Total Synthesis of Mniopetals A, B, C and D

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Dedicated to Prof. Dr. W. Steglich on the occasion of his 80th birthday

Abstract: A total synthesis of the mniopetals A, B, C and D is described. Key steps are a Sharpless asymmetric dihydroxylation and a selective esterification of an equatorial hydroxy group vicinal to an axial hydroxy function.

Key words: asymmetric synthesis, antiviral agents, chemoselectivity, intramolecular Diels–Alder reaction, natural products

In 1994, Anke and Steglich reported on the isolation, structure elucidation and determination of the absolute configuration of six new drimane-type sesquiterpenes from the culture broth of the Canadian fungus Mniopetalum sp. 87256, the mniopetals A–F (**1a**–**f**; Figure 1).[1]

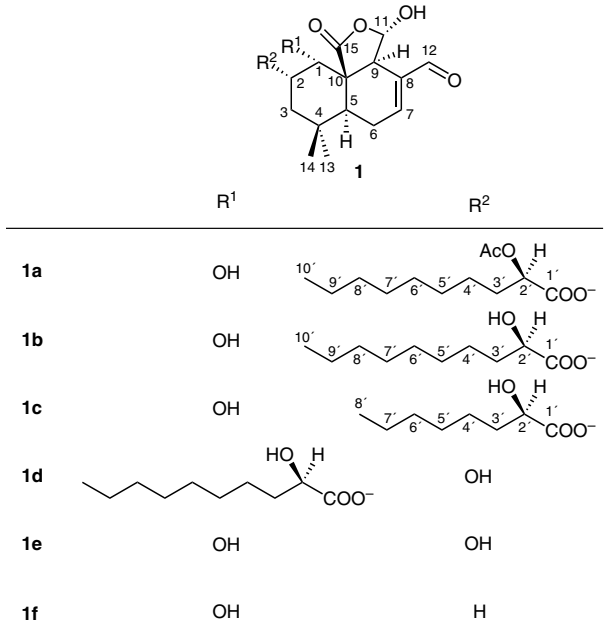
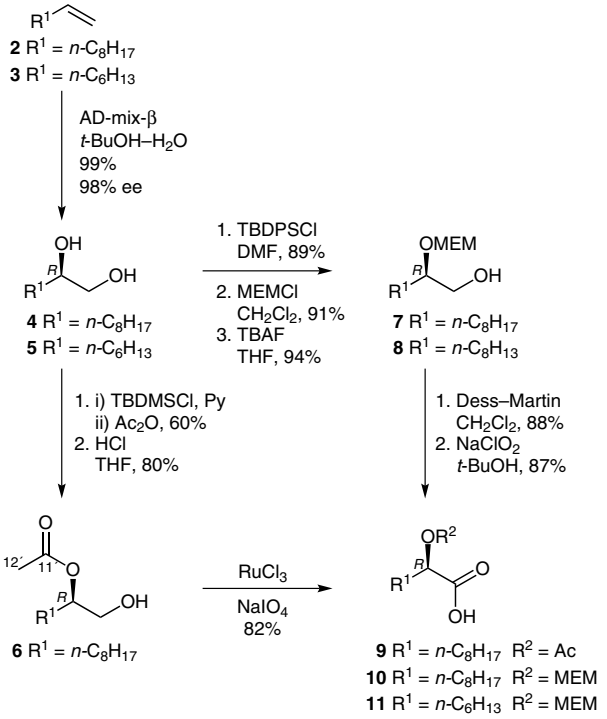


Figure 1 Structures of mniopetals A–F (**1a**–**f**)

The mniopetals inhibit the reverse transcriptase of HIV-1, which makes them attractive targets for total synthesis.[2]

Some years ago, we developed short syntheses of mniopetals E and F.[2b–d,2g] Esterification of the two secondary alcohol functions with the respective α-hydroxy or α-acetoxy carboxylic acids should lead directly to the mniopetals A–D. Therefore, it was necessary to find a simple strategy for the construction of these acids in enantiomerically pure form (Figure 1) and suitable methods for esterification with mniopetal E. Here, we wish to report our efforts in this direction.

(*R*)-2-Acetoxydecanoic acid (**9**), MEM-protected (*R*)-2-hydroxydecanoic acid (**10**) and MEM-protected (*R*)-2-hydroxyoctanoic acid (**11**) were synthesized starting with a Sharpless asymmetric dihydroxylation with AD-MIX-β of the corresponding terminal olefin (Scheme 1).[3]



Scheme 1 Common synthetic strategy for the carboxylic acid side chains **9**, **10** and **11**

In order to acetylate the secondary hydroxyl function in **4**, the primary one had to be protected temporarily. This could be accomplished in a one-pot procedure by silylation with TBDMSCl–pyridine, acetylation with Ac_2O and finally removal of the TBDMS group with dilute HCl to give **6** in good yield.[3a] Oxidation of **6** with $RuCl_3$–$NaIO_4$[3a] yielded **9** (side chain for **1a**). For the other side chains, the primary hydroxy group of **4** and **5** was silylated, then the secondary hydroxy group was protected as MEM acetal[4] and the silyl protecting group was removed under standard conditions to give **7** and **8**. Oxidation of the primary hydroxy group to the carboxylic acid in two

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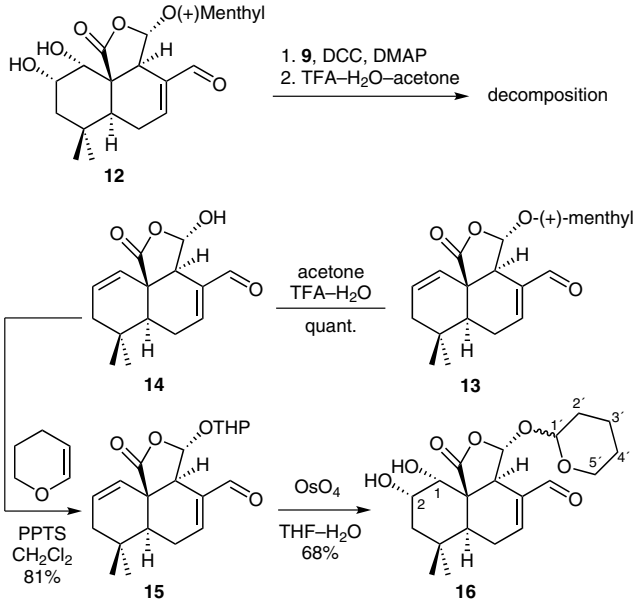
steps[4] gave **10** and **11**, respectively. The ee and the absolute configuration of hydroxyacids **10** and **11** were determined according to Mosher's method.[5] The enantiomeric excess of the synthesized acids exceeds 98%.

With the side chain acids for the mniopetals A–D in hand, esterification of **9** with the mniopetal E precursor **12**[2d] was straightforward, but the final cleavage of the menthyl acetal under standard conditions led to complete decomposition of the product (Scheme 2). Thus, we exchanged the menthyl group with a THP protecting group,[6,7] starting from **13**[2d] according to Scheme 2. Compound **15** was finally *cis*-dihydroxylated chemo- and stereoselectively[2,8] to yield **16**.

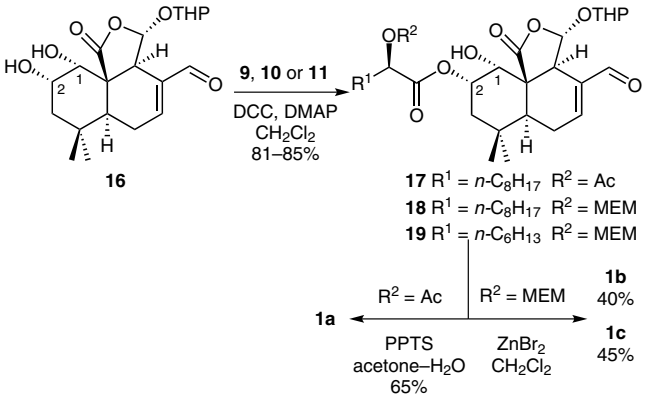


Scheme 2 Cleavage of the menthyl acetal after esterification of **12** with **9** was not possible. Therefore the menthyl group in **11** had to be exchanged with a THP group to give **16**.

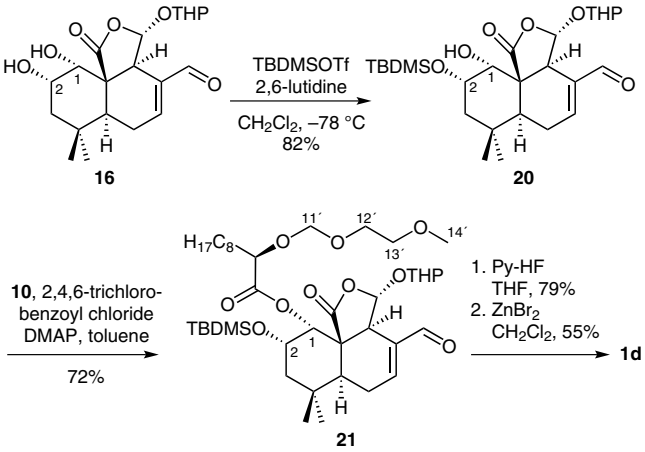
Mniopetal E precursor **16** contains equatorial and axial hydroxy groups at C2 and C1, respectively. Esterification of the equatorial hydroxy group is possible without protection of the axial hydroxy group (Scheme 3).[9] For the carboxylic acids **9**, **10** and **11** the Steglich esterification with DCC–DMAP[10] in dichloromethane is the method of choice (Scheme 3).

The THP group in **17** was cleaved with PPTS in acetone–water[11] to obtain mniopetal A (**1a**) in 65% yield. Mniopetals B and C (**1b**, **1c**) were obtained in 40% and 45% yield from **18** and **19**, respectively, after deprotection of the THP and MEM acetals in one step with $ZnBr_2$–CH_2Cl_2 (average yield for cleavage of each protecting group was 63–65%).

For the synthesis of mniopetal D (**1d**) the equatorial hydroxy group of diol **16** had to be protected selectively, which was achieved with TBDMSOTf–2,6-lutidine in dichloromethane at –78 °C (Scheme 4).[12]



Scheme 3 Syntheses of mniopetals A, B and C (**1a**, **1b** and **1c**)



Scheme 4 Synthesis of mniopetal D

After silylation of the hydroxy group at C2, [13] leading to **20**, Steglich esterification of the hydroxy group at C1 was not possible, probably due to a shielding effect of the huge silyl group and the innately lower reactivity of an axial hydroxy function. After extensive experimentation, we found that the Yamaguchi esterification with 2,4,6-trichlorobenzoyl chloride, hydroxyacid **10**, triethylamine and DMAP[14] gives **21** in 72% yield. The following desilylation has to be done with Py·HF complex, [15,16] since with TBAF migration of the acyl group to the equatorial hydroxyl group occurs. Finally, the acetal protecting groups MEM and THP were both cleaved with $ZnBr_2$–CH_2Cl_2 leading to mniopetal D (**1d**) in 55% yield (average 74% per protecting group).

All synthesized mniopetals were identical in all respects with the isolated products.

In summary, we have developed short and efficient syntheses of all known mniopetals.[17] Key features of our strategy are a straightforward construction of the side chain carboxylic acids and fine-tuned methods to manipulate an equatorial hydroxy group vicinal to an axial hydroxy group and vice versa.

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(7) **Synthesis of Compound 15**: 3,4-Dihydro-2*H*-pyran (565 µL, 6.18 mmol) was added to a mixture of **14** (324 mg, 1.24 mmol) and pyridinium *p*-toluenesulfonate (31.0 mg, 0.124 mmol) in CH_2Cl_2 (5.0 mL) and the reaction mixture was stirred at r.t. for 2 h. Sat. aq $NaHCO_3$ solution was added. Extraction with CH_2Cl_2, drying over $MgSO_4$ and purification by flash chromatography (petroleum ether–Et_2O, 2:1; silica gel, R_f 0.18 and 0.24) led to **15** (348 mg, 1.00 mmol, 81.0%). Specifications for one THP-diastereomer (R_f 0.24): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1 H, H-12), 7.17 (br d, *J* = 6.4 Hz, 1 H, H-7), 6.18 (dt, *J* = 10.2, 1.8 Hz, 1 H, H-1), 5.88 (dt, *J* = 10.2, 4.0 Hz, 1 H, H-2), 5.53 (s, 1 H, H-11), 5.07 (t, *J* = 2.8 Hz, 1 H, H-1′), 4.08 (dt, *J* = 11.1, 2.6 Hz, 1 H, H-5′$_{ax}$), 3.65 (br d, *J* = 11.5 Hz, 1 H, H-5′$_{eq}$), 3.20 (br s, 1 H, H-9), 2.55 (dm, *J* = 19.5 Hz, 1 H, H-6$_{ax}$), 2.43 (ddm, *J* = 19.5, 12.5 Hz, 1 H, H-6$_{eq}$), 2.00 (dd, *J* = 4.0, 2.1 Hz, 2 H, H-3), 1.82–1.93 (m, 1 H, H-3′$_{ax}$), 1.80–1.63 (m, 5 H, H-5, H-2′, H-4′), 1.57–1.63 (m, 1 H, H-3′$_{eq}$), 1.24 (s, 3 H, H-14), 1.04 (s, 3 H, H-13). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.7 (C-12), 175.3 (C-15), 156.0 (C-7), 138.9 (C-8), 129.5 (C-2), 126.2 (C-1), 99.2 (C-11), 94.7 (C-1′), 61.4 (C-5′), 49.9 (C-9), 48.2 (C-10), 44.9 (C-5), 41.2 (C-3), 31.14 (C-13), 31.05 (C-4), 29.8 (C-2′), 25.2 (C-4′), 24.6 (C-6), 24.2 (C-14), 18.1 (C-3′). $[\alpha]^{20}_D$ –22.2 ($CHCl_3$, *c* = 0.1). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{26}O_5Na$: 369.1678; found: 369.1634.

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(11) **Synthesis of Compound 17**: To a solution of **9** (15.7 mg, 68.0 µmol) in CH_2Cl_2 (1 mL) were added DMAP (0.64 mg, 5.26 µmol) and **16** (20.0 mg, 53.0 µmol). Then the solution was cooled to 0 °C and DCC (11.9 mg, 58.0 µmol) was added. The mixture was stirred at 0 °C for 10 min, then at r.t. overnight. The precipitate was filtered off and the filtrate was evaporated to dryness. The residue was diluted in CH_2Cl_2 (5 mL) and washed once with 0.5 M HCl solution (2 mL) and once with sat. aq $NaHCO_3$ solution. After drying with $MgSO_4$ the product was purified by flash chromatography (petroleum ether–Et_2O 1:1; silica gel, R_f 0.13 and 0.08) to yield **17** (27.0 mg, 46.0 µmol, 87.0%). Specifications for one THP-diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.45 (s, 1 H, H-12), 7.10 (br d, *J* = 6.6 Hz, 1 H, H-7), 5.34 (s, 1 H, H-11), 5.25–5.31 (m, 1 H, H-2), 5.08 (br s, 1 H, H-1″), 4.75 (br t, *J* = 6.2 Hz, 1 H, H-2′), 4.70 (br s, 1 H, H-1), 3.88 (br s, 1 H, H-9), 3.82–3.88 (m, 1 H, H-5″$_{ax}$), 3.56–3.61 (m, 1 H, H-5″$_{eq}$), 2.75 (d, *J* = 4.1 Hz, 1 H, OH), 2.42–2.50 (m, 1 H, H-6$_{ax}$), 2.20–2.30 (m, 1 H, H-6$_{eq}$), 2.09 (s, 3 H, H-12′), 2.01–2.09 (m, 1 H, H-3$_{ax}$), 1.49–1.85 (m, 10 H, H-3$_{eq}$, H-3′, H-2″, H-3″, H-4″), 1.37–1.45 (m, 2 H, H-4′), 1.34 (s, 3 H, H-14), 1.23–1.32 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.06 (s, 3 H, H-13), 0.88 (t, *J* = 7.1 Hz, 3 H, H-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.9 (C-12), 175.4 (C-15), 171.1 (C-11′), 169.7 (C-1′), 154.3 (C-7), 138.3 (C-8), 103.8 (C-11), 99.2 (C-1″), 73.4 (C-2′), 71.4 (C-2), 67.4 (C-1), 61.6 (C-5″), 52.7 (C-10), 46.6 (C-9), 39.5 (C-5), 37.4 (C-3), 33.5 (C-4), 33.4 (C-13), 31.8 (C-3′), 30.7 (C-8′), 29.7 (C-2″), 29.3 (C-5′), 29.13 (C-6′), 29.11 (C-7′), 25.1 (C-4′), 24.9 (C-4″), 24.6 (C-6), 23.3 (C-14), 22.6 (C-9′), 20.5 (C-12′), 18.1 (C-3″), 14.1 (C-10′). $[\alpha]^{20}_D$ –45.5 ($CHCl_3$, *c* = 0.2). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{48}O_{10}Na$: 615.3146; found: 615.3157.

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(14) **Synthesis of Compound 21**: Compound **10** (21.8 mg, 79.0 µmol) was diluted in toluene (900 µL). 2,4,6-Trichlorobenzoyl chloride (10.4 µL, 67.0 µmol) and Et_3N (17.0 µL, 121 µmol) were added and the solution was stirred for 2 h at r.t. After this a mixture of **20** (30 mg, 61.0 µmol) and DMAP (9.6 mg, 79 µmol) in toluene (900 µL) was added and the solution was stirred for 24 h at r.t.. Sat. aq $NaHCO_3$ solution was added and extraction with EtOAc, drying over $MgSO_4$, filtration and evaporation afforded a yellow oil,

which was purified by flash chromatography (petroleum ether–Et_2O, 1:1; silica gel, R_f 0.13 and 0.09). Yield: 31 mg (41.0 μmol, 67.9%). Specifications for one THP-diastereomer (R_f 0.09): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.43 (s, 1 H, H-12), 7.11 (br d, *J* = 6.4 Hz, 1 H, H-7), 5.86 (br s, 1 H, H-1), 5.31 (s, 1 H, H-11), 5.05 (br s, 1 H, H-1″), 4.75 (s, 2 H, H-11′), 4.36 (ddd, *J* = 12.8, 4.1, 2.4 Hz, 1 H, H-2), 4.22 (dd, *J* = 7.5, 5.0 Hz, 1 H, H-2′), 3.81–3.91 (m, 1 H, H-5″$_{ax}$), 3.76 (ddd, *J* = 11.0, 6.3, 3.2 Hz, 1 H, H-12′$_a$), 3.67 (ddd, *J* = 11.0, 5.6, 3.2 Hz, 1 H, H-12′$_b$), 3.48–3.63 (m, 3 H, H-5″$_{eq}$), 3.38 (s, 3 H, H-14′), 3.22 (br s, 1 H, H-9), 2.48 (ddd, *J* = 19.1, 5.8, 3.0 Hz, 1 H, H-6$_{ax}$), 2.18–2.29 (m, 1 H, H-6$_{eq}$), 1.99–2.12 (m, 1 H, H-3″$_{ax}$), 1.38–1.85 (m, 12 H, H-3, H-5, H-3′, H-4′, H-2″, H-3″$_{eq}$, H-4″), 1.31 (s, 3 H, H-14), 1.21–1.31 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.05 (s, 3 H, H-13), 0.86–0.90 (m, 3 H, H-10′), 0.86 (s, 9 H, *t*-Bu), 0.07 (s, 3 H, SiMe), 0.05 (s, 3 H, SiMe). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.4 (C-12), 175.2 (C-15), 170.7 (C-1′), 154.2 (C-7), 137.9 (C-8), 103.8 (C-11), 99.6 (C-1″), 95.0 (C-11′), 75.4 (C-2′), 72.7 (C-1), 71.6 (C-13′), 67.6 (C-12′), 65.9 (C-2), 61.4 (C-5″), 59.0 (C-14′), 52.2 (C-10), 47.4 (C-9), 43.0 (C-3), 40.7 (C-5), 33.6 (C-13), 33.5 (C-4), 33.2 (C-3′), 31.9 (C-8′), 29.5 (C-2″), 29.33 (C-5′), 29.31 (C-6′), 29.25 (C-7′), 25.8 (*t*-Bu), 25.07 (C-4′), 25.05 (C-4″), 24.7 (C-6), 23.5 (C-14), 22.6 (C-9′), 18.3 (*t*-Bu), 17.6 (C-3″), 14.1 (C-10′), –5.1 (SiMe), –5.3 (SiMe). $[\alpha]^{20}_D$ –25.3 ($CHCl_3$, *c* = 0.3). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd. for $C_{40}H_{68}O_{11}SiNa$: 775.4423; found: 775.4400.

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(16) **Cleavage of the Silyl Protection Group in 21**: Compound **21** (30.0 mg, 40.0 μmol) was diluted in HF·pyridine (1.14 mL, 1.59 mmol) in THF–pyridine prepared according to a procedure of Trost's (see ref. 15a). The solution was stirred at r.t. for 24 h. Sat. aq $NaHCO_3$ solution was added. Extraction with EtOAc, drying over $MgSO_4$, filtration and evaporation afforded a yellow oil, which was purified by flash chromatography (petroleum ether–acetone, 5:1; silica gel, R_f 0.12). Yield: 20.0 mg (31.0 μmol, 79.0%). Specifications for one THP-diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1 H, H-12), 7.11 (d, *J* = 6.5 Hz, 1 H, H-7), 5.76 (s, 1 H, H-1), 5.40 (s, 1 H, H-11), 4.96 (br s, 1 H, H-1″), 4.67–4.77 (m, 2 H, H-11′), 4.29–4.39 (m, 1 H, H-2), 4.21–4.28 (m, 1 H, H-2′), 3.93 (dd, *J* = 11.4, 2.5 Hz, 1 H, H-5″$_{ax}$), 3.69–3.77 (m, 1 H, H-12′$_a$), 3.56–3.62 (m, 1 H, H-12′$_b$), 3.53–3.56 (m, 1 H, H-5″$_{eq}$), 3.45–3.50 (m, 2 H, H-13′), 3.32 (s, 3 H, H-14′), 3.30 (br s, 1 H, H-9), 2.44 (dm, *J* = 19.3 Hz, 1 H, H-6$_{ax}$), 2.14–2.26 (m, 1 H, H-6$_{eq}$), 1.82 (d, *J* = 3.3 Hz, 1 H, OH), 1.66–1.77 (m, 4 H, H-3′, H-2″), 1.47–1.65 (m, 7 H, H-3, H-5, H-3″, H-4″), 1.33–1.44 (m, 2 H, H-4′), 1.24 (s, 3 H, H-14), 1.16–1.27 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.00 (s, 3 H, H-13), 0.81 (t, *J* = 7.0 Hz, 3 H, H-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.2 (C-12), 175.0 (C-15), 172.2 (C-1′), 153.8 (C-7), 137.8 (C-8), 99.9 (C-11), 94.9 (C-11′), 94.4 (C-1″), 75.4 (C-2′), 72.9 (C-1), 71.7 (C-13′), 67.6 (C-12′), 65.7 (C-2), 61.2 (C-5″), 59.0 (C-14′), 52.3 (C-10), 45.9 (C-9), 41.6 (C-5), 41.1 (C-3), 33.6 (C-13), 33.5 (C-4), 33.0 (C-3′), 31.9 (C-8′), 29.8 (C-2″), 29.4 (C-5′), 29.3 (C-6′), 29.2 (C-7′), 25.1 (C-4′), 25.0 (C-4″), 24.7 (C-6), 23.4 (C-14), 22.6 (C-9′), 17.5 (C-3″), 14.1 (C-10′). $[\alpha]^{20}_D$ –32.1 ($CHCl_3$, *c* = 1.2). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{54}O_{11}Na$: 661.3564; found: 661.3549.

(17) Mniopetal A (**1a**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.44 (s, 1 H, H-12), 7.12 (br d, *J* = 6.7 Hz, 1 H, H-7), 5.48 (br s, 1 H, H-11), 5.37 (ddd, *J* = 12.7, 4.0, 2.3 Hz, 1 H, H-2), 4.87 (dd, *J* = 6.5, 6.5 Hz, 1 H, H-2′), 4.59 (br s, 1 H, H-1), 3.89 (br s, 1 H, H-9), 2.46 (dm, *J* = 19.5 Hz, 1 H, H-6$_{ax}$), 2.24 (dm, *J* = 19.5 Hz, 1 H, H-6$_{eq}$), 2.14 (s, 3 H, H-12′), 2.08 (dd, *J* = 12.6, 12.6 Hz, 1 H, H-3$_{ax}$), 1.81–1.85 (m, 2 H, H-3′), 1.77 (dd, *J* = 12.7, 3.4 Hz, 1 H, H-5), 1.50 (dd, *J* = 12.2, 3.6 Hz, 1 H, H-3$_{eq}$), 1.37–1.44 (m, 2 H, H-4′), 1.33 (s, 3 H, H-14), 1.20–1.30 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.05 (s, 3 H, H-13), 0.88 (t, *J* = 7.1 Hz, 3 H, H-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.3 (C-12), 175.9 (C-15), 171.7 (C-11′), 169.6 (C-1′), 154.8 (C-7), 138.5 (C-8), 99.6 (C-11), 73.0 (C-2′), 71.1 (C-2), 68.1 (C-1), 53.4 (C-10), 46.2 (C-9), 39.7 (C-5), 37.5 (C-3), 33.6 (C-4), 33.3 (C-13), 31.8 (C-8′), 30.9 (C-3′), 29.3 (C-5′), 29.14 (C-6′), 29.11 (C-7′), 25.1 (C-4′), 24.7 (C-6), 23.3 (C-14), 22.6 (C-9′), 20.7 (C-12′), 14.1 (C-10′). $[\alpha]^{20}_D$ –64.0 ($CHCl_3$, *c* = 0.4); Lit.[1b] $[\alpha]^{20}_D$ –63 ($CHCl_3$, *c* = 0.05). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{40}O_9Na$: 531.2570; found: 531.2563.

Mniopetal B (**1b**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H, H-12), 7.18 (br d, *J* = 6.5 Hz, 1 H, H-7), 5.52 (br s, 1 H, H-11), 5.40 (ddd, *J* = 12.6, 4.0, 2.4 Hz, 1 H, H-2), 4.56 (br s, 1 H, H-1), 4.49 (br s, 1 H, OH), 4.18 (br s, 1 H, H-2′), 3.85 (br s, 1 H, H-9), 2.99 (br s, 1 H, OH), 2.92 (br s, 1 H, OH), 2.49 (dddm, *J* = 19.5, 6.7, 3.9 Hz, 1 H, H-6$_{ax}$), 2.26 (ddm, *J* = 19.5, 12.9 Hz, 1 H, H-6$_{eq}$), 2.02 (ddd, *J* = 12.6, 12.6, 6.7 Hz, 1 H, H-3$_{ax}$), 1.77 (dd, *J* = 12.6, 3.3 Hz, 1 H, H-5), 1.68–1.74 (m, 1 H, H-3′$_a$), 1.62–1.67 (m, 1 H, H-3′$_b$), 1.55–1.59 (m, 1 H, H-3$_{eq}$), 1.37-1.43 (m, 2 H, H-4′), 1.35 (s, 3 H, H-14), 1.20–1.30 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.07 (s, 3 H, H-13), 0.88 (t, *J* = 6.8 Hz, 3 H, H-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.2 (C-12), 175.7 (C-15), 174.4 (C-1′), 154.9 (C-7), 138.1 (C-8), 99.4 (C-11), 71.4 (C-2), 70.6 (C-2′), 68.8 (C-1), 53.4 (C-10), 46.2 (C-9), 39.6 (C-5), 37.4 (C-3), 34.5 (C-3′), 33.7 (C-4), 33.3 (C-13), 31.8 (C-8′), 29.4 (C-5′), 29.3 (C-6′), 29.2 (C-7′), 24.8 (C-4′), 24.7 (C-6), 23.2 (C-14), 22.7 (C-9′), 14.1 (C-10′). $[\alpha]^{20}_D$ –47.3 ($CHCl_3$, *c* = 0.1); Lit.[1b] $[\alpha]^{20}_D$ –46 ($CHCl_3$, *c* = 0.05). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{38}O_8Na$: 489.2465; found: 489.2475.

Mniopetal C (**1c**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.44 (s, 1 H, H-12), 7.14 (br d, *J* = 6.8 Hz, 1 H, H-7), 5.51 (br s, 1 H, H-11), 5.38 (ddd, *J* = 12.7, 4.0, 2.3 Hz, 1 H, H-2), 4.56 (br s, 1 H, H-1), 4.18 (dd, *J* = 7.5, 4.1 Hz, 1 H, H-2′), 3.83 (br s, 1 H, H-9), 2.48 (ddd, *J* = 18.6, 6.0, 3.0 Hz, 1 H, H-6$_{ax}$), 2.25 (ddm, *J* = 19.0, 12.5 Hz, 1 H, H-6$_{eq}$), 2.04 (dd, *J* = 12.6, 12.6 Hz, 1 H, H-3$_{ax}$), 1.76 (dd, *J* = 12.2, 3.9 Hz, 1 H, H-5), 1.69–1.75 (m, 1 H, H-3′$_a$), 1.63–1.68 (m, 1 H, H-3′$_b$), 1.55 (dd, *J* = 12.3, 4.2 Hz, 1 H, H-3$_{eq}$), 1.38–1.44 (m, 2 H, H-4′), 1.34 (s, 3 H, H-14), 1.24–1.33 (m, 6 H, H-5′, H-6′, H-7′), 1.06 (s, 3 H, H-13), 0.88 (t, *J* = 6.8 Hz, 3 H, H-8′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.3 (C-12), 175.9 (C-15), 174.4 (C-1′), 155.1 (C-7), 135.2 (C-8), 99.5 (C-11), 71.3 (C-2), 70.7 (C-2′), 68.6 (C-1), 53.5 (C-10), 46.2 (C-9), 39.6 (C-5), 37.4 (C-3), 34.4 (C-3′), 33.7 (C-4), 33.2 (C-13), 31.6 (C-6′), 28.9 (C-5′), 24.8 (C-4′), 24.7 (C-6), 23.2 (C-14), 22.5 (C-7′), 14.0 (C-8′). $[\alpha]^{20}_D$ –47.3 ($CHCl_3$, *c* = 0.1); Lit.[1b] $[\alpha]^{20}_D$ –45 ($CHCl_3$, *c* = 0.05). HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{34}O_8Na$: 461.2152; found: 461.2150.

Mniopetal D (**1d**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H, H-12), 7.16 (br d, *J* = 6.6 Hz, 1 H, H-7), 5.84 (br s, 1 H, H-1), 5.50 (s, 1 H, H-11), 4.49 (s, 1 H, OH), 4.39–4.44 (m, 1 H, H-2), 4.29–4.33 (m, 1 H, H-2′), 3.27 (br s, 1 H, H-9), 2.75 (d, *J* = 5.7 Hz, 1 H, OH), 2.52 (ddd, *J* = 19.6, 6.7, 3.3 Hz, 1 H, H-6$_{ax}$), 2.27 (ddd, *J* = 19.7, 12.8, 2.5 Hz, 1 H, H-6$_{eq}$), 1.95 (d, *J* = 2.8 Hz, 1 H, OH), 1.80–1.88 (m, 1 H, H-3′$_a$), 1.57–1.73 (m, 4 H, H-3, H-5, H-3′$_b$), 1.44–1.54 (m, 2 H, H-4′),

1.32 (s, 3 H, H-14), 1.23–1.30 (m, 10 H, H-5′, H-6′, H-7′, H-8′, H-9′), 1.08 (s, 3 H, H-13), 0.87 (t, J = 7.1 Hz, 3 H, H-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.6 (C-12), 176.1 (C-15), 174.4 (C-1′), 154.6 (C-7), 137.5 (C-8), 99.3 (C-11), 74.5 (C-1), 70.6 (C-2′), 65.2 (C-2), 52.3 (C-10), 47.0 (C-9), 41.3 (C-3), 40.8 (C-5), 34.6 (C-3′), 33.53 (C-4), 33.49 (C-13), 31.8 (C-8′), 29.4 (C-5′), 29.3 (C-6′), 29.1 (C-7′), 24.7 (C-6), 24.5 (C-4′), 23.4 (C-14), 22.6 (C-9′), 14.1 (C-10′). $[\alpha]^{20}_D$ –36.6 ($CHCl_3$, c = 0.1); Lit.[1b] $[\alpha]^{20}_D$ –40 ($CHCl_3$, c = 0.05). HRMS (ESI$^+$): m/z $[M + Na]^+$ calcd for $C_{25}H_{38}O_8Na$: 489.2465; found: 489.2434.

