Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Introduction of a tailor made anion receptor into the side chain of small peptides allows fine-tuning the thermodynamic signature of peptide-DNA binding

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Supporting Information

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1 General

General Remarks: Solvents were dried and distilled before use. Millipore water was obtained with a Micropure from *TKA*. All reactions were carried out in oven dried glassware. Lyophilization was carried out with an Alpha 1-4 2D plus freeze drying apparatus from *Christ*. Analytical TLC was carried out on SiO_2 aluminum foils ALUGRAM SIL G/UV_{254} from *Macherey-Nagel*. Reversed phase column chromatography was done with an *Armen Instrument* Spot Flash Liquid Chromatography MPLC apparatus with *RediSep* C-18 Reversed-Phase columns.^{1}H- and ^{13}C-NMR spectra were recorded on a DRX 500 MHz spectrometer from *Bruker* at ambient temperature. The chemical shifts are reported in parts per million (ppm) relative to the deuterated solvent $CDCl_3$ or DMSO-d_6. The following abbreviations are used for peak multiplicities: s, singlet; d, doublet, m, multiplet; br, broad. MALDI-TOF-mass spectra were received by using a *Bruker* BioTOF III. Determination of pH values was carried out with a pH-Meter 766 Calimatic from *Knick*. Isothermal Titration Calorimetry (ITC) experiments were conducted on a *Microcal* VPITC microcalorimeter. Origin 7.0 software, supplied by the manufacturer, was used for data acquisition and analysis. Microwave assisted SPPS was carried out with a *CEM* Discover. Dynamic Light Scattering (DLS) experiments were performed using a Zetasizer-Nano ZS from *Malvern* equipped with a 4 mW He-Ne laser (633 nm wavelength) at a fixed detector angle of 173° with an avalanche photodiode detector.

2 Peptide Synthesis

Microwave Assisted Solid-Phase Peptide Synthesis of (1): The reaction was carried out in a fritted, microwave-transparent 25 ml polyethylene column with a CEM Discover microwave apparatus. Rink-Amide MBHA resin (200 mg, 0.62mmol/g) was swollen in DCM (5 ml) for 2 h. Fmoc removal was achieved by irradiating the resin in 20 % piperidine/DMF (5 ml) for 1 min and 5 min at 20 W and a maximum temperature of 60°C followed by washing with DMF (6 × 5 ml). The first residue Fmoc-Alloc-Lys-OH (169 mg, 0.37 mmol, 3 eq) was attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (194 mg, 0.37 mmol, 3 eq), DIPEA (130 µl, 0.74 mmol, 6 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). Coupling and washing steps were repeated. After Fmoc deprotection the second to the fourth residues Fmoc-Alloc-Lys-OH was attached to the resin as described above, also repeating coupling and washing steps. Alloc removal was achieved by $Pd(PPh_3)_4$ (57 mg, 0.05 mmol, 0.4 eq), $PhSiH_3$ (366 µl, 2.98 mmol, 24 eq) in 7 ml DCM for 30 min at room temperature under argon bubbling and consequent washing with DMF (3 × 5 ml). The deprotection and washing process was repeated. The GCP groups (591 mg, 1.48 mmol, 12 eq) were attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (774mg, 1.48 mmol, 12 eq),

DIPEA (505 µl, 2.97 mmol, 24 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). The coupling process was repeated until Kaiser Test showed negative result. After Fmoc deprotection the resin was washed with DCM (3 × 5 ml), methanol (3 × 5 ml), and DCM (3 × 5 ml) and dried under reduced pressure for one hour. To cleave the product, the resin was transferred to a flask equipped with a frit onto a Heidolph Rotamax 120 shaker. There it was shaken under argon atmosphere in a mixture containing 95 % TFA, 2.5 % water, and 2.5 % TIS for three hours and washed twice with the cleavage mixture. The filtrates were combined and concentrated in high vacuum at room temperature. Diethyl ether (40 ml) was added and the resulting suspension was centrifuged. The supernatant solvent was decanted and the solid was washed with diethyl ether and centrifuged again. After decanting, the raw product was dissolved in little methanol, water (30 ml) was added, and the mixture was freeze-dried in vacuum. The resulting solid was purified by MPLC on C18 reversed-phase silica gel (5 % to 45 % methanol/water in 45 min, 0.1 % TFA) to obtain **1** as white solid (8 mg, 5%) with 93% purity by analytical RP-HPLC. ^{1}H-NMR (500 MHz, d^{6}-DMSO): δ [ppm] = 1.29-1.40 (m, 8H, Lys-CH2), 1.48-1.70 (m, 16H, Lys-CH2), 3.20 (s, 8H, Lys-CH2), 3.69-3.79 (m, 1H, Lys-CH), 4.16-4.22 (m, 2H, Lys-CH), 4.46 (s, 1H, Lys-CH), 5.32-5.52 (m, 1H, amino-NH), 6.83 (s, 4H, pyrrole-CH), 7.02-7.17 (m, 2H, amide-NH), 7.26-7.31 (m, 2H, amide-NH2), 7.42(s, 4H, pyrrole-CH), 7.78(s, 1H, guanidine-NH), 7.93(br. s, 1H, guanidine-NH), 8.18-8.68 (m,

19H, amide-NH, guanidine-NH), 11.88 (br.s, 3H, guanidine-NH), 12.26 (br.s, 3H, guanidine-NH). ^{13}C-NMR (125 MHz, d^{6}-DMSO): δ [ppm] = 22.7 (Lys-CH2), 22.9 (Lys-CH2), 23.1 (Lys-CH2), 28.9 (Lys-CH2), 31.4 (Lys-CH2), 31.7 (Lys-CH2), 38.7 (Lys-CH2), 52.2 (Lys-CH), 52.6 (Lys-CH), 52.9 (Lys-CH), 112.3 (pyrrole-CH), 113.4 (pyrrole-CH), 115.8 (pyrrole-CH), 125.4 (pyrrole-CH), 155.5 (Cq), 158.9 (Cq), 159.7 (Cq), 171.2 (Cq), 171.6 (Cq), 171.8 (Cq), 173.4 (Cq). MALDI-TOF-MS (pos.) m/z calculated for $C_{52}H_{76}N_{25}O_{12}$ $[M + H]^+$ 1242.61, found 1242.01

Microwave Assisted Solid-Phase Peptide Synthesis of (2): The reaction was carried out in a fritted, microwave-transparent 25 ml polyethylene column with a CEM Discover microwave apparatus. Rink-Amide MBHA resin (200 mg, 0.62mmol/g) was swollen in DCM (5 ml) for 2 h. Fmoc removal was achieved by irradiating the resin in 20 % piperidine/DMF (5 ml) for 1 min and 5 min at 20 W and a maximum temperature of 60° C followed by washing with DMF (6 × 5 ml). The first residue Fmoc-Boc-Lys-OH (173 mg, 0.37 mmol, 3 eq) was attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (194 mg, 0.37 mmol, 3 eq), DIPEA (130 µl, 0.74 mmol, 6 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). Coupling and washing steps were repeated. After Fmoc deprotection the second to the fourth residues Fmoc-Alloc-Lys-OH was attached to the resin as described above, also

repeating coupling and washing steps. Alloc removal was achieved by $Pd(PPh_3)_4$ (42 mg, 0.04 mmol, 0.3 eq), $PhSiH_3$ (366 µl, 2.98 mmol, 24 eq) in 7 ml DCM for 30 min at room temperature under argon bubbling and consequent washing with DMF (3 × 5 ml). The deprotection and washing process was repeated. The GCP groups (443 mg, 1.11 mmol, 9 eq) were attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (580 mg, 1.11 mmol, 9 eq), DIPEA (379 µl, 2.22 mmol, 18 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). The coupling process was repeated until Kaiser Test showed negative result. After Fmoc deprotection the resin was washed with DCM (3 × 5 ml), methanol (3 × 5 ml), and DCM (3 × 5 ml) and dried under reduced pressure for one hour. To cleave the product, the resin was transferred to a flask equipped with a frit onto a Heidolph Rotamax 120 shaker. There it was shaken under argon atmosphere in a mixture containing 95 % TFA, 2.5 % water, and 2.5 % TIS for three hours and washed twice with the cleavage mixture. The filtrates were combined and concentrated in high vacuum at room temperature. Diethyl ether (40 ml) was added and the resulting suspension was centrifuged. The supernatant solvent was decanted and the solid was washed with diethyl ether and centrifuged again. After decanting, the raw product was dissolved in little methanol, water (30 ml) was added, and the mixture was freeze-dried in vacuum. The resulting solid was purified by MPLC on C18 reversed-phase silica gel (5 % to

45 % methanol/water in 45 min, 0.1 % TFA) to obtain **2** as white solid (6 mg, 4%) with 95% purity by analytical RP-HPLC. ^{1}H-NMR (500 MHz, d^{6}-DMSO): δ [ppm] = 1.37-1.39 (m, 8H, Lys-CH2), 1.51-1.72 (m, 16H, Lys-CH2), 2.61-2.74 (s, 2H, Lys-CH2), 3.20 (s, 6H, Lys-CH2), 3.83 (s, 1H, Lys-CH), 4.16-4.22 (m, 2H, Lys-CH), 4.32 (s, 1H, Lys-CH), 6.85-6.87 (m, 2H, pyrrole-CH), 7.04-7.50 (m, 5H, amide-NH), 7.85(s, 4H, pyrrole-CH), 8.17-8.63 (m, 18H, amide-NH, guanidine-NH), 12.0 (s, 2H, amine-NH2), 12.29(s, 2H, amide-NH2). ^{13}C-NMR (125 MHz, d^{6}-DMSO): δ [ppm] = 21.6 (Lys-CH2), 22.8 (Lys-CH2), 22.9 (Lys-CH2), 26.5 (Lys-CH2), 28.4 (Lys-CH2), 28.7 (Lys-CH2), 30.8 (Lys-CH2), 31.4 (Lys-CH2), 31.5 (Lys-CH2), 38.5 (Lys-CH2), 51.9 (Lys-CH), 52.7 (Lys-CH), 112.3 (pyrrole-CH), 112.4 (pyrrole-CH), 115.8 (pyrrole-CH), 155.4 (Cq), 159.0 (Cq), 159.6 (Cq), 168.5 (Cq), 171.2 (Cq), 173.3 (Cq). MALDI-TOF-MS (pos.) m/z calculated for $C_{45}H_{70}N_{21}O_{10}$ $[M + H]^{+}$ 1065.55, found 1065.36

Microwave Assisted Solid-Phase Peptide Synthesis of (3): The reaction was carried out in a fritted, microwave-transparent 25 ml polyethylene column with a CEM Discover microwave apparatus. Rink-Amide MBHA resin (200 mg, 0.62mmol/g) was swollen in DCM (5 ml) for 2 h. Fmoc removal was achieved by irradiating the resin in 20 % piperidine/DMF (5 ml) for 1 min and 5 min at 20 W and a maximum temperature of 60° C followed by washing with DMF (6 × 5 ml). The first residue Fmoc-Alloc-Lys-OH (169 mg, 0.37 mmol, 3

eq) was attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (194 mg, 0.37 mmol, 3 eq), DIPEA (130 µl, 0.74 mmol, 6 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). Coupling and washing steps were repeated. After Fmoc deprotection the second to the third residues Fmoc-Boc-Lys-OH was attached to the resin as described above, also repeating coupling and washing steps. Afterwards, the fourth residue Fmoc-Alloc-Lys-OH (169 mg, 0.37 mmol, 3 eq) was attached to the resin. Alloc removal was achieved by $Pd(PPh_3)_4$ (28 mg, 0.02 mmol, 0.2 eq), $PhSiH_3$ (366 µl, 2.98 mmol, 24 eq) in 7 ml DCM for 30 min at room temperature under argon bubbling and consequent washing with DMF (3 × 5 ml). The deprotection and washing process was repeated. The GCP groups (211 mg, 0.49 mmol, 4 eq) were attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (210 mg, 0.49 mmol, 4 eq), DIPEA (168 µl, 0.98 mmol, 8 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). The coupling process was repeated until Kaiser Test showed negative result. After Fmoc deprotection the resin was washed with DCM (3 × 5 ml), methanol (3 × 5 ml), and DCM (3 × 5 ml) and dried under reduced pressure for one hour. To cleave the product, the resin was transferred to a flask equipped with a frit onto a Heidolph Rotamax 120 shaker. There it was shaken under argon atmosphere in a mixture containing 95 % TFA, 2.5 % water, and 2.5 %

TIS for three hours and washed twice with the cleavage mixture. The filtrates were combined and concentrated in high vacuum at room temperature. Diethyl ether (40 ml) was added and the resulting suspension was centrifuged. The supernatant solvent was decanted and the solid was washed with diethyl ether and centrifuged again. After decanting, the raw product was dissolved in little methanol, water (30 ml) was added, and the mixture was freeze-dried in vacuum. The resulting solid was purified by MPLC on C18 reversed-phase silica gel (5 % to 45 % methanol/water in 45 min, 0.1 % TFA) to obtain **3** as white solid (8 mg, 7%) with 88% purity by analytical RP-HPLC. ^{1}H-NMR (500 MHz, d^{6}-DMSO): δ [ppm] = 1.33-1.35 (m, 8H, Lys-CH2), 1.51-1.72 (m, 16H, Lys-CH2), 2.75 (s, 4H, Lys-CH2), 3.22 (s, 4H, Lys-CH2), 3.72-3.83 (s, 1H, Lys-CH), 4.16-4.45 (m, 3H, Lys-CH), 6.87-6.89 (m, 1H, amide-NH), 7.03-7.12 (m, 2H, pyrrole-CH), 7.20-7.47 (m, 2H, pyrrole-CH), 7.82-7.88 (m, 8H, amide-NH, amine-NH2, pyrrole-NH), 8.22-8.58 (m, 12H, amide-NH, guanidine-NH), 12.0 (s, 1H, amine-NH), 12.3 (s, 1H, amide-NH). MALDI-TOF-MS (pos.) m/z calculated for $C_{38}H_{64}N_{17}O_8$ $[M + H]^+$ 886.50, found 886.84

Microwave Assisted Solid-Phase Peptide Synthesis of (4): The reaction was carried out in a fritted, microwave-transparent 25 ml polyethylene column with a CEM Discover microwave apparatus. Rink-Amide MBHA resin (200 mg, 0.62mmol/g) was swollen in DCM (5 ml) for 2 h. Fmoc removal was achieved by irradiating the resin in 20 % piperidine/DMF

(5 ml) for 1 min and 5 min at 20 W and a maximum temperature of 60° C followed by washing with DMF (6 × 5 ml). The first residue Fmoc-Alloc-Lys-OH (169 mg, 0.37 mmol, 3 eq) was attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (194 mg, 0.37 mmol, 3 eq), DIPEA (130 µl, 0.74 mmol, 6 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). Coupling and washing steps were repeated. After Fmoc deprotection the second to the fourth residues Fmoc-Boc-Lys-OH was attached to the resin as described above, also repeating coupling and washing steps. Alloc removal was achieved by $Pd(PPh_3)_4$ (28 mg, 0.02 mmol, 0.2 eq), $PhSiH_3$ (366 µl, 2.98 mmol, 24 eq) in 7 ml DCM for 30 min at room temperature under argon bubbling and consequent washing with DMF (3 × 5 ml). The deprotection and washing process was repeated. The GCP groups (106 mg, 0.25 mmol, 2 eq) were attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (105 mg, 0.25 mmol, 2 eq), DIPEA (84 µl, 0.49 mmol, 4 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). The coupling process was repeated until Kaiser Test showed negative result. After Fmoc deprotection the resin was washed with DCM (3 × 5 ml), methanol (3 × 5 ml), and DCM (3 × 5 ml) and dried under reduced pressure for one hour. To cleave the product, the resin was transferred to a flask equipped with a frit onto a Heidolph Rotamax 120 shaker. There it was

shaken under argon atmosphere in a mixture containing 95 % TFA, 2.5 % water, and 2.5 % TIS for three hours and washed twice with the cleavage mixture. The filtrates were combined and concentrated in high vacuum at room temperature. Diethyl ether (40 ml) was added and the resulting suspension was centrifuged. The supernatant solvent was decanted and the solid was washed with diethyl ether and centrifuged again. After decanting, the raw product was dissolved in little methanol, water (30 ml) was added, and the mixture was freeze-dried in vacuum. The resulting solid was purified by MPLC on C18 reversed-phase silica gel (5 % to 45 % methanol/water in 45 min, 0.1 % TFA) to obtain **4** as white solid (6 mg, 7%) with 90% purity by analytical RP-HPLC. ^{1}H-NMR (500 MHz, d^{6}-DMSO): δ [ppm] = 1.51-1.58 (m, 8H, Lys-CH2), 1.66-1.76 (m, 16H, Lys-CH2), 2.74 (s, 6H, Lys-CH2), 3.21 (s, 2H, Lys-CH2), 3.86-3.90 (m, 1H, Lys-CH), 4.16-4.33 (m, 3H, Lys-CH), 6.91 (s, 1H, pyrrole-CH), 7.43(s, 1H, pyrrole-CH), 7.93-8.39 (m, 10H, amide-NH, guanidine-NH), 8.61 (s, 4H, amine-NH2), 8.73-8.79 (m, 3H, amide-NH), 12.2 (s, 1H, amide-NH), 12.3 (s, 1H, amide-NH). ^{13}C-NMR (125 MHz, d^{6}-DMSO): δ [ppm] = 22.0 (Lys-CH2), 22.1(Lys-CH2), 22.2 (Lys-CH2), 26.3 (Lys-CH2), 26.4 (Lys-CH2), 28.4 (Lys-CH2), 30.7 (Lys-CH2), 31.1 (Lys-CH2), 31.3 (Lys-CH2), 38.5 (Lys-CH2), 51.9 (Lys-CH), 52.5 (Lys-CH), 112.5 (pyrrole-CH), 116.0 (pyrrole-CH), 125.2 (Cq), 132.9 (Cq), 155.6 (Cq), 159.0 (Cq),159.6 (Cq), 168.5 (Cq), 171.2 (Cq),

173.4 (Cq). MALDI-TOF-MS (pos.) m/z calculated for $C_{31}H_{58}N_{13}O_6$ $[M + H]^+$ 708.46, found 708.59

Microwave Assisted Solid-Phase Peptide Synthesis of (5): The reaction was carried out in a fritted, microwave-transparent 25 ml polyethylene column with a CEM Discover microwave apparatus. Rink-Amide MBHA resin (200 mg, 0.62mmol/g) was swollen in DCM (5 ml) for 2 h. Fmoc removal was achieved by irradiating the resin in 20 % piperidine/DMF (5 ml) for 1 min and 5 min at 20 W and a maximum temperature of 60° C followed by washing with DMF (6 × 5 ml). The first residue Fmoc-Lys(Boc)-OH (175 mg, 0.37 mmol, 3 eq) was attached to the resin by microwave irradiation for 20 min at 20 W and a maximum temperature of 60° C under argon atmosphere with PyBOP (194 mg, 0.37 mmol, 3 eq), DIPEA (127 µl, 0.74 mmol, 6 eq) in DMF (5 ml) and consequent washing with DMF (3 × 5 ml). Coupling and washing steps were repeated. After Fmoc deprotection the second to the fourth residues Fmoc-Lys(Boc)-OH were attached to the resin as described above, also repeating coupling and washing steps. After Fmoc deprotection the resin was washed with DCM (3 × 5 ml), methanol (3 × 5 ml), and DCM (3 × 5 ml) and dried under reduced pressure for one hour. To cleave the product, the resin was transferred to a flask equipped with a frit onto a Heidolph Rotamax 120 shaker. There it was shaken under argon atmosphere in a mixture containing 95 % TFA, 2.5 % water, and 2.5 % TIS for three hours and washed twice

with the cleavage mixture. The filtrates were combined and concentrated in high vacuum at room temperature. Diethyl ether (40 ml) was added and the resulting suspension was centrifuged. The supernatant solvent was decanted and the solid was washed with diethyl ether and centrifuged again. After decanting, the raw product was dissolved in little methanol, water (30 ml) was added, and the mixture was freeze-dried in vacuum. The resulting solid was purified by MPLC on C18 reversed-phase silica gel (0 % to 50 % methanol/water in 50 min, 0.1 % TFA) to obtain **5** as white solid (6.6 mg, 10%) with 90% purity by analytical RP-HPLC. ^{1}H-NMR (500 MHz, d^{6}-DMSO):δ [ppm] = 1.29-1.44 (m, 8H, Lys-CH2), 1.57-1.73 (m, 16H, Lys-CH2), 2.75 (s, 8H, Lys-CH2), 3.87 (s, 1H, Lys-CH), 4.16-4.32 (m, 3H, Lys-CH), 7.12-7.48 (m, 2H, amino-NH2), 7.97-8.04 (m, 10H, amino-NH2, amide-NH), 8.26-8.27 (m, 2H, amino-NH2), 8.85 (s, 1H, amide-NH). ^{13}C-NMR (125 MHz, d^{6}-DMSO): δ [ppm] = 20.9 (Lys-CH2), 22.1 (Lys-CH2), 26.3 (Lys-CH2), 30.3 (Lys-CH2), 30.9 (Lys-CH2), 31.3 (Lys-CH2), 38.3 (Lys-CH2), 51.6 (Lys-CH), 52.1 (Lys-CH), 52.5 (Lys-CH), 52.6 (Lys-CH), 168.4 (Cq), 171.1 (Cq), 173.4 (Cq). MALDI-TOF-MS (pos.) m/z calculated for $C_{24}H_{52}N_9O_4$ $[M + H]^+$ 530.41, found 530.21

3 Binding studies

Ethidium Bromide Displacement Assay: Spectra were recorded at 25° C in aqueous sodium cacodylate buffer (0.01 M, pH 7.40 ± 0.01) in quartz fluorescence microcuvettes (1 cm) equipped with a stopper. To a solution of ethidium bromide (900 µL, 0.75 µM), 1eq ctDNA was added and incubated for 15 min. The fluorescence emission was then measured from 560 to 650 nm utilizing an excitation wavelength of 520 nm. To this mixture a stock solution (50 µM) of **1 - 5** were added in aliquots (1–32 µl). After each addition the cuvette was gently shaken and the mixture was incubated for 1 min to ensure that the equilibria were established (no change was observed with longer incubation time). An excerpt of the fluorescence emission at 600 nm was corrected for ethidium bromide´s own emission and plotted against [EB]/[**1**], [EB]/[**2**], [EB]/[**3**] [EB]/[**4**]and [EB]/[**5**], respectively. An exponential decay first order function was fitted using Origin 7.0. The reciprocal x-value at half of the maximum fluorescence emission is the IC_{50} value representing the equivalents of **1 – 5** that are necessary to displace half of the ethidium bromide from the EB/DNA complex.

peptides	**1**	**2**	**3**	**4**	**5**
IC_{50} (µM)	0.85	1.51	1.50	1.31	0.85

Tab.S1. IC_{50} value of peptides **1 - 5** from ethidium bromide displacement assay in 0.01 M sodium cacodylate buffer at pH 7.4

Isothermal Titration Calorimetry: All measurements were carried out in sodium cacodylate buffer (0.01 M, pH 7.40 ± 0.01) at 25° C. All solutions were ultrasonicated and degassed in vacuum prior to the experiments. Aliquots of fragmented ctDNA (0.7 mM, 5µL) were injected from a 297µl rotating syringe (307 rpm) into the calorimeter reaction cell containing 1.45 ml of corresponding peptide **1 - 5** solutions (0.05mM). Blank experiments were conducted to determine the heats of dilution of ctDNA. These were subtracted from the heats measured in the titration experiments. Data was analyzed using Origin 7.0 software according to a single set of sites binding mode.

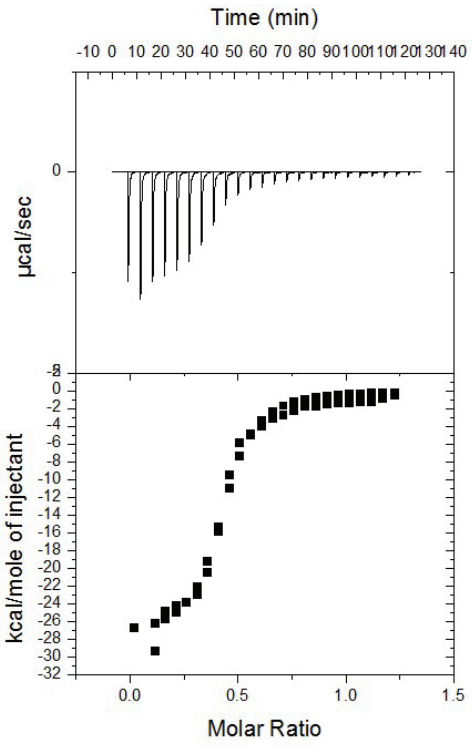


Fig.S1. ITC titration in sodium cacodylate buffer (0.01 M) at pH 7.4: ctDNA (0.7 mM) was added to **1** (0.05 mM) every 5 min.

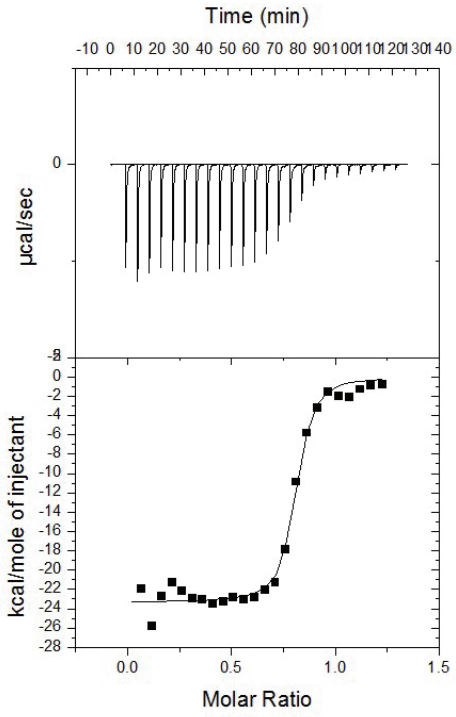


Fig.S2. ITC titration in sodium cacodylate buffer (0.01 M) at pH 7.4: ctDNA (0.7 mM) was added to **2** (0.05 mM) every 5 min.

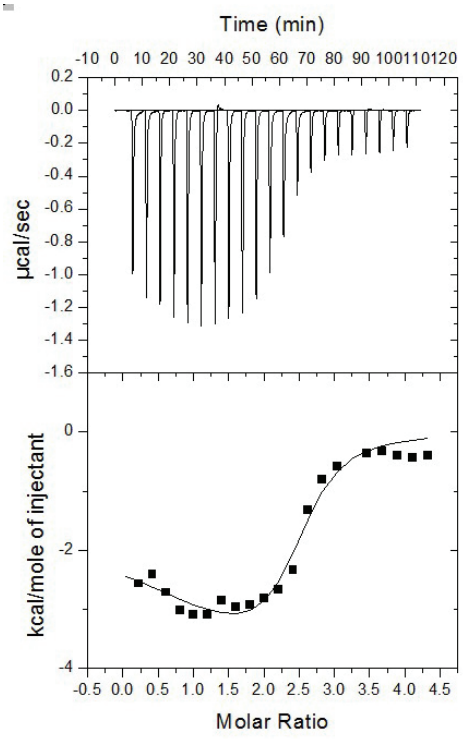


Fig.S3. ITC titration in sodium cacodylate buffer (0.01 M) at pH 7.4: ctDNA (0.7 mM) was added to **3** (0.05 mM) every 5 min.

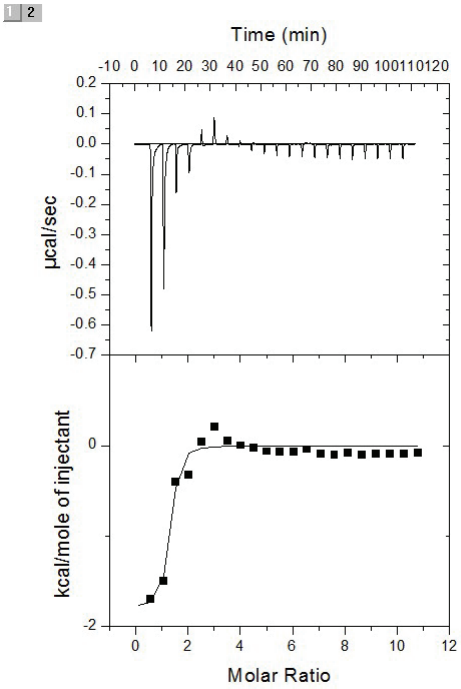


Fig.S4. ITC titration in sodium cacodylate buffer (0.01 M) at pH 7.4: ctDNA (0.7 mM) was added to**4** (0.05 mM) every 5 min.

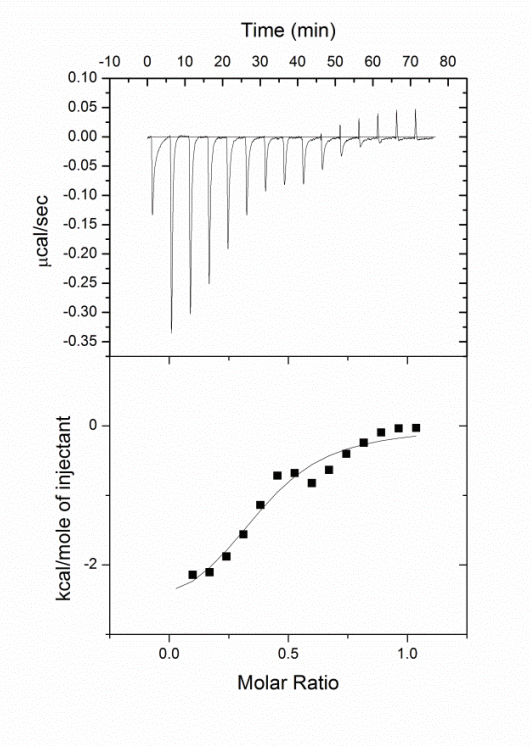


Fig.S5. ITC titration in sodium cacodylate buffer (0.01 M) at pH 7.4: ctDNA (0.7 mM) was added to **5** (0.05 mM) every 5 min.

4 DNA condensation studies

DLS experiments: All measurements were carried out in sodium cacodylate buffer (0.01 M, pH 7.40 ± 0.01) at 25° C in UV-transparent microcuvettes (1 cm) equipped with a stopper. Mixtures of fragmented ctDNA (50 μM) and **1 - 5** (150 μM) were prepared and filtered prior to measuring via 0.20 μm nylon filters. The autocorrelation functions of the backscattered light fluctuations were analyzed with the DTS 6.20 software from *Malvern* providing the hydrodynamic diameter (Z-average), polydispersity, size distribution (NNLS analysis) and Zeta potential.

5 Gene transfection experiments

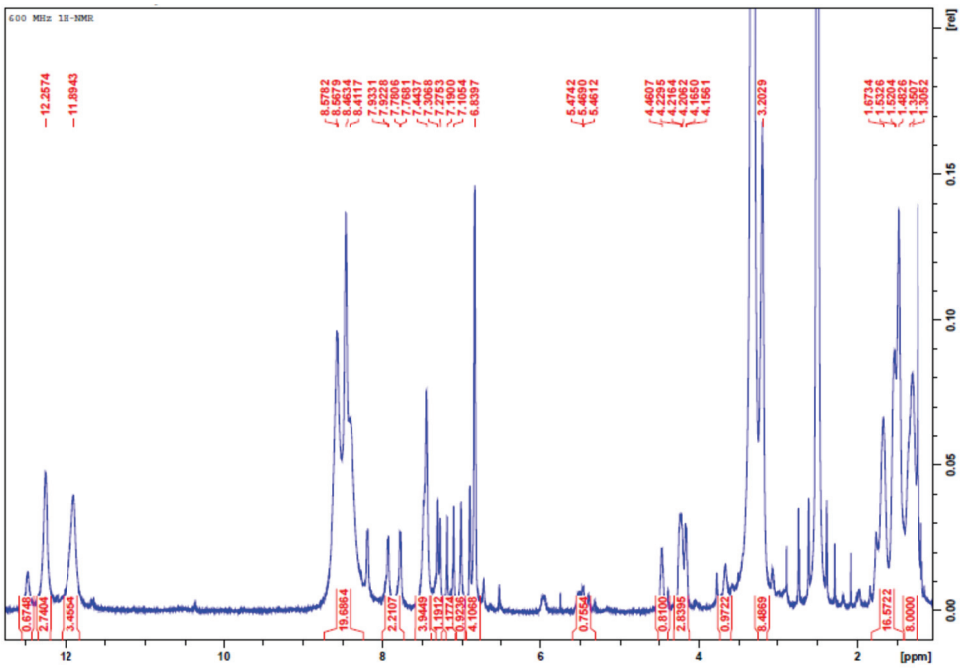
Cell lines and DNA: The human cervix carcinoma cell lines HeLa (ATCC-No.CCL-2) was obtained from the American Type Culture Collection and maintained as recommended in complete Dulbecco`s Modified Eagle Medium (DMEM) supplemented with 10 % fetal bovine serum, 1 % Glutamine and 1 % Antibiotic-Antimycotic (*Invitrogen*) at 37° C in a humidified atmosphere of 5 % CO_2. Calf thymus DNA (ctDNA) was obtained from Aldrich, dissolved in sodium cacodylate buffer (0.05 M, pH 7), cooled to 4° C for 20 h, sonicated (8 × 4 sec) and filtered through a 0.45 μm PTFE filter.

Transfection and Microscopy: Per well, 1×10^4 cells were seeded in 96 well cell culture plates (*Greiner bio-one*) in a total medium volume of 100 µl 24 h before transfection. The cationic transfection reagent polyethylenimine (PEI, pH 6.8, *Sigma-Aldrich*) was used at a concentration of 0.15 mM in PBS (*Invitrogen*) with 2 µg of plasmid DNA per well. Transfection with **1** - **5** were carried out in 0.15 mM with 2 µg plasmid DNA in a total volume of 30 µl in PBS buffer. Transfection efficiency was analyzed 24 h after transfection with an inverted fluorescence microscope (Axiovert 200M, *Carl Zeiss*) with a 10X air objective. Images were processed and analyzed using MetaMorph 6.3r6 (*Molecular Devices*) and Adobe Photoshop CS2 (*Adobe Systems*).

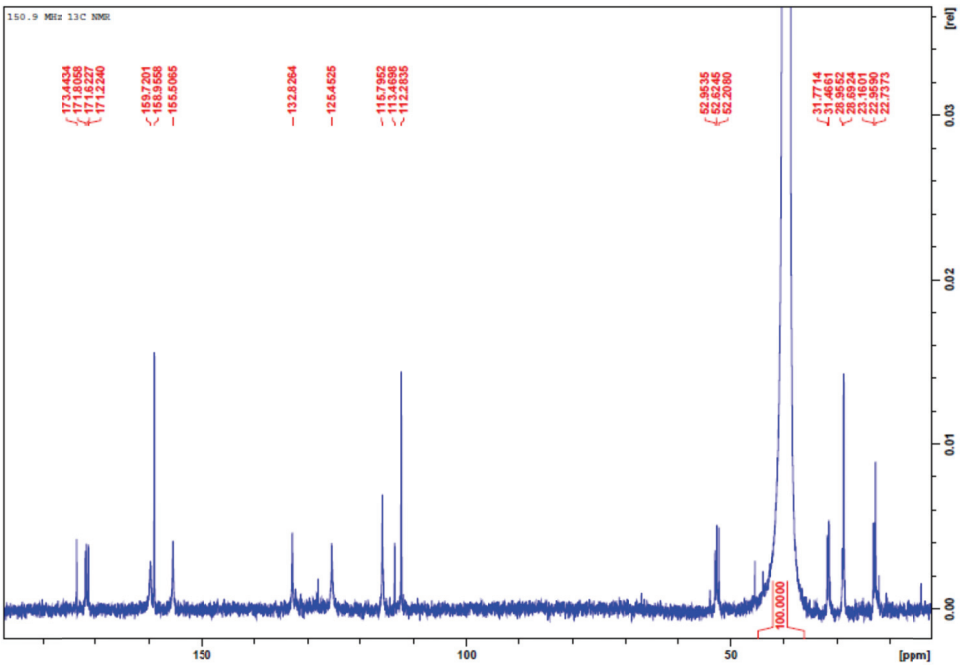
Alamar Blue Cell Viability Assay: Hela cells were grown and transfected as described above. Before transfection and 24 h after transfection cells were incubated with Alamar Blue dye (*Invitrogen*, 10 % v/v) for 3 h at 37° C at 5 % CO_2. Fluorescence was measured at 590 nm using a multimode reader (GloMax-Multi+DetectionSystem, *Promega*).

6 NMR spectra of all compounds

Fig.S6. ^{1}H NMR of **1** in DMSO-d6 recorded at 500 MHz.



^{13}C NMR of **1** in DMSO-d6 recorded at 125 MHz.



Analytical HPLC of **1** with 30 % - 50% methanol gradient (0.05% TFA).

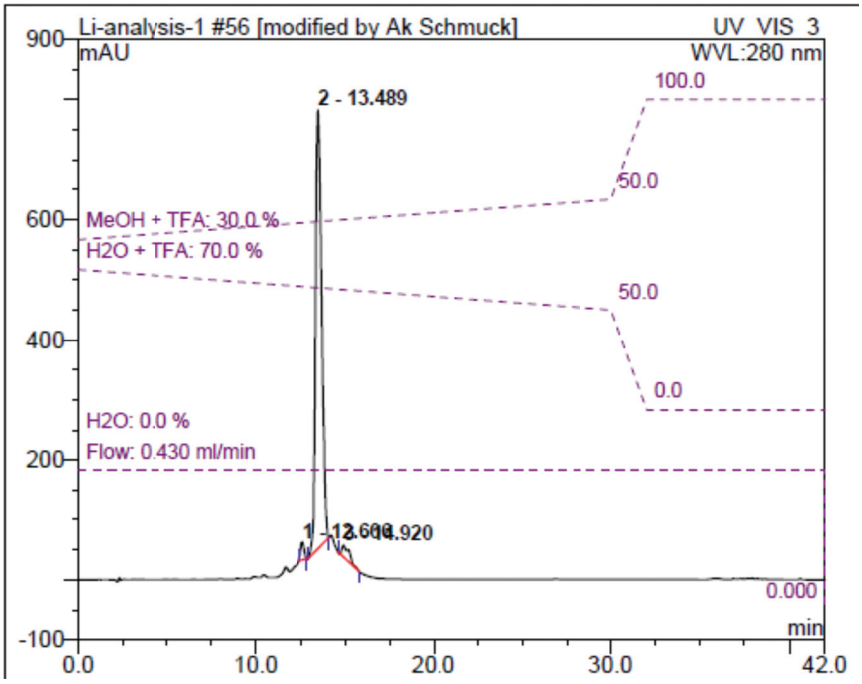
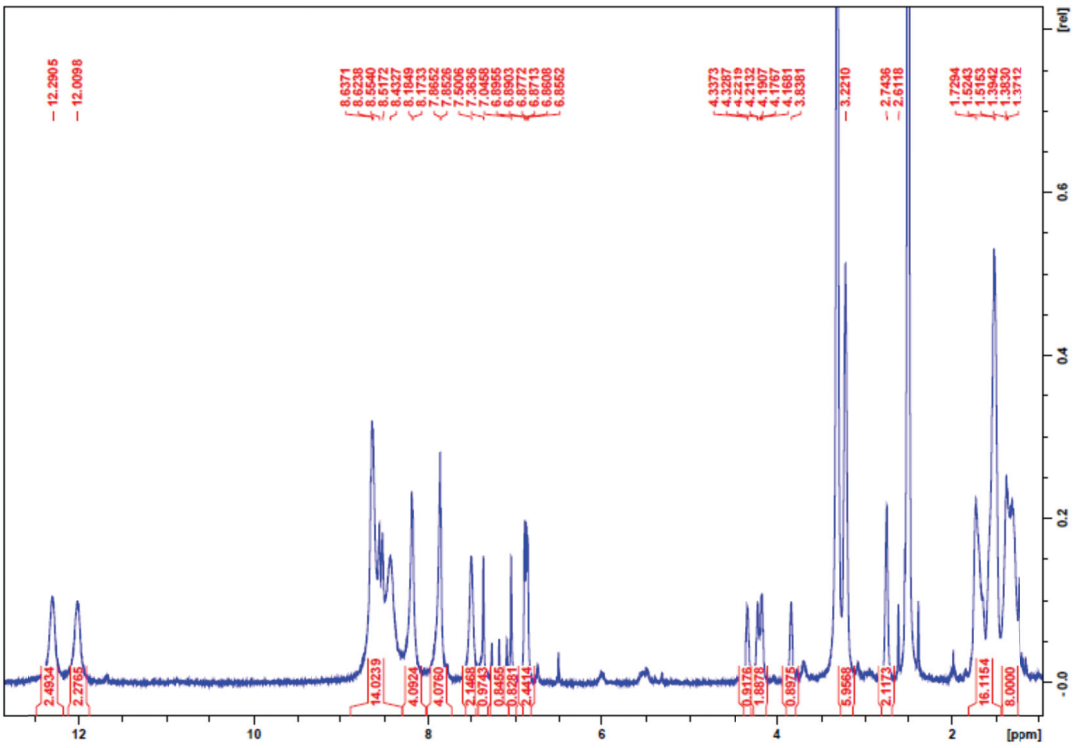
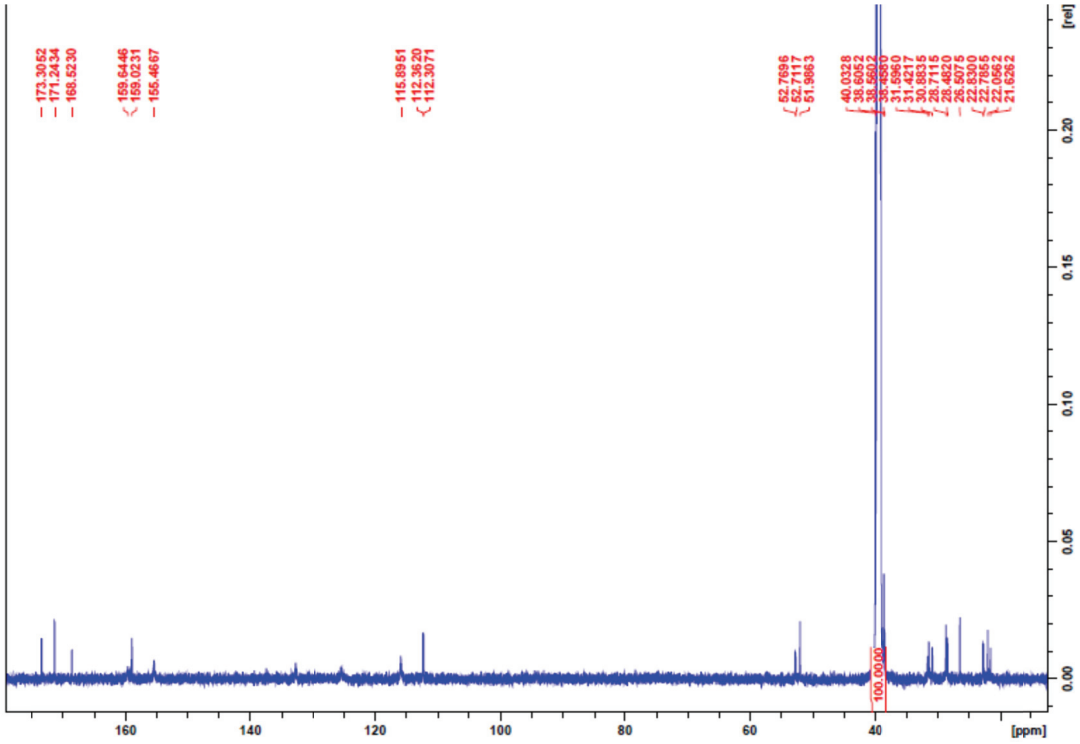


Fig.S7. ^{1}H NMR of **2** in DMSO-d6 recorded at 500 MHz.



^{13}C NMR of **2** in DMSO-d6 recorded at 125 MHz.



Analytical HPLC of **2** with 20 % - 40% methanol gradient (0.05% TFA).

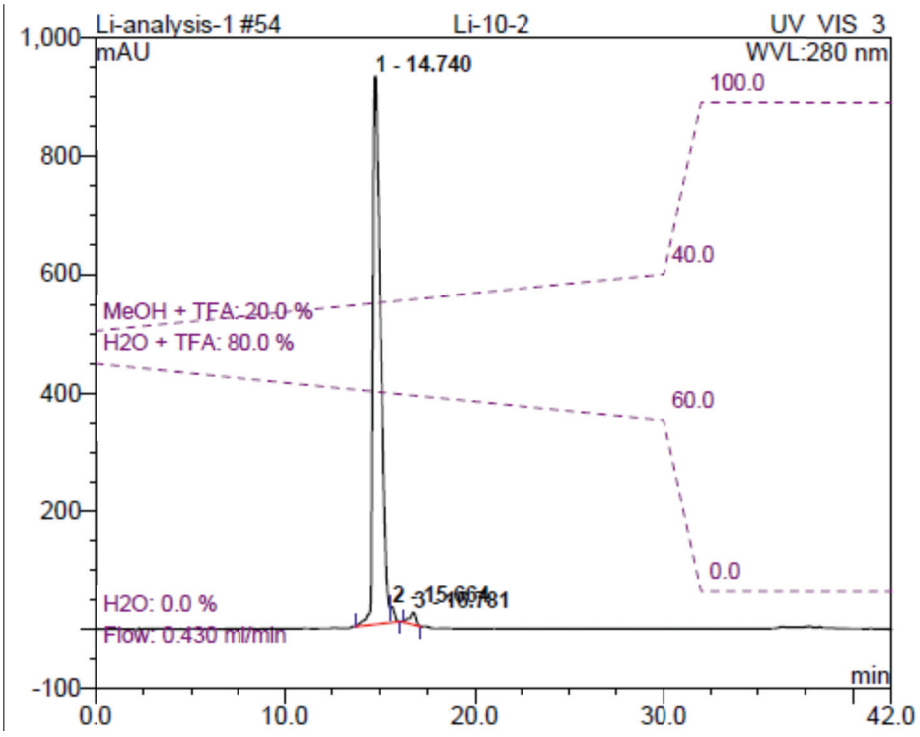
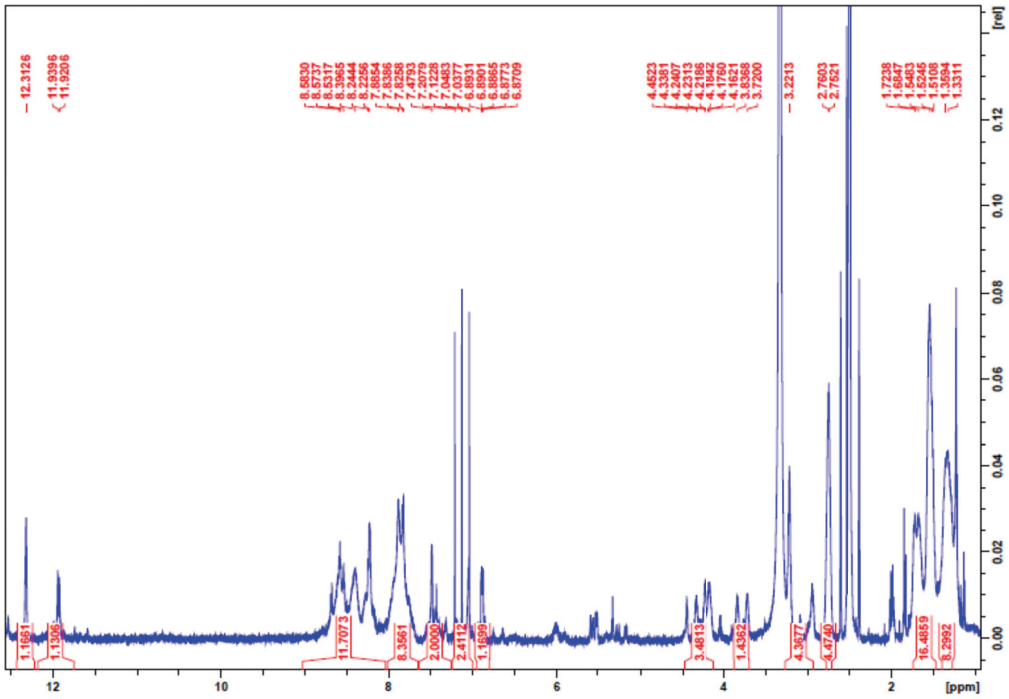


Fig.S8. [1]H NMR of **3** in DMSO-d6 recorded at 500 MHz.



Analytical HPLC of **3** with 10 % - 50% methanol gradient (0.05% TFA).

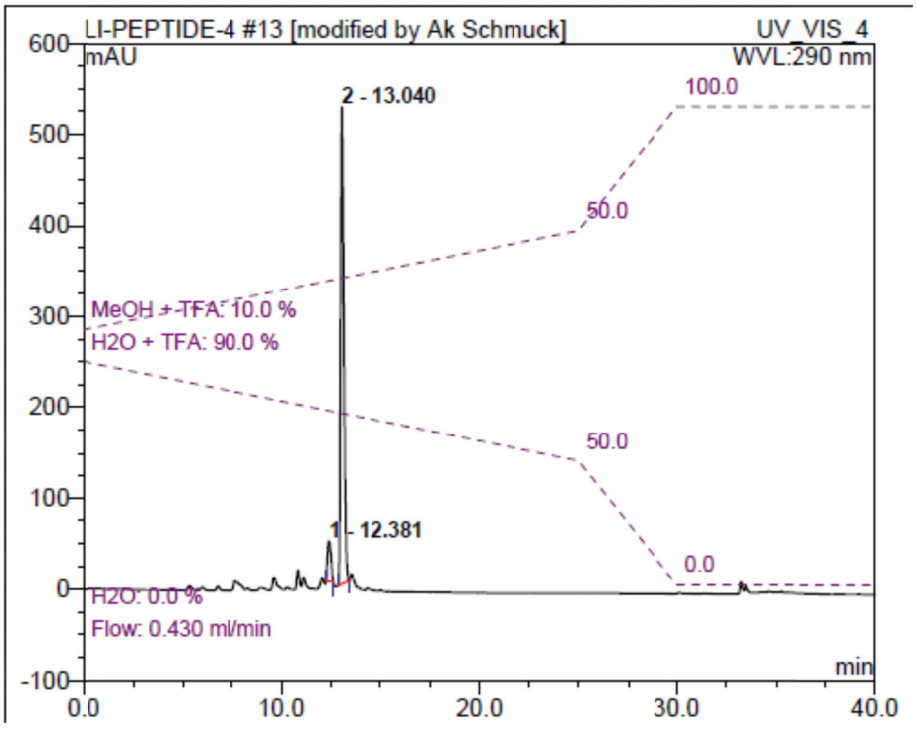
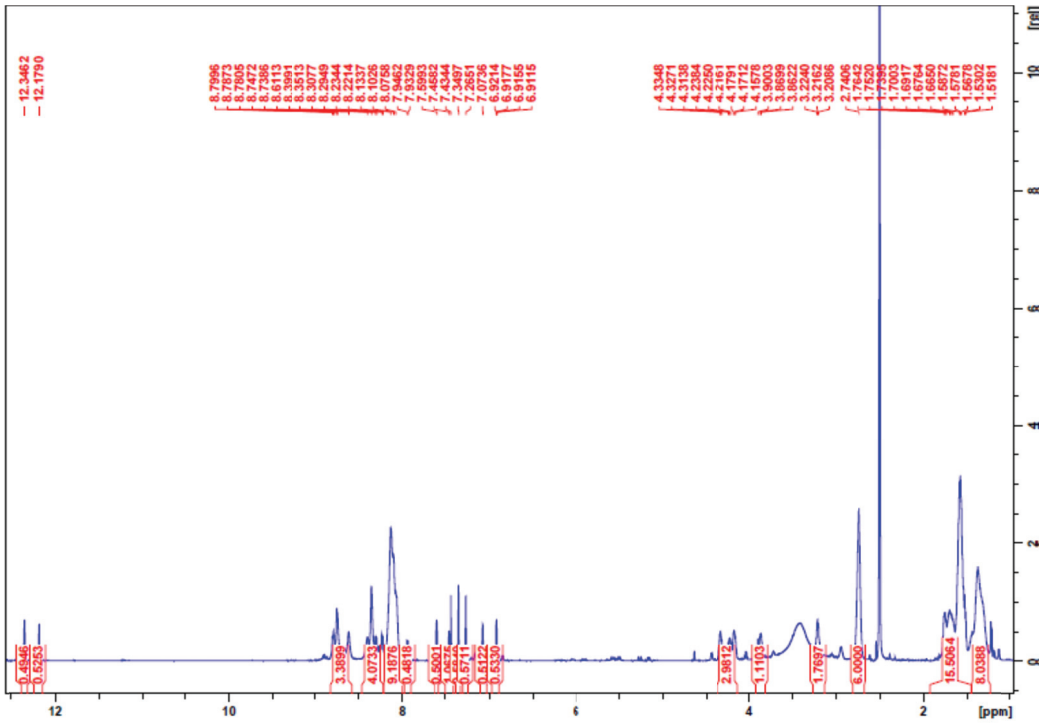
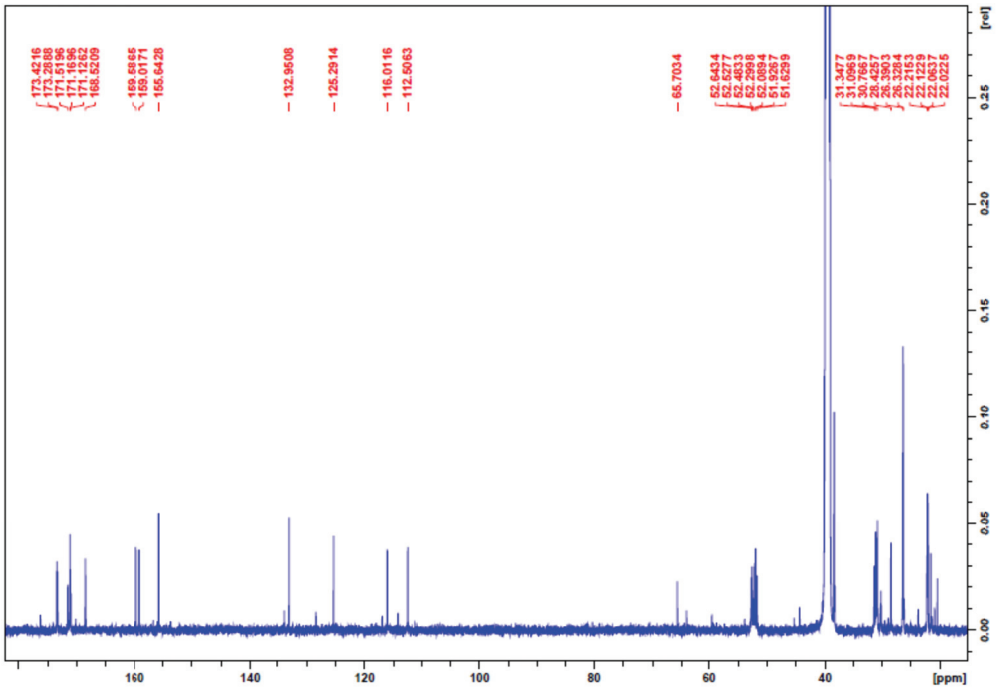


Fig.S9. ^{1}H NMR of **4** in DMSO-d6 recorded at 500 MHz.



^{13}C NMR of **4** in DMSO-d6 recorded at 125 MHz.



Analytical HPLC of **4** with 10 % - 100% methanol gradient (0.05%TFA).

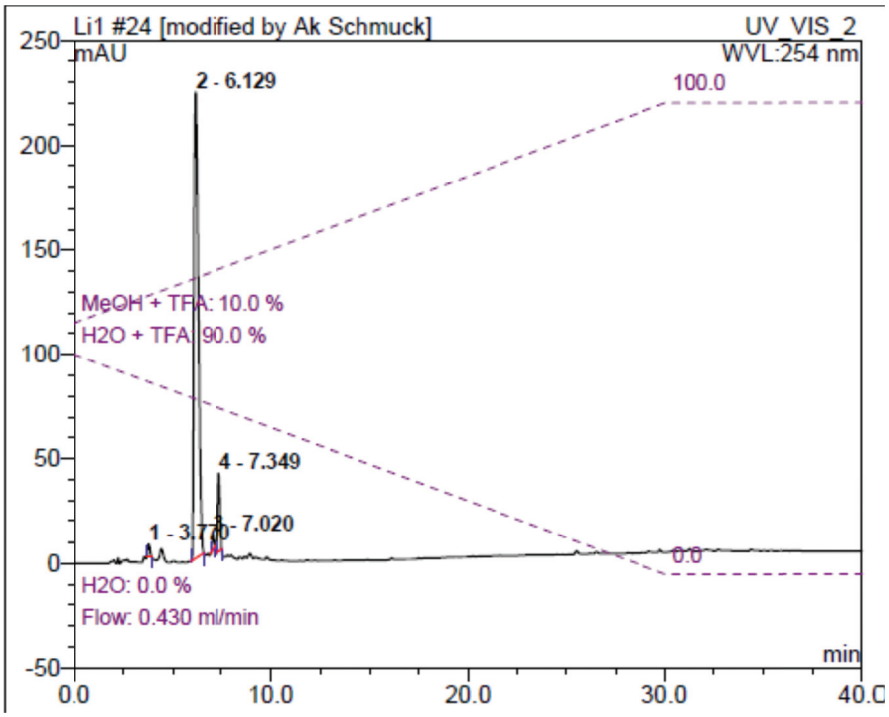
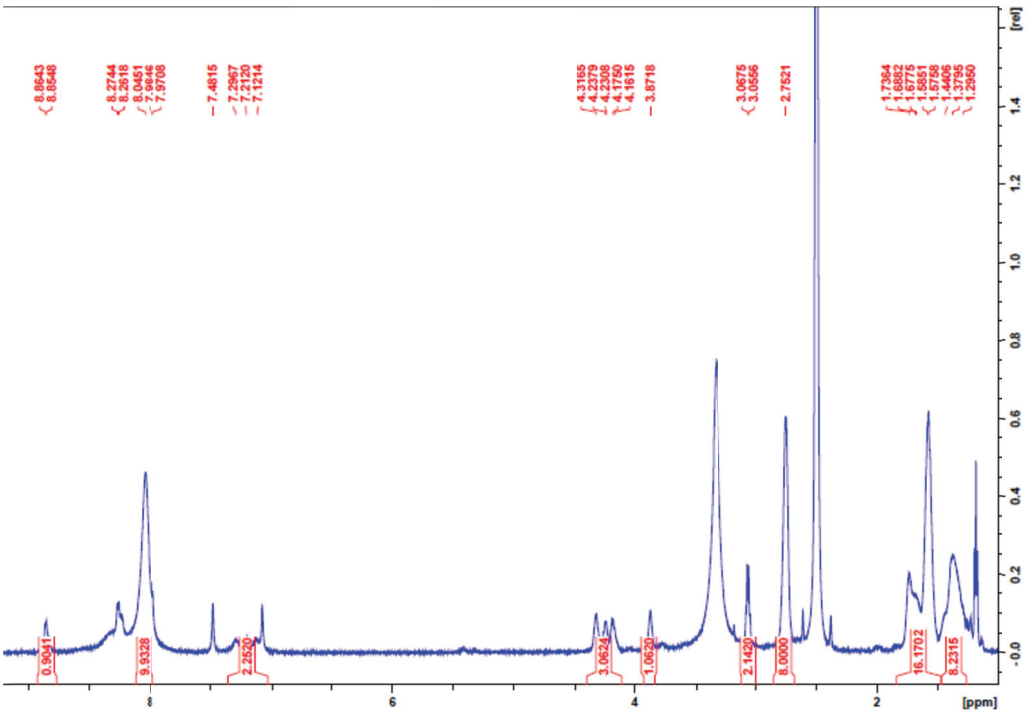
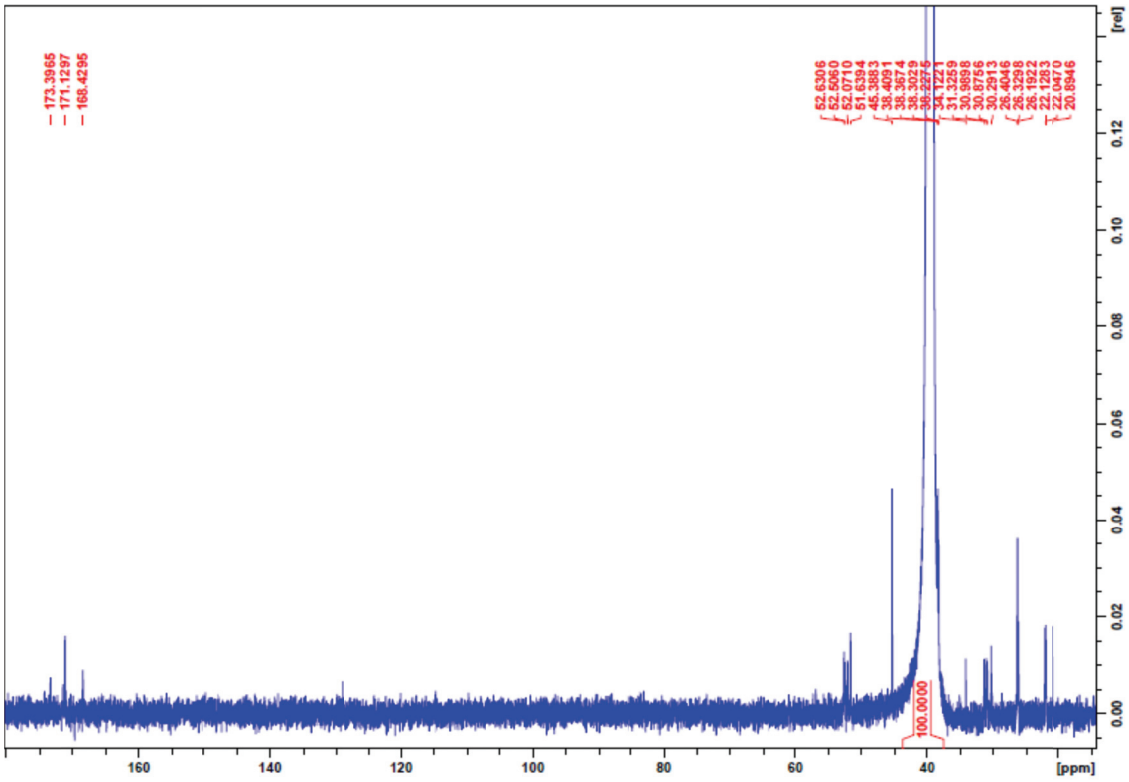


Fig.S10. ^{1}H NMR of **5** in DMSO-d6 recorded at 500 MHz.



^{13}C NMR of **5** in DMSO-d6 recorded at 125 MHz.



Analytical HPLC of **5** with 0 % - 20% methanol gradient (0.05% TFA).