Electronic Supplementary Material (ESI) for ChemComm.
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Electronic Supplementary Information

Triazole-based, optically-pure metallosupramolecules; highly potent and selective anticancer compounds

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Contents

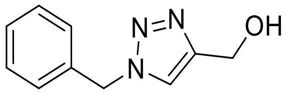
1. Synthesis

All solvents and chemicals purchased from commercial sources (Sigma-Aldrich, Acros, Fisher Scientific or Alfa Aesar) were used without further purification unless otherwise stated. Sodium hydride dispersions in mineral oil were placed in a Schlenk vessel under an inert atmosphere and washed three times with diethyl ether to remove the oil, then dried and stored under argon in an MBraun dry box. Where appropriate, reactions were carried out under argon using a dual manifold argon/vacuum line and standard Schlenk techniques or in an MBraun dry box. Necessary solvents were dried by heating to reflux for 3 d under dinitrogen over the appropriate drying agents (potassium for tetrahydrofuran, sodium/potassium alloy for diethyl ether, and calcium hydride for acetonitrile and pyridine) and degassed before use. Tetrahydrofuran and diethyl ether were additionally pre-dried over sodium wire. Dried solvents were stored in glass ampoules under argon. All glassware and cannulae were stored in an oven at > 375 K.

Deuterated solvents were purchased from Sigma-Aldrich and Cambridge Isotope Laboratories. NMR spectra were recorded on Bruker Spectrospin 300/400/500 MHz. Routine NMR assignments were confirmed by ^{1}H-^{1}H (COSY) and ^{13}C-^{1}H (HSQC) correlation experiments where necessary. The spectra were internally referenced using the residual protio solvent ($CDCl_3$, CD_3CN etc.) resonance relative to tetramethylsilane ($\delta = 0$ ppm). ESI mass spectra were recorded on an Agilent Technologies 1260 Infinity spectrometer or a Bruker Daltonics MicroTOF spectrometer. Infra-Red spectra were measured using a Bruker Alpha-P FTIR spectrometer. Elemental analyses were performed by Medac Ltd. Chobham, Surrey GU24, 8JB, UK.

The enantiomers of 2-([2,2'-bipyridin]-5-ylmethoxy)-1-phenylethan-1-amine (**2**) and aromatic azide derivatives were synthesized by known methods.[1]

(1-benzyl-1H-1,2,3-triazol-4-yl)methanol



(Azidomethyl)benzene (0.24 g, 1.79 mmol) and propargyl alcohol (0.10 g, 1.79 mmol) were dissolved into methanol, followed by addition of CuI (34 mg, 0.18 mmol). The reaction mixture was heated at 60 °C overnight. After cooling to room temperature, the reaction solution was filtered to remove CuI. The solvent was removed under reduced pressure to afford the final product as white solid.

Yield 0.30 g, 90 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 8.01 (1H, s, triazole), 7.40-7.30 (5H, m, Ph), 5.57 (2H, s, Ph-C$\underline{H}_2$), 5.15 (1H, t, $^3J_{HH}$ = 5.0 Hz, OH), 4.50 (2H, d, $^3J_{HH}$ = 5.0 Hz, C$\underline{H}_2$OH).

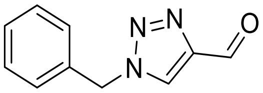
^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 136.7 (q, Ph), 129.2/ 128.6/ 128.4 (Ph), 123.3 (triazole), 55.5 (Ph-$\underline{C}H_2$), 53.2 ($\underline{C}H_2$OH).

Elemental Analysis found (Calculated for $C_{10}H_{11}N_3O$) % C 63.56 (63.48), H 5.81 (5.86), N 22.43 (22.20).

LRMS (ESI+) m/z 212.2 [M+Na]$^+$; HRMS Calculated for [M+Na]$^+$ *m/z* 212.0794, found *m/z* 212.0788.

IR *v* cm^{-1} 3237 (br, s), 1456 (w), 1220 (m), 1127 (m), 1013 (s), 838 (w), 716 (s), 690 (s), 570 (w).

1-benzyl-1H-1,2,3-triazole-4-carbaldehyde (1a)



(1-Benzyl-1H-1,2,3-triazol-4-yl)methanol (0.15 g, 0.79 mmol) was dissolved into 2-propanol, followed by addition of activated manganese dioxide (0.23 g, 2.6 mmol). The reaction mixture was heated overnight at 100 °C. After cooling down to room temperature, the suspension was filtered to remove MnO_2. The solvent was removed under reduced pressure to get crude product which was further purified by flash chromatography (DCM: MeOH =100:1) to give the 1-benzyl-1H-1,2,3-triazole-4-carbaldehyde as a white solid (0.14 g, 0.73 mmol). R_f= 0.50 (DCM: MeOH = 100:5).

Yield 0.14 g, 92 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 10.01 (1H, s, O=CH), 8.97 (1H, s, triazole), 7.42-7.32 (5H, m, Ph), 5.70 (2H, s, Ph-$C\underline{H}_2$).

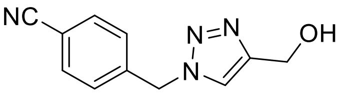
^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 185.4 (O=CH), 147.5 (q, triazole) 135.8 (q, Ph), 129.3/ 128.9/ 128.6 (Ph), 53.7 (Ph-$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{10}H_9N_3O$) % C 64.20 (64.16), H 4.69 (4.85), N 22.29 (22.44).

HRMS Calculated for $[M+Na]^+$ *m/z* 210.0638, found *m/z* 210.0633.

IR *v* cm^{-1} 3125 (w), 1691 (s), 1532 (m), 1447 (w), 1356 (w), 1236 (m), 1163 (m), 1050 (m), 876 (w), 796 (s), 764 (s), 713 (s), 699 (s), 578 (w), 461 (w).

4-((4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzonitrile



4-((4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzonitrile was synthesised using the procedure described for 1-benzyl-1H-1,2,3-triazol-4-yl)methanol, substituting 4-(azidomethyl)benzonitrile for (azidomethyl)benzene.

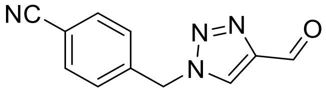
Yield 0.50 g, 90 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 8.08 (1H, s, triazole), 7.86 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 7.45 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 5.70 (2H, s, Ph-C$\underline{H}_2$), 5.18 (1H, t, $^3J_{HH}$ = 5.0 Hz, OH), 4.52 (2H, d, $^3J_{HH}$ = 5.0 Hz, C$\underline{H}_2$OH).

^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 142.2 (q, triazole), 133.2/ 129.1 (Ph), 123.7 (triazole), 119.0 (CN), 111.3 (q, Ph), 55.5 (Ph-$\underline{C}H_2$), 52.5 (CH_2OH).

LRMS (ESI+) m/z 237.2 [M+Na]$^+$, 451.3 [2M+Na]$^+$; HRMS Calculated for [M+Na]$^+$ *m/z* 237.0747, found *m/z* 237.0746.

4-((4-formyl-1H-1,2,3-triazol-1-yl)methyl)benzonitrile (1b)



1b was synthesised using the procedure described for **1a**, substituting 4-((4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzonitrile for (1-benzyl-1H-1,2,3-triazol-4-yl)methanol.

Yield 0.40 g, 88 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 10.03 (1H, s, O=CH), 9.01 (1H, s, triazole), 7.87 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 7.51 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 5.82 (2H, s, Ph-C$\underline{H}_2$).

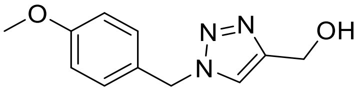
^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 185.4 (O=CH), 141.2 (q, triazole), 133.3/ 129.4 (Ph), 129.2 (triazole), 118.9 (CN), 111.6 (q, Ph), 53.0 (Ph-$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{11}H_8N_4O$) % C 61.86 (62.26), H 3.93 (3.80), N 25.79 (26.39).

LRMS (ESI+) m/z 235.2 $[M+Na]^+$; HRMS Calculated for $[M+Na]^+$ *m/z* 235.0590, found *m/z* 235.0585.

IR *v* cm^{-1} 3103 (w), 2232 (w), 1697 (s), 1534 (m), 1237 (w), 1163 (w), 1047 (w), 765 (s), 555 (s).

(1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methanol



(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)methanol was synthesised using the procedure described for 1-benzyl-1H-1,2,3-triazol-4-yl)methanol, substituting 1-(azidomethyl)-4-methoxybenzene for (azidomethyl)benzene.

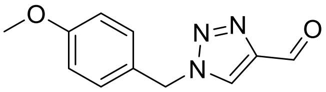
Yield 0.50 g, 85 %.

^{1}H NMR (300 MHz, 298 K, $CDCl_3$) δ_H 7.43 (1H, s, triazole), 7.27 (2H, d, $^3J_{HH}$ = 7.0 Hz, Ph), 6.92 (2H, d, $^3J_{HH}$ = 7.0 Hz, Ph), 5.47 (2H, s, Ph-C$\underline{H}_2$), 4.78 (2H, s, C$\underline{H}_2$OH), 3.83 (3H, s, OCH_3).

^{13}C {^{1}H} NMR (75 MHz, 298 K, $CDCl_3$) δ_C 129.7 (Ph), 126.4 (q, Ph), 114.5 (Ph), 56.7 (Ph-$\underline{C}H_2$), 55.4 (OCH_3), 53.8 (CH_2OH).

HRMS Calculated for $[M+Na]^+$ *m/z* 242.0900, found *m/z* 242.0898.

1-(4-methoxybenzyl)-1H-1,2,3-triazole-4-carbaldehyde (1c)



1c was synthesised using the procedure described for **1a**, substituting (1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methanol for (1-benzyl-1H-1,2,3-triazol-4-yl)methanol.

Yield 0.55 g, 87 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 10.00 (1H, s, O=CH), 8.92 (1H, s, triazole), 7.35 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 6.94 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 5.61 (2H, s, Ph-C$\underline{H}_2$), 3.74 (3H, s, OCH_3).

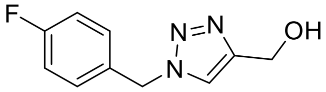
^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 185.4 (O=CH), 159.8 (q, Ph), 147.5 (q, triazole), 130.3 (Ph), 128.4 (triazole), 127.7 (q, Ph), 114.7 (Ph), 55.6 (OCH_3), 53.2 (Ph-CH_2).

Elemental Analysis found (Calculated for $C_{11}H_{11}N_3O_2$) % C 60.40 (60.82), H 4.99 (5.10), N 19.21 (19.33).

HRMS Calculated for $[M+Na]^+$ *m/z* 240.0743, found *m/z* 240.0739.

IR *v* cm^{-1} 3091 (w), 1696 (s), 1612 (w), 1514 (s), 1438 (w), 1253 (s), 1168 (m), 1029 (m), 786 (s), 552 (w).

(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methanol



1-(4-Fluorobenzyl)-1H-1,2,3-triazol-4-yl)methanol was synthesised using the procedure described for 1-benzyl-1H-1,2,3-triazol-4-yl)methanol, substituting 1-(azidomethyl)-4-fluorobenzen for (azidomethyl)benzene.

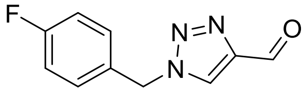
Yield 0.60 g, 92 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 8.02 (1H, s, triazole), 7.39 (2H, d, $^3J_{HH}$ = 8.0 Hz, Ph), 7.21 (2H, d, $^3J_{HH}$ = 8.0 Hz, Ph), 5.56 (2H, s, Ph-C$\underline{H}_2$), 5.16 (1H, t, $^3J_{HH}$ = 5.5 Hz, OH), 4.50 (2H, d, $^3J_{HH}$ = 5.5 Hz, C$\underline{H}_2$OH).

^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 163.9 (q, F-Ph), 160.7 (q, triazole), 133.0 (q, F-Ph), 130.8/ 130.7 (F-Ph), 123.2 (triazole), 116.2/ 115.9 (F-Ph), 55.5 (Ph-$\underline{C}H_2$), 52.4 (CH_2OH).

LRMS (ESI+) m/z 230.1 $[M+Na]^+$; HRMS Calculated for $[M+Na]^+$ *m/z* 230.0700, found *m/z* 230.0699.

1-(4-fluorobenzyl)-1H-1,2,3-triazole-4-carbaldehyde (1d)



1d was synthesised using the procedure described for **1a**, substituting ((1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methanol for (1-benzyl-1H-1,2,3-triazol-4-yl)methanol.

Yield 0.40 g, 86 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 10.01 (1H, s, O=CH), 8.96 (1H, s, triazole), 7.45 (2H, t, $^3J_{HH}$ = 8.0 Hz, Ph), 7.23 (2H, t, $^3J_{HH}$ = 8.0 Hz, Ph), 5.69 (2H, s, Ph-C$\underline{H}_2$).

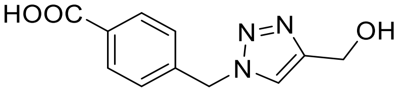
^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 185.4 (O=CH), 164.1 (q, F-Ph), 147.5 (q, triazole), 132.0 (q, F-Ph), 131.1/ 131.0 (F-Ph), 128.7 (triazole)), 116.3/ 116.0 (F-Ph), 52.9 (Ph-$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{10}H_8FN_3O$) % C 58.37 (58.54), H 3.78 (3.93), N 20.02 (20.47).

HRMS Calculated for $[M+Na]^+$ *m/z* 228.0544, found *m/z* 228.0541.

IR *v* cm^{-1} 3137 (w), 1695 (s), 1604 (m), 1508 (s), 1431 (w), 1218 (s), 1158 (m), 1045 (m), 1015 (m), 852 (m), 796 (s), 678 (w), 539 (m), 484 (m).

4-((4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzoic acid



4-((4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzoic acid was synthesised using the procedure described for 1-benzyl-1H-1,2,3-triazol-4-yl)methanol, substituting 4-azidomethyl benzoic acid for (azidomethyl)benzene.

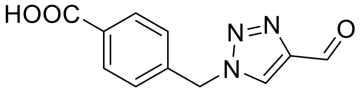
Yield 0.50 g, 87 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 13.01 (1H, s, COOH), 8.04 (1H, s, triazole), 7.94 (2H, d, $^3J_{HH}$ = 5.0 Hz, Ph), 7.40 (2H, d, $^3J_{HH}$ = 5.0 Hz, Ph), 5.67 (2H, s, Ph-C$\underline{H}_2$), 5.19 (1H, t, $^3J_{HH}$ = 5.0 Hz, OH), 4.52 (2H, d, $^3J_{HH}$ = 5.0 Hz, C$\underline{H}_2$OH).

^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 141.5 (q, triazole), 128.6 (triazole), 55.5 (Ph-$\underline{C}H_2$), 52.7 (CH$_2$OH).

LRMS (ESI+) m/z 232.0 [M-H]$^-$; HRMS Calculated for [M-H]$^-$ *m/z* 232.0728, found *m/z* 232.0725.

4-((4-formyl-1H-1,2,3-triazol-1-yl)methyl)benzoic acid (1e)



1e was synthesised using the procedure described for **1a**, substituting 4-((4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)methyl)benzoic acid for (1-benzyl-1H-1,2,3-triazol-4-yl)methanol.

Yield 0.30 g, 50 %.

^{1}H NMR (300 MHz, 298 K, DMSO) δ_H 13.09 (1H, s, COOH), 10.03 (1H, s, O=CH), 9.00 (1H, s, triazole), 7.95 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 7.44 (2H, d, $^3J_{HH}$ = 7.5 Hz, Ph), 5.80 (2H, s, Ph-C$\underline{H}_2$).

^{13}C {^{1}H} NMR (75 MHz, 298 K, DMSO) δ_C 185.4 (O=CH), 167.3 (COOH), 147.5 (q, triazole), 140.5/ 131.2 (q, Ph), 130.3 (Ph), 129.1 (triazole), 128.6 (Ph), 53.2 (Ph-$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{11}H_9N_3O_3$) % C 56.57 (57.14), H 3.77 (3.92), N 18.00 (18.17).

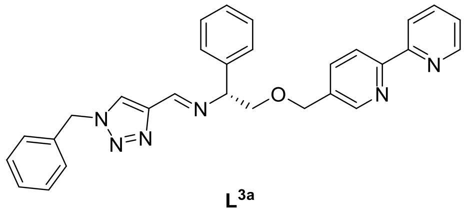
HRMS Calculated for $[M+Na]^+$ *m/z* 254.0536, found *m/z* 254.0532.

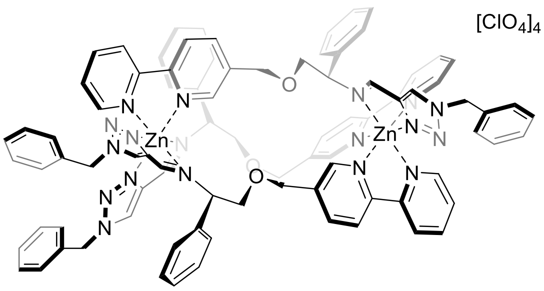
IR *v* cm^{-1} 2978 (w), 1671 (s), 1543 (m), 1423 (w), 1290 (m), 1167 (w), 1045 (w), 929 (w), 806 (m), 763 (s), 727 (s), 545 (m).

General synthesis of HHT-[$Zn_2L^n{}_3$][ClO_4]$_4$ (where n =3a-d).

$Zn(ClO_4)_2·6H_2O$ (2 equiv.) was added to a stirred solution of the desired substituted triazolyl aldehyde (3 equiv.) and (*R*)-2-(2,2'-bipyridin-5-ylmethoxy)-1-phenylethanamine (3 equiv.) in acetonitrile (20 ml) at ambient temperature for 4 h. The resulting yellow solution yielded the desired product as a white crystalline solid on the addition of ethyl acetate.

R_c,Δ_{Zn},HHT-[$Zn_2L^{\mathbf{3a}}{}_3$][ClO_4]$_4$


L^{3a}



Yield 0.29 g, 90 %

^{1}H NMR (500 MHz, 298 K, CD_3CN) δ_H ppm 9.21 (1H, s, HC=N), 9.17 (2H, s, HC=N/bpy), 9.14 (1H, s, bpy), 8.83 (1H, s, HC=N), 8.60 (1H, s, TRZ), 8.54 (1H, s, TRZ), 8.48 (1H, s, bpy), 8.45 (2H, d, $^3J_{HH}$ =8.2 Hz, bpy), 8.42 (2H, d, $^3J_{HH}$ =8.3 Hz, bpy), 8.24-7.77 (15H, m, bpy/TRZ), 7.66-7.28 (17H, m, bpy/Ph), 7.22-6.94 (10H, m, bpy/Ph), 6.89 (2H, t, $^3J_{HH}$ =7.4 Hz, Ph), 6.74 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 6.56 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 6.11 (2H, d, $^3J_{HH}$ =7.5 Hz, Ph), 5.98 (2H, d, $^3J_{HH}$ =7.5 Hz, Ph), 5.61-5.46 (6H, m, PhC$\underline{H}_2$), 5.43 (1H, dd, $^3J_{HH}$ = 11.4 Hz $^4J_{HH}$ = 3.2, C$\underline{H}$Ph), 5.26-5.10 (3H, m, C$\underline{H}_2$-bpy), 4.88 (1H, d, $^3J_{HH}$ =9.0 Hz, C$\underline{H}$Ph), 4.79 (1H, d, $^3J_{HH}$ =8.2 Hz, C$\underline{H}$Ph), 4.54-4.43 (3H, m, C$\underline{H}_2$-bpy), 4.18 (1H, t, J_{HH} =11.2 Hz, C$\underline{H}_2$-CHPh), 4.09 (1H, t, J_{HH} =10.8 Hz, C$\underline{H}_2$-CHPh), 4.03 (1H, t, J_{HH} =10.9 Hz, C$\underline{H}_2$-CHPh), 3.66 (1H, dd, $^2J_{HH}$ = 10.4 Hz $^3J_{HH}$ = 3.5, C$\underline{H}_2$-CHPh), 3.53 (1H, dd, $^2J_{HH}$ = 11.2 Hz $^3J_{HH}$ = 3.1, C$\underline{H}_2$-CHPh), 3.47 (1H, dd, $^2J_{HH}$ = 11.2 Hz $^3J_{HH}$ = 3.4, C$\underline{H}_2$-CHPh).

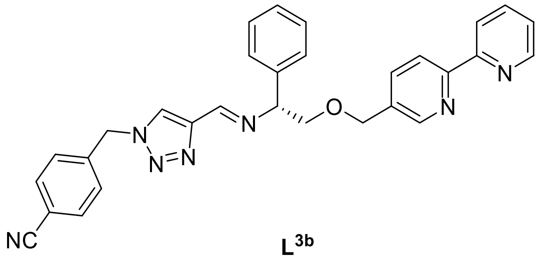
$^{13}C\{^1H\}$ NMR (125 MHz, 298 K, CD_3CN) δ_C ppm 157.1, 156.6, 156.1 (HC=N), 150.4, 150.2, 149.9 (bpy), 149.4, 149.3, 149.0, 148.7, 148.5 (q, bpy), 148.1 (bpy), 147.6 (q, bpy), 147.5 (bpy), 143.6, 143.0, 142.9, 142.1, 142.1 (bpy), 141.9, 141.8 (q, TRZ), 141.6 (bpy), 141.5 (q, TRZ), 138.0, 137.5, 137.4 (q, bpy), 135.0, 134.5, 134.4, 134.0, 133.8, 133.7 (q, Ph), 130.1, 129.7, 129.7, 129.5, 129.5, 129.5, 129.3, 129.1, 129.0, 128.8, 128.5, 128.4, 128.2 (Ph/TRZ), 127.8, 127.4, 127.3 (bpy), 127.2, 126.5, 126.4 (Ph), 123.6, 123.2, 123.1, 123.1, 122.7 (bpy), 70.0, 69.9 ($\underline{C}H_2$-bpy), 69.7 ($\underline{C}$HPh), 69.5 ($\underline{C}$HPh), 69.1 ($\underline{C}H_2$-bpy), 69.0, 68.9 ($\underline{C}H_2$-CHPh), 67.8 ($\underline{C}$HPh), 55.5, 55.3, 55.1 (Ph$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{87}H_{78}Cl_4N_{18}O_{19}Zn_2\cdot 4H_2O$) % C 51.61 (51.62), H 4.04 (4.28), N 12.39 (12.45).

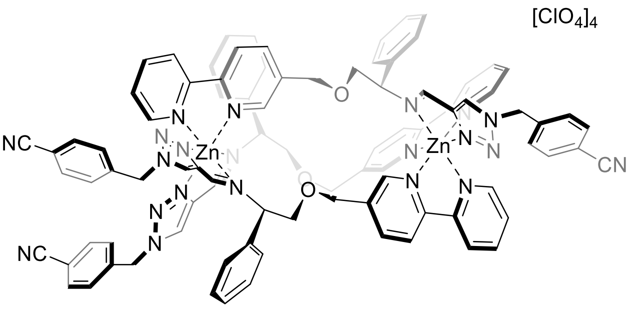
LRMS (ESI+) *m/z* 475.4 $[L+H]^+$, 497.3 $[L+Na]^+$; HRMS Calculated for $[L+H]^+$ *m/z* 475.2241, found *m/z* 475.2244.

IR *v* cm^{-1} 1603 (w), 1440 (w), 1224 (w), 1069 (s), 843 (m), 791 (m), 722 (m), 700 (m), 620 (s).

R_c,Δ_{Zn},HHT-$[Zn_2L^{\mathbf{3b}}_3][ClO_4]_4$



L^{3b}



Yield 0.28 g, 83 %

^1H NMR (500 MHz, 298 K, CD_3CN) δ_H ppm 9.24 (1H, s, HC=N), 9.21 (1H, s, HC=N), 9.18 (1H, s, bpy), 9.14 (1H, s, bpy), 8.89 (1H, s, HC=N), 8.68 (1H, s, TRZ), 8.61 (1H, s, TRZ), 8.49 (1H, s, bpy), 8.44 (2H, d, $^3J_{HH}$ =8.5 Hz, bpy), 8.42 (2H, d, $^3J_{HH}$ =8.5 Hz, bpy) 8.24-6.98 (37H, m, Ph/bpy/TRZ), 6.89 (2H, t, $^{3}J_{HH}$ =7.4 Hz, Ph), 6.75 (2H, t, $^{3}J_{HH}$ =7.7 Hz, Ph), 6.56 (2H, t, $^{3}J_{HH}$ =7.7 Hz, Ph), 6.12 (2H, d, $^{3}J_{HH}$ =7.6 Hz, Ph), 6.00 (2H, d, $^{3}J_{HH}$ =7.6 Hz, Ph), 5.72-5.55 (6H, m, $\mathrm{CNPhC\underline{H}_2}$), 5.44 (1H, dd, $^{3}J_{HH}$ = 11.3 Hz $^{4}J_{HH}$ = 3.2, $\mathrm{C\underline{H}Ph}$), 5.27-5.11 (3H, m, $\mathrm{C\underline{H}_2}$-bpy), 4.90 (1H, d, $^{3}J_{HH}$ =9.2 Hz, $\mathrm{C\underline{H}Ph}$), 4.81 (1H, d, $^{3}J_{HH}$ =8.2 Hz, $\mathrm{C\underline{H}Ph}$), 4.57-4.45 (3H, m, $\mathrm{C\underline{H}_2}$-bpy), 4.20 (1H, t, J_{HH} =11.2 Hz, $\mathrm{C\underline{H}_2}$-CHPh), 4.11 (1H, t, J_{HH} =10.8 Hz, $\mathrm{C\underline{H}_2}$-CHPh), 4.06 (1H, t, J_{HH} =10.9 Hz, $\mathrm{C\underline{H}_2}$-CHPh), 3.68 (1H, dd, $^{2}J_{HH}$ = 10.4 Hz $^{3}J_{HH}$ = 3.5, $\mathrm{C\underline{H}_2}$-CHPh), 3.54 (1H, dd, $^{2}J_{HH}$ = 11.2 Hz $^{3}J_{HH}$ = 3.0, $\mathrm{C\underline{H}_2}$-CHPh), 3.49 (1H, dd, $^{2}J_{HH}$ = 11.3 Hz $^{3}J_{HH}$ = 3.4, $\mathrm{C\underline{H}_2}$-CHPh).

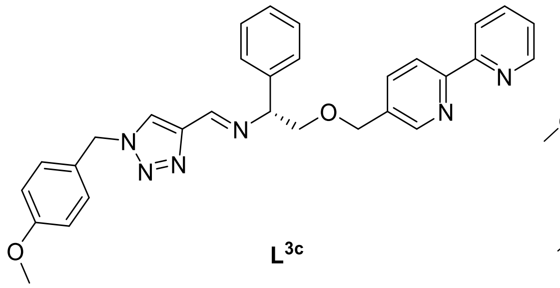
^{13}C {^{1}H} NMR (125 MHz, 298 K, CD_3CN) δ_C ppm 157.2, 156.6, 156.2 (HC=N), 150.4, 150.3, 149.9 (bpy), 149.3, 149.3, 149.0, 148.6, 148.5 (q, bpy), 148.1, 147.5 (bpy), 147.5 (q, bpy), 143.6, 143.1, 143.0, 142.1, 142.1 (bpy), 142.0, 142.0 (q, TRZ), 141.6 (bpy), 141.6 (q, TRZ), 139.6, 138.9, 138.1 (q, $\mathrm{CN\underline{Ph}}$), 137.5, 137.5, 133.9 (q, bpy), 133.8, 133.5, 133.3, 133.2 (q, Ph), 129.9, 129.2, 129.0 ($\mathrm{CN\underline{Ph}}$), 128.9, 128.9, 128.7 (Ph, TRZ), 127.9, 127.7, 127.4 (bpy), 127.3, 126.5, 126.5 (Ph), 123.6, 123.2, 123.1, 123.0, 122.6 (bpy), 118.6, 118.6, 118.5 (q, $\mathrm{CN\underline{Ph}}$), 113.1, 112.8, 112.7 (CN), 70.0, 70.0 ($\mathrm{\underline{C}H_2}$-bpy), 69.8, 69.5 ($\mathrm{\underline{C}HPh}$), 69.0 ($\mathrm{\underline{C}H_2}$-bpy), 69.0, 68.9 ($\mathrm{\underline{C}H_2}$-CHPh), 67.8 ($\mathrm{\underline{C}HPh}$), 54.7, 54.5, 54.3 (CNPh-$\mathrm{\underline{C}H_2}$).

Elemental Analysis found (Calculated for $C_{90}H_{75}Cl_4N_{21}O_{19}Zn_2\cdot 6EtOAc$) % C 53.67 (53.57), H 4.59 (4.85), N 11.54 (11.51).

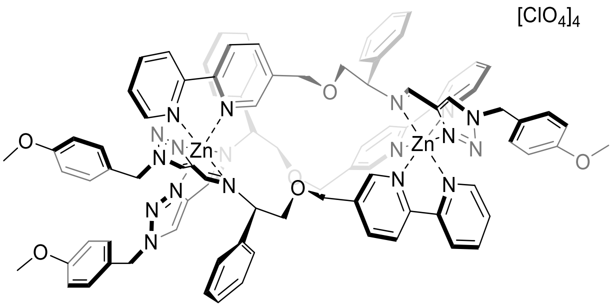
LRMS (ESI+) *m/z* 500.3 $[L+H]^+$, 522.3 $[L+Na]^+$; HRMS Calculated for $[L+H]^+$ *m/z* 500.2193, found *m/z* 500.2195.

IR *v* cm^{-1} 1602 (w), 1475 (w), 1440 (w), 1073 (s), 792 (m), 752 (m), 700 (m), 620 (s), 546 (m).

R_{c},Δ_{Zn},HHT-$[\mathrm{Zn_2L^{3c}_3}][\mathrm{ClO_4}]_4$



L^3c



Yield 0.30 g, 88 %

^{1}H NMR (500 MHz, 298 K, $\mathrm{CD_3CN}$) δ_{H} ppm 9.20 (1H, s, HC=N), 9.17 (1H, s, HC=N), 9.16 (1H, s, bpy), 9.13 (1H, s, HC=N), 8.81 (1H, s, bpy), 8.59-6.85 (55H, m, Ph/bpy/TRZ), 6.74 (2H, t, $^{3}J_{\mathrm{HH}}$ =7.7 Hz, Ph), 6.56 (2H, t, $^{3}J_{\mathrm{HH}}$ =7.7 Hz, Ph), 6.10 (2H, d, $^{3}J_{\mathrm{HH}}$ =7.6 Hz, Ph), 5.97 (2H, d, $^{3}J_{\mathrm{HH}}$ =7.6 Hz, Ph), 5.58-5.38 (7H, m, $\mathrm{PhCH_2}$ overlapping with CHPh), 5.23-5.02 (3H, m, $\mathrm{CH_2}$-bpy), 4.88 (1H, d, $^{3}J_{\mathrm{HH}}$ = 9.1 Hz CHPh), 4.78 (1H, d, $^{3}J_{\mathrm{HH}}$ =7.9 Hz, CHPh), 4.56-4.41 (3H, m, $\mathrm{CH_2}$-bpy), 4.18 (1H, t, $^{3}J_{\mathrm{HH}}$ =11.2 Hz, $\mathrm{CH_2}$-CHPh), 4.08 (1H, t, $^{3}J_{\mathrm{HH}}$ =10.8 Hz, $\mathrm{CH_2}$-CHPh), 4.04 (1H, t, $^{3}J_{\mathrm{HH}}$ =10.9 Hz, $\mathrm{CH_2}$-CHPh), 3.87 (3H, s, $\mathrm{OCH_3}$), 3.85 (3H, s, $\mathrm{OCH_3}$), 3.79 (3H, s, $\mathrm{OCH_3}$), 3.66 (1H, dd, $^{2}J_{\mathrm{HH}}$ = 10.4 Hz $^{3}J_{\mathrm{HH}}$ = 3.5, $\mathrm{CH_2}$-CHPh), 3.52 (1H, dd, $^{2}J_{\mathrm{HH}}$ = 11.1 Hz $^{3}J_{\mathrm{HH}}$ = 3.0, $\mathrm{CH_2}$-CHPh), 3.46 (1H, dd, $^{2}J_{\mathrm{HH}}$ = 11.2 Hz $^{3}J_{\mathrm{HH}}$ = 3.4, $\mathrm{CH_2}$-CHPh).

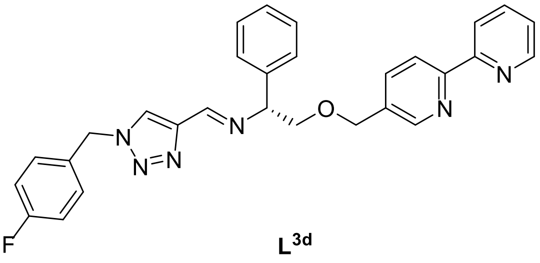
^{13}C {^{1}H} NMR (125 MHz, 298 K, $\mathrm{CD_3CN}$) δ_{C} ppm 160.9, 160.6, 160.5 (q, $\mathrm{PhOCH_3}$), 157.1, 156.6, 156.0 (HC=N), 150.4, 150.2, 149.9 (bpy), 149.4, 149.2, 149.1, 148.7, 148.5 (q, bpy), 148.1, 148.1 (bpy), 147.6 (q, bpy), 147.5 (bpy), 143.6, 143.0, 142.9, 142.3, 142.1, 142.0 (bpy), 141.9, 141.7 (q, TRZ), 141.6 (bpy), 141.5 (q, TRZ), 137.9, 137.5, 137.4 (q, bpy), 135.0, 134.0, 133.8 (q, Ph), 131.2, 130.3, 130.2, 130.1 ($\mathrm{PhOCH_3}$), 129.8, 129.4, 129.2, 129.1, 129.0, 128.9, 128.8, 128.2 (Ph/TRZ), 127.8, 127.4, 127.3 (bpy), 127.2, 126.5, 126.4 (Ph), 126.3, 126.2, 125.5 (q, $\mathrm{PhOCH_3}$), 123.6, 123.3, 123.1, 123.1, 122.7 (bpy), 114.9, 114.8, 114.7 ($\mathrm{PhOCH_3}$), 70.0, 69.9 ($\underline{C}H_2$-bpy), 69.7 ($\underline{C}$HPh), 69.4 ($\underline{C}$HPh), 69.1 ($\underline{C}H_2$-bpy), 69.0, 68.9, 68.9 ($\underline{C}H_2$-CHPh), 67.7 ($\underline{C}$HPh), 55.6, 55.5, 55.5 (OCH_3), 55.0, 54.9, 54.7 (Anisole-$\underline{C}H_2$).

Elemental Analysis found (Calculated for $C_{90}H_{84}Cl_4N_{18}O_{22}Zn_2 \cdot 8H_2O$) % C 49.38 (49.44), H 4.02 (4.61), N 11.06 (11.53).

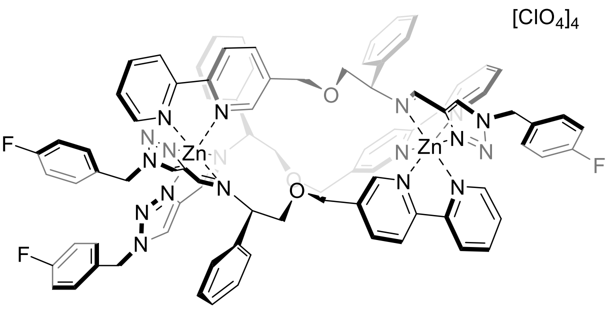
LRMS (ESI+) *m/z* 505.3 $[L+H]^+$, 527.3 $[L+Na]^+$; HRMS Calculated for $[L+H]^+$ *m/z* 505.2347, found *m/z* 505.2346.

IR *v* cm^{-1} 1604 (w), 1513 (w), 1440 (w), 1249 (w), 1070 (s), 791 (w), 750 (m), 700 (m), 620 (s).

$R_\mathrm{c},\Delta_\mathrm{Zn}$,HHT-$[\mathrm{Zn_2}\mathbf{L}^{\mathbf{3d}}_3][\mathrm{ClO_4}]_4$



L^{3d}



Yield 0.31 g, 92 %

^{1}H NMR (500 MHz, 298 K, CD_3CN) δ_H ppm 9.22 (1H, s, HC=N), 9.18 (1H, s, HC=N), 9.17 (1H, s, bpy), 9.13 (1H, s, bpy), 8.85 (1H, s, HC=N), 8.68 (1H, s, TRZ), 8.61 (1H, s, TRZ), 8.54 (1H, s, bpy), 8.50-6.98 (36H, m, Ph/bpy/TRZ), 6.89 (1H, t, $^3J_{HH}$ =7.4 Hz, Ph), 6.74 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 6.56 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 6.11 (2H, d, $^3J_{HH}$ =7.6 Hz, Ph), 5.98 (2H, d, $^3J_{HH}$ =7.6 Hz, Ph), 5.63-5.40 (7H, m, F-PhC$\underline{H}_2$ overlapping with C$\underline{H}$Ph), 5.26-5.12 (3H, m, C$\underline{H}_2$-bpy), 4.88 (1H, d, $^3J_{HH}$ =9.1 Hz, C$\underline{H}$Ph), 4.79 (1H, d, $^3J_{HH}$ =8.1 Hz, C$\underline{H}$Ph), 4.56-4.43 (3H, m, C$\underline{H}_2$-bpy), 4.19 (1H, t, $^3J_{HH}$ =11.2 Hz, C$\underline{H}_2$-CHPh), 4.10 (1H, t, $^3J_{HH}$ =10.8 Hz, C$\underline{H}_2$-CHPh), 4.04 (1H, t, $^3J_{HH}$ =10.9 Hz, C$\underline{H}_2$-CHPh), 3.67 (1H, dd, $^2J_{HH}$ = 10.4 Hz $^3J_{HH}$ = 3.5, C$\underline{H}_2$-CHPh), 3.53 (1H, dd, $^2J_{HH}$ = 11.2 Hz $^3J_{HH}$ = 3.1, C$\underline{H}_2$-CHPh), 3.47 (1H, dd, $^2J_{HH}$ = 11.2 Hz $^3J_{HH}$ = 3.4, C$\underline{H}_2$-CHPh).

^{13}C {^{1}H} NMR (125 MHz, 298 K, CD_3CN) δ_C ppm 164.5, 164.2, 164.1, 162.5, 162.3, 162.2 (q, F-$\underline{\text{Ph}}$), 157.2, 156.6, 156.1 (HC=N), 150.4, 150.2, 149.9 (bpy), 149.3, 149.3, 149.0, 148.6, 148.5 (q, bpy), 148.1 (bpy), 147.6 (q, bpy), 147.5 (bpy), 143.6, 143.0, 142.9, 142.1, 142.1 (bpy), 141.9, 141.8 (q, TRZ), 141.6 (bpy), 141.5 (q, TRZ), 138.0, 137.5, 137.4 (q, bpy), 135.0, 134.0, 133.8 (q, Ph), 131.8, 131.8, 130.8, 130.7, 130.7 (F-$\underline{\text{Ph}}$), 130.5, 130.5 (q, F-$\underline{\text{Ph}}$), 130.1 (TRZ), 129.9 (q, F-$\underline{\text{Ph}}$), 129.7 (TRZ), 129.3, 129.1, 129.0, 128.9, 128.8 (Ph), 128.5 (TRZ), 127.8, 127.4, 127.3 (bpy), 127.2, 126.5, 126.4 (Ph), 123.6, 123.2, 123.1, 123.1, 122.6 (bpy), 116.5, 116.3, 116.3, 116.3, 116.2, 116.1 (F-$\underline{\text{Ph}}$), 70.0, 70.0 ($\underline{\text{C}}H_2$-bpy), 69.7 ($\underline{\text{C}}$HPh), 69. 5 ($\underline{\text{C}}$HPh), 69.1 ($\underline{\text{C}}H_2$-bpy), 69.0, 68.9 ($\underline{\text{C}}H_2$-CHPh), 67.8 ($\underline{\text{C}}$HPh), 54.6, 54.5, 54.3 (PhF-CH_2).

Elemental Analysis found (Calculated for $C_{87}H_{75}Cl_4F_3N_{18}O_{19}Zn_2 \cdot 6H_2O$) % C 49.52 (49.42), H 3.61 (4.15), N 11.58 (11.92).

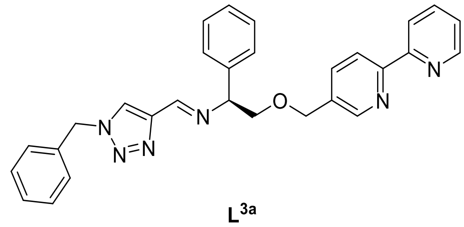
LRMS (ESI+) *m/z* 493.3 $[L+H]^+$, 515.3 $[L+Na]^+$; HRMS Calculated for $[L+H]^+$ *m/z* 493.2147, found *m/z* 493.2146.

IR *v* cm^{-1} 1603 (w), 1510 (w), 1475 (w), 1440 (w), 1224 (w), 1071 (s), 841 (m), 791 (m), 750 (m), 700 (m), 620 (s).

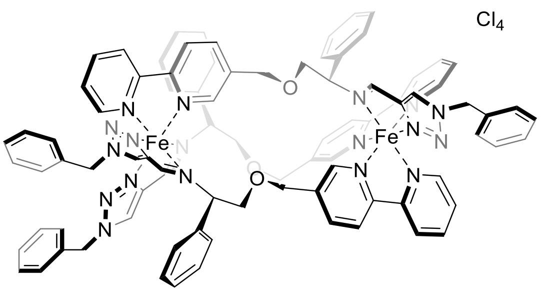
General synthesis of HHT-$[Fe_2L^{n}{}_3]Cl_4$ (where n =3a-e).

Iron(II) chloride anhydrous (2 equvi.) was added to a stirred solution of the desired substituted triazolyl aldehyde (3 equvi.) and (*S*)-2-(2,2'-bipyridin-5-ylmethoxy)-1-phenylethanamine (3 equvi.) in methanol (20 ml) at ambient temperature to give an dark orange solution that was then heated to reflux for 48 h. The reaction mixture was cooling to room temperature, filtered through a celite plug prior to the solvents being removed *in vacuo* to yield the desired product as a dark orange solid.

S_{C},Λ_{Fe},HHT-$[Fe_2L^{3a}{}_3]Cl_4$



L3a



Yield 0.58 g, 81 %

^{1}H NMR (500 MHz, 298 K, CD_3OD) δ_H ppm 9.65 (1H, s, HC=N), 9.47 (1H, s, HC=N), 9.39 (1H, s, bpy), 9.30 (1H, s, bpy), 9.20 (1H, s, HC=N), 9.19 (1H, s, TRZ), 9.01 (1H, s, TRZ), 8.75-8.56 (5H, m, bpy), 8.35 (1H, s, TRZ), 8.26-7.89 (13H, m, bpy), 7.78-7.74 (2H, m, bpy), 7.50-6.93 (42H, m, Ph/bpy), 6.78 (2H, t, $^{3}J_{HH}$ =7.6 Hz, Ph), 6.60 (2H, t, $^{3}J_{HH}$ =7.7 Hz, Ph), 5.90 (1H, s, Ph), 5.68 (2H, s, $\mathrm{PhC\underline{H}_2}$), 5.64-5.50 (4H, m, $\mathrm{PhC\underline{H}_2}$), 5.34 (1H, dt, $^{3}J_{HH}$=15.1, 7.4 Hz, $\mathrm{C\underline{H}Ph}$), 5.25 (2H, d, $^{2}J_{HH}$=13.0 Hz, $\mathrm{C\underline{H}_2}$-bpy), 5.14 (1H, d, $^{2}J_{HH}$=18.1 Hz, $\mathrm{C\underline{H}_2}$-bpy), 4.78 (1H, d, $^{3}J_{HH}$=11.3 Hz, $\mathrm{C\underline{H}Ph}$), 4.60-4.48 (6H, m, $\mathrm{C\underline{H}Ph}$/ $\mathrm{C\underline{H}_2}$-bpy), 4.28 (1H, t, $^{3}J_{HH}$=11.0 Hz), 3.54-3.51 (3H, m, $\mathrm{C\underline{H}_2}$-CHPh), 3.43-3.41 (1H, m, $\mathrm{C\underline{H}_2}$-CHPh), 3.37 (1H, $\mathrm{C\underline{H}_2}$-CHPh overlap with CD_3OD).

^{13}C {^{1}H} NMR (125 MHz, 298 K, CD_3OD) δ_C ppm 163.4, 163.1, 162.6 (HC=N), 160.1, 159.9, 159.3, 159.2, 158.5, 158.4 (q, bpy), 157.9, 157.2, 155.8, 154.3, 154.0, 153.3 (bpy), 149.5, 149.5, 149.4 (q, TRZ), 139.9, 139.8, 139.5, 138.7, 138.5, 138.3, 137.7 (bpy), 137.4, 136.8, 136.8 (q, bpy), 134.4, 134.2, 134.1, 134.0, 133.4, 132.9, 132.5 (q, Ph), 130.2 (TRZ), 129.3, 129.2, 129.0 (Ph), 129.0 (TRZ), 128.9, 128.9, 128.8, 128.7, 128.6 (Ph), 128.3 (TRZ), 127.9, 127.5, 127.3, 127.2, 127.2, 127.2 (Ph), 126.9, 126.3, 125.8, 125. 6, 123. 5, 123.0, 122.7, 122.5, 122.4, 121.6 (bpy), 72.9, 72.6 ($\underline{C}$HPh), 71.3 ($\underline{C}H_2$-bpy), 70.8 ($\underline{C}$HPh), 69.1, 69.1 ($\underline{C}H_2$-bpy), 68.7, 68.5, 68.5 ($\underline{C}H_2$-CHPh), 55.6, 55.5, 55.2 (Ph$\underline{C}H_2$).

HRMS Calculated for $[Fe_2L_3]^{4+}$ m/z 383.8803, found m/z 383.8799

Elemental Analysis found (Calculated for $C_{87}H_{78}Cl_4Fe_2N_{18}O_3\cdot 13H_2O\cdot$EtOAc) % C 54.44 (54.66), H 5.12 (5.65), N 12.31 (12.61).

IR *ν* cm^{-1} 3371 (br, s), 3028 (br, s), 1603 (m), 1468 (m), 1359 (w), 1076 (s), 1010 (w), 933 (w), 697 (s).

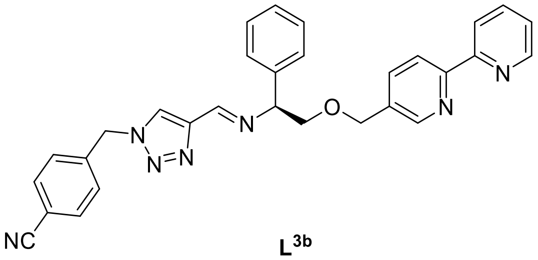
R_C,Δ_{Fe},HHT-[$Fe_2L^{3a}{}_3$]Cl_4

Data as for *S*-enantiomer

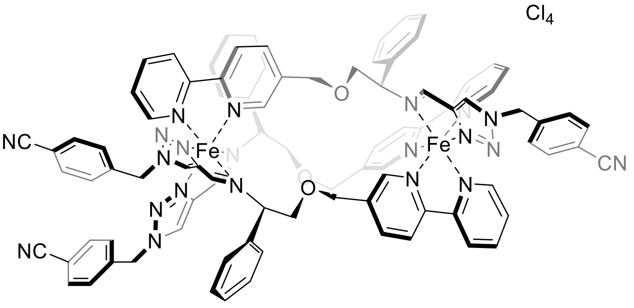
Yield 0.57 g, 79 %

Elemental Analysis found (Calculated for $C_{87}H_{78}Cl_4Fe_2N_{18}O_3\cdot 13H_2O\cdot$EtOAc) % C 54.20 (54.66), H 5.17 (5.65), N 12.24 (12.61).

S_{C},Λ_{Fe},HHT-[$Fe_2L^{3b}_3$]Cl_4



L^{3b}



Yield 0.65 g, 88 %

^{1}H NMR (500 MHz, 298 K, CD_3OD) δ_H 9.69 (1H, s, HC=N), 9.54 (1H, s, HC=N), 9.40 (1H, s, bpy), 9.31 (1H, s, bpy), 9.30 (1H, s, HC=N), 9.29 (1H, s, TRZ), 9.12 (1H, s, TRZ), 8.76-6.93 (42H, m, Ph/TRZ/bpy), 6.79 (2H, t, $^{3}J_{HH}$ =7.6 Hz, Ph), 6.61 (2H, t, $^{3}J_{HH}$ =7.6 Hz, Ph), 5.93 (1H, brs, Ph), 5.82-5.65 (6H, m, CNPhC$\underline{H}_2$), 5.42-5.32 (1H, m, C$\underline{H}$Ph), 5.28 (2H, d, $^{2}J_{HH}$=12.7 Hz, C$\underline{H}_2$-bpy), 5.18 (1H, d, $^{2}J_{HH}$=12.9 Hz, C$\underline{H}_2$-bpy), 4.79 (1H, d, $^{3}J_{HH}$=12.9 Hz, C$\underline{H}$Ph), 4.68-4.35 (8H, m, C$\underline{H}$Ph/C$\underline{H}_2$-bpy), 3.86-3.61 (3H, m, C$\underline{H}_2$-CHPh), 3.57-3.54 (1H, m, C$\underline{H}_2$-CHPh), 3.43 (1H, d, $^{3}J_{HH}$=8.6 Hz, C$\underline{H}_2$-CHPh), 3.37 (1H, C$\underline{H}_2$-CHPh overlap with CD_3OD).

^{13}C {^{1}H} NMR (125 MHz, 298 K, CD_3OD) δ_C ppm 163.5, 163.3, 162.8 (HC=N), 160.1, 159.8, 159.2, 159.1 (q, bpy), 158.4, 158.4, 158.3, 157.9, 157.3, 155.8, 154.4, 154.1, 153.9, 153.7, 153.3 (bpy), 149.8, 149.6, 149.5 (q, TRZ), 140.0, 139.9, 139.6 (bpy), 139.4, 139.2 (q, bpy), 138.7, 138.7, 138.5 (bpy), 138.4 (q, bpy), 137.8 (bpy), 137.5, 137.0, 136.8 (q, bpy), 134.5, 134.2 (q, Ph), 132.8, 132.8, 132.6, 132.5, 132.4 (CN$\underline{Ph}$), 130.7 (TRZ), 129.4, 129.3 (Ph), 129.0 (TRZ), 128.9, 128.7, 128.6, 128.4 (Ph), 128.4 (TRZ), 128.3, 127.3, 127.2, 127.2, 127.2, 126.9 (Ph), 126.4, 125.9, 125.6, 123.9, 123.7, 123.6, 123.5, 123.0, 122.7, 122.5, 122.4, 121.5 (bpy), 117.8, 117.7, 117.6 (q, CNPh), 112.8, 112.6, 112.3 (CN), 73.0 ($\underline{C}$HPh), 72.6 ($\underline{C}$HPh), 71.4 ($\underline{C}H_2$-bpy), 70.9 ($\underline{C}$HPh), 69.2, 69.0 ($\underline{C}H_2$-bpy), 68.7, 68.6, 68.5 ($\underline{C}H_2$-CHPh), 54.8, 54.6, 54.4 (Benzonitrile-$\underline{C}H_2$).

HRMS Calculated for $[Fe_2L_3]^{4+}$ m/z 402.6267, found m/z 402.6248

Elemental Analysis found (Calculated for $C_{90}H_{75}Cl_4Fe_2N_{21}O_3 \cdot 12H_2O \cdot 3EtOAc$) % C 54.81 (54.87), H 4.79 (5.55), N 13.26 (13.17).

IR *v* cm^{-1} 3394 (br, s), 3028 (br, s), 1603 (m), 1467 (m), 1078 (s), 934 (w), 790 (s), 755 (s), 698 (s).

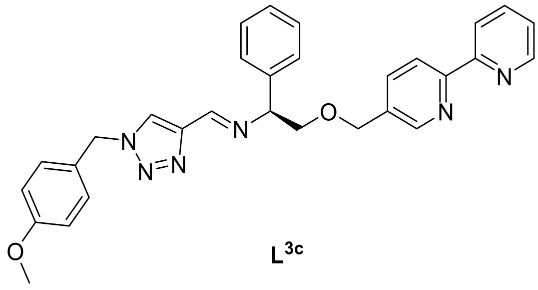
R_C,Δ_{Fe},HHT-[$Fe_2L^{3b}{}_3$]Cl_4

Data as for *S*-enantiomer

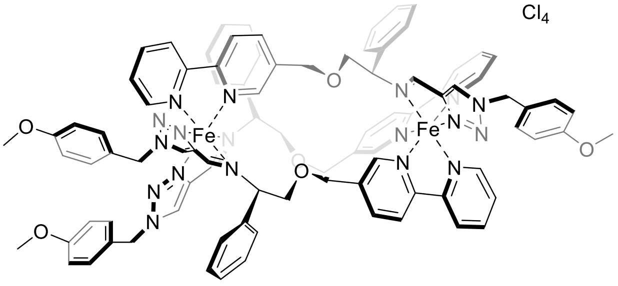
Yield 0.59 g, 80 %

Elemental Analysis found (Calculated for $C_{90}H_{75}Cl_4Fe_2N_{21}O_3 \cdot 11H_2O \cdot MeOH \cdot 2EtOAc$) % C 55.44 (55.09), H 4.73 (5.46), N 13.36 (13.63).

S_C,Λ_{Fe},HHT-[$Fe_2L^{3c}{}_3$]Cl_4



L^{3c}



Yield 0.42 g, 83 %

^{1}H NMR (500 MHz, 298 K, CD_3OD) δ_H ppm 9.65 (1H, s, HC=N), 9.47 (1H, s, HC=N), 9.39 (1H, s, bpy), 9.30 (1H, s, bpy), 9.19 (1H, s, HC=N), 9.12 (1H, s, TRZ), 8.96 (1H, s, TRZ), 8.85-8.51 (7H, m, bpy), 8.26 (1H, s, TRZ), 8.25-7.73 (18H, m, TRZ/bpy), 7.57-6.82 (50H, m, Ph/bpy), 6.78 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 6.60 (2H, t, $^3J_{HH}$ =7.7 Hz, Ph), 5.90 (1H, brs, Ph), 5.68-

5.42 (6H, m, $\mathrm{C\underline{H}_2PhOCH_3}$), 5.34 (1H, dd, $^3J_{HH}$=11.3, $^4J_{HH}$=3.7 Hz, $\mathrm{C\underline{H}Ph}$), 5.25 (2H, d, $^2J_{HH}$=11.9 Hz, $\mathrm{C\underline{H}_2}$-bpy), 5.16 (1H, d, $^2J_{HH}$=13.0 Hz, $\mathrm{C\underline{H}_2}$-bpy), 4.77 (1H, d, $^3J_{HH}$=8.6 Hz, $\mathrm{C\underline{H}Ph}$), 4.68-4.42 (6H, m, $\mathrm{C\underline{H}Ph}$ / $\mathrm{C\underline{H}_2}$-bpy), 4.29 (1H, t, $^3J_{HH}$=10.9 Hz $\mathrm{C\underline{H}_2}$-CHPh), 3.90-3.61 (9H, m, $\mathrm{OCH_3}$/ $\mathrm{C\underline{H}_2}$-CHPh), 3.56-3.49 (1H, m, $\mathrm{C\underline{H}_2}$-CHPh), 3.44-3.39 (1H, m, $\mathrm{C\underline{H}_2}$-CHPh), 3.37 (1H, $\mathrm{C\underline{H}_2}$-CHPh overlap with $\mathrm{CD_3OD}$).

^{13}C {^{1}H} NMR (125 MHz, 298 K, $\mathrm{CD_3OD}$) δ_C ppm 163.4, 163.1, 162.5 (HC=N), 160.7, 160.4, 160.3 (q, $\mathrm{\underline{Ph}OCH_3}$), 160.1, 159.9, 159.3, 159.2, 158.5, 158.4 (q, bpy), 157.9, 157.3, 155.7, 154.3, 154.0, 153.3 (bpy), 149.4, 149.4, 149.3 (q, TRZ), 139.9, 139.8, 139.5, 138.7, 138.5, 138.3, 137.7 (bpy), 137.4, 136.8 (q, bpy), 134.4, 132.9, 132.5 (q, Ph), 130.6, 129.6, 129.3, 129.0, 129.0, 128.7, 128.6, 128.3, 128.3, 127.3, 127.2, 127.2, 127.2 (TRZ/ $\mathrm{PhOCH_3}$/ Ph), 126.3 (bpy), 126.0 (q, $\mathrm{\underline{Ph}OCH_3}$), 125.8 (bpy), 125.7 (q, $\mathrm{\underline{Ph}OCH_3}$), 125.6 (bpy), 125.2 (q, $\mathrm{\underline{Ph}OCH_3}$), 123.9, 123.7, 123.5, 123.0, 122.7, 122.5, 122.4, 121.5 (bpy), 114.2, 114.1, 114.0 ($\mathrm{\underline{Ph}OCH_3}$), 72.9 ($\mathrm{\underline{C}HPh}$), 72.6 ($\mathrm{\underline{C}HPh}$), 71.5 ($\mathrm{\underline{C}H_2}$-bpy), 70.8 ($\mathrm{\underline{C}HPh}$), 69.1, 68.9 ($\mathrm{\underline{C}H_2}$-bpy), 68.8, 68.5, ($\mathrm{\underline{C}H_2}$-CHPh), 55.3, 55.1, 54.9 (Anisole-$\mathrm{\underline{C}H_2}$), 54.6, 54.5, 54.4 ($\mathrm{OCH_3}$).

HRMS Calculated for $[\mathrm{Fe_2L_3}]^{4+}$ m/z 406.3882, found m/z 406.3886

Elemental Analysis found (Calculated for $\mathrm{C_{90}H_{84}Cl_4Fe_2N_{18}O_6 \cdot 14H_2O \cdot EtOAc}$) % C 53.31 (53.57), H 5.01 (5.74), N 11.75 (11.96).

IR ν cm^{-1} 3375 (br, s), 3026 (br, s), 1604 (m), 1512 (m), 1466 (m), 1246 (m), 1076 (s), 1023 (s), 755 (s), 697 (s).

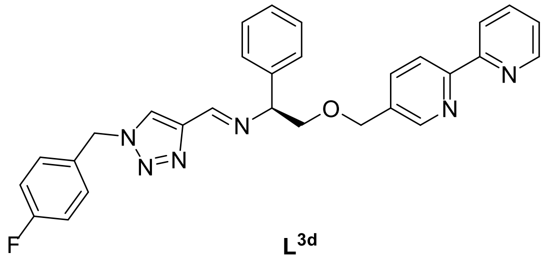
R_C,Δ_{Fe},HHT-$[\mathrm{Fe_2L^{3c}_3}]\mathrm{Cl_4}$

Data as for *S*-enantiomer

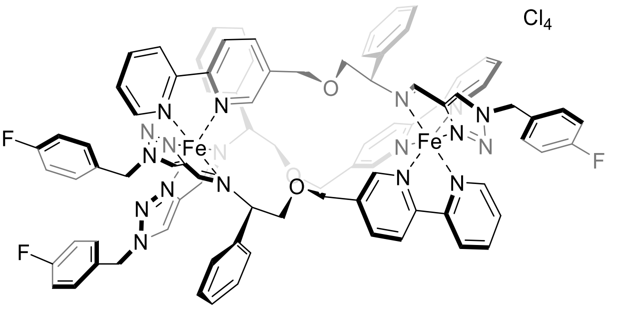
Yield 0.44 g, 87 %

Elemental Analysis found (Calculated for $C_{90}H_{84}Cl_4Fe_2N_{18}O_6 \cdot 14H_2O \cdot EtOAc$) % C 53.46 (53.57), H 5.03 (5.74), N 11.52 (11.96).

S_{C},Λ_{Fe},HHT-$[Fe_2L^{3d}_3]Cl_4$



L^{3d}



Yield 0.38 g, 78 %

^{1}H NMR (500 MHz, 298 K, CD_3OD) δ_H ppm 9.67 (1H, s, HC=N), 9.50 (1H, s, HC=N), 9.38 (1H, s, bpy), 9.30 (1H, s, bpy), 9.23 (1H, s, HC=N), 9.20 (1H, s, TRZ), 9.03 (1H, s, TRZ), 8.79-8.52 (7H, m, bpy), 8.34 (1H, s, TRZ), 8.29-7.72 (18H, m, bpy), 7.55-6.85 (50H, m, Ph/F-Ph/bpy), 6.78 (2H, t, $^3J_{HH}$ =7.6 Hz, Ph), 6.60 (2H, t, $^3J_{HH}$ =7.6 Hz, Ph), 6.19-5.82 (4H, m, Ph), 5.73-5.46 (6H, m, F-PhC$\underline{H}_2$), 5.35 (1H, dd, $^3J_{HH}$=11.4, $^4J_{HH}$=3.5 Hz, C$\underline{H}$Ph), 5.25 (2H, d, $^2J_{HH}$=13.1 Hz, C$\underline{H}_2$-bpy), 5.16 (1H, d, $^3J_{HH}$=13.0 Hz, C$\underline{H}_2$-bpy), 4.77 (1H, d, $^3J_{HH}$=8.8 Hz, C$\underline{H}$Ph), 4.67-4.43 (6H, m, C$\underline{H}$Ph/ C$\underline{H}_2$-bpy), 4.30 (1H, t, $^3J_{HH}$=11.0 Hz $\underline{C}H_2$-CHPh), 3.88-3.63 (3H, m, $\underline{C}H_2$-CHPh)3.54 (1H, dd, $^3J_{HH}$=10.4, 3.6 Hz $\underline{C}H_2$-CHPh), 3.42 (1H, d, $^3J_{HH}$=8.4 Hz $\underline{C}H_2$-CHPh), 3.37 (1H, $\underline{C}H_2$-CHPh overlap with CD_3OD).

^{13}C {^{1}H} NMR (125 MHz, 298 K, CD_3OD) δ_C ppm 164.3, 164.0, 163.9 (q, F-Ph), 163.4, 163.2, 162.6 (HC=N), 162.3, 162.1, 161.9 (q, F-Ph), 160.1, 159.8, 159.3, 159.1, 158.5, 158.4 (q, bpy), 157.9, 157.3, 155.7, 154.3, 154.0, 153.3 (bpy), 149.6, 149.5, 149.4 (q, TRZ), 139.9, 139.8, 139.5, 138.7, 138.5, 138.3, 137.7 (bpy), 137.4, 136.9, 136.8 (q, bpy), 134.4, 132.9, 132.5 (q, Ph), 131.2, 131.1, 130.4, 130.3, 130.0, 129.9 (F-Ph), 129.3, 129.0, 129.0, 128.9, 128.8, 128.7, 128.6, 128.6, 128.3, 127.3, 127.2, 127.2, 127.2, 126.9 (TRZ/ Ph), 126.3, 125.8, 125.6, 123.5, 123.0, 122.7, 122.5, 122.4, 121.5 (bpy), 115.8, 115.7, 115.6, 115.5, 115.5, 115.3 (F-Ph), 72.9 (CHPh), 72.6 (CHPh), 71.3 (CH_2-bpy), 70.8 (CHPh), 69.1, 69.0 (CH_2-bpy), 68.7, 68.5, 68.5 (CH_2-CHPh), 54.8, 54.6, 54.4 (PhF-CH_2).

HRMS Calculated for $[Fe_2L_3]^{4+}$ m/z 397.3732, found m/z 397.3726

Elemental Analysis found (Calculated for $C_{87}H_{75}Cl_4F_3Fe_2N_{18}O_3 \cdot 13H_2O \cdot EtOAc$) % C 53.23 (53.23), H 4.91 (5.35), N 11.98 (12.28).

IR *v* cm^{-1} 3374 (br, s), 3026 (br, s), 1602 (m), 1509 (m), 1468 (m), 1220 (m), 1077 (s), 1009 (m), 753 (s), 697 (s).

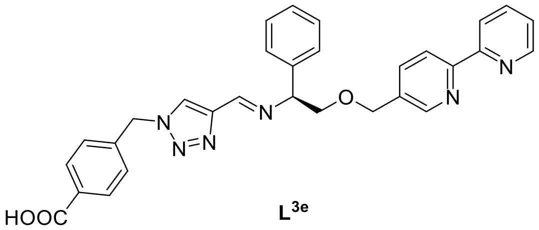
R_c,Δ_{Fe},HHT-$[Fe_2L^{3d}_3]Cl_4$

Data as for *S*-enantiomer

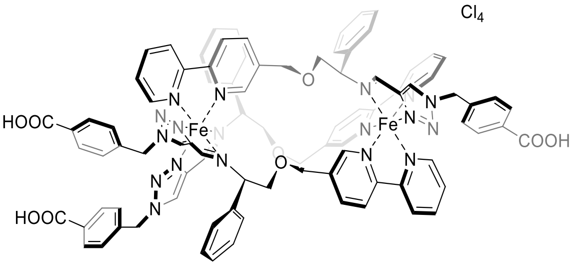
Yield 0.36 g, 75 %

Elemental Analysis found (Calculated for $C_{87}H_{75}Cl_4F_3Fe_2N_{18}O_3 \cdot 13H_2O \cdot 2EtOAc$) % C 53.45 (53.28), H 4.69 (5.51), N 11.75 (11.77).

S_c,Λ_{Fe},HHT-$[Fe_2L^{3e}_3]Cl_4$



L^{3e}



Yield 0.44 g, 86 %

$^{13}C\ \{^1H\}$ NMR (125 MHz, 298 K, CD_3OD) δ_C ppm 163.4, 163.2, 162.6 (HC=N), 160.1, 159.8, 159.3, 159.2, 159.0, 158.5, 158.4, 158.3, 158.2, 157.9 (bpy), 157.3 (bpy), 155.8 (bpy), 154.4, 153.9, 153.7, 153.3, 153.1, 152.5, 151.9, 149.6 (q, TRZ), 149.6 (q, TRZ), 149.5 (q, TRZ), 139.9, 139.8, 139.6, 138.7, 138.5, 138.3, 138.3, 138.0, 137.8, 137.5, 136.9, 136.8, 134.4, 134.0, 134.0, 133.9, 132.8, 132.5, 130.0 (TRZ), 129.3, 129.3, 129.3, 129.0 (TRZ), 129.0, 128.7, 128.6, 128.3 (TRZ), 127.7, 127.6, 127.4, 127.2, 127.2, 127.2, 126.4, 125.9, 125.6, 123.9, 123.7, 123.6, 123.5, 123.0, 122.7, 122.5, 121.5 (Ar), 73.0 ($\underline{C}$HPh), 72.6 ($\underline{C}$HPh), 71.3 ($\underline{C}H_2$-bpy), 70.8 ($\underline{C}$HPh), 69.2, 69.1 ($\underline{C}H_2$-bpy), 69.0, 68.7, 68.5 ($\underline{C}H_2$-CHPh), 55.0, 55.0, 54.7 (Ph-$\underline{C}H_2$).

HRMS Calculated for $[Fe_2L_3]^{4+}$ m/z 416.8727, found m/z 416.8725

Elemental Analysis found (Calculated for $C_{90}H_{78}Cl_4Fe_2N_{18}O_9\cdot15H_2O\cdot2EtOAc$) % C 52.05 (52.18), H 4.76 (5.54), N 11.13 (11.18).

IR *v* cm^{-1} 3371 (br, s), 2851 (br, s), 1694 (m), 1591 (m), 1525 (m), 1467 (m), 1401 (s), 1077 (s), 753 (s), 698 (s).

$\boldsymbol{R_C,\Delta_{Fe}}$,HHT-$[Fe_2L^{3e}{}_3]Cl_4$

Data as for *S*-enantiomer

Yield 0.42 g, 82 %

Elemental Analysis found (Calculated for $C_{90}H_{78}Cl_4Fe_2N_{18}O_9\cdot16H_2O\cdot EtOAc$) % C 51.49 (51.66), H 4.69 (5.44), N 11.35 (11.54).

2. NMR spectra

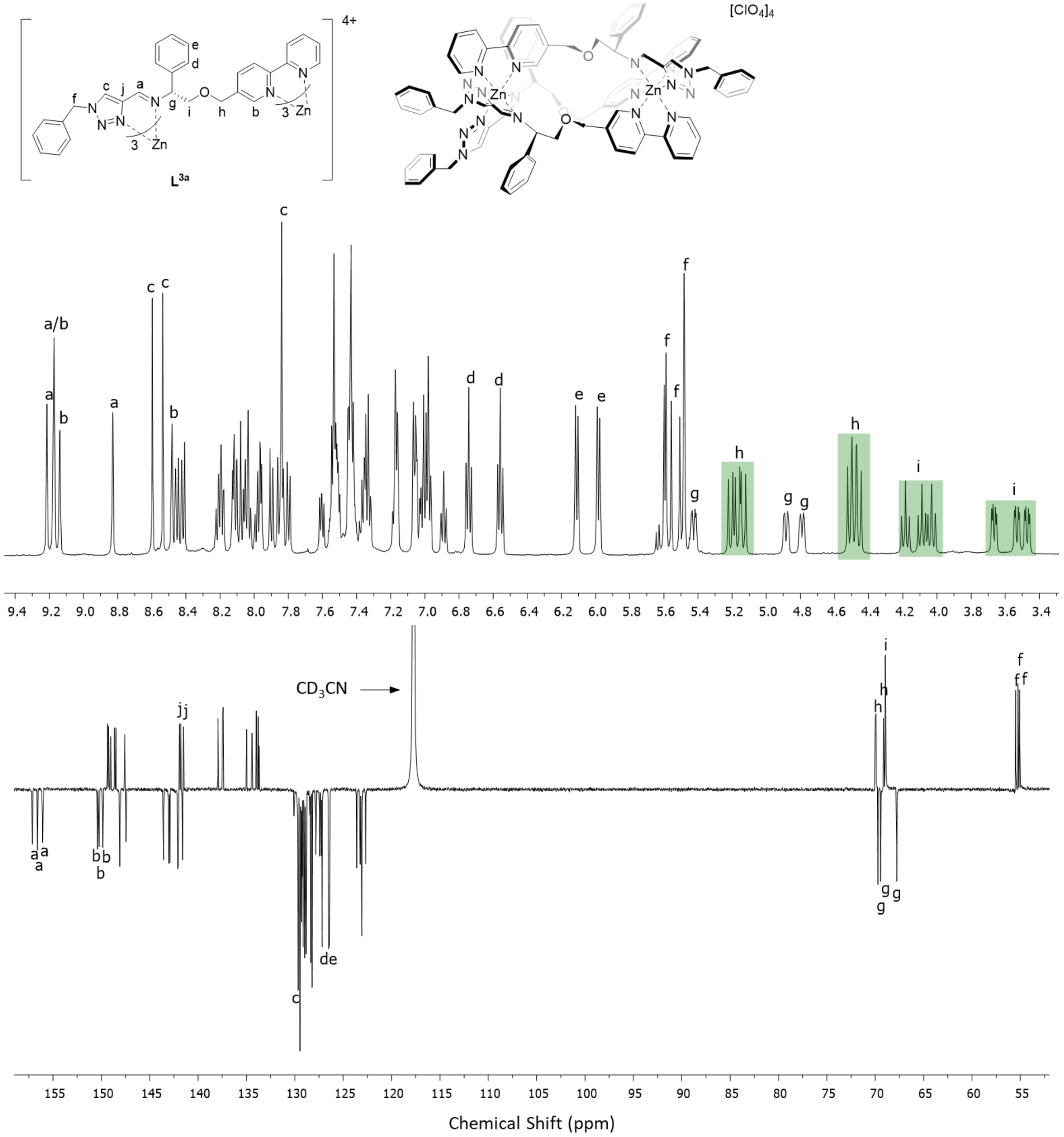


Figure S1 ^{1}H (500 MHz, CD_3CN, 298K) and ^{13}C (125 MHz, CD_3CN, 298K) NMR spectra of *R*$_c$,Δ_{Zn},HHT-[Zn_2**L**$^{3a}{}_3$][ClO_4]$_4$. Three imine carbon peaks C$^{\mathbf{a}}$ were found at 157.1-156.1 ppm, and three bpy carbon peaks C$^{\mathbf{b}}$ were observed at 150.4-149.9 ppm. The three benzylic carbon peaks C$^{\mathbf{g}}$ were detected at 69.7, 69.5 and 67.8 ppm. Bipyridine-CH_2 carbon peaks C$^{\mathbf{h}}$ were found at 70.0, 69.9 and 69.1 ppm. Benzyl-CH_2 carbon peaks C$^{\mathbf{f}}$ were assigned at 55.5-50.1 ppm.

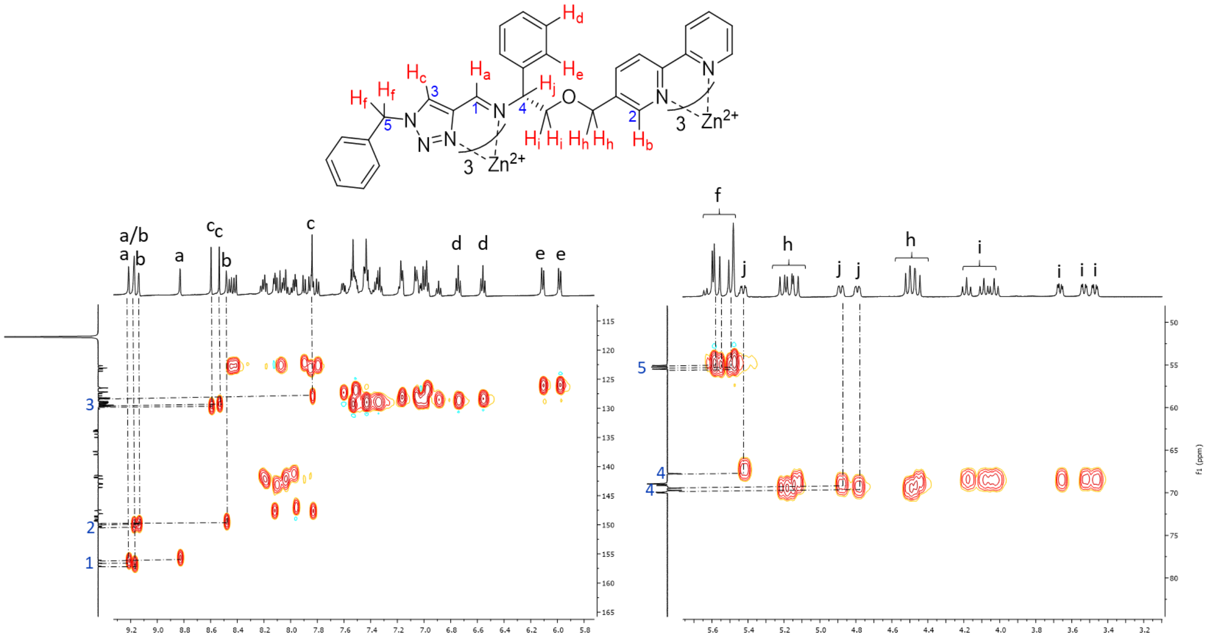


Figure S2 2D ^{1}H-^{13}C HSQC (500 MHz/125 MHz, CD$_3$CN, 298K) NMR spectra of $R_{\mathrm{c}},\Delta_{\mathrm{Zn}}$,HHT-$[\mathrm{Zn}_2\mathbf{L}^{\mathbf{3a}}{}_3][\mathrm{ClO}_4]_4$

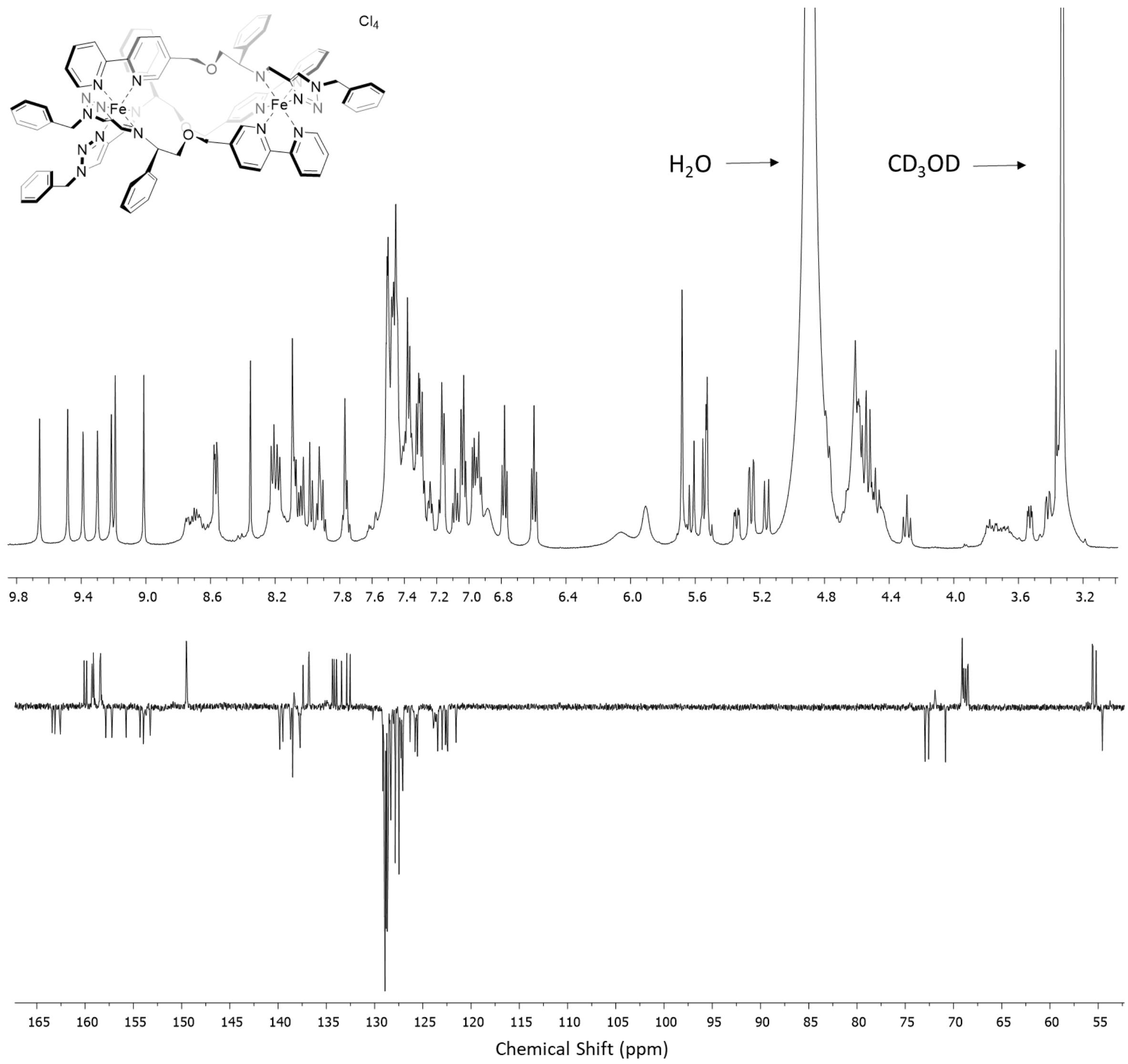


Figure S3 ^{1}H (500 MHz, CD$_3$OD, 298K) and ^{13}C (125 MHz, CD$_3$OD, 298K) NMR spectra of $R_{\mathrm{c}},\Delta_{\mathrm{Fe}}$,HHT-$[\mathrm{Fe}_2\mathbf{L}^{\mathbf{3a}}{}_3]\mathrm{Cl}_4$.

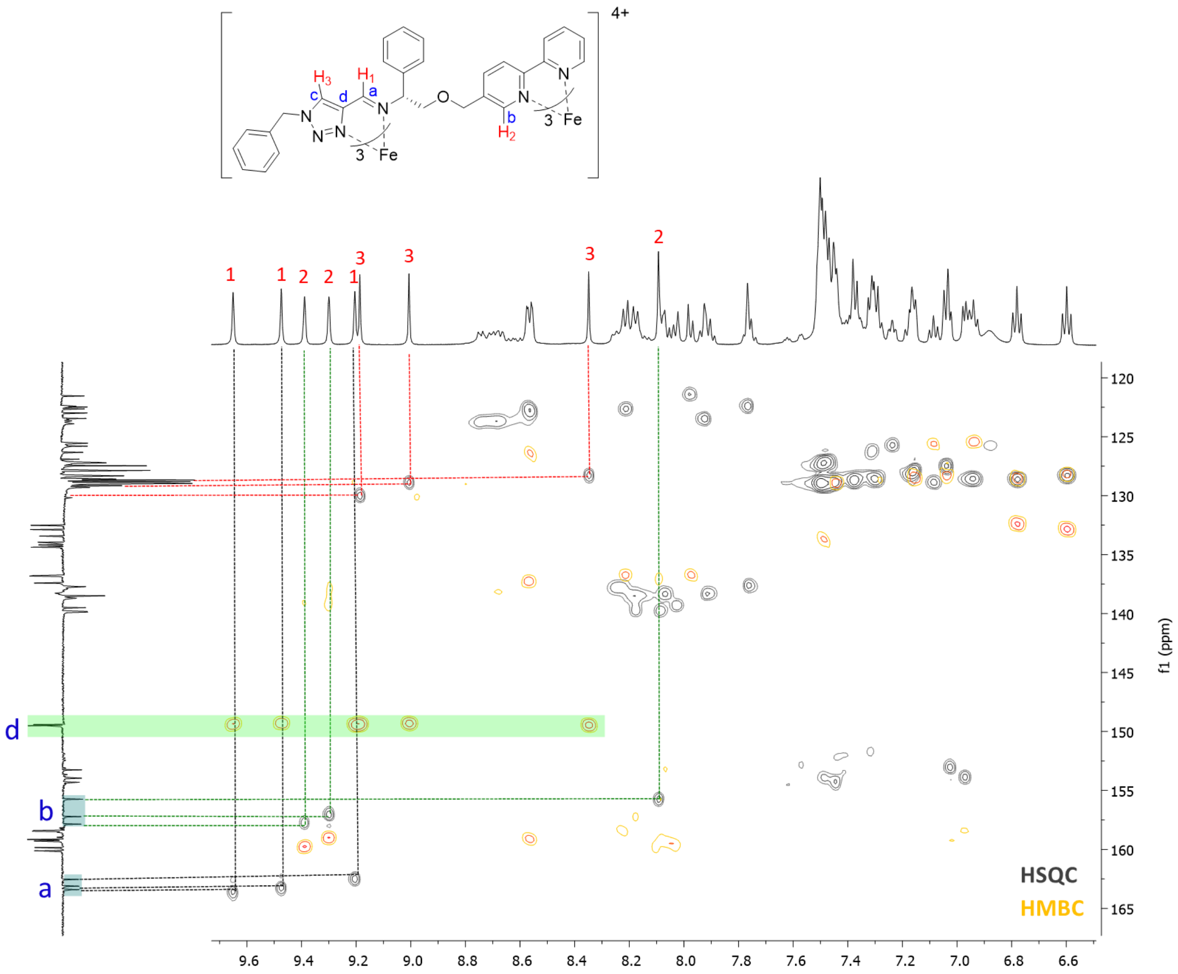


Figure S4 Partial 2D ^{1}H-^{13}C HSQC/HMBC (500 MHz/125 MHz, CD$_3$OD, 298K) spectra of (R_c,Δ_{Fe})-HHT-[Fe$_2$**L**$^{3a}{}_3$]Cl$_4$

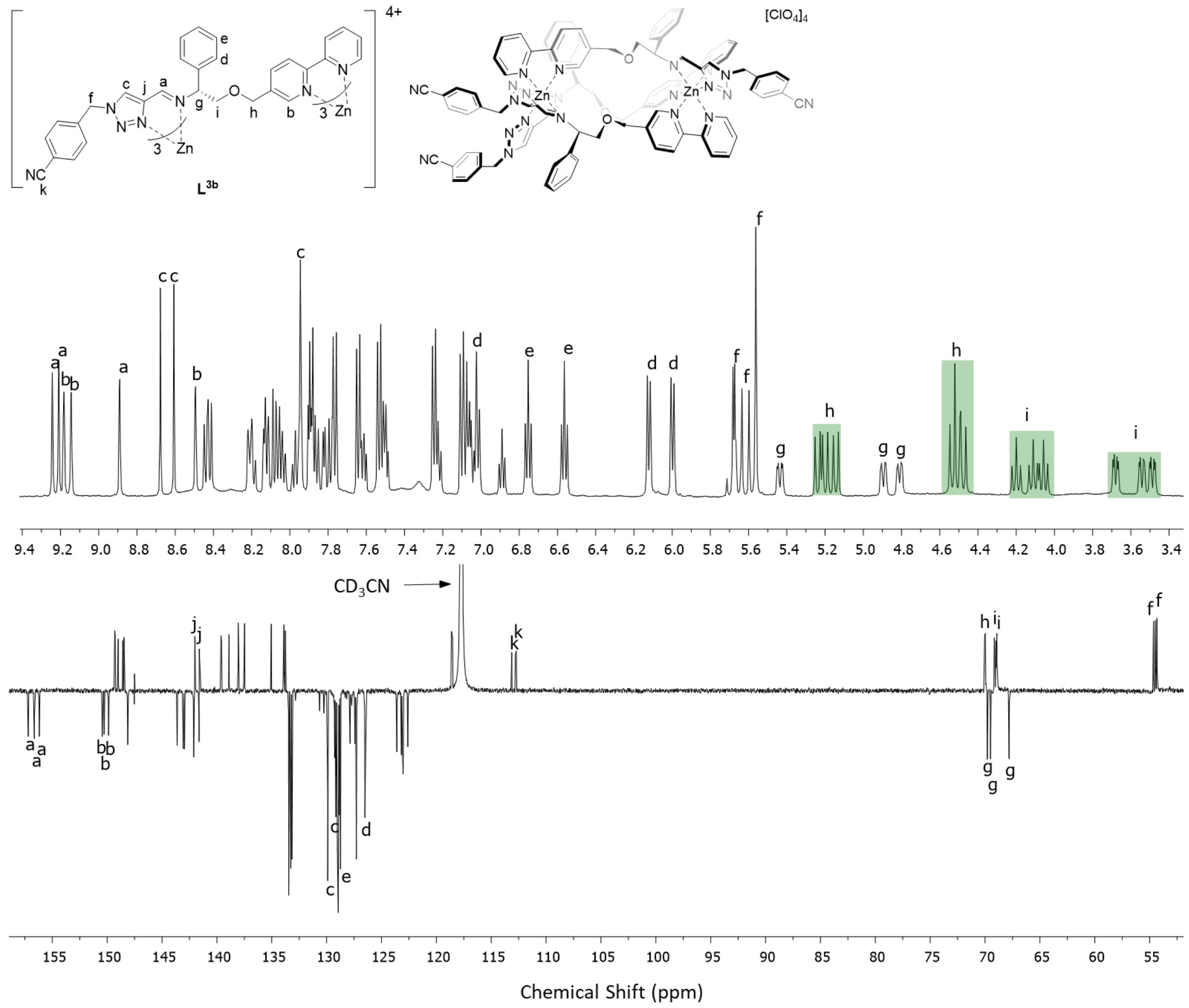


Figure S5 ^{1}H (500 MHz, CD$_3$CN, 298K) and ^{13}C (125 MHz, CD$_3$CN, 298K) NMR spectra of R_c,Δ_{Zn},HHT-[Zn$_2$**L**^{3b}$_3$][ClO$_4$]$_4$

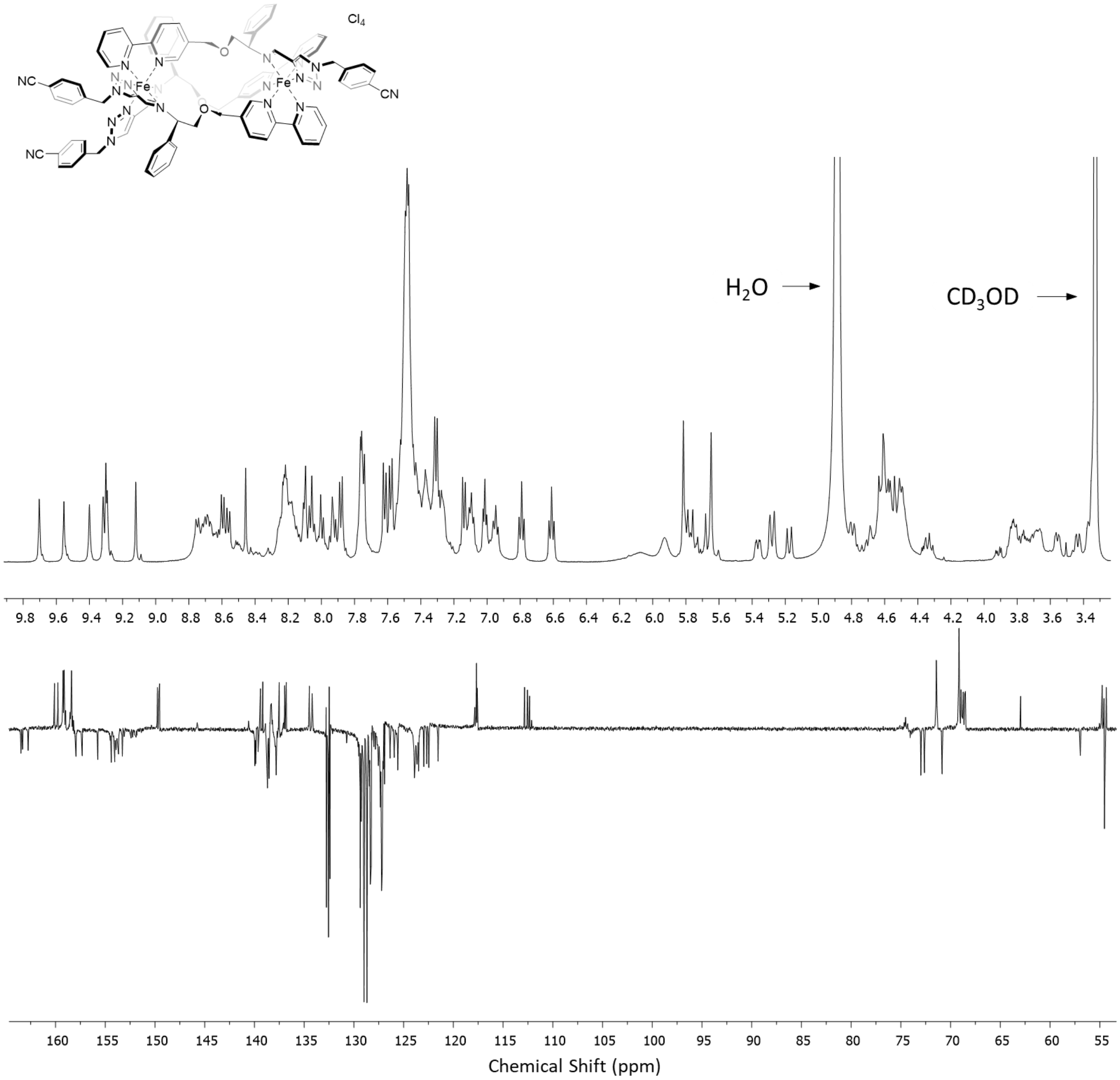


Figure S6 ^{1}H (500 MHz, CD_3OD, 298K) and ^{13}C (125 MHz, CD_3OD, 298K) NMR spectra of $R_\mathrm{c},\Delta_\mathrm{Fe}$,HHT-$[\mathrm{Fe}_2\mathbf{L}^{\mathbf{3b}}{}_3]\mathrm{Cl}_4$.

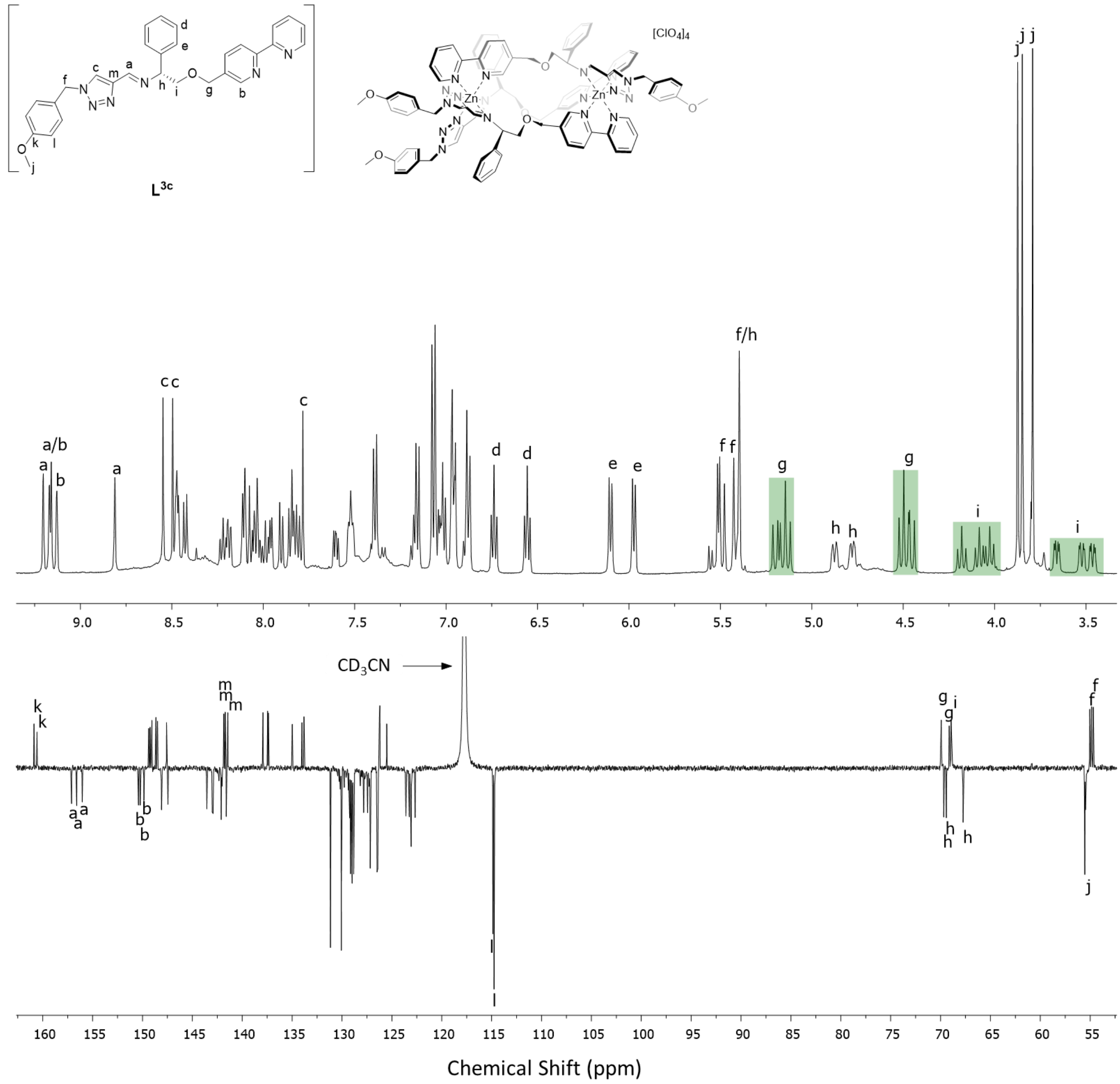


Figure S7 ^{1}H (500 MHz, CD$_3$CN, 298K) and ^{13}C (125 MHz, CD$_3$CN, 298K) NMR spectra of R_c,Δ_{Zn},HHT-[Zn$_2$**L**^{3c}$_3$][ClO$_4$]$_4$

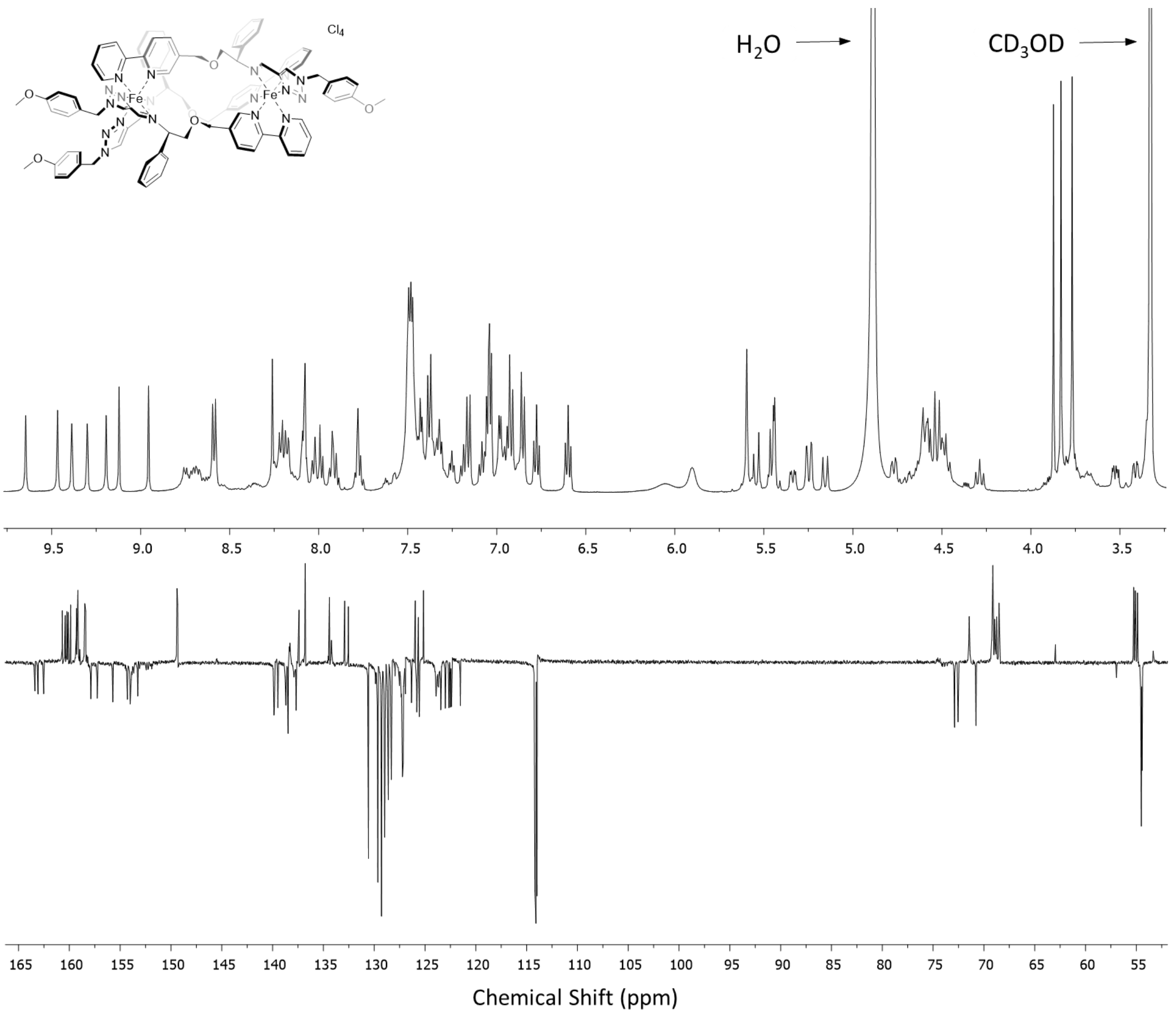


Figure S8 ^{1}H (500 MHz, $\mathrm{CD_3OD}$, 298K) and ^{13}C (125 MHz, $\mathrm{CD_3OD}$, 298K) NMR spectra of $R_{\mathrm{c}},\Delta_{\mathrm{Fe}}$,HHT-$[\mathrm{Fe}_2\mathbf{L}^{\mathbf{3c}}{}_3]\mathrm{Cl}_4$.

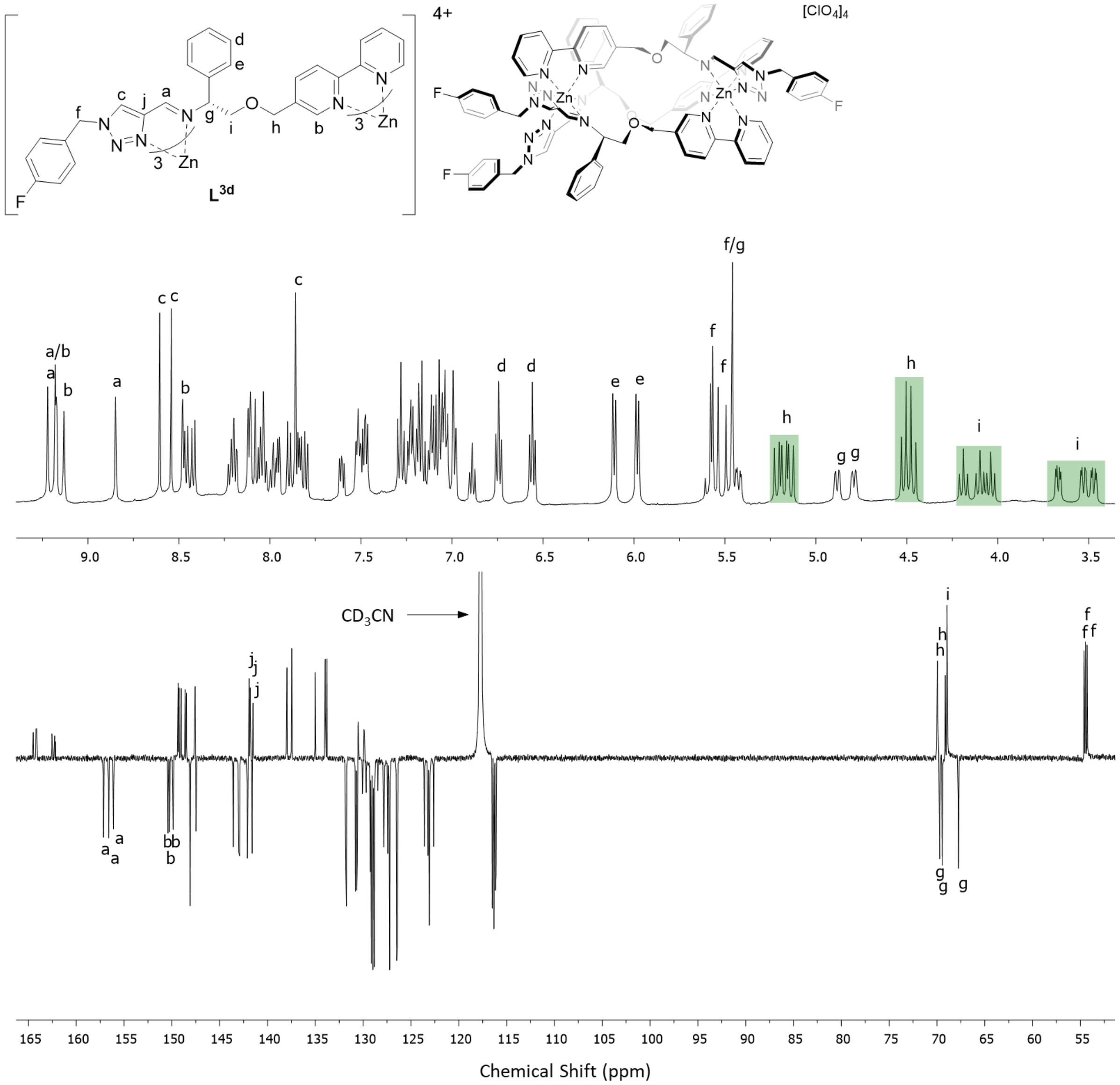


Figure S9 ^{1}H (500 MHz, CD$_3$CN, 298K) and ^{13}C (125 MHz, CD$_3$CN, 298K) NMR spectra of R_c,Δ_{Zn},HHT-[Zn$_2$**L**^{3d}$_3$][ClO$_4$]$_4$

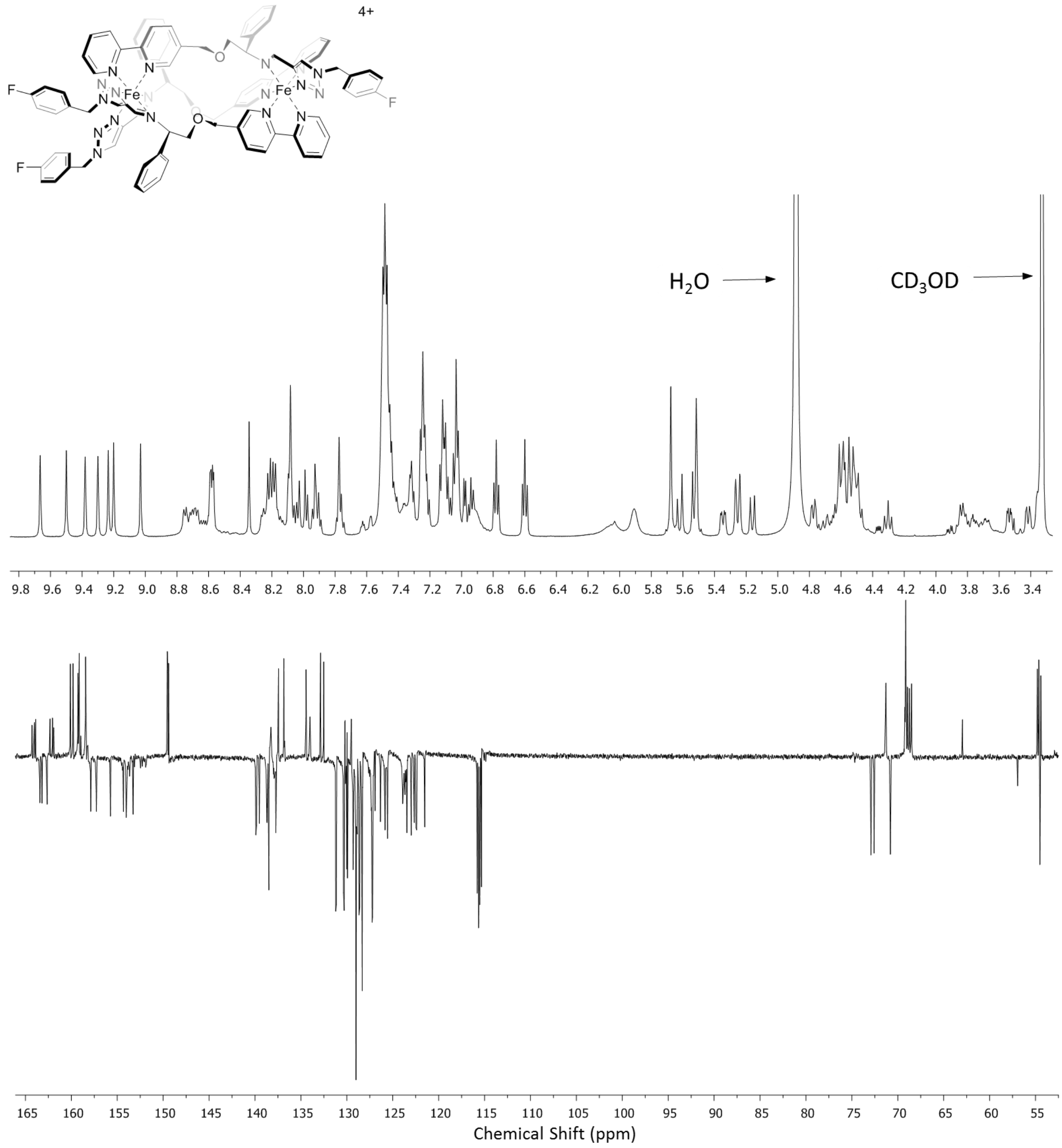


Figure S10 ^{1}H (500 MHz, CD$_3$OD, 298K) and ^{13}C (125 MHz, CD$_3$OD, 298K) NMR spectra of $R_\mathrm{c},\Delta_\mathrm{Fe}$,HHT-$[\mathrm{Fe}_2\mathbf{L}^{\mathbf{3d}}{}_3]\mathrm{Cl}_4$.

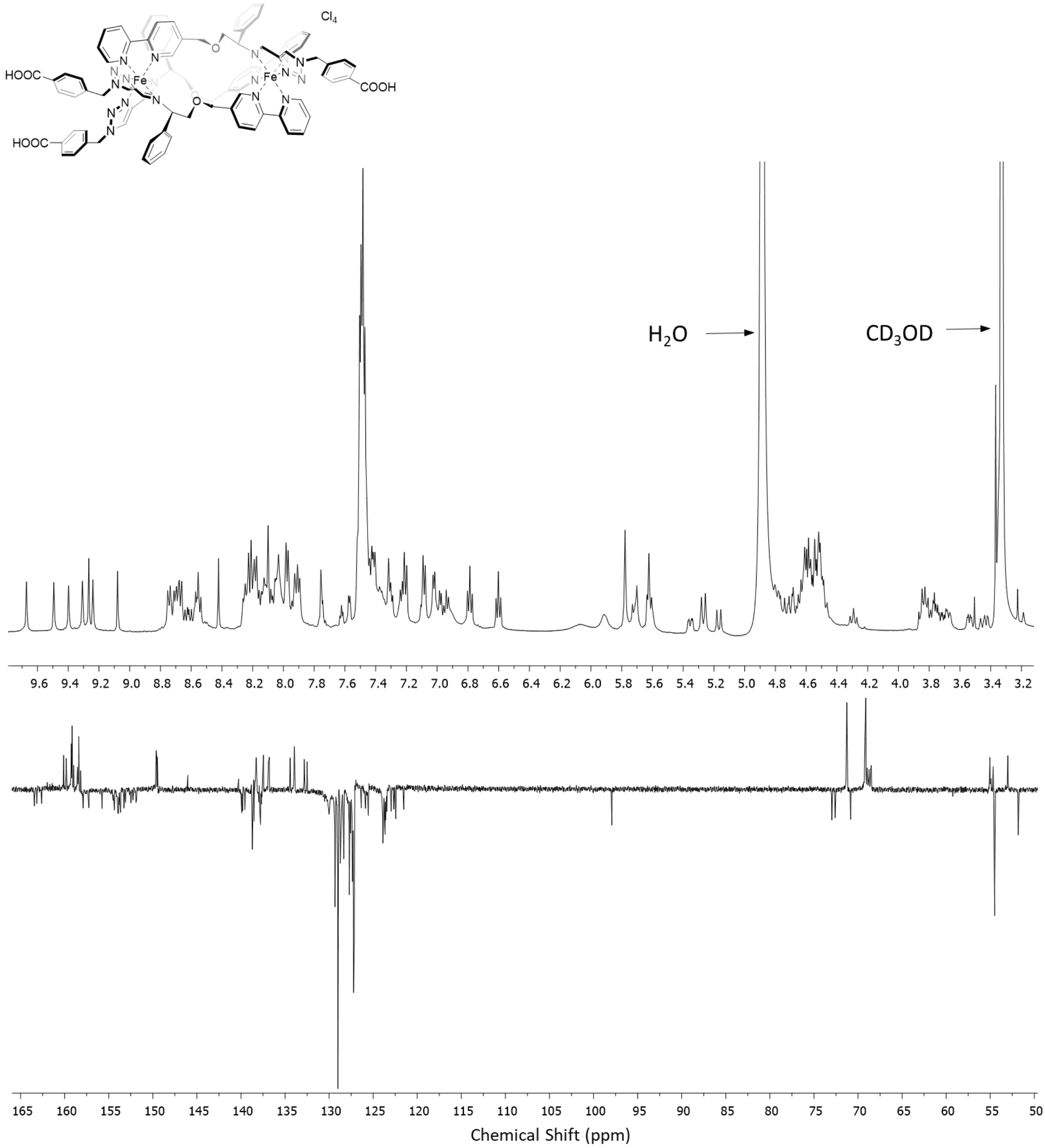


Figure S11 ^{1}H (500 MHz, CD_3OD, 298K) and ^{13}C (125 MHz, CD_3OD, 298K) NMR spectra of R_c,Δ_{Fe},HHT-$[Fe_2\mathbf{L}^{3e}{}_3]Cl_4$.

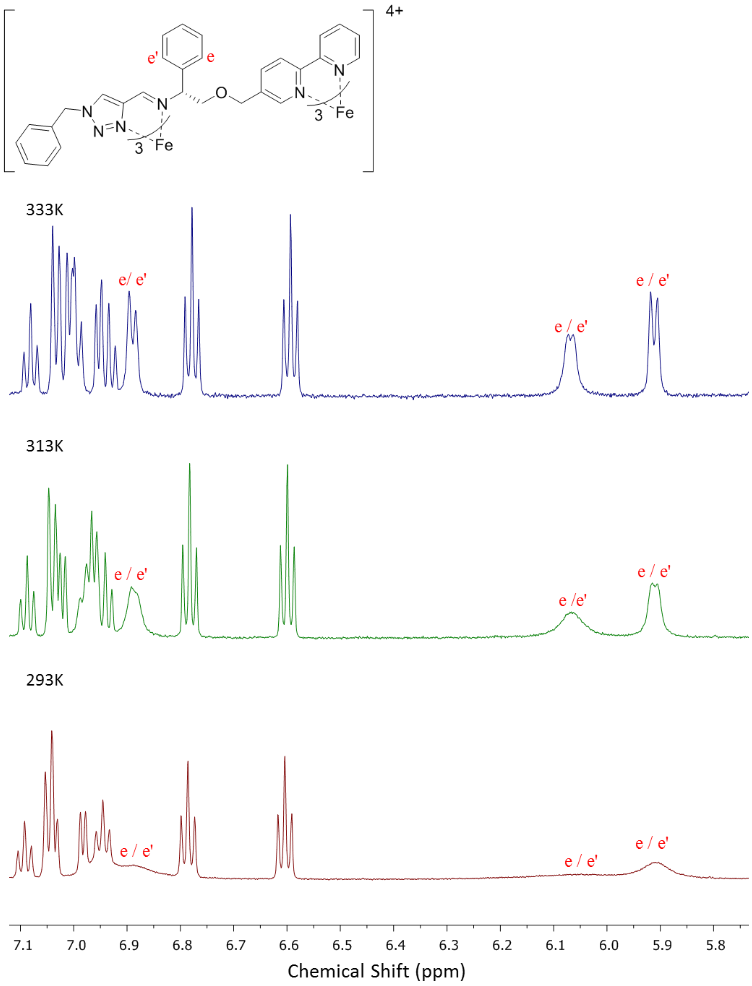


Figure S12 Variable temperature ^{1}H spectra of (R_c,Δ_{Fe})-HHT-[Fe$_2$**L**^{3a}$_3$]Cl$_4$ (600 MHz, CD$_3$OD, 298K) at 7.2-5.6 ppm. Compared with the Zn(II) counterparts, the protons (6.2-5.8 ppm) of the π-stacked phenyl rings (H^e) were much broader for the Fe(II) metallohelices at 293 K. We attribute this to the shorter expected N-Fe(II) bond lengths with respect to Zn(II),[2] resulting in stronger π-stacking between phenyl ring and bipyridine in a more compact structure, slowing the phenyl ring rotation. Variable temperature ^{1}H NMR spectra of Δ-[Fe$_2$**L**^{3a}$_3$]Cl$_4$ reveal spectral sharpening with increasing temperature, consistent with the increased phenyl ring rotation.

3. High Resolution ESI mass spectra

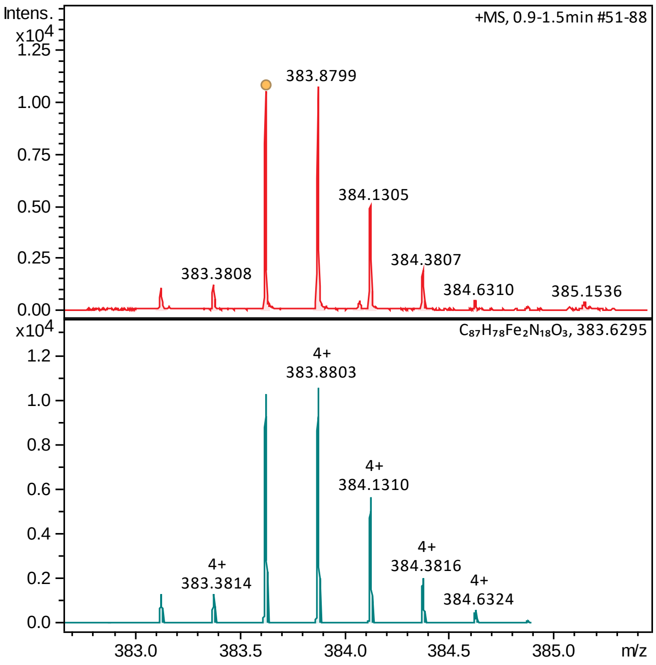


Figure S13 High resolution ESI mass spectrum of Λ_{Fe},HHT-[Fe_2**L**$^{3a}{}_3$]Cl_4 showing the observed z = +4 charge (top), compared to the theoretical isotope pattern (bottom).

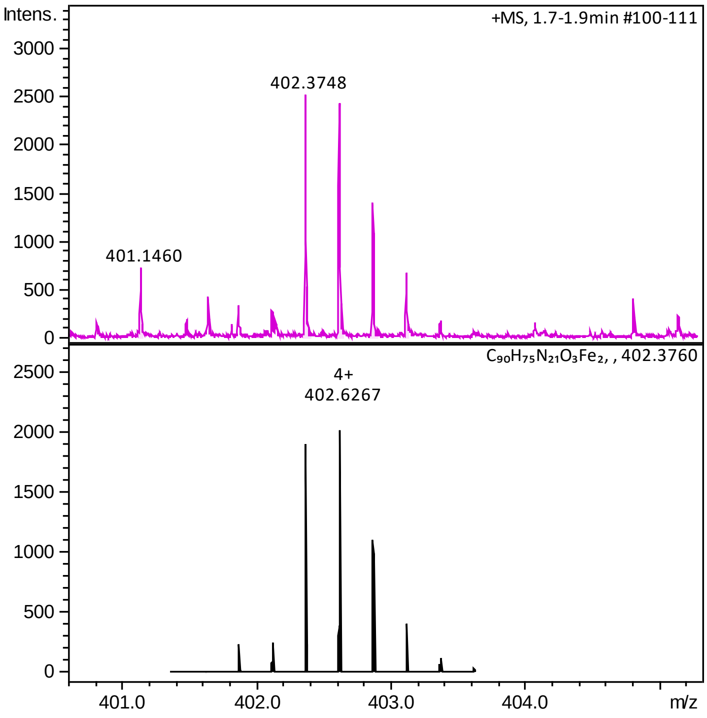


Figure S14 High resolution ESI mass spectrum of Λ_{Fe},HHT-[Fe_2**L**$^{3b}{}_3$]Cl_4 showing the observed z = +4 charge (top), compared to the theoretical isotope pattern (bottom).

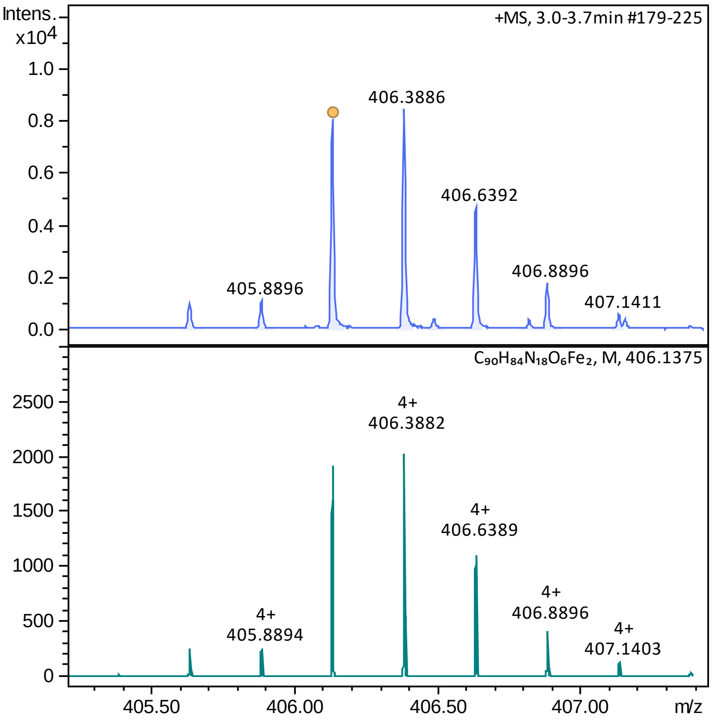


Figure S15 High resolution ESI mass spectrum of Λ_{Fe},HHT-$[Fe_2\mathbf{L}^{3c}_3]Cl_4$ showing the observed z = +4 charge (top), compared to the theoretical isotope pattern (bottom).

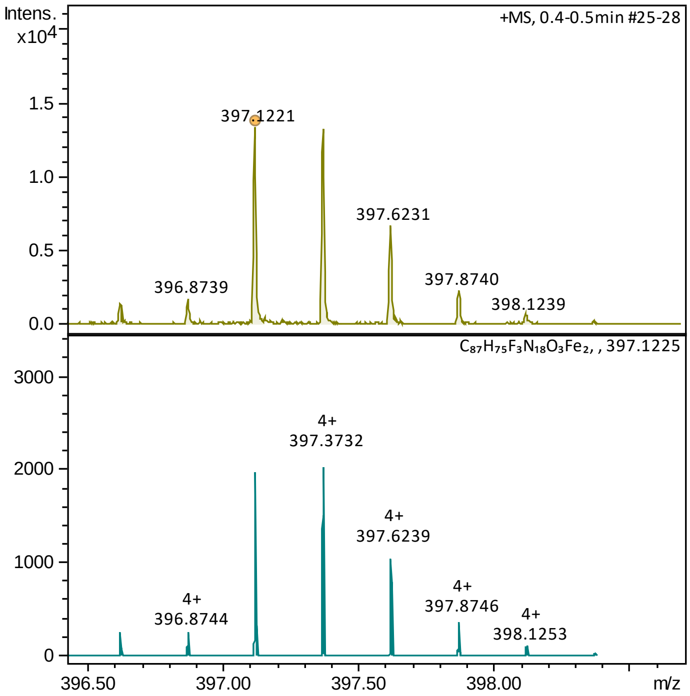


Figure S16 High resolution ESI mass spectrum of Λ_{Fe},HHT-$[Fe_2\mathbf{L}^{3d}_3]Cl_4$ showing the observed z = +4 charge (top), compared to the theoretical isotope pattern (bottom).

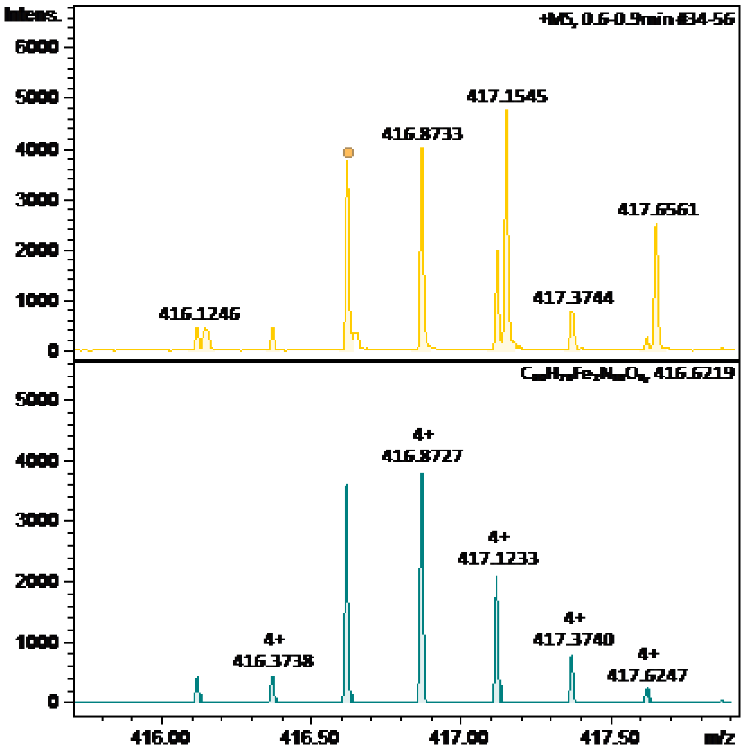


Figure S17 High resolution ESI mass spectrum of Δ_{Fe},HHT-[Fe_2**L**^{3e}$_3$]Cl_4 showing the observed z = +4 charge (top), compared to the theoretical isotope pattern (bottom).

4. Circular Dichroism Spectra

Circular Dichroism Spectra were measured on a JascoJ-815 spectrometer, calibrated conventionally using 0.060% ACS a holmium filter. Measurements were collected using a 1 cm path-length quartz cuvette. The parameters used were; bandwidth 1 nm, response time 1 sec, wavelength scan range 270 – 700 nm, data pitch 0.2 nm, scanning speed 100 nm/min and accumulation 8.

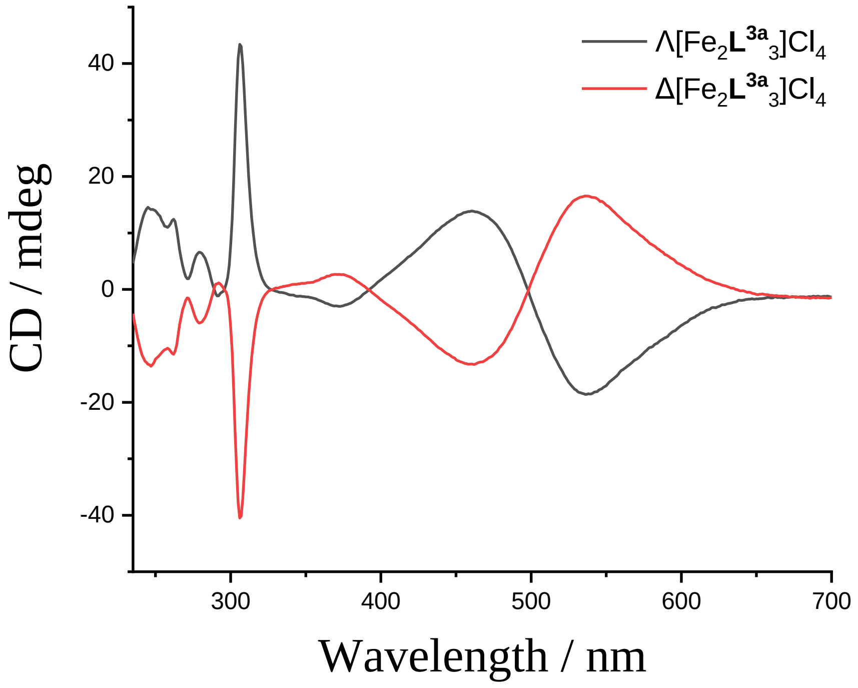


Figure S18 CD spectra of the pairs of enantiomers [Fe$_2$L^{3a}$_3$]Cl$_4$ (0.1mg/mL in methanol); each enantiomer shows an equal and opposite spectrum to its pair.

5. Stability studies

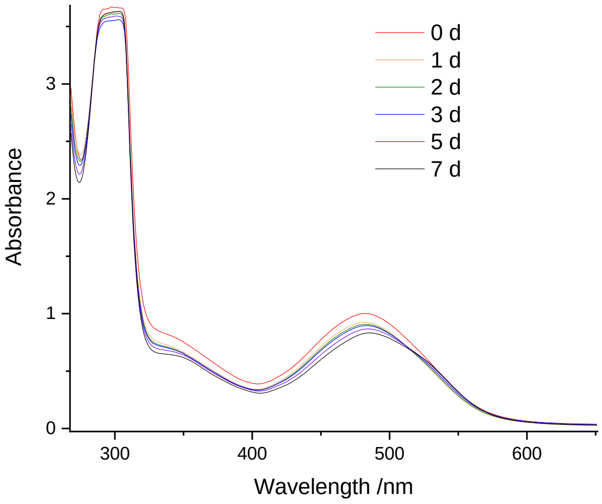


Figure S19 Time-dependent UV-Vis absorption spectra of Λ-[Fe$_2$L^{3a}$_3$]Cl$_4$ (100 μM, dissolved in deionised water), from 0-7 d.

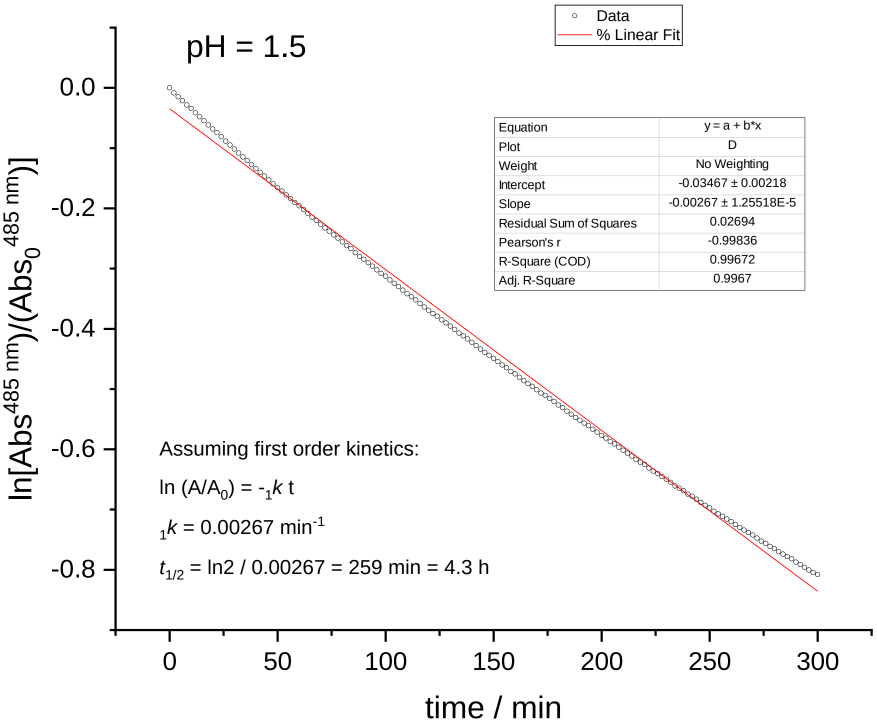


Figure S20 Time-dependent UV-Vis absorption measurements at λ = 485 nm of Λ-[$Fe_2L^{3a}_3$]Cl_4 (0.02 µg mL^{-1}, dissolved in aqueous KCl/HCl buffer at pH = 1.5), from 0-300 min.

6. In vitro antiproliferative activity screening

The human ovarian carcinoma cisplatin-sensitive A2780 cells, cisplatin-resistant A2780cisR (a cisplatin-resistant variant of A2780 cells), human cervical carcinoma HeLa cells, and human breast cancer MCF-7 cells, were kindly supplied by Professor B. Keppler, University of Vienna (Austria). Highly invasive breast carcinoma MDA-MB-231 cells and human MRC-5 pd30 cells derived from normal lung tissue were purchased from the European collection of authenticated cell cultures (ECACC; Salisbury, UK). HCT116 p53$^{+/+}$ colorectal cancer cells and ARPE-19 human retinal epithelial cells (non-cancer) were obtained from ATCC.

The A2780 and A2780cisR cells were grown in RPMI 1640 medium (Biosera, Boussens, France) supplemented with gentamycin (50 mgmL^{-1}, Serva, Heidelberg, Germany) and 10%

heat-inactivated fetal bovine serum (PAA, Pasching, Austria). The acquired resistance of A2780cisR cells was maintained by supplementing the medium with 1 µM cisplatin every second passage. The HeLa and MCF-7 were grown in DMEM medium (Dulbecco's Modified Eagle's Medium, high glucose 4.5 gL^{-1}, PAA) supplemented with gentamycin (50 $mgmL^{-1}$, Serva) and 10% heat-inactivated fetal bovine serum (PAA). The MDA-MB-231 and MRC-5 pd30 cells were grown in DMEM medium (high glucose 4.5 gL^{-1}, PAA) supplemented with gentamycin (50 $mgmL^{-1}$, Serva), 10% heat-inactivated fetal bovine serum (PAA), and 1% non-essential amino acids (Sigma–Aldrich, Prague, Czech Republic). The cells were cultured in a humidified incubator at 37°C in a 5% CO_2 atmosphere and subcultured 2–3 times a week with an appropriate plating density. ARPE-19 human retinal epithelial cells (non-cancer) were cultured in DMEM/F12 culture medium containing l-glutamine (2.5mM), sodium pyruvate (0.5mM), HEPES buffer (15mM) and foetal calf serum (10% v/v). HCT116 $p53^{+/+}$ cells were grown in DMEM containing L-glutamine (2mM) and foetal calf serum (10% v/v). All cell lines were routinely maintained as monolayer cultures and sub-cultured or harvested for chemosensitivity studies when approximately 70-80% confluent. Cells were seeded into 96-well tissue culture plates at a density of 2×10^3 cells/well for HCT116 $p53^{+/+}$and ARPE-19 cell lines, 1×10^4 cells/well for A2780, A2780cisR, and MRC-5; 5×10^3 cells/well for MCF-7, HeLa and MDA-MB-231. Plates containing cells were incubated for 24 h at 37°C in an atmosphere of 5% CO_2 prior to drug exposure. Cell media (200 µl) was added to the control cells and differing concentrations (0 to 50 µM) of drug solution (200 µl) were added to the remaining wells. All complexes were directly dissolved in cell media. The plates were incubated for a further 72 or 96 h at 37°C in an atmosphere of 5% CO_2. Due to these compounds being purple in colour, media is removed and replaced with fresh media prior to the assay for all studies. 3-(4,5-Dimethylthiazol-1-yl)-2,5-diphenyltetrazolium bromide (MTT) solution (0.5 mg/ml, 20µl per well) was added to each well and incubated for a further 4 h at 37°C in an atmosphere of

5% CO_2. Upon completion, all solutions were removed from the wells and dimethyl sulfoxide (150 µl,) was added to each well to dissolve the purple formazan crystals. A Thermo Scientific Multiskan EX microplate photometer was used to measure the absorbance at 540 nm. Lanes containing 100% cell media and untreated cells were used as a blank and 100% cell survival respectively. Cell survival was determined as the true absorbance of treated cells divided by the true absorbance of untreated controls; this value was expressed as a percentage. The IC_{50} values were determined from a plot of percentage cell survival against drug concentration (µM). All assays were conducted in triplicate and the mean IC_{50} ± standard deviation was determined.

Table S1 Cytotoxicity and selectivity index of triazole triplex $[\mathrm{Fe_2}\mathbf{L}^{3a\text{-}e}{}_3]\mathrm{Cl_4}$, ligand precursor amines (*R*/*S*)-**2** and aldehyde **1a** against HCT116 p53$^{+/+}$ and ARPE-19 cell line. Cells were treated for 96 h.

		mean IC_{50} (µM)		**Selectivity Index**
		HCT116 p53$^{+/+}$	**ARPE-19**	
$[\mathrm{Fe_2}\mathbf{L}^{3a}{}_3]\mathrm{Cl_4}$	Λ	0.19 ± 0.01	0.97 ± 0.25	5
	Δ	0.32 ± 0.14	6.31 ± 0.78	20
$[\mathrm{Fe_2}\mathbf{L}^{3b}{}_3]\mathrm{Cl_4}$	Λ	0.20 ± 0.02	1.83 ± 0.80	9
	Δ	0.35 ± 0.20	9.88 ± 3.82	28
$[\mathrm{Fe_2}\mathbf{L}^{3c}{}_3]\mathrm{Cl_4}$	Λ	0.20 ± 0.01	2.22 ± 0.58	11
	Δ	0.23 ± 0.02	7.97 ± 1.18	34
$[\mathrm{Fe_2}\mathbf{L}^{3d}{}_3]\mathrm{Cl_4}$	Λ	0.20 ± 0.01	1.92 ± 0.43	10
	Δ	0.40 ± 0.30	6.89 ± 1.94	17
$[\mathrm{Fe_2}\mathbf{L}^{3e}{}_3]\mathrm{Cl_4}$	Λ	0.30 ± 0.10	0.72 ± 0.11	2
	Δ	1.72 ± 0.07	3.05 ± 1.29	2
2	*S*	1.13 ± 0.37	2.34 ± 0.33	2
	R	2.29 ± 0.57	9.66 ± 3.61	4
1a		> 73.2	> 89.1	-
$FeCl_2$		> 100	> 100	-

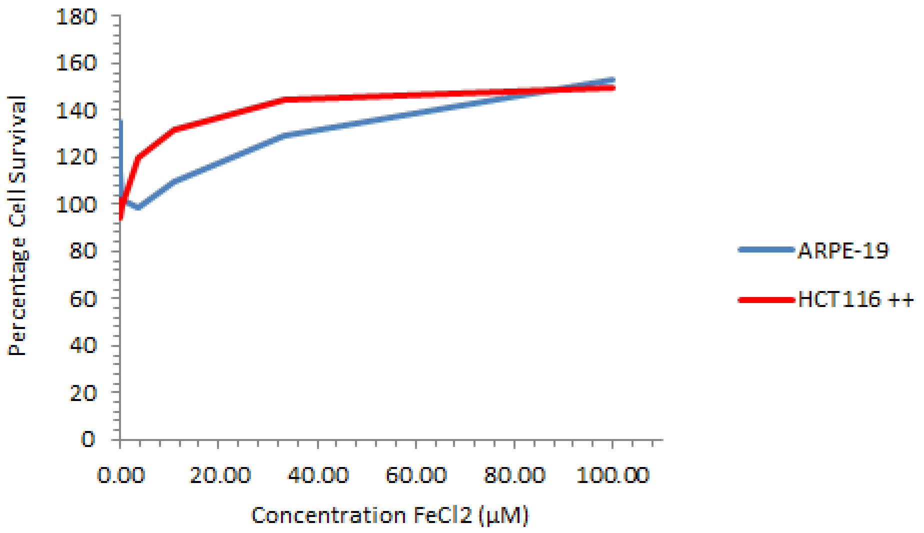


Figure S21 Percentage cell survival as a function of [$FeCl_2$]. Cell survival measured by standard MTT, by comparison with untreated cells.

Table S2 Cytotoxicity of triazole triplex Λ/Δ[$Fe_2\mathbf{L}^{3a}{}_3$]Cl_4 against HCT116 $p53^{+/+}$ using stock solutions (dissolved in cell culture medium) pre-incubated at 37 °C for 24 h, and stock solutions made up immediately before dosing cells. Cells were treated with compound for 24 h and fresh media was replaced for a further 72 h. IC_{50} was determined by SRB assay.

		mean IC_{50} (μM) - HCT116 $p53^{+/+}$	
		24 h pre-incubation	**0 h pre-incubation**
[$Fe_2\mathbf{L}^{3a}{}_3$]Cl_4	Λ	0.57±0.06	0.58±0.07
	Δ	8.6 ± 0.7	8.9 ± 0.3

7. Combined treatment

The cells were seeded and processed following the procedure mentioned above and were treated with cisplatin and Δ-[$Fe_2\mathbf{L}^{3a}{}_3$]Cl_4 at equimolar concentrations (1:1). CompuSyn software (Combo SynInc, City, State, USA) was used to determine the Combination Indexes (CI). CI < 0.9 indicated synergism, CI > 1.1 indicated antagonism and CI within the range (0.9 – 1.1) indicated additive effect. The experiments were carried out at least in triplicate.

8. Antimicrobial screening

The bacterial strains used in this study are listed in Table S3. For MIC determination the standard broth microdilution method was employed, in agreement with the Clinical and Laboratory Standards Institute (CLSI) guidelines M07-A9 and M100-S24. Cation-adjusted Mueller Hinton Broth (CAMHB) was used as the media and a 512 μg ml^{-1} stock solution of each metallohelix was prepared in water. Each measurement was performed in triplicate.

Table S3: *In vitro* antimicrobial activity (MICs) of $\Lambda/\Delta[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$ against Gram-positive strain *S. aureus* and Gram-negative strain *E. coli*. Ciprofloxacin is the control.

	MIC (μg ml^{-1})	
Compound	*Staphylococcus aureus* ATCC29213	*Escherichia coli* ATCC25922
Λ-$[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$	256	128
Δ-$[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$	256	128
Ciprofloxacin	0.25	0.008

9. Haemolysis screening

Fresh equine blood was centrifuged at 1,000 x g for 10 min and the supernatant was removed. Harvested erythrocytes were washed three times with PBS and then resuspended to a 5% erythrocyte concentration in PBS. $[Fe_2L^{3a}{}_3]Cl_4$ compounds were dissolved in PBS in a 0.5-256 μg ml^{-1} serial dilution range. The $[Fe_2L^{3a}{}_3]Cl_4$ solutions (100 μl) were added to the suspended erythrocytes (100 μl) in 96-well round bottom plates at 37 °C for 1 h without agitation. Controls included a PBS and 1% Triton X-100 as 0 and 100% haemolysis, respectively. Each measurement was performed in triplicate.

Table S4: Haemolytic activity of $\Lambda/\Delta[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$ against equine erythocytes.

Compound	**Haemolytic concentration** (μg ml^{-1})
Λ-$[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$	>256
Δ-$[Fe_2\mathbf{L}^{\mathbf{3a}}{}_3]Cl_4$	>256

10. Real-time cell growth monitoring

Real-time Cell Analyzer (RTCA) (xCELLigence RTCA SP Instrument, ROCHE) was applied for growth monitoring of cells in the absence and the presence of tested compounds. The instrument first read the background of E-plates (100 µL medium). After that, upon a 24-hour incubation period, the A2780 cells (5x10^3 cells/well; 50 µL) were treated with tested compounds at varying concentrations. The impedance was monitored for additional 80 h. An arbitrary unit CI (cell index) is a quantitative measure reflecting the status of the cells (number of attached cells and cell status such as morphology) in an electrode-containing well. Normalized CI at a given time point is given by dividing CI at the time point by CI at a reference time point. Δ-$[Fe_2\mathbf{L}^{3a}{}_3]Cl_4$ shows a very different profile to that of cisplatin in A280 cells. The complex treatment resulted in a significant increase in Cell index within 20 to 60 hours following the compound addition.

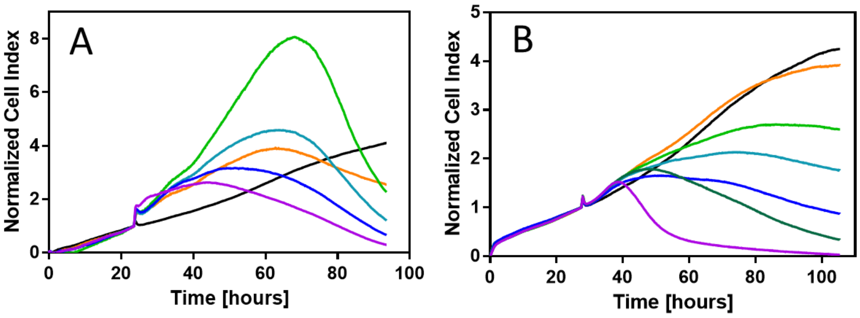


Figure S22 Time-dependent cellular response profiles of A2780 cells treated with increasing concentrations of tested compounds; Cell index in arbitrary units is a measure of cell sensor impedance: (A) Δ-$[Fe_2\mathbf{L}^{3a}{}_3]Cl_4$ (lines: orange – 0.1 µM; green – 0.2 µM; turquoise – 0.4 µM; blue – 0.8 µM; magenta – 1.6 µM); (B) cisPt (lines: orange – 1 µM; green – 2 µM; turquoise – 4 µM; blue – 8 µM; dark green – 12 µM; magenta – 20 µM).

11. Fluorescence competition assays

A solution (10 mM Tris buffer, pH 7.4, 1 mM EDTA) of 3.9 µM ct-DNA with 1.3 µM ethidium bromide was titrated by an aliquots of stock 100µM metallohelice. The DNA-EtBr complexes were excited at 520 nm and fluorescence intensity was measured at 550-700 nm after each addition of 2 μL complex until the fluorescence was reduced to 50 %. The standard parameters used were: response time 1 sec, data pitch 1 nm, scanning speed 100 nm/min and accumulation 1. The Hoechst competition assay was similar with ethidium bromide except that the DNA-Hoechst complexes were excited at 345 nm and the fluorescence intensity was measured at 360-600 nm. The methyl green competition assay was conducted in which the DNA-methyl green complexes were excited at 640 nm and the fluorescence intensity was measured at 650-750 nm.

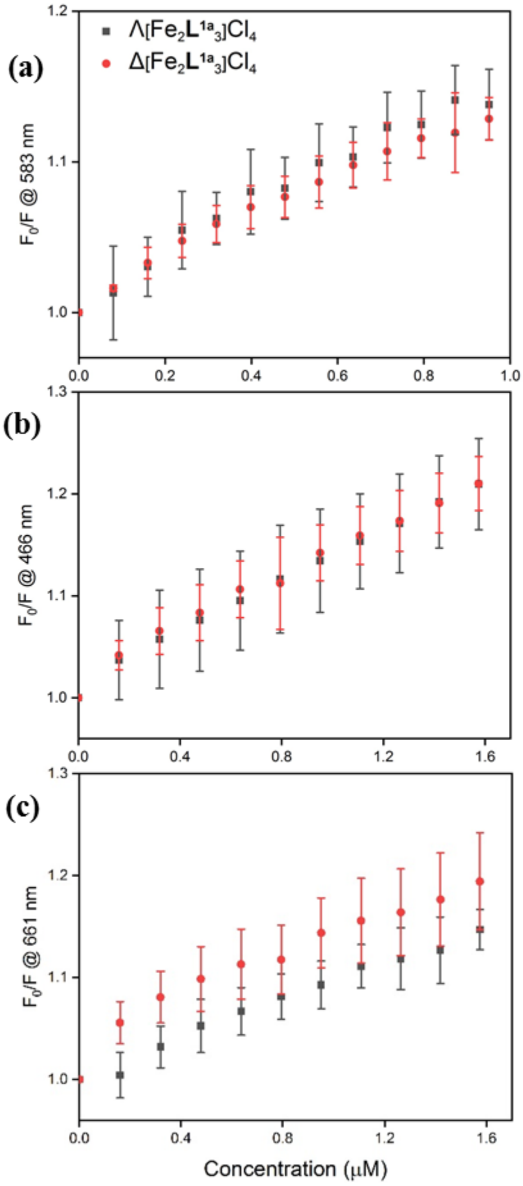
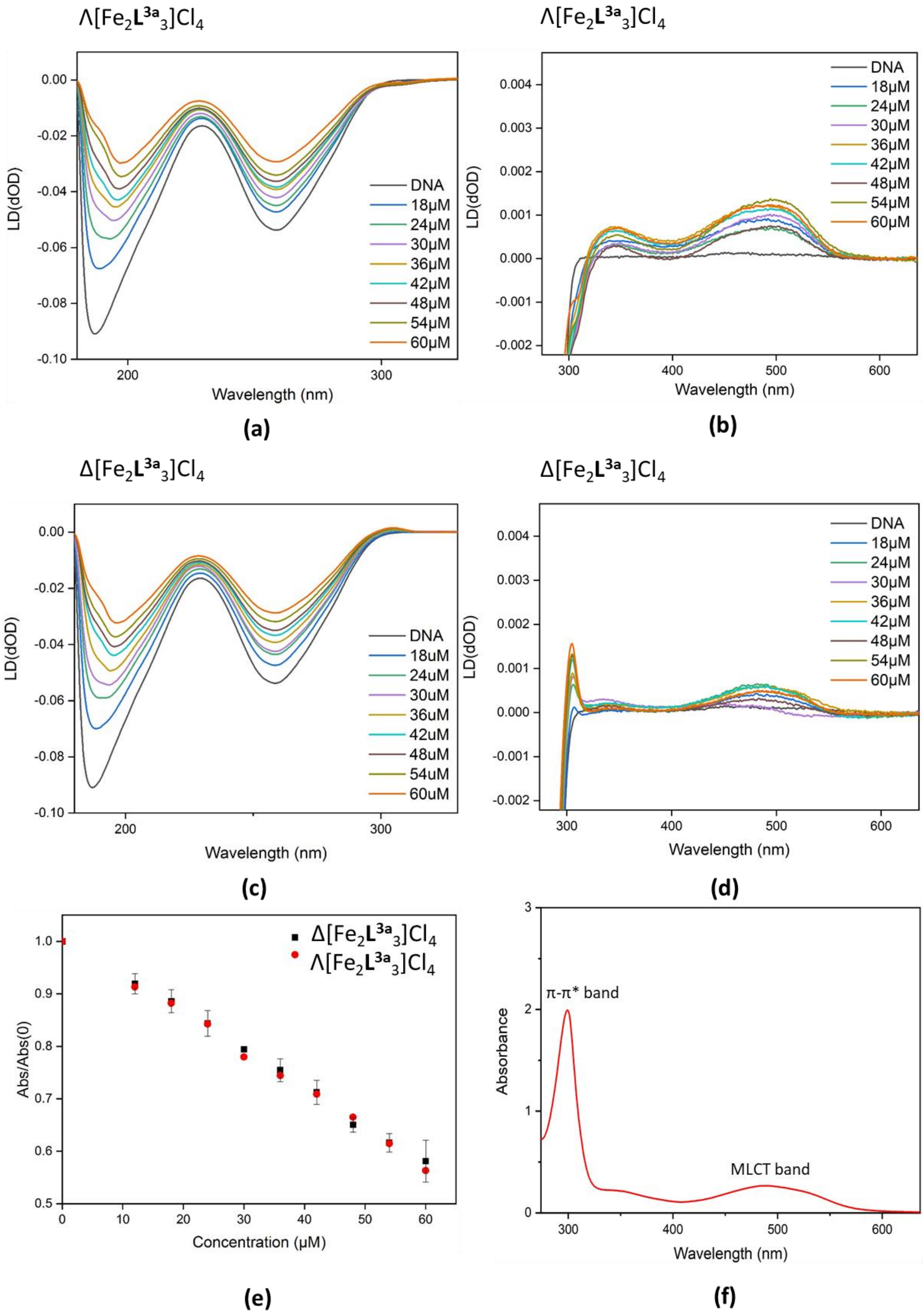


Figure S23 Fluorescence competition assay: The ct-DNA (3.9 μM) was firstly incubated with fluorescent binder (1.3 μM), then titrated with variable concentration of metallohelices (0-2.0 μM). Finally, the fluorescent ratio F$_0$/F

(F_0 equals fluorescence of control with no complex, F equals instant fluorescence intensity with the addition of complex) versus concentration of metallohelices was plotted. (a) Ethidium bromide (DNA intercalator binder), F_0/F measured at 583 nm; (b) hoechst (DNA minor grove binder), F_0/F measured at 466 nm and (c) methyl green (DNA major grove binder), F_0/F measured at 661 nm.

12. DNA binding studies using Flow LD spectra

Flow LD spectra were measured by Jasco J-815 spectrometer equipped with LD spectroscopy kit. The standard parameters used were: bandwidth 1 nm, response time 1 sec, wavelength scan range 180 – 700 nm, data pitch 0.1 nm, scanning speed 100 nm/min and accumulation 4. Calf thymus DNA (ct-DNA) (600 μM) was prepared in Trizma Buffer (pH 7.4), followed by addition of various concentration of metallohelices with the ratio to ct-DNA: 3:100, 4:100, 5:100, 6:100, 7:100, 8:100, 9:100, and 10:100. The LD spectra were obtained by subtracting the parallel absorption of the molecule from perpendicular absorption [$LD = A_{\parallel} - A_{\perp}$] in the presence of Laminar flow.



(a) (b) (c) (d) (e) (f)

Figure S24 Linear dichroism spectra of ct-DNA (600 µM) in the presence of Λ[Fe_2**L**$^{3a}{}_3$]Cl_4 at (a) 180-330 nm (b) 274-636 nm wavelength; and Δ[Fe_2**L**$^{3a}{}_3$]Cl_4 at (c) 180-330 nm (d) 274-636 nm wavelength; (e) the absorbance ratio Abs/Abs(0) [Abs(0) equals LD signal of control with no complex at 260 nm wavelength], versus concentration of metallohelices was plotted. Error bars show standard deviation for three separate repeats (f) UV-vis spectrum of Δ[Fe_2**L**$^{3a}{}_3$]Cl_4 (100 µM in H_2O).

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