Supporting Information

Expeditious synthesis of bis-β-cyclodextrinyl-diazacrown-[2]cryptorotaxanes

Florence Dumarcay-Charbonnier and Alain Marsura*

aSRSMC, Nancy Université & CNRS, Faculté des Sciences et Techniques, B. 70239, F-54506 Vandœuvre-lès-Nancy Cedex, France.
Fax: +33 (0)3 83 68 23 45; Tel: +33 (0)3 83 68 49 55; E-mail: Alain.Marsura@pharma.uhp-nancy.fr

Experimental

General

1,12-diaminododecane, octadecanedioic acid, sodium tetraphenylboron, tetraphenylphosphonium chloride and diphenyl ethylamine were purchased from Sigma-Aldrich and were used as purchased without further purification. 1H NMR (400MHz) and 13C NMR spectra (100MHz) were recorded on a Bruker DRX 400 FT-NMR spectrometer. Chemical shifts for 1H- and 13C-NMR were reported in parts per million (ppm), calibrated to the residual solvent peak set, with coupling constants reported in Hertz (Hz). High Resolution Electrospray Mass spectra (HR-ESIMS) were recorded on a Bruker Micro QTOF spectrometer. Mass spectrum of 4 was also recorded on a MALDI-TOF–TOF Bruker Daltonics Ultraflex II in positive reflectron mode with 2,5-DHB as matrix. Dialysis was performed on a Spectra/Por Float-A-lyser-MWCO 100-500D.

Synthesis of the bis-β-cyclodextrinyl-diazacrown receptor 1

1 was synthesized following our recent report 1.

Synthesis of pseudorotaxane 3.

1,12-diaminododecane (0.016g, 8.00.10^-5 mole, 1 equiv.) was added to a solution of 1,10-N,N’-Bis-[cyclomaltioheptaosyl-6A-deoxy-6A-ureido]-4,7,13,16-tetraoxa-1,10-diazacyclooctadecane 1 (8.02.10^-5 mole, 0.21g) into distilled water (42 mL). The reaction mixture was stirred during 2 days at r.t. until to obtain a clear solution and then was lyophilized. The pseudorotaxane 3 was obtained as a white powder (0.160 g, 72%). 1H NMR (400MHz, D2O): δΗ 5.06 (s, H1), 4.00-3.40 (m, H3, H5, H2, H6, H6’), 2.86 (t, α-CH2, J = 7.56 Hz, J = 15,12 Hz), 1.58 (m, β-CH2), 1.27 (s, CH2 centre). 13C NMR (100MHz, D2O): δC 160.7 (NH-CO-NH), 102.3 (C 1), 81.4 (C4), 73.6-72.3-70.6 (C2, C3, C5), 60.4 (C6), 39.8 (C6’), 28.9, 27.6, 26.4, 23.6 (CH2 chain). HR-ESIMS calcd. for [C110H192N6O74]+, [3] = 2783.1600, found 1392.0787 [3]^2+/2.


A solution of sodium tetraphenylboron (0.06g, 6.6.10^-5 mole, 2.2 equivs.) in distilled water (3mL), was added drop wise to an aqueous solution (3mL) of pseudorotaxane 3 (0.084g, 3.0.10^-5 mole, 1 equiv.). A white precipitate was immediately formed, then centrifugated and washed three time with distilled water. Pure cryptorotaxane 4 was obtained as a white amorphous powder (97%). 1H NMR (400MHz, DMSO-6d): δΗ  7.17 (s, 16H, arom.), 6.94 (t, 16H, arom.), 6.79 (t, 8H, arom.), 4.84 (s, 14H, H 1), 4.00-3.10 (m, 122H, H 2, H3, H4, H5, H 6, O-CH2 crown, N-CH2 crown), 2.75 (t, 4H, α-CH2), 1.49 (s, 4H, β-CH2), 1.25 (s, 24H, CH2 diaminododecane alkyl chain). 13C NMR (100MHz, DMSO-5d): δC 164.9, 163.9, 163.5, 163.4 (Cq arom.), 160.7 (C=ONH), 136.4, 126.2, 122.4 (C H arom.), 102.3 (C1), 73.4 (C4), 72.9 (C2), 72.8 (C3), 72.7 (C5), 70.6 (C6), 62.5 (C6’), 29.9, 29.8, 29.7, 29.5 (CH2 diaminododecane alkyl chain), 28.0 (α-CH2 diaminododecane alkyl chain), 26.7 (β-CH2, diaminododecane). HR-ESIMS calcd. for [C158H234B2N6O74]+ [4] = 3421.4900, found 2582.1870 [4]- C60H70B2N2]+, 319.1631[BPh 4]-, 202.2356 [1,12-diaminododecane]+.

Synthesis of pseudorotaxane 6.

Octadecanedioic disodium salt (0.019g, 6.15.10^-5 mole, 1 equiv.) was added to a solution of 1,10-N,N’-Bis-[cyclomaltioheptaosyl-6A-deoxy-6A-ureido]-4,7,13,16-tetraoxa-1,10-diazacyclooctadecane 1 (0.16g, 6.15.10^-5 mole, 1 equiv.) into distilled water (6 mL). The reaction mixture was stirred during 1h. at r.t. then dialyzed and lyophilized. The pseudorotaxane 6 was obtained as an amorphous white powder (97%). 1H NMR (400MHz, D2O): δΗ  4.96 (14Η, Η 1), 3.98−3.72 (m, 58H, O-CH2 crown, H 3, H 6, H 5), 3.72-3.30 (m,  64H, O-CH2 crown, N-CH2 crown), 2.75 (t, 4H, α-CH2, J = 7.52Hz), 1.49 (s, 4H, β-CH2), 1.25 (s, 24H, CH2 diaminododecane alkyl chain). 13C NMR (100MHz, DMSO-5d): δC 164.9, 163.9, 163.5, 163.4 (Cq arom.), 160.7 (CONH), 136.4, 126.2, 122.4 (CH arom.), 102.3 (C1), 73.4 (C4), 72.9 (C2), 72.8 (C3), 72.7 (C5), 70.6 (C6), 62.5 (C6’), 29.9, 29.8, 29.7, 29.5 (CH2 diaminododecane alkyl chain), 28.0 (α-CH2 diaminododecane alkyl chain), 26.7 (β-CH2, diaminododecane).
N-CH2-crown), 2.06-1.84 (m, 10H, α-CH2, CH2 chain), 1.45-1.32 (m, 4H, β-CH2), 1.22-0.85 (m, 18H, CH2 chain). 13C NMR (100MHz, D2O): δ 171.9 (COO−), 170.2 (COO−), 162.0 (NH-CO NH), 104.9 (C1), 88.9 (C6), 76.2, 75.4, 74.4 (C2, C3, C4), 72.4 (C5), 71.5, 69.7, 67.7 (α-CH2, β-CH2, CH2 chain), 62.6 (C6), 51.0 (CH2 crown), 43.6 (CH2 crown), 26.2 (CH2 chain).


Synthesis of [2]cryptorotaxane 7. An aqueous solution (2mL) of Tetraphenylphosphonium chloride (0.032g, 8.53.10−5 mole, 2.2 equivs.) was added to a solution of 6 (0.112g, 3.80.10−5 mole) in 10mL of water. The resulting solution was stirred 1.5 h more at r.t., then dialyzed and lyophilized to give 7 as an amorphous white powder (0.142g, 99%). 1H NMR (400MHz, DMSO-6d): δ 7.98 (m, 8H, arom.), 7.83 (m, 16H, arom.), 7.75 (m, 16H arom.), 6.16 (s, 2H, NHCONH), 4.84 (s, 14H, H1), 3.85-3.00 (m, 122H, H2, H3, H4, H5, H6, O-CN=Crown, N-CN=Crown), 2.04 (s, 4H, α-CH2 diacide chain), 1.77 (s, 4H, β-CH2 diacide chain), 1.23 (s large, 24H, CH2 centre diacide alkyl chain). 13C NMR (100MHz, DMSO-6d): δ 174.3, 170.7 (COO−), 158.0 (NHCONH), 135.3, 134.5, 130.5, 118.1, 117.2 (CH arom.), 101.9 (C1), 81.6 (C4), 73.0, 72.4, 71.9 (C2, C3, C5), 70.1 (C6), 59.8 (C6'), 48.0 (CH2 crown), 40.4 (CH2 crown), 23.3 (β-CH2 dicarboxylic chain), 20.5 (α-CH2 dicarboxylic chain).


Fig. 1S : Job plot for 1 with 1,12-diaminododecane 2 and octadecanedioic acid 5.
Fig. B. Job plot corresponding to the CIS of the methylene protons of the octadecanedioic acid chain for [3] in D$_2$O at 300K. ■ $\alpha$-methylen protons; ♦ $\beta$-methylene protons; ▲ methylene protons of the centre of alkyl chain.

Fig. 2S: 2D ROESY NMR spectrum of the pseudorotaxane 6 in D$_2$O.
Fig. 3S: 2D ROESY NMR spectrum of the pseudorotaxane 3 in D$_2$O.

Fig. 4S: 2D ROESY NMR spectrum of the [2]cryptorotaxane 8 in D$_2$O. Cross peaks between dicarboxylic chain, diphenylethylamine and CD cavities are indicated by arrows.
Fig. 5s. Zoom of 2D ROESY NMR spectra of the pseudorotaxanes in D$_2$O: a) 3 and b) 6.

Fig. 6S: 2D ROESY NMR spectrum of the [2]cryptorotaxane 4 in DMSO-δ$_d$. 
Fig. 7S: 2D ROESY NMR spectrum of the [2]cryptorotaxane 7 in DMSO-<sup>d</sup>.

References: