Orthogonally Protected Sugar Diamino Acids as Novel Building Blocks for Linear and Branched Oligosaccharide Mimetics

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Experimental Section

17: β-Alanine amide 13 (27 mg, 0.067 mmol) was dissolved in dry DMF (4 mL) and treated with piperidine (1 mL). After 40 min, the solvent was removed under reduced pressure followed by co-evaporation with toluene. The residue was re-dissolved in CHCl₃ (3 mL) and 2 (44 mg, 0.081 mmol) and a solution of HBTU (31 mg, 0.081 mmol) and HOBt (19 mg, 0.121 mmol) in dry DMF (3 mL) were added. iPr₂NEt (31 µL, 0.202 mmol) was added and the mixture was stirred over night. After dilution with CHCl₃ (15 mL), the organic phase was washed with 0.1 N HCl and sat aq NaHCO₃, dried with Na₂SO₄ and evaporated. Purification by flash chromatography (silica, EtOAc/MeOH 95/5) gave 17 (42 mg, 89 %): R_F = 0.5 (EtOAc/MeOH 9/1).

18: Peptide 17 (50 mg, 0.071 mmol) was dissolved in dry DMF (4 mL) and treated with piperidine (1 mL) for 30 min. After evaporation and co-evaporation with toluene, the remaining solid was dissolved in CHCl₃ (8 mL) and building block 1 (88 mg, 0.142 mmol), a solution of HATU (54 mg, 0.142 mmol) and HOAt (29 mg, 0.214 mmol) in DMF (8 mL), and iPr₂NEt (55 µL, 0.356 mmol) were added. After stirring over night, aqueous workup as described for 17 followed. Flash chromatography (silica, EtOAc/MeOH 95/5) gave 18 (61 mg, 79 %): R_F = 0.53 (EtOAc/MeOH 9/1).

19: To a solution of 18 (50 mg, 0.046 mmol) in THF (4 mL) PMe₃ (278 µL, 1 M in THF) and water (1 mL) were added. After 1 h, the mixture was evaporated and co-evaporated several times with toluene. The subsequent peptide coupling was carried out as described for 17 using 2 eq of 1. Purification by flash chromatography (silica, EtOAc/MeOH 95/5) gave 19 (56 mg, 73 %): R_F = 0.48 (EtOAc/MeOH 9/1); RP-HPLC (Vydac 218TP54 C₁₈ reversed-phase column, 4 × 250 mm, flow = 1 mL min⁻¹, 20–80 % acetonitrile in water/0.1 % TFA over 30 min): t_R = 24.0 min. HRMS (MALDI-FTICR), calcd for C₈₃H₁₁₀N₈O₂₇: 1673.73730 [M + Na⁺], found: 1673.73587, ∆m = 0.8 ppm.
Protected oligomer 19 (15 mg, 0.009 mmol) was dissolved in CHCl₃/THF 1:1 (1 mL) and stirred for 1 h. The mixture was evaporated and the remainder was dissolved in MeOH (500 µL), treated with 1 N HCl (500 µL) for 1 h, and lyophilized. Finally, stirring with 20% piperidine in DMF (500 µL) led to complete deprotection. Purification by RP-HPLC (Vydac 218TP54 C₁₈ reversed-phase column, 4 × 250 mm, flow = 1 mL min⁻¹, 1–100% acetonitrile in water/0.13% pentafluoropropionic acid over 30 min, tᵣ = 15.5 min) gave 20 • 4 F₃C-CF₂-CO₂H (3.5 mg, 28%). HRMS (ESI-FTICR, MeCN/H₂O), calcd for C₃₁H₅₀N₈O₁₃: 743.35696 [M + H⁺], found: 743.35563, Δm = 1.8 ppm (see Figure S-1).

![Figure S-1. HRMS (ESI-FTICR, MeCN/H₂O) of 20.](image-url)