Formal Synthesis of (±) Guanacastepene A: A Tandem Ring-Closing Metathesis Approach

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Supporting Information

Experimental Procedure

General: Melting points were determined on a Reichert hot stage apparatus. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer or on a Nicolet Avatar 320 FT-IR as neat or in solutions. ¹H and ¹³C NMR spectra were recorded on a Bruker AM 400 NMR spectrometer as solutions in CDCl₃, using residual protic solvent CHCl₃ (δ_H=7.27 ppm) or CDCl₃ (δ_C=77.0 ppm) as internal reference. Mass spectra were determined on a Hewlett Packard HP 5970B/5890A or on a Nermag R10-10C or linked to a Varian 3300 GC. Ionization was obtained either by electronic impact (EI) or chemical ionization with ammonia (CI, NH₃). All reactions were monitored by TLC carried out on 0.2 mm aluminium silica gel (60 F₂₅₄) pre-coated plates using UV light and 5% ethanolic phosphomolybdic acid and heat as developing agent. Flash chromatography was performed on 40-63 μm (400-230 mesh) silica gel 60 with ethyl acetate (EtOAc)-petroleum ether (PE) (bp. 40-60°C) or cyclohexane as eluents. Commercially available reagents and solvents were purified and dried when necessary by usual methods. THF, benzene and Et₂O were purified by distillation, under nitrogen, from sodium / benzophenone. CH₂Cl₂, Me₂SO were dried by distillation from calcium hydride.

$C_{12}H_{19}NO$
Mol. Wt.: 193,29

Ketone 6: To a solution of ketone **5** (2.84 g, 20.27 mmol) in anhydrous Et₂O (25 mL) at rt under argon was added sodium methylate (336 mg, 6.08 mmol). The reaction mixture was stirred for 1 h at rt. To this orange solution was added dropwise over 30 min at

18 °C (the exothermic reaction was moderated with a water bath at rt) a solution of freshly distilled acrylonitrile (1.81 mL, 27.49 mmol) in Et₂O (26 mL). Stirring was continued for 2 h at rt and sat. aq. NH₄Cl (30 mL) added. The resultant mixture was stirred for 10 min at rt and the aqueous layer was extracted with Et₂O (3 × 60 mL), the combined organic extracts washed with brine (50 mL), dried (MgSO₄) and evaporated under reduced pressure. The crude product was purified by Kugelrohr distillation (150-190 °C, 0.1 torr) to give 1.738 g (44%) of **6** as slightly yellow oil. ¹H NMR: δ = 2.38-2.32 (m, 2 H), 2.20-2.05 (m, 4 H), 1.84-1.75 (m, 1 H), 1.72-1.58 (m, 2 H), 1.52-1.40 (m, 1 H), 0.99 (d, *J* =

6.3 Hz, 3 H), 0.94 (d, J = 6.3 Hz, 3 H), 0.91 (s, 3 H). **^{13}C NMR**: δ = 222.2 (C), 119.6 (C), 50.9 (C), 48.8 (CH), 36.8 (CH₂), 32.3 (CH₂), 29.2 (CH), 23.5 (CH₂), 22.1 (CH₃), 21.2 (CH₃), 17.2 (CH₃), 12.6 (CH₂). **IR** (neat): 2963, 2874, 2246, 1731, 1459, 1077 cm⁻¹. **GC** analysis (MDN5S, 0.32 mm id. $\times$ 30 m, 50 °C – 300 °C, 10 °C/min), retention time 10.54 min. **EI MS**: m/z (%) 193 (M^+ , 1), 178 ($\text{M}^+ - \text{Me}$, 2), 41 (100).

$\text{C}_{14}\text{H}_{21}\text{N}$
Mol. Wt.: 203,32

7

Diene 7: To a solution of ketone **6** (0.816 g, 4.22 mmol) in anhydrous CH_2Cl_2 (30 mL) at 0 °C under argon was added 2,6-di-*tert*-butyl-4-methylpyridine (DBMP) (2.18 g, 10.55 mmol) and dropwise TiF_4 (1.8 mL, 10.55 mmol). The reaction mixture was stirred for 6 h at rt. Another portion of proton sponge (1.73 g, 8.44 mmol) and TiF_4 (1.1 mL, 6.33 mmol) were added at 0 °C and stirring was continued for 17 h at rt. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and poured in cold water. The aqueous layer was extracted with CH_2Cl_2 (3 $\times$ 50 mL) and the combined organic extracts washed with saturated aqueous sodium bicarbonate solution (60 mL), brine (60 mL), dried (MgSO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/cyclohexane 5:95 to 20:80) to give 1.12 g (81%) of triflate as yellow oil which was used immediately in the next step. A solution of tetrakis(triphenylphosphine)palladium (0) (100 mg, 0.086 mmol), dry LiCl (590 mg, 14.28 mmol) in anhydrous THF (13 mL) was stirred for 15 min under argon; then a solution of the triflate (1.12 g, 3.41 mmol) and tri-*n*-butyl(vinyl)tin (1.6 mL, 9.08 mmol) in anhydrous THF (13 mL) was added, followed by an additional 4 mL of THF. The resulting, slightly yellow solution was heated to a gentle reflux for 18 h. The black reaction mixture was cooled to rt, diluted with pentane (100 mL) and poured in water (100 mL). The aqueous layer was back-extracted with pentane (2 $\times$ 100 mL). The combined organic extracts were washed with saturated aqueous sodium bicarbonate solution (100 mL), brine (100 mL), dried (MgSO_4) and evaporated under reduced pressure. The crude product was purified by chromatography on silica gel (Et₃N/EtOAc/cyclohexane 1:0:99 to 1:2.5:96.5) to give 610 mg (71%, 2 steps) of diene **7** as slightly yellow oil. **^1H NMR**: δ = 6.10 (dd, J = 17.6, 11.2 Hz, 1 H), 5.75 (t, J = 2.5 Hz, 1 H), 5.35 (d, J = 17.6 Hz, 1 H), 5.01 (d, J = 11.2 Hz, 1 H), 2.33 (dd, J = 18.0, 7.9, 3.1 Hz, 1 H), 2.30-2.21 (m, 1 H), 2.14-2.06 (m, 1 H), 2.03-1.99 (m, 1 H), 1.98-1.93 (m, 2 H), 1.75-1.59 (m, 2 H), 1.03 (s, 3 H), 0.99 (d, J = 6.4 Hz, 3 H), 0.83 (d, J = 6.4 Hz, 3 H). **^{13}C NMR**: δ = 146.7 (C), 130.9 (CH), 128.5 (CH), 120.4 (C), 114.3 (CH₂), 50.7 (CH), 49.7 (C), 34.8 (CH₂), 33.9 (CH₂), 29.0 (CH), 22.5 (CH₃), 22.2 (CH₃), 19.7 (CH₃), 12.5 (CH₂). **GC** analysis (MDN5S, 0.32 mm id. $\times$ 30 m, 50 °C – 300 °C, 10 °C/min), retention time 10.12 min. **IR** (neat): 3041, 2959, 2929, 2872, 2246, 1634 cm⁻¹. **EI MS**: m/z (%) 203 (M^+ , 1), 188 ($\text{M}^+ - \text{Me}$, 2), 160 (2), 41 (100).

8
 $\text{C}_{15}\text{H}_{24}\text{O}$
 Mol. Wt.: 220,35

Ketone 8: To a solution of methylmagnesium bromide (82 mL, 133.27 mmol, 1.6 M in Et_2O) was added a solution of nitrile **7** (2.46 g, 12.1 mmol) in Et_2O (76 mL) and the mixture was stirred under reflux for 2 h 30, cooled to 0 °C, diluted with Et_2O (50 mL)

and quenched with aq. HCl 5 % (pH 1 for the aqueous phase) and the mixture stirred for 20 min. The organic layer was separated, washed with aqueous saturated sodium bicarbonate solution (50 mL), brine (50 mL), dried (MgSO_4) filtered and evaporated under reduced pressure. The crude product was purified by chromatography on silica gel (EtOAc /cyclohexane 5:95) to give 1.939 g (72%) of **8** as colorless oil. **R_f**: 0.20 (2.5% EtOAc in PE), **¹H NMR**: δ = 6.10 (dd, J = 17.6, 11.2 Hz, 1 H), 5.76 (t, J = 2.5 Hz, 1 H), 5.37 (d, J = 17.6 Hz, 1 H), 5.01 (d, J = 11.2 Hz, 1 H), 2.23-2.45 (m, 2 H), 2.12-2.22 (m, 1 H), 2.06 (s, CH_3), 1.96-2.05 (m, 1 H), 1.72-1.82 (m, 2 H), 1.55-1.60 (m, 2 H), 0.98 (s, 3 H), 0.93 (d, J = 6.4 Hz, 3 H), 0.83 (d, J = 6.4 Hz, 3 H). **¹³C NMR**: δ = 209.1 (C), 148.2 (C), 131.4 (CH), 127.1 (CH), 113.7 (CH_2), 51.1 (CH), 49.4 (C), 39.4 (CH_2), 34.9 (CH_2), 31.3 (CH_2), 29.9 (CH_3), 29.1 (CH_2), 22.6 (CH_3), 22.4 (CH_3), 20.2 (CH_3). **IR (neat)**: 1719, 1633 cm^{-1} . **CI MS**: NH_3 m/z (%) 221 ($\text{M}^+ + 1$), 238 ($\text{M}^+ + 18$).

9
 $\text{C}_{16}\text{H}_{25}\text{N}$
 Mol. Wt.: 231,38

Nitrile 9: To an ice-cooled solution of TosMIC (2.29 g, 11.74 mmol) in dry Me_2SO (13 mL) was added all at once 4.0 g (35.7 mmol) of solid *tert*-BuOK. After stirring for 5 min under N_2 0.44 □L of MeOH was added, then 1.92 g (8.76 mmol) of ketone **8**, and

the mixture was stirred for 17 h at rt. The reaction mixture was diluted with water (250 mL), acidified with 2 N HCl, and extracted with PE (bp 40-60 °C). The combined extracts were washed with saturated NaCl solution, dried over MgSO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc /PE 1.25:98.75 to 2.5:97.5) to give 1.17 g (58%) of **8** (mixture of isomers) as colorless oil. **R_f**: 0.30 (EtOAc /PE 2.5:97.5). **¹H NMR**: δ = 6.50-6.15 (m, 1 H), 5.73 (br s, 1 H), 5.37 and 5.33 (2 d, J = 17.5 Hz, 1 H), 4.99 and 4.96 (2 d, J = 11.7 Hz, 1 H), 2.42-2.57 (m, 1 H), 2.28-2.38 (m, 1 H), 1.92-2.04 (m, 1 H), 1.05-1.85 (m, 5 H), 1.24-1.40 (m, 1H), 1.26 and 1.25 (2 d, J = 6.4 Hz, 3 H), 1.00 (s, 3 H), 0.99 and 0.97 (2 d, J = 6.4 Hz, 3 H), 0.87 and 0.86 (2 d, J = 6.4 Hz, 3 H). **¹³C NMR**: δ = 148.0 (C), 131.4 and 131.2 (CH), 127.1 and 126.8 (CH), 122.7 (C), 113.8 and 113.5 (CH_2), 50.9 and 50.8 (CH), 49.5 (C), 35.3 (CH_2), 34.9 (CH_2), 29.1 and 28.9 (CH_2), 29.0 (CH), 24.7, 22.5, 22.3, 20.2, 17.8. **CI MS**: NH_3 m/z 232 ($\text{M}^+ + 1$), 249 ($\text{M}^+ + 18$).

10
 $\text{C}_{22}\text{H}_{35}\text{N}$
 Mol. Wt.: 313,52

Nitrile 10: To a solution of **9** (693 mg, 3.0 mmol) and homoprenyl iodide (2.52 g, 12 mmol) in dry THF (6 mL) was added dropwise a solution of LiHMDS (12 mL, 1.0

M in THF) at rt. After being stirred at this temperature for 1.5 h (TLC showed disappearance of the starting material), the mixture was cooled at 0 °C and quenched with water. The two phases were separated and the aqueous phase was extracted with three 15 mL portions of Et₂O. The combined organic phases were washed with brine, dried over MgSO₄ and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/PE 1.25:98.75 to 2.5:97.5) to give 867 mg (92%) of **8** as colorless oil. **R_f**: 0.75 (EtOAc/PE 2.5:97.5). **¹H NMR**: δ = 6.15 (dd, *J* = 17.6, 11.2 Hz, 1 H), 5.75 (br s, 1 H), 5.40 (dd, *J* = 17.5, 3.8 Hz, 1 H), 5.07 (tt, *J* = 5.7, 1.3 Hz, 1 H), 5.02 (dd, *J* = 11.2, 3.8 Hz, 1 H), 2.42-2.32 (m, 1 H), 2.12-2.08 (m, 1 H), 2.04-1.92 (m, 1 H), 1.80-1.70 (m, 4 H), 1.69 (s, CH₃), 1.62 (s, CH₃), 1.62-1.32 (m, 3 H), 1.29 and 1.28 (2 s, 3 H), 1.28-1.26 (m, 1 H), 1.00 (s, 3 H), 1.00 and 1.02 (2 d, *J* = 6.4 Hz, 3 H), 0.90 (d, *J* = 6.4 Hz, 3 H). **¹³C NMR**: δ = 148.3 (C), 131.4 and 132.7 (C), 131.6 (CH), 127.2 and 127.0 (CH), 124.4 (C), 122.7 (CH), 114.0 and 113.9 (CH₂), 51.0 (CH), 49.7 (C), 39.2 and 39.0 (CH₂), 35.1 (C), 34.3 (CH₂), 32.8 (CH₂), 29.3 (CH₂), 25.6 (CH), 23.5 (CH₃), 23.0 (CH₃), 22.9 (CH₃), 22.8 (CH₂), 22.6 (CH₃), 20.6 (CH₃), 17.7 (CH₃). **IR**: 2232 cm⁻¹. **CI MS**: NH₃ *m/z* 314 (M⁺ + 1), 331 (M⁺ + 18).

C₂₂H₃₆O
Mol. Wt.: 316.52

Aldehyde 11: To a solution of nitrile **10** (854 mg, 2.72 mmol) in dry Et₂O (20 mL) cooled at -70 °C and stirred under N₂ was added dropwise a solution of DIBAL-H 1.0 M in hexane (6.8 mL, 6.8 mmol). After being stirred

at this temperature for 45 min, EtOAc (0.5 mL) was added and the mixture was slowly warmed up to rt. Potassium sodium tartrate (Rochelle salt) solution (10 mL) was added and the mixture was stirred for 30 min at rt until the layers appeared clear. The phases were separated and the aqueous layer was extracted three times with Et₂O. The combined organic phases were washed with brine, dried over MgSO₄ and concentrated to give the crude **11**. Flash chromatography on silica gel (EtOAc/PE 1.25:98.75 to 2:98) gave 787 mg (91.5%) of **11** as colorless oil. **R_f**: 0.75 (EtOAc/PE 2.5:97.5). **¹H NMR**: δ = 9.37 (s, 1 H), 6.02-6.17 (m, 1 H), 5.73 (br s, 1 H), 5.38 (br d, *J* = 17.5 Hz, 1 H), 5.08-5.00 (m, 1 H), 4.94 (d, *J* = 11.2 Hz, 1 H), 2.40-2.30 (m, 1 H), 2.02-1.90 (m, 1 H), 1.90-1.70 (m, 3 H), 1.66 (s, CH₃), 1.56 (s, CH₃), 1.56-1.35 (m, 5 H), 1.35-1.15 (m, 2 H), 1.00-0.90 (9 H), 0.89 (d, *J* = 6.4 Hz, 3 H). **¹³C NMR**: δ = 206.7 and 206.5 (C), 148.4 (C), 132.6 (C), 132.0 and 131.6 (CH), 126.9 (CH), 123.9 (CH), 122.7 (C), 113.7 (CH₂), 50.5 (CH), 49.8 (C), 48.9 (C), 35.7 (CH₂), 35.1 (CH₂), 31.7 (CH₂), 30.3 and 30.1 (CH₂), 29.2 (CH), 25.6 (CH₃), 22.7 (CH₂), 22.6 (CH₃), 20.6 (CH₃), 17.7 (CH₃), 17.6 (CH₃). **IR** (CCl₄): 1728 cm⁻¹. **CI MS**: NH₃ *m/z* 317 (M⁺ + 1), 334 (M⁺ + 18).

Trienyne 4: To a solution of aldehyde **11** (777 mg, 2.45 mmol) and dimethyl 1-diazo-2-oxopropylphosphonate¹ (876 mg, 3.15 mmol) in anhyd MeOH (43 mL) was added K₂CO₃ (741 mg, 5.36 mmol) and stirring was continued under argon for 3 h. The reaction mixture was diluted

with Et₂O (20 mL), washed with an aq solution of NaHCO₃ (10%) and dried (MgSO₄). Evaporation of the solvents yields 710 mg of 1-alkyne (92%) as colorless oil. **R_f**: 0.65 (EtOAc/cyclohexane 2.5:97.5). To a cold solution (-78°C) of 1-alkyne (710 mg, 2.27 mmol) in THF (9 mL) under argon was added BuLi (3.68 mmol, 2.30 mL, 1.6 M in hexane). The resulting mixture was stirred for 40 min and freshly distilled ClCO₂Me (3.55 mmol, 0.31 mL) was added and the reaction mixture allowed to warm to 20°C. The reaction mixture was diluted with Et₂O (75 mL), washed with water (30 mL). The aqueous phase was extracted with Et₂O (2 × 50 mL) and the combined organic layers washed with brine (30 mL) and dried over MgSO₄. The residue was purified by flash chromatography on silica gel (EtOAc/cyclohexane 0:100 to 2.5:97.5) to give 742 mg (88%) of **4** as colorless oil. **R_f**: 0.45 (EtOAc/cyclohexane 2.5:97.5). **¹H NMR:** δ = 6.14 (dd, *J* = 17.7, 11.4 Hz, 1 H), 5.72 (br s, 1 H), 5.38 (br d, *J* = 17.7 Hz, 1 H), 5.08 (br t, *J* = 6.3 Hz, 1 H), 4.98 (d, *J* = 11.4 Hz, 1 H), 3.74 (s, CH₃), 2.34 (ddd, *J* = 16.5, 7.2, 2.7 Hz, 1 H), 2.12-1.94 (m, 2 H), 1.83-1.15 (m, 9 H), 1.68 (s, CH₃), 1.61 (s, CH₃), 1.20 (s, CH₃), 1.02 (s, CH₃), 1.00 (d, *J* = 6.4 Hz, 3 H), 0.89 (d, *J* = 6.4 Hz, 3 H). **¹³C NMR:** δ = 154.3 (C), 148.7 (C), 131.8 (CH + C), 126.7 and 126.6 (CH), 123.8 (CH), 113.8 and 113.7 (CH₂), 95.5 (C), 73.9 (C), 52.3 (CH), 50.9 (CH₃), 49.8 (C), 40.5 and 40.4 (C), 35.6 (CH₂), 35.1 (CH₂), 32.7 (CH₂), 29.3 (CH), 25.6 (CH₃), 25.4 and 25.3 (CH₃), 23.5 (CH₂), 22.7 and 22.5 (CH₃), 20.7 (CH₃), 17.6 (CH₃). **IR** (neat): 1716, 1633 cm⁻¹. **CI MS:** NH₃ *m/z* 371 (M⁺ + 1), 388 (M⁺ + 18).

Tricyclic triene 3: To a degassed solution of trienyne **4** (450 mg, 1.21 mmol) in dry CH₂Cl₂ (15.3 mL) under argon was added Grubbs catalyst II **12** (160 mg, 12% mol). The mixture was heated at reflux for 3 h. The solvent was removed and the residue submitted to flash

chromatography on silica gel (EtOAc/PE 1.25:98.75 to 2.5:97.5) to give the pure tricyclic compound **3** (313 mg, 82 %) as a colorless oil. 2 isomers. **¹H NMR:** δ = 6.53 (br s, 0.5 H), 6.25 (br s, 0.5 H), 6.20 (br s, 1 H), 5.55 (br s, 0.5 H), 5.46 (br s, 0.5 H), 3.76 (s, 1.5 H), 3.74 (s, 1.5 H), 2.45-2.15 (m, 3 H), 2.10-1.55 (m, 6 H), 1.50-2.10 (m, 3 H), 1.04-0.84 (2 s + 2 d, 12 H). **¹³C NMR** (key signals): δ = 169.1 (C),

¹ Eymery, F. ; Iorga, B. ; Savignac, P. *Synthesis*, **2000**, 2, 185-213.

150.9 (C), 137.8 (C), 135.6 (CH), 135.4 (CH), 133.3 (C), 132.0 (br), 129.6 (CH), 129.4 (CH), 124.5 (CH), 124.4 (CH), 59.0 (CH), 51.6 (CH₃). **IR** (CCl₄): 1722, 1618 cm⁻¹. **CI MS**: NH₃ *m/z* 315 (M⁺ + 1), 332 (M⁺ + 18).

Allyl ethers 14 and 15: *m*-CPBA (80%, 80 mg) was added to a biphasic mixture of **3** (116 mg, 0.369 mmol), CH₂Cl₂ (1.5 mL) and saturated aqueous sodium bicarbonate (1.5 mL) at 0°C. The heterogeneous mixture was stirred vigorously for 30 min and then quenched with saturated sodium sulfite (0.2 mL). The mixture was stirred for 15 min while slowly warmed up to rt. The CH₂Cl₂ layer was separated and the aqueous layer was extracted three times with CH₂Cl₂. The combined organic layers were washed with saturated NaHCO₃, brine, dried (MgSO₄) and evaporated under reduced pressure to give 132 mg of crude epoxide **13**, which was used without further purification in the next reaction.

To a solution of the above crude **13** in allyl alcohol (1.0 mL) was added at room temperature ytterbium triflate hydrate [Yb(OTf)₃] (3 mg, 4.8 μmol, 0.013 equiv). After being stirred at room temperature for 1 h, allyl alcohol was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (EtOAc/PE 1:4). Concentration of the appropriate fractions afforded 48 mg (34%) **14** (major, more polar isomer) and 32 mg (22%) of **15** as colorless oils.

Allyl ether 14 (*major isomer, more polar*): colorless oil.

R_f: 0.45 (EtOAc/PE 1:4). **¹H NMR**: δ = 6.04 (br s, 1 H), 5.95-5.84 (m, 1 H), 5.23 (d, *J* = 17.2 Hz, 1 H), 5.13 (d, *J* = 10.3 Hz, 1 H), 4.41 (br s, 1 H), 4.32 (br s, 1 H), 4.07 (dd, *J* = 12, 5.6 Hz, 1 H), 3.99 (dd, *J* = 12, 5.6 Hz, 1 H), 3.70 (s, 3 H), 2.15-1.50 (m, 10 H), 1.45-1.15 (m, 3 H), 1.04 (s, 3 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 3 H), 0.91 (d, *J* = 6.6 Hz, 3 H). **¹³C NMR**: δ = 135.5 (CH), 116.5 (CH₂), 74.8 (br), 72.7 (br), 70.2 (CH₂), 51.3 (CH₃), 39.3, 37.5, 37.0, 36.6, 34.8, 29.7, 28.1, 23.7, 22.4. All that remains of carbons were too broad to be observed. **IR** (CCl₄): 3612, 1720 cm⁻¹.

Allyl ether 15 (*minor isomer*): colorless oil. **R_f**: 0.35

(EtOAc/PE 1:4). **¹H NMR**: δ = 6.07 (br s, 1 H), 5.95-5.85 (m, 1 H), 5.23 (d, *J* = 17.2 Hz, 1 H), 5.13 (d, *J* = 10.3 Hz, 1 H), 4.55 (d, *J* = 9.6 Hz, 1 H), 4.30 (t, *J* = 5.9 Hz, 1 H), 4.09 (dd, *J* = 12, 5.6 Hz, 1 H), 3.96 (dd, *J* = 12, 5.6 Hz, 1 H), 3.72 (s, 3 H), 2.15-1.50 (m, 8 H), 1.43 (t, *J* = 7.8 Hz, 1 H), 1.35-1.15 (m, 3 H), 1.14 (s, 3 H), 1.10-1.00 (m, 1 H), 0.98 (s, 3 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 0.85 (d, *J* = 6.6 Hz, 3 H). **¹³C NMR**: δ =

169.0 (C), 155.6 (C), 149.6 (C), 135.4 (CH), 129.0 (C), 117.9 (CH₂), 116.5 (CH), 73.6 (CH), 71.3 (CH₂), 70.3 (CH), 53.3 (CH), 51.3 (CH₃), 48.8 (C), 41.0 (C), 38.0 (CH₂), 36.3 (CH₂), 36.2 (CH₂), 35.9 (CH₂), 30.6, 29.2, 24.1 (CH₂), 23.3 (CH₃), 22.1 (CH₃), 15.9 (CH₃). **IR** (CCl₄): 3612, 1720 cm⁻¹.

Diether 16: To a solution of pure **14** (46 mg, 0.118 mmol) in 0.3 mL CH₂Cl₂ were added pyridine (30 μL, 0.354 mmol) and TBSOTf (36 μL, 0.154 mmol) under N₂ at 0 °C. The mixture was stirred for 30 min and 0.25 mL of

saturated NaHCO₃ aqueous solution was added. The mixture was extracted three times with Et₂O. The combined organic layers were dried (MgSO₄) and concentrated to give the crude **16**. Flash chromatography on silica gel (2.5% EtOAc in PE) gave 48 mg (81%) of pure **16** as a colorless liquid. **R_f**: 0.30 (2.5% EtOAc in PE). **¹H NMR:** δ = 5.95-5.80 (m, 2 H), 5.23 (d, *J* = 17.2 Hz, 1 H), 5.13 (d, *J* = 10.3 Hz, 1 H), 4.45-4.25 (m, 2 H), 4.07 (dd, *J* = 12, 5.6 Hz, 1 H), 3.99 (dd, *J* = 12, 5.6 Hz, 1 H), 3.70 (s, 3 H), 1.90-1.45 (m, 10 H), 1.45-1.15 (m, 2 H), 1.04 (s, 3 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 3 H), 0.91 (d, *J* = 6.6 Hz, 3 H), 0.86 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H). **¹³C NMR:** δ = 168 (C), 135.3 (CH), 116.0 (CH₂), 74.1 (br), 72.4 (br), 70.9 (CH₂), 54.9 (CH₃), 37.4 (CH₂), 39.3, 27.8, 25.4 (3 Me, *t*-Bu), 23.5, 22.1, 17.7, -3.8. All that remains of carbons were too broad to be observed. **IR** (CCl₄): 1716 cm⁻¹.

Diol 17: To a stirred solution of **16** (46 mg, 91 μmol) and [Cl₂Ni(dppp)] (3 mg) in Et₂O (0.7 mL) under argon was added dropwise DIBAL-H (1.0 M in hexanes, 240 μL, 0.42 μmol) at 0 °C. The mixture was stirred for 10 min at the same temperature and then 2.5 h at rt. The mixture

was diluted with Et₂O (1 mL), and quenched by addition of H₂O (0.1 mL) and, after stirring for 45 min, dried over MgSO₄, filtered through a Celite pad, and concentrated under reduced pressure to leave the crude product. Flash chromatography on silica gel (EtOAc/PE 1:3, then 1:2) gave 28 mg of pure **17** (71%) as a colorless syrup. **R_f**: 0.30 (EtOAc/PE 1:3). **¹H NMR:** δ = 5.09 (s, 1 H), 4.44-4.15 (m, 4 H), 2.55 (br, 2 H, OH), 1.95-1.85 (m, 1 H), 1.86-1.55 (m, 8 H), 1.73-1.50 (br, 2 H), 1.45-1.30 (m, 3 H), 1.23 (br, 1 H), 0.99 (s, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.88 (s, 15 H), 0.06 (s, 3 H), 0.05 (s, 3 H). **¹³C NMR:** δ = 157.2, 37.7, 28.1, 25.7, 25.4, 23.8, 22.4, 18.0, -4.5. All that remains of carbons were too broad to be observed. **IR** (CCl₄): 3600-3100 cm⁻¹.

Triol 18: To a stirred solution of **17** (22 mg, 50 μ mol) in THF (0.4 mL) under N_2 was added dropwise TBAF (1.0 M in THF, 150 μ L, 150 μ mol) at 0 $^{\circ}$ C. The mixture was stirred for 6 days at room temperature and 0.5 mL of water was added. The phases were separated and the aqueous layer was extracted

three times with EtOAc. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated to give colorless residue. Flash chromatography on silica gel (EtOAc/PE 1:1) gave 4 mg of **17** (16%) followed by 13 mg of pure **18** (81%) as a white solid. **Mp** 149-151 $^{\circ}$ C (EtOAc-petroleum ether). **1H NMR:** δ = 6.12 (s, 1 H), 4.39 (br s, 2 H), 4.33 (br d, J = 12 Hz, 1 H), 4.24 (br d, J = 12 Hz, 1 H), 2.42 (br, 1 H, OH), 2.14 (br, 1 H, OH), 1.96-1.70 (m, 6 H), 1.62-1.55 (m, 4 H), 1.48-1.30 (m, 4 H), 0.99 (s, 3 H), 0.97 (d, J = 6.7 Hz, 3 H), 0.89 (d, J = 6.7 Hz, 3 H), 0.88 (s, 3 H); **^{13}C NMR:** δ = 158.5, 36.7, 28.1, 25.6 (br), 23.8, 22.4. All that remains of carbons were too broad to be observed. **IR** (CCl_4): 3600-3100. The spectra are identical to those described by Snider and coworkers.²

Triol 19: Following the same procedures than used for the preparation of **18** led to triol **19** as a white solid. **Mp** 171-173 $^{\circ}$ C (EtOAc). **1H NMR:** δ = 6.19 (s, 1 H), 4.56 (br d, J = 10 Hz, 1 H), 4.47 (d, J = 12 Hz, 1 H), 4.30 (t, J = 6.7 Hz, 1 H), 4.24 (d, J = 12 Hz, 1 H), 3.35 (br, OH), 2.80 (br, OH), 2.10-

1.80 (m, 3 H), 1.75-1.55 (m, 6 H), 1.44-1.22 (m, 4 H), 1.28 (s, 3 H), 0.99 (s, 3 H), 0.91 (d, J = 6.7, 3 H), 0.85 (d, J = 6.7, 3 H). **^{13}C NMR:** δ = 154.8 (C), 140.8 (C), 134.4 (C), 115.5 (CH), 71.1 (CH), 70.4 (CH), 60.8 (CH₂), 48.2 (C), 40.5 (C), 37.5 (CH₂), 37.3 (CH₂), 36.9 (CH₂), 36.1 (CH₂), 31.6, 29.7 (C), 29.3, 28.8 (CH₂), 23.5, 22.2, 15.8. **IR** ($CHCl_3$): 3590-3100 cm^{-1} . *The structure of this compound was confirmed by X-ray crystallographic analysis.*

² Shi, B.; Hawryluk, N. A.; Snider, B. B.; *J. Org. Chem.* **2003**, 68, 1030.