

SUPPORTING INFORMATION FOR

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

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Synthesis and characterization

General synthesis of metal complexes

[Pt(HCC-bpy)Cl₂] (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 CH₃CN (10 ml) and CH₃OH (10 ml). The solid was dried under vacuum and used without further purification. Yield: 142 mg (90%); ¹H 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; ¹³C 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, ¹⁹⁵Pt (107 MHz, DMSO-[d₆], referred to Na₂[PtCl₆]): δ = -2300 ppm; Anal. Calcd. for C₁₂H₈Cl₂N₂Pt: 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((Et₂N)₂Bpy)₂(HCC-bpy)]Cl₃ (2). A mixture of [Ru((Et₂N)₂Bpy)₂Cl₂]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 CH₃OH (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 CH₃CN 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 CH₂Cl₂ (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**. ¹H NMR (500 MHz, DMSO-[d₆]): 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); ¹³C NMR (125 MHz, DMSO-[d₆]): 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 C₄₈H₆₀Cl₃N₁₀Ru: 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 C₄₈H₆₀N₁₀Ru₁ = 439.2022; IR (solid state, KBr, cm⁻¹): ν_{C≡C} 2122.

[Re(HCC-bpy)(CO)₂Br₂] (3). A mixture of (Et₄N)₂[Re(CO)₂Br₄]^[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 CHCl₃ and purified by column chromatography on silica gel using CHCl₃/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 C₁₄H₈Br₂N₂O₂Re: 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 C₁₄H₈Br₂N₂O₂Re = 580.8510; IR (solid state, KBr, cm⁻¹): ν_{C≡C} 2119, ν_{C=O} 1994, 1842.

[Ru(HCC-bpy)(bpy)₂]Cl₂ (4). Complex **4** was obtained via anion metathesis starting from [Ru(HCC-bpy)(bpy)₂](PF₆)₂.^[3] The latter was dissolved in acetone and an aqueous solution of concentrated tetrabutylammonium chloride was added dropwise until precipitation of **4** occurred.

Characterization of the vitamin B₁₂ derivatives

B₁₂-bpy. Red powder; Yield: 52.8 mg (78%); ¹H NMR (500 MHz, MeOD-[d₄]): 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, H₃C-51), 2.60-5.58 (m, 3H, H₃C-151), 2.57 (m, 1H, H_bC-132), 2.56-2.53 (m, 2H, H₂C-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, H₃C-11N), 2.27 (s, 3H, H₃C-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, H₃C-7A), 1.83-1.78 (m, 1H, H_aC-172), 1.77 (m, 1H, H_bC-82), 1.46 (s, 3H, H₃C-12A), 1.37 (s, 3H, H₃C-2A), 1.36 (m, 1H, H_a-82), 1.32 (s, 3H, H₃C-17B), 1.31 (m, 1H, H_aC-81), 1.25 (d, *J* = 6.25 Hz, 3H, H₃C-177), 1.15 (s, 3H, H₃C-12B), 0.51 (s, 3H, H₃C-1A) ppm; ¹³C NMR (125 MHz, MeOD-[d₄]): 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 C₇₄H₉₅Cl₂Co₁N₁₅O₁₄P₁Na₂ = 1530.6144; IR (solid state, KBr, cm⁻¹): ν_{C=C} 2124.

B₁₂-1. Red powder; Yield: 52.7 mg (61%); ¹H NMR (500 MHz, MeOD-[d₄]): 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, H₃C-51), 2.71-2.67 (m, 3H, H₃C-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, H₂C-32), 2.31 (s, 3H, H₃C-11N), 2.29 (s, 3H, H₃C-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, H₃C-7A), 1.86-1.80 (m, 1H, H_aC-172), 1.78-1.71 (m, 1H, H_bC-82), 1.47 (s, 3H, H₃C-12A), 1.45 (s, 3H, H₃C-2A), 1.37 (s, 3H, H₃C-17B), 1.28 (s, 1H, H_aC-81), 1.25 (d, *J* = 6.25 Hz, 3H, H₃C-177), 1.12 (s, 3H, H₃C-12B), 0.51 (s, 3H, H₃C-1A) ppm; ¹³C NMR (125 MHz, MeOD-[d₄]): 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; ¹⁹⁵Pt (107 MHz, DMSO-[d₆], referred to Na₂[PtCl₆]): δ = -2311 ppm; HRMS (ESI⁺): [M+2Na]²⁺ = 909.7522, calculated for C₇₄H₉₅Cl₂Co₁N₁₅O₁₄P₁Pt₁Na₂ = 909.7533; IR (solid state, KBr, cm⁻¹): ν_{C=C} 2123.

B₁₂-2. The following modification was applied to the general procedure: the first crude precipitate was dissolved in CH₂Cl₂ 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%); ¹H NMR (500 MHz, MeOD-[d₄]): 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* = 7 Hz, 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, H₂C-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, H₃C-51), 2.59 (br s, 3H, H₃C-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, H₂C-32), 2.28 (s, 3H, H₃C-11N), 2.27 (s, 3H, H₃C-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, H₃C-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, H₃C-12A), 1.36 (s, 3H, H₃C-12A), 1.27 (d, *J* = 10.4 Hz, 3H, H₃C-17B), 1.26 (s, 1H, H_aC-81), 1.25 (d, *J* = 6.45 Hz, 3H, H₃C-177), 1.23-1.16 (m, 24H, H₃C-24/26/28/30/42/44/46/48L), 1.12 (d, *J* = 12.4 Hz, 3H, H₃C-12B), 0.49 (s, 3H, H₃C-1A) ppm. ¹³C NMR (125 MHz, MeOD-[d₄]): 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 C₁₁₀H₁₄₇Co₁N₂₃O₁₄P₁Ru₁ = 1102.9815; IR (solid state, KBr, cm⁻¹): ν_{C=C} 2123.

B₁₂-3. 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 C₇₆H₉₅Br₂Co₁N₁₅O₁₆P₁Re₁Na₁ = 1933.3953; IR (solid state, KBr, cm⁻¹): ν_{C=C} 2122, ν_{C=O} 1999, 1869.

B₁₂-4-CBC. The rhodamine labeled vitamin B₁₂ (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-[d₄]): 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, H₃C-51, H₃C-151, H_bC-21, H_aC-132 H_bC-71, H_bC-132, H₂C-32, H₃C-16/23Rh), 2.26 (m, 6H, H₃C-11N, H₃C-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, H₃C-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, H₃C-12A), 1.39-1.32 (m, 7H, H₃C-2A, H₃C-17B, H_aC-81), 1.26 (d, *J* = 10.0 Hz, 3H, H₃C-177), 1.10 (d, *J* = 15 Hz, 3H, H₃C-12B), 0.5 (s, 3H, H₃C-1A) ppm. ¹³C NMR (125 MHz, MeOD-[d₄]): 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 C₁₃₂H₁₅₇Co₁N₂₃O₂₂P₁Ru₁ = 1304.5013; IR (solid state, KBr, cm⁻¹): ν_{C=C} 2123.

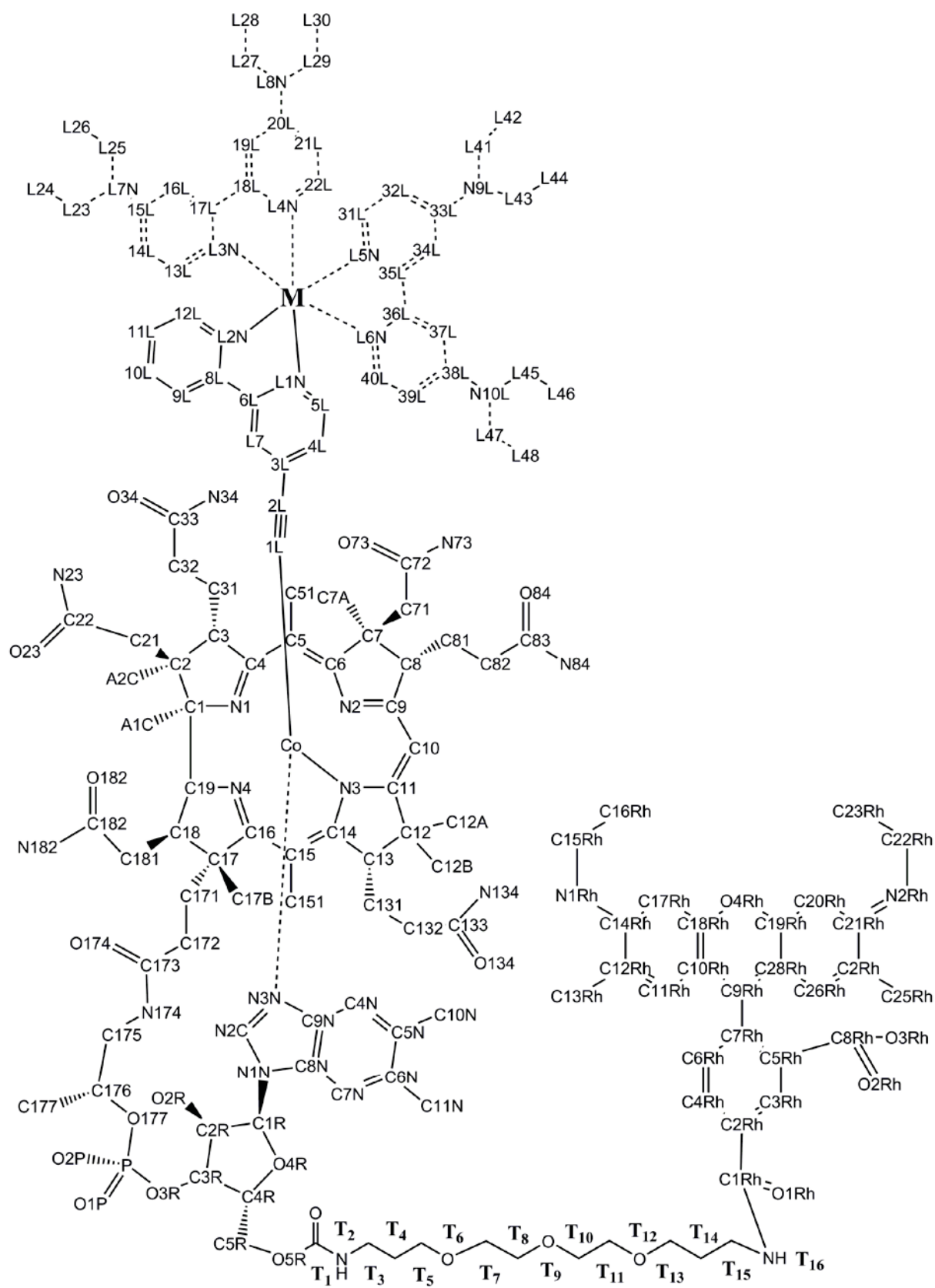


Figure S1. Atom numbering used for derivatives B₁₂-bpy/1/2/4-CBC

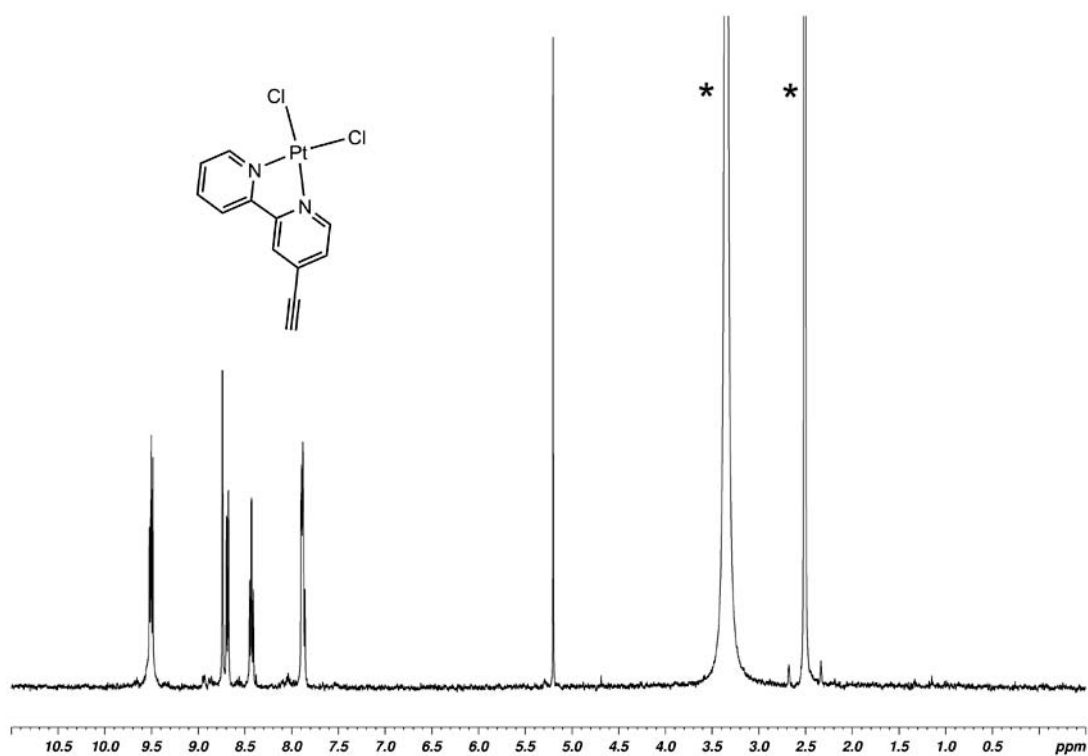


Figure S2. 500 MHz ^1H -NMR of complex 1 (in DMSO- d_6 , * = solvent signal)

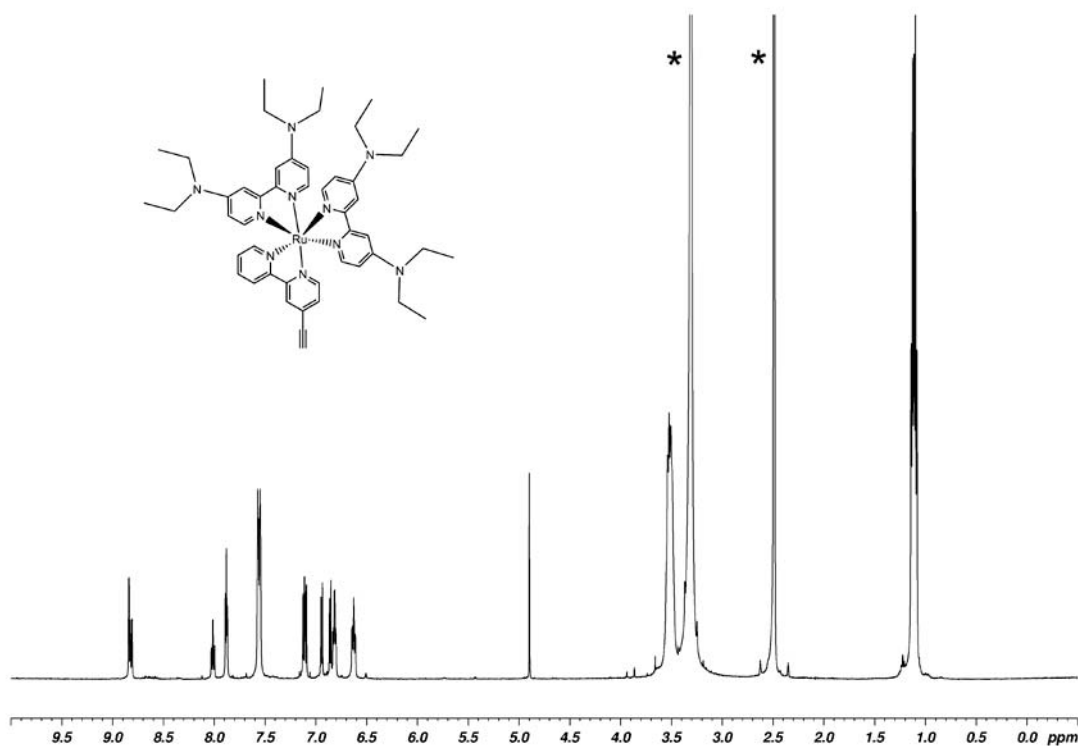


Figure S3. 500 MHz ^1H -NMR of complex 2 (in DMSO- d_6 , * = solvent signal)

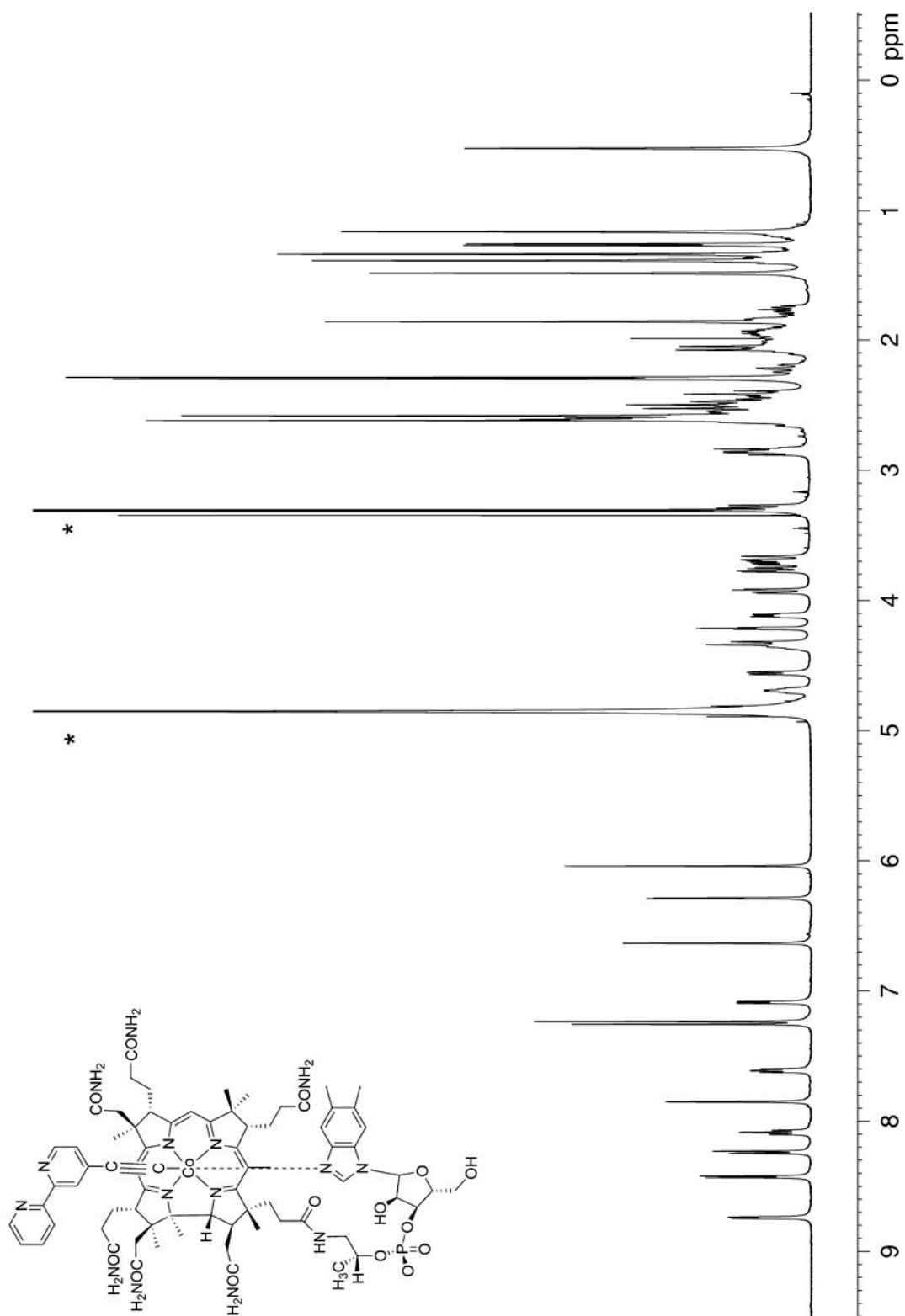


Figure S4. 500 MHz ¹H-NMR of derivative B₁₂-bpy (in MeOD-d₄, * = solvent signal)

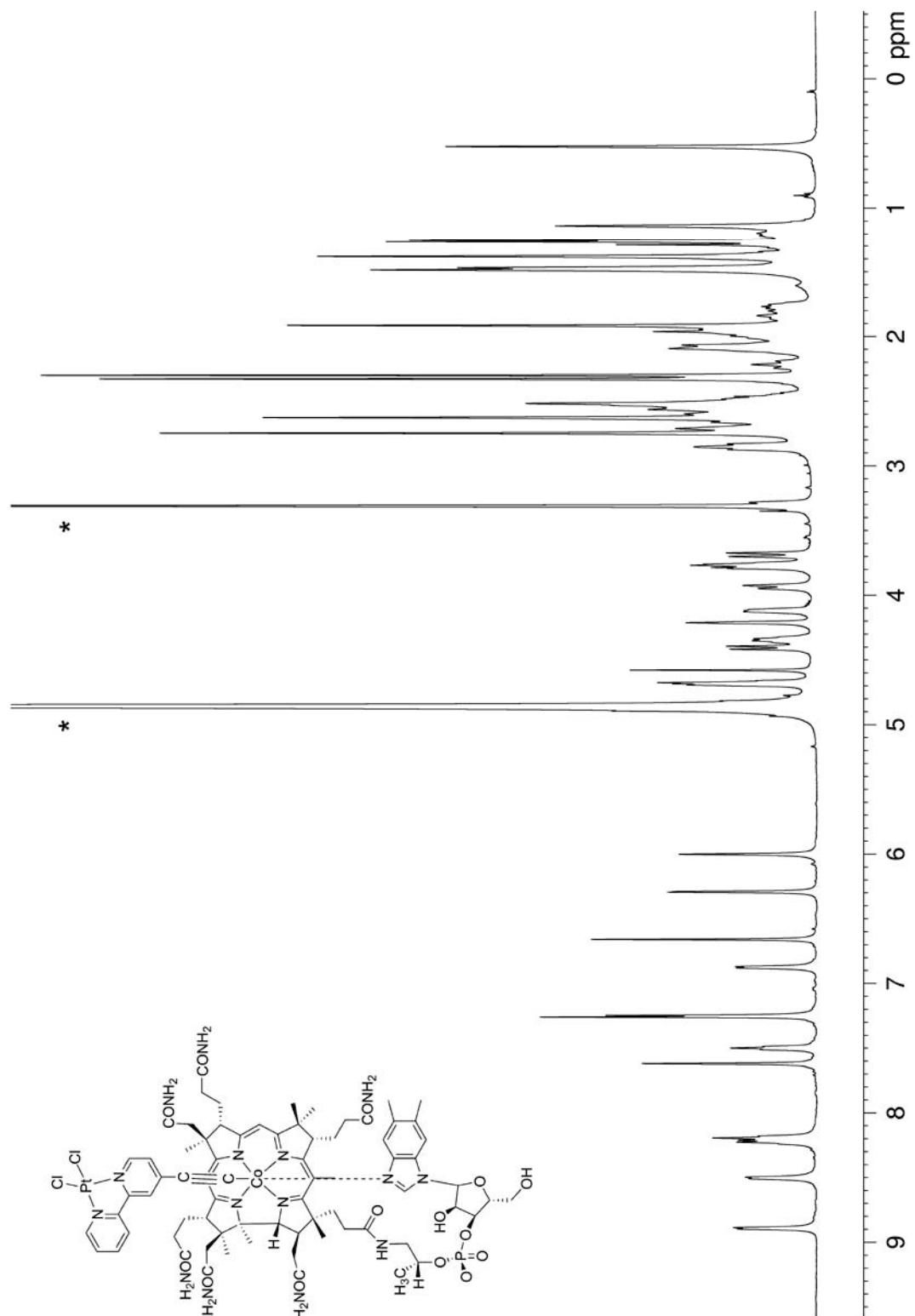


Figure S5. 500 MHz $^1\text{H-NMR}$ of derivative $\text{B}_{12}\text{-1}$ (in MeOD-d_4 , * = solvent signal)

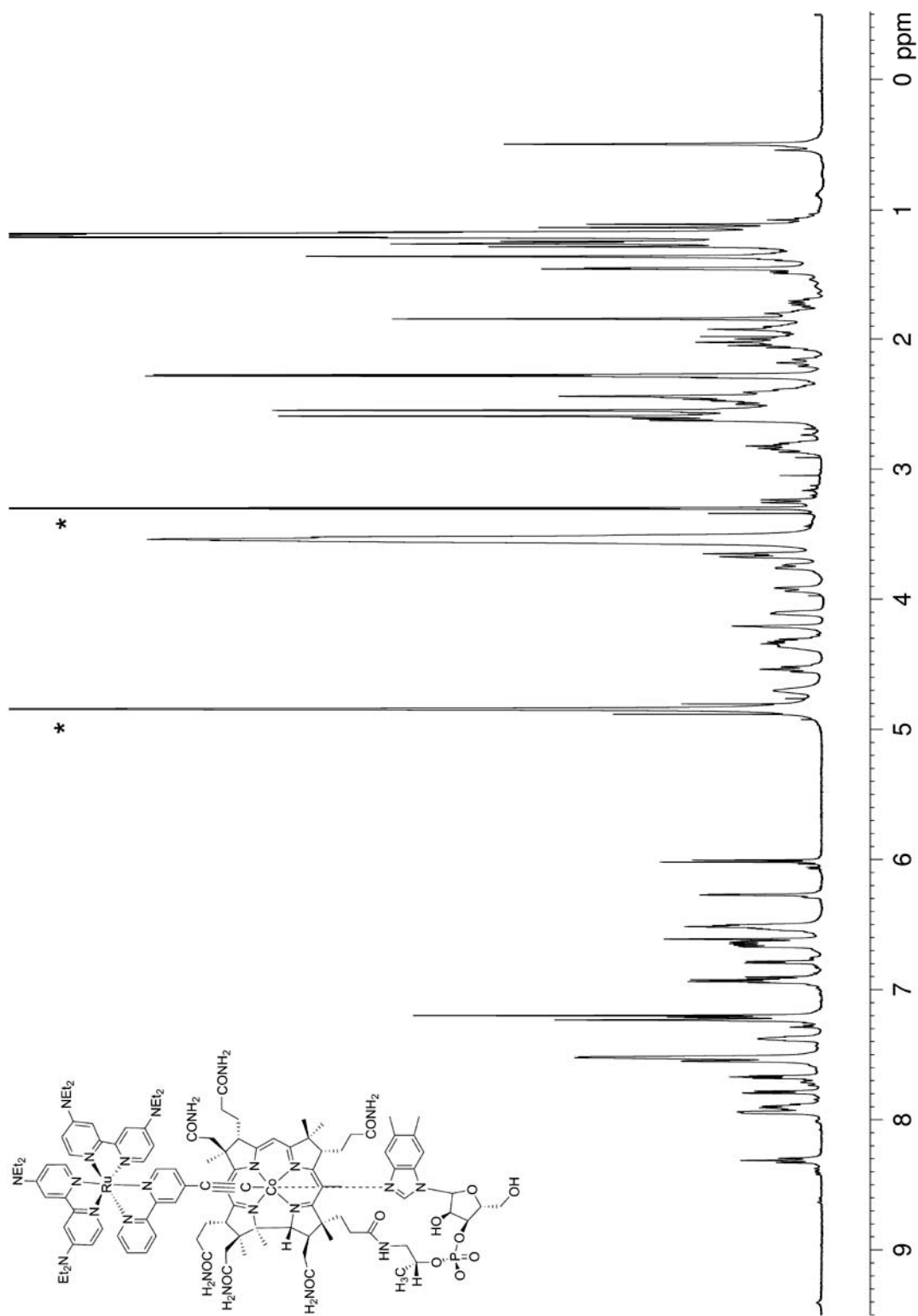


Figure S6. 500 MHz $^1\text{H-NMR}$ of derivative $\text{B}_{12}\text{-2}$ (in MeOD-d_4 , * = solvent signal)

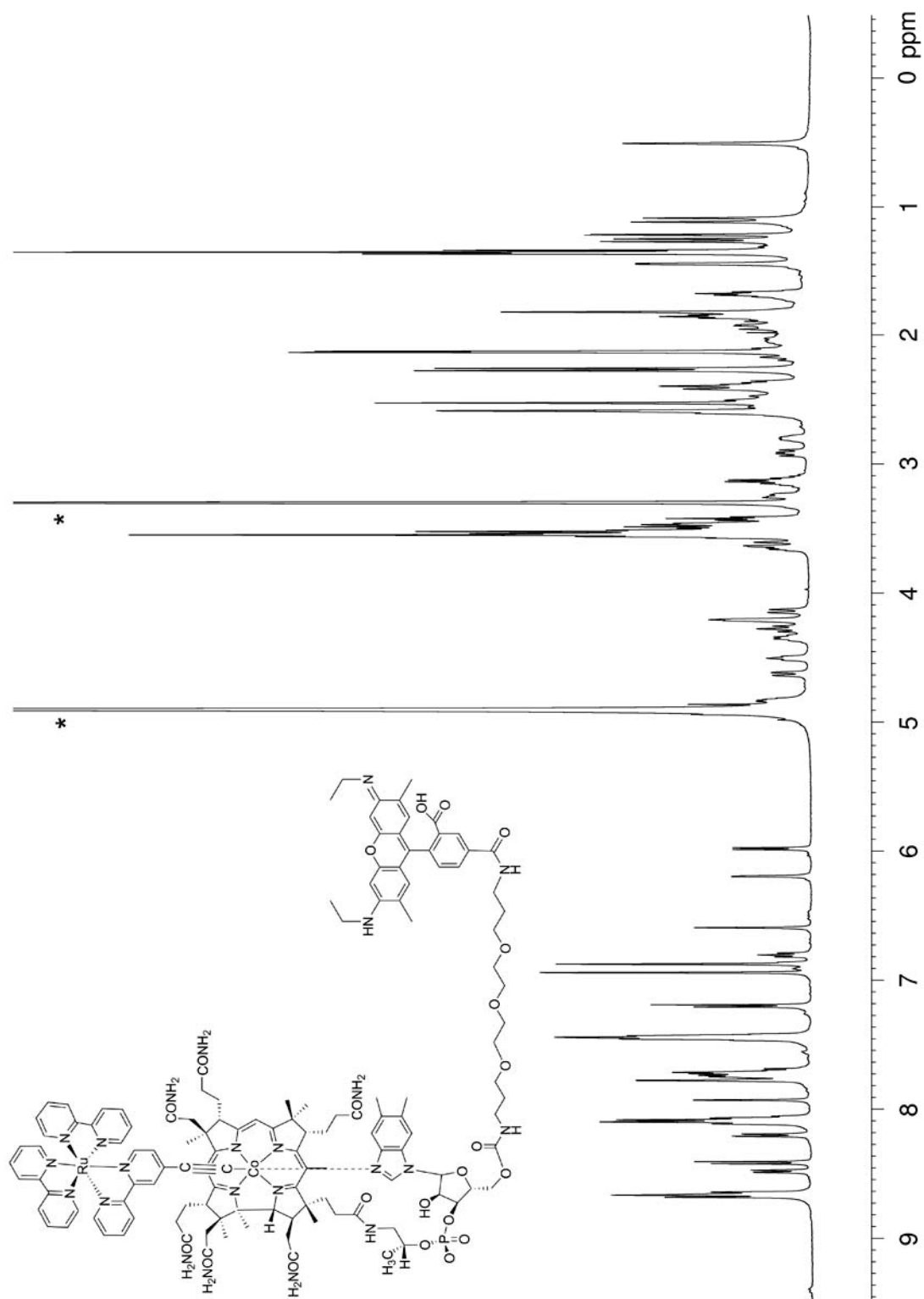


Figure S7. 500 MHz ¹H-NMR of derivative B₁₂-4-CBC (in MeOD-d₄, * = solvent signal)

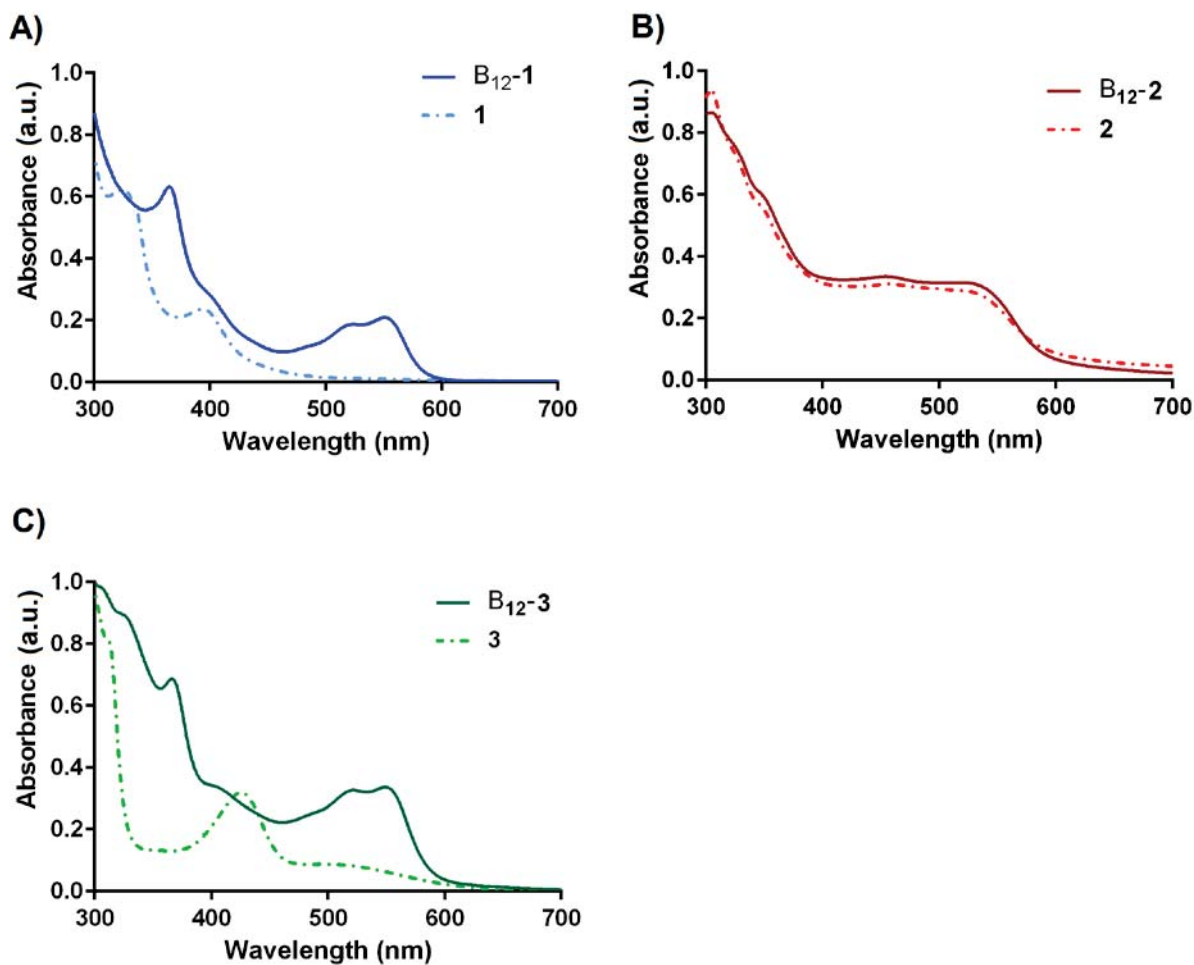


Figure S8. Normalized UV-Vis spectra of A) complex 1 and derivative B₁₂-1; B) complex 2 and derivative B₁₂-2; C) complex 3 and derivative B₁₂-3.

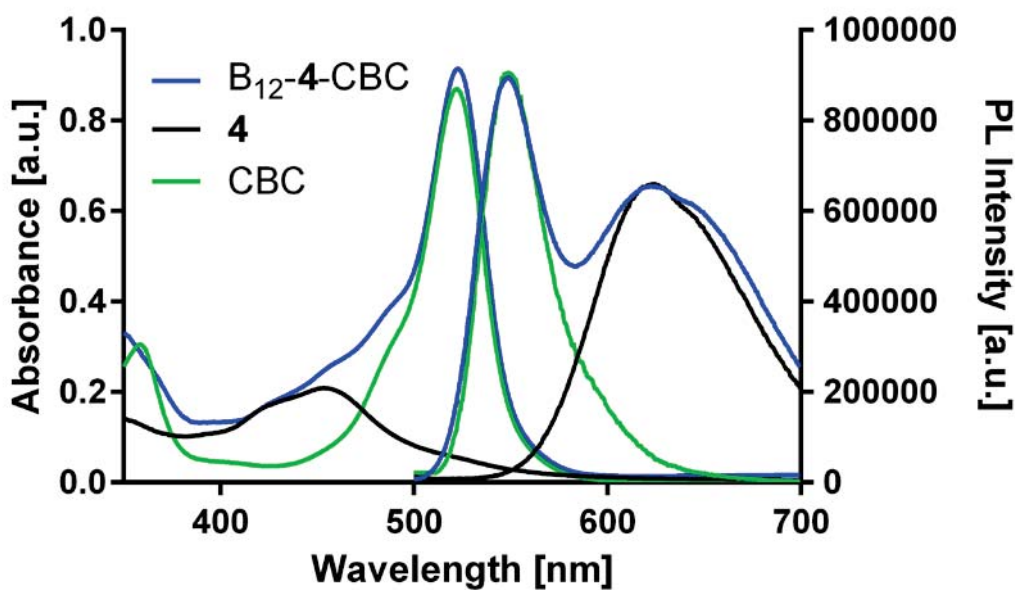


Figure S9. UV-Vis and emission spectra of B₁₂-4-CBC, complex 4 and of CBC.

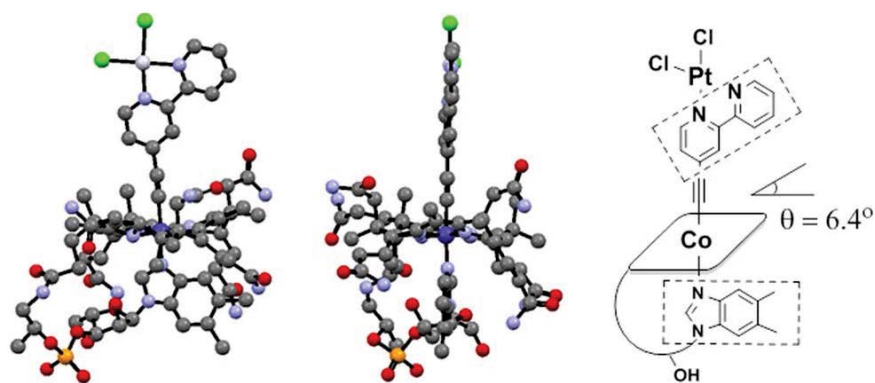


Figure S10. X-ray data-based MM model of B₁₂-1. Crystals were obtained by slow evaporation of water/methanol solution. Unfortunately, due to twinning, the structure of the derivative was only partially solved. As it appears in the figure, the bipyridine and dimethylbenzimidazole moiety are almost completely eclipsed with a measured 6.4° twist angle between their respective planes.

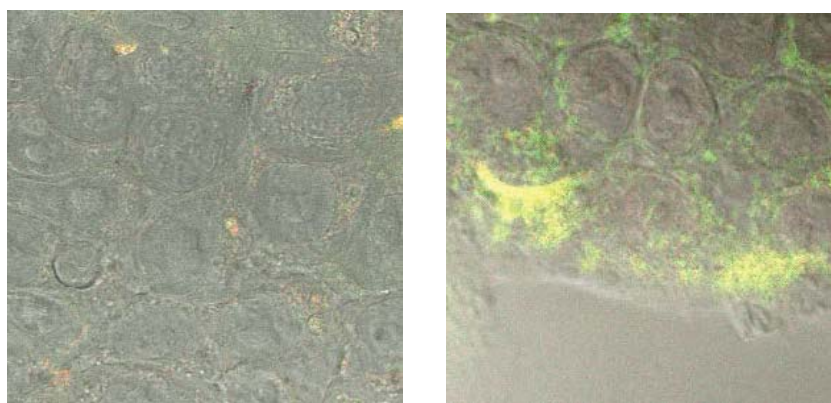


Figure S11. Left: Low temperature (4 °C) incubation (1h) of B₁₂-4-CBC with MCF7 cells and, right: Incubation (1h) at 37 °C of B₁₂-4-CBC with the same cell line. Both Rho and Ru signals of the probe are overlapped in the corresponding brightfield image.

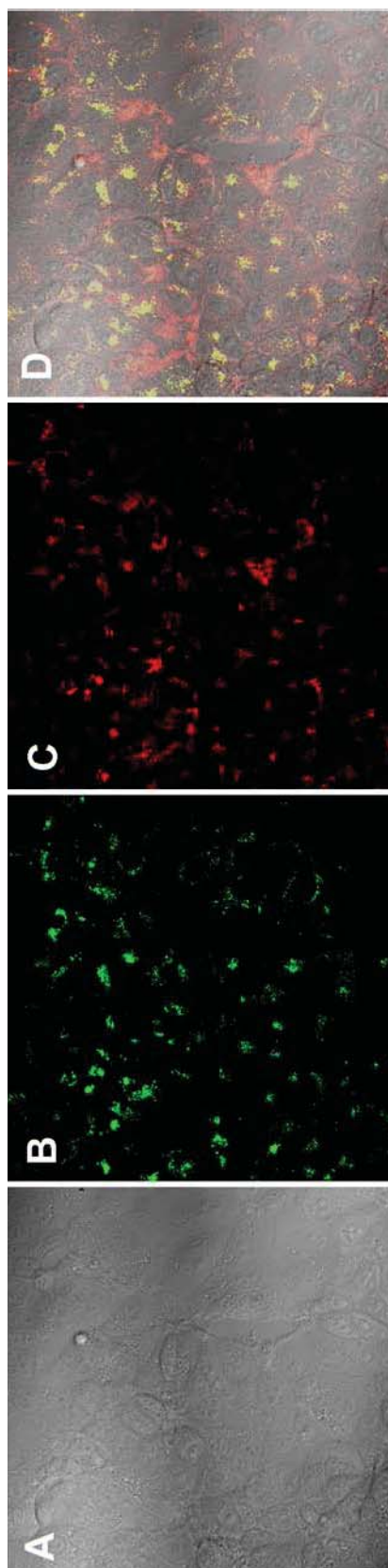


Figure S12. Co-localization images of lysotracker (LTB) and B₁₂-4-CBC in MCF7 cells after 1h of incubation at 37 °C. A) Brightfield, B) Lysotracker, C) B₁₂-4-CBC (Overlap of the Rho and Ru emission) and D) Overlap of A, B and C.

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