Supporting Information

Synthesis and Evaluation of Bifunctional DFO2K: a Modular Chelator with Ideal Properties for Zirconium-89 Chelation

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Keywords

Desferrioxamine, hydroxamic acid, chelator, radiometal, radiochemistry, PET imaging, zirconium-89, theranostic, density functional theory calculations, DFT

Disclosures: None.

DFO-Lys(Z)-Boc (1)

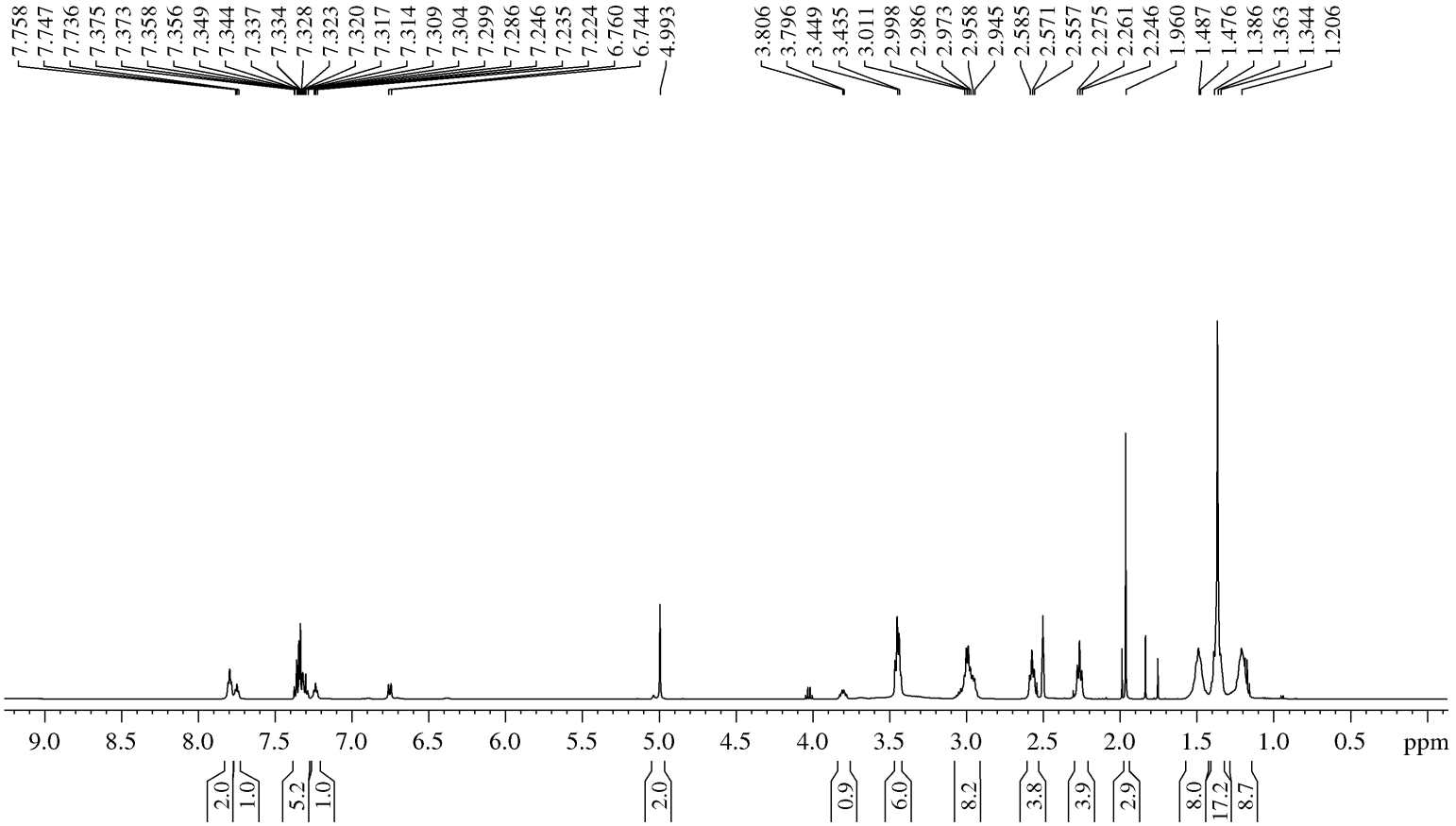

Figure S1. ^{1}H NMR spectrum of compound **1** in $(CD_3)_2SO$. The signals at 1.17, 1.99, 4.02 ppm are assigned to residual ethyl acetate and signal at 2.50 is assigned to residual DMSO in the NMR sample.

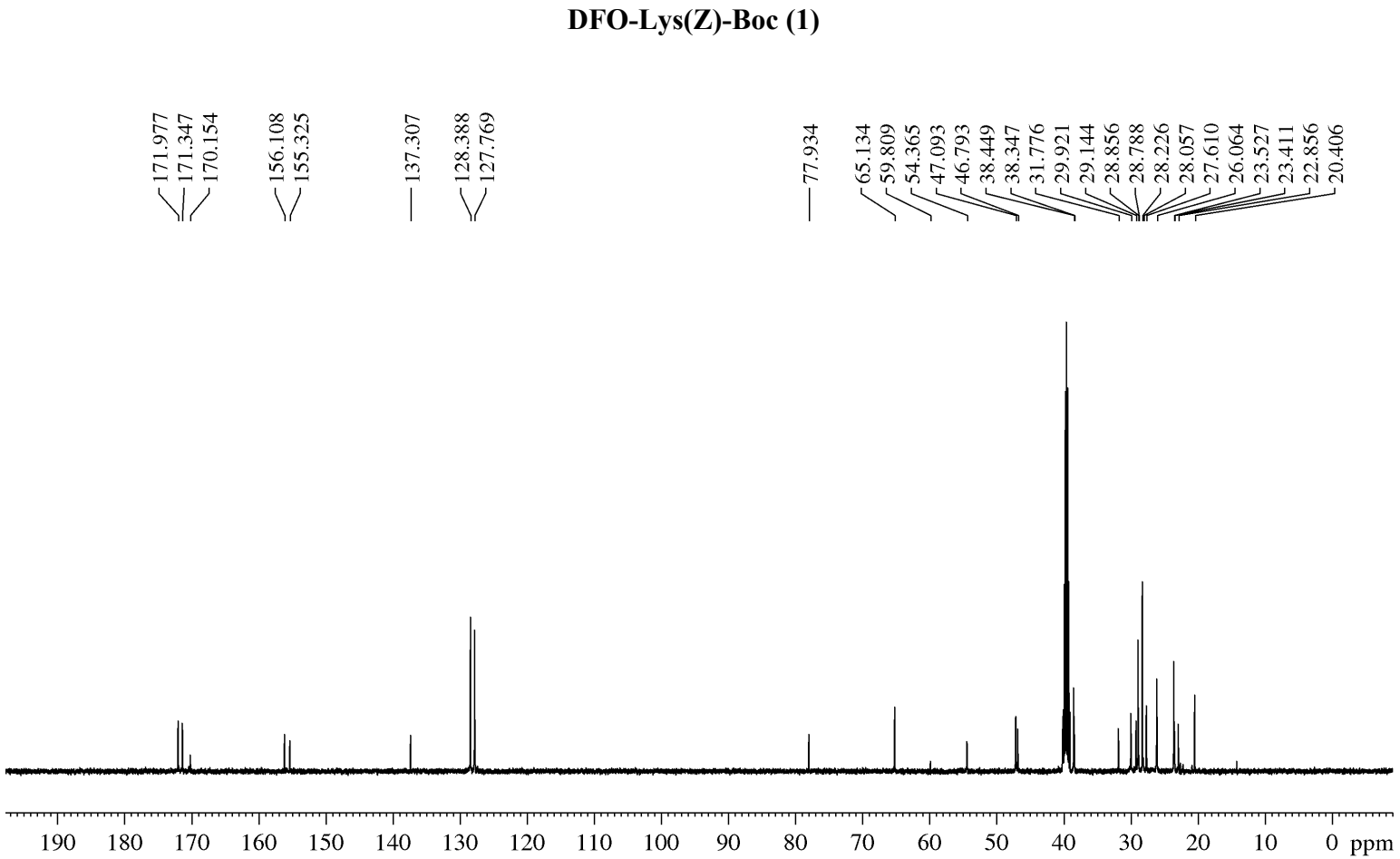

Figure S2. ^{13}C NMR spectrum of compound **1** in $(CD_3)_2SO$.

DFO-Lys(Z)-NH_2 (2)

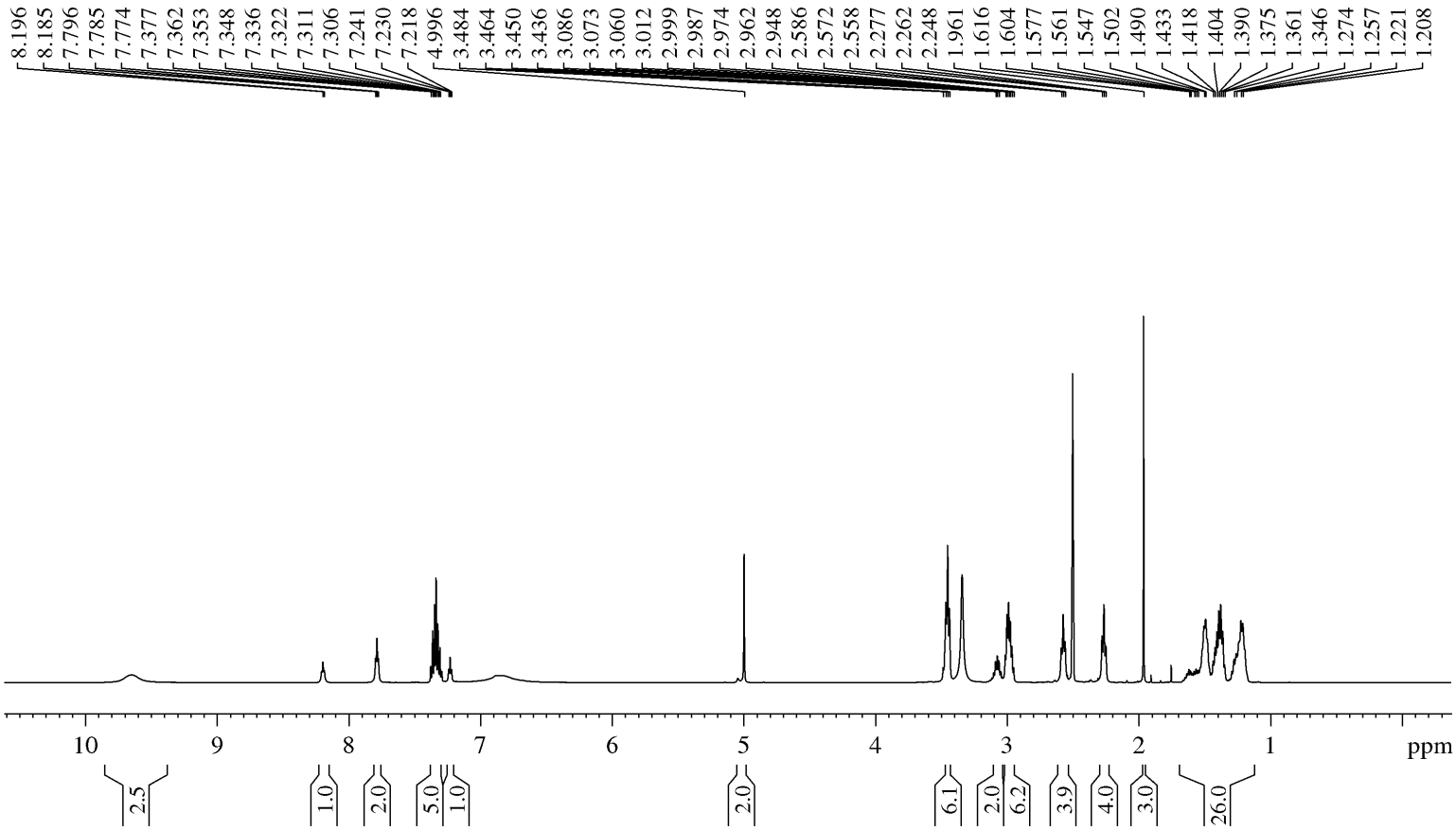

Figure S3. ^{1}H NMR spectrum of compound **2** in $(CD_3)_2SO$. The signal at 2.50 is assigned to residual DMSO in the NMR sample.

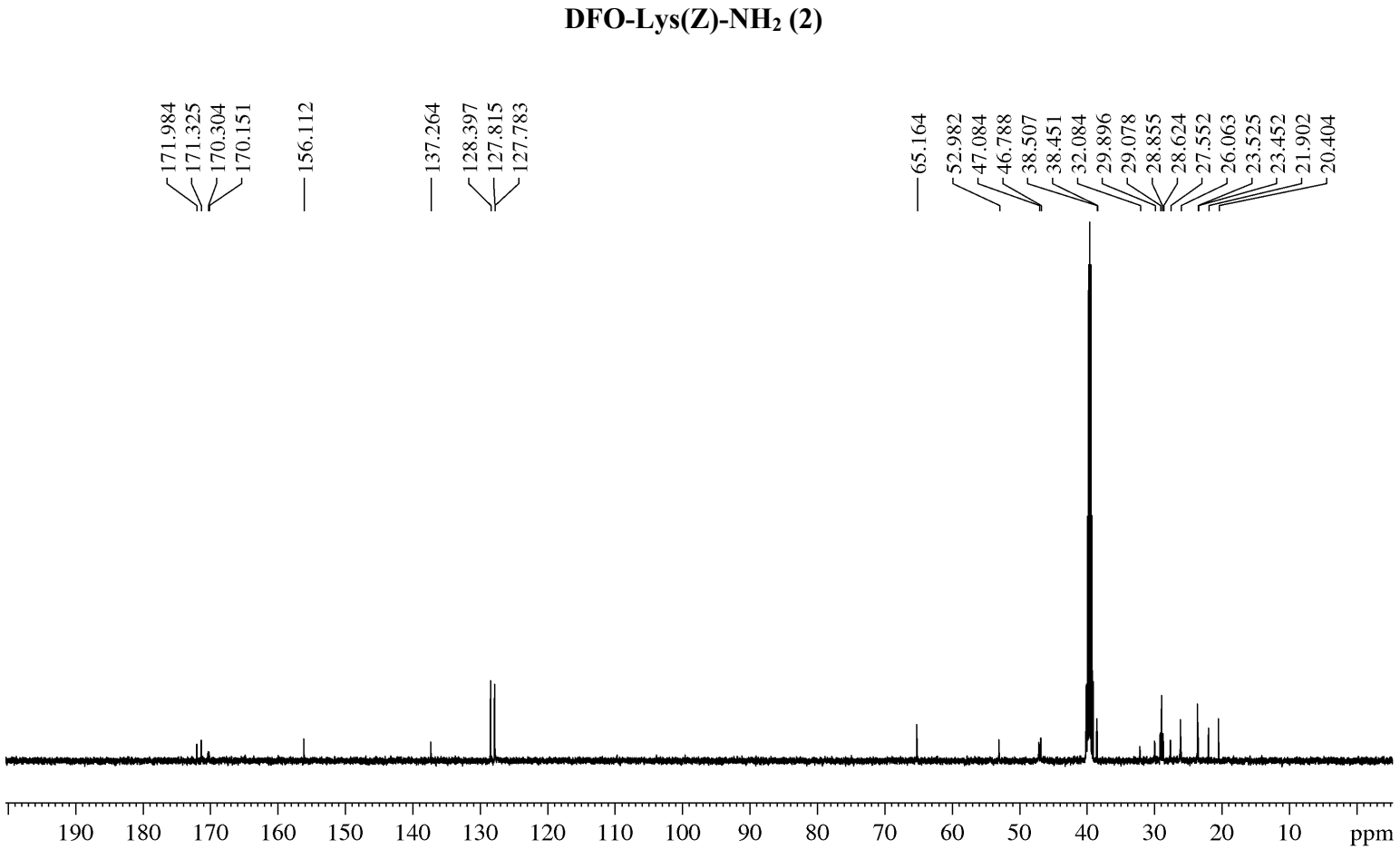

Figure S4. ^{13}C NMR spectrum of compound **2** in $(CD_3)_2SO$.

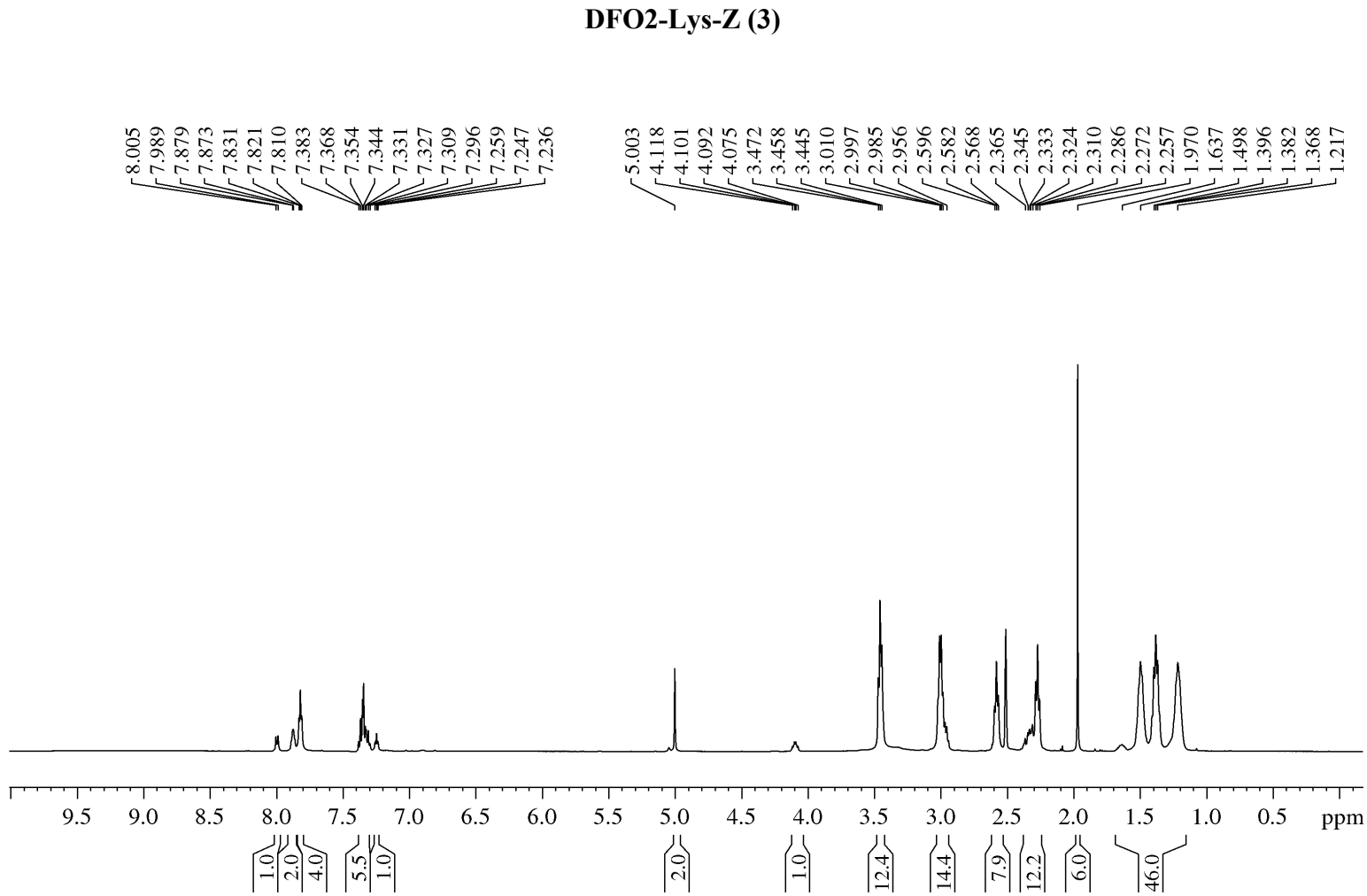

Figure S5. ^{1}H NMR spectrum of compound **3** in $(CD_3)_2SO$. The signal at 2.50 is assigned to residual DMSO in the NMR sample.

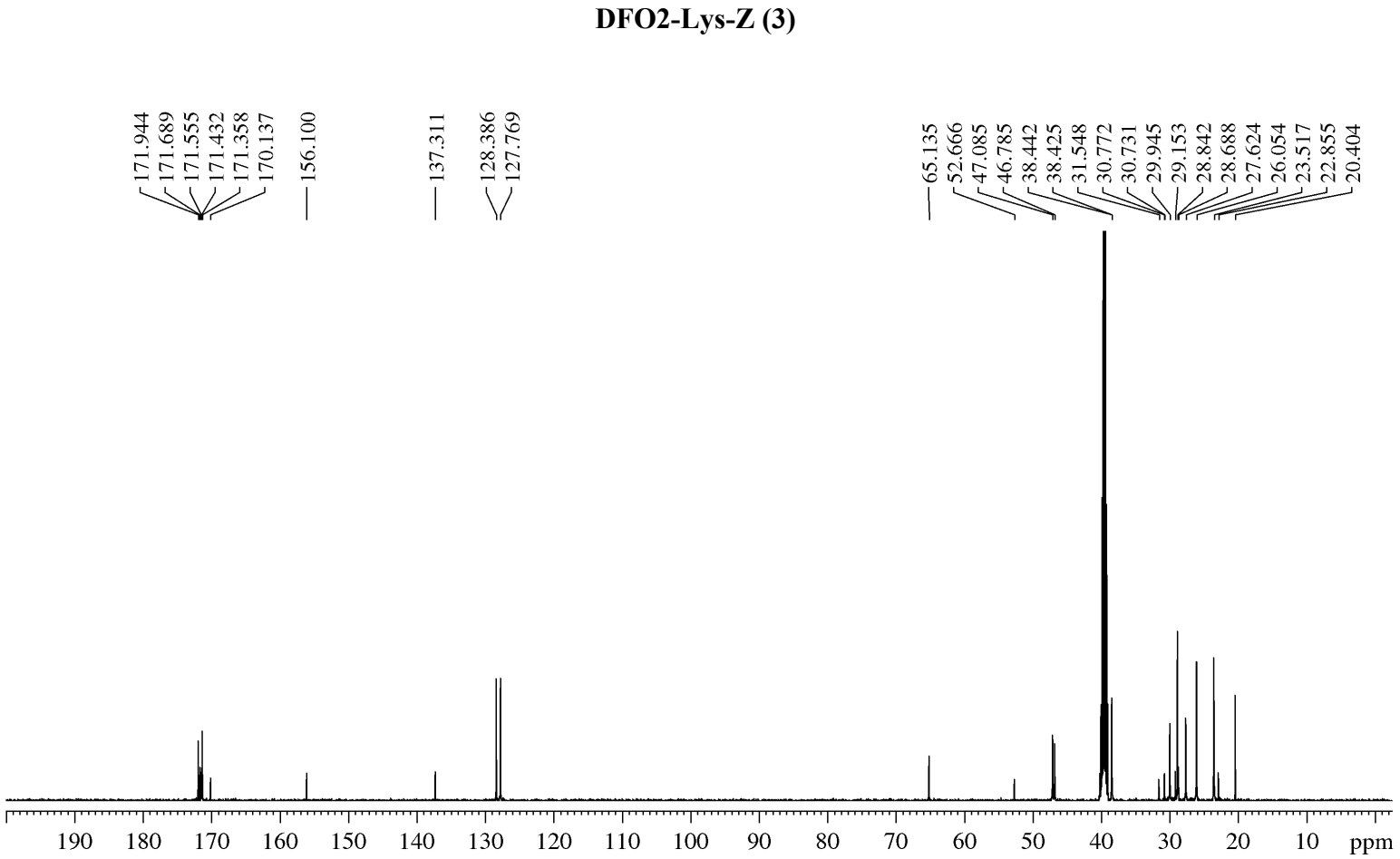

Figure S6. ^{13}C NMR spectrum of compound **3** in $(CD_3)_2SO$.

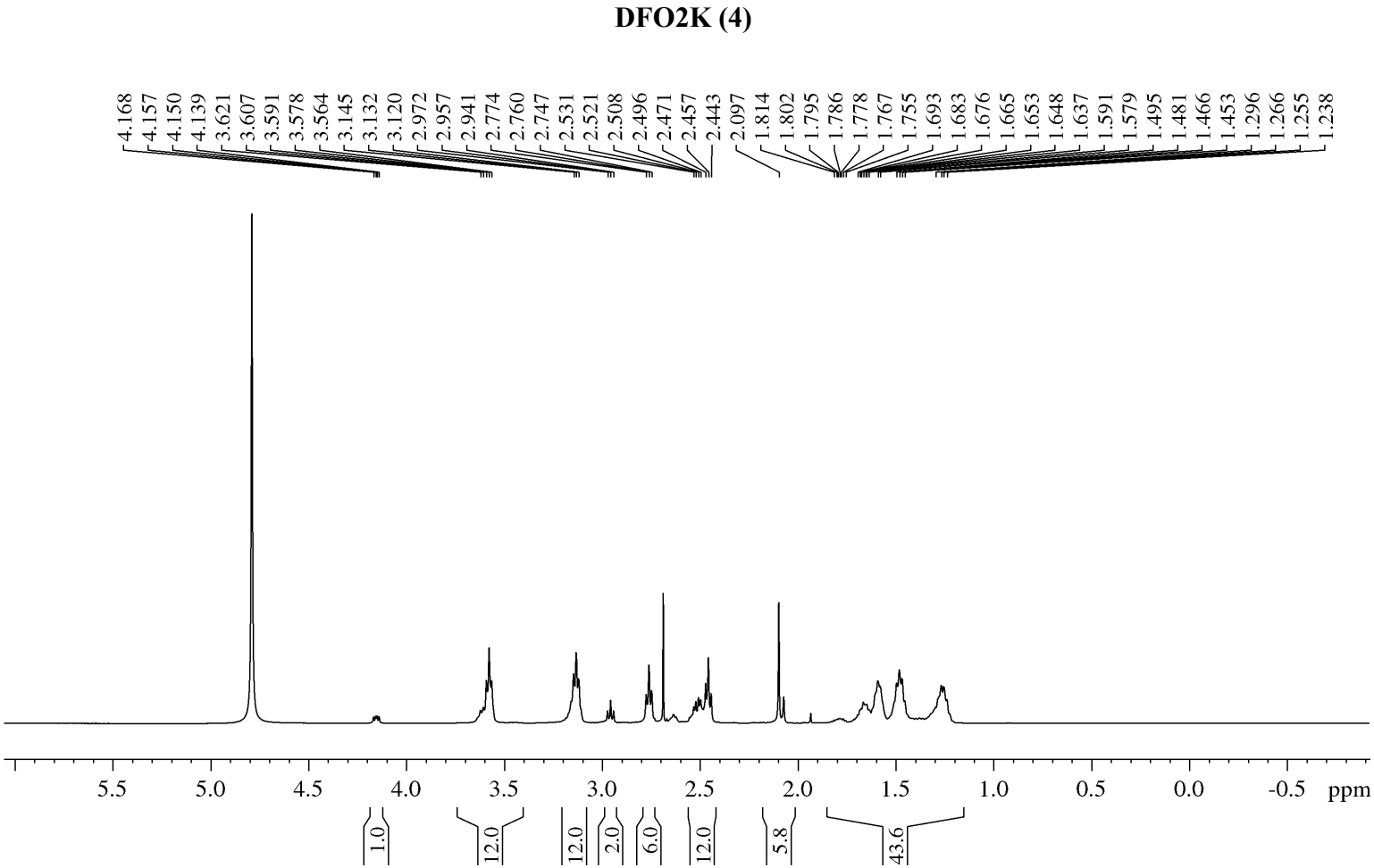

Figure S7. ^{1}H NMR spectrum of compound **4** in D_2O. The signal at 4.79 is assigned to residual H_2O in the NMR sample.

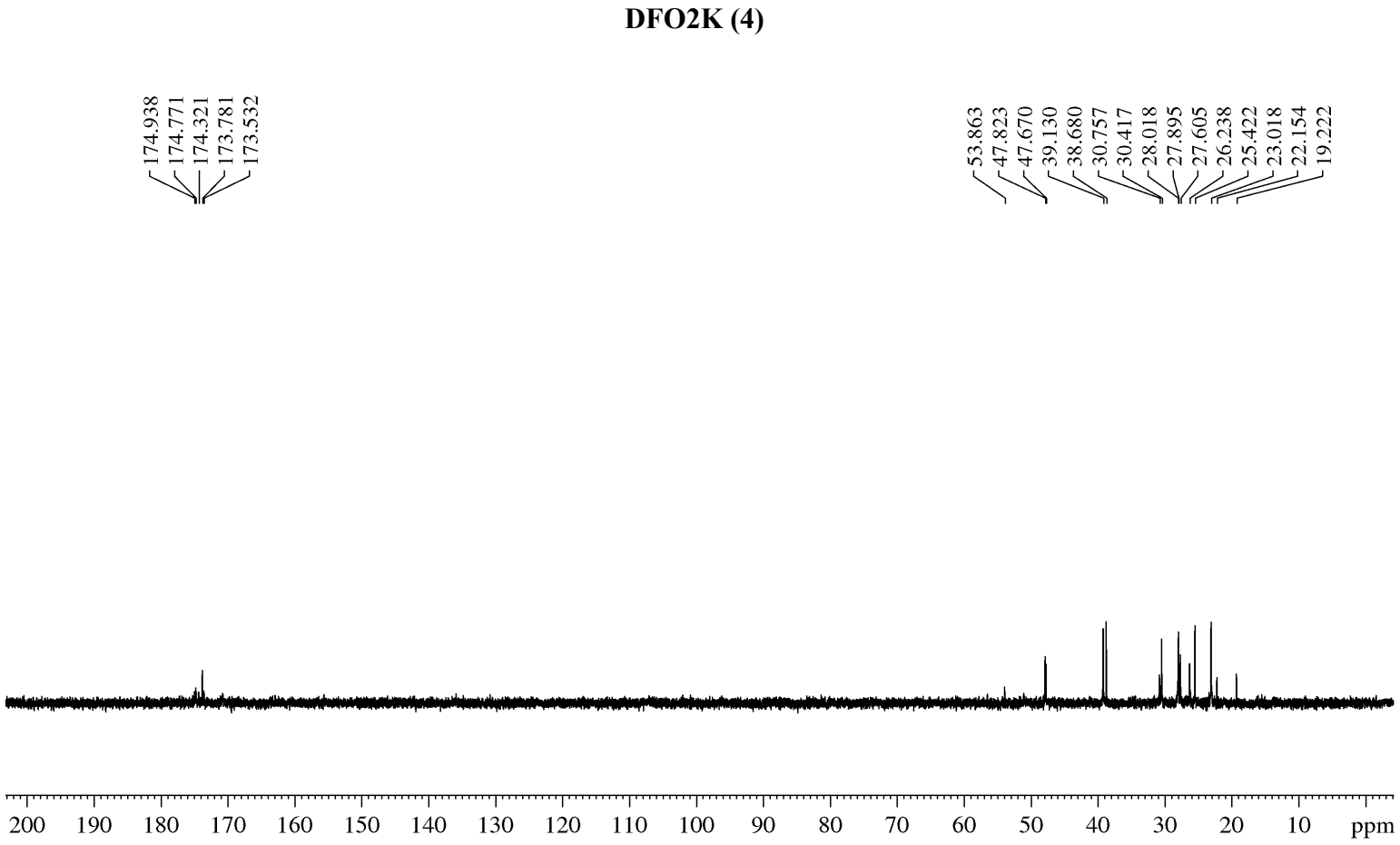

Figure S8. ^{13}C NMR spectrum of compound **4** in D_2O.

DFO2K (4)

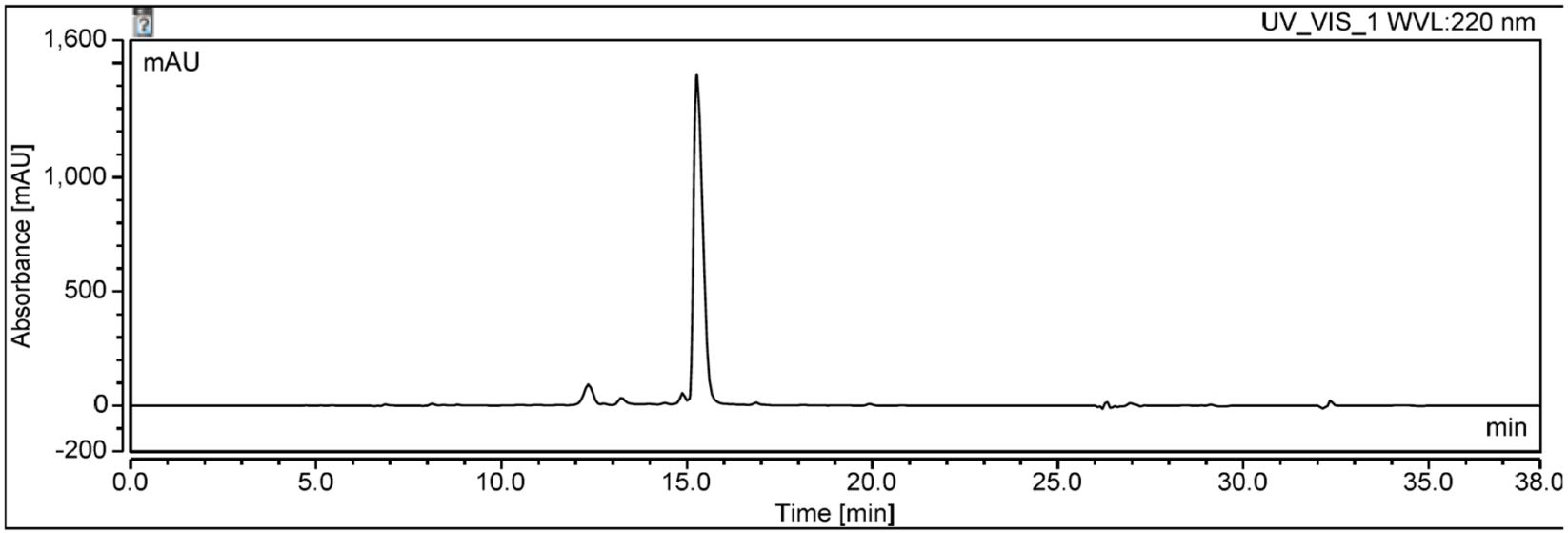

Figure S9. Analytical HPLC chromatogram for semi-pure DFO2K. HPLC conditions: C18 Inspire analytical DIKMA; 5 µm, 250 × 10.0 mm; (15 – 30% acetonitrile in water (0.1% formic acid); flow rate, 2 mL/min, t_R = 15.3 min)

[^{Nat}Zr]Zr-DFO2K (5)

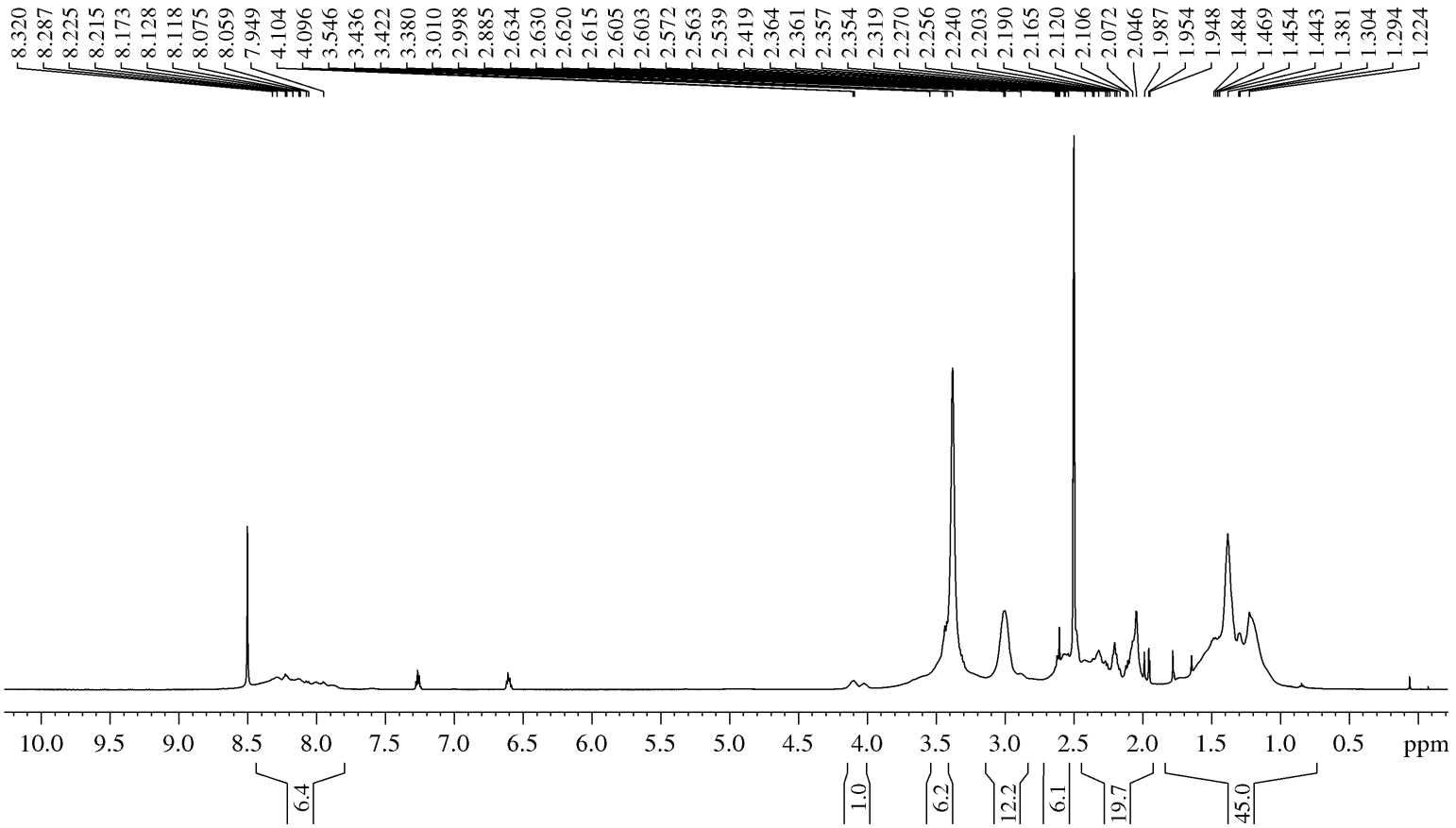

Figure S10. ^{1}H NMR spectrum of compound **5** in $(CD_3)_2SO$. The signal at 2.50 is assigned to residual DMSO and the signal at 3.33 pm is assigned to residual H_2O in the NMR sample.

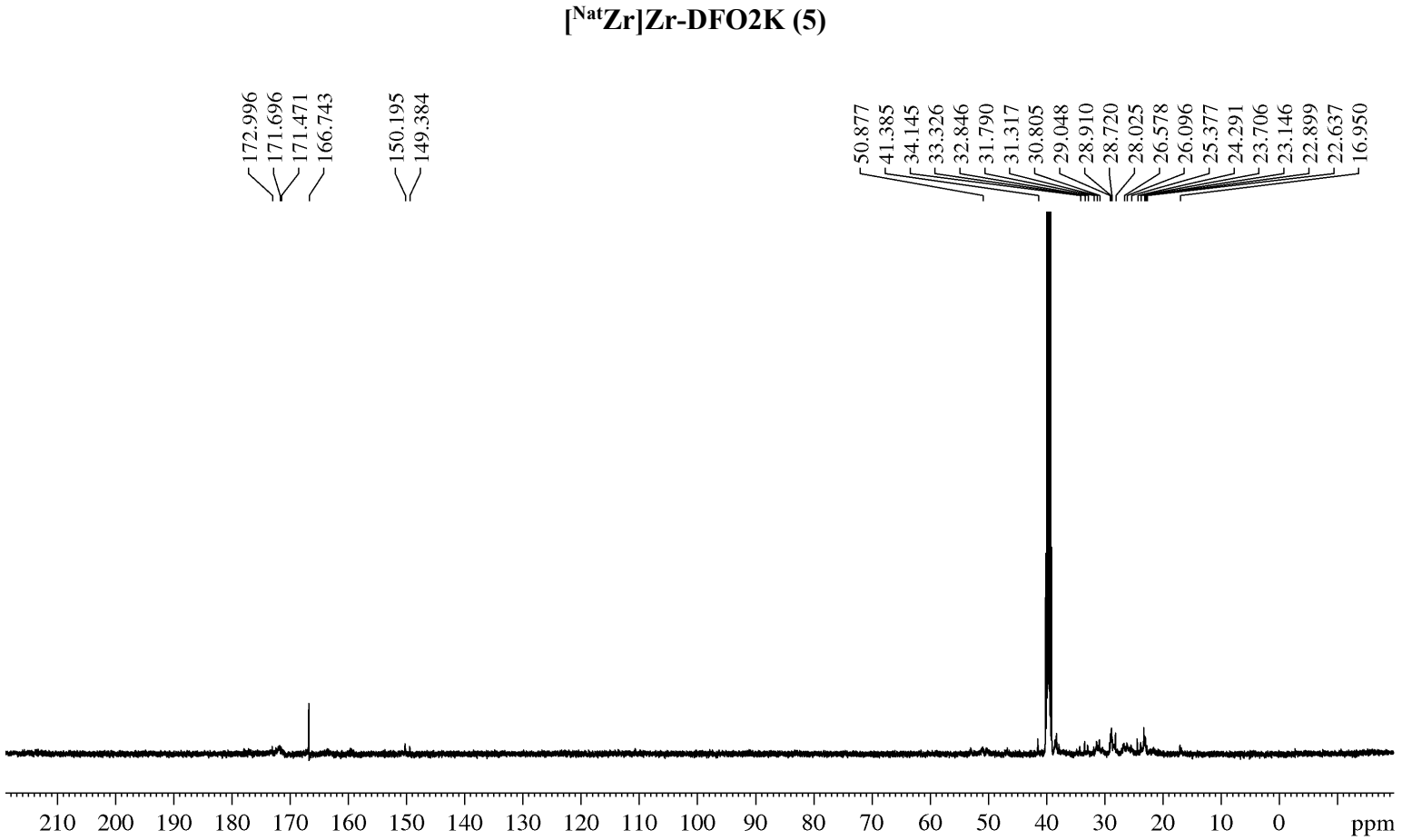

Figure S11. ^{13}C NMR spectrum of compound **5** in $(CD_3)_2SO$.

_p_-Ph-SCN-DFO2K (6)

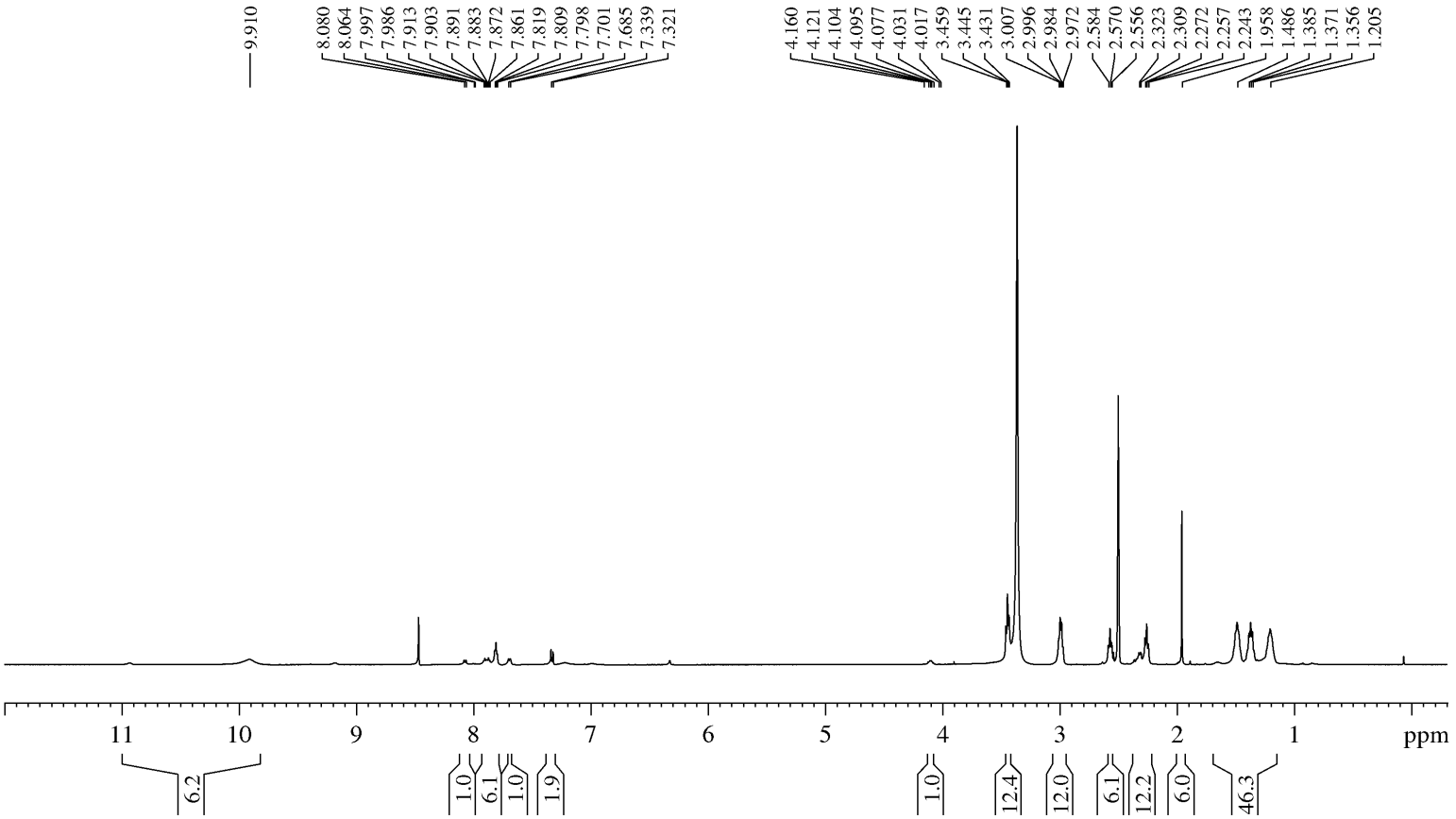

Figure S12. ^{1}H NMR spectrum of compound **6** in $(CD_3)_2SO$. The signal at 2.50 is assigned to residual DMSO and the signal at 3.33 pm is assigned to residual H_2O in the NMR sample.

_p_-Ph-SCN-DFO2K (6)

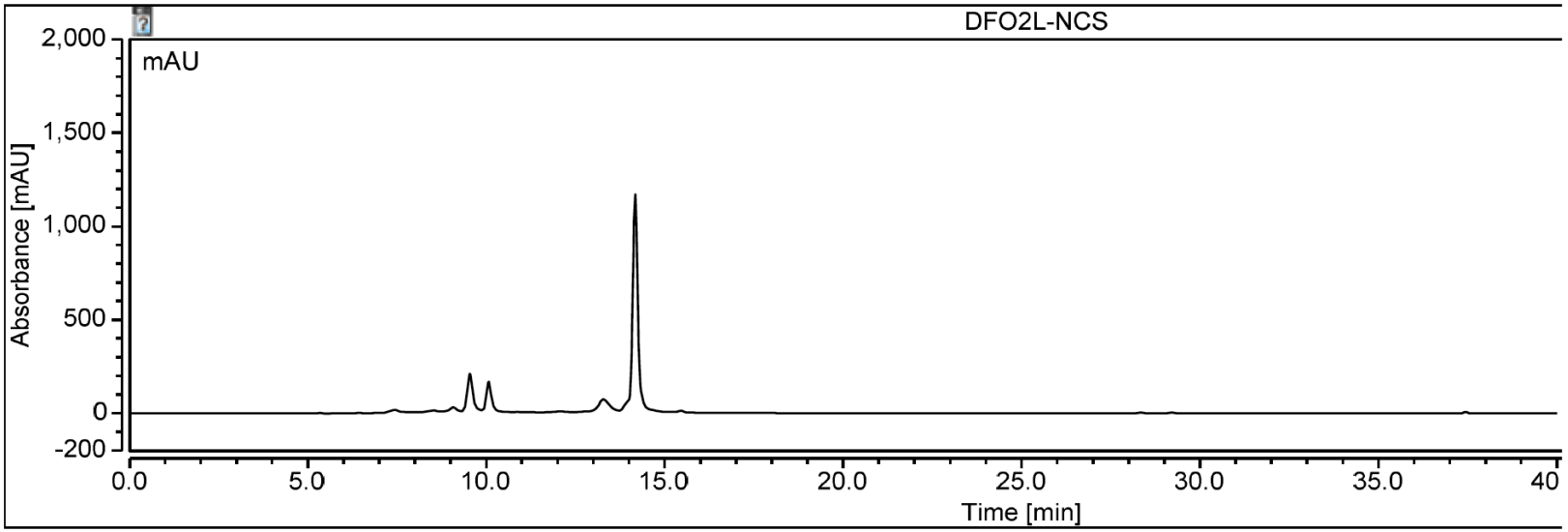

Figure S13. Analytical HPLC chromatogram for ***p*-Ph-SCN-DFO2K**. HPLC conditions: C18 Inspire analytical DIKMA; 5 µm, 250 × 10.0 mm; (30 – 60% acetonitrile in water (0.1% formic acid); flow rate, 2 mL/min, t_R = 14.3 min)

XYZ Coordinates of Zr(DFO2K) optimized structure *

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N	49.79700	-90.21100	0.67300
C	48.63600	-89.60800	0.32000
C	47.36800	-90.24200	0.95300

C	46.07400	-89.69800	0.33900
C	44.81500	-90.17400	1.06800
O	48.57500	-88.58600	-0.39000
N	47.45300	-91.70700	0.95800
C	51.11200	-89.87900	0.13100
C	51.72400	-91.08000	-0.59800
C	53.08100	-90.80800	-1.25700
C	54.23600	-90.53600	-0.28500
C	55.55200	-90.42200	-1.05200
N	56.69200	-90.03500	-0.22200
C	57.93000	-90.60200	-0.32400
C	59.09400	-89.80000	0.21200
C	60.43100	-90.49600	-0.00100
C	61.61300	-89.53700	0.07900
N	62.82500	-90.12200	-0.08300
C	64.06800	-89.36000	-0.19100
C	65.24900	-90.30500	-0.38500
C	66.57700	-89.57000	-0.58200
C	67.74800	-90.55000	-0.67100
O	56.64800	-88.68200	0.19400

O	58.07100	-91.72900	-0.85600
O	61.49100	-88.30700	0.26100
C	69.09200	-89.85900	-0.90100
N	70.20500	-90.78200	-0.68200
C	70.94600	-91.42300	-1.57300
C	70.91800	-91.15900	-3.05200
C	72.34900	-90.92300	-3.59500
C	72.96600	-89.67300	-2.98600
N	73.63500	-89.86300	-1.82200
C	74.01900	-88.77000	-0.92900
C	72.82500	-88.19500	-0.15200
C	73.25800	-87.24900	0.98800
C	72.59200	-87.51100	2.34800
C	73.09400	-88.73700	3.13400
N	72.51500	-90.03600	2.78200
C	71.55500	-90.67500	3.44100
C	70.86600	-90.05300	4.61800
O	70.42600	-91.08500	0.62700
O	71.79800	-92.28500	-1.11600
O	72.81500	-88.54600	-3.50800

O	71.21200	-91.85300	3.03600
O	73.09200	-90.69400	1.72800
N	50.72500	-95.89500	0.66700
C	51.43600	-97.15000	0.88900
C	52.89400	-97.07200	0.41600
C	53.72000	-95.99600	1.12900
C	55.16600	-95.91600	0.63200
C	55.93500	-94.77200	1.30000
N	57.30800	-94.64000	0.82000
C	58.37800	-95.24000	1.42800
C	59.67000	-95.27000	0.63300
C	60.86900	-95.71600	1.46700
C	61.99600	-96.23600	0.59000
N	63.24800	-95.81800	0.89500
C	64.41500	-96.29300	0.15200
C	65.71300	-95.61900	0.59300
C	66.86600	-96.07100	-0.31300
C	68.20200	-95.33500	-0.14000
O	57.41500	-94.32600	-0.55400
O	58.27100	-95.71800	2.57700

O	61.78300	-97.03600	-0.34800
C	69.02800	-95.75100	1.08500
N	70.35800	-95.12800	1.05800
C	71.41400	-95.50600	0.33500
C	71.55000	-96.90500	-0.20500
C	72.63200	-97.69300	0.56700
C	72.13600	-98.21700	1.90600
N	72.80700	-97.87800	3.03600
C	73.92200	-96.93800	3.20400
C	75.29900	-97.56700	2.97100
C	76.47100	-96.58300	3.12100
C	76.40200	-95.36800	2.16900
C	75.86400	-94.06800	2.81500
N	74.86800	-93.36400	1.99300
C	75.09200	-92.79600	0.81500
C	76.47600	-92.56000	0.29700
O	70.40100	-93.85100	1.56700
O	72.36700	-94.66700	0.17100
O	71.14200	-98.97800	1.95200
O	74.08500	-92.42600	0.09500

O	73.56900	-93.49700	2.41100
C	49.66000	-95.72400	-0.15800
C	49.26900	-94.27000	-0.36900
C	47.82400	-93.93900	0.04400
C	47.60300	-92.45200	-0.17200
O	49.05900	-96.66300	-0.72100
O	47.65300	-91.93700	-1.30500
Zr	72.07200	-92.54800	1.07300
C	43.53300	-89.58800	0.46800
C	42.26300	-90.09300	1.14900
N	41.05800	-89.51700	0.51800

* Density Functional Theory calculations performed by using Material Studio software via DMol^3/PBE.