A BODIPY-based fluorescent chemodosimeter for Cu(II) driven by oxidative dehydrogenation mechanism

Dongping Wang, Yasuhiro Shiraishi* and Takayuki Hirai

Research Center for Solar Energy Chemistry, and Division of Chemical Engineering, Graduate School of Engineering Science, Osaka University, Toyonaka 560-8531, Japan

E-mail: shiraish@cheng.es.osaka-u.ac.jp

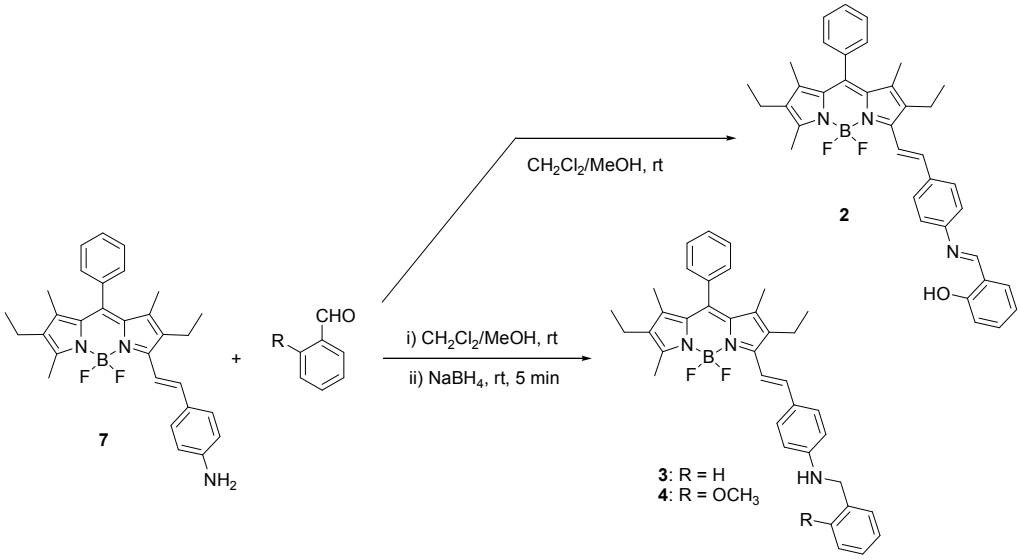
Electronic Supplementary Information (ESI)†

Contents

General

All reagents were supplied by Wako, Aldrich, and Tokyo Kasei, and used without further purification. Perchlorate (Li^+, Na^+, Mg^{2+}, Mn^{2+}, Cr^{3+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}), tetrafluoroborate (Ag^+), and iodide salts (Cu^+) were used as the metal cation source. Water was purified by the Milli-Q system. Fluorescence spectra were measured on a Hitachi F-4500 fluorescence spectrophotometer (excitation and emission slit width, 2.5 nm). Absorption spectra were measured on a UV-visible spectrophotometer (Shimadzu, Multispec-1500). All measurements were performed at 25 ºC using a 10 mm path length quartz cell in an aerated condition, after the solution was stirred for 20 min. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-AL400 and JEOL JNM-GSX270 Excalibur with TMS as standard. FAB-MS spectra were obtained from JEOL JMS 700 Mass spectrometer. IR spectra were measured on an FT-IR-610 infrared spectrophotometer (Jasco Corp.) with KBr disk. ESR spectra were performed at the X-band using a Bruker EMX-10/12 spectrometer with a 100 kHz magnetic field modulation at a microwave power level of 20 mW. Φ_F was determined with rhodamine B as a standard (Φ_F = 0.69 in ethanol) (C. A. Parker and W. T. Rees, *Analyst*, 1960, **85**, 587).

Synthesis



Compound **2**: **7**[10] (48.3 mg, 0.1 mmol) and salicylaldehyde (122.1 mg, 1 mmol) were stirred in a mixture of CH_2Cl_2 (15 mL) and MeOH (10 mL) at room temperature until the complete disappearance of **7** by TLC monitoring. The solution was concentrated to ca. 4 mL. The solid formed was recovered by filtration and washed with MeOH (5 mL × 3), affording **2** as a gray green solid (47.5 mg, 81%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 13.25 (s, 1H, PhO*H*), 8.66 (s, 1H, N=C*H*), 7.74 (d, 1H, *J* = 16.6, C*H*=CH), 7.65 (d, 2H, *J* = 8.5, Ph*H* of styryl), 7.54–7.46 (m, 3H, Ph*H*), 7.44–7.35 (m, 2H, Ph*H*OH), 7.34–7.27 (m, 4H, Ph*H* and Ph*H* of styryl), 7.21 (d, 1H, *J* = 16.8, C*H*=CH), 7.03 (d, 1H, *J* = 8.3, Ph*H*OH), 6.94 (t, 1H, *J* = 7.6, Ph*H*OH),

2.65–2.56 (m, 5H, CH_3CH_2 and CH_3), 2.32 (q, 2H, J = 7.6, CH_3CH_2), 1.32 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.16 (t, 3H, J = 7.6, CH_3CH_2),1.00 (t, 3H, J = 7.6, CH_3CH_2). ^{13}C NMR (DMSO-d_6, 67.5 MHz): δ 161.79, 161.01, 155.90, 148.23, 147.92, 139.41, 139.06, 138.11, 136.33, 135.64, 133.73, 133.51, 132.96, 132.88, 132.11, 131.70, 128.86, 128.65, 128.24, 128.01, 121.41, 120.l5, 119.14, 118.89, 117.45, 117.10, 18.31, 17.11, 14.45, 14.11, 12.83, 11.75, 11.33. MS (FAB): *m*/*z* Calcd for $C_{37}H_{36}BF_2N_3O$: 587.3; Found: 587.2. HRMS (FAB): *m*/*z* Calcd for $C_{37}H_{36}BF_2N_3O$: 587.2919; Found: 589.2926.

Compounds **3** and **4**: **7**[10] (48.3 mg, 0.1 mmol) was dissolved in a mixture of CH_2Cl_2 (15 mL) and MeOH (10 mL). Benzaldehyde (106 mg, 1 mmol for **3**) or *o*-anisaldehyde (136 mg, 1 mmol for **4**) was added to the solution and stirred at room temperature until the complete disappearance of **7** by a TLC monitoring. $NaBH_4$ (76 mg, 2 mmol) was added to the solution and stirred for 5 min. The solution was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated by evaporation. The crude product was purified by column chromatography on silica gel using CH_2Cl_2/*n*-hexane (2/1 v/v for **3**) or ethyl acetate/*n*-hexane (1/3 v/v for **4**) as eluent.

3: (42.4 mg, 78%, brown solid). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.59–7.53 (m, 3H, Ph*H*), 7.40–7.29 (m, 9H, Ph*H*, Bn*H*, Ph*H* of styryl and C*H*=CH), 7.23 (t, 1H, J = 6.8, Bn*H*), 7.16 (d, 1H, J = 16.6, C*H*=CH), 6.85 (t, 1H, J = 6.1, CH_2NH), 6.66 (d, 2H, J = 8.5, Ph*H* of styryl), 4.34 (d, 2H, J = 6.1, CH_2NH), 2.56 (q, 2H, J = 7.3, CH_3CH_2), 2.46 (s, 3H, CH_3), 2.30 (q, 2H, J = 7.6, CH_3CH_2), 1.27 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.06 (t, 3H, J = 7.3, CH_3CH_2), 0.94 (t, 3H, J = 7.6, CH_3CH_2). ^{13}C NMR (DMSO-d_6, 67.5 MHz): δ 152.06, 149.82, 149.59, 139.38, 138.29, 138.08, 136.80, 136.16, 134.73, 132.44, 132.32, 130.93, 130.23, 128.82, 128.73, 128.18, 128.00, 126.86, 126.41, 124.27, 113.37, 112.26, 45.96, 17.62, 16.33, 14.39, 13.71, 12.22, 11.15, 10.95. MS (FAB): *m*/*z* Calcd for $C_{37}H_{38}BF_2N_3$: 573.3; Found: 573.2. HRMS (FAB): *m*/*z* Calcd for $C_{37}H_{38}BF_2N_3$: 573.3127; Found: 573.3133.

4: (45.9 mg, 76%, brown solid). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.58–7.53 (m, 3H, Ph*H*), 7.40–7.29 (m, 5H, Ph*H*, Ph*H* of styryl and C*H*=CH), 7.26–7.20 (m, 2H, Ph*H*OMe), 7.16 (d, 1H, J = 16.6, C*H*=CH), 7.01 (d, 1H, J = 8.1, Ph*H*OMe), 6.88 (t, 1H, J = 7.3, Ph*H*OMe), 6.67 (t, 1H, J = 6.1, CH_2NH), 6.63 (d, 2H, J = 8.5, Ph*H* of styryl), 4.29 (d, 2H, J = 6.1, CH_2NH), 3.85 (s, 3H, OCH_3), 2.56 (q, 2H, J = 7.6, CH_3CH_2), 2.46 (s, 3H, CH_3), 2.30 (q, 2H, J = 7.6, CH_3CH_2), 1.27 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.07 (t, 3H, J = 7.6, CH_3CH_2), 0.94 (t, 3H, J = 7.8, CH_3CH_2). ^{13}C NMR (DMSO-d_6, 67.5 MHz): δ 156.55, 151.99, 149.87, 149.73, 138.29, 138.03, 136.76, 136.24, 134.74, 132.45, 132.30, 130.94, 130.22, 128.82, 128.74, 128.23, 128.01, 127.68, 127.53, 126.54, 124.15, 119.85, 113.25, 112.08, 110.35, 55.19, 40.79, 17.63, 16.33, 14.39, 13.72, 12.21, 11.15, 10.96. MS (FAB): *m*/*z* Calcd for $C_{38}H_{40}BF_2N_3O$: 603.3; Found: 603.2. HRMS (FAB): *m*/*z* Calcd for $C_{38}H_{40}BF_2N_3O$: 603.3232; Found: 603.3239.

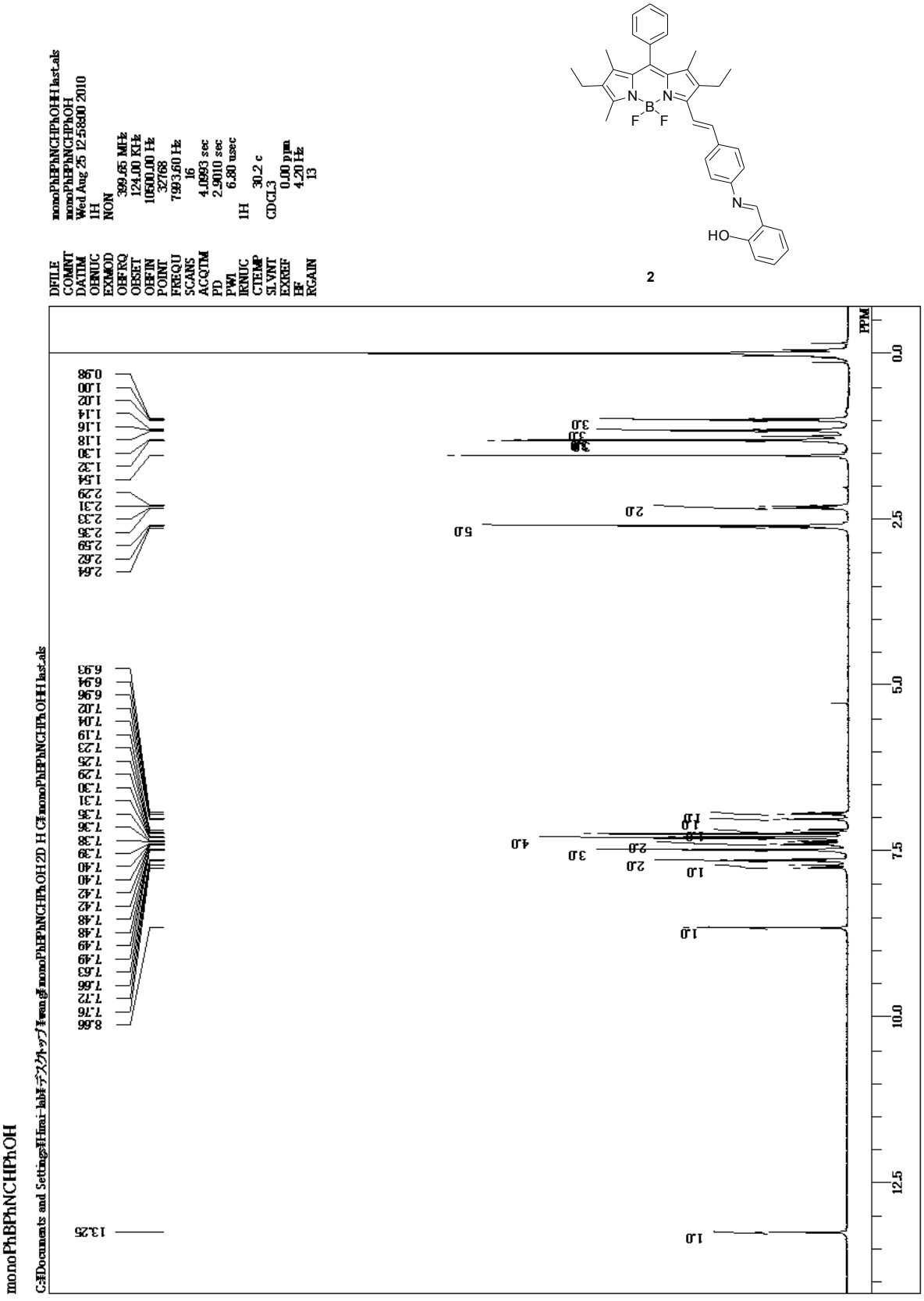


Fig. S1 ^{1}H NMR chart of **2** in $CDCl_3$ (400 MHz).

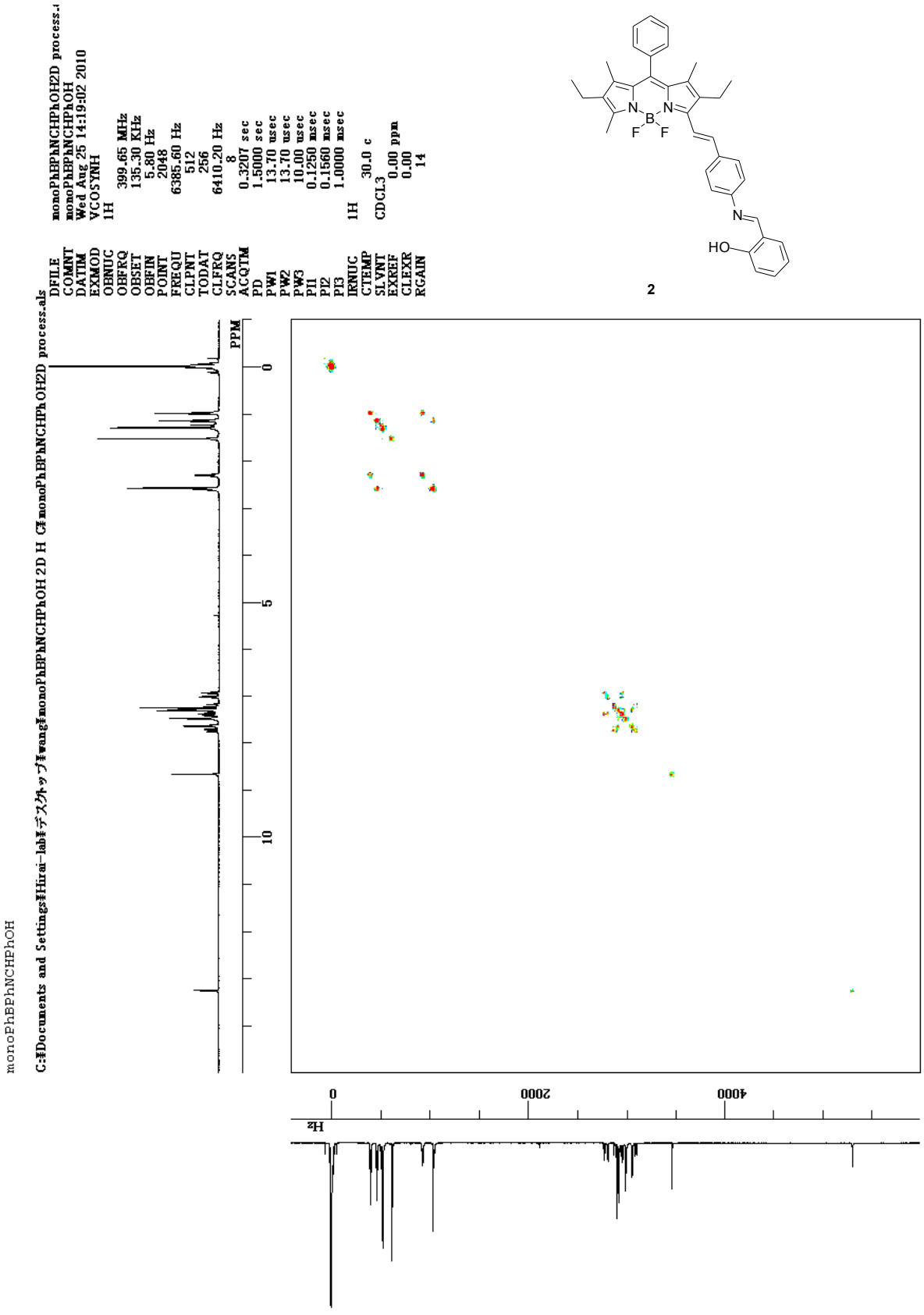


Fig. S2 gCOSY chart of **2** in $CDCl_3$ (400 MHz).

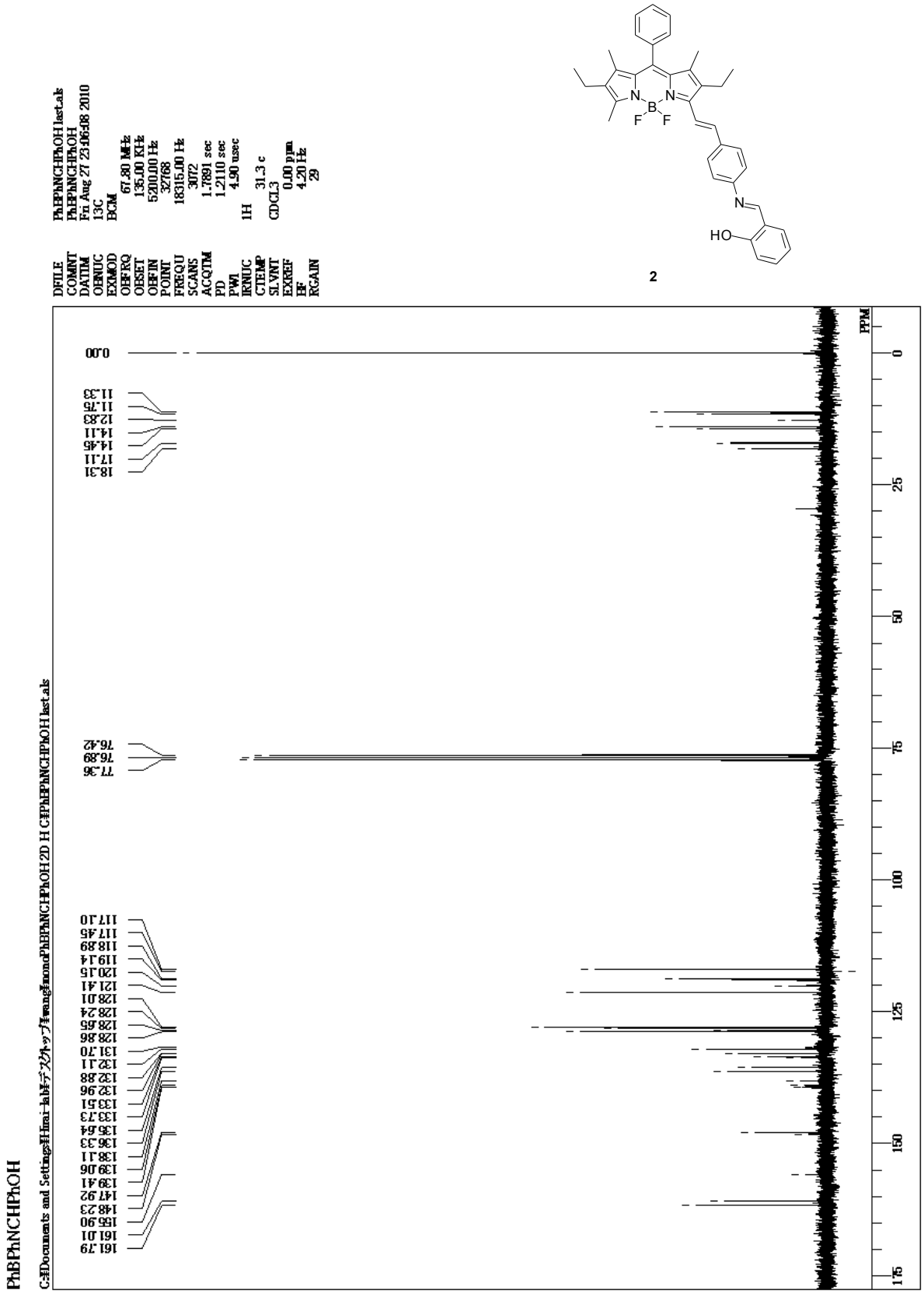


Fig. S3 ^{13}C NMR chart of **2** in $CDCl_3$ (67.5 MHz).

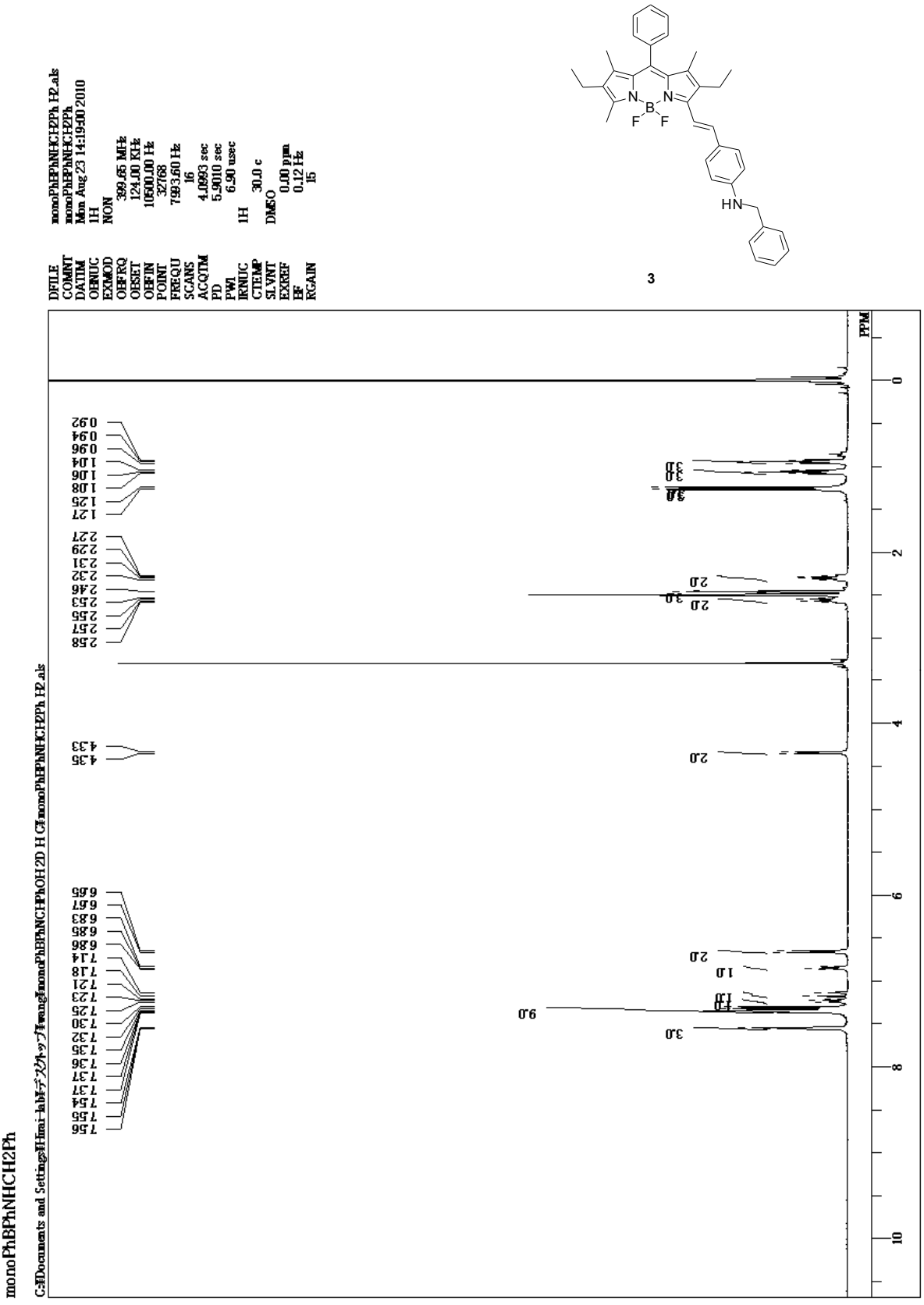


Fig. S4 ^{1}H NMR chart of **3** in DMSO-d_6 (400 MHz).

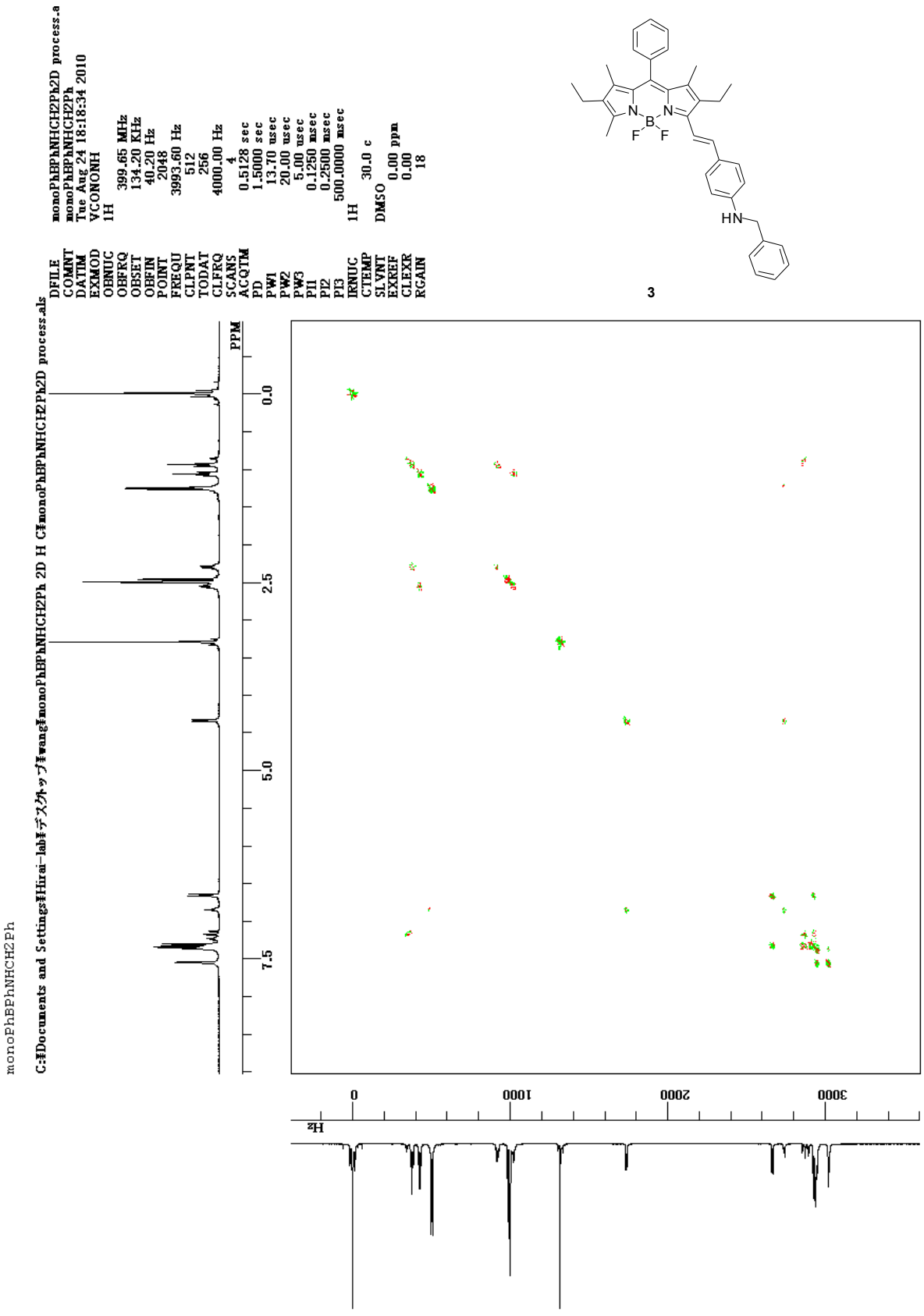


Fig. S5 gCOSY chart of **3** in DMSO-d_6 (400 MHz).

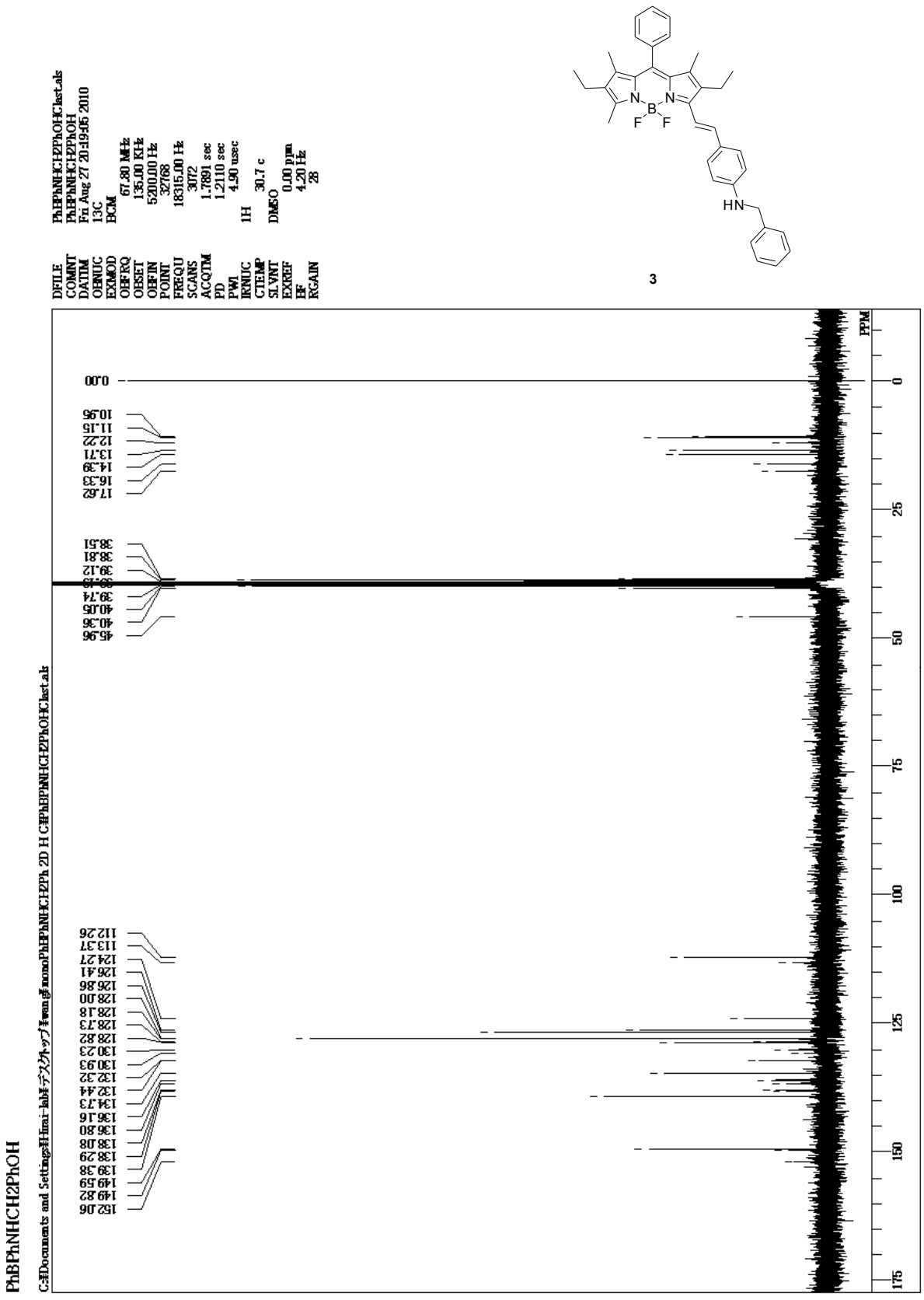


Fig. S6 ^{13}C NMR chart of **3** in DMSO-d_6 (67.5 MHz).

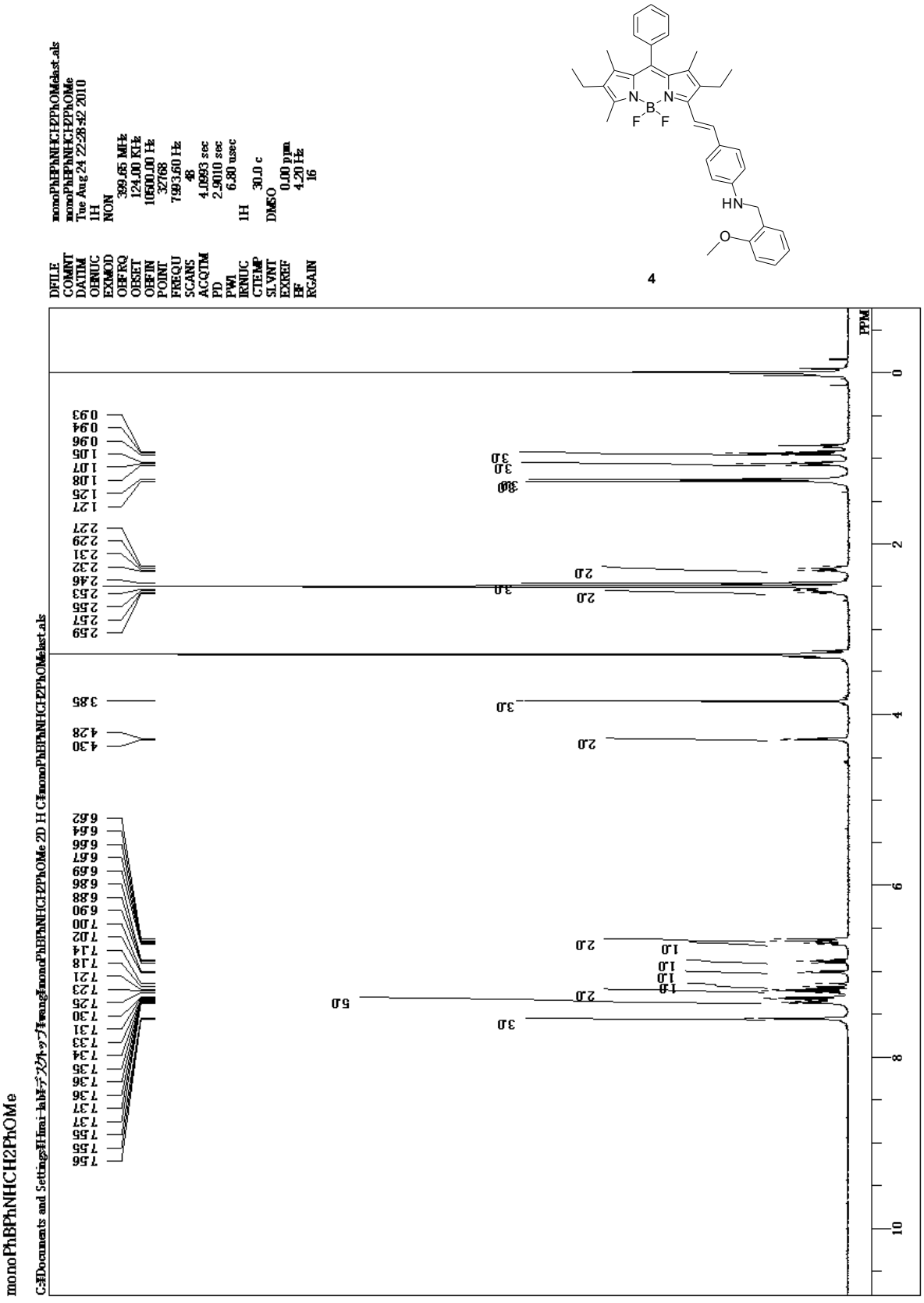


Fig. S7 ^{1}H NMR chart of **4** in DMSO-d_6 (400 MHz).

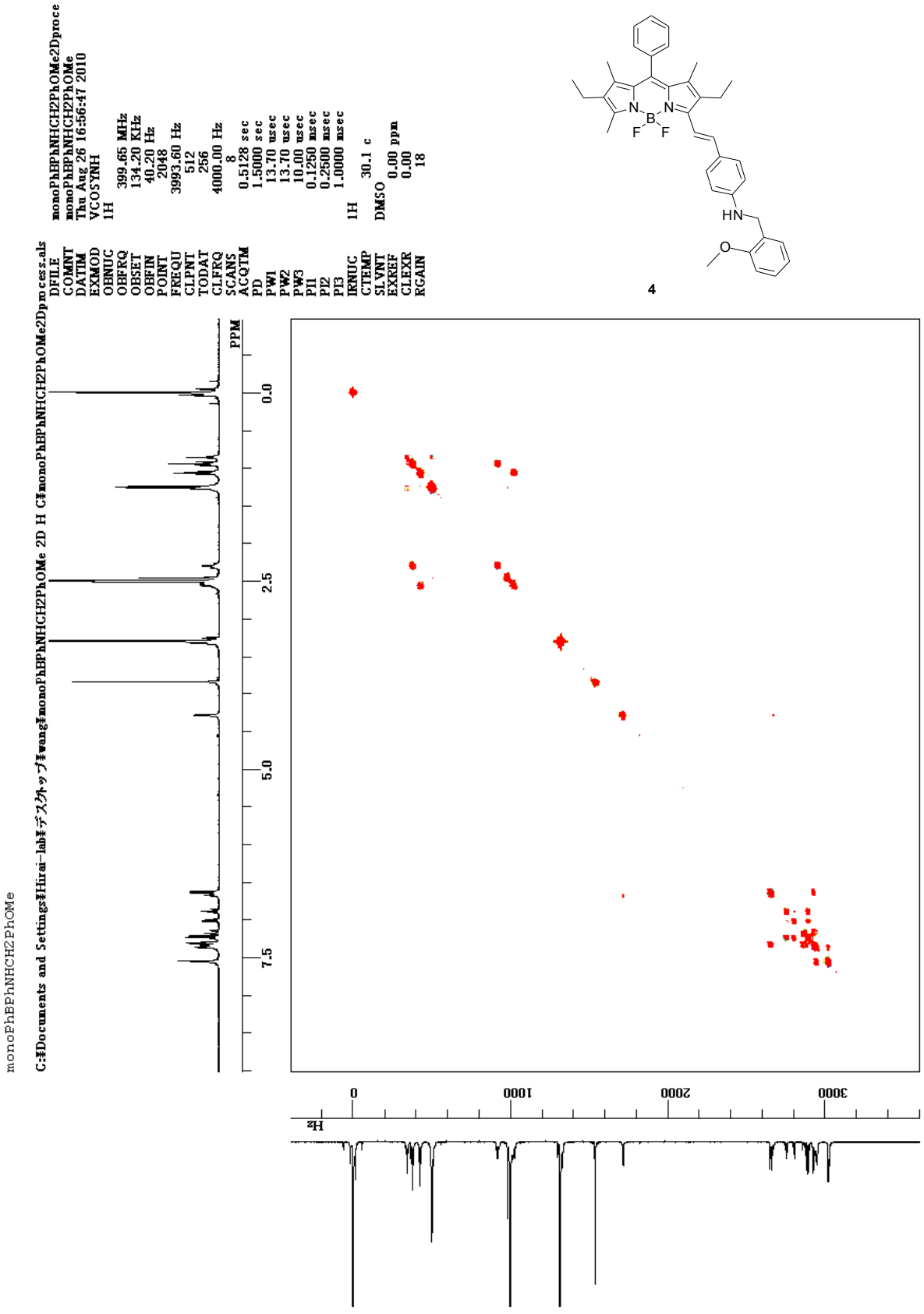


Fig. S8 gCOSY chart of **4** in DMSO-d_6 (400 MHz).

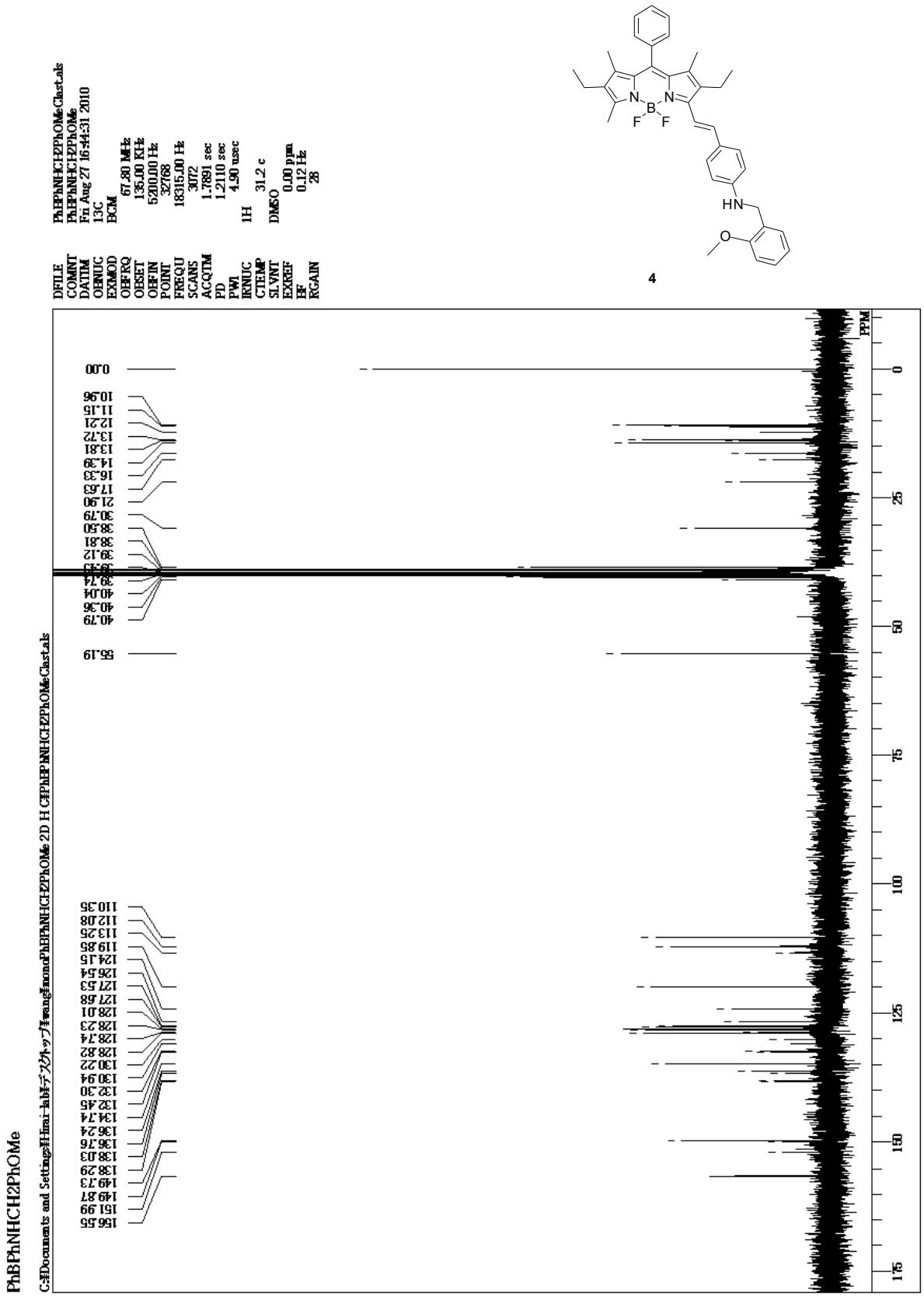


Fig. S9 ^{13}C NMR chart of **4** in DMSO-d_6 (67.5 MHz).

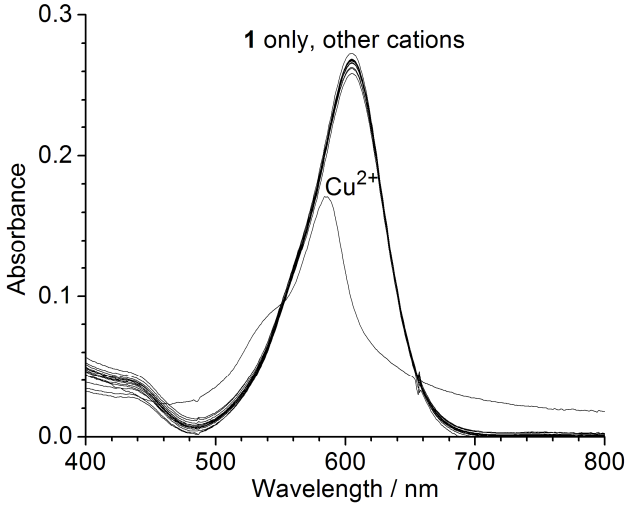


Fig. S10 Absorption spectra of **1** (5 μM) measured in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) with respective metal cations (20 equiv).

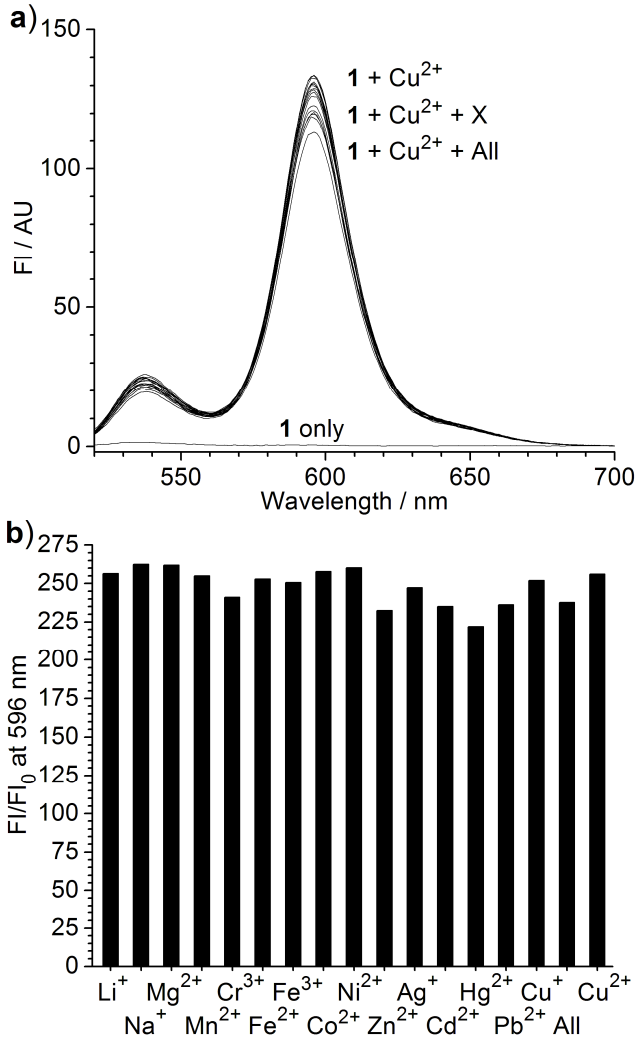


Fig. S11 (a) Fluorescence spectra (λ_{ex} = 510 nm) of **1** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) measured with 20 equiv of Cu^{2+} and 20 equiv of other respective metal cations (X). (b) The ratio of fluorescence intensity (FI/FI_0) of **1**, where FI and FI_0 are the intensity measured with Cu^{2+} and X and without metal cations, respectively.

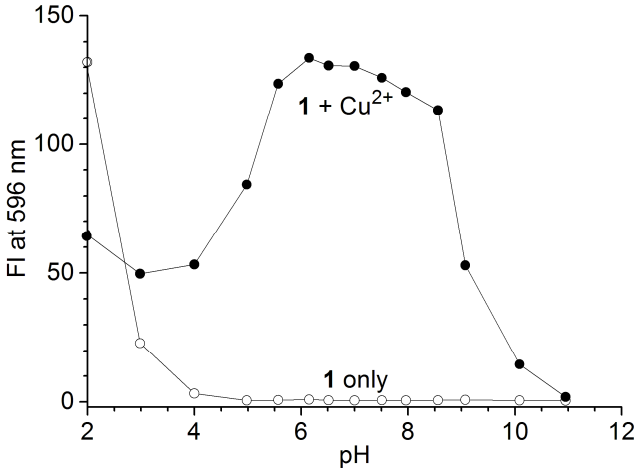


Fig. S12 pH-dependent change in fluorescence intensity (λ_{ex} = 510 nm) of **1** (5 μM) in a MeCN/water mixture (1/1 v/v) measured with and without Cu^{2+} (20 equiv). pH of the solution was adjusted with NaOH and HCl.

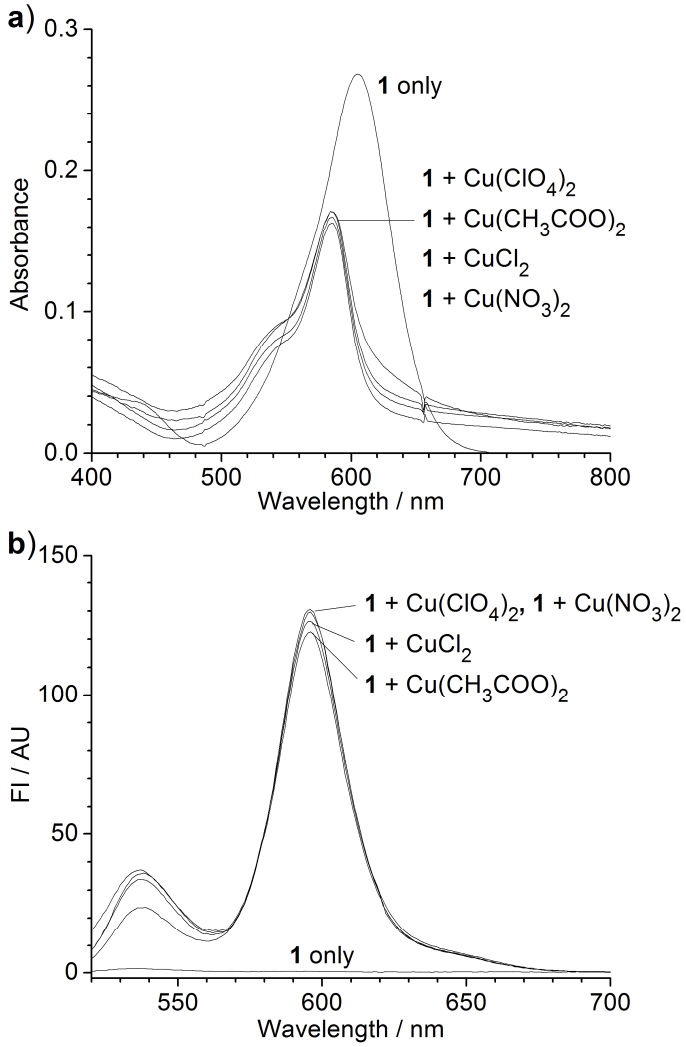


Fig. S13 (a) Absorption and (b) fluorescence spectra (λ_{ex} = 510 nm) of **1** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) measured with 20 equiv of $Cu(ClO_4)_2$, $Cu(CH_3COO)_2$, $CuCl_2$, and $Cu(NO_3)_2$.

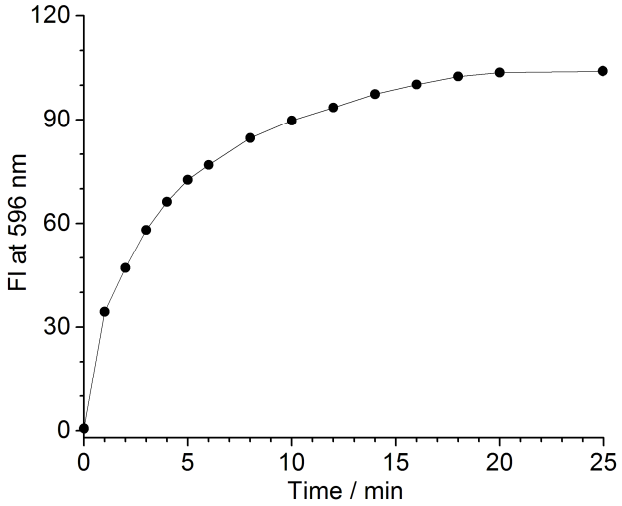


Fig. S14 Time-dependent change in fluorescence intensity (λ_{ex} = 510 nm) of **1** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) upon addition of 10 equiv of Cu^{2+}.

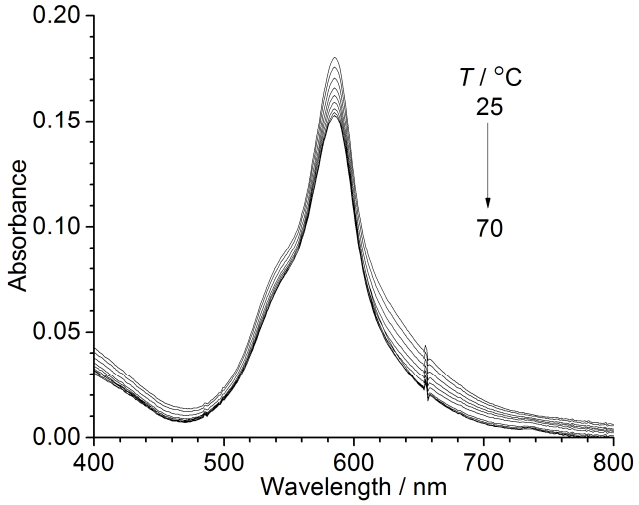


Fig. S15 Temperature-dependent change in absorption spectra (λ_{ex} = 510 nm) of **1** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) with 10 equiv of Cu^{2+}. The measurements were carried out during a heating sequence after stirring the solution at 25 ºC for 20 min.

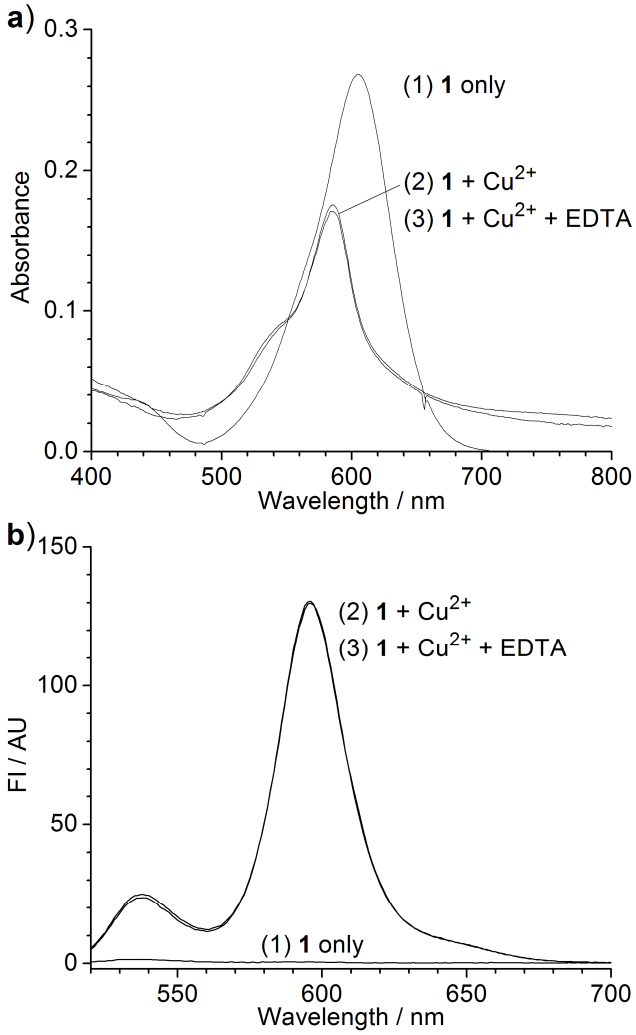
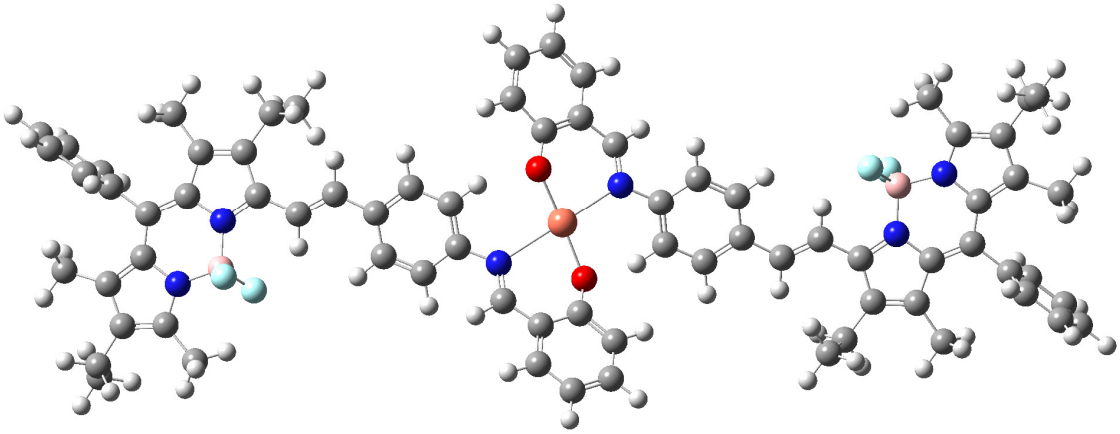


Fig. S16 (a) Absorption and (b) fluorescence spectra (λ_{ex} = 510 nm) of **1** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) measured (1) without cations, (2) with Cu^{2+} (20 equiv), and (3) after addition of EDTA (100 equiv) to the sample (2).

(Top view)



(Side view)

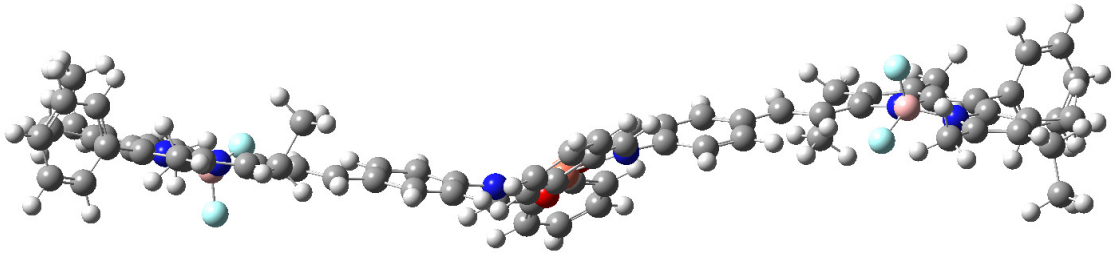


Fig. S17 Geometry optimized structure of **1**–Cu^{+} 2:1 complex determined by *ab initio* calculation within the Gaussian 03 program at the DFT level (B3LYP/3-21 basis set for all atoms except for Cu, for which LANL2DZ basis set with effective core potential was used).

Cartesian Coordinates (in Å) of 1–Cu^{+} 2:1 complex

C	-5.636324	-0.938997	0.564627	C	-12.325451	3.578799	-0.354014
C	-5.882397	0.437548	0.779223	C	-10.078029	2.374999	0.055512
C	-4.775710	1.249133	1.133462	C	-15.739231	2.518896	-2.217287
C	-3.503937	0.728759	1.281438	H	-13.983836	1.402251	-2.798518
C	-3.273187	-0.649034	1.093647	H	-14.910792	1.352873	1.386217
C	-4.366530	-1.467770	0.714712	C	-16.261709	2.491578	0.143154
N	-1.973523	-1.161960	1.257076	C	-8.347122	0.410679	0.323083
C	-0.637345	-3.130626	1.894583	H	-12.749539	3.605070	-1.363501
C	0.603702	-2.741805	1.277814	H	-11.749866	4.495027	-0.200197
C	1.711782	-3.630602	1.461688	H	-13.166567	3.577535	0.345810
C	1.599341	-4.807321	2.168101	C	-9.193687	3.596664	0.059173
C	0.370704	-5.186214	2.756791	C	-16.559304	2.911014	-1.156249
C	-0.716169	-4.349339	2.614932	H	-15.966280	2.842020	-3.226958
O	0.744419	-1.652361	0.562120	H	-16.895109	2.793837	0.969483
Cu	0.052928	0.130813	0.888066	C	-7.187272	1.049233	0.642391

O	-0.705995	1.841372	1.417261	H	-8.337262	-0.656449	0.144420
C	-0.527350	3.048518	0.943335	C	-8.413080	3.752812	-1.273640
C	-1.523253	4.054619	1.171169	H	-8.493020	3.560404	0.899789
C	-1.396273	5.338764	0.693436	H	-9.811832	4.487309	0.212915
C	-0.262473	5.724003	-0.059120	H	-17.423485	3.539016	-1.340247
C	0.719203	4.787051	-0.297729	H	-7.198471	2.115544	0.837964
C	0.628046	3.455548	0.186866	H	-7.769038	4.639340	-1.245202
C	1.735007	2.597149	-0.092392	H	-9.116898	3.855435	-2.105827
N	1.902356	1.332146	0.224484	H	-7.789231	2.873589	-1.456832
C	3.186801	0.775301	0.019377	H	16.593287	1.928328	-0.019073
C	4.368533	1.531379	0.222397	C	15.909064	1.082824	-0.139150
C	5.618673	0.983561	-0.004914	H	16.171216	0.552274	-1.059157
C	5.758370	-0.353144	-0.443631	H	16.078000	0.387491	0.691467
C	4.572023	-1.109110	-0.608407	C	14.485706	1.572313	-0.168481
C	3.318790	-0.572084	-0.372155	C	14.071991	2.890612	0.099390
H	-4.937190	2.311914	1.289148	C	13.304521	0.815273	-0.452266
H	-2.647392	1.343789	1.533320	C	12.661086	2.931329	-0.022983
H	-4.193567	-2.517324	0.508492	C	14.940262	4.055493	0.498584
H	2.655147	-3.334068	1.020279	N	12.206567	1.689574	-0.353223
H	2.465280	-5.453106	2.277994	C	13.098057	-0.548277	-0.732784
H	0.290033	-6.114121	3.310162	C	11.740499	4.104878	0.119073
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H	-2.390284	3.762090	1.750425	H	14.485856	4.990012	0.148145
H	-2.175713	6.067045	0.895542	H	15.918908	3.975520	0.009718
H	-0.169683	6.735826	-0.434602	B	10.745049	1.319531	-0.736135
H	1.603694	5.060396	-0.867473	C	11.806973	-1.062780	-0.847741
H	2.535897	3.093239	-0.656839	C	14.283387	-1.449878	-0.863472
H	4.291202	2.545289	0.595946	H	12.174978	4.866589	0.771597
H	4.654188	-2.146665	-0.919585	H	10.786779	3.757809	0.518465
H	2.420251	-1.175104	-0.416530	H	11.544017	4.556126	-0.863476
H	-2.710102	-2.822165	2.255116	H	15.771961	4.988350	2.308278
C	-1.830546	-2.350059	1.794845	H	15.621518	3.215851	2.398613
H	6.501652	1.589541	0.161684	H	14.176627	4.231647	2.539342
H	-6.452536	-1.590019	0.273660	N	10.680008	-0.237932	-0.698669
H	-16.445155	-2.268478	-1.246382	F	10.425620	1.815083	-2.010577
C	-15.796056	-1.391064	-1.166596	F	9.850204	1.873586	0.223506
H	-15.820240	-0.861284	-2.126038	C	11.331181	-2.413722	-1.036271
H	-16.218163	-0.715014	-0.417010	C	14.902236	-1.623502	-2.108499
C	-14.398075	-1.816306	-0.803655	C	14.793380	-2.117109	0.257670
C	-13.942741	-3.147085	-0.738466	C	9.541370	-1.009602	-0.753178
C	-13.286098	-0.979634	-0.471151	C	12.183134	-3.637569	-1.242026
C	-12.575779	-3.115572	-0.369342	C	9.941613	-2.382273	-0.979157
C	-14.728381	-4.394791	-1.047779	C	16.015344	-2.458628	-2.230505
N	-12.187784	-1.818620	-0.208621	H	14.506152	-1.102654	-2.972621
C	-13.133302	0.419290	-0.423135	H	14.312396	-1.978080	1.219079

C	-11.642250	-4.261774	-0.123321	C	15.906862	-2.951295	0.134101
C	-14.680917	-4.755905	-2.556657	C	8.260580	-0.405603	-0.539238
H	-15.773628	-4.262786	-0.742434	H	12.894430	-3.491124	-2.060061
H	-14.331375	-5.233351	-0.463314	H	11.558624	-4.503072	-1.477643
B	-10.818338	-1.336068	0.348010	H	12.769021	-3.870941	-0.346387
C	-11.885752	0.989785	-0.176166	C	9.032369	-3.583635	-1.041903
C	-14.321746	1.289098	-0.679507	C	16.519390	-3.124006	-1.109696
H	-11.957041	-5.149347	-0.678321	H	16.487572	-2.589677	-3.197534
H	-11.615725	-4.508877	0.947146	H	16.295032	-3.465136	1.006268
H	-10.634419	-3.965159	-0.416976	C	7.038195	-0.983588	-0.696755
H	-15.256155	-5.666824	-2.762714	H	8.324147	0.616337	-0.190068
H	-13.645218	-4.916150	-2.873947	C	8.530744	-4.006970	0.365193
H	-15.094938	-3.936453	-3.153331	H	9.576361	-4.422179	-1.489147
N	-10.751413	0.191186	0.043458	H	8.179643	-3.385315	-1.699522
F	-10.726903	-1.588349	1.726375	H	17.383119	-3.772002	-1.205017
F	-9.766075	-2.018054	-0.327142	H	7.862691	-4.873222	0.295105
C	-11.452167	2.368426	-0.158381	H	7.989259	-3.185493	0.842721
C	-14.625211	1.710156	-1.980686	H	9.383588	-4.270779	0.998752
C	-15.148038	1.682782	0.381373	H	6.967495	-2.006787	-1.047465
C	-9.643725	0.998020	0.169628				

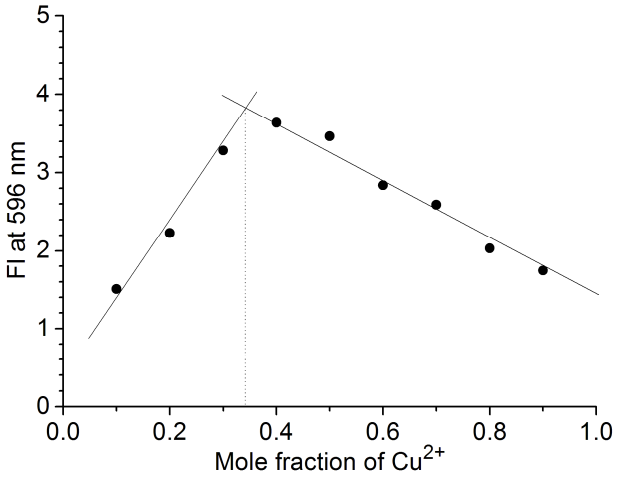

Fig. S18 Job's plot of **1** with Cu^{2+} obtained by fluorescence measurements (λ_{ex} = 510 nm). The total concentration of **1** and Cu^{2+} is 5 μM.

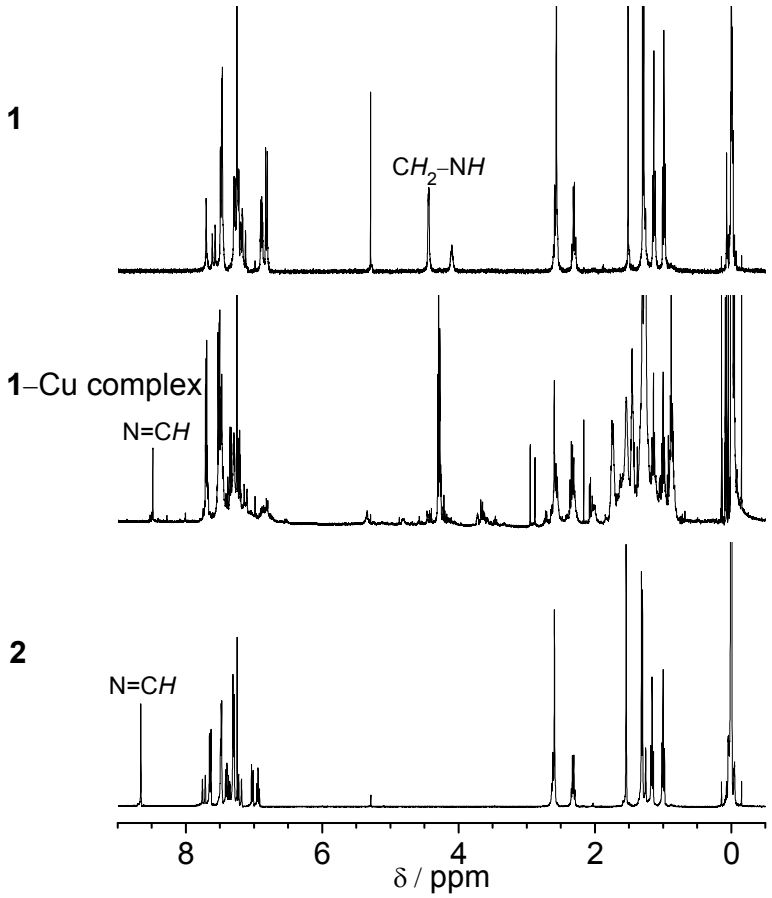

Fig. S19 ^{1}H NMR spectra of **1**, **1**–Cu complex, and **2** measured in $CDCl_3$ (400 MHz). The **1**–Cu complex sample was obtained by the following simple procedure: the buffered MeCN/water solution containing **1** was treated with Cu^{2+}. The solution was extracted with CH_2Cl_2, washed with water, and concentrated by evaporation.

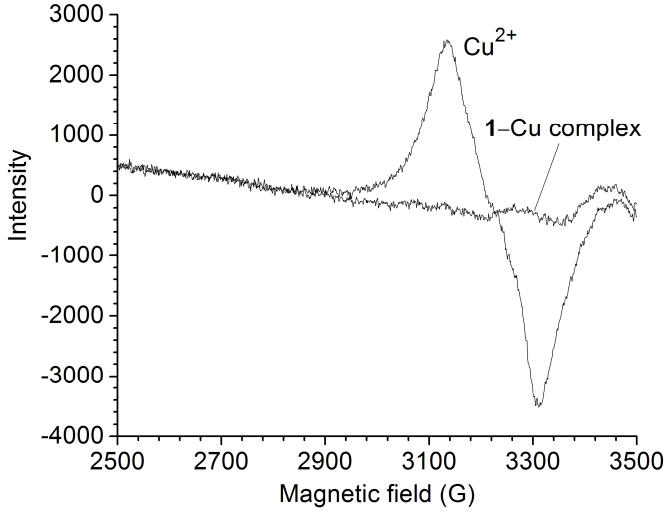

Fig. S20 ESR spectra of $Cu(ClO_4)_2$ (2 mM) and **1**–Cu complex (ca. 2 mM) in MeCN measured at 25 ºC.

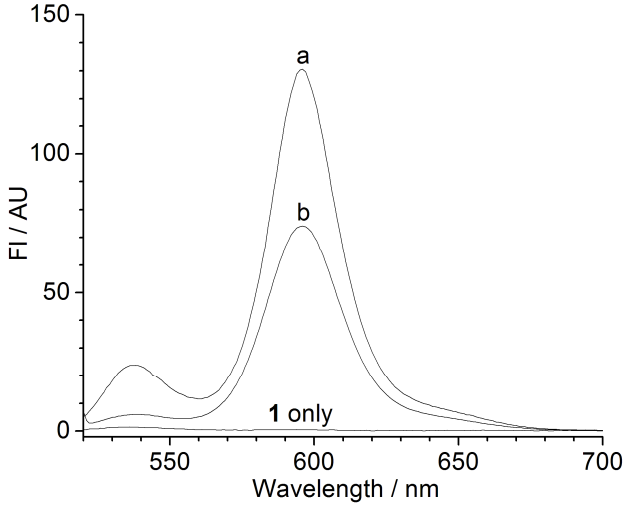

Fig. S21 Fluorescence spectra (λ_{ex} = 510 nm) of **1** (5 μM) measured in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) with 20 equiv of Cu^{2+} under (a) air and (b) argon. The sample (b) was measured by the following simple procedure: argon gas was bubbled through the solution containing **1**, and Cu^{2+} was added under argon.

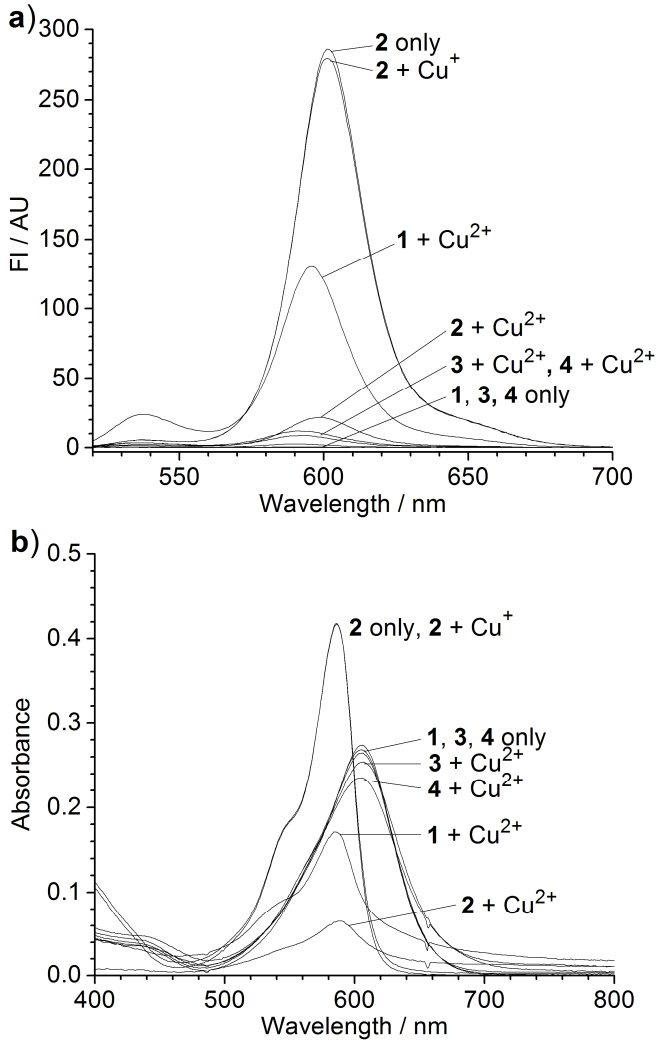

Fig. S22 (a) Fluorescence (λ_{ex} = 510 nm) and (b) absorption spectra of **1**, **2**, **3,** and **4** (5 μM) in a buffered MeCN/water mixture (1/1 v/v; HEPES 100 mM; pH 7.0) measured with and without Cu^{2+} or Cu^{+} (20 equiv).

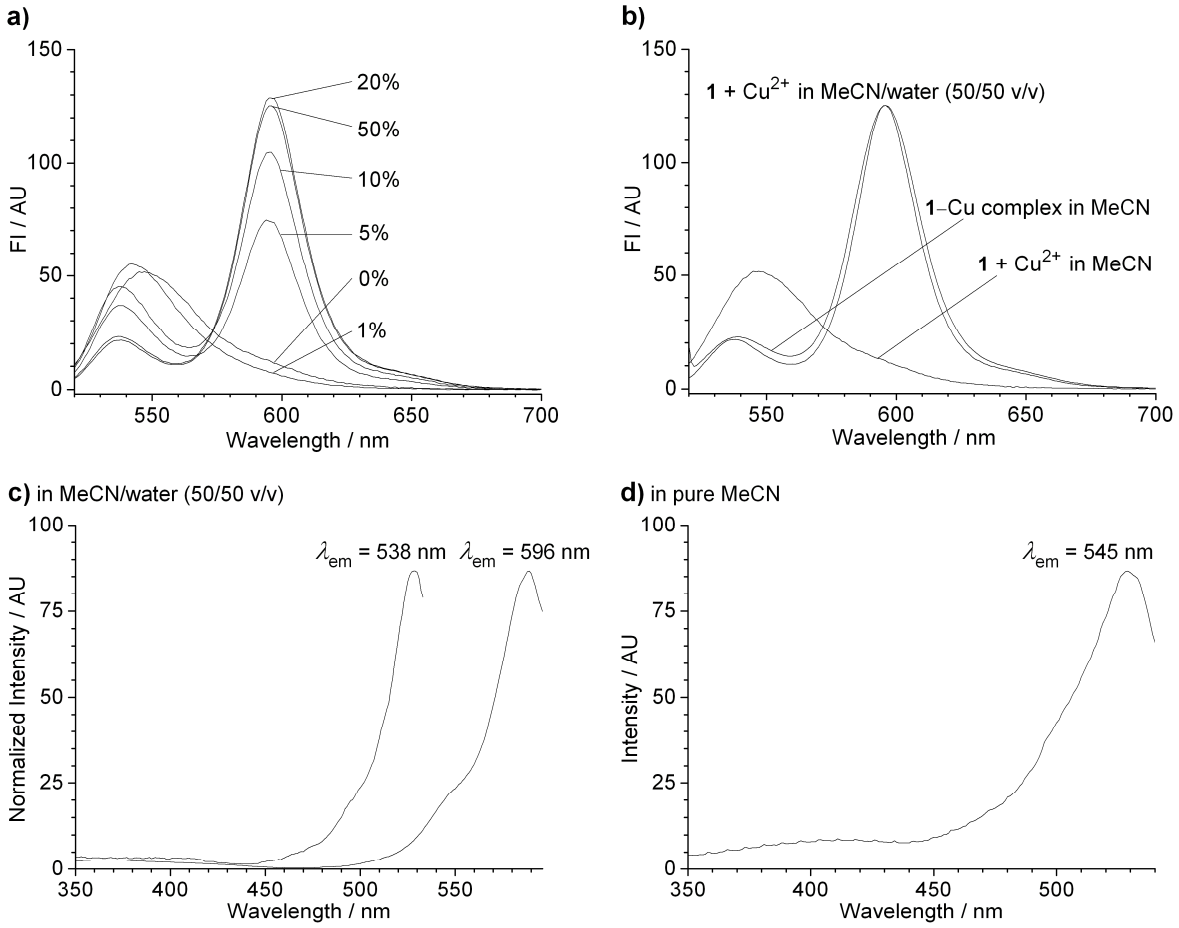

Fig. S23 (a) Fluorescence spectra (λ_{ex} = 510 nm) of **1** (5 μM) + Cu^{2+} (20 equiv) in MeCN solution with different amount of water (0−50%, pH 7). (b) Fluorescence spectrum (λ_{ex} = 510 nm) of the isolated **1**–Cu complex when dissolved in MeCN, where the spectra for **1** + Cu^{2+} in pure MeCN and in a MeCN/water mixture (50/50 v/v; pH 7.0) are also shown for comparison. (c) Excitation spectra for **1** + Cu^{2+} monitored at 538 and 596 nm in a MeCN/water mixture (50/50 v/v). (d) Excitation spectrum for **1** + Cu^{2+} monitored at 545 nm in pure MeCN.

NOTE for the emission bands:

Two emission bands (538 and 596 nm) in larger water content solution are from **the 1–Cu^{+} complex**. In contrast, the single emission band in pure MeCN (545 nm) is probably from **the intermediate**, which has a coordinated structure between **1** and Cu^{2+}.

As shown in (a), **1** + Cu^{2+} in a MeCN/water mixture (λ_{ex} = 510 nm) shows two emission bands at 538 and 596 nm. As shown in (c), the excitation spectra for these emissions show the bands at 528 and 589 nm, respectively, which correspond to the bands observed in the absorption spectra for **1** + Cu^{2+} (Fig. 4). These two emissions are therefore formed by simultaneous excitation (λ_{ex} = 510 nm) of two excitation bands; in other words, both emissions originate from the identical **1**–Cu^{+} complex. In addition, as shown in Fig. 3, the titration of **1** with Cu^{2+} leads to a simultaneous increase in both emission bands, where the intensity ratio of these bands is almost constant. This also suggests that two emission bands originate from the identical **1**–Cu^{+} complex. The MeCN/water mixture of **1** treated with Cu^{2+}

was extracted with CH_2Cl_2, washed with water, and concentrated by evaporation. It must be noted that, as shown in (b), the fluorescence spectrum of the obtained **1**–Cu^+ complex, when measured in pure MeCN, is close to that observed in a MeCN/water mixture.
In contrast, as shown in (a), **1** + Cu^{2+} in pure MeCN shows a 545 nm emission, while the 596 nm emission does not appear. As shown in (d), the excitation spectrum for this emission shows a band at ca. 530 nm. The 545 nm emission is different from the emission for the isolated **1**–Cu^+ complex in pure MeCN (538 nm). This clearly indicates that the 545 nm emission observed in pure MeCN originates from different species. The absence of main 596 nm emission indicates that the single 545 nm emission probably originates from the intermediate, which has a coordinated structure between **1** and Cu^{2+} (Scheme 2, center). The absence of water probably suppresses the subsequent dehydrogenation of imine moiety and, hence, shows the single emission band from the coordinated intermediate.