An alternative total synthesis of solamargine

WEI GuoHua, WEI DongBin* & DU YuGuo*

State Key Laboratory of Environmental Chemistry and Ecotoxicology; Research Center for Eco-Environmental Sciences (CAS),
Beijing 100085, China

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Solamargine, (25*R*)-3β-{*O*-α-*L*-rhamnopyranosyl-(1→2)-[*O*-α-*L*-rhamnopyranosyl-(1→4)]-β-*D*-glucopyranosyloxy}-22α-*N*-spiroisol-5-ene, isolated from the berries of *solanum aculeastrum*, has been synthesized in 26.8% overall yield. First glycosylation before *N*-cyclization significantly facilitated synthesis of the desired molecule. We anticipate that this work will provide a new approach to access solamargine and its diversified analogues.

solasodine, natural products, solamargine, glycosides

1 Introduction

Solamargine is a major glycoalkaloid which occurs in at least 100 *Solanum* species [1]. Pharmacological studies have indicated that solamargine and its derivatives show anti-tumor activities through inhibition of tumor cell growth, such as colon (HT-29, HCT-15), prostate (LNCap, PC-3), breast (T47D, MDA-MB-231), and human hepatoma (PLC/PRF/5) cells [2–6]. Despite its widespread occurrence and biological importance, there are surprisingly few reports of the total synthesis of solamargine or structurally related compounds [7]. Recently, we reported the total synthesis of solamargine using partially protected glucopyranosyl donor and an oxaza-spiro moiety in 13 steps in a 10.5% overall yield. The synthetic solamargine exhibited good cytotoxic activities against tumor cells HeLa, A549, MCF-7, K562, HCT116, U87, and HepG2 with IC50 ranging from 2.1 to 8.0 μM [8]. To further investigate the preclinical potential, we need a practical method toward large scale preparation of solamargine. Herein we would like to report our solution for this purpose.

2 Experimental

General methods

Optical rotations were determined at 25 °C with a Perkin-Elmer Model 241-Mc automatic polarimeter unless otherwise stated. ¹H, ¹³C NMR spectra were recorded with ARX 400 spectrometers for solutions in CDCl₃ or CD₃OD. Chemical shifts are given in ppm downfield from internal Me₄Si. Mass spectra were measured using MALDI-TOF-MS with dihydroxybenzoic acid (DHB) as the matrix. High-resolution mass spectrometry was conducted in a positive mode using ESI-source. Thin layer chromatography (TLC) was performed on silica gel HF₂₅₄ with detection by charring with 30% (v/v) H₂SO₄ in MeOH or in some cases by a UV detector.

Synthesis of compound 5

Compound 2 (185 mg, 0.38 mmol) was subjected to Ac₂O/Py. After removal of the solvent, the residue was dissolved into wet acetone (2 mL), and NBS (136 mg, 0.76 mmol) was added at –10 °C. Then, the reaction mixture was stirred for 30 min in the dark, concentrated, and extracted with methylene chloride (3 × 20 mL). The organic phase was washed successively with saturated aqueous NaHCO₃, brine, then dried over anhydrous Na₂SO₄ and concentrated

*Corresponding author (email: weidb@rcees.ac.cn; duyuguo@rcees.ac.cn)

to dryness, and then the residue was subjected to DBU/ Cl_3CCN . Purification of the residue by silica-gel column chromatography (3:1 petroleum ether-EtOAc) afforded **5** (202 mg, 88% for 3 steps); $[\alpha]_{\text{D}}^{25} -28$ (*c* 2.4, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 1.92, 2.01 (2 s, 2×3 H, CH_3CO), 3.47–3.55 (m, 2 H), 3.80 (2 s, 2×3 H, $\text{CH}_3\text{OPhCH}_2$), 4.03–4.07 (m, 2 H), 4.44 (q, 2 H, $\text{CH}_3\text{OPhCH}_2$), 4.60 (q, 2 H, $\text{CH}_3\text{OPhCH}_2$), 5.06 (dd, 1 H, J 3.5, 10.0 Hz, H-2), 5.22 (t, 1 H, J 10.0 Hz, H-4), 6.54 (d, 1 H, J 3.4 Hz, H-1), 6.53–7.24 (m, 8 H, *Ph*), 8.61 (s, 1 H, *NH*). ^{13}C NMR (100 MHz, CDCl_3): 20.5, 20.7, 55.2, 55.23, 68.3, 69.9, 71.8, 72.18, 73.1, 74.1, 75.9, 90.9, 93.5, 159.2, 159.3, 160.7, 169.2, 169.7. MALDI-TOF-MS calcd for $\text{C}_{28}\text{H}_{32}\text{Cl}_3\text{NO}_{10}$: 647.1 $[\text{M}]^+$; found, 670.2 $[\text{M}+\text{Na}]^+$.

Synthesis of compound 7

To the solution of **6** (100 mg, 0.14 mmol) in dried pyridine (3 mL) was added HF-Py complex (0.8 mL) at 0 °C. The mixture was stirred for 10 h, and extracted with methylene chloride (3×20 mL). The organic phase was washed successively with saturated aqueous NaHCO_3 , 1 N HCl, saturated aqueous NaHCO_3 , brine, then dried over anhydrous Na_2SO_4 and concentrated. The residue was subjected to column chromatography on a silica gel column with 3:1 petroleum ether-EtOAc as the eluent to yield **7** as an amorphous solid (55 mg, 85%); $[\alpha]_{\text{D}}^{25} -54$ (*c* 2.1, CHCl_3). Selected ^1H NMR (400 MHz, CDCl_3): 0.78 (s, 3 H, CH_3), 0.98 (d, 3 H, J 6.5 Hz, CH_3), 1.03 (m, 6 H, CH_3), 2.55–2.62 (m, 3 H), 2.75–2.82 (m, 1 H), 3.16 (dd, 1 H, J 5.4, 12 Hz, H-26a), 3.27 (dd, 1 H, J 5.4, 12 Hz, H-26b), 3.54 (m, 1 H, H-3 α), 5.35 (d, 1 H, J 5.1 Hz, H-6). ^{13}C NMR (100 MHz, CDCl_3): 12.9, 15.3, 17.6, 19.3, 20.5, 27.4, 29.63, 30.9, 31.7, 32.9, 36.5, 36.9, 37.2, 38.6, 39.6, 41.6, 42.1, 43.8, 49.4, 51.2, 57.5, 66.2, 71.5, 120.8, 140.9, 213.2, 218.1. ESI-HRMS calcd for $\text{C}_{27}\text{H}_{41}\text{N}_3\text{O}_3$: 455.3148 $[\text{M}]^+$; found, 456.3221 $[\text{M}+\text{H}]^+$.

Synthesis of compound 8

To a solution of compound **5** (170 mg, 0.26 mmol) and compound **7** (80 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (2 mL) at -15 °C was added AgOTf (20 mg, 0.08 mmol) under N_2 protection. The mixture was stirred under these conditions for 80 min, at the end of which TLC indicated the reaction was complete. The mixture was neutralized with Et_3N and concentrated to dryness. The residue was purified by column chromatography on a silica gel column with 3:1 petroleum ether-EtOAc as the eluent to yield **8** as an amorphous solid (155 mg, 94%); $[\alpha]_{\text{D}}^{25} -64$ (*c* 0.9, CHCl_3). Selected ^1H NMR (400 MHz, CDCl_3): 0.79 (s, 3 H, CH_3), 0.94 (d, 3 H, J 6.5 Hz, CH_3), 1.04 (m, 6 H, CH_3), 1.92, 2.01 (2 s, 2×3 H, CH_3CO), 2.55–2.61 (m, 3 H), 2.76 (m, 1 H), 3.17 (dd, 1 H, J 5.4, 12 Hz, H-26a), 3.27 (dd, 1 H, J 5.4, 12 Hz, H-26b), 3.44–3.55 (m, 4 H, H-3 α , 6a 1 , 6b 1 , 5 1), 3.66 (t, 1 H, J 9.4 Hz, H-3 1), 3.78 (2 s, 2×3 H, $\text{CH}_3\text{OPhCH}_2$), 4.48 (m, 5

H, $J_{1,2}^{1,1}$ 8.0 Hz, $\text{CH}_3\text{OPhCH}_2$, H-1 1), 5.0 (m, 2 H, H-2 1 , 4 1), 5.32 (d, 1 H, J 5.0 Hz, H-6), 6.82–7.25 (m, 8 H, *Ph*). Selected ^{13}C NMR (100 Hz, CDCl_3): 13.0, 15.4, 17.7, 19.4, 20.5, 20.9, 20.9, 27.5, 29.7, 30.9, 31.8, 32.9, 36.8, 36.9, 37.2, 38.6, 39.6, 41.7, 42.2, 43.4, 49.8, 51.3, 55.3 (2 C), 57.6, 66.3, 69.7, 71.0, 72.8, 72.9, 73.3, 73.6, 79.5, 79.7, 99.9, 121.1, 140.8, 159.2, 159.3, 169.2, 169.6, 213.2, 218.1. ESI-HRMS calcd for $\text{C}_{53}\text{H}_{71}\text{N}_3\text{O}_{12}$: 941.5038 $[\text{M}]^+$; found, 942.5111 $[\text{M}+\text{H}]^+$.

Synthesis of compound 11

The mixture of **8** (80 mg, 0.09 mmol) and NaBH_4 (100 mg, 2.63 mmol) in *i*-propanol (2 mL) and CH_2Cl_2 (0.2 mL) was stirred at room temperature for 10 h. The reaction mixture was then extracted with methylene chloride (3×20 mL). The organic phase was washed successively with saturated aqueous NaHCO_3 , brine, then dried over anhydrous Na_2SO_4 and concentrated. The residue was subjected to column chromatography on a silica gel column with 3:1 petroleum ether-EtOAc as the eluent to yield crude foamy **9** (50 mg). To the solution of **9** (50 mg, 0.05 mmol) in THF (3 mL) and H_2O (0.3 mL) was added Ph_3P (41.7 mg, 0.16 mmol). The mixture was refluxed for 4 h, and then co-evaporated with toluene to dryness to yield **10**, which was used in the next step without further purification. Compound **10** was dissolved into a mixed solvent (5 mL, $\text{CH}_2\text{Cl}_2:\text{MeOH} = 1:3$) and NaOMe was added at room temperature to make the pH around 10. The above mixture was stirred at room temperature for 36 h, and neutralized with Amberlite IR-120 (H^+) resin. The liquid phase was evaporated *in vacuo* and the residue was purified on silica gel column chromatography with 1:2 petroleum ether-EtOAc $\rightarrow$ EtOAc as the eluent to yield **11** as an amorphous solid (38 mg, 53% from **8**); $[\alpha]_{\text{D}}^{25} -43$ (*c* 0.55, CHCl_3). Selected ^1H NMR (400 MHz, CDCl_3): δ 0.81 (s, 3H, H-18), 0.86 (d, 3H, J = 6.2 Hz, H-27), 0.96 (d, 3H, J = 7.2 Hz, H-21), 1.03 (s, 3H, H-19), 2.60–2.66 (m, 2H, H-26a, H-26b), 3.36–3.49 (m, 3H), 3.55–3.60 (m, 2H), 3.66 (dd, 1H, J = 5.4, 10 Hz, H-6a 1), 3.72 (dd, 1H, J = 5.4, 10 Hz, H-6b 1), 3.80 (s, 6H, $\text{CH}_3\text{OPhCH}_2$), 4.32 (m, 1H, H-16), 4.36 (d, 1H, $J_{1,2}^{1,1} = 7.8$ Hz, H-1 1), 4.50 (s, 2H, $\text{CH}_3\text{OPhCH}_2$), 4.72 (d, 1H, J = 11 Hz, one proton of $\text{CH}_3\text{OPhCH}_2$), 4.88 (d, 1H, J = 11 Hz, one proton of $\text{CH}_3\text{OPhCH}_2$), 5.34 (d, 1H, J = 5.0 Hz, H-6), 6.85–7.32 (m, 8H, *Ph*); Selected ^{13}C NMR (100 Hz, CDCl_3): δ 15.4, 16.3, 19.2, 19.4, 20.9, 29.6, 29.7, 31.2, 31.4, 31.8, 32.1, 32.2, 36.9, 37.3, 38.9, 39.8, 40.6, 42.4, 47.7, 50.1, 55.3 (2 C), 56.4, 62.9, 70.3, 71.8, 73.3, 74.1, 74.1, 74.3, 79.1, 83.4 (2 C), 98.4, 101.3, 121.8, 140.4, 159.3, 159.4. ESI-HRMS calcd for $\text{C}_{49}\text{H}_{69}\text{NO}_9$: 815.4972 $[\text{M}]^+$; found: 816.5046 $[\text{M}+\text{H}]^+$.

Synthesis of compound 13

Compounds **11** (22 mg, 0.03 mmol) and **12** (35 mg, 0.10 mmol) and activated 4 Å molecular sieves were pre-dried in

one flask under vacuum for 4 h. The mixture was then dissolved in CH_2Cl_2 (1 mL), and AgOTf (30 mg, 0.12 mmol) and 2,6-lutidine (15 μL , 0.12 mmol) were added under an N_2 atmosphere at -30°C . The mixture was stirred under these conditions for 3 h, neutralized with triethylamine, concentrated under reduced pressure, and purified on a silica gel column with 1:2 petroleum ether-EtOAc $\rightarrow$ EtOAc as the eluent to yield **13** as a white solid (30 mg, 90%); $[\alpha]_{\text{D}}^{25} +68$ (c 0.6, CHCl_3). Selected ^1H NMR (400 Hz, CDCl_3): δ 0.81 (s, 3H, H-18), 0.88 (d, 3H, $J = 6.2$ Hz, H-27), 1.01 (m, 6H, H-21, 19), 1.19–1.26 (m, 6H, H-6^{II}, 6^{III}), 1.71, 1.72, 1.87, 2.01, 2.03, 2.05 (6 s, 6 $\times$ 3H, CH_3CO), 2.62–2.68 (m, 2H, H-26a, H-26b), 3.36–3.57 (m, 7H), 3.67–3.72 (m, 2H), 3.78 (2 s, 2 $\times$ 3H, $\text{CH}_3\text{OPhCH}_2$), 4.32–4.34 (m, 1H, H-16), 4.39 (d, 2H, $J_{1,2}^{\text{I}} = 7.8$ Hz, H-1^I), 4.48 (s, 2H, $\text{CH}_3\text{OPhCH}_2$), 4.57 (d, 1H, $J = 10.0$ Hz, one proton of $\text{CH}_3\text{OPhCH}_2$), 4.63 (dd, 1H, $J = 2.6, 4.0$ Hz, H-2^{II}), 4.68 (dd, 1H, $J = 2.6, 4.0$ Hz, H-2^{III}), 4.74 (d, 1H, $J = 10.0$ Hz, one proton of $\text{CH}_3\text{OPhCH}_2$), 4.98–5.04 (m, 3H, H-3^{III}, 4^{II}, 4^{III}), 5.10 (dd, 1H, $J = 4.0, 8.6$ Hz, H-3^{II}), 5.19 (d, 1H, $J = 2.0$ Hz, H-1^{II}), 5.23 (d, 1H, $J = 2.0$ Hz, H-1^{III}), 5.34 (d, 1H, $J = 5.0$ Hz, H-6), 6.85–7.32 (m, 8H, Ph). ^{13}C NMR (100 Hz, CDCl_3) δ 15.3, 16.4, 17.5, 17.7, 19.3, 19.4, 20.5, 20.7, 20.8, 20.9, 22.7, 25.7, 26.1, 29.7 (2 C), 29.9, 31.4, 31.9, 32.1, 32.2, 36.9, 37.3, 38.6, 39.9, 40.6, 41.3, 47.5, 50.1, 55.3 (2 C), 56.5, 62.5, 69.2, 69.3, 69.5, 70.1, 70.3, 70.4, 70.8, 72.3, 72.9 (2 C), 74.6, 74.9, 75.0, 76.0, 79.0, 81.9 (2 C), 97.1 (C-1^{II}), 97.4 (C-1^{III}), 98.3 (C-22), 100.7 (C-1^I), 121.7 (C-6), 140.7 (C-5), 159.1 (2 C), 169.7 (2 CH_3CO), 169.8 (2 CH_3CO), 170.2 (CH_3CO), 170.3 (CH_3CO). ESI-HRMS calcd for $\text{C}_{73}\text{H}_{101}\text{NO}_{23}$: 1359.6764 $[\text{M}]^+$, found: 1360.6838 $[\text{M}+\text{H}]^+$.

Synthesis of compound 1

A solution of **13** (30 mg, 0.02 mmol) in TFA: CH_2Cl_2 (1:4, V/V, 1 mL) was stirred at -15°C for 0.5 h, neutralized with saturated aqueous sodium bicarbonate, and extracted with dichloromethane (3 $\times$ 15 mL). The organic phases were combined, dried over anhydrous sodium sulfate and concentrated, which was used in the next step without further purification. To a solution of the above residue in a mixed solvent (5 mL, CH_2Cl_2 : MeOH = 1:3) aqueous 0.3 M NaOH was added until the pH was 10. The mixture was stirred at room temperature for 6 h, and neutralized with

Amberlite IR-120 (H^+). The solvents were filtered, and the filtrate was concentrated to dryness under diminished pressure. The residue was subjected to column chromatography on silica gel with 5:2 CH_2Cl_2 -MeOH as the eluent to yield **1** as a white solid (15.7 mg, 80% for 2 steps); $[\alpha]_{\text{D}}^{25} -88$ (c 0.5, MeOH: $\text{CHCl}_3 = 1:1$) [lit. [4] $[\alpha]_{\text{D}}^{24} -91$ (c 0.2, MeOH: $\text{CHCl}_3 = 1:1$)]; The diagnostic NMR signals are identical to those reported for the natural product [1]. Selected ^1H NMR (400 Hz, CDCl_3 : $\text{CD}_3\text{OD} = 1:1$): δ 0.84 (s, 3H, H-18), 0.87 (d, 3H, $J = 6.2$ Hz, H-27), 0.97 (d, 3H, $J = 7.0$ Hz, H-21), 1.05 (s, 3H, H-19), 1.22–1.26 (m, 6H, H-6^{II}, 6^{III}), 1.42–2.47 (m, 24H), 2.63–2.67 (m, 2H, H-26), 3.21–4.09 (m, 15H), 4.31–4.33 (m, 1H, H-16), 4.50 (d, 1H, $J = 7.8$ Hz, H-1^I), 4.90 (s, 1H, H-1^{II}), 5.24 (s, 1H, H-1^{III}), 5.40 (d, 1H, $J = 4.0$ Hz, H-6). Selected ^{13}C NMR (100 Hz, CDCl_3 : $\text{CD}_3\text{OD} = 1:1$): δ 15.6, 16.9, 17.4, 17.9, 19.2 (2 C), 20.8, 28.4, 28.7, 29.2, 29.6, 30.2, 31.5, 33.4, 36.2, 38.2, 39.1, 40.5, 41.5, 42.1, 47.3, 51.1, 56.0, 61.4, 62.8, 68.2, 68.9, 69.2, 69.4, 70.5, 71.5, 73.3, 73.5, 75.5, 76.8, 77.1, 79.1, 79.5, 79.6, 98.8, 100.4, 101.3, 102.4, 121.8, 141.3. ESI-HRMS calcd for $\text{C}_{45}\text{H}_{73}\text{NO}_{15}$: 867.4980 $[\text{M}]^+$, found: 868.5053 $[\text{M}+\text{H}]^+$.

3 Results and discussion

In our previous method [8], although treatment of solasodine **3** with a partially protected glycosyl donor **2** in dry methylene dichloride in the presence of AgOTf and *N*-iodosuccinimide (NIS) at -50°C afforded the desired key saponin **4** in an optimized yield around 65% (Scheme 1), significantly simplifying the solamargine synthesis, a large amount of expensive donor **2** was quickly consumed in the presence of cyclic amine (oxaza-spiro structure). Based on the phenomenon, herein we explored a new method for the total synthesis of solamargine **1** as shown in Scheme 2. First glycosylation before *N*-cyclization would favor synthesis of the desired molecule.

PMB (*p*-methoxybenzyl) in Schmidt reagent **5** was selected as the protecting groups, as it not only enhances the reactivity of the sugar moiety, but also improves the selectivity in the final deprotection step. Thus, the known compound **2** [8] was first acetylated with acetic anhydride in pyridine, which was further converted into trichloroacetim-

Scheme 1 The previous method of synthesis of Solamargine **1**.

Scheme 2 Reagents and condition: (a) Ac_2O , Pyridine; NBS, wet DCM, dark, 0°C ; DBU, Cl_3CCN , DCM, 88% (for 3 steps); (b) HF/Py , 85%; (c) AgOTf , DCM, -40°C , 94%; (d) NaBH_4 , *i*-PrOH, rt; (e) Ph_3P , $\text{THF/H}_2\text{O}$ (v/v, 10:1), reflux; (f) NaOMe , MeOH, 53% overall yield for three steps from **4**; (g) **12**, AgOTf , 2,6-lutidine, DCM, -30°C , 90%; (h) 10% TFA in DCM, -15°C ; 0.3 M NaOH, MeOH, 80% for 2 steps.

idate **5**. Treatment of compound **6** [8] with HF/Py complex provided acceptor **7**. After coupling of glycosyl donor **5** and aglycone precursor **7** in anhydrous methylene chloride with mild catalyst AgOTf [9], key intermediate **8** was obtained in 94% isolated yield. Selective reduction of 16-ketone **8** with NaBH_4 /*i*-PrOH [10] ($\rightarrow$ **9**), followed by reductive cyclization with $\text{Ph}_3\text{P/THF/H}_2\text{O}$ under refluxing ($\rightarrow$ **10**) and removal of the acetyl group with NaOMe in MeOH, afforded acceptor **11** in 53% overall yield for three steps [8]. Condensation of **11** and rhamnopyranosyl bromide **12** using AgOTf and 2,6-lutidine as catalysts [11] afforded trisaccharide alkaloid **13** in excellent yield (90%). Removal of the PMB groups of **13** with 10% TFA in DCM at -15°C , followed by deacetylation with 0.3 M NaOH in MeOH, afforded the final solamargine **1** in 80% overall yield for 2 steps [8]. The analytic data (NMR, MS, optical rotation) for the synthesized solamargine **1** were identical to those of the natural product [1, 8].

4 Conclusion

In summary, a highly efficient approach for the synthesis of solamargine **1** has been developed. First glycosylation be-

fore *N*-cyclization significantly facilitated synthesis of the desired molecule. We anticipate that this work will provide a new approach to access solamargine and its diversified analogues.

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- Wanyonyi AW, Chhabra SC, Mkoji G, Eilert U, Njue WM. Bioactive steroidal alkaloid glycosides from *Solanum aculeastrum*. *Phytochemistry*, 2002, 59: 79–84
- Kuo KW, Hsu SH, Li YP, Lin WL, Liu LF, Chang LC, Lin CC, Lin CN, Sheu HM. Triggering apoptosis in human hepatoma cells. *Biochem Pharmacol*, 2000, 60: 1865–1873
- Liu LF, Liang CH, Shiu LY, Lin W L, Lin CC, Kuo KW. Action of solamargine on human lung cancer cells—enhancement of the susceptibility of cancer cells to TNFs. *FEBS Letters*, 2004, 577: 67–74
- Al Chami L, Méndez R, Chataing B, O’Callaghan J, Usabillaga A, LaCruz L. Toxicological effects of solamargine in experimental animals. *Phytother Res*, 2003, 17: 254–258
- Maruo VM, Soares MR, Bernardi MM, Spinosa HS. Embryotoxic effects of *Solanum lycocarpum* St. Hill fruits consumption during preimplantation and organogenesis in rats. *Neurotoxicol Teratol*, 2003, 25: 627–631
- Heo KS, Lee SJ, Ko JH, Lim K, Lim KT. Glycoprotein isolated from *Solanum nigrum* L. inhibits the DNA-binding activities

- of NF- κ B and AP-1, and increases the production of nitric oxide in TPA-stimulated MCF-7 cells. *Toxicol in Vitro*, 2004, 18: 755–763
- 7 Shahid M. Synthesis of solanum glycosides. PCT Patent WO/018604, 2003
- 8 Wei G, Wang J, Du Y. Total synthesis of solamargine. *Bioorg Med Chem Lett*, 2011, 21: 2930–2933
- 9 Wei G, Gu G, Du Y. Silver Triflate. A mild alternative catalyst for glycosylation conditions using trichloroacetimidates as glycosyl donors. *J Carbohydr Chem*, 2003, 22: 385–393
- 10 Mazur Y, Danieli N, Sondheimer F. The synthesis of the steroidal sapogenins. *J Am Chem Soc*, 1960, 82: 5889–5908
- 11 Depré D, Düffels A, Green LG, Roman L, Ley SV, Wong C-H. Synthesis of glycans from the glycodefins: two undeca-, two deca-, three nona-, an octa- and a heptasaccharide. *Chem Eur J*, 1999, 5: 3326–3340