ORGANIC LETTERS

Dynamic Multivalent Lactosides Displayed on Cyclodextrin Beads Dangling from Polymer Strings

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SUPPORTING INFORMATION

(7 PAGES)

S2	General Methods and Procedures
S5	^1H NMR spectrum of 1
S6	TROESY NMR of Polytetrahydropyran
S7	TROESY NMR of Polypropylene glycol
S8	^1H NMR spectrum of 2
S9	^1H NMR spectra of 2 before and after the addition of PEG

General methods: Analytical TLC was performed on silica gel 60-F₂₅₄ (Merck) with detection by fluorescence and/or by charring following immersion in a 5% H₂SO₄/EtOH. Flash chromatography was performed with silica gel 60 (Silicycle). Preparative gel permeation chromatography was performed using (1) a 25 × 900 mm column of Sephadex[®] LH20 resin (Sigma), eluting with MeOH or (2) a 5 × 100 cm column of Sephadex[®] G-25 resin (Amersham Pharmacia Biotech), eluting with 5% *n*BuOH in water. ¹H and ¹³C NMR spectra were recorded on a Brüker Avance 500 spectrometer (at 500 MHz and 125 MHz, respectively) or Brüker Avance 600 spectrometer (at 600 MHz and 150 MHz, respectively) at ambient temperature. ¹H NMR and ¹³C NMR spectra were referenced using either their residual solvent signals or tetramethylammonium iodide as the internal standard. The following abbreviations were used to explain the signal multiplicities or characteristics: s, singlet; d, doublet; dd, double doublet; pd, pseudo-doublet; pt, pseudo-triplet; m, multiplet; b, broad. Electrospray mass spectrometry (ESI) was performed using a Sciex API IIIIR triple quadrupole electrospray mass spectrometer using H₂O/MeCN/HCOOH, 50:50:0.1 as the mobile phase. High resolution matrix assisted laser desorption ionization (HR-MALDI) spectra were recorded using dihydroxybenzoic acid as matrix and external calibration with substance P on a IonSpec Ultima 7.4 Tesla FTMS instrument.

1: The mono-amino α -CD derivative **4** (500 mg, 0.515 mmol) was added to a stirred solution of the lactosyl propionic acid **3** (634 mg, 0.88 mmol), HBTU-BF₄ (628 mg, 1.96 mmol), and *i*Pr₂NEt (150 μ L) under an argon atmosphere. The reaction mixture was stirred 24 h before being concentrated *in vacuo*, and the residue redissolved in EtOAc.

The organic layer was then washed with 1 M HCl and brine, dried (Na₂SO₄) and filtered. The organic solution was evaporated to dryness to afford an oil which was dissolved in MeOH (50 mL) to which 0.5 M methanolic NaOMe solution (0.8 mL) was added. The reaction mixture was stirred at room temperature for 5 h. The reaction mixture was neutralized using Amberlite IR-120 (H⁺ form) and the solvent evaporated to afford a crude oil. Gel filtration chromatography (G-25, 5% BuOH/H₂O) gave the desired compound **1** as a white solid in 59 % unoptimized yield over two steps. ¹H NMR (500MHz, D₂O): δ = 2.58-2.70 (m, 2H, C(O)CH₂), 2.93-3.06 (m, 2H, SCH₂), 3.33-3.40 (m, 1H), 3.44-4.05 (m, 47H), 4.44 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 4.57 (d, $J_{1,2}$ = 9.9 Hz, 1H, H-1'') 5.02-5.10 (m, 6H, H-1); Selected ¹³C NMR (150 MHz, D₂O) δ = 26.5 (C(O)CH₂), 36.4 (SCH₂), 85.8 (C-1'), 101.2 (C-1), 101.3 (4 x C-1), 101.4 (C-1), 102.9 (C-1''). MALDI-TOF: m/z = 4185 [M + Na]⁺.

2: Mono(6-amino-6-deoxy-2-*O*-methyl)-hexakis(2,6-di-*O*-methyl)- β -CD (500 mg, 0.515 mmol) was added to a stirred solution of the lactosyl propionic acid **3** (634 mg, 0.88 mmol), HBTU-BF₄ (628 mg, 1.96 mmol), and *i*Pr₂NEt (150 μ L) under an argon atmosphere. The reaction mixture was stirred 24 h before being concentrated *in vacuo*, and the residue redissolved in EtOAc. The organic layer was then washed with 1 M HCl and brine, dried (Na₂SO₄) and filtered. The organic solution was evaporated to dryness to afford an oil which was dissolved in MeOH (50 mL) to which 0.5 M methanolic NaOMe solution (0.8 mL) was added. The reaction mixture was stirred at room temperature for 5 h. The reaction mixture was neutralized using Amberlite IR-120 (H⁺ form) and the solvent evaporated to afford a crude oil. Gel filtration chromatography (G-25, 5% BuOH/H₂O) gave the desired compound **2** as a white solid in 52 % unoptimized yield

over two steps. ^1H NMR (500MHz, D_2O): δ = 2.56-2.70 (m, $\text{C}(\text{O})\text{CH}_2$), 2.92-3.06 (m, 2H, SCH_2), 3.19-3.92 (m, 57H), 4.04 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1'), 4.55 (d, $J_{1,2}$ = 9.8 Hz, 1H, H-1''), 5.08-5.28 (m, 7H, H-1).

General Procedure for Pseudopolyrotaxane Formation: The cyclodextrin derivative **1** (33 mg, 23.5 μmol) or **2** (18 mg, 10.7 μmol) was dissolved in D_2O (0.6 mL). The polymer was then added to the aqueous solution and the resulting heterogeneous solution was sonicated for 40 min. The threading process was monitored by ^1H NMR spectroscopy.

Current Data Parameters
NAME pp9
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20030815
Time 9.02
INSTRUM avance500
PROBHD 5 mm bb-Z
PULPROG zg
TD 32768
SOLVENT D2O
NS 8
DS 0
SWH 5000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2789500 sec
RG 90.5
DW 100.000 usec
DE 6.00 usec
TE 300.0 K
D1 2.0000000 sec

CHANNEL f1
NUC1 1H
P1 12.50 usec
PL1 0.00 dB
SFO1 500.3325016 MHz

F2 - Processing parameters
SI 32768
SF 500.3299382 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

TROESY
D₂O
298 K

Figure 1 displays two ^1H NMR spectra. The top spectrum is for the poly(6-methyl-2,3-O-isopropylidene-1-thio- β -D-glucopyranoside) (P6MSTG), showing a broad peak for $-\text{OCH}_2\text{CH}_2-$ at approximately 3.6 ppm and a peak for H-3 at approximately 3.9 ppm. The bottom spectrum is for the derivative, showing a peak for TMACI at approximately 3.2 ppm. Chemical structures of the repeating units are shown above each spectrum.