Supporting Information

Tetranuclear Cu(II)-chiral complexes: Synthesis, characterization and biological activity.

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1. Experimental details

General considerations. All reagents and solvents were used as received from commercial supplies without further purification. Major elemental analyses, such as C, H and N analyses, were carried out with a Vario Micro Cube. The circular dichroism spectra of **S-1** and **R-1** were recorded on a JASCO J-1500 CD-Spektrometer. IR spectra were obtained from Perkin Elmer Spectrum GX FT-IR System in the range of 400-4000 cm^{-1} in KBr pellets at room temperature. NMR spectra were collected on a Varian Inova operating at 500 MHz. All chemical shifts are reported in parts per million and referenced to tetramethylsilane for 1H. Single crystal X-ray diffraction (SCXD) data were collected at 180(2) K using a STOE IPDS II. Powder X-ray diffraction (PXRD) measurements on **R-1** and **S-1** were performed on an STOE STADI-P diffractometer with Cu-Kα radiation.

UV/Vis

The maxima absorption of **S-1** and **R-1** were recorded using 50 μM solution in MeOH. In order to compare the optical properties of these complexes to (S)-(H_2mvan)(Pheol-im) ligand the 400 μM solution of (S)-H_2L were prepared.

X-ray structural studies: X-ray crystallography measurements for *S*-[Cu_4(mvan)(Pheol-im)$_4$ ($CH_3OH)_2$]($NO_3)_2$] (**S-1**) and *R*-[Cu_4(mvan)(Pheol-im)$_4$($CH_3OH)_2$]($NO_3)_2$] (***R*-1**) were determined at 180(2) K STOE IPDS II diffractometer with Mo-Kα radiation from a microfocus source, and corrected semi empirically for absorption. Structure solution was by dual-space directed methods (SHELXT-2016), with anisotropic thermal parameters for all ordered non-H atoms. Further details of the crystal structures investigation may be obtained either from FIZ Karlsruhe, 76344 Eggenstein-Leopoldshafen, Germany (FAX: (+49)7247-808-666; email:

crysdata@fiz-karlsruhe.de on quoting the deposition numbers CCDC-1, CCDC-2, CCDC-3,) or CS 1, CS2, CS3.

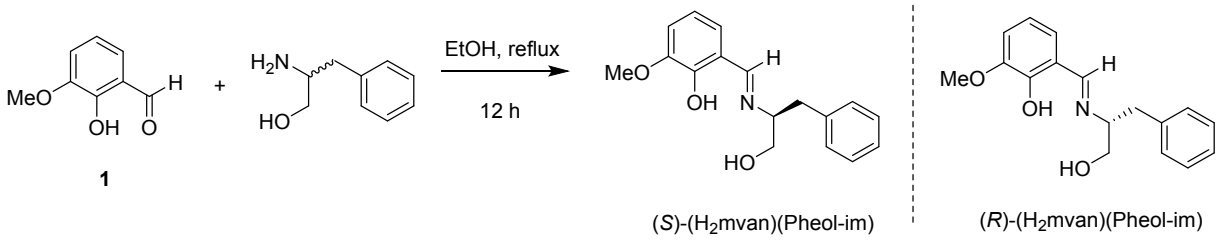
Cell Culture: Cell culture flasks, dishes and plates (CELLSTARS) were supplied by Greiner Bio-One GmbH. The epidermoid human cancer cell line A431 (ATCCS number: CRL-1555) and the human embryonic kidney cell line HEK293 (DMSZ number: ACC 305) were cultured as previously reported [22,23]. All cell lines were confirmed to be mycoplasma-negative using the Venor®GeM Advance Mycoplasma Detection Kit (Minerva Biolabs) and were tested monthly.

In vitro Cytotoxicity Evaluation: For the cytotoxicity assessment of **S-1** and **R-1**, the MTS (CellTiter 96 Aqueous one Solution Cell Proliferation Assay, Promega) assay was performed as detailed previously [23]. Briefly, 5000 A431 or HEK293 cells, respectively, per well were seeded in sterile 96-well microtiter plates. After 48 h incubation, increasing concentrations of either **S-1** or **R-1** were added to the cells in quintuplicate. After exposure for 48 h, 20 µL of MTS assay solution were added to the wells and incubated for 90 min. Optical densities at 492 nm were measured with a microplate reader (Sunrise, Tecan). The viability of the cells is expressed as a percentage of viable cells grown in the absence of the compounds, but in the presence of the corresponding volume of DMSO (vehicle-treated control, final concentration 0.4%). IC50 values were calculated using GraphPad Prism 7.04 (GraphPad Software).

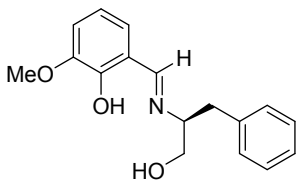
Antibacterial Testing: The antibacterial potential of **S-1** and **R-1** against Gram-negative *E. coli* and Gram-positive *B. subtilis* was assessed by monitoring their growth in LB broth over 6 h in the presence of 10, 50 or 100 µM of either **S-1**, **R-1** or the corresponding volume of DMSO (vehicle-treated control) as recently described [23]. Briefly, 200 µL of an overnight culture of each strain were used to inoculate 20 mL of LB broth and cultivation was continued at 37°C in an orbital shaker with 50 mm offset and shaking speed of 200 rpm (Multitron Cell, Infors).

Cell growth was monitored repeatedly by measurement of optical density in 1 mL cuvettes at 600 nm using a spectrophotometer (Ultrospec 10, Biochrom Ltd).

Synthesis Chiral Schiff-base ligands. Synthesis of the Schiff-base ligands S/R-(H_2mvan)(Pheol-im)$_4$(CH_3OH)$_2$](NO_3)$_2$] was performed by the condensation reaction between 2-hydroxy-3-methoxybenzaldehyde and the corresponding amino alcohol of R/S- 2-amino-3-phenyl-1-propanol under reflux in absolute ethanol. After completion of the reaction, yellow solid was filtered, washed with cooled ethanol and dried under reduced pressure.



(βS)-β-[(E)-[(2-Hydroxy-3-methoxyphenyl)methylene]amino]benzenepropanol (S)-(H_2mvan)(Pheol-im) : (*S*)-2-amino-3-phenyl-1-propanol (10.91 mmol, 1.650 g) and 2-hydroxy-3-methoxybenzaldehyde (8.71 mmol, 1.326 g) were dissolved in absolute EtOH (100 mL). The resulting mixture was brought to reflux 12 h. After completion of the reaction, the yellow solid was filtered, washed with cooled ethanol and dried under reduced pressure to obtain (86% yield).



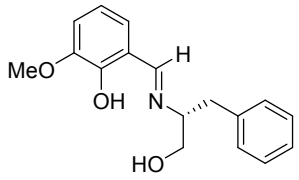
(*S*)-(H_2mvan)(Pheol-im)

^{1}H NMR (500 MHz, DMSO-d_6) = δ 13.78 (s, 1 H), 7.25 (t, J = 7.5 Hz, 1H), 7.20-7.12 (m, 2H), 6.99 (dd, J = 8.0, 1.5 Hz, 1H), 6.91 (dd, J = 7.8, 1.5 Hz, 1H), 6.74 (t, J = 7.9 Hz, 1H), 4.93 (s, 1H), 3.65

(dd, J = 10.4, 3.6 Hz, 1H), 3.51 (ddt, J = 17.6, 9.9, 5.6 Hz, 1H), 3.00 (dd, J = 13.5, 4.4 Hz, 1H), 2.80 (dd, J = 13.5, 8.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) = δ 165.51 (CH), 151.81 (C), 148.03 (C), 138.54 (C), 129.32 (2×CH), 128.21 (2×CH), 126.07 (CH), 123.14 (CH), 118.23 (CH), 117.49 (CH), 114.58 (CH), 71.65 (*CH), 64.20 (CH), 55.72 (CH_3), 38.33 (CH_2). FT-IR (cm^{-1}) in KBr: 3436m, 3225m, 3020w, 2920w, 2850w, 1638s, 1503s, 1458m, 1242s, 1088s, 1042m, 972m, 903m, 762s, 707s.

(βR)-β-[(E)-[(2-Hydroxy-3-methoxyphenyl)methylene]amino]benzenepropanol

(*R*)-(H_2mvan)(Pheol-im): (*R*)-2-amino-3-phenyl-1-propanol (8.5 mmol, 0.8872 g) and 2-hydroxy-3-methoxybenzaldehyde (6.36 mmol, 0.9682 g) were dissolved in absolute EtOH (100 mL). The resulting mixture was brought to reflux 12 h. After completion of reaction, the yellow solid was filtered, washed with cooled ethanol and dried under reduced pressure to obtain (82% yield).



(*R*)-(H_2mvan)(Pheol-im)

^{1}H NMR (500 MHz, DMSO-d_6) = δ 13.75 (s, 1H), 8.24 (s, 1H), 7.27-7.20 (m, 2H), 7.20-7.11 (m, 3H), 6.98 (dd, J = 8.0, 1.5 Hz, 1H), 6.90 (dd, J = 7.8, 1.5 Hz, 1H), 6.73 (t, J = 7.8 Hz, 1H), 4.98-4.83 (m, 1H), 3.76 (s, 3H), 3.68-3.57 (m, 1H), 3.57-3.41 (m, 2H), 2.99 (dd, J = 13.5, 4.4 Hz, 1H), 2.78 (dd, J = 13.5, 8.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) = δ 165.33 (CH), 151.61 (C), 147.84 (C), 138.37 (C), 129.14 (2×CH), 128.03 (2×CH), 125.89 (CH), 122.96 (CH), 118.05 (CH), 117.31 (CH), 114.41 (CH), 71.46 (*CH), 64.01 (CH), 55.55 (CH_3), 38.13 (CH_2). FT-IR (cm^{-1}) in KBr:

3436m, 3210m, 3015w, 2925w, 2855w, 1643s, 1498s, 1458s, 1242s, 1218s, 1157w, 1088s, 957w, 901m, 756m, 707m.

Synthesis of Cu(II)-cluster $C_{70}H_{78}Cu_4N_6O_{20}$ (S-1); (*S*)-[Cu_4(mvan)(Pheol-im)$_4$($CH_3OH)_2$]($NO_3)_2$: A solution of the Schiff-base ligand *S*-(H_2mvan)(Pheol-im) (0.2 mmol, 57 mg) in methanol (10 mL) was added a solution of $Cu(NO_3)_2.5H_2O$ (0.1 mmol, 24 mg) in methanol (5 mL). The resulting mixture was stirred at room temperature for 15 min then a solution of $NaOAc.3H_2O$ (0.5 mmol, 68 mg) in methanol (5 mL) was added and the reaction mixture was allowed to stir for another 30 min. After being filtered the green solution was left to stand at ambient temperature to allow for solvent evaporation. After 7 days, green crystals of the complex S-[$Cu_4L_4(CH_3OH)_2](NO_3)_2$ were obtained. The crystals were isolated by filtration and air-dried. Yield: 72% (based on $Cu(NO_3)_2$•$5H_2O$). Elemental analysis calcd for S-1 ($C_{70}H_{78}N_6O_{20}Cu_4$): C, 53.29%; H, 4.98%; N, 5.33%. Found: C, 52.51%; H, 4.52%; N, 5.34%. FT-IR (cm^{-1}) in KBr: 3360m, 2927m, 1619s, 1446s, 1297s, 1221s, 1089s, 1035s, 978s, 854m, 737s, 703s, 639m.

Synthesis of Cu(II)-cluster $C_{70}H_{78}Cu_4N_6O_{20}$ (R-1); (*R*)-[Cu_4(mvan)(Pheol-im)$_4$($CH_3OH)_2$]($NO_3)_2$: A solution of the Schiff-base ligand *R*-(H_2mvan)(Pheol-im) (0.2 mmol, 57 mg) in methanol (10 mL) was added a solution of $Cu(NO_3)_2$.5H2O (0.1 mmol, 24 mg) in methanol (5 mL). The resulting mixture was stirred at room temperature for 15 min then a solution of $NaOAc.3H_2O$ (0.5 mmol, 68 mg) in methanol (5 mL) was added and the reaction mixture was allowed to stir for further 30 min. After being filtered the green solution was left to stand at ambient temperature to allow for solvent evaporation. After 7 days, green crystals of the complex R-[$Cu_4L_4(CH_3OH)_2](NO_3)_2$ were obtained. R-H_2L. Yield 70% (based on $Cu(NO_3)_2$•$5H_2O$). Elemental analysis calcd for **R-1** ($C_{70}H_{78}N_6O_{20}Cu_4$): C, 53.29%; H, 4.98%; N,

5.33%. Found: C, 52.07%; H, 4.78%; N, 5.31%. FT-IR (cm^{-1}) KBr: 3367m, 2935m, 1630s, 1549m, 1439s, 1299s, 1219s, 1084s, 1039s, 979s, 858m, 743s, 698s, 633m.

2.Supporting experimental results

Crystallographic data

Table S1. Crystallographic data of complexes S-1 and R-1

	S-1	**R-1**
Empirical formula	$C_{71}H_{82}Cu_4N_6O_{21}$	$C_{70.7}H_{80.8}Cu_4N_6O_{21}$
Formula weight	1609.58	1604.77
Temperature/K	180(2)	180.15
Crystal system	monoclinic	monoclinic
Space group	$P2_1$	$P2_1$
A [Å]	10.6198(7)	10.5835(8)
B [Å]	21.4213(14)	21.529(2)
C [Å]	15.6347(12)	15.5711(12)
α [°]	90	90
β [°]	94.833(6)	94.696(6)
γ [°]	90	90
Volume [$Å^3$]	3544.1(4)	3536.0(5)
Z	2	2
ρ_{calc}g [cm^3]	1.508	1.507
μ [mm^{-1}]	1.263	1.266
F(000)	1668	1662
Crystal size [mm^3]	0.34 × 0.18 × 0.16	0.58 × 0.23 × 0.18
Radiation	MoKα (λ = 0.71069)	MoKα (λ = 0.71073)
2Θ range for data collection [°]	3.232 to 53.462	3.784 to 52.742
Index ranges	-13 ≤ h ≤ 13, -24 ≤ k ≤ 27, -16 ≤ l ≤ 19	-11 ≤ h ≤ 13, -26 ≤ k ≤ 26, -19 ≤ l ≤ 19
Reflections collected	29165	28025
Independent reflections	14517 [R_{int} = 0.0493, R_{sigma} = 0.0652]	14367 [R_{int} = 0.0873, R_{sigma} = 0.0750]
Data/restraints/parameters	14517/29/940	14367/34/935
Goodness-of-fit on F^2	0.938	0.978
Final R indexes [I>=2σ (I)]	R_1 = 0.0380, wR_2 = 0.0829	R_1 = 0.0431, wR_2 = 0.1067
Final R indexes [all data]	R_1 = 0.0648, wR_2 = 0.0936	R_1 = 0.0624, wR_2 = 0.1200
Largest diff. peak/hole [e $Å^{-3}$]	0.53/-0.62	0.73/-0.63
Flack parameter	-0.010(7)	0.0+G1:I2903(15)

Table S2. Crystallographic data of complexes S-1: bond lengths

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cu1	O2	1.934(4)	C11	C12	1.512(8)
Cu1	O3	1.996(4)	C12	C13	1.374(9)
Cu1	O6	1.929(4)	C12	C17	1.388(9)
Cu1	O13	2.324(5)	C13	C14	1.381(9)
Cu1	N1	1.941(5)	C14	C15	1.367(11)
Cu2	O5	1.904(4)	C15	C16	1.365(12)
Cu2	O6	1.976(4)	C16	C17	1.393(10)
Cu2	O7	2.380(4)	C18	C19	1.418(8)
Cu2	O8	2.002(4)	C18	C23	1.399(10)
Cu2	O12	2.504(4)	C19	C20	1.362(9)
Cu2	N2	1.930(5)	C20	C21	1.389(12)
Cu3	O8	1.936(4)	C21	C22	1.365(10)
Cu3	O9	1.971(5)	C22	C23	1.405(9)
Cu3	O12	1.951(4)	C23	C24	1.443(9)
Cu3	O14	2.305(4)	C26	C27	1.507(9)
Cu3	N3	1.948(5)	C26	C28	1.525(9)
Cu4	O1	2.423(4)	C28	C29	1.501(9)
Cu4	O2	1.985(4)	C29	C30	1.397(10)
Cu4	O6	2.444(4)	C29	C34	1.369(10)
Cu4	O11	1.926(4)	C30	C31	1.378(9)
Cu4	O12	1.991(4)	C31	C32	1.355(10)
Cu4	N4	1.931(5)	C32	C33	1.382(10)
O1	C2	1.351(8)	C33	C34	1.388(9)
O1	C8	1.444(8)	C35	C36	1.422(9)
O2	C1	1.325(7)	C35	C40	1.391(8)
O3	C10	1.429(8)	C36	C37	1.374(9)
O4	C19	1.375(8)	C37	C38	1.373(10)
O4	C25	1.424(8)	C38	C39	1.379(10)
O5	C18	1.314(7)	C39	C40	1.400(9)
O6	C27	1.431(8)	C40	C41	1.450(9)
O7	C36	1.350(8)	C43	C44	1.524(10)
O7	C42	1.434(8)	C43	C45	1.531(9)
O8	C35	1.324(7)	C45	C46	1.516(10)
O9	C44	1.438(9)	C46	C47	1.387(10)
O10	C53	1.353(9)	C46	C51	1.374(11)
O10	C59	1.427(9)	C47	C48	1.383(11)
O11	C52	1.321(8)	C48	C49	1.356(13)
O12	C61	1.407(7)	C49	C50	1.366(14)
O13	C69	1.420(10)	C50	C51	1.387(12)
O14	C70	1.415(8)	C52	C53	1.434(9)
O18	N6	1.242(10)	C52	C57	1.394(9)
O19	N6	1.209(11)	C53	C54	1.374(10)

O20	N6	1.202(9)	C54	C55	1.389(12)
N1	C7	1.299(8)	C55	C56	1.363(10)
N1	C9	1.454(8)	C56	C57	1.410(9)
N2	C24	1.282(7)	C57	C58	1.439(9)
N2	C26	1.481(8)	C60	C61	1.512(9)
N3	C41	1.277(8)	C60	C62	1.518(9)
N3	C43	1.482(8)	C62	C63	1.499(8)
N4	C58	1.287(8)	C63	C64	1.379(10)
N4	C60	1.483(8)	C63	C68	1.395(10)
C1	C2	1.407(9)	C64	C65	1.377(10)
C1	C6	1.402(9)	C65	C66	1.352(11)
C2	C3	1.391(10)	C66	C67	1.379(12)
C3	C4	1.374(10)	C67	C68	1.385(10)
C4	C5	1.357(10)	O71A	C71A	1.49(2)
C5	C6	1.421(9)	O15	N5	1.271(8)
C6	C7	1.437(9)	O16	N5	1.237(9)
C9	C10	1.524(8)	O17	N5	1.216(10)
C9	C11	1.535(8)	C71B	O71B	1.44(3)

Table S3. Crystallographic data of complexes S-1: bond angles

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O2	Cu1	O3	173.84(19)	C3	C2	C1	120.5(6)
O2	Cu1	O13	88.29(18)	C4	C3	C2	119.9(7)
O2	Cu1	N1	91.98(19)	C5	C4	C3	121.8(6)
O3	Cu1	O13	95.05(18)	C4	C5	C6	119.5(6)
O6	Cu1	O2	86.59(17)	C1	C6	C5	119.9(6)
O6	Cu1	O3	98.28(17)	C1	C6	C7	123.1(5)
O6	Cu1	O13	94.58(17)	C5	C6	C7	116.7(6)
O6	Cu1	N1	164.20(18)	N1	C7	C6	126.1(6)
N1	Cu1	O3	82.31(19)	N1	C9	C10	107.0(5)
N1	Cu1	O13	101.11(18)	N1	C9	C11	109.8(5)
O5	Cu2	O6	174.67(19)	C10	C9	C11	111.8(5)
O5	Cu2	O7	95.25(17)	O3	C10	C9	108.8(5)
O5	Cu2	O8	91.03(18)	C12	C11	C9	112.0(5)
O5	Cu2	O12	92.64(16)	C13	C12	C11	120.8(6)
O5	Cu2	N2	93.39(19)	C13	C12	C17	118.7(6)
O6	Cu2	O7	90.08(16)	C17	C12	C11	120.5(6)
O6	Cu2	O8	90.67(16)	C12	C13	C14	121.2(6)
O6	Cu2	O12	83.08(15)	C15	C14	C13	119.7(7)
O7	Cu2	O12	144.01(14)	C16	C15	C14	120.3(7)
O8	Cu2	O7	72.90(16)	C15	C16	C17	120.2(7)
O8	Cu2	O12	71.91(15)	C12	C17	C16	119.9(7)
N2	Cu2	O6	85.52(19)	O5	C18	C19	118.1(6)
N2	Cu2	O7	100.08(19)	O5	C18	C23	124.3(5)

N2	Cu2	O8	172.0(2)	C23	C18	C19	117.6(5)
N2	Cu2	O12	114.44(18)	O4	C19	C18	113.3(5)
O8	Cu3	O9	171.39(19)	C20	C19	O4	124.9(6)
O8	Cu3	O12	87.04(18)	C20	C19	C18	121.8(7)
O8	Cu3	O14	93.58(16)	C19	C20	C21	119.7(6)
O8	Cu3	N3	91.1(2)	C22	C21	C20	120.5(7)
O9	Cu3	O14	92.79(18)	C21	C22	C23	120.6(7)
O12	Cu3	O9	98.3(2)	C18	C23	C22	119.9(6)
O12	Cu3	O14	94.22(16)	C18	C23	C24	123.2(5)
N3	Cu3	O9	82.5(2)	C22	C23	C24	116.9(6)
N3	Cu3	O12	169.30(19)	N2	C24	C23	125.3(6)
N3	Cu3	O14	96.41(19)	N2	C26	C27	106.0(5)
O1	Cu4	O6	143.56(15)	N2	C26	C28	116.4(5)
O2	Cu4	O1	71.31(16)	C27	C26	C28	112.8(6)
O2	Cu4	O6	72.64(15)	O6	C27	C26	110.1(5)
O2	Cu4	O12	90.87(17)	C29	C28	C26	109.9(5)
O11	Cu4	O1	94.33(18)	C30	C29	C28	119.5(6)
O11	Cu4	O2	91.68(18)	C34	C29	C28	122.1(7)
O11	Cu4	O6	91.86(17)	C34	C29	C30	118.2(6)
O11	Cu4	O12	174.62(19)	C31	C30	C29	120.6(7)
O11	Cu4	N4	93.0(2)	C32	C31	C30	120.3(7)
O12	Cu4	O1	90.97(17)	C31	C32	C33	120.3(6)
O12	Cu4	O6	84.39(15)	C32	C33	C34	119.3(7)
N4	Cu4	O1	102.85(19)	C29	C34	C33	121.2(7)
N4	Cu4	O2	172.8(2)	O8	C35	C36	118.6(5)
N4	Cu4	O6	112.65(19)	O8	C35	C40	123.1(6)
N4	Cu4	O12	84.94(19)	C40	C35	C36	118.4(6)
C2	O1	Cu4	109.7(4)	O7	C36	C35	114.6(5)
C2	O1	C8	119.6(5)	O7	C36	C37	124.9(6)
C8	O1	Cu4	129.6(4)	C37	C36	C35	120.5(6)
Cu1	O2	Cu4	106.90(19)	C38	C37	C36	120.5(7)
C1	O2	Cu1	128.6(4)	C37	C38	C39	120.2(6)
C1	O2	Cu4	124.3(4)	C38	C39	C40	120.5(6)
C10	O3	Cu1	113.3(4)	C35	C40	C39	119.9(6)
C19	O4	C25	117.3(5)	C35	C40	C41	123.2(6)
C18	O5	Cu2	126.8(4)	C39	C40	C41	116.8(6)
Cu1	O6	Cu2	123.7(2)	N3	C41	C40	125.4(6)
Cu1	O6	Cu4	91.32(15)	N3	C43	C44	106.1(6)
Cu2	O6	Cu4	94.63(17)	N3	C43	C45	109.7(5)
C27	O6	Cu1	118.9(4)	C44	C43	C45	111.0(6)
C27	O6	Cu2	106.7(3)	O9	C44	C43	108.7(5)
C27	O6	Cu4	118.5(4)	C46	C45	C43	112.9(6)
C36	O7	Cu2	110.8(4)	C47	C46	C45	119.8(7)
C36	O7	C42	118.6(5)	C51	C46	C45	121.1(7)
C42	O7	Cu2	130.7(5)	C51	C46	C47	119.1(7)

Cu3	O8	Cu2	107.04(19)	C48	C47	C46	120.1(8)
C35	O8	Cu2	122.9(4)	C49	C48	C47	120.2(9)
C35	O8	Cu3	129.0(4)	C48	C49	C50	120.4(9)
C44	O9	Cu3	113.8(4)	C49	C50	C51	120.1(9)
C53	O10	C59	116.7(6)	C46	C51	C50	120.1(8)
C52	O11	Cu4	125.3(4)	O11	C52	C53	117.2(6)
Cu3	O12	Cu2	89.70(15)	O11	C52	C57	125.2(5)
Cu3	O12	Cu4	127.1(2)	C57	C52	C53	117.6(6)
Cu4	O12	Cu2	92.43(16)	O10	C53	C52	114.5(6)
C61	O12	Cu2	116.9(4)	O10	C53	C54	125.2(6)
C61	O12	Cu3	118.8(4)	C54	C53	C52	120.3(7)
C61	O12	Cu4	107.0(4)	C53	C54	C55	121.4(7)
C69	O13	Cu1	135.6(5)	C56	C55	C54	119.0(7)
C70	O14	Cu3	134.3(4)	C55	C56	C57	121.6(7)
C7	N1	Cu1	126.1(4)	C52	C57	C56	120.1(6)
C7	N1	C9	119.7(5)	C52	C57	C58	123.3(6)
C9	N1	Cu1	114.2(4)	C56	C57	C58	116.6(6)
C24	N2	Cu2	125.7(5)	N4	C58	C57	124.9(6)
C24	N2	C26	122.3(5)	N4	C60	C61	105.3(5)
C26	N2	Cu2	112.0(4)	N4	C60	C62	115.8(5)
C41	N3	Cu3	127.5(4)	C61	C60	C62	112.8(6)
C41	N3	C43	118.0(6)	O12	C61	C60	109.9(5)
C43	N3	Cu3	114.5(4)	C63	C62	C60	111.2(5)
C58	N4	Cu4	126.1(5)	C64	C63	C62	122.3(6)
C58	N4	C60	122.1(6)	C64	C63	C68	117.8(6)
C60	N4	Cu4	111.8(4)	C68	C63	C62	119.8(7)
O19	N6	O18	119.1(9)	C65	C64	C63	121.6(7)
O20	N6	O18	126.4(10)	C66	C65	C64	119.8(8)
O20	N6	O19	114.4(11)	C65	C66	C67	120.9(7)
O2	C1	C2	118.3(6)	C66	C67	C68	119.3(8)
O2	C1	C6	123.2(5)	C67	C68	C63	120.6(8)
C6	C1	C2	118.4(5)	O16	N5	O15	119.4(8)
O1	C2	C1	114.3(6)	O17	N5	O15	116.9(8)
O1	C2	C3	125.2(6)	O17	N5	O16	123.8(7)

Table S4. Crystallographic data of complexes R-1: bond lengths

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cu1	O2	1.931(5)	C16	C17	1.381(11)
Cu1	O3	2.004(5)	C18	C19	1.428(10)
Cu1	O6	1.938(4)	C18	C23	1.393(10)
Cu1	O13	2.302(5)	C19	C20	1.363(11)
Cu1	N1	1.942(5)	C20	C21	1.387(13)
Cu2	O5	1.911(5)	C21	C22	1.365(12)
Cu2	O6	1.972(4)	C22	C23	1.416(10)
Cu2	O7	2.387(5)	C23	C24	1.433(10)
Cu2	O8	1.995(4)	C26	C27	1.523(9)
Cu2	N2	1.928(5)	C26	C28	1.519(10)
Cu3	O8	1.933(5)	C28	C29	1.493(10)
Cu3	O9	1.969(5)	C29	C30	1.378(11)
Cu3	O12	1.948(4)	C29	C34	1.404(11)
Cu3	O14	2.301(5)	C30	C31	1.373(11)
Cu3	N3	1.944(6)	C31	C32	1.382(12)
Cu4	O1	2.425(5)	C32	C33	1.385(12)
Cu4	O2	1.984(4)	C33	C34	1.372(11)
Cu4	O11	1.922(5)	C35	C36	1.408(10)
Cu4	O12	1.981(5)	C35	C40	1.394(9)
Cu4	N4	1.940(6)	C36	C37	1.367(10)
O1	C2	1.358(9)	C37	C38	1.394(12)
O1	C8	1.423(9)	C38	C39	1.372(12)
O2	C1	1.326(8)	C39	C40	1.417(10)
O3	C10	1.428(9)	C40	C41	1.436(10)
O4	C19	1.375(9)	C43	C44	1.515(12)
O4	C25	1.418(9)	C43	C45	1.528(11)
O5	C18	1.303(8)	C45	C46	1.506(12)
O6	C27	1.427(8)	C46	C47	1.370(13)
O7	C36	1.367(8)	C46	C51	1.383(12)
O7	C42	1.421(9)	C47	C48	1.398(16)
O8	C35	1.333(8)	C48	C49	1.373(18)
O9	C44	1.447(9)	C49	C50	1.339(16)
O10	C53	1.368(11)	C50	C51	1.368(14)
O10	C59	1.426(11)	C52	C53	1.425(10)
O11	C52	1.305(9)	C52	C57	1.396(11)
O12	C61	1.421(8)	C53	C54	1.367(13)
O13	C69A	1.414(13)	C54	C55	1.384(14)
O14	C70	1.421(9)	C55	C56	1.382(13)
N1	C7	1.292(9)	C56	C57	1.418(11)
N1	C9	1.455(8)	C57	C58	1.442(11)
N2	C24	1.297(9)	C60	C61	1.513(10)
N2	C26	1.474(9)	C60	C62	1.512(10)
N3	C41	1.296(10)	C62	C63	1.495(11)

N3	C43	1.472(9)	C63	C64	1.393(12)
N4	C58	1.278(9)	C63	C68	1.374(11)
N4	C60	1.482(9)	C64	C65	1.380(13)
C1	C2	1.411(10)	C65	C66	1.381(14)
C1	C6	1.406(10)	C66	C67	1.359(14)
C2	C3	1.382(11)	C67	C68	1.385(12)
C3	C4	1.377(12)	O18A	N6A	1.162(13)
C4	C5	1.367(11)	O18B	N6B	1.249(18)
C5	C6	1.423(10)	O19A	N6A	1.251(15)
C6	C7	1.439(10)	O19B	N6B	1.245(19)
C9	C10	1.533(10)	O20A	N6A	1.234(14)
C9	C11	1.527(9)	O20B	N6B	1.253(19)
C11	C12	1.499(9)	O71A	C71	1.43(2)
C12	C13	1.388(11)	O71B	C71	1.38(2)
C12	C17	1.389(10)	O15	N5	1.259(9)
C13	C14	1.394(12)	O16	N5	1.247(10)
C14	C15	1.374(14)	O17	N5	1.211(11)
C15	C16	1.371(13)			

Table S5. Crystallographic data of complexes R-1: bond angles

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O2	Cu1	O3	173.9(2)	C13	C12	C11	121.5(6)
O2	Cu1	O6	86.78(19)	C13	C12	C17	117.7(7)
O2	Cu1	O13	89.1(2)	C17	C12	C11	120.8(6)
O2	Cu1	N1	91.9(2)	C12	C13	C14	121.2(8)
O3	Cu1	O13	94.5(2)	C15	C14	C13	119.3(8)
O6	Cu1	O3	97.8(2)	C16	C15	C14	120.6(8)
O6	Cu1	O13	95.01(19)	C15	C16	C17	119.7(8)
O6	Cu1	N1	164.6(2)	C16	C17	C12	121.5(7)
N1	Cu1	O3	82.6(2)	O5	C18	C19	117.7(6)
N1	Cu1	O13	100.3(2)	O5	C18	C23	125.3(6)
O5	Cu2	O6	174.4(2)	C23	C18	C19	117.0(6)
O5	Cu2	O7	95.52(19)	O4	C19	C18	113.1(6)
O5	Cu2	O8	90.64(19)	C20	C19	O4	125.1(7)
O5	Cu2	N2	93.7(2)	C20	C19	C18	121.8(7)
O6	Cu2	O7	90.09(18)	C19	C20	C21	120.2(7)
O6	Cu2	O8	91.28(18)	C22	C21	C20	120.2(8)
O8	Cu2	O7	73.20(18)	C21	C22	C23	120.4(8)
N2	Cu2	O6	85.0(2)	C18	C23	C22	120.4(7)
N2	Cu2	O7	99.8(2)	C18	C23	C24	123.0(6)
N2	Cu2	O8	172.1(2)	C22	C23	C24	116.5(7)
O8	Cu3	O9	171.8(2)	N2	C24	C23	125.7(6)
O8	Cu3	O12	86.71(19)	N2	C26	C27	105.5(5)

O8	Cu3	O14	92.96(19)	N2	C26	C28	116.0(6)
O8	Cu3	N3	91.5(2)	C28	C26	C27	111.8(6)
O9	Cu3	O14	92.9(2)	O6	C27	C26	108.5(5)
O12	Cu3	O9	98.5(2)	C29	C28	C26	110.0(6)
O12	Cu3	O14	94.88(18)	C30	C29	C28	121.6(7)
N3	Cu3	O9	82.1(2)	C30	C29	C34	117.4(7)
N3	Cu3	O12	168.9(2)	C34	C29	C28	120.8(7)
N3	Cu3	O14	96.2(2)	C31	C30	C29	122.1(8)
O2	Cu4	O1	71.72(18)	C30	C31	C32	120.2(8)
O11	Cu4	O1	94.9(2)	C31	C32	C33	118.8(8)
O11	Cu4	O2	91.7(2)	C34	C33	C32	120.8(8)
O11	Cu4	O12	174.1(2)	C33	C34	C29	120.7(8)
O11	Cu4	N4	92.8(2)	O8	C35	C36	119.4(6)
O12	Cu4	O1	90.97(19)	O8	C35	C40	121.9(6)
O12	Cu4	O2	90.80(19)	C40	C35	C36	118.7(6)
N4	Cu4	O1	101.9(2)	O7	C36	C35	114.6(6)
N4	Cu4	O2	172.5(2)	O7	C36	C37	123.9(7)
N4	Cu4	O12	85.3(2)	C37	C36	C35	121.6(7)
C2	O1	Cu4	109.4(4)	C36	C37	C38	119.6(7)
C2	O1	C8	118.6(6)	C39	C38	C37	120.3(7)
C8	O1	Cu4	131.2(5)	C38	C39	C40	120.5(7)
Cu1	O2	Cu4	106.8(2)	C35	C40	C39	119.1(7)
C1	O2	Cu1	128.9(4)	C35	C40	C41	124.2(6)
C1	O2	Cu4	124.0(4)	C39	C40	C41	116.6(6)
C10	O3	Cu1	112.8(4)	N3	C41	C40	125.7(6)
C19	O4	C25	117.5(6)	N3	C43	C44	106.7(6)
C18	O5	Cu2	126.2(4)	N3	C43	C45	109.3(6)
Cu1	O6	Cu2	123.8(2)	C44	C43	C45	112.8(7)
C27	O6	Cu1	117.8(4)	O9	C44	C43	107.8(6)
C27	O6	Cu2	107.2(4)	C46	C45	C43	114.3(7)
C36	O7	Cu2	110.2(4)	C47	C46	C45	121.1(9)
C36	O7	C42	119.1(6)	C47	C46	C51	118.2(9)
C42	O7	Cu2	130.8(5)	C51	C46	C45	120.7(8)
Cu3	O8	Cu2	107.3(2)	C46	C47	C48	119.8(11)
C35	O8	Cu2	122.6(4)	C49	C48	C47	120.6(10)
C35	O8	Cu3	129.5(4)	C50	C49	C48	119.1(11)
C44	O9	Cu3	114.1(5)	C49	C50	C51	121.3(11)
C53	O10	C59	117.2(8)	C50	C51	C46	121.0(9)
C52	O11	Cu4	126.3(5)	O11	C52	C53	118.8(7)
Cu3	O12	Cu4	127.5(2)	O11	C52	C57	124.7(6)
C61	O12	Cu3	118.0(4)	C57	C52	C53	116.6(7)
C61	O12	Cu4	106.8(4)	O10	C53	C52	113.8(7)
C69A	O13	Cu1	139.0(8)	C54	C53	O10	124.0(7)
C70	O14	Cu3	133.5(5)	C54	C53	C52	122.1(8)
C7	N1	Cu1	125.9(5)	C53	C54	C55	120.9(8)

C7	N1	C9	119.7(5)	C56	C55	C54	118.9(8)
C9	N1	Cu1	114.4(4)	C55	C56	C57	120.8(9)
C24	N2	Cu2	124.9(5)	C52	C57	C56	120.6(7)
C24	N2	C26	122.8(6)	C52	C57	C58	123.2(6)
C26	N2	Cu2	112.3(4)	C56	C57	C58	116.2(7)
C41	N3	Cu3	126.5(5)	N4	C58	C57	125.5(7)
C41	N3	C43	118.9(6)	N4	C60	C61	105.3(6)
C43	N3	Cu3	114.6(5)	N4	C60	C62	116.1(6)
C58	N4	Cu4	125.3(5)	C62	C60	C61	113.2(6)
C58	N4	C60	122.9(6)	O12	C61	C60	110.3(6)
C60	N4	Cu4	111.7(4)	C63	C62	C60	111.1(6)
O2	C1	C2	118.6(6)	C64	C63	C62	119.8(7)
O2	C1	C6	122.9(6)	C68	C63	C62	121.6(8)
C6	C1	C2	118.5(6)	C68	C63	C64	118.5(8)
O1	C2	C1	114.3(6)	C65	C64	C63	120.3(9)
O1	C2	C3	125.4(7)	C64	C65	C66	119.6(9)
C3	C2	C1	120.3(7)	C67	C66	C65	120.8(8)
C4	C3	C2	120.7(7)	C66	C67	C68	119.4(9)
C5	C4	C3	121.0(7)	C63	C68	C67	121.3(9)
C4	C5	C6	119.6(7)	O18A	N6A	O19A	121.0(14)
C1	C6	C5	119.9(6)	O18A	N6A	O20A	127.8(14)
C1	C6	C7	122.6(6)	O20A	N6A	O19A	109.8(12)
C5	C6	C7	117.2(6)	O18B	N6B	O20B	125.8(18)
N1	C7	C6	126.7(6)	O19B	N6B	O18B	116.3(16)
N1	C9	C10	106.7(5)	O19B	N6B	O20B	117.9(17)
N1	C9	C11	109.4(5)	O16	N5	O15	119.3(8)
C11	C9	C10	111.9(6)	O17	N5	O15	117.8(9)
O3	C10	C9	109.7(6)	O17	N5	O16	122.8(7)
C12	C11	C9	112.3(6)				

Powder X-ray diffraction (PXRD) pattern

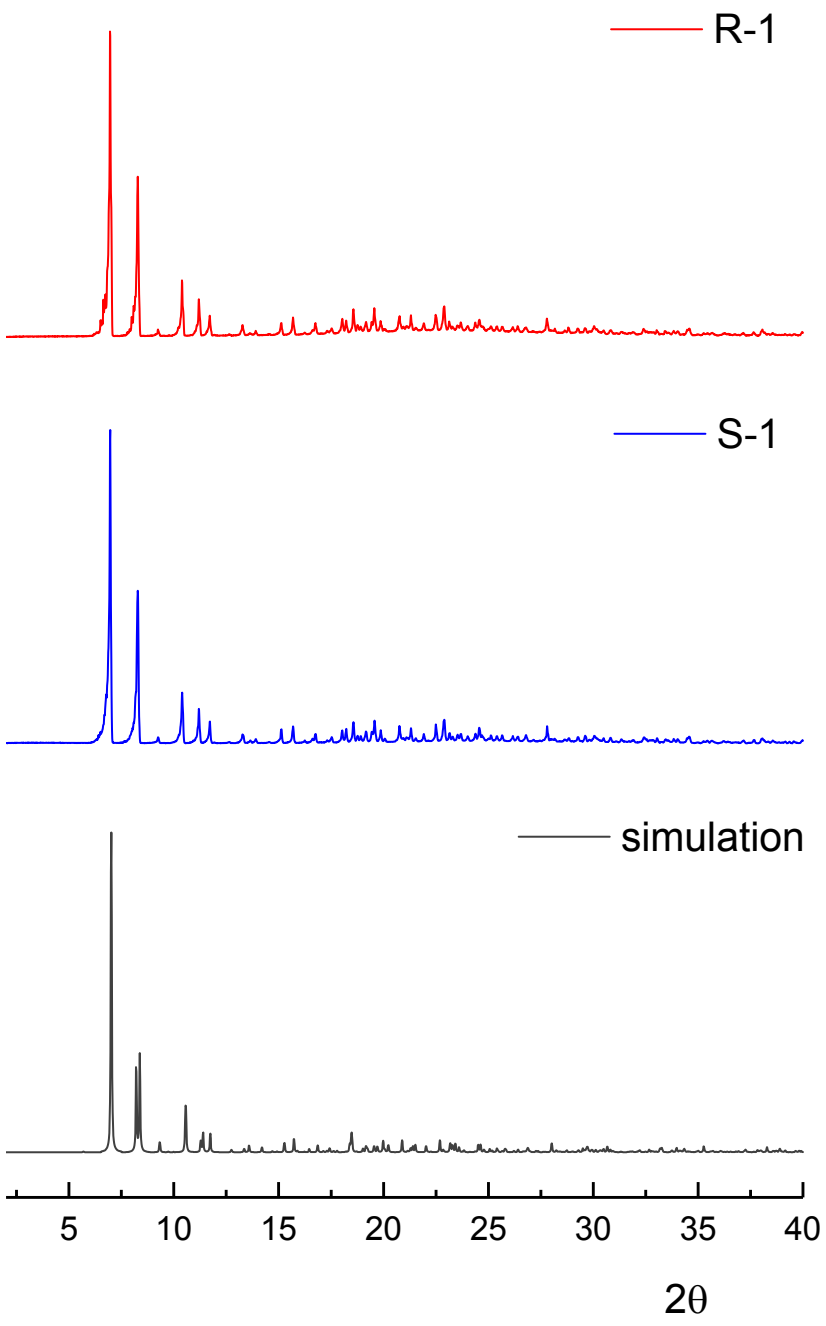


Figure S1 Comparison of PXRD pattern of **S-1** and **R-1** to simulation pattern.

NMR and IR spectrums

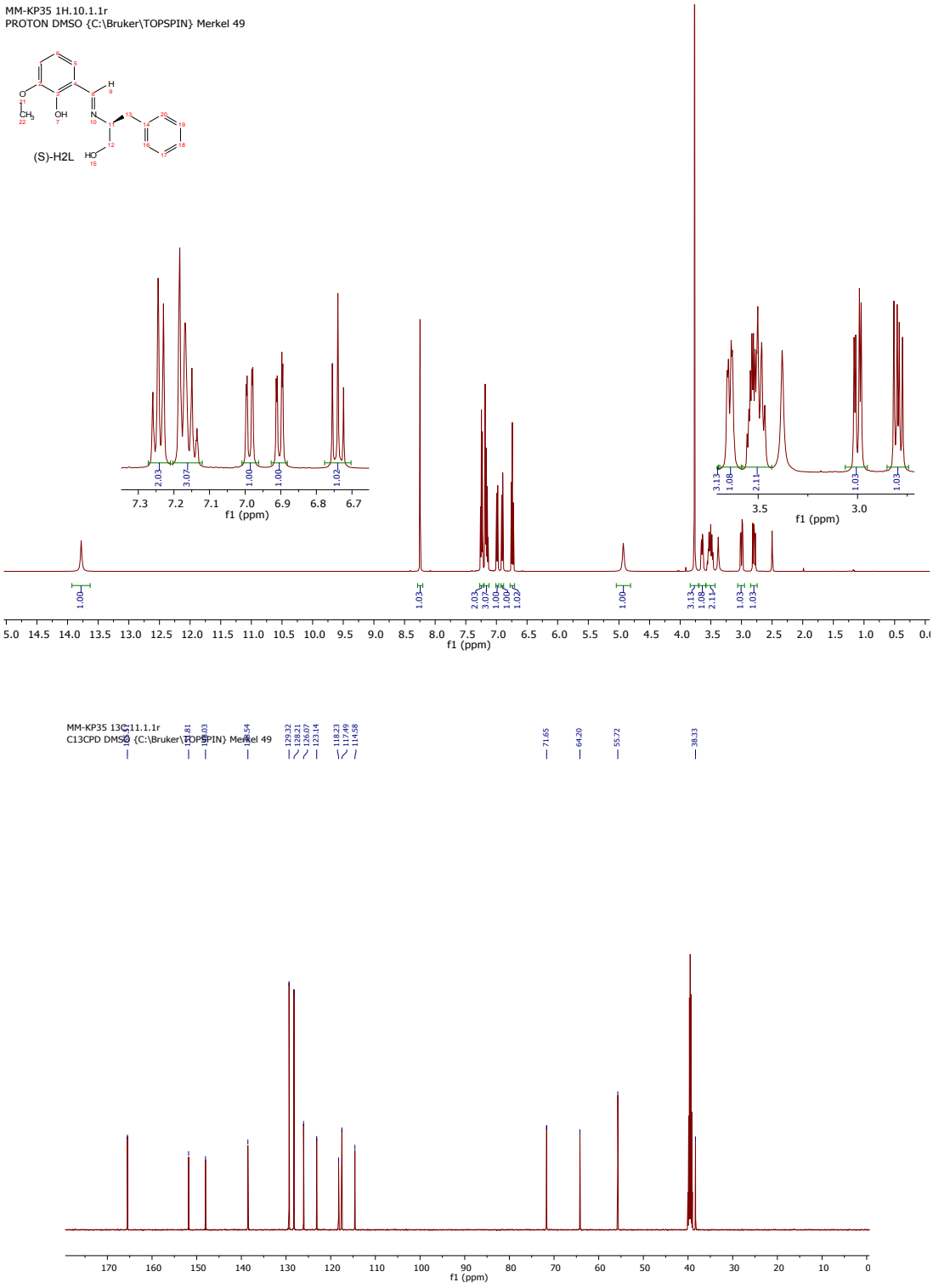


Figure S2. ^{1}H and ^{13}C NMR of chiral Schiff-base (S)-H_2L.

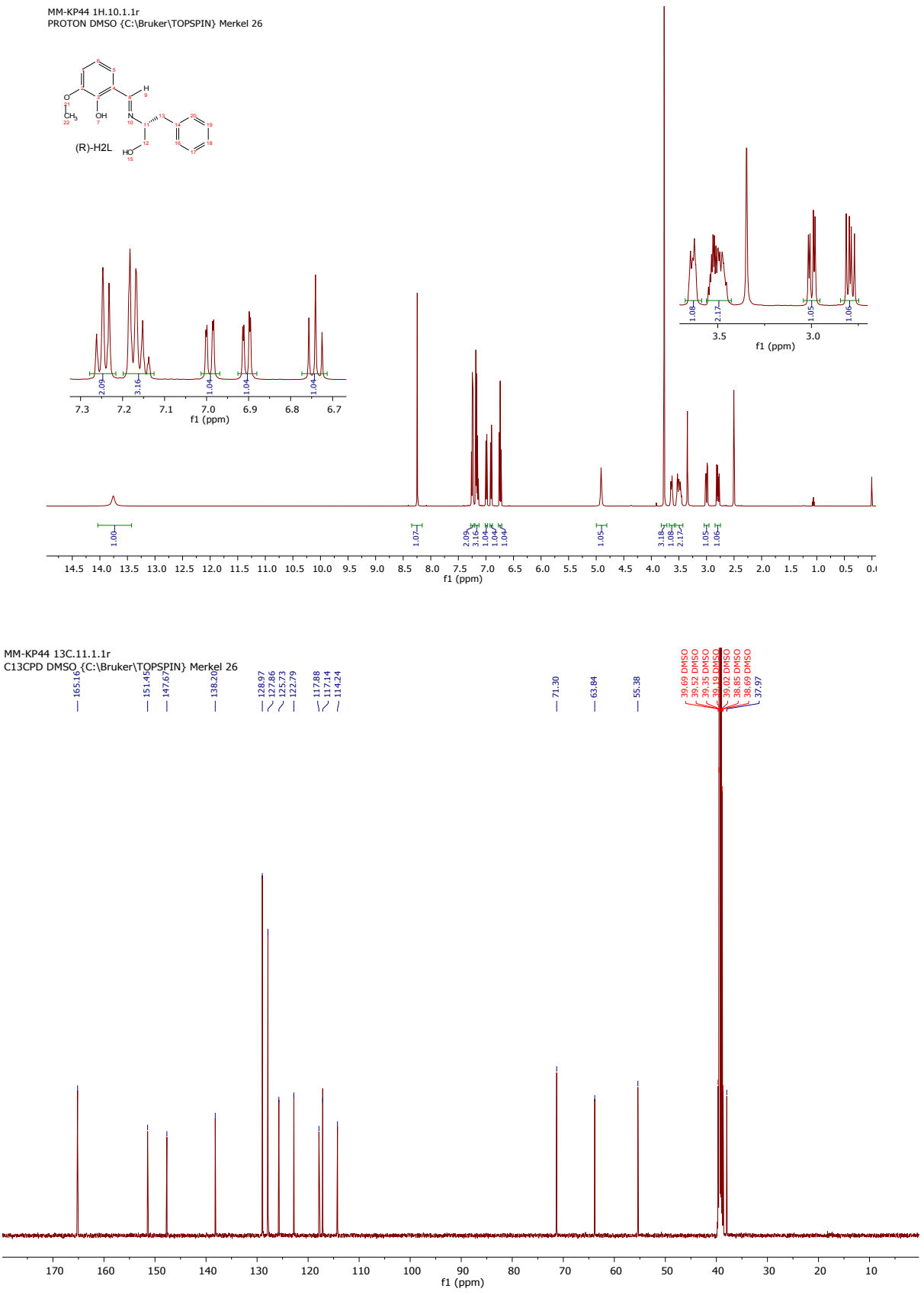


Figure S3.^{1}H and ^{13}C NMR of chiral Schiff-base (R)-H_2L.

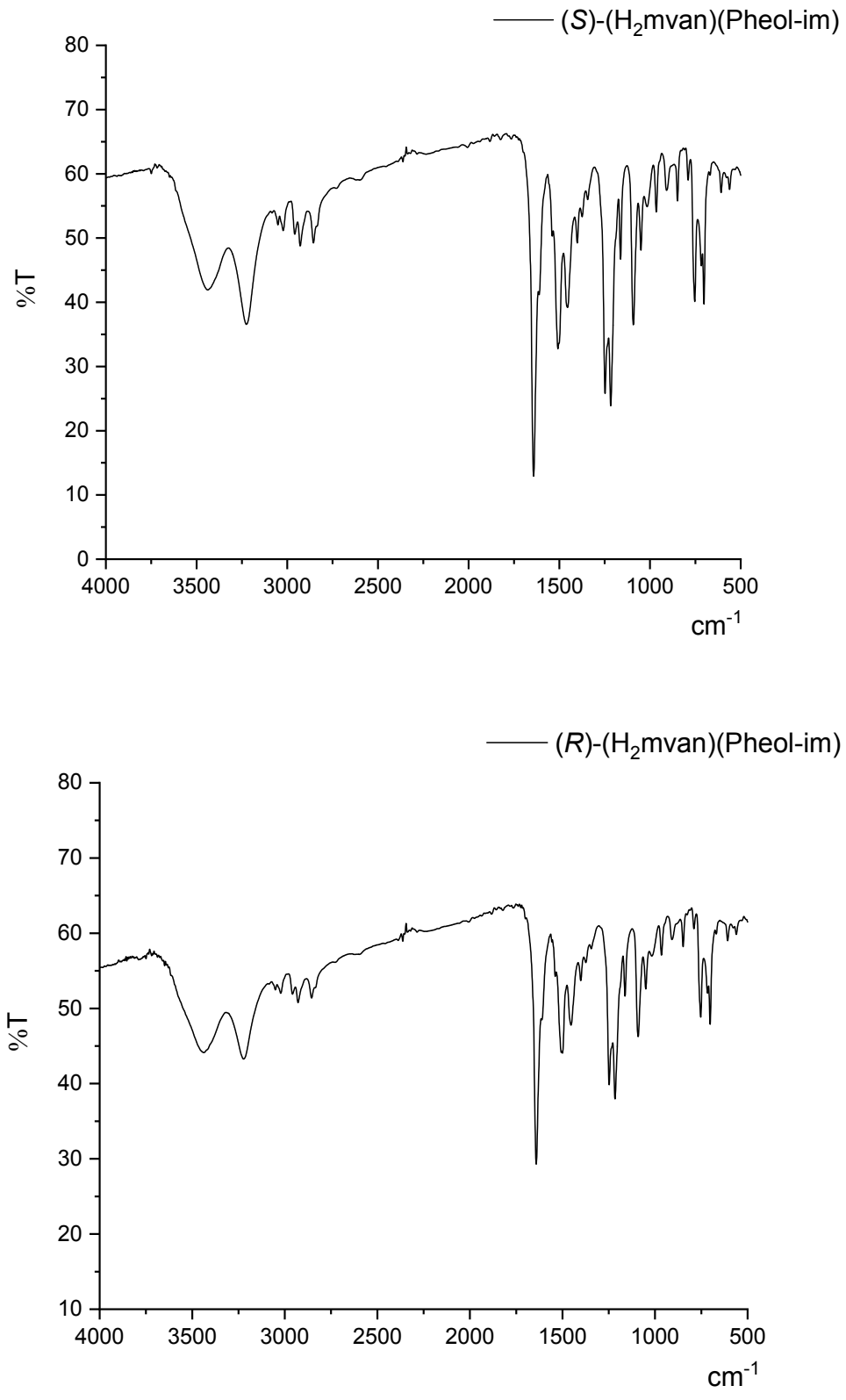


Figure S4. IR spectra of chiral Schiff-base (*S*)-H_2L and (*R*)-H_2L in KBr pallet.

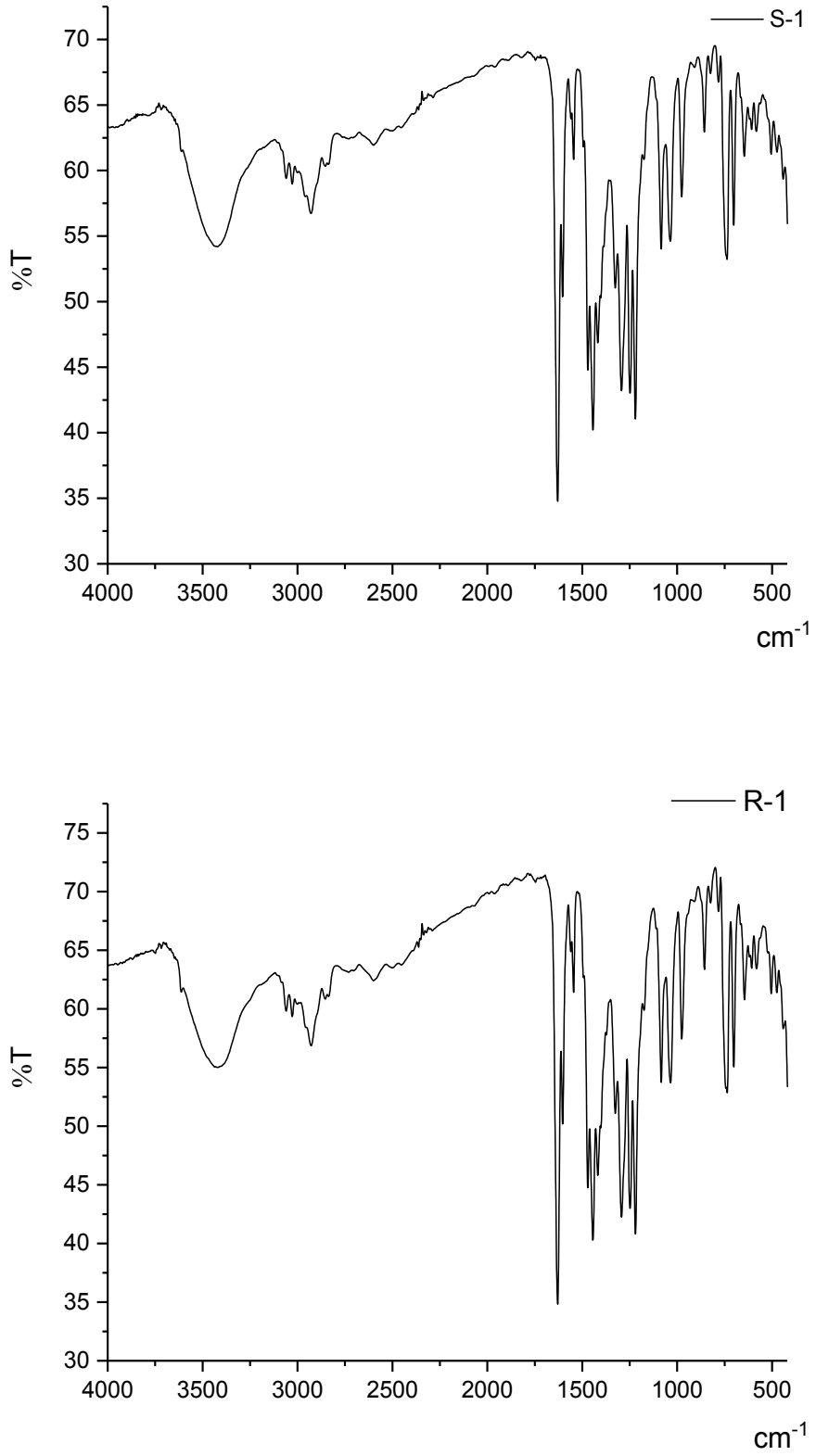


Figure S5. IR spectra of **S-1** and **R-1** in KBr pallet.

UV-Vis of Complex S-1 and R-1 comparison to S-H_2L

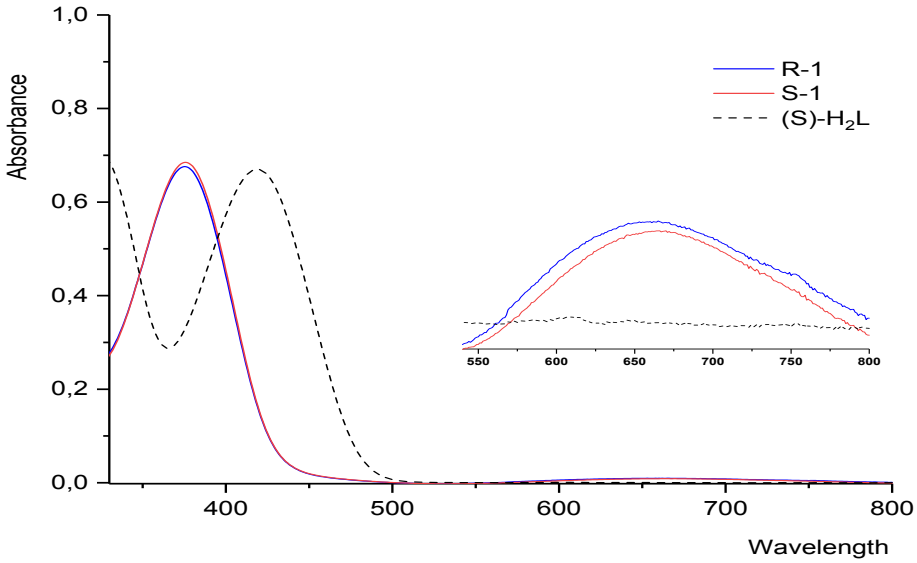
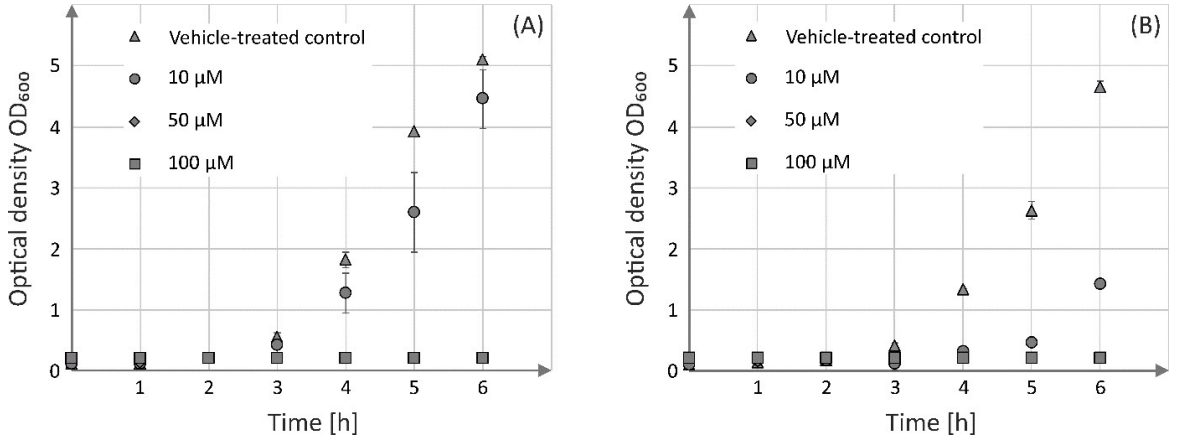


Figure S6. Absorption spectra of **S-1** and **R-1** compare to (*S*)-H_2L ligand.

Antibacterial studies

The antibacterial activity of **S-1** and **R-1** was evaluated in batch cultures. Gram-positive *B. subtilis* as well as Gram-negative *E. coli* were chosen as model systems for this investigation. After direct addition of the complexes dissolved in DMSO to the bacterial media, growth was monitored over time in comparison to vehicle control cultures. These analyses showed that both enantiomers possess comparable growth inhibitory effects towards the Gram-positive strain, but have no bactericidal activity against its Gram-negative counterpart. Incubation of *B. subtilis* in the presence of 50 or 100 μM of either **S-1** or **R-1** prevents their growth entirely, whereas addition of 10 μM of both substances only led to growth delay.

a)



b)

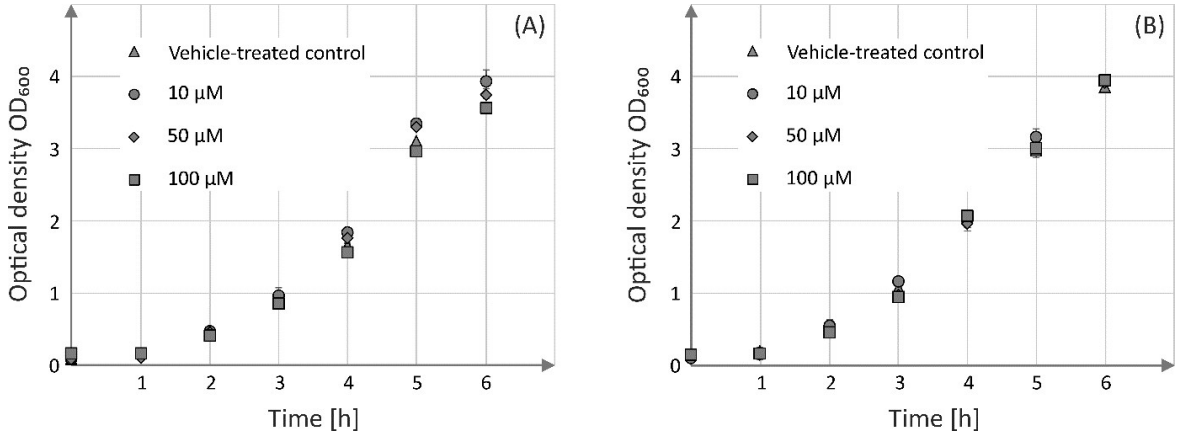


Figure S7. Cell densities measured at a wavelength of 600 nm (OD_{600}) during cultivation of Gram-positive *B. subtilis* (a) and Gram-negative *E. coli* (b) in the presence of 10 μM (circle), 50 μM (rhombus) or 100 μM (square) of **S-1** (A) and **R-1** (B), respectively.

Stability test of Cu(II)-cluster $C_{70}H_{78}Cu_4N_6O_{20}$ (S-1) and (R-1)

The stability of these complexes were investigated by the following of the change of molecular mass over 48h at 37 °C in the presence of 0.4% DMSO in water. The mass spectroscopy analysis reveals the molecular mass of **S-1** and **R-1** at 1735 m/z (plus water molecule and DMSO) and the fragment of two methanol ligand at 1389 m/z. These analysis evidence that both Cu(II)-complexes are stable over 48h in the presence of water (Figure S8)

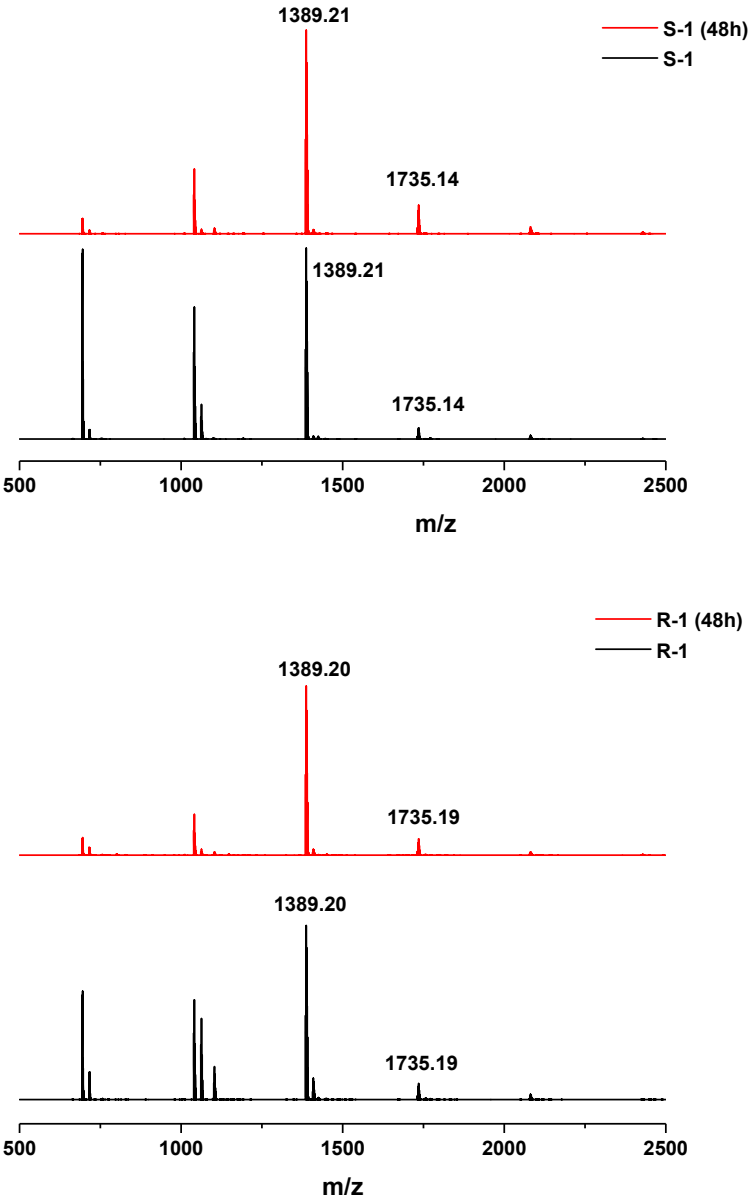


Figure S8. ESI analysis of **S-1** and **R-1** in 0.4% DMSO in H_2O at 37 °C for 48h.