Supporting Information

Enantioselective Inhibition of the SARS-CoV-2 Main Protease with a Rhenium(I) Picolinic Acid Complex

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EXPERIMENTAL SECTION

Materials and Methods

All reagents and solvents were obtained from commercial sources and used without further purification. Solvents were dried over molecular sieves if necessary. NMR spectra were recorded at apparatus from the nuclear magnetic resonance facility located in the Department of Chemistry and Biochemistry at the University of California, San Diego. ^{1}H and ^{13}C NMR spectra were measured on a 500 MHz NMR spectrometer. The spectra were analyzed by chemical shifts (δ) in parts per million (ppm) referenced to tetramethylsilane (δ 0.00) ppm using the residual proton solvent peaks as internal standards and coupling constants (*J*) in Hertz (Hz). The multiplicity of the peaks is abbreviated as follows: br (broad), s (singlet), d (doublet), t (triplet), m (multiplet). Mass spectra were recorded at the molecular mass spectrometry facility located in the Department of Chemistry and Biochemistry at the University of California, San Diego. High resolution mass spectrometry (HR-MS) was measured with an Agilent 6230 time-of-flight mass spectrometer using a jet stream electrospray ionization source (ESI). The jet stream source was operated under positive ionization mode with the following parameters: VCap: 3500V; fragmentor voltage: 160 V; nozzle voltage: 500 V; drying gas temperature: 325 °C, sheath gas temperature: 325 °C, drying gas flow rate: 7.0 L/min; sheath gas flow rate: 10 L/min; nebulizer pressure: 40 psi. For analytic HPLC the following system was used: Agilent 1200 series degasser and pump system with with an Agilent Ecplise XDB-C18 (5 μm 150×4.6 mm) column. The solvents (HPLC grade) were millipore water (solvent A) and acetonitrile (solvent B). The following solvent gradient was used: 0-3 minutes: isocratic 95% A (5% B); 3-17 minutes: linear gradient from 95% A (5% B) to 50% A (50% B); 17-20 minutes: isocratic 50% A (50% B). All metal complexes were found with at least 95% purity as confirmed by HPLC analysis. The enzymatic assay kits were commercially purchased from BPS Bioscience.

Synthesis

Picolinic acid

The compound was commercially obtained from Alfa Aesar and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.70 (dd, J = 4.8, 1.0 Hz, 1H), 8.04 (dt, J =7.7, 1.1 Hz, 1H), 7.97 (td, J = 7.7, 1.0 Hz, 1H), 7.61 (ddd, J = 7.7, 4.8, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.3, 149.6, 148.4, 137.7, 127.3, 124.8; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_6H_4N_1O_2$, 122.0248; found, 122.0246.

3-Fluoropicolinic acid

3-Chloropicolinic acid (100 mg, 0.63 mmol), 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) and dichloro(1,5-cyclooctadiene)palladium(II) (9 mg, 0.03 mmol) were suspended in pentane (25 mL). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The obtained solid and silver(I) fluoride (799 mg, 6.3 mmol) were dissolved in dichloromethane (50 mL). The mixture was protected from light and stirred at room temperature overnight. After this time, the solution was filtered through celite and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 100%/0%). The fractions containing the product were combined and the compound dried. Yield: 15 mg (0.11 mmol, 17%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.51 (dt, J = 4.3, 1.4 Hz, 1H), 7.88 (ddd, J = 10.5, 8.5, 1.4 Hz, 1H), 7.69 (dt, J = 8.5, 4.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.4 (d, J = 6 Hz), 158.3 (d, J = 266 Hz), 145.5 (d, J = 5 Hz), 137.8 (d, J = 10 Hz), 128.8 (d, J = 5 Hz), 125.8 (d, J = 20 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3F_1N_1O_2$, 140.0153; found, 140.0151.

3-Chloropicolinic acid

3-Hydroxypicolinic acid (50 mg, 0.36 mmol) was dissolved in phosphoryl chloride (2 mL) and heated at 120 °C for 4 h. After this time the reaction was cooled down with an ice bath. The excess of phosphoryl chloride was quenched with an aqueous sodium hydroxide solution until pH 9 was reached. The crude product was extracted with dichloromethane (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 12 mg (0.08 mmol, 22%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.56 (dd, J = 4.6, 1.4 Hz, 1H), 8.07 (dd, J = 8.3, 1.4 Hz, 1H), 7.57 (dd, J = 8.3, 4.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.2, 149.7, 147.6, 138.5, 127.9, 126.7; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3Cl_1N_1O_2$, 155.9858; found, 155.9856.

3-(Trifluoromethyl)picolinic acid

3-Chloropicolinic acid (100 mg, 0.63 mmol), copper(I) iodide (120 mg, 0.63 mmol), methyl fluorosulfonyldifluoroacetate (2.4 mL, 18.9 mmol) were dissolved in 1-methylpyrrolidin-2-one (20 mL). The mixture was heated at 80 °C overnight under nitrogen atmosphere. The solution was filtered over celite and thoroughly washed with ethyl acetate. The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 41 mg (0.21 mmol, 33%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.88 (dd, J = 5.0, 1.4 Hz, 1H), 8.34 (dd, J = 8.1, 1.4 Hz, 1H), 7.76 (ddd, J = 8.1, 5.0, 1.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.8, 152.8, 150.0 (q, J = 2 Hz), 135.5 (q, J = 5 Hz), 125.3, 123.0 (q, J = 285 Hz), 122.1 (q, J = 22 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3F_3N_1O_2$, 190.0121; found, 190.0123.

3-Methylpicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.47 (dd, J = 4.7, 1.6 Hz, 1H), 7.79 (dd, J = 7.8, 1.6 Hz, 1H), 7.48 (dd, J = 7.8, 4.7 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.5, 148.4, 146.2, 140.1, 133.4, 126.0, 19.0; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_2$, 136.0404; found, 136.0405.

3-Cyanopicolinic acid

3-Chloropicolinic acid (100 mg, 0.63 mmol), sodium cyanide (31 mg, 0.63 mmol), palladium acetate (7 mg, 0.03 mmol) and 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) were dissolved in 1,3,5-trimethylbenzene (50 mL) and *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (142 µL, 0.95 mmol) was added under nitrogen atmosphere. The reaction mixture was heated to reflux overnight. Water (10 mL) was added and the solution stirred for 10 min. The solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 100%/0%). The fractions containing the product were combined and the compound dried. Yield: 35 mg (0.23 mmol, 38%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.92 (dd, J = 4.7, 1.4 Hz, 1H), 8.58 (dd, J = 8.4, 1.4 Hz, 1H), 7.84 (dd, J = 8.4, 4.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.9, 154.0, 146.6,

143.8, 133.5, 126.7, 117.6; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_7H_3N_2O_2$, 147.0200; found, 147.0198.

3-Carboxylic acid picolinic acid

The compound was commercially obtained from Sigma Aldrich and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.73 (dd, J = 4.8, 1.6 Hz, 1H), 8.23 (dd, J = 7.9, 1.6 Hz, 1H), 7.61 (dd, J = 7.9, 4.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.0, 166.6, 152.5, 151.7, 137.9, 125.6, 124.9; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_7H_4N_1O_4$, 166.0146; found, 166.0148.

3-Hydroxypicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.13 (d, J = 4.7 Hz, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.79 (dd, J = 8.5, 4.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.4, 160.3, 148.6, 133.3, 132.2, 129.7; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_3N_1O_3$, 138.0197; found, 138.0199.

3-Methoxypicolinic acid

3-Hydroxypicolinic acid (200 mg, 1.44 mmol) was suspended with potassium carbonate (596 mg, 4.31 mmol) in dry acetone (25 mL). Over a time of 15 min, a solution of iodomethane in *tert*-butyl methyl ether (2.0 M, 1.0 mL, 2.00 mmol) was added. The reaction mixture was heated to reflux overnight. The solvent was removed under reduced pressure and the residue redissolved in dichloromethane (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 157 mg (1.02 mmol, 71%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.16 (dd, J = 4.6, 1.2 Hz, 1H), 7.66 (dd, J = 8.6, 1.2 Hz, 1H), 7.54 (dd, J = 8.6, 4.6 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.4, 153.4, 140.7, 139.9, 126.7, 121.0, 56.0; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_7H_6N_1O_3$, 152.0353; found, 152.0355.

3-Aminopicolinic acid

Quinolinimide (200 mg, 1.35 mmol) was dissolved in a 10% aqueous sodium hydroxide solution (20 mL). An aqueous hypobromite solution (10 mL, 1.35 mmol) was added dropwise over 10 min. The mixture was stirred at 0 °C for 2 h, slowly warmed up to room temperature and then heated at 85 °C for 2 h. After this time, the solution was cooled down to room temperature and the pH adjusted to 5 using hydrochloric acid. The mixture was stirred at room temperature overnight. After this time, the solution was filtered and an aqueous solution (10 mL) containing copper(II) acetate monohydrate (136 mg, 0.68 mmol) and acetic acid (0.1 mL) added to the solution. The mixture was filtered and the solid thoroughly washed with water (3×10 mL). The precipitate was suspended in an aqueous solution (30 mL) and a hydrogen sulfide solution in tetrahydrofuran (3.4 mL, 0.8 M) was added dropwise. The mixture was filtered and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 11 mg (0.08 mmol, 6%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.82 (dd, J = 4.3, 1.4 Hz, 1H), 7.35 (dd, J = 8.5, 4.3 Hz, 1H), 7.29 (dd, J = 8.5, 1.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.7, 147.8, 134.9, 128.4, 126.3, 125.5; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_5N_2O_2$, 137.0357; found, 137.0358.

3-Nitropicolinic acid

2-Methyl-3-nitropyridine (100 mg, 0.72 mmol) and potassium permanganate (228 mg, 1.44 mmol) were dissolved in water (20 mL) and heated at reflux for 2 h. After this time, the reaction was cooled down to 50 °C and filtered hot through filter paper. The precipitate was thoroughly washed with water (3×10 mL). The aqueous solution was washed with ethyl acetate (3×10 mL). The solution was concentrated to 5 mL and then acidified with an aqueous solution of hydrogen chloride until pH 5 was reached. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 19 mg (0.11 mmol, 15%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.92 (dd, J = 4.8, 1.4 Hz, 1H), 8.58 (dd, J = 8.4, 1.4 Hz, 1H), 7.84 (dd, J = 8.4, 4.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.6, 153.6, 146.2, 143.4, 133.1, 126.4; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3N_2O_4$, 167.0098; found, 167.0099.

4-Fluoropicolinic acid

4-Chloropicolinic acid (100 mg, 0.63 mmol), 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) and dichloro(1,5-cyclooctadiene)palladium(II) (9 mg, 0.03 mmol) were suspended in pentane (25 mL). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The obtained solid and silver(I) fluoride (799 mg, 6.3 mmol) were dissolved in dichloromethane (50 mL). The mixture was protected from light and stirred at room temperature overnight. After this time, the solution was filtered through celite and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 100%/0%). The fractions containing the product were combined and the compound dried. Yield: 11 mg (0.08 mmol, 12%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.74 (dd, J = 8.5, 5.6 Hz, 1H), 7.87 (dd, J = 9.6, 2.6 Hz, 1H), 7.60 (ddd, J = 8.8, 5.6, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.7 (d, J = 261 Hz), 165.3 (d, J = 4 Hz), 152.5 (d, J = 7 Hz), 151.7 (d, J = 6 Hz), 114.8 (d, J = 16 Hz), 112.7 (d, J = 18 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3F_1N_1O_2$, 140.0153; found, 140.0152.

4-Chloropicolinic acid

4-Hydroxypicolinic acid (50 mg, 0.36 mmol) was dissolved in phosphoryl chloride (2 mL) and heated at 120 °C for 4 h. After this time the reaction was cooled down with an ice bath. The excess of phosphoryl chloride was quenched with an aqueous sodium hydroxide solution until pH 9 was reached. The crude product was extracted with dichloromethane (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 26 mg (0.17 mmol, 47%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.67 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 7.78 (d, J = 5.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2, 151.1, 150.2, 144.1, 127.1, 124.8; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3Cl_1N_1O_2$, 155.9858; found, 155.9857.

4-(Trifluoromethyl)picolinic acid

4-Chloropicolinic acid (100 mg, 0.63 mmol), copper(I) iodide (120 mg, 0.63 mmol), methyl fluorosulfonyldifluoroacetate (2.4 mL, 18.9 mmol) were dissolved in 1-methylpyrrolidin-2-one (20 mL). The mixture was heated at 80 °C overnight under nitrogen atmosphere. The solution was filtered over celite and thoroughly washed with ethyl acetate. The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 54 mg (0.28 mmol, 44%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.00 (d, J = 5.0 Hz, 1H), 8.23 (s, 1H), 8.04 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2, 151.4, 150.1, 137.8 (q, J = 34 Hz), 122.7 (q, J = 273 Hz), 122.7 (q, J = 4 Hz), 120.0 (q, J = 4 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3F_3N_1O_2$, 190.0121; found, 190.0120.

4-Methylpicolinic acid

The compound was commercially obtained from Sigma Aldrich and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.55 (d, J = 4.9 Hz, 1H), 7.91 (s, 1H), 7.48 (d, J = 4.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.2, 149.0, 149.0, 148.0, 127.9, 125.6, 20.5; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_2$, 136.0404; found, 136.0404.

4-Cyanopicolinic acid

4-Fluoropicolinic acid (50 mg, 0.35 mmol) was dissolved in dimethyl sulfoxide (2 mL) and potassium cyanide (68 mg, 1.05 mmol) added. The mixture was heated at 120 °C overnight. After this time, the solution was diluted with ethyl acetate (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 31 mg (0.21 mmol, 60%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.95 (dd, J = 4.9, 0.9 Hz, 1H), 8.39 (dd, J = 1.6, 0.9 Hz, 1H), 8.11 (dd, J = 4.9, 1.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.4, 151.3, 150.0, 129.3, 126.9, 121.3, 116.8; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3N_2O_2$, 147.0200; found, 147.0200.

4-Carboxylic acid picolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.89 (d, J = 5.0 Hz, 1H), 8.38 (s, 1H), 8.02 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.8, 165.7, 150.9, 149.6, 139.5, 126.0, 123.6; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_4N_1O_4$, 166.0146; found, 166.0147.

4-Hydroxypicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.34 (d, J = 6.7 Hz, 1H), 7.53 (d, J = 2.6 Hz, 1H), 7.17 (dd, J = 6.7, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.6, 162.0, 144.0, 143.8, 115.8, 114.6; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3N_1O_3$, 138.0197; found, 138.0197.

4-Methoxypicolinic acid

4-Hydroxypicolinic acid (200 mg, 1.44 mmol) was suspended with potassium carbonate (596 mg, 4.31 mmol) in dry acetone (25 mL). Over a time of 15 min, a solution of iodomethane in *tert*-butyl methyl ether (2.0 M, 1.0 mL, 2.00 mmol) was added. The reaction mixture was heated to reflux overnight. The solvent was removed under reduced pressure and the residue redissolved in dichloromethane (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 10%/90%). The fractions containing the product were combined and the compound dried. Yield: 124 mg (0.81 mmol, 56%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.50 (d, J = 5.7 Hz, 1H), 7.55 (d, J = 2.6 Hz, 1H), 7.21 (dd, J = 5.7, 2.6 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.6, 165.6, 150.3, 150.1, 113.0, 110.7, 55.9; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_3$, 152.0353; found, 152.0350.

4-Aminopicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.25 (s, 2H), 7.99 (d, J = 6.8 Hz, 1H), 7.30 (d, J = 2.5 Hz, 1H), 6.84 (dd, J = 6.8, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.8,

160.6, 143.8, 140.1, 109.3, 109.1; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_5N_2O_2$, 137.0357; found, 137.0355.

4-Nitropicolinic acid

2-Methyl-4-nitropyridine (100 mg, 0.72 mmol) and potassium permanganate (228 mg, 1.44 mmol) were dissolved in water (20 mL) and heated at reflux for 2 h. After this time, the reaction was cooled down to 50 °C and filtered hot through filter paper. The precipitate was thoroughly washed with water (3×10 mL). The aqueous solution was washed with ethyl acetate (3×10 mL). The solution was concentrated to 5 mL and then acidified with an aqueous solution of hydrogen chloride until pH 5 was reached. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 12 mg (0.07 mmol, 10%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.07 (d, J = 5.3 Hz, 1H), 8.52 (d, J = 2.3 Hz, 1H), 8.35 (dd, J = 5.3, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.8, 154.6, 152.5, 151.1, 119.6, 117.2; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_3N_2O_4$, 167.0098; found, 167.0099.

5-Fluoropicolinic acid

5-Chloropicolinic acid (100 mg, 0.63 mmol), 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) and dichloro(1,5-cyclooctadiene)palladium(II) (9 mg, 0.03 mmol) were suspended in pentane (25 mL). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The obtained solid and silver(I) fluoride (799 mg, 6.3 mmol) were dissolved in dichloromethane (50 mL). The mixture was protected from light and stirred at room temperature overnight. After this time, the solution was filtered through celite and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 100%/0%). The fractions containing the product were combined and the compound dried. Yield: 21 mg (0.15 mmol, 24%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.68 (d, J = 2.9 Hz, 1H), 8.68 (dd, J = 8.8, 4.6 Hz, 1H), 8.68 (dd, J = 8.8, 2.9 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.3, 160.8 (d, J = 260 Hz), 145.0 (d, J = 4 Hz), 138.1 (d, J = 25 Hz), 127.1 (d, J = 6 Hz), 124.2 (d, J = 19 Hz); HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_3F_1N_1O_2$, 140.0153; found, 140.0152.

5-Chloropicolinic acid

5-Hydroxypicolinic acid (50 mg, 0.36 mmol) was dissolved in phosphoryl chloride (2 mL) and heated at 120 °C for 4 h. After this time the reaction was cooled down with an ice bath. The excess of phosphoryl chloride was quenched with an aqueous sodium hydroxide solution until pH 9 was reached. The crude product was extracted with dichloromethane (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 21 mg (0.13 mmol, 36%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.75 (dd, J = 2.4, 0.7 Hz, 1H), 8.11 (dd, J = 8.4, 2.4 Hz, 1H), 8.05 (dd, J = 8.4, 0.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.5, 148.3, 146.9, 137.3, 134.6, 126.2; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3Cl_1N_1O_2$, 155.9858; found, 155.9856.

5-(Trifluoromethyl)picolinic acid

5-Chloropicolinic acid (100 mg, 0.63 mmol), copper(I) iodide (120 mg, 0.63 mmol), methyl fluorosulfonyldifluoroacetate (2.4 mL, 18.9 mmol) were dissolved in 1-methylpyrrolidin-2-one (20 mL). The mixture was heated at 80 °C overnight under nitrogen atmosphere. The solution was filtered over celite and thoroughly washed with ethyl acetate. The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 67 mg (0.35 mmol, 56%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.11 (d, J = 2.3 Hz, 1H), 8.41 (dd, J = 8.2, 2.3 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2, 152.1, 146.4, 135.3, 130.2 (q, J = 34 Hz), 124.8, 122.7 (q, J = 270 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3F_3N_1O_2$, 190.0121; found, 190.0120.

5-Methylpicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.62 (s, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.8, 148.1, 143.8, 140.2, 138.5, 125.1, 18.1; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_2$, 136.0404; found, 136.0405.

5-Cyanopicolinic acid

5-Fluoropicolinic acid (50 mg, 0.35 mmol), palladium acetate (7 mg, 0.03 mmol) and 1,5-bis(diphenylphosphino)-pentane (154 mg, 0.35 mmol) were dissolved in dimethyl sulfoxide (2 mL) and potassium cyanide (68 mg, 1.05 mmol) added under nitrogen atmosphere. The mixture was heated at 120 °C overnight. After this time, the solution was diluted with ethyl acetate (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 27 mg (0.18 mmol, 51%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.14 (s, 1H), 8.51 (d, J = 8.2 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2, 152.5, 151.2, 141.8, 124.5, 116.7, 111.8; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_7H_3N_2O_2$, 147.0200; found, 147.0201.

5-Carboxylic acid picolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.14 (d, J = 2.1 Hz, 1H), 8.42 (dd, J = 8.1, 2.1 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.7, 165.7, 151.4, 150.1, 138.5, 129.1, 124.7; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_7H_4N_1O_4$, 166.0146; found, 166.0145.

5-Hydroxypicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (d, J = 2.8 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.25 (d, J = 8.5, 2.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.0, 156.7, 139.1, 137.9, 126.6, 122.3; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_6H_3N_1O_3$, 138.0197; found, 138.0198.

5-Methoxypicolinic acid

5-Hydroxypicolinic acid (200 mg, 1.44 mmol) was suspended with potassium carbonate (596 mg, 4.31 mmol) in dry acetone (25 mL). Over a time of 15 min, a solution of iodomethane in

tert-butyl methyl ether (2.0 M, 1.0 mL, 2.00 mmol) was added. The reaction mixture was heated to reflux overnight. The solvent was removed under reduced pressure and the residue redissolved in dichloromethane (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 10%/90%). The fractions containing the product were combined and the compound dried. Yield: 98 mg (0.64 mmol, 44%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.37 (d, J = 2.9 Hz, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.51 (dd, J = 8.7, 2.9 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.8, 157.9, 140.4, 137.8, 126.4, 120.4, 56.0; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_7H_6N_1O_3$, 152.0353; found, 152.0353.

5-Aminopicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.95 (d, J = 2.7 Hz, 1H), 7.74 (d, J = 8.5 Hz, 1H), 6.92 (dd, J = 8.5, 2.7 Hz, 1H), 6.17 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.3, 148.1, 135.3, 134.7, 126.3, 118.5; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_6H_5N_2O_2$, 137.0357; found, 137.0359.

5-Nitropicolinic acid

2-Methyl-5-nitropyridine (100 mg, 0.72 mmol) and potassium permanganate (228 mg, 1.44 mmol) were dissolved in water (20 mL) and heated at reflux for 2 h. After this time, the reaction was cooled down to 50 °C and filtered hot through filter paper. The precipitate was thoroughly washed with water (3×10 mL). The aqueous solution was washed with ethyl acetate (3×10 mL). The solution was concentrated to 5 mL and then acidified with an aqueous solution of hydrogen chloride until pH 5 was reached. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 9 mg (0.05 mmol, 7%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.44 (d, J = 2.6 Hz, 1H), 8.74 (dd, J = 8.6, 2.6 Hz, 1H), 8.26 (d, J = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.9, 152.8, 145.7, 144.8, 133.2, 125.5; HRMS (*m*/*z*): $[M-H]^-$ calcd. for $C_6H_3N_2O_4$, 167.0098; found, 167.0097.

6-Fluoropicolinic acid

6-Chloropicolinic acid (100 mg, 0.63 mmol), 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) and dichloro(1,5-cyclooctadiene)palladium(II) (9 mg, 0.03 mmol) were suspended in pentane (25 mL). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The obtained solid and silver(I) fluoride (799 mg, 6.3 mmol) were dissolved in dichloromethane (50 mL). The mixture was protected from light and stirred at room temperature overnight. After this time, the solution was filtered through celite and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 100%/0%). The fractions containing the product were combined and the compound dried. Yield: 12 mg (0.09 mmol, 14%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.17 (dd, J = 8.2, 7.4 Hz, 1H), 7.99 (dd, J = 7.4, 2.5 Hz, 1H), 7.46 (dd, J = 8.2, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.9, 162.4 (d, J = 238 Hz), 146.7 (d, J = 13 Hz), 143.6 (d, J = 8 Hz), 123.1 (d, J = 4 Hz), 113.9 (d, J = 37 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3F_1N_1O_2$, 140.0153; found, 140.0151.

6-Chloropicolinic acid

6-Hydroxypicolinic acid (50 mg, 0.36 mmol) was dissolved in phosphoryl chloride (2 mL) and heated at 120 °C for 4 h. After this time the reaction was cooled down with an ice bath. The excess of phosphoryl chloride was quenched with an aqueous sodium hydroxide solution until pH 9 was reached. The crude product was extracted with dichloromethane (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 11 mg (0.07 mmol, 19%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.04 (dd, J = 7.6, 6.3 Hz, 1H), 8.03 (dd, J = 7.6, 2.5 Hz, 1H), 7.76 (dd, J = 6.3, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.9, 150.2, 148.9, 141.2, 128.0, 124.1; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3Cl_1N_1O_2$, 155.9858; found, 155.9856.

6-(Trifluoromethyl)picolinic acid

6-Chloropicolinic acid (100 mg, 0.63 mmol), copper(I) iodide (120 mg, 0.63 mmol), methyl fluorosulfonyldifluoroacetate (2.4 mL, 18.9 mmol) were dissolved in 1-methylpyrrolidin-2-one (20 mL). The mixture was heated at 80 °C overnight under nitrogen atmosphere. The solution was filtered over celite and thoroughly washed with ethyl acetate. The organic phase was three-

times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 27 mg (0.14 mmol, 21%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.31 (dd, J = 7.8, 1.6 Hz, 1H), 8.29 (d, J = 7.8, 7.3 Hz, 1H), 8.14 (dd, J = 7.3, 1.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.1, 149.1, 146.5 (q, J = 35 Hz), 140.3, 128.1, 123.9 (q, J = 3 Hz), 121.4 (q, J = 275 Hz); HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3F_3N_1O_2$, 190.0121; found, 190.0119.

6-Methylpicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.92-7.85 (m, 2H), 7.52 (d, J = 7.2 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.9, 158.0, 147.1, 138.3, 127.0, 122.1, 23.5; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_2$, 136.0404; found, 136.0403.

6-Cyanopicolinic acid

6-Chloropicolinic acid (100 mg, 0.63 mmol), sodium cyanide (31 mg, 0.63 mmol), palladium acetate (7 mg, 0.03 mmol) and 1,5-bis(diphenylphosphino)-pentane (278 mg, 0.63 mmol) were dissolved in 1,3,5-trimethylbenzene (20 mL) and *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (142 µL, 0.95 mmol) was added under nitrogen atmosphere. The mixture was heated at 120 °C overnight. After this time, the solution was diluted with ethyl acetate (50 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 38 mg (0.26 mmol, 41%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.30 (dd, J = 7.0, 2.1 Hz, 1H), 8.27-8.22 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.8, 149.9, 139.8, 132.6, 131.9, 128.4, 117.1; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_3N_2O_2$, 147.0200; found, 147.0201.

6-Carboxylic acid picolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.24 (d, J = 8.7 Hz, 1H), 8.23 (d, J = 6.7 Hz, 1H), 8.17 (dd, J = 8.7, 6.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.6, 148.2, 139.4, 127.7; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_4N_1O_4$, 166.0146; found, 166.0147.

6-Hydroxypicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.56 (dd, J = 9.1, 6.8 Hz, 1H), 6.97 (dd, J = 6.8, 1.1 Hz, 1H), 6.64 (dd, J = 9.1, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.0, 162.3, 140.1, 137.6, 123.7, 110.1; HRMS (m/z): [M-H]$^-$ calcd. for $C_6H_3N_1O_3$, 138.0197; found, 138.0199.

6-Methoxypicolinic acid

6-Hydroxypicolinic acid (200 mg, 1.44 mmol) was suspended with potassium carbonate (596 mg, 4.31 mmol) in dry acetone (25 mL). Over a time of 15 min, a solution of iodomethane in *tert*-butyl methyl ether (2.0 M, 1.0 mL, 2.00 mmol) was added. The reaction mixture was heated to reflux overnight. The solvent was removed under reduced pressure and the residue redissolved in dichloromethane (25 mL). The organic phase was three-times washed with water (3×25 mL) and brine (3×25 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 10%/90%). The fractions containing the product were combined and the compound dried. Yield: 142 mg (0.93 mmol, 65%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.85 (dd, J = 8.3, 7.3 Hz, 1H), 7.66 (dd, J = 7.3, 0.8 Hz, 1H), 7.04 (dd, J = 8.3, 0.8 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.0, 163.3, 146.0, 140.1, 118.5, 114.9, 53.4; HRMS (m/z): [M-H]$^-$ calcd. for $C_7H_6N_1O_3$, 152.0353; found, 152.0353.

6-Aminopicolinic acid

The compound was commercially obtained from Combi Blocks and used without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.59 (dd, J = 8.3, 7.1 Hz, 1H), 7.16 (d, J = 7.1 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 6.57 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 165.3,

158.2, 146.1, 139.2, 112.5, 112.2; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_5N_2O_2$, 137.0357; found, 137.0358.

6-Nitropicolinic acid

2-Methyl-6-nitropyridine (100 mg, 0.72 mmol) and potassium permanganate (228 mg, 1.44 mmol) were dissolved in water (20 mL) and heated at reflux for 2 h. After this time, the reaction was cooled down to 50 °C and filtered hot through filter paper. The precipitate was thoroughly washed with water (3×10 mL). The aqueous solution was washed with ethyl acetate (3×10 mL). The solution was concentrated to 5 mL and then acidified with an aqueous solution of hydrogen chloride until pH 5 was reached. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of ethyl acetate/hexane (0%/100% - 20%/80%). The fractions containing the product were combined and the compound dried. Yield: 15 mg (0.08 mmol, 11%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.51 (d, J = 7.8 Hz, 1H), 8.44 (dd, J = 7.8, 7.3 Hz, 1H), 8.42 (d, J = 7.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 164.5, 156.1, 147.7, 142.5, 130.3, 121.4; HRMS (*m*/*z*): [M-H]$^-$ calcd. for $C_6H_3N_2O_4$, 167.0098; found, 167.0099.

General Procedure for the Synthesis of [Re(pic)(H_2O)(CO)$_3$]

Pentacarbonylchlororhenium (50 mg, 0.138 mmol, 1.0 equiv) was suspended in acetonitrile (25 mL) and the mixture heated at reflux for 6 h. After this time, the solvent was removed under reduced pressure. The solid was suspended in water (25 mL) and the picolinic acid derivative (0.138 mmol, 1.0 equiv) was added. The mixture was heated at reflux for 4 h. After this time, the solution was placed in a fridge at 4 °C overnight. The precipitate was collected by filtration and thoroughly washed with water (3×10 mL) and diethyl ether (3×10 mL). The solid was again recrystallized from water in a fridge at 4 °C overnight. The precipitate was collected by filtration, washed with diethyl ether (3x10 mL) and dried.

[Re(picolinic acid)(H_2O)(CO)$_3$] (1)

Yield: 81%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.90-8.80 (m, 1H), 8.29 (td, J = 7.7, 1.6 Hz, 1H), 8.22 (d, J = 7.3 Hz, 1H), 7.82 (ddd, J = 7.3, 5.3, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-

d$_4$): δ 197.7, 197.5, 194.5, 175.4, 153.6, 151.0, 142.3, 130.2, 128.3; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_5N_1O_5Re_1$, 393.9720; found, 393.9718.

[Re(3-fluoropicolinic acid)(H_2O)(CO)$_3$] (2)

Yield: 73%. ^{1}H NMR (500 MHz, MeOH-*d*$_4$): δ 8.78 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.12 (ddd, *J* = 9.8, 8.7, 1.2 Hz, 1H), 7.85 (ddd, *J* = 8.7, 5.2, 4.3 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-*d*$_4$): δ 197.6, 197.2, 194.2, 172.5 (d, *J* = 6 Hz), 162.7 (d, *J* = 268 Hz), 150.4 (d, *J* = 5 Hz), 139.0 (d, *J* = 13 Hz), 132.2 (d, *J* = 8 Hz), 131.7 (d, *J* = 21 Hz); HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_4F_1N_1O_5Re_1$, 411.9626; found, 411.9631.

[Re(3-chloropicolinic acid)(H_2O)(CO)$_3$] (3)

Yield: 68%. ^{1}H NMR (500 MHz, MeOH-*d*$_4$): δ 8.89 (dd, *J* = 5.2, 1.3 Hz, 1H), 8.34 (dd, *J* = 9.8, 8.3, 1.3 Hz, 1H), 7.75 (ddd, *J* = 8.3, 5.2 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-*d*$_4$): δ 197.8, 197.3, 194.3, 172.7, 152.9, 146.6, 145.7, 137.9, 130.3; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_4Cl_1N_1O_5Re_1$, 427.9321; found, 427.9326.

[Re(3-(trifluoromethyl)picolinic acid)(H_2O)(CO)$_3$] (4)

Yield: 71%. ^{1}H NMR (500 MHz, MeOH-*d*$_4$): δ 9.12 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.65 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.96 (dd, *J* = 8.3, 5.4 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-*d*$_4$): δ 197.7, 197.2, 194.1, 171.5, 156.8, 150.1 (q, *J* = 2 Hz), 141.1, (q, *J* = 7 Hz), 131.3 (q, *J* = 36 Hz), 129.9, 123.5 (q, *J* = 273 Hz); HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_{10}H_4F_3N_1O_5Re_1$, 461.9594; found, 461.9596.

[Re(3-methylpicolinic acid)(H_2O)(CO)$_3$] (5)

Yield: 92%. ^{1}H NMR (500 MHz, MeOH-*d*$_4$): δ 8.77 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.09 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.65 (dd, *J* = 7.9, 5.3 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR (125 MHz, MeOH-*d*$_4$): δ 198.3, 197.7, 194.8, 175.8, 151.8, 148.0, 145.8, 141.9, 129.3, 20.2; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_{10}H_7N_1O_5Re_1$, 407.9876; found, 407.9874.

[Re(3-cyanopicolinic acid)(H_2O)($CO)_3$] (6)

Yield: 61%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.91 (dd, J = 5.1, 1.3 Hz, 1H), 8.52 (dd, J = 8.3, 1.3 Hz, 1H), 8.17 (dd, J = 8.3, 5.1 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.5, 197.2, 193.7, 173.7, 153.9, 149.4, 136.1, 132.7, 130.4, 116.5; HRMS (m/z): [M-H_2O+H+CH_3OH]$^+$ calcd. for $C_{10}H_4N_2O_5Re_1$+CH_3OH, 450.9935; found, 450.9933.

[Re(3-carboxylic acid picolinic acid)(H_2O)($CO)_3$] (7)

Yield: 69%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.96 (dd, J = 5.4, 1.5 Hz, 1H), 8.30 (dd, J = 7.9, 1.5 Hz, 1H), 7.88 (dd, J = 7.9, 5.4 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.5, 197.2, 194.3, 173.8, 169.6, 154.4, 147.3, 140.7, 137.0, 130.1; HRMS (m/z): [M-H_2O-H]$^-$ calcd. for $C_{10}H_3N_1O_7Re_1$, 435.9473; found, 435.9477.

[Re(3-hydroxypicolinic acid)(H_2O)($CO)_3$] (8)

Yield: 74%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.43 (dd, J = 5.0, 1.2 Hz, 1H), 7.73 (dd, J = 8.7, 1.2 Hz, 1H), 7.65 (dd, J = 8.7, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.5, 197.3, 194.3, 179.4, 160.6, 145.2, 133.9, 131.9, 130.7; HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_9H_5N_1O_6Re_1$, 409.9669; found, 409.9672.

[Re(3-methoxypicolinic acid)(H_2O)($CO)_3$] (9)

Yield: 82%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.50 (dd, J = 5.1, 1.1 Hz, 1H), 8.00 (dd, J = 8.8, 1.1 Hz, 1H), 7.74 (dd, J = 8.8, 5.1 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.2, 197.6, 194.6, 174.5, 160.7, 145.5, 138.3, 131.4, 126.6, 57.0; HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 423.9826; found, 423.9828.

[Re(3-aminopicolinic acid)(H_2O)($CO)_3$] (10)

Yield: 57%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.09 (dd, J = 4.8, 1.3 Hz, 1H), 7.46 (dd, J = 8.7, 1.3 Hz, 1H), 7.37 (dd, J = 8.7, 4.8 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.4, 197.9, 195.0, 178.8, 150.6, 141.5, 130.2, 129.5, 128.9; HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_9H_6N_2O_5Re_1$, 408.9829; found, 408.9832.

[Re(3-nitropicolinic acid)(H_2O)($CO)_3$] (11)

Yield: 67%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.08 (dd, J = 5.3, 1.3 Hz, 1H), 8.49 (dd, J = 8.3, 1.3 Hz, 1H), 8.00 (dd, J = 8.3, 5.3 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.1, 196.9, 193.8, 170.6, 155.7, 150.3, 142.7, 136.2, 131.5; HRMS (m/z): [M-H_2O+Na]$^+$ calcd. for $C_9H_3N_2O_7Re_1Na_1$, 460.9387; found, 460.9390.

[Re(4-fluoropicolinic acid)(H_2O)($CO)_3$] (12)

Yield: 53%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.91 (dd, J = 6.3, 2.9 Hz, 1H), 7.98 (dd, J = 7.6, 2.8 Hz, 1H), 7.66 (ddd, J = 7.6, 6.1, 2.9 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.4, 197.2, 194.3, 174.1 (d, J = 3 Hz), 172.2 (d, J = 271 Hz), 156.7 (d, J = 10 Hz), 155.1 (d, J = 9 Hz), 118.1 (d, J = 20 Hz), 116.5 (d, J = 21 Hz); HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_9H_4F_1N_1O_5Re_1$, 411.9626; found, 411.9625.

[Re(4-chloropicolinic acid)(H_2O)($CO)_3$] (13)

Yield: 81%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.82 (d, J = 5.8 Hz, 1H), 8.22 (d, J = 2.3 Hz, 1H), 7.89 (dd, J = 5.8, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.4, 197.3, 194.2, 174.1, 154.4, 152.5, 150.3, 130.3, 128.7; HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_9H_4Cl_1N_1O_5Re_1$, 427.9321; found, 427.9324.

[Re(4-(trifluoromethyl)picolinic acid)(H_2O)($CO)_3$] (14)

Yield: 64%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.14 (d, J = 5.6 Hz, 1H), 8.44 (d, J = 2.0 Hz, 1H), 8.14 (dd, J = 5.6, 2.0 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.2, 197.2, 194.0, 173.8, 155.3, 153.1, 142.9 (q, J = 36 Hz), 126.2 (q, J = 4 Hz), 124.1 (q, J = 4 Hz), 123.5 (q, J = 273 Hz); HRMS (m/z): [M-H_2O+H]$^+$ calcd. for $C_{10}H_4F_3N_1O_5Re_1$, 461.9594; found, 461.9592.

[Re(4-methylpicolinic acid)(H_2O)($CO)_3$] (15)

Yield: 93%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.70 (d, J = 5.5 Hz, 1H), 8.05 (d, J = 1.9 Hz, 1H), 7.64 (dd, J = 5.5, 1.9 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.8,

197.6, 194.6, 175.6, 155.5, 152.9, 150.4, 130.8, 129.0, 21.5; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_5Re_1$, 407.9876; found, 407.9878.

[Re(4-cyanopicolinic acid)(H_2O)($CO)_3$] (16)

Yield: 86%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.09 (d, J = 5.6, 0.8 Hz, 1H), 8.49 (d, J = 1.8, 0.8 Hz, 1H), 8.14 (dd, J = 5.6, 1.8 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.1, 197.1, 193.9, 173.6, 154.7, 152.6, 132.1, 130.4, 125.8, 116.3; HRMS (*m*/*z*): $[M\text{-}H_2O+H+CH_3OH]^+$ calcd. for $C_{10}H_4N_2O_5Re_1+CH_3OH$, 450.9935; found, 450.9931.

[Re(4-carboxylic acid picolinic acid)(H_2O)($CO)_3$] (17)

Yield: 59%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.05 (d, J = 5.5, 0.8 Hz, 1H), 8.62 (d, J = 1.9, 0.8 Hz, 1H), 8.28 (dd, J = 5.5, 1.9 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.3, 197.3, 194.2, 174.6, 165.7, 154.7, 152.2, 144.0, 129.5, 127.4; HRMS (*m*/*z*): $[M\text{-}H_2O\text{-}H]^-$ calcd. for $C_{10}H_3N_1O_7Re_1$, 435.9473; found, 435.9474.

[Re(4-hydroxypicolinic acid)(H_2O)($CO)_3$] (18)

Yield: 53%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.52 (d, J = 6.2 Hz, 1H), 7.58 (d, J = 2.7 Hz, 1H), 7.12 (dd, J = 6.2, 2.7 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.3, 198.2, 191.8, 175.3, 168.8, 154.5, 143.8, 117.7, 116.8; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_5N_1O_6Re_1$, 409.9669; found, 409.9674.

[Re(4-methoxypicolinic acid)(H_2O)($CO)_3$] (19)

Yield: 84%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.65 (d, J = 6.3 Hz, 1H), 7.71 (d, J = 2.9 Hz, 1H), 7.32 (dd, J = 6.3, 2.9 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.9, 197.6, 194.8, 175.5, 170.6, 154.6, 152.7, 115.7, 114.2, 57.3; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 423.9826; found, 423.9825.

[Re(4-aminopicolinic acid)(H_2O)($CO)_3$] (20)

Yield: 67%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.16 (d, J = 6.3 Hz, 1H), 7.26 (d, J = 2.6 Hz, 1H), 6.74 (dd, J = 6.3, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.4, 198.1, 195.4, 176.7, 159.2, 152.7, 150.4, 141.5, 112.5; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_6N_2O_5Re_1$, 408.9829; found, 408.9833.

[Re(4-nitropicolinic acid)(H_2O)($CO)_3$] (21)

Yield: 85%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.23 (d, J = 5.9 Hz, 1H), 8.78 (d, J = 2.5 Hz, 1H), 8.51 (dd, J = 5.9, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.1, 197.0, 193.8, 173.4, 157.3, 156.4, 154.7, 123.1, 121.2; HRMS (*m*/*z*): $[M\text{-}H_2O+Na]^+$ calcd. for $C_9H_3N_2O_7Re_1Na_1$, 460.9387; found, 460.9388.

[Re(5-fluoropicolinic acid)(H_2O)($CO)_3$] (22)

Yield: 79%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.85 (dd, J = 5.6, 2.3 Hz, 1H), 8.27 (dd, J = 8.8, 5.2 Hz, 1H), 8.13 (ddd, J = 8.8, 7.7, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.3, 197.2, 194.2, 174.1, 163.4 (d, J = 259 Hz), 148.0, 142.5 (d, J = 32 Hz), 130.1 (d, J = 8 Hz), 129.1 (d, J = 19 Hz); HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_4F_1N_1O_5Re_1$, 411.9626; found, 411.9624.

[Re(5-chloropicolinic acid)(H_2O)($CO)_3$] (23)

Yield: 86%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.88 (d, J = 2.2 Hz, 1H), 8.35 (dd, J = 8.4, 2.2 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.3, 197.1, 194.1, 174.3, 152.2, 149.6, 142.1, 138.2, 129.1; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_4Cl_1N_1O_5Re_1$, 427.9321; found, 427.9320.

[Re(5-(trifluoromethyl)picolinic acid)(H_2O)($CO)_3$] (24)

Yield: 74%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.09 (d, J = 2.2 Hz, 1H), 8.66 (dd, J = 8.2, 2.2 Hz, 1H), 8.41 (d, J = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.2, 197.0, 193.9, 173.7, 154.4, 150.4 (q, J = 4 Hz), 139.9 (q, J = 3 Hz), 132.2 (q, J = 35 Hz), 128.7, 123.7 (q, J = 273 Hz); HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_4F_3N_1O_5Re_1$, 461.9594; found, 461.9595.

[Re(5-methylpicolinic acid)(H_2O)($CO)_3$] (25)

Yield: 86%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.71-8.69 (m, 1H), 8.11-8.09 (m, 2H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.8, 197.5, 194.6, 175.6, 153.5, 148.5, 142.6, 141.8, 127.8, 18.4; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_5Re_1$, 407.9876; found, 407.9874.

[Re(5-cyanopicolinic acid)(H_2O)($CO)_3$] (26)

Yield: 74%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.24 (dd, J = 1.8, 0.8 Hz, 1H), 8.66 (dd, J = 8.1, 1.8 Hz, 1H), 8.34 (dd, J = 8.1, 0.8 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 196.9, 196.9, 193.9, 173.6, 156.4, 153.6, 145.9, 128.3, 116.1, 115.6; HRMS (*m*/*z*): $[M\text{-}H_2O+H+CH_3OH]^+$ calcd. for $C_{10}H_4N_2O_5Re_1+CH_3OH$, 450.9935; found, 450.9926.

[Re(5-carboxylic acid picolinic acid)(H_2O)($CO)_3$] (27)

Yield: 72%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.31 (d, J = 1.9 Hz, 1H), 8.79 (dd, J = 8.0, 1.9 Hz, 1H), 8.32 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.5, 197.3, 194.2, 174.3, 165.4, 154.3, 153.6, 143.0, 133.0, 128.2; HRMS (*m*/*z*): $[M\text{-}H_2O\text{-}H]^-$ calcd. for $C_{10}H_3N_1O_7Re_1$, 435.9473; found, 435.9479.

[Re(5-hydroxypicolinic acid)(H_2O)($CO)_3$] (28)

Yield: 61%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.46 (d, J = 2.6 Hz, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 8.7, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.9, 197.8, 191.1, 178.9, 161.4, 142.8, 138.5, 131.0, 125.8; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_5N_1O_6Re_1$, 409.9669; found, 409.9674.

[Re(5-methoxypicolinic acid)(H_2O)($CO)_3$] (29)

Yield: 84%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.48 (dd, J = 2.7, 0.5 Hz, 1H), 8.15 (dd, J = 8.7, 0.5 Hz, 1H), 7.84 (dd, J = 8.7, 2.7 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4):

δ 197.8, 197.4, 194.5, 175.5, 161.3, 143.1, 142.1, 129.4, 124.7, 57.2; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 423.9826; found, 423.9828.

[Re(5-aminopicolinic acid)(H_2O)($CO)_3$] (30)

Yield: 81%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.21 (d, J = 2.5 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.26 (dd, J = 8.7, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.2, 197.7, 195.0, 176.9, 151.5, 138.8, 137.8, 129.1, 123.0; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_6N_2O_5Re_1$, 408.9829; found, 408.9831.

[Re(5-nitropicolinic acid)(H_2O)($CO)_3$] (31)

Yield: 88%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 9.54 (d, J = 2.3 Hz, 1H), 9.05 (dd, J = 8.5, 2.3 Hz, 1H), 8.43 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.5, 196.9, 193.8, 173.1, 155.0, 149.2, 148.6, 137.2, 128.8; HRMS (*m*/*z*): [M-H_2O+Na]$^+$ calcd. for $C_9H_3N_2O_7Re_1Na_1$, 460.9387; found, 460.9386.

[Re(6-fluoropicolinic acid)(H_2O)($CO)_3$] (32)

Yield: 77%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.44-8.39 (m, 1H), 8.13 (dt, J = 7.5, 1.1 Hz, 1H), 7.72 (dt, J = 8.3, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 196.7, 196.5 (d, J = 11 Hz), 193.5, 174.2 (d, J = 1 Hz), 164.5 (d, J = 260 Hz), 149.6, 147.5 (d, J = 10 Hz), 125.2 (d, J = 3 Hz), 115.7 (d, J = 30 Hz); HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_4F_1N_1O_5Re_1$, 411.9626; found, 411.9628.

[Re(6-chloropicolinic acid)(H_2O)($CO)_3$] (33)

Yield: 89%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.24 (dd, J = 7.6, 7.4 Hz, 1H), 8.23 (dt, J = 7.6, 1.9 Hz, 1H), 8.04 (dd, J = 7.4, 1.9 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.7, 196.4, 193.7, 174.9, 155.7, 153.4, 144.3, 130.7, 126.9; HRMS (*m*/*z*): [M-H_2O+H]$^+$ calcd. for $C_9H_4Cl_1N_1O_5Re_1$, 427.9321; found, 427.9321.

[Re(6-(trifluoromethyl)picolinic acid)(H_2O)($CO)_3$] (34)

Yield: 82%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.59 (dd, J = 7.8, 1.6 Hz, 1H), 8.52 (dd, J = 7.8, 7.8 Hz, 1H), 8.41 (dd, J = 7.8, 1.6 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 196.6, 195.4, 194.1, 173.9, 154.0, 148.7 (q, J = 34 Hz), 144.2, 131.9, 127.9 (q, J = 5 Hz), 122.0 (q, J = 275 Hz); HRMS (m/z): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_4F_3N_1O_5Re_1$, 461.9594; found, 461.9594.

[Re(6-methylpicolinic acid)(H_2O)($CO)_3$] (35)

Yield: 86%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.11 (dd, J = 7.6, 7.2 Hz, 1H), 8.09 (dd, J = 7.6, 2.1 Hz, 1H), 7.81 (dd, J = 7.2, 2.1 Hz, 1H), 2.95 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.4, 196.7, 194.1, 176.0, 162.8, 151.6, 141.9, 130.4, 125.9, 28.6; HRMS (m/z): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_5Re_1$, 407.9876; found, 407.9875.

[Re(6-cyanopicolinic acid)(H_2O)($CO)_3$] (36)

Yield: 75%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.49-8.43 (m, 2H), 8.37 (dd, J = 6.6, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 196.2, 196.1, 193.5, 173.7, 153.5, 143.7, 136.6, 135.5, 131.6, 116.6; HRMS (m/z): $[M\text{-}H_2O+H+CH_3OH]^+$ calcd. for $C_{10}H_4N_2O_5Re_1$+CH_3OH, 450.9935; found, 450.9933.

[Re(6-carboxylic acid picolinic acid)(H_2O)($CO)_3$] (37)

Yield: 53%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.40-8.31 (m, 2H), 8.03 (dd, J = 7.3, 1.8 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 196.9, 196.6, 194.3, 174.7, 167.7, 156.0, 151.5, 143.2, 129.1, 128.1; HRMS (m/z): $[M\text{-}H_2O\text{-}H]^-$ calcd. for $C_{10}H_3N_1O_7Re_1$, 435.9473; found, 435.9478.

[Re(6-hydroxypicolinic acid)(H_2O)($CO)_3$] (38)

Yield: 77%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.00 (dd, J = 8.4, 7.3 Hz, 1H), 7.66 (dd, J = 7.3, 1.1 Hz, 1H); 7.18 (dd, J = 8.4, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.9, 197.8, 194.6, 176.4, 165.8, 148.8, 143.7, 119.5, 115.4; HRMS (m/z): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_5N_1O_6Re_1$, 409.9669; found, 409.9671.

[Re(6-methoxypicolinic acid)(H_2O)($CO)_3$] (39)

Yield: 83%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.22 (dd, J = 8.5, 7.4 Hz, 1H), 7.82 (d, J = 7.4 Hz, 1H); 7.48 (d, J = 8.5 Hz, 1H), 4.16 (s, 3H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 197.9, 197.6, 194.3, 175.9, 165.9, 149.3, 145.0, 120.7, 111.9, 57.7; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 423.9826; found, 423.9826.

[Re(6-aminopicolinic acid)(H_2O)($CO)_3$] (40)

Yield: 49%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 7.73 (dd, J = 8.5, 7.1 Hz, 1H), 7.39 (d, J = 7.1 Hz, 1H); 7.07 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 198.2, 196.7, 194.0, 161.4, 155.5, 145.1, 141.0, 117.0, 115.7; HRMS (*m*/*z*): $[M\text{-}H_2O+H]^+$ calcd. for $C_9H_6N_2O_5Re_1$, 408.9829; found, 408.9833.

[Re(6-nitropicolinic acid)(H_2O)($CO)_3$] (41)

Yield: 76%. ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.61 (dd, J = 7.9, 7.8 Hz, 1H), 8.53 (dd, J = 7.8, 1.3 Hz, 1H); 8.30 (d, J = 7.9, 1.3 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4): δ 195.6, 195.4, 193.4, 173.2, 161.1, 151.6, 146.8, 131.0, 122.9; HRMS (*m*/*z*): $[M\text{-}H_2O+Na]^+$ calcd. for $C_9H_3N_2O_7Re_1Na_1$, 460.9389; found, 460.9390.

General Procedure for the Synthesis of [Re(picolinic acid derivative)(DMSO)($CO)_3$]

[Re(picolinic acid derivative)(H_2O)($CO)_3$] (20 mg) was dissolved in dry dimethyl sulfoxide (5 mL) and stirred overnight at room temperature in the dark. The solution was dropwise added to an excess of diethyl ether (200 mL). The precipitate was collected by centrifugation. The solid was thoroughly washed with diethyl ether (3×25 mL). The solid was dried under vacuum.

[Re(picolinic acid)(DMSO)($CO)_3$] ($\mathbf{1_{DMSO}}$)

Yield: 17%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.81 (ddd, J = 5.3, 1.5, 0.8 Hz, 1H), 8.29 (ddd, J = 7.7, 7.7, 1.5 Hz, 1H), 8.10 (ddd, J = 7.7, 1.5, 0.8 Hz, 1H), 7.81 (ddd, J = 7.7, 5.3, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.8, 197.7, 194.5, 171.9, 152.1, 149.7, 141.1, 129.0, 126.7; MS (*m*/*z*): $[M+H]^+$ calcd. for $C_{11}H_{11}N_1O_6S_1Re_1$, 472.0; found, 472.3; HRMS (*m*/*z*): $[M\text{-}DMSO+H]^+$ calcd. for $C_9H_5N_1O_5Re_1$, 393.9720; found, 393.9719.

[Re(4-methoxypicolinic acid)(DMSO)(CO)$_3$] (19$_{DMSO}$)

Yield: 12%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.57 (d, J = 6.3 Hz, 1H), 7.55 (d, J = 2.8 Hz, 1H), 7.32 (d, J = 6.3, 2.8 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.8, 197.6, 194.6, 171.8, 168.3, 152.9, 148.7, 114.8, 112.2, 56.8; MS (*m*/*z*): $[M+H]^+$ calcd. for $C_{12}H_{13}N_1O_7S_1Re_1$, 502.0; found, 502.2; HRMS (*m*/*z*): $[M\text{-}DMSO+H]^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 423.9826; found, 423.9825.

Separation of Enantiomeric Mixture of [Re(4-methoxypicolinic acid)(H$_2$O)(CO)$_3$] (19)

[Re(4-methoxypicolinic acid)(H$_2$O)(CO)$_3$] (50 mg, 0.114 mmol, 1.0 equiv) and *N*-(tert-butoxycarbonyl)-L-cysteine methyl ester (24 µL, 0.114 mmol, 1.0 equiv) were dissolved in methanol (35 mL) and the mixture stirred at room temperature overnight. The generated diastereomeric mixture of [Re(4-methoxypicolinic acid)(*N*-(tert-butoxycarbonyl)-L-cysteine methyl ester)(CO)$_3$] was separated by reverse phase liquid chromatography. Column chromatography was performed on a CombiFlash Rf Teledyne ISCO system equipped with a High Perfomance RediSepRf GOLD C18 column (50 g, Particle Size: 20-40 µm spherical, Mesh Size: 400-632, Pore Size: 100 Å, Surface Area: 300±50 m²/g, Carbon Content: 15±2 %) using millipore water (solvent A) and methanol (solvent B). The following solvent gradient was used: 0-5 min: isocratic 100% A (0% B); 5-50 min: linear gradient from 100% A (0% B) to 80% A (20% B); 50-55 min: isocratic 20% A (80% B). The flow rate was 20 mL/min and the separation was performed under pressure of approximately 22-25 psi. The chromatogram was detected at 254 and 280 nm. The fractions containing the product were combined and the compound dried.

The respective isomers (10 mg, 0.114 mmol, 1.0 equiv) and 1-phenylprop-2-en-1-one (10 mg, 0.114 mmol, 1.0 equiv) were separately suspended in water and the mixture heated at reflux for 4 h. The solvent was removed under reduced pressure. The crude product was purified by reverse phase column chromatography. Column chromatography was performed on a CombiFlash Rf Teledyne ISCO system equipped with a High Perfomance RediSepRf GOLD C18 column (50 g, Particle Size: 20-40 µm spherical, Mesh Size: 400-632, Pore Size: 100 Å, Surface Area: 300±50 m²/g, Carbon Content: 15±2 %) using millipore water (solvent A) and methanol (solvent B). The following solvent gradient was used: 0-2 min: isocratic 50% A (50% B); 2-20 min: linear gradient from 50% A (50% B) to 10% A (90% B); 20-25 min:

isocratic 10% A (90% B). The flow rate was 20 mL/min and the separation was performed under pressure of approximately 22-25 psi. The chromatogram was detected at 254 and 280 nm. The fractions containing the product were combined and the compound dried.

(*A*)-19: ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.65 (d, J = 6.3 Hz, 1H), 7.71 (d, J = 2.9 Hz, 1H), 7.32 (dd, J = 6.3, 2.9 Hz, 1H), 4.04 (s, 3H); MS (m/z): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 424.0; found, 423.9 CD (CH_3OH): λ, nm (Δε, M^{-1} cm^{-1}) 290 (+16), 490 (-3).

(*C*)-19: ^{1}H NMR (500 MHz, MeOH-d_4): δ 8.65 (d, J = 6.3 Hz, 1H), 7.71 (d, J = 2.9 Hz, 1H), 7.32 (dd, J = 6.3, 2.9 Hz, 1H), 4.04 (s, 3H); MS (m/z): $[M\text{-}H_2O+H]^+$ calcd. for $C_{10}H_7N_1O_6Re_1$, 424.0; found, 424.0. CD (CH_3OH): λ, nm (Δε, M^{-1} cm^{-1}) 290 (-15), 490 (+3).

Single Crystal X-ray Diffraction

Crystals were grown using the vapor diffusion technique. Metal complexes were dissolved in methanol (0.5 mL) at a concentration of ~3-5 mg/mL. The solutions were filtered through a 0.2 uM syringe filter and placed inside a small vial. The small vial containing the solution of the complex was placed in a larger, outer vial that was partially filled with the cyclohexane (3 mL, antisolvent). The samples were sealed and stored at 4 °C in the dark. Within 2-3 weeks crystals suitable for single crystal X-ray diffraction formed.

All single crystal X-ray diffraction analyses were performed at 160(1) K on Rigaku OD diffractometers (Synergy-Pilatus and Supernova-Atlas) using the copper X-ray radiation (l = 1.54184 Å) from a dual wavelength X-ray source and an Oxford Instruments Cryojet XL cooler. The provided single crystals were covered with a polybutene oil, selected, and mounted on a loop fixed on a goniometer head. Pre-experiments, data collections, data reductions and analytical absorption corrections (Clark, R. C.; Reid, J. S. *Acta Cryst. A* **1995**, 51, 887) were performed with the program suite *CrysAlisPro* (*CrysAlisPro* (version 1.171.40.68a), Rigaku Oxford Diffraction Ltd, Yarnton, Oxfordshire, England, **2021**). Using *Olex2* (Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, 42, 339), the structures were solved with the *SHELXT* (Sheldrick, G. M. *Acta Cryst. A* **2015**, 71, 3) small molecule structure solution program and refined with the *SHELXL* program package (Sheldrick, G. M. *Acta Cryst. C* **2015**, 71, 3) by full-matrix least-squares minimization on F^2. *PLATON* (Spek, A. L. *Acta Cryst. D* **2009**, *65*, 148) was used to check the result of the X-ray analyses. The crystal data collections and structure refinement parameters are shown in Tables S1 – S15. CCDC 2205502 – 2205530 contain the supplementary crystallographic data for these

compounds, and can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

In the crystal structures of compounds **2**, **3**, **9**, **11**, **13**, **15**, **19**, **23**, **34**, **36**, **37** and **38**, the asymmetric unit contains only one organometallic molecule. In the crystal structures of compounds **12**, **24** and **33**, the asymmetric unit contains two independent organometallic molecules. In the crystal structures of compounds **25**, **29**, **30**, **31**, **32**, **35** and **39**, the organometallic molecules cocrystallize with solvent molecules of water in a 1:1 ratio. In the crystal structures of compounds **5**, **8** and **10**, the asymmetric unit contains two independent organometallic molecules and one solvent molecule of water. In the crystal structures of compounds **4** and **26**, the asymmetric unit contains two independent organometallic molecules and three solvent molecules of water. In the crystal structure of compound **41**, the asymmetric unit contains three independent organometallic molecules and one solvent molecule of water. The oxygen atoms of one NO_2 group are disordered over two sets of positions with site-occupancy factors of 0.416(17) and 0.584(17). In the crystal structure of compound **22**, the asymmetric unit contains two organometallic molecules and one solvent molecule of methanol.

Reaction of 1 with DMSO or DMF

The metal complex **1** was dissolved in deuterated dry dimethyl sulfoxide or dimethylformamide (0.5 mL, 2 mg/mL). ^{1}H NMR spectra were measured at selected times (5, 10, 15, 20, 25, 30, 40, 50, 60, 65, 70 min) using a Jeol ECZ-402 instrument located in the Department of Chemistry and Biochemistry at U.C. San Diego.

Reaction of $\mathbf{1_{DMSO}}$ with Water

The metal complex $\mathbf{1_{DMSO}}$ was dissolved in 2:8 DMSO-d_6:H_2O (0.5 mL, 6 mg/mL). ^{1}H NMR spectra were measured at selected times (5, 10, 15, 20, 25, 30, 40, 45, 120, 180, 240, 300, 360 min) using a Jeol ECZ-402 instrument located in the Department of Chemistry and Biochemistry at U.C. San Diego.

Aqueous Solubility Tests

The aqueous solubility of complex **1** was assessed by dynamic light scattering. The metal complexes were dissolved in DMSO or DMF with a final concentration of 20 mM. The stock solution was diluted with PBS buffer in ratios 1:250 – 1:1000. The obtained mixtures were analysed by dynamic light scattering using a Malvern Instruments Zetasizer Nano apparatus. All metal complexes remained clear solutions and did not show any precipitation. As a negative control zinc oxide which principates in an aqueous solution was used.

Aqueous Stability Tests

The stability of a compound was assessed by HPLC analysis. The compound was dissolved in water or phosphate buffered saline (1% DMF, *v*%) at a concentration of 1 mg/mL and incubated at 37 °C for 24 h in the dark. After this time, the solution was analyzed using a HPLC system. For analytic HPLC the following system was used: Agilent 1200 series degasser and pump system with an Agilent Ecplise XDB-C18 (5 µm 150×4.6 mm) column. The solvents (HPLC grade) were millipore water (solvent A) and acetonitrile (solvent B). The following solvent gradient was used: 0-3 minutes: isocratic 95% A (5% B); 3-17 minutes: linear gradient from 95% A (5% B) to 50% A (50% B); 17-20 minutes: isocratic 50% A (50% B).

Covalent Protein Binding studied by Mass Spectrometry

The protein (0.5 µg/µL) was incubated with the Re(I) tricarbonyl complex (50 µM, DMF <1%) for 2 h at room temperature with slow shaking. For the binding competition with GC376, the protein (0.5 µg/µL) was incubated with GC376 (50 µM) for 2 h at room temperature with slow shaking, followed by an additional incubation for 2 h with the Re(I) tricarbonyl complex (50 µM) for 2 h at room temperature with slow shaking. After this time, the $3CL^{pro}$-inhibitor mixture was analyzed by liquid chromatography electrospray ionization time-of-flight mass spectrometry (LC-ESI-TOFMS). An Agilent 6230 time-of-flight mass spectrometer with a Jet Stream electrospray ionization source was used. The chromatographic separation was performed at room temperature on a Phenomenex Aeris widepore XB-C18 column (2.1 mm ID × 50 mm length, 3.6 µm particle size) using HPLC-grade water with 0.1% TFA and HPLC grade acetonitrile with 0.1% TFA as mobile phases. The measured molecular weight of $3CL^{pro}$ (33797 Da) was found to be in agreement with the predicted molecular weight (33796.5 Da) from the protein sequence using the online mass protein calculator v3.4

(http://www.protcalc.sourceforge.net) as well as the information provided by the commercial supplier ($3CL^{pro}$ ~34 kDa).

Coordinate Covalent Binding studied by Inductively Coupled Plasma Mass Spectrometry

The protein (50 µg) was incubated with the Re(I) tricarbonyl complex (50 µM, DMF <1%) in 200 µL of buffer for 2 h at room temperature with slow shaking. After this time, the protein-inhibitor mixture was placed in a Pierce protein PES concentrator (0.1-0.5 mL) with a molecular-weight cutoff of 10 kDa. The solution was centrifuged at 10000 rpm for 10 min. The concentrated protein was mixed with 0.5 mL of trace metal free water. The mixture was washed five times with trace metal free water. After this procedure the protein was digested in concentrated trace metal free nitric acid. Each sample was diluted to a final volume of 1 mL with trace metal free water to a 5% aqueous nitric acid solution. The metal content of the sample was determined using an iCAP RQ inductively coupled plasma-mass spectrometer (ICP-MS) and compared with reference standards. The obtained data analyzed with Qtegra analysis software.

Prediction of Binding Pose

The prediction of the binding pose was done in two independent steps. In the first step, the geometry of the metal complex was calculated using density-functional theory (DFT) calculations with the Gaussian software package. The metal atom was described using the Los Alamos (LANL2) effective core potential with the corresponding triple-zeta basis set while all other atoms were described with the Pople double-zeta basis set with a single set of polarization functions on non-hydrogen atoms (6-31G(d)). Solvent effects were included using a polarizable continuum model (PCM). The structure of the calculated molecule corresponds to ground state minima on the ground state potential energy surfaces with no imaginary frequencies present. During these calculations, the molecular parameters of the metal complex including its shape, charge, and three-dimensional geometry were characterized. Afterwards, the water molecule which was placed as a capping group for the metal-cysteine interaction was removed and the obtained structure fixed. The structure of the SARS-CoV-2 main protease (PDB: 6Y2F) was prepared using the molecular operating environment (MOE) software package by removal of the bound ligand, water molecules and protonation. In the second step, the metal complex fragment was covalently docked towards thiol residues in the protein. During these calculations

the specifics of the metal complex were not considered. The compound was merely considered as a rigid body and was docked as such towards the enzyme. The generated docking poses were energetically minimized and scored using the GBVI/WSA dG force fields in MOE.

3CL^{pro} Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. Dithiothreitol was substituted with tris(2-carboxyethyl)phosphine (TCEP), the latter of which was found to not alter the activity of the enzyme in the assay. The 3CL^{pro} protease was thawed on ice and diluted to 10 ng/µL with the assay buffer containing 50 µM TCEP. The enzyme was treated with increasing concentrations of the complex (DMF <1%) diluted in assay buffer achieving a total volume of 25 µL. The mixture was incubated for 30 min at 37 °C with slow shaking. The substrate (Dabcyl-KTSAVLQSGFRKM-E(Edans)-NH_2) was added to the reaction mixture to a final concentration of 50 µM and the mixture was incubated at 37 °C for 4 h. The generated fluorescence signal (λ_{ex} = 360 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. The difference in fluorescence signals was correlated to the concentration of the complex and the IC_{50} values determined. As a control substance, the well-known inhibitor GC376 (IC_{50} = 140±20 nM) was used.

DPP4 Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. The DPP4 enzyme was thawed on ice and diluted to 0.1 ng/µL with assay buffer and the substrate (Ala-Pro-AMC dipeptide) diluted to 100 µM with assay buffer. 80 µL of the assay buffer was mixed with 5 µL of the substrate, 5 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer and 10 µL of the DPP4 enzyme. This yields a mixture containing 10 mM Tris-HCl, 10 mM $MgCl_2$, 0.05% Tween 20, and 20 µM DPP4 substrate at pH 7.4. The mixture was incubated for 60 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 360 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. The difference in fluorescence signals was correlated to the concentration of the complex and the IC_{50} values determined. As a control substance, the well-known inhibitor Sitaglipin (IC_{50} = 23±9 nM) was used.

BACE1 Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. The BACE1 enzyme was thawed on ice and diluted to 7.5 ng/µL with assay buffer. 69 µL of the assay buffer was mixed with 1 µL of the FRET substrate, 10 µL of increasing concentrations of the complex (DMF <1%) diluted in inhibitor buffer and 20 µL of the BACE1 enzyme. This yields a mixture containing 10 mM NaOAc, HOAc and BACE1 substrate at pH 7.4. The fluorescence signal (λ_{ex} = 320 nm; λ_{em} = 405 nm) was recorded with a Synergy H4 (BioTek) microplate reader. The plate was immediately covered with aluminum foil, kept in the dark and incubated for 20 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 320 nm; λ_{em} = 405 nm) was recorded with a Synergy H4 (BioTek) microplate reader. The difference in fluorescence intensity was correlated to the concentration of the complex and the IC_{50} values determined. As a control substance, the well-known inhibitor Verubecestat (IC_{50} = 37±8 nM) was used.

Cathepsin B Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. Dithiothreitol was substituted with tris(2-carboxyethyl)phosphine (TCEP), the latter of which was found to not alter the activity of the enzyme in the assay. The Cathepsin B enzyme was thawed on ice and activated by dilution to 10.0 ng/µL with assay buffer. The enzyme solution was further diluted with assay buffer to 0.02 ng/µL. 20 µL of the enzyme solution was mixed with 5 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer. The mixture was incubated for 10 min at 37 °C with slow shaking. The substrate (Z-Leu-Arg-AMC) was diluted to 10 µM and 25 µL were added to the enzyme mixture. This yields a mixture containing 10 mM Tris-HCl, 0.05% glycerol, 300 µM TCEP, and 10 µM Cathepsin B substrate. The mixture was incubated for 60 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 360 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. As a control substance, the well-known inhibitor E-64 (IC_{50} = 4±2 nM) was used.

Cathepsin L Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. Dithiothreitol was substituted with tris(2-carboxyethyl)phosphine (TCEP), the latter of

which was found to not alter the activity of the enzyme in the assay. The Cathepsin L enzyme was thawed on ice and activated by dilution to 10.0 ng/µL with assay buffer. The enzyme solution was further diluted with assay buffer to 0.02 ng/µL. 20 µL of the enzyme solution was mixed with 5 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer. The substrate (Z-Leu-Arg-AMC) was diluted to 10 µM and 25 µL were added to the enzyme mixture. This yields a mixture containing 10 mM Tris-HCl, 0.05% glycerol, 300 µM TCEP, and 10 µM Cathepsin L substrate. The mixture was incubated for 60 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 360 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. As a control substance, the well-known inhibitor E-64 (IC_{50} = 33±9 nM) was used.

Furin Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. The Furin enzyme was thawed on ice and activated by dilution to 10.0 ng/µL with assay buffer. The enzyme solution was further diluted with assay buffer to 0.5 ng/µL. 50 µL of the enzyme solution was mixed with 10 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer. The substrate was diluted to 5 µM and 40 µL were added to the enzyme mixture. The mixture was incubated for 30 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 380 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. As a control substance, the well-known inhibitor Chloromethylketone (IC_{50} = 4±0.5 nM) was used.

PL^{pro} Enzymatic Assay

A slightly modified protocol from a previous publication (*Chem. Eur. J.* **2020,** *26* (66), 15140-15144) was used. The PL^{pro} enzyme (Elabscience) was thawed on ice and activated by dilution to 10.0 ng/µL with HEPES buffer. The enzyme solution was further diluted with HEPES buffer to 0.02 ng/µL. 20 µL of the enzyme solution was mixed with 5 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer. The substrate (Z-Arg-Leu-Arg-Gly-Gly-AMC, Bachem Bioscience) was diluted to 10 µM and 25 µL were added to the enzyme mixture. The mixture was incubated for 60 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 355 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. As a control substance, the well-known inhibitor GRL-0617 (IC_{50} = 5±2 µM) was used.

TMPRSS2 Enzymatic Assay

A slightly modified protocol from the commercially available assay (BPS Bioscience) was used. The TMPRSS2 enzyme was thawed on ice and activated by dilution to 5.0 ng/µL with assay buffer. The enzyme solution was further diluted with assay buffer to 0.5 ng/µL. 30 µL of the enzyme solution was mixed with 10 µL of increasing concentrations of the complex (DMF <1%) diluted in assay buffer. The substrate was diluted to 50 µM and 10 µL were added to the enzyme mixture. The mixture was incubated for 30 min at 37 °C with slow shaking. The generated fluorescence signal (λ_{ex} = 380 nm; λ_{em} = 460 nm) was recorded with a Synergy H4 (BioTek) microplate reader. As a control substance, the well-known inhibitor Camostat (IC_{50} = 5±2 nM) was used.

Computational Prediction of the Circular Dichroism Spectra

The geometry of a metal complex was determined using density-functional theory calculations with the Gaussian software package. The metal atom was described using the Los Alamos (LANL2) effective core potential with the corresponding triple-zeta basis set while all other atoms were described with the Pople double-zeta basis set with a single set of polarization functions on non-hydrogen atoms (6-31G(d)). Solvent effects were included using a polarizable continuum model (PCM). The structure of the calculated molecule corresponds to ground state minima on the ground state potential energy surfaces with no imaginary frequencies present. Excited states of all compounds were probed using time dependent density functional theory combined with the same exchange correlation functional and basis set. All transitions (singlet-singlet) were calculated vertically with respect to the singlet ground state.

Antiviral Activity in SARS-CoV-2 Infected Human Cells

Vero E6 and Huh 7.5.1 cells were cultivated in DMEM medium (Gibco, 11995-065) supplemented with 5% FBS (SigmaAldrich, F2442) and 1x Penicillin/Streptomycin (100 units/mL and 100 µg/mL, respectively) (Gibco 15140122). SARS-CoV-2 infection was conducted in Biosafety Level-3 at the University of California San Diego following the guidelines approved by the Institutional Biosafety Committee. SARS-CoV-2 Washington isolate (USA-WA1/2020) was acquired from BEI Resources (cat# NR-52281), amplified in one

infection cycle, harvests and frozen in DMEM + 1% FBS + 1x Penicillin/Streptomycin, and stored at -80 until use.

To test antiviral activity, compounds were dissolved in DMSO and spotted to 384-well plates using ATS (EDC Biosystems) in 10-point 2-fold serial dilutions starting at 80uM final concentration. VeroE6 cells or Huh 7.5.1 cells were seeded at 2000 cells/well in the presence of the compounds and allowed to adhere overnight in an incubator at 37°C and 5% CO2. Cells were then infected with SARS-CoV-2 in a total volume of 30 µL of medium at 1 MOI and incubated for an additional 48h at 37°C and 5% CO2. Plates were fixed for 1h in the presence of 4% paraformaldehyde solution. Cells were then submitted to an immunofluorescence assay using a 1:2000 dilution of the Rabbit IgG antibody against SARS-CoV-2 nucleocapsid (Genetex, GTX135357) as the primary antibody, and anti-Rabbit AlexaFluor488 (Invitrogen, A-11008) diluted 1:1000 as the secondary antibody. Plates were imaged using ImageXpress (Molecular Devices). DAPI staining at 0.5 µg/ml (Sigma, D9542) was used to count total number of cells, while immunofluorescence signals were used to detect viral infection.

To calculate the antiviral activity, the average infection ratio from the untreated controls (0.1% DMSO) was normalized as 0% antiviral activity. The average infection ratio from the uninfected controls (no SARS-CoV-2) was normalized to 100% antiviral activity. A linear regression was applied to calculate the antiviral activity of each well related to the normalized controls. Dose-response curves of the reference compounds Remdesivir and K777 were also added as positive controls for these assays. Serial dilutions of the testing compounds were performed in order to assess the antiviral effect and potency (EC_{50}) in both Vero E6 and Huh 7.5.1 cell lines. EC_{50} values were calculated based on a curve fit model extrapolating the concentration in which the curve crossed the 50% antiviral efficacy using Prism GraphPad software.

SUPPORTING FIGURES AND TABLES

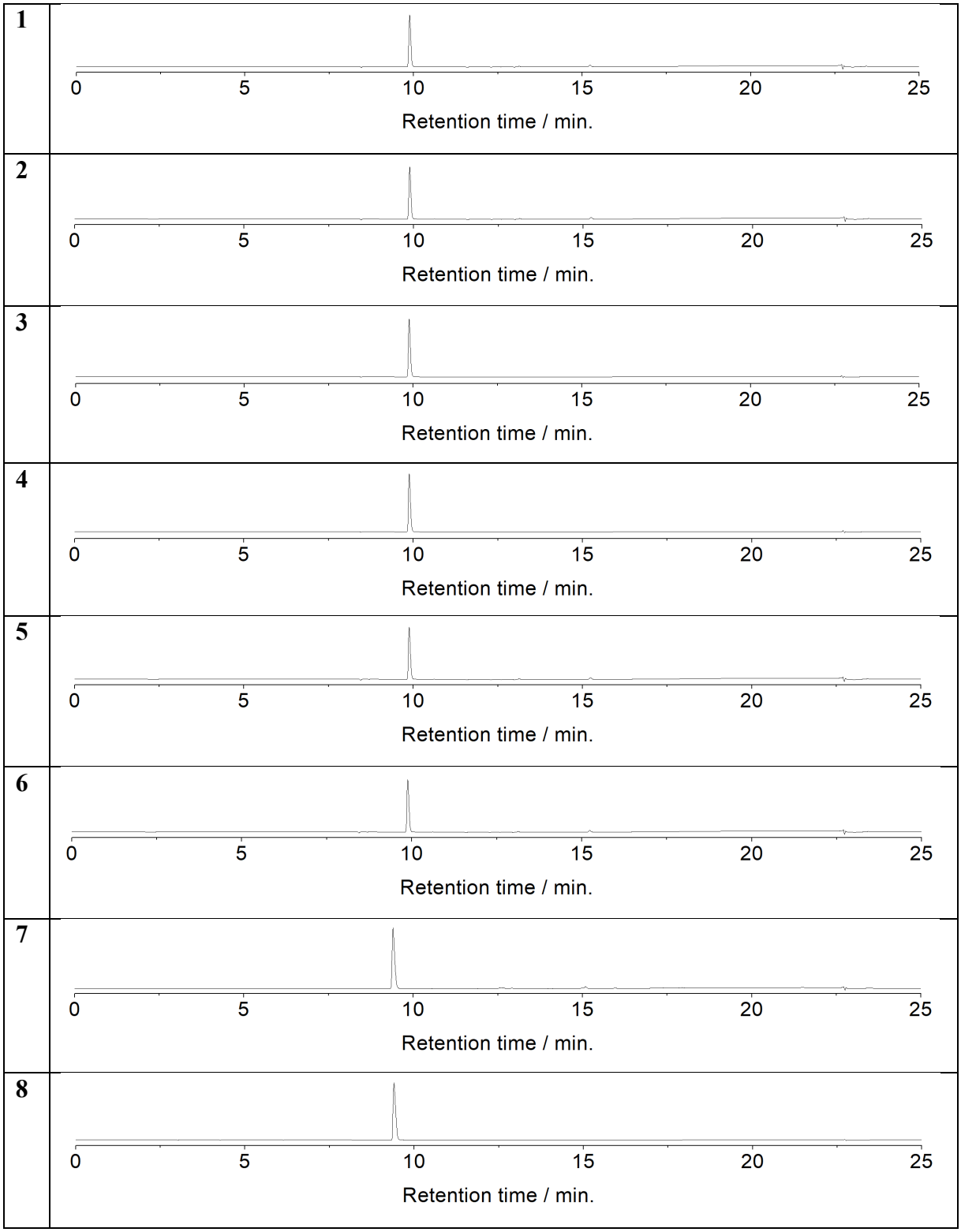

Figure S1. HPLC chromatogram of compounds **1**, **2**, **3**, **4**, **5**, **6**, **7** and **8**, monitored at 250 nm.

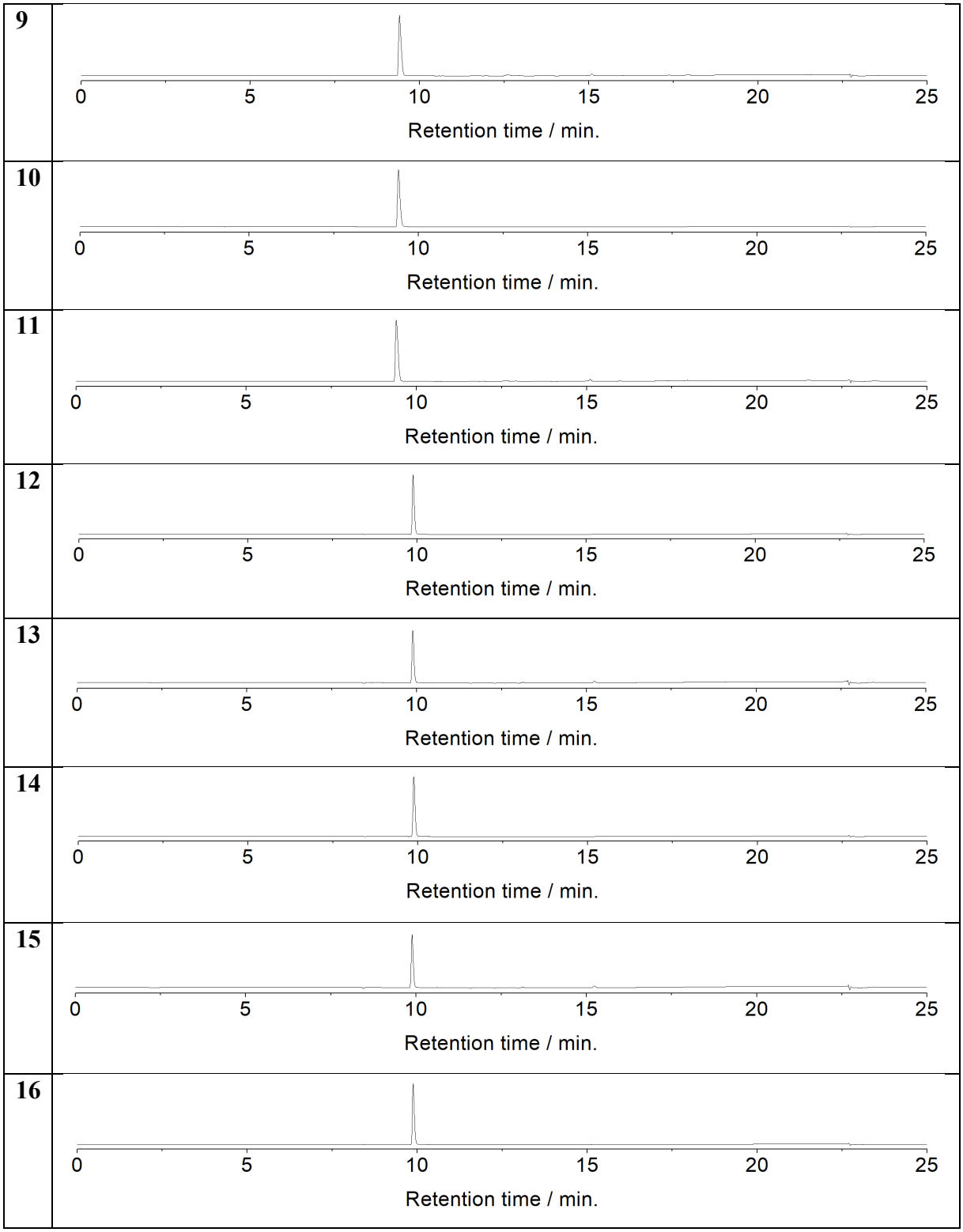

Figure S2. HPLC chromatogram of **9**, **10**, **11**, **12**, **13**, **14**, **15** and **16** at 250 nm.

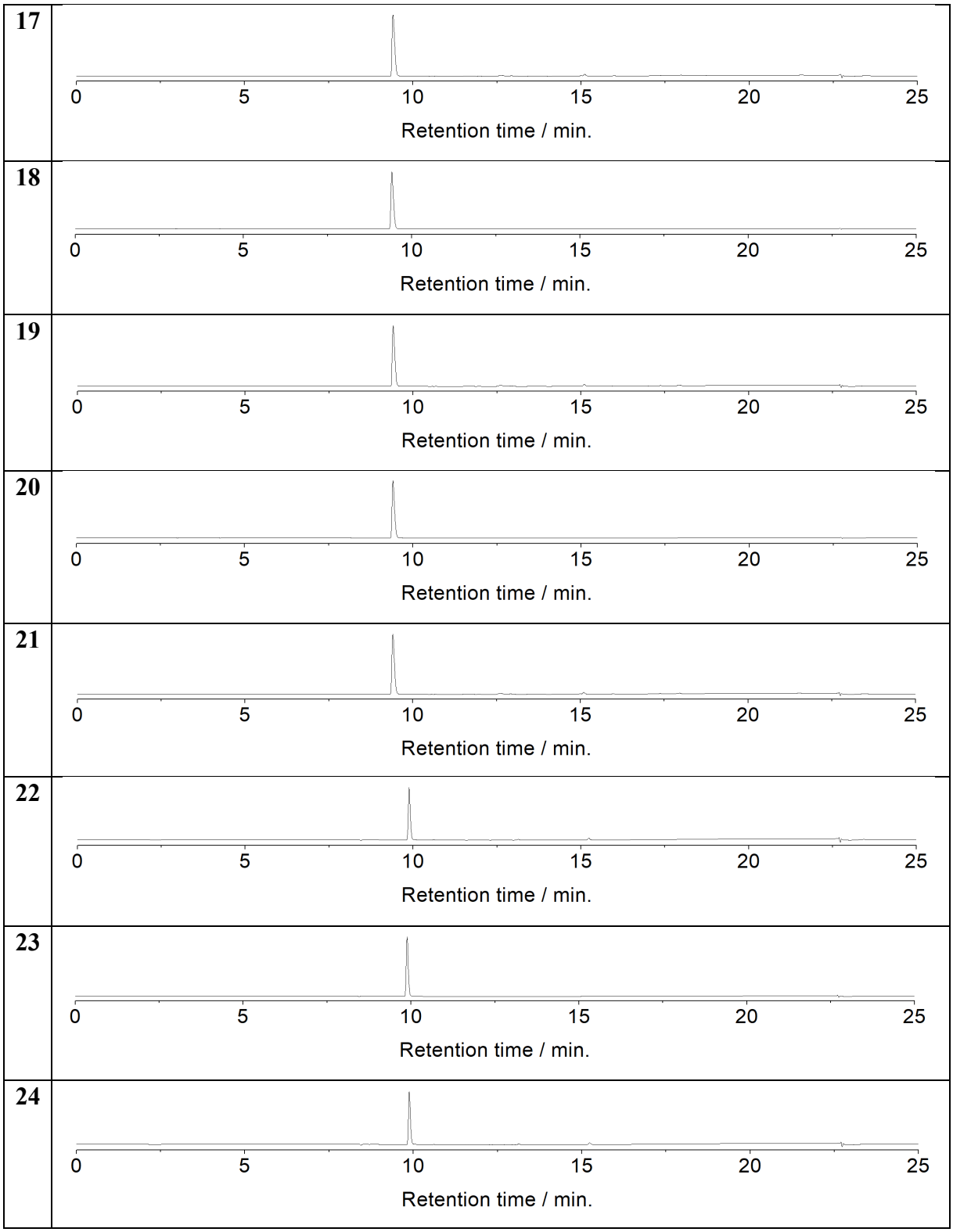

Figure S3. HPLC chromatogram of **17**, **18**, **19**, **20**, **21**, **22**, **23** and **24** at 250 nm.

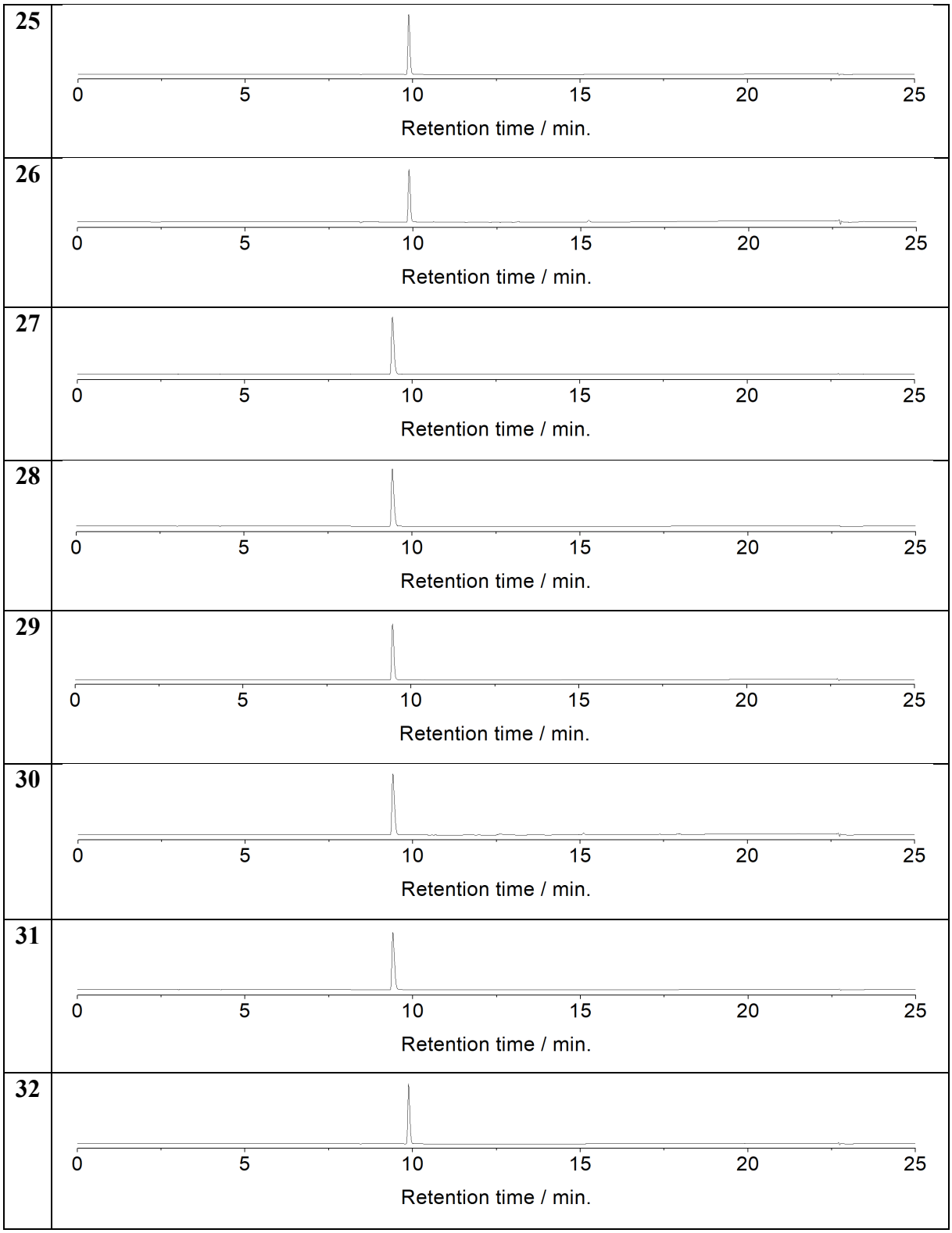

Figure S4. HPLC chromatogram of **25**, **26**, **27**, **28**, **29**, **30**, **31** and **32** at 250 nm.

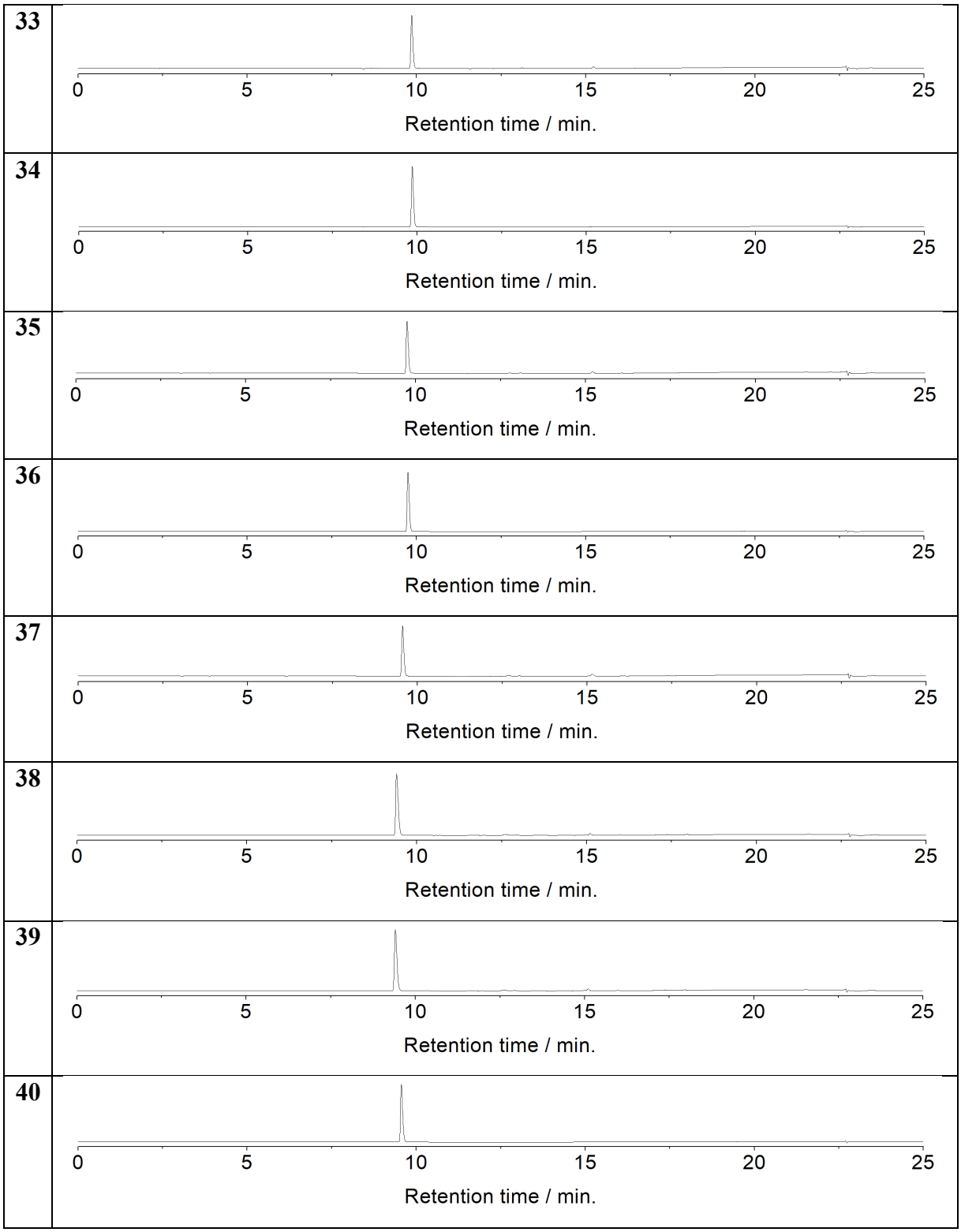

Figure S5. HPLC chromatogram of **33**, **34**, **35**, **36**, **37**, **38**, **39** and **40** at 250 nm.

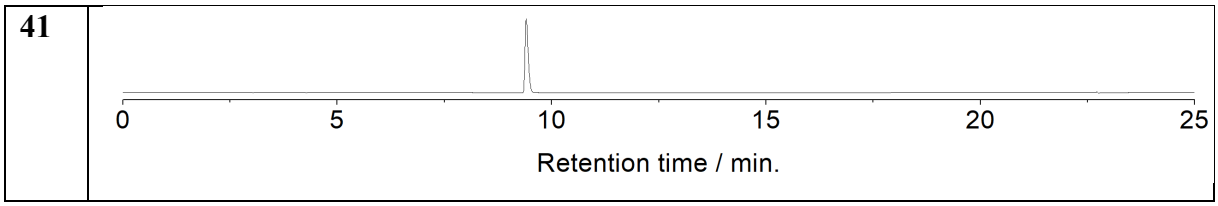

Figure S6. HPLC chromatogram of compound **41** monitored at 250 nm.

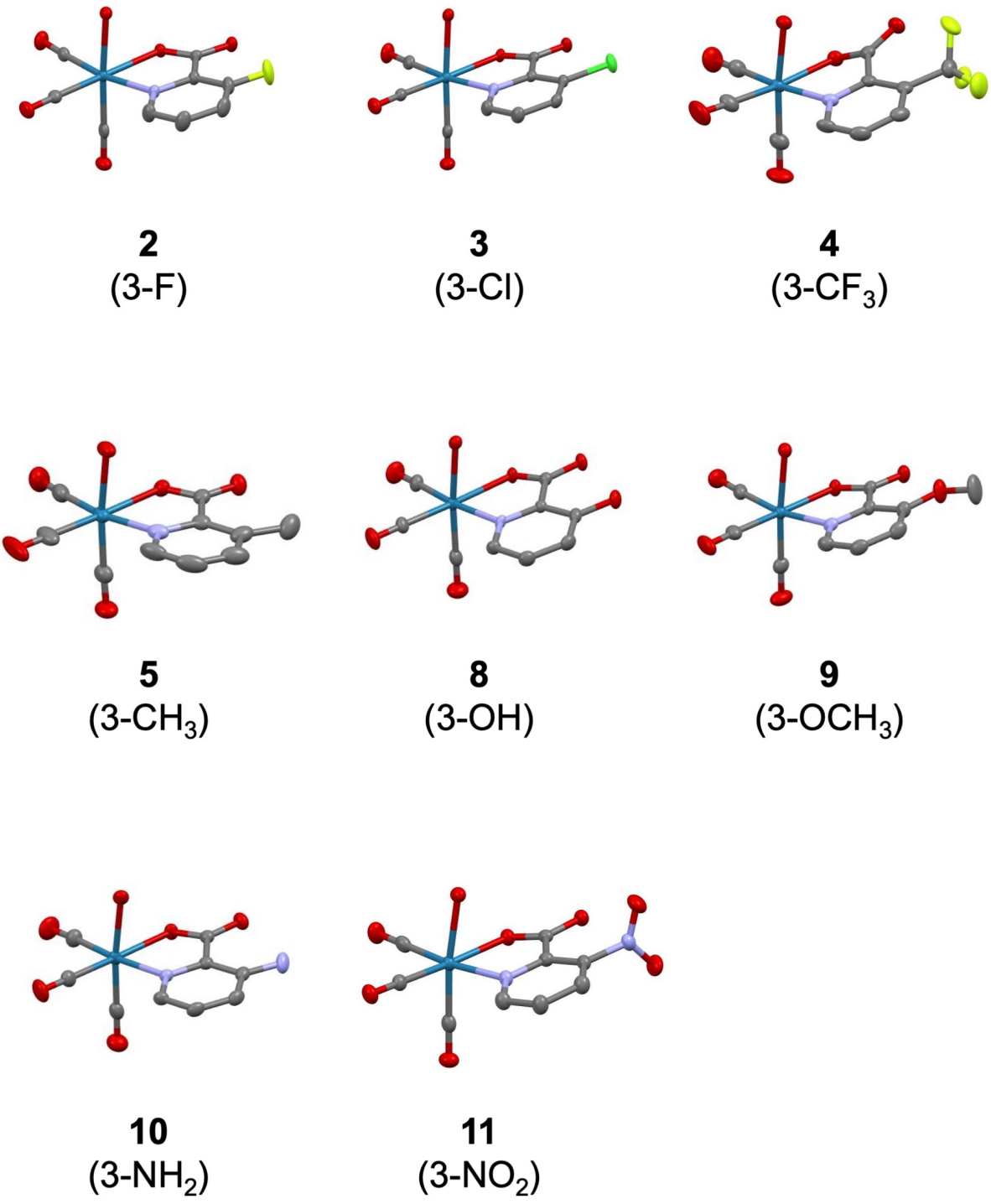

Figure S7. Single crystal X-ray diffraction structures (50% probability ellipsoids) of [Re(pic)$(CO)_3(H_2O)$] complexes with substituents in the 3-position of the picolinic acid ligand. Hydrogen atoms and co-crystallized solvent molecules are omitted for clarity.

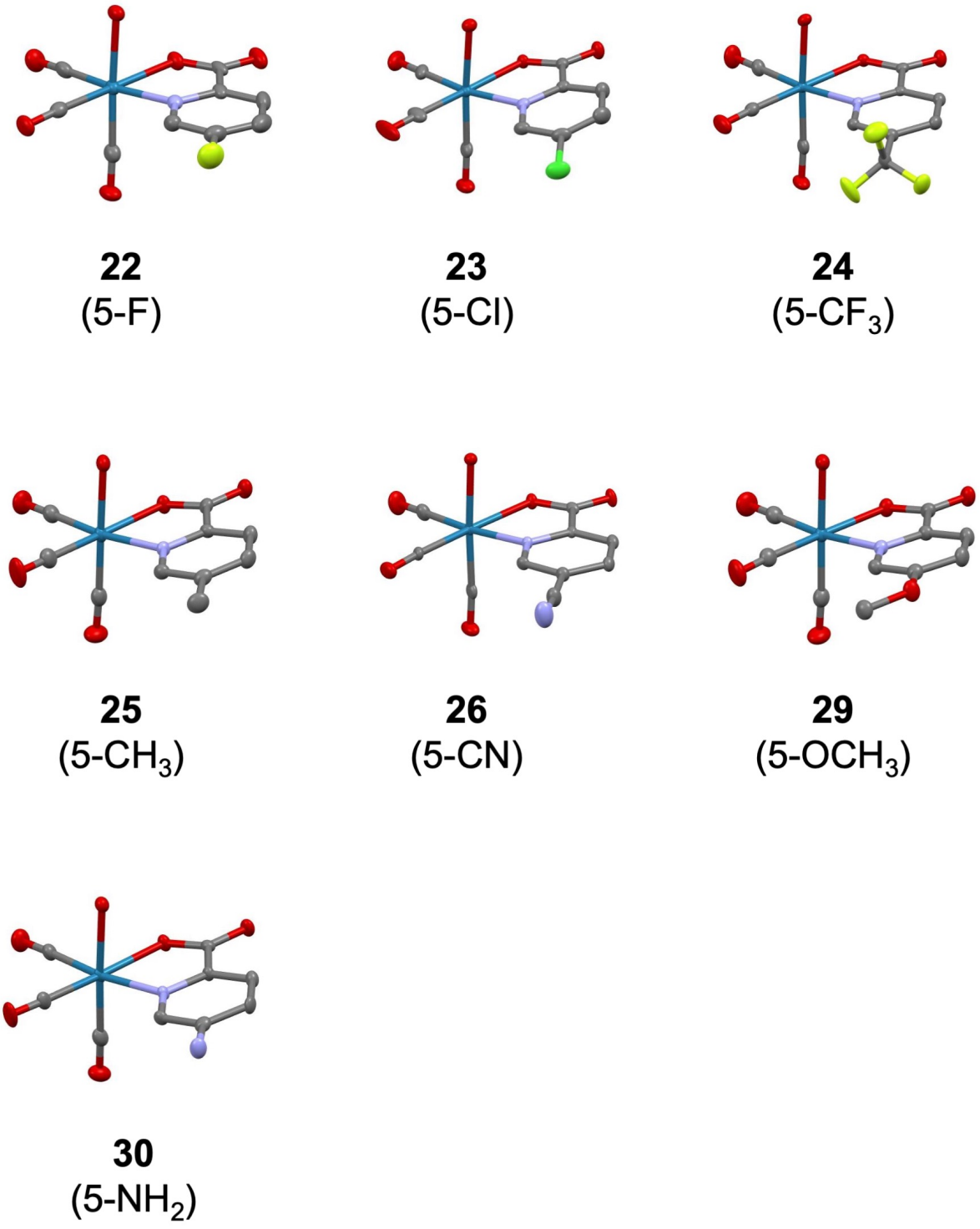

Figure S8. Single crystal X-ray diffraction structures (50% probability ellipsoids) of [Re(pic)$(CO)_3(H_2O)$] complexes with substituents in the 5-position of the picolinic acid ligand. Hydrogen atoms and co-crystallized solvent molecules are omitted for clarity.

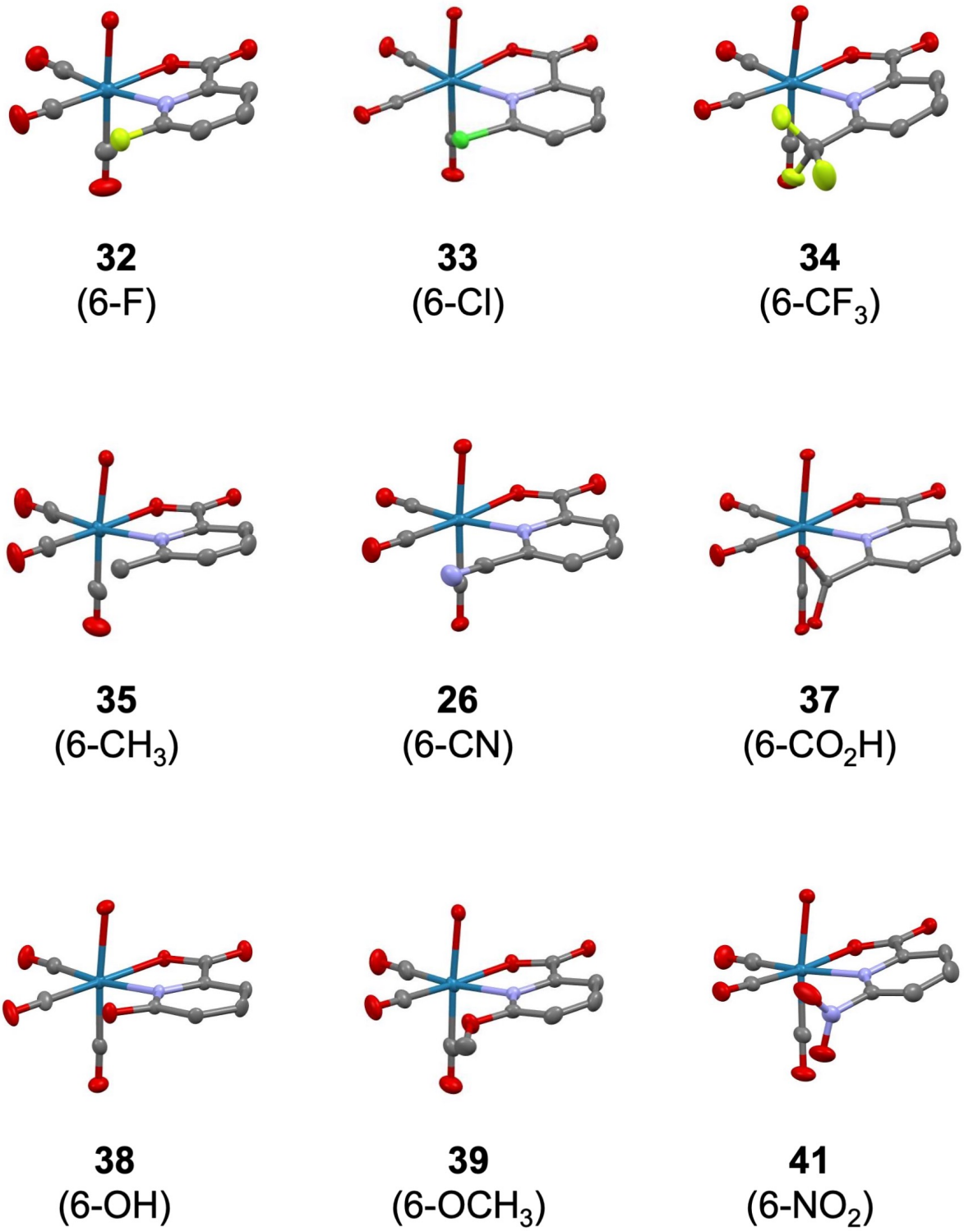

Figure S9. Single crystal X-ray diffraction structures (50% probability ellipsoids) of [Re(pic)$(CO)_3(H_2O)$] complexes with substituents in the 6-position of the picolinic acid ligand. Hydrogen atoms and co-crystallized solvent molecules are omitted for clarity.

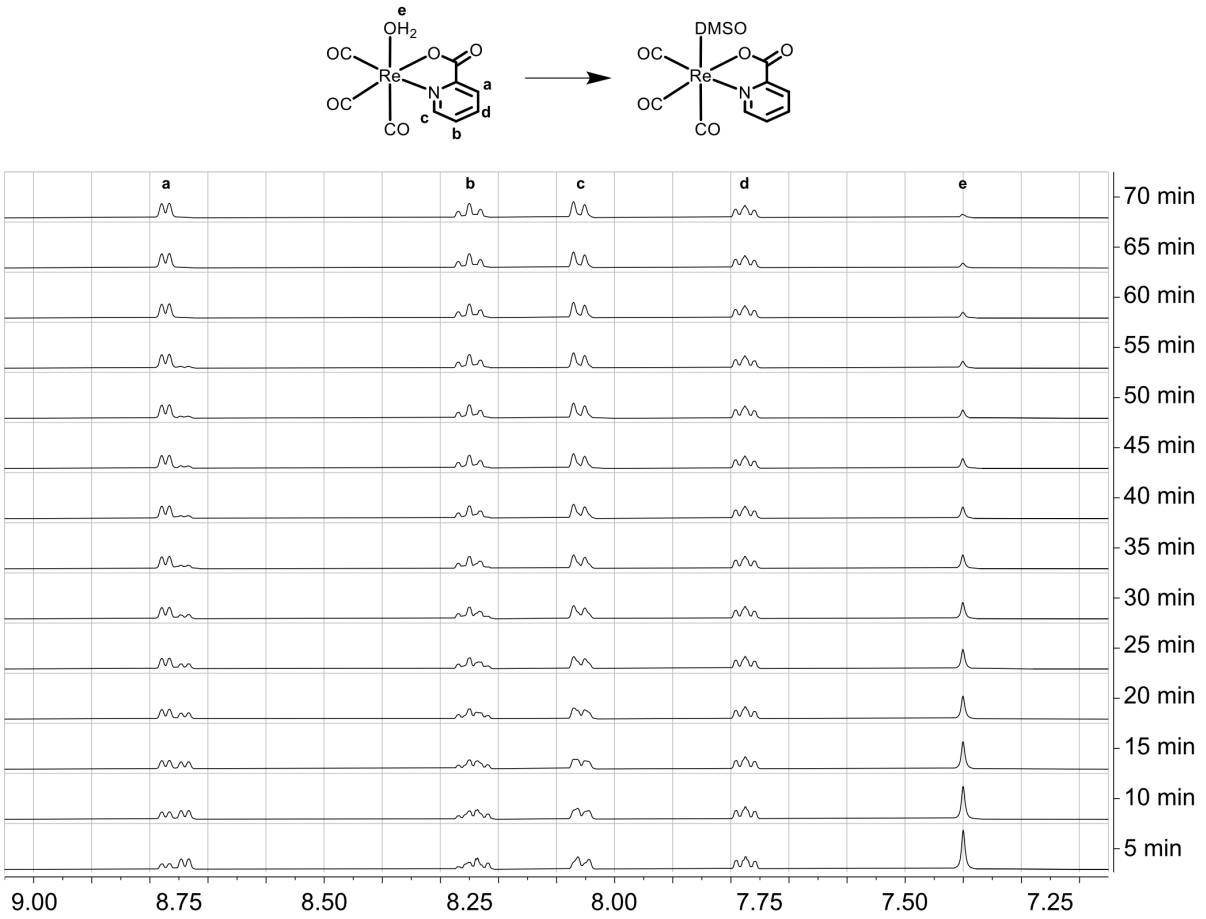

Figure S10. Time-dependent ^{1}H NMR spectroscopy of the conversion of complex **1** to complex $\mathbf{1_{DMSO}}$ in DMSO-d_6. The Re(I)-coordinated water molecule is observed at 7.4 ppm.

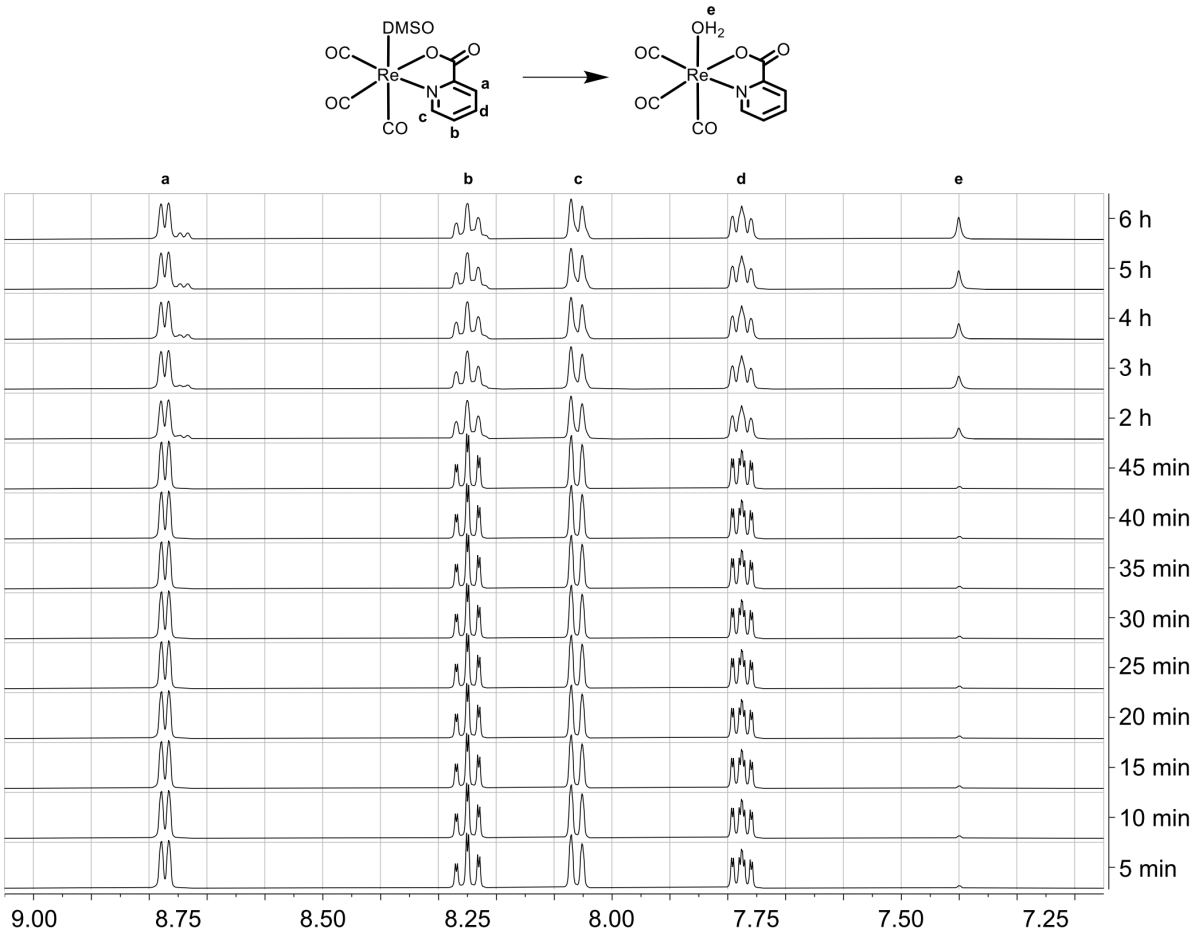

Figure S11. Time-dependent ^{1}H NMR spectroscopy of the reaction of complex $\mathbf{1_{DMSO}}$ in 2:8 DMSO-d_6:H_2O.

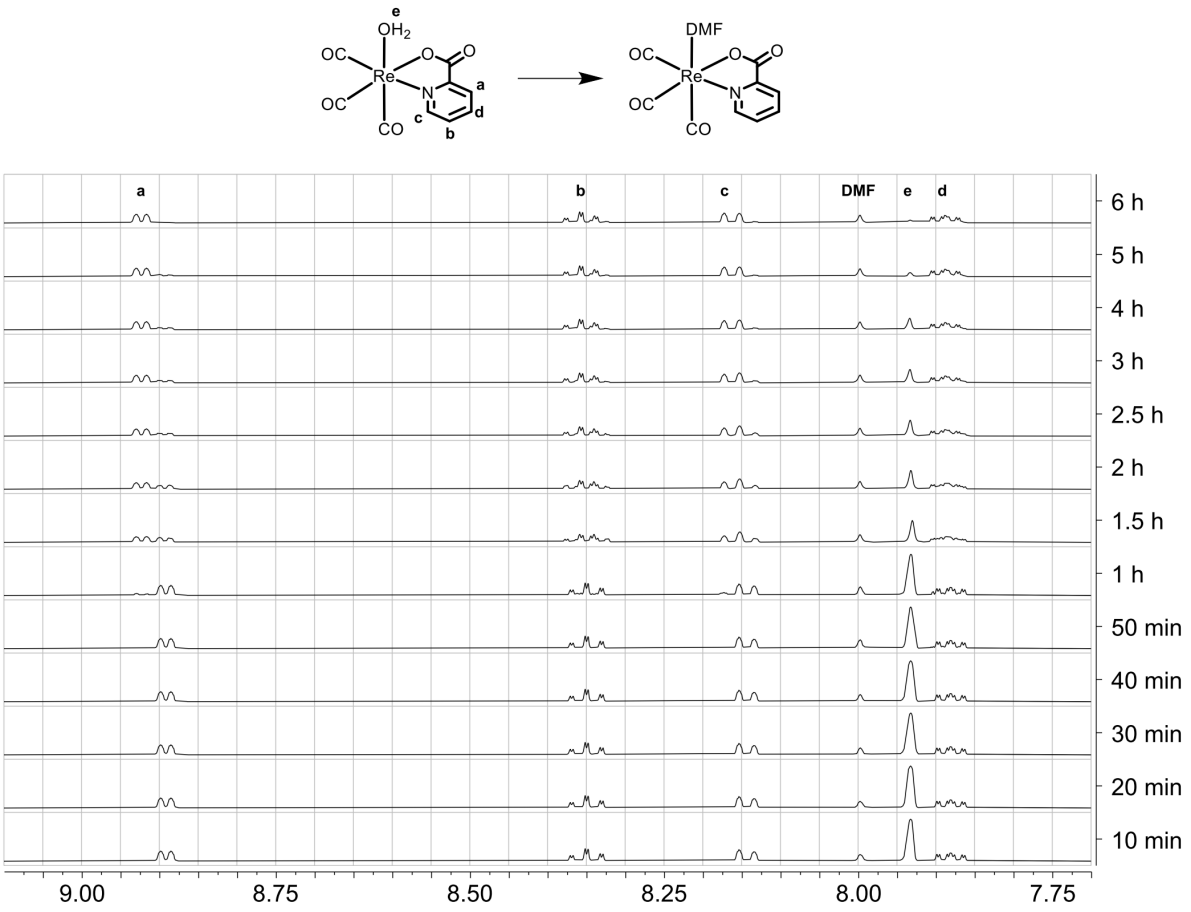

Figure S12. Time-dependent ^{1}H NMR spectroscopy of the reaction of complex **1** in DMF-d_7. The Re(I)-coordinated water molecule is observed at 7.93 ppm.

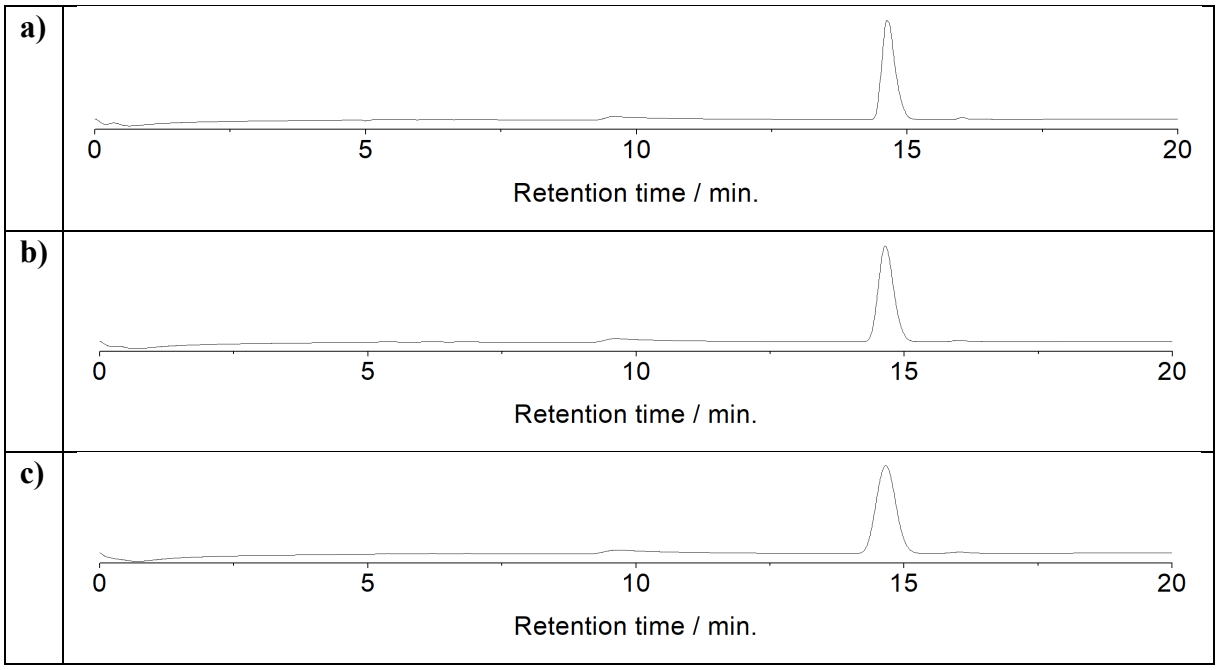

Figure S13. HPLC chromatogram at 250 nm of complex **1** upon incubation at: a) 0 h and b) after 24 h in H_2O, or c) after 24 h in PBS (1% DMF).

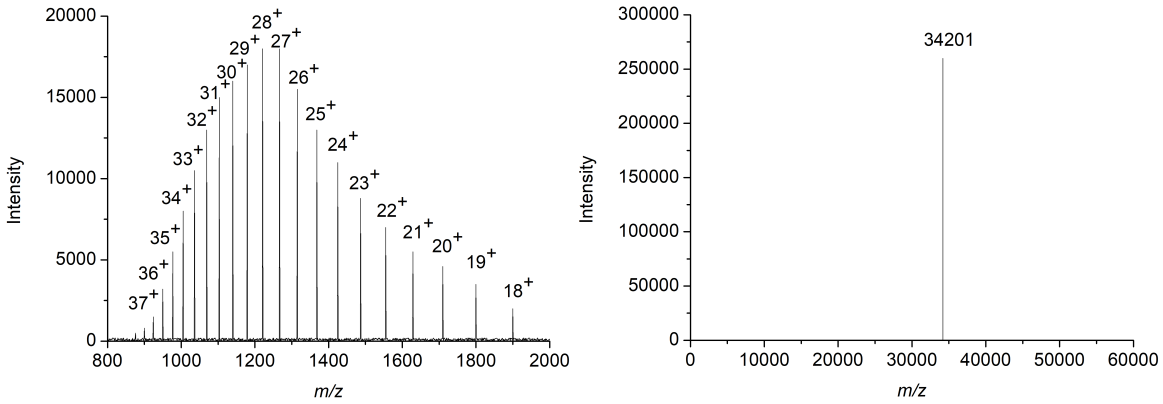

Figure S14. Measured ESI-TOF (*left*) and deconvoluted (*right*) spectrum of 3CL^{pro} incubated with GC376.

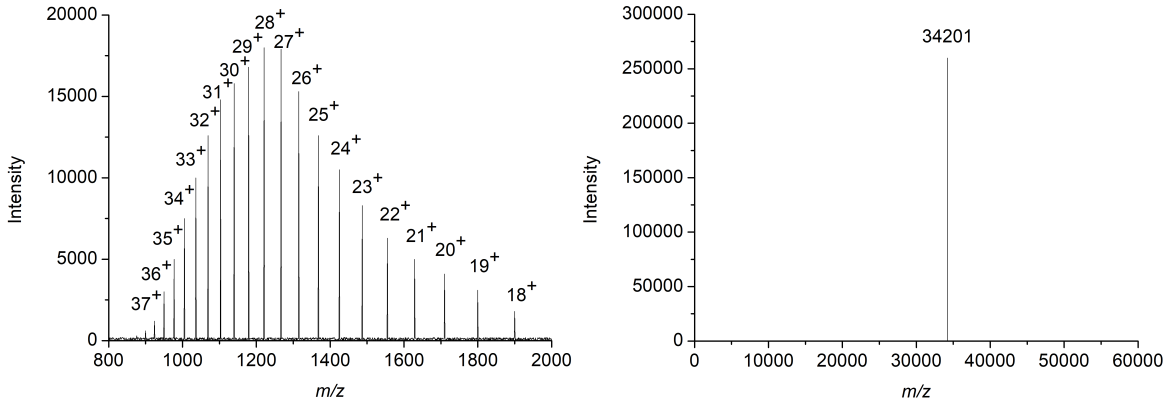

Figure S15. Measured ESI-TOF (*left*) and deconvoluted (*right*) spectrum of $3CL^{pro}$ first incubated with GC376 and then with the Re(I) tricarbonyl complex **1**.

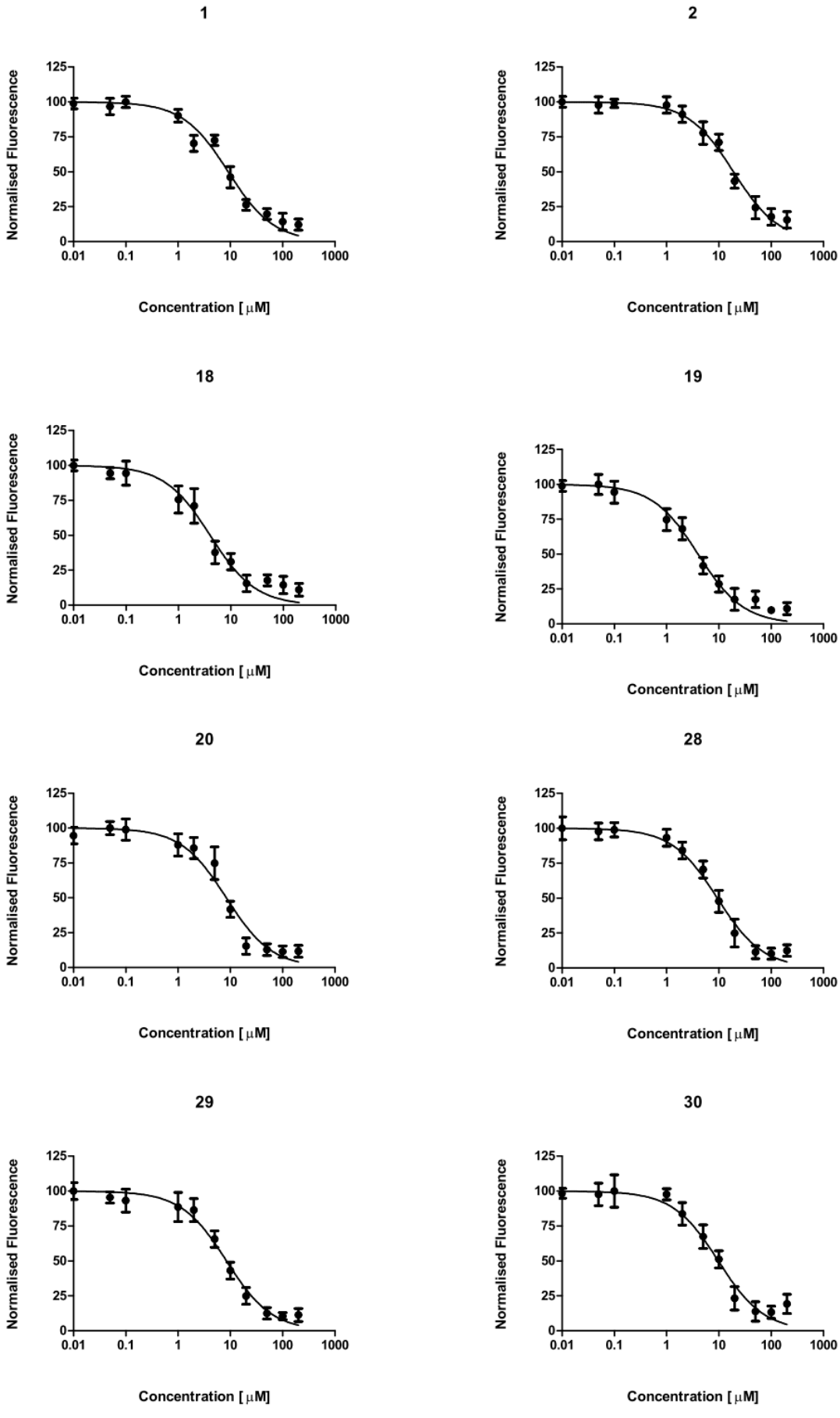

Figure S16. Dose-response curves of the inhibition of $3CL^{pro}$ of **1**, **2**, **18**-**20**, **28**-**30**.

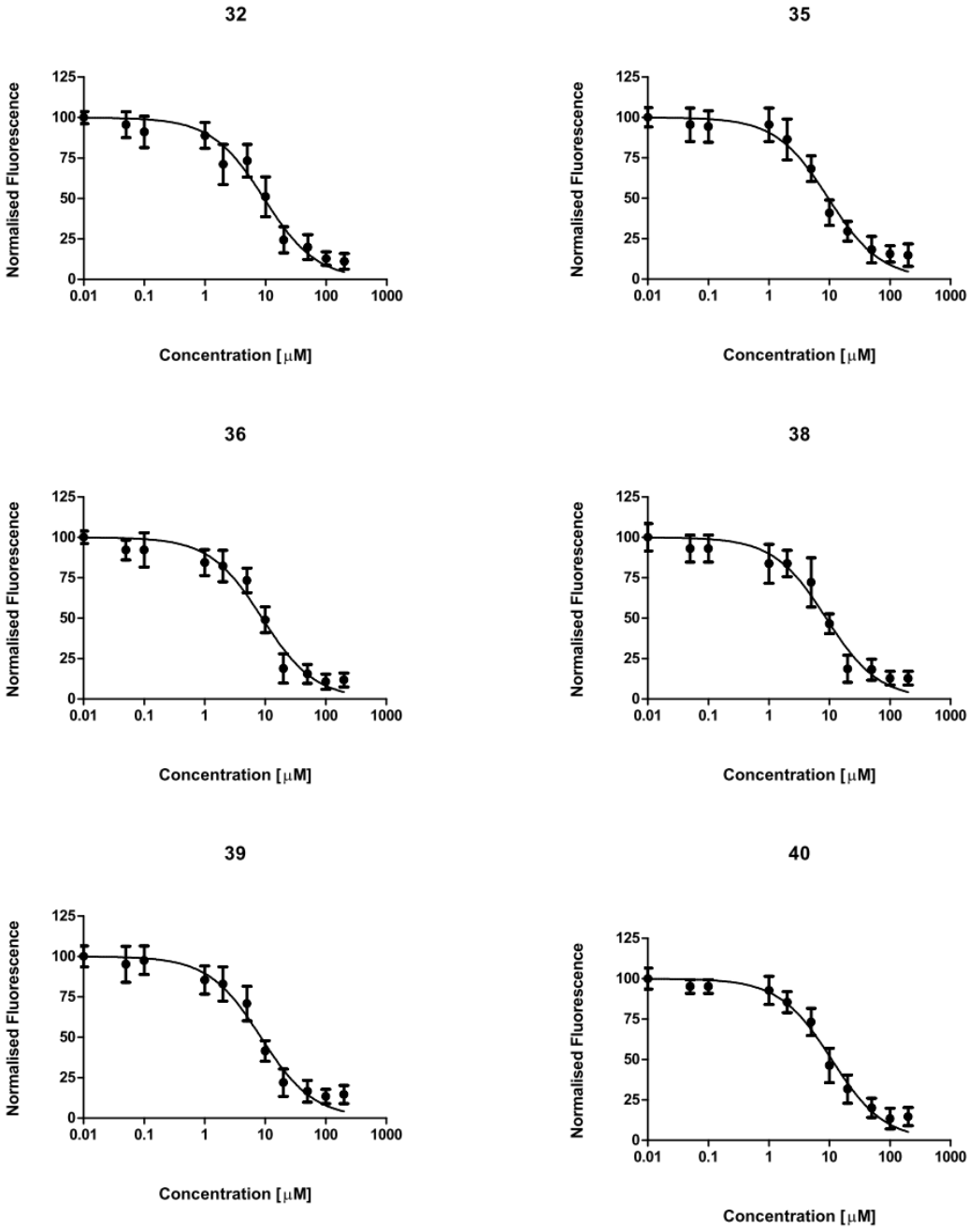

Figure S17. Dose-response curves of the inhibition of $3CL^{pro}$ of **32**, **35**-**36**, **38**-**40**.

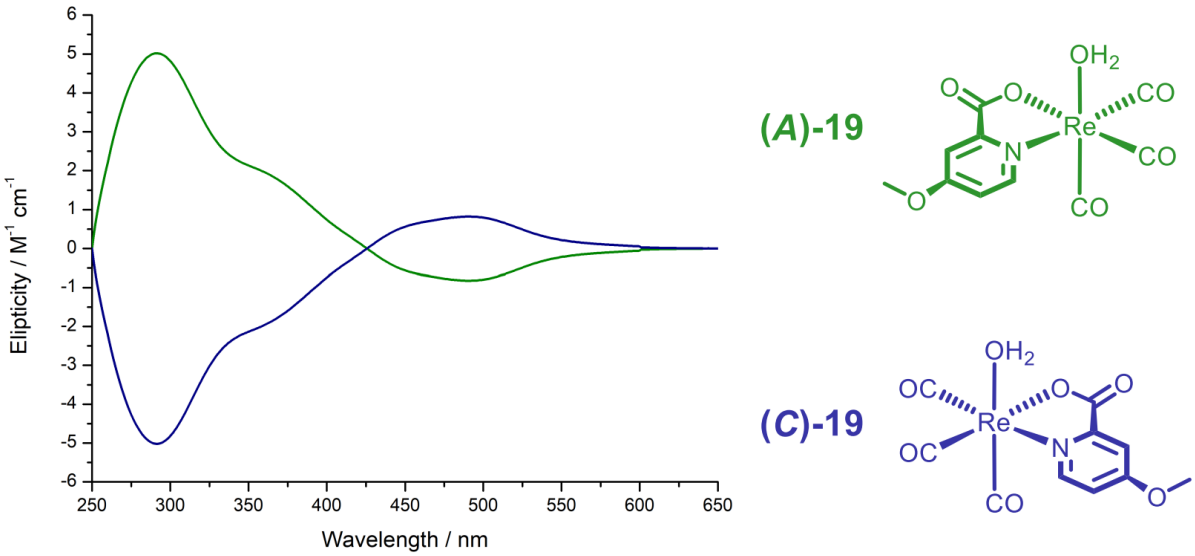

Figure S18. Calculated circular dichroism spectra of the enantiomers **(*A*)-19** and **(*C*)-19** in methanol.

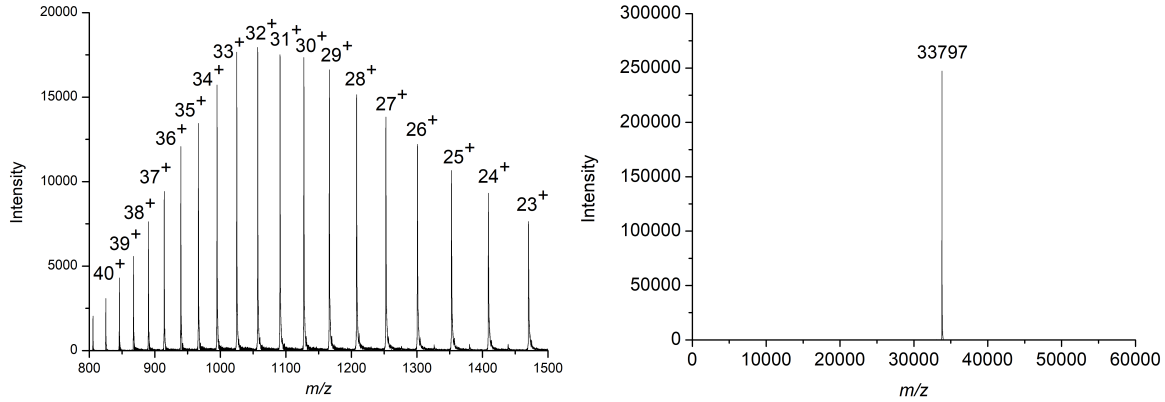

Figure S19. Measured ESI-TOF (*left*) and deconvoluted (*right*) spectrum of 3CL^{pro} incubated with **(*C*)-19**.

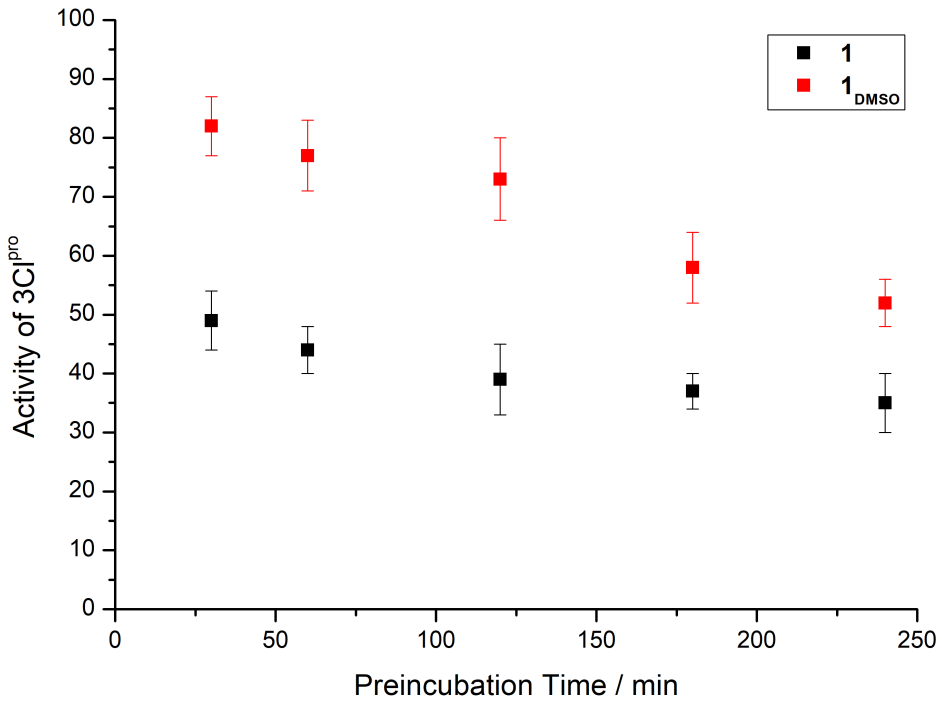

Figure S20. Inhibition of 3CL^{pro} upon variation of the preincubation time with **1** (black) or **1**$_{DMSO}$ (red) at an inhibitor concentration of 10 μM.

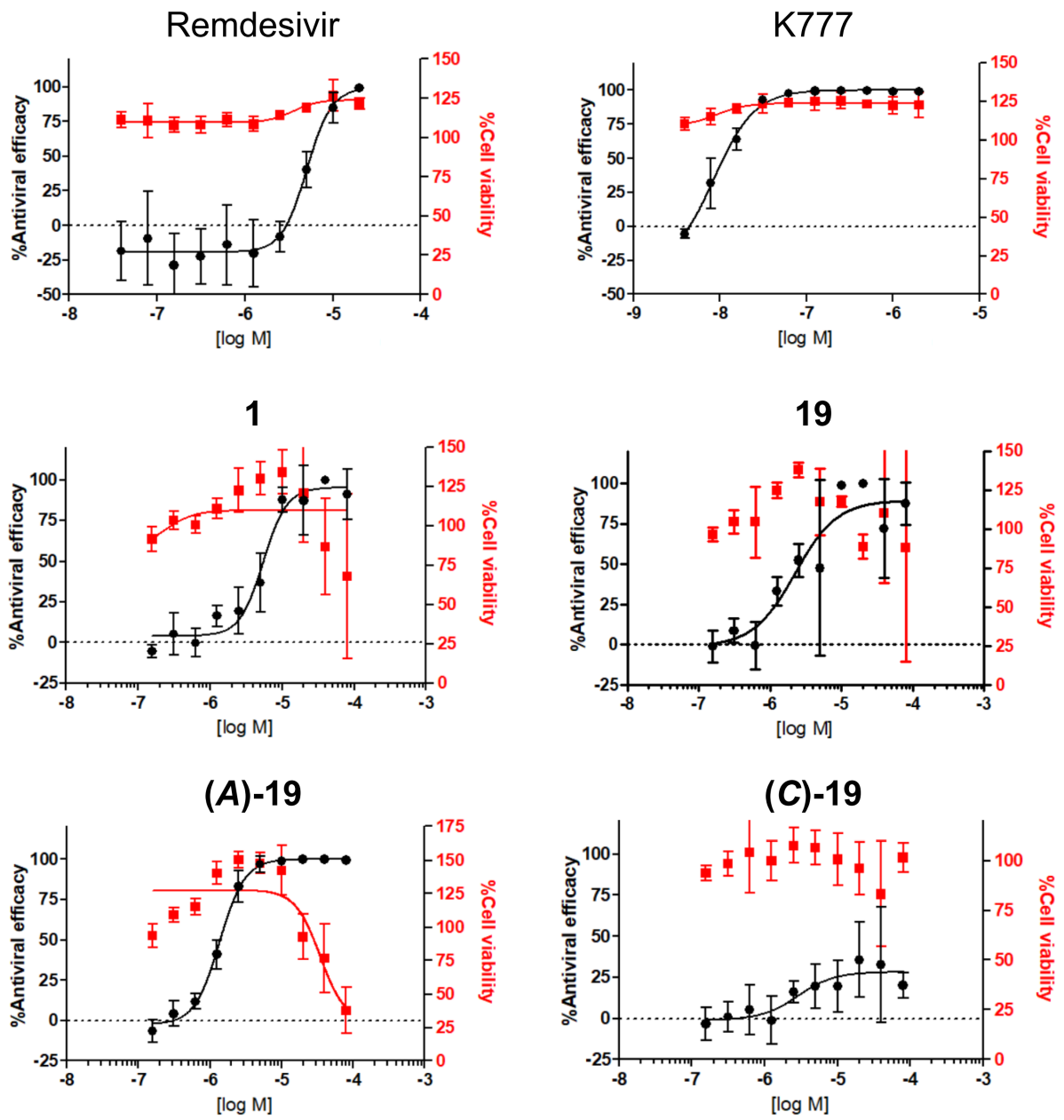

Figure S21. Dose-response curves of SARS-CoV-2 infected Vero E6 cells treated with **1**, **19**, **(*A*)-19**, and **(*C*)-19** and the control compounds Remdesivir and K777.

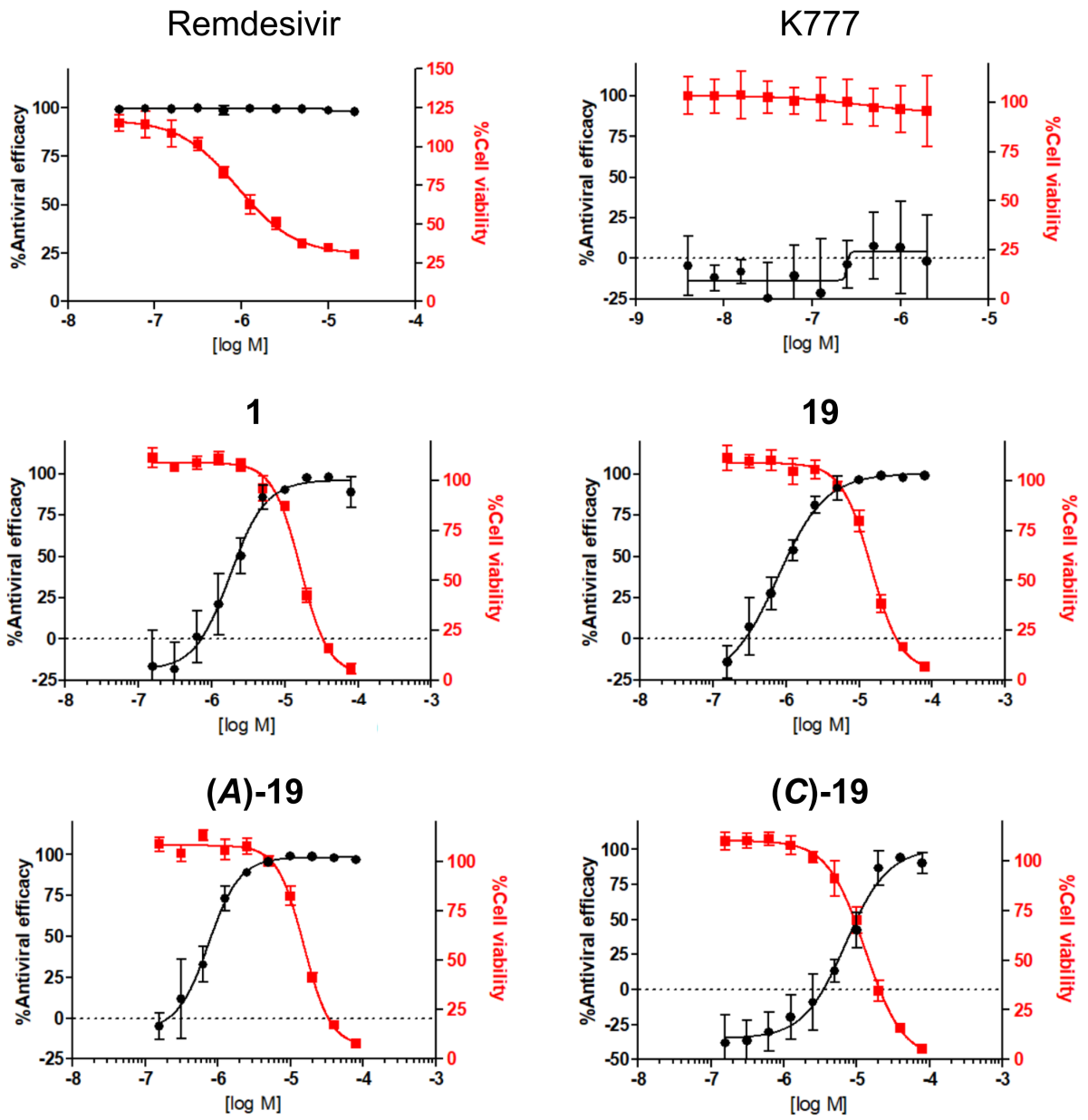

Figure S22. Dose-response curves of SARS-CoV-2 infected Huh 7.5.1 cells treated with **1**, **19**, **(*A*)-19**, and **(*C*)-19** and the control compounds Remdesivir and K777.

Table S1. Selected crystal data and structure refinement parameters for **2** and **3**.

	2	**3**
CCDC number	2205502	2205505
Empirical formula	$C_9H_5FNO_6Re$	$C_9H_5ClNO_6Re$
Formula weight	428.34	444.79
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	$P2_1/c$
a/Å	7.1094(2)	8.25530(10)
b/Å	8.1861(3)	7.15140(10)
c/Å	9.3662(3)	19.0448(2)
α/°	92.147(3)	90
β/°	94.856(2)	92.8380(10)
γ/°	90.442(3)	90
Volume/Å^3	542.73(3)	1122.97(2)
Z	2	4
ρ_{calc}g/cm^3	2.621	2.631
μ/mm^{-1}	22.298	23.598
F(000)	396.0	824.0
Crystal size/mm^3	0.18 × 0.11 × 0.07	0.25 × 0.17 × 0.05
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.484 to 148.922	9.298 to 148.83
Index ranges	$-8 \le h \le 8$, $-10 \le k \le 9$, $-11 \le l \le 11$	$-10 \le h \le 10$, $-8 \le k \le 8$, $-23 \le l \le 17$
Reflections collected	8892	11053
Independent reflections	2196 [R_{int} = 0.0178, R_{sigma} = 0.0121]	2287 [R_{int} = 0.0277, R_{sigma} = 0.0133]
Data/restraints/parameters	2196/0/172	2287/2/172
Goodness-of-fit on F^2	1.201	1.227
Final R indexes [I>=2σ (I)]	R_1 = 0.0145, wR_2 = 0.0358	R_1 = 0.0193, wR_2 = 0.0519
Final R indexes [all data]	R_1 = 0.0145, wR_2 = 0.0358	R_1 = 0.0194, wR_2 = 0.0519
Largest diff. peak/hole / e Å^{-3}	0.68/-0.64	0.83/-0.73

Table S2. Selected crystal data and structure refinement parameters for **4** and **5**.

	4	**5**
CCDC number	2205504	2205511
Empirical formula	$C_{20}H_{16}F_6N_2O_{15}Re_2$	$C_{20}H_{18}N_2O_{13}Re_2$
Formula weight	1010.75	866.76
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	C2/c	I2/a
a/Å	24.2151(2)	22.7527(2)
b/Å	10.28390(10)	10.61400(10)
c/Å	11.55570(10)	21.7337(2)
α/°	90	90
β/°	90.5060(10)	109.9160(10)
γ/°	90	90
Volume/Å^3	2877.55(4)	4934.72(8)
Z	4	8
ρ_{calc}g/cm^3	2.333	2.333
μ/mm^{-1}	17.251	19.536
F(000)	1896.0	3248.0
Crystal size/mm^3	0.33 × 0.25 × 0.15	0.15 × 0.1 × 0.03
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.302 to 148.994	8.266 to 148.964
Index ranges	-29 ≤ h ≤ 30, -12 ≤ k ≤ 11, -14 ≤ l ≤ 14	-28 ≤ h ≤ 28, -13 ≤ k ≤ 13, -27 ≤ l ≤ 24
Reflections collected	14283	25330
Independent reflections	2953 [R_{int} = 0.0302, R_{sigma} = 0.0141]	5046 [R_{int} = 0.0222, R_{sigma} = 0.0147]
Data/restraints/parameters	2953/0/225	5046/0/356
Goodness-of-fit on F^2	1.164	1.141
Final R indexes [I>=2σ (I)]	R_1 = 0.0249, wR_2 = 0.0651	R_1 = 0.0179, wR_2 = 0.0429
Final R indexes [all data]	R_1 = 0.0250, wR_2 = 0.0652	R_1 = 0.0183, wR_2 = 0.0431
Largest diff. peak/hole / e Å^{-3}	1.12/-1.26	0.58/-0.86

Table S3. Selected crystal data and structure refinement parameters for **8** and **9**.

	8	**9**
CCDC number	2205518	2205503
Empirical formula	$C_{18}H_{14}N_2O_{15}Re_2$	$C_{10}H_8NO_7Re$
Formula weight	870.71	440.37
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	$P2_1/c$
a/Å	9.8967(3)	11.9487(3)
b/Å	10.5952(3)	6.8332(2)
c/Å	12.8653(2)	16.0682(4)
α/°	106.448(2)	90
β/°	105.596(3)	108.801(3)
γ/°	103.191(3)	90
Volume/Å^3	1176.61(6)	1241.93(6)
Z	2	4
ρ_{calc}g/cm^3	2.458	2.355
μ/mm^{-1}	20.556	19.455
F(000)	812.0	824.0
Crystal size/mm^3	0.17 × 0.16 × 0.1	0.27 × 0.08 × 0.02
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.67 to 148.97	7.816 to 148.864
Index ranges	$-12 \le h \le 12$, $-11 \le k \le 13$, $-15 \le l \le 16$	$-14 \le h \le 14$, $-8 \le k \le 8$, $-15 \le l \le 20$
Reflections collected	21833	11246
Independent reflections	4784 [R_{int} = 0.0274, R_{sigma} = 0.0184]	2499 [R_{int} = 0.0381, R_{sigma} = 0.0261]
Data/restraints/parameters	4784/8/359	2499/2/180
Goodness-of-fit on F^2	1.182	1.124
Final R indexes [I>=2σ (I)]	R_1 = 0.0221, wR_2 = 0.0562	R_1 = 0.0309, wR_2 = 0.0896
Final R indexes [all data]	R_1 = 0.0234, wR_2 = 0.0565	R_1 = 0.0337, wR_2 = 0.0939
Largest diff. peak/hole / e Å^{-3}	1.04/-1.45	1.84/-1.02

Table S4. Selected crystal data and structure refinement parameters for **10** and **11**.

	10	**11**
CCDC number	2205521	2205510
Empirical formula	$C_{18}H_{16}N_4O_{13}Re_2$	$C_9H_5N_2O_8Re$
Formula weight	868.75	455.35
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	$P2_1/c$
a/Å	10.5868(2)	6.79860(10)
b/Å	13.4770(3)	18.1770(3)
c/Å	18.0923(3)	9.65140(10)
α/°	82.284(2)	90
β/°	87.5270(10)	94.9710(10)
γ/°	68.815(2)	90
Volume/Å^3	2385.09(9)	1188.22(3)
Z	4	4
ρ_{calc}g/cm^3	2.419	2.545
μ/mm^{-1}	20.238	20.464
F(000)	1624.0	848.0
Crystal size/mm^3	0.12 × 0.08 × 0.02	0.26 × 0.13 × 0.12
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	4.93 to 146.74	9.732 to 148.972
Index ranges	$-13 \le h \le 11$, $-16 \le k \le 16$, $-22 \le l \le 22$	$-8 \le h \le 8$, $-22 \le k \le 22$, $-11 \le l \le 12$
Reflections collected	44910	11577
Independent reflections	9457 [R_{int} = 0.0191, R_{sigma} = 0.0119]	2423 [R_{int} = 0.0278, R_{sigma} = 0.0139]
Data/restraints/parameters	9457/0/729	2423/1/190
Goodness-of-fit on F^2	1.142	1.225
Final R indexes [I>=2σ (I)]	R_1 = 0.0150, wR_2 = 0.0353	R_1 = 0.0212, wR_2 = 0.0554
Final R indexes [all data]	R_1 = 0.0157, wR_2 = 0.0355	R_1 = 0.0214, wR_2 = 0.0556
Largest diff. peak/hole / e Å^{-3}	1.31/-0.85	0.89/-1.19

Table S5. Selected crystal data and structure refinement parameters for **12** and **13**.

	12	**13**
CCDC number	2205507	2205506
Empirical formula	$C_9H_5FNO_6Re$	$C_9H_5ClNO_6Re$
Formula weight	428.34	444.79
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	I2/a
a/Å	10.0882(2)	9.33670(10)
b/Å	19.6105(3)	11.12590(10)
c/Å	12.6146(3)	22.2200(2)
α/°	90	90
β/°	112.846(3)	99.6720(10)
γ/°	90	90
Volume/Å^3	2299.81(9)	2275.39(4)
Z	8	8
ρ_{calc}g/cm^3	2.474	2.597
μ/mm^{-1}	21.048	23.293
F(000)	1584.0	1648.0
Crystal size/mm^3	0.31 × 0.1 × 0.06	0.11 × 0.08 × 0.04
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.842 to 136.468	8.072 to 148.974
Index ranges	$-12 \le h \le 12$, $-23 \le k \le 23$, $-15 \le l \le 14$	$-11 \le h \le 11$, $-13 \le k \le 13$, $-26 \le l \le 27$
Reflections collected	21410	11613
Independent reflections	4214 [R_{int} = 0.0300, R_{sigma} = 0.0157]	2318 [R_{int} = 0.0163, R_{sigma} = 0.0097]
Data/restraints/parameters	4214/0/338	2318/0/172
Goodness-of-fit on F^2	1.276	1.289
Final R indexes [I>=2σ (I)]	R_1 = 0.0264, wR_2 = 0.0628	R_1 = 0.0134, wR_2 = 0.0330
Final R indexes [all data]	R_1 = 0.0264, wR_2 = 0.0629	R_1 = 0.0136, wR_2 = 0.0336
Largest diff. peak/hole / e Å^{-3}	1.99/-1.28	0.50/-0.46

Table S6. Selected crystal data and structure refinement parameters for **15** and **19**.

	15	**19**
CCDC number	2205509	2205508
Empirical formula	$C_{10}H_8NO_6Re$	$C_{10}H_8NO_7Re$
Formula weight	424.37	440.37
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	I2/a	C2/c
a/Å	9.2924(2)	25.3206(6)
b/Å	11.1464(3)	11.8306(2)
c/Å	22.2675(6)	9.3609(2)
α/°	90	90
β/°	100.090(2)	121.786(3)
γ/°	90	90
Volume/Å^3	2270.72(10)	2383.57(11)
Z	8	8
ρ_{calc}g/cm^3	2.483	2.454
μ/mm^{-1}	21.174	20.274
F(000)	1584.0	1648.0
Crystal size/mm^3	0.2 × 0.12 × 0.05	0.14 × 0.11 × 0.02
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.066 to 148.794	8.216 to 148.848
Index ranges	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, -26 ≤ l ≤ 27	-31 ≤ h ≤ 31, -14 ≤ k ≤ 14, -11 ≤ l ≤ 11
Reflections collected	10677	12287
Independent reflections	2298 [R_{int} = 0.0293, R_{sigma} = 0.0197]	2434 [R_{int} = 0.0187, R_{sigma} = 0.0098]
Data/restraints/parameters	2298/0/173	2434/2/182
Goodness-of-fit on F^2	1.089	1.102
Final R indexes [I>=2σ (I)]	R_1 = 0.0246, wR_2 = 0.0638	R_1 = 0.0237, wR_2 = 0.0661
Final R indexes [all data]	R_1 = 0.0257, wR_2 = 0.0645	R_1 = 0.0241, wR_2 = 0.0668
Largest diff. peak/hole / e Å^{-3}	0.91/-1.49	1.71/-1.38

Table S7. Selected crystal data and structure refinement parameters for **22** and **23**.

	22	**23**
CCDC number	2205516	2205513
Empirical formula	$C_{19}H_{14}F_2N_2O_{13}Re_2$	$C_9H_5ClNO_6Re$
Formula weight	888.72	444.79
Temperature/K	160(1)	160(1)
Crystal system	triclinic	triclinic
Space group	P-1	P-1
a/Å	9.7973(2)	6.3055(2)
b/Å	10.6398(3)	9.8069(2)
c/Å	12.7440(3)	10.5545(2)
α/°	78.502(2)	102.051(2)
β/°	68.184(2)	100.494(2)
γ/°	73.235(2)	105.893(2)
Volume/Å^3	1174.53(5)	593.68(3)
Z	2	2
ρ_{calc}g/cm^3	2.513	2.488
μ/mm^{-1}	20.674	22.318
F(000)	828.0	412.0
Crystal size/mm^3	0.21 × 0.06 × 0.02	0.29 × 0.1 × 0.03
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.512 to 148.9	8.858 to 148.962
Index ranges	$-12 \le h \le 10$, $-13 \le k \le 13$, $-15 \le l \le 15$	$-7 \le h \le 7$, $-12 \le k \le 12$, $-13 \le l \le 13$
Reflections collected	24608	11168
Independent reflections	4747 [R_{int} = 0.0326, R_{sigma} = 0.0229]	2415 [R_{int} = 0.0280, R_{sigma} = 0.0159]
Data/restraints/parameters	4747/0/363	2415/7/170
Goodness-of-fit on F^2	1.068	1.109
Final R indexes [I>=2σ (I)]	R_1 = 0.0191, wR_2 = 0.0483	R_1 = 0.0185, wR_2 = 0.0480
Final R indexes [all data]	R_1 = 0.0221, wR_2 = 0.0495	R_1 = 0.0187, wR_2 = 0.0482
Largest diff. peak/hole / e Å^{-3}	1.17/-0.85	0.97/-0.74

Table S8. Selected crystal data and structure refinement parameters for **24** and **25**.

	24	**25**
CCDC number	2205514	2205512
Empirical formula	$C_{10}H_5F_3NO_6Re$	$C_{10}H_{10}NO_7Re$
Formula weight	478.35	442.39
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	C2/c
a/Å	6.42250(10)	24.6859(3)
b/Å	10.7862(3)	11.41920(10)
c/Å	18.6703(5)	9.1451(2)
α/°	83.339(2)	90
β/°	85.503(2)	97.3100(10)
γ/°	79.429(2)	90
Volume/Å^3	1260.68(5)	2556.99(7)
Z	4	8
ρ_{calc}g/cm^3	2.520	2.298
μ/mm^{-1}	19.543	18.899
F(000)	888.0	1664.0
Crystal size/mm^3	0.19 × 0.03 × 0.02	0.26 × 0.2 × 0.06
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	4.774 to 149	7.22 to 149
Index ranges	$-6 \le h \le 8$, $-13 \le k \le 13$, $-23 \le l \le 23$	$-26 \le h \le 30$, $-14 \le k \le 14$, $-11 \le l \le 11$
Reflections collected	25823	12718
Independent reflections	5099 [R_{int} = 0.0294, R_{sigma} = 0.0199]	2609 [R_{int} = 0.0204, R_{sigma} = 0.0097]
Data/restraints/parameters	5099/4/392	2609/5/189
Goodness-of-fit on F^2	1.023	1.216
Final R indexes [I>=2σ (I)]	R_1 = 0.0146, wR_2 = 0.0331	R_1 = 0.0204, wR_2 = 0.0519
Final R indexes [all data]	R_1 = 0.0162, wR_2 = 0.0336	R_1 = 0.0205, wR_2 = 0.0519
Largest diff. peak/hole / e Å^{-3}	0.67/-0.43	0.76/-0.92

Table S9. Selected crystal data and structure refinement parameters for **26** and **29**.

	26	**29**
CCDC number	2205522	2205517
Empirical formula	$C_{20}H_{16}N_4O_{15}Re_2$	$C_{10}H_{10}NO_8Re$
Formula weight	924.77	458.39
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	C2/c
a/Å	10.9380(3)	24.61350(10)
b/Å	11.4782(3)	11.21590(10)
c/Å	12.8234(3)	9.56510(10)
α/°	101.726(2)	90
β/°	111.100(3)	94.0710(10)
γ/°	109.637(3)	90
Volume/Å^3	1314.84(7)	2633.90(4)
Z	2	8
ρ_{calc}g/cm^3	2.336	2.312
μ/mm^{-1}	18.475	18.440
F(000)	868.0	1728.0
Crystal size/mm^3	0.34 × 0.13 × 0.05	0.09 × 0.08 × 0.03
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.952 to 148.99	7.202 to 148.92
Index ranges	-13 ≤ h ≤ 13, -14 ≤ k ≤ 14, -15 ≤ l ≤ 15	-30 ≤ h ≤ 30, -13 ≤ k ≤ 14, -11 ≤ l ≤ 11
Reflections collected	23312	25893
Independent reflections	5341 [R_{int} = 0.0236, R_{sigma} = 0.0140]	2686 [R_{int} = 0.0161, R_{sigma} = 0.0060]
Data/restraints/parameters	5341/8/401	2686/3/200
Goodness-of-fit on F^2	1.135	1.216
Final R indexes [I>=2σ (I)]	R_1 = 0.0198, wR_2 = 0.0563	R_1 = 0.0123, wR_2 = 0.0309
Final R indexes [all data]	R_1 = 0.0201, wR_2 = 0.0566	R_1 = 0.0123, wR_2 = 0.0309
Largest diff. peak/hole / e Å^{-3}	1.20/-0.95	0.51/-0.57

Table S10. Selected crystal data and structure refinement parameters for **30** and **31**.

	30	**31**
CCDC number	2205515	2205520
Empirical formula	$C_9H_9N_2O_7Re$	$C_9H_7N_2O_9Re$
Formula weight	443.38	473.37
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	C2/c	$P2_1/n$
a/Å	24.23071(18)	6.46680(10)
b/Å	11.28656(8)	24.4678(3)
c/Å	8.98742(7)	8.21830(10)
α/°	90	90
β/°	98.0757(8)	102.6050(10)
γ/°	90	90
Volume/Å^3	2433.52(3)	1269.03(3)
Z	8	4
ρ_{calc}g/cm^3	2.420	2.478
μ/mm^{-1}	19.885	19.257
F(000)	1664.0	888.0
Crystal size/mm^3	0.43 × 0.23 × 0.13	0.37 × 0.09 × 0.08
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.37 to 148.842	7.226 to 148.976
Index ranges	$-30 \le h \le 22$, $-14 \le k \le 14$, $-11 \le l \le 11$	$-8 \le h \le 7$, $-30 \le k \le 26$, $-10 \le l \le 10$
Reflections collected	11222	13269
Independent reflections	2483 [R_{int} = 0.0266, R_{sigma} = 0.0151]	2590 [R_{int} = 0.0358, R_{sigma} = 0.0191]
Data/restraints/parameters	2483/3/200	2590/3/203
Goodness-of-fit on F^2	1.252	1.257
Final R indexes [I>=2σ (I)]	R_1 = 0.0272, wR_2 = 0.0705	R_1 = 0.0290, wR_2 = 0.0774
Final R indexes [all data]	R_1 = 0.0273, wR_2 = 0.0706	R_1 = 0.0297, wR_2 = 0.0777
Largest diff. peak/hole / e Å^{-3}	0.99/-1.96	1.09/-1.28

Table S11. Selected crystal data and structure refinement parameters for **32** and **33**.

	32	**33**
CCDC number	2205530	2205528
Empirical formula	$C_9H_7FNO_7Re$	$C_9H_5ClNO_6Re$
Formula weight	446.36	444.79
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	I2/a	C2/c
a/Å	9.04380(10)	22.8800(2)
b/Å	11.1598(2)	9.98140(10)
c/Å	23.9385(4)	20.3649(2)
α/°	90	90
β/°	96.2130(10)	91.5910(10)
γ/°	90	90
Volume/Å^3	2401.85(6)	4649.03(8)
Z	8	16
ρ_{calc}g/cm^3	2.469	2.542
μ/mm^{-1}	20.255	22.800
F(000)	1664.0	3296.0
Crystal size/mm^3	0.18 × 0.11 × 0.07	0.18 × 0.07 × 0.04
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.43 to 148.958	7.73 to 149.006
Index ranges	$-11 \le h \le 11$, $-13 \le k \le 13$, $-29 \le l \le 29$	$-27 \le h \le 28$, $-12 \le k \le 12$, $-20 \le l \le 25$
Reflections collected	12376	24897
Independent reflections	2446 [R_{int} = 0.0222, R_{sigma} = 0.0117]	4750 [R_{int} = 0.0211, R_{sigma} = 0.0140]
Data/restraints/parameters	2446/3/191	4750/1/340
Goodness-of-fit on F^2	1.154	1.238
Final R indexes [I>=2σ (I)]	R_1 = 0.0174, wR_2 = 0.0463	R_1 = 0.0152, wR_2 = 0.0355
Final R indexes [all data]	R_1 = 0.0180, wR_2 = 0.0467	R_1 = 0.0156, wR_2 = 0.0356
Largest diff. peak/hole / e Å^{-3}	0.81/-0.71	0.64/-0.53

Table S12. Selected crystal data and structure refinement parameters for **34** and **35**.

	34	**35**
CCDC number	2205519	2205527
Empirical formula	$C_{10}H_5F_3NO_6Re$	$C_{10}H_{10}NO_7Re$
Formula weight	478.35	442.39
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	I2/a
a/Å	12.92600(10)	9.18810(10)
b/Å	6.81770(10)	11.06790(10)
c/Å	15.2153(2)	25.0097(3)
α/°	90	90
β/°	112.2060(10)	97.9890(10)
γ/°	90	90
Volume/Å^3	1241.41(3)	2518.63(5)
Z	4	8
ρ_{calc}g/cm^3	2.559	2.333
μ/mm^{-1}	19.846	19.187
F(000)	888.0	1664.0
Crystal size/mm^3	0.38 × 0.11 × 0.04	0.25 × 0.11 × 0.1
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.676 to 152.624	7.138 to 148.986
Index ranges	-15 ≤ h ≤ 16, -8 ≤ k ≤ 8, -19 ≤ l ≤ 19	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, -25 ≤ l ≤ 31
Reflections collected	12810	13080
Independent reflections	2583 [R_{int} = 0.0263, R_{sigma} = 0.0142]	2565 [R_{int} = 0.0274, R_{sigma} = 0.0172]
Data/restraints/parameters	2583/0/199	2565/1/189
Goodness-of-fit on F^2	1.117	1.203
Final R indexes [I>=2σ (I)]	R_1 = 0.0167, wR_2 = 0.0436	R_1 = 0.0222, wR_2 = 0.0574
Final R indexes [all data]	R_1 = 0.0173, wR_2 = 0.0440	R_1 = 0.0228, wR_2 = 0.0575
Largest diff. peak/hole / e Å^{-3}	0.65/-0.57	1.45/-1.10

Table S13. Selected crystal data and structure refinement parameters for **36** and **37**.

	36	**37**
CCDC number	2205524	2205526
Empirical formula	$C_{10}H_5N_2O_6Re$	$C_{10}H_6NO_8Re$
Formula weight	435.36	454.36
Temperature/K	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a/Å	10.3332(3)	10.54130(10)
b/Å	6.6448(2)	6.84780(10)
c/Å	17.7601(4)	17.1068(2)
α/°	90	90
β/°	102.862(2)	103.5150(10)
γ/°	90	90
Volume/Å^3	1188.85(6)	1200.65(3)
Z	4	4
ρ_{calc}g/cm^3	2.432	2.514
μ/mm^{-1}	20.279	20.225
F(000)	808.0	848.0
Crystal size/mm^3	0.46 × 0.12 × 0.05	0.25 × 0.19 × 0.11
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.778 to 148.95	8.628 to 148.86
Index ranges	$-12 \le h \le 12$, $-8 \le k \le 8$, $-19 \le l \le 22$	$-13 \le h \le 13$, $-8 \le k \le 8$, $-21 \le l \le 18$
Reflections collected	11482	14353
Independent reflections	2423 [R_{int} = 0.0280, R_{sigma} = 0.0149]	2457 [R_{int} = 0.0364, R_{sigma} = 0.0151]
Data/restraints/parameters	2423/0/181	2457/3/194
Goodness-of-fit on F^2	1.150	1.274
Final R indexes [I>=2σ (I)]	R_1 = 0.0197, wR_2 = 0.0512	R_1 = 0.0232, wR_2 = 0.0595
Final R indexes [all data]	R_1 = 0.0197, wR_2 = 0.0512	R_1 = 0.0232, wR_2 = 0.0595
Largest diff. peak/hole / e Å^{-3}	0.95/-0.97	1.09/-1.16

Table S14. Selected crystal data and structure refinement parameters for **38** and **39**.

	38	**39**
CCDC number	2205523	2205525
Empirical formula	$C_9H_6NO_7Re$	$C_{10}H_{10}NO_8Re$
Formula weight	426.35	458.39
Temperature/K	160(1)	160(1)
Crystal system	triclinic	monoclinic
Space group	P-1	I2/a
a/Å	7.2397(3)	8.88210(10)
b/Å	8.0044(4)	11.1360(2)
c/Å	9.5362(2)	26.3990(4)
α/°	88.048(3)	90
β/°	76.353(3)	93.4570(10)
γ/°	84.465(4)	90
Volume/Å^3	534.48(4)	2606.40(7)
Z	2	8
ρ_{calc}g/cm^3	2.649	2.336
μ/mm^{-1}	22.569	18.634
F(000)	396.0	1728.0
Crystal size/mm^3	0.24 × 0.04 × 0.02	0.2 × 0.16 × 0.07
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.544 to 148.984	6.708 to 149.006
Index ranges	$-8 \le h \le 9$, $-9 \le k \le 9$, $-11 \le l \le 9$	$-11 \le h \le 11$, $-13 \le k \le 13$, $-32 \le l \le 28$
Reflections collected	10649	13294
Independent reflections	2165 [R_{int} = 0.0375, R_{sigma} = 0.0215]	2652 [R_{int} = 0.0227, R_{sigma} = 0.0108]
Data/restraints/parameters	2165/0/166	2652/3/197
Goodness-of-fit on F^2	1.126	1.156
Final R indexes [I>=2σ (I)]	R_1 = 0.0218, wR_2 = 0.0584	R_1 = 0.0164, wR_2 = 0.0419
Final R indexes [all data]	R_1 = 0.0226, wR_2 = 0.0589	R_1 = 0.0165, wR_2 = 0.0420
Largest diff. peak/hole / e Å^{-3}	1.54/-1.16	0.61/-0.73

Table S15. Selected crystal data and structure refinement parameters for **41**.

	41
CCDC number	2205529
Empirical formula	$C_{27}H_{17}N_6O_{25}Re_3$
Formula weight	1384.06
Temperature/K	160(1)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.13580(10)
b/Å	18.60120(10)
c/Å	16.12660(10)
α/°	90
β/°	90.2970(10)
γ/°	90
Volume/Å^3	3640.38(4)
Z	4
ρ_{calc}g/cm^3	2.525
μ/mm^{-1}	20.072
F(000)	2584.0
Crystal size/mm^3	0.29 × 0.1 × 0.06
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.254 to 148.99
Index ranges	$-15 \leq h \leq 15$, $-22 \leq k \leq 23$, $-20 \leq l \leq 20$
Reflections collected	71970
Independent reflections	7431 [R_{int} = 0.0309, R_{sigma} = 0.0121]
Data/restraints/parameters	7431/42/600
Goodness-of-fit on F^2	1.263
Final R indexes [I>=2σ (I)]	R_1 = 0.0180, wR_2 = 0.0445
Final R indexes [all data]	R_1 = 0.0181, wR_2 = 0.0446
Largest diff. peak/hole / e Å^{-3}	0.75/-1.15