Electronic Supplementary Information

1. Materials and general methods.

All chemicals and solvents were purchased from Sigma–Aldrich, Fisher, Alfa Aesar, or Fluorochem and used as received. Deuterated solvents for NMR were supplied by Goss Scientific. Resin, Fmoc-Arg(Pbf)-OH (L and D configurations) and reagents for the peptide synthesis were Novabiochem products supplied by Merck Biosciences Ltd. Fe(II) parent cylinder $[Fe_2(L1)_3](Cl)_4$ was synthesised according with previously reported procedures.[1] Thin layer chromatography (TLC) was carried out on silica gel pre-coated aluminium sheets (Silica Gel 60 F254), supplied by MERCK KGaA. Visualisation used UV light (254/365). Column chromatography was performed using laboratory grade solvents on Silica Gel 60 (0.043–0.063 mm, supplied by Fluorochem, Glossop, UK) under gravity or with gentle pressure applied using nitrogen flow. All reverse phase high performance liquid chromatography (RP-HPLC) analyses and purifications were performed on Dionex Summit HPLC systems with Chromoleon software, using HPLC grade solvents, supplied by Fisher. Analytical HPLC were acquired with the aid of a Summit P580 quaternary low pressure gradient pump with built in vacuum degasser while, for the preparative HPLC, a high pressure gradient pump was employed on the same machine. Phenomenex Luna 10l C18 (2) columns were used for analytical (250 x 4.6 mm, 1 ml/min flow) and preparative (250 x 21.2 mm, 21 ml/min flow) RP-HPLC.

Coupling constants for ^{1}H NMR analysis are given in Hz and multiplicities of the spectroscopic data are recorded as follows: s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, dt= double triplet, br = broaden. Electrospray Ionisation (ESI) analyses, including accurate mass calculation (High Resolution Mass Spectrometry, HRMS) where possible, were carried out on a Micromass LCT Time of Flight Mass Spectrometer in positive ionisation mode and processed by MassLynx software. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer as neat films and wavelengths (ν) are quoted in cm^{-1}.

UV-Vis analysis and complexes concentration measurements were carried out at 20 °C in a Varian Cary 5000 spectrophotometer with Cary temperature controller, using 10 mm cuvettes. CD analyses were carried out at 20 °C in 10 mm pathlength cuvettes using a Jasco J-715 spectropolarimeter supported with Jasco PTC-423S temperature controller and RTE 111 bath circulator from Neslab. The chirality of the complexes was analysed by CD in acetonitrile for hexafluorophospate complexes and in water for chloride complexes. Complexes concentrations were determed by UV-Vis using the measured molar extinction coefficient ε_{599} = 12,900 M^{-1} cm^{-1}.

2. Synthesis of D and L-arginine conjugated cylinders.

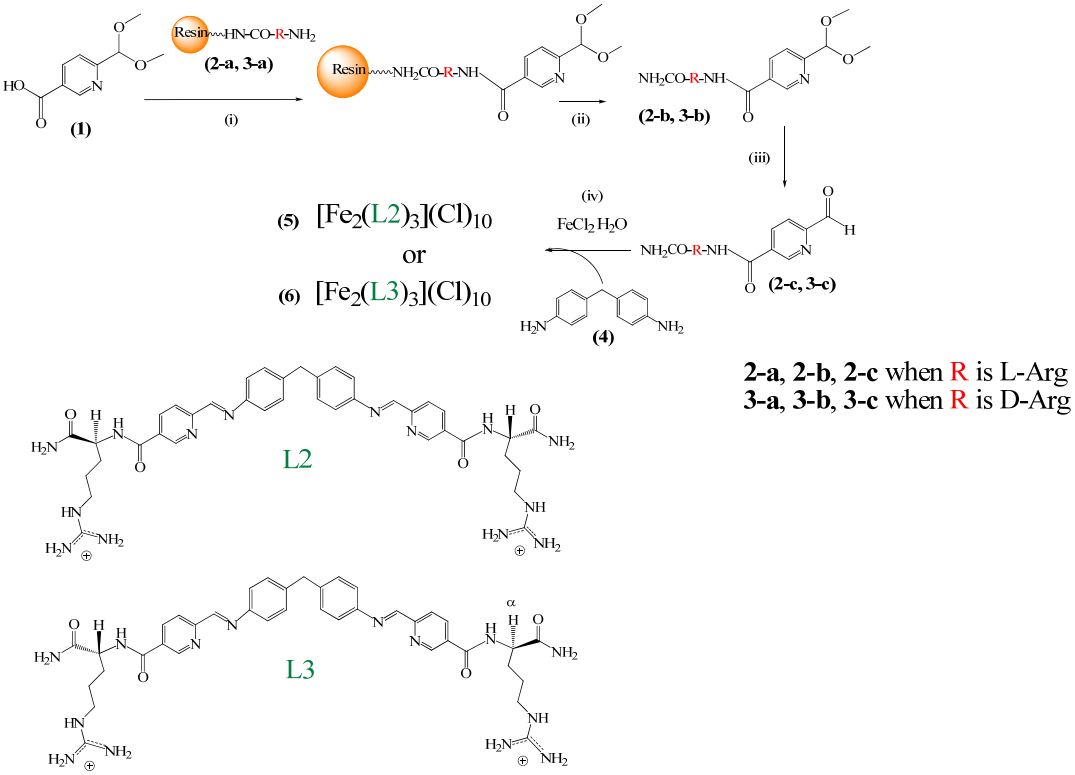
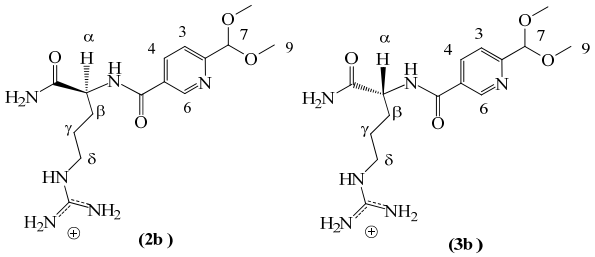


Fig. ESI.1 Scheme of synthesis of the D and L-Arginine conjugated Fe(II) cylinders. (i) HBTU, DIEA, in DMF; (ii) 95% TFA, 2.5% Water, 2.5% TIS; (iii) 1M HCl in THF, 3 days; (iv) in MeOH and N_2 atmosphere.

2.1 Synthesis of 2-Dimethoxymethyl-5-(arginine)-pyridine (2-b and 3-b).



The synthetic methods described below refer to Fig. ESI.1

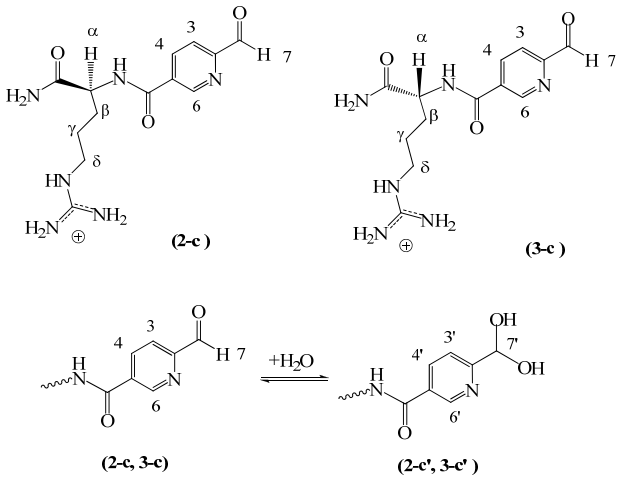
6-dimethoxymethyl-nicotinic acid **(1)** was synthesised according with the previously reported procedure.[2] Standard manual solid phase synthesis with fluorenylmethoxcarbonil (Fmoc) chemistry was applied. Rink Amide MHBA resin (loading grade 0.525 mmol/g, 2.8 mmol synthesis scale, 60 mL

volume for each of the following coupling/washing/deprotection steps) was swollen in dimethylformamide (DMF) for 1 hour, followed by treatment with 20% piperidine in DMF to remove the Fmoc group from the resin (1 treatment for 3 min followed by a second treatment for 7 min). After standard cycles of resin washing, with DMF and isopropanol, the coupling reaction was performed by using Fmoc-L-Arg(Pbf)-OH (to achieve compound **2a-2b**) or Fmoc-D-Arg(Pbf)-OH (for compound **3a-3b**). The reaction was carried out using amino acid/HBTU/DIEA = 3:3:6 in relation to the synthesis scale, in DMF for 2 hours. Cycles of washing with DMF and DCM, treatment with 20% piperidine in DMF to remove the Fmoc group from the amino acid and again washing with DMF and isopropanol were performed. 6-dimethoxymethyl-nicotinic acid **(1)** was coupled to the resin using standard coupling conditions (step (i) in Fig. ESI.1): 6-dimethoxymethyl-nicotinic acid/HBTU/DIEA=1.5/1.5/3, in relation to the synthesis scale, in DMF for 2 hours. A standard Kaiser test was used to verify that each coupling reaction was complete. The resin was washed with DMF, DCM and diethyl ether, dried and treated with 50 mL of cleavage solution (trifluoroacetic acid (TFA)/H_2O/triisopropylsilane = 9.5:0.25:0.25) for 3 h at room temperature. The mixture was filtrated, and the volume of the collected solution was reduced to few millilitres by evaporation. The crude compound was obtained by cold precipitation with diethyl ether and then analysed and purified by RP-HPLC. From 0 to 100% of acetonitrile 0.05% TFA in H_2O 0.05% TFA in 40 min was the gradient used for this analysis. Pure **2b** or **3b** were achieved with 66% and 57% yield respectively.

2-dimethoxymethyl-5-(L-Arg)-pyridine (2-b): ^{1}H NMR (400 MHz, MeOD, 298 K) δ 9.01 (1H, d, ^{4}J = 2.0 H_{6py}), 8.37 (1H, dd, ^{3}J and ^{4}J = 8.2, 2.0 Hz, H_{4py}), 7.75 (1H, d, ^{3}J = 8.2 Hz, H_{3py}), 5.45 (1H, s, H_7), 4.59 (1H, dd, ^{3}J = 5.3, 8.8 Hz, H_α), 3.32 (6H, s, H_9), 3.24 (2H, td, ^{3}J = 2.9, 7.0 Hz, H_δ), 1.99 (1H, m, H_β), 1.83 (1H, m, H_β), 1.72 (2H, m, H_γ). HRMS (ESI) analysis calcd. for $C_{15}H_{25}N_6O_4$, 353.1937 $[M]^+$; found 353.1931. IR (ν) = 3187 (br m), 2892 (w), 1648 (vs), 1533 (s), 1422 (w), 1293 (w), 1198 (s), 1130 (vs), 914 (w), 839 (m), 799 (w), 722 (m) cm^{-1}.

2-dimethoxymethyl-5-(D-Arg)-pyridine (3-b): ^{1}H NMR (400 MHz, MeOD, 298 K) δ 9.03 (1H, d, ^{4}J = 2.0 H_{6py}), 8.36 (1H, dd, ^{3}J and ^{4}J = 8.2, 2.0 Hz, H_{4py}), 7.75 (1H, d, ^{3}J = 8.2 Hz, H_{3py}), 5.41 (1H, s, H_7), 4.62 (1H, dd, ^{3}J = 5.3, 8.8 Hz, H_α), 3.32 (6H, s, H_9), 3.26 (2H, td, ^{3}J = 2.9, 7.0 Hz, H_δ), 1.99 (1H, m, H_β), 1.83 (1H, m, H_β), 1.72 (2H, m, H_γ). HRMS (ESI) analysis calcd. for $C_{15}H_{25}N_6O_4$, 353.1937 $[M]^+$; found 353.1933. IR (ν) = 3194 (br m), 2892 (w), 1651 (vs), 1532 (s), 1424 (w), 1321 (br w), 1179 (s), 1126 (vs), 914 (w), 836 (m), 799 (w), 720 (m) cm^{-1}.

2.2 2-formyl-5-(arginine)-pyridine (2-c, 3-c).



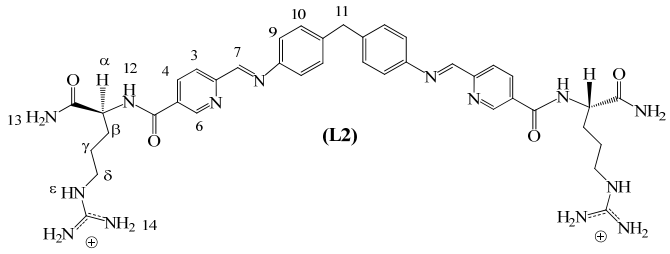
Deprotection of aldehyde group was achieved using the same procedure for all 2-dimethoxymethyl-R-pyridine compounds where R is L-Arg (**2-b**) or D-Arg (**3-b**). 2-Dimethoxymethyl-R-pyridine (1 mmol) was partially dissolved in 18 mL of THF and 3 mL of 1M HCl were added in 1 hour time at 0 °C. The mixture was stirred at room temperature and the reaction was monitored by analytical RP-HPLC every 24 h (from 0 to 100% of acetonitrile in water in 40 min). The peak corresponding to the unprotected aldehyde (~3 min earlier than starting protected compound) was present in the chromatogram after 24 h, but the reaction was promoted by adding small quantities (~ 1 mL) of 1M HCl until the chromatogram showed the unprotected aldehyde as the main compound. 3 days were sufficient to have a complete reaction. The crude was purified by preparative RP-HPLC (from 0 to 100% of acetonitrile in water in 70 min, 22 mL/min flow). Yields: 38% **2-c,** 31% **3-c**).

All the ^{1}H NMR spectra, both in D_2O and in MeOD, of 2-formyl-5-(arginine)-pyridine (**2-c**, **3-c**), shows two set of signals, because in solution the aldehyde group is in equilibrium with the hydrate form (as showed in the scheme above). Consequently the spectra present the resonances of the protons of the pyridine rings of both the species: the resonances of the aldehyde proton and those from the hydrate species. In the region of the signals due to the protons in the peptide chain, there is the contribution of both the species.

2-formyl-5-(L-Arg)-pyridine (2-c): ^{1}H NMR (400 MHz, MeOD, 298 K) δ 9.00 (1H, d, ^{4}J=2.4 $H_{6'py}$), 8.32 (1H, dd, ^{3}J and ^{4}J = 2.4, 8.3 Hz, $H_{4'py}$), 7.75 (1H, d, ^{3}J = 8.3 Hz $H_{3'py}$), 5.59 (1H, s, $H_{7'}$), 4.62 (1H, dd, ^{3}J = 5.3, 8.8 Hz, H_{α}), 3.27 (2H, dt, ^{3}J = 2.3, 6.8, Hz, H_{δ}), 1.99 (1H, m H_{β}), 1.83 (1H, m H_{β}), 1.70 (2H, m H_{γ}). Only less than 10% of aldeyde form was present in the spectrum δ 10.07 (s, H_7), 9.20 (d, ^{4}J=2.4 H_{6py}), 8.42 (dd, ^{3}J and ^{4}J = 2.4, 8.3, Hz, H_{4py}), 8.06 (d, ^{3}J = 8.3 Hz, H_{3py}). HRMS (ESI) analysis calcd. for $C_{13}H_{19}N_6O_3$, 307.1519 $[M]^+$; found 307.1511. IR (ν) = 3163 (br m), 2952 (w), 1643 (vs), 1530 (s), 1417 (w), 1291 (w), 1175 (m), 1040 (br s), 910 (m), 865 (br m) cm^{-1}.

2-formyl-5-(D-Arg)-pyridine (3-c): ^{1}H NMR (400 MHz, MeOD, 298 K) δ 8.98 (1H, d, ^{4}J=2.4 $H_{6'py}$), 8.33 (1H, dd, ^{3}J and ^{4}J = 2.4, 8.3 Hz, $H_{4'py}$), 7.77 (1H, d, ^{3}J = 8.3 Hz, $H_{3'py}$), 5.57 (1H, s, $H_{7'}$), 4.62 (1H, dd, ^{3}J = 5.3, 8.8 Hz, H_{α}), 3.27 (2H, dt, ^{3}J = 2.3, 6.8, Hz, H_{δ}), 1.99 (1H, m H_{β}), 1.83 (1H, m H_{β}), 1.70 (2H, m H_{γ}). Only less than 10% of aldeyde form was present in the spectrum δ 10.08 (s, H_7), 9.20 (d, ^{4}J=2.4 H_{6py}), 8.43 (dd, ^{3}J and ^{4}J = 2.4, 8.3 Hz, H_{4py}), 8.07 (d, ^{3}J = 8.3 Hz, H_{3py}). HRMS (ESI) analysis calcd. for $C_{13}H_{19}N_6O_3$, 307.1519 $[M]^+$; found 307.1511. IR (ν) = 3186 (br m), 2892 (w), 1640 (vs), 1536 (s), 1422 (w), 1292 (w) 1198 (s), 1127 (br s), 915 (m), 836 (br m) cm^{-1}.

2.3 $[Fe_2(L2)_3](Cl)_{10}$ (5).

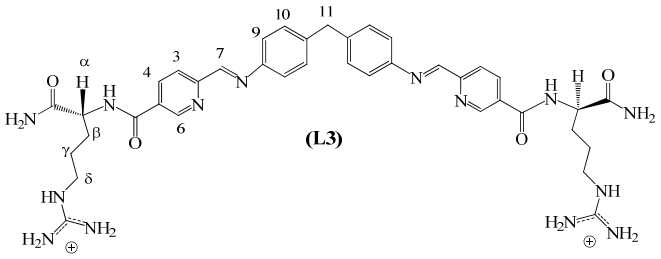


1 mL of 4,4'-methylenedianiline (**4**) (12.9 mg, 0.065 mmol) in methanol was added dropwise to a stirring solution of 2-formyl-5-(L-Arg)-pyridine (**2-c**) (40mg, 0.130 mmol) in 2 ml of methanol at 50°C in nitrogen atmosphere. In few minute an intense yellow mixture is formed. Temperature was raised to reflux and solid $FeCl_2$ x $4H_2O$ (8.5 mg, 0.0043 mmol) was added to the mixture, causing immediate formation of dark blue solution. The solution was stirred in nitrogen atmosphere in reflux for 1 hour and at room temperature overnight. Diethyl ether was added to the solution to afford the precipitation of a blue solid which was collected by filtration and washed with ethanol and diethyl ether, dried overnight on P_2O_5 to achieve 30.7 mg of chloride complex (51% yield). ^{1}H NMR (500 MHz, D_2O, 298 K) δ 9.04 (1H, s, H_7), 8.66-8.61 (overlapped 1H, dd ^{3}J = 8.1 Hz, H_{4py}+ 1H, d, ^{3}J = 8.1 Hz, H_{3py}), 7.57 (1H, s, H_{6py}), 7.03 (2H, br, H_{10}), 5.50 (2H, br, H_9), 4.31 (1H, dd, ^{3}J and ^{4}J = 5.8, 8.0 H_{α}), 3.93 (1H, s, H_{11}), 3.14 (2H, t, ^{3}J = 7.2 Hz, H_{δ}), 1.80 (2H, br m, H_{β}), 1.58 (2H, br m, H_{γ}). UV–Vis (water) λ_{max} (nm) = 599 (with a shoulder at 546), 340, 282 (shoulder), 238. ε_{599} = 12,900 M^{-1} cm^{-1}.

Saturated methanolic solution of NH_4PF_6 was added drop wise to 20 mg of chloride complex dissolved in the minimum volume of methanol to obtain dark-blue precipitate $[Fe_2(L2)_3](PF_6)_{10}$, which was filtrated and washed with diethyl ether, cold methanol/ethanol (1/1) and diethyl ether (16 mg, 57% yield). ^{1}H NMR (400 MHz, CD_3CN, 298 K) δ 9.33 (1H, d, ^{3}J = 6.7 Hz, H_{12}), 8.98 (1H, s, H_7), 8.57 (1H, d, ^{3}J = 8.0 Hz, H_{4py}), 8.54 (1H, d, ^{3}J = 8.0 Hz, H_{3py}), 8.01 (1H, s, H_{6py}), 7.09 (2H, br, $H_{9/10}$), 6.73 (1H, s, H_{13}), 6.61 (1H, br, H_{ε}), 6.21(1H, s, H_{13}), 6.17 (overlapped, br, H_{14}), 5.44 (2H, br, $H_{9/10}$), 4.13 (1H, br dt, H_{α}), 4.02 (1H, s, H_{11}), 3.14 (2H, m, H_{δ}), 1.72 (2H, br, H_{β}), 1.47 (2H, br H_{γ}). IR (ν) =

3160 (br m), 2912 (w), 1643 (vs), 1536 (m), 1500 (w shoulder), 1415 (w), 1318 (w), 1290 (w), 1200 (m), 1172 (m) 1129 (m), 1017 (w), 916 (w), 861 (w), 719 (w) cm^{-1}.

2.4 $[Fe_2(L3)_3](Cl)_{10}$ (6).



The same procedure used for the synthesis of $[Fe_2(L2)_3](Cl)_{10}$ was herein applied, but using 2-formyl-5-(D-Arg)-pyridine (**3-c**) (28.3 mg, 47% yield). ^{1}H NMR (500 MHz, D_2O, 298 K) δ 9.08 (1H, s, H_7), 8.69-8.67 (overlapped 1H, dd, ^3J = 8.1 Hz, H_{4py}+ 1H, d, ^3J = 8.1 Hz, H_{3py}), 7.60 (1H, s, H_{6py}), 7.03 (2H, br, H_{10}), 5.50 (2H, br, H_9), 4.36 (1H, dd, ^3J and ^4J = 5.8, 8.0 H_α), 3.97 (1H, s, H_{11}), 3.18 (2H, t, ^3J = 7.2 Hz, H_δ), 1.85 (2H, br m, H_β), 1.61 (2H, br m, H_γ). UV–Vis (water) λ_{max} (nm) = 599 (with a shoulder at 546), 340, 282 (shoulder), 238. ε_{599} = 12,900 M^{-1} cm^{-1}.

^{1}H NMR (400 MHz, CD_3CN, 298 K) δ 9.33 (1H, d, ^3J = 6.7 Hz, H_{12}), 8.95 (1H, s, H_7), 8.60 (1H, d ^3J = 8.0 Hz, H_{4py}), 8.57 (1H, d, ^3J = 8.0 Hz, H_{3py}), 8.01 (1H, s, H_{6py}), 7.10 (2H, br, $H_{9/10}$), 6.78 (1H, s, H_{13}), 6.66 (1H, br, H_ε), 6.20 (1H, s, H_{13}), 6.19 (overlapped, br, H_{14}), 5.44 (2H, br, $H_{9/10}$), 4.17 (1H, br dt, H_α), 4.05 (1H, s, H_{11}), 3.18 (2H, m, H_δ), 1.72 (2H, br, H_β), 1.47 (2H, br H_γ). IR (ν) = 3167 (br m), 2912 (w), 1646 (vs), 1536 (m), 1500 (w shoulder), 1478 (w), 1412 (w), 1319 (w), 1290 (w), 1203 (m), 1166 (m) 1112 (w), 1017 (w), 918 (w), 862 (w), 719 (w) cm^{-1}.

3. ^{1}H NMR analysis with Δ-TRISPHAT.

^{1}H NMR experiments with Δ-TRISPHAT (purchased from Sigma-Aldrich) were carried out as follows: NMR spectra of the complexes alone in CD_3CN were run (spectrum (4) and (3) in Fig. ESI.2), then 2 equivalents of solid Δ-TRISPHAT were added to each complex solution directly in the NMR tube. NMR spectra were run 15 min after that Δ-TRISPHAT was completely dissolved (spectrum (2) and (1) in Fig. ESI.2). Any comparison between D and L-Arg conjugate cylinders, both by NMR and CD, was carried out using complex solutions with the same concentration, measured by UV-Vis.

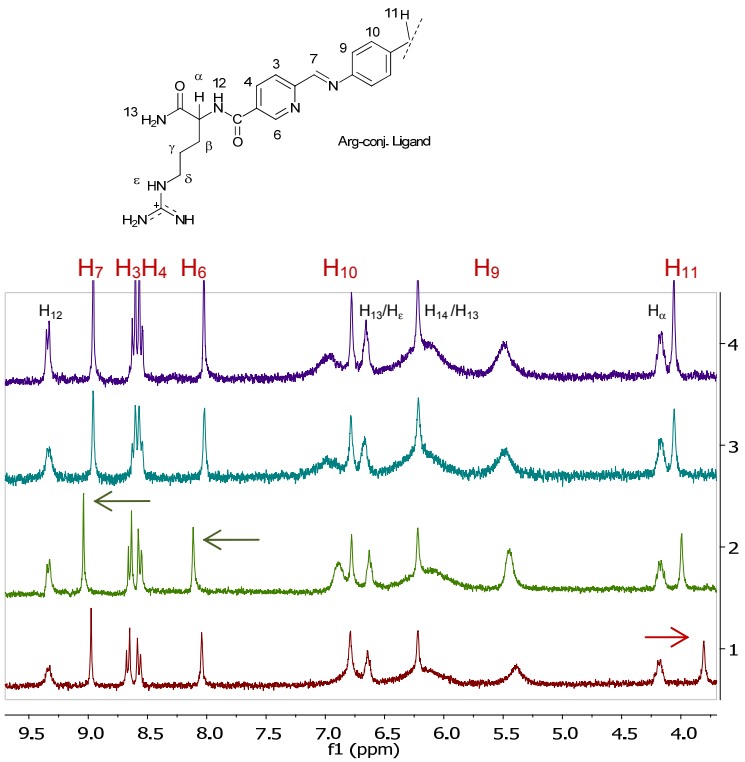


Fig.ESI.2 ^{1}H NMR (400 MHz, CD_3CN, 298K) of (4) $[Fe_2(\mathbf{L2})_3](PF_6)_{10}$, (3) $[Fe_2(\mathbf{L3})_3](PF_6)_{10}$, (2) $[Fe_2(\mathbf{L2})_3](PF_6)_{10}$ with 2 eq. of Δ-TRISPHAT and (1) $[Fe_2(\mathbf{L3})_3](PF_6)_{10}$ with 2 eq. of Δ-TRISPHAT. The signals indicated in red correspond to the protons of the helicate core and arrows show the peaks affected by the presence of TRISPHAT.

4. Polyacrylamide gel electrophoresis.

The formations of DNA three way junction by the complexes were probed using 15% native polyacrylamide gel electrophoresis run in TB buffer pH 8.3 comprising of 89 mM tris(hydroxymethy) amino methane, 89 mM boric acid. The oligonucleotides were purchased from MWG Eurosin, which provided the three sequences purified by PAGE. One strand of DNA (S3) was labeled with ^{32}P at 5' terminus by using T4 polynucleotide kinase (by New England BioLab) and [γ-^{32}P] adenosine 5'-triphosphate (by Perkin Elmer). The labeled strand was purified by QIA quick nucleotide removal kit. Briefly, 10 volumes of Buffer PN were added to 1 volume of the reaction sample. Then the mixture was transferred onto spin column and centrifuged column at 6,000 rpm for 1 minute. The supernatant was discarded. The column was transferred into a new elution tube and buffer PE was added (500 µL). Then discard the flow-through and repeat wash with another 500 µL of Buffer PE. The column was centrifuged again at 13,000 rpm for 1 minute to get rid of the buffer residual. The column was transferred into 1.5 mL eppendorf. Then 30 µL of milliQ water were added to the column and allowed to stand for 5 min before centrifuged at 13,000 rpm for 2 minutes to obtain 8 µM of stock radiolabeled DNA. Stock solutions of complexes were freshly prepared and both concentrations and chirality of the

conjugates were checked by UV-vis and CD right before the gel experiment. Stechiometric amounts of oligonucleotide were mixed with complexes to have final concentrations to load on the gel of 0.4 μM of each single strand (1.2 μM total concentration of DNA) and 0.4 μM of complex (so that the theoretical 3 way junction: complex is 1:1) in the TBN buffer containing mM tris(hydroxymethy) amino methane, 89 mM boric acid and 100 μM NaCl. The solutions were incubated at room temperature for 1 h and followed on ice for 15 minutes. The samples were run in 15% polyacrylamide gel electrophoresis for 3.5 h at 5 W at room temperature. Then the gel was exposed on phosphor plate for 1 h. The image was obtained from Molecular imager FX (Bio-Rad). The experiment was repeated 3 times and the images were quantified by Quantity one to calculate the percent of three way junction that was formed for each complex. It is not possible to estimate how that precipitate would have contribute if it was free to run in the gel and whether the DNA that run in those lanes is entirely involved in the formation of the 3WJ. For this reason the percent of 3WJ relatively to the single strands only (Fig. ESI.3) was calculated as follows:

$$\% \text{ 3WJ} = [I_{3WJ}/(I_{ss}+I_{3WJ})]*100$$

where $I_{3WJ,}$ and I_{ss} are the measured intensities of the bands relative to the three way junctions and the single strands for each lane. In each case, the values of the intensity were the calculated as the averages of the intensities from the bands of each of the 3 experiments (1-sigma error limit, paired T-test $p<0.05$).

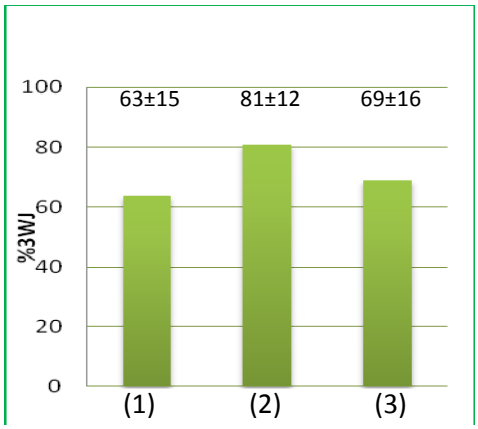


Fig. ESI.3. Quantification of the intensity of the bands from the gel in Fig. 4. % of three way junction formed in presence of each complex only relative to the bands of single strands. (1) $[Fe_2(\mathbf{L1})_3]^{4+}$ (2) $[Fe_2(\mathbf{L3})_3]^{10+}$ (3) $[Fe_2(\mathbf{L2})_3]^{10+}$.

4. Cell cultures and MTT assay.

DMEM medium and FBS were obtained from Invitrogen. Antibiotic antimycotic solution, L-glutamine, trypsin-EDTA, HEPES buffer solution, sodium pyruvate, MTT (3-(4,5-dimethylthiazol-2-

yl)-2,5-diphenyltetrazolium bromide) and DMSO were purchased from Sigma, UK. Tissue culture flasks, 96 well microtitre plates were obtained from Appleton Woods, UK.

The cytotoxic activity of the synthesized compounds was tested in a human A2780 ovarian cancer cell line. The cells growing as monolayers in DMEM medium supplemented with 10% FBS, 1% L-glutamine, 1% HEPES buffer, 1% sodium piruvate and 1% antibiotic were maintained in the incubator at 37 C° and humidified atmosphere and regularly checked for the absence of contamination. The cells were collected from the tissue culture flaks using 10% trypsin-PBS solution. Single cell suspensions were prepared, cells counted using cell counting chamber and placed in 96 microlitre plates at the concentration of 4000 cells/well to a total volume of 100 µL per well. Plates with cells were placed in the incubator for 24 hours to allow cells to attach to the surface. The A2780 cancer cells were treated with five different concentrations (200, 100, 50, 25, 12.5 µM) of the synthesized complexes dissolved in a fresh medium and incubated for 72 hours.

The MTT solution was prepared by dissolving yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) 0.25 g in 50 mL of phosphate-buffered saline. 20 µL of MTT solution was added in each well of 96 well plates except three wells of the control and cells were further incubated for 2 hours. The medium was carefully removed and 200 µL of DMSO was added in each well to dissolve the formed purple crystals of formazan. Absorbance was measured in 15-20 minutes after the addition of DMSO using a 96-well microtitre plate reader (BioRad) set at 590 nm. All the experiments were repeated at least three times for more accurate results.

5. References

1. I. Meistermann, V. Moreno, M. J. Prieto, E. Moldrheim, E. Sletten, S. Khalid, P. M. Rodger, J. C. Peberdy, C. J. Isaac, A. Rodger and M. J. Hannon, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 5069.
2. L. Cardo and M. J. Hannon, *Inorg. Chim. Acta*, 2009, **362**, 784.