Electronic Supplementary Information

New Strategies towards Advanced CT Contrast Agents. Development of Neutral and Monoanionic Sulfur-bridged W(V) Dimeric Complexes

Hristo P. Varbanov,*[a] Toma Glasnov,[b] Ferdinand Belaj,[a] Simon Herbert,[c]
Thomas Brumby [c] and Nadia C. Mösch-Zanetti*[a]

[a.] Institute of Chemistry - Inorganic Chemistry, University of Graz, Schubertstraße 1/III, 8010 Graz, Austria

[b.] Institute of Chemistry - Medicinal Chemistry, University of Graz, Schubertstraße 1/IV, 8010 Graz, Austria

[c.] Research & Development, Pharmaceuticals Laboratory, Bayer AG, 13342 Berlin, Germany

Contents

Page S2 Reactivity of histidine towards complexes **1b** and **9b** (Figures S1 and S2)

Page S3 Crystal structure determination of **2** and **3**

Page S12 ESI-HRMS of the crude products obtained after the reaction of **1a** and L2 or L4, respectively (Fig. S6 and S7)

Page S13 ESI-HRMS evidence for the formation of $[W_2O_2S_2(L6)]^-$ and the double-charged dimer $[W_2O_2S_2(L6)]_2^{2-}$ (Fig. S8)

Page S13 Reactivity of **1b** towards EDTA, HEDTA, L5, and L6 (Fig. S9)

Page S14 ESI-HRMS spectra of complexes **5b**, **7a** and **8a** (Fig. S10-S13)

Page S16 Approximate solubility, retention times and HPLC purity of the investigated W(V) complexes (Table S5, Fig. S14)

Page S17 ^{1}H NMR spectra of complex **7b** in D_2O and in DMSO-d_6 (Fig. S15)

Page S18 Synthesis and characterization of L1-8

Page S24 ^{1}H and ^{13}C NMR spectra of the investigated W(V) dinuclear complexes

Reactivity of histidine towards $Na_2[W_2O_2S_2(Cys)_2]$ (1b) and $Na_2[W_2O_2S_2(EDTA)]$ (9b)

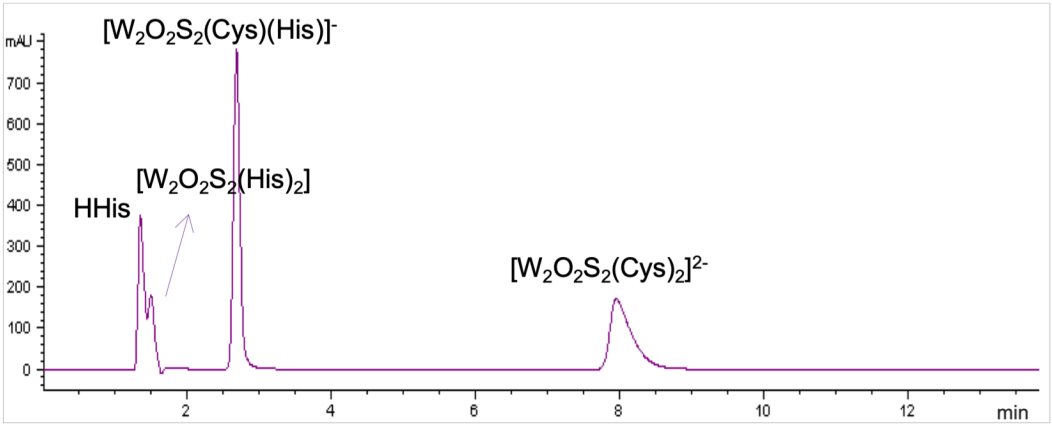


Fig. S1 Reactivity of $Na_2[W_2O_2S_2(Cys)_2]$ (**1b**) towards histidine (HHis) at pH 7.5 after 4 h of incubation at 90 °C as followed by RPIP-HPLC. Mobile phase consisted of 0.1% Bu_4NCl/MeOH (65/35); a chromatogram recorded at 230 nm is shown. A mixture of products was formed regardless of the reaction conditions (pH, reaction time and temperature, conventional or microwave heating) used.

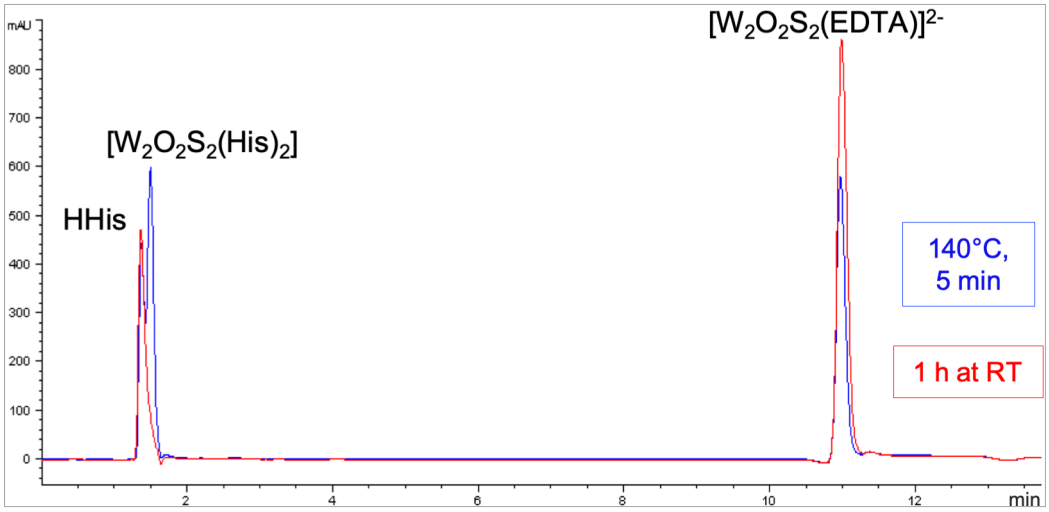


Fig. S2 RP-HPLC chromatograms of the reaction mixture of $Na_2[W_2O_2S_2(EDTA)]$ (**9b**) and histidine at pH 8 after 1 h at rt (red) or 5 min at 140 °C microwave heating (blue). Mobile phase consisted of 0.1% Bu_4NCl/MeOH (65/35); overlay of chromatograms recorded at 230 nm is shown. The formed complex $[W_2O_2S_2(His)_2]$ (**2**) precipitates after cooling the reaction mixture to 4° C and can be collected via filtration.

Crystal Structure Determination

All the measurements were performed using monochromatized Mo K_α radiation at 100 K. The structures were solved by direct methods (SHELXS-97)[1] and refined by full-matrix least-squares techniques against F^2 (SHELXL-2014/6).[2] Crystal data, data collection parameters and structure refinement details are given in Table S1 and in the deposited cif files.

Crystal Structure Determination of 2. The absolute configuration was established by anomalous dispersion effects in the diffraction measurements on the crystal. The same anisotropic displacement parameters were used for the ring atoms of the same imidazole rings to keep the number of parameters low. The equivalent bonds in the histidinato ligands were restrained to have the same lengths. Two of the seventeen water molecules were disordered over two orientations which refined to site occupation factors of 0.518(17) and 0.482(17), respectively. Some of the positions of the H atoms of the water molecules were taken from a difference Fourier map, the others were put at directions towards the nearest acceptor atoms. The O–H distances were fixed to 0.84 Å and for eight water molecules the H···H distances were restrained to 1.40 Å to obtain realistic H–O–H bond angles. Moreover, seven 'antibumping' restraints between H atoms were generated. Common isotropic displacement parameters were refined for the H atoms of the same water molecule. The H atoms of the imidazole rings were put at the external bisectors of the X–C–N angles (X = C or N) at C–H distances of 0.95 Å or of the C–N–C angles at N–H distances of 0.88 Å, resp., and a common isotropic displacement parameter was refined for these H atoms. The H atoms of the tertiary C–H groups were refined with a common isotropic displacement parameter and all X–C–H angles equal at a C–H distance of 1.00 Å. The H atoms of the CH_2 groups were refined with a common isotropic displacement parameter and idealized geometries with approx. tetrahedral angles and C–H distances of 0.99 Å. The H atoms of the NH_2 groups were refined with a common isotropic displacement parameter and idealized geometries with approx. tetrahedral angles and N–H distances of 0.91 Å. The largest peaks in a final difference Fourier map (0.95 - 1.21 $eÅ^{-3}$) were in the vicinity (1.12 - 1.28 Å) of the W atoms. For 1531 parameters final *R* indices of R1 = 0.0387 and wR^2 = 0.0636 (GOF = 1.014) were obtained.

Crystal Structure Determination of 3. Since twinning was detected a twin matrix (0 0 1 / 0 1 0 / -1 0 -1) was applied. The two scale factors between the three unequal components refined to 0.00164(7) and 0.00101(4) lowering R1 from 0.0253 to 0.0246. The diaminopropionato ligands were disordered over two orientations which refined to site occupation factors of 0.637(3) / 0.363(3) and 0.642(3) / 0.358(3), respectively. In these ligands the same anisotropic displacement parameters were used for atoms whose positions are close together, and the equivalent bonds were restrained to have the same lengths. The $[WS_4]^{2-}$ ion lying on a three-fold rotation axis was ordered, the other one at a general position was slightly disordered refining to site occupation factors of 0.9574(3) / 0.0426(3). The same anisotropic displacement parameters were used for equivalent atoms of the disordered dianion and the bond lengths of the less prominent occupied ion were fixed to those of the other one. Two potassium cations together with three coordinating water molecules were ordered, the other two potassium cations and the remaining water molecules were heavily disordered. The same anisotropic displacement parameters were used for the disordered O atoms O41-O46. The H atoms of the tertiary C–H groups were included with all X–C–H angles equal at C–H distances of 1.00 Å, the H atoms of the CH_2 groups were included with idealized geometries with approximately tetrahedral angles and C–H distances of 0.99 Å. A common isotropic displacement parameter was refined for the H atoms bonded to carbon. The H atoms of the NH_2 groups were included with idealized geometries with approximately tetrahedral angles and N–H distances of 0.91 Å and a common isotropic displacement parameter was refined for these H atoms. The positions of the H atoms of the water molecules were taken from a difference Fourier map, the O–H distances were fixed to 0.84 Å, and common isotropic displacement parameters were refined for the H atoms of the same ordered water molecule. The isotropic displacement parameters were fixed to 1.2 times U_{eq} of the O atom they are bonded to for the disordered water molecules. The largest peaks in a final difference Fourier map (1.38 - 2.05 $eÅ^{-3}$) were in the vicinity (0.40 - 0.79 Å) of the W atoms. For 516 parameters final *R* indices of R1 = 0.0246 and wR^2 = 0.0570 (GOF = 1.037) were obtained.

Table S1 Crystallographic data and structure refinement for complexes **2** and **3**.

Crystal Data	**$[W_2O_2S_2(His)_2]$ (2)**	**$[W_2O_2S_2(DAP)_2]$ (3)**
Empirical formula	$6C_{12}H_{16}N_6O_6S_2W_2 \cdot 17H_2O$	$3C_6H_{14}N_4O_6S_2W_2 \cdot 4K_2WS_4 \cdot 14H_2O$
Formula weight	4939.03	3823.48
Crystal description	plate, yellow	plate, yellow
Crystal size	0.12 x 0.12 x 0.03 mm	0.30 x 0.17 x 0.11 mm
Crystal system, space group	orthorhombic, P 2_1 2_1 2_1	trigonal, R -3
Unit cell dimensions:	a = 10.0553(5) Å b = 31.7945(16) Å c = 39.5192(19) Å	a = 18.0697(7) Å b = 18.0697(7) Å c = 45.2783(18) Å
Volume	12634.4(11) $Å^3$	12803.3(13) $Å^3$
Z	4	6
Calculated density	2.597 Mg/m^3	2.975 Mg/m^3
F(000)	9272	10572
Linear absorption coefficient μ	11.173 mm^{-1}	14.416 mm^{-1}
Absorption correction	semi-empirical from equivalents	semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.725	1.000 and 0.349
Unit cell determination	2.40° < Θ < 25.48° 9173 reflections used at 100 K	2.63° < Θ < 35.55° 9988 reflections used at 100 K
Data collection		
Θ range for data collection	1.28 to 25.00°	1.38 to 35.0°
Reflections collected / unique	49623 / 21953	48598 / 12558
Significant unique reflections	18585 with I > 2σ (I)	11195 with I > 2σ (I)
R(int), R(sigma)	0.0559, 0.0820	0.0458, 0.0434
Completeness to Θ = 25.0°/35.0°	99.9%	100.0%
Refinement		
Data / parameters / restraints	21953 / 1531 / 380	12558 / 516 / 79
Goodness-of-fit on F^2	1.014	1.037
Final R indices [I > 2σ (I)]	R1 = 0.0387, wR2 = 0.0588	R1 = 0.0246, wR2 = 0.0556
R indices (all data)	R1 = 0.0550, wR2 = 0.0636	R1 = 0.0292, wR2 = 0.0570
Weighting scheme	$w = 1/[\sigma^2(F_o^2)+(aP)^2+bP]$ where $P = (F_o^2+2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2)+(aP)^2+bP]$ where $P = (F_o^2+2F_c^2)/3$
Weighting scheme parameters a,b	0.0008, 2.6043	0.0128, 2.6029
Largest Δ/σ in last cycle	0.004	0.006
Largest difference peak and hole	1.213 and -1.365 e/$Å^3$	2.052 and -1.799 e/$Å^3$
CCDC deposition number	2160190	2160191

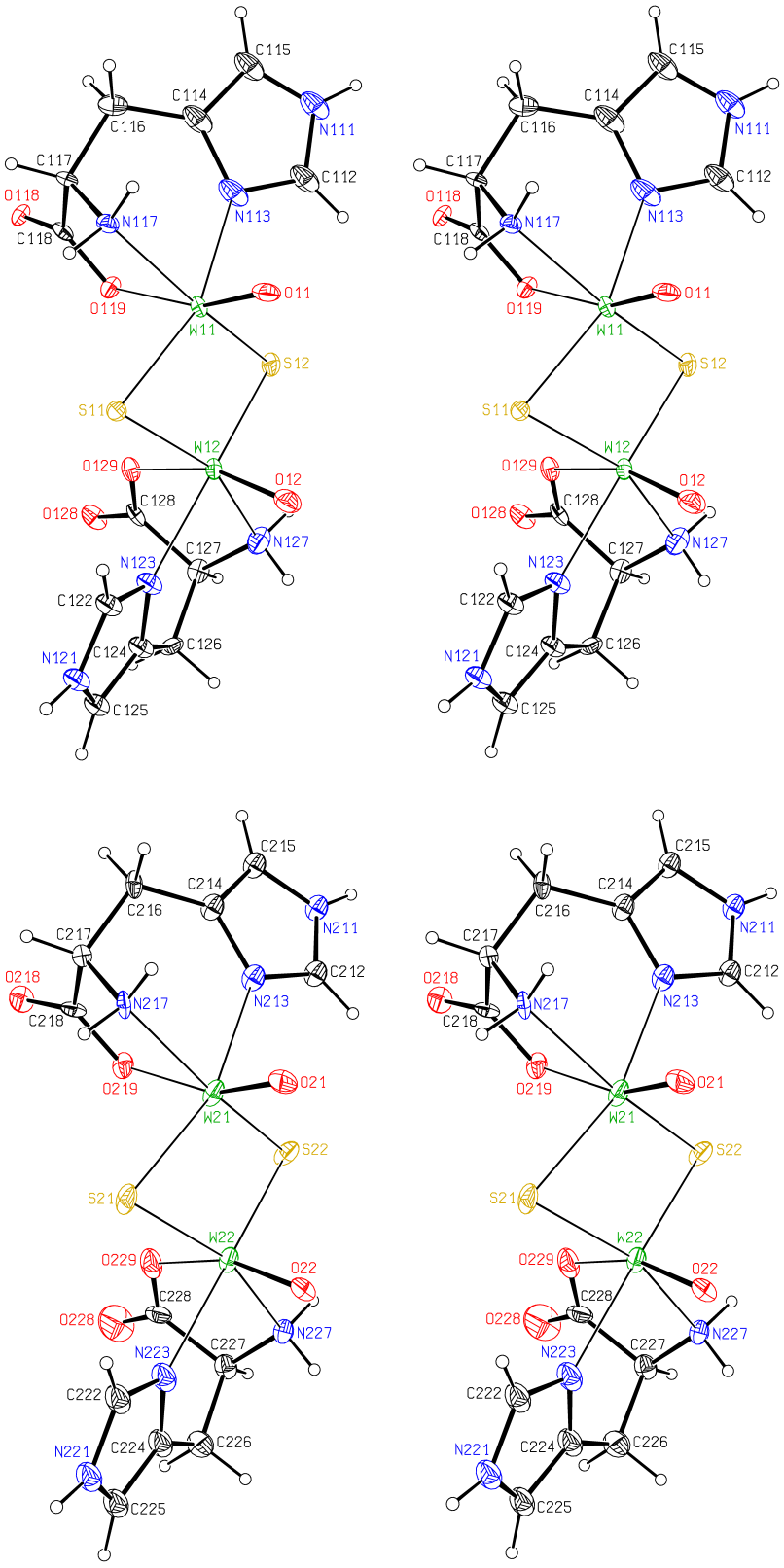


Fig. S3 Stereoscopic ORTEP[3] plot of complex **2** showing the atomic numbering scheme. The probability ellipsoids are drawn at the 50% probability level. The H atoms are drawn with arbitrary radii. Water molecules are omitted for clarity.

Table S2 Selected bond lengths [Å] and angles [°] for complex **2**.

W11-O11	1.701(11)	W31-O31	1.694(11)	W51-O51	1.706(11)
W11-O119	2.149(10)	W31-O319	2.188(10)	W51-O519	2.157(9)
W11-N113	2.233(11)	W31-N313	2.240(11)	W51-N513	2.218(11)
W11-N117	2.224(11)	W31-N317	2.222(12)	W51-N517	2.229(11)
W11-S11	2.329(4)	W31-S31	2.343(4)	W51-S51	2.332(4)
W11-S12	2.335(4)	W31-S32	2.328(4)	W51-S52	2.324(4)
W12-O12	1.705(11)	W32-O32	1.692(11)	W52-O52	1.718(10)
W12-O129	2.166(10)	W32-O329	2.162(10)	W52-O529	2.137(10)
W12-N123	2.232(11)	W32-N323	2.252(13)	W52-N523	2.234(11)
W12-N127	2.236(12)	W32-N327	2.237(13)	W52-N527	2.237(11)
W12-S11	2.322(4)	W32-S31	2.337(4)	W52-S51	2.321(4)
W12-S12	2.344(4)	W32-S32	2.334(5)	W52-S52	2.320(4)
C118-O118	1.228(8)	C318-O318	1.228(8)	C518-O518	1.230(8)
C118-O119	1.282(8)	C318-O319	1.283(8)	C518-O519	1.284(8)
C128-O128	1.228(8)	C328-O328	1.228(8)	C528-O528	1.230(8)
C128-O129	1.283(8)	C328-O329	1.283(8)	C528-O529	1.284(8)
W21-O21	1.700(11)	W41-O41	1.722(10)	W61-O61	1.703(10)
W21-O219	2.173(10)	W41-O419	2.181(10)	W61-O619	2.203(10)
W21-N213	2.236(11)	W41-N413	2.242(12)	W61-N613	2.209(12)
W21-N217	2.237(12)	W41-N417	2.212(11)	W61-N617	2.224(12)
W21-S21	2.330(4)	W41-S41	2.322(4)	W61-S61	2.348(4)
W21-S22	2.338(4)	W41-S42	2.336(4)	W61-S62	2.325(4)
W22-O22	1.706(11)	W42-O42	1.700(11)	W62-O62	1.700(10)
W22-O229	2.187(11)	W42-O429	2.168(10)	W62-O629	2.179(9)
W22-N223	2.226(11)	W42-N423	2.236(11)	W62-N623	2.229(10)
W22-N227	2.239(12)	W42-N427	2.237(11)	W62-N627	2.226(12)
W22-S21	2.324(4)	W42-S41	2.313(4)	W62-S61	2.322(4)
W22-S22	2.335(4)	W42-S42	2.338(4)	W62-S62	2.324(4)
C218-O218	1.228(8)	C418-O418	1.229(8)	C618-O618	1.229(8)
C218-O219	1.283(8)	C418-O419	1.283(8)	C618-O619	1.283(8)
C228-O228	1.228(8)	C428-O428	1.229(8)	C628-O628	1.230(8)
C228-O229	1.283(8)	C428-O429	1.284(8)	C628-O629	1.284(8)

O11-W11-O119	161.9(4)	O31-W31-O319	161.9(5)	O51-W51-O519	161.4(4)
N113-W11-S11	159.9(3)	N313-W31-S31	161.6(3)	N513-W51-S51	161.1(3)
N117-W11-S12	158.8(3)	N317-W31-S32	158.6(3)	N517-W51-S52	157.5(3)
S11-W11-S12	104.29(14)	S31-W31-S32	103.73(16)	S51-W51-S52	103.64(14)
O12-W12-O129	160.8(5)	O32-W32-O329	159.7(5)	O52-W52-O529	158.4(4)
N123-W12-S12	162.3(3)	N323-W32-S32	160.0(3)	N523-W52-S52	163.8(3)
N127-W12-S11	157.6(3)	N327-W32-S31	158.9(3)	N527-W52-S51	158.3(3)
S11-W12-S12	104.27(14)	S31-W32-S32	103.73(16)	S51-W52-S52	104.14(14)
W11-S11-W12	74.62(11)	W31-S31-W32	74.71(12)	W51-S51-W52	74.77(13)
W11-S12-W12	74.10(12)	W31-S32-W32	75.03(13)	W51-S52-W52	74.94(13)
C112-N113-C114	105.2(11)	C312-N313-C314	105.4(11)	C512-N513-C514	106.0(11)
C112-N113-W11	122.4(9)	C312-N313-W31	122.5(9)	C512-N513-W51	123.3(8)
C114-N113-W11	129.7(9)	C314-N313-W31	131.5(8)	C514-N513-W51	130.6(9)
C117-N117-W11	111.5(8)	C317-N317-W31	112.2(8)	C517-N517-W51	112.6(8)
C118-O119-W11	121.5(8)	C318-O319-W31	119.7(9)	C518-O519-W51	122.4(8)
C122-N123-C124	105.9(11)	C322-N323-C324	105.7(12)	C522-N523-C524	105.5(11)
C122-N123-W12	122.8(9)	C322-N323-W32	123.5(10)	C522-N523-W52	122.1(8)
C124-N123-W12	131.3(8)	C324-N323-W32	130.7(9)	C524-N523-W52	130.8(9)
C127-N127-W12	112.0(8)	C327-N327-W32	112.3(8)	C527-N527-W52	111.7(8)
C128-O129-W12	122.2(8)	C328-O329-W32	122.5(8)	C528-O529-W52	121.6(8)
O21-W21-O219	160.2(5)	O41-W41-O419	160.9(4)	O61-W61-O619	159.3(4)
N213-W21-S21	160.4(3)	N413-W41-S41	162.0(3)	N613-W61-S61	159.2(3)
N217-W21-S22	159.6(3)	N417-W41-S42	158.6(3)	N617-W61-S62	161.1(3)
S21-W21-S22	102.88(16)	S41-W41-S42	103.49(14)	S61-W61-S62	102.15(14)
O22-W22-O229	160.3(5)	O42-W42-O429	161.2(4)	O62-W62-O629	156.5(4)
N223-W22-S22	160.8(3)	N423-W42-S42	161.0(3)	N623-W62-S62	160.2(3)
N227-W22-S21	160.0(3)	N427-W42-S41	157.5(3)	N627-W62-S61	163.7(3)
S21-W22-S22	103.15(15)	S41-W42-S42	103.72(14)	S61-W62-S62	102.97(15)
W21-S21-W22	75.20(12)	W41-S41-W42	75.27(13)	W61-S61-W62	74.33(13)
W21-S22-W22	74.83(12)	W41-S42-W42	74.54(13)	W61-S62-W62	74.72(13)
C212-N213-C214	105.5(11)	C412-N413-C414	105.3(12)	C612-N613-C614	105.9(12)
C212-N213-W21	122.9(9)	C412-N413-W41	122.7(9)	C612-N613-W61	123.8(9)
C214-N213-W21	130.1(8)	C414-N413-W41	132.0(9)	C614-N613-W61	130.3(9)
C217-N217-W21	113.1(8)	C417-N417-W41	112.1(8)	C617-N617-W61	113.4(9)
C218-O219-W21	122.3(8)	C418-O419-W41	119.5(8)	C618-O619-W61	121.6(8)
C222-N223-C224	105.5(11)	C422-N423-C424	106.4(11)	C622-N623-C624	105.6(10)
C222-N223-W22	122.8(9)	C422-N423-W42	123.2(8)	C622-N623-W62	124.1(8)
C224-N223-W22	131.6(8)	C424-N423-W42	130.2(9)	C624-N623-W62	130.3(8)
C227-N227-W22	112.2(9)	C427-N427-W42	112.8(8)	C627-N627-W62	113.1(8)
C228-O229-W22	121.3(9)	C428-O429-W42	121.9(8)	C628-O629-W62	121.7(8)

O11-W11-W12-O12	-2.5(6)	O31-W31-W32-O32	-1.8(5)	O51-W51-W52-O52	-2.9(5)
O11-W11-W12-O129	178.6(7)	O31-W31-W32-O329	-179.4(5)	O51-W51-W52-O529	178.5(5)
O119-W11-W12-O12	-179.4(10)	O319-W31-W32-O32	-179.6(16)	O519-W51-W52-O52	178.9(7)
O119-W11-W12-O129	1.7(4)	O319-W31-W32-O329	2.8(4)	O519-W51-W52-O529	0.0(7)
N113-W11-W12-N123	-155.3(6)	N313-W31-W32-N323	-154.4(7)	N513-W51-W52-N523	-159.1(6)
N113-W11-W12-N127	-4.5(6)	N313-W31-W32-N327	-5.4(6)	N513-W51-W52-N527	-3.7(6)
N117-W11-W12-N123	-6.4(6)	N317-W31-W32-N323	-3.2(7)	N517-W51-W52-N523	-12.4(6)
N117-W11-W12-N127	144.4(6)	N317-W31-W32-N327	145.7(6)	N517-W51-W52-N527	143.0(6)
S12-W11-S11-W12	12.70(15)	S32-W31-S31-W32	12.82(15)	S52-W51-S51-W52	12.09(14)
S11-W11-S12-W12	-12.61(13)	S31-W31-S32-W32	-12.81(15)	S51-W51-S52-W52	-12.08(16)
S12-W12-S11-W11	-12.65(14)	S32-W32-S31-W31	-12.78(16)	S52-W52-S51-W51	-12.14(15)
S11-W12-S12-W11	12.65(14)	S31-W32-S32-W31	12.84(17)	S51-W52-S52-W51	12.17(15)
O21-W21-W22-O22	-1.4(5)	O41-W41-W42-O42	-3.3(4)	O61-W61-W62-O62	-1.4(4)
O21-W21-W22-O229	-177.5(6)	O41-W41-W42-O429	178.4(5)	O61-W61-W62-O629	-174.3(5)
O219-W21-W22-O22	-178.5(4)	O419-W41-W42-O42	178.8(3)	O619-W61-W62-O62	-173.3(5)
O219-W21-W22-O229	5.4(4)	O419-W41-W42-O429	0.5(13)	O619-W61-W62-O629	13.8(4)
N213-W21-W22-N223	-156.4(7)	N413-W41-W42-N423	-157.4(7)	N613-W61-W62-N623	-157.9(6)
N213-W21-W22-N227	-1.1(8)	N413-W41-W42-N427	-8.8(7)	N613-W61-W62-N627	9.5(6)
N217-W21-W22-N223	-2.9(7)	N417-W41-W42-N423	-4.4(6)	N617-W61-W62-N623	2.3(6)
N217-W21-W22-N227	152.5(6)	N417-W41-W42-N427	144.2(6)	N617-W61-W62-N627	169.7(6)
S22-W21-S21-W22	15.16(15)	S42-W41-S41-W42	13.23(15)	S62-W61-S61-W62	18.34(14)
S21-W21-S22-W22	-15.11(15)	S41-W41-S42-W42	-13.13(14)	S61-W61-S62-W62	-18.28(15)
S22-W22-S21-W21	-15.20(14)	S42-W42-S41-W41	-13.23(14)	S62-W62-S61-W61	-18.41(15)
S21-W22-S22-W21	15.17(14)	S41-W42-S42-W41	13.19(14)	S61-W62-S62-W61	18.56(14)

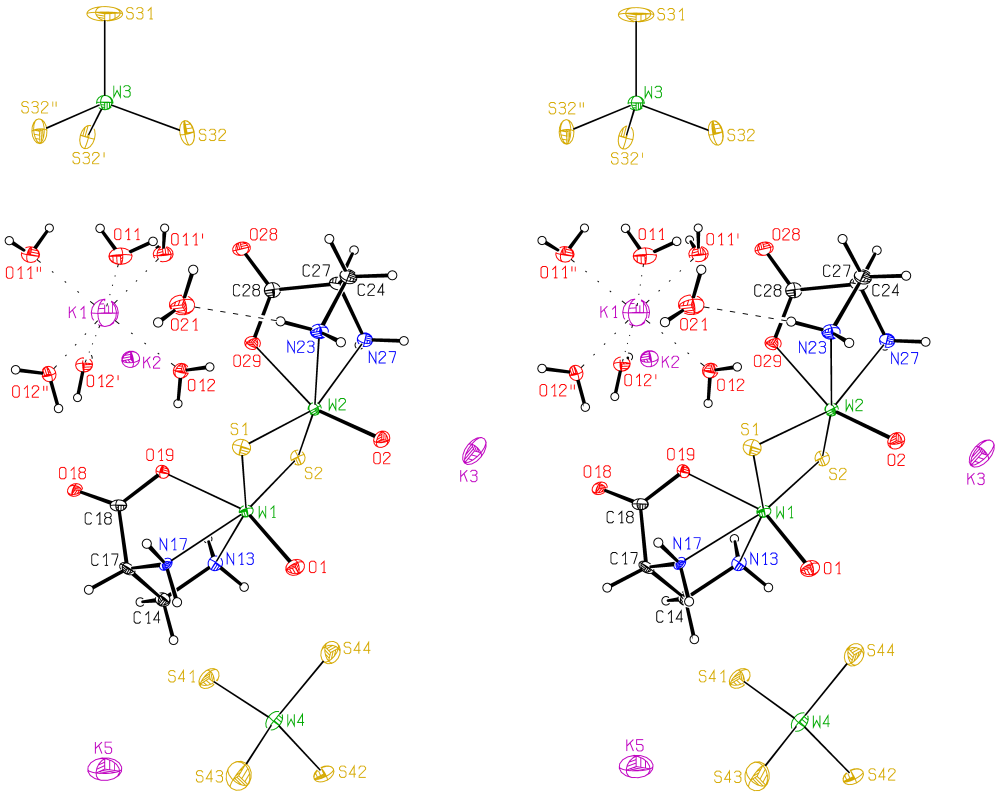


Fig. S4 Stereoscopic ORTEP[3] plot of **3** (together with co-crystallized K^+, H_2O and WS_4^{2-}) normal to the three-fold rotation axis through the atoms S31, W3, K1, K5 showing the atomic numbering scheme. The probability ellipsoids are drawn at the 50% probability level, the H atoms are drawn with arbitrary radii. The atoms with site occupation factors less than 0.5 were omitted for clarity. The hydrogen bond is indicated by a dashed line, the coordination of K1 by dotted lines.

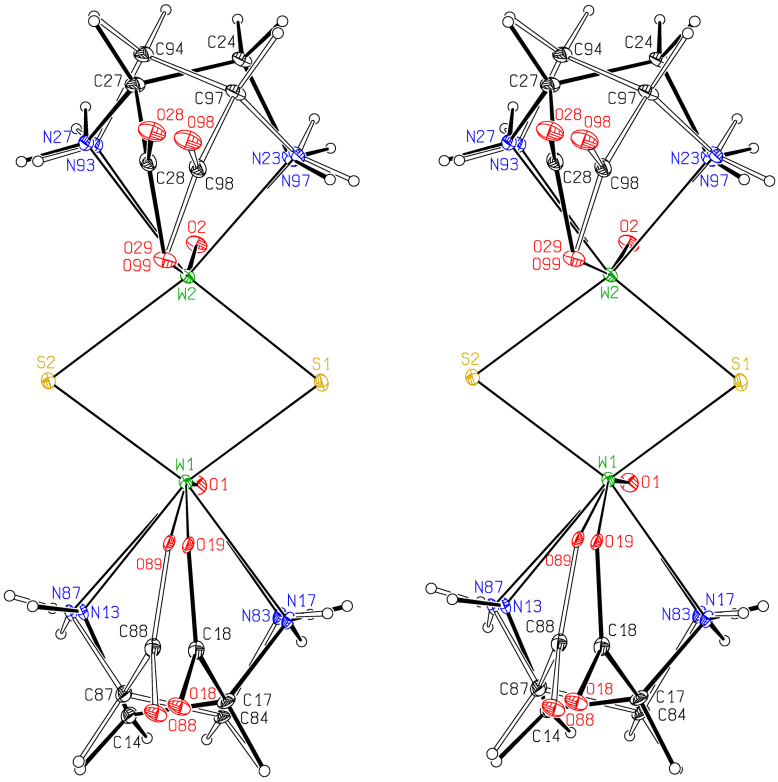


Fig. S5 Stereoscopic ORTEP[3] plot of complex **3**. The probability ellipsoids are drawn at the 20% probability level, the H atoms are drawn with arbitrary radii. The ligands in the less prominent occupied orientations were plotted with open bonds.

Table S3 Selected bond lengths [Å] and angles [°] for **3**.

W1-O1	1.7236(15)	W2-O2	1.7225(14)
W1-O19	2.1820(19)	W2-O29	2.1942(19)
W1-N13	2.184(4)	W2-N23	2.189(4)
W1-N17	2.301(4)	W2-N27	2.288(4)
W1-S1	2.3280(5)	W2-S1	2.3230(5)
W1-S2	2.3294(5)	W2-S2	2.3297(5)
N13-C14	1.492(10)	N23-C24	1.505(14)
C14-C17	1.527(4)	C24-C27	1.516(4)
C17-N17	1.483(8)	C27-N27	1.496(15)
C17-C18	1.517(4)	C27-C28	1.535(4)
C18-O18	1.227(3)	C28-O28	1.220(3)
C18-O19	1.292(3)	C28-O29	1.313(12)
W3-S31	2.1489(13)	W4-S41	2.1810(6)
W3-S32	2.1982(6)	W4-S42	2.1863(6)
W3-S32[i)]	2.1982(6)	W4-S43	2.1885(8)
W3-S32[ii)]	2.1982(6)	W4-S44	2.2190(7)

O1-W1-O19	156.97(11)	O2-W2-O29	159.0(4)
N13-W1-S1	158.26(18)	N27-W2-S1	157.1(4)
N17-W1-S2	157.9(2)	N23-W2-S2	158.0(3)
S1-W1-S2	104.040(18)	S1-W2-S2	104.186(17)
W1-S1-W2	74.122(14)	W1-S2-W2	73.972(14)
C14-N13-W1	115.1(4)	C24-N23-W2	115.1(6)
C17-N17-W1	102.9(3)	C27-N27-W2	102.6(5)
C18-O19-W1	119.3(2)	C28-O29-W2	116.8(6)

S1-W1-S2-W2	14.67(3)	S1-W2-S2-W1	-14.71(4)
S2-W1-S1-W2	-14.70(3)	S2-W2-S1-W1	14.71(4)
O1-W1-W2-O2	1.18(9)	O19-W1-W2-O29	-8.4(10)
W1-N13-C14-C17	27.7(9)	W2-N23-C24-C27	26.4(12)
C14-C17-N17-W1	58.8(4)	C24-C27-N27-W2	59.7(10)
C18-C17-N17-W1	-55.8(4)	C28-C27-N27-W2	-53.3(10)
C17-C18-O19-W1	12.7(5)	C27-C28-O29-W2	7.6(23)
O18-C18-O19-W1	-166.6(4)	O28-C28-O29-W2	-166.3(9)

Symmetry transformations used to generate equivalent atoms:

[i] 1-y, x-y+1, z [ii] y-x, 1-x, z

Table S4 Hydrogen bonds for **3** [Å, °].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
N13-H131···O18[i]	0.91	2.05	2.951(17)	170.4
N17-H171···O2[ii]	0.91	2.19	3.089(8)	168.8
N17-H172···O1[ii]	0.91	2.5	3.158(6)	129.3
N83-H831···O2[ii]	0.91	2.22	2.982(15)	140.6
N87-H871···O88[i]	0.91	2.04	2.75(3)	134.4
N23-H231···O21	0.91	2.21	3.12(2)	174.5
N23-H232···S32[iii]	0.91	2.5	3.332(15)	151.9
N97-H971···O21	0.91	2.26	3.04(4)	144.3
O11-H111···O28	0.84	2.068(4)	2.831(4)	150.9(5)
O11-H111···O98	0.84	1.855(9)	2.616(8)	150.0(8)
O12-H121···O18[i]	0.84	1.961(8)	2.789(8)	168.4(9)
O12-H121···O88[i]	0.84	2.084(15)	2.923(15)	176.1(10)
O12-H122···O29	0.84	2.151(18)	2.918(14)	151.6(10)
O12-H122···O99	0.84	2.17(3)	2.93(2)	151.8(15)
O21-H211···O28[iv]	0.84	1.993(5)	2.799(5)	160.6(6)
O21-H211···O98[iv]	0.84	1.843(9)	2.679(9)	173.4(7)

Symmetry transformations used to generate equivalent atoms:

[i] 1-y, x-y+1, z [ii] x-y+1/3, x-1/3, 2/3-z [iii] x-y+1, x, 1-z [iv] 1-x, 1-y, 1-z

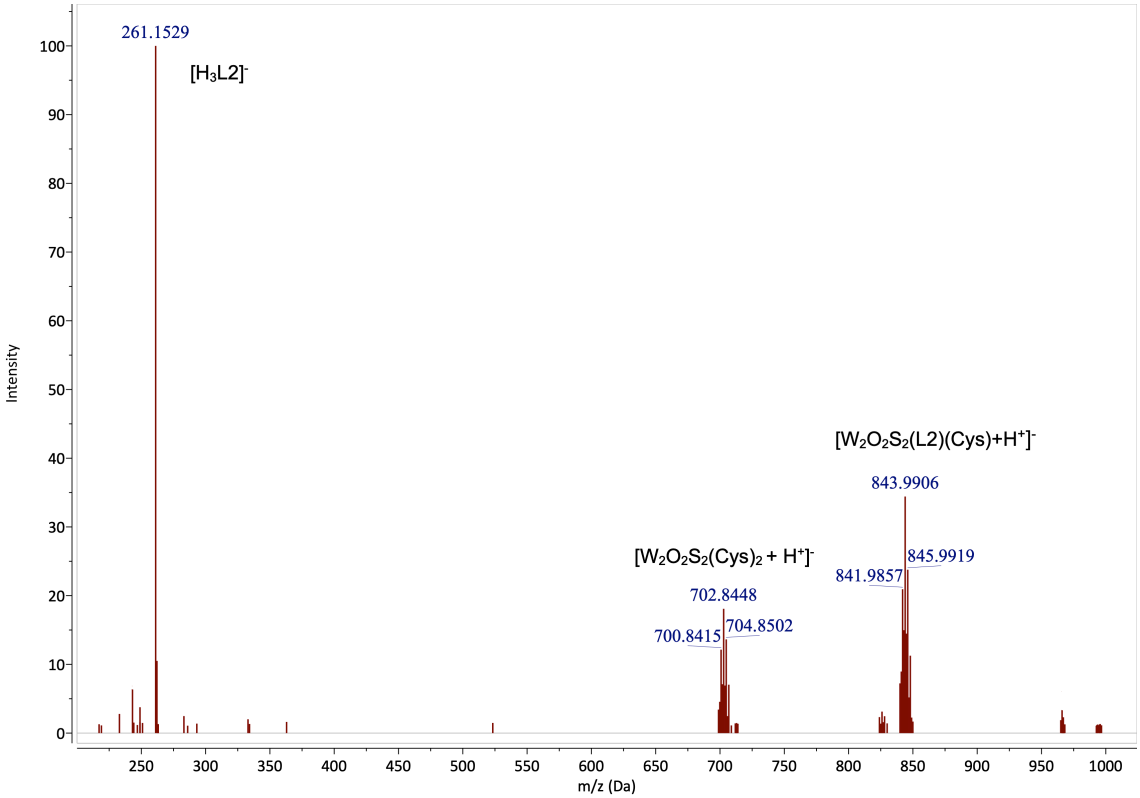


Fig. S6 ESI-HRMS (-) spectra of the poorly soluble crude product obtained after the reaction of **1a** and **L2** conducted at pH 1.

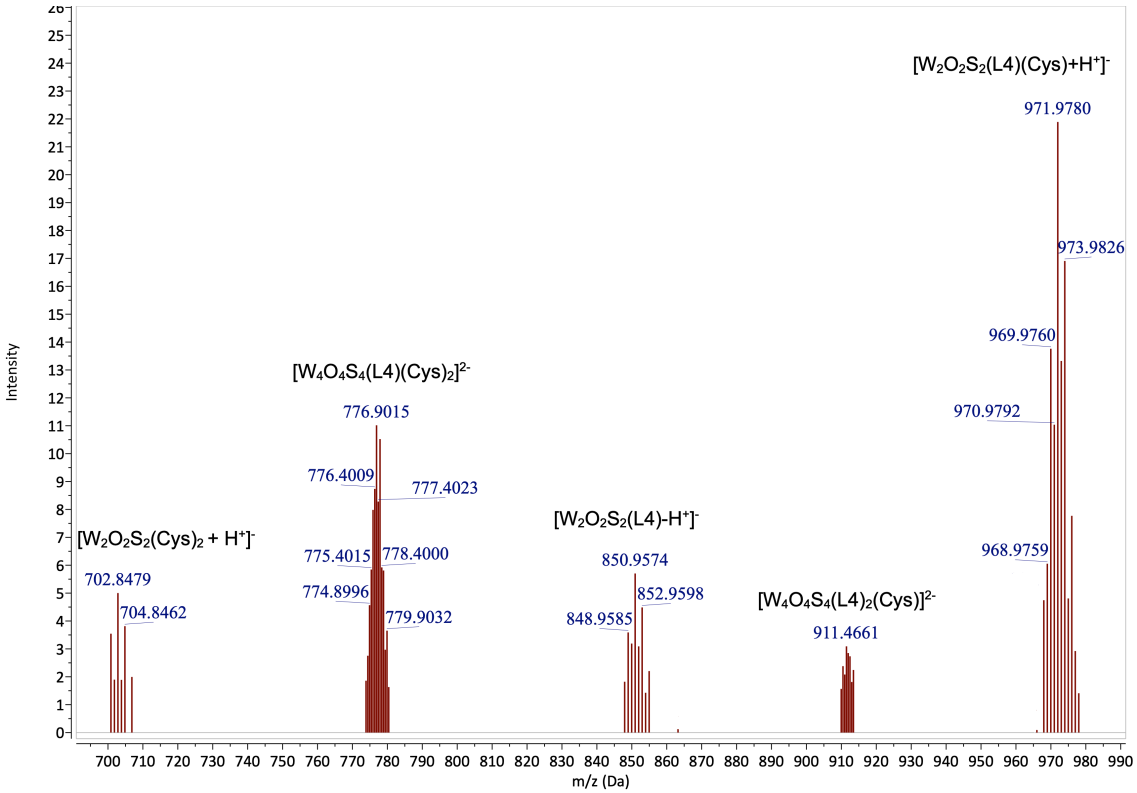


Fig. S7 Main tungsten-containing species observed in the ESI-HRMS (-) spectra of the poorly soluble crude product obtained after the reaction of **1a** and **L4** conducted at pH 1.

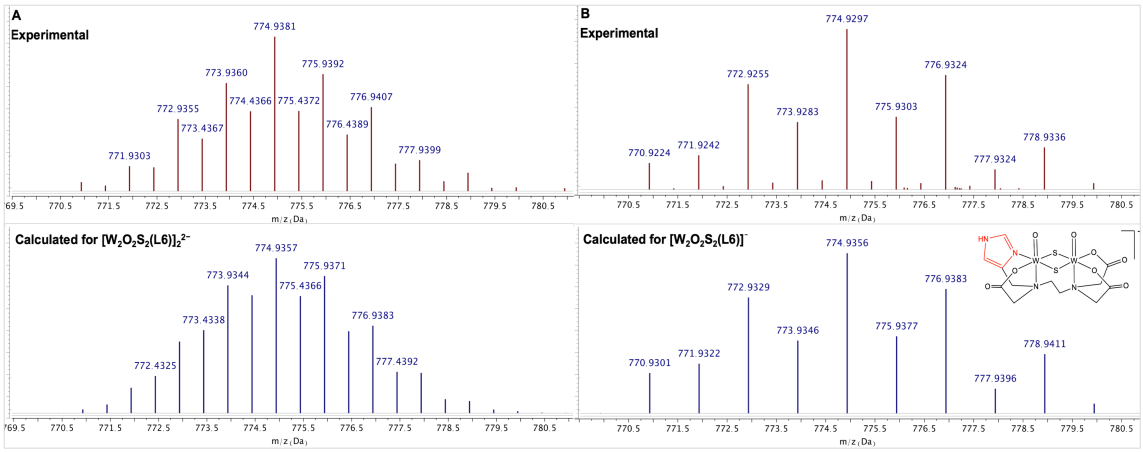


Fig. S8 ESI-HRMS (-) spectra of the crude product obtained after the reaction of **1a** and **L6** conducted at pH 1. A) sample, dissolved in acetate buffer at pH= 4.5 and rt; B) sample, dissolved in water at ~ 80 °C. Experimental spectrum vs. simulated isotopic pattern for $[W_2O_2S_2(L6)]_2^{2-}$ (A) and $[W_2O_2S_2(L6)]^-$ (B) are shown.

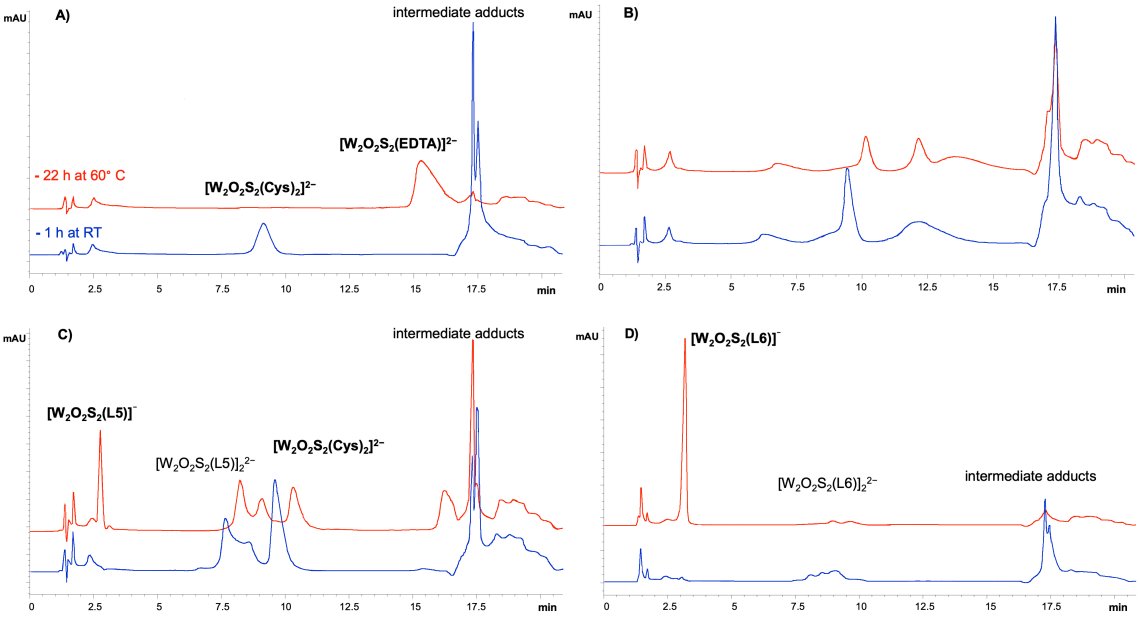


Fig. S9 Reactivity of **1b** towards EDTA (A), HEDTA (B), L5 (C), and L6 (D) at pH 4 after 1 h of incubation at rt (blue) and 22 h at 60 °C (red) as followed by RPIP-HPLC. Mobile phase consisted of 0.1% Bu_4NCl/MeOH (65/35 at 0-14 min and 40/60 at 14.5-18.5 min). Overlay of HPLC chromatograms recorded at 230 nm is shown.

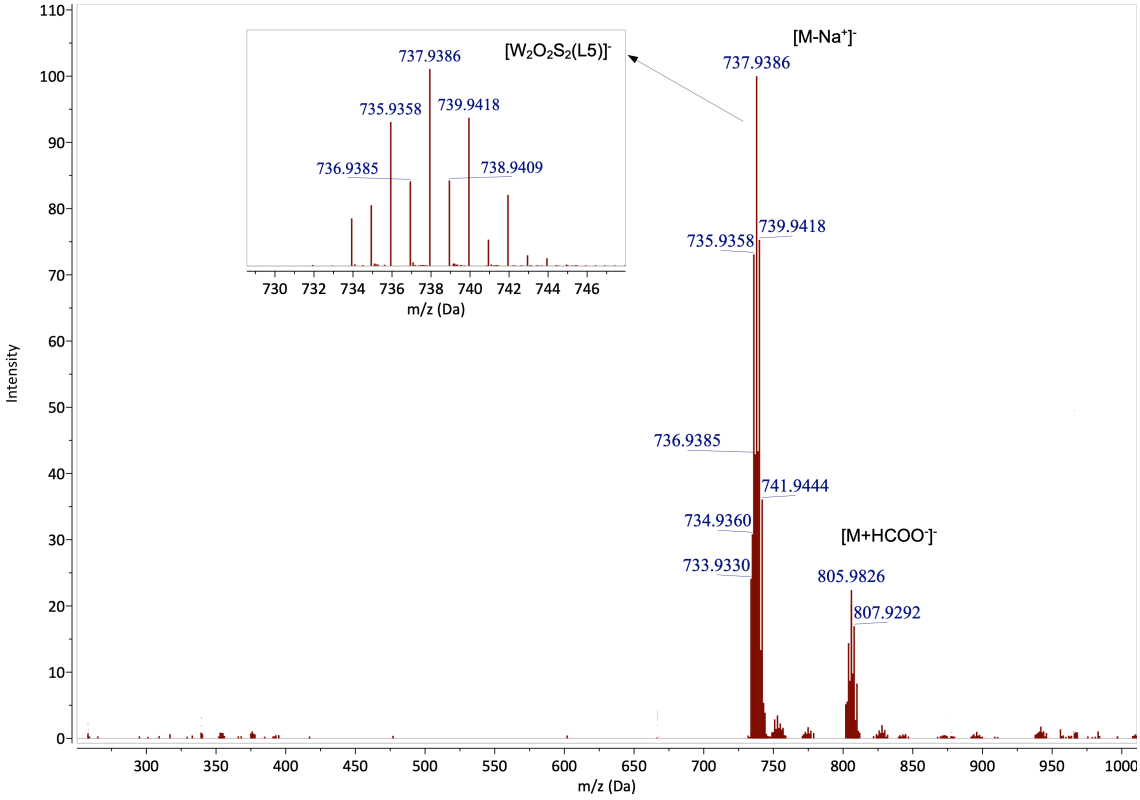


Fig. S10 ESI-HRMS (-) spectra of Na[$W_2O_2S_2$(L5)] (**5b**).

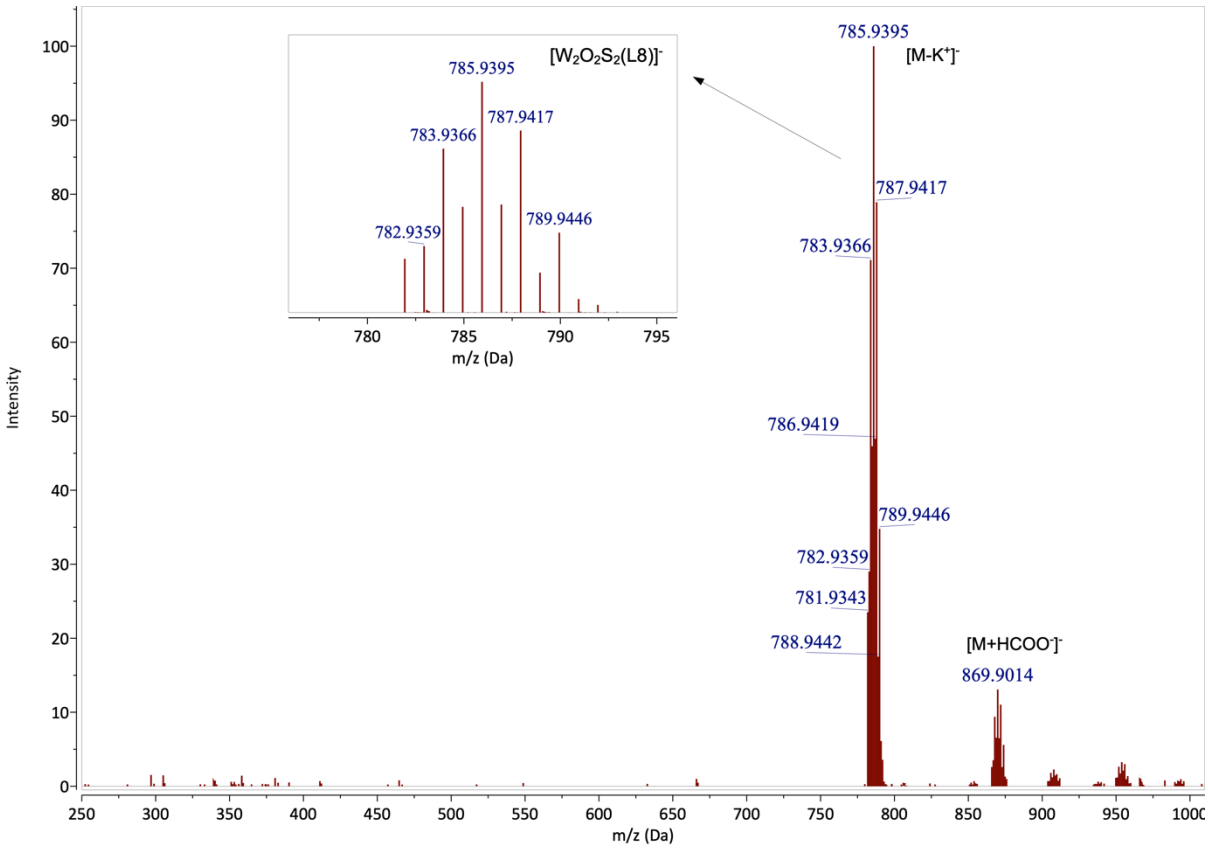


Fig. S11 ESI-HRMS (-) spectra of K[$W_2O_2S_2$(L8)] (**8a**)

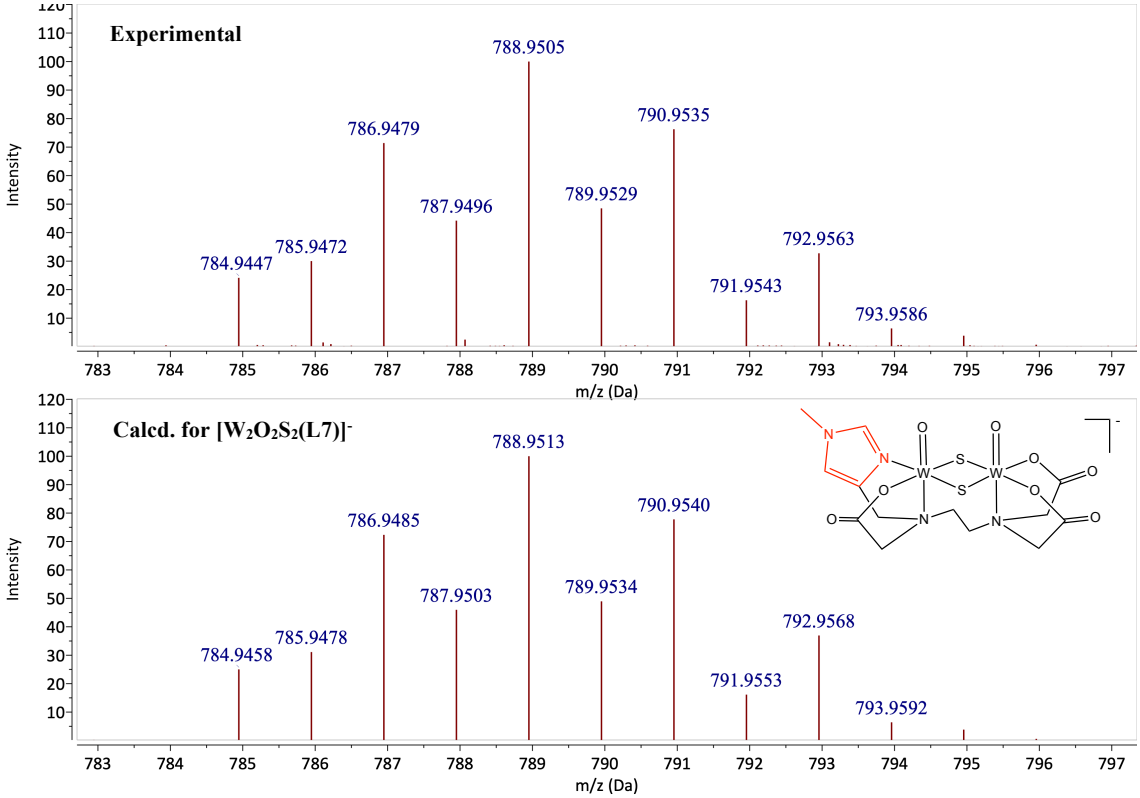


Fig. S12 ESI-HRMS (-) spectra of K[$W_2O_2S_2$(L7)] (**7a**). Experimental spectrum vs. simulated isotopic pattern for [$W_2O_2S_2$(L7)]$^-$ is shown.

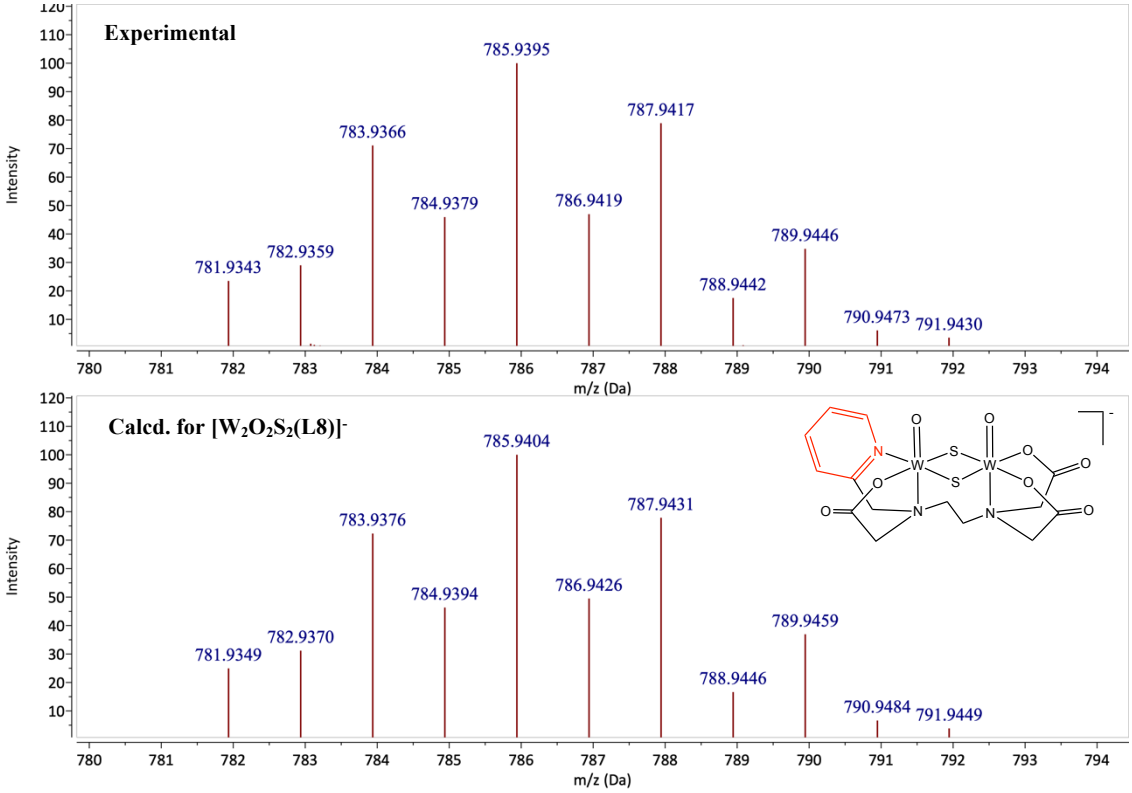


Fig. S13 ESI-HRMS (-) spectra of K[$W_2O_2S_2$(L8)] (**8a**). Experimental spectrum vs. simulated isotopic pattern for [$W_2O_2S_2$(L8)]$^-$ is shown.

Table S5 Approximate water solubility, retention time and HPLC purity of sulfido-bridged W(V) dinuclear complexes under investigation. A mobile phase containing 0.1% Bu_4NCl in water/MeOH (62/38 at 0-12 min, 40/60 at 12.5-16 min) was used in the HPLC experiments. HPLC purity was calculated from the chromatograms recorded at 230 nm.

Compound	Formula	Aq. solubility (mg/ml)[a]	t_R (min)	HPLC purity (%)
2	$[W_2O_2S_2(His)_2]$	< 0.5	1.5	> 99
3	$[W_2O_2S_2(DAPA)_2]$	< 0.5	1.5	95
4	$[W_2O_2S_2(L1)]$	< 0.5	-[b]	-[b]
5a	$K[W_2O_2S_2(L5)]$	1.5	2.8	> 98
5b	$Na[W_2O_2S_2(L5)]$	1.8	2.8	> 96
6a	$K[W_2O_2S_2(L6)]$	1.5	3.1	> 99
6b	$Na[W_2O_2S_2(L6)]$	1.6	3.0	100
6c	$(NH_4)[W_2O_2S_2(L6)]$	1.5	3.1	> 99
7a	$K[W_2O_2S_2(L7)]$	8.2	3.2	> 99
7b	$Na[W_2O_2S_2(L7)]$	5.1	3.2	> 99
8a	$K[W_2O_2S_2(L8)]$	8.4	3.6	> 99
8b	$Na[W_2O_2S_2(L8)]$	10	3.6	100
1a	$K_2[W_2O_2S_2(Cys)_2]$	28	7.7	> 99
1b	$Na_2[W_2O_2S_2(Cys)_2]$	150	7.8	> 99
1c	$(NH_4)_2[W_2O_2S_2(Cys)_2]$	60	7.8	> 99
9a	$K_2[W_2O_2S_2(EDTA)]$	18	10.6	100
9b	$Na_2[W_2O_2S_2(EDTA)]$	42	10.6	> 99

[a] approximate water solubility was determined at room temperature by pipetting of minimal amounts of Milli-Q water to a weighted amount of substance until a clear solution is obtained (after gentle warming, shaking and sonication for 2-5 minutes). The obtained solutions were stable for several days at room temperature without signs of precipitation.

[b] aqueous solubility of **4** was insufficient to get a distinguished signal in the chromatogram.

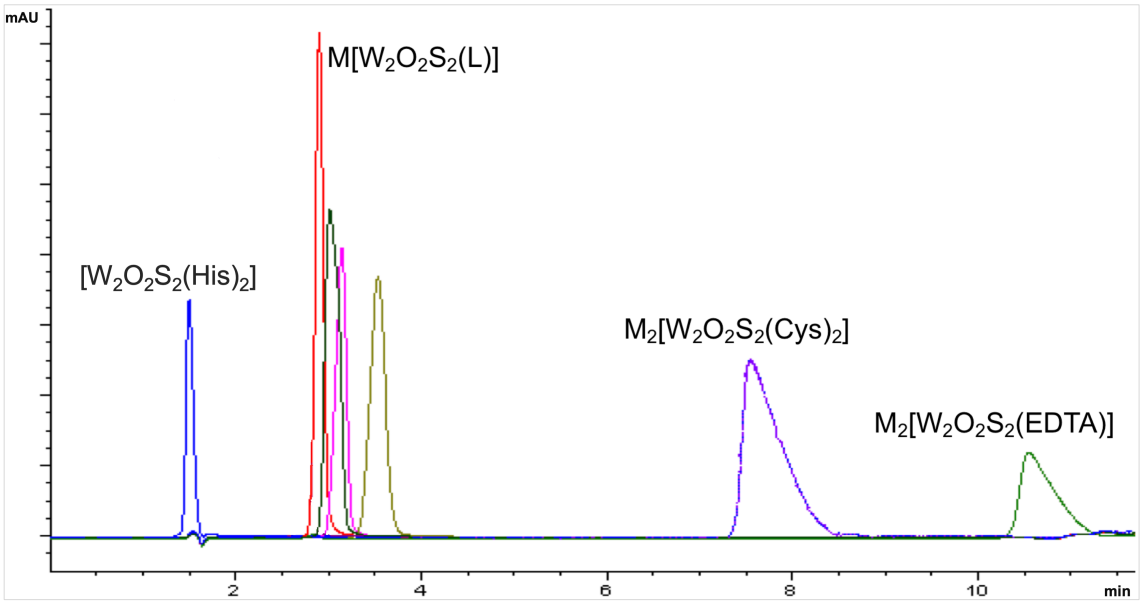


Fig. S14 HPLC chromatograms of sulfido-bridged W(V) dimeric complexes; L = L5-8, $M^+ = K^+$ or Na^+. Mobile phase consisted of 0.1% Bu_4NCl/MeOH (62/38); overlay of chromatograms recorded at 230 nm is shown.

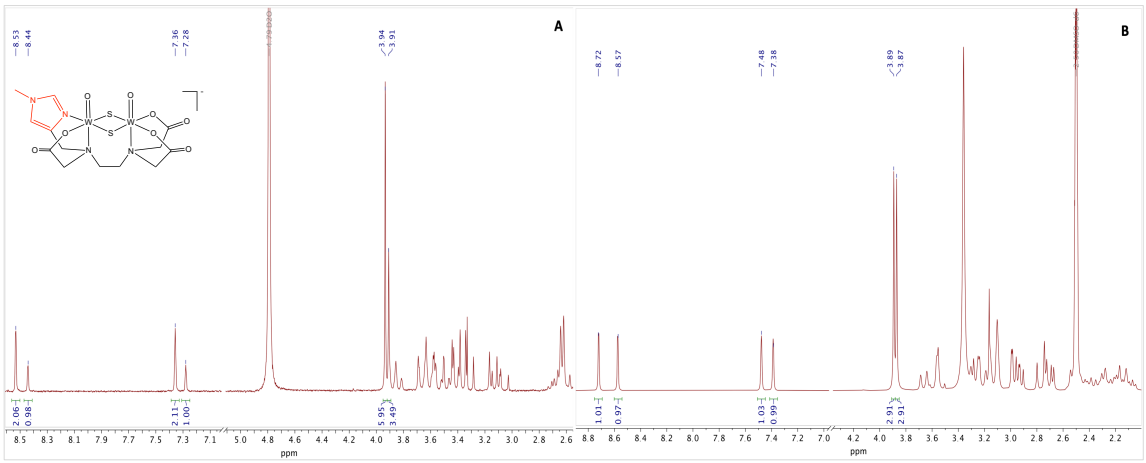


Fig. S15 ^1H NMR spectra of complex **7b** in D_2O (A) and in DMSO-d_6 (B); measurements were carried out at ambient temperature.

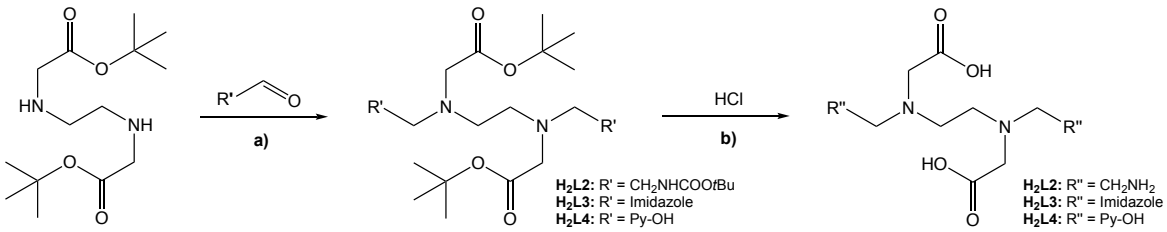
Synthesis and characterization of L1-8

EDTA analogues L1-8 were synthesized by WuXi AppTec Co., Ltd at the request of T. Brumby. Their identity and purity were verified by ^{1}H and ^{13}C NMR spectroscopy, ESI-HRMS, and ion chromatography (Instrument: Thermo Scientific ICS 5000+; Capillary IC Column: IonPac AS11-HC and IonPac CS16; Gradient Eluent $[H]^{+}$ $[OH]^{-}$; Detector: conductivity detection) at Bayer AG and at the Institute of Chemistry, University of Graz.

N,N'-1,2-ethanediylbis[N-(2-amino-2-oxoethyl)-glycine] hydrochloride (H_2L1·HCl)

Synthesis was carried out according to the published procedure[4] with minor revisions; the compound was isolated as a hydrochloride salt in 60% yield. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.74 (s, 2H, NH_2), 7.42 (s, 2H, NH_2), 3.78 (s, 4H, CH_2COO), 3.64 (s, 4H, CH_2CON), 3.12 (s, 4H, CH_2N) ppm. ^{13}C NMR (DMSO-d_6, 101 MHz): δ 170.5 (COOH), 170.3 ($CONH_2$), 55.8 (CH_2COO), 54.4 (CH_2CON), 51.2 (CH_2N) ppm. ESI-HRMS(-) found (calculated): *m/z* $[M\text{-}H^{+}]^{-}$, 289.1148 (289.1154). Ion chromatography gave 8.5% (0.76 equiv) of chloride.

H_2L2-4 were synthesized according to **Scheme S1.** The precursor, N,N'-1,2-ethanediylbis-glycine, 1,1'-bis(1,1-dimethylethyl) ester, was prepared as described in literature.[5,6]



Scheme S1. Synthesis of H_2L2-4

***N,N'*-1,2-ethanediyl-bis[N-(2-aminoethyl)-glycine] tetrahydrochloride (H_2L2·4HCl)**

***a) N,N'*-1,2-ethanediylbis[N-{2-[(1,1-dimethyl-ethoxycarbonyl)amino]ethyl}-glycine] 1,1'-bis(1,1-dimethyl-ethyl)ester.**

Sodium triacetoxyborohydride (26.5 g, 125.03 mmol) was added to a solution of N,N'-1,2-ethanediylbis-glycine, 1,1'-bis(1,1-dimethylethyl) ester (7 g, 24.27 mmol) and tert-butyl *N*-(2-oxoethyl)carbamate (16 g, 100.51 mmol) in DCM (200 mL). The mixture was stirred at room temperature for 2.5 hours, after which LC-MS indicated the reaction to be complete. The mixture was treated with K_2CO_3 (aq., 20%) until pH 9 was reached, and combined with another batch (2.25 g, 7.81 mmol obtained in the same way as above). The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuum. The residue was purified by column chromatography on silica gel (petroleum ether : ethyl acetate = 15:1 to 5:1) to afford the title compound (12.5 g, 68%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.76 (br s, 2H), 3.31 (s, 4H), 3.17 (s, 4H), 2.77-2.74 (m, 8H), 1.53 (s, 18H), 1.51 (s, 18H) ppm.

***b) N,N'*-1,2-ethanediyl-bis[N-(2-aminoethyl)-glycine] tetrahydrochloride**

A mixture of N,N'-1,2-ethanediylbis[N-{2-[(1,1-dimethyl-ethoxycarbonyl)amino]ethyl}-glycine] 1,1'-bis(1,1-dimethyl-ethyl)ester (12.3 g, 21.40 mmol) and HCl/dioxane (4 M, 125 mL) was stirred at room temperature for 16 h. The mixture was concentrated in vacuum. The residue was dissolved in water (125 mL) and lyophilized to afford the title compound (8.7 g, 99%) as a grey solid. ^{1}H NMR (D_2O, 400 MHz): δ 3.77 (s, 4H), 3.17-3.25 (m, 12H) ppm. ^{13}C NMR (D_2O, 101 MHz): δ 175.1, 172.5, 54.3, 52.1, 52.1, 35.4 ppm. ESI-HRMS(-) found (calculated): *m/z* [M-H$^+$]$^-$, 261.1562 (261.1568). Ion chromatography gave 34.75% (4.0 equiv.) of chloride. An impurity (ca. 5%, possibly a lactam) is present. The material was used as such for further experiments.

***N,N'*-1,2-ethanediyl-bis[N-(1H-imidazol-4-ylmethyl)-glycine] tetrahydrochloride (H_2L3·4HCl)**

***a) N,N'*-1,2-ethanediyl-bis[N-(1H-imidazol-4-ylmethyl)-glycine] 1,1'-bis(1,1-dimethyl-ethyl)ester.**

Sodium triacetoxyborohydride (85.1 g, 401.53 mmol) and 1*H*-imidazole-4-carbaldehyde (17 g, 176.92 mmol) were added to a mixture of N,N'-1,2-ethanediylbis-glycine, 1,1'-bis(1,1-dimethylethyl) ester (23 g, 79.76 mmol) in DCM (600 mL). The reaction mixture was stirred at room temperature (rt) for 16 h, after which LC-MS indicated the reaction to be completed. The reaction mixture was diluted with saturated aq. NH_4Cl (200 mL) and K_2CO_3 was added until pH of the aqueous phase exceeded 9. Two phases were separated, and the aqueous phase was extracted with DCM (300 mL). The combined organic phase was washed with brine (200 mL), dried over $MgSO_4$, filtered through a pad of celite and concentrated under reduced pressure to give 50 g of crude product as a yellow oil. The later was purified by reversed phase column chromatography (0.5% HCOOH in H_2O /ACN = 90/10). Solid K_2CO_3 was added to the obtained colorless solution until pH > 9. The resulting solution was concentrated under reduced pressure to remove ACN. The residue was extracted by DCM (300 mL x 2). The combined organic phase was washed with brine (200 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the title compound (10.5 g, 29%) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.57 (d, 2H), 6.82 (s, 2H), 3.66 (s, 4H), 3.19 (s, 4H), 2.65 (s, 4H), 1.40 (s, 18H) ppm.

***b) N,N'*-1,2-ethanediyl-bis[N-(1H-imidazol-4-ylmethyl)-glycine] tetrahydrochloride**

N,N'-1,2-ethanediyl-bis[N-(1H-imidazol-4-ylmethyl)-glycine] 1,1'-bis(1,1-dimethyl-ethyl)ester (10.5 g, 23.41 mmol) was suspended in HCl/dioxane (4 M, 200 mL) and stirred at rt for 20 hours. LC-MS indicated the reaction to be completed. A white solid was collected via filtration and subsequently dissolved in H_2O (60 mL). The resulting solution was lyophilized to give the title compound (9.1 g, 81%) as an off-white solid. ^{1}H NMR (D_2O, 400 MHz): δ 8.67 (d, *J*=1.3 Hz, 2H), 7.55 (d, *J*=1.3 Hz, 2H), 4.26 (s, 4H), 3.70 (s, 4H), 3.27 (s, 4H) ppm. ^{13}C NMR (D_2O, 101 MHz): δ 172.1, 135.0, 125.0, 120.6, 53.9, 51.0, 47.9 ppm. ESI-HRMS(-) found (calculated): *m/z* [M-H$^+$]$^-$, 335.1464 (335.1473). Ion chromatography gave 28.6% (3.8 equiv.) of chloride.

***N*,*N*'-1,2-ethanediylbis[*N*-((5-hydroxypyridin-2-yl)methyl)-glycine] tetrahydrochloride (H_2L4·4HCl)**

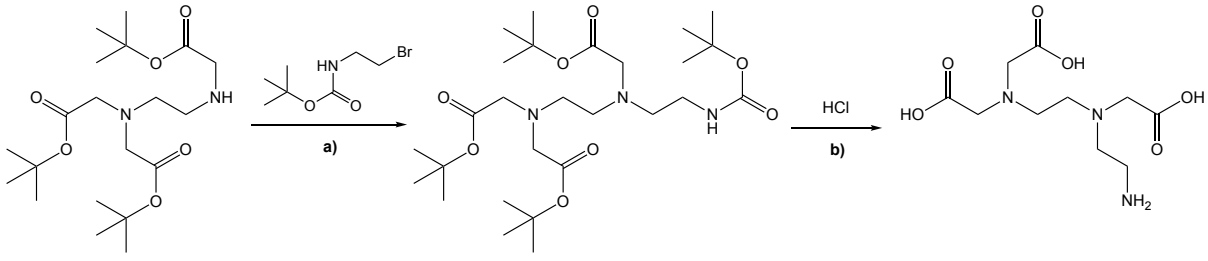
***a) N*,*N*'-1,2-ethanediylbis[*N*-(5-hydroxypyridin-2-yl)methyl)-glycine] 1,1'-bis(1,1-dimethyl-ethyl)ester**

Sodium triacetoxyborohydride (17.2 g, 81.2 mmol) and molecular sieves (2.50 g) were added to a solution of 5-hydroxy-2-pyridinecarboxaldehyde (5 g, 40.6 mmol) in DCM (150 mL). Then N,N'-1,2-ethanediylbis-glycine, 1,1'-bis(1,1-dimethylethyl) ester (3.51 g, 12.2 mmol) in DCM (50 mL) was added dropwise at 15 °C and the reaction was stirred at 15 °C for 12 h. The mixture was concentrated under reduced pressure and the residue was dissolved in 1 M HCl (100 ml). Subsequently, saturated aqueous K_2CO_3 was added until reaching pH 9 and the crude product was collected via filtration. The crude product was triturated with DCM (150 ml) at 15 °C for 4 h and filtered under reduced pressure to give the title compound (10.7 g) as a grey solid. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.99 (d, *J* = 2.8 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.10-7.06 (m, 2H), 3.67 (s, 4H), 3.22 (s, 4H), 2.63 (s, 4H), 1.38 (s, 18H) ppm.

***b) N*,*N*'-1,2-ethanediylbis[*N*-((5-hydroxypyridin-2-yl)methyl)-glycine] tetrahydrochloride**

N,*N*'-1,2-ethanediylbis[*N*-(5-hydroxypyridin-2-yl)methyl)-glycine]-1,1'-bis(1,1-dimethyl-ethyl)ester (16.6 g, 33.0 mmol) was dissolved in 6 M HCl (170 mL) and the reaction mixture was stirred at 70 °C for 20 h. Subsequently, the mixture was concentrated under vacuum to give the title compound (14.5 g, 82%) as a gray solid. ^{1}H NMR (D_2O, 400 MHz): δ 8.13 (dd, J=2.3, 0.8 Hz, 2H), 7.68-7.74 (m, 4H), 4.28 (s, 4H), 3.66 (s, 4H), 3.28 (s, 4H) ppm. ^{13}C NMR (D_2O, 101 MHz): δ 172.1, 155.4, 139.8, 131.9, 131.3, 128.5, 55.5, 54.4, 51.1 ppm. ESI-HRMS(-) found (calculated): *m/z* [M-H^+]$^-$, 389.1463 (389.1467); [M+Cl^-]$^-$, 425.1231 (425.1233). Ion chromatography gave 34.1% (> 4 equiv.) of chloride.

H_3L5 was synthesized according to **Scheme S2.** The precursor, *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]-amino]ethyl]-glycine, 1,1-dimethylethyl ester, was prepared as described in literature.[7]



Scheme S2. Synthetic pathway to H_3L5.

***N*-[2-aminoethyl]-*N*-[2-[bis[carboxymethyl]amino]ethyl]-glycinehydrochloride (H_3L5·HCl)**

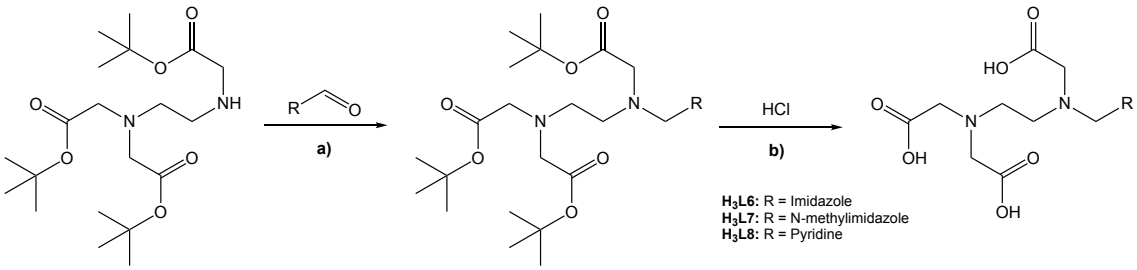
***a) N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-*N*-[2-[(1,1-dimethyl-ethoxy-carbonyl)amino]ethyl]-glycine, 1,1-dimethylethyl ester**

N-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-glycine, 1,1-dimethylethyl ester (120 g, 298 mmol), *N*-(2-bromoethyl)-carbamic acid 1,1-dimethyl-ethyl ester (86.8 g, 387 mmol) and K_2CO_3 (41.2 g, 298 mmol) in ACN (1.0 L) were stirred at 80 °C for 16 h, after which LC-MS indicated the reaction to be complete. The mixture was filtered and concentrated to give a residue. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate 100:1 to 0:1) to give the title compound (88.0 g, 48%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.44 (s, 4H), 3.29 (s, 2H), 3.17-3.14 (m, 2H), 2.86-2.73 (m, 6H), 1.46-1.44 (m, 36H) ppm.

***b) N*-[2-aminoethyl]-*N*-[2-[bis[carboxymethyl]amino]ethyl]-glycine hydrochloride**

To a mixture of N-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-N-[2-[(1,1-dimethyl-ethoxy-carbonyl)amino]ethyl]-glycine, 1,1-dimethylethyl ester (43.0 g, 78.8 mmol) in dioxane (220 mL) was added 4 M HCl (200 ml in dioxane) and stirred at 25 °C for 3 h. The mixture was filtered to give a residue, which was triturated with ethyl acetate (600 mL) to give the title compound (40.6 g, crude product) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.33 (br s, 3H, NH_3), 3.97 (s, 4H), 3.90 (s, 2H), 3.35 (br t, *J*=5.07 Hz, 2H), 3.24 (br t, *J*=6.21 Hz, 4H), 3.03-3.12 (m, 2H) ppm. ^{13}C NMR (DMSO-d_6, 101 MHz) δ 170.3, 170.1 (2C), 54.7 (2C), 53.2, 51.5, 51.0, 50.1, 35.2 ppm. ESI-HRMS(-) found (calculated): *m/z* $[M\text{-}H^+]^-$, 276.1188 (276.1201). Ion chromatography gave 17.1% (1.5 equiv.) of chloride. The preparation contains dioxane, EDTA and cyclic lactam (< 5%) as impurities. The material was used as such for further reactions towards tungsten complexes.

H_3L6-8 were prepared from *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]-amino]ethyl]-glycine, 1,1-dimethylethyl ester[7], according to **Scheme S3.**



Scheme S3. Synthesis of H_3L6-8.

***N*-[2-[bis[carboxymethyl]amino]ethyl]-*N*-[1H-imidazol-4-ylmethyl]-glycine trihydrochloride (H_3L6·3HCl)**

***a) N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-*N*-[1H-imidazol-4-ylmethyl]-glycine, 1,1-dimethylethyl ester**

Sodium triacetoxyborohydride (94.7 g, 447 mmol) was added to a solution of *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]-amino]ethyl]-glycine,1,1-dimethylethyl ester (120 g, 298 mmol) and 1*H*-Imidazole-5-carboxaldehyde (37.2 g, 387 mmol) in DCM (1.20 L). The reaction mixture was stirred at 25 °C for 16 h. Subsequently, 1 N NaOH (150 ml in water) was added and the organic layer was separated, washed with H_2O (700 mL x 3), brine (650 mL), dried over Na_2SO_4,

filtered and concentrated under reduced pressure to give a residue. The residue was further purified with silica gel chromatography column by eluting with petroleum ether : ethyl acetate = 10 : 1 to ethyl acetate : methanol = 10 : 1 (TLC: ethyl acetate : MeOH = 10:1, Rf = 0.4) to give the title compound (100 g, 70%) as yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65 (s, 1H), 6.88 (s, 1H), 3.80 (s, 2H), 3.42 (s, 4H), 3.24 (s, 2H), 2.90-2.80 (m, 2H), 2.80-2.70 (m, 2H), 1.44-1.46 (m, 27H) ppm.

b) ***N*-[2-[bis[carboxymethyl]amino]ethyl]-*N*-[1H-imidazol-4-ylmethyl]-glycine trihydrochloride**

4 M HCl in dioxane (250 mL) was added to a mixture of *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-*N*-[1H-imidazol-4-ylmethyl]-glycine,1,1-dimethylethyl ester (48.0 g, 99.4 mmol) in dioxane (240 mL). The mixture was stirred at 25 °C for 12 h, after which the reaction was essentially completed (LC-MS control). The suspension was filtered to give a residue, which was dissolved in H_2O (100 mL). The solution was concentrated at 60 °C to give the title compound (34.8 g, 83%) as a white solid. ^{1}H NMR (D_2O, 400 MHz): δ 8.62 (d, *J*=1.27 Hz, 1H), 7.46 (d, *J*=1.01 Hz, 1H), 4.08 (s, 2H), 3.96 (s, 4H), 3.55 (s, 2H), 3.36-3.42 (m, 2H), 3.09-3.15 (m, 2H) ppm. ^{13}C NMR (D_2O, 101 MHz): δ 172.7, 170.5 (2C), 134.7, 126.7, 119.6, 55.3 (2C), 53.5, 52.3, 49.7, 47.3 ppm. ESI-HRMS(-) found (calculated): *m/z* $[M\text{-}H^+]^-$, 313.1144 (313.1154). Ion chromatography gave 22.9% (2.7 equiv.) chloride.

N-{2-[bis(carboxymethyl)amino]ethyl}-N-[(1-methyl-1H-imidazol-4-yl)methyl]glycine trihydrochloride (H_3L7·3HCl)

a) ***N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-*N*-[(1-methyl-1H-imidazol-4-yl)methyl]-glycine, 1,1-dimethylethyl ester**

A solution of 1-methyl-1H-imidazole-4-carbaldehyde (7.46 g, 67.7 mmol) and *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]-amino]ethyl]-glycine, 1,1-dimethylethyl ester (30.0 g, 74.5 mmol) in DCM (200 mL) was adjusted to pH 6 with acetic acid, then sodium triacetoxyborohydride (21.5 g, 101 mmol) was added. The reaction mixture was stirred under N_2 at 25 °C for 24 h, then heated to 35 °C and stirred for another 12 h, after which LC-MS showed the starting amine to be entirely consumed. The reaction mixture was diluted with water (300 ml) and extracted with DCM (200 mL x 3). The organic layer was washed with brine (300 mL x 2), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography twice on silica gel (petroleum ether: ethyl acetate, 1:0 to 0:1) to give the title compound as a yellow oil (18.5 g, 55%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 (d, *J* = 0.8 Hz, 1H), 6.79 (d, *J* = 0.8 Hz, 1H), 3.74 (s, 2H), 3.60 (s, 3H), 3.42 (s, 4H), 3.30 (s, 2H), 2.86 - 2.82 (m, 2H), 2.77 - 2.74 (m, 2H), 1.42 - 1.41 (m, 27H) ppm.

b) **N-{2-[bis(carboxymethyl)amino]ethyl}-N-[(1-methyl-1H-imidazol-4-yl)methyl]glycine trihydrochloride**

36% HCl (45 ml, 503 mmol) was added to a solution of N-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-N-[(1-methyl-1H-imidazol-4-yl)methyl]-glycine, 1,1-dimethylethyl ester

(17.5 g, 35.2 mmol) in H_2O (50.0 mL). The reaction mixture was stirred at 25 °C for 12 h, after which TLC (petroleum ether: ethyl acetate = 0:1) showed the starting material (R_f = 0.3) to be entirely consumed. Hydrochloric acid and water were removed under reduced pressure and the title compound was obtained as a light-yellow solid (15.42 g, 98%). ^{1}H NMR (DMSO-d_6, 400 MHz,): δ 9.16 (s, 1H), 7.71 (d, *J*=1.3 Hz, 1H), 4.13 (s, 6H), 3.84 (s, 3H), 3.61 (s, 2H), 3.46 (br t, *J*=5.7 Hz, 2H), 3.15 (br t, *J*=5.6 Hz, 2H) ppm. ^{13}C NMR (DMSO-d_6, 101 MHz): δ = 170.93, 168.72 (2C), 136.11, 127.54, 123.04, 54.36 (2C), 53.04, 51.65, 48.53, 46.17, 35.70 ppm. ESI-HRMS(-) found (calculated): *m/z* [M-H$^+$]$^-$, 327.1300 (327.1310). Ion chromatography gave 26.0% (3.3 equiv.) of chloride.

N-{2-[bis(carboxymethyl)amino]ethyl}-N-(pyridin-2-ylmethyl)glycine dihydrochloride (H_3L8·3HCl)

a) ***N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-*N*-[pyridin-2-ylmethyl]-glycine, 1,1-dimethylethyl ester**

A solution of *N*-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]-amino]ethyl]-glycine, 1,1-dimethylethyl ester (30.0 g, 74.5 mmol) and 2-pyridinecarboxaldehyde (12.0 g, 111 mmol) in DCM (200 mL) was adjusted to pH 6 with acetic acid. Sodium triacetoxyborohydride (23.7 g, 112 mmol) was added and the reaction mixture was stirred under N_2 at 25 C for 20 h. The reaction mixture was diluted with H_2O (300 mL) and extracted with ethyl acetate (300 mL x 3). The combined organic layers were washed with brine (500 mL x 2), dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel eluted with petroleum ether: ethyl acetate = (1:0 to 0:1). The title compound (18.0 g, 49%) was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.50 (dd, *J* = 0.8, 4.8 Hz, 1H), 7.64 - 7.60 (m, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.12 (dt, *J* = 1.0, 6.2 Hz, 1H), 3.94 (s, 2H), 3.42 (s, 4H), 3.36 (s, 2H), 2.87 - 2.81 (m, 4H), 1.45 - 1.41 (m, 27H) ppm.

b) **N-{2-[bis(carboxymethyl)amino]ethyl}-N-(pyridin-2-ylmethyl)glycine dihydrochloride**

36% HCl (35 ml, 403 mmol) was added to a solution of N-[2-[bis[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]ethyl]-N-[pyridin-2-ylmethyl]-glycine, 1,1-dimethylethyl ester (17.9 g, 36.3 mmol) in H_2O (40 mL). The mixture was stirred at 25 °C for 12 h, after which LC-MS indicated the reaction to be completed. The solvent was removed under reduced pressure and the title compound was obtained as a light-yellow solid (14.2 g, 90%). ^{1}H NMR (DMSO-d_6, 400 MHz,): δ 8.78 (dd, *J*=0.8, 5.8 Hz, 1H), 8.51 (dt, *J*=1.5, 7.9 Hz, 1H), 8.05 (d, *J*=8.1 Hz, 1H), 7.94 (t, *J*=6.7 Hz, 1H), 4.39 (s, 2H), 4.25 (s, 2H), 3.52 (br t, *J*=5.6 Hz, 2H), 3.56 (s, 4H), 3.25 (br t, *J*=5.6 Hz, 2H) ppm. ^{13}C NMR (DMSO-d_6, 101 MHz): δ 171.88, 167.81 (2C), 153.56, 145.73, 141.68, 126.52, 125.83, 54.22 (2C), 54.03, 53.47, 52.47, 48.78 ppm. ESI-HRMS(-) found (calculated): *m/z* [M-H$^+$]$^-$, 324.1199 (324.1201). Ion chromatography gave 23.6% (2.9 equiv) of chloride.

NMR spectra of sulfido-bridged W(V) dinuclear complexes

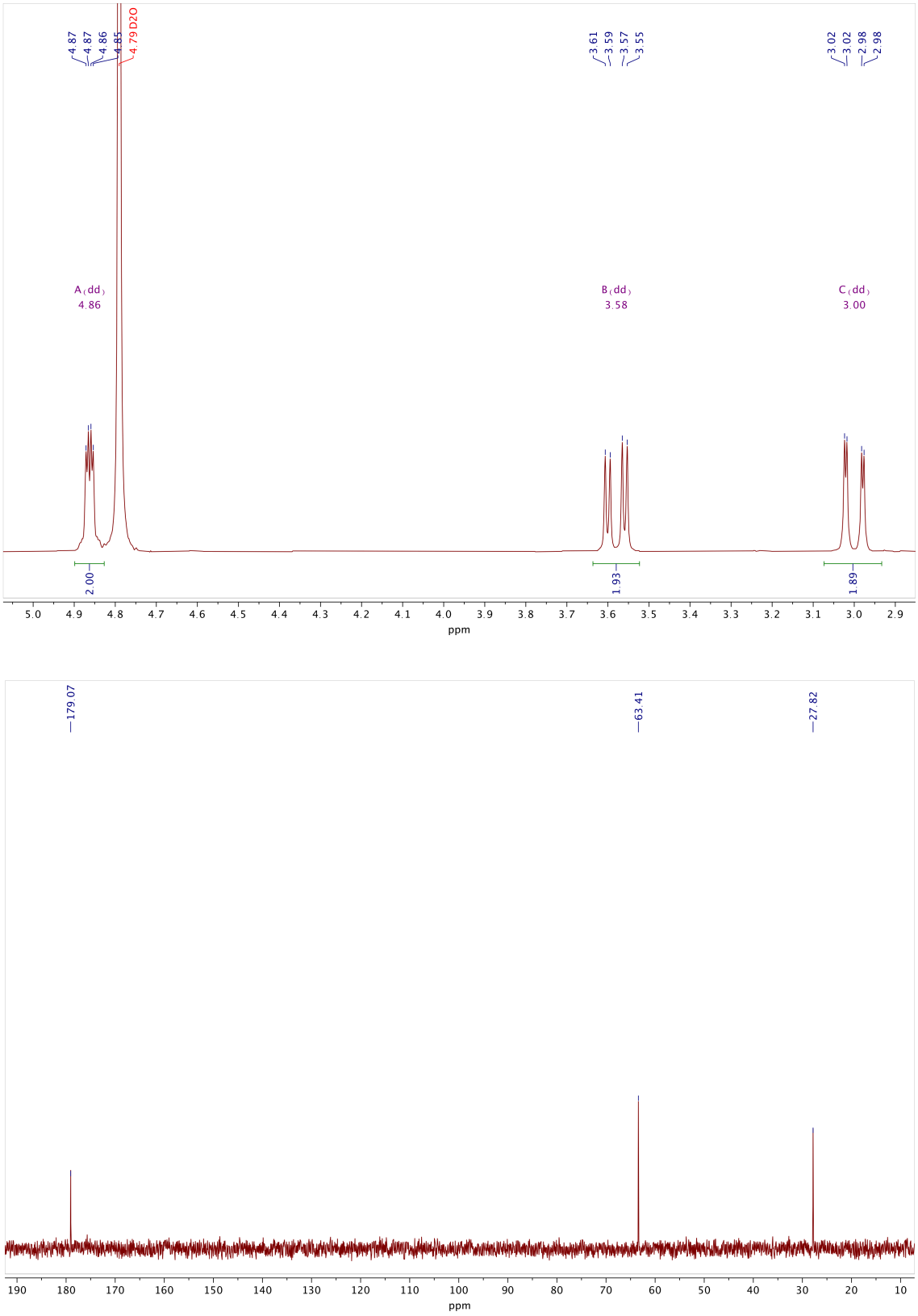


Fig. S16 ^{1}H and ^{13}C NMR spectra of $K_2[W_2O_2S_2(Cys)_2]$ (**1a**) in D_2O at 26° C.

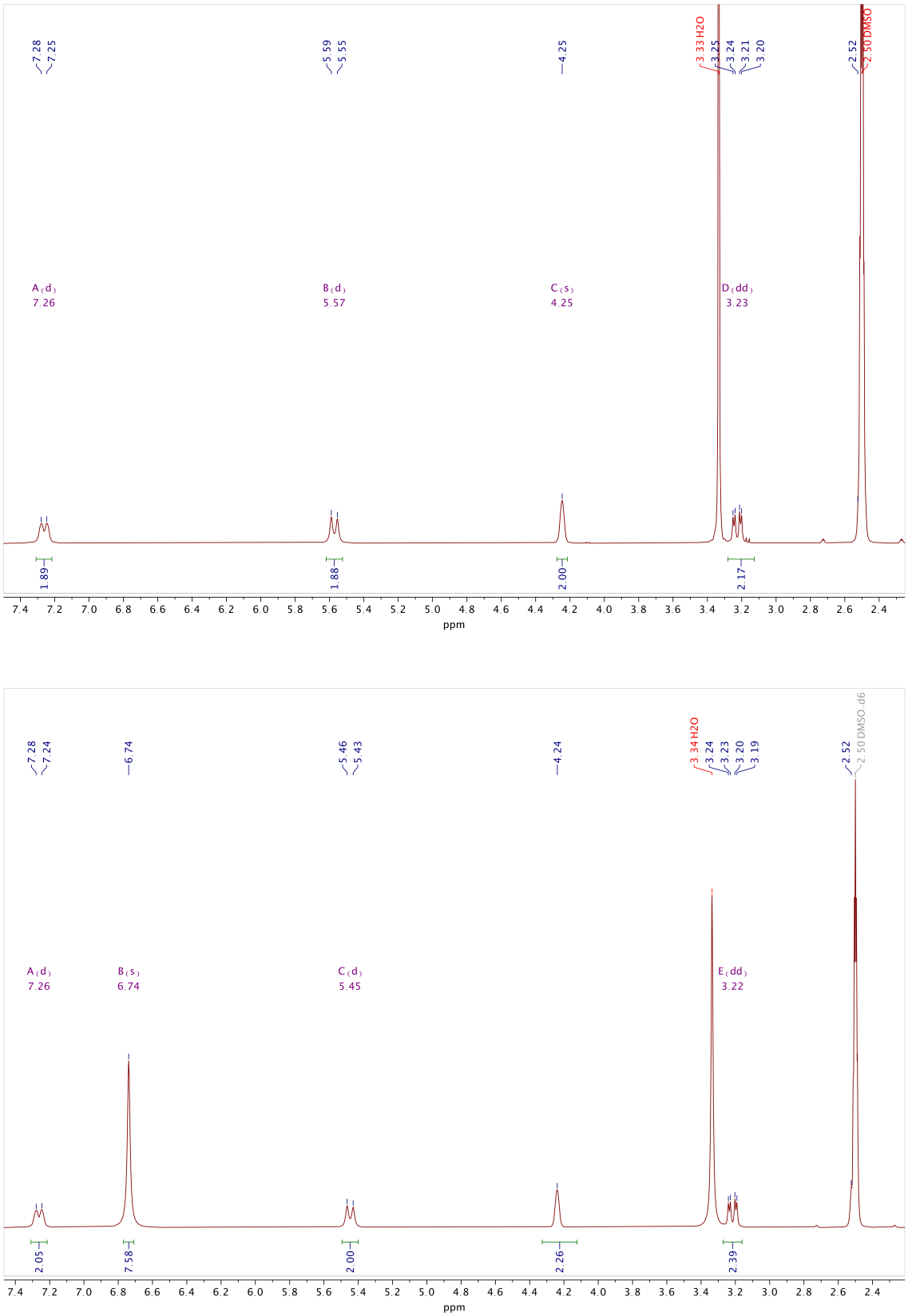


Fig. S17 ^{1}H NMR spectra of complexes **1b** (top) and **1c** (bottom) in DMSO-d_6 at 24° C.

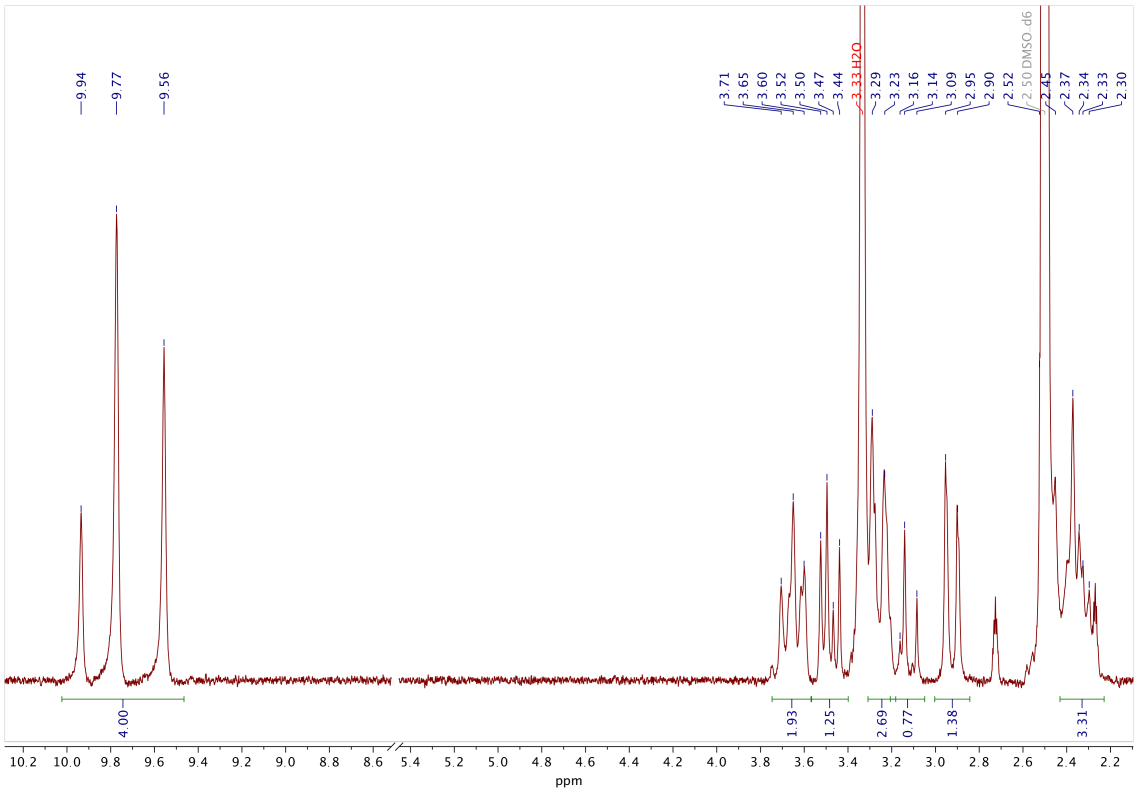


Fig. S18 ^{1}H NMR spectra of $[W_2O_2S_2(L1)]$ (**4**) in DMSO-d_6 at 24° C.

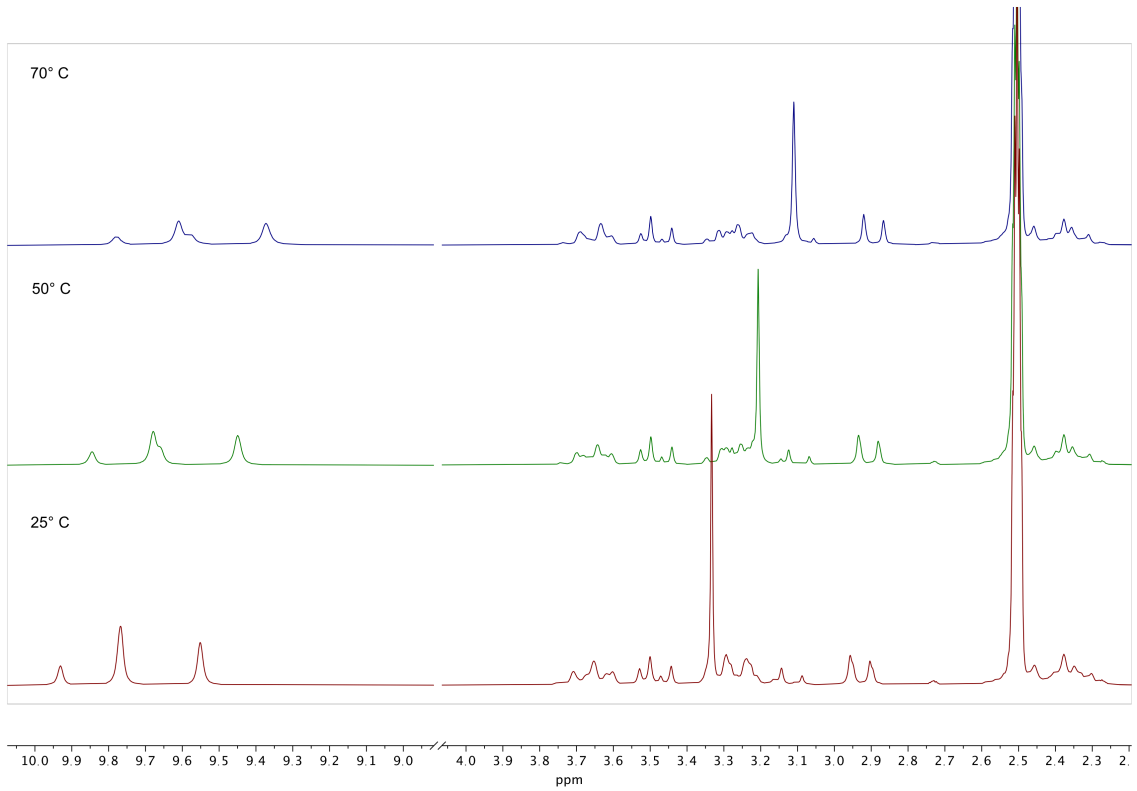


Fig. S19 Variable temperature ^{1}H NMR spectra of $[W_2O_2S_2(L1)]$ (**4**) in DMSO-d_6 at 25°C, 50°C and 70°C

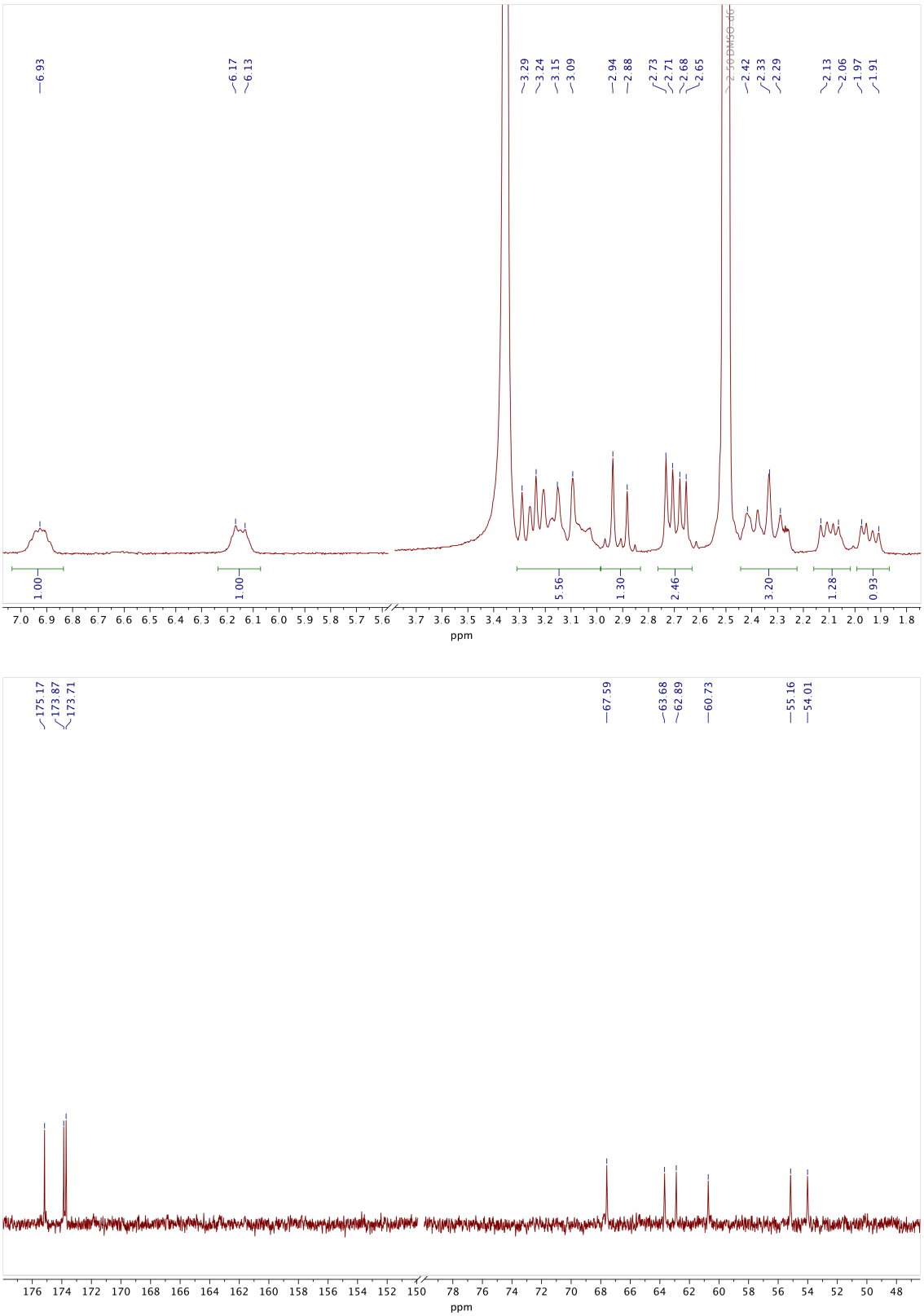


Fig. S20 ^{1}H and ^{13}C NMR spectra of Na[$W_2O_2S_2$(L5)] (**5b**) in DMSO-d_6 at 24° C.

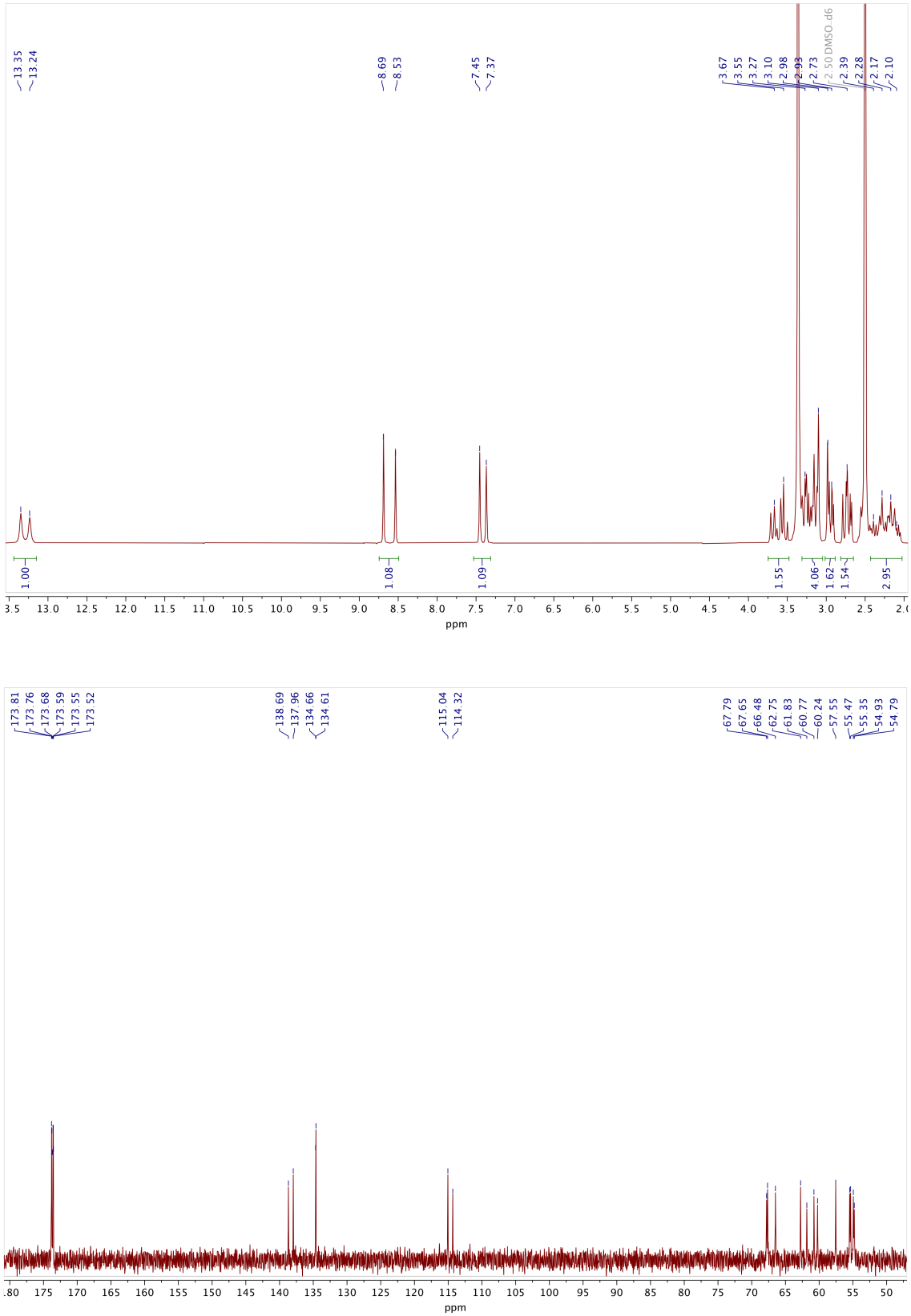


Fig. S21 ^{1}H and ^{13}C NMR spectra of $K[W_2O_2S_2(L6)]$ (**6a**) in DMSO-d_6 at 24° C.

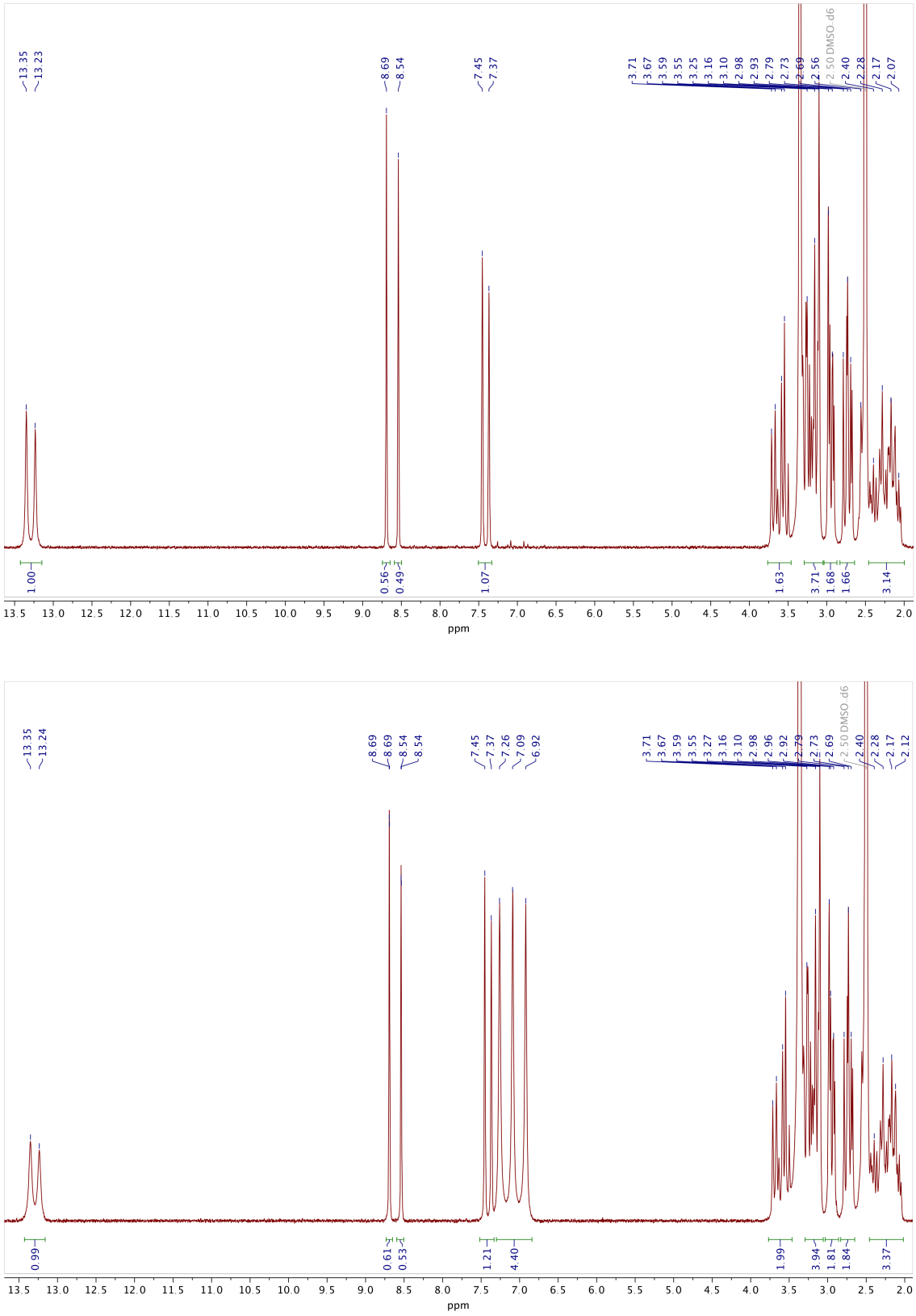


Fig. S22 ^{1}H NMR spectra of Na[$W_2O_2S_2$(L6)] (**6b**) and (NH_4)[$W_2O_2S_2$(L6)] (**6c**) in DMSO-d_6 at 24° C.

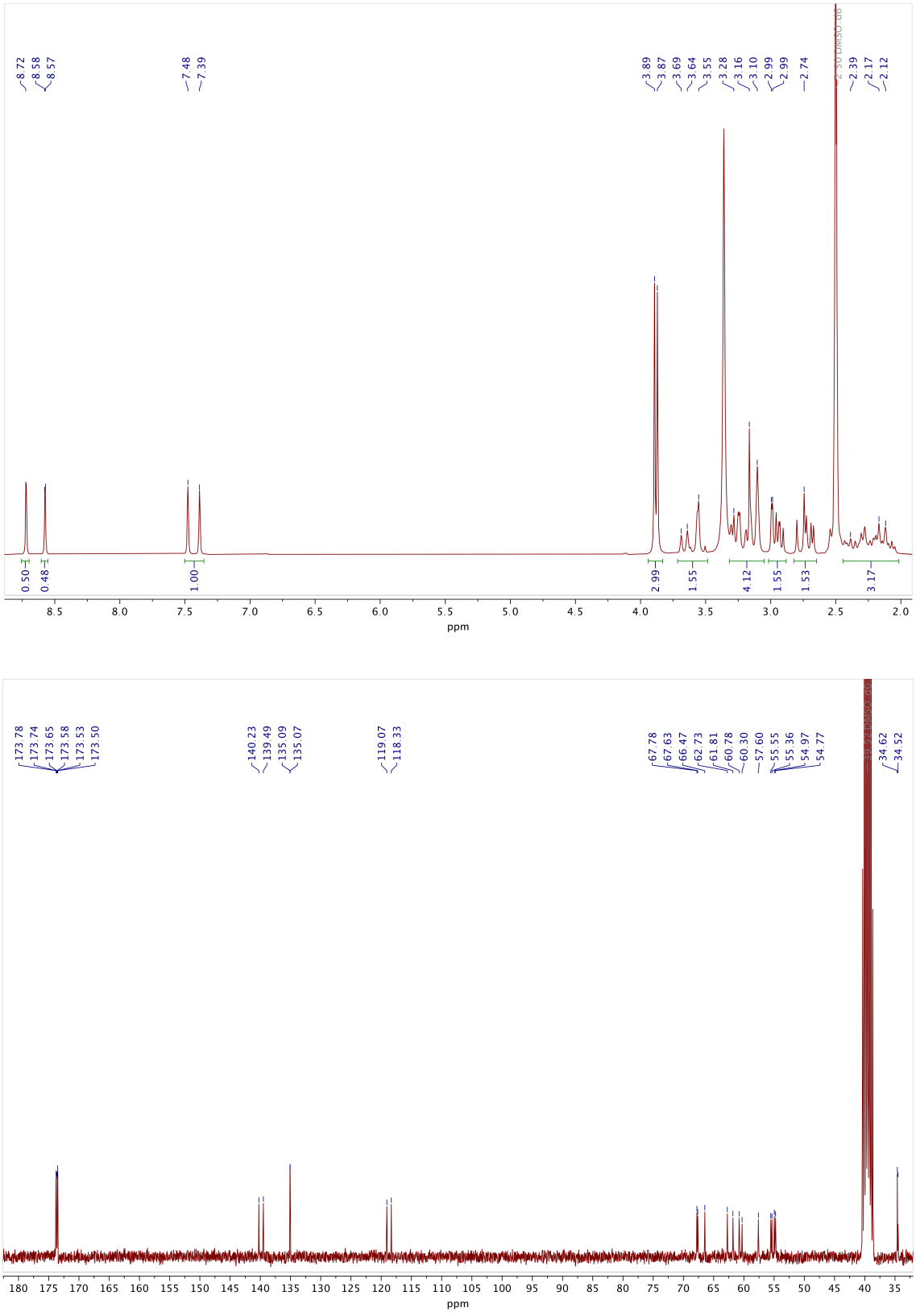


Fig. S23 ^{1}H and ^{13}C NMR spectra of $Na[W_2O_2S_2(L7)]$ (**7b**) in DMSO-d_6 at 24° C.

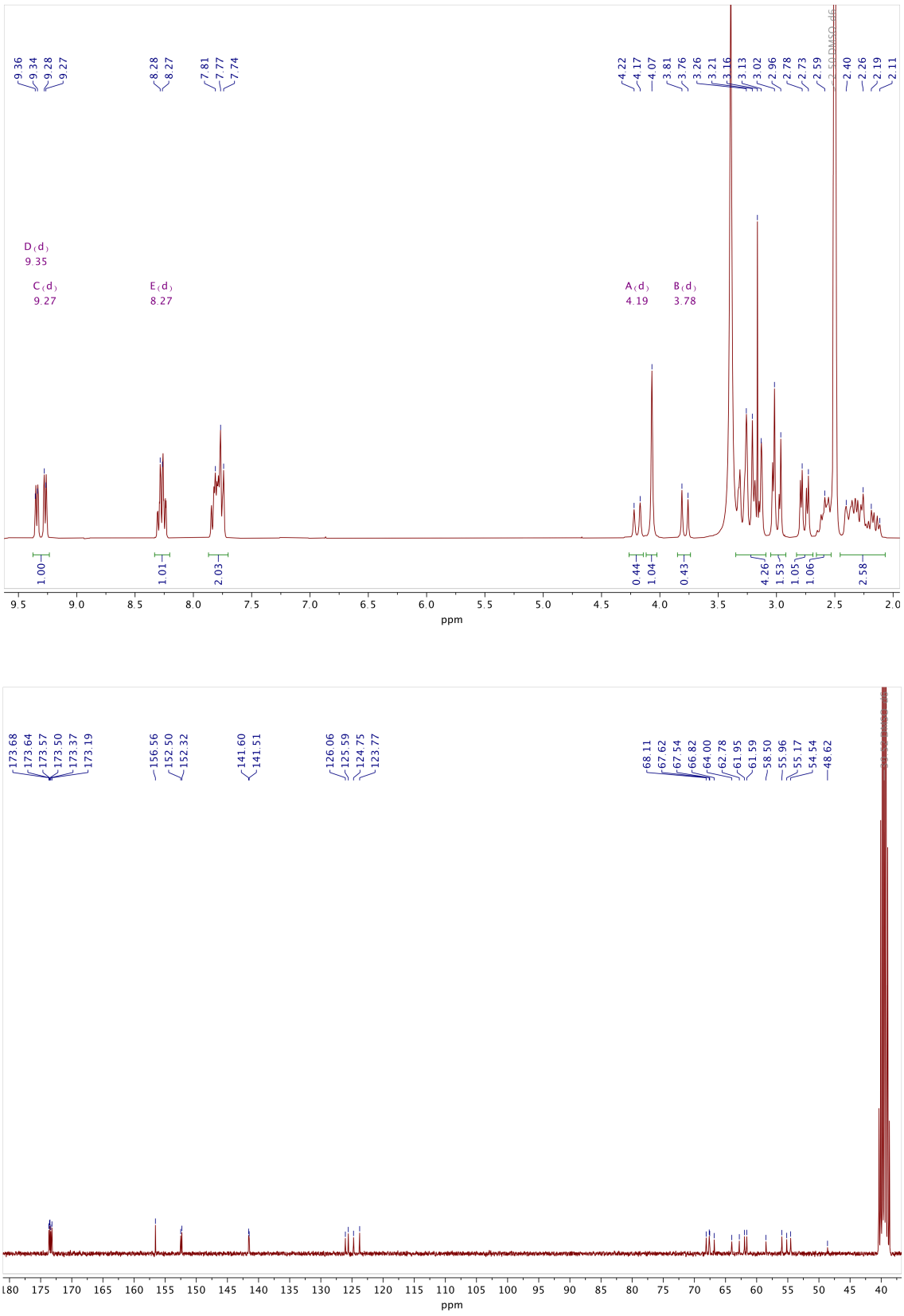


Fig. S24 ^{1}H and ^{13}C NMR spectra of $Na[W_2O_2S_2(L8)]$ (**8b**) in DMSO-d_6 at 23° C.

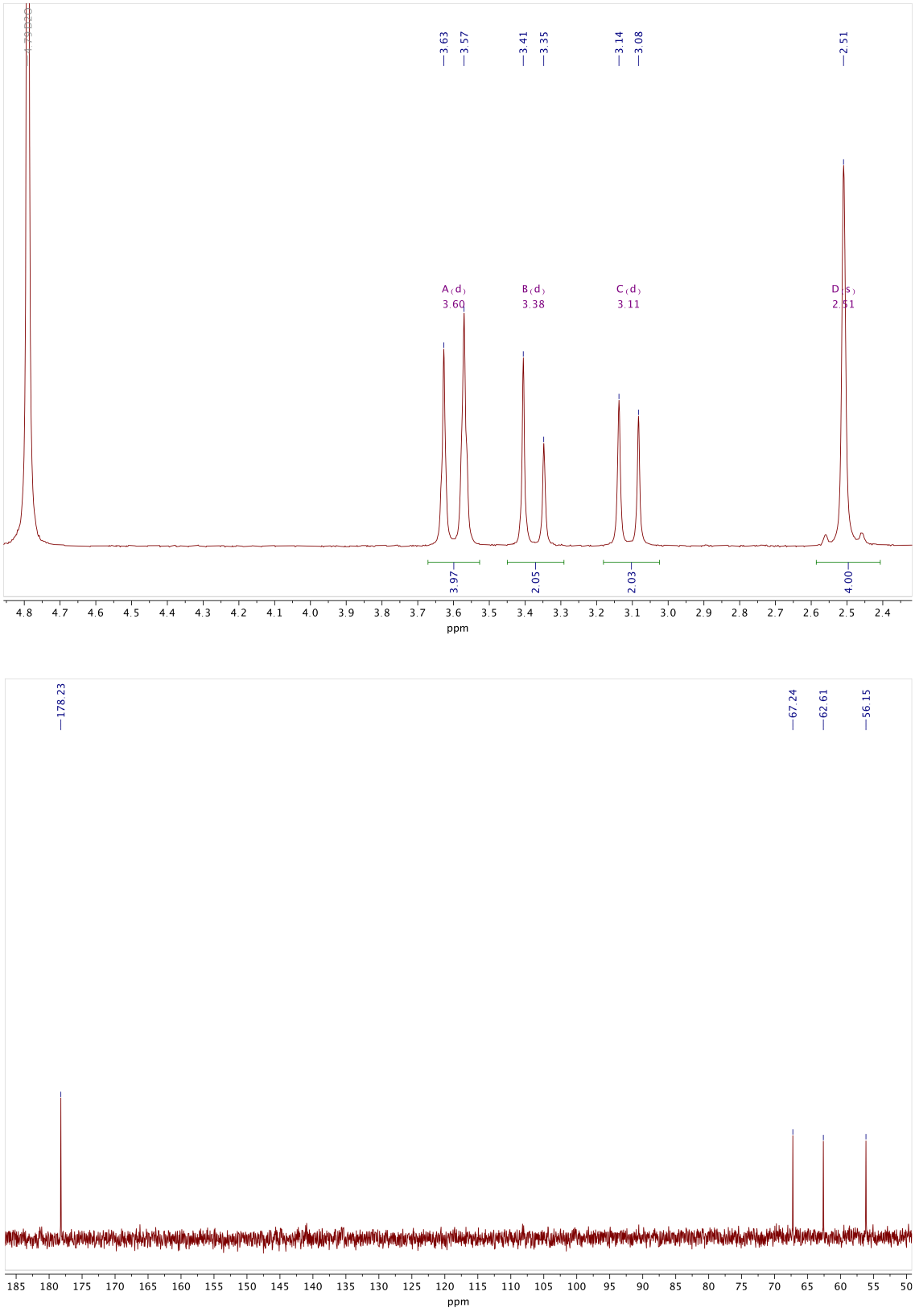


Fig. S25 ^{1}H and ^{13}C NMR spectra of $Na_2[W_2O_2S_2(EDTA)]$ (**9b**) in D_2O at 23° C.

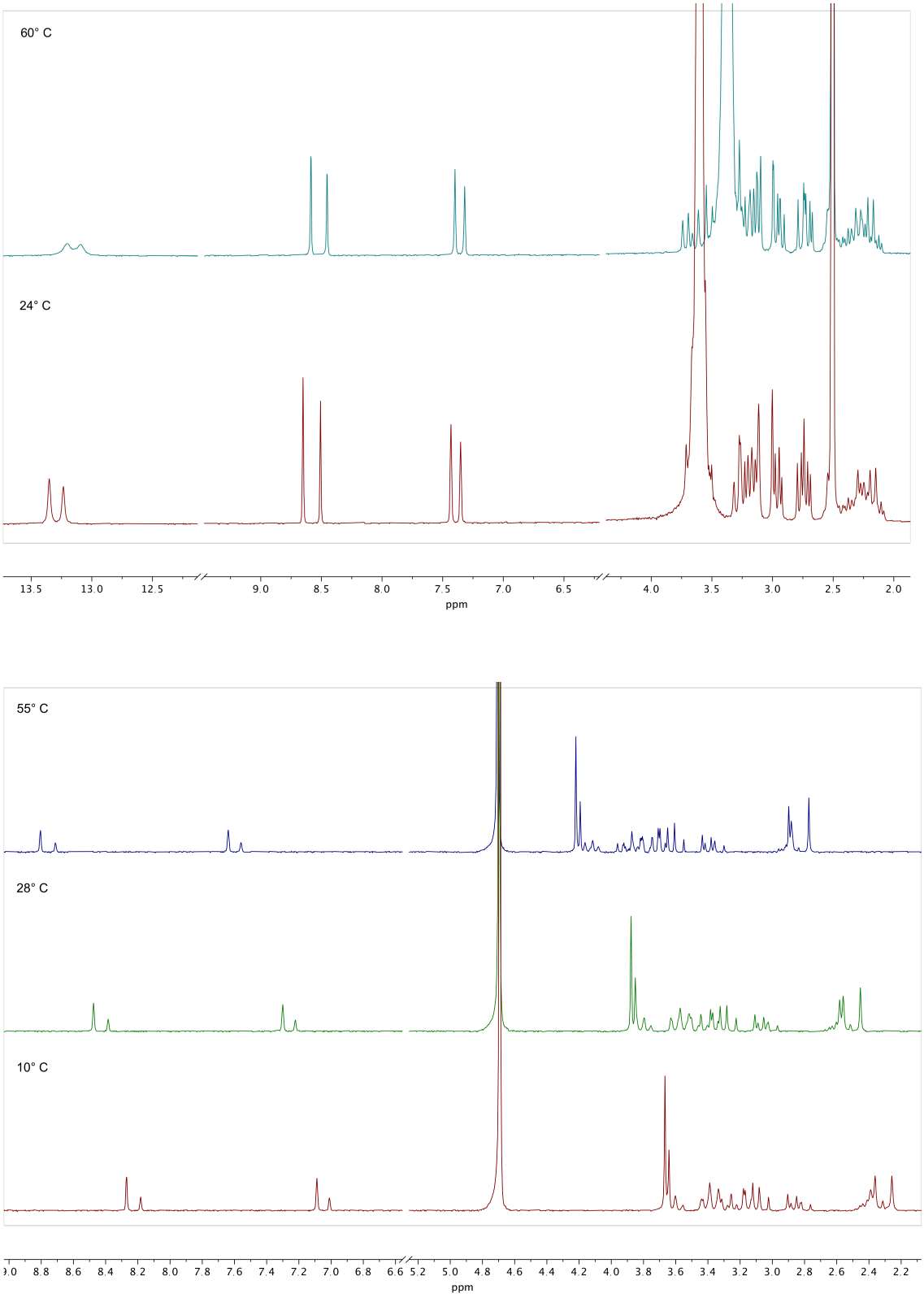


Fig. S26 Variable temperature ^{1}H NMR spectra of Na[$W_2O_2S_2$(L6)] (**6b**) in DMSO-d_6 (top) and K[$W_2O_2S_2$(L7)] (**7a**) in D_2O (bottom).

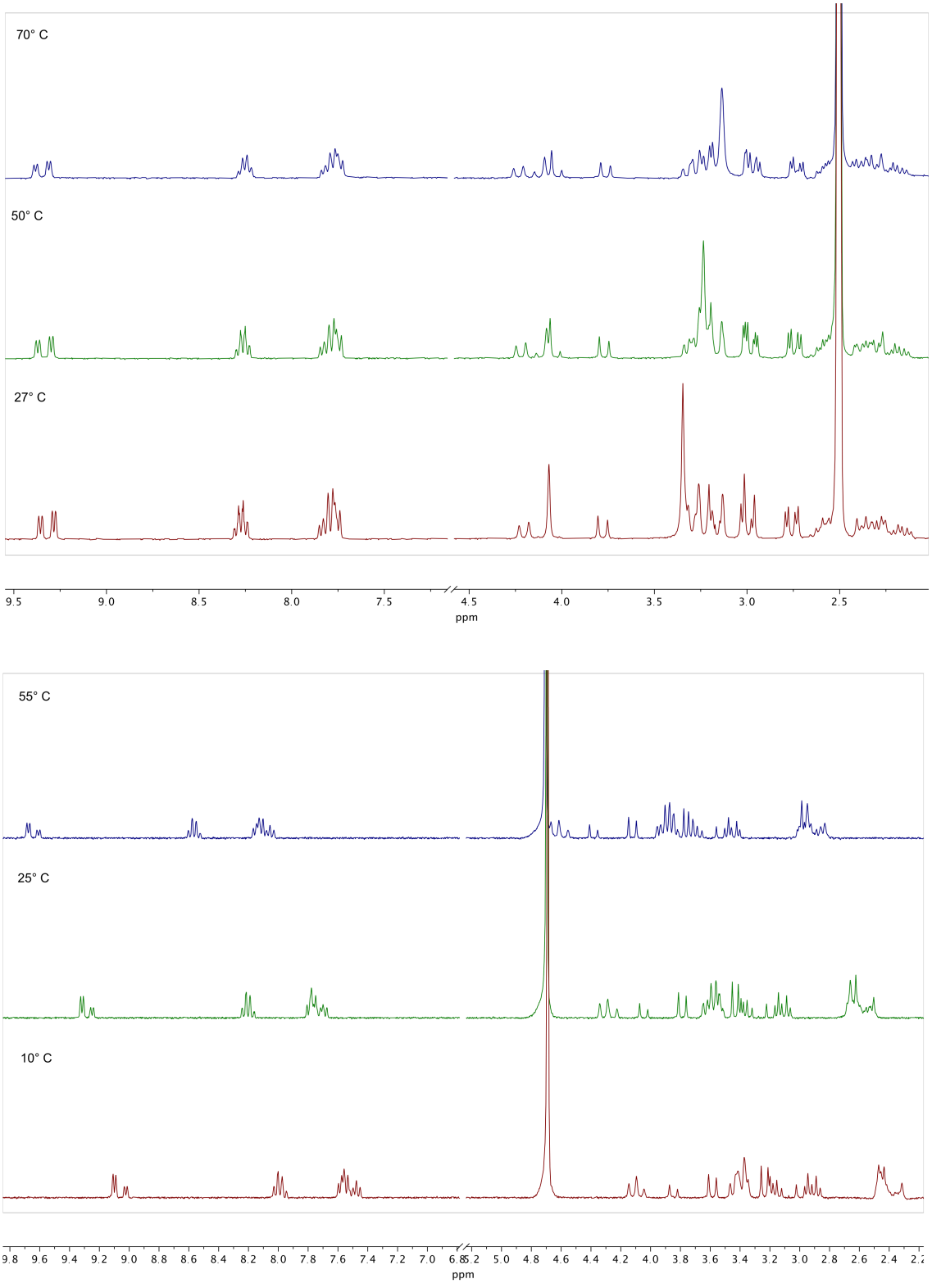


Fig. S27 Variable temperature ^{1}H NMR spectra of Na[$W_2O_2S_2$(L8)] (**8b**) in DMSO-d_6 (top) and in D_2O (bottom).

References

1. G. M. Sheldrick, *Acta Crystallogr. Sect. A Found. Crystallogr.*, 2008, **64**, 112–122.
2. G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.*, 2015, **71**, 3–8.
3. C. K. Johnson, *ORTEP. Report ORNL–3794.*, United States, 1965.
4. E. S. Claudio, M. A. ter Horst, C. E. Forde, C. L. Stern, M. K. Zart and H. A. Godwin, *Inorg. Chem.*, 2000, **39**, 1391–1397.
5. E. W. Price, J. F. Cawthray, G. A. Bailey, C. L. Ferreira, E. Boros, M. J. Adam and C. Orvig, *J. Am. Chem. Soc.*, 2012, **134**, 8670–8683.
6. R. S. Mulla, M. S. Beecroft, R. Pal, J. A. Aguilar, J. Pitarch-Jarque, E. García-España, E. Lurie-Luke, G. J. Sharples and J. A. Gareth Williams, *Chem. - A Eur. J.*, 2018, **24**, 7137–7148.
7. S. Achilefu, R. R. Wilhelm, H. N. Jimenez, M. A. Schmidt and A. Srinivasan, *J. Org. Chem.*, 2000, **65**, 1562–1565.