

Supporting Information

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

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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 ^{13}C NMR spectra (100MHz) were recorded on a Bruker DRX 400 FT-NMR spectrometer. Chemical shifts for ^1H - and ^{13}C -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 **2** (0,016g, $8.00 \cdot 10^{-5}$ mole, 1 equiv.) was added to a solution of 1,10-N,N'-Bis-[cyclomaltoheptaosyl-6A-deoxy-6A-ureido]-4,7,13,16-tetraoxa-1,10-diazacyclooctadecane **1** ($8.02 \cdot 10^{-5}$ 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, D_2O): δ_{H} 5.06 (s, H1), 4.00-3.40 (m, H3, H5, H2, H6, H6'), 2.86 (t, $\alpha\text{-CH}_2$, $J = 7.56$ Hz, $J = 15,12$ Hz), 1,58 (m, $\beta\text{-CH}_2$), 1.27 (s, CH_2 centre). ^{13}C NMR (100MHz, D_2O): δ_{C} 160.7 (NH-CO-NH), 102.3 (C_1), 81.4 (C_4), 73.6-72.3-70.6 (C_2 , C_3 , C_5), 60.4 (C_6), 39.8 (C_6'), 28.9, 27.6, 26.4, 23.6 (CH_2 chain). HR-ESIMS calcd. for $[\text{C}_{110}\text{H}_{192}\text{N}_6\text{O}_{74}]^+$, $[\mathbf{3}] = 2783.1600$, found 1392,0787 $[\mathbf{3}]^{2+}/2$.

Synthesis of [2]cryptorotaxane 4. A solution of sodium tetraphenylboron (0.06g, $6.6 \cdot 10^{-5}$ mole, 2.2 equiv.) in distilled water (3mL), was added dropwise to an aqueous solution (3mL) of pseudorotaxane **3** (0.084g, $3.0 \cdot 10^{-5}$ 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 (0.10g, 97%). ^1H NMR (400MHz, $\text{DMSO-}d_6$): δ_{H} 7.17 (s, 16H, arom.), 6.94 (t, 16H, arom.), 6.79 (t, 8H, arom.), 4.84 (s, 14H, H₁), 4.00-3.10 (m, 122H, H₂, H₃, H₄, H₅, H₆, O- CH_2 crown, N- CH_2 crown), 2.75 (t, 4H, $\alpha\text{-CH}_2$, $J = 7.52$ Hz), 1.49 (s, 4H, $\beta\text{-CH}_2$), 1.25 (s, 24H, CH_2 diaminododecane alkyl chain). ^{13}C NMR (100MHz, $\text{DMSO-}d_6$): δ_{C} 164.9, 163.9, 163.5, 163.4 (C_q arom.), 160.7 (CONH), 136.4, 126.2, 122.4 (CH arom.), 102.3 (C_1), 73.4 (C_4), 72.9 (C_2), 72.8 (C_3), 72.7 (C_5), 70.6 (C_6), 62.5 (C_6'), 29.9, 29.8, 29.7, 29.5 (CH_2 diaminododecane alkyl chain), 28.0 ($\alpha\text{-CH}_2$ diaminododecane), 26.7 ($\beta\text{-CH}_2$, diaminododecane). HR-ESIMS calcd. for $[\text{C}_{158}\text{H}_{234}\text{B}_2\text{N}_6\text{O}_{74}]^+$ $[\mathbf{4}] = 3421.4900$, found 2582.1870 $[\mathbf{4} - \text{C}_{60}\text{H}_{70}\text{B}_2\text{N}_2]^+$, 1392,0787 $[\mathbf{3}]^{2+}/2$, 319.1631 $[\text{BPh}_4]$, 202.2356 $[\text{1,12-diaminododecane}]^+$.

Synthesis of pseudorotaxane 6. Octadecanedioic disodium salt (0.019g, $6.15 \cdot 10^{-5}$ mole, 1equiv.) was added to a solution of 1,10-N,N'-Bis-[cyclomaltoheptaosyl-6A-deoxy-6A-ureido]-4,7,13,16-tetraoxa-1,10-diazacyclooctadecane **1** (0.16g, $6.15 \cdot 10^{-5}$ mole, 1equiv.) 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 (0158g, 97%). ^1H NMR (400MHz, D_2O): δ_{H} 4.96 (14H, H₁), 3.98-3.72 (m, 58H, O- CH_2 crown, H₃, H₆, H₅), 3.72-3.30 (m, 64H, H₆, H₄, H₂,

N-CH₂crown), 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_C 171.9 (COO⁻), 170.2 (COO⁻), 162.0 (NH-CO NH), 104.9 (C₁), 88.9 (C₄), 76.2, 75.4, 74.4 (C₂, C₃, C₅), 72.4 (C₆), 71.5, 69.7, 67.7 (α-CH₂, β-CH₂, CH₂ chain), 62.6 (C_{6'}), 51.0 (CH₂ crown), 43.6 (CH₂ crown), 26.2 (CH₂ chain). HR-ESIMS calcd. for [C₁₁₆H₁₉₆N₄Na₂O₇₈]⁺ [6] = 2940.7600, found 1447.0743 [6]²⁺/2; 1313.9470 [6 - C₁₈H₃₂N₂O₄]²⁺/2 + Na⁺; 337.2332 [C₁₈H₃₂O₄²⁻ + Na⁺ + 2H⁺].

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_H 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-CH₂ crown, N-CH₂ 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_C 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 (C_{6'}), 48.0 (CH₂ crown), 40.4 (CH₂ crown), 23.3 (β-CH₂ dicarboxylic chain), 20.5 (α-CH₂ dicarboxylic chain) □ HR-ESIMS calcd. for [C₁₆₄H₂₃₆N₄O₇₈P₂]⁺ [7] = 3571.4100, found 1447.0743 [7 - C₂₄H₂₀P⁺]²⁺/2, 339.1301 [C₂₄H₂₀P⁺].

Synthesis of [2]cryptorotaxane 8. 2,2-Diphenylethylammonium chloride (0.0073g, 3.7.10⁻⁵ mole, 2.2equivs.) were added to a solution of pseudorotaxane 6 (0.050g, 1.7.10⁻⁵ mole), in water (3mL). The resulting solution was stirred 1h. more at r.t. under argon, then dialyzed and lyophilized to give 8 as an amorphous white powder (0.020g, 37%). ¹H NMR (400MHz, D₂O): δ_H 7.40-7.21 (m, 10H, arom.), 5.37-5.34 (br m, 2H, NH), 5.02 (s, 14H, H₁), 4.12 (t, 2H, J = 8Hz, CH amine), 3.95-3.32 (m, complex 126H, H₂, H₃, H₄, H₅, O-CH₂ crown, N-CH₂ crown, N-CH₂ diphenylethylammonium), 2.16 (s, 4H, α-CH₂ dicarboxylic chain), 1.55 (s, 4H, β-CH₂ dicarboxylic chain), 1.36-1.08 (m, 24H, CH₂ centre dicarboxylic alkyl chain). ¹³C NMR (100MHz, D₂O): δ_C 160.3 (NCONH), 129.0, 127.6, 125.4 (CH arom.), 102.0 (C₁), 80.6 (C₄), 73.3, 72.1, 70.3 (C₂, C₃, C₅), 60.5, 59.7 (C₆, C_{6'}), 52.0 (CH diphenylethylammonium), 49.5 (CH₂ crown), 44.8 (CH₂ crown), 37.7 (α-CH₂ dicarboxylic chain), 28.6 (β-CH₂ dicarboxylic chain) 26.0 (CH₂ centre dicarboxylic alkyl chain). HR-ESIMS calcd. for [C₁₄₄H₂₂₈N₆O₇₈]⁺ [8] = 3289.4100, found 1447.0657 [6]²⁺/2, 1313.9504 [6 - C₁₈H₃₂N₂O₄]²⁺/2 + Na⁺, 337.2332 [C₁₈H₃₂O₄²⁻ + Na⁺ + 2H⁺], 198.1291 [C₁₄H₁₆N]⁺.

Fig. 1S : Job plot for 1 with 1,12-diaminododecane 2 and octadecanedioic acid 5.

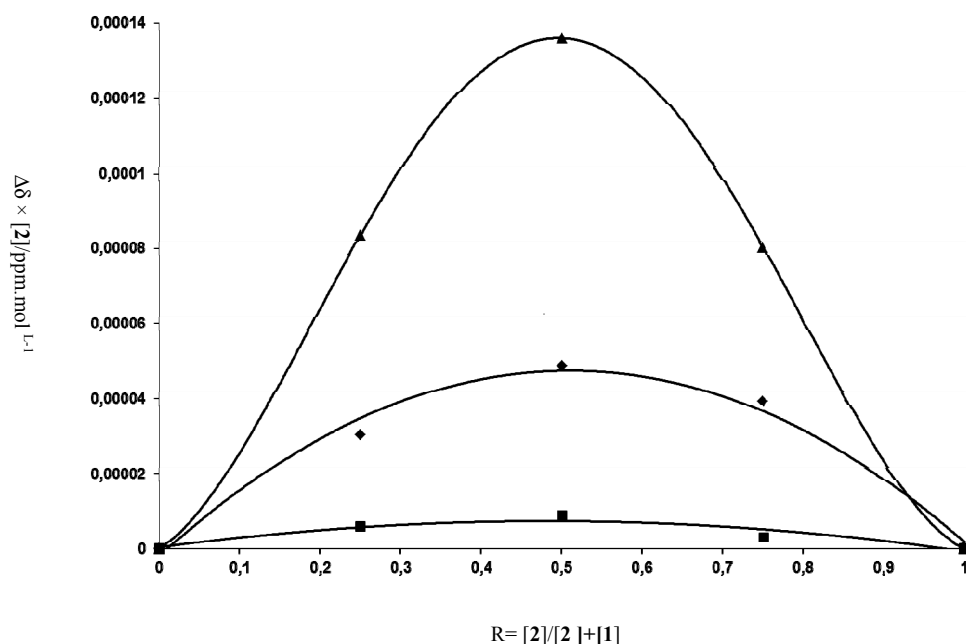


Fig. A. Job plot corresponding to the CIS of the methylene protons of the 1,12-diaminododecane chain for [1/2] in D₂O at 300K. ■ α-methylene protons; ◆ β-methylene protons; ▲ methylene protons of the centre of alkyl chain.

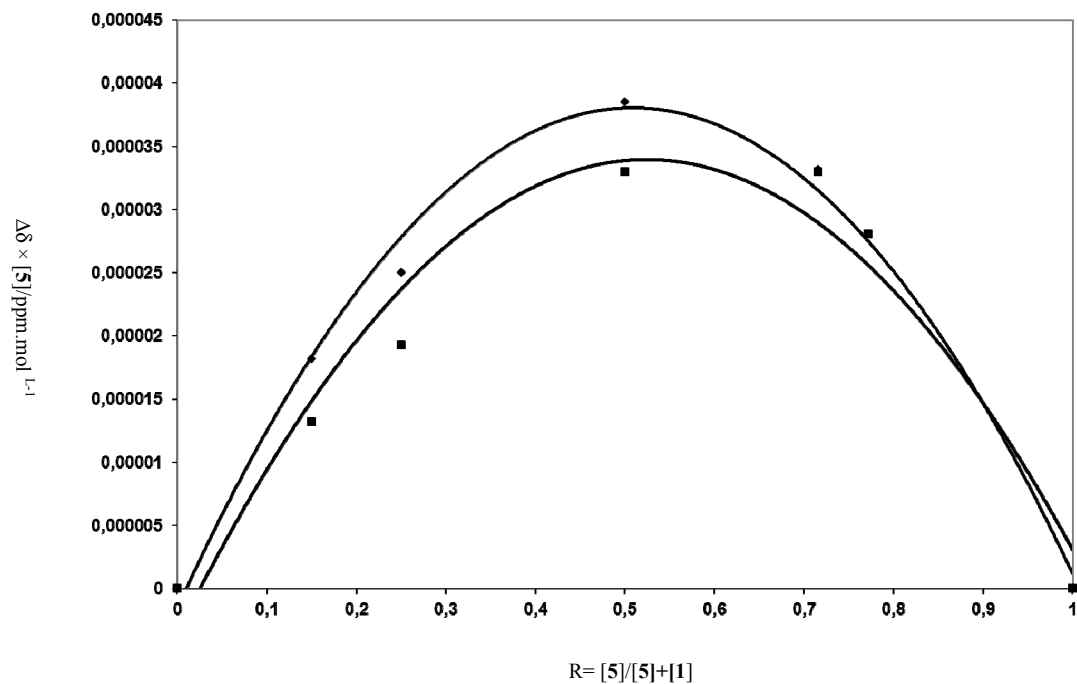


Fig. B. Job plot corresponding to the CIS of the methylene protons of the octadecanedioic acid chain for [1/5] in D_2O at 300K. ■ α -methylene protons; ◆ β -methylene protons; ▲ methylene protons of the centre of alkyl chain.

Fig. 2S: 2D ROESY NMR spectrum of the pseudorotaxane **6** in D_2O .

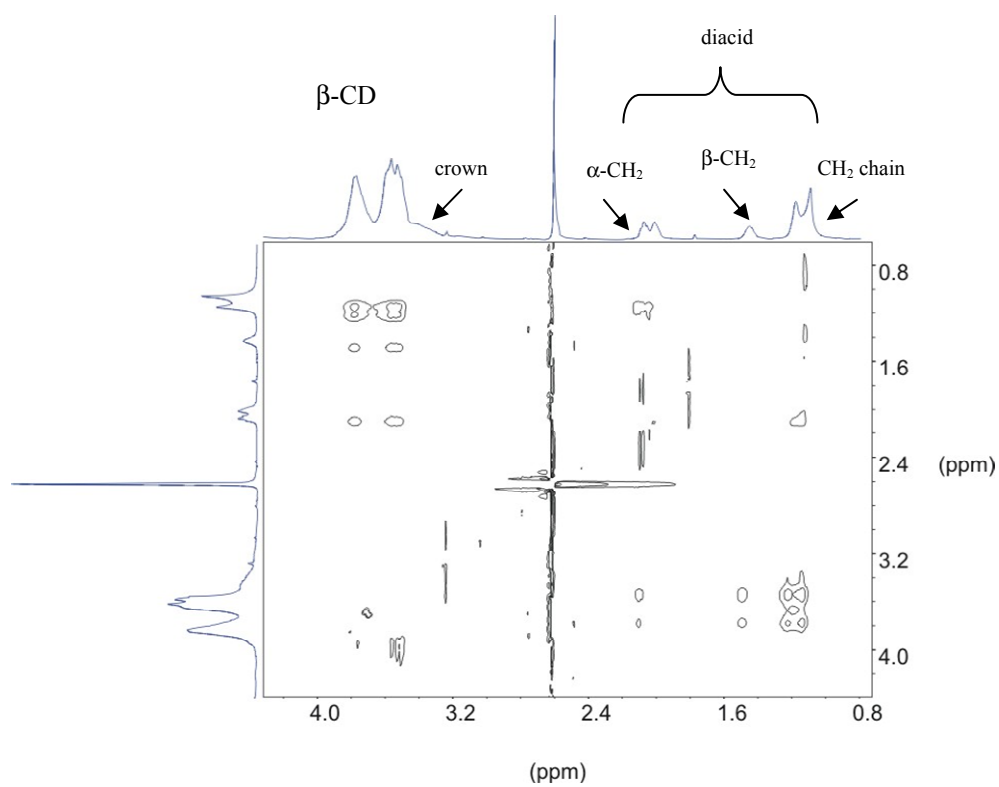


Fig. 3S: 2D ROESY NMR spectrum of the pseudorotaxane **3** in D₂O.

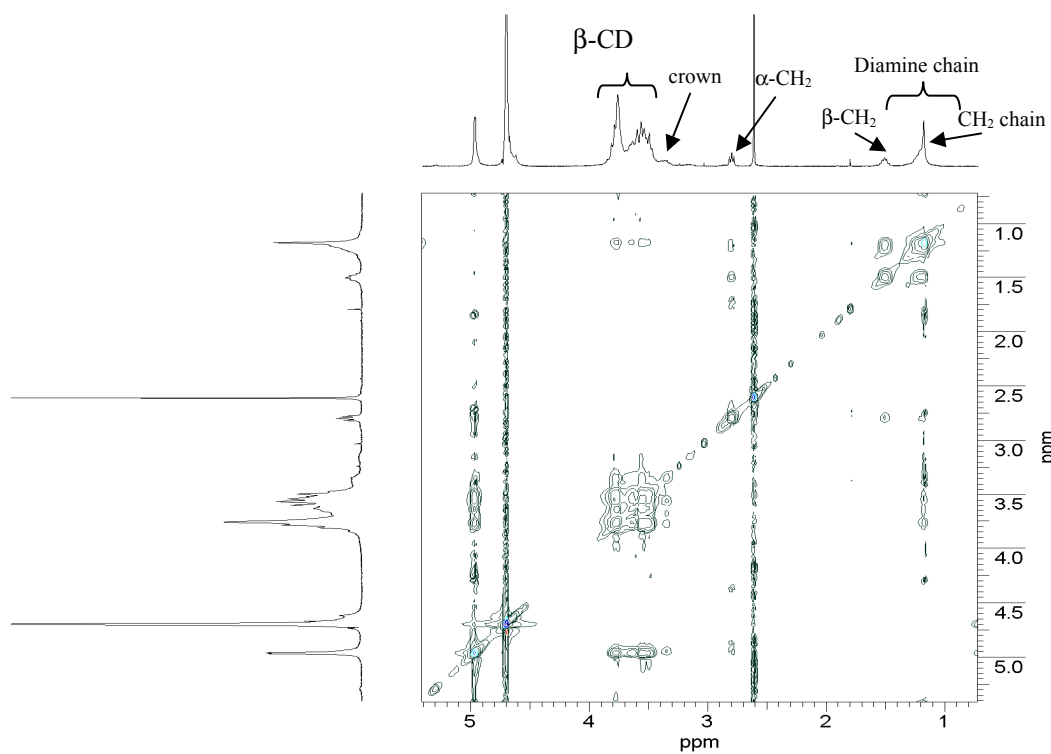


Fig. 4S: 2D ROESY NMR spectrum of the [2]cryptorotaxane **8** in D₂O. Cross peaks between dicarboxylic chain, diphenylethylamine and CD cavities are indicated by arrows.

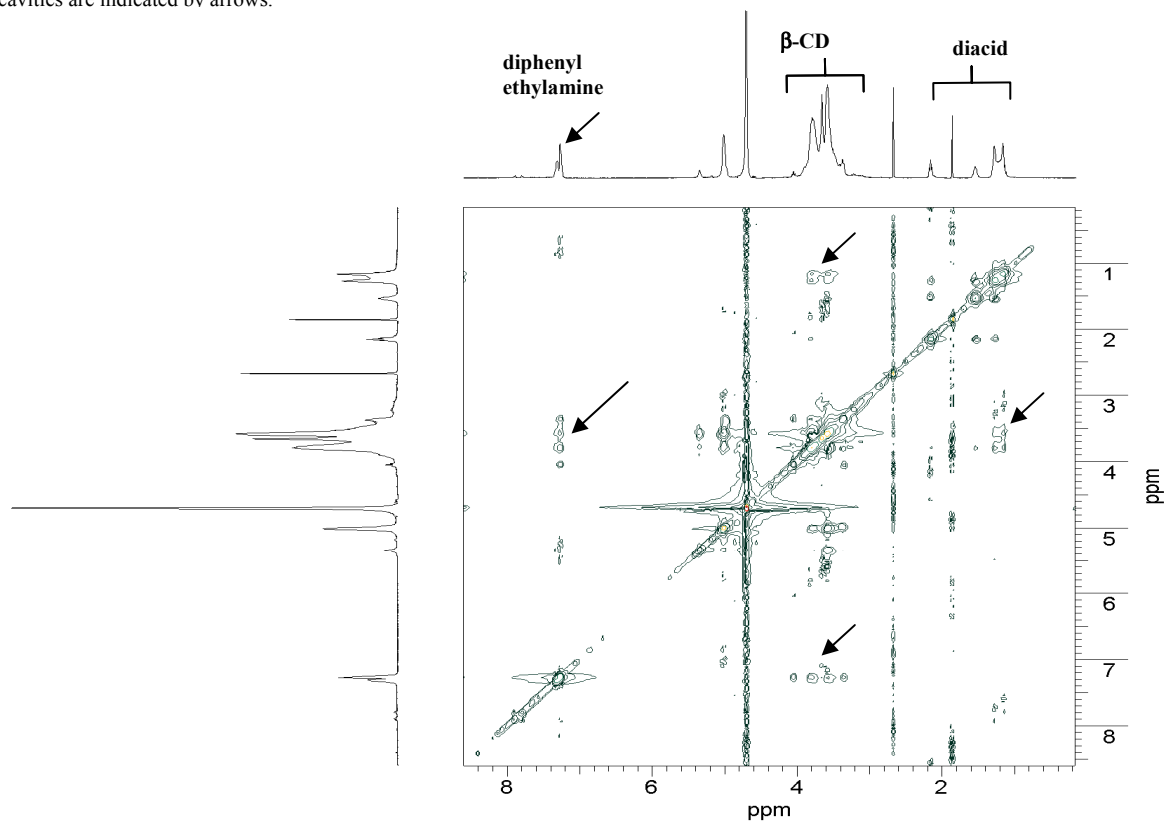


Fig. 5s. Zoom of 2D ROESY NMR spectra of the pseudorotaxanes in D₂O: a) **3** and b) **6**.

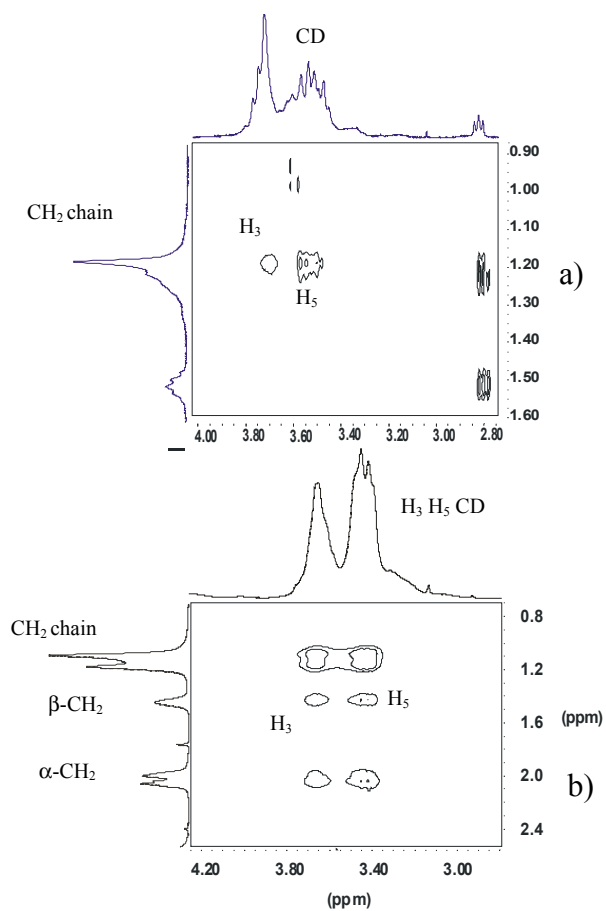


Fig. 6S: 2D ROESY NMR spectrum of the [2]cryptorotaxane **4** in DMSO-⁶d.

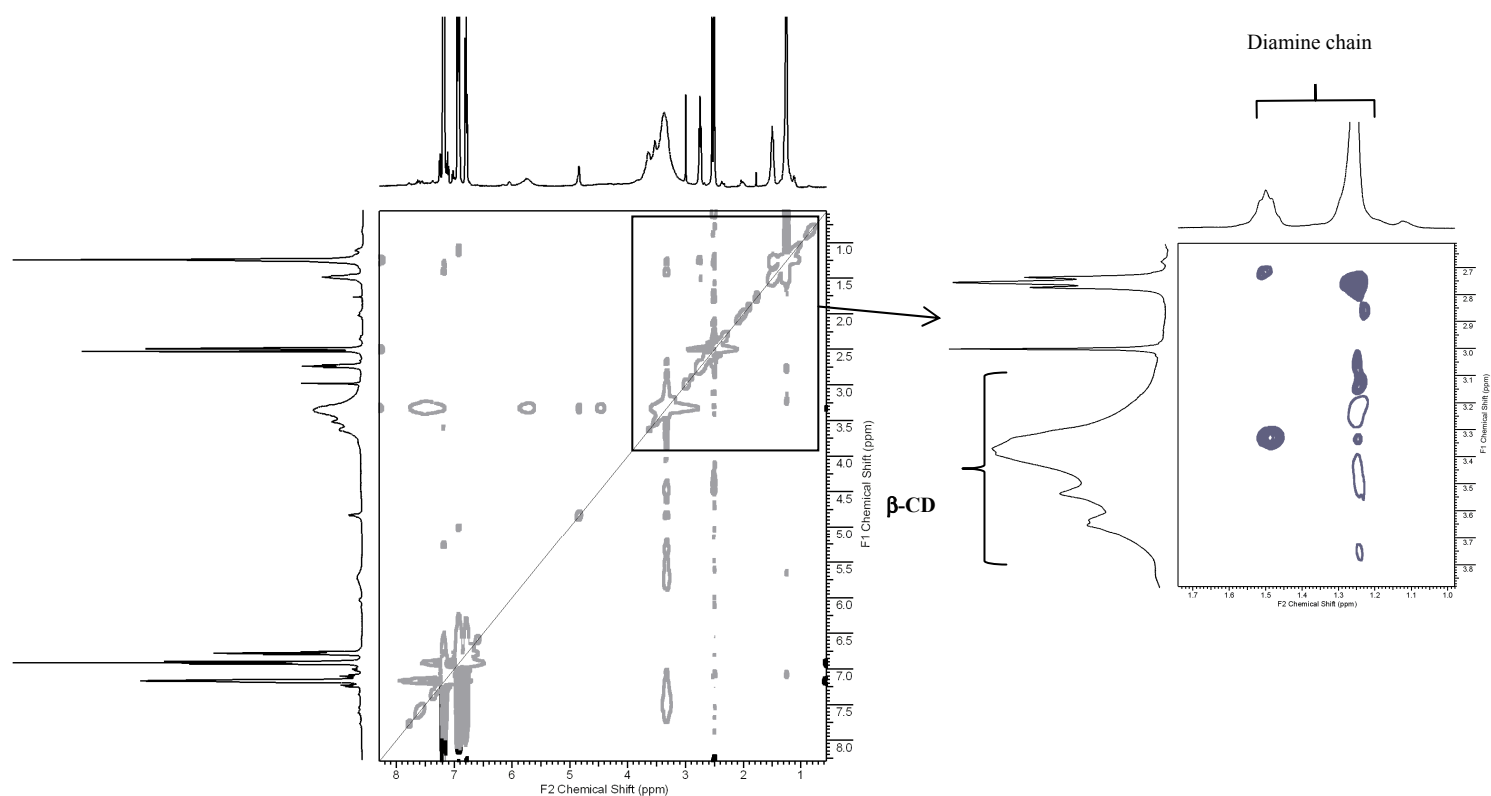
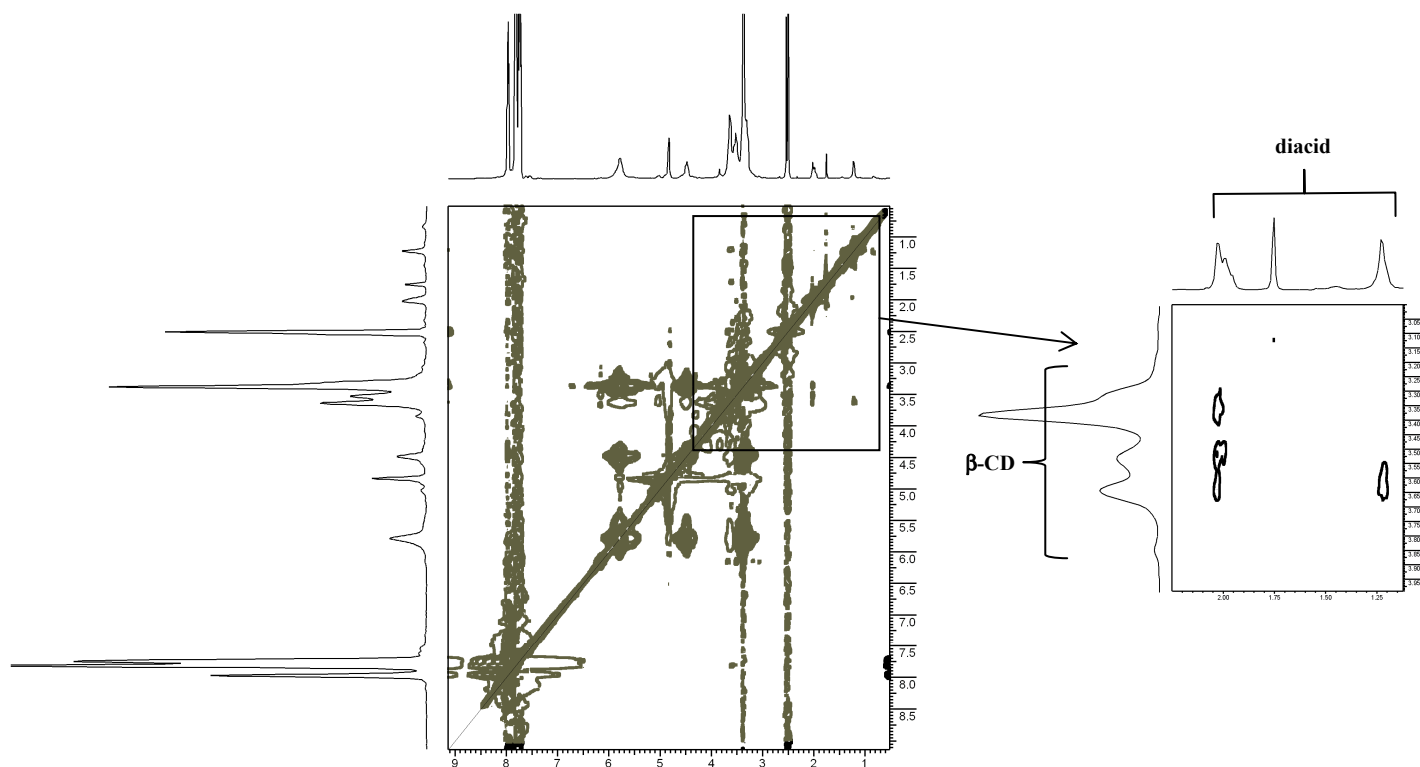


Fig.7S : 2D ROESY NMR spectrum of the [2]cryptorotaxane **7** in DMSO- d_6 .



References :

- (1). S. Manuel, J.-P. Joly, B. Courcot, J. Elysée, N.-E. Ghermani, and Alain Marsura, *Tetrahedron*, 2007, **63**, 1706-1714