: 208.1095; found: 208.1099 [M⁺].

1.2 — Synthesis of Compound 9.

See typical experimental procedure.
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.75\) (s, 1H), 5.58-5.45 (dttd, 1H, J = 16.8 Hz, 8.4 Hz and 8.4 Hz), 4.95-4.85 (m, 2H), 2.81-2.70 (m, 1H), 2.65-2.55 (m, 1H), 2.55-2.40 (m, 1H), 2.35-2.05 (m, 5H), 2.00-1.92 (dd, 1H, J = 13.6 Hz and 4.8 Hz), 1.59-1.48 ppm (ddd, 1H, J = 14.6 Hz, 14.6 Hz and 9.2 Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 215.2, 197.5, 168.8, 131.6, 124.0, 119.1, 52.1, 38.3, 35.6, 32.1, 26.8, 26.7 ppm; \)EI MS (70 eV): m/z (%): 190 (49) [M]\(^+\), 148 (37), 106 (56), 105 (45), 91 (100), 79 (37); \)HRMS (ESI): m/z calcd for C\(_{12}\)H\(_{14}\)O\(_2\): 190.0990; found: 190.0988 [M]\(^+\); \(\alpha\)\(^{20}\)D -244 (c 1.00, CHCl\(_3\)); HPLC Chiralpak AS column, hexane/iPrOH 65:35 1 mL/min, \(t_1 = 32.2\) min (minor), \(t_2 = 37.1\) min (major) (83% ee)

1.3 —— Synthesis of Compound 10.

To a solution of 9 (900 mg, 4.74 mmol) in dry CHCl\(_3\) (5 mL) was added HS(CH\(_2\))\(_3\)SH (0.526 mL, 5.21 mmol) and TMSCl (0.18 mL, 1.42 mmol). The mixture was stirred at room temperature for 7 h. The resulting mixture was extracted with EtOAc (40 \(\times\) 2 mL). The combined extracts were washed with 5% NaOH solution (5 \(\times\) 3 mL) and dried over Na\(_2\)SO\(_4\), and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 8:1 to 6:1) afforded 10 (994 mg, 75% yield).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.78\) (s, 1H), 5.78-5.62 (dttd, 1H, J = 16.8 Hz, 8.4 Hz and 8.4 Hz), 5.18-5.01 (m, 2H), 3.04-2.88 (m, 2H), 2.88-2.80 (m, 1H), 2.80-2.70 (m, 2H), 2.60-2.53 (m, 1H), 2.53-2.42 (m, 2H), 2.37-2.21 (m, 3H), 2.21-2.11 (ddd, 1H, J = 13.6 Hz, 13.6 Hz and 3.2 Hz), 2.11-2.00 (m, 1H), 1.96-1.82 (m, 2H), 1.64-1.53 ppm (ddd, 1H, J = 13.2 Hz, 13.2 Hz and 3.2 Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 216.9, 144.6, 132.6, 123.7, 118.6, 52.2, 48.2, 39.1, 36.5, 32.8, 27.5, 26.8, 26.3, 24.7, 23.8 ppm; \)EI MS (70 eV): m/z (%): 280 (27) [M]\(^+\), 239 (41), 91 (70), 84 (100), 77 (48), 45 (45); \)HRMS (ESI): m/z calcd for C\(_{15}\)H\(_{20}\)OS\(_2\): 280.0951; found: 280.0956 [M]\(^+\); \(\alpha\)\(^{20}\)D -231 (c 1.00, CHCl\(_3\)).

1.4 —— Synthesis of Compound 11.

To a dried 10 mL flask, 2mol/L BH\(_3\) • Me\(_2\)S (1.07 mL, 2.14 mmol), cyclohexene (0.434 mL,
4.28 mmol) and THF (1 mL) was added under argon atmosphere at 0°C. The mixture was stirred at 0°C for 1 h. Then 10 (600 mg, 2.14 mmol) was added. The mixture was stirred at room temperature for 3 h. The resulting solution was quenched by addition of NaBO₃ • 4H₂O (989 mg, 6.42 mmol) and H₂O (1 mL), then it was stirred at room temperature for 4 h. The resulting mixture was extracted with EtOAc (40 × 2 mL). The combined extracts were dried over Na₂SO₄, and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 2:1) afforded 11 (607 mg, 95% yield).

**1H NMR** (400 MHz, CDCl₃): δ = 5.65 (s, 1H), 3.50-3.40 (m, 2H), 2.94-2.80 (m, 2H), 2.78-2.62 (m, 3H), 2.60-2.33 (m, 4H), 2.23-2.11 (m, 1H), 2.11-1.92 (m, 2H), 1.86-1.70 (m, 2H), 1.60-1.33 ppm (m, 5H); **13C NMR** (100 MHz, CDCl₃): δ = 217.5, 145.0, 123.0, 62.0, 51.4, 47.9, 36.1, 32.6, 30.1, 27.1, 26.8, 26.2, 26.0, 24.4, 22.9 ppm; **EI MS** (70 eV): m/z (%): 298 (11), 123 (14), 91 (24), 83 (32), 43 (100), 41 (32); **HRMS** (ESI): m/z calcd for C₁₅H₂₂O₂S₂: 298.1056; found: 298.1060 [M⁺]; [α]²⁰D -143 (c 1.00, CHCl₃).

**1.5 Synthesis of Compound 12.**

To a solution of 11 (300 mg, 1 mmol) in EtOH (10 mL) was added W-2 Raney Ni a little every 10 minutes until the solution, which turned red at first, finally got colorless again. It took about 2 h. The mixture was purified through column chromatography first on Al₂O₃ (EtOAc) then on silica gel (petroleum/EtOAc 2:1) afforded 12 (160 mg, 82% yield).

**1H NMR** (300 MHz, CDCl₃): δ = 5.58 (m, 1H), 3.60-3.45 (m, 2H), 2.75-2.60 (m, 1H), 2.52-2.40 (m, 2H), 2.25-2.10 (m, 2H), 2.00-1.80 (m, 3H), 1.80-1.20 ppm (m, 7H); **13C NMR** (75 MHz, CDCl₃): δ = 220.5, 141.2, 121.4, 62.7, 50.4, 36.6, 30.6, 27.1, 26.8, 25.6, 24.3, 17.9 ppm; **EI MS** (70 eV): m/z (%): 194 (40) [M⁺], 150 (47), 135 (90), 107 (57), 93 (100), 91 (98); **HRMS** (ESI): m/z calcd for C₁₂H₁₈O₂: 194.1302; found: 194.1299 [M⁺]; [α]²⁰D -126 (c 1.00, CHCl₃).

**1.6 Synthesis of Compound 13.**
To a solution of 12 (135 mg, 0.7 mmol) in dry CH₂Cl₂ (14 mL) was added Et₃N (0.107 mL, 0.77 mmol) and then MsCl (0.06 mL, 0.77 mmol). The mixture was stirred at room temperature for 10 minutes. The reaction was quenched by H₂O. The mixture was extracted with CH₂Cl₂ (30 × 2 mL). The combined extracts were dried over Na₂SO₄, and concentrated under reduced pressure to give the product quantitatively. The product was dissolved in dry DMF (3 mL), then NaN₃ (228 mg, 3.5 mmol) was added. The mixture was stirred at room temperature for 2 days. The reaction was quenched by H₂O. The resulting mixture was extracted with EtOAc: CH₂Cl₂ = 10:1 (30 × 2 mL). The combined extracts were washed with H₂O (2 × 5 mL) dried over Na₂SO₄, and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 16:1) afforded 13 (133 mg, 87% 2 steps).

**¹H NMR** (300 MHz, CDCl₃): δ = 5.60 (m, 1H), 3.25-3.15 (m, 2H), 2.75-2.60 (m, 1H), 2.60-2.60 (m, 2H), 2.29-2.09 (m, 1H), 2.10-1.80 (m, 3H), 1.70-1.10 ppm (m, 7H); **¹³C NMR** (75 MHz, CDCl₃): δ = 219.7, 140.9, 121.7, 51.5, 50.2, 36.7, 31.3, 26.8, 25.6, 24.3, 23.5, 17.9 ppm; **EI MS** (70 eV): m/z (%): 219 (12) [M]+, 191 (16), 190 (32), 162 (96), 135 (83), 91 (100); [α]₂⁰D -170 (c 1.00, CHCl₃).

**1.7 Synthesis of Compound 14.**

To a dried 5mL flask, compound 13 (224 mg, 1.02 mmol) was added under argon atmosphere, then BF₃·Et₂O (0.258 mL, 2.04 mmol) was added. The mixture was stirred at room temperature for 1 minute. The reaction was quenched by H₂O. The resulting mixture was extracted with EtOAc: CH₂Cl₂ = 10:1 (30 × 2 mL). The combined extracts were dried over Na₂SO₄, and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 1:1) afforded 14 (138 mg, 70% yield).

**¹H NMR** (300 MHz, CDCl₃): δ = 4.15-4.00 (m, 1H), 3.20-3.10 (m, 1H), 2.50-2.38 (m, 1H), 2.38-2.20 (m, 2H), 2.20-2.10 (m, 1H), 2.10-2.00 (m, 2H), 1.95-1.70 (m, 6H), 1.70-1.48 (m, 2H), 1.35-1.20 ppm (m, 1H); **¹³C NMR** (75 MHz, CDCl₃): δ = 169.5, 135.5, 123.8, 63.2, 41.5, 34.7, 33.0, 31.5, 27.7, 23.7, 20.1, 19.1 ppm; **EI MS** (70 eV): m/z (%): 191 (29) [M]+, 164 (12), 163 (100), 135 (21), 134 (30), 41 (16); **HRMS** (ESI): m/z calcd for C₁₂H₁₇NO: 191.1306; found: 191.1309 [M]+; [α]₂⁰D -133 (c 1.00, CHCl₃).

**1.8 Synthesis of Compound 15.**
To a solution of 14 (115 mg, 0.6 mmol) in EtOAc (30 mL) was added Pd-C (65 mg). The mixture was stirred under H₂ atmosphere at room temperature for 10 h. Then the Pd-C was filtrated and the resulting mixture was concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (EtOAc) afforded 15 (96 mg, 83% yield).

\[ ^1H \text{ NMR (300 MHz, CDCl}_3): \delta = 3.75-3.60 \ (m, \ 1H), \ 3.35-3.20 \ (m, \ 1H), \ 2.45-2.30 \ (m, \ 1H), \ 2.30-2.19 \ (m, \ 2H), \ 2.19-2.00 \ (m, \ 1H), \ 1.85-1.70 \ (m, \ 2H), \ 1.65-1.10 \ \text{ppm (m, 11H)}; \]
\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3): \delta = 168.5, \ 63.8, \ 43.6, \ 39.9, \ 35.7, \ 30.7, \ 29.7, \ 28.6, \ 23.2, \ 22.6 \]
\[ 19.9, \ 19.4 \ \text{ppm}; \]
\[ \text{El MS (70 eV): } m/z (\%): 193 (12) [M]^+, 150 (100), 137 (11), 108 (14); \]
\[ \text{HRMS (ESI): } m/z \ \text{calcd for } C_{12}H_{19}NO: 193.1462; \text{ found: 193.1467 } [M]^+; \]
\[ [\alpha]_{20}^{D} +15 (c 1.00, \text{CHCl}_3). \]

1.9 Synthesis of Compound 16.

To a solution of 15 (54 mg, 0.28 mmol) in toluene (5 mL) was added Lawesson's Reagent (85 mg, 0.21 mmol). The mixture was heated to reflux for 30 minutes. The resulting mixture was concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (petroleum/EtOAc 20:1 to 16:1) afforded 16 (56 mg, 96% yield).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3): \delta = 4.25-4.15 \ (m, \ 1H), \ 3.82-3.70 \ (m, \ 1H), \ 3.22-3.10 \ (m, \ 1H), \ 3.00-2.85 \ (m, \ 1H), \ 2.52-2.40 \ (m, \ 1H), \ 2.20-2.00 \ (m, \ 1H), \ 2.00-1.85 \ (m, \ 2H), \ 1.80-1.05 \ \text{ppm (m, 11H)}; \]
\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta = 195.2, \ 67.6, \ 52.0, \ 39.9, \ 39.1, \ 35.3, \ 28.9, \ 28.7, \ 23.2, \ 22.2 \ 19.3, \ 19.3 \ \text{ppm}; \]
\[ \text{El MS (70 eV): } m/z (\%): 209 (52) [M]^+, 176 (22), 166 (100), 152 (16), 133 (14), 120 (10); \]
\[ [\alpha]_{20}^{D} -62 (c 1.00, \text{CHCl}_3). \]

References:
