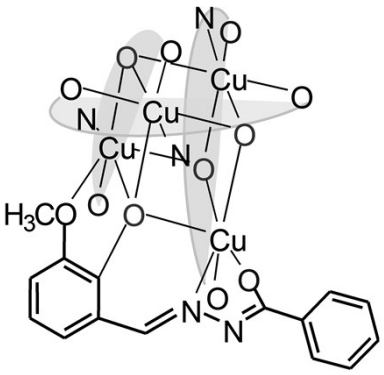
Electronic Supplementary Information **(ESI)**

Copper(II) complexes with benzhydrazone-related ligands: synthesis, structural studies and cytotoxicity assay

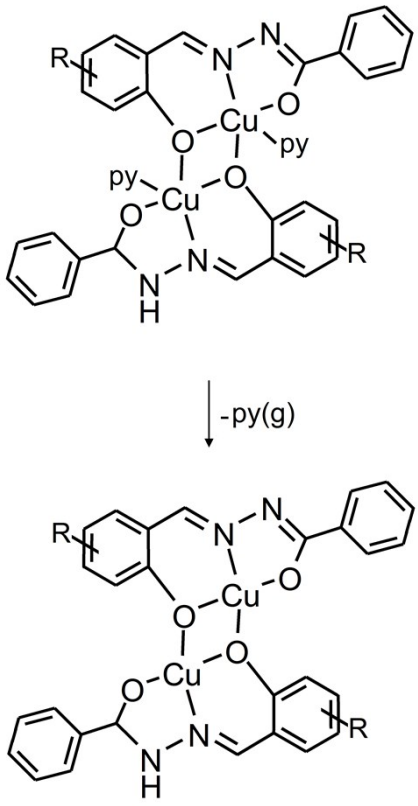
Marina Cindrić, Alen Bjelopetrović, Gordana Pavlović, Vladimir Damjanović, Jasna Lovrić, Dubravka Matković-Čalogović and Višnja Vrdoljak

Contents

Scheme



Scheme S1 The structural formula of the tetranuclear complex $[Cu_4(L^{3OMe})_4]$



Scheme S2 Dinuclear $[Cu_2(L)_2(py)_2]$ (in the upper half of the Scheme) and $[Cu_2(L)_2]$ complexes (in the lower half of the Scheme). The R substituent is shown in red colour in Scheme 1.

Powder X-ray diffraction patterns

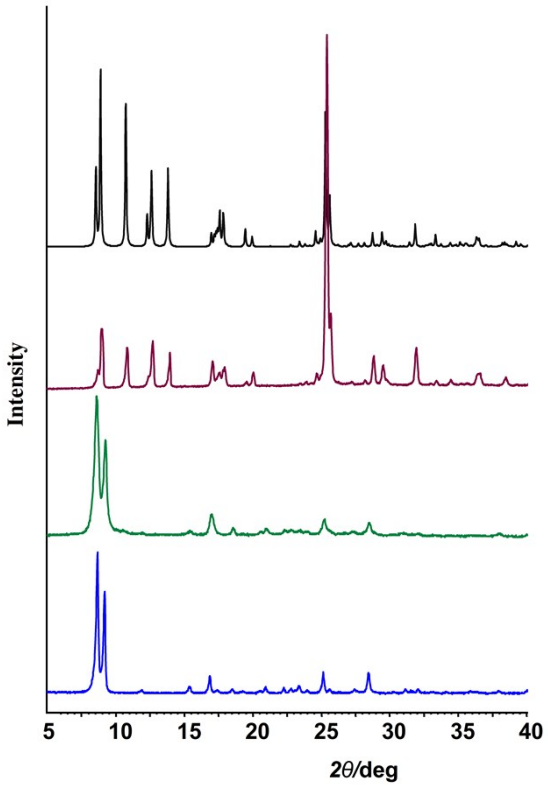


Fig. S1 PXRD patterns (form top to bottom) for: **1py** calculated from the X-ray single-crystal structure (refcode UKEVEL01); **1py** obtained by the solution-based method; **1** obtained by the solid-state thermally induced synthesis; **1** obtained by the conventional solution-based method.

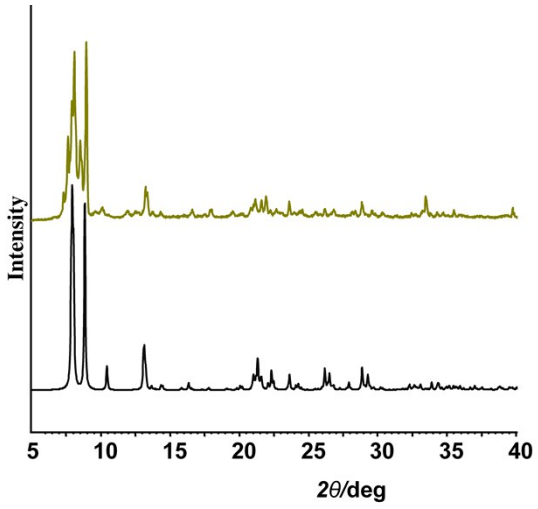


Fig. S2 PXRD patterns of sample obtained upon standing of **2a·4MeOH·2H$_2$O** at room temperature for 5 min (top); and PXRD pattern of **2a·4MeOH·2H$_2$O** calculated from the X-ray single-crystal structure (bottom).

X-Ray Crystallography. Single crystal diffraction.

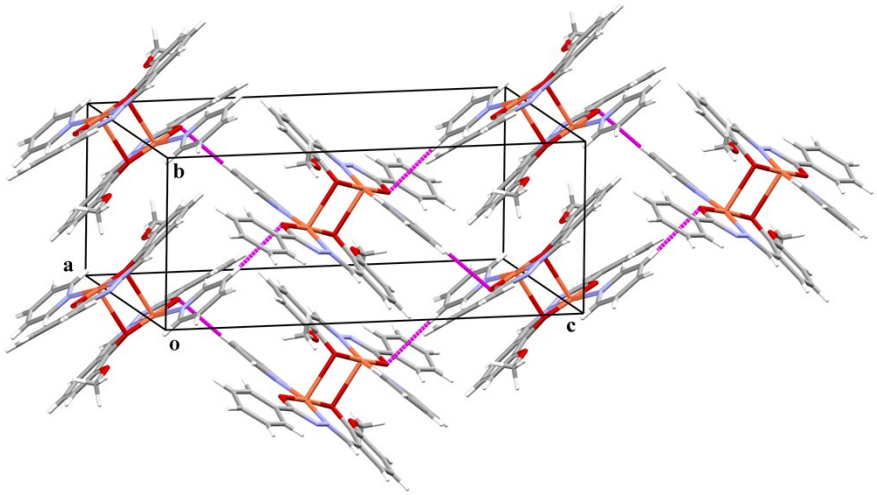


Fig. S3. Layers of 2D infinite chains of rings in **2py·3H$_2$O** structure.

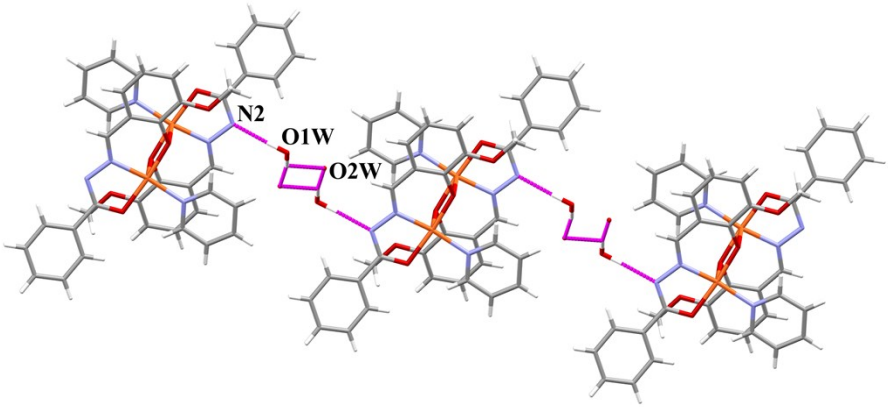


Fig. S4. Supramolecular assembling of **2py·3H$_2$O** *via* hydrogen bonds between H_2O and complex molecules.

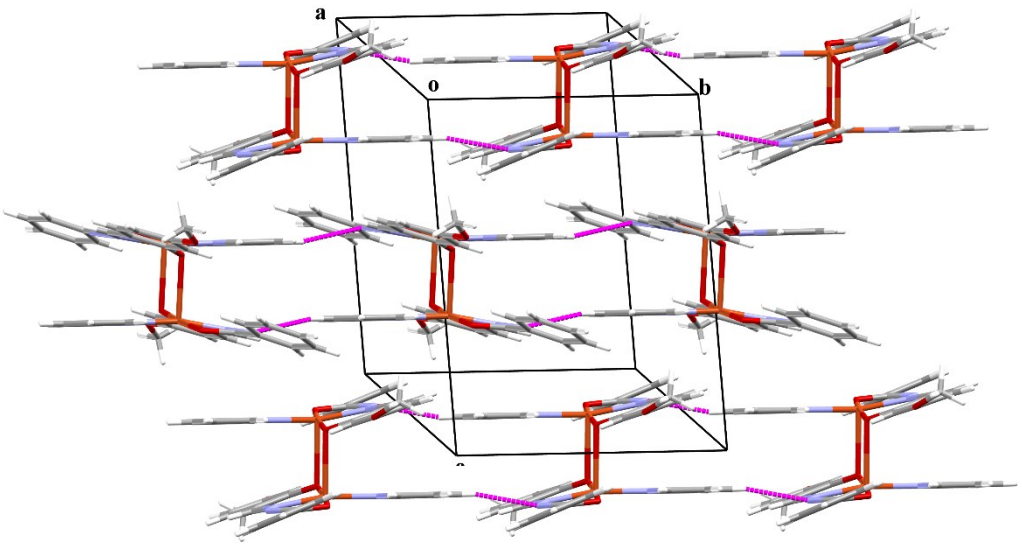
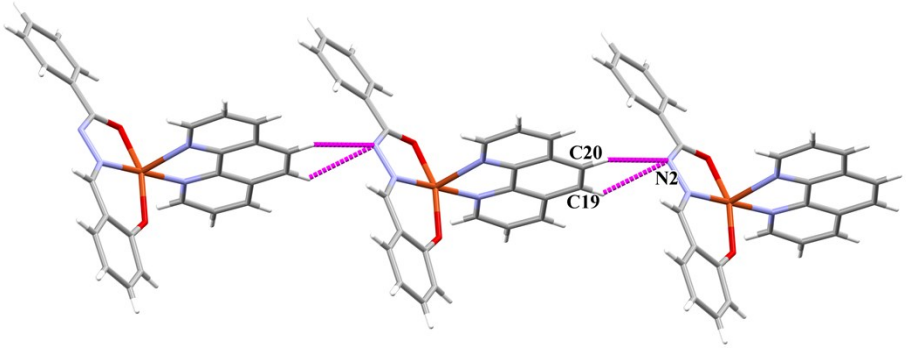
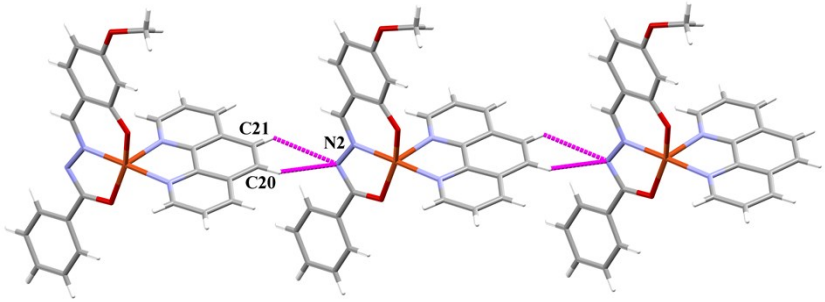


Fig. S5. Layers of 2D infinite chains of rings spreading along *c* axis in **3py** structure.



(a)



(b)

Fig. S6. Partial crystal structure of **1phen** (a) and **3phen** (b) structures showing bifurcation at N2 proton acceptor of C-H···N hydrogen bonds along *b* axis.

Table S1. Selected bond lengths [Å] and angles [°] for complexes: **2py·3H$_2$O**, **3py**, **1bpy*·2MeOH** and **2bpy.**

Complex	2py·3H$_2$O	3py	1bpy*·2MeOH	2bpy
		Bond distances		
Cu1–N1	1.927(2)	1.9265(19)	1.9248(15)	1.9227(16)
Cu1–O1	1.943(2)	1.9425(17)	1.9370(14)	1.9144(15)
Cu1–O2	1.906(2)	1.9086(18)	1.9033(14)	1.8752(15)
Cu1–N3	2.008(2)	2.0091(19)	2.0039(15)	2.0228(17)
Cu1–O2^{i}	2.515(2)	2.567(2)	2.6019(14)	-
Cu1···Cu1^{i}	3.367(1)	3.260(1)	3.348(1)	-
N1–C8	1.293(3)	1.286(3)	1.290(2)	1.292(3)
N1–N2	1.400(2)	1.392(3)	1.391(2)	1.397(2)
N2–C1	1.315(3)	1.309(3)	1.322(2)	1.320(3)
O1–C1	1.293(3)	1.295(3)	1.289(2)	1.296(2)
O2–C10	1.320(3)	1.329(3)	1.320(2)	1.312(2)
		Bond angles		
N1–Cu1–O1	81.01(8)	81.00(8)	81.23(6)	81.53(7)
N1–Cu1–O2	93.10(8)	92.27(7)	93.14(6)	94.03(7)
O1–Cu1–O2	174.01(7)	172.83(7)	171.95(5)	174.91(6)
N1–Cu1–O2^{i}	98.32(7)	100.13(7)	104.15(6)	-
O1–Cu1–O2^{i}	100.14(6)	91.05(8)	90.49(5)	-
O2–Cu1–O2^{i}	81.74(6)	87.69(8)	85.29(5)	-
O2–Cu1–N3	92.89(8)	92.74(8)	92.69(6)	91.08(7)
N1–Cu1–N3	169.69(8)	168.49(9)	167.75(7)	173.59(7)
O1–Cu1–N3	92.89(8)	94.33(8)	93.94(6)	93.19(7)
N3-Cu1-O2^{i}	90.85(8)	90.42(6)	87.06(5)	
τ parameter*	0.07	0.07	0.07	-

Symmetry code: **2py·3H$_2$O**: (i):-x+1,-y+1, -z+1; **3py**: i =2-x,1-y,-z; **1bpy*·2MeOH**: i =2-x,-y,2-z.

*Ideal τ (calculated as ($\angle$(O1–Cu1–O2) – $\angle$(N1–Cu1–N3)]/60°) is 0 and 1 for the perfect square pyramid and trigonal bipyramid geometries, respectively.

Table S2. Selected bond lengths [Å] and angles [°] for mononuclear complexes: **3phen** and **1phen**.

Complex	**3phen**	**1phen**
	Bond length	
Cu1–N1	1.911(3)	1.914(6)
Cu1–O1	1.989(3)	1.987(5)
Cu1–O2	1.917(3)	1.931(6)
Cu1–N3	2.013(3)	2.012(6)
Cu1-N4	2.266(3)	2.271(7)
N1–C8	1.292(5)	1.272(9)
N1–N2	1.387(4)	1.406(8)
N2–C1	1.319(4)	1.306(9)
O1–C1	1.301(4)	1.295(9)
O2–C10	1.301(4)	1.293(10)
	Bond angles	
N1–Cu1–O1	80.81(12)	81.3(2)
N1–Cu1–O2	92.85(13)	92.0(2)
O1–Cu1–O2	161.01(10)	158.5(2)
O2–Cu1–N3	88.87(12)	87.5(2)
N1–Cu1–N3	178.27(14)	179.4(3)
O1–Cu1–N3	97.58(11)	99.2(2)
N1-Cu1-N4	101.91(11)	101.5(2)
O2-Cu1-N4	99.94(11)	101.7(2)
O1-Cu1-N4	98.88(10)	99.7(2)
N3-Cu1-N4	77.68(11)	78.2(3)
τ parameter*	0.29	0.35

*Ideal τ (calculated as ($\angle$(O1–Cu1–O2) – $\angle$(N1–Cu1–N3)]/60°) is 0 and 1 for the perfect square pyramid and trigonal bipyramid geometries, respectively.

Table S3. Selected bond lengths [Å] and angles [°] for tetranuclear complex **2a·4MeOH·2H$_2$O**

Complex	**2a·4MeOH·2H$_2$O**
Bond distances	
Cu1–O11	1.922(5)
Cu1–N11	1.930(5)
Cu1–O12	1.940(5)
Cu1–O22	1.979(5)
Cu1–O23	2.281(5)
Cu1–O12^{i}	2.716(5)
Cu2–N21	1.909(7)
Cu2–O21	1.931(5)
Cu2–O22^{i}	1.970(4)
Cu2–O12	2.004(4)
Cu2–O13	2.306(5)
Cu2–O22	2.653(5)
Bond angles	
O11–Cu1–N11	82.2(2)
O11–Cu1–O12	173.7(2)
N11–Cu1–O12	92.9(2)
O11–Cu1–O22	96.1(2)
N11–Cu1–O22	172.0(2)
O12–Cu1–O22	88.19(19)
O11–Cu1–O23	87.3(2)
N11–Cu1–O23	111.9(2)
O12–Cu1–O23	98.2(2)
O22–Cu1–O23	75.72(18)
N21–Cu2–O21	82.1(2)
N21–Cu2–O22^{i}	91.8(2)
O21–Cu2–O22^{i}	172.5(2)
N21–Cu2–O12	172.0(2)
O21–Cu2–O12	96.2(2)
O22–Cu2–O12^{i}	89.30(19)
N21–Cu2–O13	112.8(2)
O21–Cu2–O13	89.2(2)
O22–Cu2–O13^{i}	97.25(19)
O12–Cu2–O13	74.95(18)

i: -x,y,1/2-z

Table S4. Dihedral angles between best planes defined by chosen atoms (°) in complexes **3py**, **2py·3H$_2$O**, **1bpy*·2MeOH, 2bpy**, **1phen** and **3phen**

∠	**3py**	**2py·3H$_2$O**	**1bpy*·2MeOH**	**2bpy**	**1phen**	**3phen**
I,II	18.16(8)	18.49(14)	4.2(1)	3.9(1)	17.8(5)	11.7(2)
I,III	20.63(7)	15.98(15)	4.0(1)	7.8(1)	15.9(4)	10.4(2)
I,IV	18.93(8)	9.51(15)	8.2(1)	6.0(2)	12.2(5)	9.7(2)
II,III	11.30(7)	3.99(17)	1.0 (1)	3.9(1)	3.3(5)	2.7(2)
III, IV		15.31(15)	9.3(1)	1.9(2)	8.9(6)	
I,V	51.82(9)	15.60(11)	-	-	70.4(2)	75.3(2)
II,V	50.51(8)	13.53(11)	-	-	87.6(2)	86.9(2)

Atoms define planes:
I: C2-C7
II: C9-C14
III: six-membered chelate ring atoms: O2,N1,C8,C9,C10
IV: five-membered chelate ring atoms: O1,N1,N2,C1
V: py ring atoms in pyridine dinuclear complexes and 1,10-phen ring atoms in **1phen** and **3phen** complexes.

Table S5. Hydrogen bonds and interactions for complexes: **3py**, **2py·3H$_2$O, 1bpy*·2MeOH, 2bpy, 1phen**, **3phen** and **2a·4MeOH·2H$_2$O**

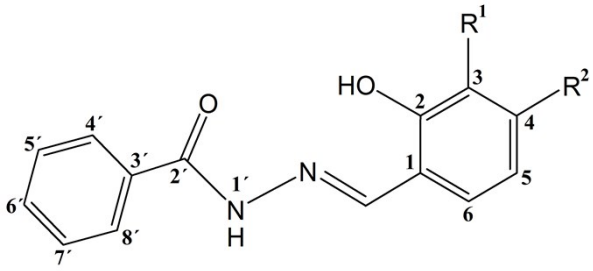
D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)	Symmetry code
3py					
C17-H17…N2	0.93	2.537	3.452(3)	168	x,+y+1,+z
C15–H15···O1	0.93	2.415	2.974(3)	119	-
C19–H19···O2	0.93	2.363	2.912(3)	118	-
2py·3H$_2$O					
O1W–H11A···N2	0.97	1.920	2.884(4)	171	-
O1W–H11B···O2W	0.89(7)	2.13(6)	2.650(18)	117(5)	-
O1W–H11A···N1	0.97	2.839	3.737(4)	154	-
C7–H7···O1W	0.95	2.648	3.480(5)	147	-
C8–H8···O2W	0.95	2.788	3.690(19)	159	-x+2, -y+2, -z+1
C19-H19···O1W	0.95	2.820	3.751(5)	167	x-1,y,z
C16–H16···O1	0.95	2.330	2.912(3)	119	-
C20–H20···O2	0.95	2.380	2.920(3)	116	-
C15–H15B···N2	0.98	2.885	3.846(4)	167	-x+1,-y+2,-z+1
C17–H17···O1	0.95	2.857	3.806(3)	177	-x+1,+y-1/2,-z+3/2
1bpy*·2MeOH					
O3–H3O···N2	0.83(2)	2.02(2)	2.832(2)	167(2)	-
O3–H3O···N1	0.83(2)	2.82(2)	3.495(2)	140(2)	-
C5–H5···O3	0.95	2.628	3.504(3)	154	-x+3/2,+y+1/2,-z+3/2
C16–H16···O3	0.95	2.663	3.331(3)	128	x-1,+y,+z
C19–H19···O2	0.95	2.317	2.883(2)	118	-
C15–H15···O1	0.95	2.359	2.941(2)	119	-
C8–H8···O3	0.95	2.770	3.376(2)	122	-
C18–H18···O3	0.95	2.512	3.504(3)	122	-x+2,-y,-z+2
2bpy					
C16–H16···O2	0.93	2.300	2.852(3)	118	-
C20–H20···O1	0.93	2.357	2.928(3)	119	-
C13–H13···N2	0.93	2.804	3.524(3)	135	-x+1,+y-1/2,-z+3/2
C16–H16···O3	0.93	2.856	3.391(3)	118	-x+1/2,+y,-z+1
C17–H17···O3	0.93	2.632	3.275(3)	127	-x+1/2,+y,-z+1
C15–H15B···O3	0.93	2.717	3.447(3)	133	-x+1/2,+y,-z+1
1phen					
C8–H8···O1	0.93	2.805	3.63(1)	148	x,-y,+z+1/2
C12–H12···N4	0.93	2.912	3.81(1)	162	x+1/2,-y+1/2,+z+1/2
C19–H19···N2	0.93	2.697	3.32(1)	126	x,+y+1,+z
C20–H20···N2	0.93	2.772	3.37(1)	123	x,+y+1,+z
3phen					
C5–H5···N4	0.93	2.963	3.790(5)	149	–x+1,+y–1/2, –z+1/2
C20–H20···N2	0.93	2.721	3.381(5)	129	x,+y+1,+z
C21–H21···N2	0.93	2.857	3.450(5)	123	x,+y+1,+z
C8–H8···O1	0.93	2.825	3.616(5)	144	x, –y+1/2,+z–1/2
C15B–H15D···O3	0.96	2.710	3.430(15)	132	–x, –y+1, –z–1
C16–H16···O3	0.93	2.981	3.559(6)	122	–x, –y+1, –z
C17–H17···O3	0.93	2.797	3.455(7)	129	–x, –y+1, –z
2a·4MeOH·2H$_2$O					

C114–H114···N22	0.95	2.620	3.556(10)	168	-x,1+y,1/2-z
C113–H113···O1ME	0.95	2.686	3.41(3)	134	-
C115–H11B···O1W	0.98	2.974	3.57(6)	120	-
C14–H14··· O1ME	0.95	2.964	3.78(3)	145	x+1/2,-y+1/2+2,+z+1/2
C14–H14···O1W	0.95	2.957	3.88(5)	165	-x,+y+1,-z+1/2
C26–H26···O21	0.95	2.892	3.80(1)	159	-x,-y+1,-z
C113–H113···O1W	0.95	2.810	3.60(6)	141	-x-1/2,-y+1/2+1,-z
C114–H114···N22	0.95	2.622	3.56(1)	168	x,+y+1,+z

Ligands

Table S6. ^{1}H and ^{13}C chemical shifts (ppm) of H_2L^{H}, $H_2L^{3OMe}\cdot H_2O$ and $H_2L^{4OMe}\cdot H_2O$

Atom	H_2L^{H}		$H_2L^{3OMe}\cdot H_2O$		$H_2L^{4OMe}\cdot H_2O$	
	δ/ppm (^{1}H)	δ/ppm (^{13}C)	δ / ppm (^{1}H)	δ / ppm (^{1}H)	δ / ppm (^{1}H)	δ / ppm (^{13}C)
α	8.69	148.86	8.68	148.42	8.57	149.33
1	–	119.15	–	119.39	–	112.23
2	–	157.99	–	148.42	–	159.93
3	6.93	119.82	–	147.67	6.52	101.66
4	7.33	131.84	7.17	121.31	–	162.56
5	6.97	116.92	6.88	119.51	6.55	106.96
6	7.58	130.07	7.05	114.29	7.44	131.67
1'	12.16	–	12.11	–	12.02	–
2'	–	163.35	–	163.30	–	163.09
3'	–	133.29	–	133.33	–	133.38
4', 8'	7.99	128.14	7.96	128.12	7.94	128.06
5', 7'	7.56	129.03	7.55	129.03	7.55	129.01
6'	7.64	132.46	7.62	132.45	7.61	132.35
OH-2	11.37	–	11.02	–	11.66	–
OMe			3.38	56.29	3.37	55.79



R^1	R^2	ligand
H	H	H_2L^{H}
OCH_3	H	$H_2L^{3OMe}\cdot H_2O$
H	OCH_3	$H_2L^{4OMe}\cdot H_2O$

Scheme S3 The structural formula of H_2L with the NMR numbering scheme