Electronic Supplementary Material (ESI) for Dalton Transactions.

Supplementary Information

A Study of ^{99m}Tc/Re-Tricarbonyl Complexes of 4-Amino-1,8-Naphthalimides

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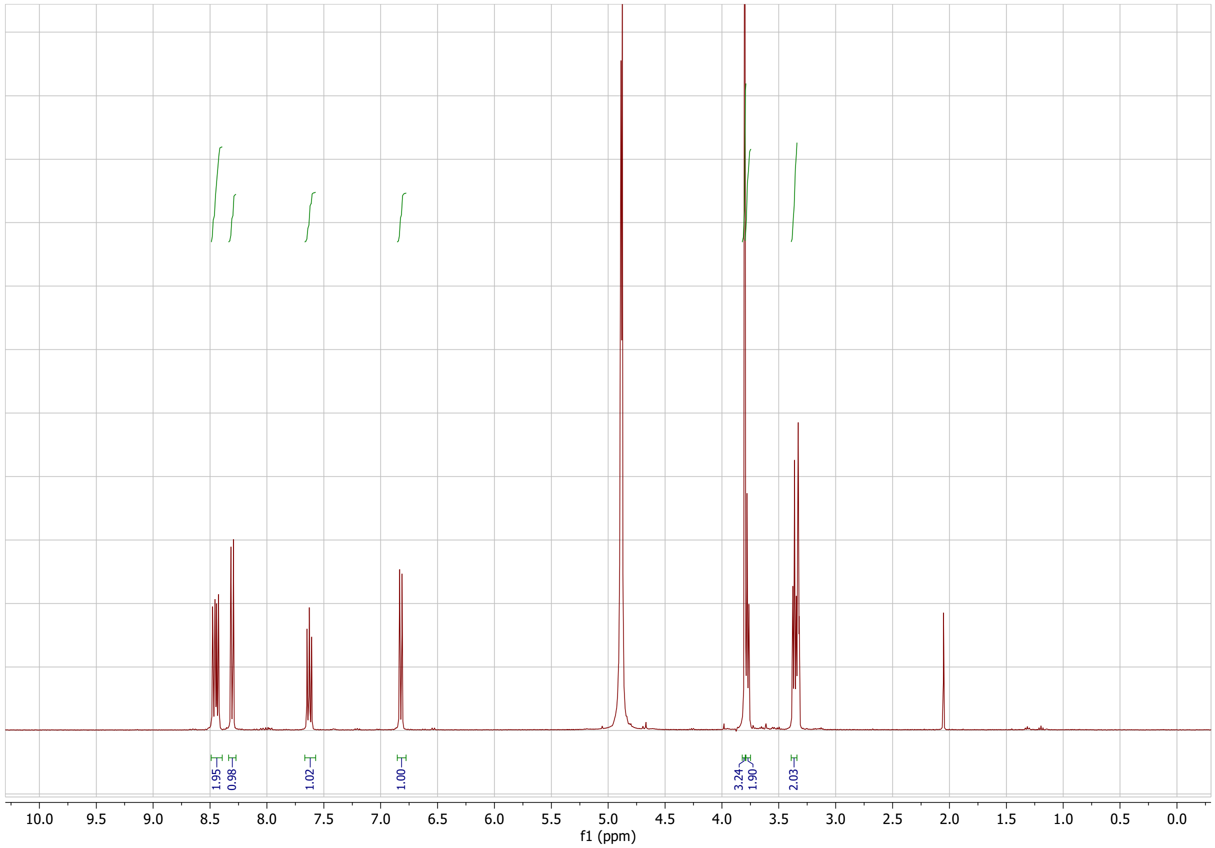

Figure S1 – ^{1}H NMR spectrum (400 MHz; CD_3OD) of **3**.

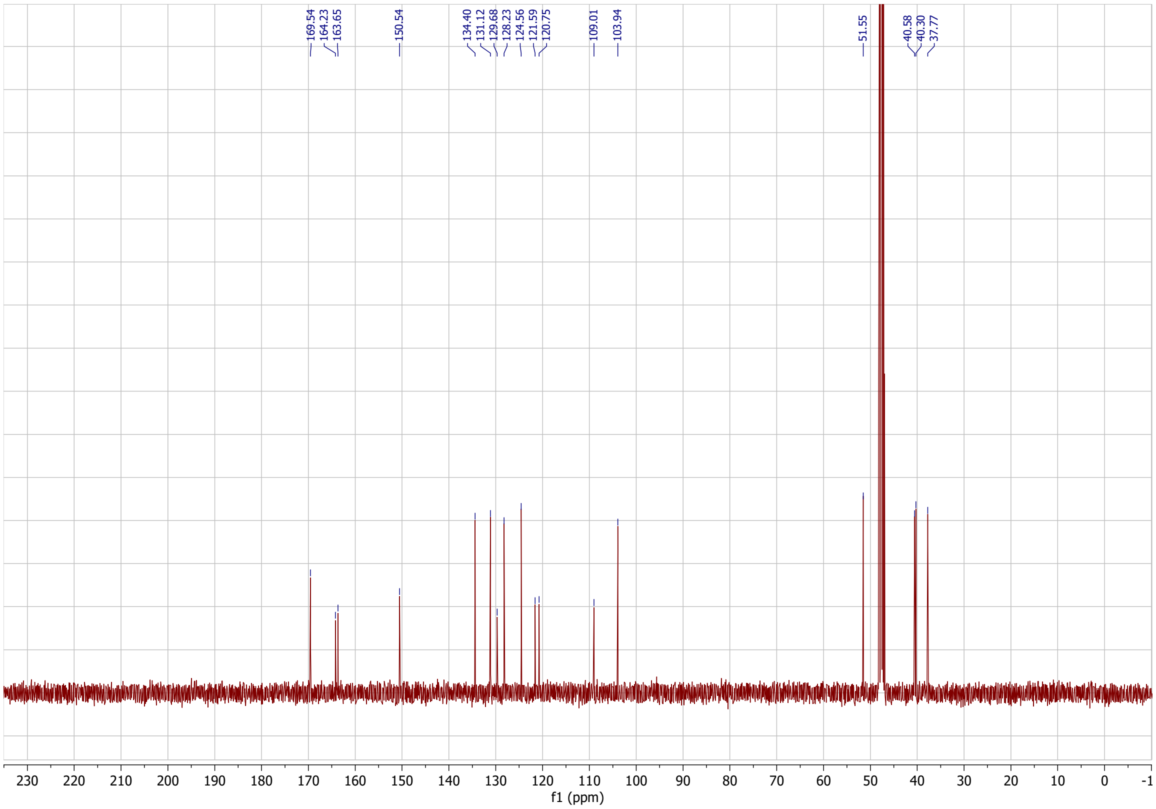

Figure S2 – ^{13}C NMR spectrum (100 MHz; CD_3OD) of **3**.

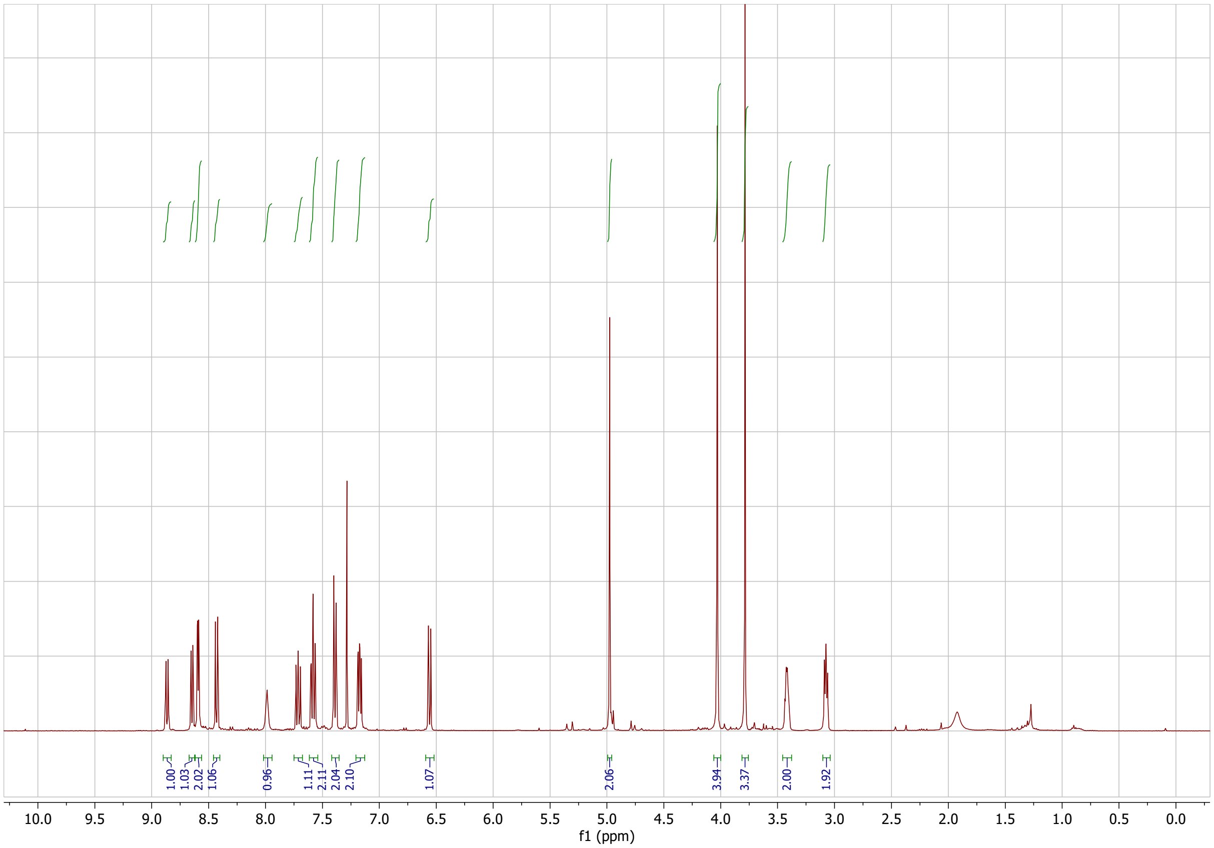

Figure S3 – ^{1}H NMR spectrum (400 MHz; $CDCl_3$) of **L1**.

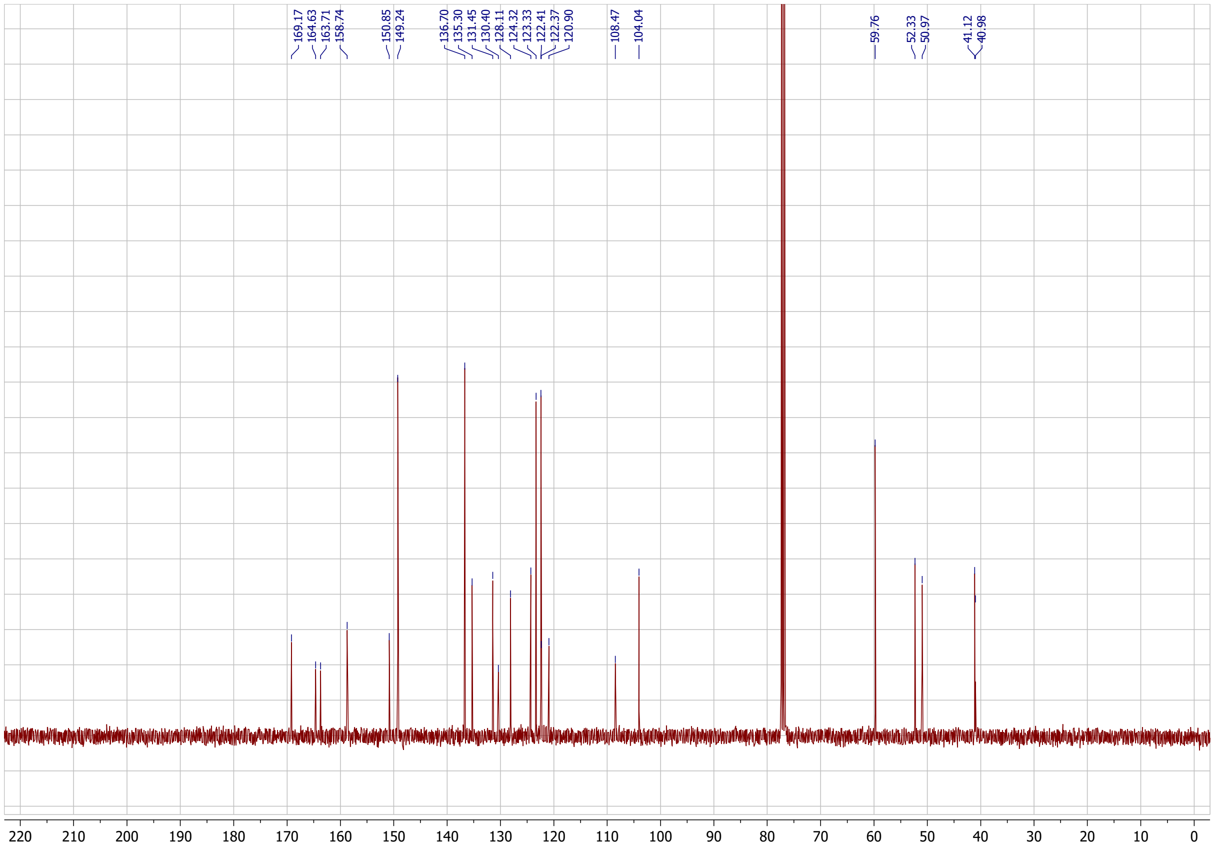

Figure S4 – ^{13}C NMR spectrum (100 MHz; $CDCl_3$) of **L1**.

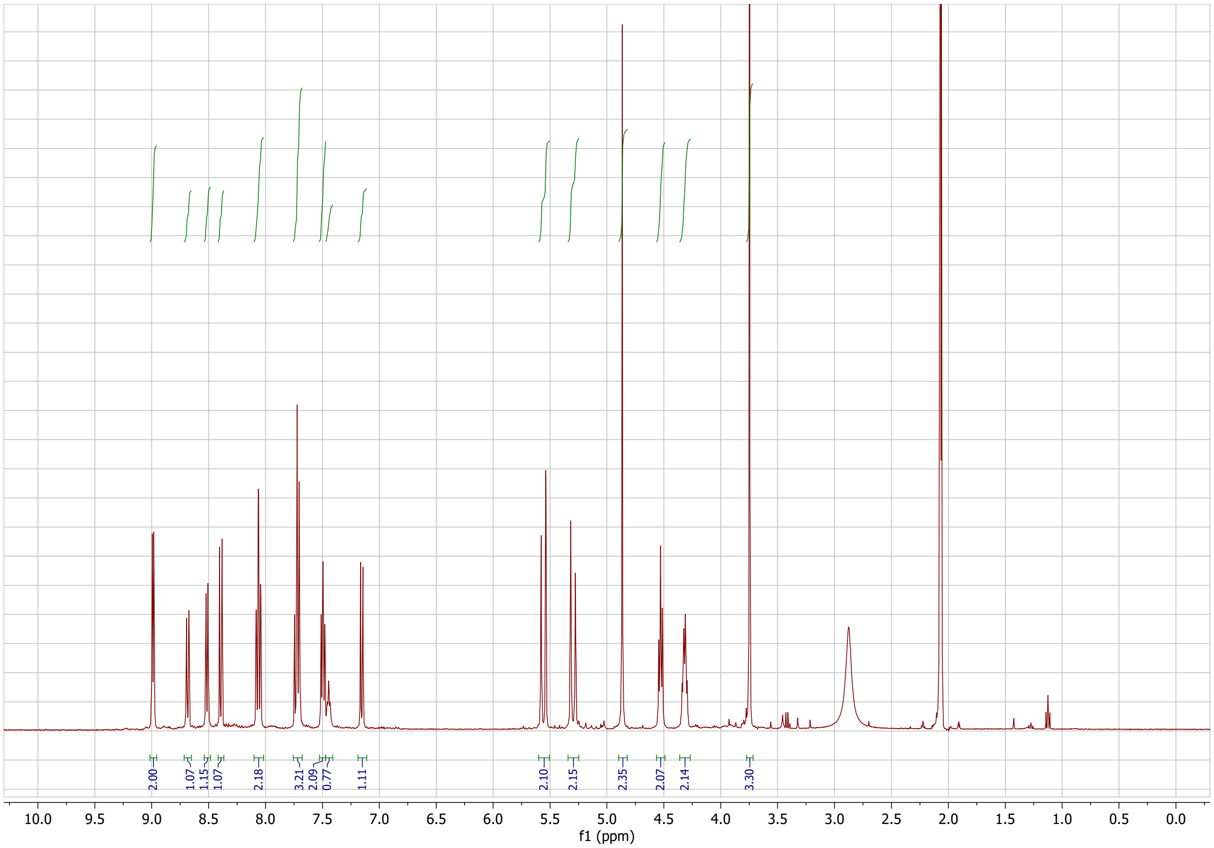

Figure S5 – ^{1}H NMR spectrum (400 MHz; acetone-d_6) of **Re-L1**.

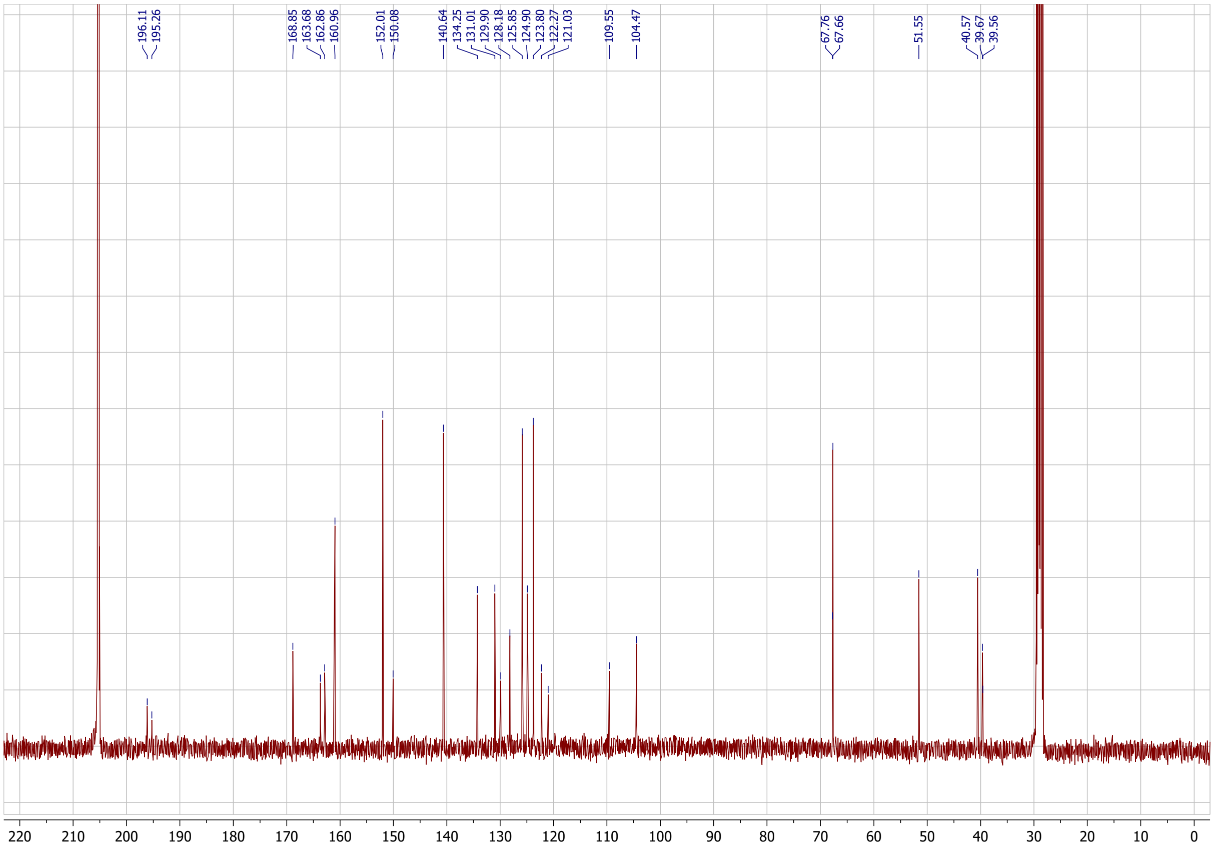

Figure S6 – ^{13}C NMR spectrum (100 MHz; acetone-d_6) of **Re-L1**.

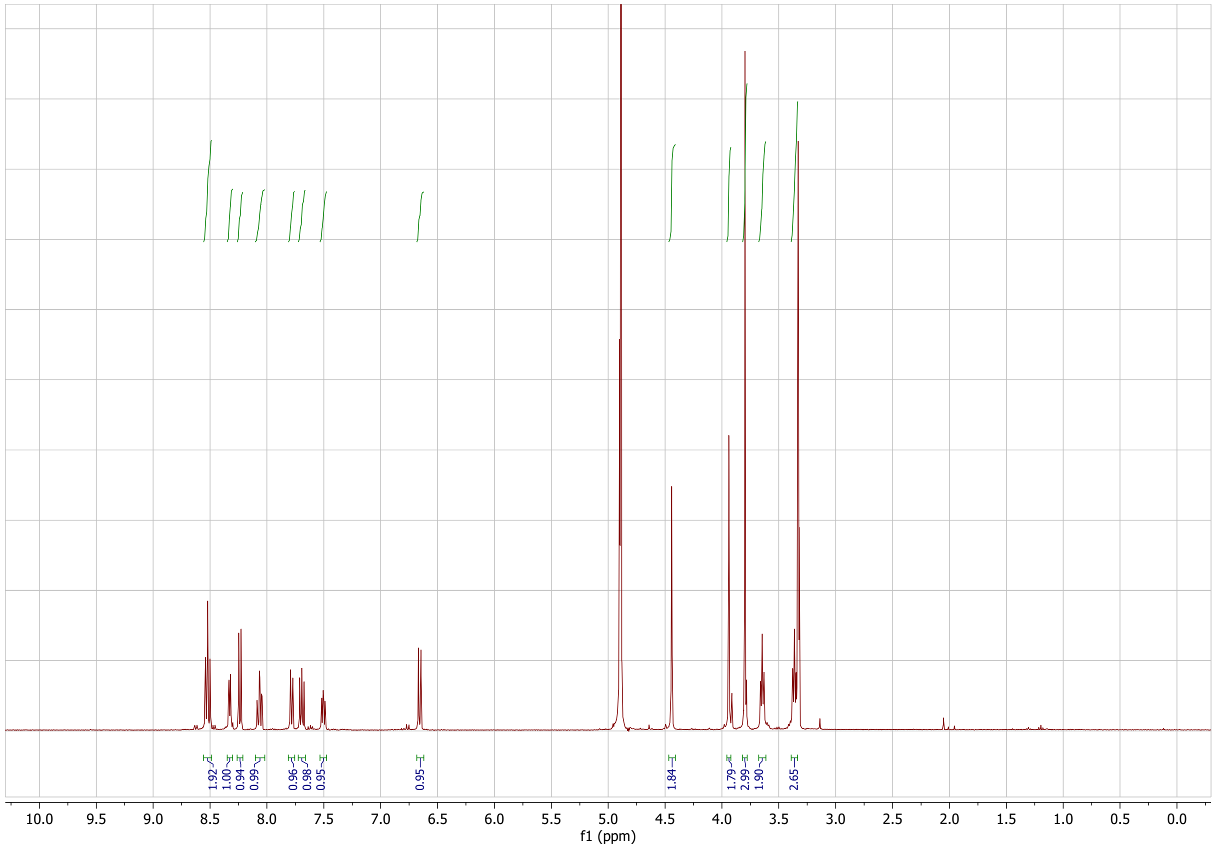

Figure S7 – ^{1}H NMR spectrum (400 MHz; CD_3OD) of **L2**.

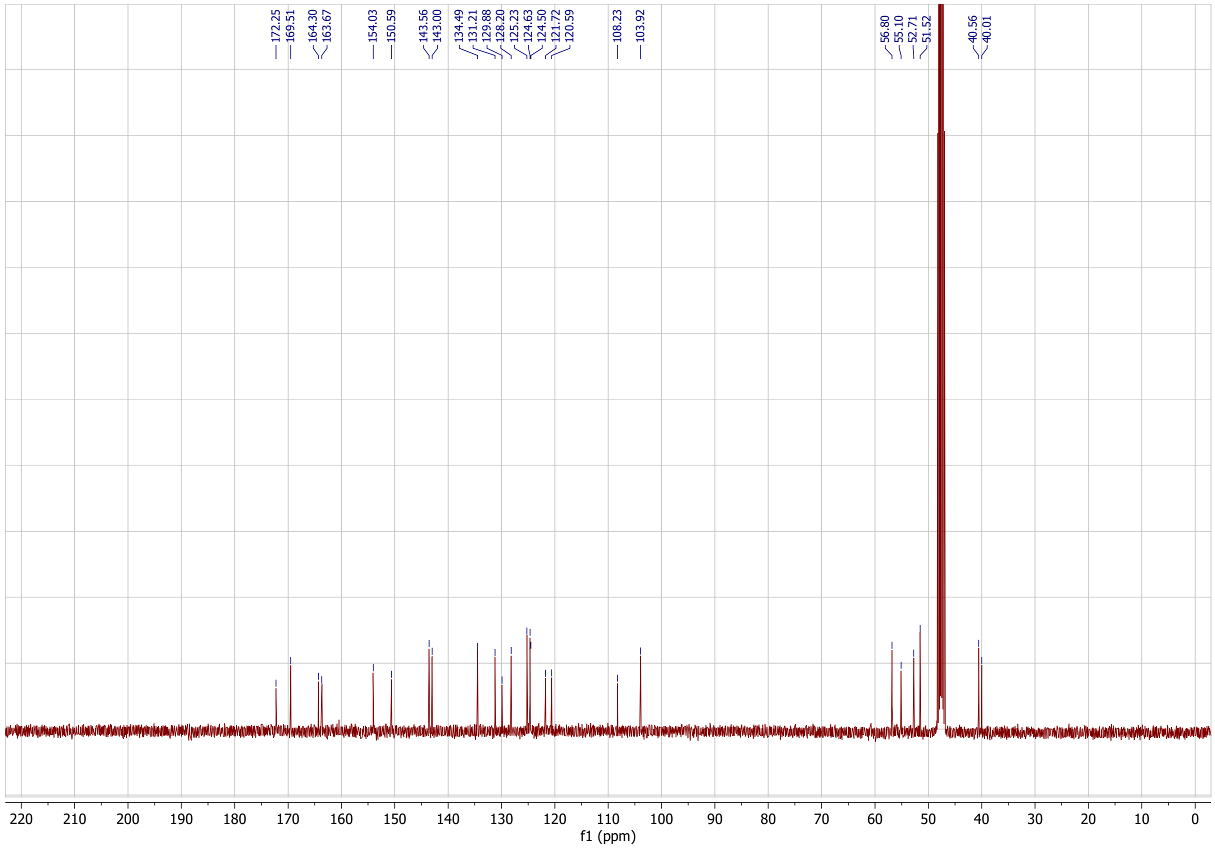

Figure S8 – ^{13}C NMR spectrum (100 MHz; CD_3OD) of **L2**.

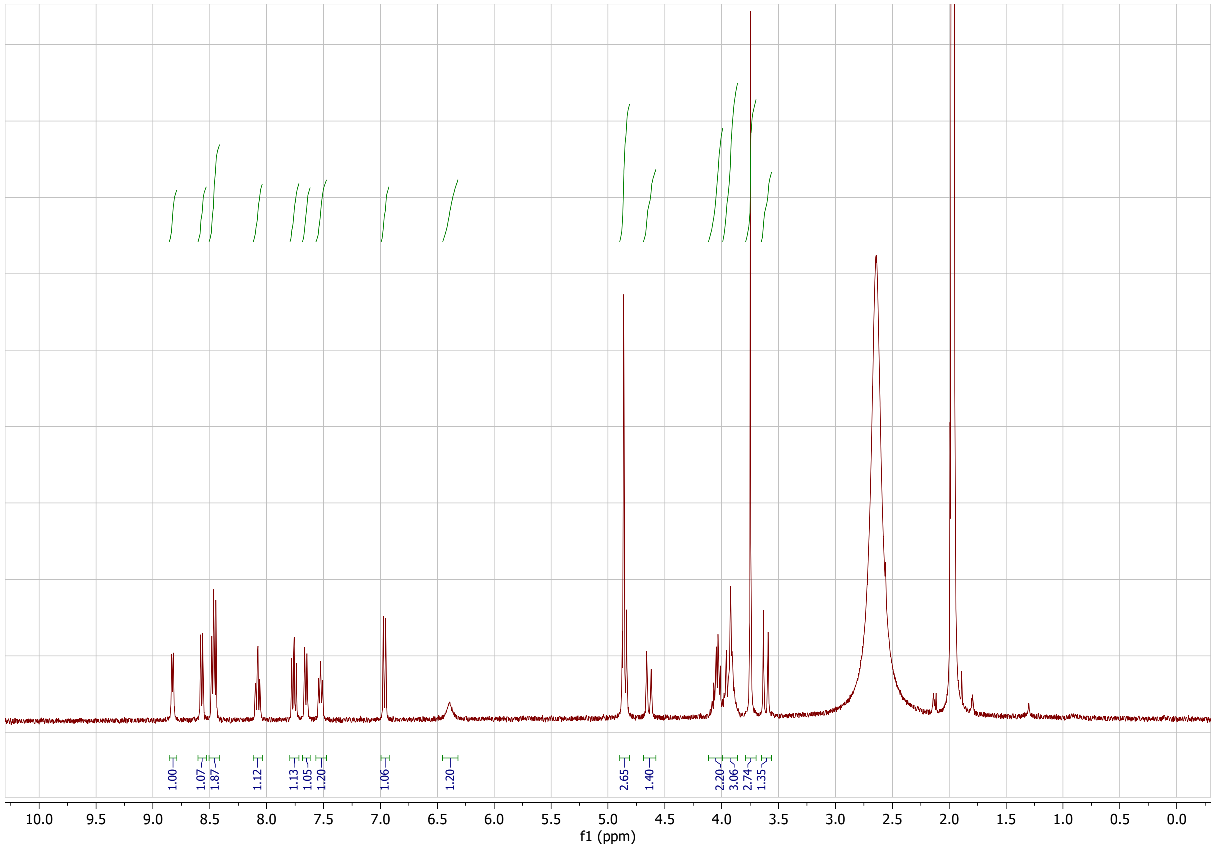

Figure S9 – ^{1}H NMR spectrum (400 MHz; CD_3CN) of **Re-L2**.

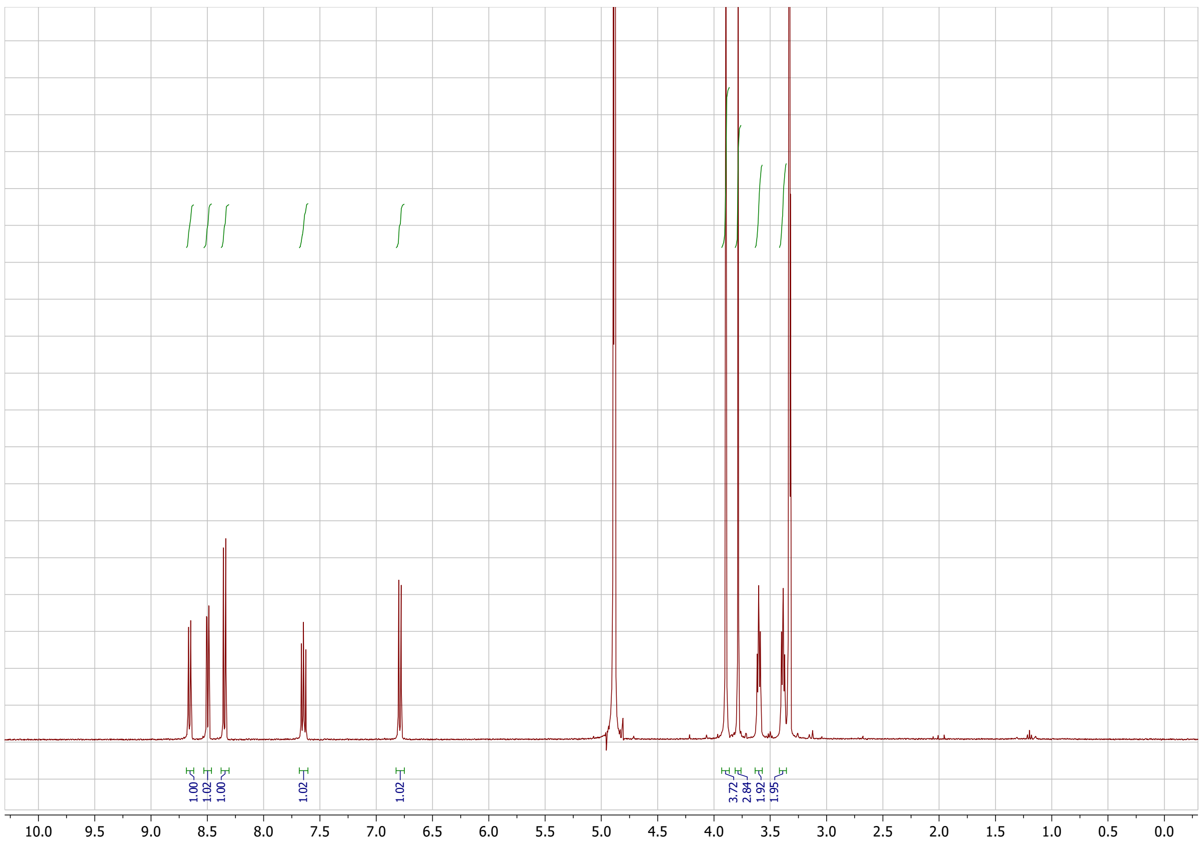

Figure S10 – ^{1}H NMR spectrum (400 MHz; CD_3OD) of **L3**.

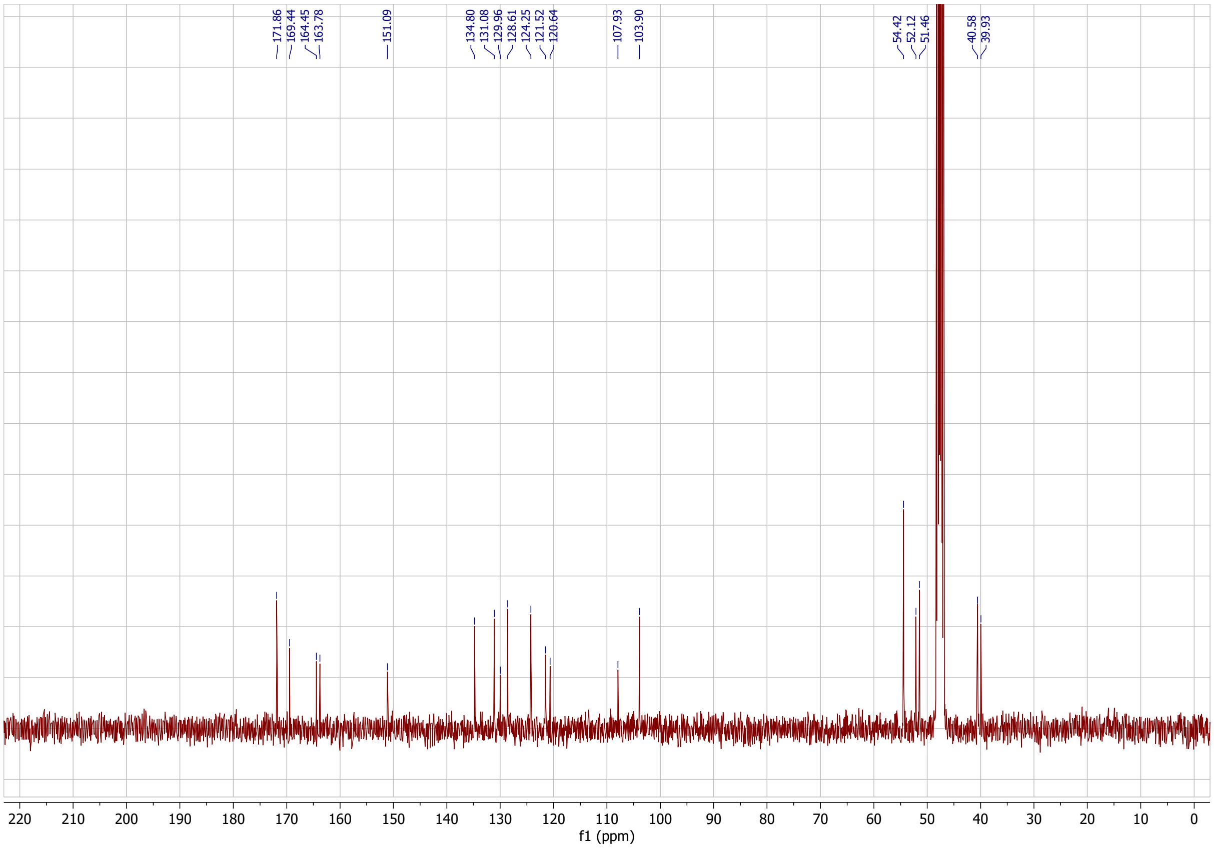

Figure S11 – ^{13}C NMR spectrum (100 MHz; CD_3OD) of **L3**.

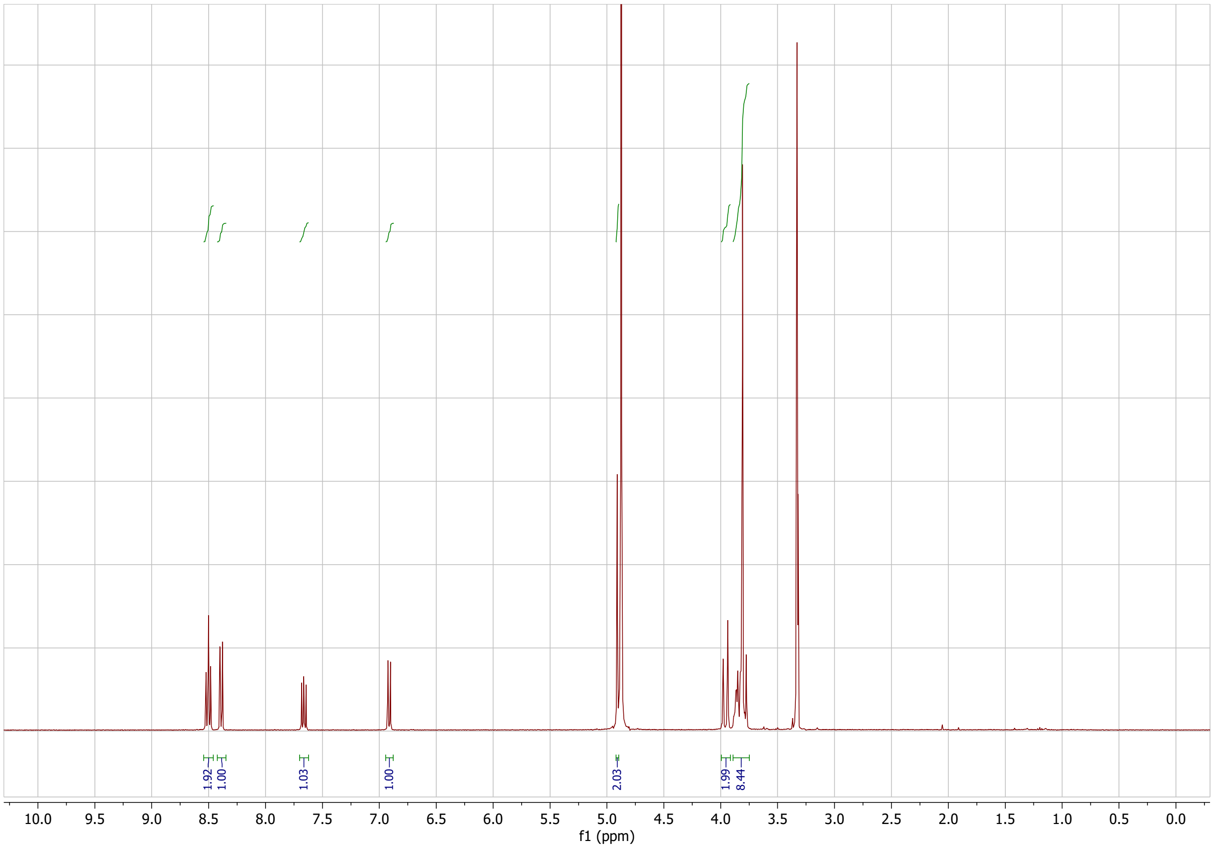

Figure S12 – ^{1}H NMR spectrum (400 MHz; CD_3OD) of **Re-L3**.

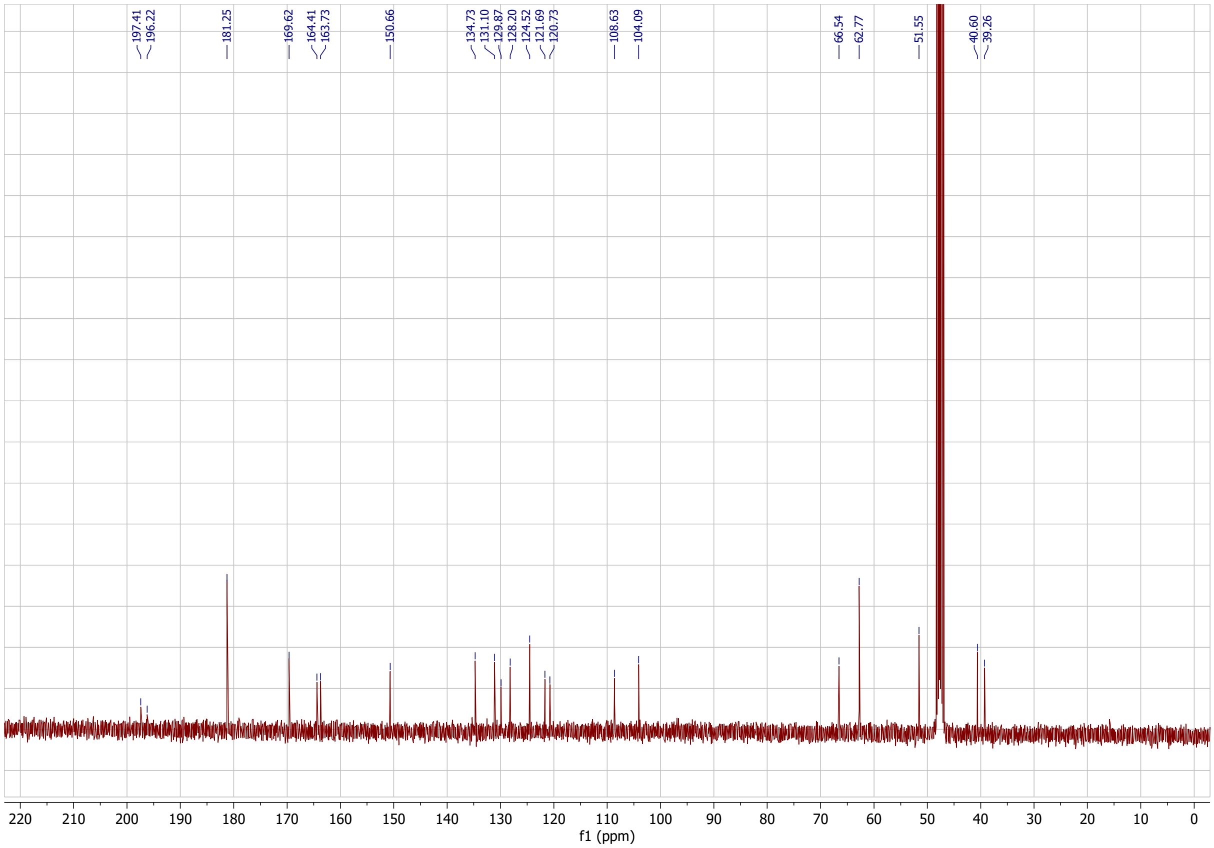

Figure S13 – ^{13}C NMR spectrum (100 MHz; CD_3OD) of **Re-L3**.

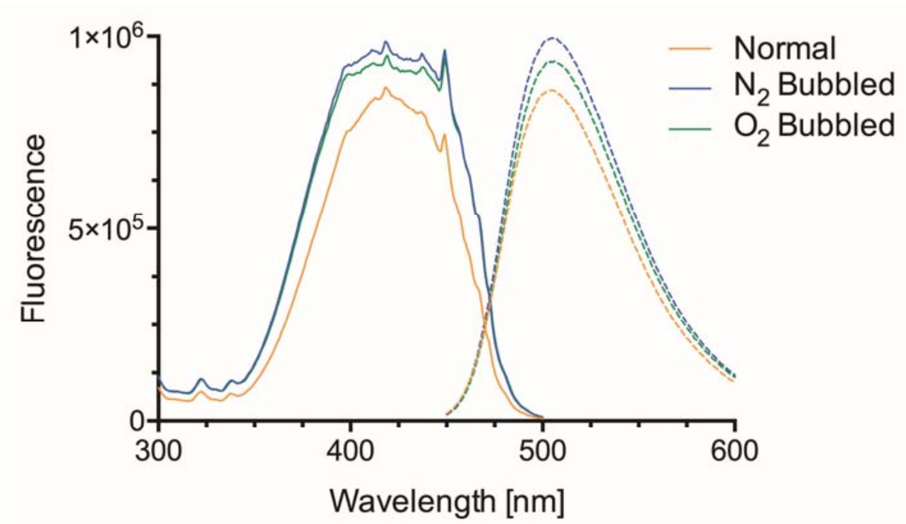

Figure S14 – Fluorescence Spectra of **Re-L1** in acetonitrile before degassing (orange), after bubbling N_2 gas through the solution (blue) and after bubbling O_2 gas through the solution (green).

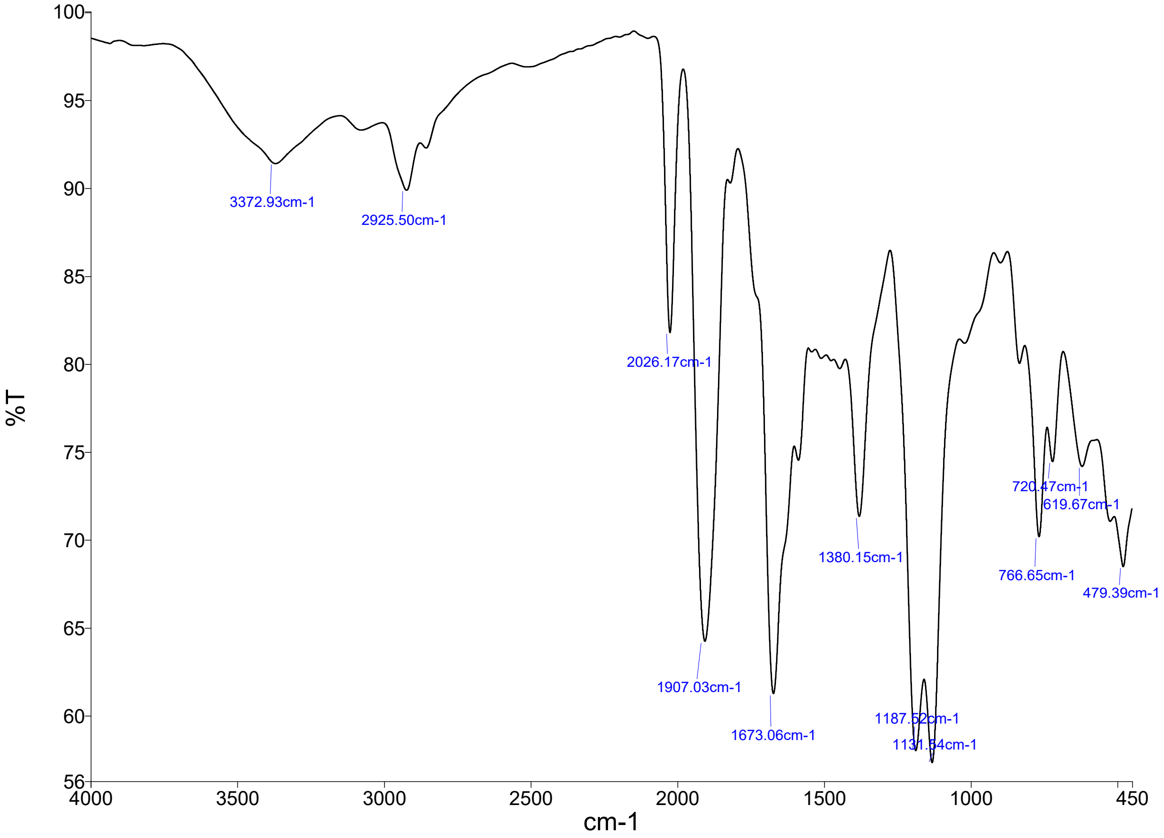

Figure S15 – Infrared spectrum of **Re-L1** (solid).

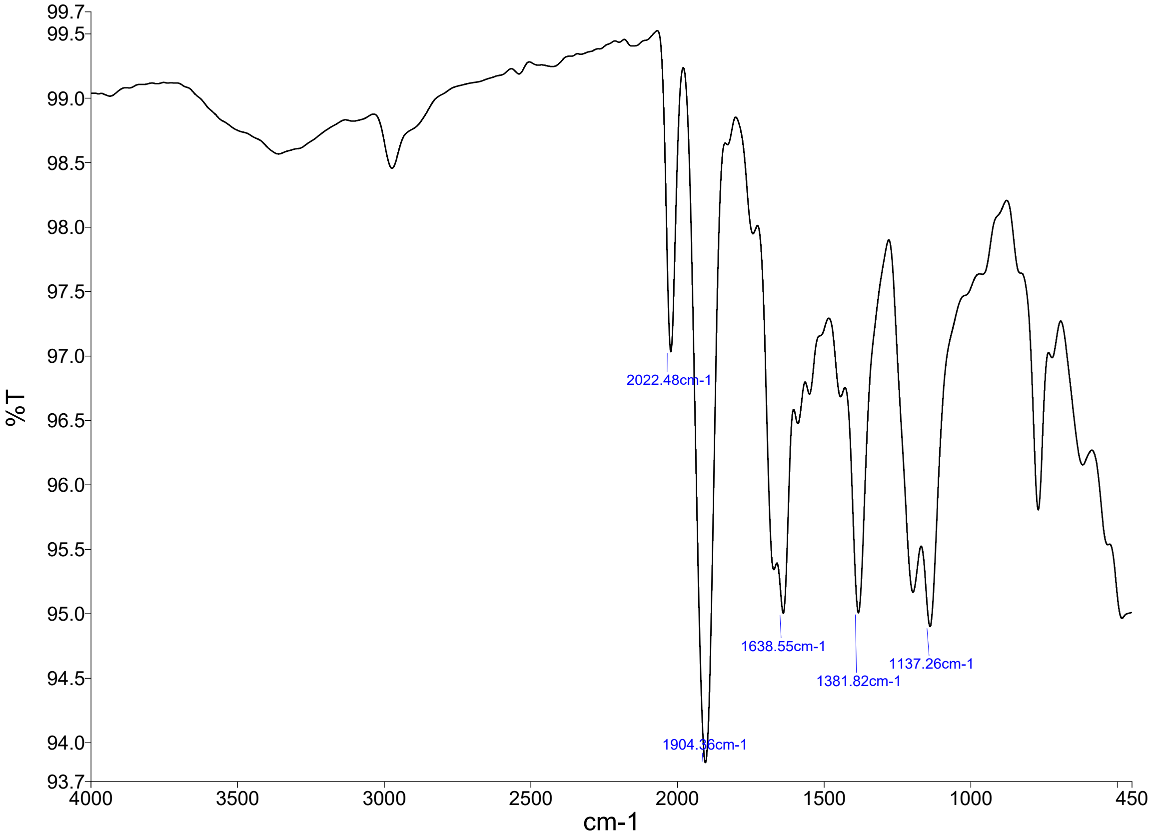

Figure S16 – Infrared spectrum of **Re-L2** (solid).

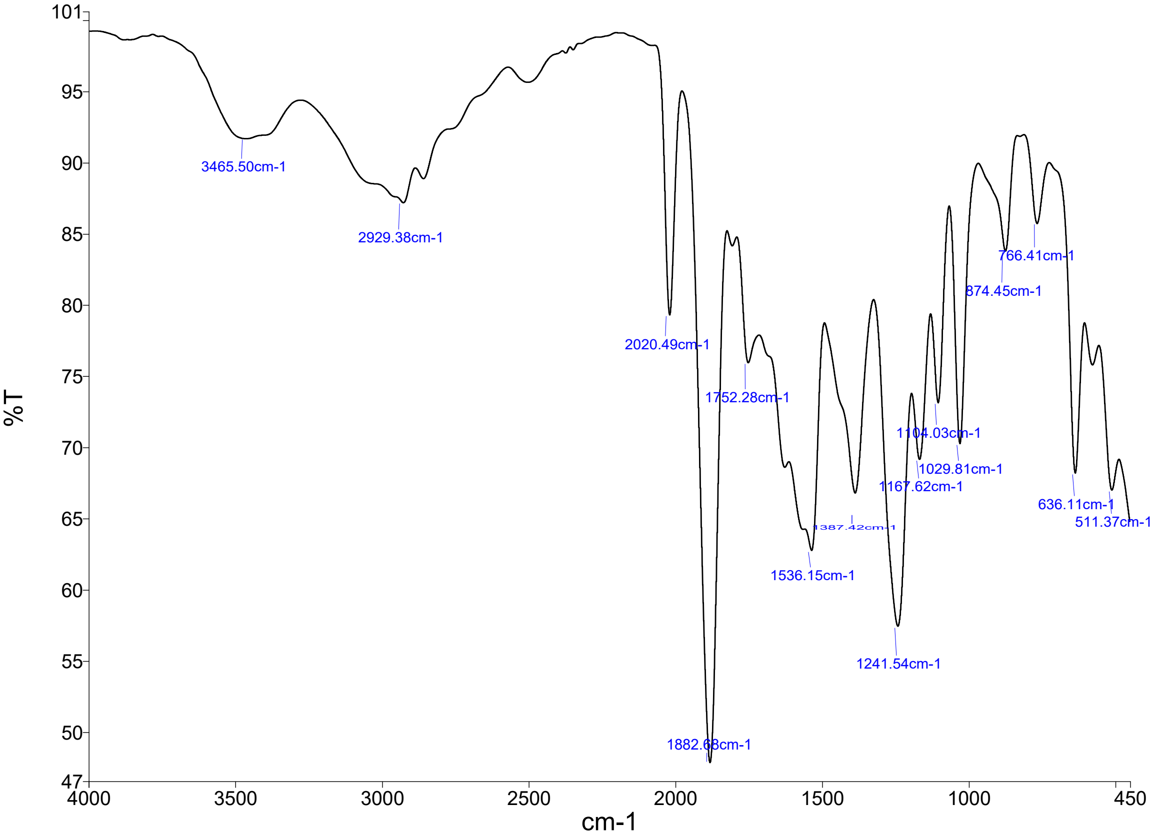

Figure S17 – Infrared spectrum of **Re-L3** (solid).

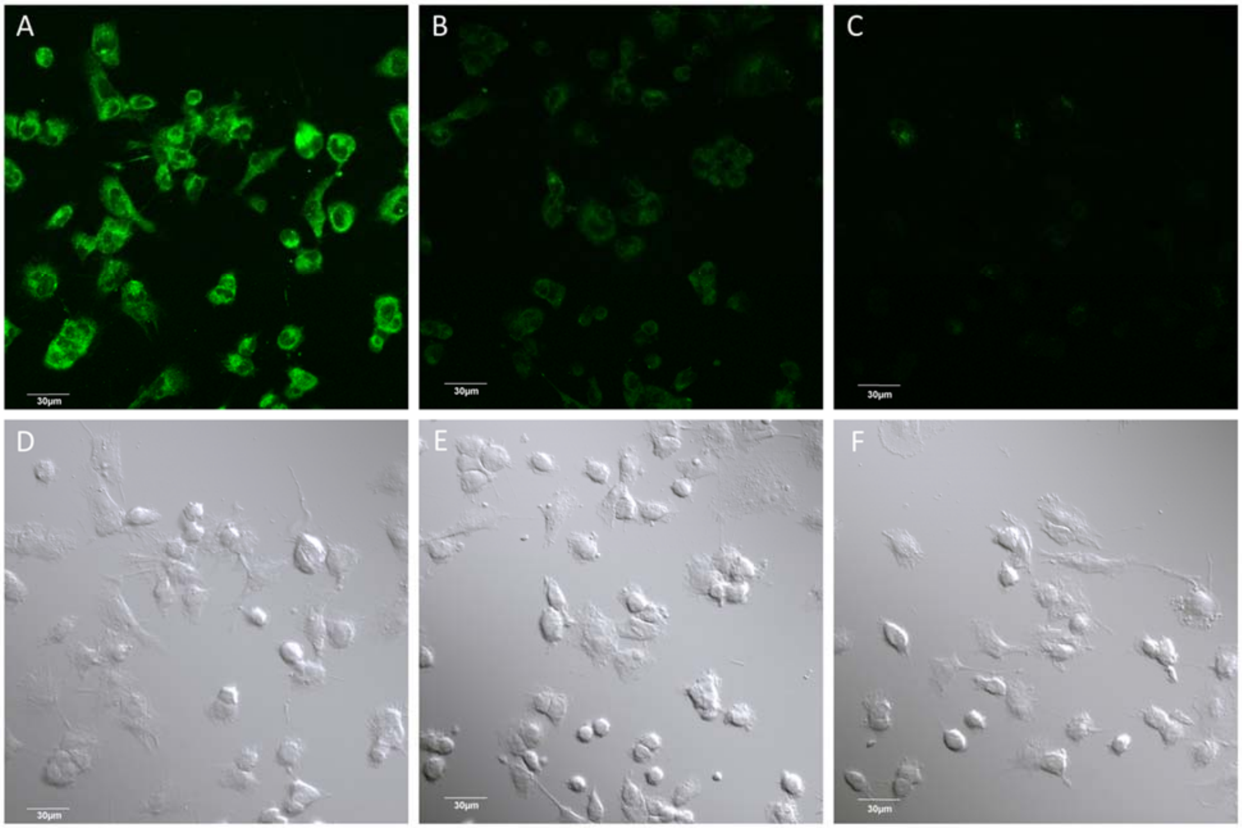

Figure S18 - Confocal microscope images of OVCAR-8 cells incubated with **Re-L1** (A, D) **Re-L2** (B, E) and **Re-L3** (C, F) at a concentration of 20 µM (λ_{Ex} = 458 nm, 40x objective).

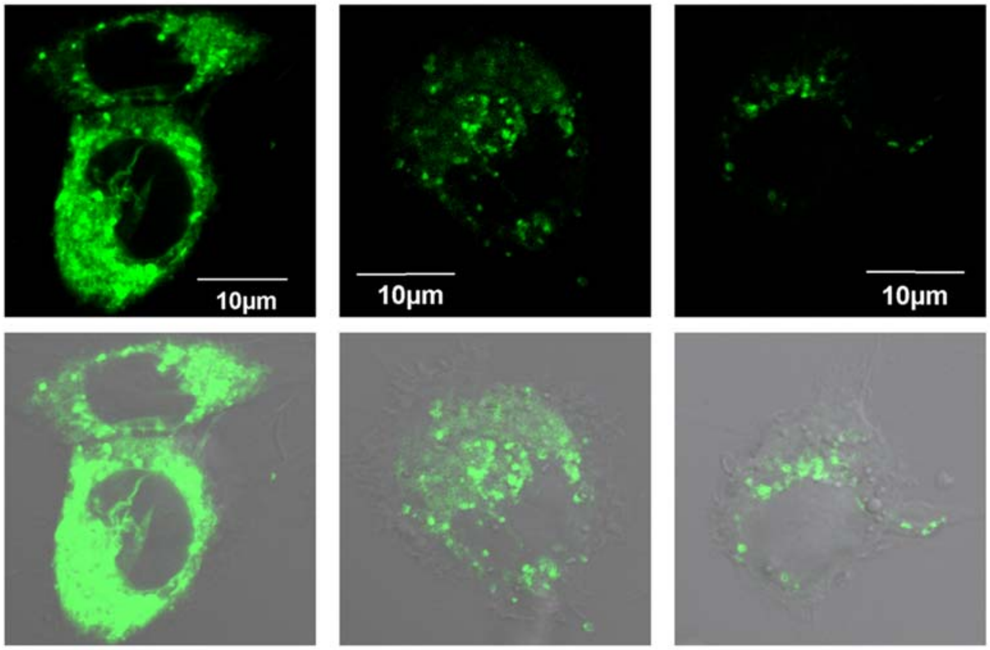

Figure S19 – Confocal microscope images (λ_{Ex} = 458 nm, 100x objective) of OVCAR-8 cells incubated with **Re-L1** (left), **Re-L2** (middle) and **Re-L3** (right). Top panel are fluorescence images, bottom panel are fluorescence images overlaid with DIC images.

Experimental

General

All reagents were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Bruker AvIII HD 400 spectrometer at 400 and 100 MHz for ^{1}H and ^{13}C experiments respectively. All chemical shifts are reported in ppm and referenced to the residual solvent peaks. High resolution mass spectra were recorded on a Thermo Scientific Double Focusing Sector mass spectrometer for EI or a Bruker micrOTOF II for ESI in either positive or negative mode. Analytical reversed-phase HPLC-MS was performed on a system consisting of an Agilent Zorbax SB-C18 column (5 μm, 4.6 x 150 mm), Waters 600 controller and binary solvent pump and a Waters Quattro Micro API mass spectrometer (System I). Mass spectra were collected using an ESI source in positive ion mode. The linear gradient solvent system comprised of solvent A (CH_3CN + 0.1 % TFA) and solvent B (H_2O + 0.1 % TFA) at a flow rate of 1.5 mL/min over 10 minutes with a 5-minute wash cycle at 95% solvent A. The UV/Vis absorbance was detected using a Waters 2998 photodiode array detector. Preparative reversed-phase HPLC-MS was performed on the same system using an Agilent Zorbax PrepHT SB-C18 column (5 μm, 21.2 x 150 mm) at a flow rate of 20 mL/min. After purification, the collected fractions were frozen at -78 °C, and lyophilized.

Methyl 2-(6-chloro-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)acetate (1)

4-Chloro-1,8-napthalic anhydride (2.00 g, 8.6 mmol), triethylamine (0.85 g, 8.5 mmol) and glycine methyl ester hydrochloride (1.53 g, 17.2 mmol) were added to ethanol (50 mL) and heated to reflux for 16 hours. The orange solution was cooled to room temperature, resulting in the formation of the product as an off-white precipitate that was collected by filtration, washed with ice cold ethanol and then dried under vacuum (2.20 g, 84%). ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.64 (dd, *J* = 7.3, 1.0 Hz, 1H), 8.58 (dd, *J* = 8.5, 1 Hz, 1H), 8.48 (d, *J* = 7.3 Hz, 1H), 7.89 – 7.76 (m, 2H), 4.94 (s, 2H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$; 100 MHz) δ 168.5, 163.5, 163.2, 139.7, 132.5, 131.6, 131.2, 129.5, 129.3, 128.0, 127.5, 122.7, 121.2, 52.7, 41.4. HRMS (EI): *m/z* calculated for $C_{15}H_{10}ClNO_4$ $[M]^+$ 303.0298; found 303.0284.

Methyl 2-(6-((2-((*tert*-butoxycarbonyl)amino)ethyl)amino)-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)acetate (2)

tert-Butyl (2-aminoethyl)carbamate (3.5 g, 21.7 mmol) and compound **1** (2.2 g, 7.2 mmol) were dissolved in DMSO (10 mL) and heated to 70 °C for 16 hours. The resulting deep red solution was cooled to room temperature and the pH neutralized with 0.1 M HCl. The solution was diluted with dichloromethane and washed with water. After drying with $MgSO_4$ the dichloromethane layer was reduced to a minimal volume under vacuum. Hexanes was added, resulting in the precipitation of the product as an orange solid which was collected by filtration, washed with cold hexanes, and dried under vacuum (3.07 g, quant.). ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.45 (d, *J* = 7.3 Hz, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.04 (br. s, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 4.95 (s, 2H), 3.79 (s, 3H), 3.61 (q, *J* = 5.6 Hz, 2H), 3.43 (q, *J* = 4.4 Hz, 2H), 1.48 (s, 9H). ^{13}C NMR (100 MHz; $CDCl_3$) δ 169.7, 164.6, 163.8, 158.4, 150.8, 135.1, 131.5, 127.7, 124.7, 120.5, 109.1, 103.6, 80.7, 52.6, 46.4, 41.2, 39.6, 29.8, 28.5. HRMS (ESI+): *m/z* calculated for $C_{22}H_{25}N_3O_6$ $[M+Na]^+$ 450.1641; found 450.1644.

Methyl 2-(6-((2-aminoethyl)amino)-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)acetate (3)

Compound **2** (3.0 g, 7.02 mmol) was dissolved in dichloromethane (10 mL) and trifluoroacetic acid (10 mL) and the solution was stirred for 24 hours at room temperature. The solvent was removed under vacuum and the resulting TFA salt was dissolved in water and the pH was neutralized with saturated sodium bicarbonate. The product was extracted into DCM, the organic layer was collected and dried with Na_2SO_4. The solvent was then removed under reduced pressure producing a yellow solid (0.95 g, 41%). ^{1}H NMR (400 MHz; CD_3OD) δ 8.50 – 8.38 (m, 2H), 8.29 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 8.3, 7.5 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 4.86 (s, 2H), 3.78 (s, 3H), 3.75 (t, *J* = 6.2 Hz, 2H), 3.34 (t, *J* = 6.2 Hz, 2H). ^{13}C NMR (100 MHz; CD_3OD) δ 170.9, 165.6, 165.1, 151.9, 135.8, 132.5, 131.1, 129.6, 126.0, 123.0, 122.2, 110.4, 105.3, 52.9, 42.0, 41.7, 39.2. HRMS (ESI+): *m/z* calculated for $C_{17}H_{17}N_3O_4$ $[M+H]^+$ 328.1297; found 328.1284.

L1

To a solution of compound **3** (50 mg, 0.15 mmol) in DMF (4 mL) was added K_2CO_3 (84 mg, 0.61 mmol), KI (51 mg, 0.31 mmol) and 2-picolylchloride hydrochloride (50 mg, 0.31 mmol). The orange solution was heated to 50 °C for 48 hours. The solution was partitioned into water (30 mL) and chloroform (50 mL). The aqueous layer was extracted 3 times with chloroform, and the combined organics were dried over Na_2SO_4 and concentrated under reduced pressure to give the product as a yellow-orange solid (**L1**) (53 mg, 68%). UV/Vis (CH_3CN): λ_{max}/nm (ε/L·mol^{-1}cm^{-1}) = 439 (14 500) 340 (2750) 324 (3450) 282 (19 000) 269 (29 500) 263 (33 000) 256 (32 000). ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.85 (dd, *J* = 8.4, 1.0 Hz, 1H), 8.63 (dd, *J* = 7.4, 1.0 Hz, 1H), 8.59 – 8.56 (m, 2H), 8.42 (d, *J* = 8.5 Hz, 1H), 7.98 (s, 1H), 7.69 (dd, *J* = 8.4, 7.4 Hz, 1H), 7.56 (td, *J* = 7.8, 1.8 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.15 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 2H), 6.55 (d, *J* = 8.5 Hz, 1H), 4.96 (s, 2H), 4.01 (s, 4H), 3.77 (s, 3H), 3.43 – 3.36 (m, 2H), 3.09 – 3.02 (m, 2H). ^{13}C NMR (100 MHz; $CDCl_3$) δ 169.3, 164.8, 163.8, 158.9, 151.0, 149.4, 136.8, 135.4, 131.6, 130.5, 128.2, 124.4, 123.4, 122.5, 121.0, 108.6, 104.2, 59.9, 52.5, 51.1, 41.3, 41.1. HRMS (ESI+): *m/z* calculated for $C_{29}H_{27}N_5O_4$ $[M+H]^+$ 510.2142; found 510.2139.

fac-[Re(CO)$_3$(L1)]OTf (Re-L1)

L1 (53 mg, 104 μmol) and *fac*-[Re(CO)$_3$(CH_3CN)$_3$]OTf (56 mg, 104 μmol) were added to chloroform (5 mL) and heated to 60 °C for 18 hours. The solution was cooled to room temperature and diethyl ether was added to induce precipitation of the product as a yellow solid, which was collected by filtration, washed with diethyl ether and dried under vacuum giving **Re-L1** (72 mg, 74%). UV/Vis (CH_3CN): λ_{max}/nm (ε/L·mol^{-1}cm^{-1}) = 424 (14 100) 338 (4150) 321 (5700) 276 (25 500) 268 (34 800) 259 (35 500) 253 (34 000). ^{1}H NMR (400 MHz; acetone-*d*$_6$) δ 8.99 – 8.96 (m, 2H), 8.67 (d, *J* = 8.5 Hz, 1H), 8.50 (dd, *J* = 7.3, 1.0 Hz, 1H), 8.38 (d, *J* = 8.5 Hz, 1H), 8.05 (td, *J* = 7.3, 1.6 Hz, 2H), 7.74 – 7.67 (m, 3H), 7.48 (t, *J* = 6.0 Hz, 2H), 7.43 (t, *J* = 5.3 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 5.54 (d, *J* = 16.4 Hz, 2H), 5.28 (d, *J* = 16.4 Hz, 2H), 4.85 (s, 2H), 4.51 (t, *J* = 6.6 Hz, 2H), 4.33 – 4.27 (m, 2H), 3.73 (s, 3H). ^{13}C NMR (100 MHz; acetone-*d*$_6$) δ 197.0, 196.1, 169.7, 164.6, 163.7, 161.9, 152.9, 151.0, 141.5, 135.1, 131.9, 130.8, 129.1, 126.7, 125.8, 124.7, 123.2, 121.9, 110.4, 105.4, 68.7, 68.6, 52.4, 41.5, 40.6, 40.5. HRMS (ESI+): *m/z* calculated for $C_{32}H_{27}N_5O_7{}^{185}Re$ $[M]^+$ 778.1440; found 778.1471.

L2

Compound **3** (50 mg, 0.15 mmol) sodium acetate (50 mg, 0.61 mmol), acetic acid (70 μL, 1.22 mmol) and 2-pyridinecarboxaldehyde (16 mg, 0.15 mmol) were dissolved in methanol (5 mL) and heated to 65 °C for 16 hours. Upon cooling to room temperature, glyoxylic acid monohydrate (21 mg, 0.23 mmol) and $NaBH_3CN$ (21 mg, 0.34 mmol) were added, and the solution stirred at room temperature for 24 hours. The solvent was removed under reduced pressure and the crude was purified by preparative HPLC (System I, 20-80%) to give the product as a hygroscopic orange solid (27 mg, 37%). UV/Vis (CH_3CN): λ_{max}/nm (ε /L·mol^{-1}cm^{-1}) = 436 (9950) 339 (1930) 322 (2350) 279 (13 000) 268 (22 700) 261 (25 500) 255 (24 500). ^{1}H NMR (400 MHz; CD_3OD) δ 8.53 – 8.47 (m, 2H), 8.33 – 8.29 (m, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.05 (td, *J* = 7.9, 1.6 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.67 (dd, *J* = 8.5, 7.4 Hz, 1H), 7.51 – 7.46 (m, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 4.88 (s, 2H), 4.42 (s, 2H), 3.92 (s, 2H), 3.78 (s, 3H), 3.63 (t, J = 6.0 Hz, 2H), 3.34 (t, J = 6.0 Hz, 2H). ^{13}C NMR (100 MHz; CD_3OD) δ 173.7, 170.9, 165.7, 165.1, 155.4, 152.0, 145.0, 144.4, 135.9, 132.6, 131.3, 129.6, 126.6, 126.0, 125.9, 123.1, 122.0, 109.6, 105.3, 58.2, 56.5, 54.1, 52.9, 42.0, 41.4. HRMS (ESI+): *m/z* calculated for $C_{25}H_{24}N_4O_6$ $[M+H]^+$ 477.1774; found 477.1776.

***fac*-Re(CO)$_3$(L2) (Re-L2)**

Prepared as for **Re-L1** but using **L2** (22 mg, 46 μmol) and *fac*-[$Re(CO)_3(CH_3CN)_3$]OTf (25 mg, 46 μmol). Precipitation with diethyl ether gave crude product which was purified by preparative HPLC (System I, 35-85%) to give the pure product as a yellow solid (10 mg, 29%). UV/Vis (CH_3CN): λ_{max}/nm (ε /L·mol^{-1}cm^{-1}) = 425 (14 750) 340 (3800) 323 (4950) 277 (23 500) 268 (29 000) 262 (34 500) 255 (34 000). ^{1}H NMR (400 MHz; CD_3CN) δ 8.80 (d, *J* = 5.6 Hz, 1H), 8.56 – 8.53 (m, 1H), 8.47 – 8.40 (m, 2H), 8.09 – 8.02 (m, 1H), 7.77 – 7.70 (m, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.46 (m, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.36 (br. s, 1H), 4.83 (d, *J* = 16 Hz 1H), 4.83 (s, 2H) 4.61 (d, *J* = 16 Hz, 1H), 4.09 – 3.98 (m, 2H), 3.95 – 3.85 (m, 3H), 3.72 (s, 3H), 3.58 (d, *J* = 16.6 Hz, 1H). HRMS (ESI+): *m/z* calculated for $C_{28}H_{23}N_4O_9{}^{185}Re$ $[M+H]^+$ 745.1073; found 745.1082.

L3

Compound **3** (50 mg, 0.15 mmol), sodium acetate (50 mg, 0.61 mmol), acetic acid (70 μL, 1.22 mmol) glyoxylic acid monohydrate (42 mg, 0.46 mmol) and $NaBH_3CN$ (21 mg, 0.34 mmol) were dissolved in methanol (5 mL) and stirred at room temperature for 48 hours. The solvent was removed under reduced pressure and the crude product purified by preparative HPLC (System I, 15-70%) to give the product as a yellow solid (34 mg, 50%). UV/Vis (CH_3CN): λ_{max}/nm (ε/L·mol^{-1}cm^{-1}) = 436 (8700) 339 (1900) 322 (2300) 279 (11 300) 269 (20 900) 261 (22 500) 255 (21 500).

^{1}H NMR (400 MHz; CD_3OD) δ 8.64 (dd, *J* = 8.4, 1 Hz, 1H), 8.48 (dd, *J* = 7.4, 1.0 Hz, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 7.62 (dd, *J* = 8.4, 7.4 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 1H), 4.87 (s, 2H), 3.87 (s, 4H), 3.77 (s, 3H), 3.58 (t, *J* = 5.8 Hz, 2H), 3.37 (t, *J* = 5.8 Hz, 2H). ^{13}C NMR (100 MHz; CD_3OD) δ 173.3, 170.8, 165.9, 165.2, 152.5, 136.2, 132.5, 131.4, 130.0, 125.7, 122.9, 122.0, 109.3, 105.3, 55.8, 53.5, 52.9, 42.0, 41.3. HRMS (ESI-): *m/z* calculated for $C_{21}H_{21}N_3O_8$ $[M-H]^-$ 442.1250; found 442.1262.

***fac*-Na[Re(CO)$_3$(L3)] (Re-L3)**

L3 (25 mg, 56 μmol), *fac*-[Re(CO)$_3$(CH$_3$CN)$_3$]OTf (31 mg, 56 μmol) and sodium bicarbonate (10 mg, 113 μmol) were added to chloroform (5 mL) and heated to 60 °C for 18 hours then cooled to room temperature. The solvent was removed, and the residue taken up in methanol (2 mL) and the residual salts were removed by filtration. Precipitation was induced by the addition of diethyl ether (10 mL) to give the product as a yellow-orange solid that was collected by filtration and dried under vacuum (16 mg, 39%). UV/Vis (CH_3CN): λ_{max}/nm (ε /L·mol^{-1}cm^{-1}) = 428 (15 000) 340 (2500) 324 (3200) 278 (22 500) 269 (31 500) 262 (33 000) 256 (32 000). ^{1}H NMR (400 MHz; CD_3OD) δ 8.53 – 8.44 (m, 2H), 8.37 (d, *J* = 8.6 Hz, 1H), 7.64 (dd, *J* = 8.4, 7.4 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 4.89 (s, 2H), 3.94 (d, *J* = 15.8 Hz, 2H), 3.88 – 3.72 (m, 9H). ^{13}C NMR (100 MHz; CD_3OD) δ 198.8, 197.6, 182.7, 171.0, 165.8, 165.1, 152.1, 136.1, 132.5, 131.3, 129.6, 125.9, 123.1, 122.1, 110.0, 105.5, 67.9, 64.2, 52.9, 42.0, 40.7. HRMS (ESI-): *m/z* calculated for $C_{24}H_{19}N_3O_{11}{}^{185}Re$ $[M]^-$ 710.0549; found 710.0540.