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Supporting Information

69451 Weinheim, Germany

Sequence-specific DNA Binding by Non-covalent Peptide-Tripyrrol Conjugates

Juan B. Blanco, Verónica I. Dodero, M. Eugenio Vázquez, Manuel Mosquera, Luis Castedo, and José L. Mascareñas*

Fax (+34) 981 595012

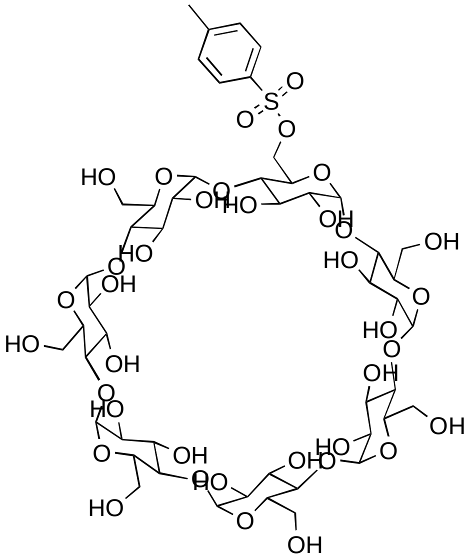
E-mail: qojoselm@usc.es

Peptide synthesis was performed using standard Fmoc-solid phase methods on a Rink-MBHA amide resin (~0.62 mmol/g), using mixtures of HBTU/HOBt as coupling agents, DIEA as base and DMF as solvent. The cleavage/deprotection step was performed by treatment of the resin-bound peptide with the following mixture: 940 μL TFA, 25 μL EDT, 25 μL H_2O and 10 μL triisopropylsilane (1 mL of this mixture for each 40 mg of resin).

CD measurements were made in a 2 mm-cell at 4ºC. Samples contained 10 mM phosphate buffer (pH 7.5), 100 mM NaCl, 5 μM peptide and 5 μM ds-oligo when present. The peptide-DNA mixtures were incubated for 5 min before registering. The spectra are the average of 5 scans and were processed using the “smooth” macro implemented in the program *Kaleidagraph* (v 3.5 by Synergy Software). Spectra of the peptides in the presence of DNA were calculated as the difference between the spectra of the peptide-DNA mixture and the spectrum of free DNA.

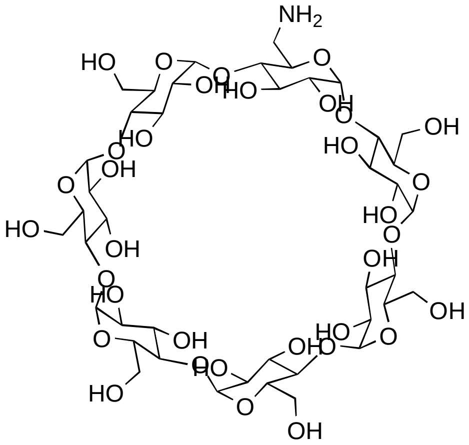
For **gel mobility shift assays**, binding reactions were performed over 30 min in a binding mixture (20 or 40 μL) containing 18 mM Tris (pH 7.5), 90 mM KCl, 1.8 mM $MgCl_2$, 1.8 mM EDTA, 9% glycerol, 0.11 mg/mL BSA and 2.2% NP-40. In the experiments analyzed by fluorescent revealing with SyBrGold we used 30 nM of the unlabeled dsDNAs and a total incubation volume of 40 μL. In the experiments with ^{32}P-labelled DNAs we used ~45 pM of labeled dsDNAs and 100 nM of unlabeled dsDNAs in a 20 μL binding mixture. Products were resolved by PAGE using a 10% nondenaturing poliacrylamide gel and 0.5XTBE buffer, and analyzed by autoradiography (when radioactivity was used) or by staining with SyBrGold (Molecular Probes: 5 μL in 50 mL of 1XTBE) for 10 min and visualized with fluorescence.

Synthesis of bCD-OTs.[12]



A solution of aqueous NaOH (1.84 mL, 15.1 mmol, 8.2 M) was added to a suspension of βCD (5 g, 4.4 mmol) in H_2O (42 mL). This mixture was stirred for 30 min and other solution of TsCl (809 mg, 4.3 mmol) in CH_3CN (2.5 mL) was added. The mixture was shaken for 2 hours at room temperature, filtered and refrigerated at 4ºC. The precipitated was filtered and the solid was dried to vacuum over P_2O_5 to give a white solid that was confirmed as the monotosylated βCD (567 mg, 10%). MS (MALDI-TOF, M+H+Na): calcd. for $C_{49}H_{77}O_{37}SNa$ 1312.4, found 1312.2.

Synthesis of bCD-NH_2.[12]



KI (16 mg, 0.097 mmol) and NaN_3 (124 mg, 1.90 mmol) were added to a solution of βCD-OTs (250 mg, 0.194 mmol) in DMF (1 mL). The mixture was stirred at 60ºC for 20 h and then treated with amberlite IR-40 (200 mg) for 30 min. The resin removed by filtration and the solution was diluted in acetone (20 mL) appearing a precipitated that was filtered to gravity. The isolated solid was dried and used in the next step without further purification.

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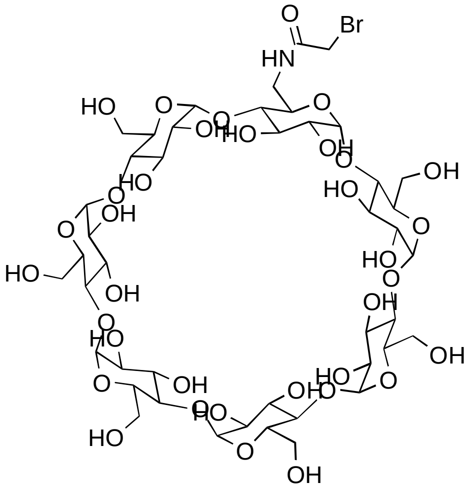
[12] Petter, R. C.; Salek, J. S.; Sikorski, T. C.; Kumaravel, G.; Lin, F-T. *J. Am. Chem. Soc.* **1990**, *112*, 3860.

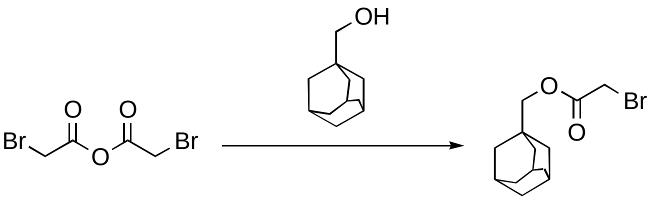
A solution of the above azide (150 mg, 0.129 mmol) in H_2O (45 mL) was hydrogenated over Pd/C (50 mg, 10%) for 12 h at room temperature (balloon pressure). The catalyst was filtered over celite and lyophilized to obtain a white solid identified as the desired βCD-NH_2. MS ((MALDI-TOF, M+H): calcd. for $C_{42}H_{72}NO_{34}$ 1134.4, found 1135.3, (M+H+Na): calcd. 1156.4, found 1157.4.

Synthesis of the bromoacetyl derivative of bCD-NH_2.



To a solution of bromoacetic acid (14.7 mg, 0.106 mmol) in DMF (0.53 mL) were added HBTU (40.2 mg, 0.106 mmol), HOBt (14.3 mg, 0.106 mmol) and a solution of DIEA (37 µL, 0.212 mmol, 0.2 M in DMF). The mixture was stirred for 3 min and added over a solution of βCD-NH_2 (30 mg, 0.0265 mmol) in DMF (1 mL). The mixture was stirred for 2 h and diluted with acetone (30 mL) to induce the precipitation of a white solid that was filtered to gravity. The residue was dried and identified by MS as the desired product (βCD-$NHCOCH_2Br$) (30 mg, 91%). MS (MALDI-TOF, M+H): calcd. for $C_{44}H_{73}BrNO_{35}$ 1238.3, found 1238.9, (M+H+Na): calcd. 1277.3, found 1276.3.

Synthesis of o-(bromoacetyl)-1-hydroximethyladamantane.

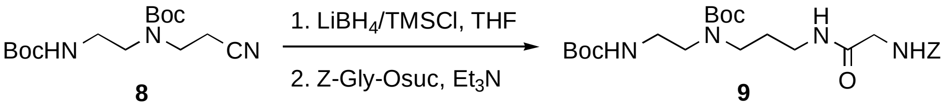


1-hydroximethyladamantane (382 mg, 2.3 mmol) was added to a solution of bromoacetic anhydride (598 mg, 2.3 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 2 h at room temperature, poured into an aqueous solution of $NaHCO_3$ (20 mL, 5%) and extracted with CH_2Cl_2 (2x20 mL). The combined organic phases were collected and dried over Na_2SO_4, and the solvents evaporated. The residue was purified by flash column chromatography on silica gel (40% EtOAc/hexane) to afford the desired compound as a colorless oil (597 mg, 90%). ^{1}H-NMR δ ($CDCl_3$): 1.51 (broad s, 6H), 1.59-1.72 (m, 6H), 1.95 (broad s, 3H), 3.73 (s, 2H), 3.82 (s, 2H). ^{13}C-NMR δ ($CDCl_3$): 25.8 (CH_2), 27.8 (CH), 33.2 (C), 36.7 (CH_2), 38.9 (CH_2), 75.4 (CH_2), 167.2 (C). MS_(CI+): *m/z* 287 (3), 149 (100). HRMS: calcd. for $C_{13}H_{20}BrO_2$ 287.0647, found 287.0471.

Synthesis of the adamantyl derivative 4.

8

Acrylonitrile (0.891 mL, 13.5 mmol) was added to an ice-water cooled solution of *tert*-butyl-2-aminoethylcarbamate (1.9 g, 12.3 mmol) in EtOH (30 mL). The mixture was stirred for 12 h at rt, the solvent evaporated and the residue redissolved in CH_2Cl_2 (30 mL). To the resulting solution was added Et_3N (2.55 mL, 18.4 mmol) and Boc_2O (3.23 g, 14.8 mmol). The reaction mixture was allowed to stir for 0.5 h, poured into aqueous HCl (20 mL, 3%) and extracted with CH_2Cl_2 (2x30 mL). The organic fractions were collected, dried over Na_2SO_4 and concentrated under vacuum to afford a white solid that was used in the next step without purification (3.6 g, 94%). ^{1}H-NMR δ ($CDCl_3$): 1.40 (s, 9H), 1.45 (s, 9H), 2.56-2.63 (m, 2H), 3.20-3.27 (m, 2H), 3.36 (m, 2H), 3.47 (t, *J*= 6.7 Hz, 2H), 4.76-4.94 (2 s, 1H). ^{13}C-NMR δ ($CDCl_3$): 16.8 (CH_2), 17.4 (CH_2), 28.2 (CH_3), 28.3 (CH_3), 39.2 (CH_2), 44.2 (CH_2), 47.0 (CH_2), 48.0 (CH_2), 79.4 (C), 80.9 (C), 117.7 (C), 118.2 (C), 155.1 (C), 155.8 (C). MS (CI+): *m/z* 314 (27), 258 (48), 202 (84), 158 (100), 114 (74). HRMS: calcd. for $C_{15}H_{28}N_3O_4$ 314.2080, found 314.2078.

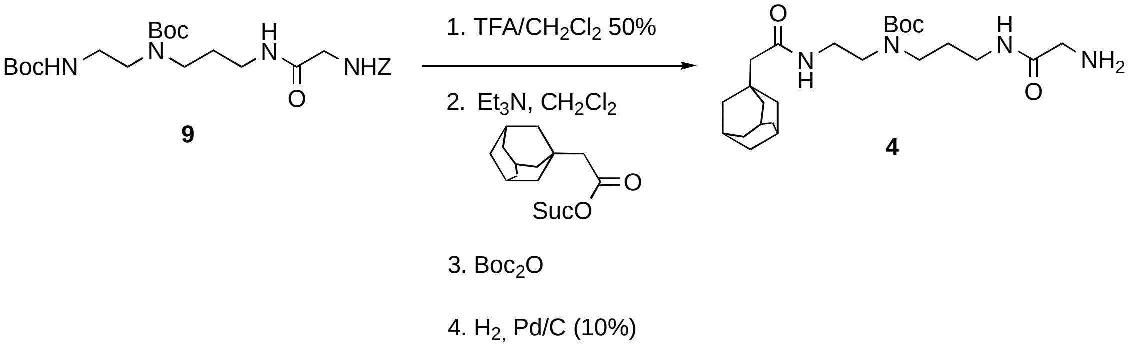


8 **9**

TMSCl (2.11 mL, 16.6 mmol) was slowly added to a suspension of $LiBH_4$ (0.181 g, 8.3 mmol) in THF (15 mL). The mixture was stirred at room temperature for 45 min and cooled in a ice-water bath. Over this suspension, a solution of the above nitrile (1.3 g, 4.15 mmol) in THF (5 mL) was added and after 12 h stirring at room temperature, the reaction was quenched by slow addition of MeOH. Solvents were removed under vacuum and the residue was poured in a aqueous solution of KOH (10 mL, 10%). The resulting suspension was extracted with CH_2Cl_2 (4x40 mL) and the organic phases were collected, dried over Na_2SO_4 and concentrated to afford a oily residue (676 mg, 51%) which was submitted to the next step without further purification.

Et_3N (0.591 mL, 4.26 mmol) and benzyloxycarbonylglycine succinic ester (782 mg, 2.56 mmol) were added to a solution of the above amine (676 mg, 2.13 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 1 h, poured into aqueous HCl (20 mL, 3%) and extracted with CH_2Cl_2 (2x20 mL). The organic phases were collected, dried over Na_2SO_4

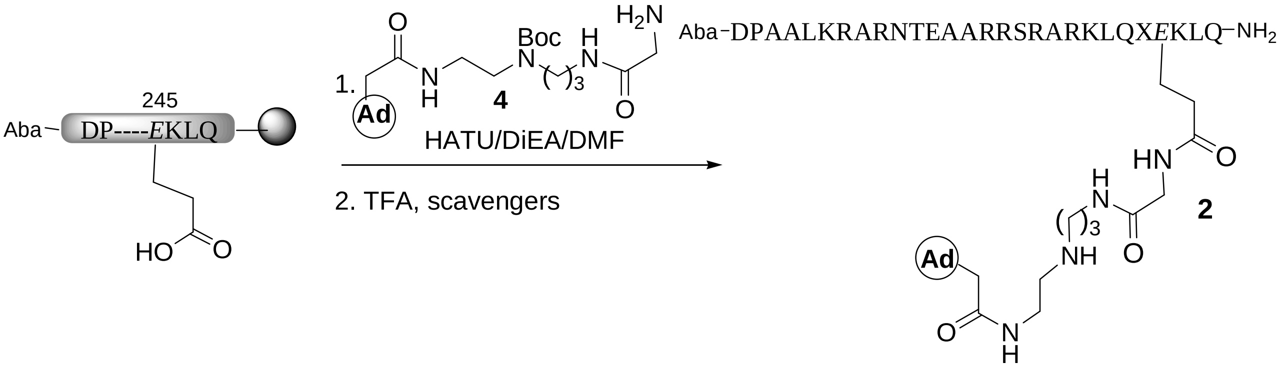
and concentrated. The residue was purified by flash column chromatography on silica gel (5% MeOH/CH_2Cl_2) to afford the desired product **9** (960 mg, 89%).



TFA (3 mL) was added to a solution of compound **9** (960 mg, 1.9 mmol) in CH_2Cl_2 (3 mL) cooled in a ice-water bath. The solution was stirred for 15 min in the bath and then other 2 h at room temperature. Solvents were evaporated and the residual TFA was removed by codestillation with CH_2Cl_2. The residue was redissolved in CH_2Cl_2 (20 mL) and Et_3N (0.626 mL, 4.51 mmol) and admantylacetate succinic ester (393 mg, 1.35 mmol) were added. After stirring for 2 h Boc_2O (394 mg, 1.8 mmol) was added and the reaction was allowed to stir for another 1 h. The solution was poured into aqueous HCl (20 mL, 3%) and extracted with CH_2Cl_2 (2x20 mL). The organic phases were collected, dried and concentrated. The residue was purified by flash column chromatography on silica gel (5% MeOH/CH_2Cl_2) and submitted to the next step.

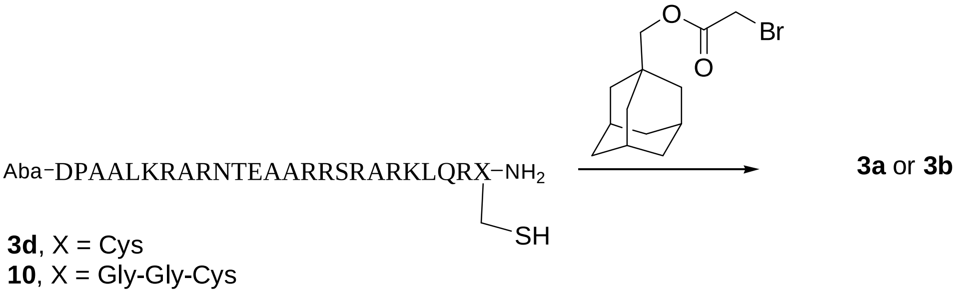
The solid was dissolved in MeOH (30 mL) and hydrogenated (H_2) over Pd/C (150 mg, 10%, balloon presure) at room temperature for 2 h. The suspension was filtered through celite and the filtered was concentrated to afford a white solid whose spectroscopic data matched the desired amine-adamantyl derivate **4** (135 mg, 33% from **9**). ^{1}H-NMR δ ($CDCl_3$): 1.23 (m, 3H), 1.41-1.44 (m, 11H), 1.57-1.70 (m, 10H), 1.88-1.93 (m, 4H), 3.24-3.45 (m, 10H). ^{13}C-NMR δ ($CDCl_3$): 25.2 (CH_2), 28.2 (CH_3), 28.4 (CH_3), 29.5 (CH_2), 32.5 (C), 36.5 (CH_2), 39.2 (CH_2), 42.4 (CH_2), 43.1 (CH_2), 45.4 (CH_2), 51.4 (CH_2), 80.0 (C), 155.8 (C), 171.5 (C), 175.8 (C). MS (FAB+): *m/z* 451 (44), 351 (100). HRMS: calcd. for $C_{24}H_{42}N_4O_4$ 450.3206, found 450.2242.

Coupling of the adamantyl derivate 4 to the peptide. Synthesis of 2.



The resin-bound peptide[8a(main manuscript)] (25 mg, ~$3.5x10^{-3}$ mmol, Eppendorf tube) was suspended in DMF (1 mL) and the mixture was shaken for 1 h to ensure a good resin swelling. The DMF was removed and a solution of HATU in DMF (2.66 mg in 170 μL, $7.0x10^{-3}$ mmol, 2 equiv) and DIEA (35 μL, 0.5 M en DMF, $1.75x10^{-2}$ mmol, 5 equiv) were added. The resulting mixture was shaked for 5 min and the resin washed with DMF (3x0.6 mL). A solution of the adamantyl derivate **4** (7.9 mg in 70 μL of DMF, $1.75x10^{-2}$ mmol, 5 equiv) and DIEA (35 μL, 0.5 M in DMF) were added. The reaction mixture was shaken for 2 h, and the resin washed with DMF (3x0.6 mL, for 5 min), and Et_2O (2x0.5 mL). Cleavage/deprotection of the bound peptide under standard conditions afforded a major product that was purified by RP-HPLC (Merck 300 column at a flow rate of 1 $mLmin^{-1}$, 270 nm, gradient 10->35% B ½ h, A: H_2O 0.1% TFA, B: CH_3CN 0.1% TFA, R_t=29.0 min) and identified as the desired adamantyl-containing peptide **2** (~23%, also considering peptide synthesis). MS: MALDI-TOF (M+H): calcd. for calcd. for $C_{135}H_{231}N_{48}O_{36}$ 3100.8, found 3101.0. UV(H_2O) λ_{max} (ε) 270 nm= 18069 $M^{-1}cm^{-1}$.

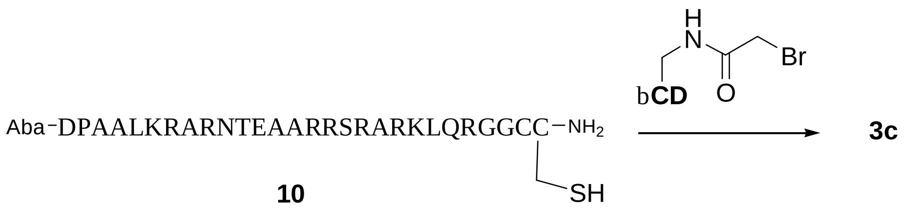
Alkylation of peptides 3d and 10 with o-(bromoacetyl)-1-hydroximethyladamantane. Synthesis of 3a and 3b.



A solution of o-(bromoacetyl)-1-hydroximethyladamantane (9 μL, 0.79 mg, $2.8x10^{-3}$ mmol) in CH_3CN was added to desoxygenated solution of the peptide **3a** (2 mg, $6.9x10^{-4}$ mmol) in buffer phosphate (150 μL, 100 mM, pH= 8.0) and CH_3CN (50 μL). The mixture was stirred at room temperature for 1 h and the reaction monitored by HPLC. A new compound was collected and its mass registered by MALDI-TOF corresponding to the desired alkylated peptide **3a** (1.6 mg, 76%, Merck 300 column at a flow rate of 1 mLmin^{-1}, 270 nm, gradient 5->75% B ½ h, A: H_2O 0.1% TFA, B: CH_3CN 0.1% TFA, R_t=18.0 min). MALDI-TOF: calcd. for $C_{133}H_{227}N_{48}O_{36}S$ 3104.7, found 3104.5. UV(H_2O) λ_{max} (ε) 270 nm= 18069 $M^{-1}cm^{-1}$.

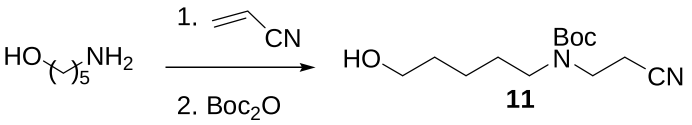
The same procedure was used to synthesize **3b** (0.9 mg, 53%): Merck 300 column at a flow rate of 1 mLmin^{-1}, 270 nm, gradient 5->75% B ½ h, A: H_2O 0.1% TFA, B: CH_3CN 0.1% TFA, R_t=18.0 min). MALDI-TOF: calcd. for $C_{137}H_{233}N_{50}O_{38}S$ 3218.8, found 3218.6. UV(H_2O) λ_{max} (ε) 270 nm= 18069 $M^{-1}cm^{-1}$.

Alkylation of peptide 10 with bromoacetic acid. Synthesis of 3c.



A desoxygenated solution of the **10** (1 mg, 3.3x10^{-4} mmol) and b**CD-NHCOCH$_2$Br** (1.6 mg, 1.28x10^{-3} mmol, ~4 equiv) in buffer phosphate (100 μL, 100 mM, pH= 8.0) was stirred at room temperature for 4 h under Ar atmosphere. The majoritary product was collected and lyophilized and proved by MS to be the alkylated peptide **3c** (1.0 mg, 71%). HPLC conditions: Merck 300 column at a flow rate of 1 mLmin^{-1}, 270 nm, gradient 5->75% B ½ h, A: H_2O 0.1% TFA, B: CH_3CN 0.1% TFA, R_t=12.2 min). MS (MALDI-TOF): calcd. for $C_{168}H_{286}N_{51}O_{71}S$ 4186.0, found 4186.0. UV(H_2O) $\lambda_{máx}$ (ε) 270 nm= 18069 $M^{-1}cm^{-1}$.

Synthesis of the yodo derivative 6.[8d]



Acrylonitrile (6.38 mL, 96.9 mmol) was added dropwise to an ice-cooled solution of 5-aminopentanol (10 g, 96.9 mmol) in EtOH (100 mL). The mixture was allowed to reach room temperature and stirred overnight. The solvent were removed under reduced pressure and the residue was redissolved in CH_2Cl_2 (100 mL). Et_3N (27 mL, 0.194 mol) and Boc_2O (21.1 g, 96.9 mmol) were added and the mixture stirred at room temperature. After 1 h the mixture was poured into aqueous HCl (60 mL, 3%) and extracted with CH_2Cl_2 (2x60 mL). The organic layers were collected, dried over Na_2SO_4 and concentrated under vacuo. The resulting oily residue was observed by NMR to consist

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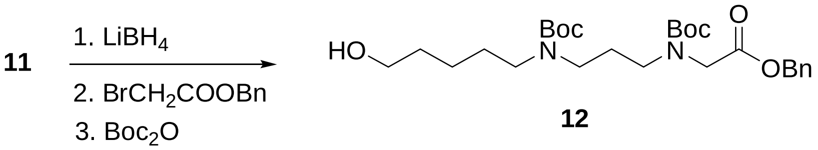
[8d] Blanco, J. B.; Vázquez, M. E.; Castedo, L.; Mascareñas, J. L. *ChemBioChem* **2005**, *6*, 2173.

majoritarily of the desired addition product **11**, and was used in the next step without further purification. ^{1}H-NMR ($CDCl_3$): 1.23-1.32 (m, 2H), 1.38 (s, 9H), 1.44-1.52 (m, 4H), 2.52 (br s, 2H), 3.17 (t, *J*= 7.3 Hz, 2H), 3.37 (t, *J*= 6.7 Hz, 2H), 3.52 (t, *J*= 6.4 Hz, 2H). ^{13}C NMR (62.89 MHz, $CDCl_3$, 25^{o}C, TMS): *d* 16.7 (CH_2), 17.2 (CH_2), 22.7 (CH_2), 27.7 (CH_2), 28.1 (CH_3), 28.3 (CH_2), 31.9 (CH_2), 43.1 (CH_2), 43.6 (CH_2), 47.3 (CH_2), 48.2 (CH_2), 62.0 (CH_2), 80.0 (C), 80.3 (C), 117.8 (C), 118.2 (C), 154.6 (C), 155.1 (C). MS (CI+): *m/z* 257 (1), 201 (26), 184 (53), 157 (100), 139 (36), 116 (72). HRMS: calcd for $C_{13}H_{25}N_2O_3$ 257.1865, found 257.1876.

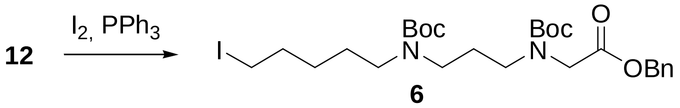


TMSCl (43.5 mL, 0.343 mol) was slowly added to a suspension of $LiBH_4$ (3.66 g, 0.168 mol) in THF (50 mL). The solution was stirred at room temperature for 45 min and cooled in an ice-water bath. A solution of the above nitrile **11** (24.8 g, 96.9 mmol) in THF (50 mL) was added dropwise to this mixture. After 12 h the reaction mixture was cooled again and quenched by the slow addition of MeOH. Solvents were partially removed under vacuo and the residue was poured into aqueous KOH (30 mL, 10%). The resulting suspension was extracted with CH_2Cl_2 (4x40 mL), and the organic layers were dried and concentrated to give a residue (20.3 g, 81%) which was submitted to the next step without further purification.

To a solution of the resulting amine (1.7 g, 6.5 mmol) in dry CH_3CN (50 mL) was added K_2CO_3 (3.5 g) and the suspension was cooled in a ice-water bath. Benzyl bromoacetate (1.3 g, 5.77 mmol) was added and the mixture was stirred for 12 h and allowed to reach room temperature. Solvents were partially removed and the solution was poured into H_2O (20 mL) and extracted with CH_2Cl_2 (3x20 mL). Organic phases were collected, dried over Na_2SO_4, concentrated in a rotary-evaporator and the residue was purified by silica gel column chromatography (10% MeOH/CH_2Cl_2).

The crude product was dissolved in CH_2Cl_2 (20 mL), and Et_3N (2.71 mL, 19.5 mmol) and Boc_2O (2.84 g, 13 mmol) were added. The mixture was stirred for 1 h, poured into aqueous HCl (20 mL, 3%) and extracted with CH_2Cl_2 (2x20 mL). The organic phases were collected, dried and concentrated and the product purified by silica gel column chromatography (5% MeOH/CH_2Cl_2) and identified as the title alcohol **12** (1.68 g, 51%, viscous oil). ^{1}H-NMR δ ($CDCl_3$): 1.19 (m, 4H), 1.28-1.31 (2s, 18H), 1.36-1.60 (m, 4H), 2.11 (s, 1H), 2.87-3.16 (m, 6H), 3.45 (t, *J*= 6.45 Hz, 2H), 3.75-3.84 (2s, 2H), 5.0 (s, 2H), 7.19 (s, 5H). ^{13}C-NMR δ ($CDCl_3$): *d* 22.8 (CH_2), 28.0 (CH_3), 28.3 (CH_3), 32.2 (CH_2), 44.6 (CH_2), 46.1 (CH_2), 46.4 (CH_2), 46.7 (CH_2), 48.9 (CH_2), 49.4 (CH_2), 62.3 (CH_2), 66.6 (CH_2), 79.1 (C), 80.2 (C), 128.1 (CH), 128.2 (CH), 128.4 (CH), 135.3 (C), 155.0 (C), 155.5 (C), 169.8 (C). MS (FAB+, M+H): *m/z* 509 (35), 409 (100), 353 (97), 309 (69). HRMS: calcd. For $C_{27}H_{44}N_2O_7$ 508.3149, found 508.3134.

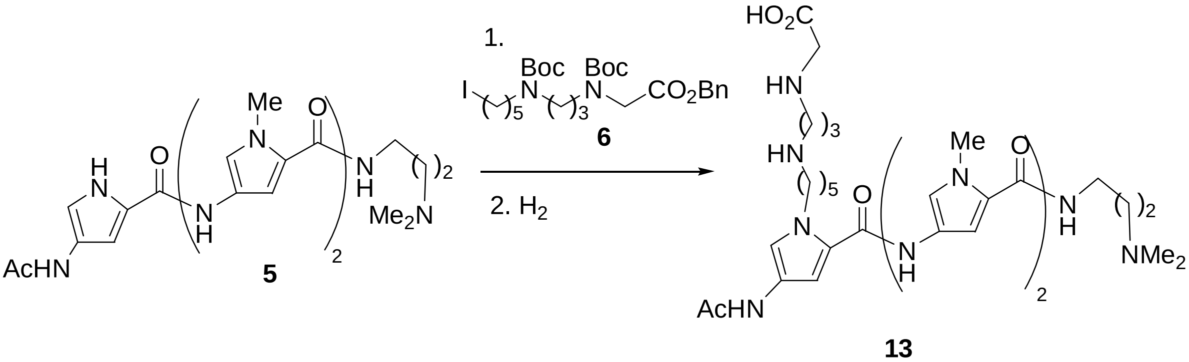
Di-*tert*-butoxycarbonyl derivative of benzyl 2-(3-(5-hydroxypentylamino) propylamino)acetate (**6**)



6

I_2 (840 mg, 3.31 mmol) was added to a solution of Ph_3P (955 mg, 3.64 mmol), imidazol (337 mg, 4.96 mmol) and the above alcohol **12** (1.68 g, 3.31 mmol) in CH_2Cl_2 (40 mL). After 10 min at room temperature the mixture was poured into an aqueous solution of sodium bisulfite (20 mL, 5%) and extracted with CH_2Cl_2 (2x20 mL). The organic layers were collected, dried and concentrated and the residue chromatographied in EtOAc/Hexane to give the iodide **6** as an oily liquid (1.94 g, 95%). ^{1}H-NMR δ ($CDCl_3$): 1.20 (m, 4H), 1.29-1.32 (2s, 18H), 1.50-1.72 (m, 4H), 2.98-3.14 (m, 8H), 3.76-3.85 (2s, 2H), 5.01 (s, 2H), 7.19 (s, 5H). ^{13}C-NMR δ ($CDCl_3$): 6.57 (CH_2), 27.4 (CH_2), 27.8 (CH_3), 28.2 (CH_3), 32.8 (CH_2), 44.4 (CH_2), 45.9 (CH_2), 46.4 (CH_2), 48.8 (CH_2), 49.2 (CH_2), 66.4 (CH_2), 78.8 (C), 79.9 (C), 127.8 (CH), 128.0 (CH), 128.2 (CH), 135.2 (C), 154.7 (C), 155.1 (C), 169.6 (C). MS (FAB+, M+H): *m/z* 619 (49), 519 (61), 419 (40). HRMS: calcd. for $C_{27}H_{43}IN_2O_6$ 618.2166, found 618.2135.

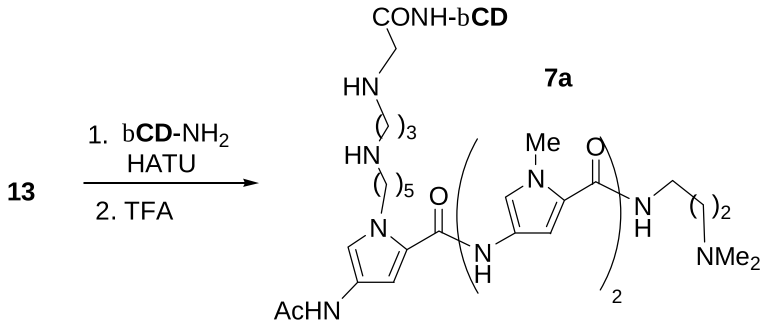
Synthesis of the tripirrole 13.



K_2CO_3 (300 mg) and iodide **6** (500 mg, 0.8 mmol) were added to a solution of tripyrrole **5**^{8d} (100 mg, 0.2 mmol) in dry acetone (6 mL). The reaction mixture was refluxed for 8 h and the resulting suspension was filtered through celite. The filtrate was concentrated and the residue purified by RP-HPLC (Scharlau 120 column at a flow rate of 4 mLmin^{-1}, 304 nm, gradient 5->95% B ½ h, A: H_2O 0.1% TFA, B: CH_3CN 0.1% TFA, R_t=24.5 min) to afford the expected alkylated tripyrrole as a pale-yellow solid (167 mg, 84%).

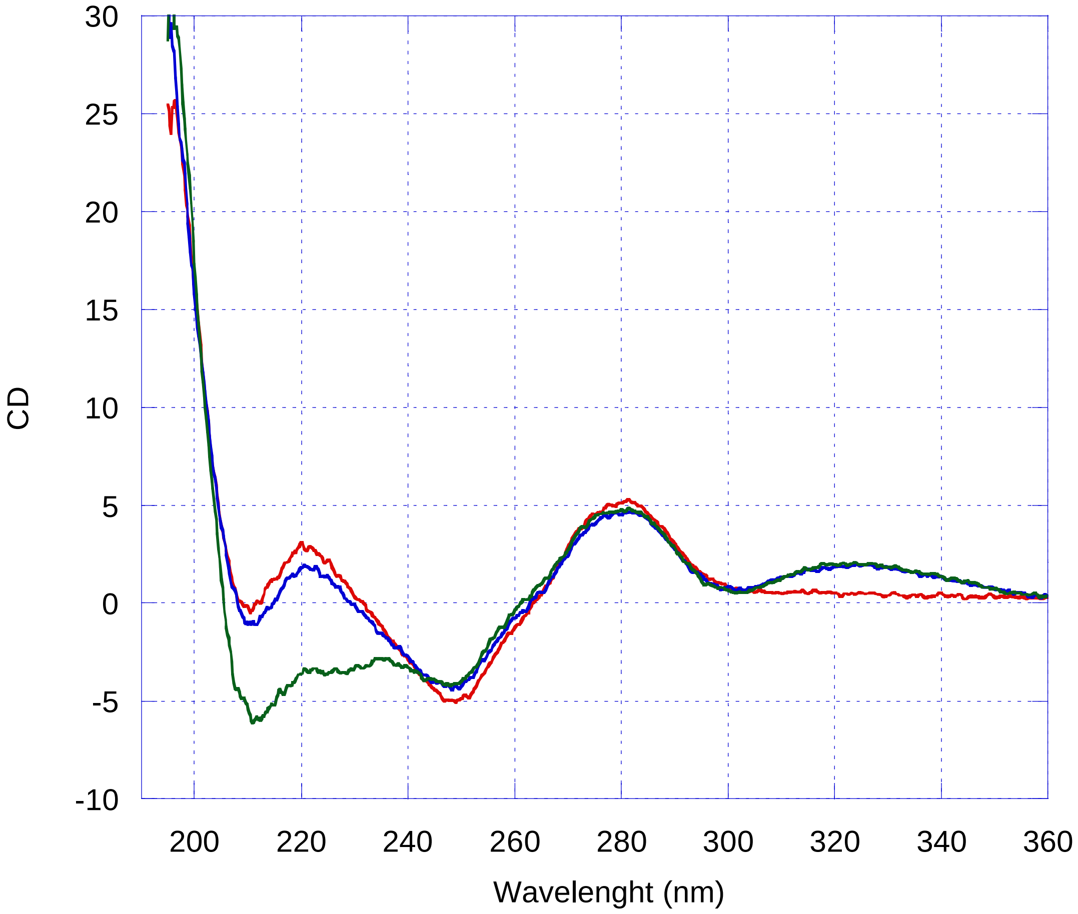
A solution of this tripyrrole (160 mg, 0.16 mmol) in MeOH (10 mL) was hydrogenated over 10% palladium on charcoal (130 mg) at room temperature for 2 h (balloon pressure). The catalyst was removed by filtration through celite, and the filtrate concentrated under reduced pressure to afford the desired acid **13** (133 mg, 93%). ^{1}H-NMR δ (CD_3OD): 1.13-1.25 (m, 2H), 1.30-1.33 (2s, 18H), 1.39-1.74 (m, 6H), 1.97 (s, 3H), 2.97 (s, 6H), 3.09-3.28 (m, 14H), 3.77-3.82 (m, 8H), 6.73-6.92 (m, 3H), 7.07-7.11 (m, 3H). HRMS (FAB+, M+H): *m/z* calcd. for $C_{44}H_{69}N_{10}O_{10}$ 897.5198, found 897.5182.

Coupling of tripyrrole-acid 13 with bCD-NH$_2$. Synthesis of 7a.



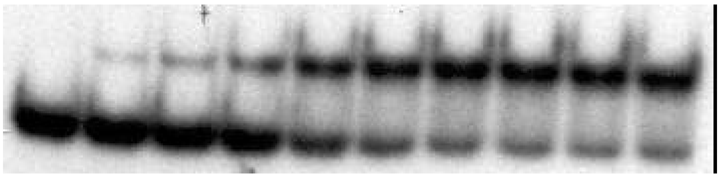
A solution of DIEA (90 μL, 0.045 mmol, 0.5 M in DMF) and HATU (4.18 mg, 0.011 mmol) in DMF (140 μL) was added to a solution of acid **13** (10 mg, 0.011 mmol) in DMF (100 μL). The mixture was stirred at room temperature for 4 min and then added to a solution of b**CD**-NH_2 (33 mg, 0.029 mmol) in DMF (400 μL). After stirring for 1 h the solvents were removed and the residue was purified by RP-HPLC (semipreparative Scharlau column 4 mL.min^{-1}, 5->95% B ½ h, R_t= 11.8 min). The product was dissolved in CH_2Cl_2 (3 mL) and to this solution, cooled in a ice-water bath, was added TFA (3 mL) dropwise. The solution was stirred for 30 min in the ice-water bath for 1 h at room temperature, the solvents evaporated and the residual TFA was removed by codestillation with CH_2Cl_2. The resulting product was identified by mass spectrometry as the desired compound (12 mg, 61%). MALDI-TOF: cald. for $C_{76}H_{122}N_{11}O_{39}$ 1812.8, found 1812.8. UV(H_2O) $\lambda_{max}(\varepsilon)$ 304 nm= 32274 M^{-1}cm^{-1}.

CIRCULAR DICHROISM CONTROL EXPERIMENTS, CARRIED OUT WITHOUT SUBSTRACTING THE CONTRIBUTIONS OF dsDNA



Red curve: 5 µM CRE^{hs}/A
Blue curve: 5 µM CRE^{hs}/A + 4,9 µM **7a**
Green curve**:** 5 µM CRE^{hs}/A + 4,8 µM **7a** + 4,8 µM **3a**

TITRATION OF PEPTIDE 3a FOR A MIXTURE OF dsDNA (CRE^{hs}/A) AND EXCESS OF TRIPYRROLE 7a



Titration autoradiogram of peptide **3a** in the presence of a mixture of ^{32}P-labelled CRE^{hs}/A (50 nM) saturated with **7a** (1 µM). [**3a**] = 0, 10, 20, 50, 80, 100, 150, 200, 250, 300 nM. Graph shows the best fit of the data to a 1:1 binding model using KaleidaGraph 3.6 data analysis software (analysis of data of three experiments). Kd = 63 ± 7 nM.