Design, synthesis and DNA interaction of chimera between a platinum complex and an IHF mimicking peptide

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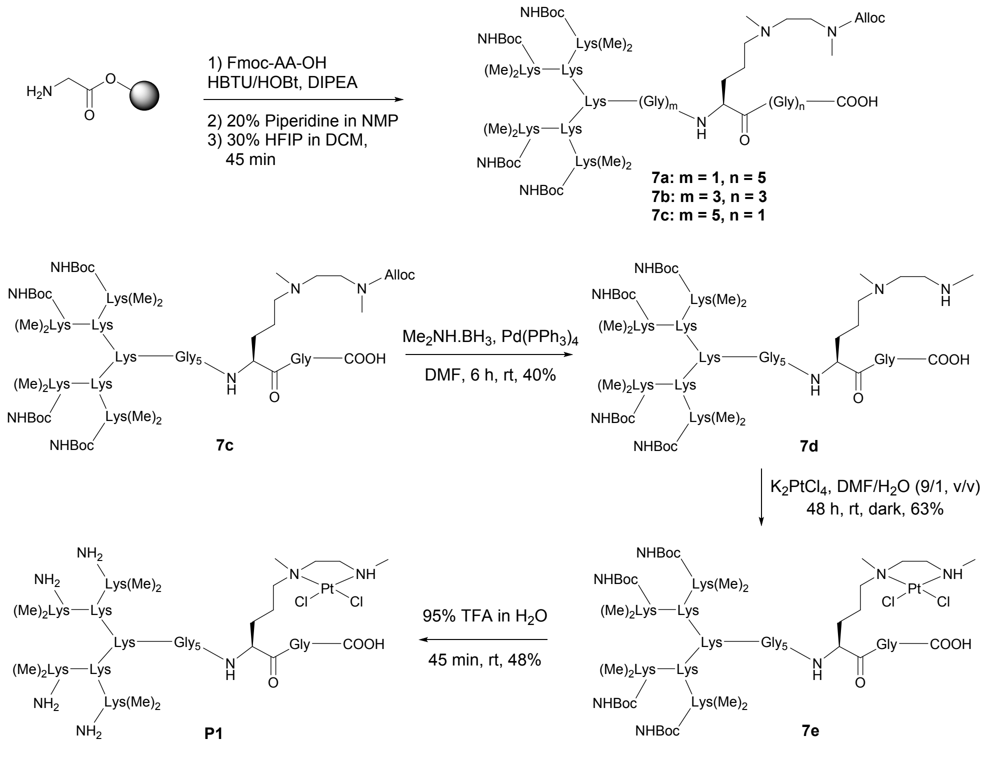
Supporting Information

Synthesis of the platinated dendrimeric units of IHF



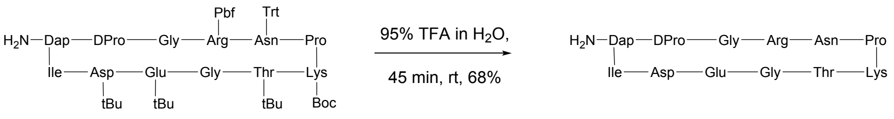
Scheme S1: Synthesis of the dendrimeric peptides **7a-c** and **P1** connected to the glycine linker containing the platinum chelating unit.

Synthesis of peptide 7d: Peptide **7c** (45 mg, 22 µmol, 1 eq) was dissolved in dry DMF (4.5 mL) under argon atmosphere. To this solution $Me_2NH.BH_3$ (52 mg, 0.88 mmol, 40 eq) and $Pd(PPh_3)_4$ (2.55 mg, 2.2 µmol, 0.1 eq) were added. After stirring the reaction mixture for 6 h at room temperature the solvent was removed under vacuum and the residue was purified by RP-HPLC. Yield (17 mg, 8.7 µmol, 40%). HPLC (10-60% B in 30 min) t_R = 21.81 min. MS (ESI): *m/z* = 978.7 $[M+2H]^{+2}$, 652.8 $[M+3H]^{+3}$, 489.8 $[M+4H]^{+4}$, 392.1 $[M+5H]^{+5}$. HRMS (ESI) = calculated for $[C_{95}H_{176}N_{23}O_{23}]^{+5}$ $[M+5H]^{+5}$) = 392.0663, found = 392.0660.

Synthesis of peptide 7e: Peptide **7d** (17 mg, 8.7 µmol, 1 eq) and K_2PtCl_4 (108.34 mg, 0.261 mmol, 30 eq) were dissolved in DMF/H_2O (4 mL, 9/1, v/v). After stirring the reaction mixture for 48 h at room temperature in dark the solvent was removed under vacuum and the residue was purified by RP-HPLC. Yield (12.18 mg, 5.48 µmol, 63%). HPLC (5-60% B in 30 min) t_R = 25.33 min. MS (ESI): *m/z* = 1111.6 $[M+2H]^{+2}$, 741.1 $[M+3H]^{+3}$, 556.1 $[M+4H]^{+4}$, 446.1 $[M+5H]^{+5}$. HRMS (ESI): calculated for $[C_{91}H_{173}Cl_2N_{23}O_{23}Pt]^{+2}$ ($[M+2H]^{+2}$) = 1111.6052, found = 1111.6068.

Synthesis of peptide P1: After stirring a solution of peptide **7e** in aqueous 95% TFA (1.5 mL) at room temperature for 45 min in dark the solvent was evaporated by argon bubbling. Thereafter, the residue was purified by RP-HPLC. Yield: (4.78 mg, 2.63 µmol, 48%). HPLC (5-30% B in 30 min) t_R = 17.91, 19.38, 20.74 min. MS (ESI): *m/z* = 911.0 $[M+2H]^{+2}$, 607.7 $[M+3H]^{+3}$, 456.0 $[M+4H]^{+4}$, 366.0 $[M+5H]^{+5}$. HRMS (ESI): calculated for $[C_{71}H_{142}Cl_2N_{23}O_{15}Pt]^{+3}$ ($[M+3H]^{+3}$) = 607.6689, found = 607.6694.

Synthesis of the cyclic recognition unit of IHF



6 **P2**

Scheme S2. Synthesis of the cyclic peptide **P2** mimicking the minor grove intercalating loop of IHF.

Synthesis of P2: Peptide **6** (5 mg, 2.48 µmol, 1 eq) was dissolved in 95% TFA (1.5 mL). After stirring the reaction mixture for 45 min at room temperature the solvent was evaporated by drying with argon. The crude product was precipitated in cold diethylether and the residue obtained after cold centrifugation and lyophilization from water was purified by RP-HLPC. Yield: (2.12 mg, 1.69 µmol, 68%). HPLC (60-100% B in 30 min) t_R = 13.2 min. MS (ESI): *m/z* = 1251.7 $[M+H]^{+}$, 626.3 $[M+2H]^{+2}$. HRMS (ESI) = calculated for $[C_{52}H_{88}N_{18}O_{18}]^{+2}$ ($[M+2H]^{+2}$) = 626.3257, found = 626.3260.

Polyacrylamide gel electrophoresis after incubation of IHF-4 with various DNA duplexes containing a GG site

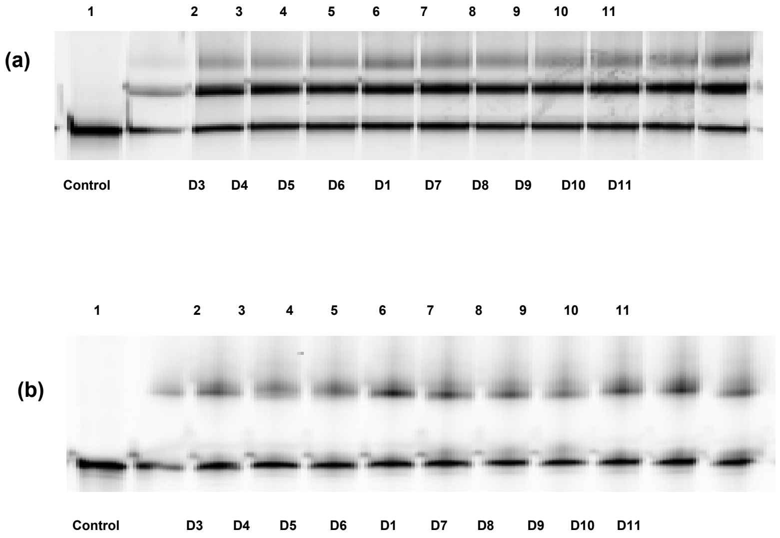


Figure S1. Gel electrophoresis assay to study the interaction of the IHF mimicking peptides with the 34-mer DNA duplex consisting of a GG site. The duplexes **D1** and **D3-D10** consist of the IHF consensus sequence, whereas the duplex **D11** is a random sequence. The samples were incubated for 17 h at 37 ˚C in 10 mM Na_2HPO_4/NaH_2PO_4, 100 mM $NaClO_4$, pH 5.8. Lane 1-11 contains 0.5 µM DNA duplex with 10 µM of **IHF-4**. (a) Performed under native conditions (20% PAA, 1xTBE). (b) Performed under denaturing conditions (20% PAA, 7 M urea, 1x TBE).

DNA sequences used in this study:

5’TAAAAAAGCATTGCCTATCAATTTGTTGCAACGA3’ (D1)
3’ATTTTTTCGTAAC**GG**ATAGTTAAACAACGTTGCT5’

5’TAAAAAA**GG**ATTGCTTATCAATTTGTTGCAACGA3’ (D3)
3’ATTTTTTCCTAACGAATAGTTAAACAACGTTGCT5’

5’TAAAAAACCATTGCTTATCAATTTGTTGCAACGA3’ (D4)
3’ATTTTTT**GG**TAACGAATAGTTAAACAACGTTGCT5’

5’TAAAAAAGCCTTGCTTATCAATTTGTTGCAACGA3’ (D5)
3’ATTTTTTC**GG**AACGAATAGTTAAACAACGTTGCT5’

5’TAAAAAAGCATTCCTTATCAATTTGTTGCAACGA3’ (D6)
3’ATTTTTTCGTAA**GG**AATAGTTAAACAACGTTGCT5’

5’TAAAAAAGCATTGCTTATCAACCTGTTGCAACGA3’ (D7)
3’ATTTTTTCGTAACGAATAGTT**GG**ACAACGTTGCT5’

5’TAAAAAAGCATTGCTTATCAATCCGTTGCAACGA3’ (D8)
3’ATTTTTTCGTAACGAATAGTTA**GG**CAACGTTGCT5’

5’TAAAAAAGCATTGCTTATCAATTCCTTGCAACGA3’ (D9)
3’ATTTTTTCGTAACGAATAGTTAA**GG**AACGTTGCT5’

5’TAAAAAAGCATTGCTTATCAATTTCCTGCAACGA3’ (D10)
3’ATTTTTTCGTAACGAATAGTTAAA**GG**ACGTTGCT5’

5’ACTAGTTACTGCATA**GG**ATCTAGCATTCAGATCA3’ (D11)
3’TGATCAATGACGTATCCTAGATCGTAAGTCTAGT5’