Electronic Supplementary Material (ESI) for Dalton Transactions.

Supporting Information

Synthesis of Tetranuclear Rhenium(I) Tricarbonyl Metallacycles

Johannes Karges[a,*], *Hyeonglim Seo*[a], *and Seth M. Cohen*[a]

[a] Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093, United States.

* Corresponding author: jkarges@ucsd.edu

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 300 MHz or 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: 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.

Synthesis

$[Re(H_2O)_2Cl(CO)_3]$ (1)

Pentacarbonylchlororhenium (100 mg, 0.28 mmol) was suspended in water (25 mL) and heated to reflux overnight. The solvent was removed under reduced pressure. The compound was used without further purification. Yield: 93 mg (0.27 mmol, 98%). MS (*m/z*): $[M\text{-}Cl]^+$ calcd. for $C_3H_4O_5Re$, 306.96; found, 307.23.

$[Re(H_2O)_3(CO)_3][CF_3SO_3]$ (2)

$[Re(H_2O)_2Cl(CO)_3]$ (**1**, 100 mg, 0.29 mmol) was dissolved in water (25 mL) and silver(I) trifluoromethanesulfonate (75 mg, 0.29 mmol) added. The mixture was heated at 60 °C for 4 h in the dark. After this time, the generated precipitated silver(I) chloride was removed by filtration. The solvent was removed under reduced pressure. The compound was used without

further purification. Yield: 134 mg (0.28 mmol, 97%). MS (*m/z*): $[M\text{-}H_2O]^+$ calcd. for $C_3H_4O_5Re$, 306.96; found, 307.38; $[CF_3SO_3]^-$ calcd. for CF_3SO_3, 148.95; found, 149.13.

$[Re(CH_3CN)_2Cl(CO)_3]$ (3)

Pentacarbonylchlororhenium (100 mg, 0.28 mmol) was suspended in acetonitrile (25 mL) and heated to reflux overnight. The solvent was removed under reduced pressure. The compound was used without further purification. Yield: 104 mg (0.27 mmol, 97%). MS (*m/z*): $[M\text{-}Cl]^+$ calcd. for $C_7H_6N_2O_3Re$, 387.96; found, 388.34.

$[Re(Br)_3(CO)_3][NEt_4]_2$ (4)

Tetraethylammonium bromide (155 mg, 0.74 mmol) was suspended in 1-methoxy-2-(2-methoxyethoxy)ethane (10 mL) under nitrogen atmosphere and heated at 80 °C. A solution of pentacarbonylbromorhenium (100 mg, 0.25 mmol) in 1-methoxy-2-(2-methoxyethoxy)ethane (1 mL) was added dropwise. The mixture was heated at 120 °C for 6 h during which a white precipitate was observed. The solid was obtained upon filtration and washed with 1-methoxy-2-(2-methoxyethoxy)ethane (40 mL), diethyl ether (40 mL) and ethanol (3 mL). The solid was dried under vacuum. The compound was used without further purification. Yield: 134 mg (0.17 mmol, 71%). MS (*m/z*): $[M\text{-}Br]^-$ calcd. for $C_3Br_2O_3Re$, 428.78; found, 428.54.

2-(1*H*-tetrazol-5-yl)pyridine (5)

2-Pyridinecarbonitrile (250 mg, 2.40 mmol), ammonium chloride (193 mg, 3.60 mmol) and sodium azide (234 mg, 3.60 mmol) were dissolved in dry *N*,*N*-dimethylformamide (2 mL). The mixture was heated at 110 °C for 4 h under argon atmosphere. The solution was concentrated nearly to dryness and water was added (20 mL). The aqueous solution was acidified to pH ~2 with a diluted hydrochloric acid solution (2 M). The product precipitated and was collected by filtration. The solid was washed with water (20 mL) and dried under vacuum. Yield: 222 mg (1.51 mmol, 63%). ^{1}H-NMR (300 MHz, $(CD_3)_2CO$): δ 8.80 (d, J = 4.8 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 8.09 (td, J = 7.9, 1.8 Hz, 1H), 7.64 (m, 1H); HRMS (*m/z*): $[M\text{-}H]^-$ calcd. for $C_6H_4N_5$, 146.0472; found, 146.0471.

Multinuclear Complexes based on [Re(2-(1*H*-tetrazol-5-yl)pyridine)(CO)$_3$] moiety (6-8)

5 (97 mg, 0.25 mmol, 1.0 equivalent) and **3** (37 mg, 0.25 mmol, 1.0 equivalent) were mixed in acetonitrile (25 mL) under nitrogen atmosphere and heated at reflux for 6 h. After this time, the solvent was removed under reduced pressure. The crude product was purified by recrystallisation from methanol in fridge. The precipitated solid was obtained by filtration and washed with diethyl ether. The respective species **6-8** were isolated by reverse phase column chromatography with a linear gradient (0%:100% - 100%:0% methanol/water). The fractions containing the product were united and the compound dried under vacuum.

6: Yield: 34%. ^{1}H-NMR (500 MHz, CD_3OD): δ 8.76 (dd, J = 4.8, 1.7 Hz, 1H), 8.25 (dt, J = 7.8, 1.0 Hz, 1H), 8.03 (td, J = 7.8, 1.7 Hz, 1H), 7.57 (ddd, J = 7.8, 4.8, 1.0 Hz, 1H); ^{13}C-NMR (125 MHz, CD_3OD): δ 151.5, 151.4, 145.2, 139.1, 127.2, 123.7; HRMS (*m/z*): [M-axial ligand]$^+$ calcd. for $C_9H_5N_5O_3Re$, 417.9943; found, 417.9945.

7: Yield: 28%. ^{1}H-NMR (500 MHz, CD_3OD): δ 8.78 (d, J = 4.2 Hz, 2H), 8.24 (d, J = 7.9 Hz, 2H), 8.08 (dd, J = 7.9, 7.8 Hz, 2H), 7.62 (t, J = 7.8, 4.2 Hz, 2H); ^{13}C-NMR (125 MHz, CD_3OD): δ 156.9, 151.2, 144.7, 139.6, 127.5, 123.9; HRMS (*m/z*): [M-axial ligand]$^+$ calcd. for $C_{18}H_9N_{10}O_6Re_2$, 834.9822; found, 834.9821.

8: Yield: 16%. ^{1}H-NMR (500 MHz, CD_3OD): δ 8.87 (d, J = 4.7, 1.6 Hz, 4H), 8.30 (d, J = 7.8, 1.3 Hz, 4H), 8.16 (ddd, J = 7.8, 7.6, 1.6 Hz, 4H), 7.71 (ddd, J = 7.6, 4.7, 1.3 Hz, 4H); ^{13}C-NMR (125 MHz, CD_3OD): δ 156.8, 151.2, 143.8, 141.5, 127.6, 124.4; HRMS (*m/z*): [M+H]$^+$ calcd. for $C_{36}H_{17}N_{20}O_{12}Re_4$, 1668.9565; found, 1668.9563.

3-(1*H*-tetrazol-5-yl)-1*H*-indazole (9)

1*H*-Indazole-3-carbonitrile (250 mg, 1.75 mmol), ammonium chloride (187 mg, 3.49 mmol) and sodium azide (227 mg, 3.49 mmol) were dissolved in dry *N*,*N*-dimethylformamide (5 mL). The mixture was heated at 110 °C for 6 h under argon atmosphere. The solution was concentrated nearly to dryness and water was added (20 mL). The aqueous solution was acidified to pH ~2 with a diluted hydrochloric acid solution (2 M). The product precipitated and was collected by filtration. The solid was washed with water (20 mL) and dried under vacuum. Yield: 220 mg (1.19 mmol, 68%). ^{1}H-NMR (300 MHz, $(CD_3)_2CO$): δ 13.94 (s, 1H),

8.28 (d, *J* = 8.2 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.54-7.50 (m, 1H), 7.39-7.31 (m, 1H); HRMS (*m/z*): [M-H]$^-$ calcd. for $C_8H_5N_6$, 185.0581; found, 185.0579.

2-(1*H*-tetrazol-5-yl)-1*H*-benzo[*d*]imidazole (10)

1*H*-benzo[*d*]imidazole-2-carbonitrile (250 mg, 1.75 mmol), ammonium chloride (187 mg, 3.49 mmol) and sodium azide (227 mg, 3.49 mmol) were dissolved in dry *N*,*N*-dimethylformamide (5 mL). The mixture was heated at 110 °C for 6 h under argon atmosphere. The solution was concentrated nearly to dryness and water was added (20 mL). The aqueous solution was acidified to pH ~2 with a diluted hydrochloric acid solution (2 M). The product precipitated and was collected by filtration. The solid was washed with water (20 mL) and dried under vacuum. Yield: 247 mg (1.33 mmol, 76%). ^{1}H-NMR (300 MHz, $(CD_3)_2CO$): δ 7.71 (d, *J* = 6.1 Hz, 2H), 7.43 (d, *J* = 6.1 Hz, 2H); HRMS (*m/z*): [M-H]$^-$ calcd. for $C_8H_5N_6$, 185.0581; found, 185.0578.

3-(1*H*-tetrazol-5-yl)benzo[*d*]isothiazole (11)

Benzo[*d*]isothiazole-3-carbonitrile (250 mg, 1.56 mmol), ammonium chloride (167 mg, 3.12 mmol) and sodium azide (203 mg, 3.12 mmol) were dissolved in dry *N*,*N*-dimethylformamide (5 mL). The mixture was heated at 110 °C for 6 h under argon atmosphere. The solution was concentrated nearly to dryness and water was added (20 mL). The aqueous solution was acidified to pH ~2 with a diluted hydrochloric acid solution (2 M). The product precipitated and was collected by filtration. The solid was washed with water (20 mL) and dried under vacuum. Yield: 257 mg (1.26 mmol, 81%). ^{1}H-NMR (300 MHz, $(CD_3)_2CO$): δ 8.96 (d, *J* = 7.3 Hz, 1H), 8.40 (d, *J* = 7.5 Hz, 1H), 7.79-7.69 (m, 2H); HRMS (*m/z*): [M-H]$^-$ calcd. for $C_8H_5N_5S$, 202.0193; found, 202.0191.

General synthetic protocol for preparation of tetranuclear Re(I) tricarbonyl complexes

9-11 (0.25 mmol, 1.0 equivalent) and **3** (37 mg, 0.25 mmol, 1.0 equivalent) were mixed in acetonitrile (25 mL) under nitrogen atmosphere and heated at reflux for 6 h. After this time, the solvent was removed under reduced pressure. The crude product was purified by recrystallisation from methanol in fridge. The precipitated solid was obtained by filtration and washed with diethyl ether. The tetranuclear metallacycle was isolated by reverse phase column

chromatography with a linear gradient (0%:100% - 100%:0% methanol/water). The fractions containing the product were united and the compound dried under vacuum.

[Re(3-(1*H*-tetrazol-5-yl)-1*H*-indazole)(CO)$_3$]$_4$ (12)

Yield: 33%. ^{1}H-NMR (500 MHz, CD_3OD): δ 8.42 (dt, J = 8.2, 1.0 Hz, 1H), 7.75 (dt, J = 8.4, 1.0 Hz, 1H), 7.60 (ddd, J = 8.4, 6.9, 1.0 Hz, 1H), 7.44 (ddd, J = 8.2, 6.8, 1.0 Hz, 1H); ^{13}C-NMR (125 MHz, CD_3OD): δ 155.3, 142.8, 131.9, 128.5, 123.7, 122.2, 122.0, 111.6; MS (*m/z*): $[M+H]^+$ calcd. for $C_{44}H_{21}N_{24}O_{12}Re_4$, 1825.00; found, 1825.71.

[Re(2-(1*H*-tetrazol-5-yl)-1*H*-benzo[*d*]imidazole)(CO)$_3$]$_4$ (13)

Yield: 38%. ^{1}H-NMR (500 MHz, CD_3OD): δ 9.10 (dt, J = 8.0, 1.0 Hz, 1H), 8.26 (dt, J = 8.1, 1.0 Hz, 1H), 7.80-7.73 (m, 2H); ^{13}C-NMR (125 MHz, CD_3OD): δ 155.1, 148.4, 146.8, 134.5, 129.9, 127.4, 126.5, 121.2; MS (*m/z*): $[M+H]^+$ calcd. for $C_{44}H_{21}N_{24}O_{12}Re_4$, 1825.00; found, 1825.54.

[Re(3-(1*H*-tetrazol-5-yl)benzo[*d*]isothiazole)(CO)$_3$]$_4$ (14)

Yield: 36%. ^{1}H-NMR (500 MHz, CD_3OD): δ 9.03 (d, J = 7.2 Hz, 1H), 8.65 (d, J = 8.2 Hz, 1H), 7.93-7.85 (m, 2H); ^{13}C-NMR (125 MHz, CD_3OD): δ 155.1, 151.5, 150.9, 134.5, 129.9, 127.4, 126.5, 121.2; MS (*m/z*): $[M+H]^+$ calcd. for $C_{44}H_{21}N_{24}O_{12}Re_4$, $C_{44}H_{17}N_{20}O_{12}Re_4S_4$, 1892.84; found, 1893.17.

Single Crystal X-ray Diffractometry

Single crystals of **8** were grown upon vapor diffusion of a solution of the metal complex in methanol with toluene at 4 °C. A suitable crystal of **8** was selected and data was collected at 100 K on a Bruker APEX-II Ultra diffractometer with a Mo-Kα Microfocus Rotating Anode and a APEX-II CCD area detector or a Bruker Kappa diffractometer equipped with a Bruker X8 APEX II Mo sealed tube and a Bruker APEX-II CCD. The data was integrated and merged within the APEXIII software suite (Bruker, 2017). The structure was refined with the XL refinement package using least squares minimization with Olex2. (O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann *J. Appl. Cryst.* **2009**, *42*, 339-341).

Crystallographic data collection and refinement information is listed in Table S1. The solvent in the pores was disordered and accounted for with the SQUEEZE (A. Spek *Acta Crystallogr. C* **2015**, *71*, 9-18) function. The diffraction was weak, but still suitable for structural determination. The structure was refined with a cutoff of 0.9 angstroms. The crystal data file of the complex was deposited into the Cambridge Crystallographic Data Centre (CCDC).

Optimization of the reaction conditions for synthesis of the tetranuclear metallacycle

The reactions were performed under various conditions to optimize the yield of the synthesis of the tetranuclear metallacycle. The obtained mixture of compounds was analysed by high-performance liquid chromatography–mass spectrometry (HPLC–MS) on an Eclipse Plus C8 analytical column. The solvents (HPLC grade) were millipore water (solvent A) and methanol (solvent B) with 0.1% formic acid. 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 0% A (100% B); 17-20 minutes: isocratic 0% A (100% B). The chromatogram was detected at 220 nm and the mass spectrum measured with an Agilent 6230 electrospray ionization time-of-flight mass spectrometer.

Precursor

5 (0.05 mmol, 1.0 equivalent) and the Re(I) tricarbonyl precursors **1** and **2** were dissolved in water (25 mL) while **5** was dissolved with the precursors **3** and **4** (0.05 mmol, 1.0 equivalent) in acetonitrile (25 mL) under nitrogen atmosphere. The mixture heated at reflux for 6 h and after this time analyzed by HPLC–MS.

Solvent

5 (19.4 mg, 0.05 mmol, 1.0 equivalent) and **3** (7.4 mg, 0.05 mmol, 1.0 equivalent) were mixed in methanol, acetonitrile, toluene or water (25 mL) under nitrogen atmosphere. The mixture heated at reflux for 6 h and after this time analyzed by HPLC–MS.

Temperature

5 (19.4 mg, 0.05 mmol, 1.0 equivalent) and **3** (7.4 mg, 0.05 mmol, 1.0 equivalent) were mixed in acetonitrile (25 mL) under nitrogen atmosphere. The solution was heated at -78 °C, 0 °C, 25 °C or 82°C (reflux temperature) for 24 h. After this time, the mixture was analyzed by HPLC–MS.

Concentration

5 (1.0 equivalent) and **3** (1.0 equivalent) with various amount of starting material (0.0125 mmol, 0.05 mmol, 0.25 mmol or 2.5 mmol) were mixed in acetonitrile (25 mL) under nitrogen atmosphere. The solution heated at reflux for 6 h. After this time, the mixture was analyzed by HPLC–MS.

SUPPLEMENTARY FIGURES AND TABLES

Table S1. Crystal data and structure refinement for **8**.

Compound	**8**
Identification code	2092925
Empirical formula	$C_{36}H_{16}N_{20}O_{12}Re_4$
Formula weight	1665.49
Temperature/K	100
Crystal system	orthorhombic
Space group	Pbca
a/Å	19.9283(7)
b/Å	18.5408(7)
c/Å	30.9067(12)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	11419.6(7)
Z	8
ρ_{calc}g/cm^3	1.937
μ/mm^{-1}	8.519
F(000)	6144
Crystal size/mm^3	0.1 × 0.1 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.276 to 46.614
Index ranges	$-22 \leq h \leq 22$, $-19 \leq k \leq 20$, $-25 \leq l \leq 34$
Reflections collected	58915
Independent reflections	8226 [R_{int} = 0.0851, R_{sigma} = 0.0603]
Data/restraints/parameters	8226/672/643
Goodness-of-fit on F^2	1.109
Final R indexes [I>=2σ (I)]	R_1 = 0.0825, wR_2 = 0.1768
Final R indexes [all data]	R_1 = 0.1130, wR_2 = 0.1904
Largest diff. peak/hole / e Å^{-3}	1.73/-2.06

Table S2. Selected bond distances (Å) and angles (°) for **8**.

Compound	**8**	
Bond lengths (Å)	Re1-N1	2.15(2)
	Re1-N5	2.16(2)
	Re1-N3c	2.15(2)
	Re2-N1a	2.16(2)
	Re2-N5a	2.20(2)
	Re2-N3	2.226(19)
	Re3-N1b	2.121(19)
	Re3-N5b	2.13(2)
	Re3-N3a	2.17(2)
	Re4-N1c	2.15(2)
	Re4-N5c	2.212(18)
	Re4-N3b	2.192(19)
Bond angles (°)	N1-Re1-N5	74.5(8)
	N1-Re1-N3c	81.8(7)
	N1a-Re2-N5a	74.8(8)
	N1a-Re2-N3	85.2(7)
	N1b-Re3-N5b	72.0(7)
	N1b-Re3-N3a	82.5(7)
	N1c-Re4-N5c	75.1(7)
	N1c-Re4-N3b	79.8(8)

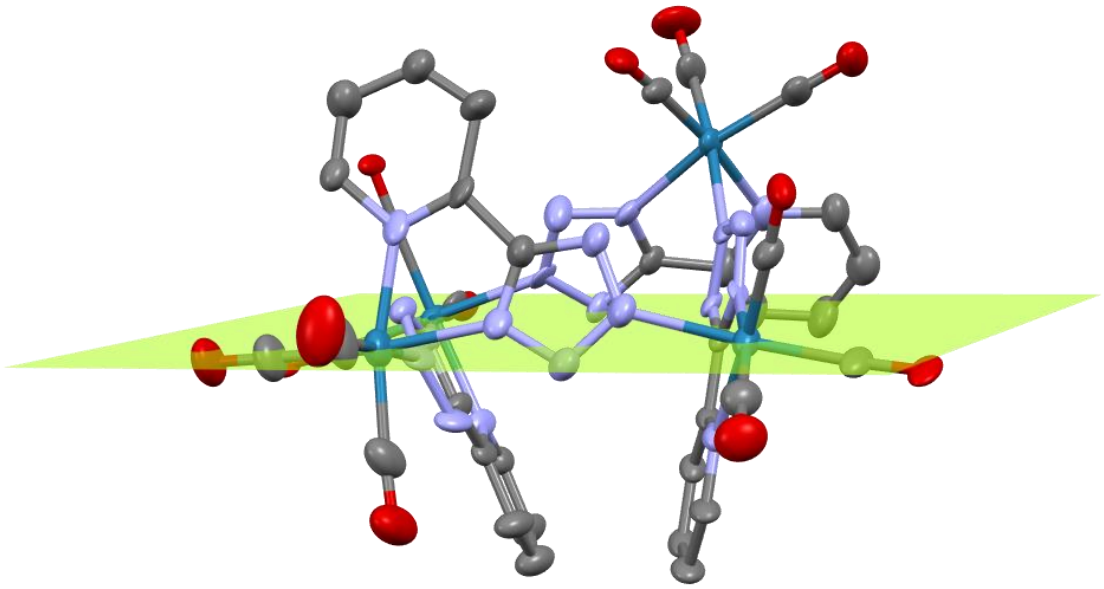

Figure S1. Presentation of the distortion and out-of-plane conformation of **8**. Hydrogen atoms have been omitted for clarity. Color scheme: carbon = grey, oxygen = red, nitrogen = blue, rhenium = blue.

Table S3. Overview of conditions investigated for the preparation of the metallacycle **8**.

Precursor	Time	Solvent	Temperature	Concentration	Integrated HPLC Signal
1	6 h	H_2O	reflux	2 mM	10%
2	6 h	H_2O	reflux	2 mM	9%
3	6 h	CH_3CN	reflux	2 mM	12%
4	6 h	CH_3CN	reflux	2 mM	>1%
4	24 h	CH_3CN	reflux	2 mM	10%
3	6 h	H_2O	reflux	2 mM	13%
3	6 h	CH_3OH	reflux	2 mM	10%
3	6 h	$(CH_3)_2CHOH$	reflux	2 mM	11%
3	6 h	CH_3CN	reflux	2 mM	11%
3	6 h	$(CH_3)_2NCHO$	reflux	2 mM	12%
3	6 h	$CH_3C_6H_6$	reflux	2 mM	>1%
3	24 h	CH_3CN	-78 °C	2 mM	>1%
3	24 h	CH_3CN	0 °C	2 mM	>1%
3	24 h	CH_3CN	25 °C	2 mM	6%
3	24 h	CH_3CN	reflux/82 °C	2 mM	12%
3	6 h	CH_3CN	reflux/82 °C	0.5 mM	>1%
3	6 h	CH_3CN	reflux/82 °C	2 mM	11%
3	6 h	CH_3CN	reflux/82 °C	10 mM	27%
3	6 h	CH_3CN	reflux/82 °C	100 mM	26%

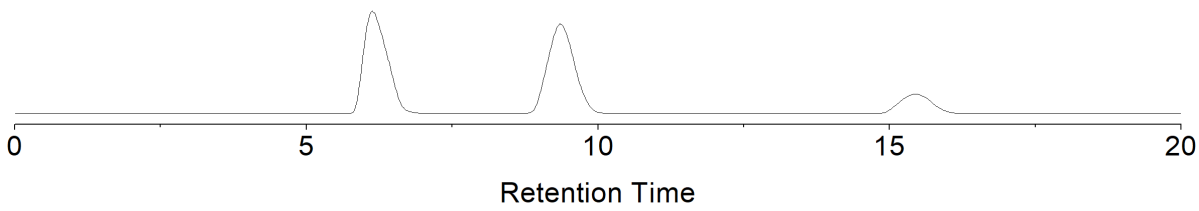

Figure S2. HPLC-MS analysis of the reaction of **4** with **5** for 24 h at a concentration of 2 mM.

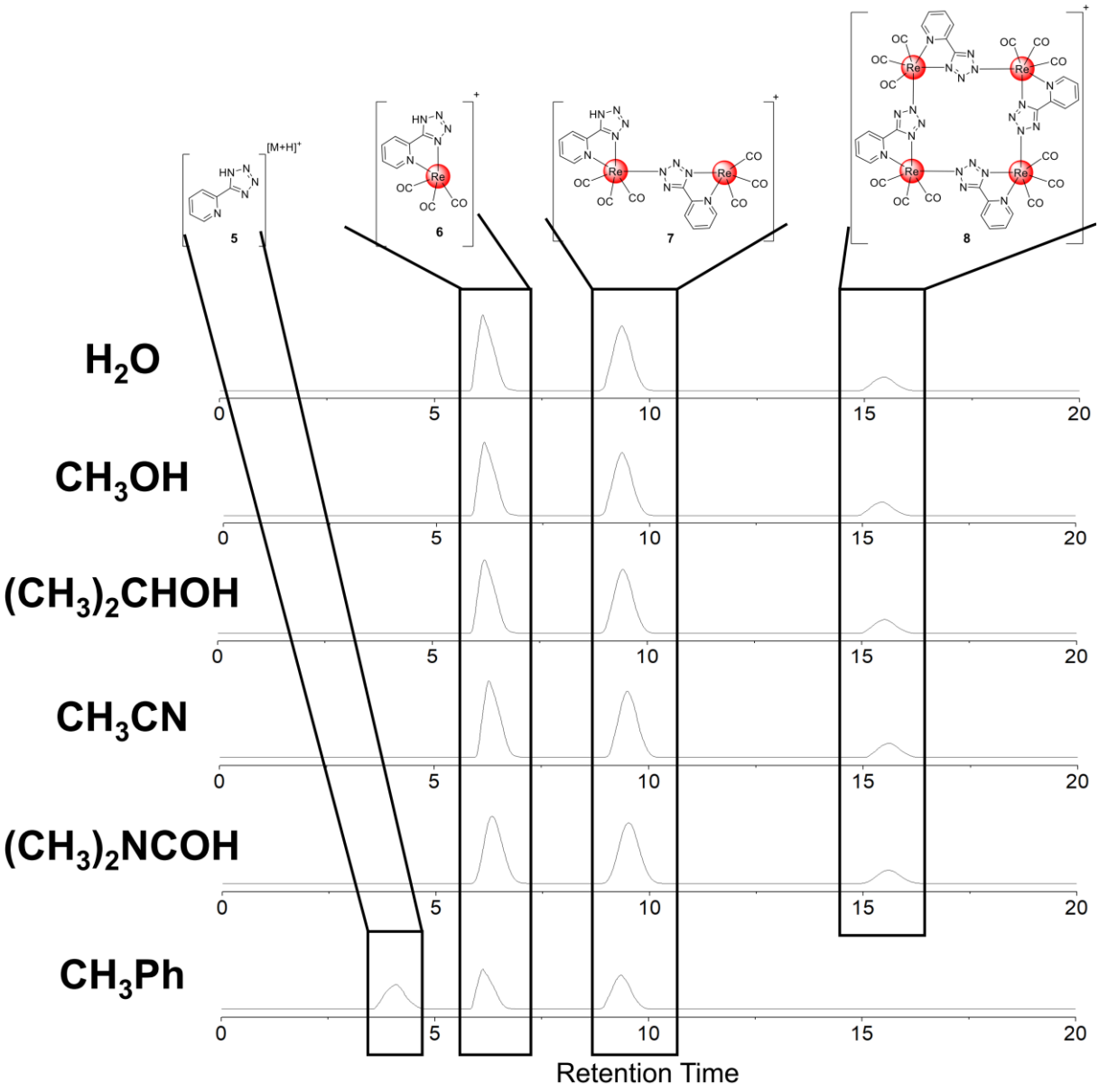

Figure S3. HPLC-MS analysis of the reaction of **3** with **5** in various solvents at a concentration of 2 mM.

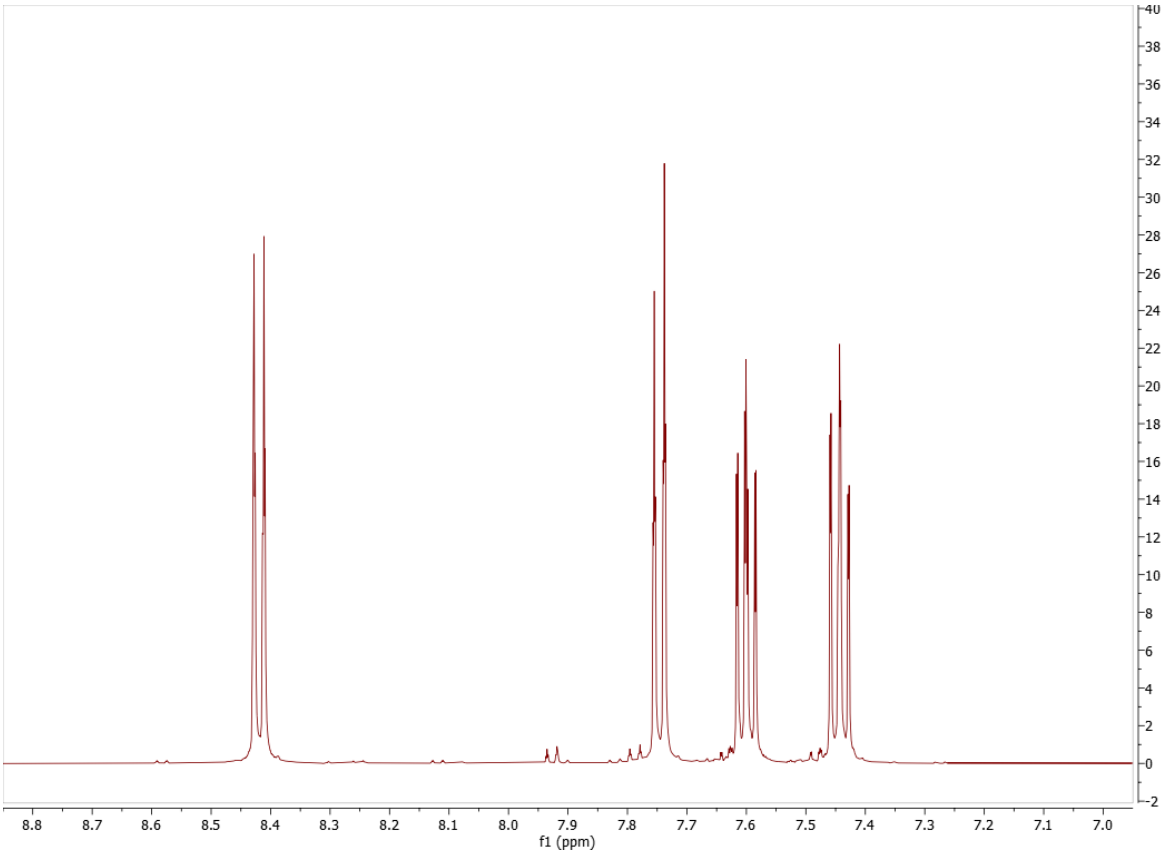

Figure S4. ^{1}H-NMR of **12** in CD_3OD.

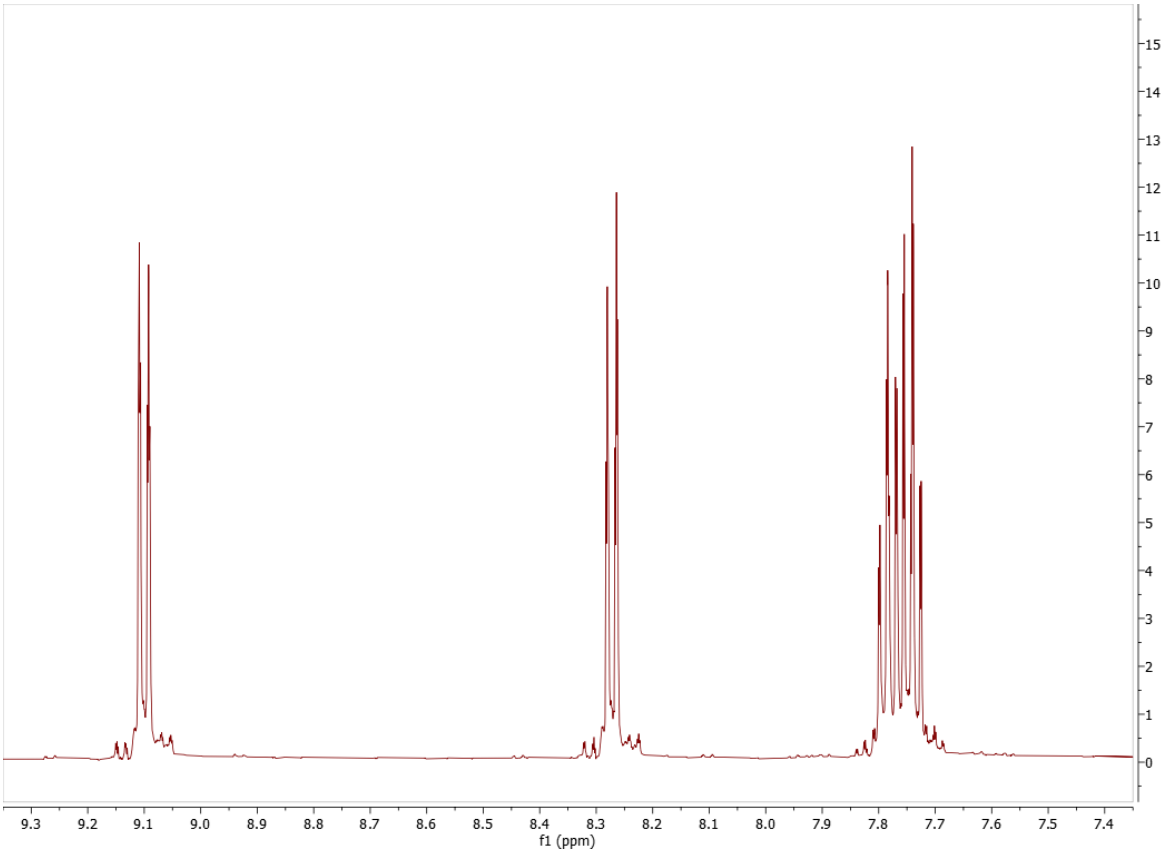

Figure S5. ^{1}H-NMR of **13** in CD_3OD.

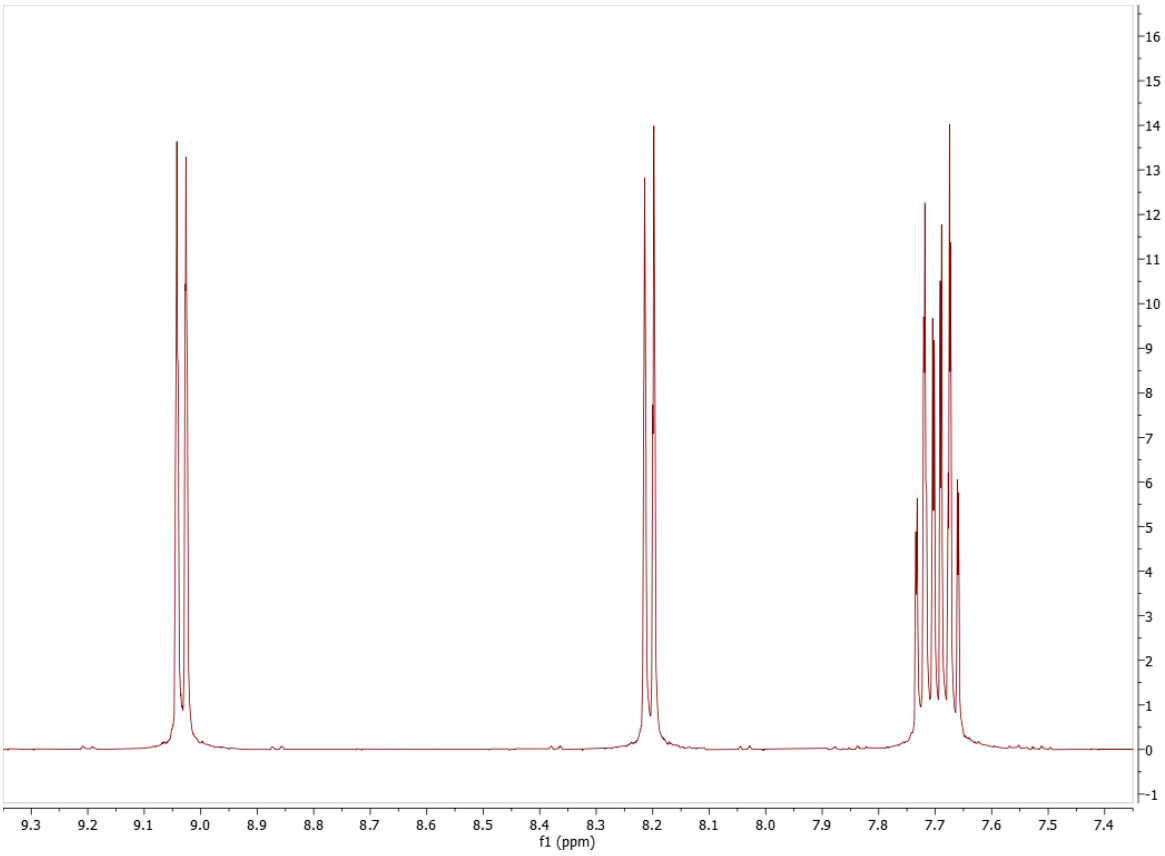

Figure S6. ^{1}H-NMR of **14** in CD_3OD.