SUPPORTING INFORMATION FOR

Organometallic Cobalamin Anticancer Derivatives for Targeted Prodrug Delivery via Transcobalamin-Mediated Uptake

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Contents

Synthesis and characterization

General synthesis of metal complexes

[Pt(HCC-bpy)Cl_2] (**1**). A mixture of cis-Dichlorobis(dimethyl sulfoxide)platinum(II) (150 mg, 35.5 mmol, 1.0 eq.) and 4-ethynyl-2,2'-bipyridine (76.7 mg, 43.0 mmol, 1.2 eq.) was dissolved in DMF (10 ml) and stirred overnight at room temperature. Upon addition of water (2 ml), a bright yellow precipitate formed. The precipitate was filtered and washed with CH_3CN (10 ml) and CH_3OH (10 ml). The solid was dried under vacuum and used without further purification. Yield: 142 mg (90%); ^{1}H NMR (500 MHz, DMSO-[d6]): δ = 9.51 (dd, *J* = 5.84, 1.1 Hz, 1H, HC-11L), 9.49 (d, *J* = 6.35 Hz, 1H, HC-7L) 8.73 (d, *J* = 1.6 Hz, 1H, HC-4L), 8.68 (d, *J* = 7.95 Hz, 1H, HC-9L), 8.42 (dt, *J* = 7.95, 1.4 Hz, 1H, HC-10L), 7.91-7.84 (m, 2H, HC-5L, HC-12L), 5.20 (s, 1H, HC-1L) ppm; ^{13}C NMR (125 MHz, DMSO-[d6]): δ= 157.2, 156.3, 148.4, 148.1, 140.6, 133.3, 129.5, 128.0, 126.4, 124.6, 90.7, 80.2 ppm, ^{195}Pt (107 MHz, DMSO-[d6], referred to $Na_2[PtCl_6]$): δ = -2300 ppm; Anal. Calcd. for $C_{12}H_8Cl_2N_2Pt$: C, 32.30; H, 1.81; N, 6.28. Found: C, 32.17; H, 1.91; N, 6.40; IR (solid state, KBr, cm^{-1}): $ν_{C≡C}$ 2113.

[Ru($(Et_2N)_2$Bpy)$_2$(HCC-bpy)]Cl_3 (**2**). A mixture of [Ru($(Et_2N)_2$Bpy)$_2Cl_2$]Cl[1] (250 mg, 0.32 mmol, 1.0 eq.), 4-ethynyl-2,2'-bipyridine (175 mg, 0.97 mmol, 3.0 eq.) and trimethylamine (0.01 ml, 0.14 mmol, 0.5 eq.) was dissolved in CH_3OH (20 ml) and heated at reflux under an argon atmosphere for 4h. The solution was allowed to cool and the solvent removed by rotary evaporation. The crude product (460 mg) was redissolved in the minimum amount of CH_3CN and purified by column chromatography on silica gel using acetonitrile, water, methanol and saturated NaCl (0.6:0.149:0.25:0.1%). The first band to elute (purple) was discarded and the second band (deep red) collected. After evaporation of the solvent, the solid was redissolved in CH_2Cl_2 (10 ml) and suction filtered to remove insolubles (presumably NaCl). The filtrate was dried under vacuum to yield 233 mg (82%) of the compound **2**. ^{1}H NMR (500 MHz, DMSO-[d_6]): δ = 8.84 (s, 1H, HC-7L), 8.82 (d, *J* = 8.0 Hz, 1H, HC-12L), 8.01 (td, *J* = 8.0, 1.2 Hz, 1H, HC-11L), 7.87 (m, 2H, HC-9L, HC-4L), 7.58-7.53 (m, 6H, HC-16/19/34/37L, HC-10L, HC-5L), 7.12 (d, *J* = 3.3 Hz, 1H, HC-40L), 7.10 (d, *J* = 3.3 Hz, 1H, HC-13L), 6.94 (d, *J* = 6.8 Hz, 1H, HC-31L), 6.85 (d, *J* = 6.8 Hz, 1H, HC-22L), 6.81 (td, *J* = 6.8, 2.7 Hz, 2H, HC-14L, HC-39L), 6.63 (m, 2H, HC-21L, HC-32L), 4.90 (s, 1H, HC-1L), 3.56-3.46 (m, 16H, HC-23/25/27/29/41/43/45/47L), 1.16-1.06 (m, 24H, HC-24/26/28/30/42/44/46/48L); ^{13}C NMR (125 MHz, DMSO-[d_6]): δ = 158.3, 157.1, 156.6, 156.5, 156.2, 156.1, 152.0, 151.9, 151.8, 151.7, 151.0, 150.8, 149.2, 149.0, 148.7, 148.5, 135.5, 128.8, 127.7, 127.5, 125.8, 124.3, 109.6, 109.4, 105.2, 105.1, 88.2, 80.6, 43.5, 12.0, 11.9; Anal. Calcd. for $C_{48}H_{60}Cl_3N_{10}Ru$: C, 58.56; H, 6.14; N, 14.23. Found: C, 58.91; H, 6.11; N, 13.77; HRMS (ESI^+): $[M]^{2+}$ = 439.2020, calculated for $C_{48}H_{60}N_{10}Ru_1$ = 439.2022; IR (solid state, KBr, cm^{-1}): $ν_{C≡C}$ 2122.

[Re(HCC-bpy)$(CO)_2Br_2$] (**3**). A mixture of $(Et4N)_2[Re(CO)_2Br_4]$[2] (100 mg, 0.12 mmol, 1.0 eq.) and 4-ethynyl-2,2'-bipyridine (27 mg, 0.15 mmol, 1.25 eq.) was dissolved in DME (10 ml) and stirred during 4h at 60 °C. The solution was dried under vacuum, dissolved in a minimum amount of $CHCl_3$ and purified by column chromatography on silica gel using $CHCl_3$/Ethanol (200:1). The first band to elute (dark brown) was determined to be complex **3**. Yield: 43 mg (61%); NMR spectrum is not reported because the compound is paramagnetic; Anal. Calcd. for $C_{14}H_8Br_2N_2O_2Re$: C, 28.88; H, 1.38; N, 4.81. Found: C, 28.71; H, 1.28; N, 4.81; MS MALDI-TOF (POS, DCTB): $[M]^+$ = 580.8433, calculated for $C_{14}H_8Br_2N_2O_2Re$ = 580.8510; IR (solid state, KBr, cm^{-1}): $ν_{C≡C}$ 2119, $ν_{C=O}$ 1994, 1842.

[Ru(HCC-bpy)$(bpy)_2$]Cl_2 (**4**). Complex **4** was obtained via anion metathesis starting from [Ru(HCC-bpy)$(bpy)_2$]$(PF_6)_2$.[3] The latter was dissolved in acetone and an aqueous solution of concentrated tetrabuthylammonium chloride was added dropwise until precipitation of **4** occurred.

Characterization of the vitamin B_{12} derivatives

B_{12}-bpy. Red powder; Yield: 52.8 mg (78%); ^{1}H NMR (500 MHz, MeOD-[d_4]): δ = 8.73 (d, *J* = 4.6 Hz, 1H, HC-9L), 8.41 (d, *J* = 5.7 Hz, 1H, HC-5L), 8.23 (d, *J* = 8.0 Hz, 1H, HC-12L), 8.07 (t, *J* = 8 Hz, 1H, HC-11L), 7.84 (s, 1H, HC-7L), 7.60 (dd, *J* = 5.2, 2.0 Hz, 1H, HC-10L), 7.24 (s, 1H, HC-7N), 7.22 (s, 1H, HC-2N), 7.07 (d, *J* = 5.7 Hz, 1H, HC-4L), 6.62 (s, 1H, HC-4N), 6.27 (d, *J* = 3.2 Hz, 1H, HC-1R), 6.03 (s, 1H, HC-10), 4.72-4.63 (m, 1H,HC-3R), 4.55 (d, *J* = 9 Hz, 1H, HC-3), 4.38-4.28 (m, 1H, HC-19), 4.20 (t, *J* = 3.6 Hz, 1H, HC-176), 4.13-4.08 (m, 1H, HC-2R), 3.92 (dd, *J* = 9.5, 3.2, 1H, HC-4R), 3.78-3.64 (m, 3H, H_bC-5R, H_aC-5R, H_bC-175), 3.27 (m, 2H, HC-8, HC-13), 2.88-2.80 (m, 2H, H_aC-175, HC-18), 2.66-2.62 (m, 1H, HC-8), 2.6 (s, 3H, H_3C-51), 2.60-5.58 (m, 3H, H_3C-151), 2.57 (m, 1H, H_bC-132), 2.56-2.53 (m, 2H, H_2C-32), 2.52-2.47 (m, 3H, H_bC-21, H_aC-132 H_bC-71), 2.45-2.36 (m, 2H, H_bC-181, H_aC-21), 2.29 (s, 3H, H_3C-11N), 2.27 (s, 3H, H_3C-10N), 2.24-2.16 (m, 1H, H_aC-171), 2.10-2.01 (m, 3H, H_aC-181, H_bC-131, H_aC-71), 2.00-1.96 (m, 1H, H_bC-81), 1.95-1.87 (m, 3H, H_bC-31, H_aC-31, H_aC-131), 1.85 (s, 3H, H_3C-7A), 1.83-1.78 (m, 1H, H_aC-172), 1.77 (m, 1H, H_bC-82), 1.46 (s, 3H, H_3C-12A), 1.37 (s, 3H, H_3C-2A), 1.36 (m, 1H, H_a-82), 1.32 (s, 3H, H_3C-17B), 1.31 (m, 1H, H_aC-81), 1.25 (d, *J* = 6.25 Hz, 3H, H_3C-177), 1.15 (s, 3H, H_3C-12B), 0.51 (s, 3H, H_3C-1A) ppm; ^{13}C NMR (125 MHz, MeOD-[d_4]): δ = 180.2, 178.7, 177.7, 177.3, 176.8, 176.5, 175.8, 175.5, 174.5, 174.4, 166.6, 166.4, 150.1, 146.4, 143.7, 140.3, 138.7, 135.2, 131.6, 128.0, 127.1, 125.2, 123.4, 118.4, 112.2, 108.1, 104.9, 102.3, 95.5, 87.9, 86.3, 83.6, 75.9, 75.6, 73.8, 73.7, 70.8, 62.7, 60.0, 57.1, 56.3, 55.1, 52.1, 46.7, 43.9, 43.9, 43.8, 40.1, 36.4, 35.3, 33.4, 33.1, 32.9, 32.5, 32.0, 29.6, 27.5, 27.4, 20.9, 20.8, 20.3, 20.1, 20.0, 17.6, 17.2, 16.4, 16.1 ppm; HRMS (ESI$^+$): $[M+Na]^+$ = 1530.6148, calculated for $C_{74}H_{95}Cl_2Co_1N_{15}O_{14}P_1Na_2$ = 1530.6144; IR (solid state, KBr, cm^{-1}): $\nu_{C\equiv C}$ 2124.

B_{12}-1. Red powder; Yield: 52.7 mg (61%); ^{1}H NMR (500 MHz, MeOD-[d_4]): δ = 8.88 (d, *J* = 5.0 Hz, 1H, HC-9L), 8.50 (d, *J* = 5.0 Hz, 1H, HC-5L), 8.25-8.15 (m, 2H, HC-11, HC-12L), 7.60 (s, 1H, HC-7L), 7.49 (m, 1H, HC-10L), 7.25 (s, 1H, HC-7N), 7.23 (s, 1H, HC-2N), 6.86 (d, *J* = 5.0 Hz, 1H, HC-4L), 6.65 (s, 1H, HC-4N), 6.28 (d, *J* = 2.5 Hz, 1H, HC-1R), 6.0 (s, 1H, HC-10), 4.70-4.63 (m, 1H, HC-3R), 4.57 (s, 1H, HC-3), 4.39 (d, *J* = 11.3 Hz, 1H, HC-19), 4.36-4.29 (m, 1H, HC-176), 4.22-4.18 (m, 1H, HC-2R), 4.14-4.08 (m, 1H, HC-4R), 3.92 (d, *J* = 11.3 Hz, 1H, H_bC-5R), 3.80-3.71 (m, 2H, H_aC-5R, H_bC-175), 3.67 (m, 2H, HC-8, HC-13), 2.83 (m, 2H, H_aC-175, HC-18), 2.73 (m, 3H, H_3C-51), 2.71-2.67 (m, 3H, H_3C-151), 2.61 (s, 3H, H_bC-21, H_aC-132 H_bC-71), 2.57-2.53 (m, 1H, H_bC-132), 2.53-2.48 (m, 2H, H_2C-32), 2.31 (s, 3H, H_3C-11N), 2.29 (s, 3H, H_3C-10N), 2.20 (t, *J* = 12.9 Hz, 1H, H_aC-171), 2.13-2.04 (m, 3H, H_aC-181, H_bC-131, H_aC-71), 2.03-1.94 (m, 4H, H_bC-81, H_bC-31, H_aC-31, H_aC-131), 1.90 (s, 3H, H_3C-7A), 1.86-1.80 (m, 1H, H_aC-172), 1.78-1.71 (m, 1H, H_bC-82), 1.47 (s, 3H, H_3C-12A), 1.45 (s, 3H, H_3C-2A), 1.37 (s, 3H, H_3C-17B), 1.28 (s, 1H, H_aC-81), 1.25 (d, *J* = 6.25 Hz, 3H, H_3C-177), 1.12 (s, 3H, , H_3C-12B), 0.51 (s, 3H, H_3C-1A) ppm; ^{13}C NMR (125 MHz, MeOD-[d_4]): δ = 180.3, 178.8, 177.8, 177.3, 176.9, 176.4, 176.3, 175.9, 174.9, 174.6, 174.5, 166.5, 166.4, 158.4, 158.4, 157.9, 149.2, 148.5, 143.8, 141.6, 139.1, 138.7, 135.1, 133.6, 131.6, 129.3, 128.1, 127.2, 126.2, 118.4, 112.2, 108.0, 105.0, 101.9, 95.3, 87.9, 86.4, 83.6, 83.5, 76.0, 75.6, 73.6, 73.5, 70.8, 62.8, 60.3, 56.9, 56.3, 55.0, 52.0, 46.7, 45.1, 43.5, 40.2, 36.6, 35.4, 33.7, 33.2, 33.1, 33.0, 32.3, 30.7, 29.7, 27.5, 20.9, 20.6, 20.4, 20.3, 20.2, 20.1, 20.0, 18.2, 17.7, 16.8, 16.4 ppm, ^{195}Pt (107 MHz, DMSO-[d_6], referred to $Na_2[PtCl_6]$): δ = -2311 ppm; HRMS (ESI$^+$): $[M+2Na]^{2+}$ = 909.7522, calculated for $C_{74}H_{95}Cl_2Co_1N_{15}O_{14}P_1Pt_1Na_2$ = 909.7533; IR (solid state, KBr, cm^{-1}): $\nu_{C\equiv C}$ 2123.

B_{12}-2. The following modification was applied to the general procedure: the first crude precipitate was dissolved in CH_2Cl_2 and filtered to remove the excess of **2**. The remaining mixture was then purified as described above. Deep red powder; Yield: 71.2 mg (73%); ^{1}H NMR (500 MHz, MeOD-[d_4]): δ = 8.31 (t, *J* = 8.25 Hz, 1H, HC-9L), 7.94 (br d, *J* = 5.15 Hz, 1H, HC-12L), 7.90 (dd, *J* = 7.2, 6.0 Hz, 1H, HC-10L), 7.78 (d, *J* = 7Hz, 1H, HC-5L), 7.67 (dd, *J* = 4, 1.65 Hz, 1H, HC-7L), 7.57-7.59 (m, 4H, HC-16/19/34/37L), 7.41-7.34 (m, 1H, HC-11L), 7.25-7.18 (m, 4H, HC-7N, HC-2N, HC-13/40L), 6.96-6.88 (m, 2H, HC-22/31L), 6.79 (d, *J* = 6 Hz, 1H, HC-4L), 6.68-6.20 (m, 2H, HC-14/39L), 6.61 (s, 1H, HC-4N), 6.56-6.47 (m, 2H, HC-21/32L), 6.27 (d, *J* = 3 Hz, 1H, HC-1R), 6.01 (d, *J* = 7.30 Hz, 1H, HC-10), 4.70 (br s, 1H, HC-3R), 4.56-4.49 (m, 1H, HC-3), 4.40-4.27 (m, 2H, HC-19, HC-176), 4.23-4.18 (m, 1H, HC-2R), 4.13-4.07 (m, 1H, HC-4R), 3.92 (br d, *J* = 11 Hz, 1H, H_bC-5R), 3.75 (br d, *J* = 11 Hz, 2H, H_aC-5R, H_bC-175), 3.69-3.62 (m, 2H, HC-8, HC-13), 3.59-3.49 (m, 16H, H_2C-23/25/27/29/41/43/45/47L), 2.88-2.77 (m, 2H, H_aC-175, HC-18), 2.64-2.60 (m, 3H, H_3C-51), 2.59 (br s, 3H, H_3C-151), 2.58-2.56 (m, 1H, H_bC-132), 2.54 (s, 3H, H_bC-21, H_aC-132 H_bC-71), 2.50-2.34 (m, 3H, H_bC-132, H_2C-32), 2.28 (s, 3H, H_3C-11N), 2.27 (s, 3H, H_3C-10N), 2.18 (t, *J* = 13 Hz, 1H, H_aC-171), 2.09-1.96 (m, 4H, H_aC-181, H_bC-131, H_aC-71, H_bC-81), 1.95-1.87 (m, 4H, H_bC-31, H_aC-31, H_bC-31, H_aC-31), 1.84 (s, 3H, H_3C-7A), 1.82-1.76 (m, 2H, H_aC-172), 1.76-1.67 (m, 1H, H_bC-82), 1.45 (d, J = 3.85 Hz, 3H, H_3C-12A), 1.36 (s, 3H, H_3C-12A), 1.27 (d, *J* = 10.4 Hz, 3H, H_3C-17B), 1.26 (s, 1H, H_aC-81), 1.25 (d, *J* = 6.45 Hz, 3H, H_3C-177), 1.23-1.16 (m, 24H, H_3C-24/26/28/30/42/44/46/48L), 1.12 (d, *J* = 12.4 Hz, 3H, H_3C-12B), 0.49 (s, 3H, H_3C-1A) ppm. ^{13}C NMR (125 MHz, MeOD-[d_4]): δ = 180.2, 178.6, 177.8, 177.3, 176.8, 176.4, 176.1, 175.7, 174.8, 174.7, 174.4, 174.2, 166.5, 166.2, 166.1, 159.3, 159.2, 158.7, 158.6, 158.3, 153.9, 153.8, 153.7, 152.4, 151.7, 150.5, 150.4, 143.7, 138.7, 136.5, 135.2, 134.2, 133.4, 131.6, 129.3, 127.9, 125.6, 124.6, 124.5, 118.4, 112.2, 110.4, 110.3, 106.4, 106.3, 106.2, 104.9, 101.2, 95.5, 87.9, 86.3, 75.7, 75.6, 73.8, 70.8, 62.8, 60.6, 57.1, 56.3, 54.9, 52.2, 52.1, 46.7, 45.2, 44.2, 40.1, 36.5, 35.3, 33.4, 33.0, 32.9, 32.6, 32.1, 32.0, 29.7, 27.4, 27.3, 20.9, 20.7, 20.3, 20.2, 20.1, 20.0, 17.7, 17.3, 16.4, 16.2, 12.4, 12.3 ppm; HRMS (ESI^+): $[M]^{2+}$ = 1102.9715, calculated for $C_{110}H_{147}Co_1N_{23}O_{14}P_1Ru_1$ = 1102.9815; IR (solid state, KBr, cm^{-1}): $\nu_{C\equiv C}$ 2123.

B_{12}-3. Red powder; Yield: 65.9 mg (78%); NMR spectrum is not reported because the compound is paramagnetic; HRMS (ESI^+): $[M+Na]^+$ = 1933.3912, calculated for $C_{76}H_{95}Br_2Co_1N_{15}O_{16}P_1Re_1Na_1$ = 1933.3953; IR (solid state, KBr, cm^{-1}): $\nu_{C\equiv C}$ 2122, $\nu_{C=O}$ 1999, 1869.

B_{12}-4-CBC. The rhodamine labeled vitamin B_{12} (CBC, 10 mg) previously described[4] was reacted with **4** and purified similarly as for the other derivatives. Red powder; Yield: 13.9 mg (72%); ^1H NMR (500 MHz, MeOD-[d_4]): δ = 8.69-8.63 (m, 4H, HC-13/22/31/40L), 8.48 (d, *J* = 8.4 Hz, 1H, HC-9L), 8.41 (d, *J* = 8.2 Hz, 1H, HC-3Rh), 8.20 (dd, *J* = 8.25, 1.73 Hz, 1H, HC-4Rh), 8.12-8.05 (m, 5H, HC-12L, HC-16/19/34/37L), 7.93 (d, *J* = 1.25 Hz,1H, HC-7L), 7.77 (d, *J* = 1.8 Hz, 1H, HC-6Rh), 7.76-7.68 (m, 5H, HC-10L, HC-15/20/33/38L), 7.48-7.40 (m, 6H, HC-5/11L, HC-14/21/32/39L), 7.20 (s, 1H, HC-7N), 7.19 (s, 1H, HC-2N), 6.94 (d, *J* = 1.65 Hz, 2H, HC-11/26Rh), 6.87 (br s, 2H, HC-17/20Rh), 6.80 (m, 1H, HC-4L), 6.59 (s, 1H, HC-4N), 6.19 (d, *J* = 2.9 Hz, 1H, HC-1R), 5.98 (d, *J* = 6.6 Hz, 1H, HC-10), 4.85-4.80 (m, 1H, HC-3R), 4.62 (d, *J* = 11.6 Hz, 1H, HC-3), 4.50 (t, *J* = 6.4 Hz, 1H, HC-19), 4.39-4.32 (m, 1H, HC-176), 4.27 (d, *J* = 10.5 Hz, 1H, HC-2R), 4.20 (m, 2H, HC-4R, H_bC-5R), 4.14 (d, *J* = 11.6 Hz, 1H, H_aC-5R), 3.68-3.50 (m, 15H, H_bC-175, HC-8, HC-13, HC-$T_{5,7,8,10,11,13}$), 3.50-3.40 (m, 6H, $T_{4,5,13,14}$), 3.18-3.08 (m, 4H, $T_{3,15}$), 2.91 (dd, *J* = 8.30, 5.35 Hz, 1H, H_aC-175), 2.84-2.76 (m, 1H, HC-18), 2.65-2.34 (m, 15H, H_3C-51, H_3C-151, H_bC-21, H_aC-132 H_bC-71, H_bC-132, H_2C-32, H_3C-16/23Rh), 2.26 (m, 6H, H_3C-11N, H_3C-10N), 2.13 (m, 5H, H_aC-181, H_bC-131, H_aC-71, HC-15/22Rh), 2.08-1.78 (m, 16H, H_aC-171, H_aC-181, H_bC-131, H_aC-71, H_bC-81, H_3C-7A, H_aC-172, H_bC-82, HC-13/25Rh), 1.74-1.64 (m, 3H, H_bC-31, H_aC-31, H_aC-131), 1.44 (d, *J* = 3.35 Hz, 3H, H_3C-12A), 1.39-1.32 (m, 7H, H_3C-2A, H_3C-17B, H_aC-81), 1.26 (d, *J* = 10.0 Hz, 3H, H_3C-177), 1.10 (d, *J* = 15 Hz, 3H, H_3C-12B), 0.5 (s, 3H, H_3C-1A) ppm. ^{13}C NMR (125 MHz, MeOD-[d_4]): δ = 180.2, 178.6, 178.5, 177.3, 176.8, 176.4, 176.0, 175.7, 174.6, 174.3, 174.2, 167.9, 167.5, 166.5, 166.3, 161.8, 161.4, 159.2, 158.9, 158.6, 158.5, 158.2, 158.0, 157.7, 152.6, 152.5, 152.4, 152.3, 152.2, 151.8, 151.7, 143.5, 139.5, 139.2, 138.6, 136.9, 136.6, 135.9, 135.3, 134.7, 133.9, 133.5, 132.9, 131.5, 130.2, 130.0, 128.9, 126.9, 126.4, 126.4, 125.6, 126.5, 118.5, 114.8, 104.9, 101.2, 95.4, 94.9, 88.1, 86.3, 81.1, 73.6, 71.3, 71.2, 71.1, 70.6, 76.3, 69.6, 63.9, 59.9, 57.0, 56.0, 54.9, 52.1, 52.1, 40.1, 39.4, 39.1, 39.0, 36.4, 35.1, 33.2, 33.0, 32.7, 32.5, 32.2, 31.0, 30.2, 29.6, 27.4, 20.9, 20.8, 20.5, 20.4, 20.1, 20.0, 17.7, 17.6, 17.3, 16.4, 16.20, 14.0 ppm; HRMS (ESI^+): $[M]^{2+}$ = 1304.5040, calculated for $C_{132}H_{157}Co_1N_{23}O_{22}P_1Ru_1$ = 1304.5013; IR (solid state, KBr, cm^{-1}): $\nu_{C\equiv C}$ 2123.

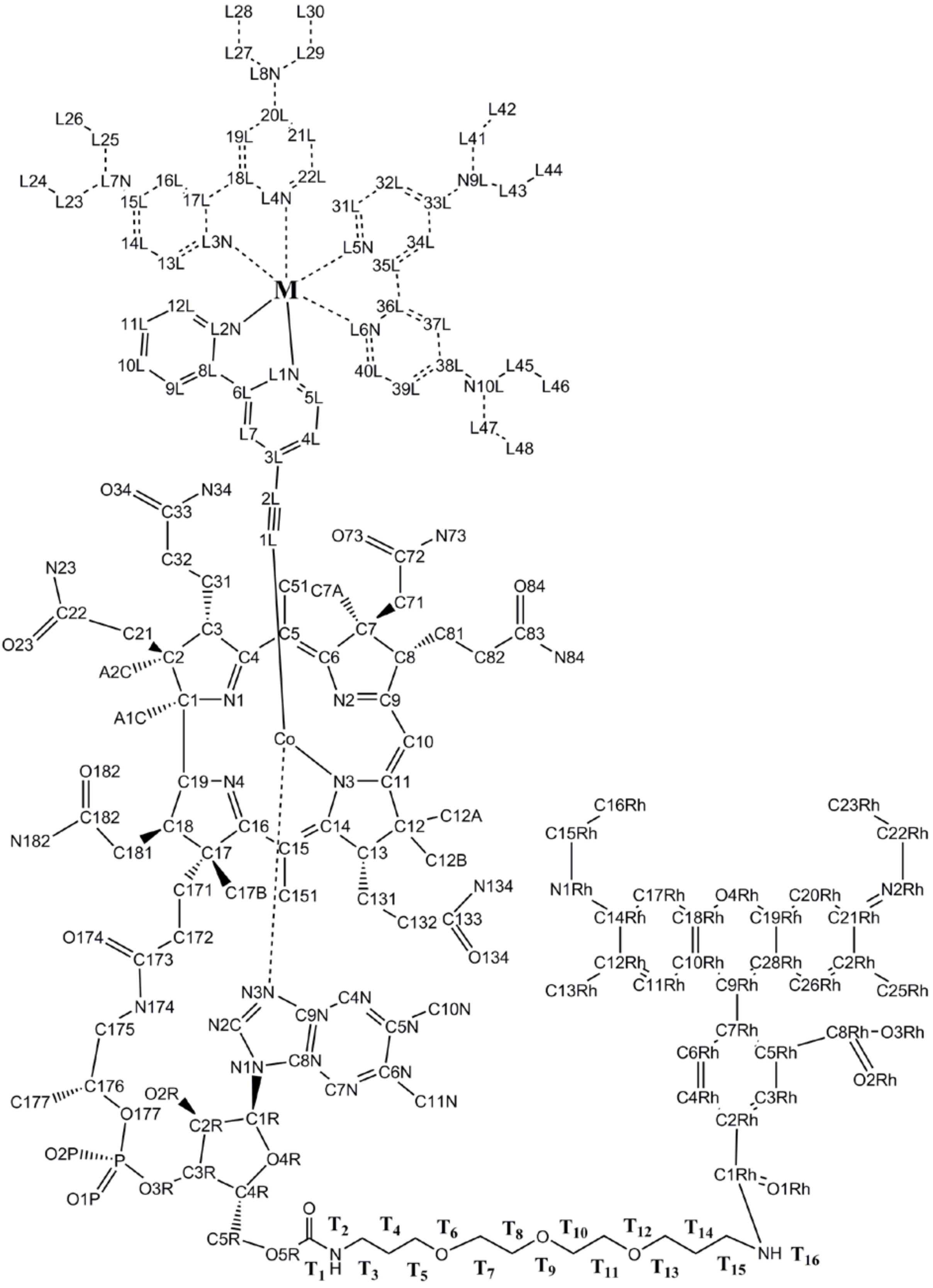

Figure S1. Atom numbering used for derivatives B_{12}-**bpy/1/2/4**-CBC

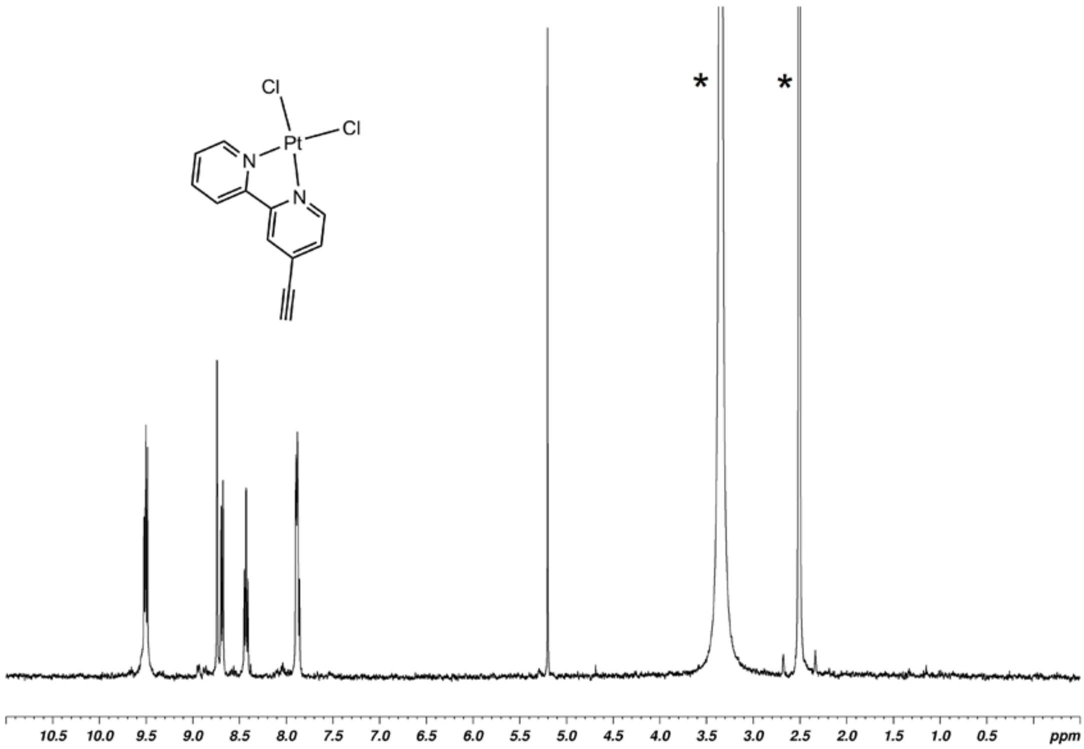

Figure S2. 500 MHz [1]H-NMR of complex **1** (in DMSO-d6, ✱= solvent signal)

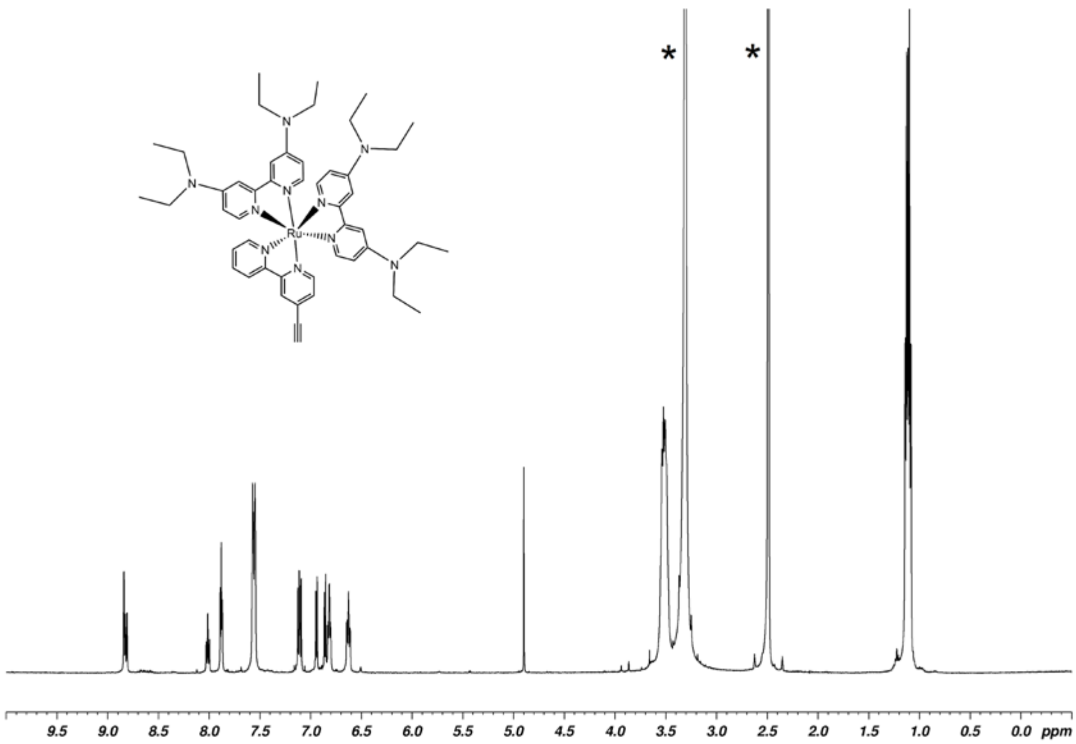

Figure S3. 500 MHz [1]H-NMR of complex **2** (in DMSO-d6, ✱= solvent signal)

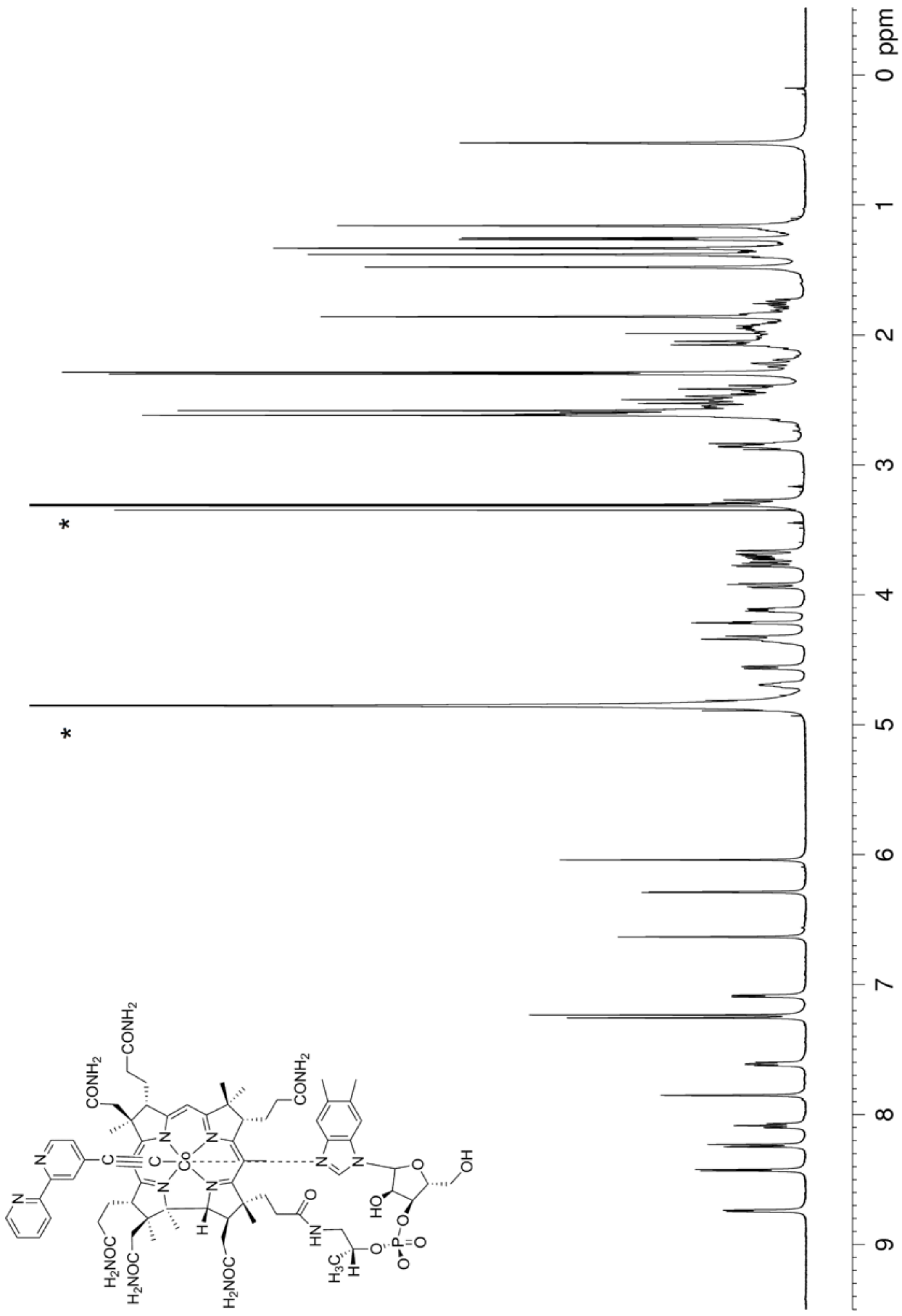

Figure S4. 500 MHz ^{1}H-NMR of derivative B_{12}-**bpy** (in MeOD-d4, ✱= solvent signal)

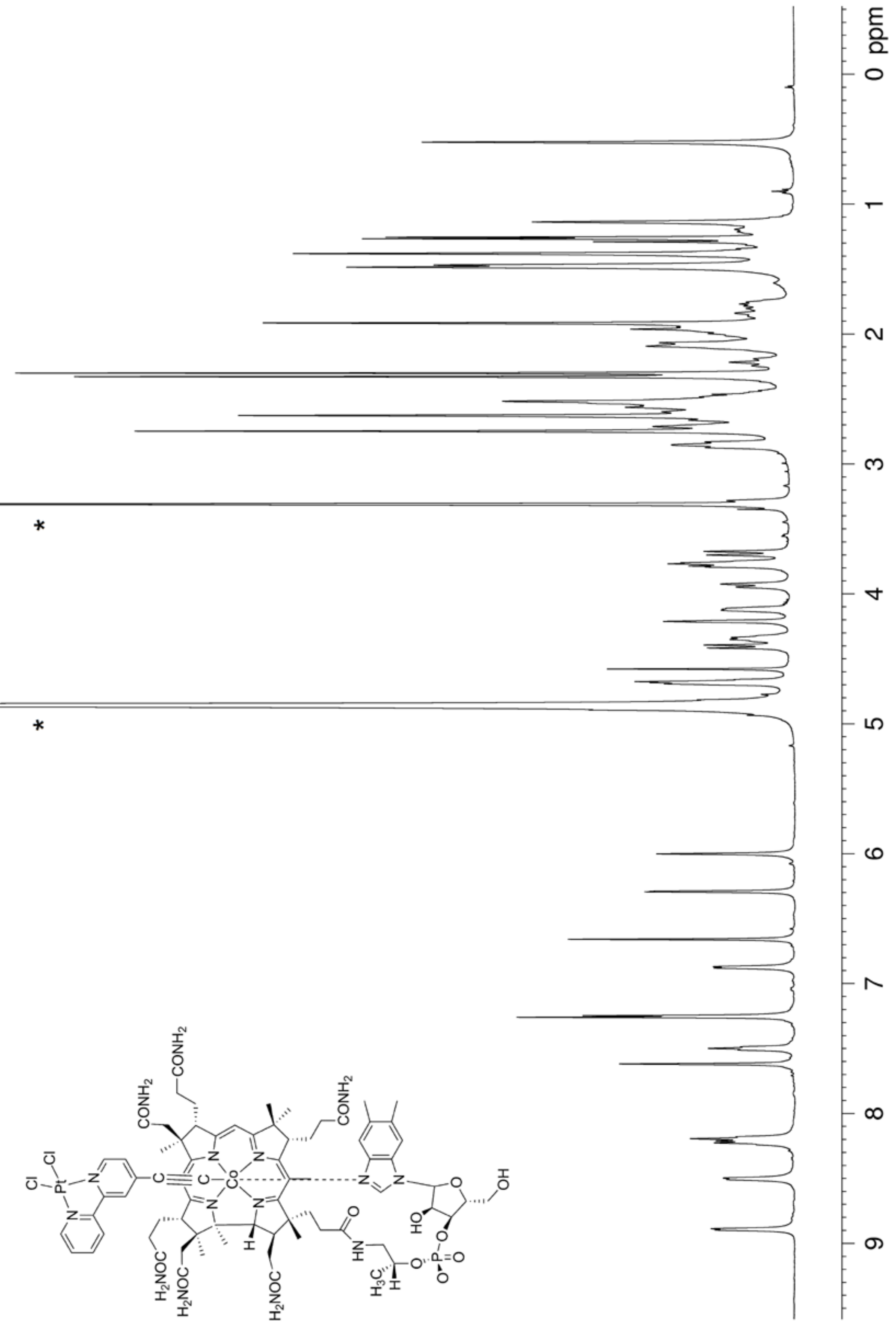

Figure S5. 500 MHz ^{1}H-NMR of derivative B_{12}-**1** (in MeOD-d4, ✱= solvent signal)

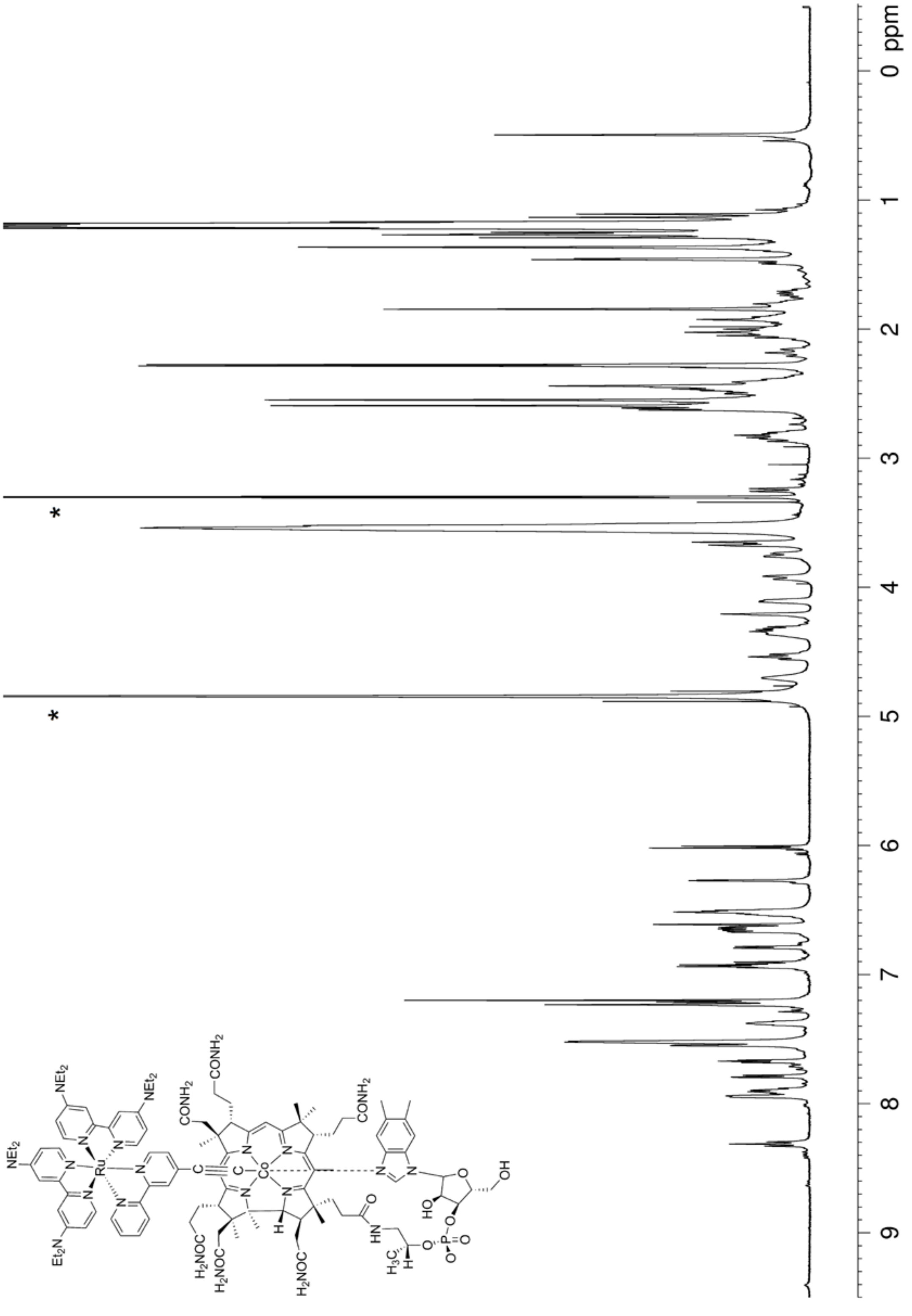

Figure S6. 500 MHz [1]H-NMR of derivative B_{12}-**2** (in MeOD-d4, ✱= solvent signal)

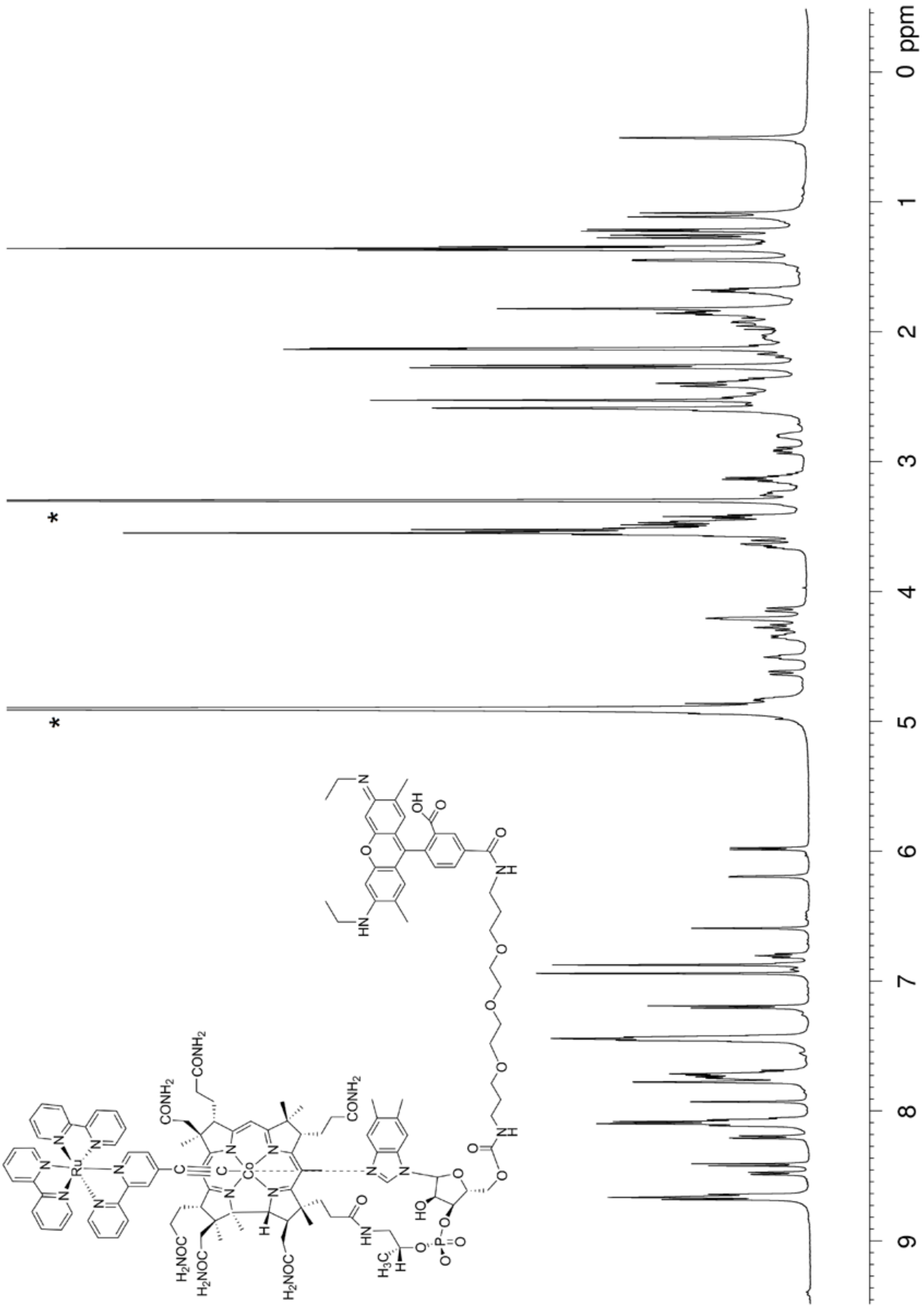

Figure S7. 500 MHz ^{1}H-NMR of derivative B_{12}-**4**-CBC (in MeOD-d4, ✱ = solvent signal)

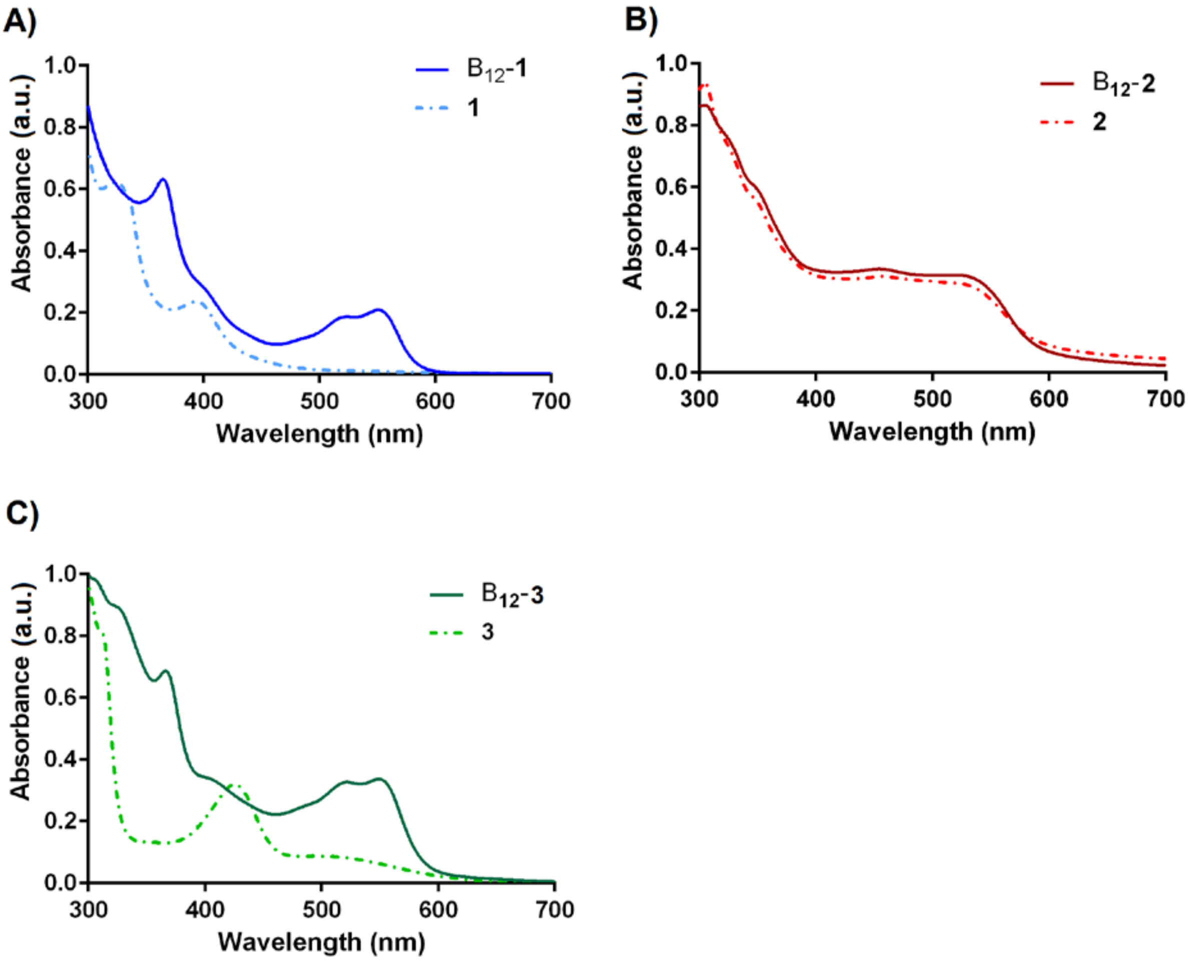

Figure S8. Normalized UV-Vis spectra of A) complex **1** and derivative B_{12}-**1**; B) complex **2** and derivative B_{12}-**2**; C) complex **3** and derivative B_{12}-**3.**

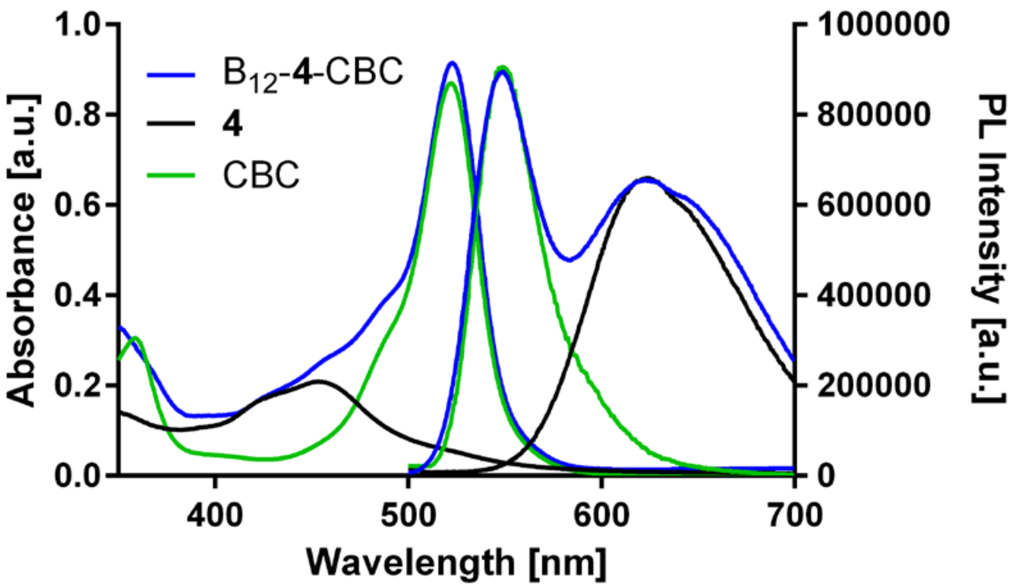

Figure S9. UV-Vis and emission spectra of B_{12}-**4**-CBC, complex **4** and of CBC.

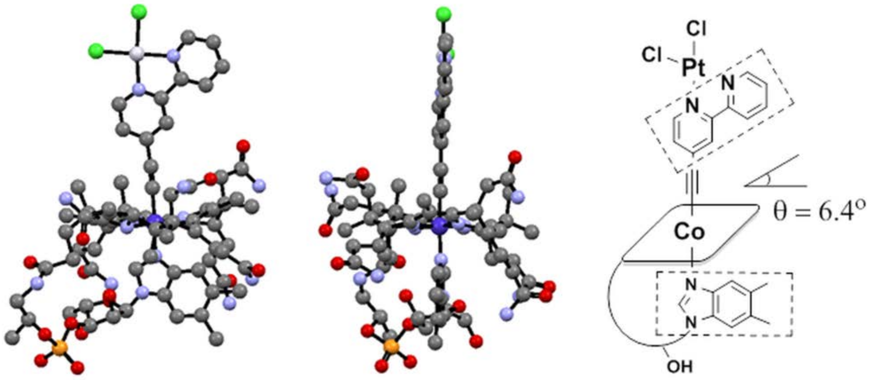

Figure S10. X-ray data-based MM model of B_{12}-**1.** Crystals were obtained by slow evaporation of water/methanol solution. Unfortunately, due to twinning, the structure of the derivative was only partially solved. As it appears in the figure, the bipyridine and dimethylbenzamidazole moiety are almost completely eclipsed with a measured 6.4° twist angle between their respective planes.

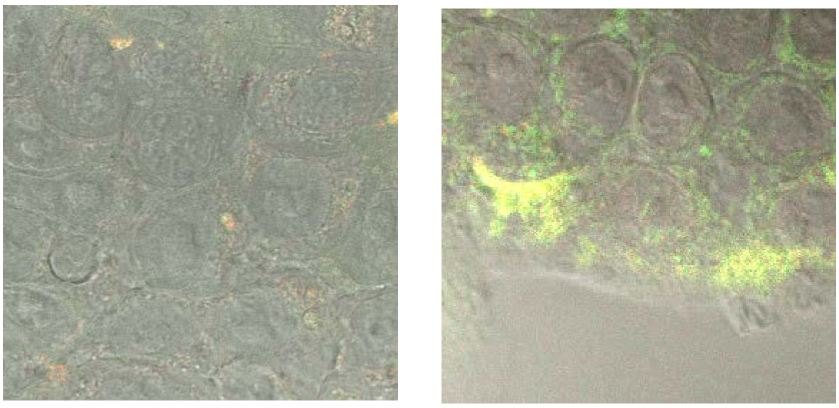

Figure S11. Left: Low temperature (4 °C) incubation (1h) of B_{12}-**4**-CBC with MCF7 cells and, right: Incubation (1h) at 37 °C of B_{12}-**4**-CBC with the same cell line. Both Rho and Ru signals of the probe are overlapped in the corresponding brightfield image.

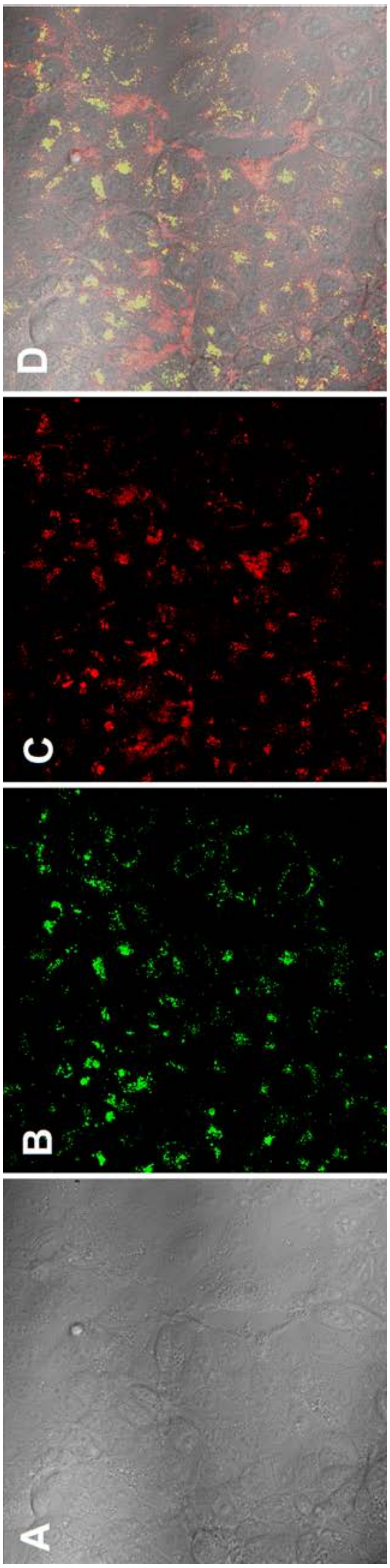

Figure S12. Co-localization images of lysotracker (LTB) and B_{12}-**4**-CBC in MCF7 cells after 1h of incubation at 37 °C. A) Brightfield, B) Lysotracker, C) B_{12}-**4**-CBC (Overlap of the Rho and Ru emission) and D) Overlap of A, B and C.

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