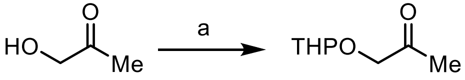
Supporting Information

Table of Contents:

Summary of Prior Synthesis of Andrographolide

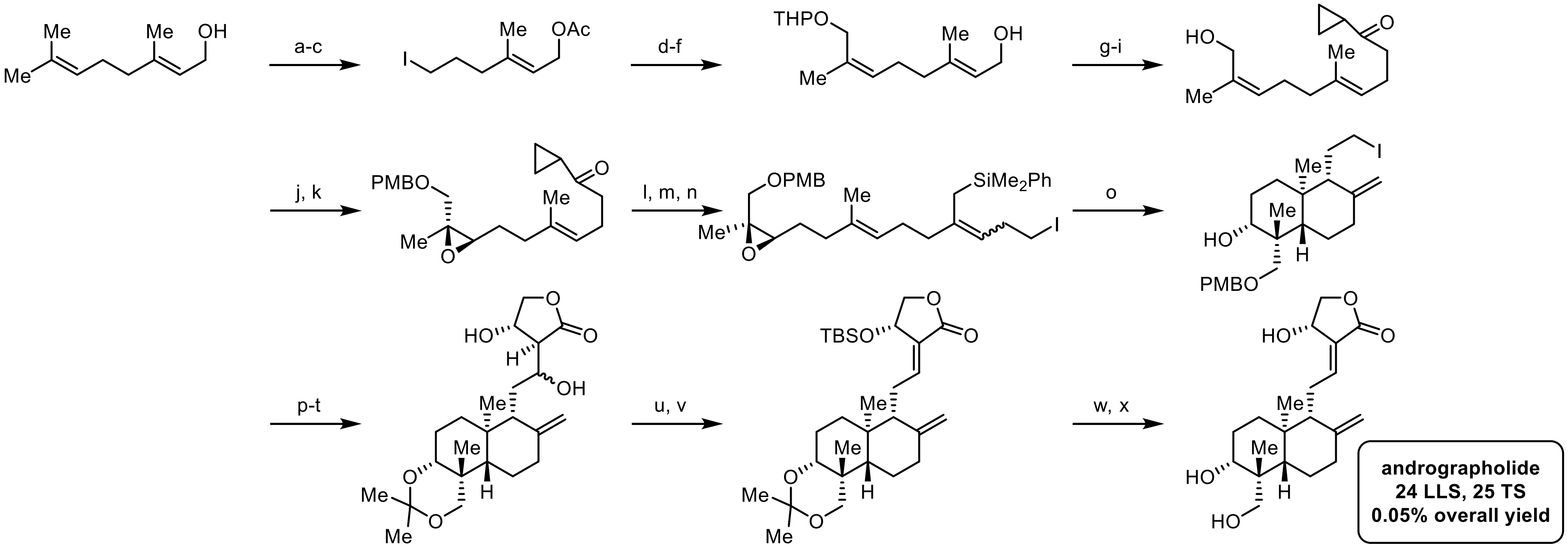
Li, W.-D. Z. *et al. Tetrahedron* **2014**, *70*, 9436.

Fragment 1



Key: (a) DHP, PPTS

Completion of Synthesis



Key: (a) Ac_2O, Pyridine; (b) O_3, then $NaBH_4$; (c) I_2, PPh_3 imid.; (d) K_2CO_3; (e) PPh_3; (f) **1**, ^nBuLi; (g) I_2, PPh_3, imid.; (h) cyclopropyl methyl ketone, LDA; (i) PTSA; (j) $Ti(OiPr)_4$, (+)-DIPT, ^tBuOOH, 86% ee; (k) PMBBr, NaH, TBAI; (l) $PhMe_2SiCH_2MgCl$, $CeCl_3$; (m) $MgI_2\bullet(OEt_2)_n$; (n) K_2CO_3; (o) $SnCl_4$; (p) DDQ; (q) K_2CO_3; (r) $Me_2C(OMe)_2$, PPTS (s) $NaHCO_3$, DMSO; (t) (*S*)-β-Hydroxy-γ-butyrolactone, LDA; (u) TBSCl, imid.; (v) MsCl, TEA; (w) TBAF; (x) HOAc.

General Information

All reactions were run under an atmosphere of argon, unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fisher Scientific (catalog number 14–959–35C) and were flame dried followed by cooling in a desiccator or under a stream of argon prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Strem Chemicals, Fisher Scientific, Sigma Aldrich and Combi Blocks) without further purification. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still. Analytical thin layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F254). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or KMnO4 stain solution followed by heating. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in $CHCl_3$. Solution concentrations are given in the units of 10^{-2} g mL^{-1}.

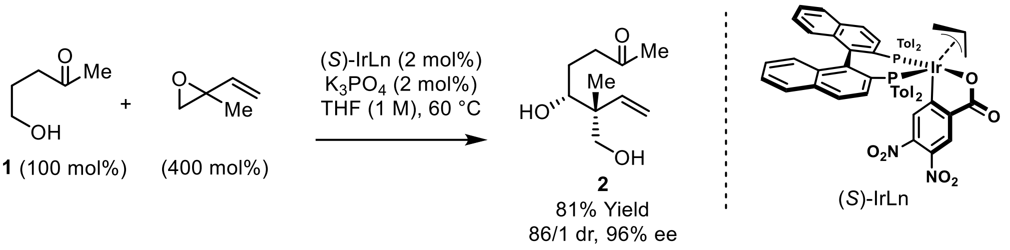
Spectroscopy, Spectrometry, and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Proton nuclear magnetic resonance (1H NMR) spectra were recorded with a Varian INOVA (500 MHz) spectrometer equipped with a Bruker AVANCE III cryoprobe.

Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for $CHCl_3$. Data reported as multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Carbon-13 nuclear magnetic resonance (13C NMR) spectra were recorded with a Varian INOVA (125 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.16 ppm for deuteriochloroform.

Detailed Procedures and Spectral Data for Asymmetric Synthesis of Andrographolide

(5*R*,6*R*)-5-Hydroxy-6-(hydroxymethyl)-6-methyloct-7-en-2-one (2)



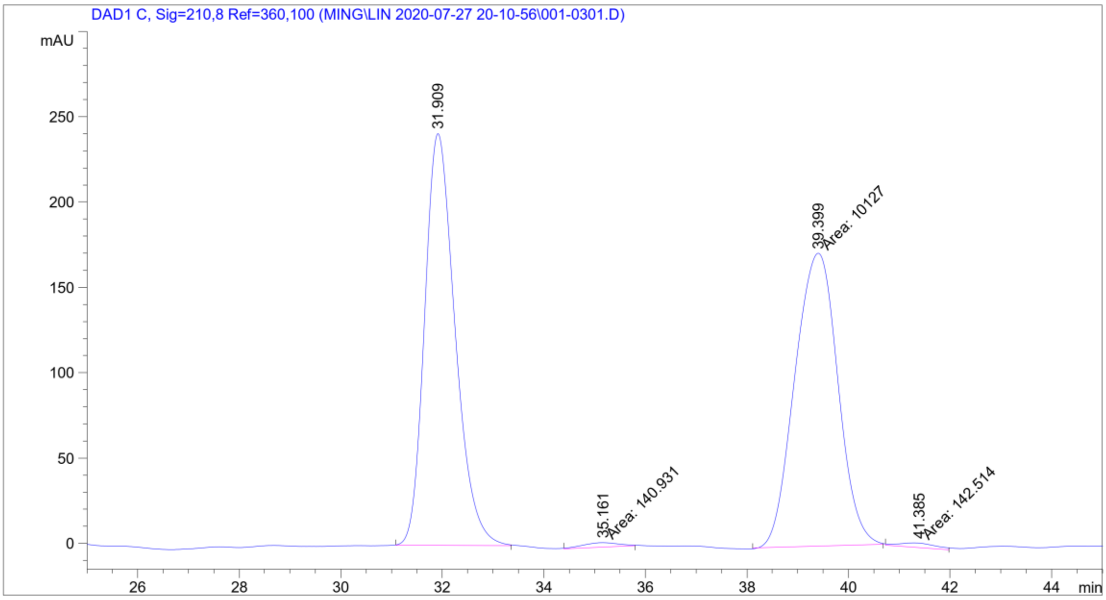
Detailed Procedures

Catalyst (*S*)-IrLn[1] (1.00 g, 0.98 mmol, 2 mol%) and K_3PO_4 (0.21 g, 0.98 mmol, 2 mol%) were added to a flame-dried seal tube and purged with argon. Anhydrous THF (49 mL) was added, followed by 5-hydroxypentan-2-one **1** (5.01 g, 10 mmol, 100 mol%) and isoprene monoxide (19.3 mL, 196 mmol, 400 mol%) via syringe. (**Caution:** K_3PO_4 is hygroscopic. Please make sure all the base solid is placed at the bottom of reaction vial and submerged by solvent). After sealed with cap, the resulting mixture was allowed to stir at 60 °C for 5 days. The solution was cooled to ambient temperature and concentrated under reduced pressure. The residue was submitted to flash column chromatography on silica gel (pretreated with triethylamine, DCM (CH_2Cl_2)/acetone = 10/1 to 5/1). *Cautions: product starts converting to ketal upon gently heating (>30 ˚C) under neutral or acidic condition!* The title compound **2** was isolated as a brown oil (7.37 g, 39.6 mmol) in 81% yield. *Product exists as an equilibrating mixture between hydroxyl ketone and two diastereomeric lactols (equilibrated ratio 0.5:0.3:0.2).*

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07* (dd, *J* = 18.0, 11.3 Hz, 1H (minor2)), 6.00 (dd, *J* = 17.8, 11.1 Hz, 1H, (major)), 5.95* (dd, *J* = 17.8, 11.0 Hz, 1H, (minor1)), 5.30-5.21 (m, 1H (major, minor1, minor2)), 5.19* (dd, *J* = 8.7, 1.4 Hz, 1H (minor1)), 5.15* (dd, *J* = 8.8, 1.4 Hz, 1H (minor2)), 5.14 (dd, *J* = 17.8, 1.4 Hz, 1H (major)), 4.19* (t, *J* = 6.8 Hz, 1H (minor1)), 4.00* (dd, *J* = 10.0, 5.8 Hz, 1H (minor2)), 3.69 (d, *J* =10.9 Hz, 1H (major)), 3.61-3.48 (m, 2H (major, minor1, minor2)), 3.25 (br, 1H (major)), 2.96* (br, 2H (minor1, minor2)), 2.66 (td, *J* = 6.7, 4.0 Hz, 2H (major)), 2.17 (s, 3H (major)), 2.12-1.90 (m, 1H (major) + 2H (minor1, minor2)), 1.87-1.54 (m, 2H (major, minor1, minor2)), 1.52* (s, 3H (minor1, minor2)), 1.00 (s, 3H (major)), 0.98* (s, 3H (minor2)), 0.96* (s, 3H (minor1)).

The spectral data recorded for the compound was in complete agreement with the literature.[2]

HPLC Diastereomeric ratio and enantiomeric excess was determined by HPLC analysis of the dibenzoate of product (Chiralcel AD-H column, hexanes/i-PrOH = 97:3, 0.50 mL/min, 230 nm), *anti:syn* = 86:1, ee = 96%.



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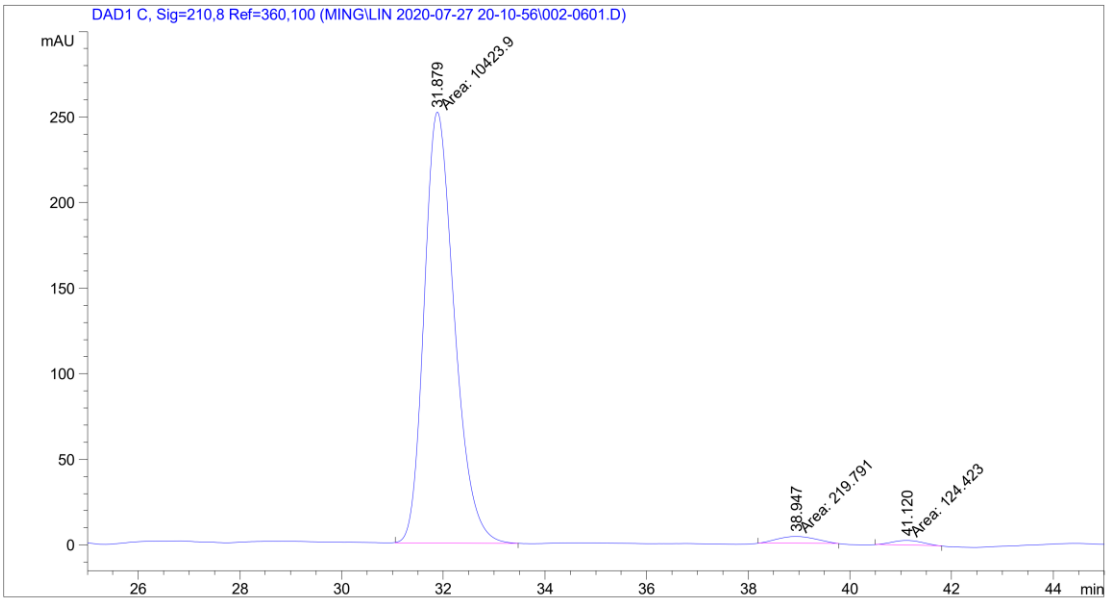

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   2  38.947 MM    0.8948  219.79094    4.09401   2.0411
   3  41.120 MM    0.7166  124.42339    2.89389   1.1555
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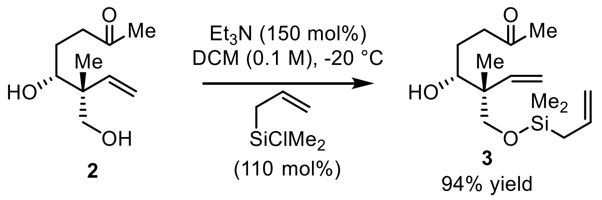
(5*R*,6*R*)-6-(((Allyldimethylsilyl)oxy)methyl)-5-hydroxy-6-methyloct-7-en-2-one (3)



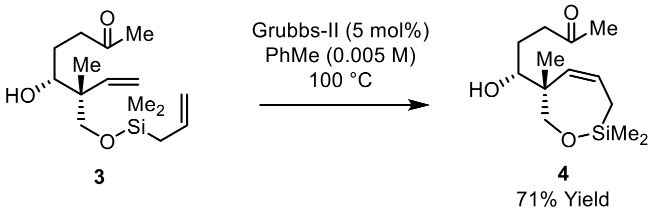
Detailed Procedures

To a solution of **2** (4.88 g, 26 mmol, 100 mol%) in anhydrous DCM (268 mL), freshly distilled triethylamine (5.45 mL, 39 mmol, 150 mol%) was added and the resulting mixture was cooled to -20 °C. Allyl(chloro)dimethylsilane (4.0 mL, 28 mmol, 105 mol%) was added dropwise via syringe over 1.5 hours. The mixture was allowed to stir for 30 min at the same temperature and quenched by addition of saturated $NaHCO_3$ aqueous solution. The two layers were separated. The organic layer was washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was subjected to flash column chromatography on silica gel (hexanes/acetone = 15/1). The title compound **3** was obtained as a light yellow liquid (7.01 g, 25 mmol) in 94% yield. *Product exists as an equilibrating mixture between hydroxy ketone and two diastereomeric lactols (equilibrated ratio 0.74:0.13:0.13).*

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (dd, *J* = 17.8, 11.1 Hz, 1H (major)), 5.94* (dd, *J* = 17.8, 11.0 Hz, 1H (minor1)), 5.88-5.72 (m, 1H (major, minor1, minor2)), 5.21* (dd, *J* = 11.0, 1.5 Hz, 1H (minor1)), 5.17 (dd, *J* = 11.1, 1.3 Hz, 1H (major)), 5.16* (dd, *J* = 11.0, 1.6 Hz, 1H (minor2)), 5.12* (dd, *J* = 17.8, 1.6 Hz, 1H (minor1)), 5.09* (dd, *J* = 17.7, 1.7 Hz, 1H (minor2)), 5.06 (dd, *J* = 17.8, 1.3 Hz, 1H (major)), 4.96-4.82 (m, 2H (major, minor1, minor2)), 4.23-4.16* (m, 1H (minor2)), 4.05-3.96* (m, 1H (minor1)), 3.71 (d, *J* = 9.7 Hz, 1H (major)), 3.61* (d, *J* = 9.7 Hz, 1H (minor1)), 3.60* (d, *J* = 9.6 Hz, 1H (minor2)), 3.51 (d, *J* = 9.7 Hz, 1H (major)), 3.51-3.46 (m, 1H (major, minor2)), 3.48* (d, *J* = 9.6 Hz, 1H (minor1)), 3.40 (dd, *J* = 4.7, 1.0 Hz, 1H (major)), 3.38* (d, *J* = 9.6 Hz, 1H (minor2)), 2.72 (ddd, *J* = 17.6, 8.4, 5.8 Hz, 1H (major)), 2.53* (br, 1H (minor1)), 2.53 (ddd, *J* = 17.8, 8.2, 6.7 Hz, 1H (major)), 2.15 (s,3H (major)), 2.11* (t, *J* = 0.9 Hz, 1H (minor2)), 2.07-1.88* (m, 2H (minor1, minor2)), 1.85-1.73 (m, 1H (major, minor1) + 2H (minor2)), 1.73-1.66* (m, 1H (minor1)), 1.65-1.60 (m, 2H (major, minor1, minor2)), 1.59-1.47 (m, 1H (major1)), 1.50 (s, 1H (minor2)), 1.49 (s, 1H (minor1)), 0.98 (s, 3H (major)), 0.97* (s, 3H (minor1)), 0.93* (s, 3H (minor2)), 0.13 (s, 6H (major)), 0.11* (s, 6H (minor1)), 0.09* (s, 6H (minor2)).

The spectral data recorded for the compound was in complete agreement with the literature.[2]

(*R*)-5-Hydroxy-5-((*R*)-2,2,6-Trimethyl-2,3,6,7-tetrahydro-1,2-oxasilepin-6-yl)pentan-2-one (4)



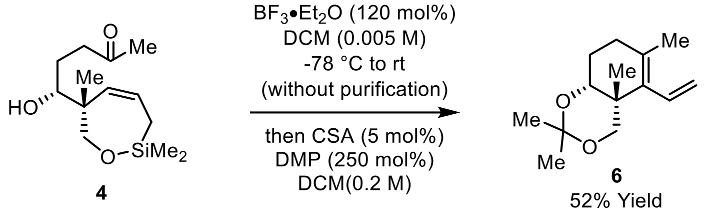
Detailed Procedures

A solution of **3** (2.3 g, 8.1 mmol, 100 mol%) in toluene (1570 mL) was degassed by freeze-pump-thaw cycle three times. The solution was heated to 100 ˚C, and a freshly made solution of Grubbs-II catalyst (0.343 g, 0.4 mmol, 5 mol%) in toluene (36 mL) was added via syringe pump over a 2 hour period. The reaction mixture was allowed to stir at the same temperature for 3 hours. The reaction mixture was allowed to cool to ambient temperature and was cooled further in an ice bath, at which point DMSO (1.43 mL, 20 mmol, 250 mol%) was added. After stirring for 12 hours, the solvent was removed under reduced pressure. The residue was subjected to flash column chromatography on silica gel (pretreated with triethylamine, hexanes/acetone = 15/1). The title compound **4** was obtained as a brown oil (1.48 g, 5.75 mmol) in 71% yield, which solidified upon standing in a -20 ˚C freezer. *Product exists as an equilibrating mixture between hydroxy ketone and two diastereomeric lactols (equilibrated ratio 0.55:0.26:0.19).*

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.78 (dt, J = 11.6, 7.3 Hz, 1H (major)), 5.74* (dt, J = 11.7, 7.3 Hz, 1H (minor2)), 5.66* (ddd, J = 11.7, 7.8, 6.8 Hz, 1H (minor1)), 5.21 (d, J = 12.4 Hz, 1H (major)), 5.17* (d, J = 12.0 Hz, 1H (minor2)), 5.15* (d, J = 12.0 Hz, 1H (minor1)), 4.23* (dd, J = 11.9, 0.8 Hz, 1H (minor1)), 4.07* (d, J = 11.7 Hz, 1H (minor2)), 4.05* (dd, J = 8.1, 5.6 Hz, 1H (minor1)), 4.00 (dd, J = 11.9, 0.9 Hz, 1H (major)), 3.88* (dd, J = 10.3, 6.4 Hz, 1H (minor2)), 3.81 (d, J = 11.9 Hz, 1H (major)), 3.65* (dd, J = 12.0, 0.7 Hz, 1H (minor1)), 3.57* (dd, J = 11.7, 0.9 Hz, 1H (minor2)), 3.39 (ddd, J = 11.0, 4.7, 2.2 Hz, 1H (major)), 3.27* (br, 1H (minor1)), 2.97 (dd, J = 4.7, 0.7 Hz, 1H (major)), 2.70 (ddd, J = 17.8, 7.8, 6.1 Hz, 1H (major)), 2.55 (dt, J = 17.7, 7.2 Hz, 1H (major)), 2.25-2.14* (m, 1H (minor1)), 2.16 (s, 3H (major)), 2.13-2.03* (m, 1H (minor2)), 2.01-1.74 (m, 1H (major) + 3H (minor1, minor2)), 1.70-1.56 (m, 3H (major) + 2H (minor1, minor2)), 1.54-1.44* (m, 1H (minor2)), 1.51* (s, 3H (minor2)), 1.50* (s, 3H (minor1)), 0.99* (s, 3H (minor1)), 0.98* (s, 3H (minor2)), 0.92 (s, 3H (major)), 0.16* (s, 3H (minor1)), 0.15 (s, 3H (major)), 0.14 (s, 3H (major)), 0.14* (s, 3H (minor1)), 0.13* (s, 3H (minor2)), 0.13* (s, 3H (minor2)).

The spectral data recorded for the compound was in complete agreement with the literature.[2]

(4a*R*,8a*R*)-2,2,4a,6-Tetramethyl-5-vinyl-4a,7,8,8a-tetrahydro-4H-benzo[d][1,3]dioxine (6)



Detailed Procedures

To a solution of **4** (1.20 g, 4.46 mmol, 100 mol%) in DCM (940 mL) at -78 ˚C, $BF_3{\cdot}OEt_2$ (0.69 mL, 5.57 mmol, 120 mol%) was added dropwise. The resulting solution was allowed to warm to room temperature over an hour and was allowed to stir for 24 hours. $NaHCO_3$ (aq., sat., 400 mL) was added and the reaction mixture was allowed to stir vigorously overnight. The reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted with DCM (150 mL × 2). The combined organic layers were washed with brine (150 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure (<30 ˚C), and the crude residue was dissolved in DCM (20 mL). 2,2-Dimethoxypropane (DMP, 1.4 mL, 11.2 mmol, 250 mol%) and (+)-10-camphorsulfonic acid (CSA, 54 mg, 0.23 mmol, 5 mol%) were added at room temperature, and the reaction mixture was allowed to stir for 5 hours. $NaHCO_3$ (aq., sat., 10 mL) was added to the reaction mixture. The reaction mixture was transferred to a separatory funnel, and the aqueous layer was extracted with DCM (20 mL × 2). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure (<30 ˚C), and the residue was submitted to flash column chromatography on a short plug of basic alumina (DCM). The title compound **6** was obtained as a colorless oil (0.537 g, 2.32 mmol) in 52% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (dd, J = 17.8, 11.3 Hz, 1H), 5.24 (dd, J = 11.3, 2.4 Hz, 1H), 5.00 (dd, J = 17.8, 2.4 Hz, 1H), 3.80 – 3.75 (m, 2H), 3.45 (d, J = 11.8 Hz, 1H), 2.29 (td, J = 14.8, 13.7, 9.4 Hz, 1H), 1.84 – 1.75 (m, 2H), 1.72 (s, 3H), 1.69 – 1.64 (m, 1H), 1.41 (s, 3H), 1.29 (s, 3H), 0.90 (s, 3H).

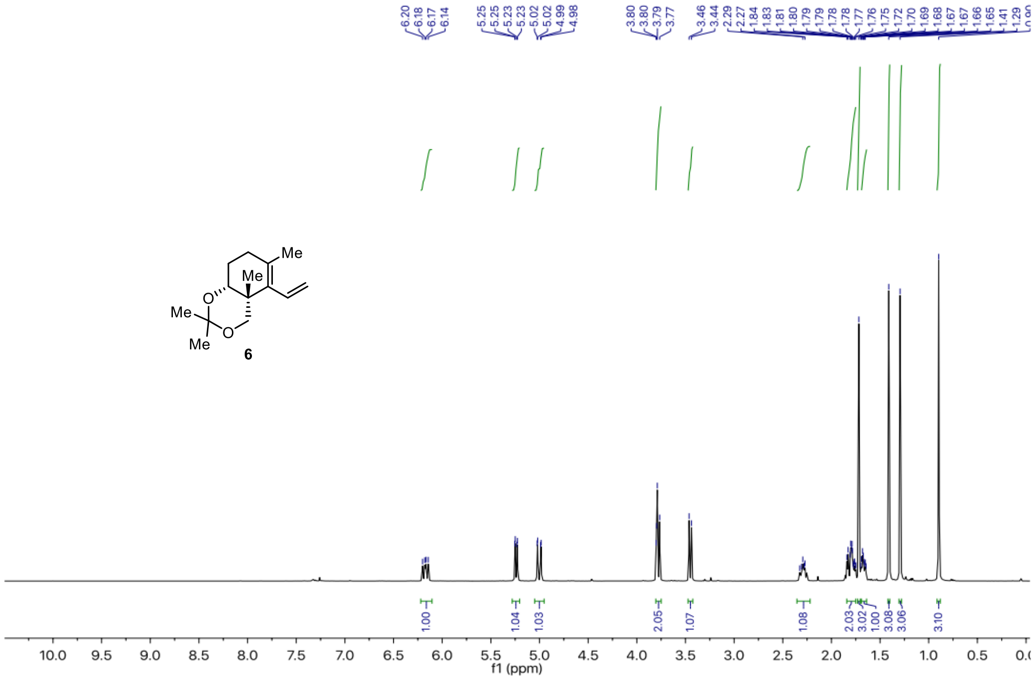
^{13}C NMR (125 MHz, $CDCl_3$) δ 134.6, 132.1, 130.6, 118.4, 98.0, 71.8, 67.3, 36.6, 28.2, 27.3, 23.5, 22.2, 21.1, 20.1.

R_f 0.69 (DCM, UV/$KMnO_4$)

HRMS (CI) Calcd. for $C_{14}H_{22}O_2$ $[M]^+$: 222.1620, found: 222.1615.

FTIR (neat): 2989, 2932, 2864, 1447, 1240, 1227, 1197, 1122, 1085 cm^{-1}.

Optical Rotation $[\alpha]_D^{26}$ = -124° (c = 1.0, $CHCl_3$)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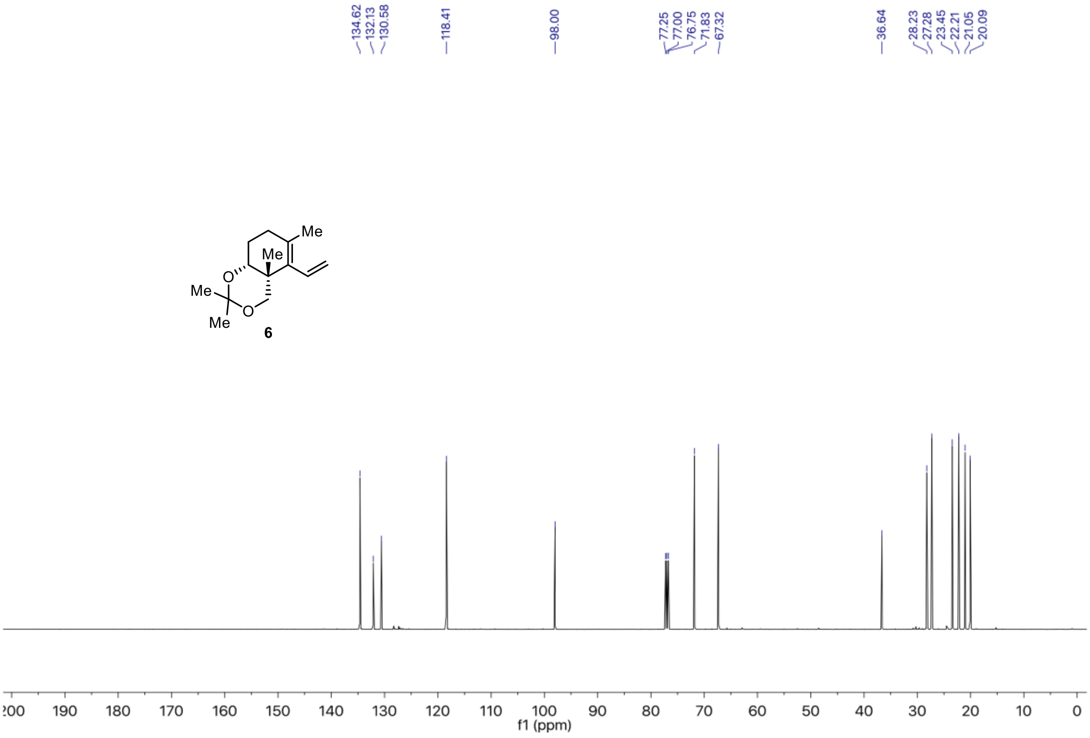
6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20.09
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Me
O
O
Me
Me
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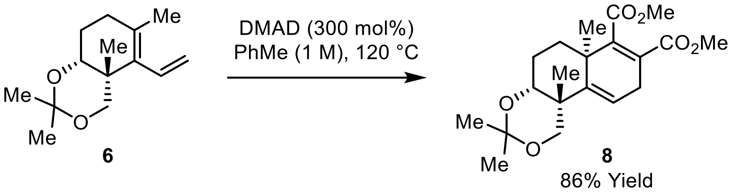
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

6

Dimethyl (4a*R*,6a*R*,10b*R*)-3,3,6a,10b-tetramethyl-4a,5,6,6a,9,10b-hexahydro-1H-naphtho[2,1-d][1,3]dioxine-7,8-dicarboxylate (8)



Detailed Procedures

To a solution of **6** (165 mg, 0.74 mmol, 100 mol%) in toluene (0.7 mL) was added dimethyl acetylenedicarboxylate (DMAD, 316 mg, 2.23 mmol, 300 mol%). The mixture was heated to 120 ˚C in seal tube for 24 hours with stirring. The reaction mixture was allowed to cool to ambient temperature. The solvent was removed and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 15/1 to 5/1). The title compound **8** was obtained as a colorless oil (207 mg, 0.64 mmol) in 86% yield.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.84 (dd, *J* = 6.3, 1.7 Hz, 1H), 3.97 (d, *J* = 12.0 Hz, 1H), 3.82 (s, 3H), 3.80 (dd, *J* = 7.4, 1.5 Hz, 1H), 3.74 (s, 3H), 3.50 (d, *J* = 12.1 Hz, 1H), 3.20 (dd, *J* = 22.0, 6.3 Hz, 1H), 2.89 (dd, *J* = 22.0, 1.7 Hz, 1H), 2.20 – 2.07 (m, 1H), 1.92 – 1.75 (m, 2H), 1.63 – 1.55 (m, 2H), 1.51 (s, 3H), 1.42 (s, 3H), 1.36 (s, 3H), 1.01 (s, 3H).

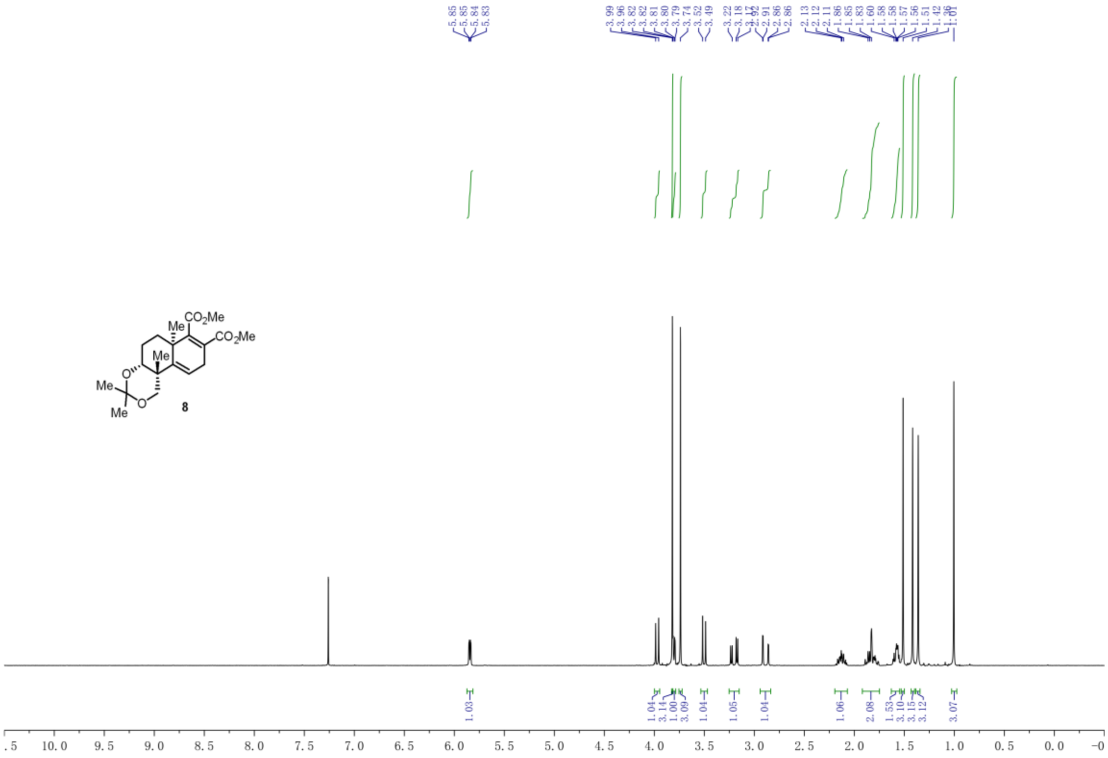
^{13}C NMR (125 MHz, CDCl$_3$) δ 169.7, 166.3, 152.3, 144.8, 126.5, 119.8, 98.7, 72.4, 68.4, 52.3, 52.1, 38.8, 38.6, 28.3, 28.3, 27.0, 26.2, 25.2, 24.7, 20.9.

Rf 0.35 (hexanes/ethyl acetate = 7:3, UV/KMnO$_4$)

HRMS (ESI) Calcd. for (M+Na)$^+$ 387.1778, found: 387.1779.

FTIR (neat): 3465, 2953, 1731, 1438, 1378, 1262, 1203 cm^{-1}.

Optical Rotation $[\alpha]_D^{26}$ = +84° (*c* = 1.0, CHCl$_3$)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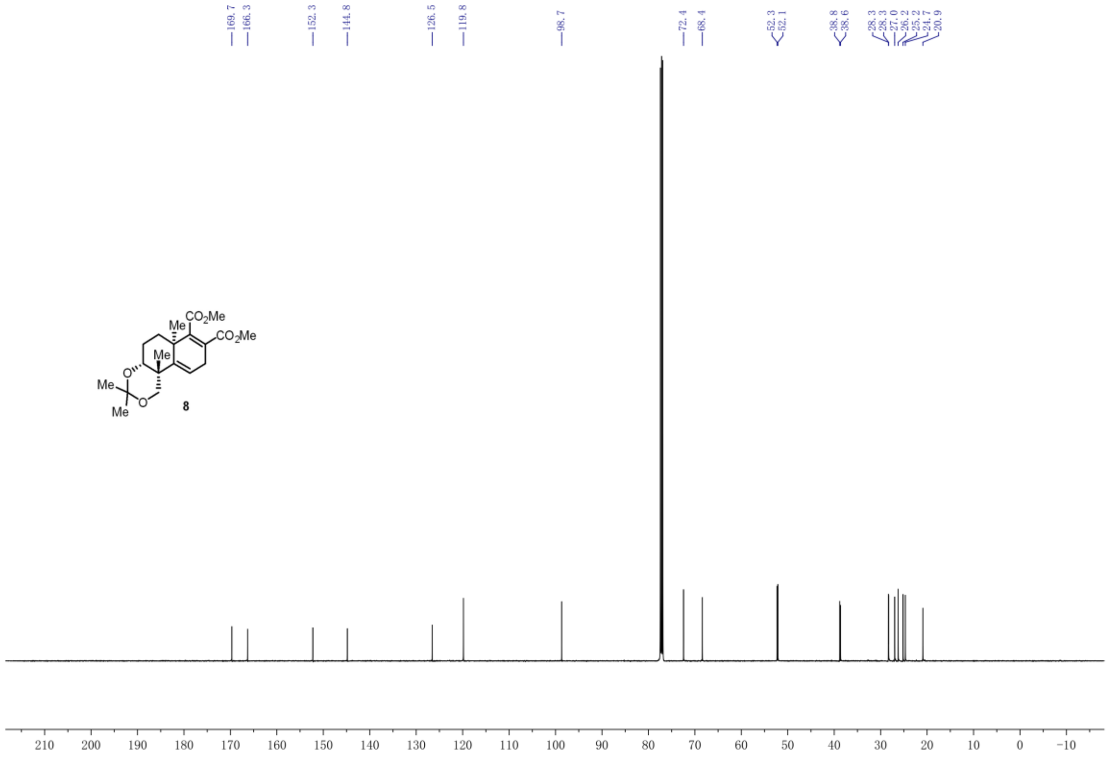
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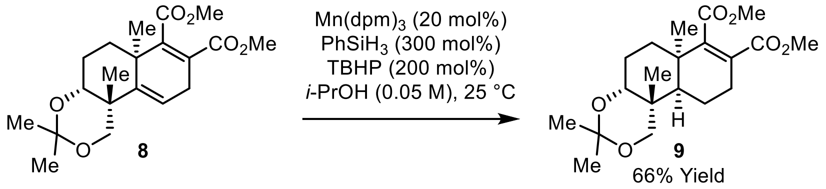
144.8
126.5
119.8
98.7
72.4
68.4
52.3
52.1
38.8
38.6
28.3
28.3
27.0
26.2
25.2
24.7
20.9
CO2Me
Me
CO2Me
Me
O
Me
Me
O
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10

Dimethyl (4a*R*,6a*R*,10a*R*,10b*R*)-3,3,6a,10b-tetramethyl-4a,5,6,6a,9,10,10a,10b-octahydro-1H-naphtho[2,1-d][1,3]dioxine-7,8-dicarboxylate (9)



Detailed Procedures

To a reaction vessel charged with a solution of olefin **8** (54 mg, 0.15 mmol, 100 mol%) in anhydrous *i*-PrOH (3 mL) under argon, was added phenylsilane (54 µL, 0.44 mmol, 300 mol%) and TBHP (5.5 M in decane, 53 µL, 0.29 mmol, 200 mol%). The resulting mixture was degassed by bubbling argon through the solution for 20 minutes. Mn(dpm)$_3$ (133 mg, 0.22 mmol, 20 mol%) was then added in one portion and the reaction was then degassed for an additional 30 seconds, and was allowed to stir at ambient temperature for 8 hours. After completion, the solvent was removed and subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 4/1). The title compound **9** was obtained as a white solid (36 mg, 0.10 mmol) in 66% yield.

^{1}H NMR (500 MHz, CDCl$_3$) δ 3.82 (s, 3H), 3.70 (s, 3H), 3.69 (d, J = 12.2 Hz, 1H), 3.62 (s, 1H), 3.35 (d, J = 12.2 Hz, 1H), 2.49 – 2.39 (m, 1H), 2.37 – 2.29 (m, 2H), 2.17 – 2.06 (m, 1H), 1.83 (qd, J = 15.7, 5.9 Hz, 3H), 1.46 – 1.42 (m, 1H), 1.42 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 0.81 (s, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 170.1, 166.9, 151.0, 128.6, 98.3, 74.0, 67.9, 52.2, 52.0, 37.0, 35.8, 35.7, 33.2, 30.7, 29.9, 24.7, 23.0, 19.0, 17.6, 16.5.

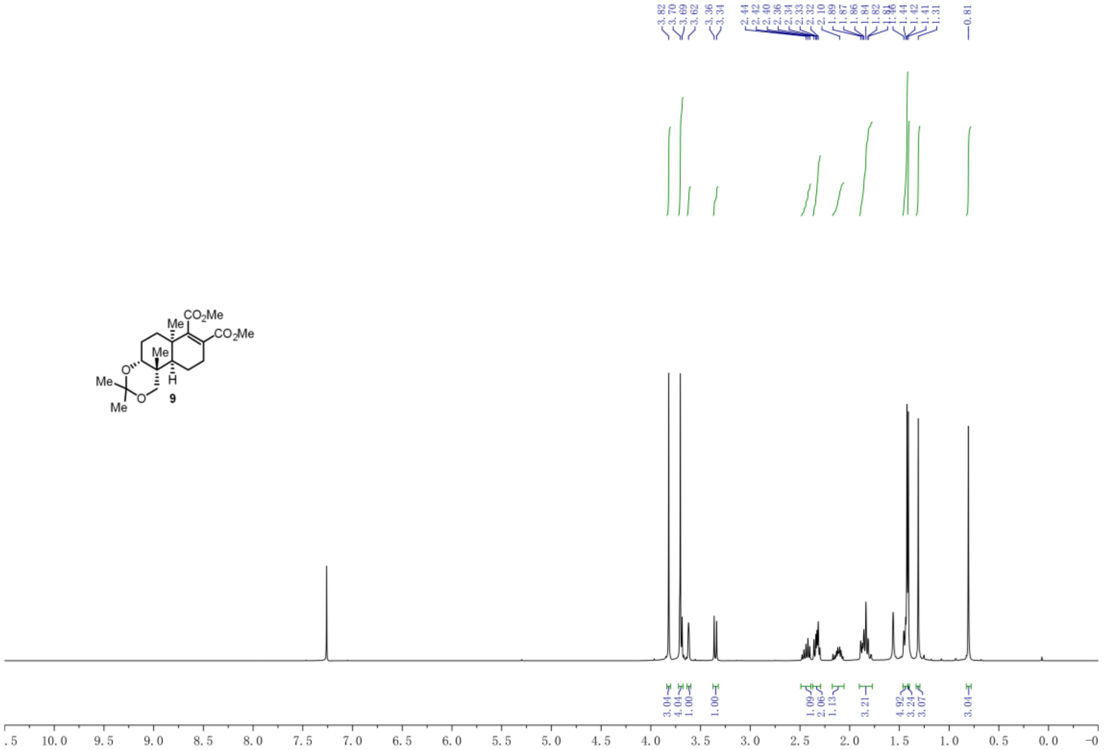
Rf 0.2 (hexanes/ethyl acetate = 5/1, UV/KMnO$_4$)

HRMS (ESI) Calcd. for (M+Na)$^+$ 389.1935, found: 389.1938.

FTIR (neat): 2948, 1721, 1433, 1378, 1251, 1199, 1136, 1090, 1073, 1057, 730 cm^{-1}.

MP 120-122 ˚C

Optical Rotation $[\alpha]_D^{26}$ = -44° (c = 0.32, CHCl$_3$)


CO2Me
Me
CO2Me
Me
O
Me
Me
O
H
9
3.82
3.70
3.69
3.62
3.36
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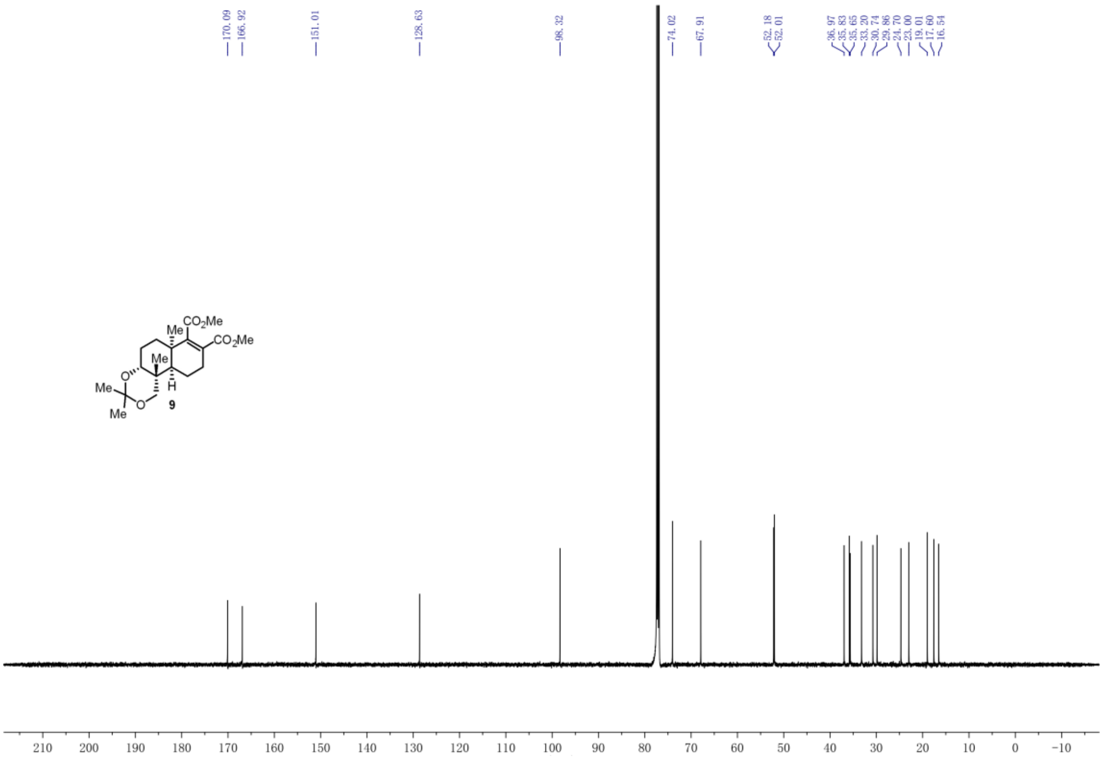
2.44
2.42
2.40
2.36
2.34
2.33
2.32
2.10
1.89
1.87
1.86
1.84
1.82
1.81
1.56
1.44
1.42
1.41
1.31
0.81
3.04
4.04
1.00
1.00
1.09
2.06
1.13
3.21
4.92
3.24
3.07
3.04
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0


170.09
166.92
151.01
128.63
98.32
74.02
67.91
52.18
52.01
36.97
35.83
35.65
33.20
30.74
29.86
24.70
23.00
19.01
17.60
16.54
CO2Me
Me
CO2Me
Me
O
Me
Me
O
H
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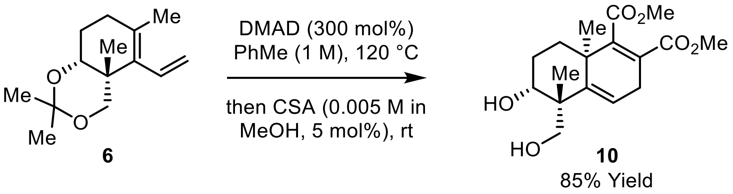
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

Dimethyl (5*R*,6*R*,8a*R*)-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-3,5,6,7,8,8a hexahydronaphthalene-1,2-dicarboxylate (10)



<u>Detailed Procedures</u>

To a solution of **6** (332 mg, 1.49 mmol, 100 mol%) in toluene (1.5 mL) was added dimethyl acetylenedicarboxylate (DMAD, 640 mg, 4.5 mmol, 300 mol%). The mixture was heated to 120 °C in seal tube for 24 hours. The reaction mixture was allowed to cool to ambient temperature and a solution of (+)-10-camphorsulfonic acid (CSA, 0.005 M in MeOH, 14 mL, 5 mol%) was added. The resulted mixture was allowed to stir at the same temperature for 3 hours. The solvent was removed and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 2/1 to 1/1). The title compound **10** was obtained as a colorless oil (412 mg, 1.27 mmol) in 85% yield.

<u>^{1}H NMR</u> (500 MHz, $CDCl_3$) δ 5.80 (dd, *J* = 5.8, 2.1 Hz, 1H), 4.13 (d, *J* = 11.1 Hz, 1H), 3.84 (d, *J* = 32.7 Hz, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 3.44 (dd, *J* = 11.8, 4.3 Hz, 1H), 3.27 (d, *J* = 11.0 Hz, 1H), 3.14 (dd, *J* = 22.7, 5.8 Hz, 1H), 2.00 – 1.85 (m, 1H), 1.81 – 1.73 (m, 1H), 1.61 (td, *J* = 13.6, 3.7 Hz, 1H), 1.51 (dt, *J* = 13.3, 3.7 Hz, 1H), 1.32 (s, 3H), 1.28 (s, 3H).

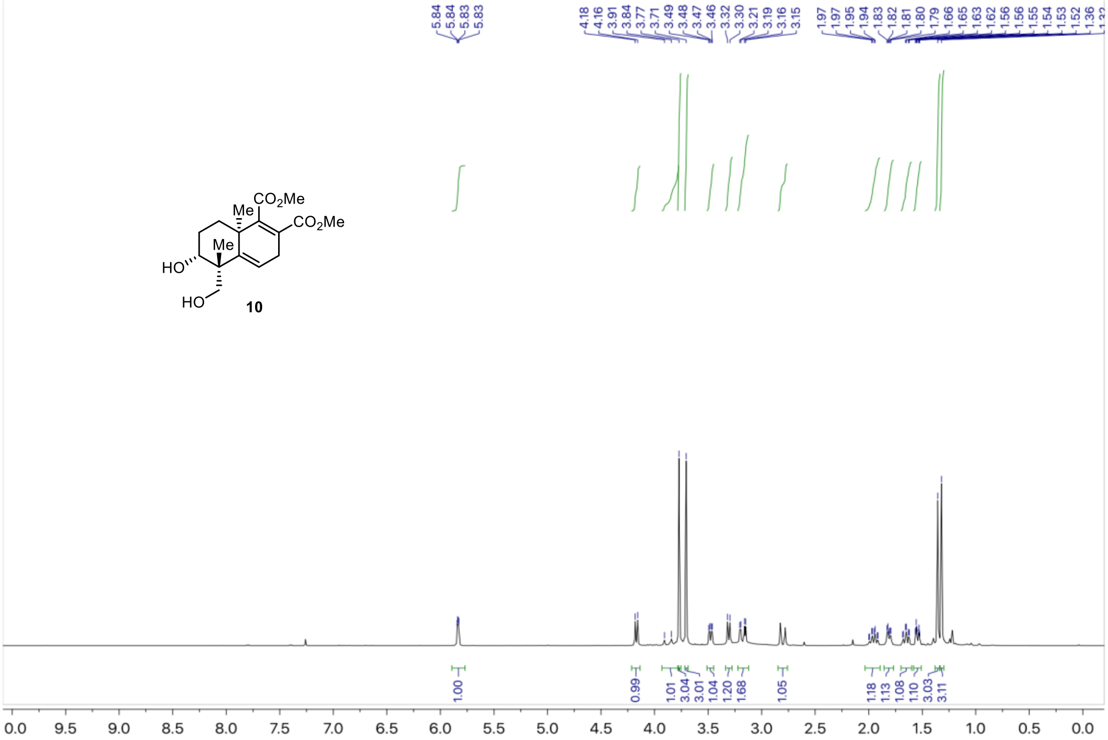
<u>^{13}C NMR</u> (125 MHz, $CDCl_3$) δ 169.3, 166.1, 149.6, 143.4, 125.4, 122.6, 77.5, 77.0, 68.5, 52.3, 52.1, 46.4, 38.1, 32.6, 27.1, 26.9, 26.0, 22.2.

<u>Rf</u> 0.2 (hexanes/ethyl acetate = 1:1, UV/$KMnO_4$)

<u>HRMS</u> (ESI) Calcd. for $(M+Na)^+$ 347.1465, found: 347.1474.

<u>FTIR</u> (neat): 3426, 2949, 2880, 2360, 1720, 1668, 1634, 1434, 1259 cm^{-1}.

<u>Optical Rotation</u> $[\alpha]_D^{26}$ = +180° (*c* = 1.0, $CHCl_3$)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5.84
5.83
5.83
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3.91
3.84
3.77
3.71
3.49
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3.46
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3.19
3.16
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1.81
1.80
1.79
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1.65
1.63
1.62
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1.56
1.55
1.54
1.53
1.52
1.36
CO2Me
Me
CO2Me
Me
HO
HO
10
1.00
0.99
1.01
3.04
3.01
1.04
1.20
1.68
1.05
1.18
1.13
1.08
1.10
3.03
3.11
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
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3.0
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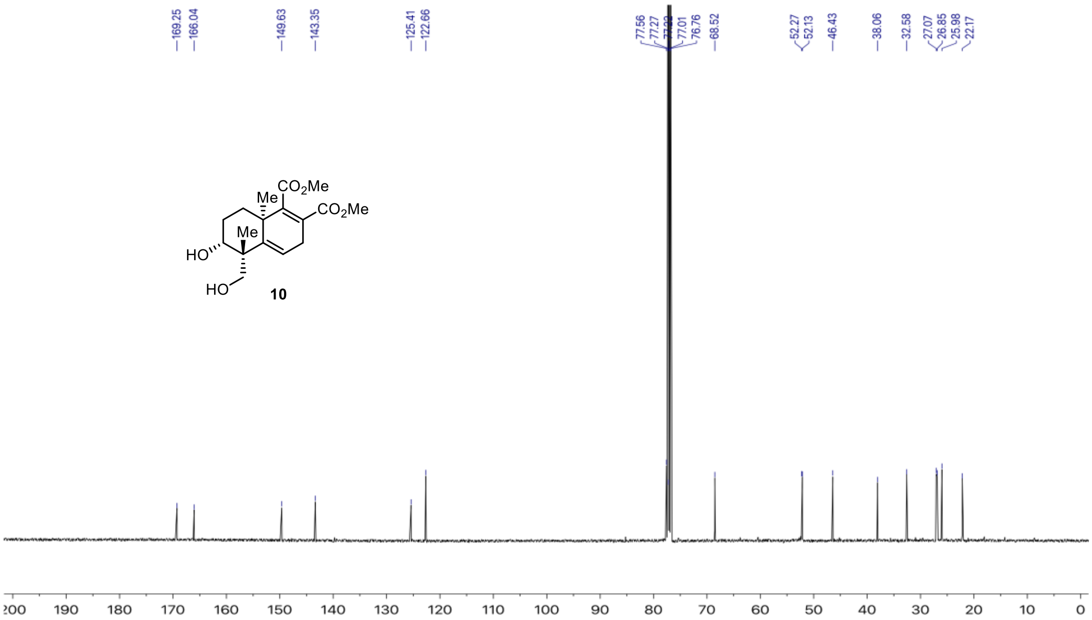
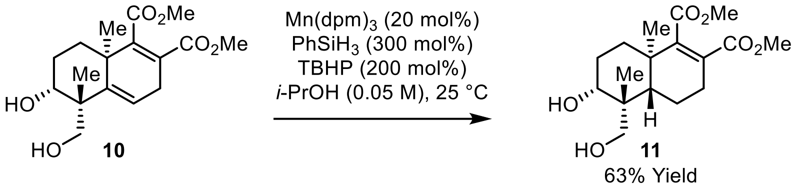
2.0
1.5
1.0
0.5
0.0


169.25
166.04
149.63
143.35
125.41
122.66
77.56
77.27
77.01
76.76
68.52
52.27
52.13
46.43
38.06
32.58
27.07
26.85
25.98
22.17
CO2Me
Me
CO2Me
Me
HO
HO
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

Dimethyl (4a*S*,5*R*,6*R*,8a*R*)-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydronaphthalene-1,2-dicarboxylate (11)



Detailed Procedures

To a reaction vessel charged with a solution of olefin **10** (356 mg, 1.1 mmol, 100 mol%) in anhydrous *i*-PrOH (22 mL) under argon, was added phenylsilane (402 µL, 3.3 mmol, 300 mol%) and TBHP (5.5 M in decane, 396 µL, 2.2 mmol, 200 mol%). The resulting mixture was degassed by bubbling argon through the solution for 20 minutes. $Mn(dpm)_3$ (133 mg, 0.22 mmol, 20 mol%) was then added in one portion and the reaction was then degassed for an additional 30 seconds. The reaction mixture was allowed to stir at ambient temperature for 8 hours. The solvent was removed and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 2/1 to 1/1). The title compound **11** was obtained as a colorless oil (226 mg, 0.69 mmol) in 63% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.20 (d, *J* = 11.2 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.63 (d, *J* = 4.3 Hz, 1H), 3.46 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.38 – 3.28 (m, 1H), 2.95 (s, 1H), 2.87 – 2.77 (m, 1H), 2.47 (ddd, *J* = 19.0, 6.5, 1.2 Hz, 1H), 2.35 (ddd, *J* = 19.0, 11.2, 7.5 Hz, 1H), 1.98 – 1.72 (m, 3H), 1.59 – 1.40 (m, 3H), 1.26 (s, 3H), 1.20 (s, 3H).

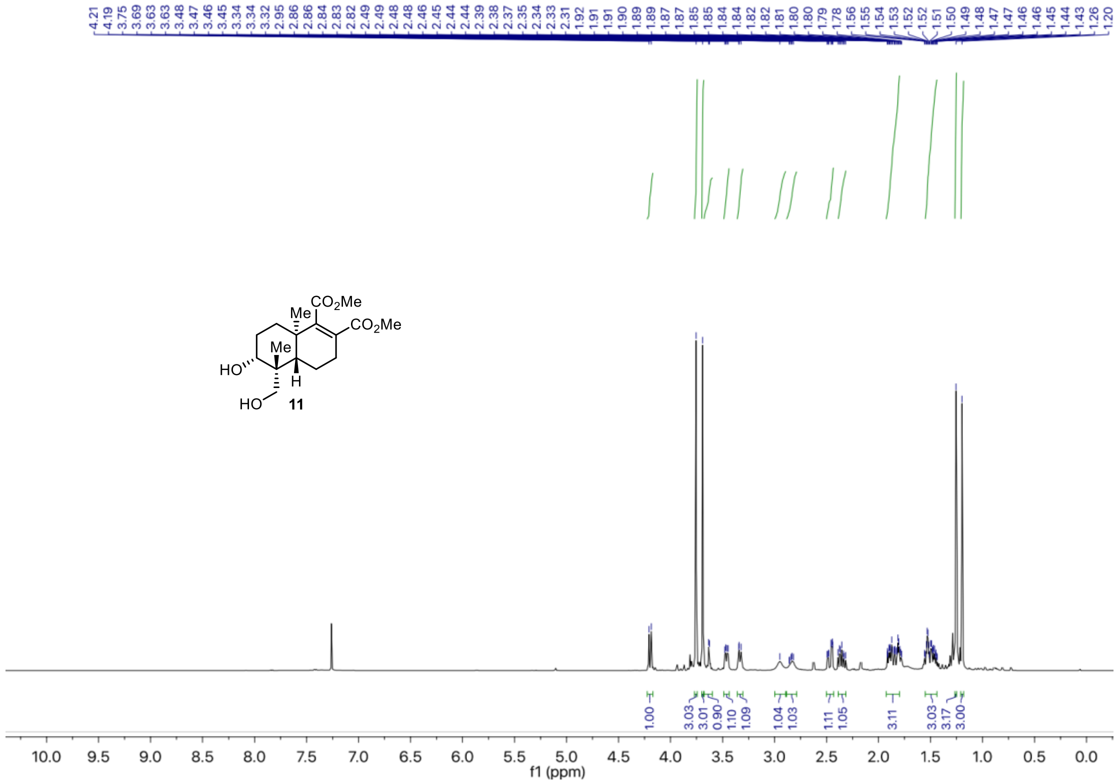
^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 167.2, 150.6, 127.0, 77.2, 52.1, 52.0, 49.6, 42.8, 37.2, 33.7, 27.6, 26.6, 22.4, 20.9, 17.7.

Rf 0.2 (hexanes/ethyl acetate = 1/1, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 349.1622, found: 349.1632.

FTIR (neat): 3400, 2950, 1726, 1434, 1379, 1255, 1039 cm^{-1}.

Optical Rotation $[\alpha]_D^{26}$ = +76° (*c* = 1.0, $CHCl_3$)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3.47
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1.52
1.51
1.50
1.49
1.48
1.47
1.46
1.46
1.45
1.44
1.43
1.26
1.20
CO2Me
Me
CO2Me
Me
HO
H
HO
11
1.00
3.03
3.01
0.90
1.10
1.09
1.04
1.03
1.11
1.05
3.11
3.03
3.17
3.00
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9.5
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
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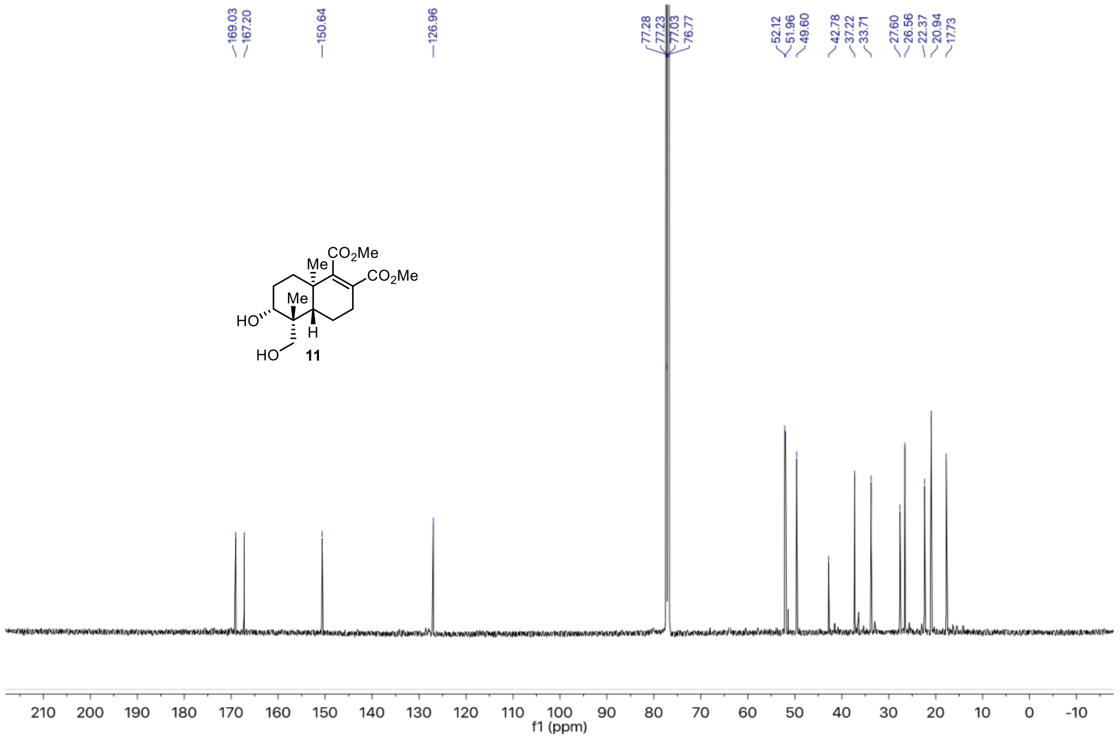
1.5
1.0
0.5
0.0
f1 (ppm)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150.64
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77.23
77.03
76.77
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49.60
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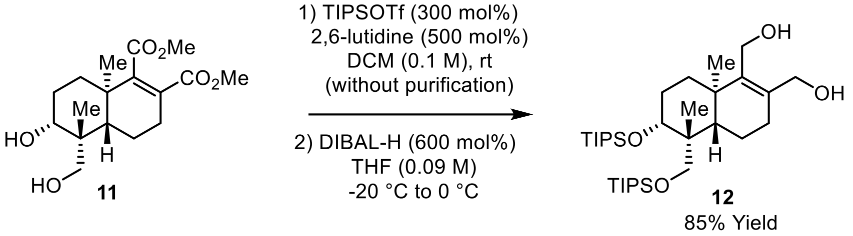
37.22
33.71
27.60
26.56
22.37
20.94
17.73
CO2Me
Me
CO2Me
Me
HO
H
HO
11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

((4a*S*,5*R*,6*R*,8a*R*)-5,8a-Dimethyl-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)-3,4,4a,5,6,7,8,8a-octahydronaphthalene-1,2-diyl)dimethanol (12)



Detailed Procedures

To a solution of **11** (190 mg, 0.59 mmol, 100 mol%) in DCM (8 mL) was added 2,6-lutidine (343 μL, 2.95 mmol, 500 mol%) and TIPSOTf (478 μL, 1.78 mmol, 300 mol%) at 0 ˚C. The mixture was warmed to room temperature and stirred for 3 hours. Water (10 mL) was added and the reaction mixture was transferred to a separatory funnel. The aqueous layer was extracted with DCM (10 mL × 2). The combined organic layers were washed with HCl (aq., 1N, 8 mL), $NaHCO_3$ (aq., sat., 8 mL), brine (10 mL) and dried (Na_2SO_4). The solvent was removed and the crude residue was dissolved in THF (9 mL). DIBAL-H (1 M in hexane, 3.6 mL, 3.6 mmol, 600 mol%) was added at -20 ˚C. The reaction mixture was warmed to 0 ˚C and stirred for 2 hours. The reaction mixture was diluted with ethyl acetate and a solution of Rochelle's salt (1.0 M aqueous solution) was added. The reaction mixture was transferred to a separatory funnel and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 3/1 to 1/1). The title compound **12** was obtained as a white solid (293 mg, 0.5 mmol) in 85% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26 – 4.06 (m, 4H), 4.01 (d, *J* = 11.6 Hz, 1H), 3.82 (d, *J* = 10.5 Hz, 1H), 3.49 (dd, *J* = 11.4, 4.8 Hz, 1H), 2.30 – 2.08 (m, 5H), 1.99 – 1.85 (m, 2H), 1.84 – 1.66 (m, 3H), 1.39 (td, *J* = 13.2, 4.0 Hz, 1H), 1.19 (s, 3H), 1.14 (s, 3H), 1.07 – 1.04 (m, 42H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 136.6, 80.2, 65.7, 64.3, 58.4, 51.8, 44.5, 38.2, 34.9, 32.9, 28.1, 23.8, 21.5, 20.2, 18.5, 18.4, 18.3, 18.3, 13.1, 12.1.

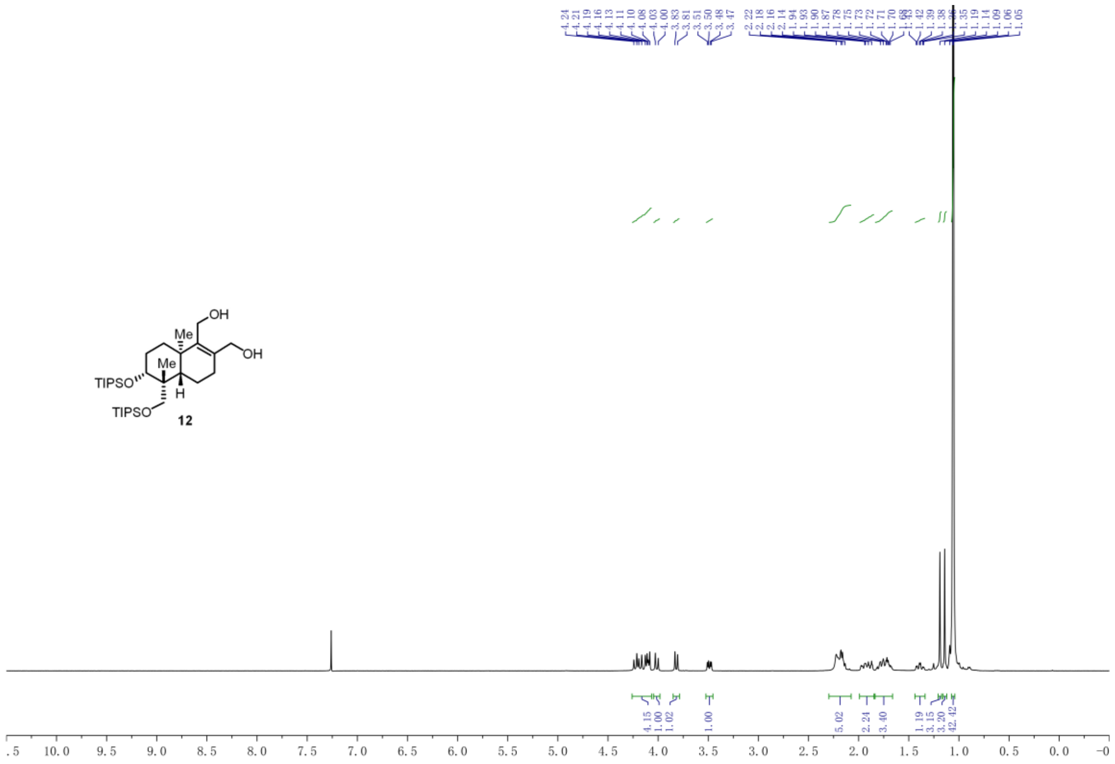
Rf 0.25 (hexanes/ethyl acetate = 3/1, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 605.4392, found: 605.4391.

FTIR (neat): 2942, 2866, 1463, 1366, 1264, 1093, 1064, 994, 882, 742 cm^{-1}.

MP 164-166 ˚C

Optical Rotation $[\alpha]_D^{26}$ = -61° (*c* = 0.14, $CHCl_3$)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1.42
1.39
1.38
1.36
1.35
1.19
1.14
1.09
1.06
1.05
OH
Me
OH
Me
TIPSO
H
TIPSO
12
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1.00
1.02
1.00
5.02
2.24
3.40
1.19
3.15
3.20
42.42
.5
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9.5
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8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
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1.5
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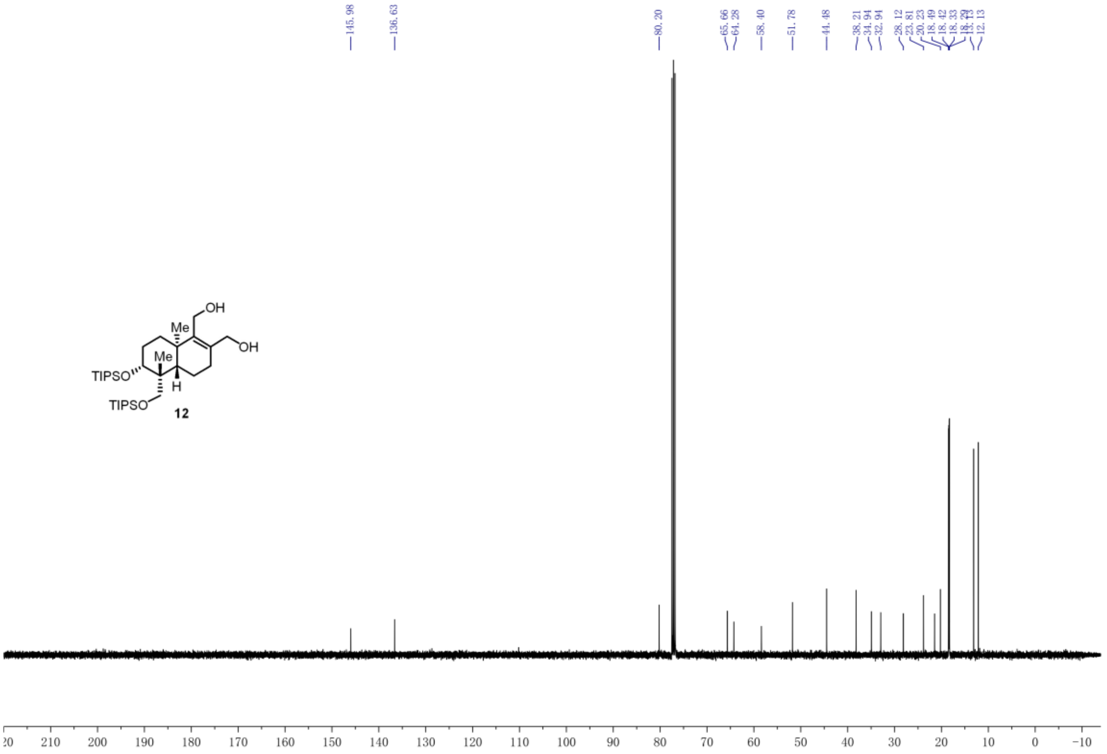
−0


145.98
136.63
80.20
65.66
64.28
58.40
51.78
44.48
38.21
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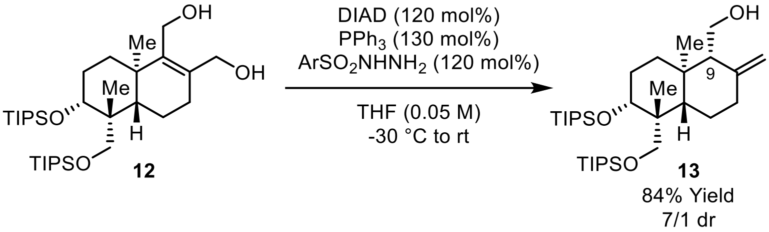
32.94
28.12
23.81
20.23
18.49
18.42
18.33
18.29
13.13
12.13
OH
Me
OH
Me
TIPSO
H
TIPSO
12
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10

((1*R*,4a*S*,5*R*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)decahydronaphthalen-1-yl)methanol (13)



Detailed Procedures

Following the known procedure,[3] diisopropylazodicarboxylate (DIAD, 53 µL, 0.268 mmol, 120 mol%) was added to a solution of triphenylphosphine (76 mg, 0.290 mmol, 130 mol%) in THF (0.9 mL) at -30 °C. After 10 min, diol **12** (130 mg, 0.223 mmol, 100 mol%) in 0.9 ml THF was added to the cold reaction mixture, followed 10 min later by a solution of 2-nitrobenzenesulfonohydrazide (NBSH, 58 mg, 0.268 mmol, 120 mol%) in THF (0.4 mL). The reaction mixture was held at -30 °C for 2.5 hours, at which point the reaction mixture was warmed to 23 ˚C then stirred at this temperature for another 5 hours. The solvent was removed and the residue was subjected to flash silica gel chromatography (hexanes/ethyl acetate = 10/1 to 5/1). The title compound was obtained as a colorless oil (105 mg, 0.187 mmol) in 84% yield as a 7/1 diastereomeric mixture at the newly formed C9 stereocenter.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (s, 1H), 4.62 (s, 1H), 4.02 (d, *J* = 10.4 Hz, 1H), 3.86 – 3.73 (m, 3H), 3.52 – 3.43 (m, 1H), 2.43 – 2.33 (m, 1H), 1.92 – 1.82 (m, 4H), 1.75 – 1.65 (m, 2H), 1.66 – 1.56 (m, 3H), 1.33 (d, *J* = 5.2 Hz, 1H), 1.14 (s, 3H), 1.06 – 1.01 (m, 42H), 0.83 (s, 3H).

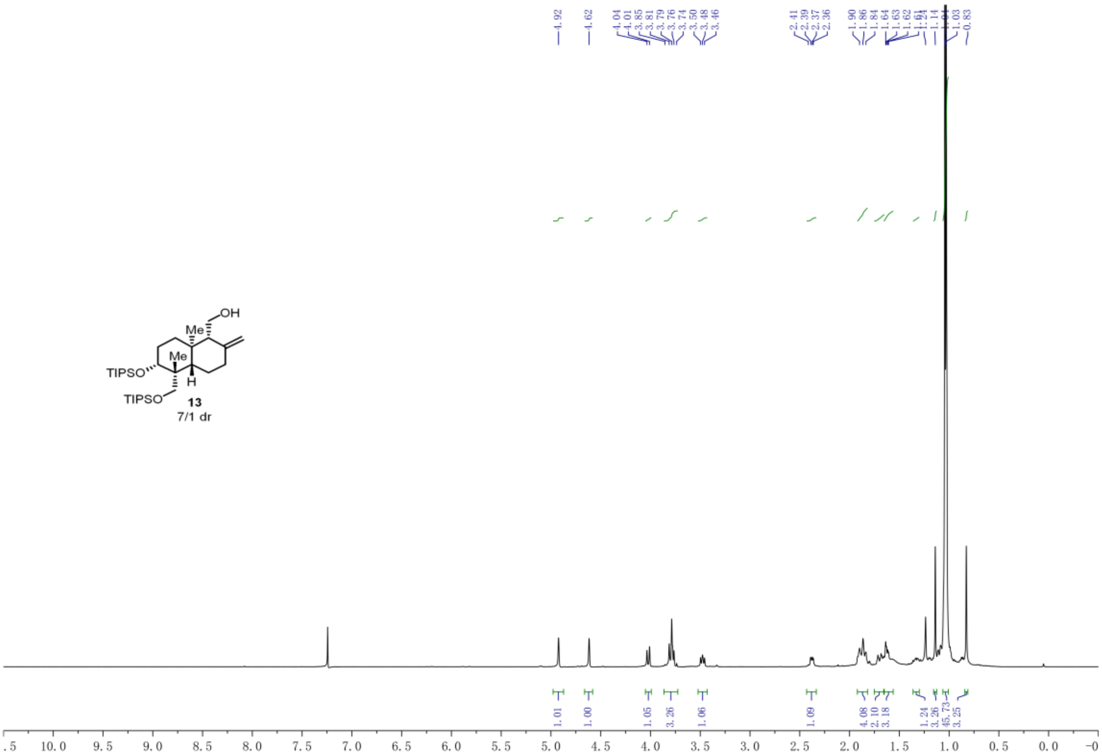
^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 106.2, 80.2, 65.1, 59.4, 59.0, 55.7, 44.8, 38.9, 38.8, 37.63, 28.4, 26.6, 23.8, 18.5, 18.4, 18.3, 18.3, 15.7, 13.1, 12.1.

Rf 0.29 (hexanes/ethyl acetate = 5/1, $KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 589.4443, found: 589.4453.

FTIR (neat): 3286, 2927, 2865, 1463, 1382, 1259, 1135, 1098, 1058, 1012, 882 cm^{-1}.

Optical Rotation $[\alpha]_D^{23}$ = +40° (*c* = 0.10, $CHCl_3$)


4.92
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4.01
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3.81
3.79
3.76
3.74
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3.48
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2.39
2.37
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1.84
1.64
1.63
1.62
1.61
1.24
1.14
1.03
0.83
OH
Me
Me
H
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TIPSO
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1.01
1.00
1.05
3.26
1.06
1.09
4.08
2.10
3.18
1.24
3.26
45.73
3.25
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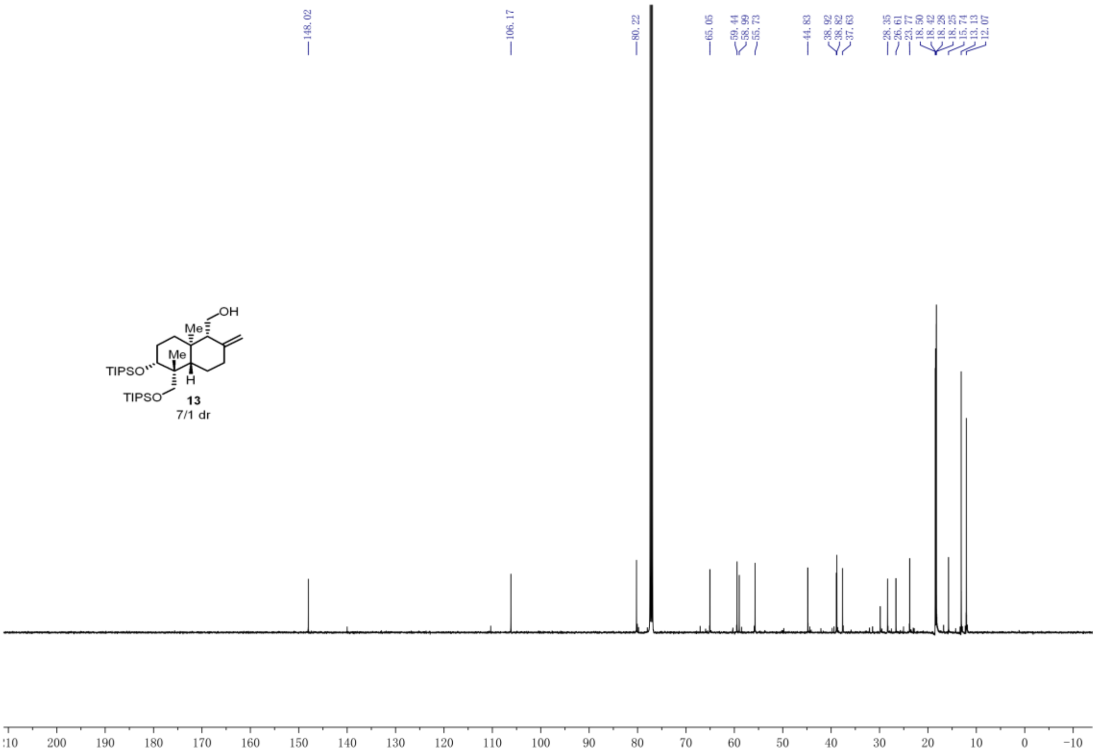
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18.25
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H
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80
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40
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20
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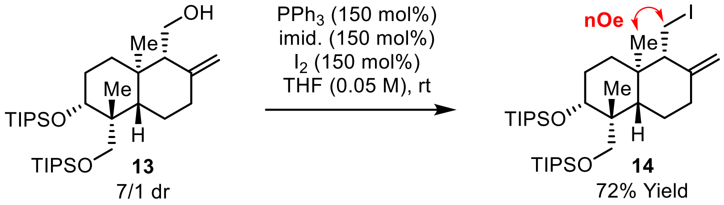
0
-10

(((1*R*,2*R*,4a*R*,5*R*,8a*S*)-5-(Iodomethyl)-1,4a-dimethyl-6-methylene-1-(((triisopropylsilyl)oxy)methyl)decahydronaphthalen-2-yl)oxy)triisopropylsilane (14)



Detailed Procedures

To a solution of PPh_3 (69.2 mg, 0.264 mmol, 150 mol%) and imidazole (20 mg, 0.264 mmol, 150mol%) in THF (0.6 mL) was added iodine (67 mg, 0.264 mmol, 150 mol%) at 0 °C. After 20 min, a solution of alcohol **13** (100 mg, 7/1 dr, 0.176 mmol, 100 mol%) in THF (0.6 mL) was added dropwise. The reaction was allowed to warm to room temperature and was stirred for 24 hours. The reaction mixture was diluted with Et_2O and $NaHCO_3$ (aq., sat., 1 mL) and $Na_2S_2O_3$ (aq., sat., 1 mL) were added. The reaction mixture was transferred to a separatory funnel, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (hexanes). The title compound **14** was obtained as a colorless oil (85.7 mg, 0.127 mmol) in 72% yield as a single diastereomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (s, 1H), 4.63 (s, 1H), 4.03 (d, *J* = 10.4 Hz, 1H), 3.81 (d, *J* = 10.4 Hz, 1H), 3.65 – 3.59 (m, 1H), 3.53 – 3.46 (m, 1H), 3.05 (t, *J* = 10.6 Hz, 1H), 2.41 (d, *J* = 12.7 Hz, 1H), 2.12 (d, *J* = 11.1 Hz, 1H), 1.98 – 1.76 (m, 4H), 1.67 (dd, *J* = 9.7, 6.5 Hz, 2H), 1.41 – 1.31 (m, 1H), 1.15 (s, 3H), 1.12 – 1.02 (m, 42H), 0.82 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1, 108.0, 80.1, 65.0, 60.7, 55.6, 44.9, 41.4, 38.7, 37.8, 28.3, 26.7, 23.7, 18.5, 18.4, 18.3, 18.2, 14.2, 13.1, 12.1, 2.3.

Rf 0.7 (hexanes, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M)^+$ 677.3646, found: 677.3629.

FTIR (neat): 2942, 2891, 2865, 1462, 1096, 1057, 882, 678 cm^{-1}.

Optical Rotation $[\alpha]_D^{24}$ = -42° (*c* = 0.70, $CHCl_3$)


5.01
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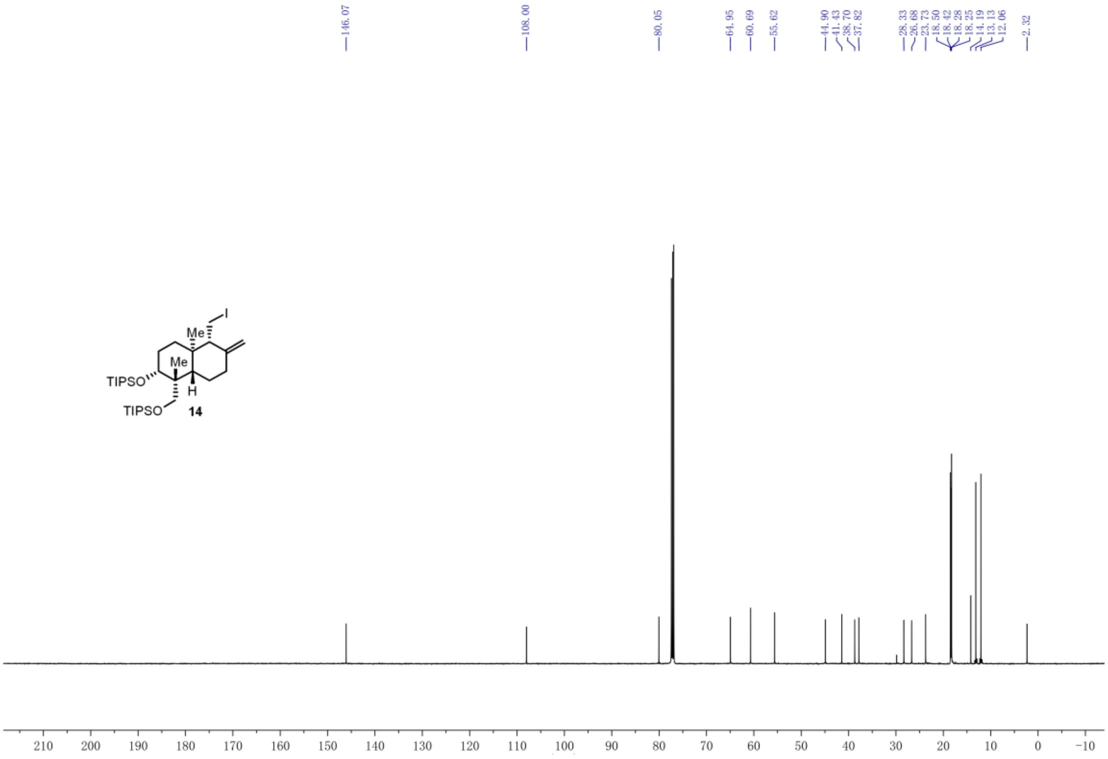
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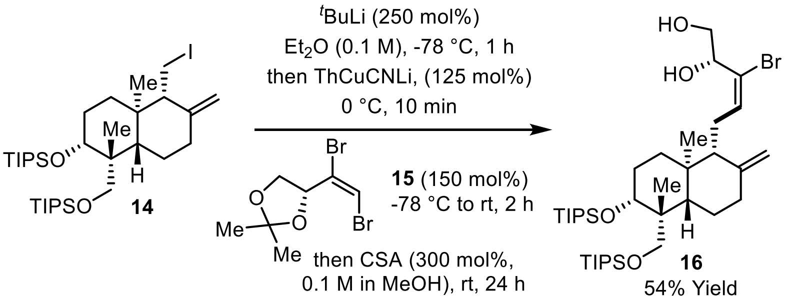
(*R*,*E*)-3-Bromo-5-((1*R*,4a*S*,5*R*,6*R*,8a*S*)-5,8a-dimethyl-2-methylene-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)decahydronaphthalen-1-yl)pent-3-ene-1,2-diol (16)



Detailed Procedures

Following the known procedure to prepare ThCuCNLi,[4] a 10-mL round-bottomed flask equipped with a stirring bar and a rubber septum was evacuated and flame-dried under vacuum, then flushed with dry argon. This process was repeated 3 times. Anhydrous THF (3.6 mL) and distilled thiophene (291 μL, 3.63 mmol, 110 mol%) were injected via syringe and the resulting solution was cooled to -78 °C. Butyllithium (2.5 M in hexanes, 1.45 mL, 3.63 mmol, 110 mol%) was added dropwise via syringe. The resulting light-yellow solution was warmed to -20 °C and stirred for 20 min. Another 10-mL round-bottomed flask equipped with a stirring bar and a rubber septum was charged with copper(I) cyanide (295 mg, 3.3 mmol, 100 mol%). The flask was evacuated and gently flame-dried under vacuum, then flushed with dry argon. The process was repeated 3 times. Anhydrous THF (3.3 mL) was injected and the resulting slurry was cooled to -78 °C. At this time, the previously prepared solution of 2-lithiothiophene in THF (at -20 °C) was added via cannula to the stirring slurry. At the end of the addition, the acetone–dry ice bath was exchanged for an ice bath. After 5 min, the flask was again placed in a dry ice–acetone bath.

A solution of **14** (48 mg, 0.071 mmol, 100 mol%) in 0.7 mL of Et$_2$O at –78 °C was treated with *t*-BuLi (104 μL of 1.7 M in pentane, 0.18 mmol, 250 mol%) dropwise over 2 min. After 1 h, freshly prepared ThCuCNLi (222 μL of 0.4 M in THF, 0.089 mmol, 125 mol%) was added and the mixture was immediately warmed to 0 °C. After 5 min, the reaction was cooled to -78 °C and a solution of **15** (30.5 mg, 0.106 mmol, 150 mol%) in 0.3 mL of Et$_2$O was added dropwise over 5 min, and the mixture was stirred at -78 °C for 10 min, warmed to 0 °C, and then stirred at 0 °C for 2 h. The reaction was warm to room temperature, and a solution of (+)-10-camphorsulfonic acid (CSA, 50 mg, 0.215 mmol, 300 mol%) in 2.1 mL of MeOH was added. Then the resulting mixture was stirred for 24 h. NaHCO$_3$ (aq., sat., 1 mL) was added and the reaction mixture was transferred to a separatory funnel and extracted with ethyl acetate. The combined organic extracts were washed with brine and dried (Na$_2$SO$_4$). The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 5/1). The title compound **16** was obtained as a colorless oil (27.6 mg, 0.038 mmol) in 54% yield.

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.04 (t, *J* = 6.8 Hz, 1H), 4.88 (s, 1H), 4.57 (d, *J* = 5.1 Hz, 1H), 4.45 (s, 1H), 4.04 (d, *J* = 10.4 Hz, 1H), 3.82 (d, *J* = 10.4 Hz, 1H), 3.77 – 3.69 (m, 1H), 3.62 (s, 1H), 3.51 – 3.42 (m, 1H), 2.40 – 2.30 (m, 2H), 2.28 – 2.20 (m, 1H), 2.16 (d, *J* = 5.7 Hz, 1H), 1.92 – 1.78 (m, 4H), 1.76 – 1.63 (m, 4H), 1.56 (s, 2H), 1.15 (s, 3H), 1.08 – 1.01 (m, 42H), 0.82 (s, 3H).

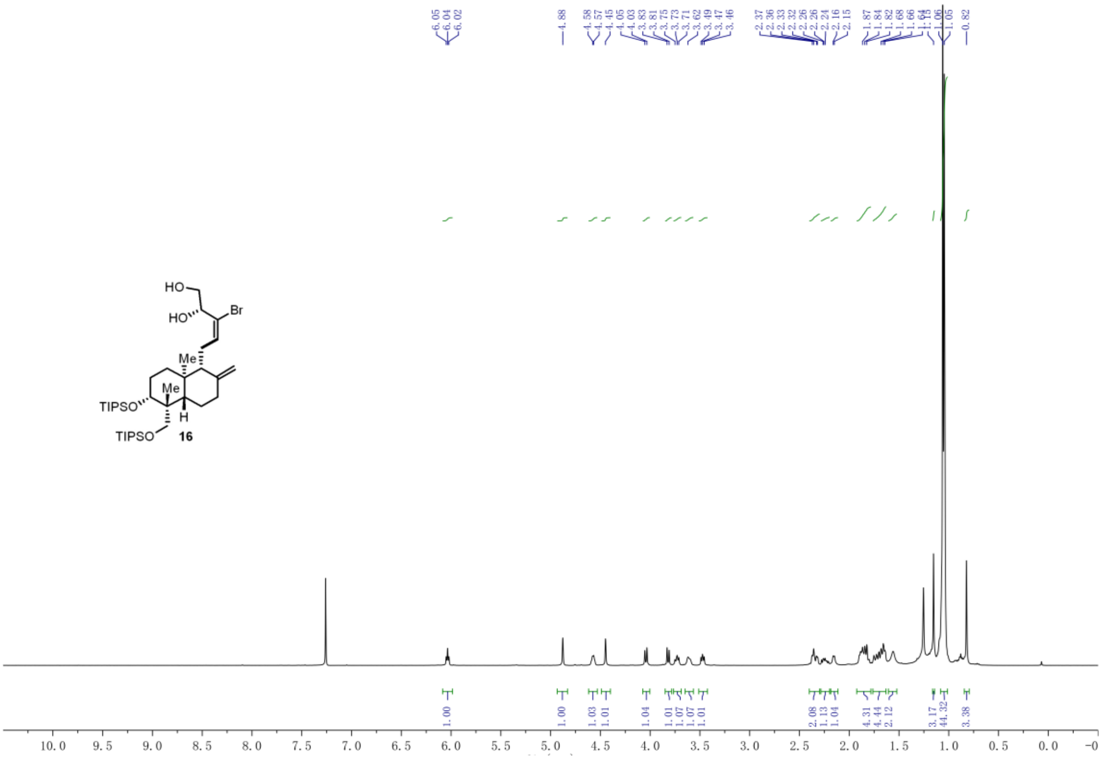
^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 137.4, 124.0, 107.8, 80.2, 70.2, 65.6, 65.0, 57.0, 55.8, 44.8, 39.5, 39.1, 37.8, 28.4, 26.6, 25.0, 23.8, 18.5, 18.4, 18.3, 18.3, 14.9, 13.1, 12.1.

Rf 0.30 (hexanes/ethyl acetate = 2/1, $KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 737.3966, found: 737.3968.

FTIR (neat): 3288, 2941, 2865, 1462, 1098, 1057, 1009, 881, 803 cm^{-1}.

Optical Rotation $[\alpha]_D^{23}$ = +6° (c = 0.17, $CHCl_3$)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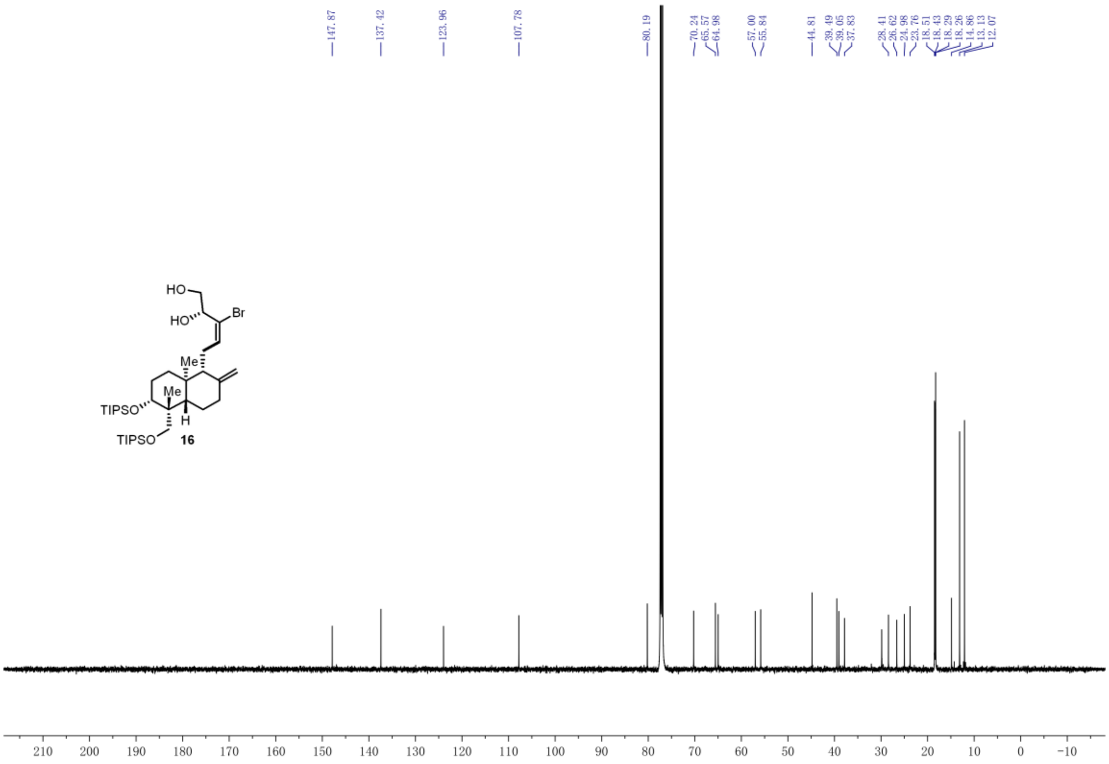
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24.98
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18.51
18.43
18.29
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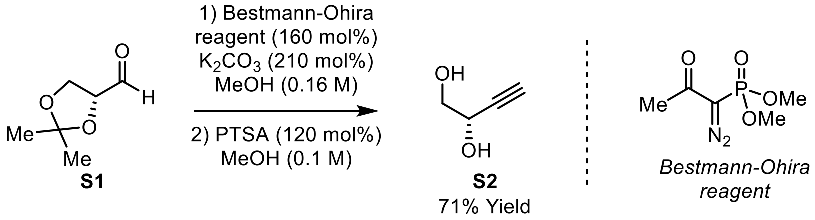
16

(*S*)-But-3-yne-1,2-diol (S2)



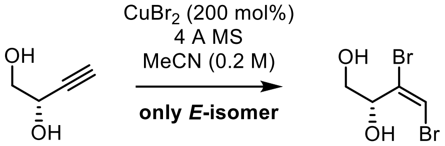
Detailed Procedures

A solution of (*R*)-glyceraldehyde acetonide **S1** (2.06 g, 15.8 mmol, 100 mol%) and the Bestmann–Ohira reagent (4.55 g, 23.7 mmol, 150 mol%) in methanol (100 mL) was cooled to 0 ºC. Anhydrous potassium carbonate (4.58 g, 33.2 mmol, 210 mol%) was gradually added (30 min). The mixture was stirred for 12 h, allowing it to warm to room temperature. The reaction was diluted with Et_2O (150 mL) and transferred to a separatory funnel. The organic layer was washed with NH_4Cl (aq., sat., 50 mL). The two layers were separated and the aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with brine, and dried (Na_2SO_4). To the resulting solution of crude product was added MeOH (100 mL) and PTSA (3.27 g, 19.0 mmol, 120 mol%) at room temperature. The reaction mixture was allowed to stir overnight. Triethylamine (2.6 mL) was added and the solvent was removed under reduced pressure. The residue was subjected to flash column chromatography on silica gel (pentane/diethyl ether = 1/1 to 0/1). The title compound **S2** was obtained as a yellow oil (966 mg, 11.2 mmol,) in 71% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 4.46 (ddd, *J* = 6.2, 3.7, 2.2 Hz, 1H), 3.77 (dd, *J* = 11.4, 3.8 Hz, 1H), 3.71 (dd, *J* = 11.4, 6.3 Hz, 1H), 2.50 (t, *J* = 6.2 Hz, 1H), 2.43 (s, 2H).

The spectral data recorded for the compound was in complete agreement with the literature.[5]

(***R***,***E***)-3,4-Dibromobut-3-ene-1,2-diol (S3)



S2

S3
92% Yield

Detailed Procedures

Following the modified procedure,[6] CuBr$_2$ (1.72 g, 7.71 mmol, 200 mol%) was added to a solution of alkyne **S2** (332 mg, 3.85 mmol, 100 mol%) and 200 mg of 4 Å molecular sieves in acetonitrile (19 mL) at room temperature. The reaction mixture was allowed to stir at room temperature for 4 h. The reaction mixture was concentrated and the residue was subjected to chromatography on silica gel (pentane/diethyl ether = 2/1 to 1/1) to afford the comound **S3** as a colorless oil (900 mg, 3.54 mmol) in 92% yield.

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.65 (s, 1H), 4.89 (dd, J = 7.7, 4.6 Hz, 1H), 3.74 (dd, J = 11.3, 7.7 Hz, 1H), 3.69 (dd, J = 11.4, 4.6 Hz, 1H), 2.39 (s, 2H).

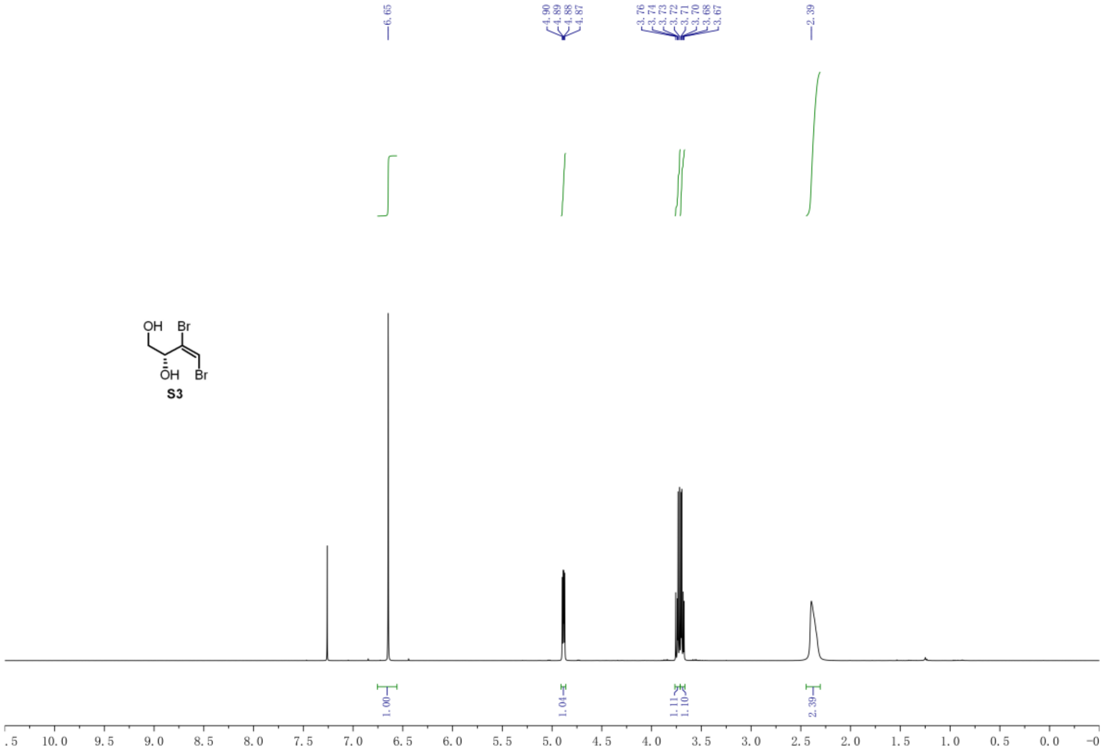
^{13}C NMR (125 MHz, CDCl$_3$) δ 126.3, 105.1, 71.3, 64.6.

Rf 0.34 (hexanes/ethyl acetate = 1/1, UV/KMnO$_4$)

HRMS (ESI) Calcd. for (M+Na)$^+$ 266.8627, found: 266.8623.

FTIR (neat): 3357, 3080, 2930, 1398, 1320, 1247, 1032, 883, 793 cm^{-1}.

Optical Rotation $[\alpha]_D^{24}$ = +12° (c = 0.51, CHCl$_3$)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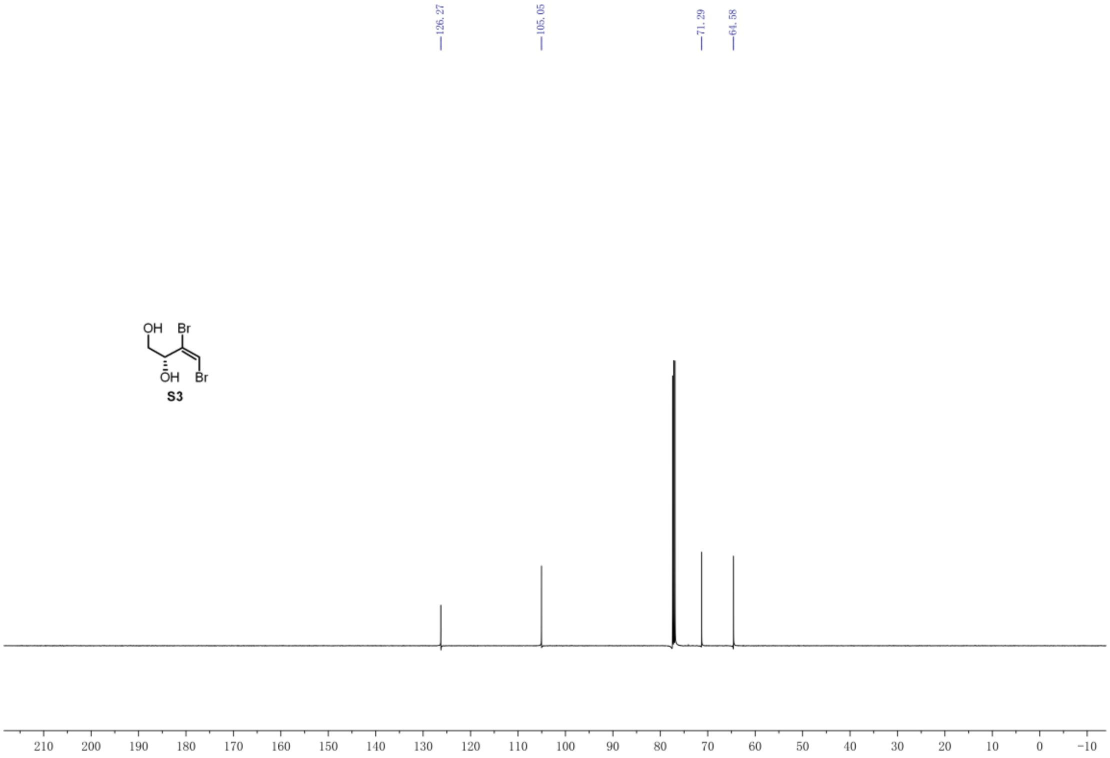
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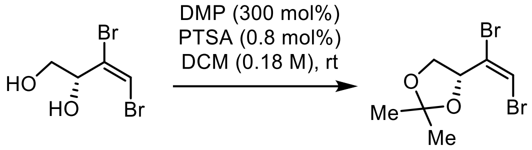
(***R***,***E***)-4-(1,2-Dibromovinyl)-2,2-dimethyl-1,3-dioxolane (S4)



S3

S4
88% Yield

Detailed Procedures

To a solution of **S3** (905 mg, 3.68 mmol, 100 mol%) in DCM (20 mL) was added 2,2-dimethoxypropane (DMP, 1.35 mL, 11.0 mmol, 300 mol%) and PTSA (5 mg, 0.03 mmol, 0.8 mol%) at room temperature. The reaction mixture was allowed to stir for 1.5 hours at room temperature. $NaHCO_3$ (aq., sat., 10 mL) was added to the reaction mixture. The reaction mixture was transferred to a separatory funnel and the aqueous layer was extracted with DCM (20 mL × 2). The combined organic extracts were washed with brine (10 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure (<30 ˚C) and the residue was subjected to flash column chromatography on silica gel (pentane/diethyl ether = 20/1 to 10/1) to afford compound **S4** as a colorless oil (919 mg, 3.24 mmol) in 88% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, *J* = 0.6 Hz, 1H), 5.19 (dt, *J* = 6.7, 3.4 Hz, 1H), 4.17 (dd, *J* = 8.4, 6.7 Hz, 1H), 3.83 (dd, *J* = 8.5, 6.8 Hz, 1H), 1.55 (s, 4H), 1.42 (s, 3H).

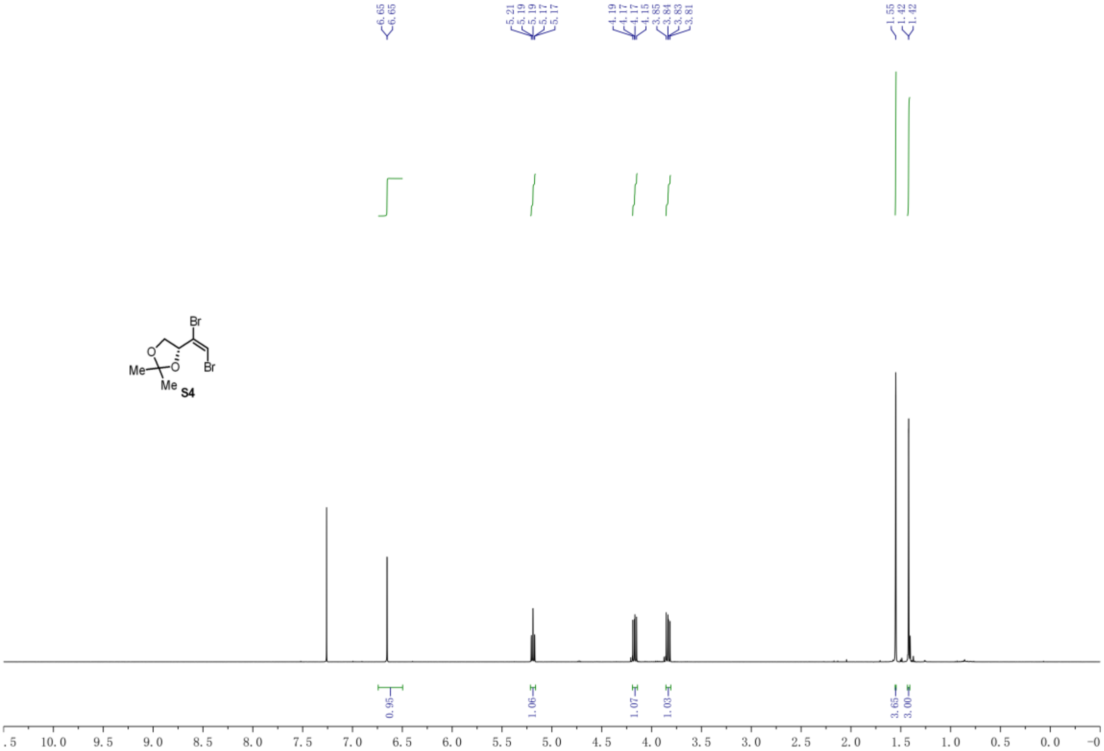
^{13}C NMR (125 MHz, $CDCl_3$) δ125.4, 111.2, 105.9, 74.5, 67.8, 26.3, 25.9.

Rf 0.48 (hexanes/ethyl acetate = 10/1, UV/$KMnO_4$)

HRMS (CI) Calcd. for $(M)^+$ 284.9126, found: 284.9127.

FTIR (neat): 3084, 2987, 2934, 1454, 1380, 1372, 1250, 1153, 1213, 1103, 1064, 850 cm^{-1}.

Optical Rotation $[\alpha]_D^{23}$ = +14° (*c* = 0.22, $CHCl_3$)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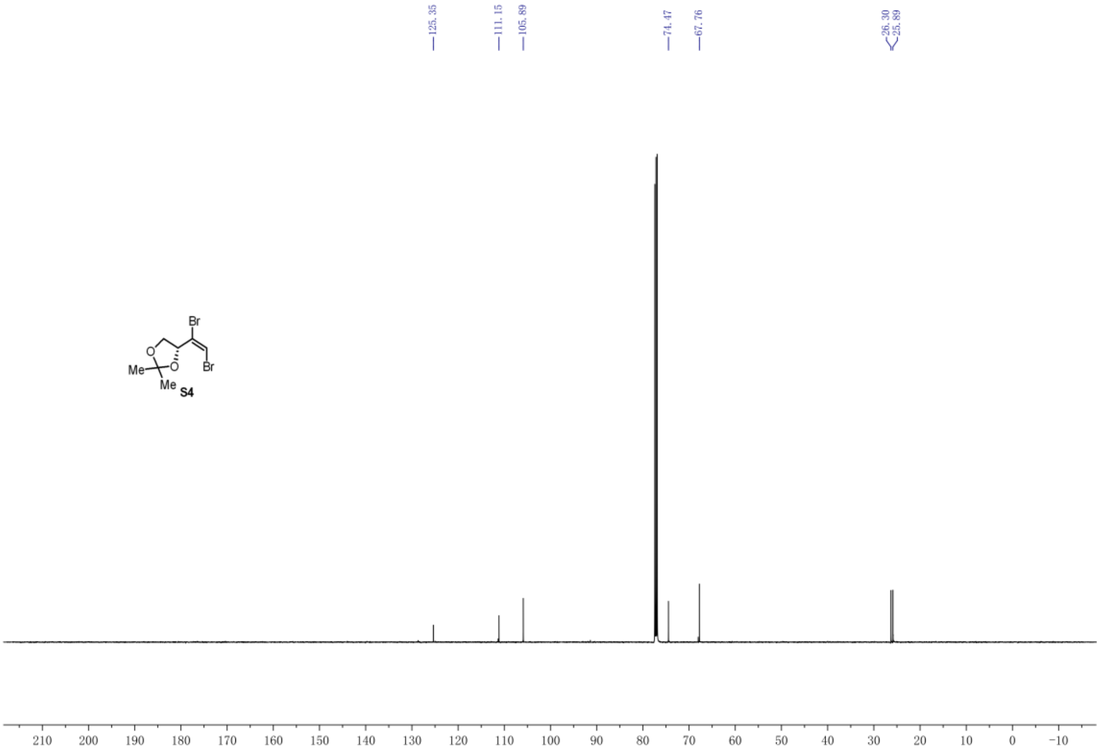
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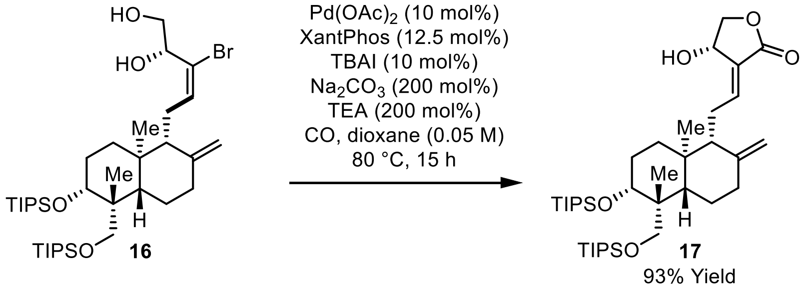
(*S*,*E*)-3-(2-((1*R*,4a*S*,5*R*,6*R*,8a*S*)-5,8a-Dimethyl-2-methylene-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)decahydronaphthalen-1-yl)ethylidene)-4-hydroxydihydrofuran-2(3H)-one (17)



Detailed Procedures

Following the modified procedure,[7] an oven dried Schlenk tube fitted with a Youngs tap was charged with alcohol **16** (14.2 mg, 0.02 mmol, 100 mol%), Pd(OAc)$_2$ (0.4 mg, 0.002 mmol, 10 mol%, XantPhos (1.5 mg, 0.0025 mmol, 13 mol%), tetra-*n*-butylammonium iodide (0.7 mg, 0.002 mmol, 10 mol%), and Na$_2$CO$_3$ (4.2 mg, 0.04 mmol, 200 mol%) under an argon atmosphere. Dry 1,4-dioxane (0.4 mL) was then added to the tube, and the solvent was degassed by a freeze-pump-thaw method (3 cycles). The tube was then backfilled with CO gas and dry NEt$_3$ (5.5 µL, 0.04 mmol, 200 mol%) was added. Then, whilst stirring vigorously, the tube was evacuated and back filled with CO gas three times, turning the mixture a deep purple color. The tube was then sealed and heated to 80 °C whilst stirring vigorously for 15 h. The reaction mixture was allowed to cool to room temperature. The solvent was removed under reduced pressure. The crude residue was subjected to flash column chromatography (hexanes/acetone = 5/1) to give lactone **17** as a colorless oil (12.2 mg, 0.017 mmol) in 93% yield.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.00 (t, *J* = 6.8 Hz, 1H), 5.03 (s, 1H), 4.89 (s, 1H), 4.56 (s, 1H), 4.45 (dd, *J* = 10.4, 5.9 Hz, 1H), 4.26 (d, *J* = 10.4 Hz, 1H), 4.05 (d, *J* = 10.5 Hz, 1H), 3.83 (d, *J* = 10.4 Hz, 1H), 3.49 (dd, *J* = 10.5, 5.4 Hz, 1H), 2.61 – 2.48 (m, 2H), 2.43 – 2.32 (m, 1H), 2.02 (d, *J* = 6.4 Hz, 1H), 1.94 – 1.78 (m, 4H), 1.78 – 1.63 (m, 3H), 1.22 – 1.17 (m, 1H), 1.16 (s, 3H), 1.08 – 1.03 (m, 42H), 0.87 (s, 3H).

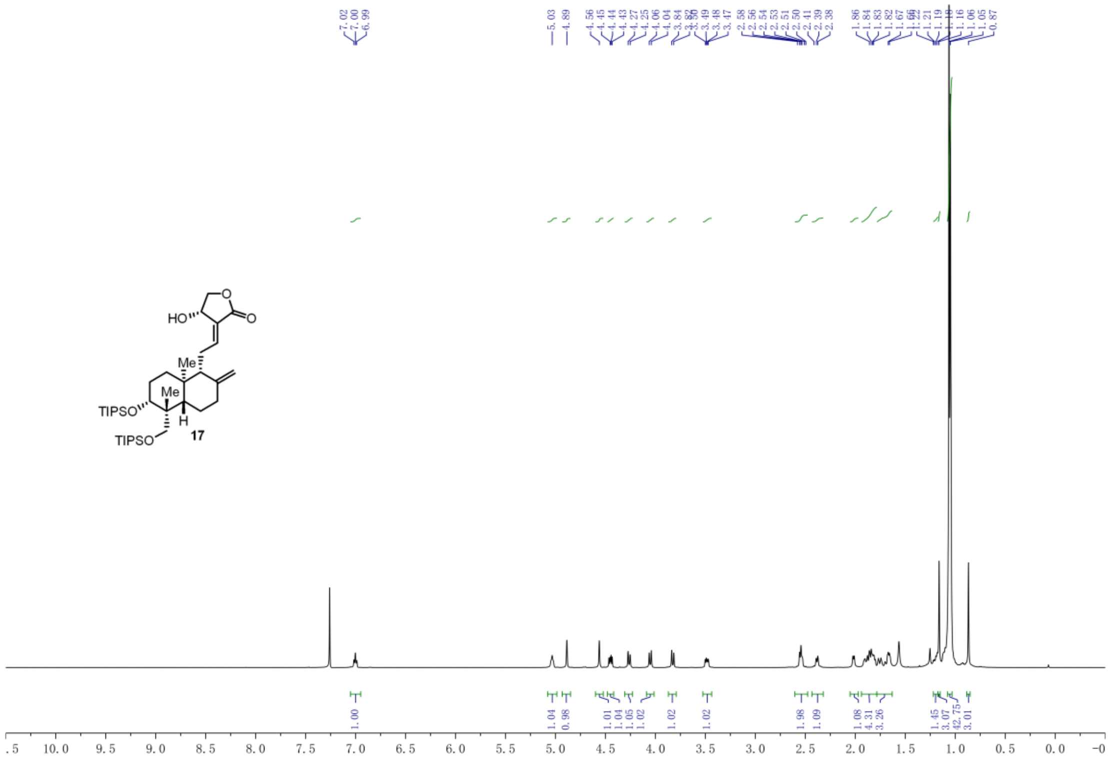
^{13}C NMR (125 MHz, CDCl$_3$) δ 170.0, 149.6, 148.0, 127.9, 107.9, 80.2, 74.3, 66.4, 65.0, 56.6, 55.8, 44.8, 39.5, 38.9, 38.0, 28.4, 26.6, 25.1, 23.8, 18.5, 18.4, 18.3, 18.3, 14.8, 13.1, 12.1.

Rf 0.41 (hexanes/ethyl acetate = 2/1, UV/KMnO$_4$)

HRMS (ESI) Calcd. for (M+Na)$^+$ 685.4654, found: 685.4653.

FTIR (neat): 3434, 2936, 1759, 1467, 1370, 1162, 1082, 1020, 965 cm^{-1}.

Optical Rotation $[\alpha]_D^{23}$ = -59° (*c* = 0.11, CHCl$_3$)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1.02
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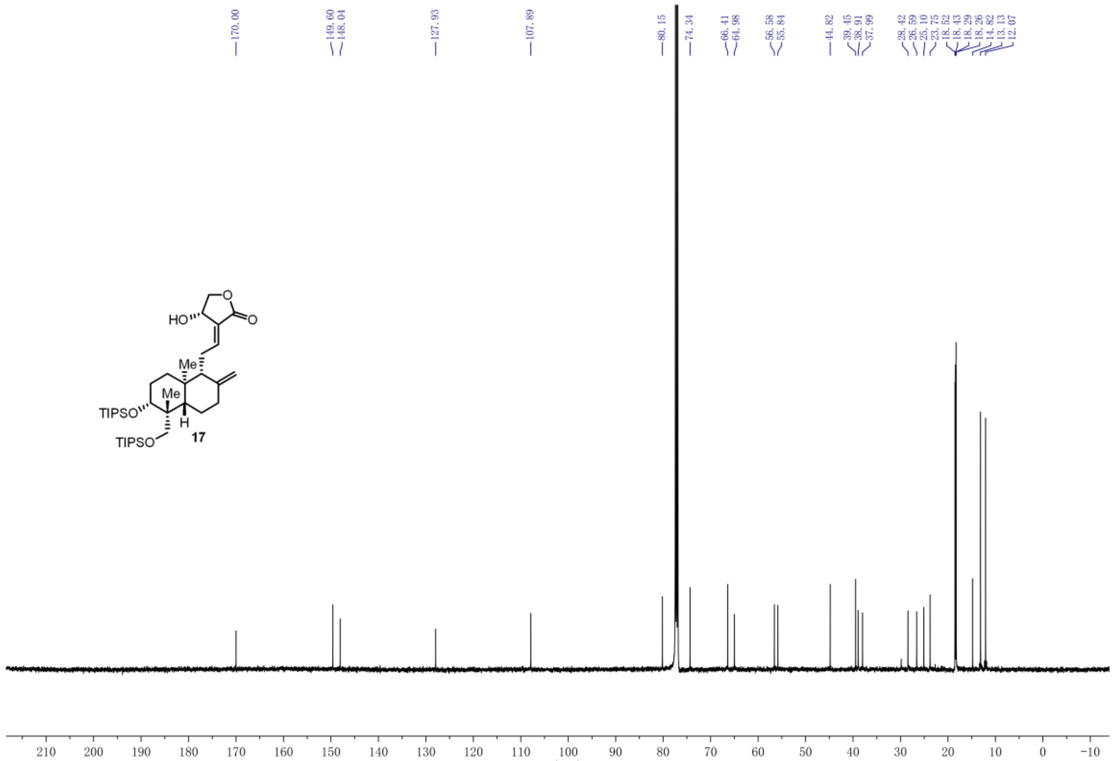
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26.59
25.10
23.75
18.52
18.43
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180
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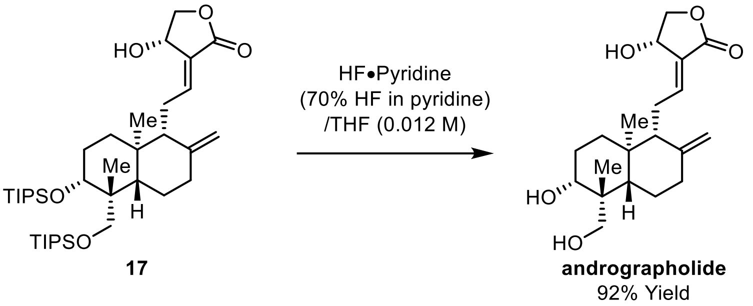
Andrographolide



Detailed Procedures

To a solution of **17** (11.8 mg, 0.018 mmol, 100 mol%) in THF (0.5 mL) was added hydrogen fluoride•pyridine (70% HF in pyridine, 497 µL) at 0 ºC. Then the reaction mixture was allowed to warm to room temperature and was stirred for 34 hours. The reaction mixture was diluted with ethyl acetate and $NaHCO_3$ (aq., sat., 5 mL) was added. The reaction mixture was transferred to separatory funnel and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (DCM/MeOH = 20/1 to15/1). The title compound **andrographolide** was obtained as colorless plates (5.7 mg, 0.0166 mmol) in 92% yield.

^{1}H NMR (500 MHz, CD3OD) δ 6.75 (td, J = 6.8, 1.5 Hz, 1H), 4.91 (d, J = 6.0 Hz, 1H), 4.79 (s, 1H), 4.57 (s, 1H), 4.37 (dd, J = 10.2, 6.1 Hz, 1H), 4.06 (dd, J = 10.2, 2.0 Hz, 1H), 4.02 (d, J = 11.0 Hz, 1H), 3.27 (d, J = 11.0 Hz, 1H), 3.32 – 3.19 (m, 1H), 2.58 – 2.43 (m, 2H), 2.36 – 2.30 (m, 1H), 1.98 – 1.90 (m, 1H), 1.83 – 1.64 (m, 5H), 1.28 – 1.18 (m, 4H), 1.12 (s, 3H), 0.66 (s, 3H).

^{13}C NMR (125 MHz, CD3OD) δ 172.67, 149.36, 148.80, 129.84, 109.24, 80.94, 76.17, 66.67, 65.00, 57.42, 56.35, 43.71, 39.99, 39.00, 38.16, 29.06, 25.73, 25.24, 23.40, 15.55.

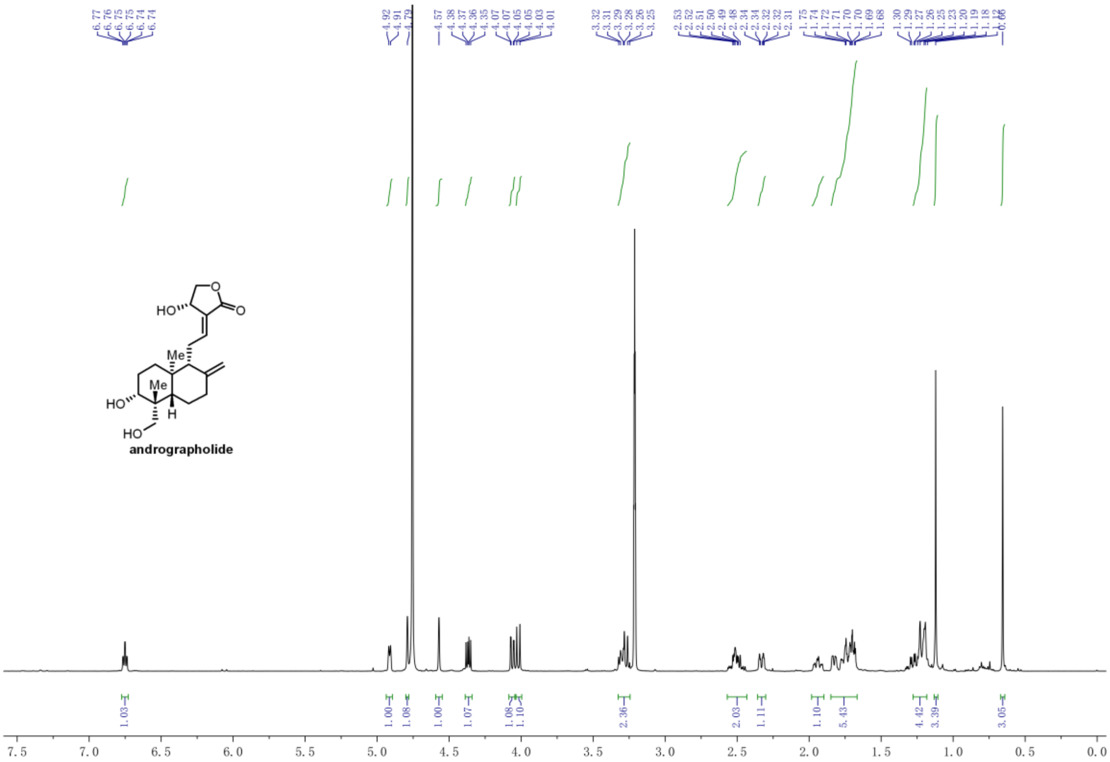
Rf 0.32 (DCM/MeOH = 10/1, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 373.1985, found: 373.1989.

FTIR (neat): 3483, 3417, 2951, 1732, 1673, 1464, 1058, 838, 779 cm^{-1}.

MP 229-231 ˚C

Optical Rotation $[\alpha]_D^{26}$ = -105° (c = 0.19, MeOH)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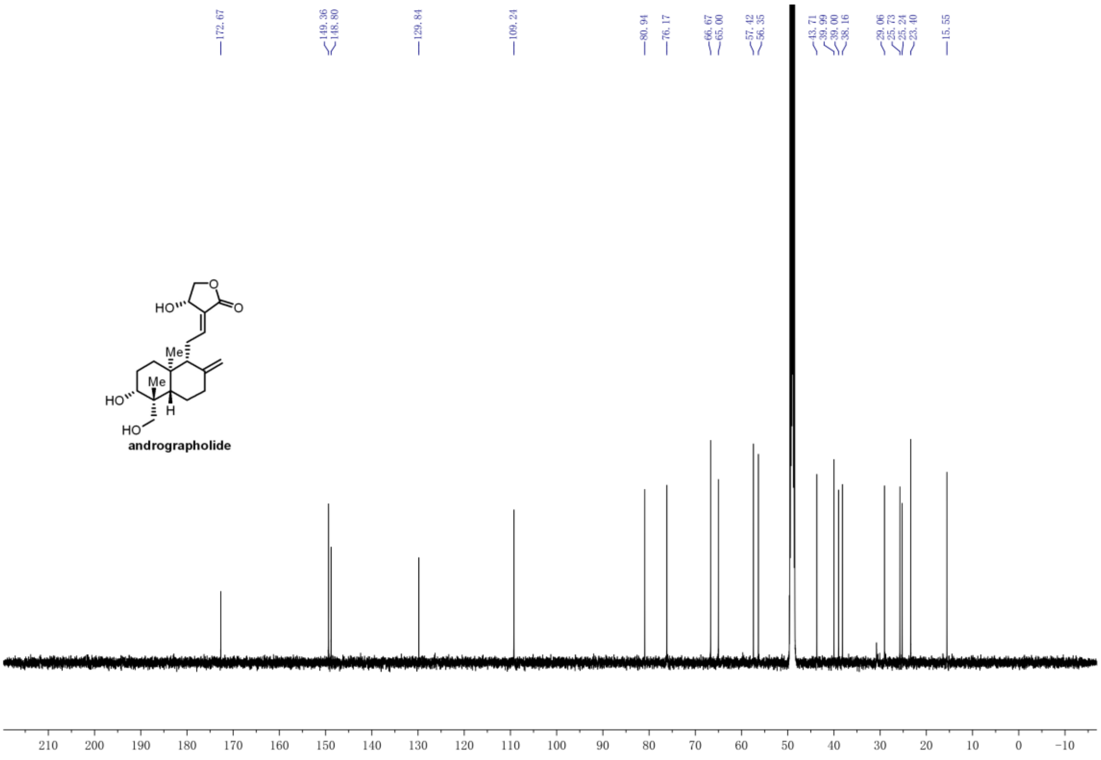
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HO
H
HO
andrographolide
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200
190
180
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160
150
140
130
120
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100
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60
50
40
30
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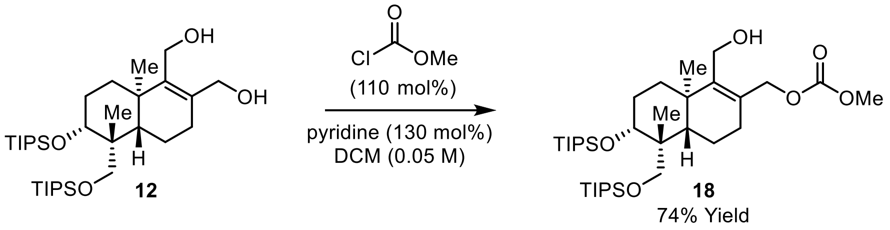
10
0
−10

Detailed Procedures and Spectral Data for Asymmetric Synthesis of 14-Hydroxy-colladonin

((4a*S*,5*R*,6*R*,8a*R*)-1-(Hydroxymethyl)-5,8a-dimethyl-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)-3,4,4a,5,6,7,8,8a-octahydronaphthalen-2-yl)methyl methyl carbonate (18)



Detailed Procedures

To a solution of **12** (146 mg, 0.25 mmol, 100 mol%) in DCM (5 mL) was added pyridine (24 µL, 0.30 mmol, 130 mol%) and methyl chloroformate (20 µL, 0.26 mmol, 110 mol%) at -20 °C. The reaction mixture was allowed to stir for 8 hours at the same temperature, then warmed to 0 °C and stirred for 4 hours. MeOH (50µL) was added to the reaction mixture. The solvent was removed under reduced pressure, and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 5/1) to afford the title compound **18** as a colorless oil (119.2 mg, 0.18 mmol) in 74% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.85 (d, *J* = 11.9 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.27 (d, *J* = 12.1 Hz, 1H), 4.09 (d, *J* = 10.6 Hz, 1H), 4.01 (d, *J* = 12.1 Hz, 1H), 3.82 (d, *J* = 10.5 Hz, 1H), 3.79 (s, 3H), 3.48 (dd, J = 11.3, 4.9 Hz, 1H), 2.17 – 1.99 (m, 2H), 1.98 – 1.88 (m, 2H), 1.84 – 1.67 (m, 3H), 1.45 (td, *J* = 13.2, 4.1 Hz, 1H), 1.18 (s, 3H), 1.13 (s, 3H), 1.07 – 1.04 (m, 42H), 0.94 – 0.87 (m, 1H).

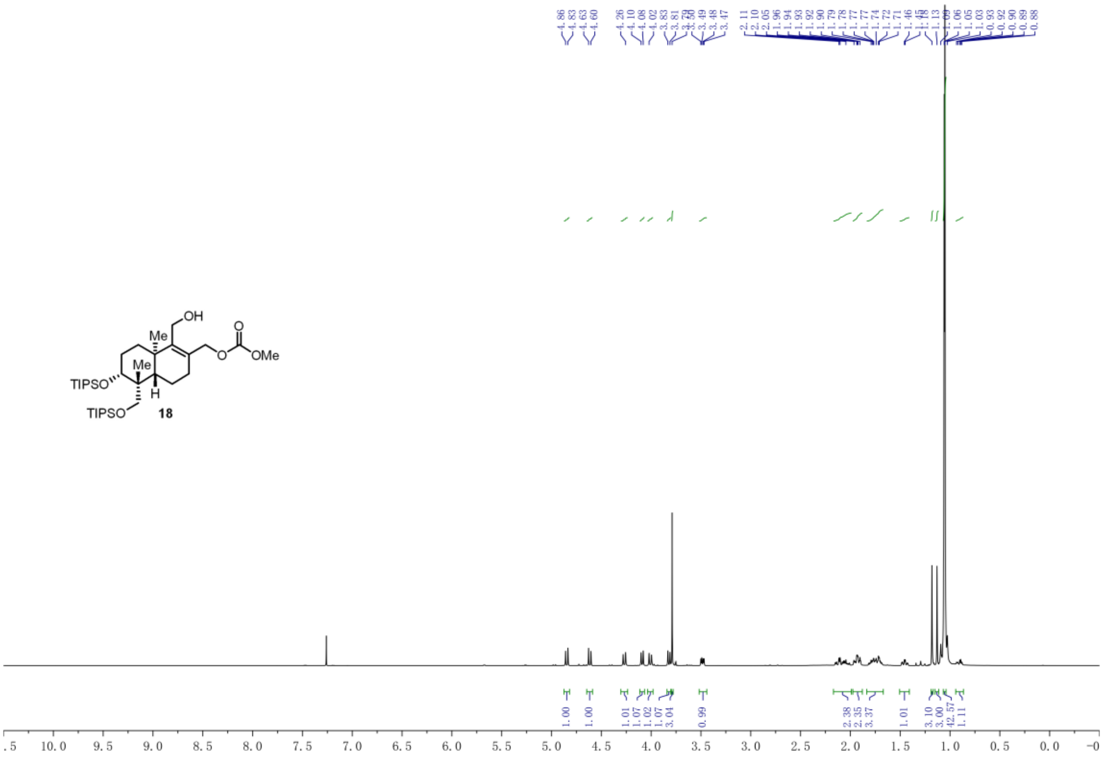
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 147.2, 130.2, 80.1, 69.1, 65.7, 57.4, 55.1, 51.7, 44.5, 38.4, 34.7, 30.9, 28.1, 23.8, 21.0, 20.3, 18.5, 18.4, 18.3, 18.3, 13.1, 12.1.

Rf 0.76 (hexanes/ethyl acetate = 2/1, $KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 663.4447, found: 663.4451.

FTIR (neat): 2943, 2865, 1748, 1462, 1260, 1100, 1065, 881 cm^{-1}.

Optical Rotation $[\alpha]_D^{24}$ = -41° (*c* = 0.23, $CHCl_3$)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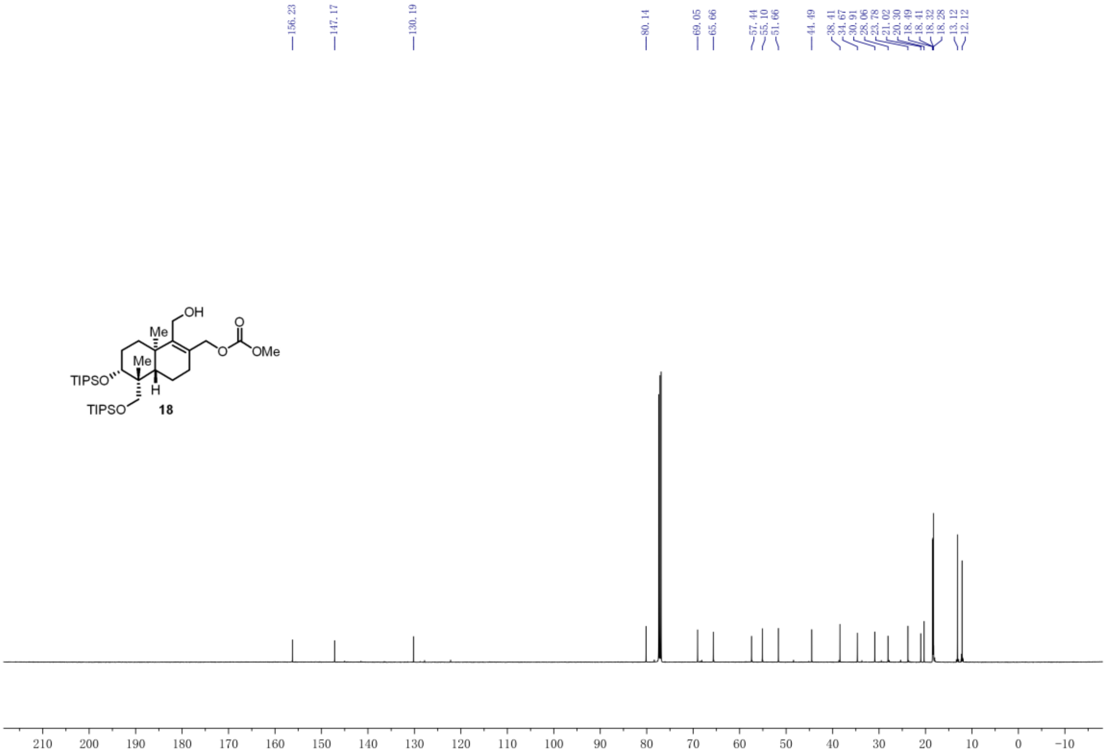
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H
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90
80
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60
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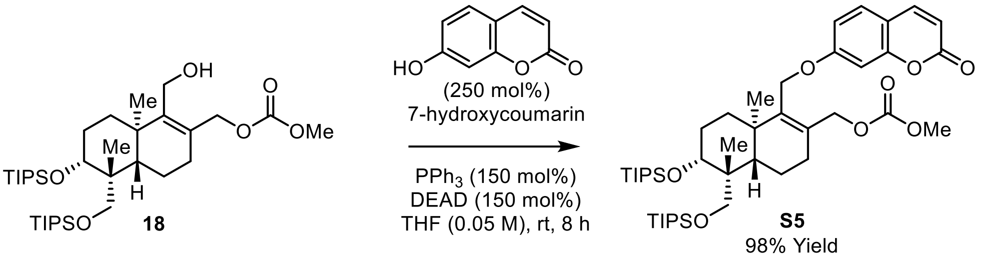
40
30
20
10
0
-10

((4a*S*,5*R*,6*R*,8a*R*)-5,8a-Dimethyl-1-(((2-oxo-2H-chromen-7-yl)oxy)methyl)-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)-3,4,4a,5,6,7,8,8a-octahydronaphthalen-2-yl)methyl methyl carbonate (S5)



Detailed Procedures

To a solution of **18** (124 mg, 0.19 mmol, 100 mol%), 7-hydroxycoumarin (78 mg, 0.48 mmol, 250 mol%) and PPh_3 (75 mg, 0.29 mmol, 150 mol%) in THF (4 mL) was added DEAD (40 wt. % in toluene, 134 μL, 0.29 mmol, 150 mol%) at 0 °C. The resulting mixture was allowed to stir for 8 h at the same temperature. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 5/1). The title compound **S5** was obtained as a colorless oil (149 g, 0.19 mmol) in 98% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 9.5 Hz, 1H), 7.37 (d, *J* = 9.3 Hz, 1H), 6.89 – 6.82 (m, 2H), 6.26 (d, *J* = 9.5 Hz, 1H), 4.74 (d, *J* = 12.3 Hz, 1H), 4.63 (d, *J* = 10.2 Hz, 1H), 4.52 (d, *J* = 12.3 Hz, 1H), 4.43 (d, *J* = 10.2 Hz, 1H), 4.09 (d, *J* = 10.6 Hz, 1H), 3.83 (d, *J* = 10.6 Hz, 1H), 3.76 (s, 3H), 3.51 (dd, *J* = 11.4, 4.3 Hz, 1H), 2.31 (dd, *J* = 18.0, 5.4 Hz, 1H), 2.13 – 1.97 (m, 2H), 1.84 (ddd, *J* = 26.2, 12.5, 5.7 Hz, 1H), 1.78 – 1.63 (m, 3H), 1.48 – 1.40 (m, 1H), 1.21 (s, 3H), 1.20 (s, 3H), 1.08 – 1.04 (m, 43H).

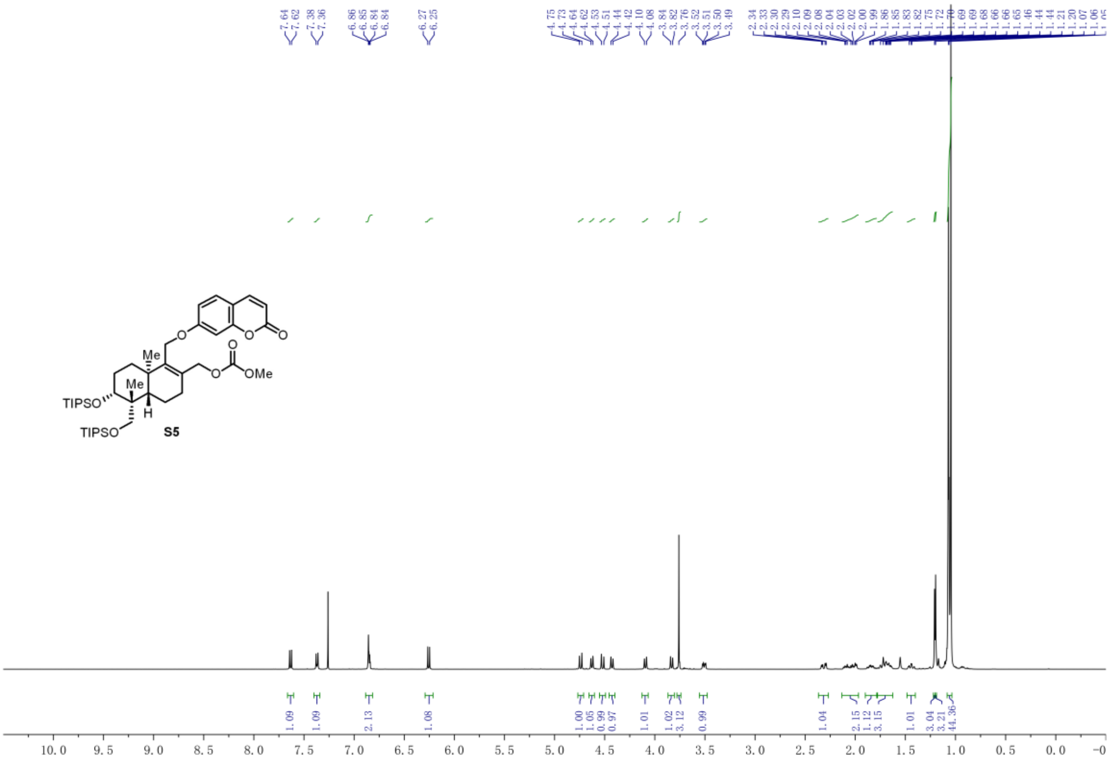
^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 161.3, 156.0, 156.0, 143.5, 141.2, 134.1, 128.9, 113.4, 113.0, 112.9, 101.8, 80.0, 67.8, 65.6, 63.7, 55.0, 51.5, 44.5, 38.4, 34.5, 30.8, 28.0, 23.8, 21.0, 20.4), 18.5, 18.4, 18.3, 18.3, 13.1, 12.1.

Rf 0.27 (hexanes/ethyl acetate = 5/1, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 807.4658, found: 807.4661.

FTIR (neat): 2943, 2865, 1739, 1612, 1463, 1383, 1276, 1196, 1119, 1065, 998 cm^{-1}.

Optical Rotation $[\alpha]_D^{24}$ = -33° (*c* = 0.21, $CHCl_3$)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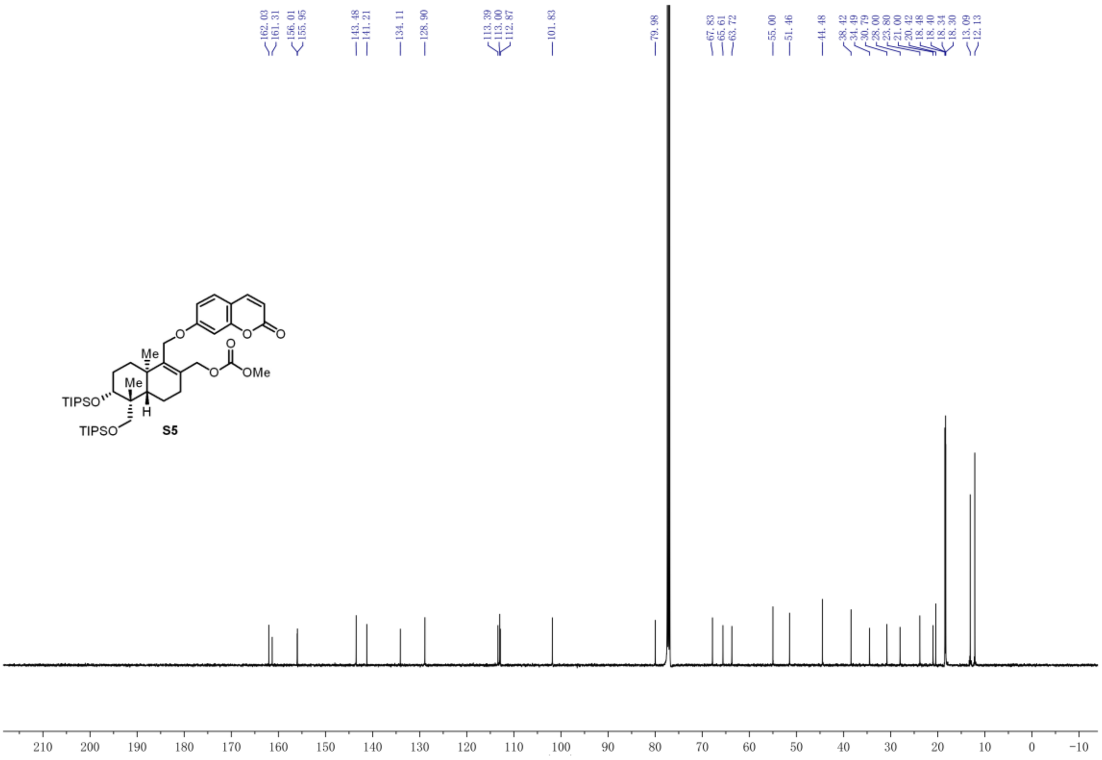
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O
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O
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OMe
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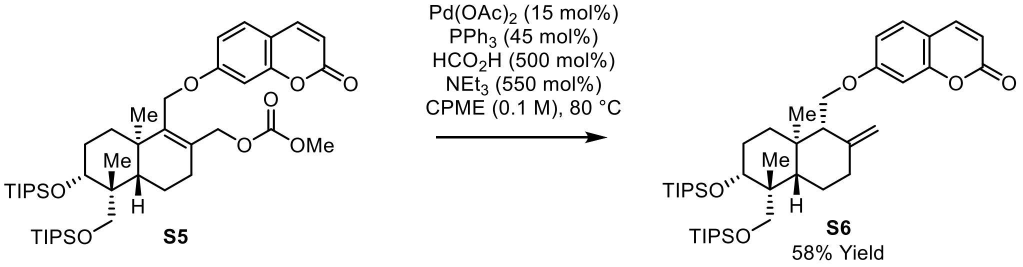
TIPSO
H
TIPSO
S5

7-(((1*R*,4a*S*,5*R*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-6-((triisopropylsilyl)oxy)-5-(((triisopropylsilyl)oxy)methyl)decahydronaphthalen-1-yl)methoxy)-2H-chromen-2-one (S6)



Detailed Procedures

S5 (52.1 mg, 0.066 mmol, 100 mol%), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 15 mol%) and PPh_3 (7.9 mg, 0.030 mmol, 45 mol%) were added to a flame-dried seal tube. The vessel was purged with argon and a solution of triethylamine (51.8 µL, 0.36 mmol, 550 mol%) and formic acid (14.7 µL, 0.033 mmol, 500 mol%) in CPME (0.7 mL) was added. The vessel was sealed and the resulting mixture was allowed to stir at 80 °C for 16 hours. The reaction mixture was allowed to cool to ambient temperature and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (hexanes/ethyl acetate = 10/1). The title compound **S6** was isolated as a colorless oil (27.2 mg, 0.038 mmol) in 58% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 9.5 Hz, 1H), 7.35 (d, *J* = 9.2 Hz, 1H), 6.86 – 6.79 (m, 2H), 6.24 (d, *J* = 9.5 Hz, 1H), 4.90 (s, 1H), 4.52 (s, 1H), 4.24 – 4.14 (m, 2H), 4.08 (d, *J* = 10.5 Hz, 1H), 3.85 (d, *J* = 10.5 Hz, 1H), 3.56 – 3.48 (m, 1H), 2.42 (d, J = 12.6 Hz, 1H), 2.19 (s, 1H), 1.99 – 1.85 (m, 3H), 1.84 – 1.78 (m, 1H), 1.76 – 1.64 (m, 2H), 1.42 (td, *J* = 12.8, 4.8 Hz, 1H), 1.19 – 1.14 (m, 1H), 1.18 (s, 3H), 1.06 (m, 42H), 0.96 (s, 3H).

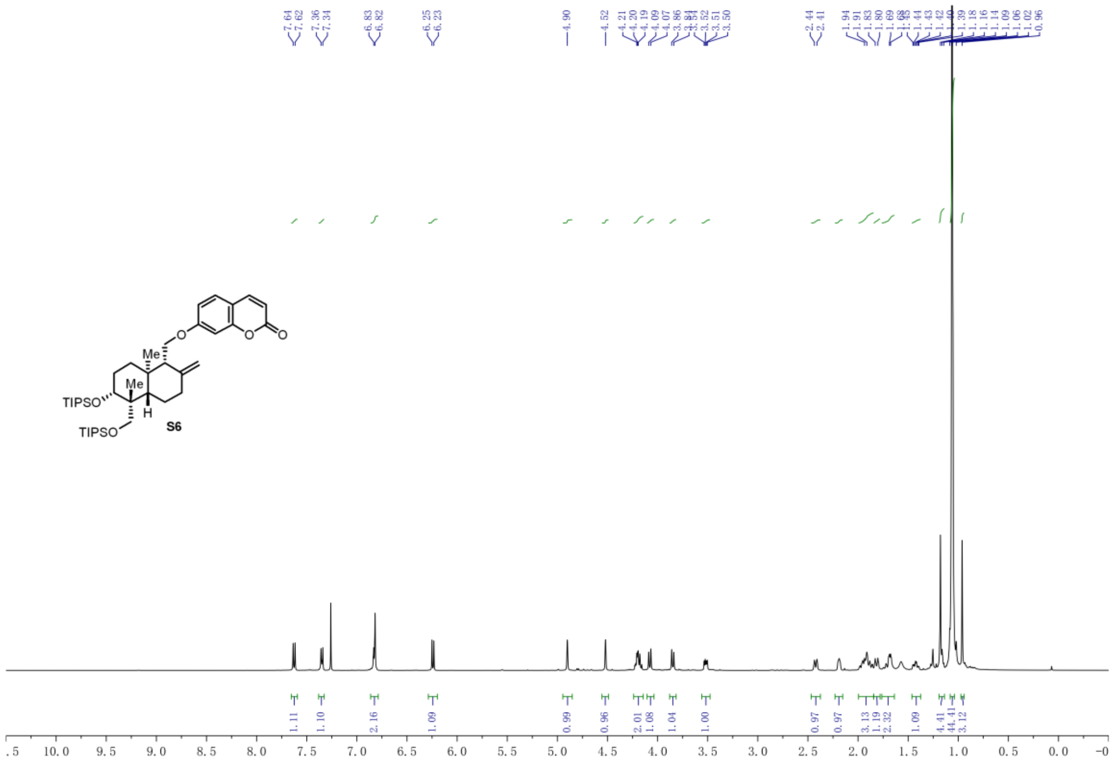
^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 161.4, 156.1, 147.1, 143.6, 128.8, 113.3, 113.1, 112.6, 107.3, 101.5, 80.1, 66.0, 65.0, 55.7, 55.4, 44.9, 38.9, 38.7, 37.9, 28.3, 26.3, 23.8, 18.5, 18.4, 18.30, 18.27, 15.9, 13.1, 12.1.

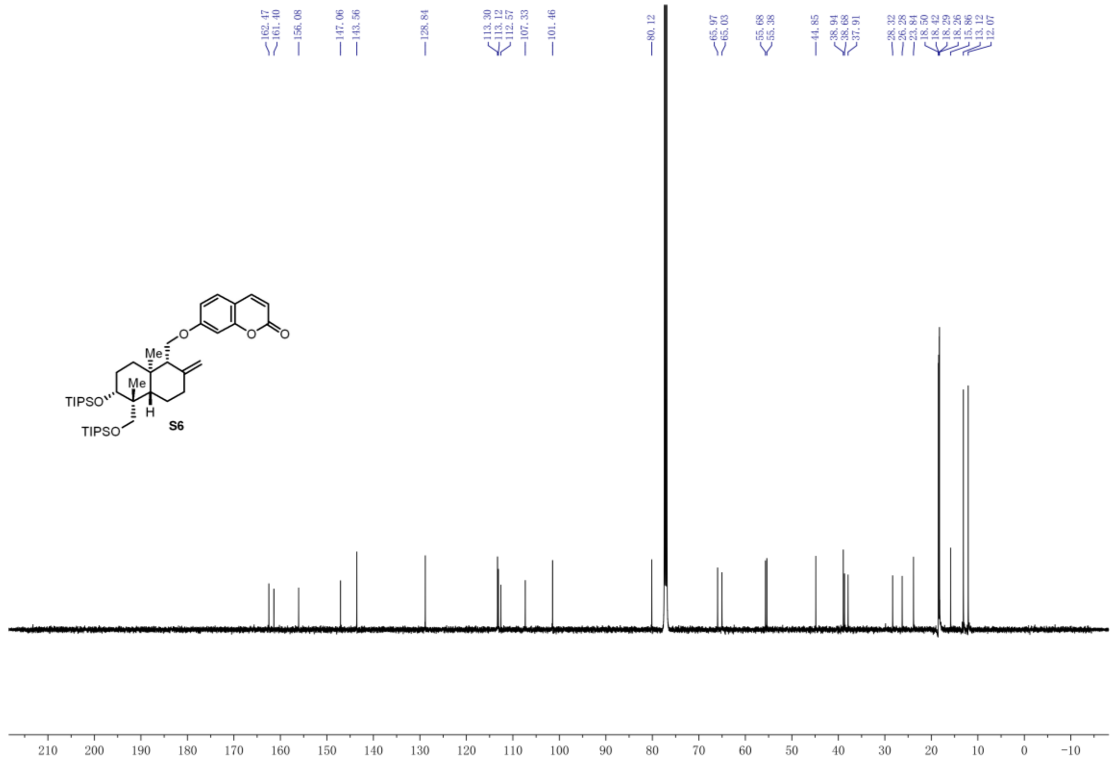
Rf 0.49 (hexanes/ethyl acetate = 5/1, UV/$KMnO_4$)

HRMS (ESI) Calcd. for $(M+Na)^+$ 733.4654, found: 733.4658.

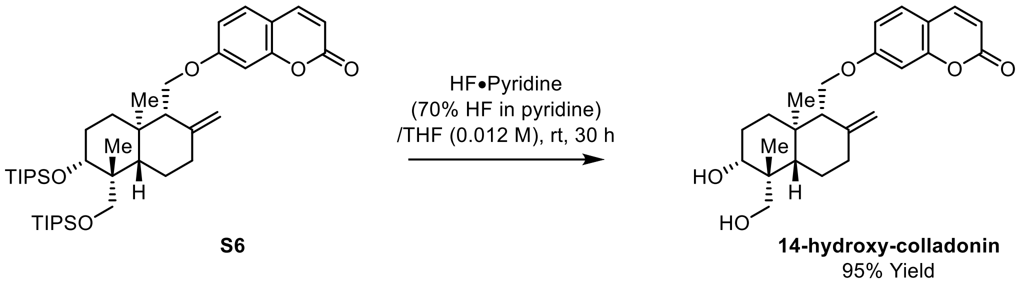
FTIR (neat): 2940, 2865, 1736, 1612, 1280, 1220, 1096, 1006 cm^{-1}.

Optical Rotation $[\alpha]_D^{24}$ = -17° (*c* = 0.21, $CHCl_3$)


7.64
7.62
7.36
7.34
6.83
6.82
6.25
6.23
4.90
4.52
4.21
4.20
4.19
4.09
4.07
3.86
3.84
3.54
3.52
3.51
3.50
2.44
2.41
1.94
1.91
1.83
1.80
1.69
1.68
1.45
1.44
1.43
1.42
1.40
1.39
1.18
1.16
1.14
1.09
1.06
1.02
0.96
Me
Me
H
TIPSO
TIPSO
O
O
O
O
S6
1.11
1.10
2.16
1.09
0.99
0.96
2.01
1.08
1.04
1.00
0.97
0.97
3.13
1.19
2.32
1.09
4.41
44.41
3.12
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0


162.47
161.40
156.08
147.06
143.56
128.84
113.30
113.12
112.57
107.33
101.46
80.12
65.97
65.03
55.68
55.38
44.85
38.94
38.68
37.91
28.32
26.28
23.84
18.50
18.42
18.29
18.26
15.86
13.12
12.07
Me
Me
H
TIPSO
TIPSO
O
O
O
O
S6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

14-Hydroxy-colladonin



Detailed Procedures

To a solution of **S6** (10.1 mg, 0.014 mmol, 100 mol%) in THF (0.5 mL) was added hydrogen fluoride•pyridine (70% HF in pyridine, 376 μL) at 0 ºC. The reaction mixture was allowed to warm to room temperature and was stirred for 30 hours. The reaction was diluted with ethyl acetate. NaHCO$_3$ (aq., sat., 5 mL) was added and the reaction mixture was transferred to a separatory funnel. The aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with brine, and dried (Na$_2$SO$_4$). The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel (PE/ ethyl acetate = 1/1 to1/2). The title compound **14-hydroxycolladonin** was obtained as colorless plates (5.4 mg, 0.0136 mmol) in 95% yield.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, J = 9.5 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 6.84 – 6.79 (m, 2H), 6.25 (d, J = 9.5 Hz, 1H), 4.91 (s, 1H), 4.54 (s, 1H), 4.24 – 4.13 (m, 3H), 3.53 (dd, J = 10.9, 4.5 Hz, 1H), 3.35 (d, J = 11.1 Hz, 1H), 2.46 (dd, J = 13.5, 3.2 Hz, 1H), 2.22 – 2.18 (m, 1H), 2.12 – 2.02 (m, 2H), 1.89 – 1.80 (m, 4H), 1.46 (td, J = 13.8, 5.4 Hz, 1H), 1.39 – 1.32 (m, 1H), 1.27 (s, 3H), 0.79 (s, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 162.2, 161.4, 156.1, 145.9, 143.5, 128.9, 113.2, 113.2, 112.7, 108.4, 101.5, 80.6, 65.8, 64.3, 55.3, 54.8, 43.2, 38.6, 37.7, 37.1, 28.3, 23.7, 22.9, 16.3.

^{1}H NMR (400 MHz, CDCl$_3$/DMSO-d_6 (v/v) = 10/1) δ 7.53 (d, J = 9.5 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 6.69 – 6.65 (m, 2H), 6.08 (d, J = 9.5 Hz, 1H), 4.75 (s, 1H), 4.39 (s, 1H), 4.09 – 3.92 (m, 3H), 3.21 (s, 3H), 3.15 (d, J = 10.8 Hz, 1H), 2.35 – 2.27 (m, 1H), 2.08 – 2.01 (m, 1H), 1.99 – 1.82 (m, 1H), 1.74 – 1.62 (m, 4H), 1.33 – 1.12 (m, 4H), 1.11 (s, 3H), 0.64 (s, 3H).

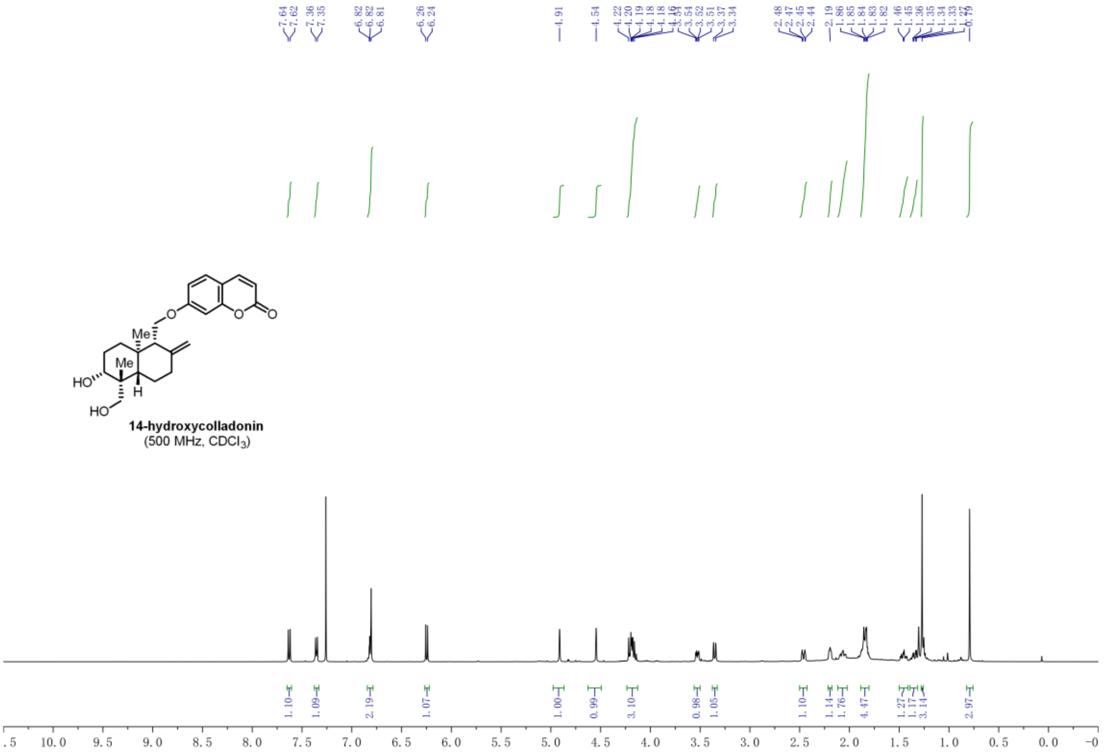
^{13}C NMR (125 MHz, CDCl$_3$/DMSO-d_6 (v/v) = 10/1) δ 161.8, 160.8, 155.4, 145.5, 143.2, 128.5, 112.5, 112.5, 112.1, 107.6, 101.0, 79.3, 65.3, 63.6, 54.7, 54.3, 42.3, 39.5, 37.2, 36.6, 27.6, 23.1, 22.7, 15.8.

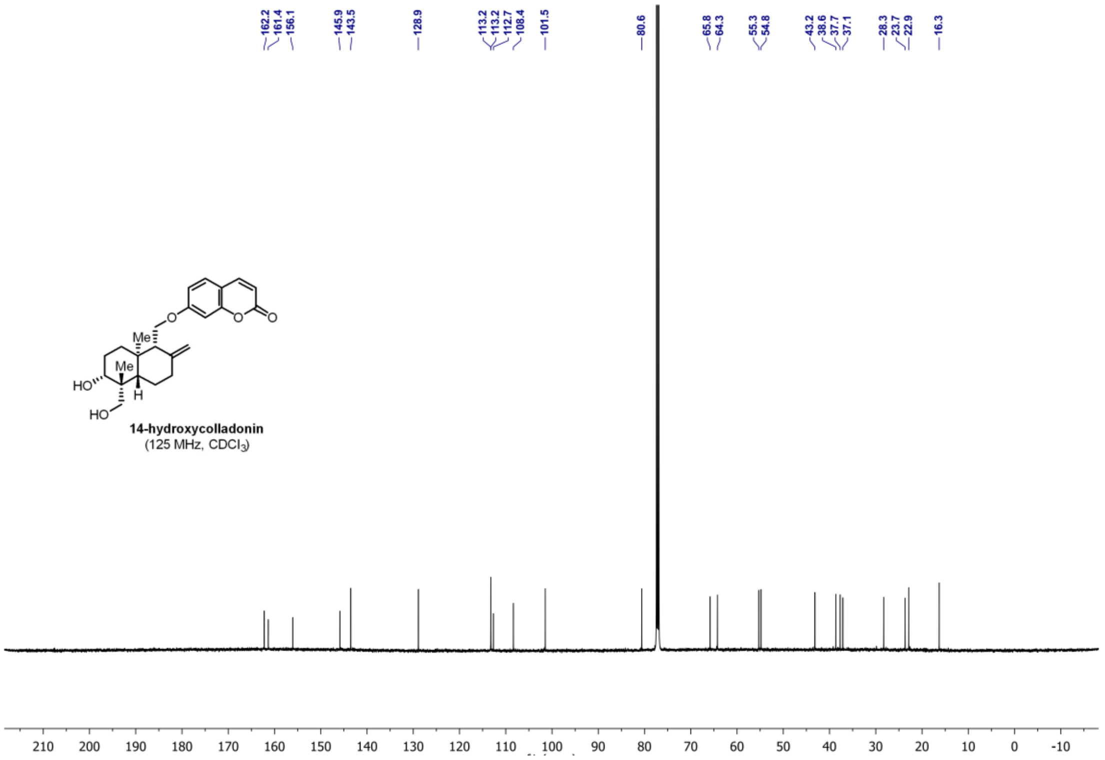
Rf 0.31 (hexanes/ethyl acetate = 1/2, UV/KMnO$_4$)

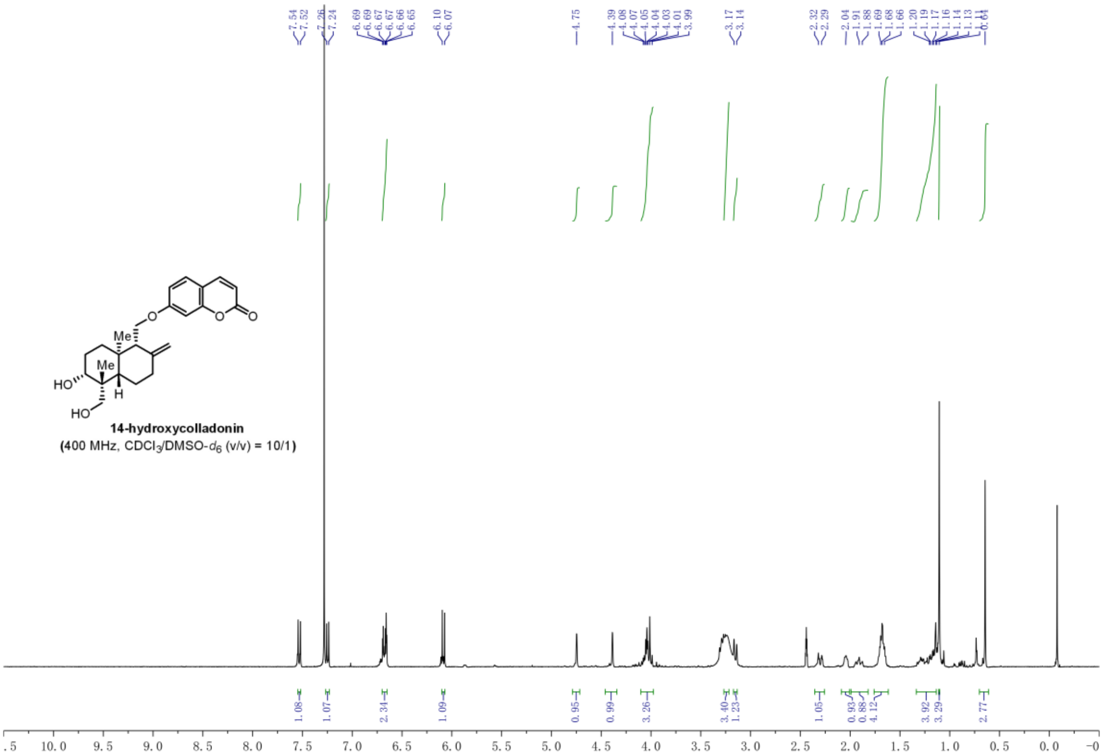
HRMS (ESI) Calcd. for (M+Na)$^+$ 421.1985, found: 421.1992.

FTIR (neat): 3314, 2929, 2852, 1708, 1612, 1285, 1240, 1121, 1155, 1034, 825 cm^{-1}.

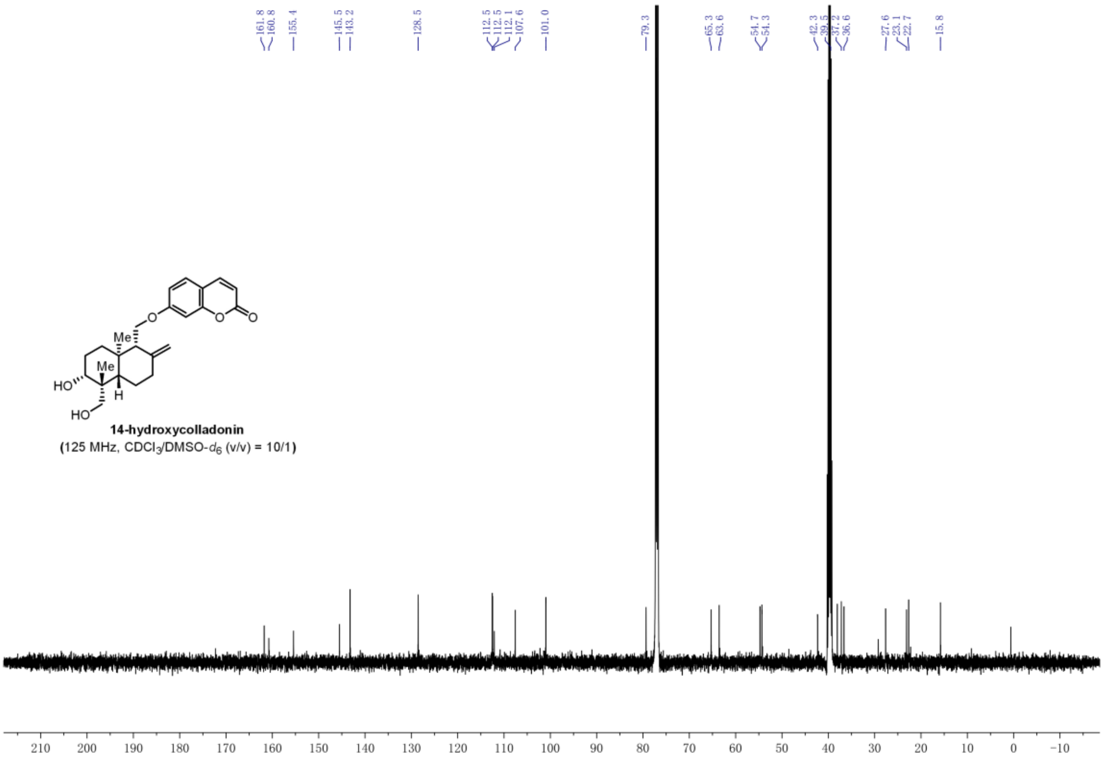
Optical Rotation $[\alpha]_D^{24}$ = -36.4° (c = 0.11, CH$_2$Cl$_2$)


14-hydroxycolladonin
(500 MHz, $CDCl_3$)


14-hydroxycolladonin
(125 MHz, $CDCl_3$)

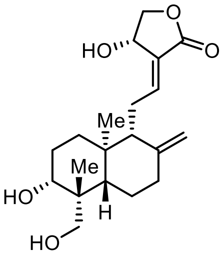


14-hydroxycolladonin
(400 MHz, $CDCl_3$/DMSO-d_6 (v/v) = 10/1)



14-hydroxycolladonin
(125 MHz, $CDCl_3$/DMSO-d_6 (v/v) = 10/1)

Comparison of NMR Data between Natural and Synthetic Andrographolide and 14-Hydroxy-colladonin



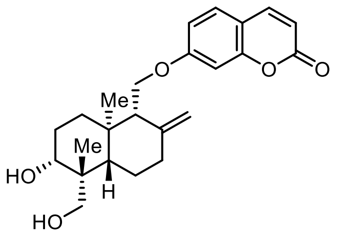
andrographolide

Table S1. ^{1}H NMR data of natural[8] and synthetic andrographolide

Natural		Synthetic (This Work)	
δ_H (ppm)	multiplicity, *J*(Hz), integration	δ_H (ppm)	multiplicity, *J*(Hz), integration
6.75	td, 6.0, 1.0, 1H	6.75	td, 6.8, 1.5, 1H
4.92	d, 6.0, 1H	4.91	d, 6.0, 1H
4.79	brs, 1H	4.79	brs, 1H
4.57	brs, 1H	4.57	brs, 1H
4.37	dd, 10.0, 6.0, 1H	4.37	dd, 10.2, 6.1, 1H
4.07	dd, 10.0, 2.0, 1H	4.06	dd, 10.2, 2.0, 1H
4.02	d, 11.0, 1H	4.02	d, 11.0, 1H
3.27	d, 11.0, 1H	3.27	d, 11.0, 1H
3.23-3.17	m, 1H	3.32-3.19	m, 1H
2.58-2.43	m, 2H	2.58-2.43	m, 2H
2.33	dt, 7.0, 2.0, 1H	2.38-2.28	m, 1H
1.98-1.64	m, 5H	1.98-1.64	m, 5H
1.35-1.15	m, 4H	1.34-1.15	m, 4H
1.12	s, 3H	1.12	s, 3H
0.65	s, 3H	0.66	s, 3H

Table S2. ^{13}C NMR data of natural[8] and synthetic andrographolide

Natural	**Synthetic (This Work)**
δ_H (ppm)	δ_H (ppm)
172.7	172.7
149.5	149.4
148.8	148.8
129.7	129.8
109.2	109.2
80.9	80.9
76.2	76.2
66.6	66.7
65.0	65.0
57.4	57.4
56.3	56.3
43.7	43.7
40.0	40.0
39.0	39.0
38.1	38.2
29.0	29.1
25.7	25.7
25.2	25.2
23.4	23.4
15.5	15.5



14-hydroxycolladonin

Table S3. ^{1}H NMR data of natural[9] and synthetic 14-hydroxy-colladonin

Natural[1] 300 MHz $CDCl_3$/DMSO-d_6 (unknown)		**Synthetic (This Work)** 400 MHz $CDCl_3$/DMSO-d_6 (v/v) = 10/1	
δ_H (ppm)	multiplicity, *J*(Hz), integration	δ_H (ppm)	multiplicity, *J*(Hz), integration
7.53	d, 9.4, 1H	7.53	d, 9.5, 1H
7.24	d, 8.4, 1H	7.25	d, 8.5, 1H
6.66	m, 2H	6.69-6.65	m, 2H
6.08	d, 9.4, 1H	6.08	d, 9.5, 1H
4.75	s, 1H	4.75	s, 1H
4.39	s, 1H	4.39	s, 1H
4.04	m, 2H	4.09-3.92	m, 3H
3.84*	brs, 1H		
3.19	brs, 1H	3.21	brs, 3H
3.15	t, 9.6, 1H	3.15	d, 10.8, 1H
not shown#		2.35-2.27	m, 1H
not shown#		2.08-2.01	m, 1H
not shown#		1.99-1.82	m, 1H
not shown#		1.74-1.62	m, 4H
not shown#		1.33-1.12	m, 3H
1.11	s, 3H	1.11	s, 3H
064	s, 3H	0.64	s, 3H

* Alcoholic proton

The authors in ref. 1 did not give the chemical shifts of H1, H2, H6, H7 and H9.

Table S4. ^{13}C NMR data of natural[9] and synthetic 14-hydroxy-colladonin

Natural 75 MHz $CDCl_3$/DMSO-d_6 (unknown)	**Synthetic (This Work)** 125 MHz $CDCl_3$/DMSO-d_6 (v/v) = 10/1	$\Delta\delta = \delta_N - \delta_S$ (ppm)
δ_H (ppm)	δ_H (ppm)	$\Delta\delta$ (ppm)
161.8	161.8	0
160.8	160.8	0
155.4	155.4	0
145.5	145.5	0
143.2	143.2	0
128.5	128.5	0
112.5	112.5	0
112.5	112.5	0
112.1	112.1	0
107.6	107.6	0
101.0	101.0	0
79.4	79.3	0.1
65.3	65.3	0
63.6	63.6	0
54.8	54.7	0.1
54.3	54.3	0
42.3	42.3	0
39.5	39.5	0
37.2	37.2	0
36.6	36.6	0
27.6	27.6	0
23.1	23.1	0
22.7	22.7	0
15.8	15.8	0

Crystallographic Material for 9

X-ray Experimental for $C_{20}H_{30}O_6$ (9)

Crystals grew as clusters of colorless prisms by slow evaporation from dichloromethane. The data crystal was cut from a larger crystal and had approximate dimensions; 0.40 x 0.20 x 0.15 mm. The data were collected on a Rigaku AFC12 diffractometer with a Saturn 724+CCD using a graphite monochromator with MoKα□ radiation (= 0.71073Å). A total of 1293 frames of data were collected using □ω-scans with a scan range of 0.5° and a counting time of 25 seconds per frame. The data were collected at 100 K using a Rigaku XStream Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 5. Data reduction were performed using the Rigaku Americas Corporation's Crystal Clear version 1.40.[10] The structure was solved by direct methods using SUPERFLIP[11] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.[12] Structure analysis was aided by use of the programs PLATON98[13] and WinGX.[14] The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms).

There are three crystallographically unique molecules in the asymmetric unit. The molecules all have the same configuration and differ only slightly in their conformation. The absolute structure was assigned on the basis of the known configuration of the starting material.

The function, $\Sigma w(|F_O|^2 - |F_C|^2)^2$, was minimized, where $w = 1/[(\sigma(F_O))^2 + (0.0352*P)^2]$ and $P = (|F_O|^2 + 2|F_C|^2)/3$. $R_W(F^2)$ refined to 0.0958, with R(F) equal to 0.0339 and a goodness of fit, S, = 1.07. Definitions used for calculating R(F), $R_W(F^2)$ and the goodness of fit, S, are given below.[15] The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[16] All figures were generated using SHELXTL/PC.[17] Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found elsewhere.

Table S5. Crystal data and structure refinement for **9**.

Empirical formula	C20 H30 O6	
Formula weight	366.44	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 21	
Unit cell dimensions	a = 12.3296(18) Å	□= 90°.
	b = 10.4946(16) Å	□= 90.083(4)°.
	c = 22.352(3) Å	□ = 90°.
Volume	2892.2(8) Å^3	
Z	6	
Density (calculated)	1.262 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	1188	
Crystal size	0.400 x 0.200 x 0.150 mm^3	
Theta range for data collection	3.132 to 27.483°.	
Index ranges	-15<=h<=16, -13<=k<=12, -29<=l<=29	
Reflections collected	41107	
Independent reflections	12456 [R(int) = 0.0428]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.837	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12456 / 1 / 722	
Goodness-of-fit on F^2	1.072	
Final R indices [I>2sigma(I)]	R1 = 0.0339, wR2 = 0.0835	
R indices (all data)	R1 = 0.0738, wR2 = 0.0958	
Absolute structure parameter	0.5(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.268 and -0.158 e.Å^{-3}	

Table S6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **9**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O1	3716(4)	-138(4)	1473(2)	26(1)
O2	4257(4)	798(5)	574(2)	26(1)
O3	9069(4)	-36(4)	-14(2)	24(1)
O4	8804(4)	1791(4)	489(2)	23(1)
O5	10236(4)	304(5)	1223(2)	28(1)
O6	9741(4)	-23(5)	2171(2)	27(1)
C1	3360(6)	525(7)	958(3)	25(2)
C2	5132(5)	1474(7)	857(3)	22(2)
C3	5993(6)	1634(7)	373(3)	29(2)
C4	6426(6)	337(8)	176(3)	30(2)
C5	6886(5)	-482(6)	685(3)	21(2)
C6	8011(6)	-38(6)	885(3)	18(1)
C7	8387(5)	-270(6)	1438(3)	18(2)
C8	7732(6)	-835(7)	1933(3)	23(2)
C9	6590(6)	-1269(6)	1748(3)	25(2)
C10	6075(5)	-539(6)	1218(3)	21(2)
C11	5543(6)	763(6)	1402(3)	19(2)
C12	4542(6)	507(7)	1793(3)	24(2)
C13	2736(5)	1736(7)	1115(3)	29(2)
C14	2659(6)	-386(8)	614(4)	39(2)
C15	7060(6)	-1829(7)	434(4)	39(2)
C16	8711(5)	533(6)	409(3)	17(1)
C17	9507(6)	2448(7)	65(4)	33(2)
C18	9551(6)	45(6)	1585(3)	20(2)
C19	10847(6)	218(7)	2360(3)	29(2)
C20	6302(6)	1657(7)	1763(3)	26(2)
O7	10928(4)	795(5)	3907(2)	26(1)
O8	10375(4)	-131(5)	4808(2)	26(1)
O9	15737(4)	-36(5)	3318(2)	26(1)
O10	15473(4)	1793(4)	3825(2)	21(1)
O11	16907(4)	291(5)	4559(2)	28(1)

O12	16405(4)	-31(5)	5508(2)	26(1)
C21	10014(6)	528(8)	4285(3)	26(2)
C22	11800(5)	1466(7)	4193(3)	23(2)
C23	12665(6)	1624(7)	3704(3)	30(2)
C24	13081(6)	344(8)	3510(3)	34(2)
C25	13551(6)	-466(6)	4025(3)	24(2)
C26	14684(5)	-39(6)	4222(3)	17(1)
C27	15065(5)	-262(6)	4773(3)	18(2)
C28	14395(6)	-843(7)	5267(3)	23(2)
C29	13251(6)	-1265(6)	5075(3)	26(2)
C30	12747(5)	-543(6)	4561(3)	20(2)
C31	12225(5)	771(6)	4734(3)	19(2)
C32	11220(6)	513(7)	5125(3)	24(2)
C33	9396(6)	1737(7)	4449(3)	31(2)
C34	9320(6)	-401(8)	3945(4)	39(2)
C35	13739(6)	-1831(7)	3765(4)	39(2)
C36	15379(5)	540(6)	3742(3)	18(2)
C37	16177(6)	2431(6)	3406(3)	30(2)
C38	16206(6)	44(6)	4916(3)	20(2)
C39	17507(6)	219(7)	5689(3)	27(2)
C40	12972(6)	1640(6)	5090(3)	27(2)
O13	12407(4)	5792(5)	2760(2)	25(1)
O14	12953(4)	4864(5)	1859(2)	27(1)
O15	7599(4)	4970(5)	3347(2)	25(1)
O16	7855(4)	6796(4)	2844(2)	22(1)
O17	6430(4)	5304(5)	2109(2)	28(1)
O18	6925(4)	4974(5)	1160(2)	26(1)
C41	13316(6)	5542(7)	2381(3)	27(2)
C42	12115(5)	5511(7)	1535(3)	24(2)
C43	11099(6)	5753(6)	1927(3)	19(2)
C44	10587(6)	4469(6)	2119(3)	20(2)
C45	10079(6)	3725(6)	1591(3)	25(2)
C46	8946(6)	4167(7)	1397(3)	24(2)
C47	8269(5)	4734(6)	1889(3)	18(2)
C48	8665(5)	4963(6)	2438(3)	18(1)
C49	9779(6)	4524(6)	2651(3)	22(2)

C50	10253(6)	5341(8)	3158(3)	31(2)
C51	10671(6)	6637(8)	2962(3)	32(2)
C52	11530(5)	6481(7)	2492(3)	22(2)
C53	13943(6)	6743(7)	2216(3)	30(2)
C54	14009(6)	4600(8)	2732(4)	39(2)
C55	10371(6)	6650(6)	1570(3)	26(2)
C56	7115(5)	5041(6)	1751(3)	19(2)
C57	5822(5)	5213(7)	978(3)	28(2)
C58	7960(5)	5527(7)	2921(3)	19(2)
C59	7162(6)	7441(7)	3266(3)	31(2)
C60	9601(7)	3180(7)	2903(4)	41(2)

Table S7. Bond lengths [Å] and angles [°] for **9**.

O1-C1	1.413(8)	C10-C11	1.571(9)
O1-C12	1.417(8)	C10-H10	1.00
O2-C1	1.430(8)	C11-C12	1.537(8)
O2-C2	1.437(8)	C11-C20	1.550(8)
O3-C16	1.203(7)	C12-H12A	0.99
O4-C16	1.337(7)	C12-H12B	0.99
O4-C17	1.458(7)	C13-H13A	0.98
O5-C18	1.202(7)	C13-H13B	0.98
O6-C18	1.333(7)	C13-H13C	0.98
O6-C19	1.448(8)	C14-H14A	0.98
C1-C14	1.500(10)	C14-H14B	0.98
C1-C13	1.526(9)	C14-H14C	0.98
C2-C11	1.516(9)	C15-H15A	0.98
C2-C3	1.526(9)	C15-H15B	0.98
C2-H2	1.00	C15-H15C	0.98
C3-C4	1.528(10)	C17-H17A	0.98
C3-H3A	0.99	C17-H17B	0.98
C3-H3B	0.99	C17-H17C	0.98
C4-C5	1.534(9)	C19-H19A	0.98
C4-H4A	0.99	C19-H19B	0.98
C4-H4B	0.99	C19-H19C	0.98
C5-C6	1.530(9)	C20-H20A	0.98
C5-C15	1.536(9)	C20-H20B	0.98
C5-C10	1.557(9)	C20-H20C	0.98
C6-C7	1.340(9)	O7-C22	1.436(8)
C6-C16	1.497(9)	O7-C21	1.438(7)
C7-C8	1.494(9)	O8-C32	1.428(8)
C7-C18	1.509(9)	O8-C21	1.429(8)
C8-C9	1.536(9)	O9-C36	1.209(7)
C8-H8A	0.99	O10-C36	1.333(7)
C8-H8B	0.99	O10-C37	1.442(7)
C9-C10	1.546(9)	O11-C38	1.206(8)
C9-H9A	0.99	O12-C38	1.348(7)
C9-H9B	0.99	O12-C39	1.441(8)

C21-C34	1.502(10)	C35-H35A	0.98
C21-C33	1.525(9)	C35-H35B	0.98
C22-C31	1.506(9)	C35-H35C	0.98
C22-C23	1.537(9)	C37-H37A	0.98
C22-H22	1.00	C37-H37B	0.98
C23-C24	1.502(10)	C37-H37C	0.98
C23-H23A	0.99	C39-H39A	0.98
C23-H23B	0.99	C39-H39B	0.98
C24-C25	1.543(10)	C39-H39C	0.98
C24-H24A	0.99	C40-H40A	0.98
C24-H24B	0.99	C40-H40B	0.98
C25-C26	1.531(10)	C40-H40C	0.98
C25-C30	1.558(9)	O13-C41	1.430(8)
C25-C35	1.563(9)	O13-C52	1.433(7)
C26-C27	1.339(9)	O14-C42	1.433(8)
C26-C36	1.501(9)	O14-C41	1.437(8)
C27-C38	1.478(9)	O15-C58	1.205(7)
C27-C28	1.508(9)	O16-C58	1.348(8)
C28-C29	1.538(10)	O16-C59	1.443(7)
C28-H28A	0.99	O17-C56	1.197(8)
C28-H28B	0.99	O18-C56	1.343(7)
C29-C30	1.511(9)	O18-C57	1.440(8)
C29-H29A	0.99	C41-C54	1.524(10)
C29-H29B	0.99	C41-C53	1.524(10)
C30-C31	1.570(8)	C42-C43	1.551(9)
C30-H30	1.00	C42-H42A	0.99
C31-C40	1.520(9)	C42-H42B	0.99
C31-C32	1.541(9)	C43-C55	1.526(9)
C32-H32A	0.99	C43-C44	1.548(9)
C32-H32B	0.99	C43-C52	1.567(8)
C33-H33A	0.98	C44-C45	1.547(9)
C33-H33B	0.98	C44-C49	1.554(9)
C33-H33C	0.98	C44-H44	1.00
C34-H34A	0.98	C45-C46	1.534(10)
C34-H34B	0.98	C45-H45A	0.99
C34-H34C	0.98	C45-H45B	0.99

C46-C47	1.504(9)	C53-H53B	0.98
C46-H46A	0.99	C53-H53C	0.98
C46-H46B	0.99	C54-H54A	0.98
C47-C48	1.340(8)	C54-H54B	0.98
C47-C56	1.491(9)	C54-H54C	0.98
C48-C58	1.507(9)	C55-H55A	0.98
C48-C49	1.525(9)	C55-H55B	0.98
C49-C60	1.534(9)	C55-H55C	0.98
C49-C50	1.535(10)	C57-H57A	0.98
C50-C51	1.519(10)	C57-H57B	0.98
C50-H50A	0.99	C57-H57C	0.98
C50-H50B	0.99	C59-H59A	0.98
C51-C52	1.502(9)	C59-H59B	0.98
C51-H51A	0.99	C59-H59C	0.98
C51-H51B	0.99	C60-H60A	0.98
C52-H52	1.00	C60-H60B	0.98
C53-H53A	0.98	C60-H60C	0.98

C1-O1-C12	113.4(5)	C4-C3-H3A	109.5
C1-O2-C2	114.5(5)	C2-C3-H3B	109.5
C16-O4-C17	115.5(5)	C4-C3-H3B	109.5
C18-O6-C19	116.1(5)	H3A-C3-H3B	108.1
O1-C1-O2	110.4(5)	C3-C4-C5	114.5(5)
O1-C1-C14	106.3(6)	C3-C4-H4A	108.6
O2-C1-C14	105.4(6)	C5-C4-H4A	108.6
O1-C1-C13	112.3(6)	C3-C4-H4B	108.7
O2-C1-C13	111.2(5)	C5-C4-H4B	108.6
C14-C1-C13	111.0(6)	H4A-C4-H4B	107.6
O2-C2-C11	111.2(6)	C6-C5-C4	112.3(6)
O2-C2-C3	105.4(6)	C6-C5-C15	105.1(6)
C11-C2-C3	113.0(6)	C4-C5-C15	107.3(6)
O2-C2-H2	109.1	C6-C5-C10	111.7(5)
C11-C2-H2	109.1	C4-C5-C10	110.6(5)
C3-C2-H2	109.1	C15-C5-C10	109.5(5)
C2-C3-C4	110.5(6)	C7-C6-C16	122.0(6)
C2-C3-H3A	109.5	C7-C6-C5	121.8(6)

C16-C6-C5	115.9(6)
C6-C7-C8	124.6(6)
C6-C7-C18	119.2(6)
C8-C7-C18	116.1(6)
C7-C8-C9	114.4(6)
C7-C8-H8A	108.6
C9-C8-H8A	108.7
C7-C8-H8B	108.6
C9-C8-H8B	108.7
H8A-C8-H8B	107.6
C8-C9-C10	115.8(5)
C8-C9-H9A	108.3
C10-C9-H9A	108.3
C8-C9-H9B	108.3
C10-C9-H9B	108.3
H9A-C9-H9B	107.4
C9-C10-C5	110.0(5)
C9-C10-C11	113.6(6)
C5-C10-C11	115.9(5)
C9-C10-H10	105.5
C5-C10-H10	105.5
C11-C10-H10	105.5
C2-C11-C12	106.0(6)
C2-C11-C20	108.7(6)
C12-C11-C20	107.2(5)
C2-C11-C10	110.9(5)
C12-C11-C10	109.4(5)
C20-C11-C10	114.3(6)
O1-C12-C11	112.0(5)
O1-C12-H12A	109.2
C11-C12-H12A	109.2
O1-C12-H12B	109.2
C11-C12-H12B	109.2
H12A-C12-H12B	107.9
C1-C13-H13A	109.5
C1-C13-H13B	109.5
H13A-C13-H13B	109.5
C1-C13-H13C	109.5
H13A-C13-H13C	109.5
H13B-C13-H13C	109.5
C1-C14-H14A	109.5
C1-C14-H14B	109.5
H14A-C14-H14B	109.5
C1-C14-H14C	109.5
H14A-C14-H14C	109.5
H14B-C14-H14C	109.5
C5-C15-H15A	109.5
C5-C15-H15B	109.5
H15A-C15-H15B	109.5
C5-C15-H15C	109.5
H15A-C15-H15C	109.5
H15B-C15-H15C	109.5
O3-C16-O4	124.3(6)
O3-C16-C6	125.0(6)
O4-C16-C6	110.5(6)
O4-C17-H17A	109.5
O4-C17-H17B	109.5
H17A-C17-H17B	109.5
O4-C17-H17C	109.5
H17A-C17-H17C	109.5
H17B-C17-H17C	109.5
O5-C18-O6	123.5(6)
O5-C18-C7	124.9(6)
O6-C18-C7	111.6(6)
O6-C19-H19A	109.5
O6-C19-H19B	109.5
H19A-C19-H19B	109.5
O6-C19-H19C	109.5
H19A-C19-H19C	109.5
H19B-C19-H19C	109.5
C11-C20-H20A	109.5
C11-C20-H20B	109.5

H20A-C20-H20B	109.5	C24-C25-C35	106.5(6)
C11-C20-H20C	109.5	C30-C25-C35	109.4(6)
H20A-C20-H20C	109.5	C27-C26-C36	121.9(6)
H20B-C20-H20C	109.5	C27-C26-C25	122.1(6)
C22-O7-C21	114.9(5)	C36-C26-C25	115.8(6)
C32-O8-C21	113.8(5)	C26-C27-C38	119.6(6)
C36-O10-C37	114.8(5)	C26-C27-C28	123.5(7)
C38-O12-C39	115.8(5)	C38-C27-C28	116.9(6)
O8-C21-O7	109.3(6)	C27-C28-C29	114.6(6)
O8-C21-C34	106.1(6)	C27-C28-H28A	108.6
O7-C21-C34	105.9(6)	C29-C28-H28A	108.6
O8-C21-C33	111.2(6)	C27-C28-H28B	108.6
O7-C21-C33	111.8(6)	C29-C28-H28B	108.6
C34-C21-C33	112.2(6)	H28A-C28-H28B	107.6
O7-C22-C31	112.3(6)	C30-C29-C28	116.3(6)
O7-C22-C23	104.8(5)	C30-C29-H29A	108.2
C31-C22-C23	112.5(6)	C28-C29-H29A	108.2
O7-C22-H22	109.0	C30-C29-H29B	108.2
C31-C22-H22	109.0	C28-C29-H29B	108.2
C23-C22-H22	109.0	H29A-C29-H29B	107.4
C24-C23-C22	110.3(6)	C29-C30-C25	110.5(6)
C24-C23-H23A	109.6	C29-C30-C31	114.9(5)
C22-C23-H23A	109.6	C25-C30-C31	113.9(5)
C24-C23-H23B	109.6	C29-C30-H30	105.5
C22-C23-H23B	109.6	C25-C30-H30	105.5
H23A-C23-H23B	108.1	C31-C30-H30	105.5
C23-C24-C25	113.9(6)	C22-C31-C40	109.8(5)
C23-C24-H24A	108.8	C22-C31-C32	105.1(5)
C25-C24-H24A	108.8	C40-C31-C32	107.2(5)
C23-C24-H24B	108.8	C22-C31-C30	111.7(5)
C25-C24-H24B	108.8	C40-C31-C30	114.1(5)
H24A-C24-H24B	107.7	C32-C31-C30	108.4(5)
C26-C25-C24	113.2(6)	O8-C32-C31	112.8(5)
C26-C25-C30	112.1(6)	O8-C32-H32A	109.0
C24-C25-C30	111.3(6)	C31-C32-H32A	109.0
C26-C25-C35	103.8(6)	O8-C32-H32B	109.0

C31-C32-H32B	109.0	H39A-C39-H39C	109.5
H32A-C32-H32B	107.8	H39B-C39-H39C	109.5
C21-C33-H33A	109.5	C31-C40-H40A	109.5
C21-C33-H33B	109.5	C31-C40-H40B	109.5
H33A-C33-H33B	109.5	H40A-C40-H40B	109.5
C21-C33-H33C	109.5	C31-C40-H40C	109.5
H33A-C33-H33C	109.5	H40A-C40-H40C	109.5
H33B-C33-H33C	109.5	H40B-C40-H40C	109.5
C21-C34-H34A	109.5	C41-O13-C52	115.8(5)
C21-C34-H34B	109.5	C42-O14-C41	113.6(5)
H34A-C34-H34B	109.5	C58-O16-C59	115.9(5)
C21-C34-H34C	109.5	C56-O18-C57	115.6(5)
H34A-C34-H34C	109.5	O13-C41-O14	109.2(6)
H34B-C34-H34C	109.5	O13-C41-C54	104.6(6)
C25-C35-H35A	109.5	O14-C41-C54	105.7(6)
C25-C35-H35B	109.5	O13-C41-C53	113.0(6)
H35A-C35-H35B	109.5	O14-C41-C53	111.7(6)
C25-C35-H35C	109.5	C54-C41-C53	112.2(6)
H35A-C35-H35C	109.5	O14-C42-C43	111.9(5)
H35B-C35-H35C	109.5	O14-C42-H42A	109.2
O9-C36-O10	124.8(7)	C43-C42-H42A	109.2
O9-C36-C26	124.6(6)	O14-C42-H42B	109.2
O10-C36-C26	110.5(6)	C43-C42-H42B	109.2
O10-C37-H37A	109.5	H42A-C42-H42B	107.9
O10-C37-H37B	109.5	C55-C43-C44	116.2(6)
H37A-C37-H37B	109.5	C55-C43-C42	106.2(5)
O10-C37-H37C	109.5	C44-C43-C42	110.1(5)
H37A-C37-H37C	109.5	C55-C43-C52	108.6(5)
H37B-C37-H37C	109.5	C44-C43-C52	109.9(5)
O11-C38-O12	122.2(7)	C42-C43-C52	105.2(5)
O11-C38-C27	125.9(6)	C45-C44-C43	113.2(5)
O12-C38-C27	111.9(6)	C45-C44-C49	110.1(6)
O12-C39-H39A	109.5	C43-C44-C49	116.2(5)
O12-C39-H39B	109.5	C45-C44-H44	105.4
H39A-C39-H39B	109.5	C43-C44-H44	105.4
O12-C39-H39C	109.5	C49-C44-H44	105.4

C46-C45-C44	115.4(6)	O13-C52-C51	107.1(5)
C46-C45-H45A	108.4	O13-C52-C43	110.2(5)
C44-C45-H45A	108.4	C51-C52-C43	112.2(6)
C46-C45-H45B	108.4	O13-C52-H52	109.1
C44-C45-H45B	108.4	C51-C52-H52	109.1
H45A-C45-H45B	107.5	C43-C52-H52	109.1
C47-C46-C45	114.8(6)	C41-C53-H53A	109.5
C47-C46-H46A	108.6	C41-C53-H53B	109.5
C45-C46-H46A	108.6	H53A-C53-H53B	109.5
C47-C46-H46B	108.6	C41-C53-H53C	109.5
C45-C46-H46B	108.6	H53A-C53-H53C	109.5
H46A-C46-H46B	107.6	H53B-C53-H53C	109.5
C48-C47-C56	119.8(6)	C41-C54-H54A	109.5
C48-C47-C46	122.6(6)	C41-C54-H54B	109.5
C56-C47-C46	117.6(6)	H54A-C54-H54B	109.5
C47-C48-C58	121.1(6)	C41-C54-H54C	109.5
C47-C48-C49	123.9(6)	H54A-C54-H54C	109.5
C58-C48-C49	114.4(5)	H54B-C54-H54C	109.5
C48-C49-C60	105.3(6)	C43-C55-H55A	109.5
C48-C49-C50	113.8(6)	C43-C55-H55B	109.5
C60-C49-C50	107.4(6)	H55A-C55-H55B	109.5
C48-C49-C44	110.4(5)	C43-C55-H55C	109.5
C60-C49-C44	109.8(6)	H55A-C55-H55C	109.5
C50-C49-C44	110.0(6)	H55B-C55-H55C	109.5
C51-C50-C49	114.6(6)	O17-C56-O18	123.1(6)
C51-C50-H50A	108.6	O17-C56-C47	125.9(6)
C49-C50-H50A	108.6	O18-C56-C47	111.0(5)
C51-C50-H50B	108.6	O18-C57-H57A	109.5
C49-C50-H50B	108.6	O18-C57-H57B	109.5
H50A-C50-H50B	107.6	H57A-C57-H57B	109.5
C52-C51-C50	110.1(6)	O18-C57-H57C	109.5
C52-C51-H51A	109.6	H57A-C57-H57C	109.5
C50-C51-H51A	109.6	H57B-C57-H57C	109.5
C52-C51-H51B	109.6	O15-C58-O16	123.0(7)
C50-C51-H51B	109.6	O15-C58-C48	126.2(6)
H51A-C51-H51B	108.2	O16-C58-C48	110.6(6)

O16-C59-H59A	109.5	C49-C60-H60A	109.5
O16-C59-H59B	109.5	C49-C60-H60B	109.5
H59A-C59-H59B	109.5	H60A-C60-H60B	109.5
O16-C59-H59C	109.5	C49-C60-H60C	109.5
H59A-C59-H59C	109.5	H60A-C60-H60C	109.5
H59B-C59-H59C	109.5	H60B-C60-H60C	109.5

Table S8. Anisotropic displacement parameters ($Å^2$x 10^3) for **9**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O1	21(3)	30(3)	26(3)	6(2)	5(2)	-1(2)
O2	15(3)	42(3)	19(3)	-1(2)	1(2)	-2(2)
O3	24(3)	27(3)	22(3)	-6(2)	2(2)	1(2)
O4	31(3)	21(3)	18(3)	0(2)	5(2)	-3(2)
O5	18(3)	41(3)	25(3)	4(3)	0(2)	-5(2)
O6	21(3)	37(3)	23(3)	3(2)	-5(2)	-3(2)
C1	13(4)	35(4)	26(4)	-2(3)	4(3)	0(3)
C2	16(4)	31(4)	20(3)	4(3)	4(3)	0(3)
C3	16(4)	47(5)	24(4)	17(4)	0(3)	-1(4)
C4	16(4)	60(5)	15(4)	-3(4)	-1(3)	-2(4)
C5	13(3)	29(4)	22(4)	-5(3)	-2(3)	-5(3)
C6	17(4)	17(3)	20(3)	-5(3)	-1(3)	0(3)
C7	11(3)	16(3)	26(4)	-1(3)	1(3)	-4(3)
C8	21(4)	24(4)	24(4)	7(3)	-1(3)	0(3)
C9	19(4)	24(4)	33(4)	10(3)	0(3)	-3(3)
C10	13(4)	26(4)	23(4)	2(3)	-1(3)	-4(3)
C11	19(4)	19(4)	19(4)	-3(3)	-2(3)	-2(3)
C12	22(4)	37(4)	14(3)	5(3)	4(3)	2(3)
C13	20(4)	43(5)	23(4)	7(3)	6(3)	2(4)
C14	20(4)	55(5)	42(5)	-12(4)	5(4)	-1(4)
C15	26(5)	42(5)	48(5)	-28(4)	16(4)	-11(4)
C16	16(4)	16(3)	18(3)	-1(3)	-2(3)	-2(3)
C17	37(5)	33(4)	29(5)	-2(3)	13(4)	-11(4)
C18	17(4)	20(4)	23(4)	1(3)	-4(3)	1(3)
C19	22(4)	36(4)	29(4)	-1(4)	-10(3)	3(4)
C20	25(4)	32(4)	21(4)	-7(3)	-5(3)	1(3)
O7	16(3)	46(3)	17(3)	3(2)	3(2)	0(2)
O8	20(3)	31(3)	28(3)	6(2)	2(2)	-4(2)
O9	23(3)	29(3)	24(3)	-7(2)	5(2)	5(2)
O10	25(3)	18(3)	19(3)	-3(2)	5(2)	-4(2)
O11	17(3)	43(3)	23(3)	3(3)	1(2)	-3(2)

O12	20(3)	42(3)	18(2)	4(2)	-4(2)	-2(2)
C21	14(4)	43(5)	22(4)	2(3)	5(3)	0(4)
C22	14(4)	32(4)	24(4)	2(3)	4(3)	-4(3)
C23	23(4)	47(5)	19(4)	19(4)	0(3)	-3(4)
C24	17(4)	68(6)	17(4)	-1(4)	0(3)	-1(4)
C25	23(4)	26(4)	21(4)	-6(3)	-1(3)	-1(3)
C26	17(4)	14(3)	21(3)	-4(3)	0(3)	1(3)
C27	18(4)	15(3)	22(4)	-1(3)	0(3)	0(3)
C28	20(4)	24(4)	26(4)	9(3)	2(3)	1(3)
C29	23(4)	20(4)	35(5)	6(3)	5(3)	-1(3)
C30	16(3)	22(4)	21(3)	-6(3)	10(3)	-7(3)
C31	14(4)	21(4)	21(4)	2(3)	5(3)	1(3)
C32	25(4)	31(4)	16(3)	2(3)	2(3)	3(3)
C33	25(4)	44(5)	25(4)	7(4)	4(3)	3(4)
C34	21(4)	58(6)	38(5)	-15(4)	3(4)	-11(4)
C35	27(5)	38(5)	53(6)	-25(4)	7(4)	-12(4)
C36	14(4)	25(4)	17(3)	-1(3)	-2(3)	1(3)
C37	43(5)	25(4)	22(4)	2(3)	14(4)	-5(4)
C38	24(4)	17(3)	19(3)	0(3)	-1(3)	1(3)
C39	20(4)	40(5)	22(4)	2(3)	-6(3)	1(3)
C40	29(4)	23(4)	27(4)	-6(3)	-3(3)	7(3)
O13	14(3)	45(3)	16(3)	-2(2)	-1(2)	3(2)
O14	21(3)	30(3)	29(3)	-2(2)	5(2)	1(2)
O15	28(3)	26(2)	21(3)	7(2)	6(2)	-5(2)
O16	24(3)	23(3)	18(2)	2(2)	6(2)	5(2)
O17	17(3)	41(3)	27(3)	-4(2)	-1(2)	4(2)
O18	18(3)	40(3)	22(3)	-5(2)	-3(2)	3(2)
C41	21(4)	40(5)	20(4)	-3(3)	1(3)	3(4)
C42	22(4)	30(4)	22(4)	-3(3)	-3(3)	-2(3)
C43	18(4)	28(4)	11(3)	-6(3)	-1(3)	-1(3)
C44	20(4)	20(4)	21(4)	2(3)	-8(3)	1(3)
C45	22(4)	22(4)	32(4)	-7(3)	1(3)	4(3)
C46	21(4)	25(4)	26(4)	-9(3)	1(3)	1(3)
C47	18(4)	19(3)	19(3)	-1(3)	-2(3)	-1(3)
C48	17(4)	19(3)	17(3)	0(3)	5(3)	1(3)
C49	15(4)	31(4)	20(4)	10(3)	2(3)	5(3)

C50	16(4)	63(5)	13(3)	4(4)	1(3)	1(4)
C51	16(4)	53(6)	27(4)	-12(4)	0(3)	-3(4)
C52	19(4)	28(4)	19(3)	-12(3)	-8(3)	1(3)
C53	19(4)	39(5)	31(4)	-6(4)	4(3)	-10(3)
C54	13(4)	63(6)	42(5)	17(4)	3(3)	8(4)
C55	26(4)	25(4)	27(4)	4(3)	-1(3)	0(3)
C56	19(4)	18(4)	20(3)	-1(3)	-2(3)	-2(3)
C57	21(4)	38(4)	25(4)	-1(3)	-7(3)	1(4)
C58	16(4)	23(4)	18(4)	4(3)	-2(3)	-3(3)
C59	36(5)	32(5)	26(4)	-4(3)	10(4)	6(4)
C60	31(5)	42(5)	49(6)	27(4)	9(4)	14(4)

Table S9. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **9**.

	x	y	z	U(eq)
H2	4869	2335	983	27
H3A	6598	2158	530	35
H3B	5676	2083	25	35
H4A	7003	473	-125	36
H4B	5832	-139	-21	36
H8A	7665	-197	2257	28
H8B	8129	-1577	2098	28
H9A	6105	-1184	2098	30
H9B	6622	-2184	1642	30
H10	5462	-1086	1077	25
H12A	4759	-13	2143	29
H12B	4255	1327	1944	29
H13A	2180	1539	1414	43
H13B	2389	2075	754	43
H13C	3238	2372	1278	43
H14A	3064	-1173	538	58
H14B	2449	2	233	58
H14C	2007	-581	847	58
H15A	7568	-1792	98	58
H15B	6365	-2175	296	58
H15C	7358	-2379	748	58
H17A	10252	2136	110	49
H17B	9487	3366	144	49
H17C	9255	2282	-344	49
H19A	11326	-433	2191	43
H19B	10889	190	2797	43
H19C	11074	1061	2219	43
H20A	6970	1804	1536	40
H20B	6480	1261	2147	40
H20C	5936	2472	1833	40
H22	11538	2328	4318	28

H23A	12348	2075	3357	35
H23B	13274	2143	3860	35
H24A	13651	471	3205	40
H24B	12480	-133	3320	40
H28A	14326	-213	5595	28
H28B	14787	-1591	5428	28
H29A	13283	-2178	4965	31
H29B	12765	-1189	5426	31
H30	12132	-1086	4418	24
H32A	11438	-9	5474	29
H32B	10938	1334	5278	29
H33A	8720	1509	4652	47
H33B	9230	2219	4085	47
H33C	9843	2261	4716	47
H34A	9737	-1177	3865	58
H34B	9093	-17	3565	58
H34C	8678	-614	4183	58
H35A	14258	-1786	3434	59
H35B	13049	-2176	3619	59
H35C	14028	-2387	4080	59
H37A	16849	1940	3361	45
H37B	16349	3285	3556	45
H37C	15813	2499	3018	45
H39A	17997	-365	5480	41
H39B	17577	91	6122	41
H39C	17697	1100	5590	41
H40A	13642	1784	4865	40
H40B	13147	1239	5475	40
H40C	12609	2457	5161	40
H42A	11905	4992	1183	29
H42B	12397	6336	1387	29
H44	11205	3933	2262	24
H45A	10571	3792	1243	30
H45B	10037	2814	1703	30
H46A	9026	4808	1076	29
H46B	8551	3429	1227	29

H50A	9686	5469	3465	37
H50B	10856	4866	3347	37
H51A	10064	7151	2800	38
H51B	10977	7095	3311	38
H52	11794	7342	2367	26
H53A	13513	7253	1935	44
H53B	14631	6505	2028	44
H53C	14087	7243	2577	44
H54A	14225	4984	3114	59
H54B	14658	4387	2501	59
H54C	13590	3824	2809	59
H55A	9694	6792	1789	39
H55B	10208	6268	1180	39
H55C	10744	7465	1511	39
H57A	5335	4633	1191	42
H57B	5753	5073	546	42
H57C	5629	6097	1072	42
H59A	6422	7104	3233	47
H59B	7157	8356	3180	47
H59C	7434	7299	3673	47
H60A	10292	2838	3048	61
H60B	9315	2625	2587	61
H60C	9082	3218	3234	61

Table S10. Torsion angles [°] for **9**.

C12-O1-C1-O2	55.5(7)	C15-C5-C10-C11	-162.6(6)
C12-O1-C1-C14	169.3(5)	O2-C2-C11-C12	-53.1(7)
C12-O1-C1-C13	-69.2(7)	C3-C2-C11-C12	-171.4(6)
C2-O2-C1-O1	-54.8(7)	O2-C2-C11-C20	-168.0(5)
C2-O2-C1-C14	-169.2(6)	C3-C2-C11-C20	73.7(7)
C2-O2-C1-C13	70.5(7)	O2-C2-C11-C10	65.6(7)
C1-O2-C2-C11	56.1(7)	C3-C2-C11-C10	-52.7(8)
C1-O2-C2-C3	178.9(5)	C9-C10-C11-C2	175.7(5)
O2-C2-C3-C4	-63.9(7)	C5-C10-C11-C2	46.9(8)
C11-C2-C3-C4	57.7(8)	C9-C10-C11-C12	-67.8(7)
C2-C3-C4-C5	-56.1(8)	C5-C10-C11-C12	163.4(5)
C3-C4-C5-C6	-76.5(7)	C9-C10-C11-C20	52.4(7)
C3-C4-C5-C15	168.5(6)	C5-C10-C11-C20	-76.4(7)
C3-C4-C5-C10	49.1(8)	C1-O1-C12-C11	-58.1(8)
C4-C5-C6-C7	154.8(6)	C2-C11-C12-O1	54.8(7)
C15-C5-C6-C7	-88.9(8)	C20-C11-C12-O1	170.8(5)
C10-C5-C6-C7	29.8(9)	C10-C11-C12-O1	-64.8(7)
C4-C5-C6-C16	-32.0(8)	C17-O4-C16-O3	-8.0(10)
C15-C5-C6-C16	84.3(7)	C17-O4-C16-C6	177.5(6)
C10-C5-C6-C16	-157.0(5)	C7-C6-C16-O3	107.0(8)
C16-C6-C7-C8	179.9(6)	C5-C6-C16-O3	-66.1(9)
C5-C6-C7-C8	-7.3(10)	C7-C6-C16-O4	-78.5(8)
C16-C6-C7-C18	-0.4(10)	C5-C6-C16-O4	108.3(6)
C5-C6-C7-C18	172.4(6)	C19-O6-C18-O5	-0.9(10)
C6-C7-C8-C9	5.8(10)	C19-O6-C18-C7	177.9(5)
C18-C7-C8-C9	-174.0(5)	C6-C7-C18-O5	-12.5(10)
C7-C8-C9-C10	-28.1(9)	C8-C7-C18-O5	167.2(7)
C8-C9-C10-C5	50.1(8)	C6-C7-C18-O6	168.7(6)
C8-C9-C10-C11	-81.7(7)	C8-C7-C18-O6	-11.6(8)
C6-C5-C10-C9	-49.1(7)	C32-O8-C21-O7	54.1(8)
C4-C5-C10-C9	-175.1(6)	C32-O8-C21-C34	168.0(5)
C15-C5-C10-C9	66.9(7)	C32-O8-C21-C33	-69.8(7)
C6-C5-C10-C11	81.4(7)	C22-O7-C21-O8	-54.3(8)
C4-C5-C10-C11	-44.5(8)	C22-O7-C21-C34	-168.2(6)

C22-O7-C21-C33	69.3(8)
C21-O7-C22-C31	57.3(7)
C21-O7-C22-C23	179.6(6)
O7-C22-C23-C24	-63.7(7)
C31-C22-C23-C24	58.5(8)
C22-C23-C24-C25	-56.8(8)
C23-C24-C25-C26	-76.7(7)
C23-C24-C25-C30	50.6(8)
C23-C24-C25-C35	169.8(6)
C24-C25-C26-C27	154.7(6)
C30-C25-C26-C27	27.8(9)
C35-C25-C26-C27	-90.2(8)
C24-C25-C26-C36	-30.6(8)
C30-C25-C26-C36	-157.5(5)
C35-C25-C26-C36	84.5(7)
C36-C26-C27-C38	-1.1(10)
C25-C26-C27-C38	173.2(6)
C36-C26-C27-C28	-179.9(6)
C25-C26-C27-C28	-5.5(10)
C26-C27-C28-C29	4.7(9)
C38-C27-C28-C29	-174.1(6)
C27-C28-C29-C30	-28.1(8)
C28-C29-C30-C25	50.0(8)
C28-C29-C30-C31	-80.6(7)
C26-C25-C30-C29	-48.3(7)
C24-C25-C30-C29	-176.2(6)
C35-C25-C30-C29	66.3(7)
C26-C25-C30-C31	82.8(7)
C24-C25-C30-C31	-45.2(8)
C35-C25-C30-C31	-162.6(6)
O7-C22-C31-C40	-168.2(5)
C23-C22-C31-C40	73.8(7)
O7-C22-C31-C32	-53.2(7)
C23-C22-C31-C32	-171.2(6)
O7-C22-C31-C30	64.2(7)
C23-C22-C31-C30	-53.8(8)
C29-C30-C31-C22	176.6(6)
C25-C30-C31-C22	47.7(8)
C29-C30-C31-C40	51.3(7)
C25-C30-C31-C40	-77.6(7)
C29-C30-C31-C32	-68.0(7)
C25-C30-C31-C32	163.1(6)
C21-O8-C32-C31	-57.3(7)
C22-C31-C32-O8	54.0(7)
C40-C31-C32-O8	170.8(5)
C30-C31-C32-O8	-65.6(7)
C37-O10-C36-O9	-8.3(10)
C37-O10-C36-C26	176.6(6)
C27-C26-C36-O9	107.3(8)
C25-C26-C36-O9	-67.4(9)
C27-C26-C36-O10	-77.7(8)
C25-C26-C36-O10	107.6(6)
C39-O12-C38-O11	0.8(10)
C39-O12-C38-C27	178.4(5)
C26-C27-C38-O11	-13.1(11)
C28-C27-C38-O11	165.8(7)
C26-C27-C38-O12	169.4(6)
C28-C27-C38-O12	-11.7(8)
C52-O13-C41-O14	-56.6(7)
C52-O13-C41-C54	-169.4(6)
C52-O13-C41-C53	68.3(8)
C42-O14-C41-O13	56.1(7)
C42-O14-C41-C54	168.1(5)
C42-O14-C41-C53	-69.6(7)
C41-O14-C42-C43	-58.9(7)
O14-C42-C43-C55	169.7(5)
O14-C42-C43-C44	-63.7(7)
O14-C42-C43-C52	54.6(7)
C55-C43-C44-C45	52.9(8)
C42-C43-C44-C45	-68.0(7)
C52-C43-C44-C45	176.6(6)
C55-C43-C44-C49	-76.0(7)

C42-C43-C44-C49	163.1(6)
C52-C43-C44-C49	47.7(8)
C43-C44-C45-C46	-80.4(8)
C49-C44-C45-C46	51.6(8)
C44-C45-C46-C47	-29.5(9)
C45-C46-C47-C48	7.0(10)
C45-C46-C47-C56	-172.9(5)
C56-C47-C48-C58	0.1(10)
C46-C47-C48-C58	-179.7(6)
C56-C47-C48-C49	171.4(6)
C46-C47-C48-C49	-8.5(11)
C47-C48-C49-C60	-87.9(8)
C58-C48-C49-C60	83.9(7)
C47-C48-C49-C50	154.8(7)
C58-C48-C49-C50	-33.4(8)
C47-C48-C49-C44	30.6(9)
C58-C48-C49-C44	-157.6(6)
C45-C44-C49-C48	-49.7(7)
C43-C44-C49-C48	80.7(7)
C45-C44-C49-C60	66.0(7)
C43-C44-C49-C60	-163.7(6)
C45-C44-C49-C50	-176.1(6)
C43-C44-C49-C50	-45.7(8)
C48-C49-C50-C51	-74.4(8)
C60-C49-C50-C51	169.5(6)
C44-C49-C50-C51	50.1(8)
C49-C50-C51-C52	-58.0(8)
C41-O13-C52-C51	179.9(6)
C41-O13-C52-C43	57.6(7)
C50-C51-C52-O13	-62.3(7)
C50-C51-C52-C43	58.9(8)
C55-C43-C52-O13	-166.3(5)
C44-C43-C52-O13	65.6(7)
C42-C43-C52-O13	-52.9(7)
C55-C43-C52-C51	74.4(7)
C44-C43-C52-C51	-53.7(8)
C42-C43-C52-C51	-172.2(6)
C57-O18-C56-O17	-1.4(10)
C57-O18-C56-C47	178.0(5)
C48-C47-C56-O17	-12.3(11)
C46-C47-C56-O17	167.6(7)
C48-C47-C56-O18	168.3(6)
C46-C47-C56-O18	-11.8(8)
C59-O16-C58-O15	-7.6(10)
C59-O16-C58-C48	177.6(5)
C47-C48-C58-O15	106.6(8)
C49-C48-C58-O15	-65.5(9)
C47-C48-C58-O16	-78.9(8)
C49-C48-C58-O16	109.1(6

Figure S1. View of molecule 1 of **9** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

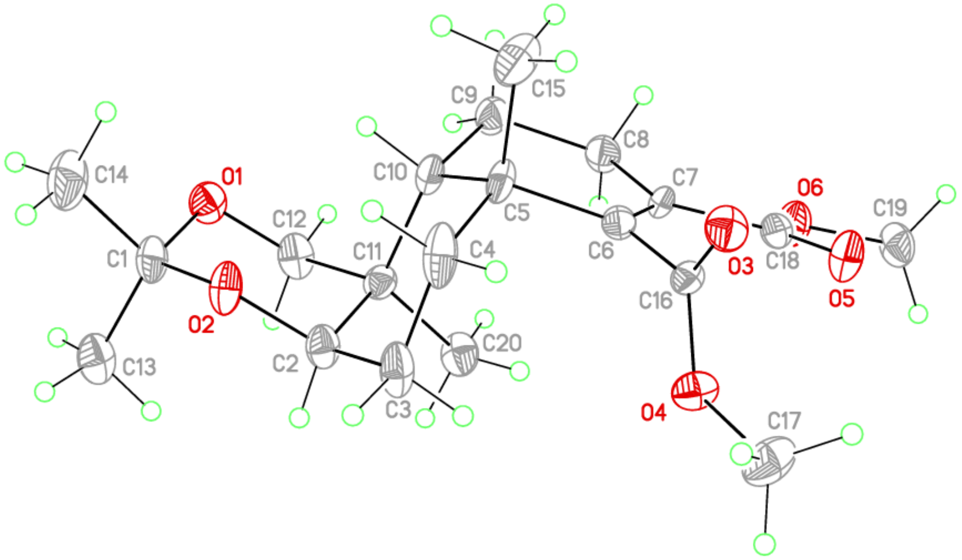


Figure S2. View of molecule 2 of **9** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

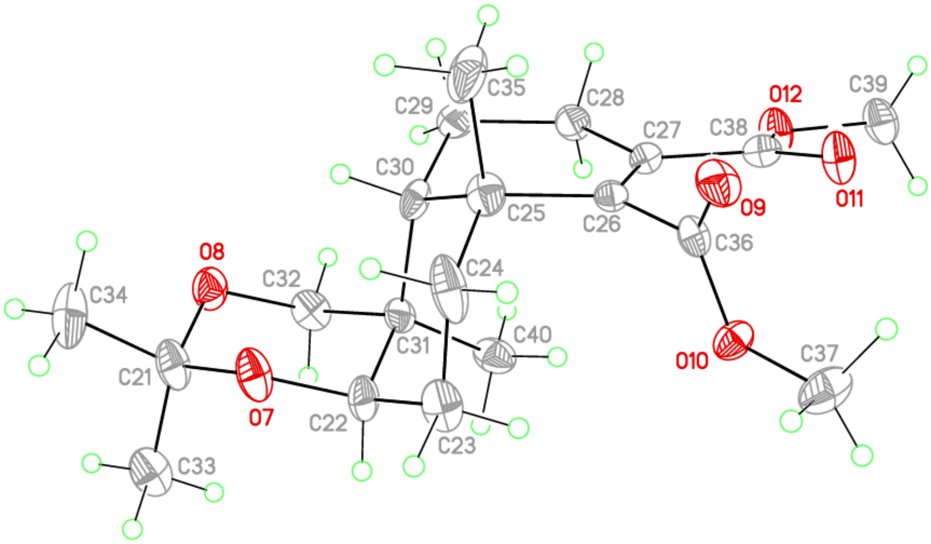
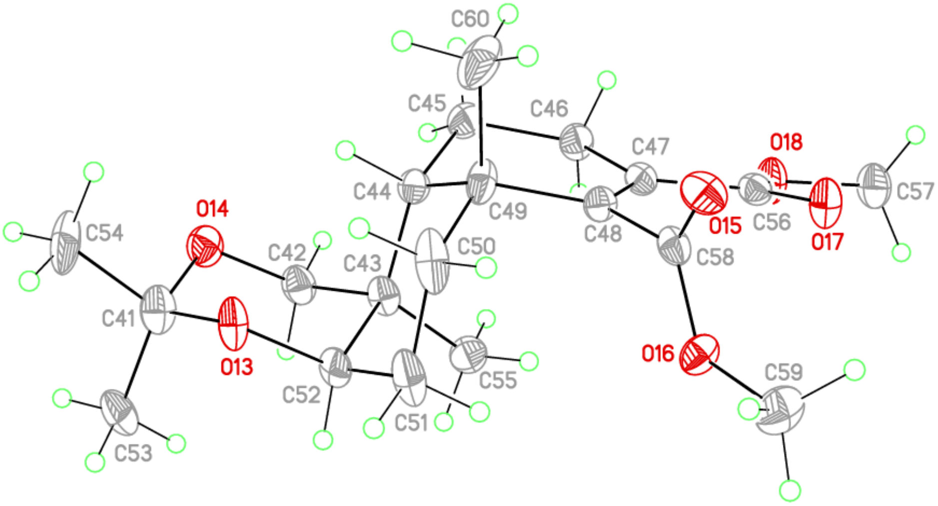


Figure S3. View of molecule 3 of **9** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



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