Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

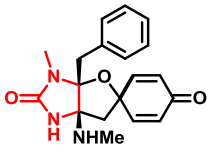
Electronic Supporting Information

Metal-free C(sp^2)–H Functionalization of Azoles: K_2CO_3/I_2 Mediated Oxidation, Imination, and Amination

Ranajit Das, Mainak Banerjee, Rakesh Kumar Rai, Ramesh karri and Gouriprasanna Roy*
Department of Chemistry, School of Natural Sciences, Shiv Nadar University, NH91, Dadri, Gauntam Buddha Nagar, UP 201314, India

Contents:

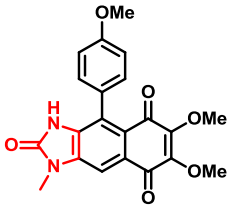
I.1 C2-Functionalized azole containing Bio-Active Natural Products and Drugs



(-) Spiroleucettadine

antibacterial activity against Enterococcus durans with an MIC < 6.25 μg/mL

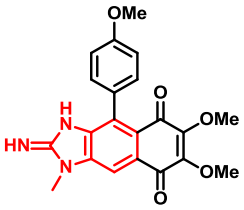
Crews et al.
J. Org. Chem., **2004**, 69, 9025–9029



Kealiiquinone

Cytotoxic against KB cells, MIC = 5 pg/mL

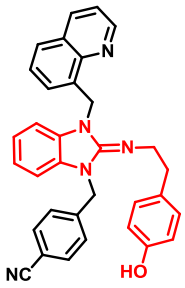
Scheuer et al.,
J. Org.Chem. **1990**,55, 1944-1946



2-Amino-2-deoxy-Kealiiquinone

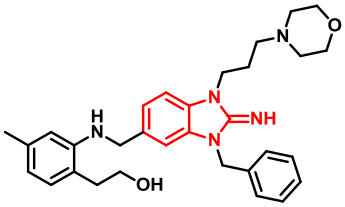
cytotoxicity against murine leukemia P-388 cell lines (IC_{50} 2 μg/mL)

Schmitz et al.,
*J. Nat. Prod.***1997**, 60, 497-498



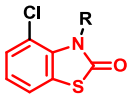
CXCR3 Invibitors

Roth et al.
US 2007/0232673 A1, 2007



RSV Inhibitor

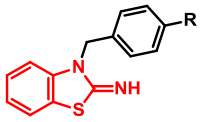
Bonfanti et al. US patent: **WO2006/097534, 2006**



(a) R= CH_2COOH **Benazolin**
(b) R= CH_3 **Chlobenthiazone**

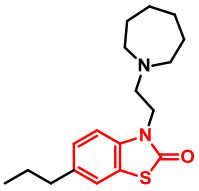
Herbicides and Fungicides

T. J.Kato et al. *Pestic. Sci.* **1983**, 8, 333
T. J.Kato et al. *Pestic. Sci.* **1984**, 9, 689



potent antiapoptotic activity EC_{50} of 1.31 μM

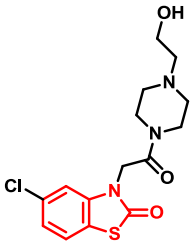
Cottam et. al.,
J. Med. Chem.. **2005,** 48, 6409 - 6422



(SN56)

Sigma-1 receptor ligand

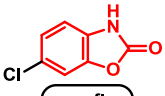
J.H. Poupaert, et al.
Med. Chem. Res. **2005**, 14, 158



Tiaramide

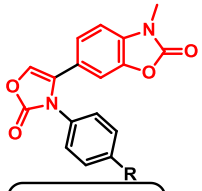
Antiinflammatory and analgesic drug

M. Matsuoet al.
Chem. Pharm. Bull., **1993**, 41,301



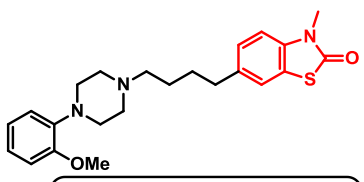
paraflex

A. H. Conne et. al.
Pharmacol. Exp. Ther. **1960**, 128, 340–343



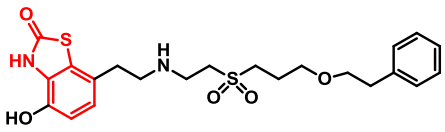
COX-2 Inhivitor

Sahin et al.,
Bioorganic Med. Chem. **2010**, 18, 6367-6376



Atypical antipsychotic property

Pfeiffer, B., *J. Med. Chem.*, **2010**, 1998, 41

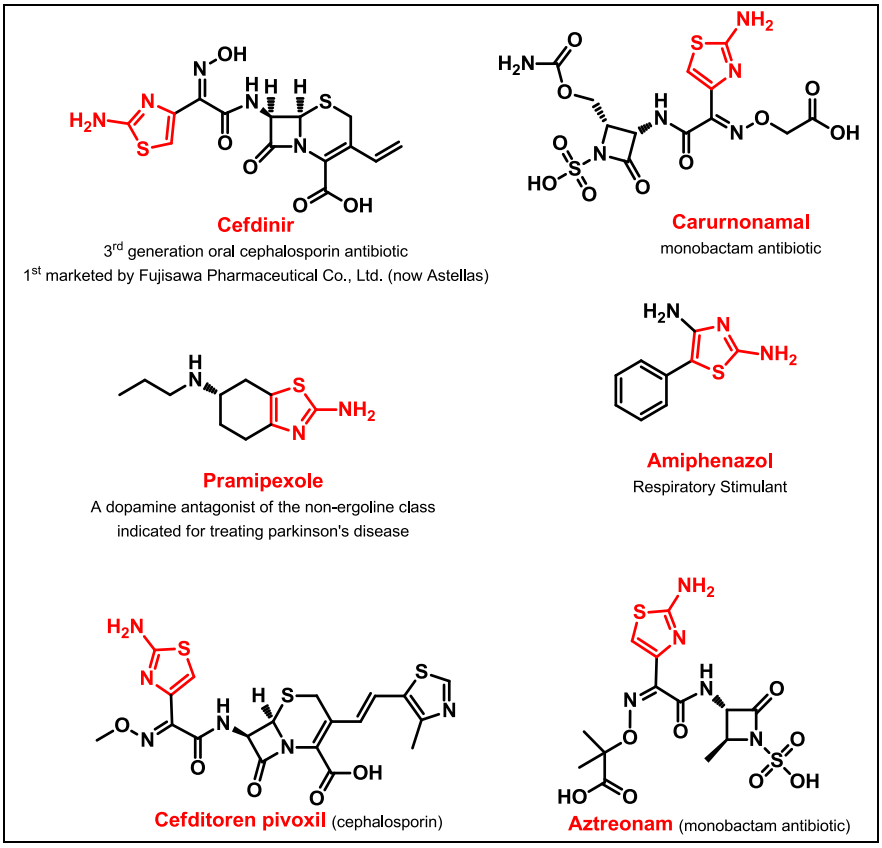


Sibenadet

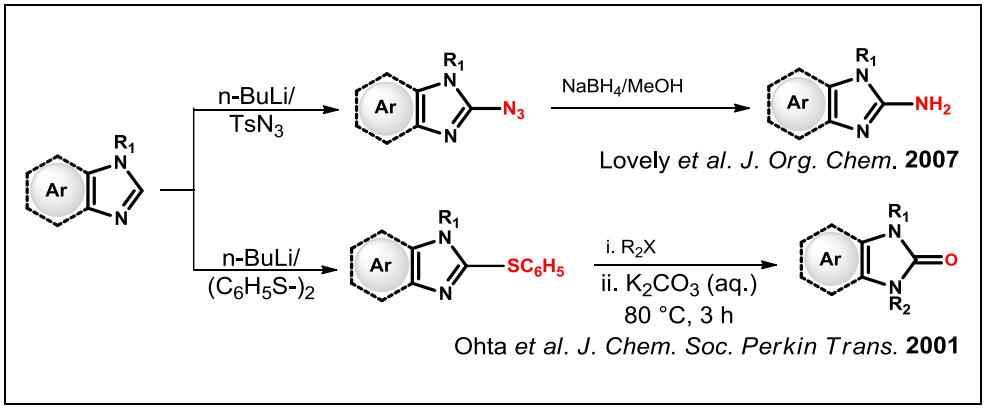
Development by **Astra Zeneca** for the treatment asthama

Young et al., *J. Med. Chem.,* **2003**, 46, 3210

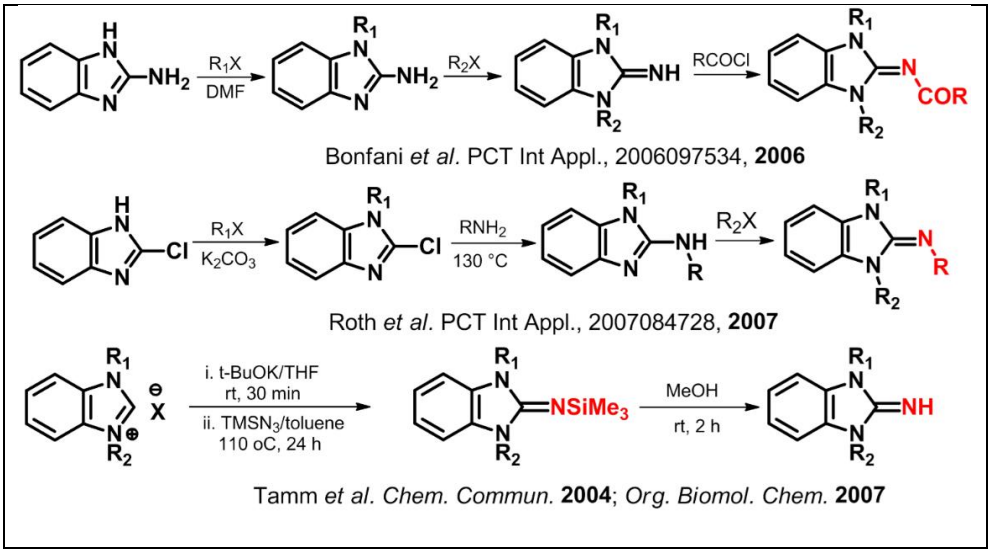
I.2. C2-Functionalized thiazole containing Bio-Active Natural Products and Drugs



II. Previous Work:



Scheme S1: Previously reported work on C2-H oxidation and imination of imidazole and benzimidazole.



Scheme S2: Previously reported work on C2-H imination of imidazole and benzimidazole.

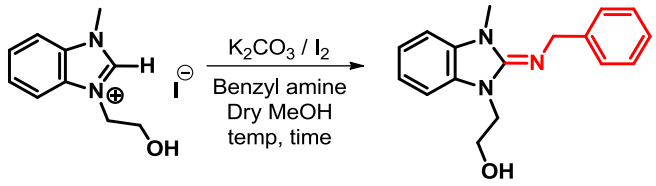
III. Reaction Condition Optimization:

Table S1: Reaction Condition Optimization for C2-H oxidation[a].

Entry	Iodine Sources	Solvent	Base	Time	Temp	Yield[b]
21	NIS	MeOH/ H_2O	K_2CO_3	30 min	40 °C	-
22	PIDA	MeOH/ H_2O	K_2CO_3	30 min	40 °C	-

[a]Reagents and conditions: 1.12 mmol (**7c**) was reacted with 1.12 mmol Iodinated Sources, in presences of 2.24 mmol of K_2CO_3 at 40 °C in MeOH/H_2O (9:1) as a solvent mixture. [b]Isolated yields are displayed over here.

Table S2: Reaction Condition Optimization for C2-H imination with benzyl amine reaction[a].

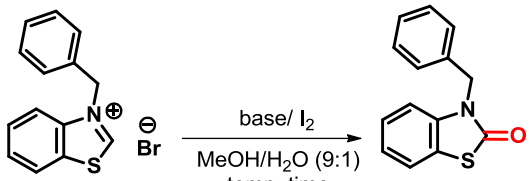


7r 12a

Entry	Time	temp	Yield[b] (%)
1	12 h	rt	-
2	12 h	40 °C	31
3	12 h	50 °C	63[c]
4	6 h	50 °C	72[c]
5	**2 h**	**50 °C**	**81**

[a]Reagents and conditions: 2-(2-(benzylimino)-3-methyl-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)ethanol was obtained in 81% yield by using 2 equiv. of K_2CO_3, 1.0 equiv. of I_2, 1.2 equiv. of $BnNH_2$ and in MeOH. [b]Isolated yields of chromatographically pure products displayed. [c]Multiple products.

Table S3: Reaction Condition Optimization for C2-H oxidation of azoles other than imidazole and benzimidazole[a]

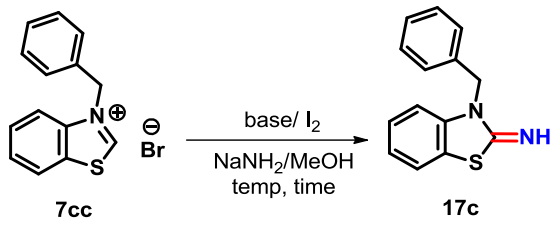


7cc 16c

Entry	Bases	Time	temp	Yield[b] (%)
1	K_2CO_3	2 h	rt	-
2	K_2CO_3	2 h	40 °C	59
3	K_2CO_3	2 h	50 °C	71[c]
4	**K_2CO_3**	**30 mins**	**50 °C**	**79**
5	Et_3N	30 mins	50 °C	51

[a]Reagents and conditions: 3-benzylbenzo[*d*]thiazol-2(3*H*)-one was obtained in 81% yield by using 2 equiv. of K_2CO_3, 1.0 equiv. of I_2, in MeOH/H_2O (9:1). [b]Isolated yields of chromatographically pure products displayed. [c]Multiple products.

Table S4: Reaction Condition Optimization for C2-H Imination of azoles other than imidazole and benzimidazole[a]



Entry	Bases	Time	temp	Yield[b] (%)
1	K_2CO_3	30 min	rt	61[c]
2	K_2CO_3	30 min	-2 °C	65[c]
3	**K_2CO_3**	**10 min**	**-5 °C**	**76**
4	Et_3N	10 mins	-5 °C	59

[a]Reagents and conditions: 3-benzylbenzo[*d*]thiazol-2(3*H*)-imine was obtained in 81% yield by using 2 equiv. of K_2CO_3, 1.0 equiv. of I_2, 1.2 equiv. of $NaNH_2$ and in MeOH. [b]Isolated yields of chromatographically pure products displayed. [c]Multiple products

V. HRMS Analyses:

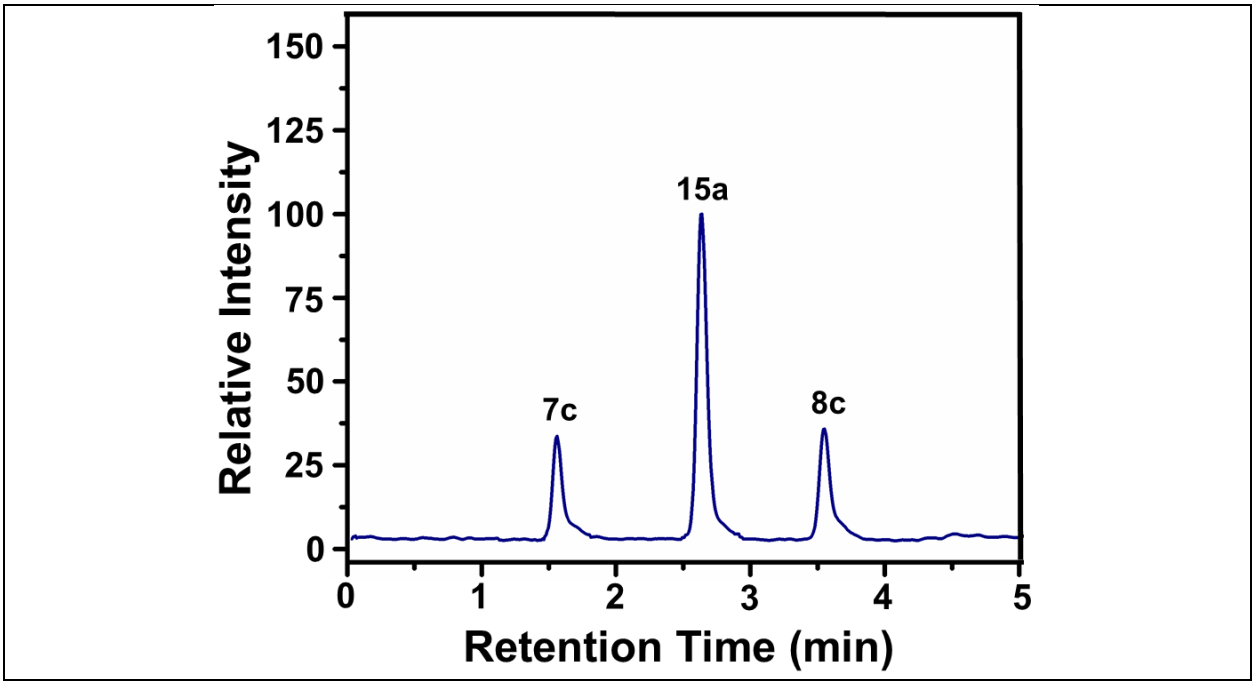
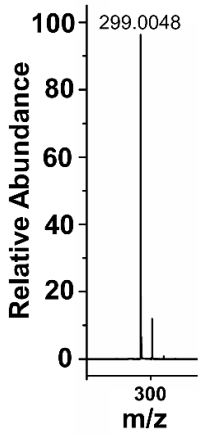
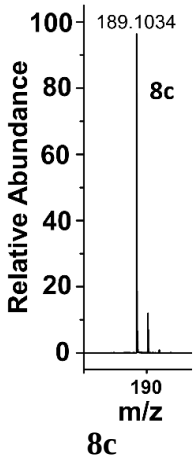


Figure S1: LCMS Chromatogram of compounds **7c**, **15a** and **8c** isolated from crude reaction mixture.



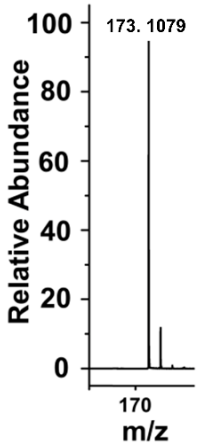
15a

Chemical Formula: $C_{11}H_{12}IN_2^+$
Calculated For : $[M]^+$
299.004
Found : 299.0048



8c

Chemical Formula: $C_{11}H_{12}N_2O$
Calculated For : $[M+H]^+$
189.1022
Found : 189.1034

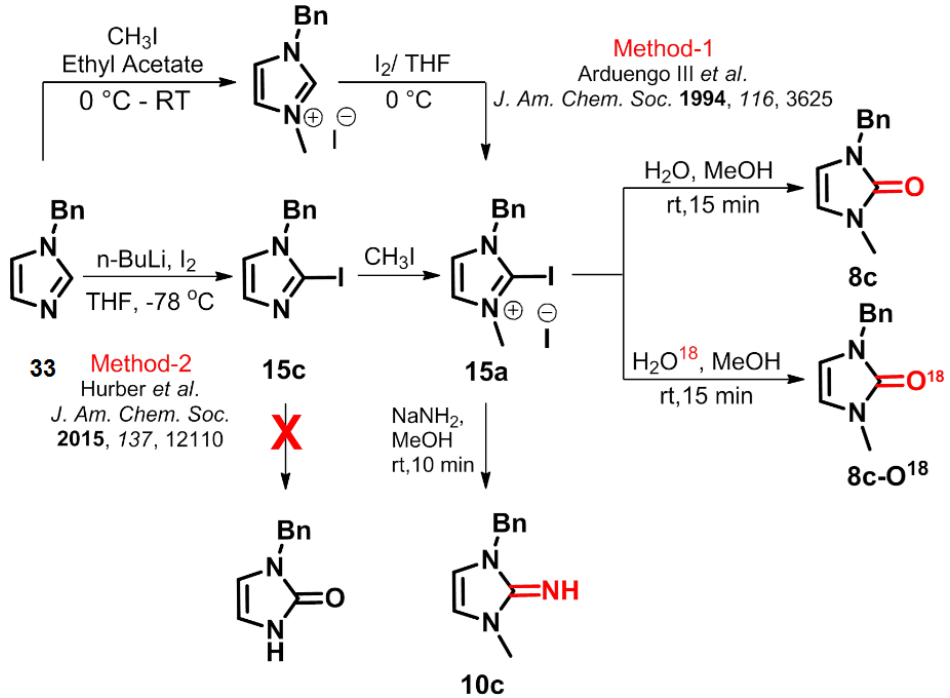


7c

Chemical Formula: $C_{11}H_{13}IN_2^+$
Calculated For : $[M]^+$
173.1073
Found : 173.1079

Figure S2: HRMS values of **2**-iodo-1,3-dimethyl-1*H*-imidazol-3-ium iodide **(15a),** 3-benzyl-1-methyl-1*H*-imidazol-3-ium bromide (**7c**) and 1-benzyl-3-methyl-1*H*-imidazol-2(3*H*)-one **(8c).**

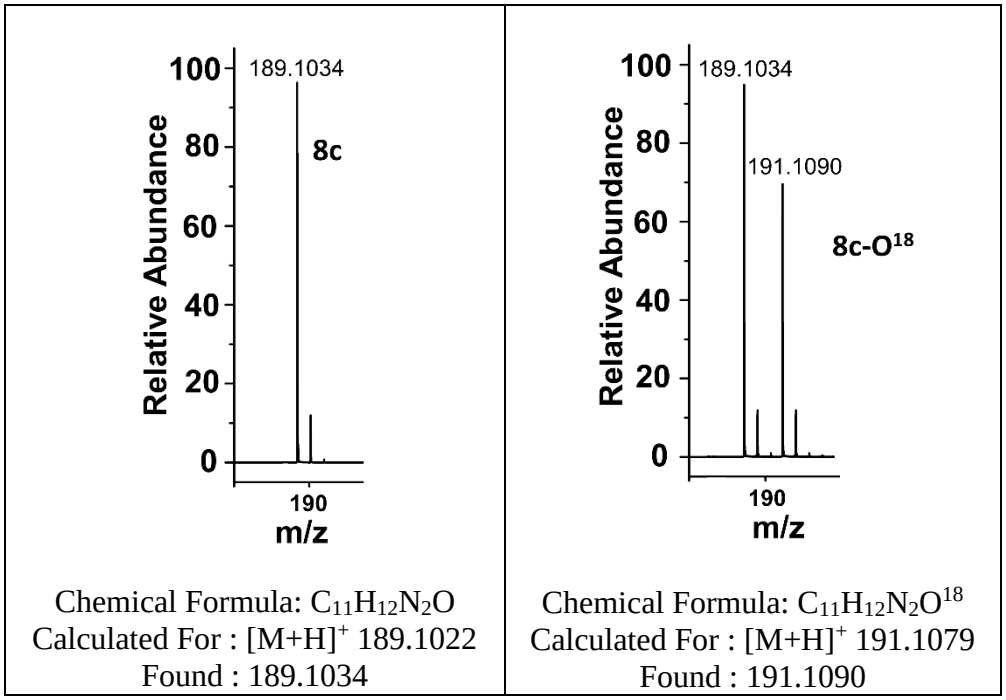
V.1: Control Experiments:



Scheme S3: Control Experiments for Mechanistic Investigation of the C(sp^2-H) functionalization reaction

Synthesis of 1-benzyl-2-iodo-1H-imidazole (**15c**)[S1]

The title compound was prepared by a modified procedure reported in the literature. To a two-necked round bottom flask,1-benzyl-1*H*-imidazole (900 mg, 5.68 mmol) was added. To the flask, THF (30 mL) was injected, and the resulting solution was cooled to –60˚C. Then a hexane solution of n-BuLi (1.6 M, 4.62 mL, 7.39 mmol) was added dropwise to the cooled mixture over 1.5 h. A THF solution (10 mL) of iodine (1.89 g, 7.39 mmol) was added to the mixture at –60 ˚C, and the resulting mixture was slowly allowed to warm up to room temperature and stirred for 30 min. Volatile components were evaporated under reduced pressure, and the resulting residue was dissolved in CH_2Cl_2 (200 mL). The organic layer was washed with water (100 mL × 2), $Na_2S_2O_3$ aq. (1M, 100 mL × 2), and brine (100 mL × 2). The combined organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure to give crude solid. The crude was purified by column chromatography on silica gel (eluent: EtOAc) to afford 2-iodo-1-phenyl-1*H*-imidazole as yellowish white solid (1.2 g, 74%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.16 (s, 2H), 7.01 (m, 1H), 7.16 (m, 2H), 7.36 (m, 2H) 7.46 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ. 51.22, 124.35, 127.08, 127.74, 132.02, 136.97. HR-ESIMS (m/z): Calcd for $[M+H]^+$ $C_{10}H_9IN_2$ 284.9883 observed value: 284.9878.



Chemical Formula: $C_{11}H_{12}N_2O$
Calculated For : $[M+H]^+$ 189.1022
Found : 189.1034

Chemical Formula: $C_{11}H_{12}N_2O^{18}$
Calculated For : $[M+H]^+$ 191.1079
Found : 191.1090

Figure S3: HRMS values of compound **(8c)** and **(8c-O^{18})** for isotope labeling study.

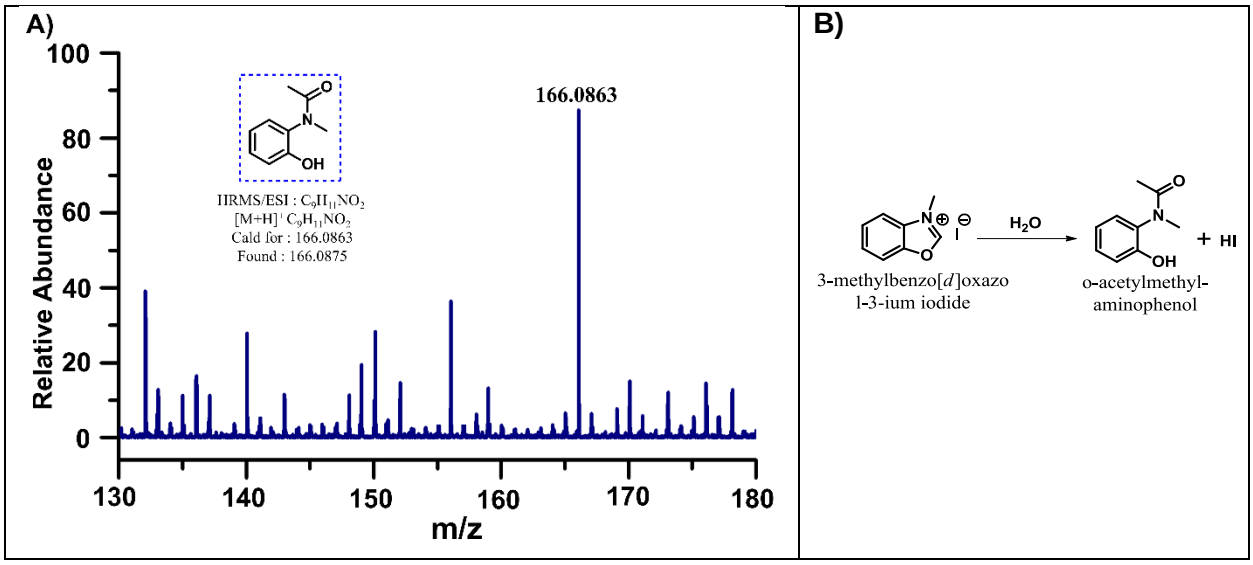
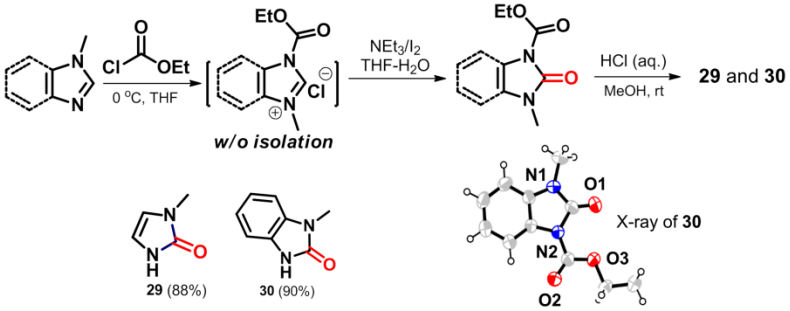


Figure S4: A) HRMS spectra of 3-(2-aminobenzoyl)-1-(2-hydroxyethyl)-1*H*-benzo[*d*]imidazol-3-ium chloride. B) Reaction scheme of hydrolysis of methyl benzoxazole salt.

General synthetic strategy to make compound 28 and 29

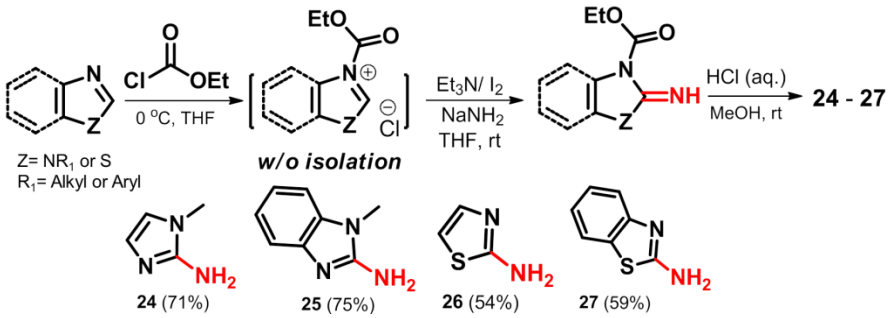


Scheme S4: General synthetic strategy for the synthesis of *N*-methyl-2-benz(imid)azolone

Characterization data of compound (**30**)

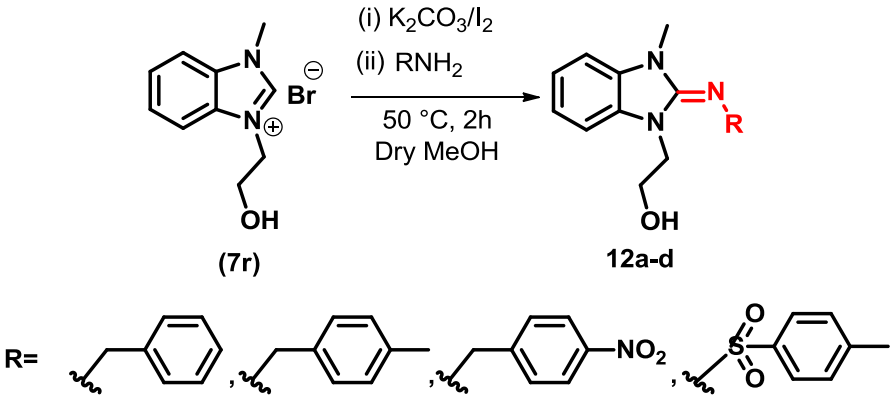
^{1}H NMR (400 MHz, $CHCl_3$-d_3): δ 7.85-7.87 (d, 1H), 7.20-7.24 (m, 1H), 7.16-7.12 (m, 1H), 6.94 (d, 1H), 4.51 (q, J= 7.12 Hz, 2H), 3.38 (s, 3H), 1.47 (t, *J*= 7.12 Hz, 2H). ^{13}C NMR (100 MHz, $CHCl_3$-d_3): 151.03, 150.71, 130.29, 126.09, 124.31, 122.50, 114.58, 107.60, 63.75, 27.19, 14.40. HR-ESIMS (m/z): Calcd for $[M+H]^+$ $C_{11}H_{12}N_2O_3$: 221.0921 observed value: 221.0927.

General synthetic strategy to make compounds 24, 25, 26, and 27



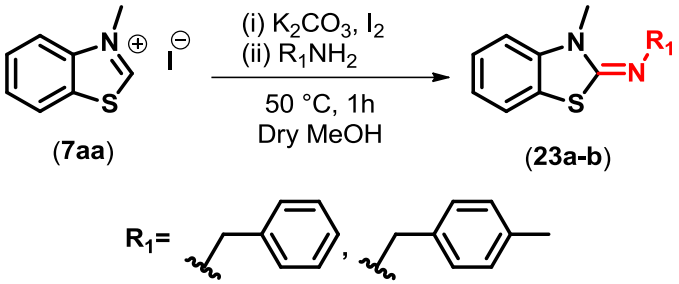
Scheme S5: General synthetic strategy for the synthesis of (*N*-methyl)-2-amino-azole

General procedures for the synthesis of substituted Imines (12a-d)



Scheme S6: General synthetic procedure for the synthesis of *N,N'*-disubstituted benzimidazoloimino compounds (**12a-d**)

General procedures for the synthesis of substituted imines (23a-b)



Scheme S7: General synthetic procedure for the synthesis of *N,N'*-disubstituted benzimidazoloimino compounds **(23a-b)**

VI. X-ray crystallography:

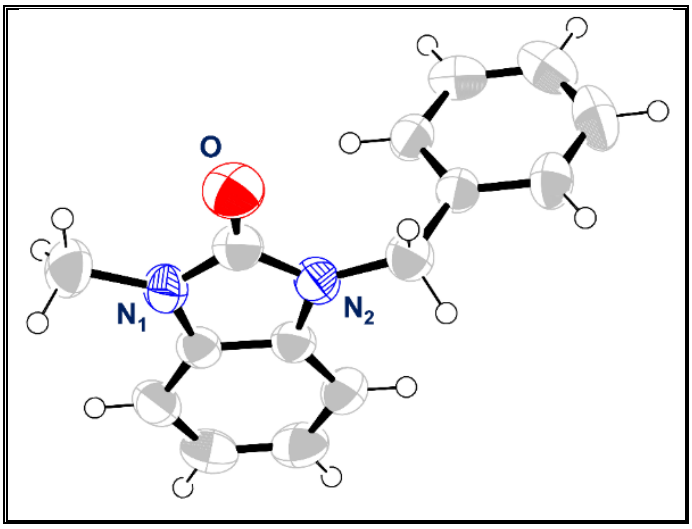


Figure S5: ORTEP diagram of 1-benzyl-3-methyl-1*H*-benzo[*d*]imidazol-2(3H)-one **(9e)**

CCDC No : 1520599	Radiation (λ)/A° : 0.71073
Lattice : monoclinic	ρ/ (g cm^{-3}) : 1.45
Formula: $C_{15}H_{14}N_2O$	μ (Mo K_α) mm^{-1} : 0.295
Formula Weight : 238.28	θ_{max}/deg : 26.4
Space Group : P $2_1/c$	No. of data collected : 42477
a/ A° : 10.5352(5)	No. of data : 2492
b/ A° : 5.6590(3)	No. of parameters : 165
c/ A° : 20.7179(8)	R_1 [I> 2σI] : 0.071
α/ ° : 90.000	wR_2 [I> 2σI] : 0.130
β/ ° : 95.495 (2)	R_1 [all data]: 0.043
γ/ ° : 90.000	wR_2 [all data] : 0.111
V/ $A^{°3}$: 1229.50(10)	R_{int} [all data] : 0.0697
Z : 4	GOF : 2.890
Temperature (K) : 299(2)	Dr_{min} and Dr_{max} (e$Å^{-3}$): -0.129 and 0.132.

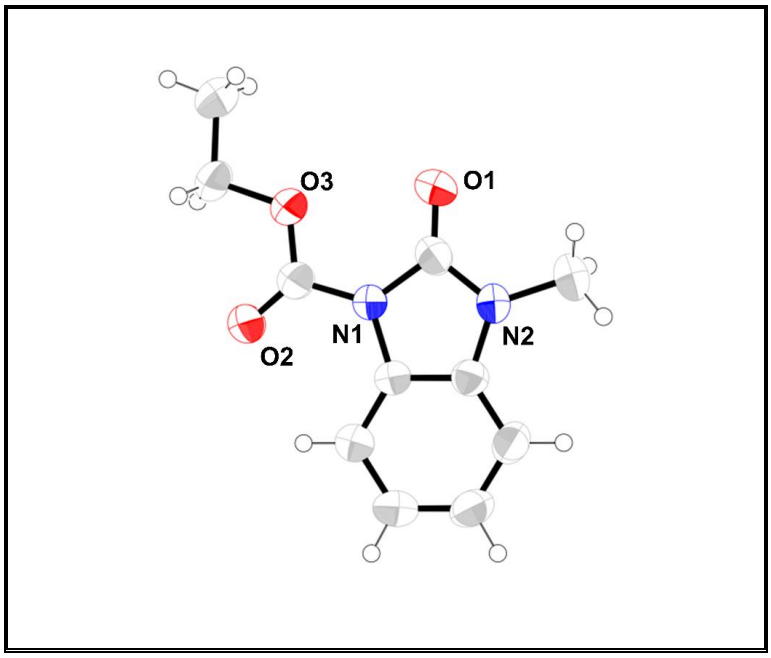


Figure S6: ORTEP diagram of ethyl 2-(3-methyl-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)acetate **(30)**

CCDC No : 1520600	Radiation (λ)/A° : 0.71073
Lattice : monoclinic	ρ/ (g cm^{-3}) : 1.45
Formula: $C_{11}H_{12}N_2O_3$	μ (Mo K_α) mm^{-1} : 0.101
Formula Weight : 222.22	θ_{max}/deg : 26.4
Space Group : P $2_1/c$	No. of data collected : 19365
a/ A° : 4.6419(3)	No. of data : 2121
b/ A° : 24.9757(17)	No. of parameters : 148
c/ A° : 9.9967(6)	R_1 [I> 2σI] : 0.127
α/ ° : 90.000	wR_2 [I> 2σI] : 0.137
β/ ° : 97.3710 (2)	R_1 [all data]: 0.060
γ/ ° : 90.000	wR_2 [all data] : 0.112
V/ $A^{°3}$: 1073.50(3)	R_{int} [all data] : 0.0829
Z : 4	GOF : 2.890
Temperature (K) : 293(2)	Dr_{min} and Dr_{max} ($eÅ^{-3}$): -0.172 and 0.184.

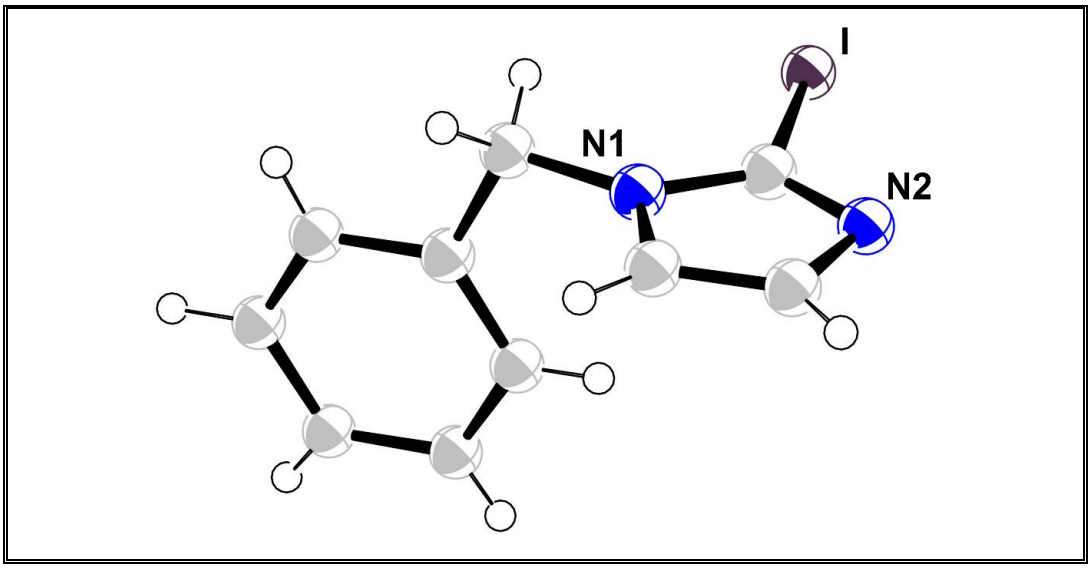


Figure S7: ORTEP diagram of 1-benzyl-2-iodo-1*H*-imidazole **(15c)**

CCDC No : 1520602

Lattice : Orthorhombic
Formula: $C_{10}H_9IN_2$
Formula Weight : 284.10
Space Group : P $2_12_12_1$
a/ A° : 8.7463(3)
b/ A° : 9.1092(3)
c/ A° : 13.1444(5)
α/ ° : 90
β/ ° : 90
γ/ ° : 90
V/ $A^{°3}$: 1047.24(3)
Z : 4
Temperature (K) : 297(2)

Radiation (λ)/A° : 0.71073

ρ/ (g cm^{-3}) : 3.66
μ (Mo K_α) mm^{-1} : 0.295
θ_{max}/deg : 26.4
No. of data collected : 22036
No. of data : 2146
No. of parameters : 119
R_1 [I> 2σI] : 0.015
wR_2 [I> 2σI] : 0.031
R_1 [all data]: 0.060
wR_2 [all data] : 0.014
R_{int} [all data] : 0.0272
GOF : 1.060
Dr_{min} and Dr_{max} (e$Å^{-3}$): -0.295 and 0.372.

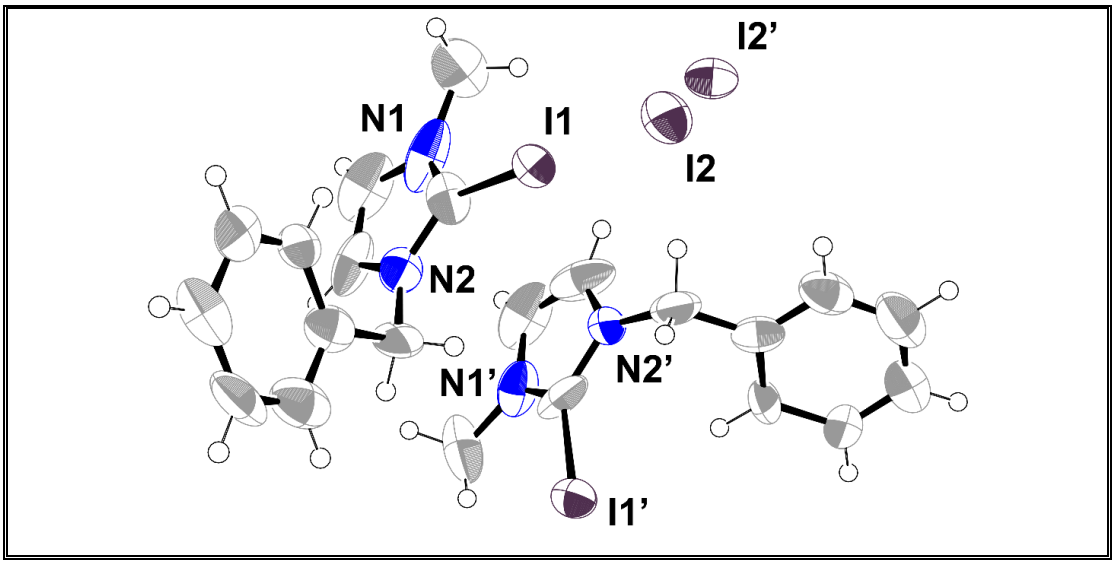


Figure S8: ORTEP diagram of 1-benzyl-2-iodo-3-methyl-1*H*-imidazol-3-ium iodide **(15a)**

CCDC No : 1520603

Lattice : Orthorhombic
Formula: $C_{11}H_{12}I_2N_2$
Formula Weight : 426.10
Space Group : P-1
a/ A° : 10.1088(11)
b/ A° : 10.1122(11)
c/ A° : 15.6369(16)
α/ ° : 106.118(4)
β/ ° : 90.8624(4)
γ/ ° : 117.901(4)
V/ $A^{°3}$: 1337.2(3)
Z : 4
Temperature (K) : 293(2)

Radiation (λ)/A° : 0.71073

ρ/ (g cm^{-3}) : 2.116
μ (Mo K_α) mm^{-1} : 4.676
θ_{max}/deg : 26.4
No. of data collected : 26112
No. of data : 5073
No. of parameters : 268
R_1 [I> 2σI] : 0.139
wR_2 [I> 2σI] : 0.248
R_1 [all data]: 0.096
wR_2 [all data] : 0.228
R_{int} [all data] : 0.0781
GOF : 1.088
Dr_{min} and Dr_{max} (e$Å^{-3}$): -1.425 and 2.659.

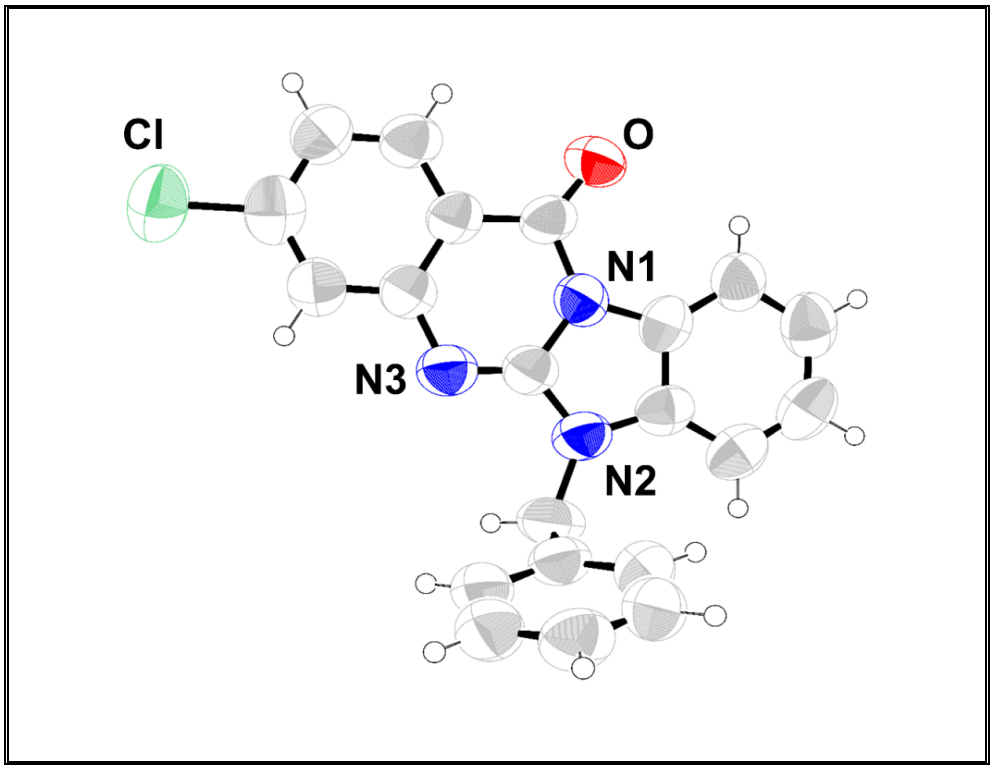


Figure S9: ORTEP diagram of 6-benzyl-3-chlorobenzo[4,5]imidazo[2,1-*b*]quinazolin-12(6*H*)-one **(32i)**

CCDC No: 1587815.

Lattice : Monoclinic
Formula: $C_{21}H_{14}ClN_3O$
Formula Weight : 359.8084
Space Group : P-1
a/ A° : 5.0704 (37)
b/ A° : 20.6683 (**)
c/ A° : 16.0005(**)
α/ ° : 90.000
β/ ° : 93.393 (21)
γ/ ° : 90.000
V/ $A^{°3}$: 1673.86(30)
Z : 2
Temperature (K) : 297(2)

Radiation (λ)/A° : 0.71073

ρ/ (g cm^{-3}) : 1.416
μ (Mo K_α) mm^{-1} : 0.967
θ_{max}/deg : 25
No. of data collected : 14899
No. of data : 3144
No. of parameters : 236
R_1 [I> 2σI] : 0.0.118
wR_2 [I> 2σI] : 0.310
R_1 [all data]: 0.225
wR_2 [all data] : 0.396
R_{int} [all data] : 0.445
GOF : 1.118
Dr_{min} and Dr_{max} ($eÅ^{-3}$): -0.384 and 0.752.

VII. Computational Details:

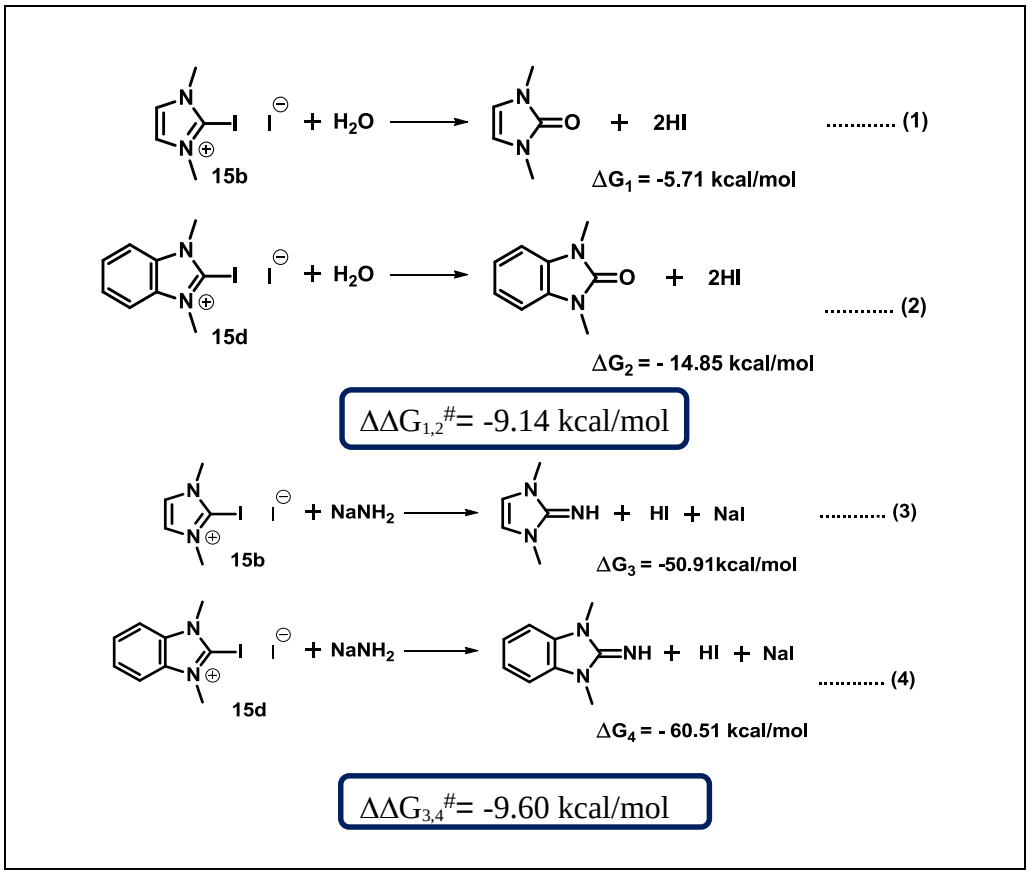


Table S5: Theoretical calculation for 2-imidazolones, 2 benzimidazolones, 2-aminoimidazole and 2-aminobenzimidazole.

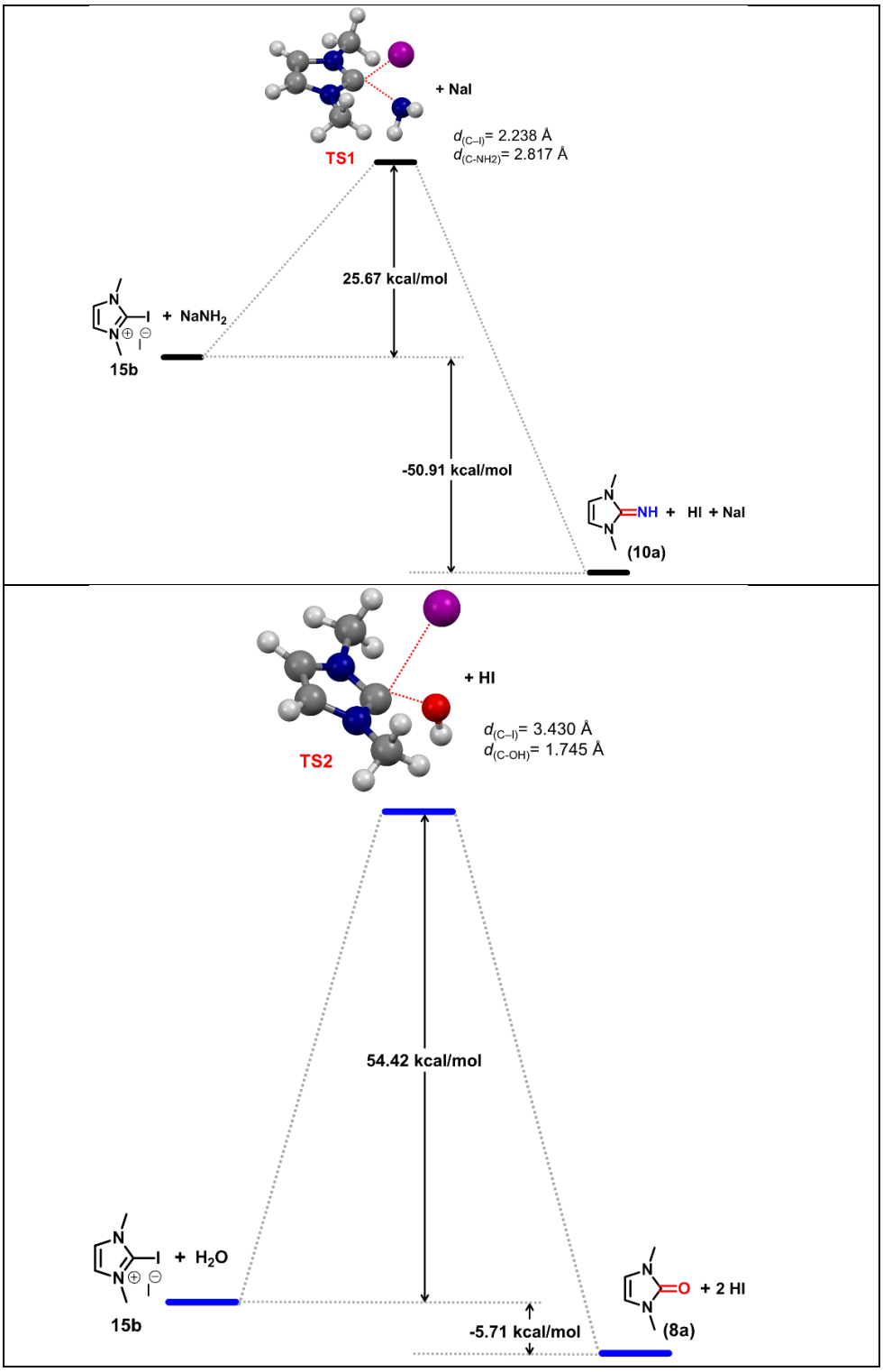
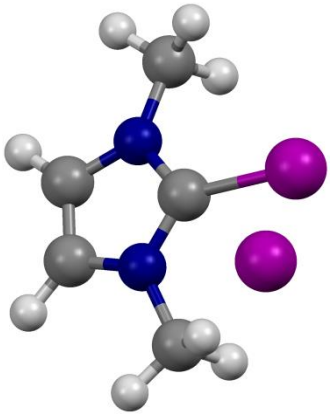


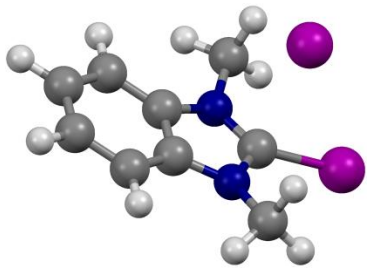
Figure S10: Gibbs free energy profile (kcal/mol) of C(sp^2)-H oxidation and imination of imidazole obtained at the M06-2X/6- 311G (d,p), def2-TZVPP (iodine) level of theory.

Optimized Geometries:



E = -900.0513489 HF

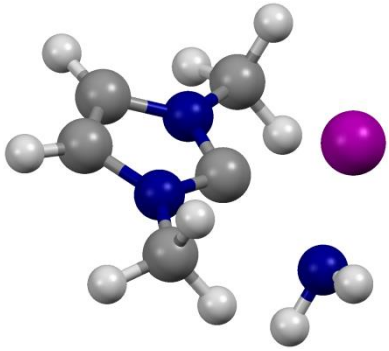
7	-0.314068000	1.536854000	1.086394000
7	-0.314485000	1.537466000	-1.086016000
6	0.477567000	2.585138000	0.677230000
6	0.477363000	2.585491000	-0.676547000
6	-0.730326000	0.878398000	0.000083000
6	-0.358882000	0.999930000	2.441999000
1	-1.385760000	0.757722000	2.711057000
1	0.029724000	1.757487000	3.118070000
6	-0.359100000	1.000807000	-2.441774000
1	0.278808000	0.111908000	-2.459369000
1	0.029091000	1.758697000	-3.117708000
1	-1.385865000	0.758106000	-2.710805000
1	0.278552000	0.110690000	2.459532000
1	0.983951000	3.219584000	-1.381753000
1	0.984487000	3.218775000	1.382606000
53	2.071577000	-0.761852000	-0.000142000
53	-1.929178000	-0.776106000	-0.000051000



E = -1053.6726602 HF

7	0.473820000	-0.979639000	-1.100838000
7	0.473783000	-0.979619000	1.100757000
6	1.802758000	-0.943156000	-0.697459000
6	1.802723000	-0.943194000	0.697454000
6	-0.287047000	-0.890577000	-0.000040000
6	0.025584000	-0.669591000	-2.450885000
1	-0.933588000	-1.148142000	-2.635466000
1	0.758495000	-1.058213000	-3.154336000
6	0.025494000	-0.669827000	2.450841000
1	-0.065901000	0.418045000	2.529980000
1	0.758633000	-1.058154000	3.154213000
1	-0.933470000	-1.148772000	2.635469000
1	-0.065405000	0.418316000	-2.529977000
53	-0.086366000	2.252337000	0.000039000
53	-2.335324000	-0.999902000	-0.000020000

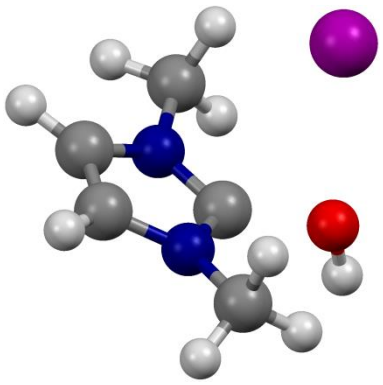
	6	2.985557000	-0.895958000	-1.427578000
	6	4.163522000	-0.856524000	-0.701625000
	1	2.988493000	-0.870425000	-2.508777000
	1	5.107523000	-0.808901000	-1.229112000
	6	4.163486000	-0.856570000	0.701637000
	6	2.985520000	-0.896040000	1.427584000
	1	2.988522000	-0.870489000	2.508780000
	1	5.107452000	-0.808906000	1.229188000



E = -658.2218063 HF

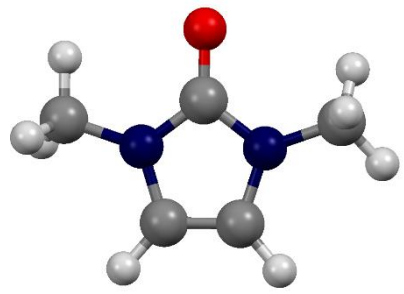
7	-1.410545000	1.083543000	0.360433000
6	-0.695878000	-0.064824000	0.308972000
7	-1.448238000	-0.961166000	-0.359633000
6	-2.607661000	0.909452000	-0.318691000
1	-3.354790000	1.682727000	-0.363415000
6	-0.950140000	2.318493000	0.968494000
6	-2.623797000	-0.364968000	-0.771374000
1	-3.390993000	-0.915234000	-1.288075000
6	-1.005789000	-2.328508000	-0.575797000
1	-0.437115000	-2.399815000	-1.504971000
1	-1.880361000	-2.976615000	-0.619759000
1	-0.379388000	-2.572367000	0.292503000
1	-0.398386000	2.923182000	0.245714000
1	-1.814797000	2.871431000	1.333685000
1	-0.300983000	2.069347000	1.805801000
53	1.426556000	0.214439000	-0.344887000
7	0.389137000	-1.847343000	2.202454000
1	-0.120358000	-1.715737000	3.080752000
1	1.056811000	-1.075298000	2.204383000

	7	-1.781187000	1.093842000	-0.066758000
	6	-1.496034000	-0.003616000	0.654221000



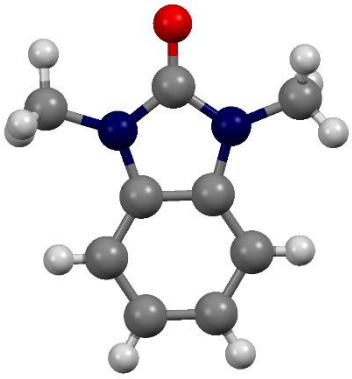
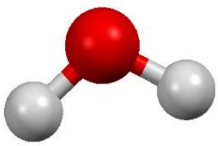
E = -678.1527749 HF

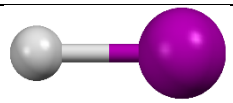
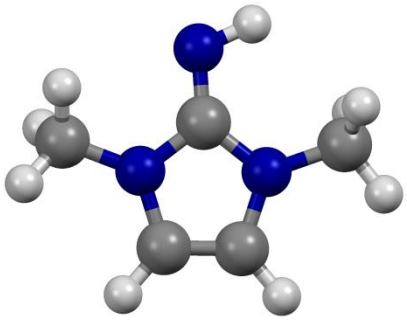
7	-1.804401000	-1.070657000	-0.101466000
6	-2.195851000	0.713701000	-1.317811000
1	-2.430210000	1.432012000	-2.083408000
6	-1.356374000	2.438940000	0.296806000
6	-2.210124000	-0.642792000	-1.339373000
1	-2.462613000	-1.330737000	-2.126691000
6	-1.409271000	-2.432040000	0.237868000
1	-0.345369000	-2.533322000	0.009100000
1	-2.008750000	-3.124618000	-0.349036000
1	-1.576938000	-2.595368000	1.299071000
1	-0.398812000	2.629527000	-0.193749000
1	-2.123096000	3.149175000	-0.005813000
1	-1.216197000	2.467625000	1.373247000
53	1.833966000	-0.004627000	-0.167971000
1	-1.373661000	-0.064531000	3.043136000
8	-0.769934000	-0.048996000	2.240490000

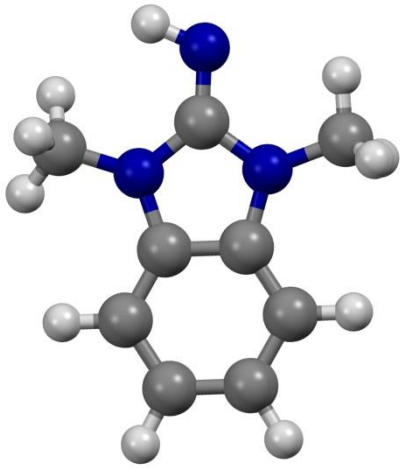
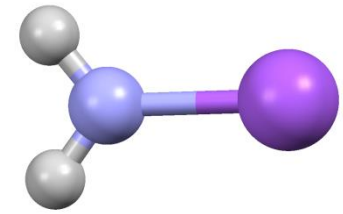


E = -360.0245015 HF

6	-0.000008000	-0.664004000	0.000040000
7	-1.092826000	0.183730000	-0.000007000
7	1.092849000	0.183837000	0.000092000
6	-0.673151000	1.508733000	-0.000023000
6	0.673068000	1.508753000	0.000016000
6	-2.452901000	-0.303639000	-0.000036000
1	-2.398963000	-1.391534000	0.000036000
1	-2.986713000	0.031322000	-0.891756000
6	2.452896000	-0.303580000	-0.000080000
1	2.986571000	0.031109000	-0.891985000
1	2.986979000	0.031694000	0.891359000
1	2.398898000	-1.391472000	0.000285000
8	0.000077000	-1.881087000	0.000033000
1	1.370952000	2.327857000	0.000128000

	1	-1.371152000	2.327729000	-0.000029000
	1	-2.986779000	0.031445000	0.891596000
 **E = -533.6603077 HF**	8	-2.906334000	-0.000011000	0.000150000
	7	-0.856441000	-1.106465000	0.000409000
	7	-0.856457000	1.106455000	-0.000408000
	6	-1.696760000	-0.000024000	0.000075000
	6	0.467582000	-0.702835000	0.000157000
	6	0.467548000	0.702836000	-0.000245000
	6	1.648667000	-1.421001000	0.000406000
	1	1.647183000	-2.504035000	0.000696000
	6	-1.341944000	2.465585000	0.000298000
	1	-1.000939000	2.996008000	0.892509000
	1	-2.429870000	2.419184000	-0.000772000
	6	-1.341938000	-2.465556000	-0.000480000
	1	-1.000494000	-2.997188000	0.890820000
	1	-0.999801000	-2.996221000	-0.892123000
	1	-2.429875000	-2.419132000	-0.000842000
	6	2.843764000	-0.695604000	0.000183000
	1	3.785563000	-1.229660000	0.000323000
	6	1.648640000	1.421002000	-0.000341000
	1	1.647133000	2.504032000	-0.000591000
	6	2.843744000	0.695620000	-0.000140000
	1	3.785536000	1.229683000	-0.000221000
	1	-0.999294000	2.997345000	-0.890471000
 **E = -76.4123628 HF**	8	0.000000000	0.000000000	0.117887000
	1	0.000000000	0.756290000	-0.471547000
	1	0.000000000	-0.756290000	-0.471547000
	1	0.000000000	0.000000000	-1.575645000

 **E = -298.2241748 HF**	53	0.000000000	0.000000000	0.029729000
 **E = -360.1196723 HF**	7	-1.091450000	-0.205091000	-0.017426000
	7	1.099098000	-0.196355000	-0.030040000
	6	2.447278000	0.313082000	0.024777000
	1	2.503221000	1.208975000	-0.598299000
	1	3.135608000	-0.446965000	-0.352664000
	1	2.731234000	0.588539000	1.047293000
	6	0.003697000	0.647184000	-0.017931000
	6	-0.662409000	-1.533721000	0.003400000
	1	-1.360265000	-2.356805000	0.005583000
	6	-2.446902000	0.277933000	0.020629000
	6	0.684455000	-1.522946000	0.000413000
	1	1.390747000	-2.338999000	0.001254000
	1	-2.666220000	0.896217000	-0.858311000
	1	-3.128670000	-0.574609000	0.025666000
	1	-2.624911000	0.876490000	0.922842000
	7	0.091707000	1.930580000	-0.004368000
	1	-0.832946000	2.354019000	-0.018264000
	7	-0.835866000	-1.117192000	0.013448000
	7	-0.864414000	1.099463000	0.007205000
	6	-1.695006000	-0.023223000	-0.005925000
	6	0.480943000	-0.697509000	0.010174000
	6	0.469636000	0.709422000	-0.003016000
	6	1.669463000	-1.407567000	0.014744000
	1	1.674160000	-2.493508000	0.026904000
	6	-1.351323000	2.454479000	0.025749000
	1	-0.609554000	3.093995000	0.511258000
	1	-2.271906000	2.500897000	0.615632000
	6	-1.291029000	-2.485265000	-0.001212000

 **E = -513.7566066 HF**	1	-0.965035000	-3.012133000	0.902843000
	1	-0.902888000	-3.010301000	-0.881616000
	1	-2.381346000	-2.463359000	-0.038471000
	6	2.862083000	-0.672369000	0.002840000
	1	3.810241000	-1.201600000	0.005228000
	6	1.646821000	1.436292000	-0.021675000
	1	1.642864000	2.522005000	-0.048514000
	6	2.851238000	0.719148000	-0.015348000
	1	3.790356000	1.263896000	-0.029523000
	1	-1.550925000	2.839329000	-0.981660000
	7	-2.968054000	-0.128384000	-0.027094000
	1	-3.414589000	0.783119000	-0.074974000
 **E = -218.1799690 HF**	7	-0.000313000	1.072531000	0.000000000
	1	0.002817000	1.695549000	0.802179000
	1	0.002817000	1.695549000	-0.802179000
	11	-0.000313000	-0.990801000	0.000000000
 **E = -459.9686144 HF**	53	0.000000000	0.000000000	0.464559000
	11	0.000000000	0.000000000	-2.238330000

General synthetic scheme for the synthesis of *N*,*N*′-disubstituted imidazolium and benzimidazolium salts:

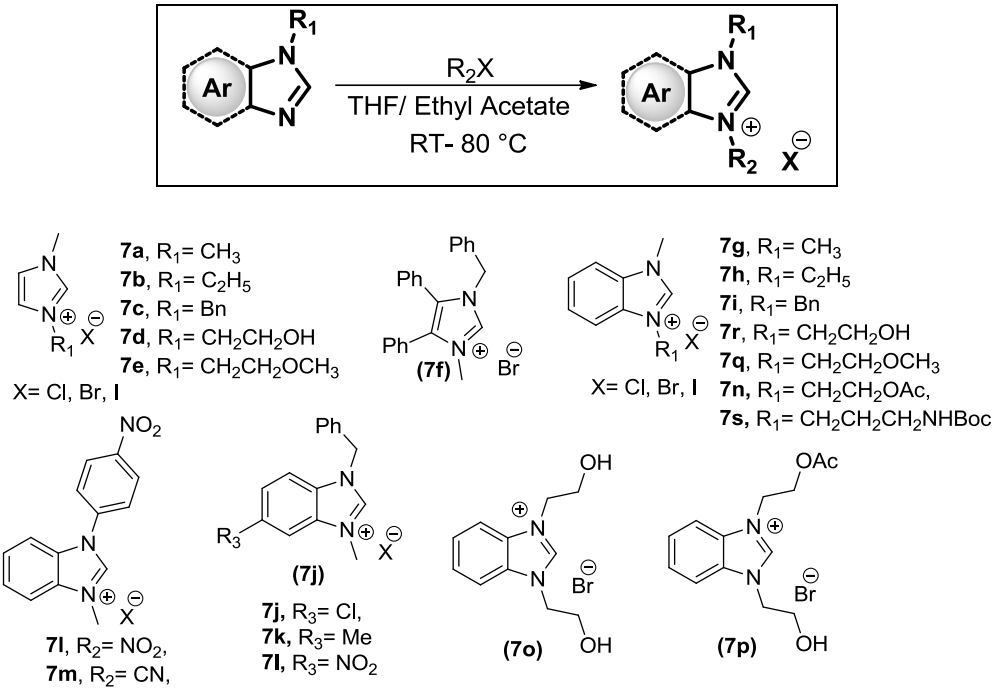
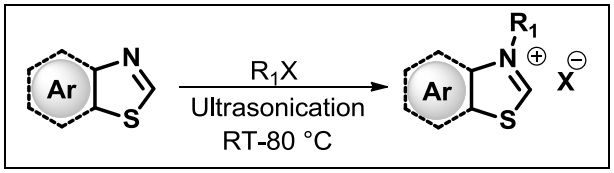


Figure S11: List of synthesized *N*,*N*′-disubstituted imidazolium and benzimidazolium salts.

General synthetic strategy for the synthesis of N-substituted benzothiazoles and thiazoles:



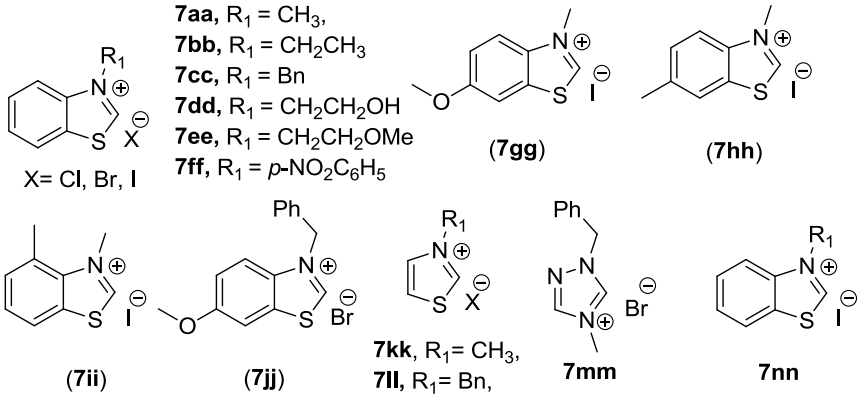


Figure S12: list of synthesized *N*′-substituted benzothiazolium salts.

X. References:

(S1) S. H. Jungbauer, S. M. Huber, *J. Am. Chem. Soc.* 2015, **137**, 12110–2120.

(S1) Full Citation of Reference 14 (main manuscript): Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G . A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H .P.; Izmaylov, A . F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.;Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, N. K.; Staroverov, V .N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V,; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.

IX. ^{1}H and ^{13}C NMR Data

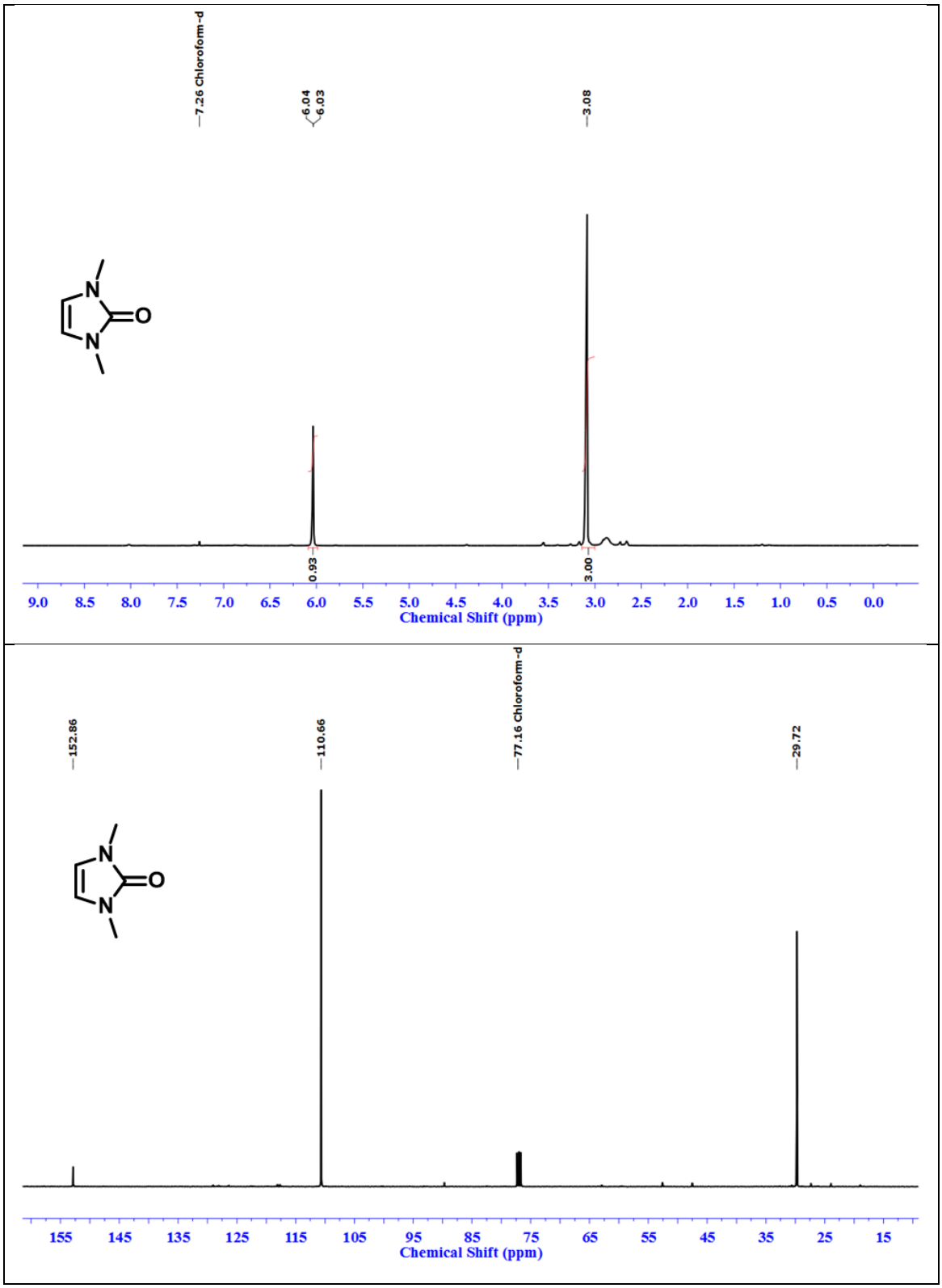


Figure S13: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **8a** in $CDCl_3$

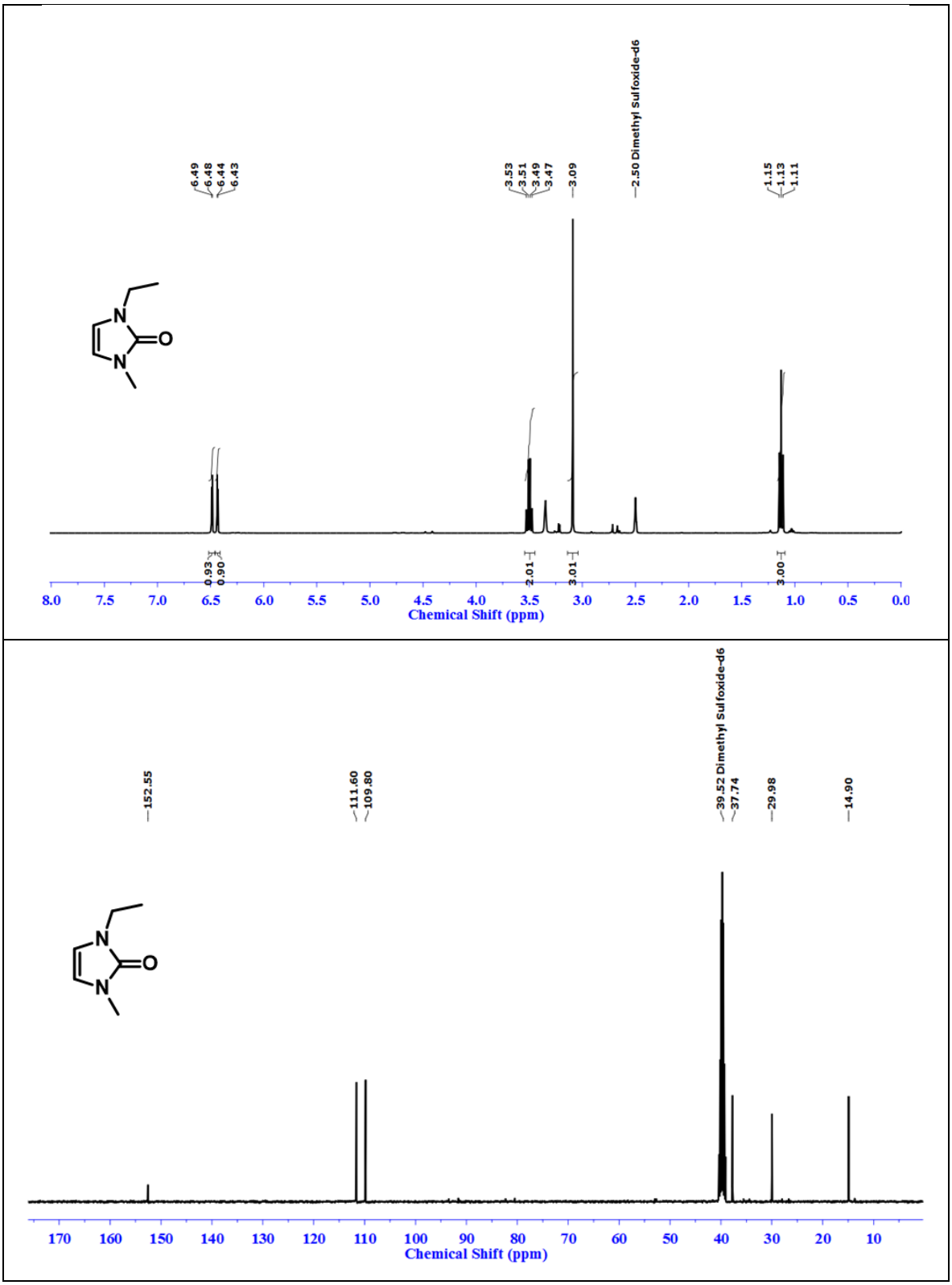


Figure S14: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **8b** in $CDCl_3$.

.

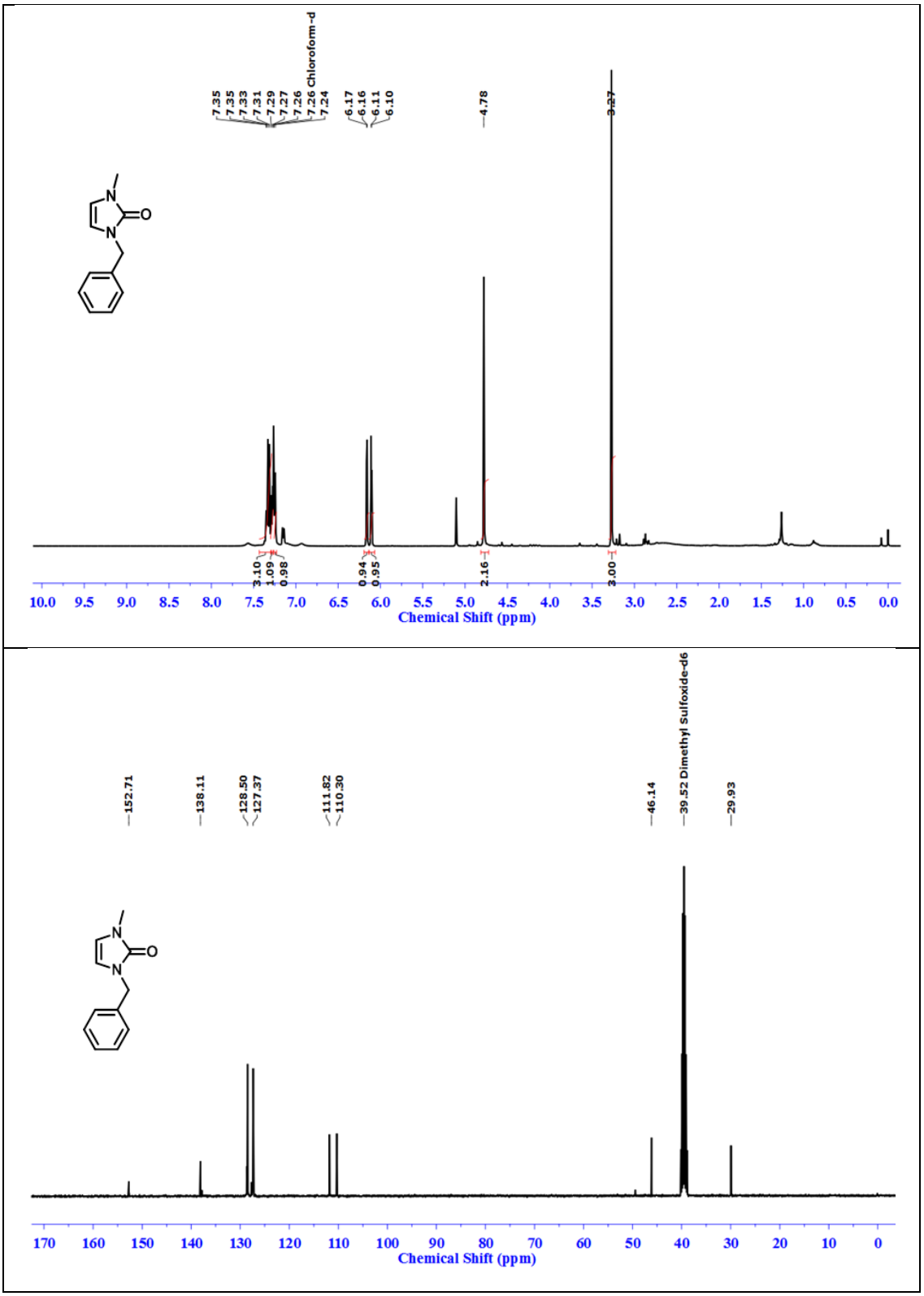


Figure S15: ^{1}H NMR in $CDCl_3$-*d* and ^{13}C NMR in DMSO-d_6 of **8c**.

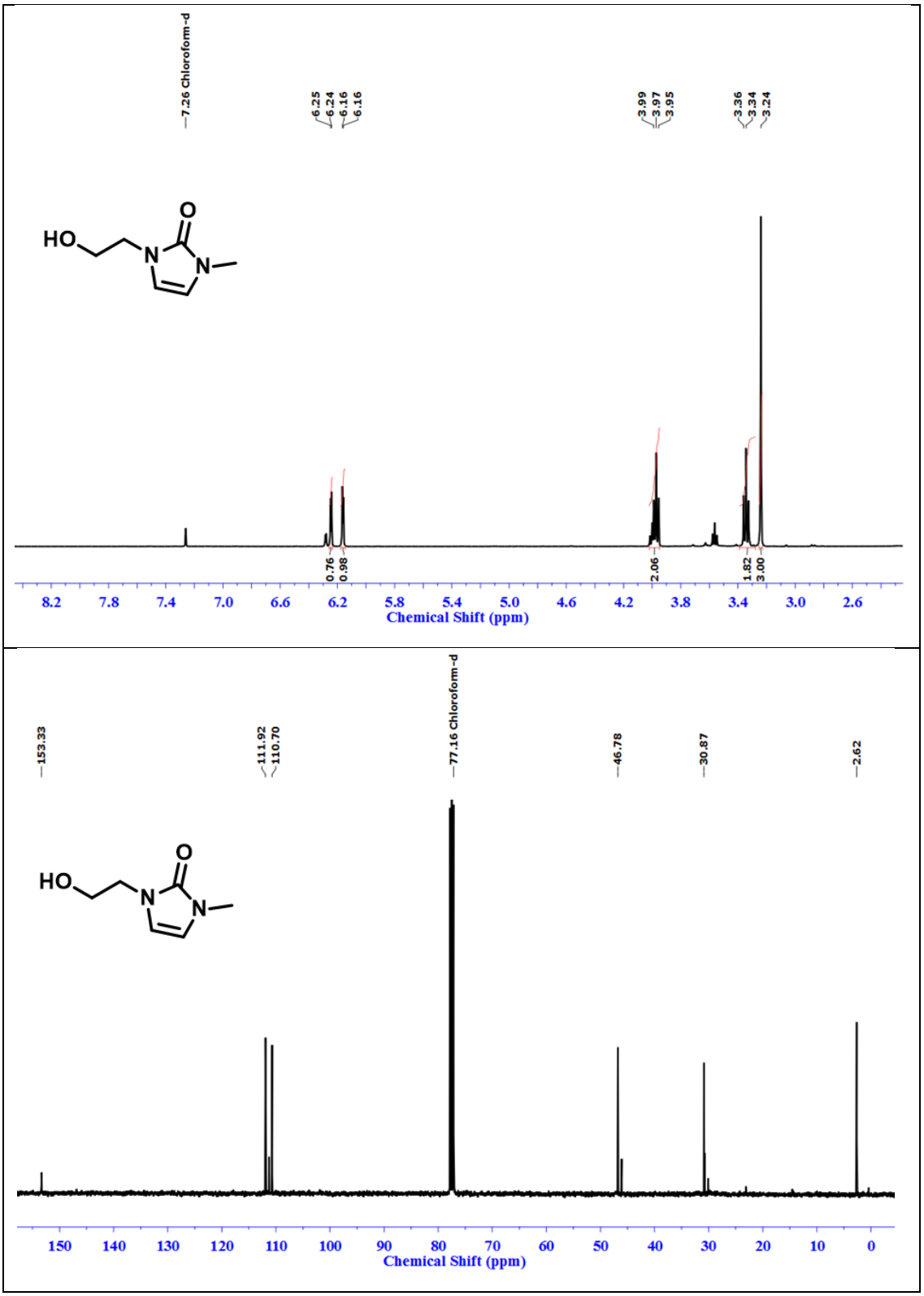


Figure S16: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **8d** in $CDCl_3$-*d*.

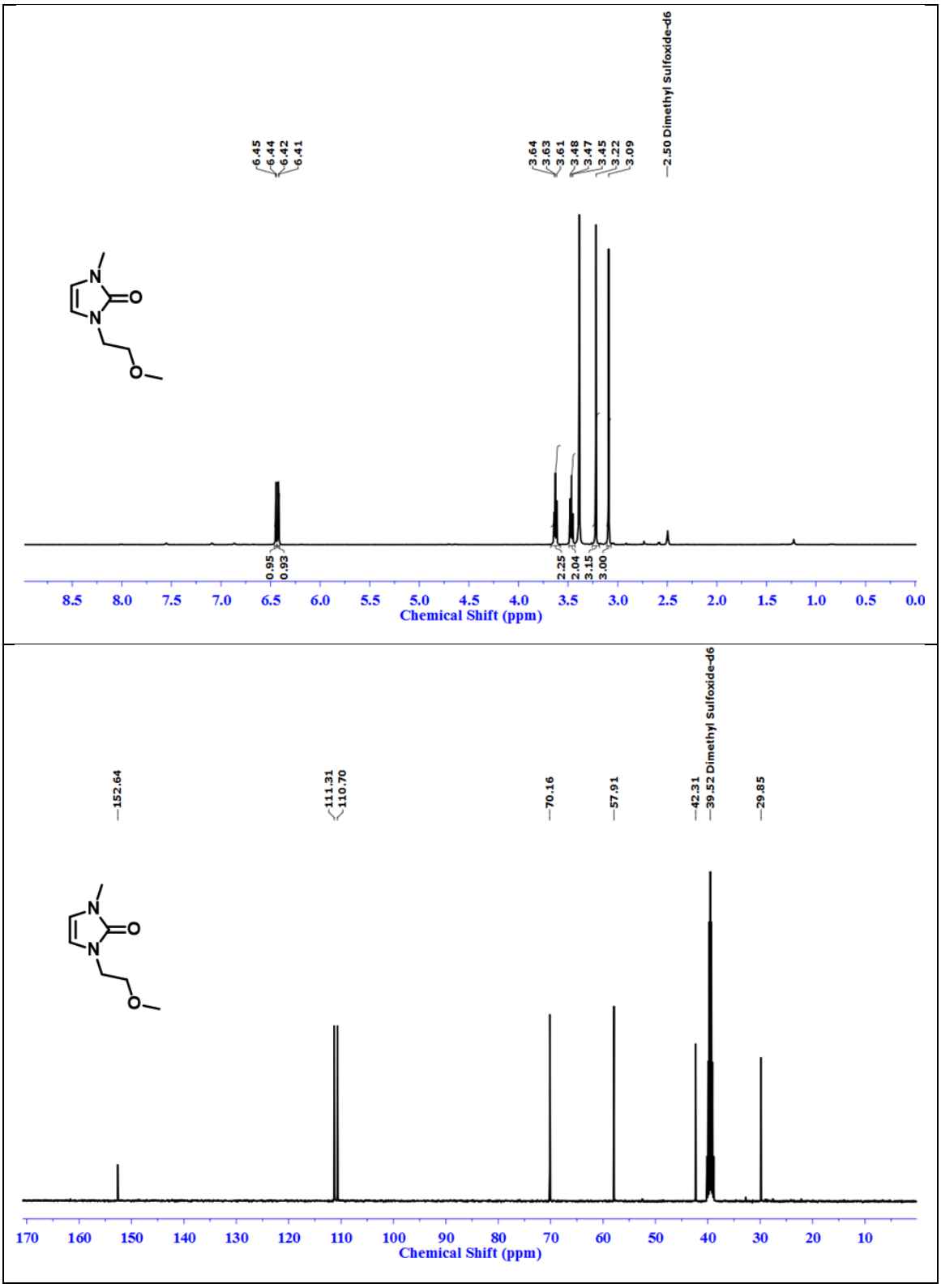


Figure S17: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **8e** in DMSO-d_6.

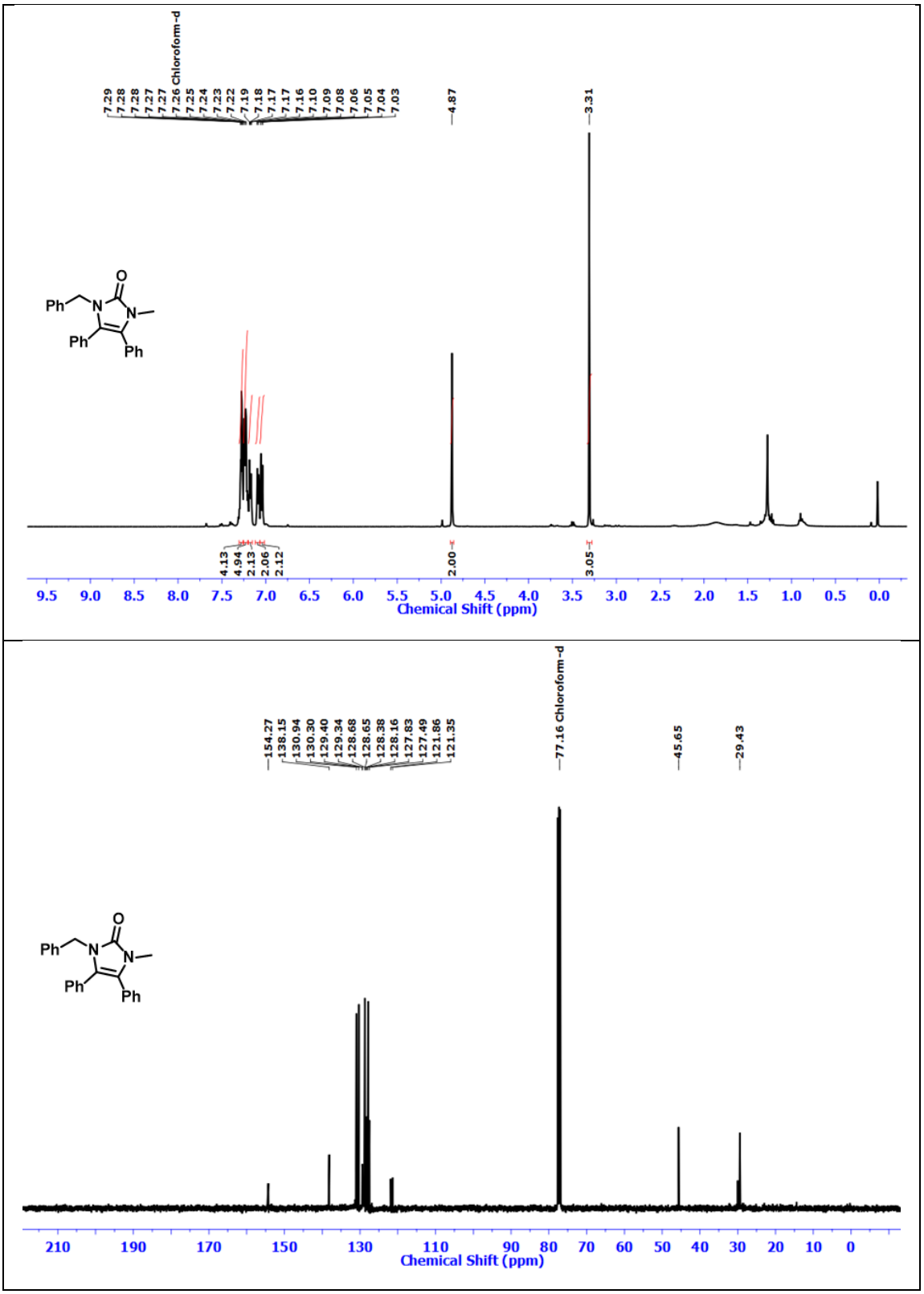


Figure S18: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **8f** in $CDCl_3$-*d*.

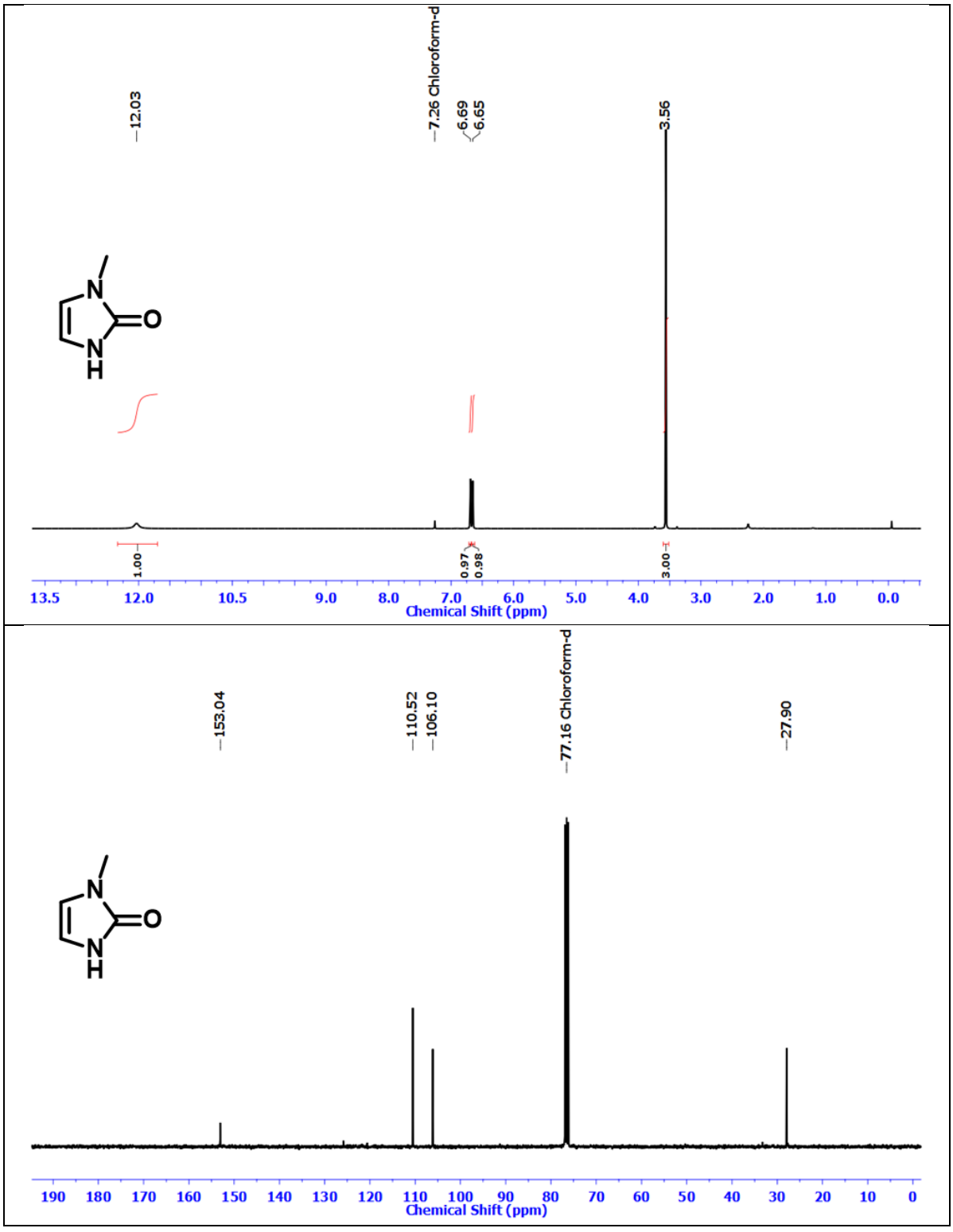


Figure S19: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **28** in $CDCl_3$-*d*.

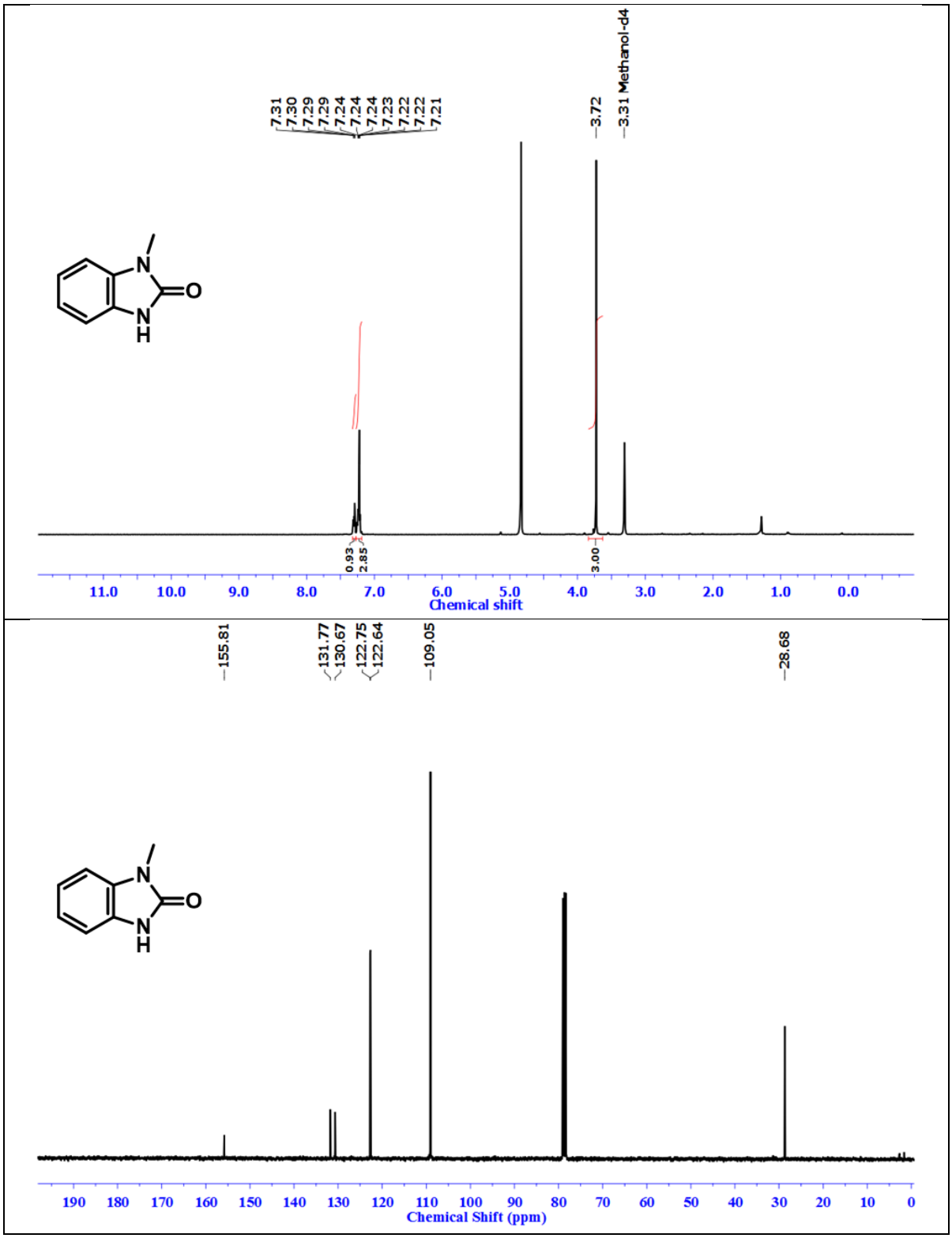


Figure S20: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **29** in $CDCl_3$-*d*.

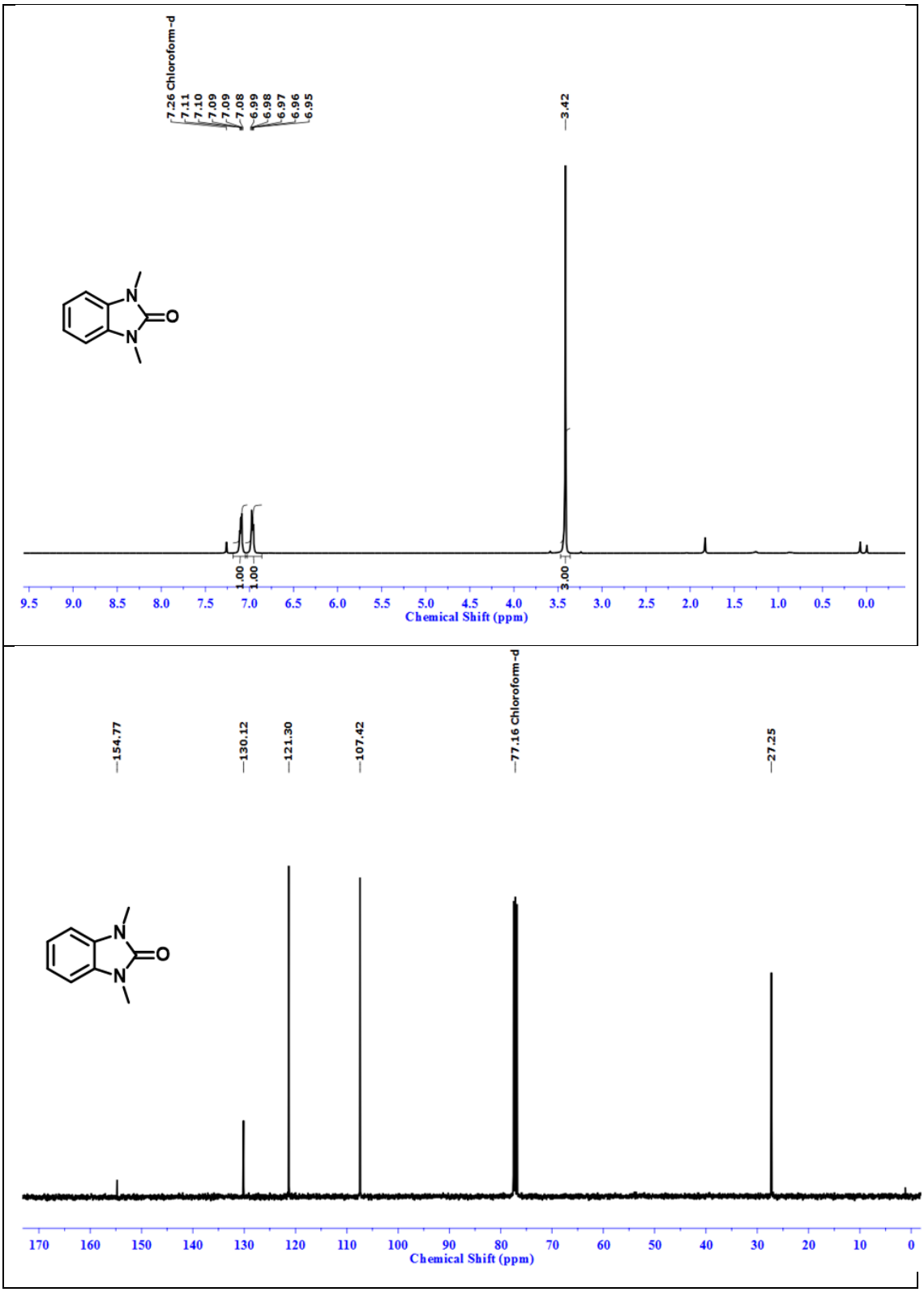


Figure S21: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9c** in $CDCl_3$-*d*.

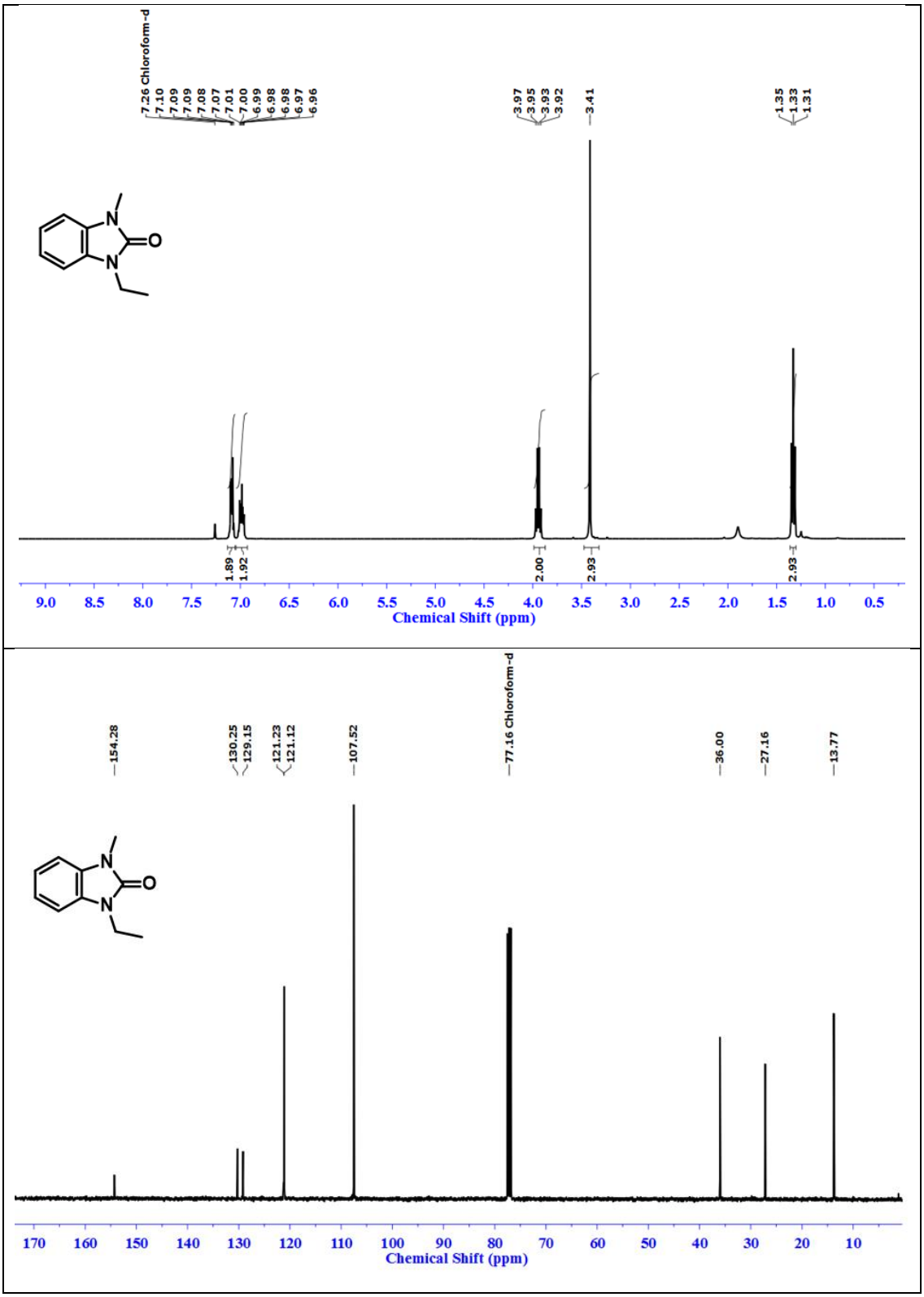


Figure S22: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9d** in $CDCl_3$-*d*.

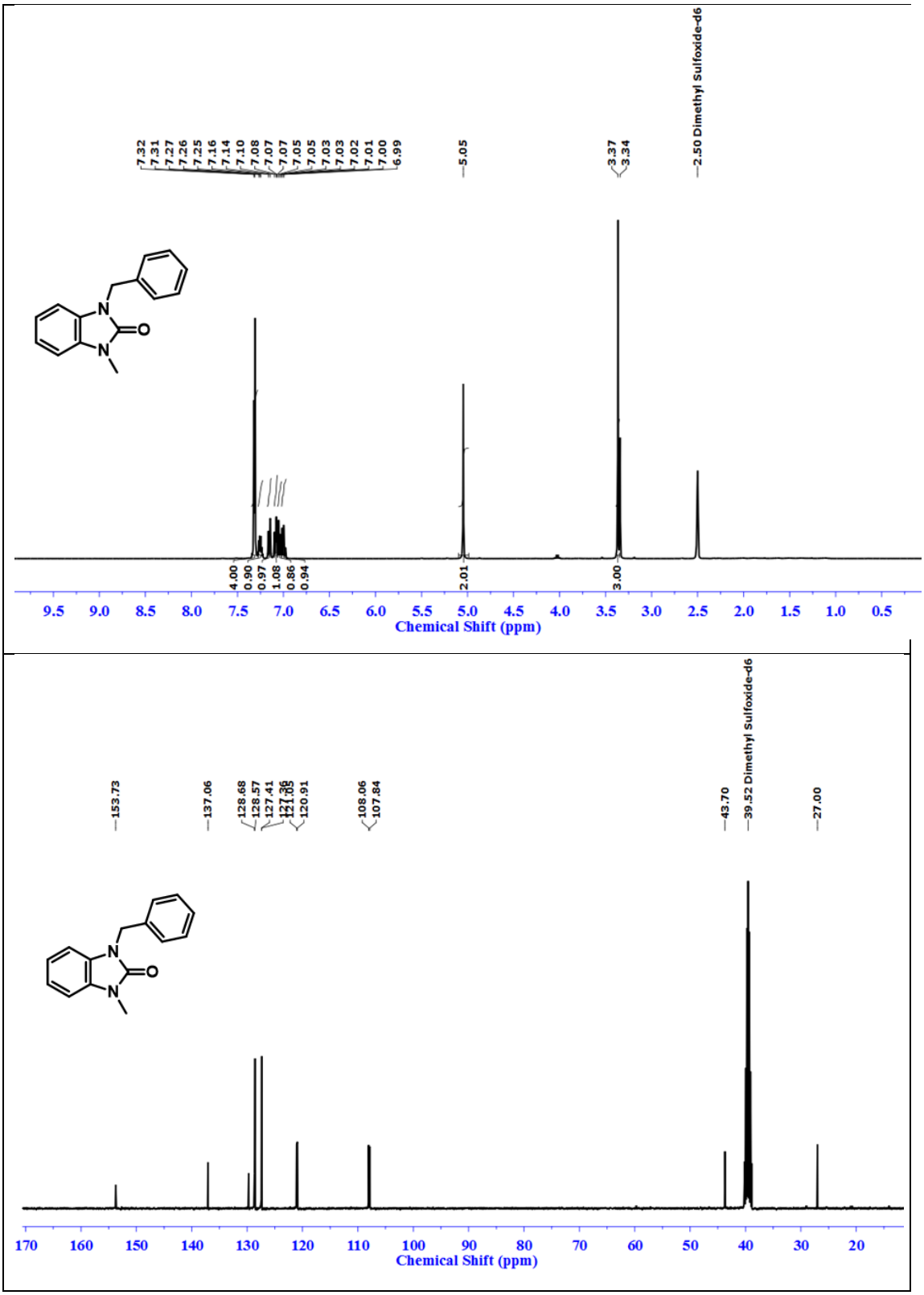


Figure S23: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9e** in DMSO-d_6.

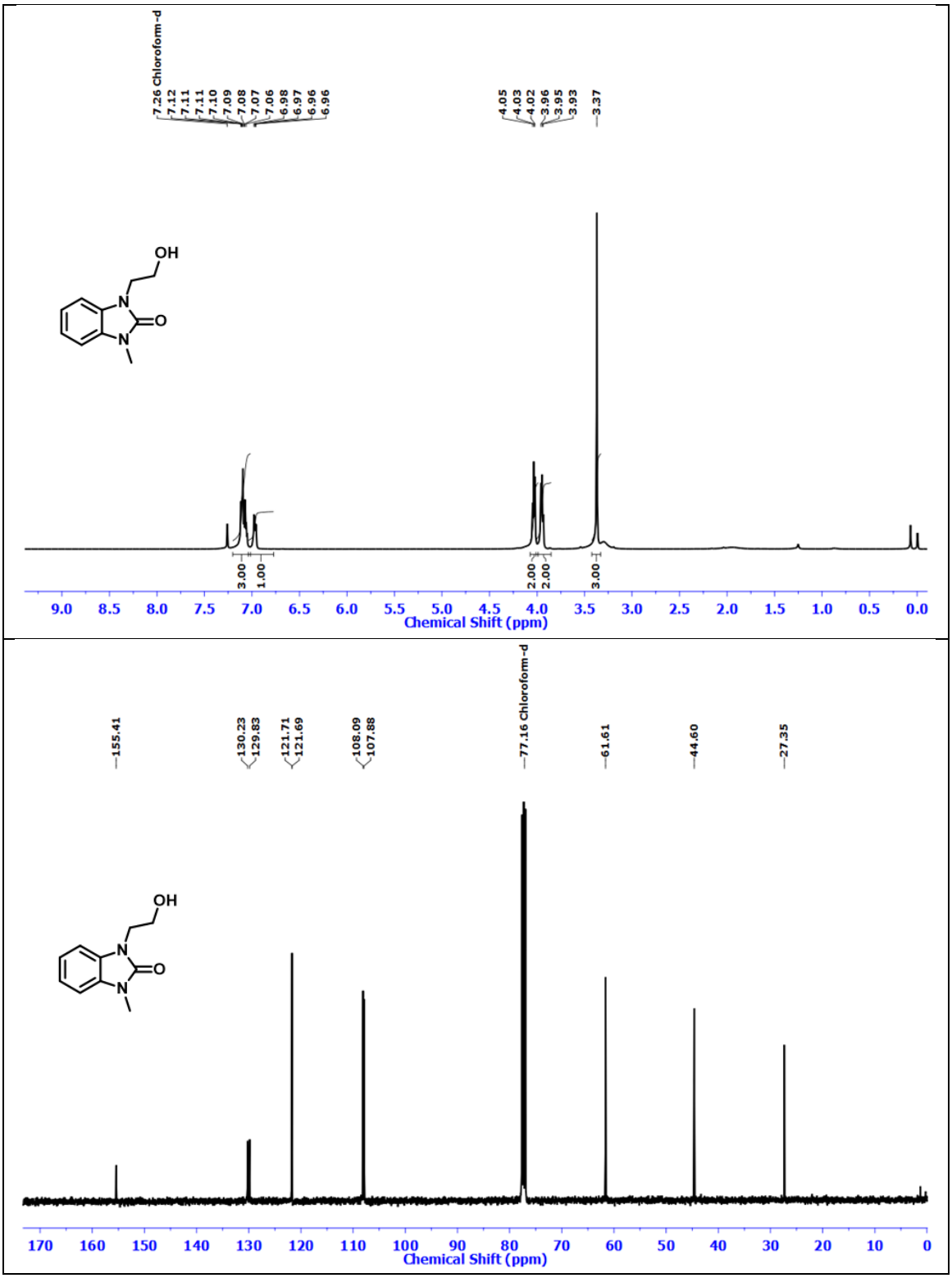


Figure S24: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9f** in $CDCl_3$-*d*.

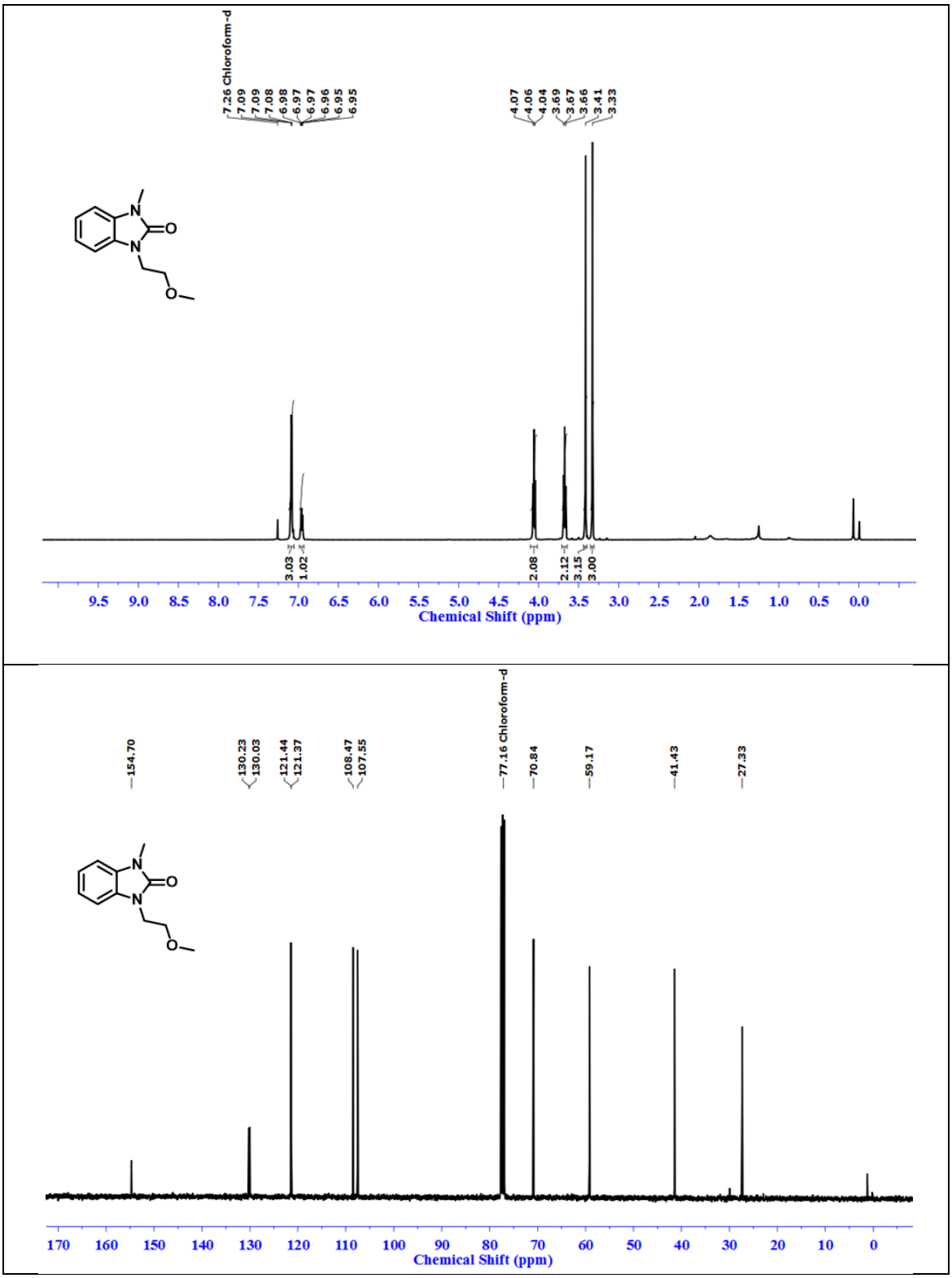


Figure S25: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9g** in $CDCl_3$-*d*.

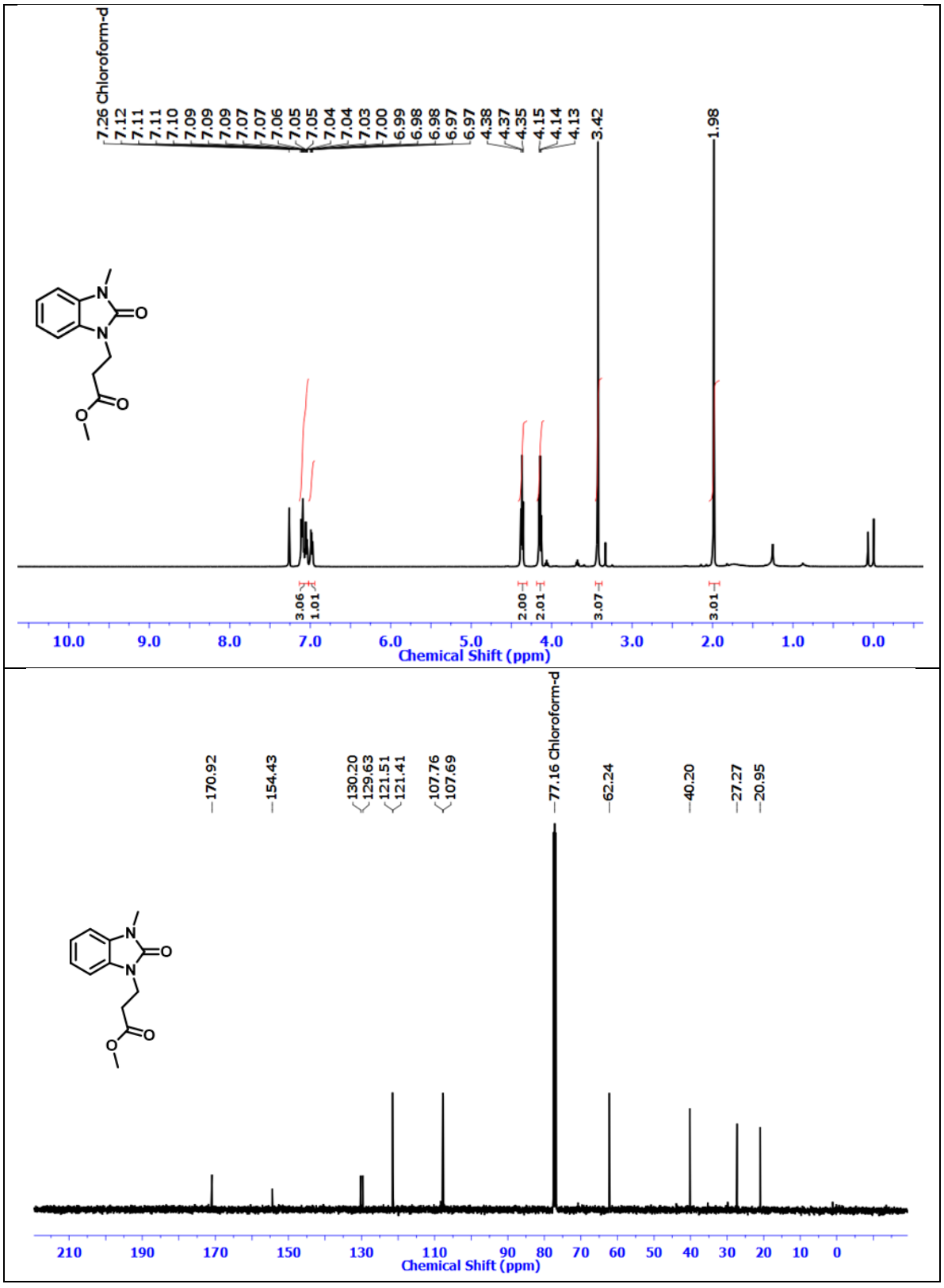


Figure S26: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9h** in $CDCl_3$-*d*.

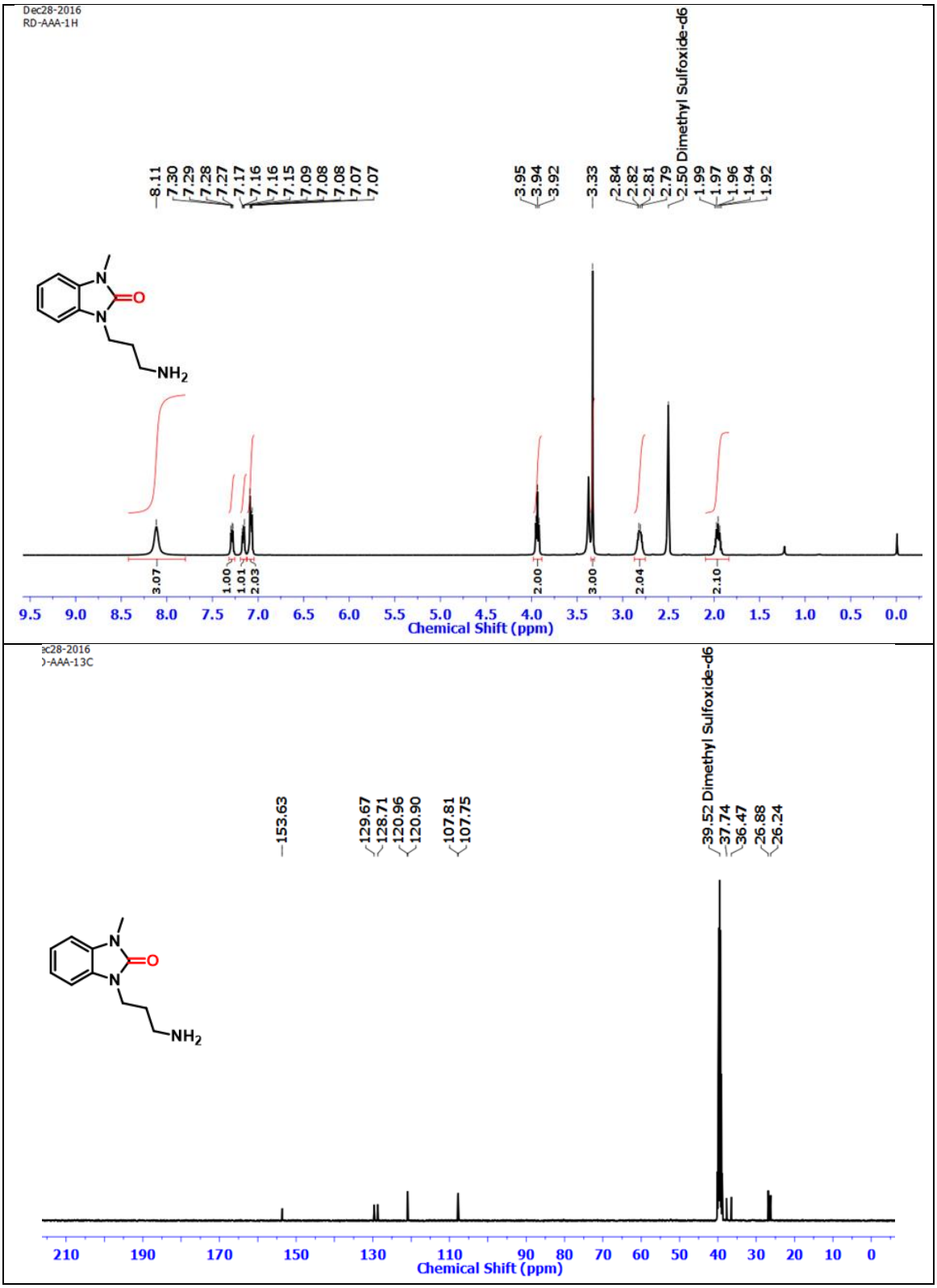


Figure S27: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9i** in DMSO-d_6

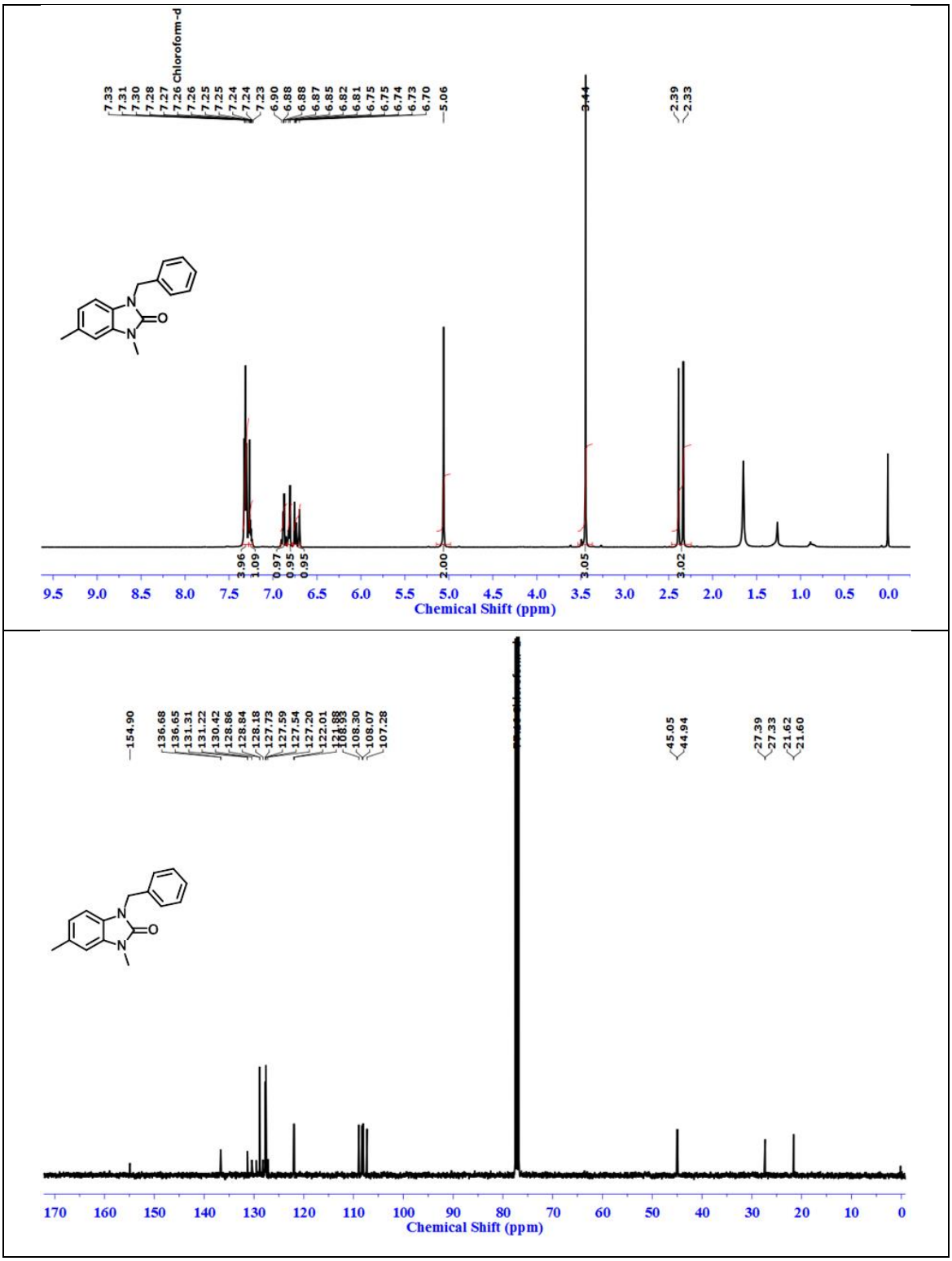


Figure S28: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9l** in $CDCl_3$-*d*.

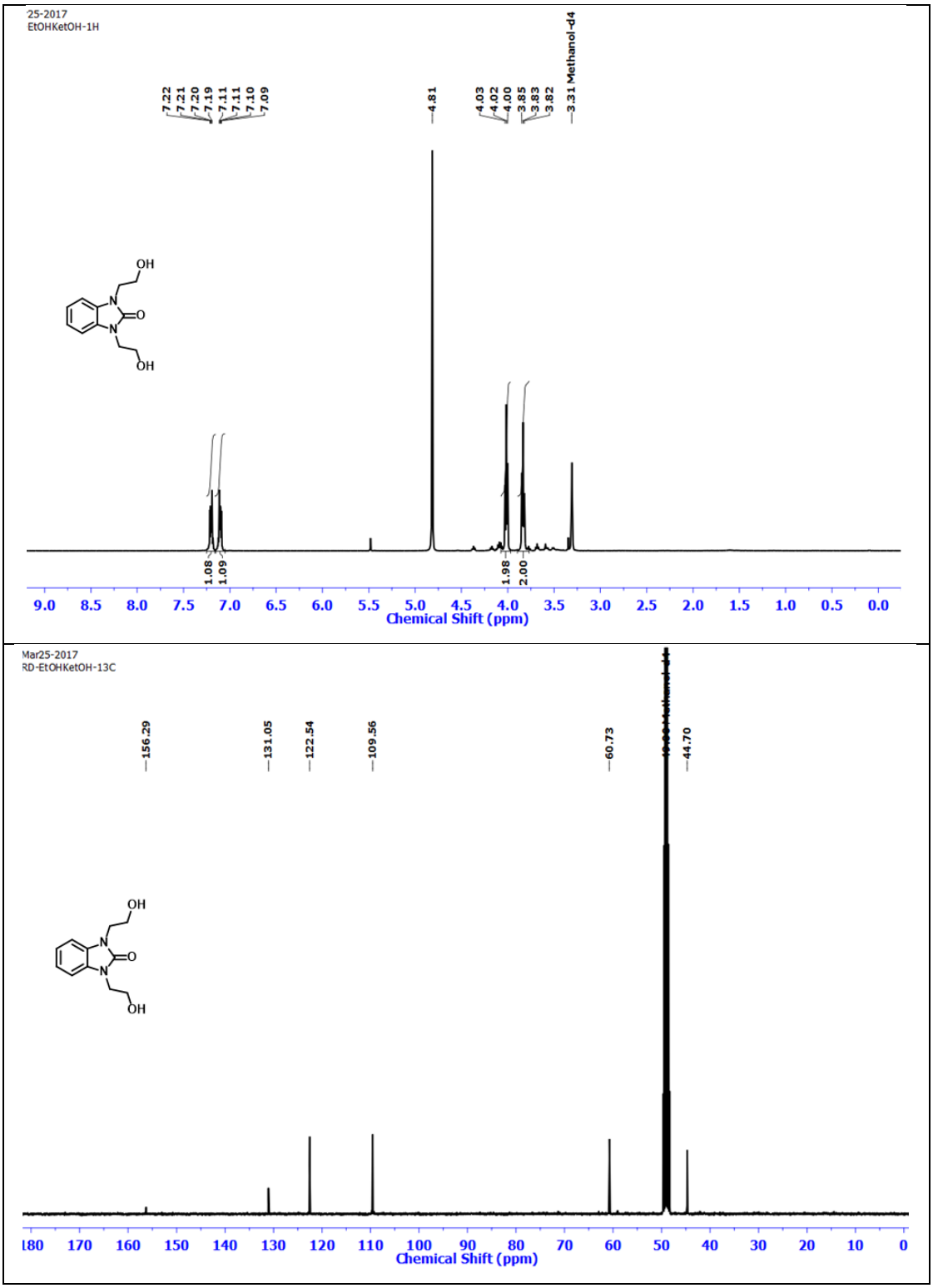


Figure S29: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9a** in MeOH-d_4.

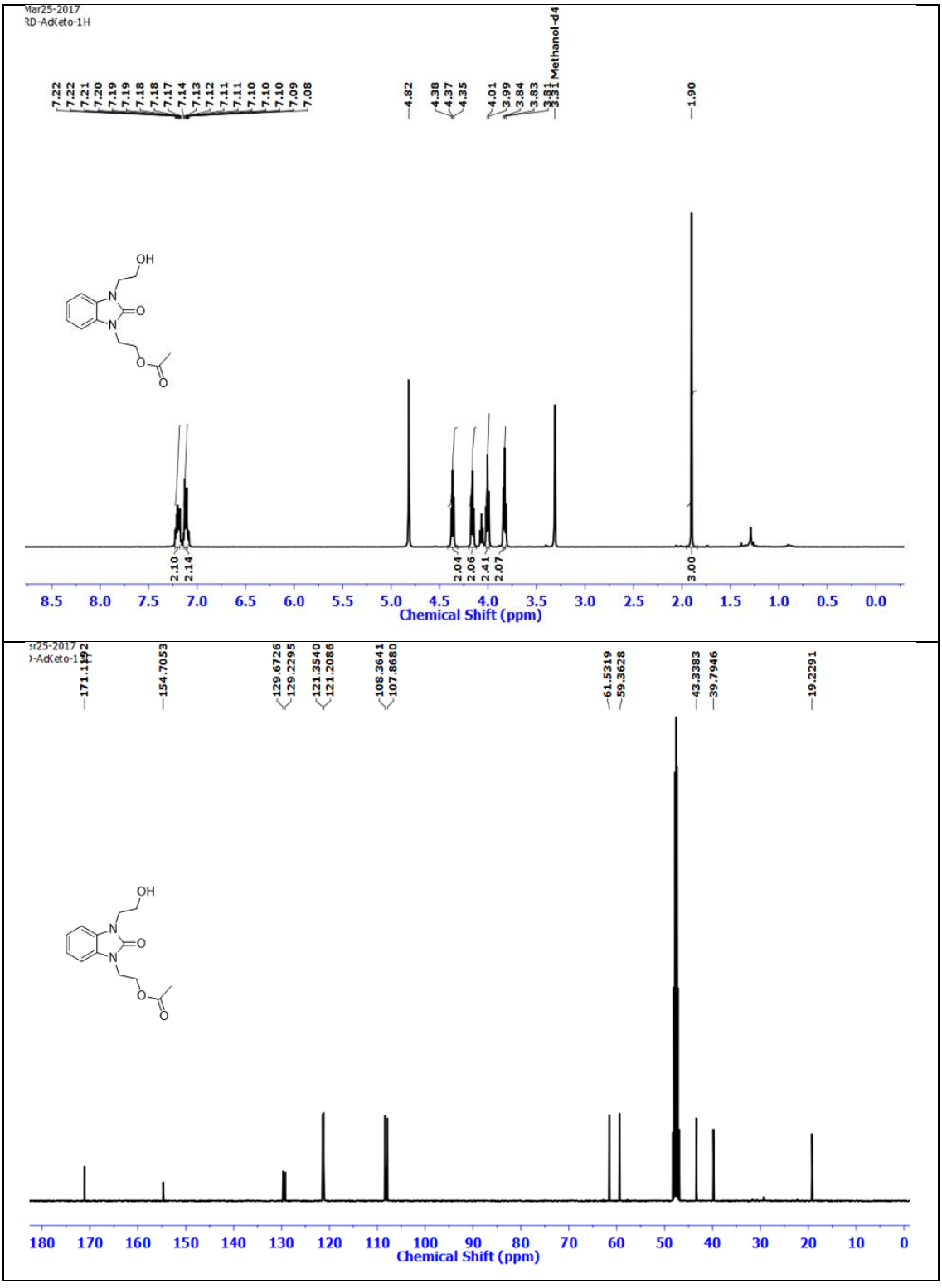


Figure S30: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9b** in MeOH-d_4.

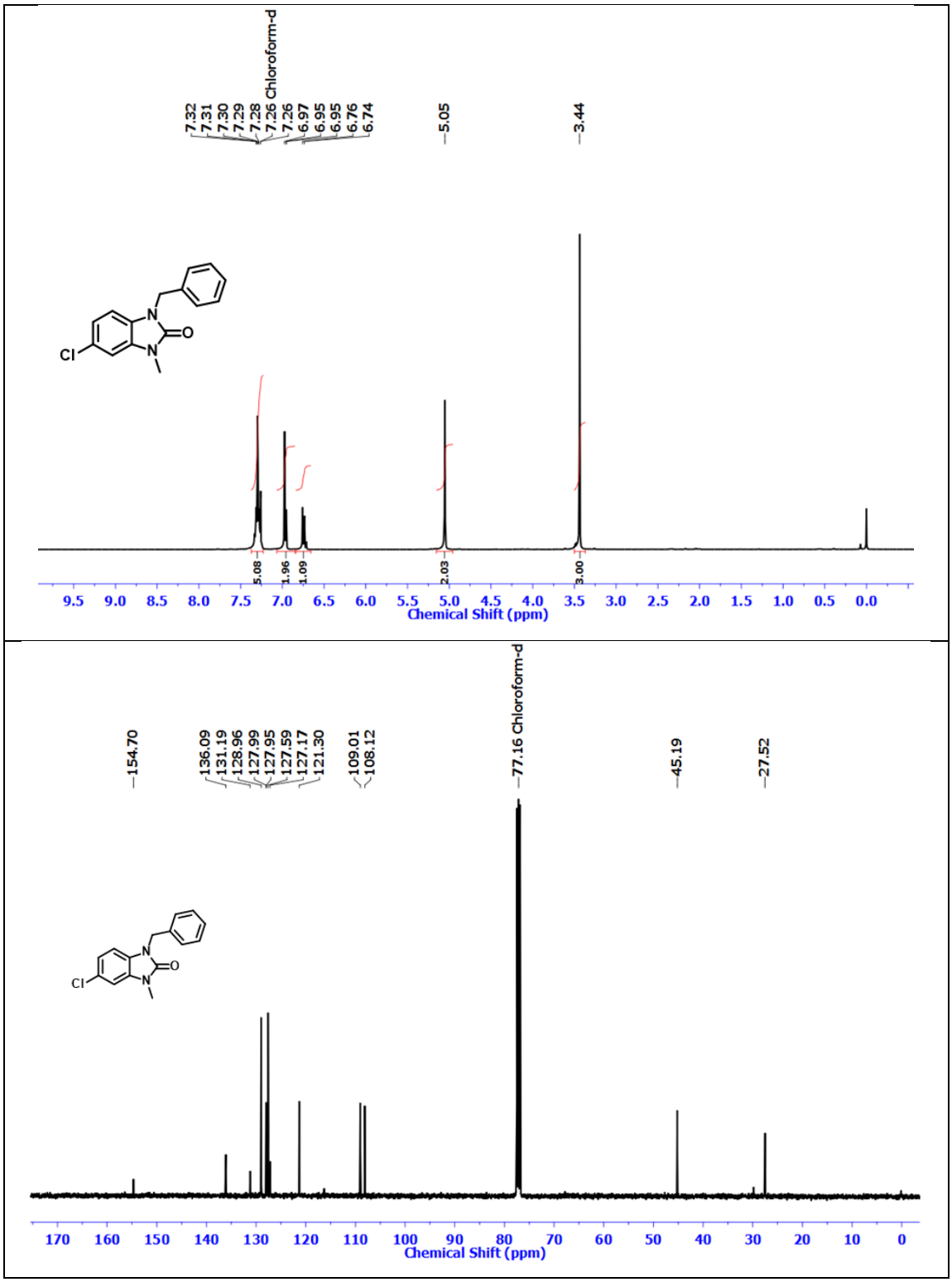


Figure S31: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9m** in $CDCl_3$-*d*.

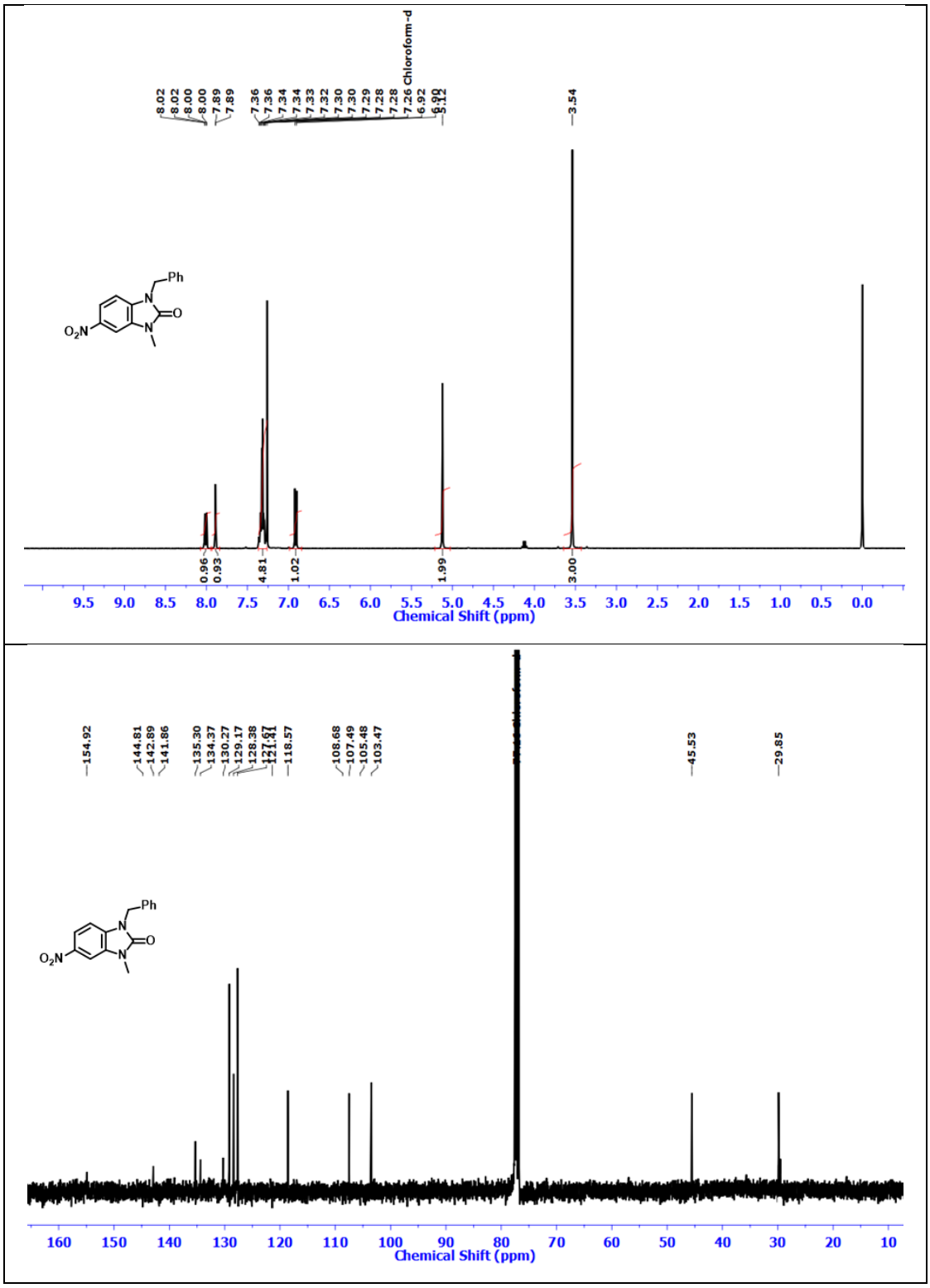


Figure S32: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9n** in $CDCl_3$-*d*.

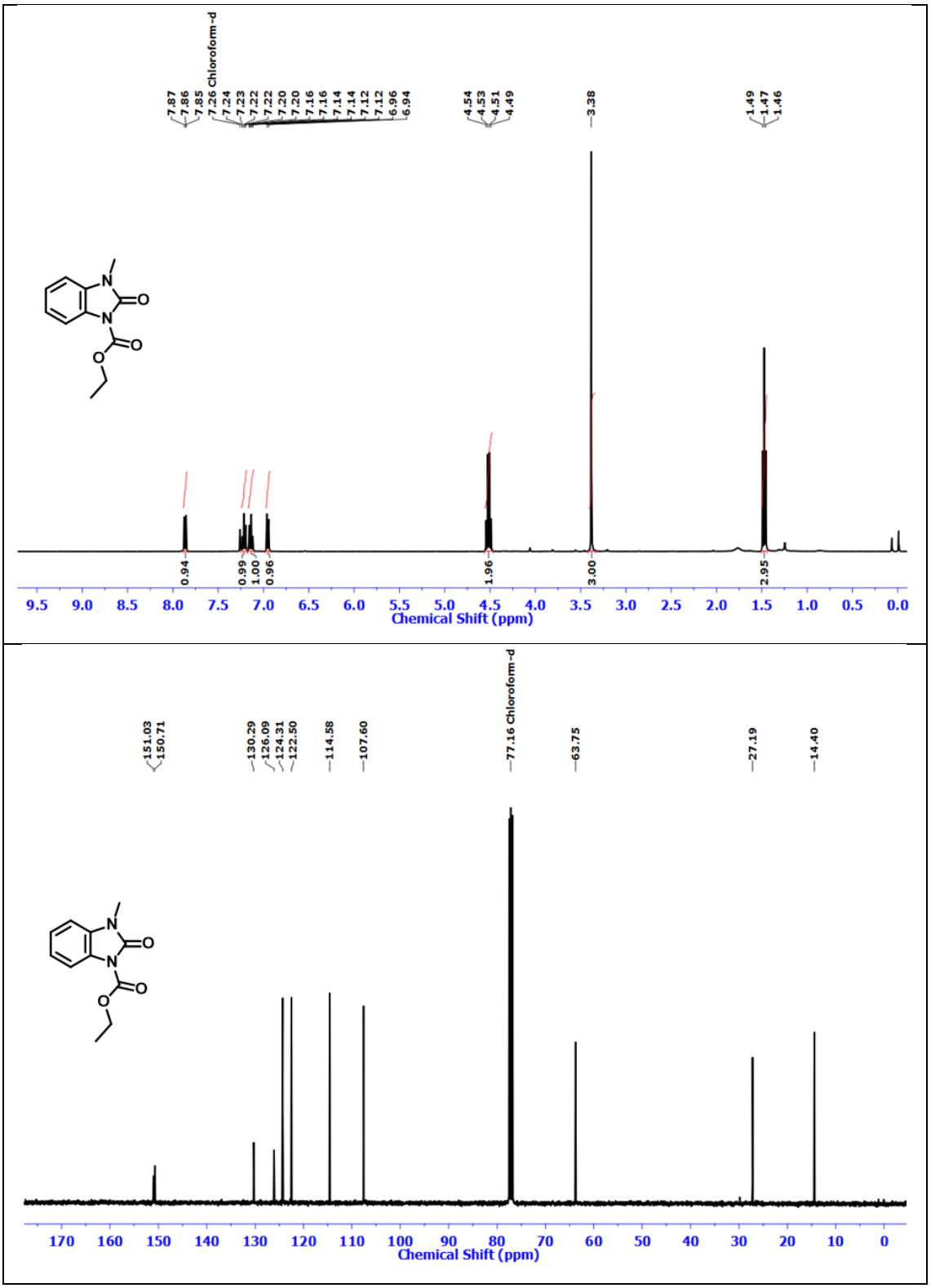


Figure S33: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **30** in $CDCl_3$-*d*.

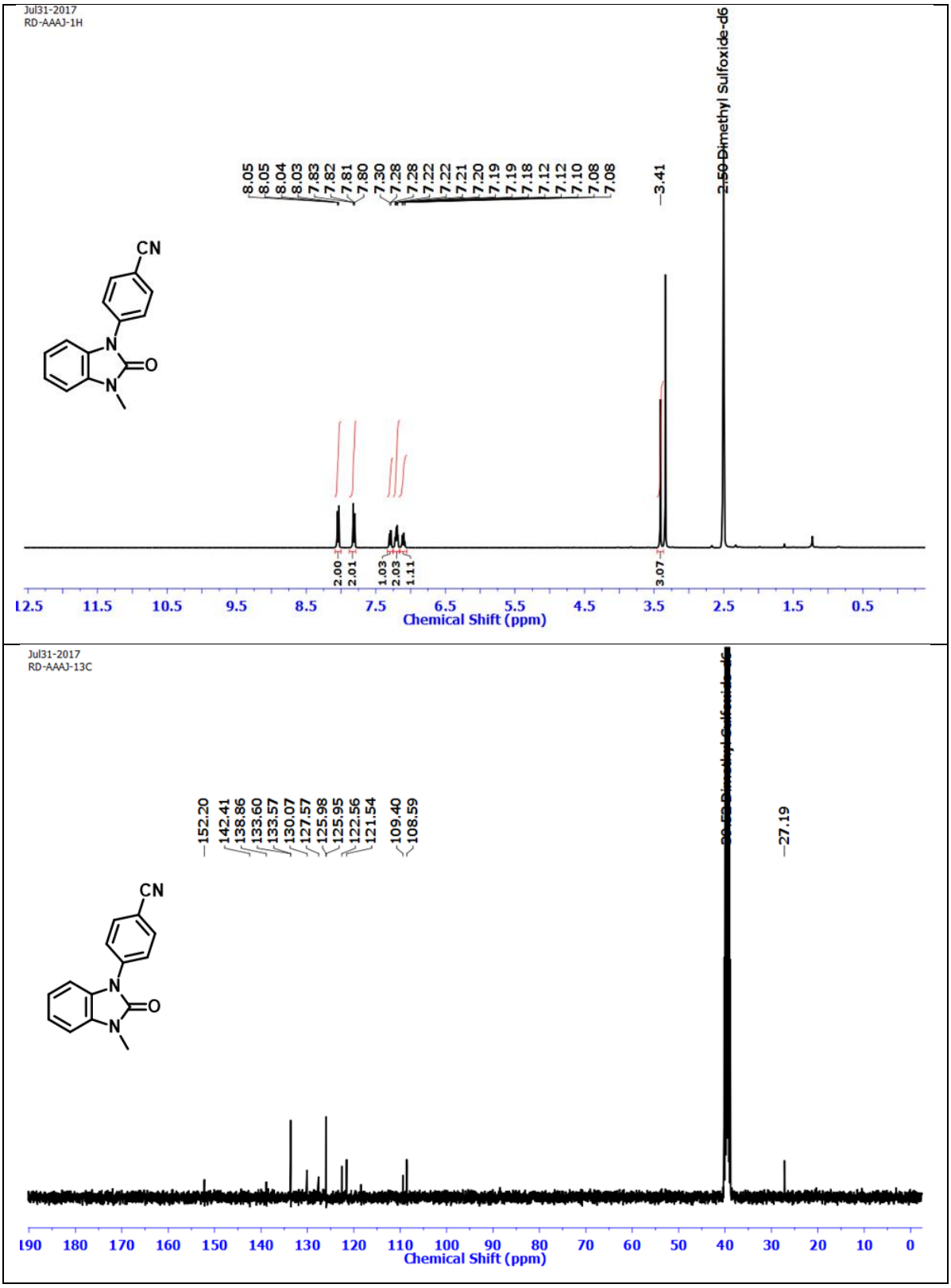


Figure S34: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9k** in DMSO-d_6.

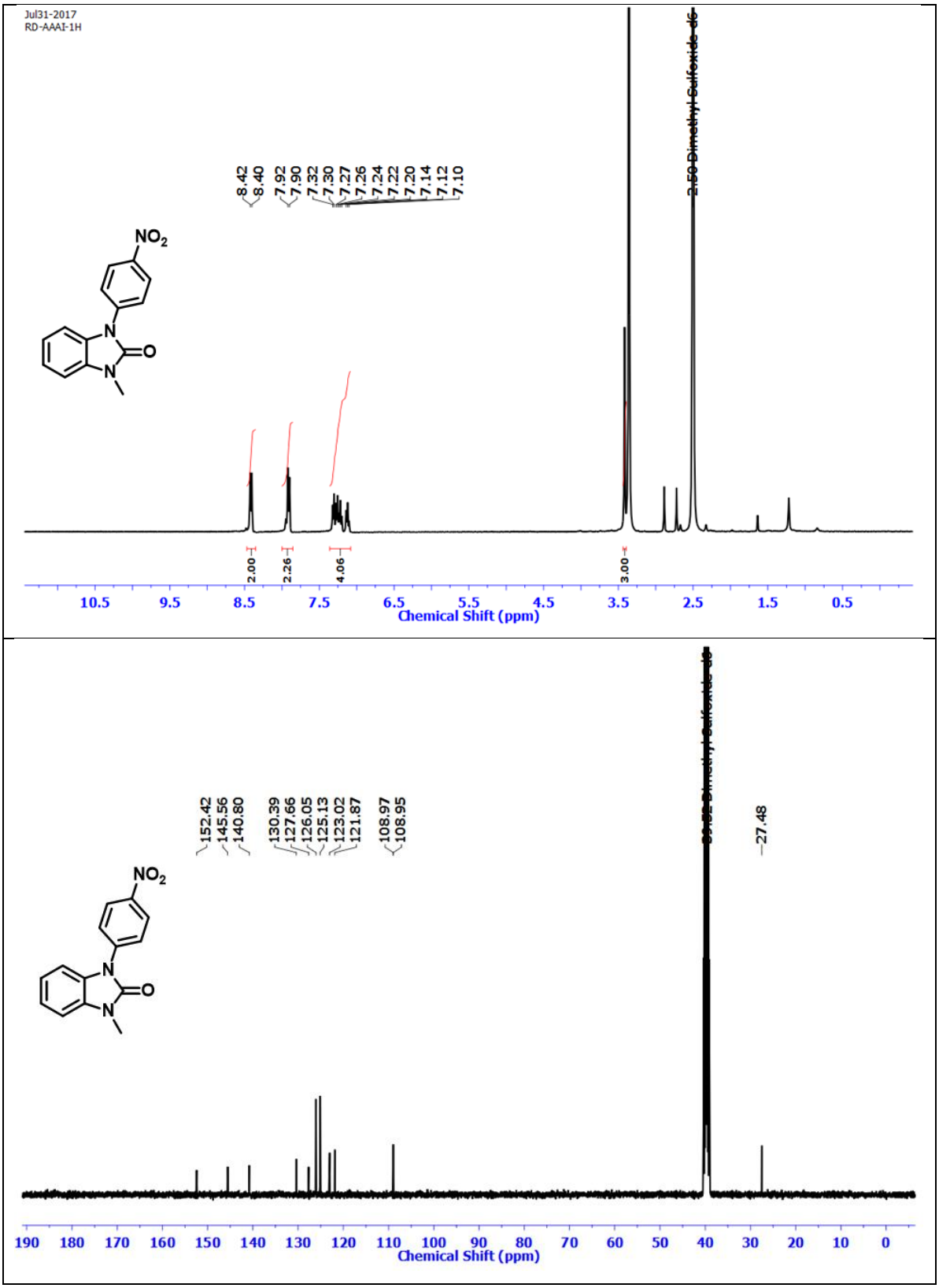


Figure S35: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **9j** in DMSO-d_6

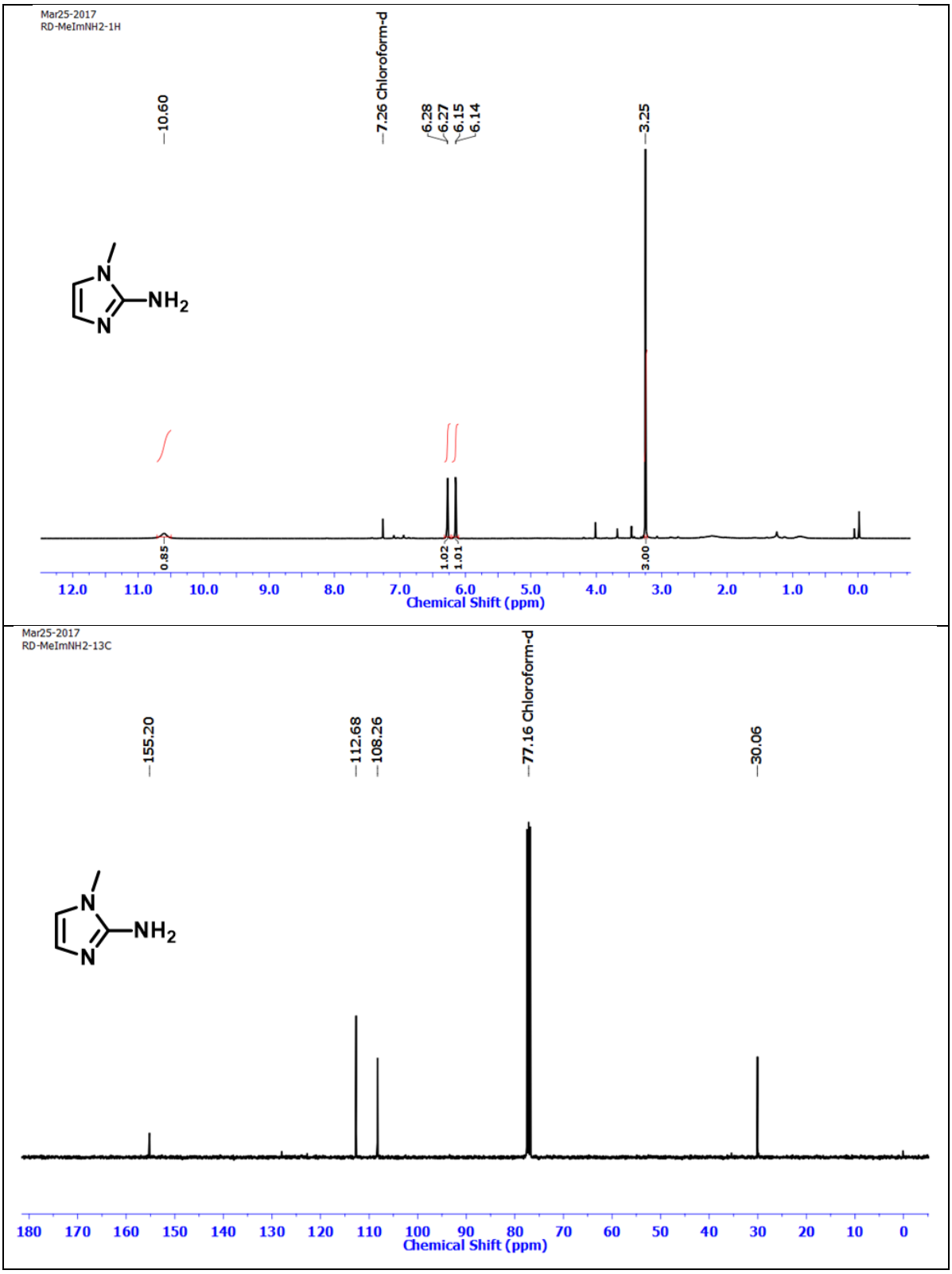


Figure S36: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **24** in $CDCl_3$-*d*.

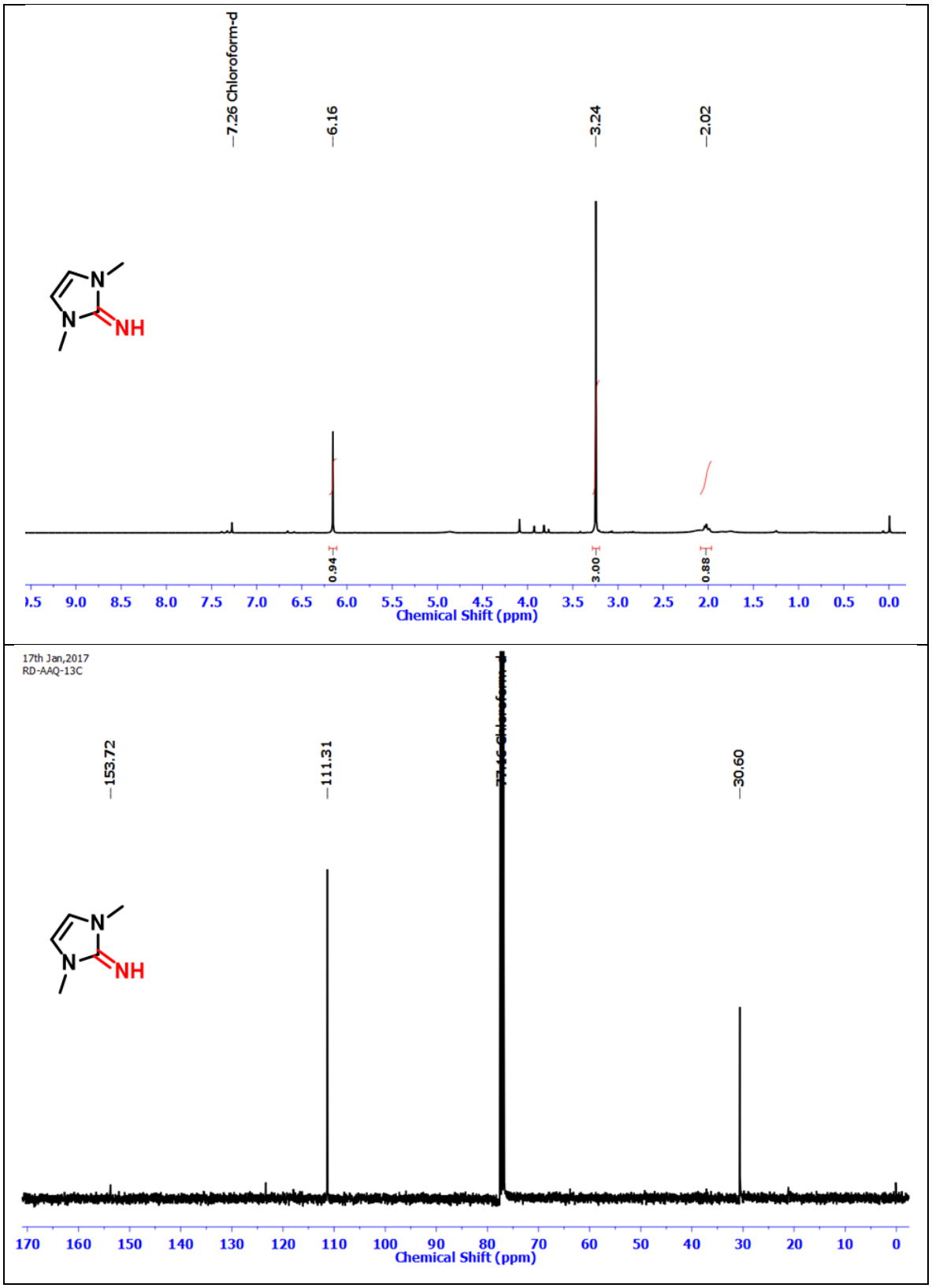


Figure S37: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **10a** in $CDCl_3$-*d*.

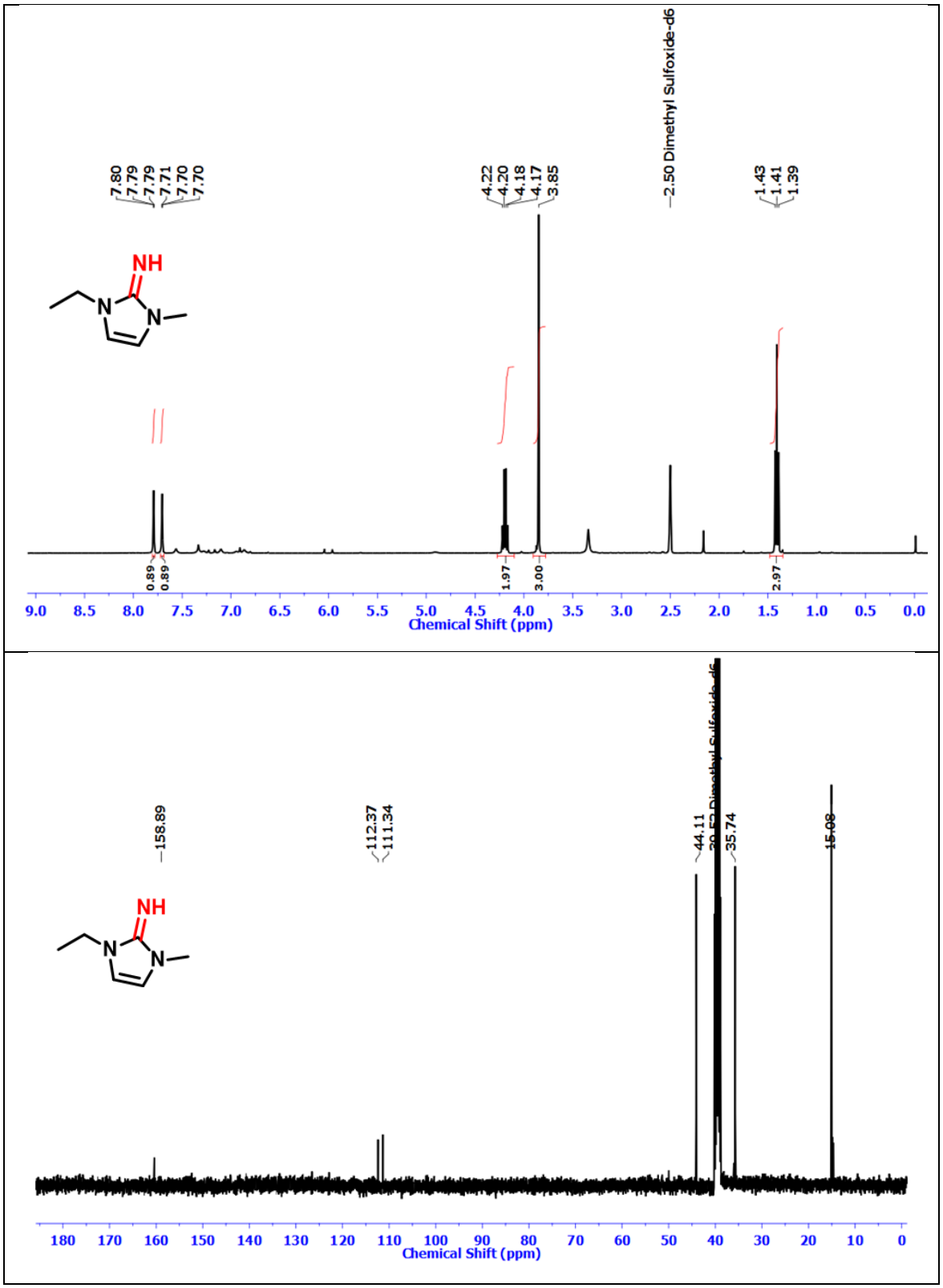


Figure S36: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **10b** in DMSO-d_6.

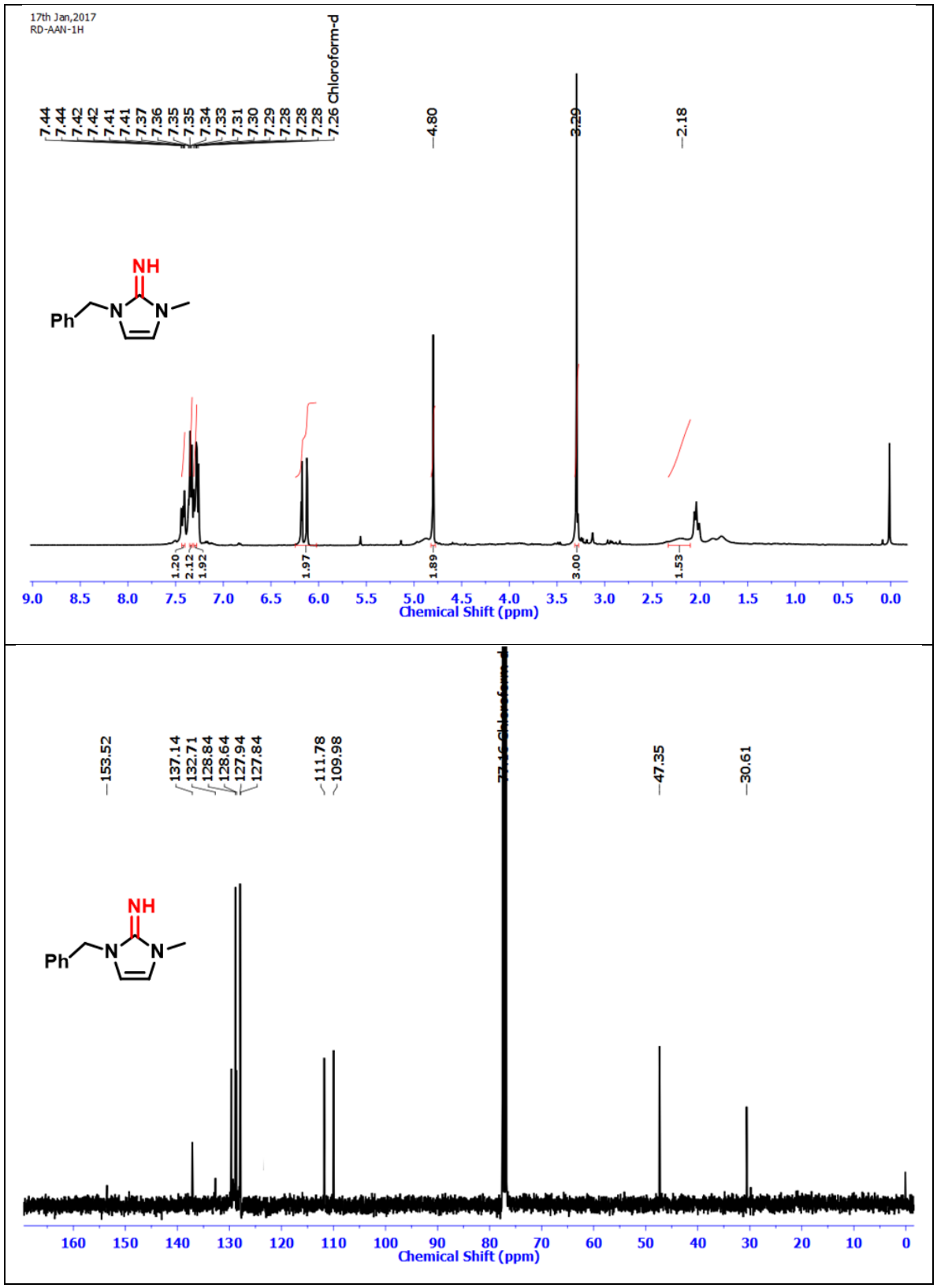


Figure S39: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **10c** in $CDCl_3$.

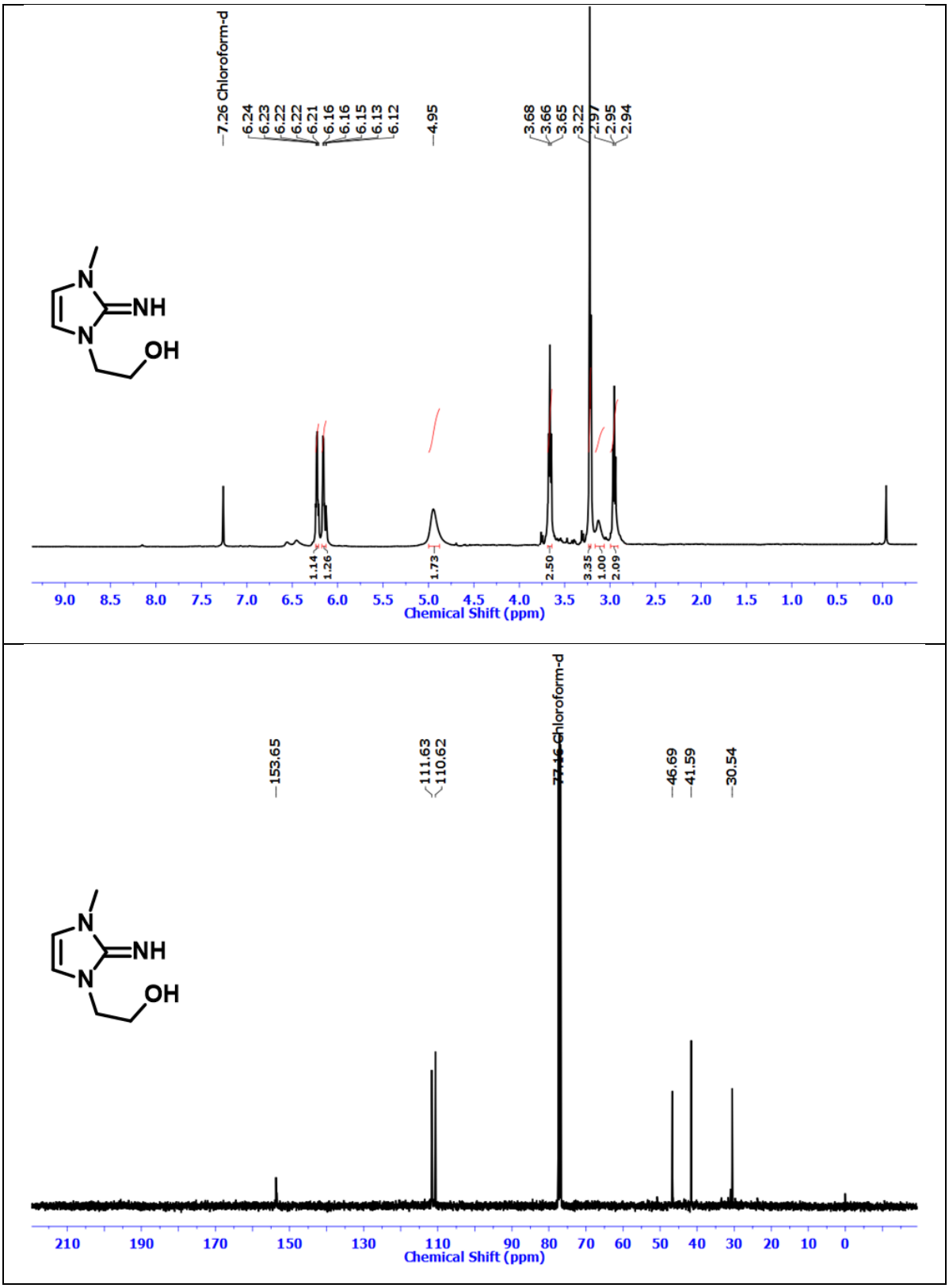


Figure S40: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **10d** in $CDCl_3$-*d*.

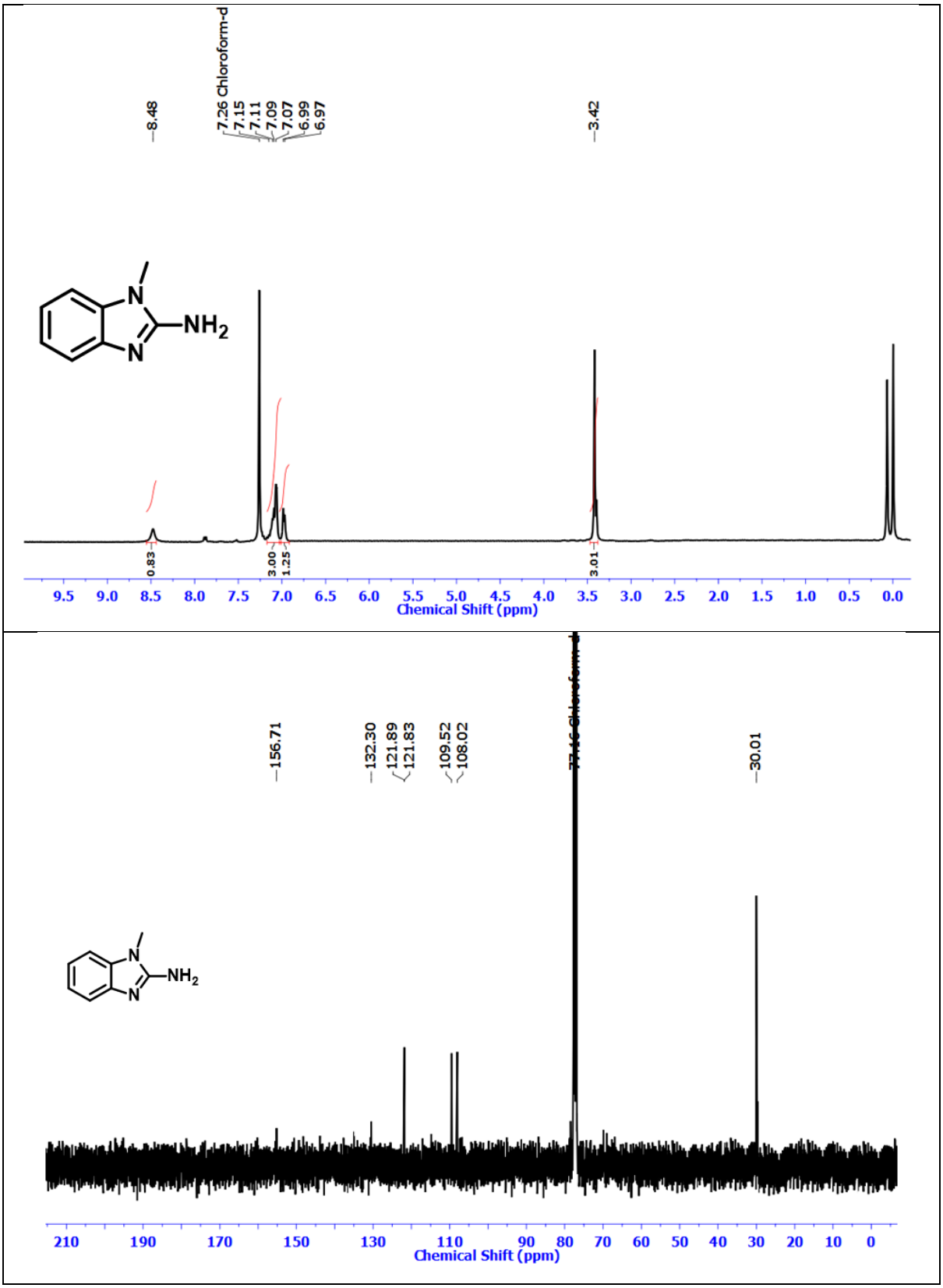


Figure S41: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **25** in $CDCl_3$-*d*.

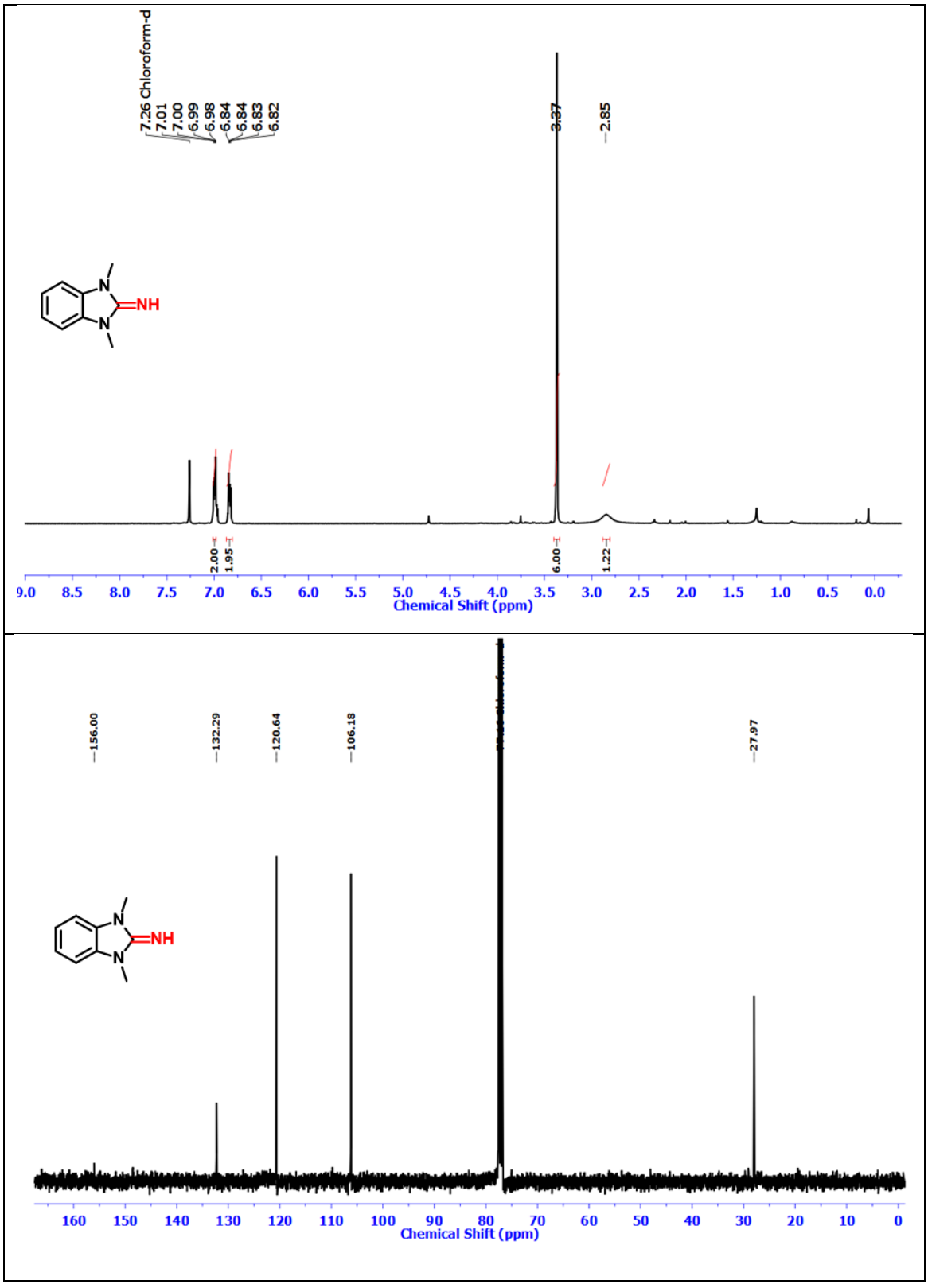


Figure S42: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **11a** in $CDCl_3$.

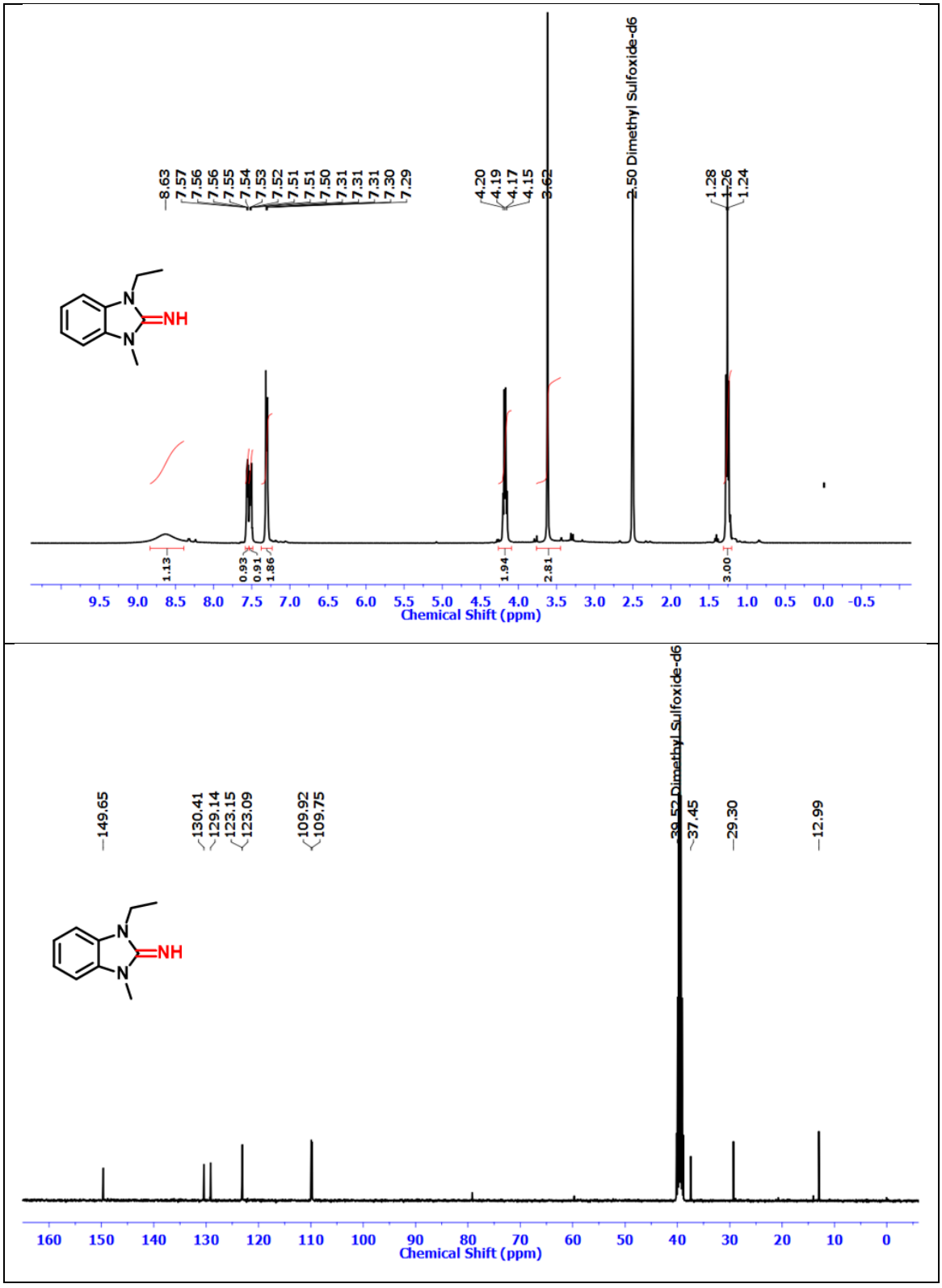


Figure S43: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **11b** in $CDCl_3$.

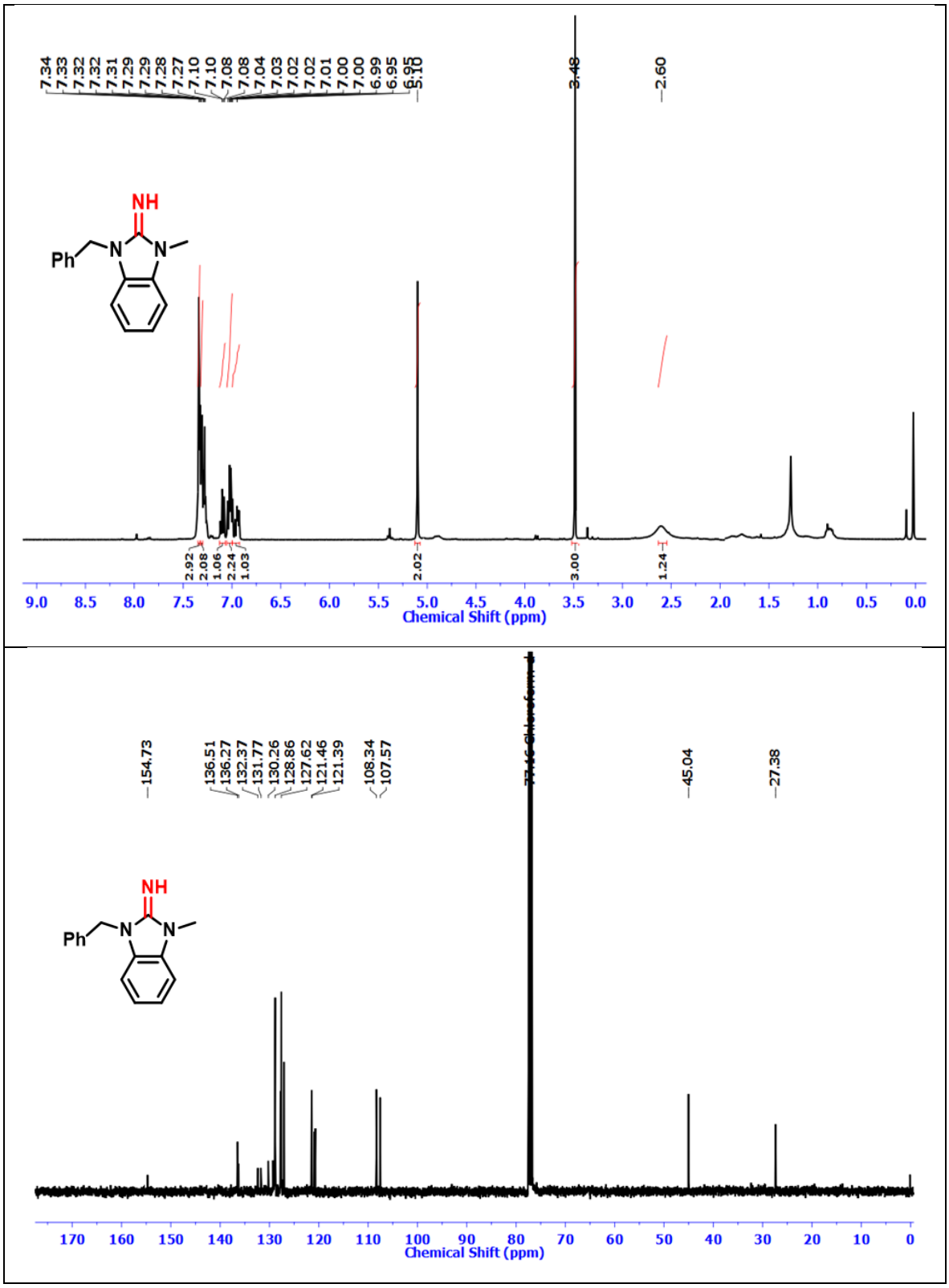


Figure S44: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **11c** in $CDCl_3$-*d*.

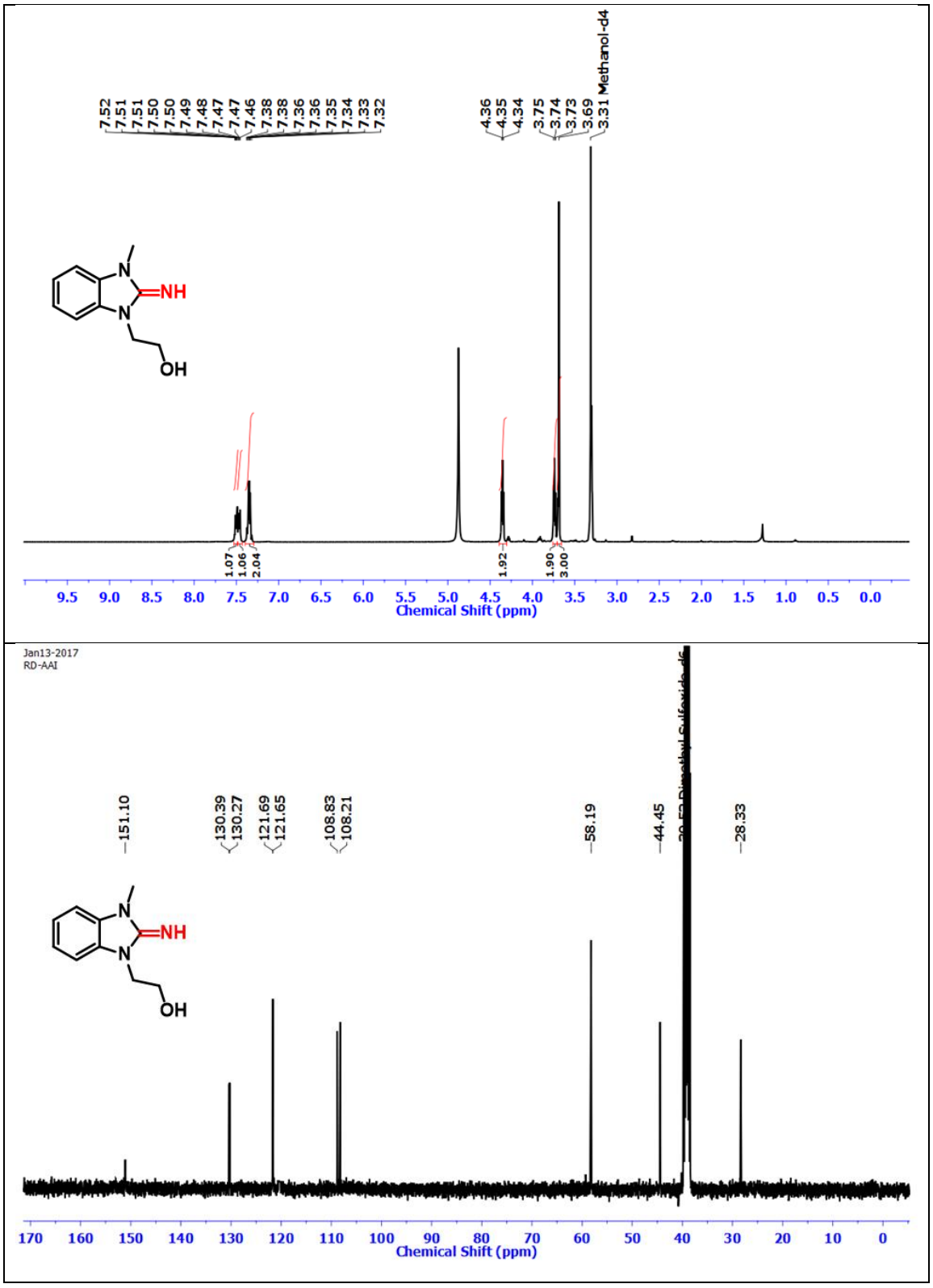


Figure S45: ^{1}H NMR spectrum in MeOH-d_4 and ^{13}C NMR spectrum of **11d** in DMSO-d_6.

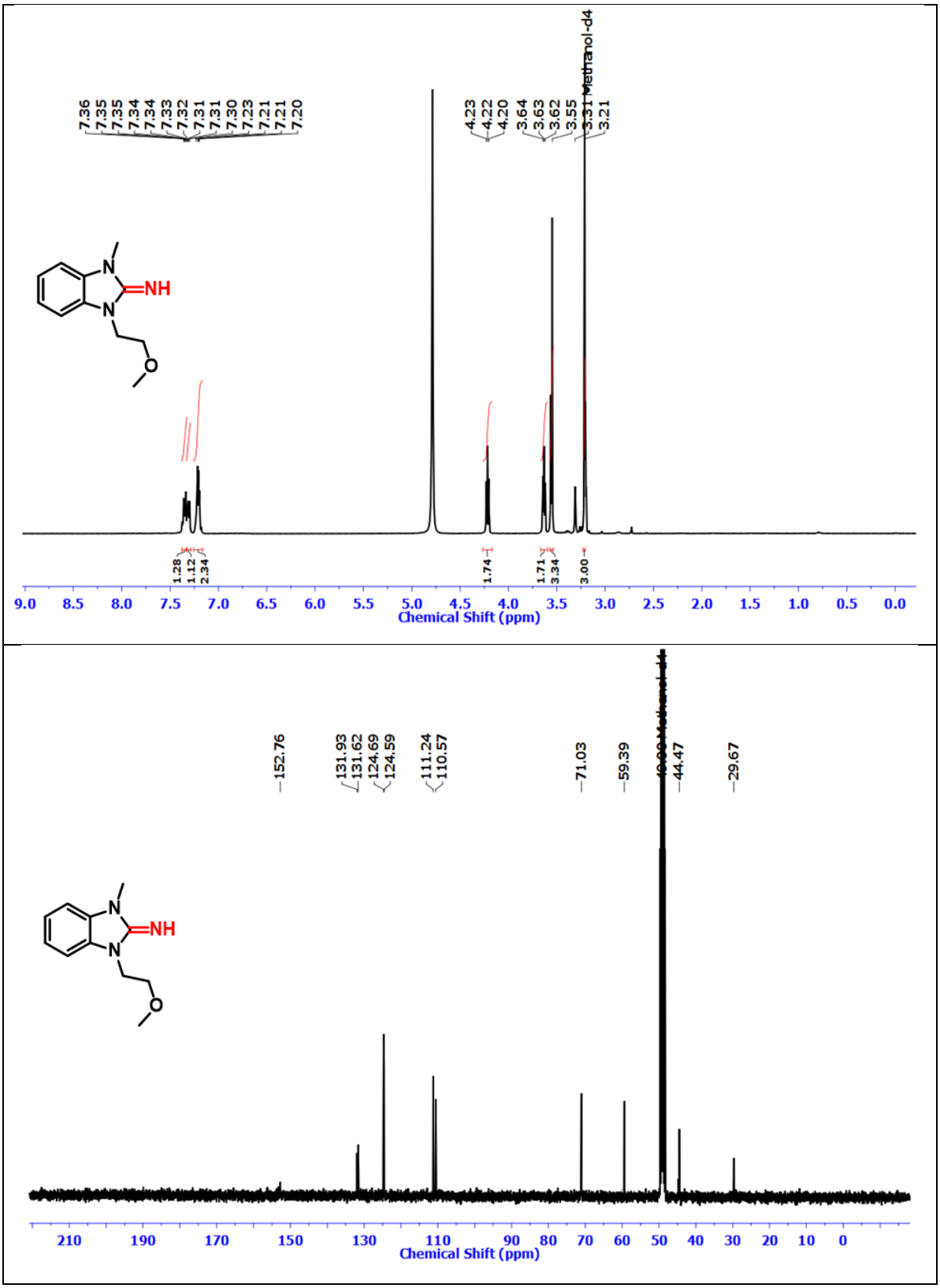


Figure S46: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **11e** in MeOH-d_4.

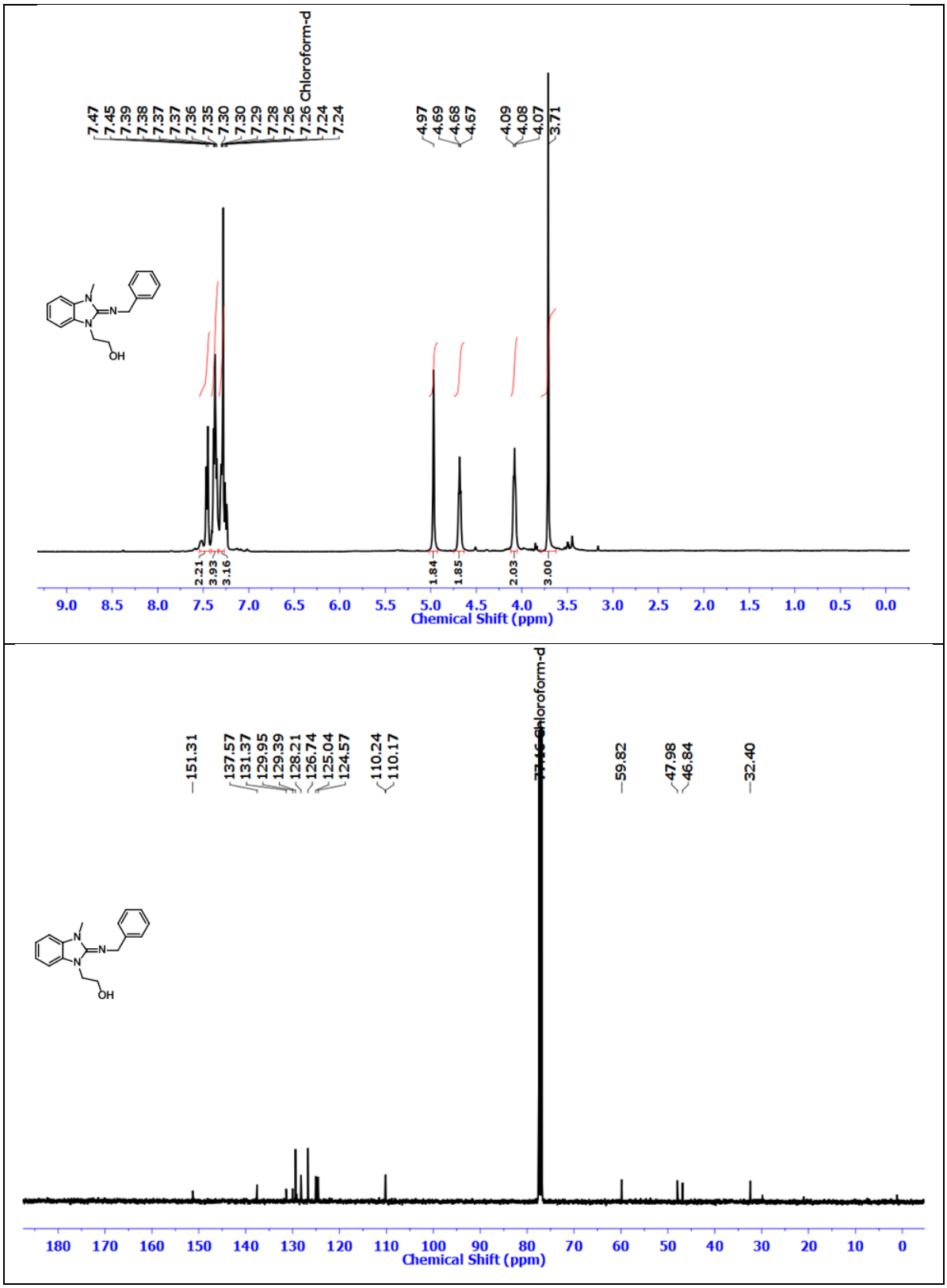


Figure S47: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **12a** in $CDCl_3$-*d*.

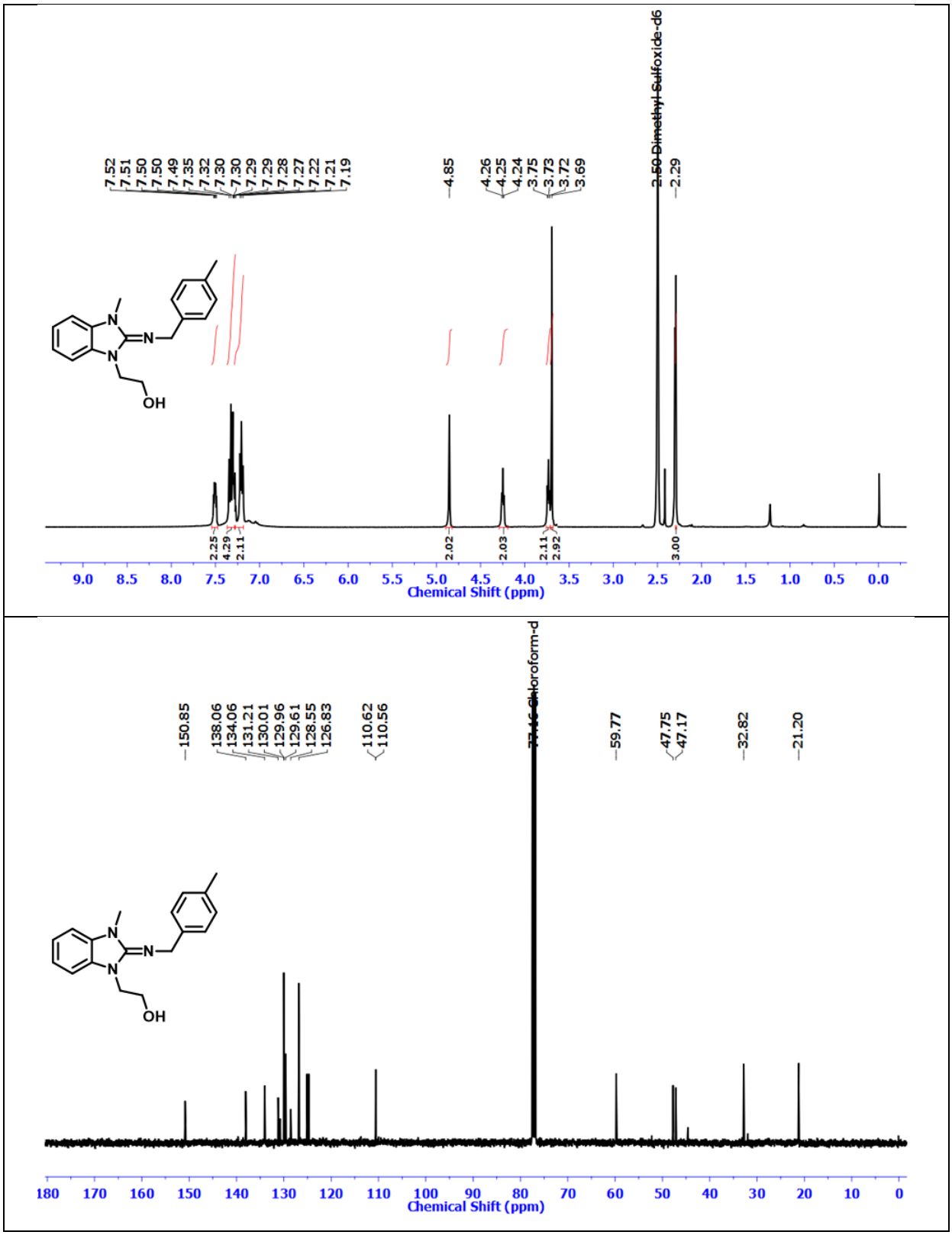


Figure S48: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **12b** in $CDCl_3$-*d*.

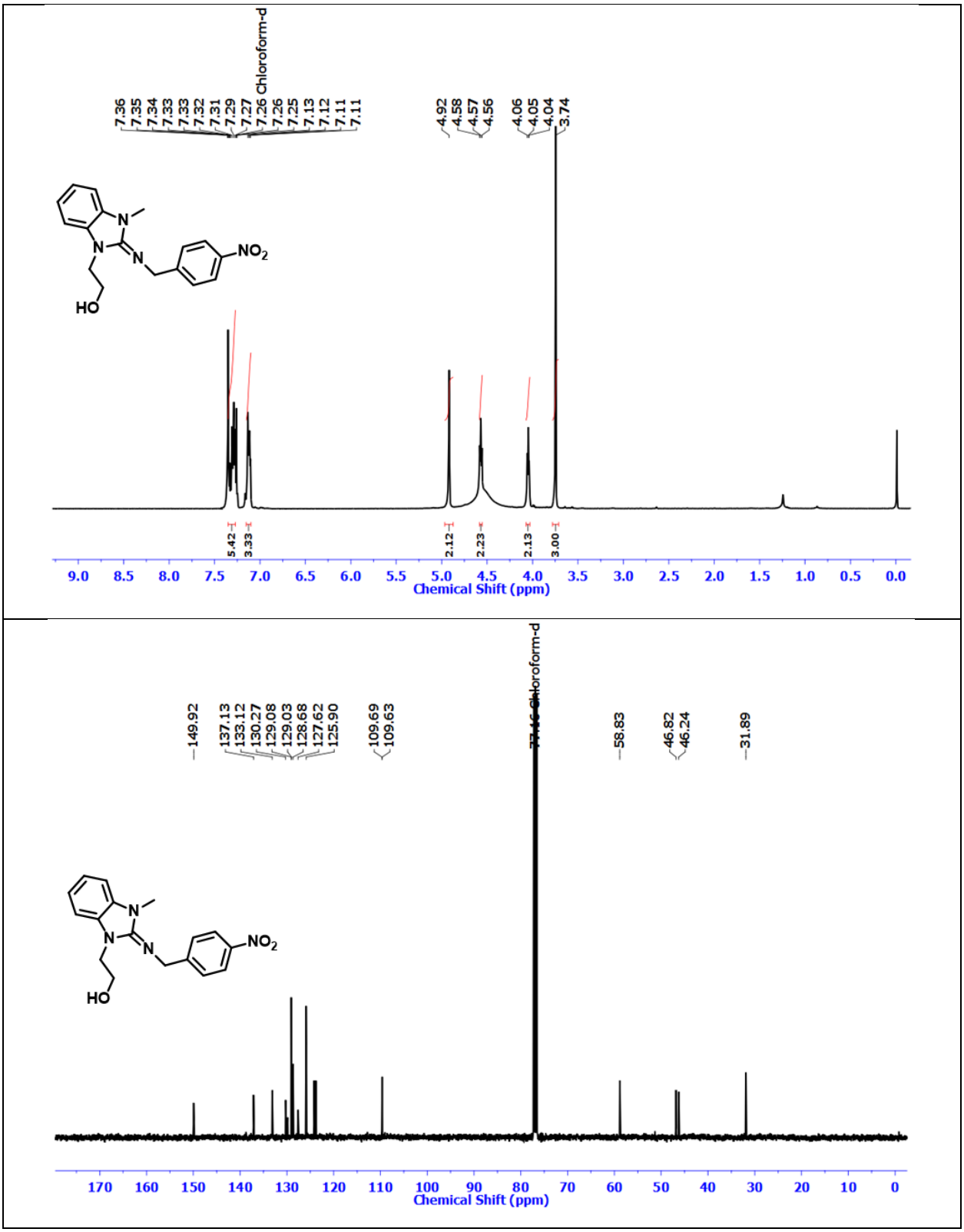


Figure S49: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **12c** in $CDCl_3$- *d*.

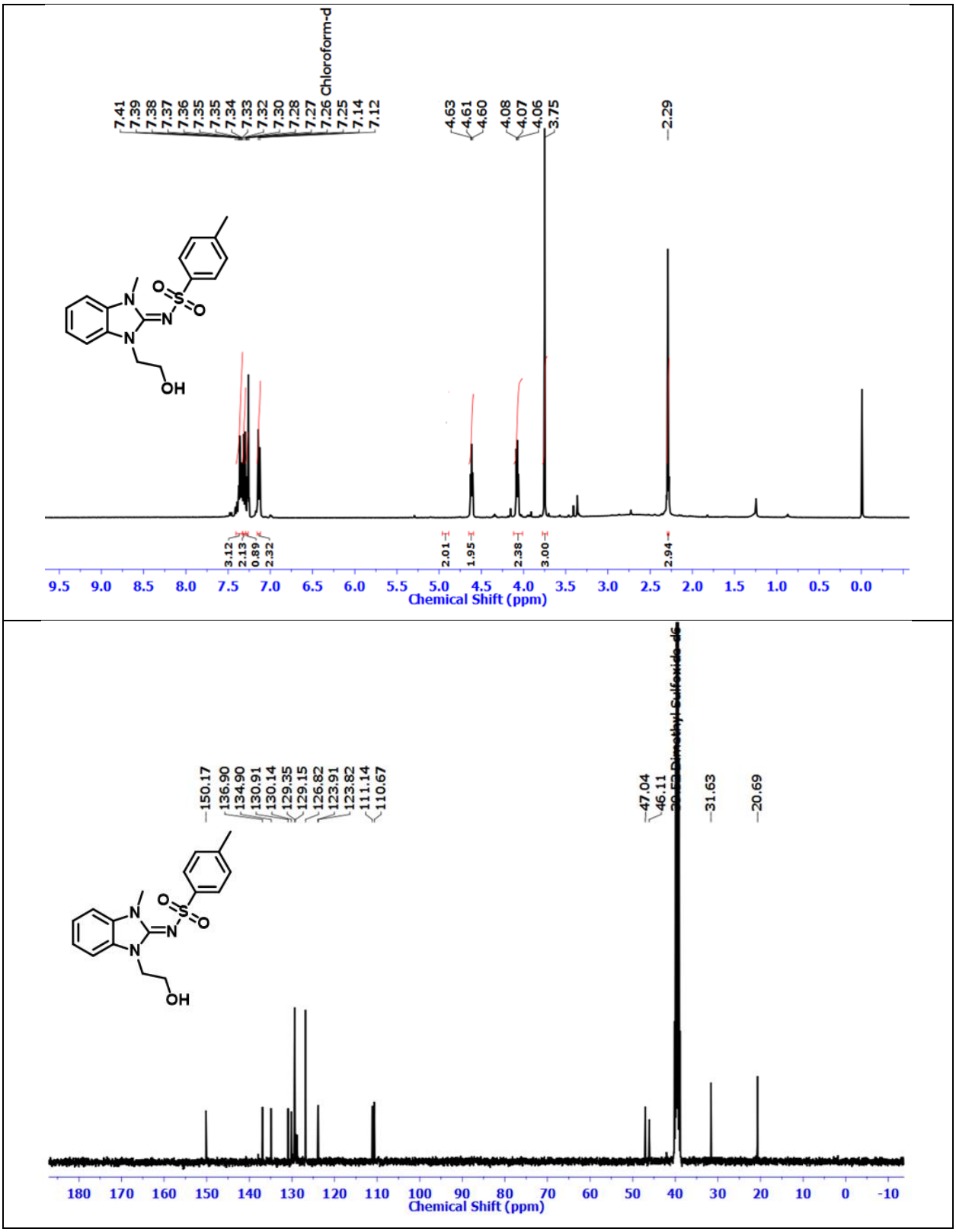


Figure S50: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **12d** in DMSO-d_6.

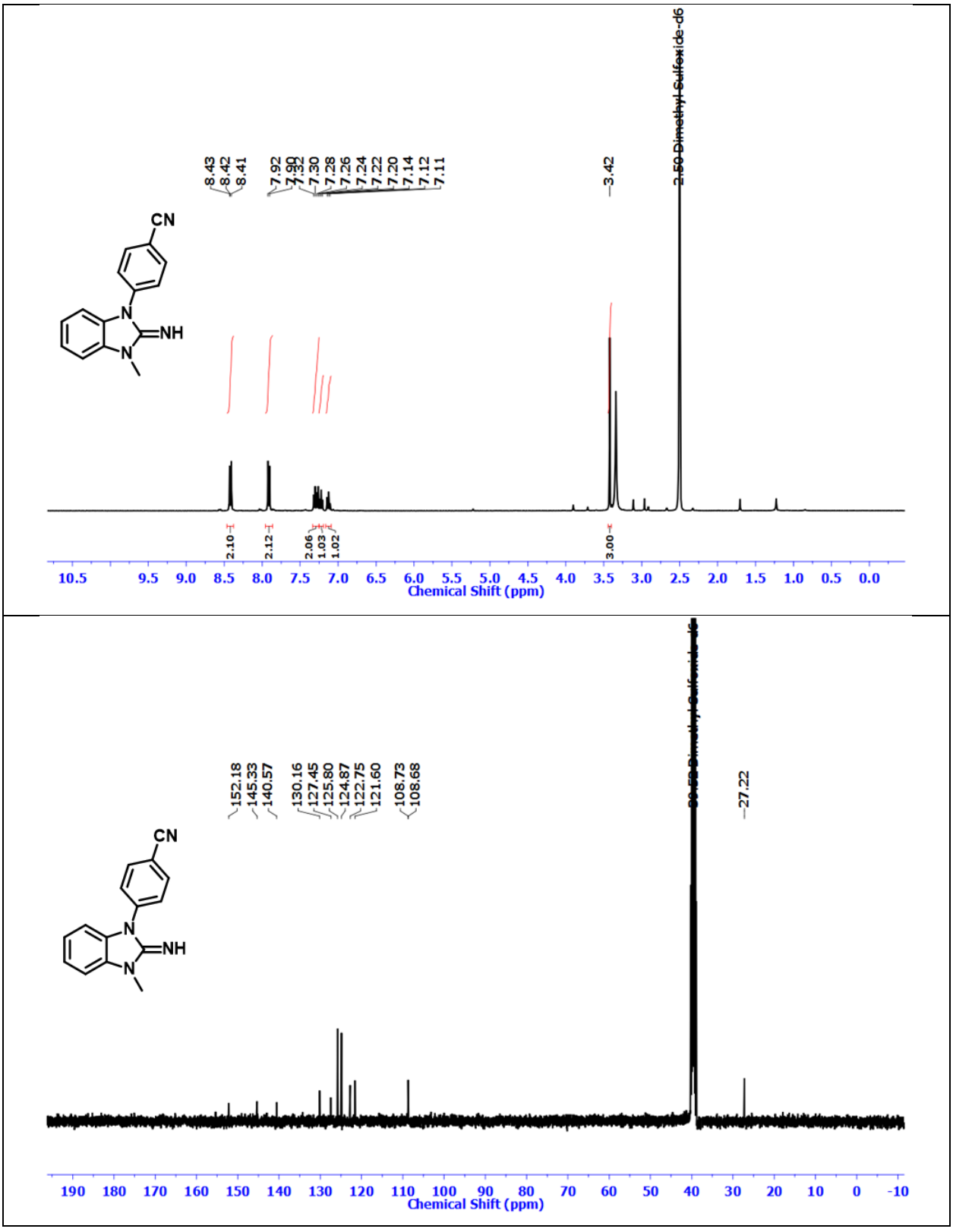


Figure S51: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **13a** in DMSO-d_6.

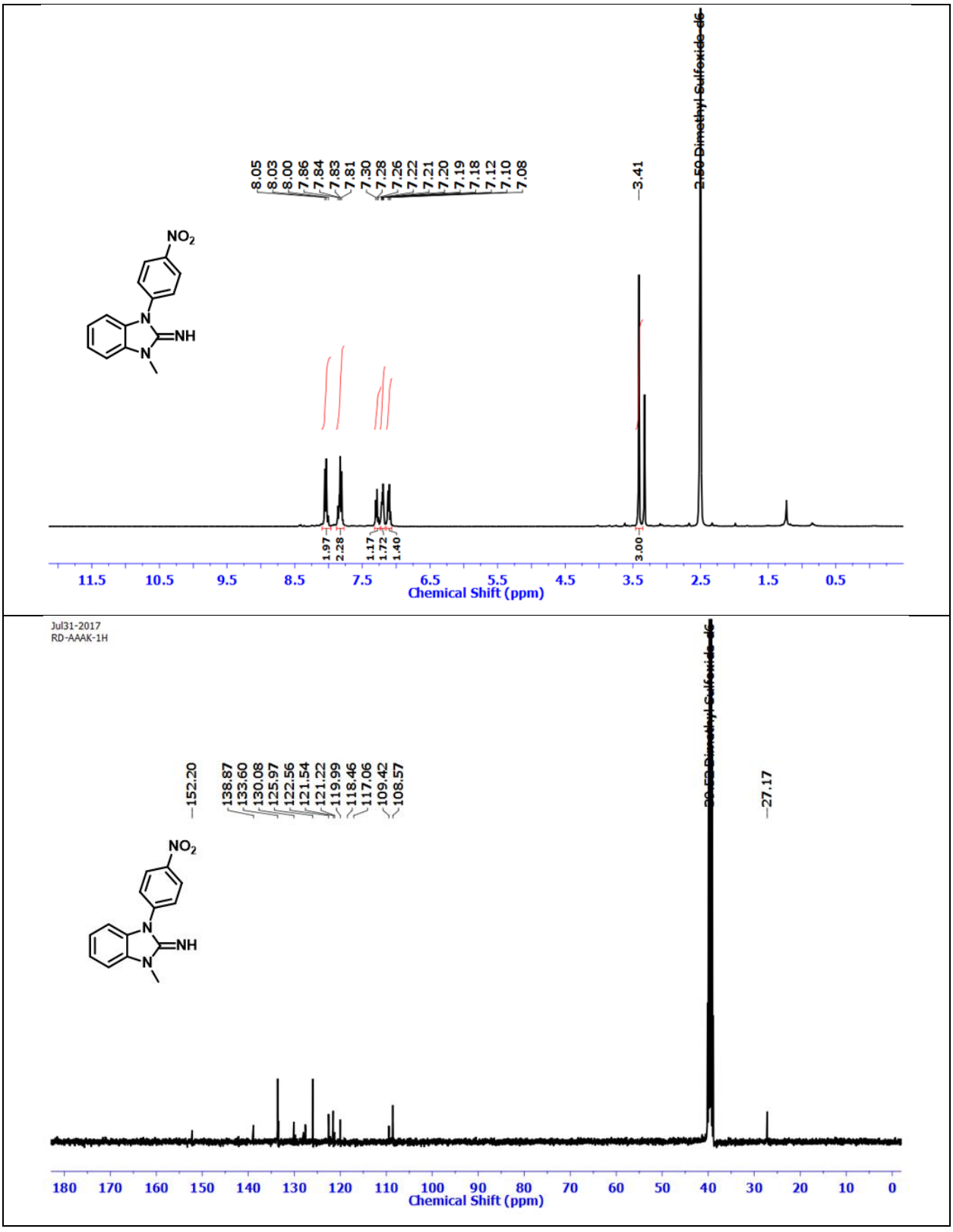


Figure S52: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **13b** in DMSO-d_6.

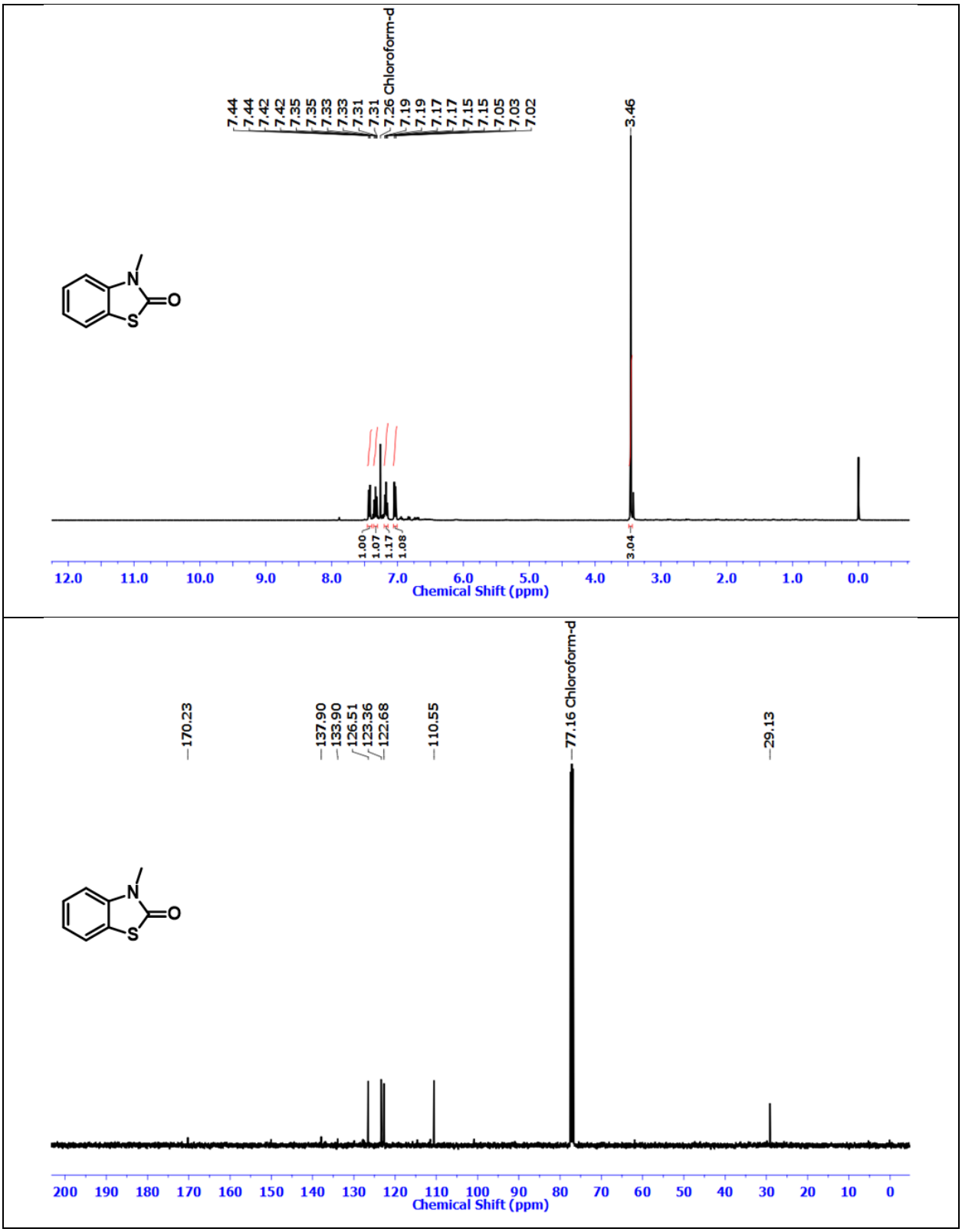


Figure S53: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16a** in $CDCl_3$-*d*.

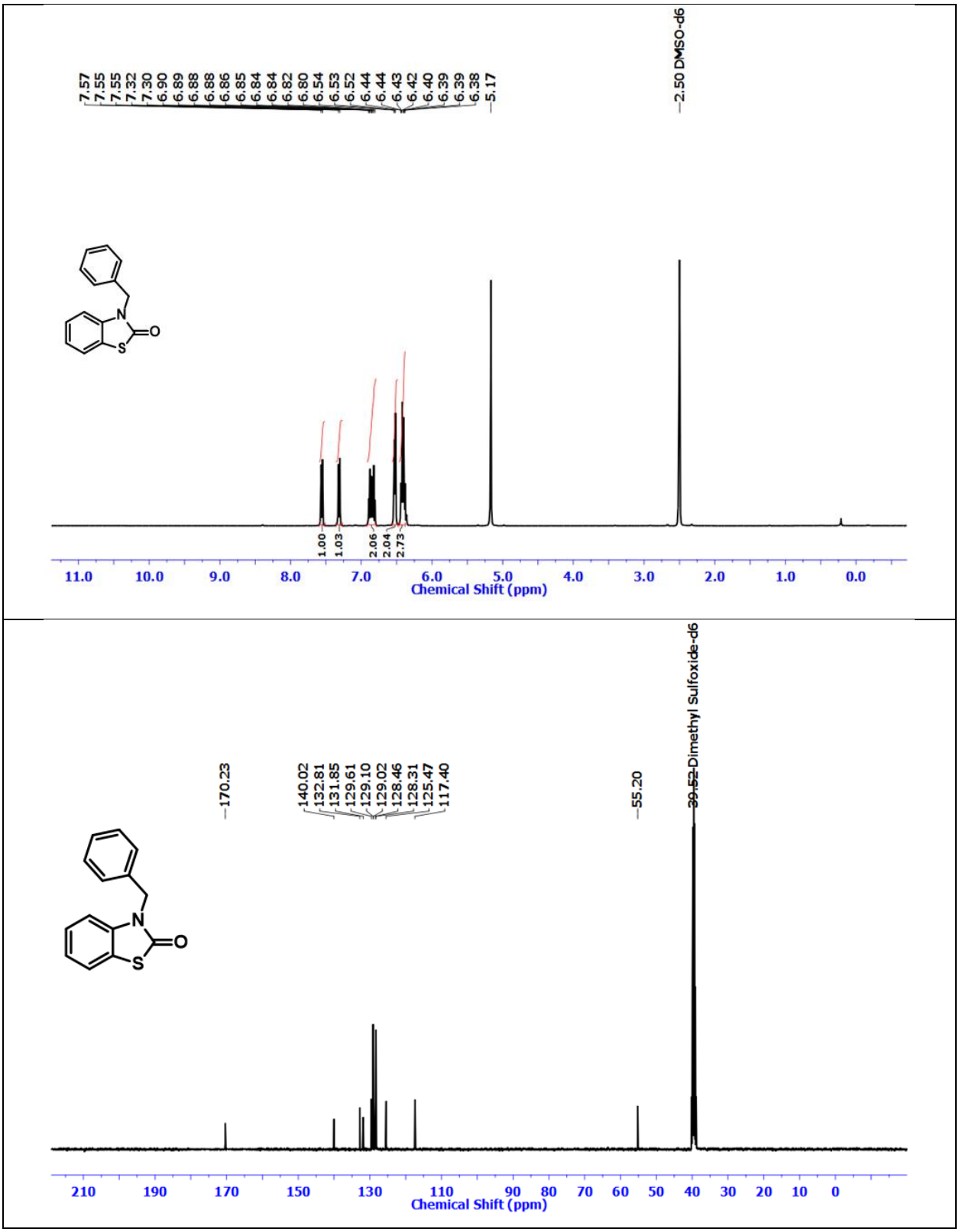


Figure S54: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16c** in DMSO-d_6.

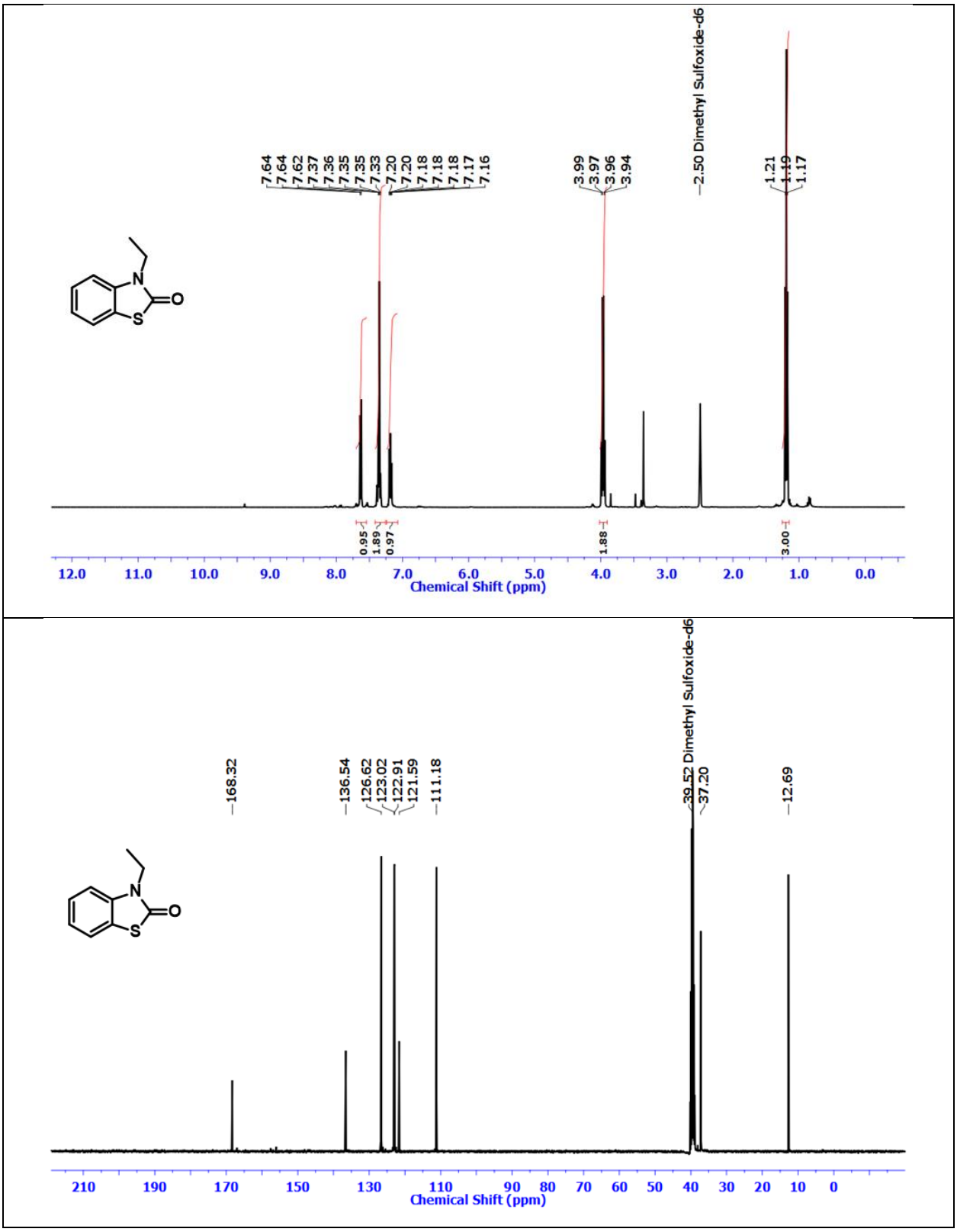


Figure S55: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16b** in DMSO-d_6.

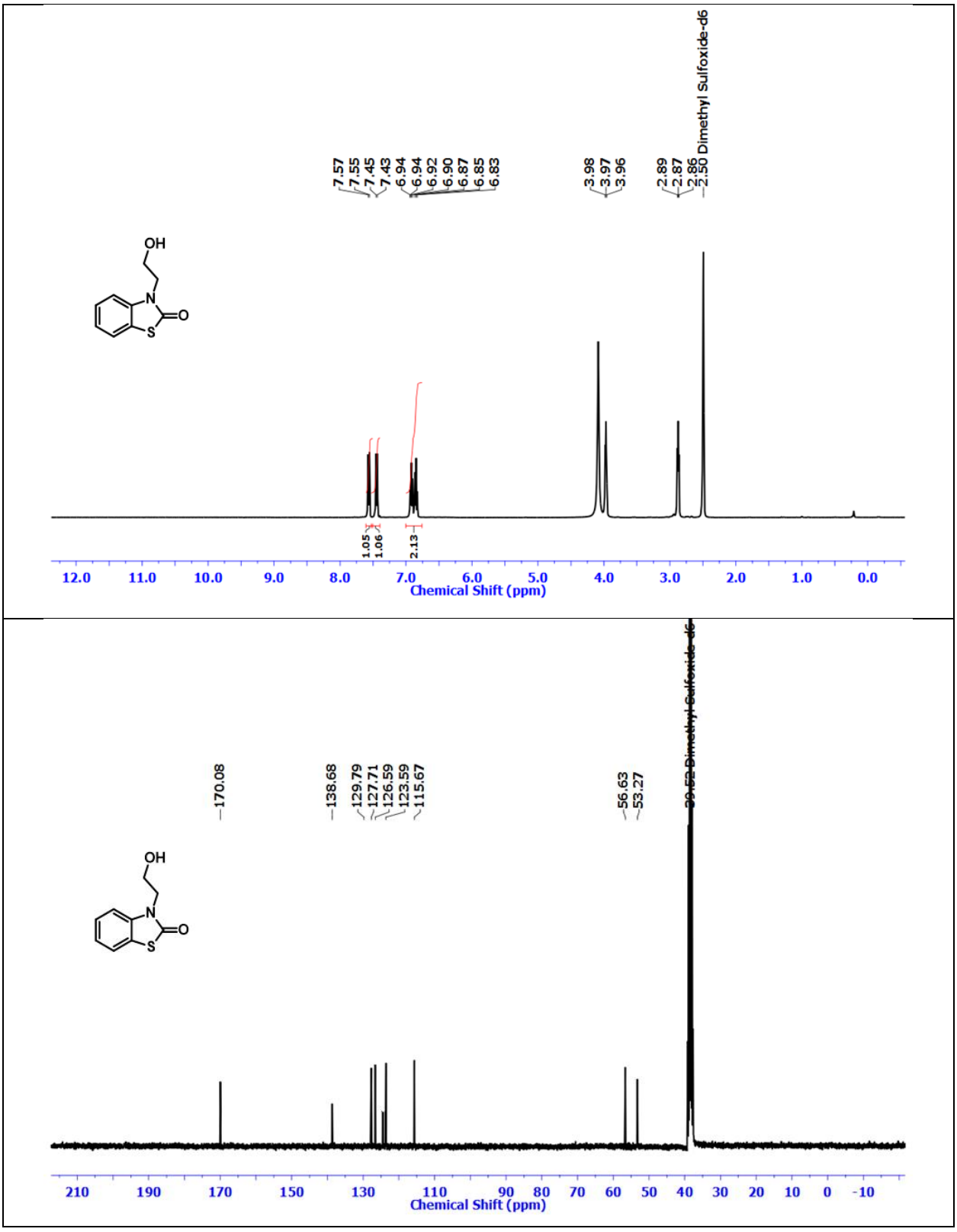


Figure S56: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16d** in DMSO-d_6.

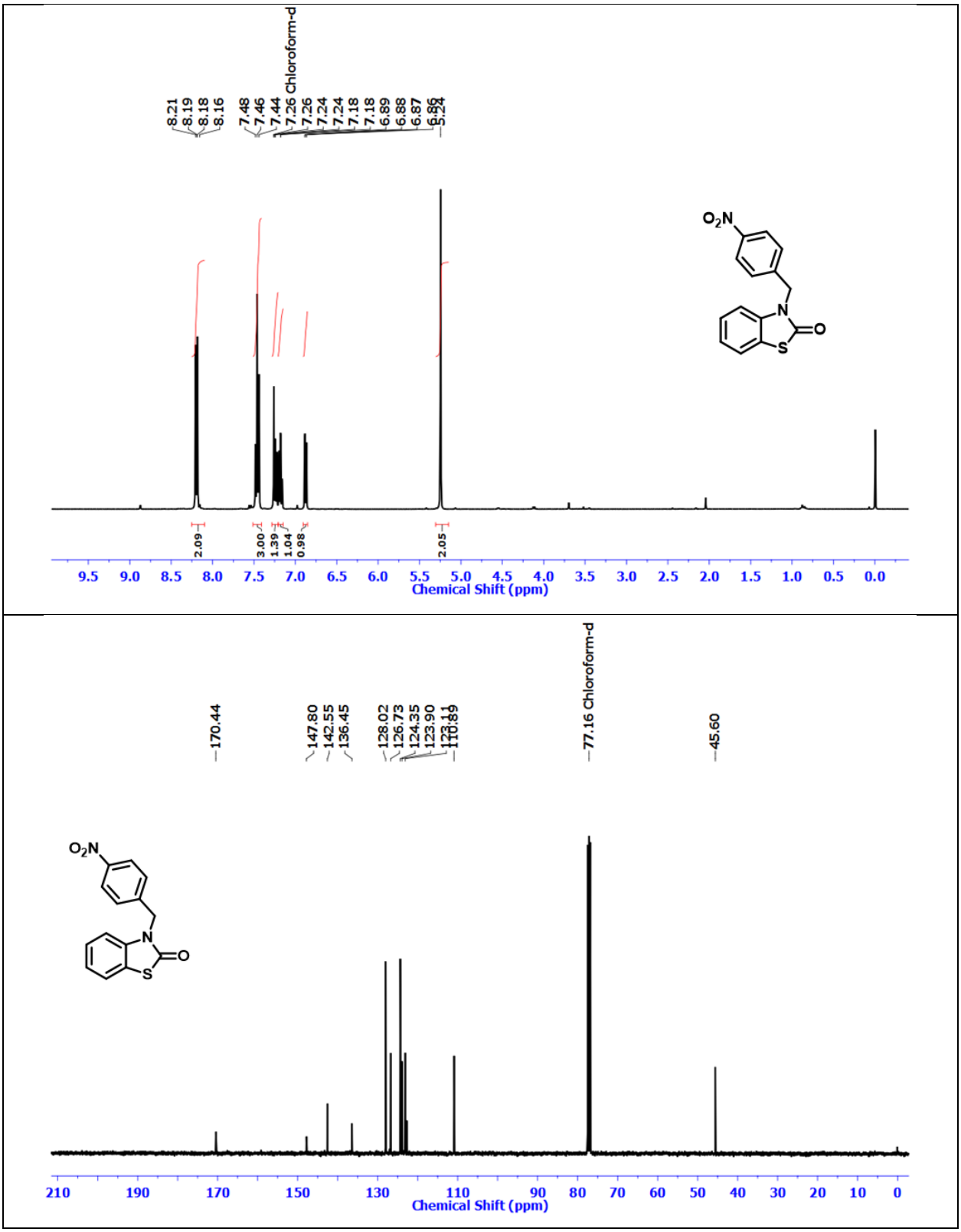


Figure S57: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16f** in $CDCl_3$.*d*.

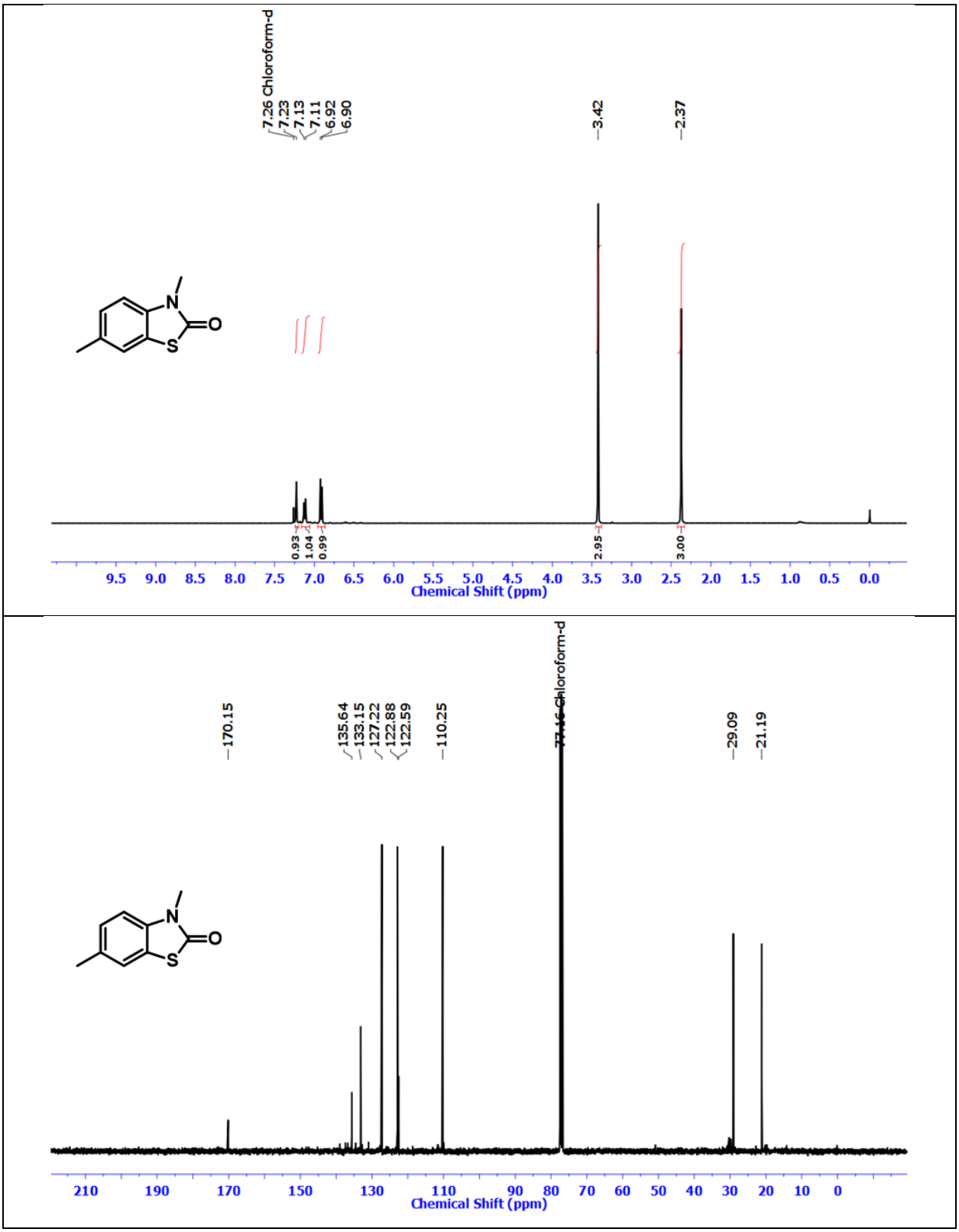


Figure S58: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16j** in $CDCl_3$-*d*.

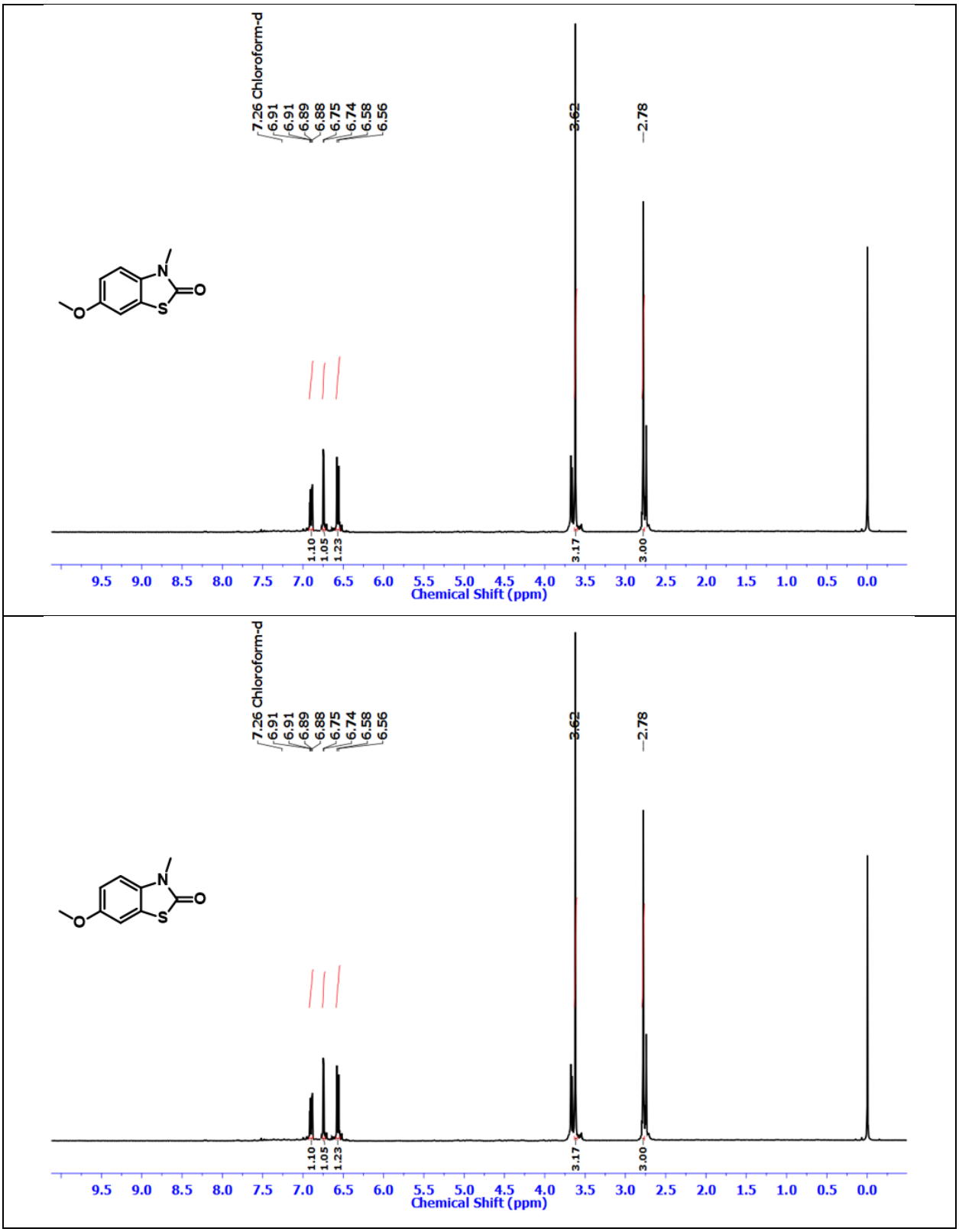


Figure S59: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16k** in $CDCl_3$-*d*

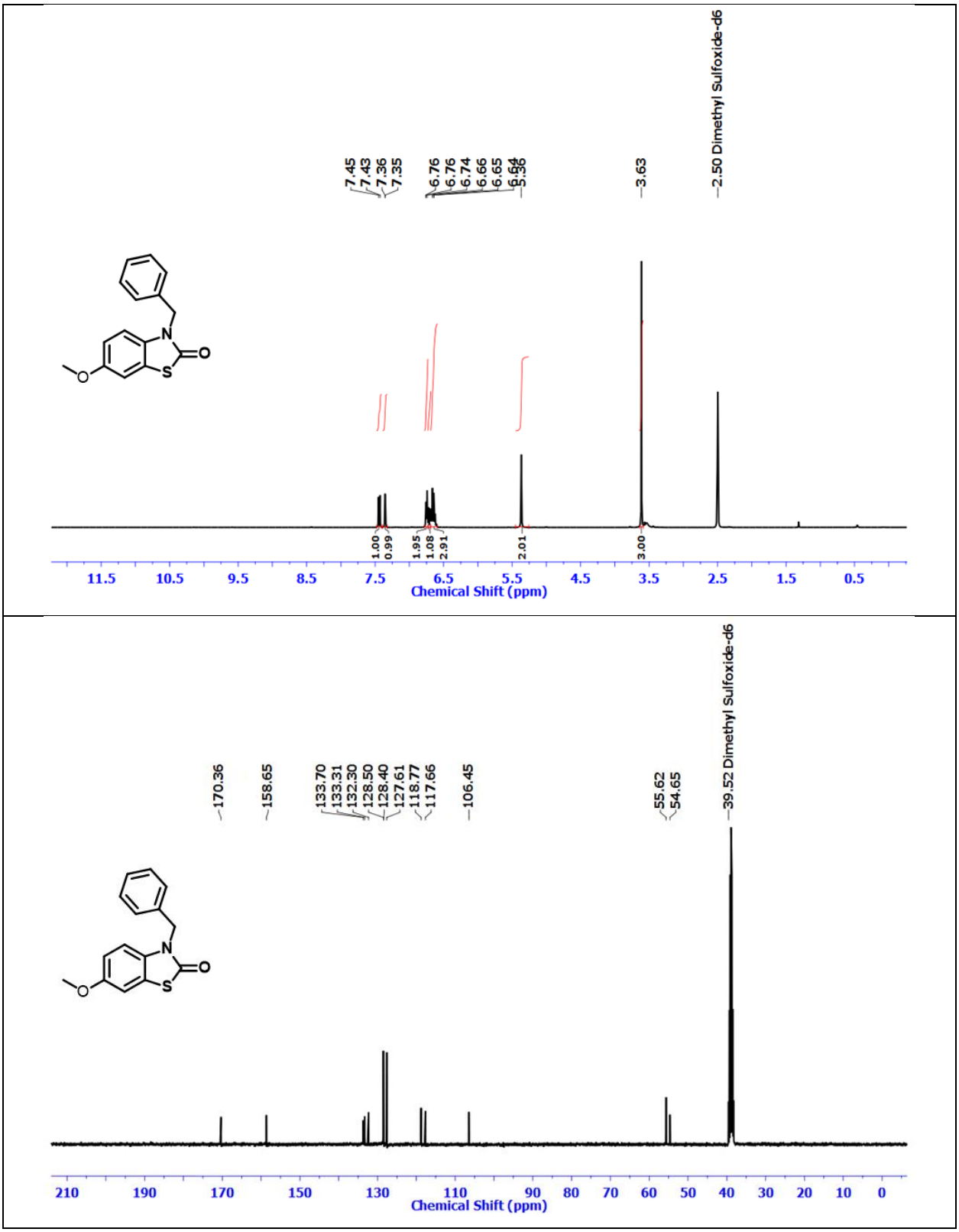


Figure S60: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16h** in DMSO-d_6.

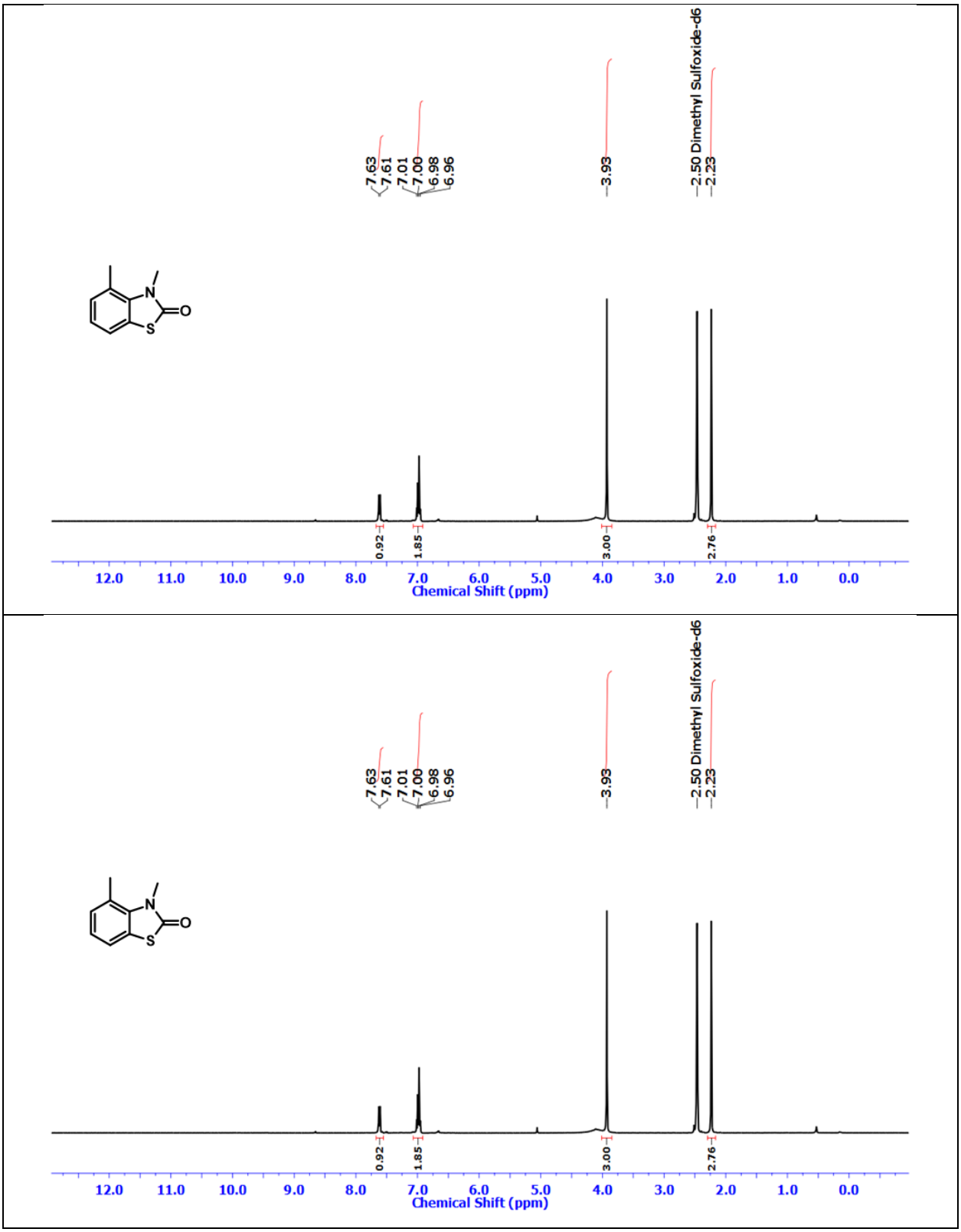


Figure S61: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **16i** in DMSO-d_6.

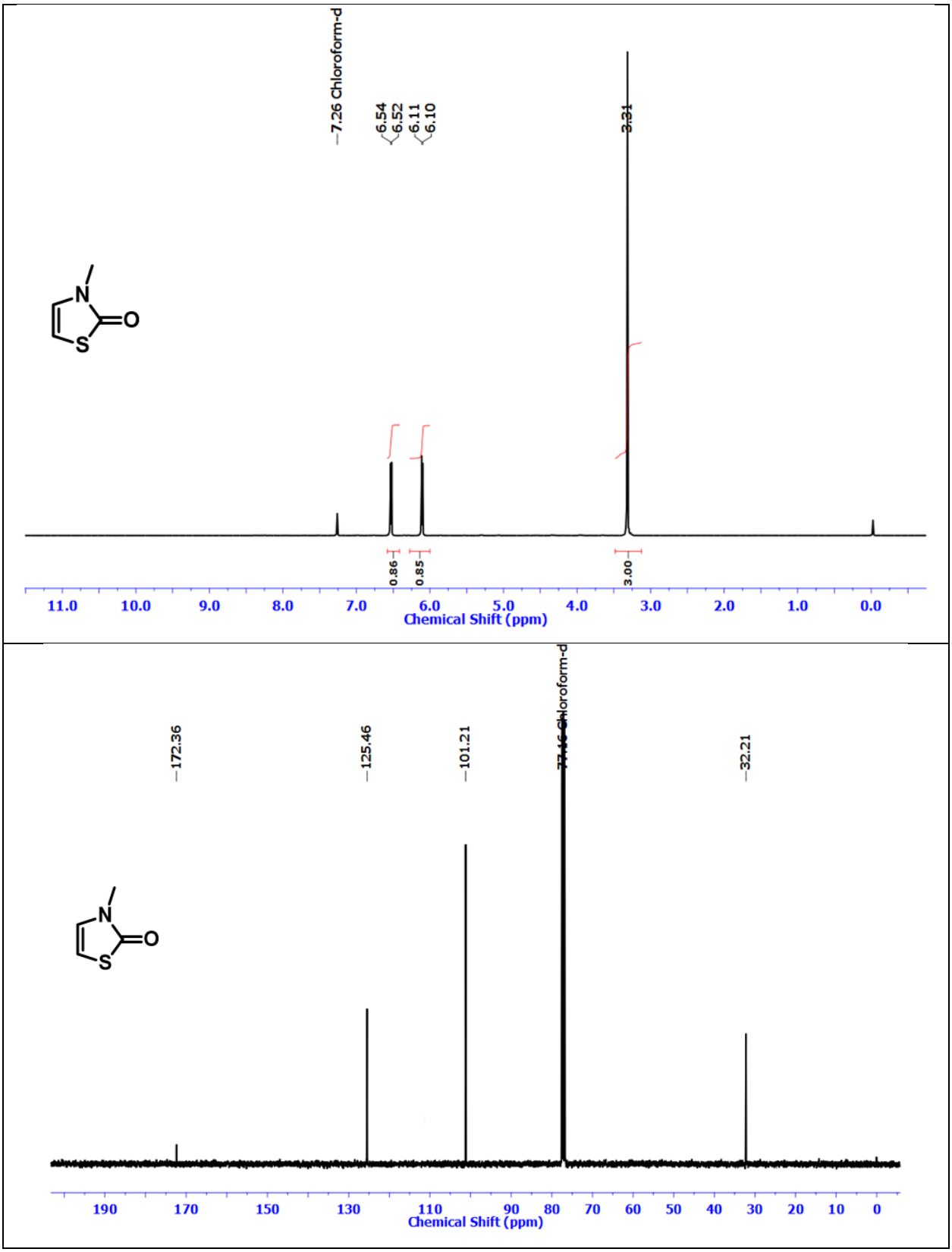


Figure S62: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **18a** in $CDCl_3$-*d*.

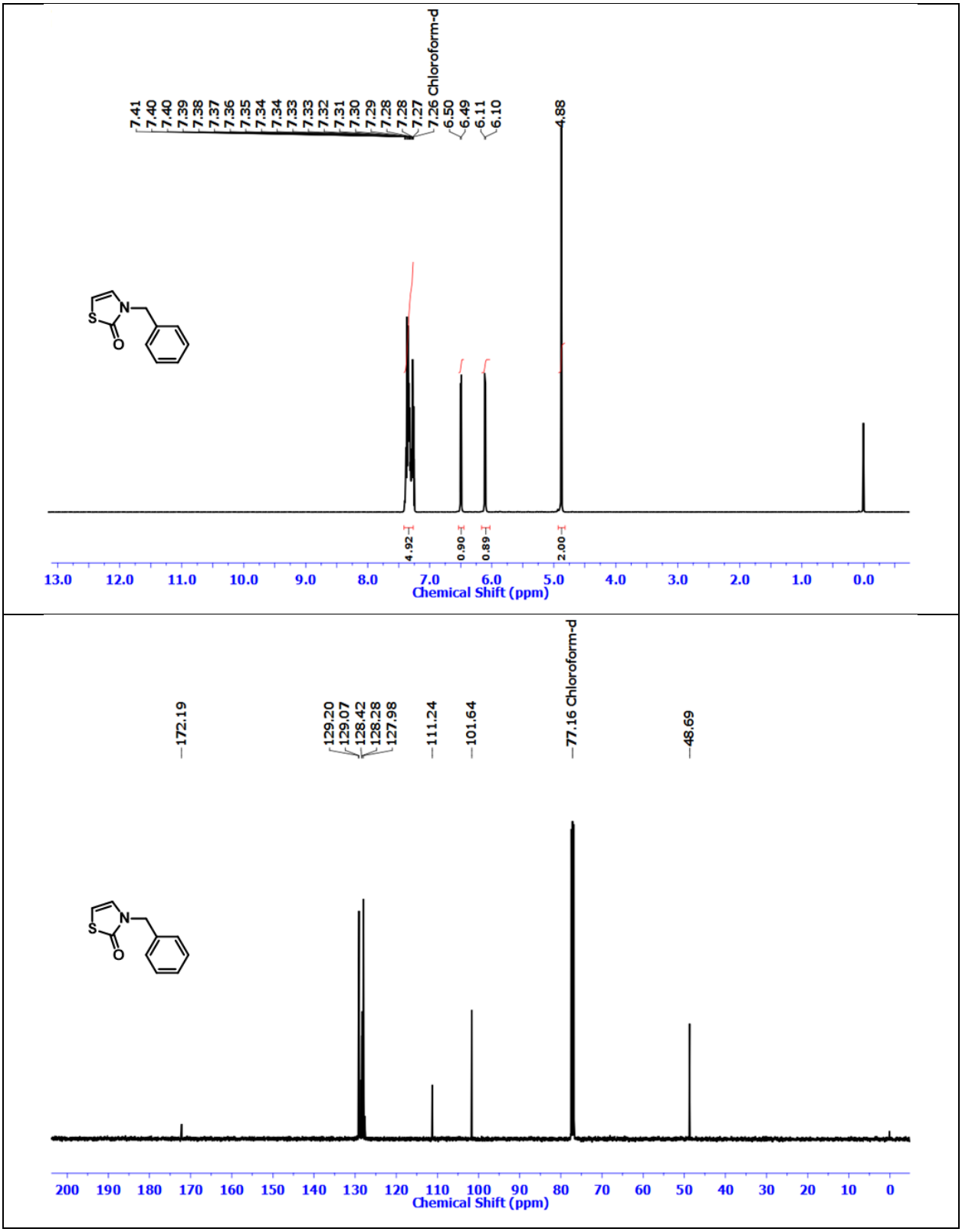


Figure S63: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **18b** in $CDCl_3$-*d*.

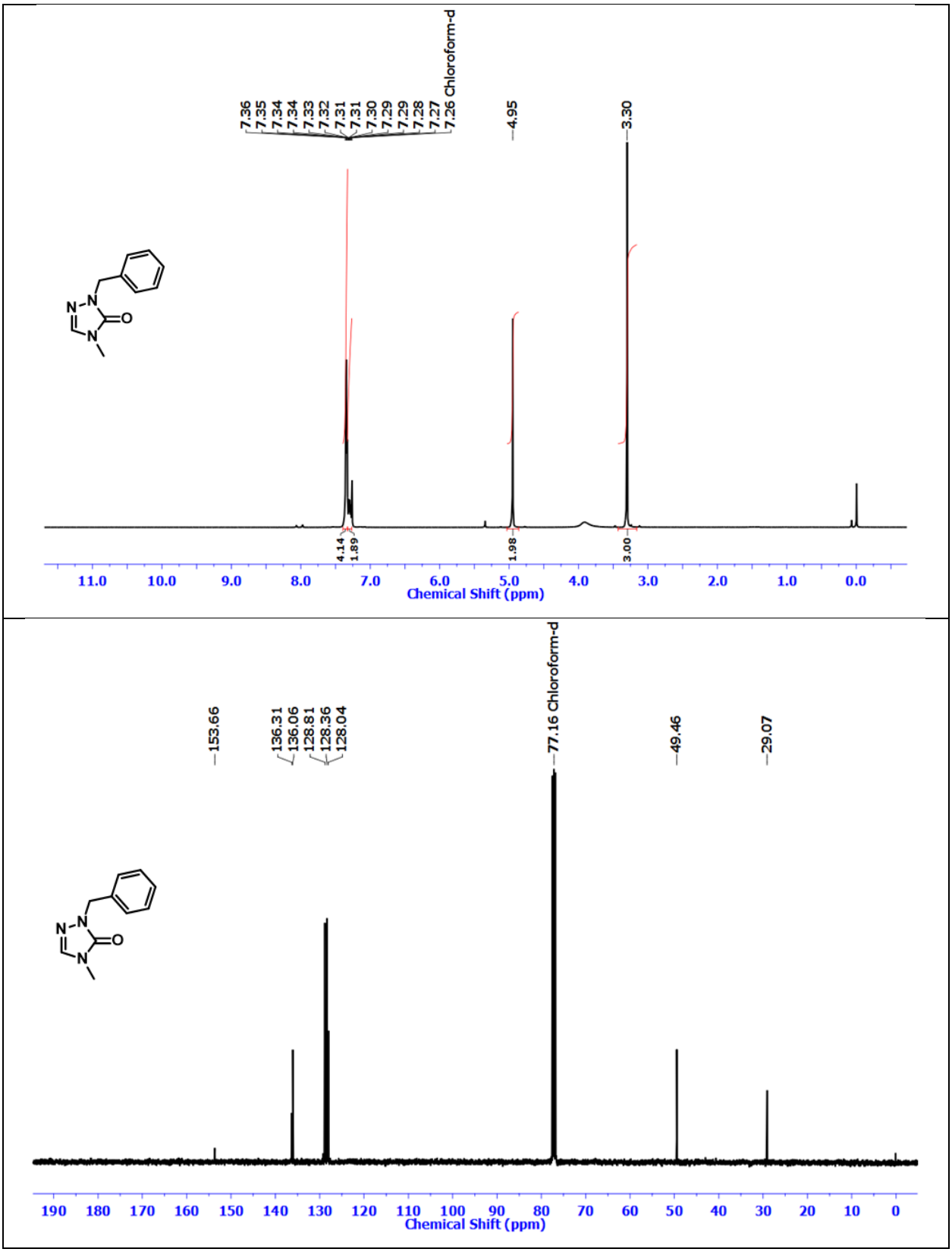


Figure S64: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **20** in $CDCl_3$-*d*.

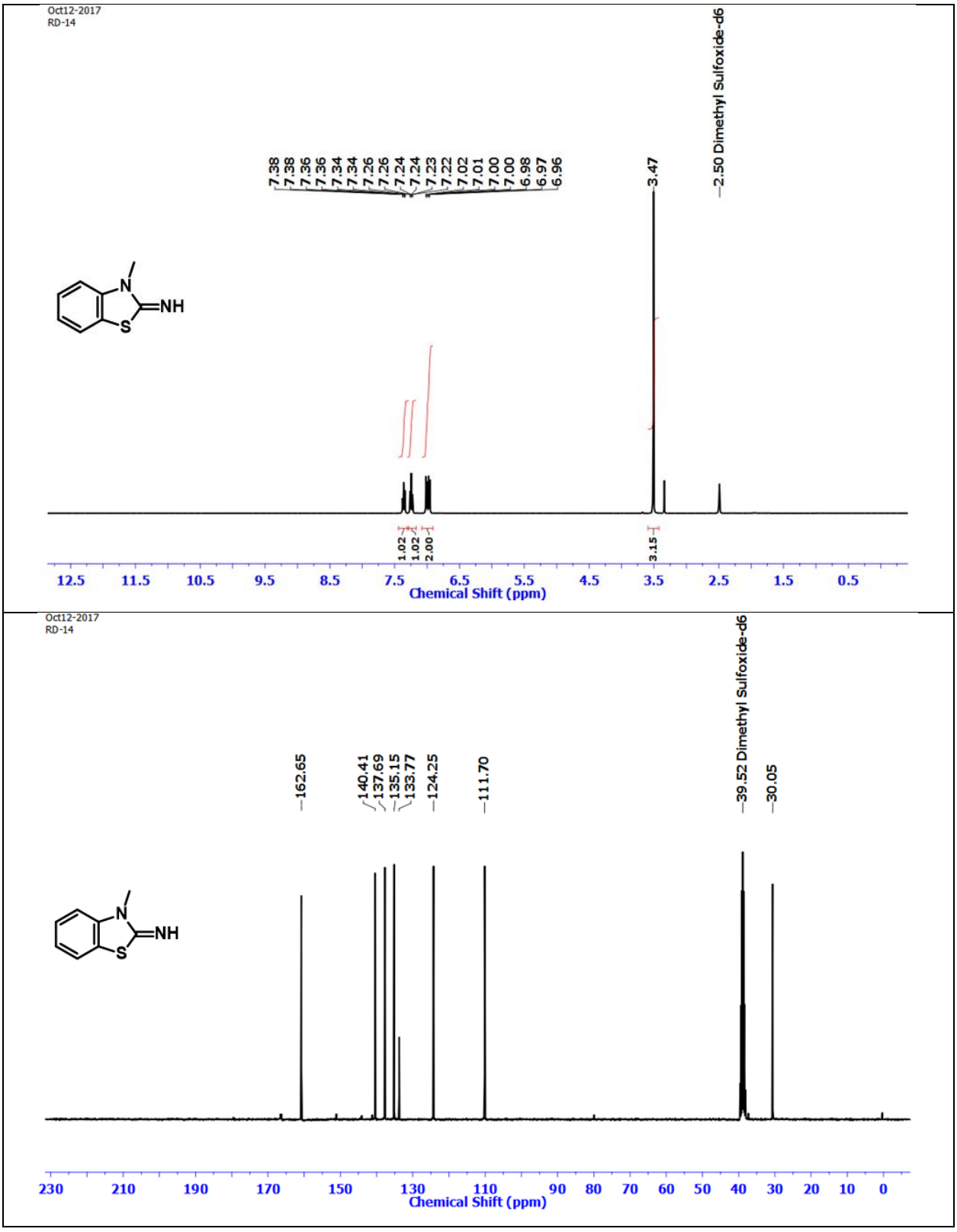


Figure S65: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17a** in DMSO-d_6.

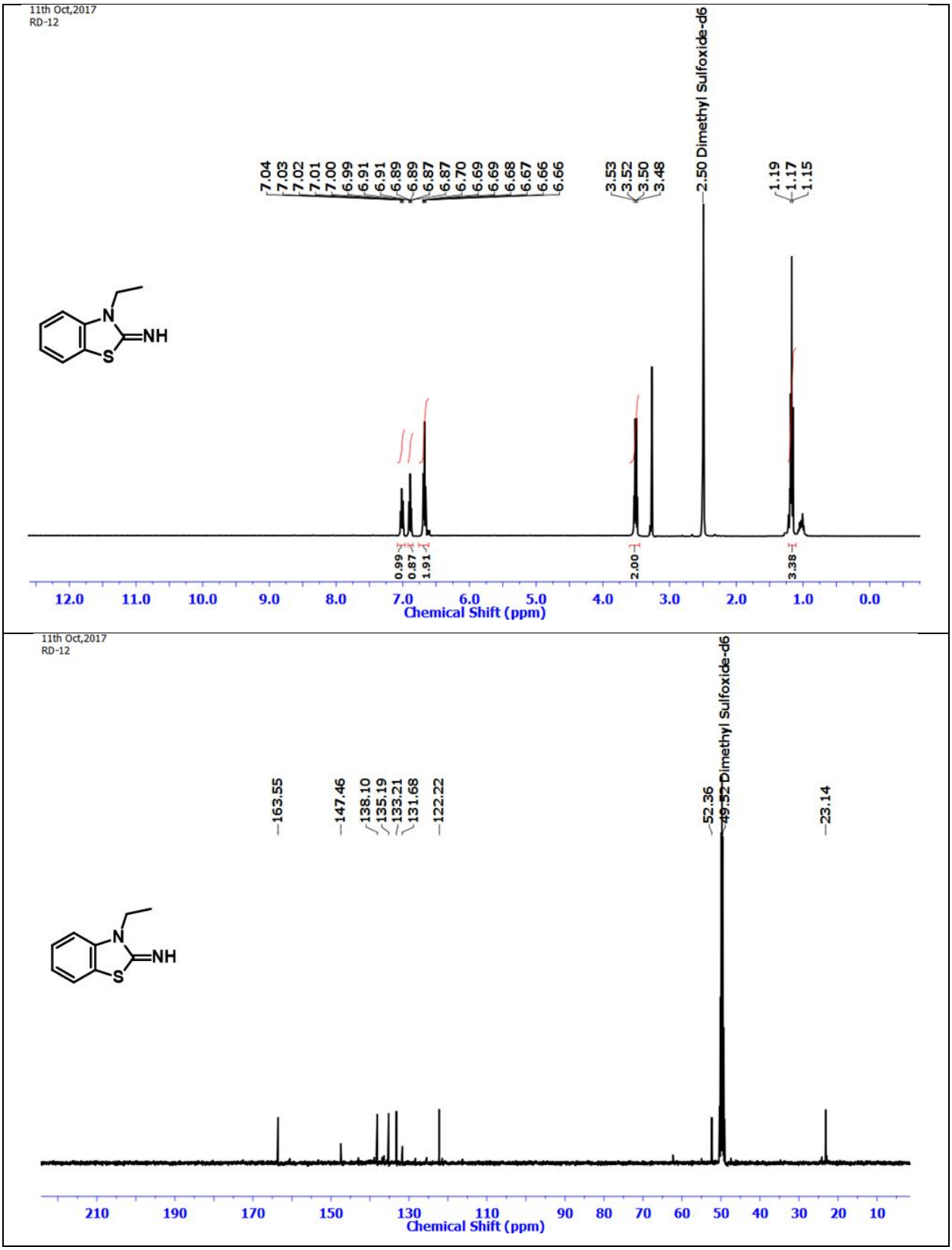


Figure S66: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17b** in DMSO-d_6.

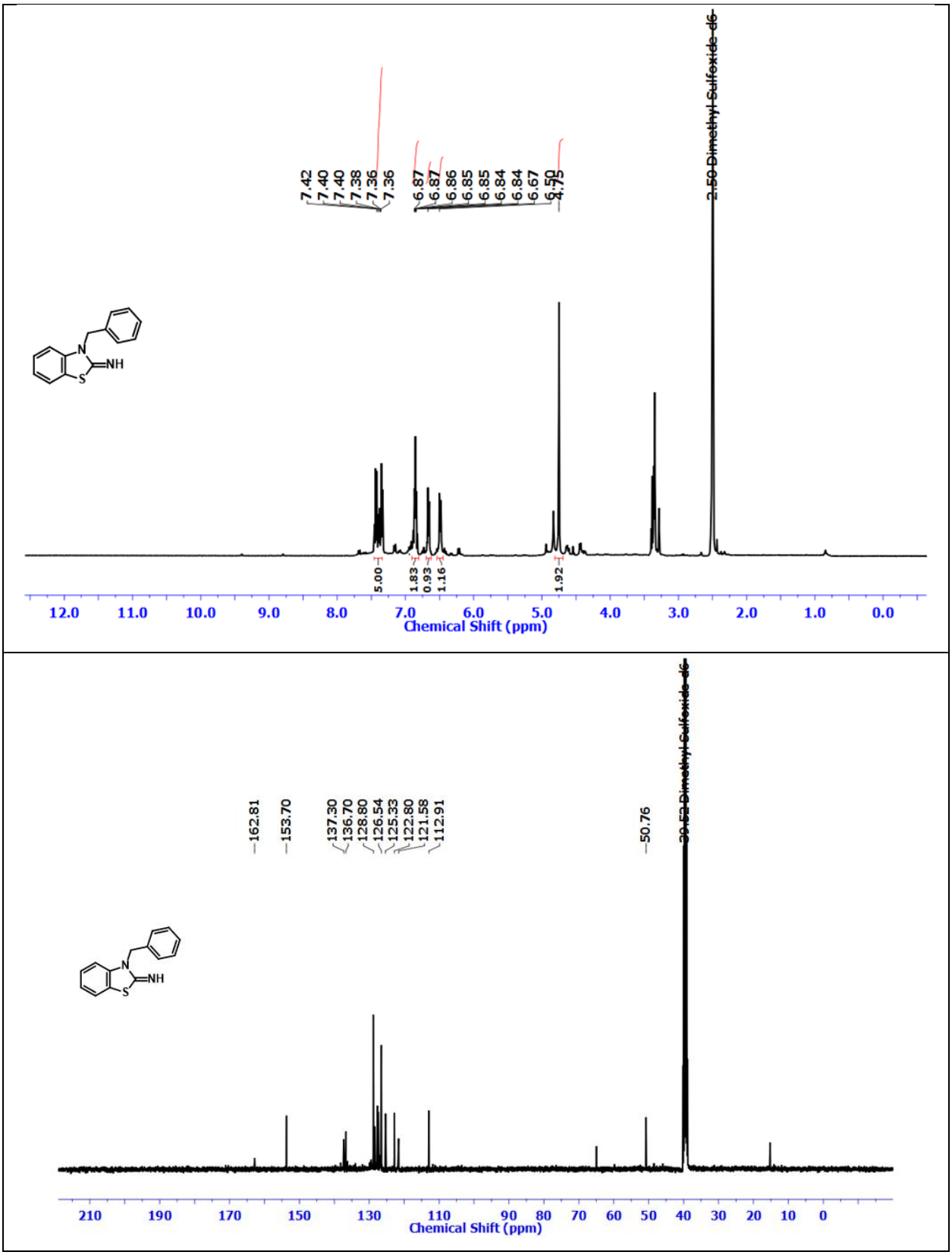


Figure S67: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17c** in DMSO-d_6.

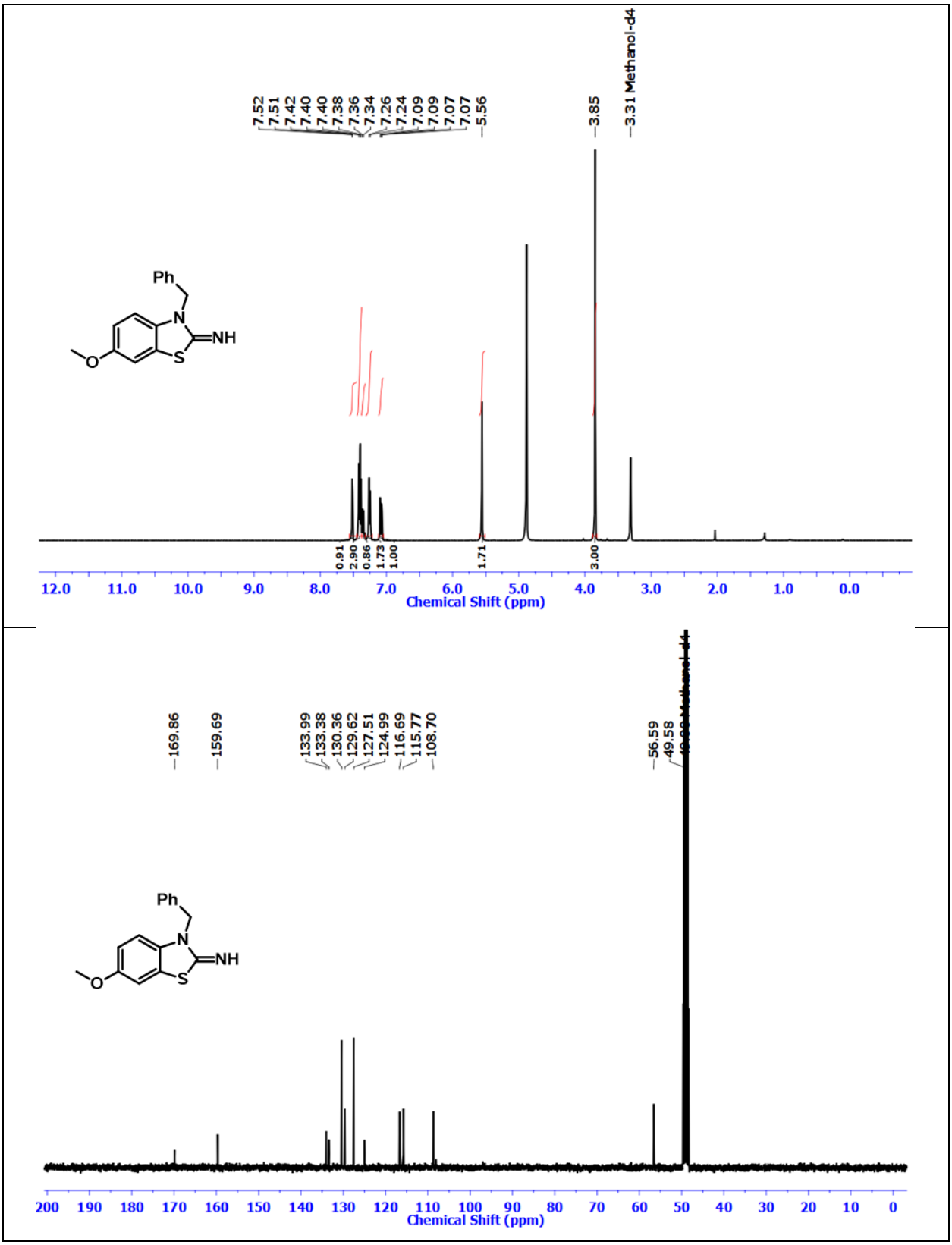


Figure S68: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17f** in MeOH-d_4.

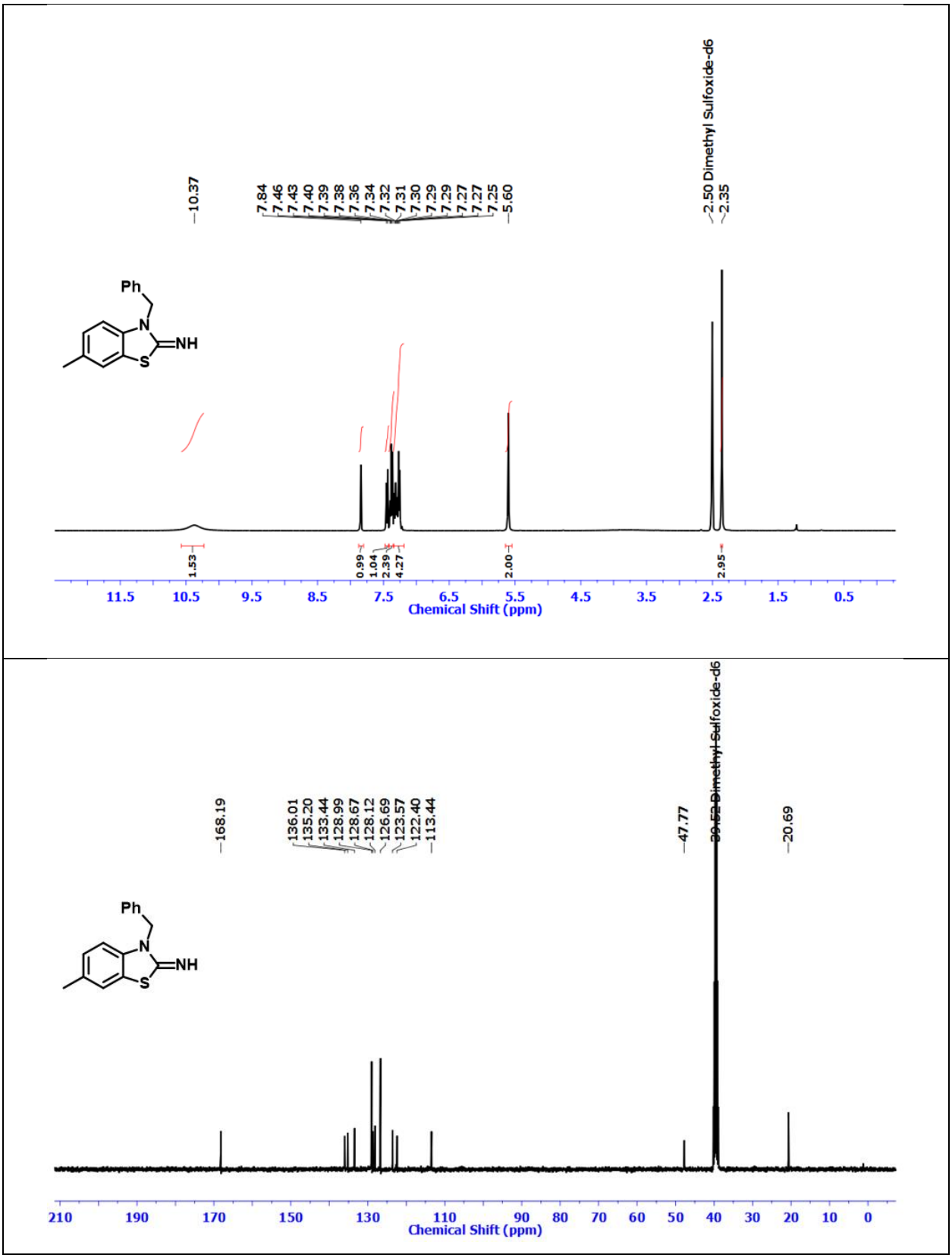


Figure S69: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17e** in DMSO-d_6.

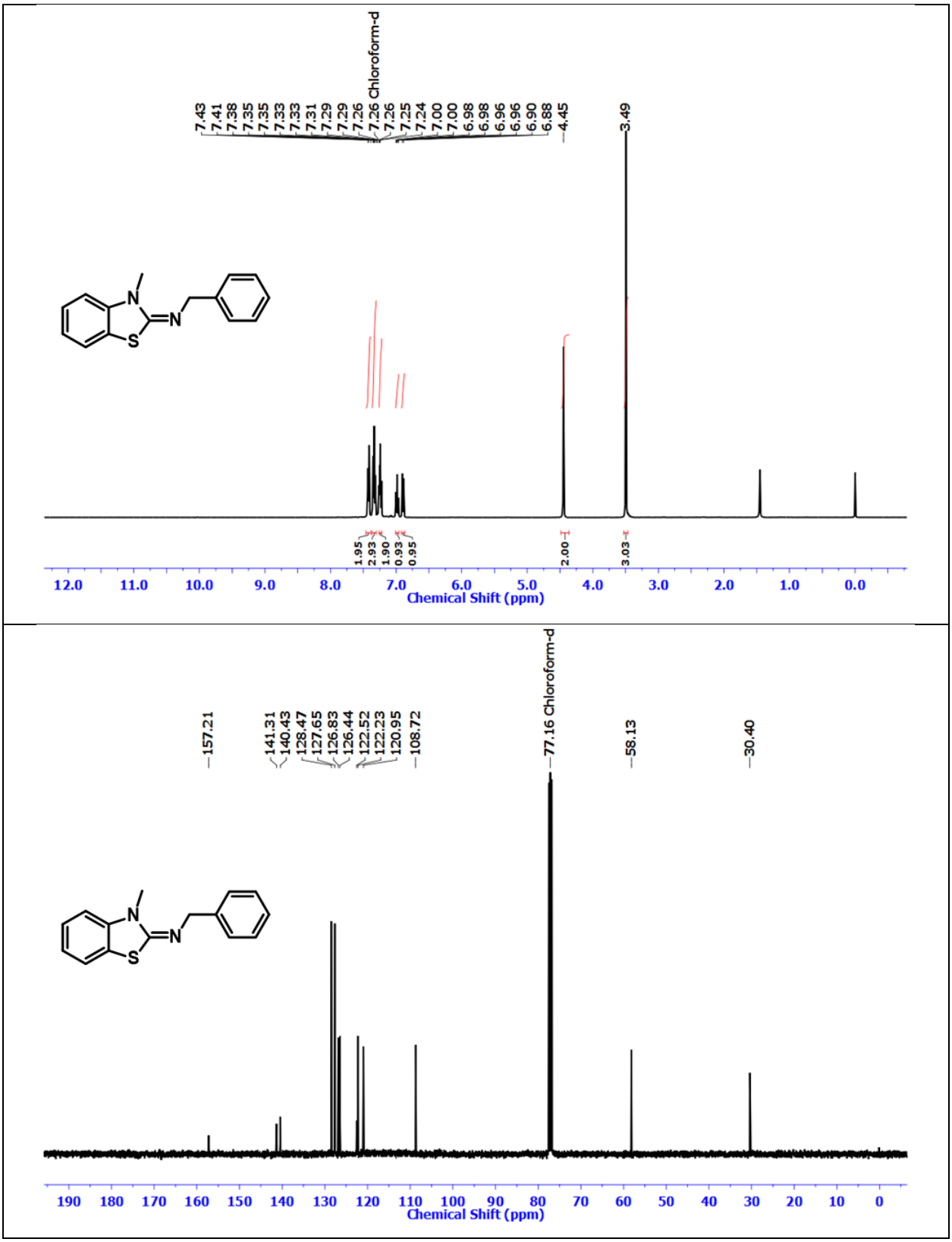


Figure S70: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **23a** in $CDCl_3$.

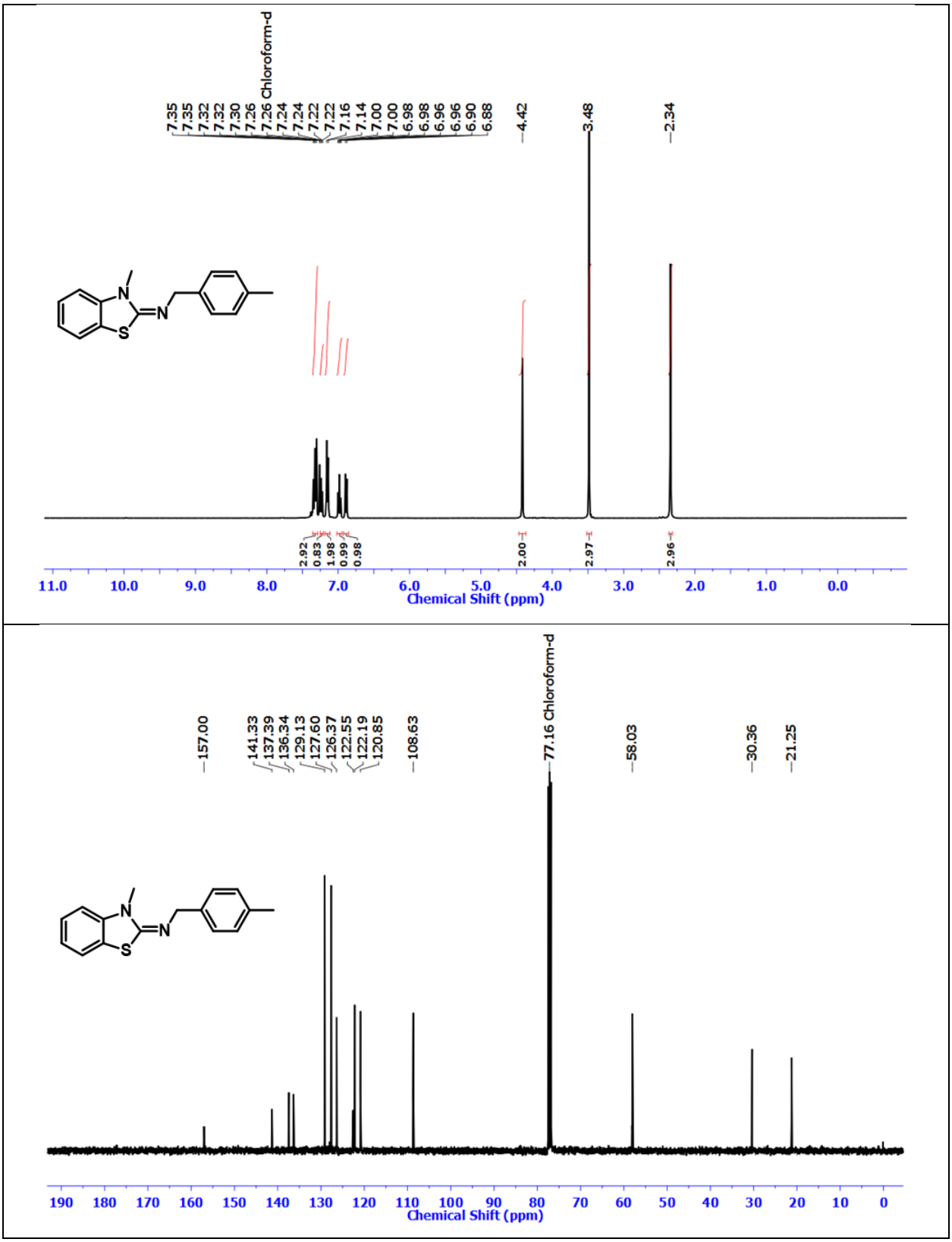


Figure S71: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **23b** in $CDCl_3$.

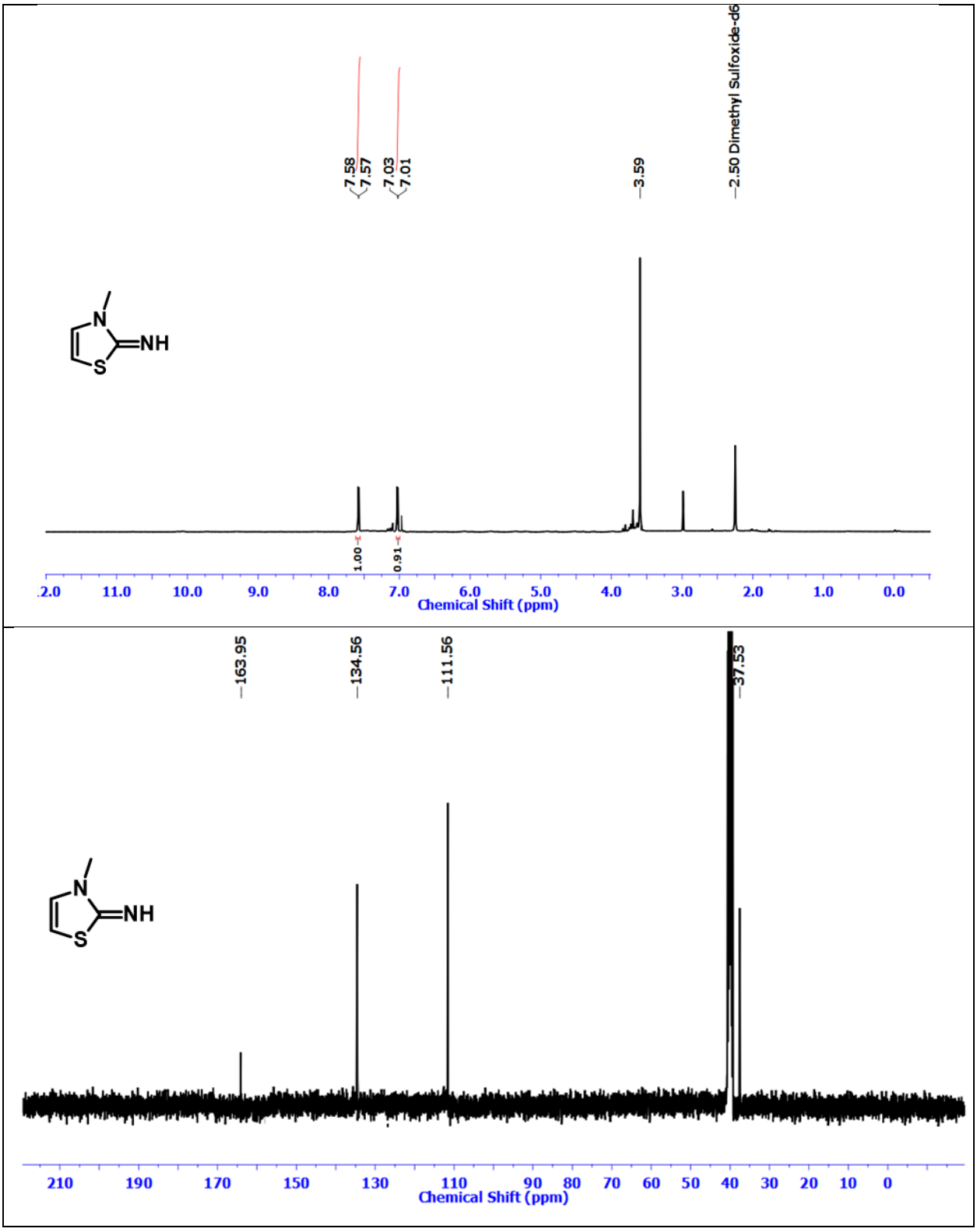


Figure S72: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **19a** in DMSO-d_6.

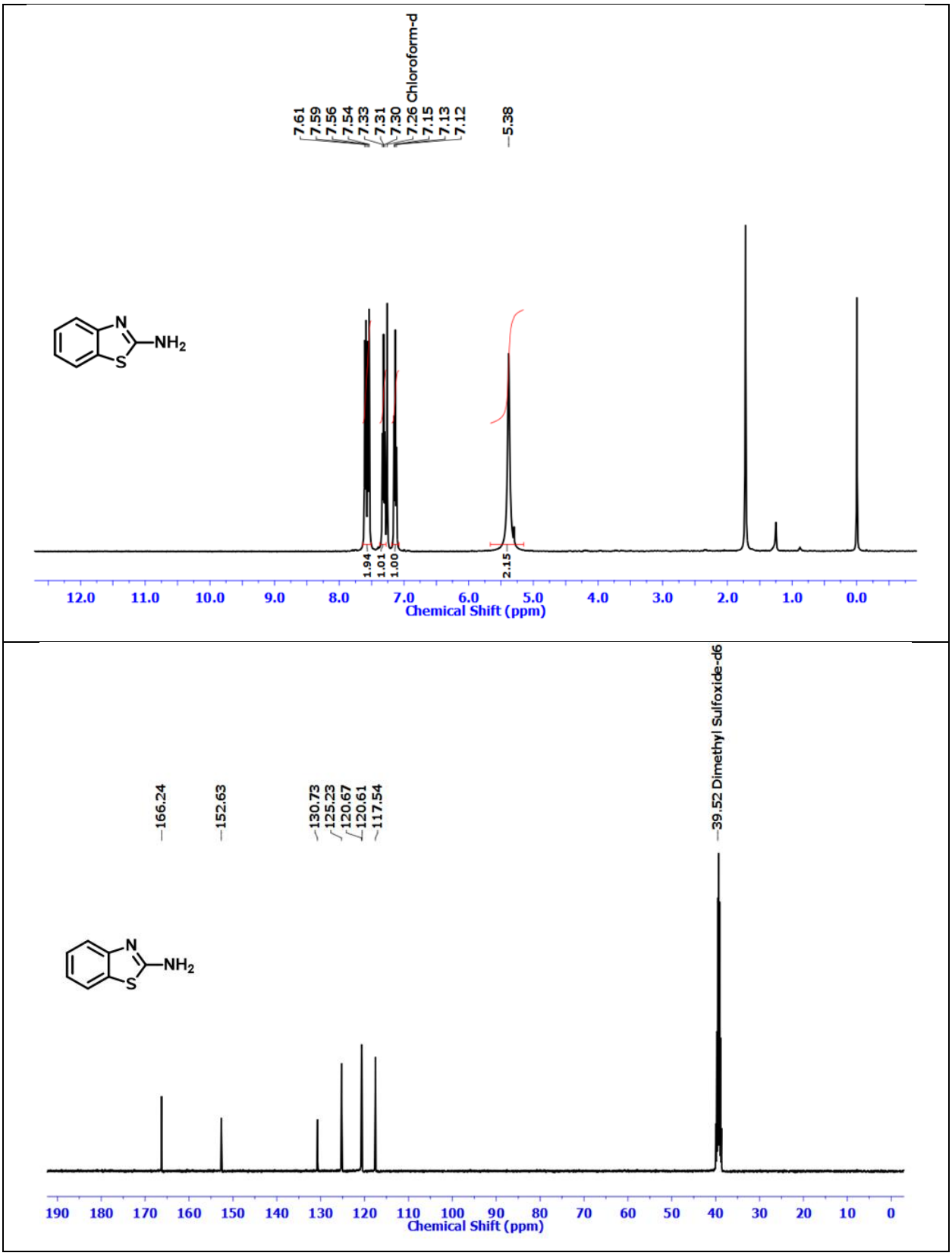


Figure S73: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **27** in DMSO-d_6

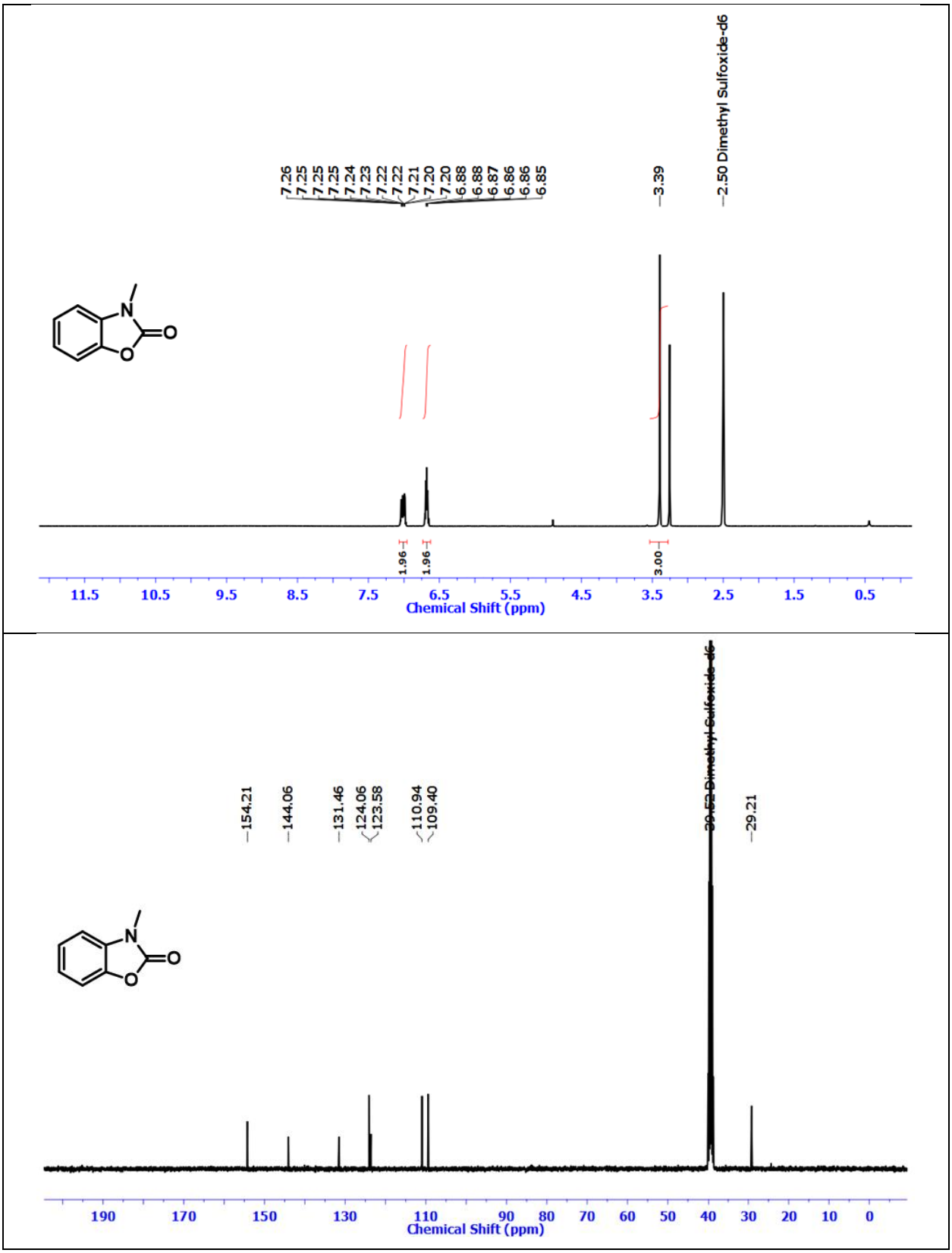


Figure S74: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **22** in DMSO-d_6.

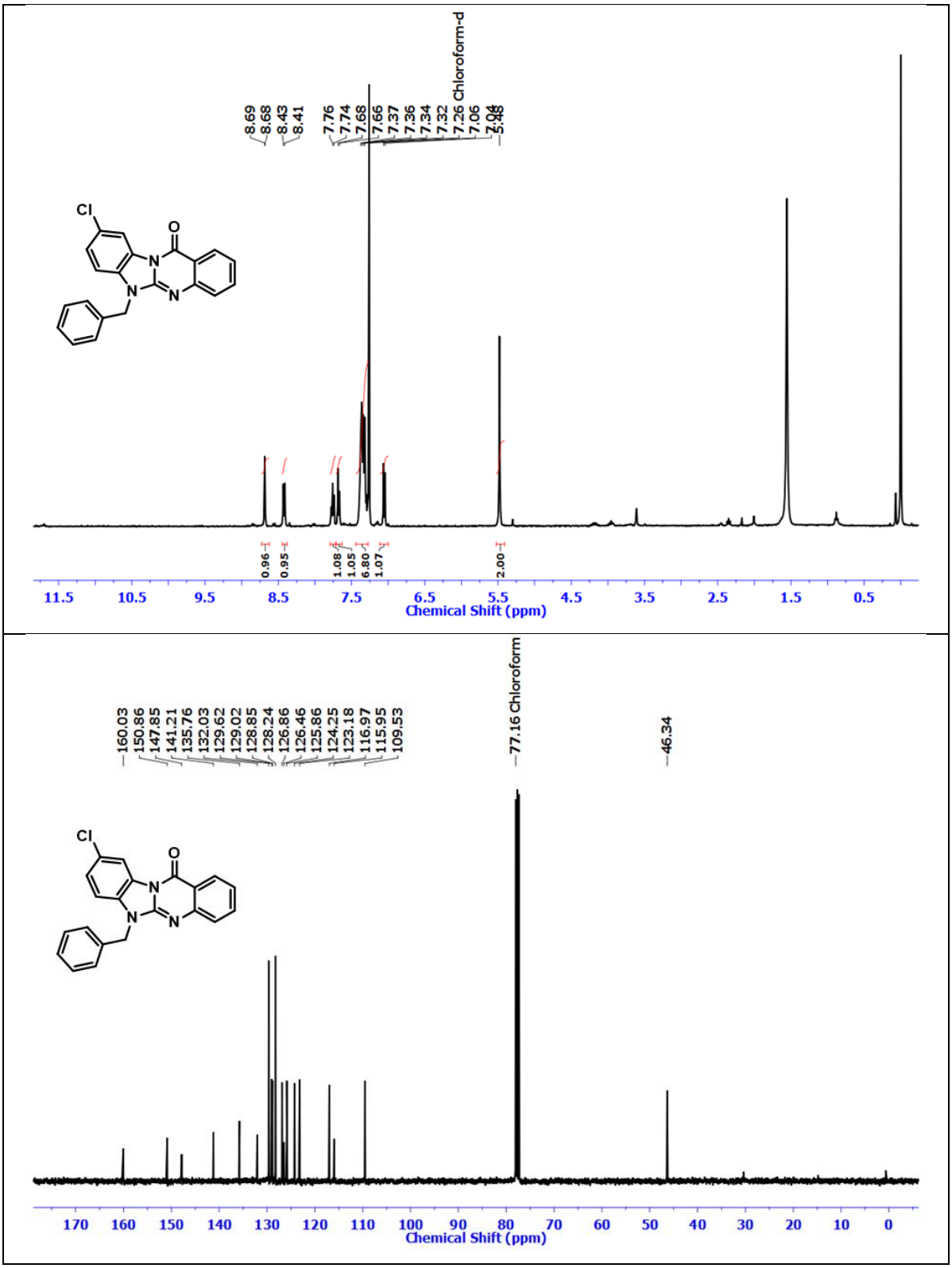


Figure S75: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **31d** in $CDCl_3$-*d*.

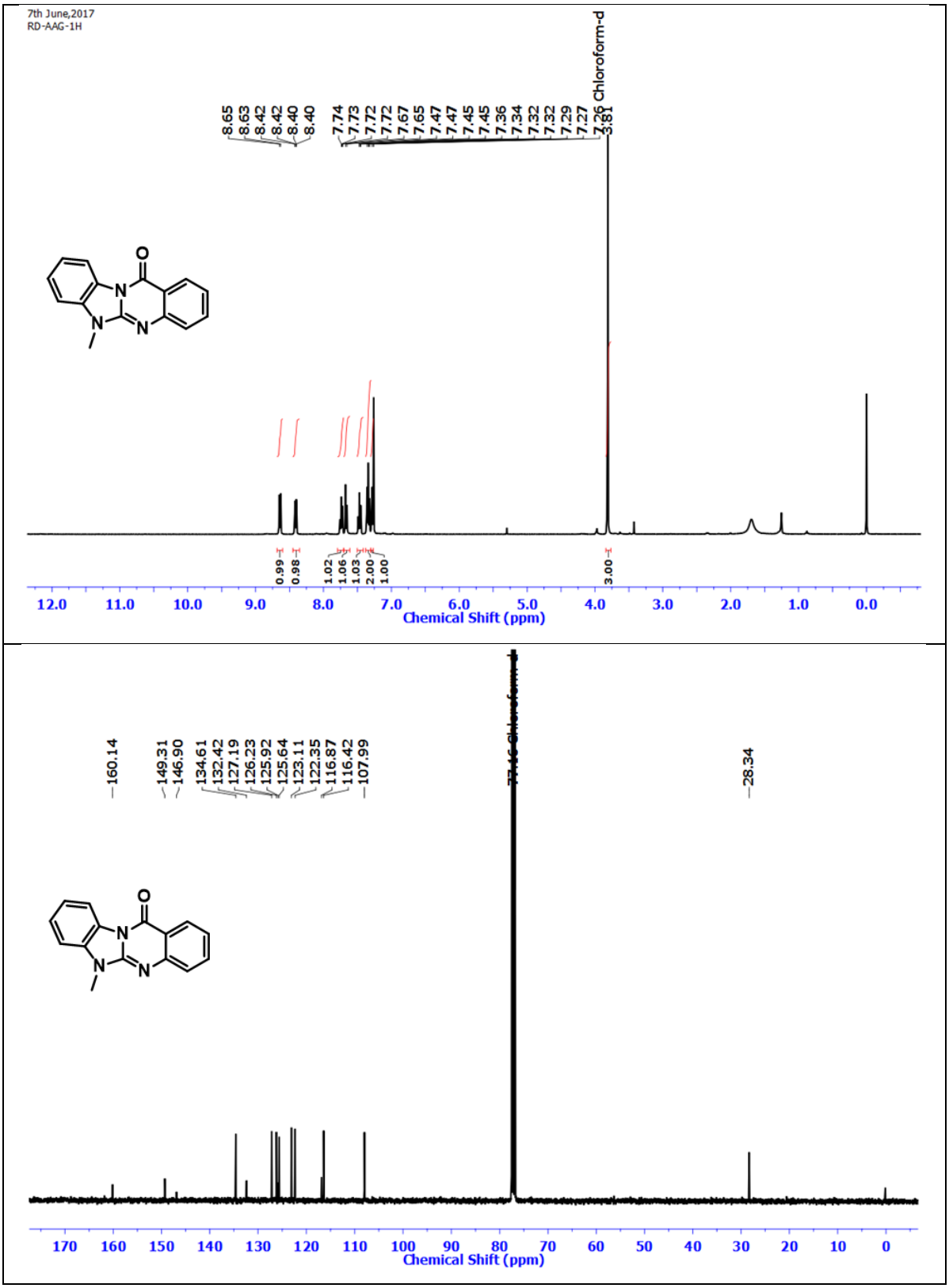


Figure S76: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32a** in $CDCl_3$-*d*.

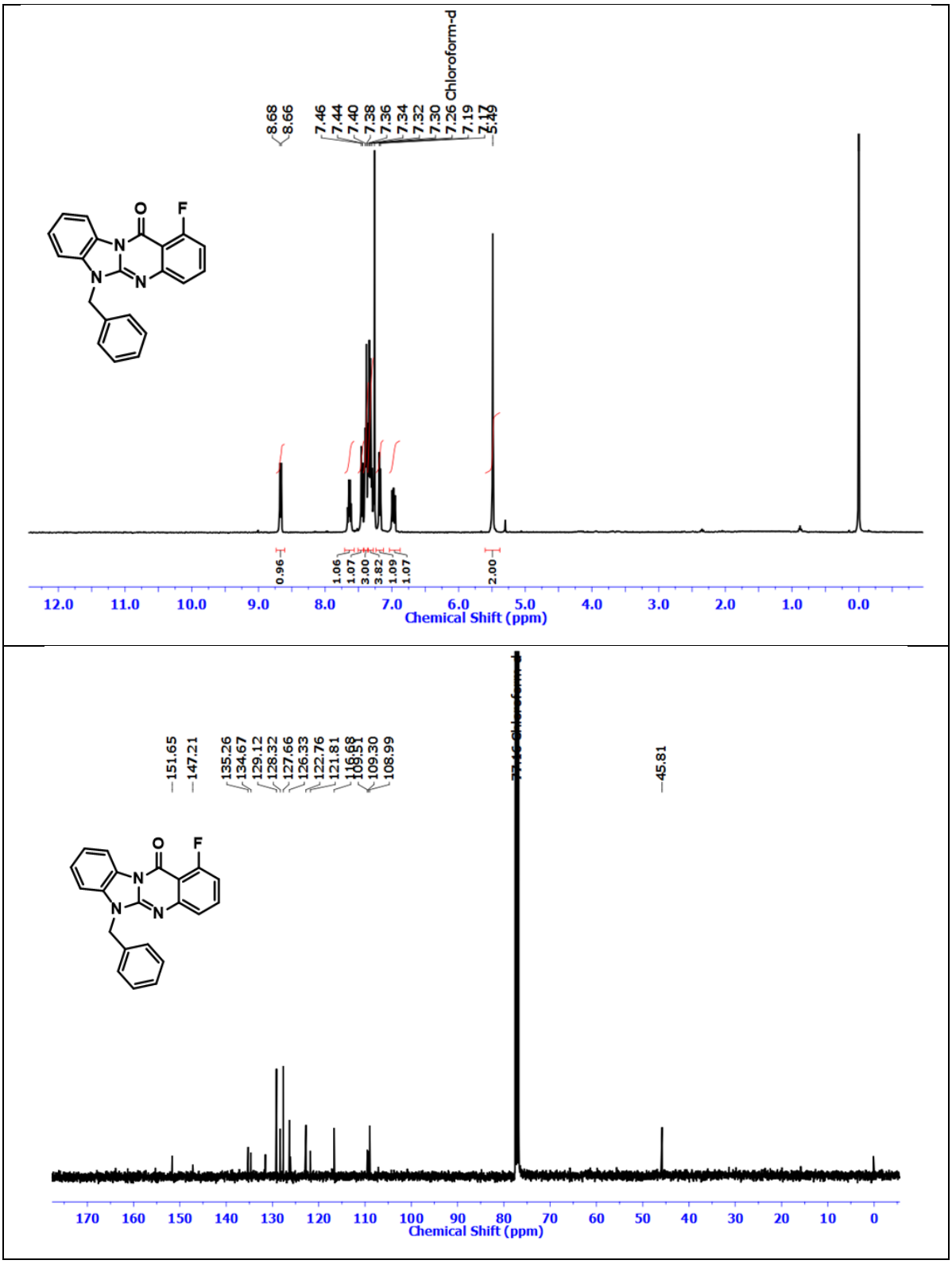


Figure S77: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32j** in $CDCl_3$-*d*.

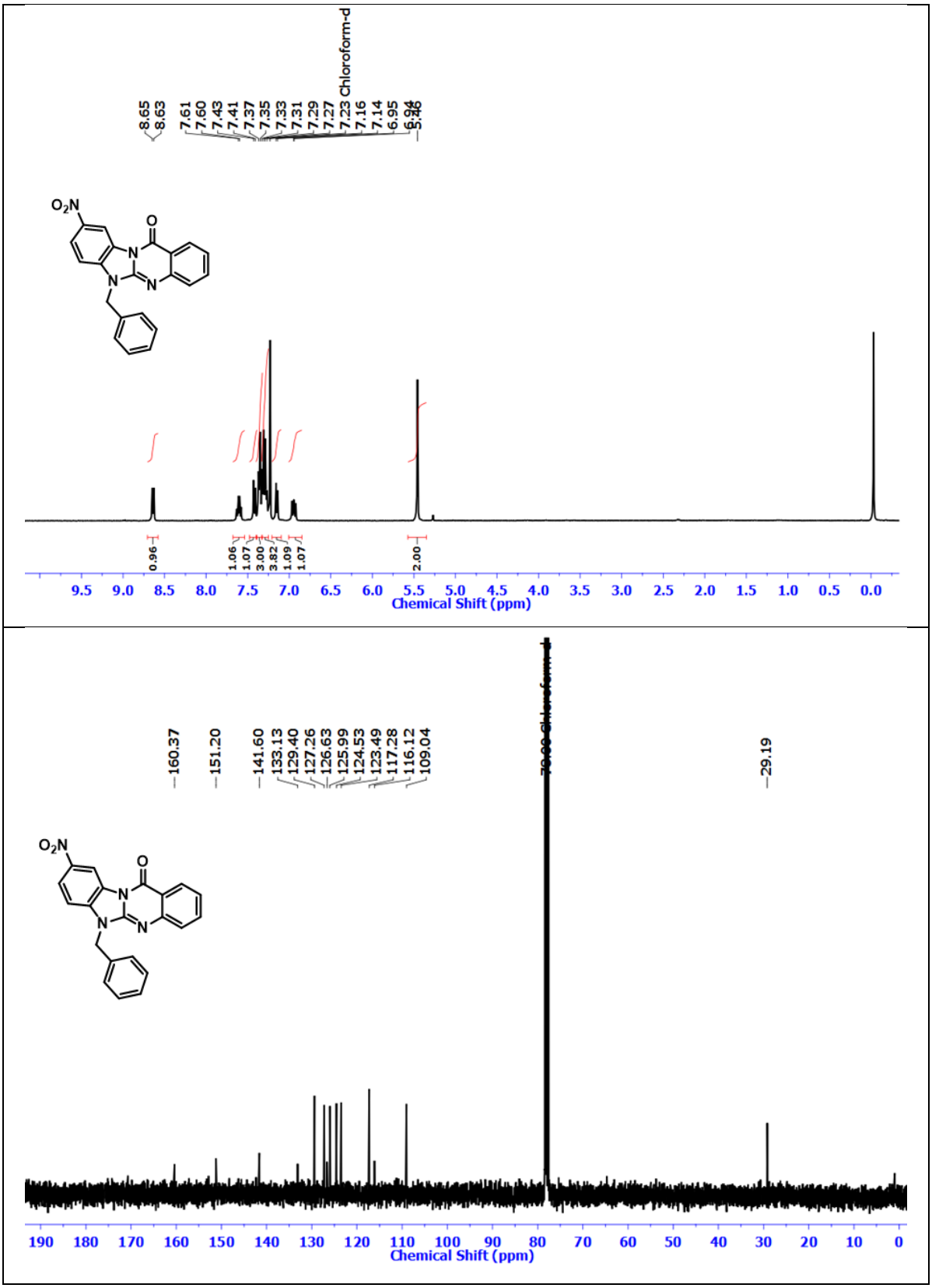


Figure S78: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32i** in $CDCl_3$-*d*.

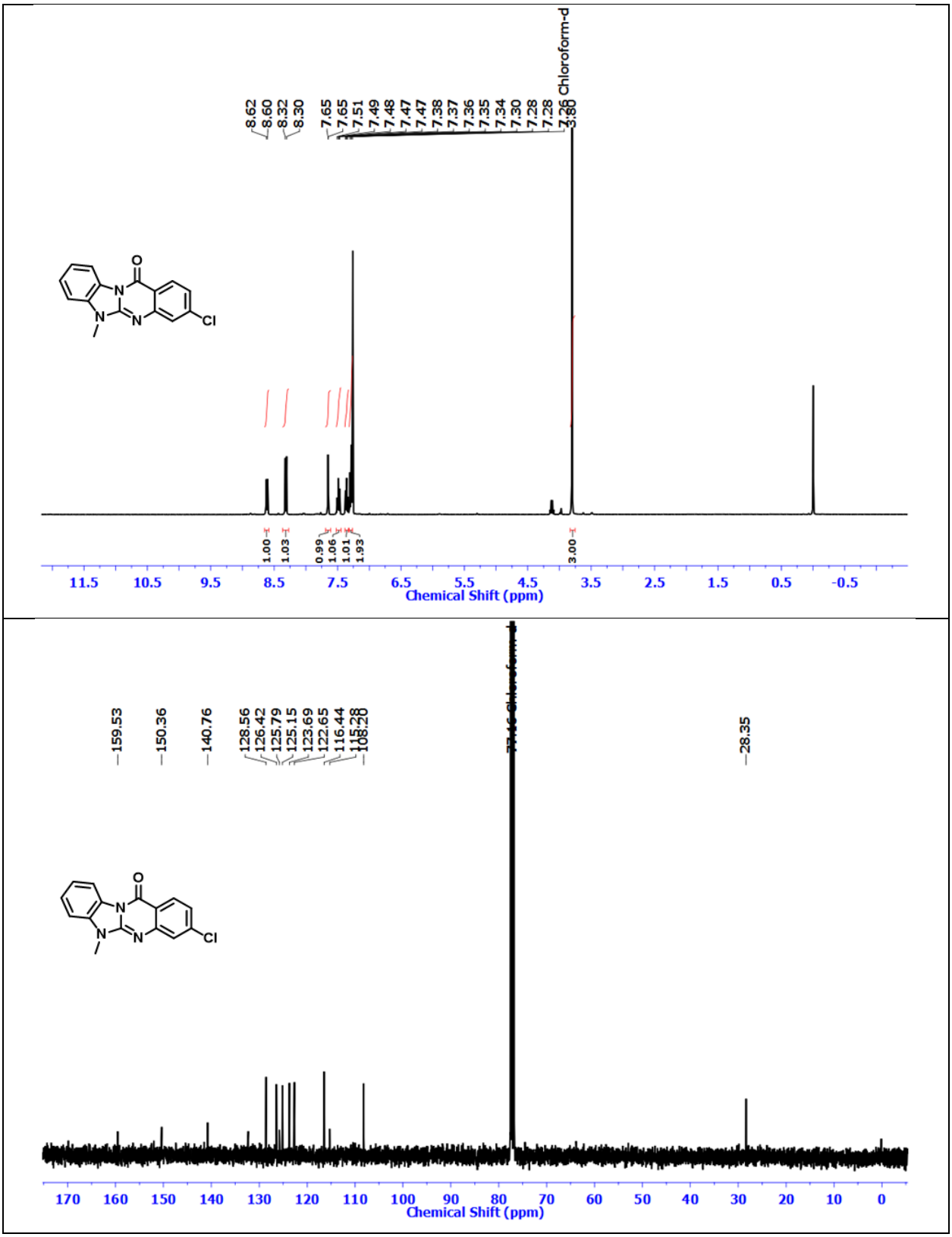


Figure S79: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32k** in $CDCl_3$-*d*.

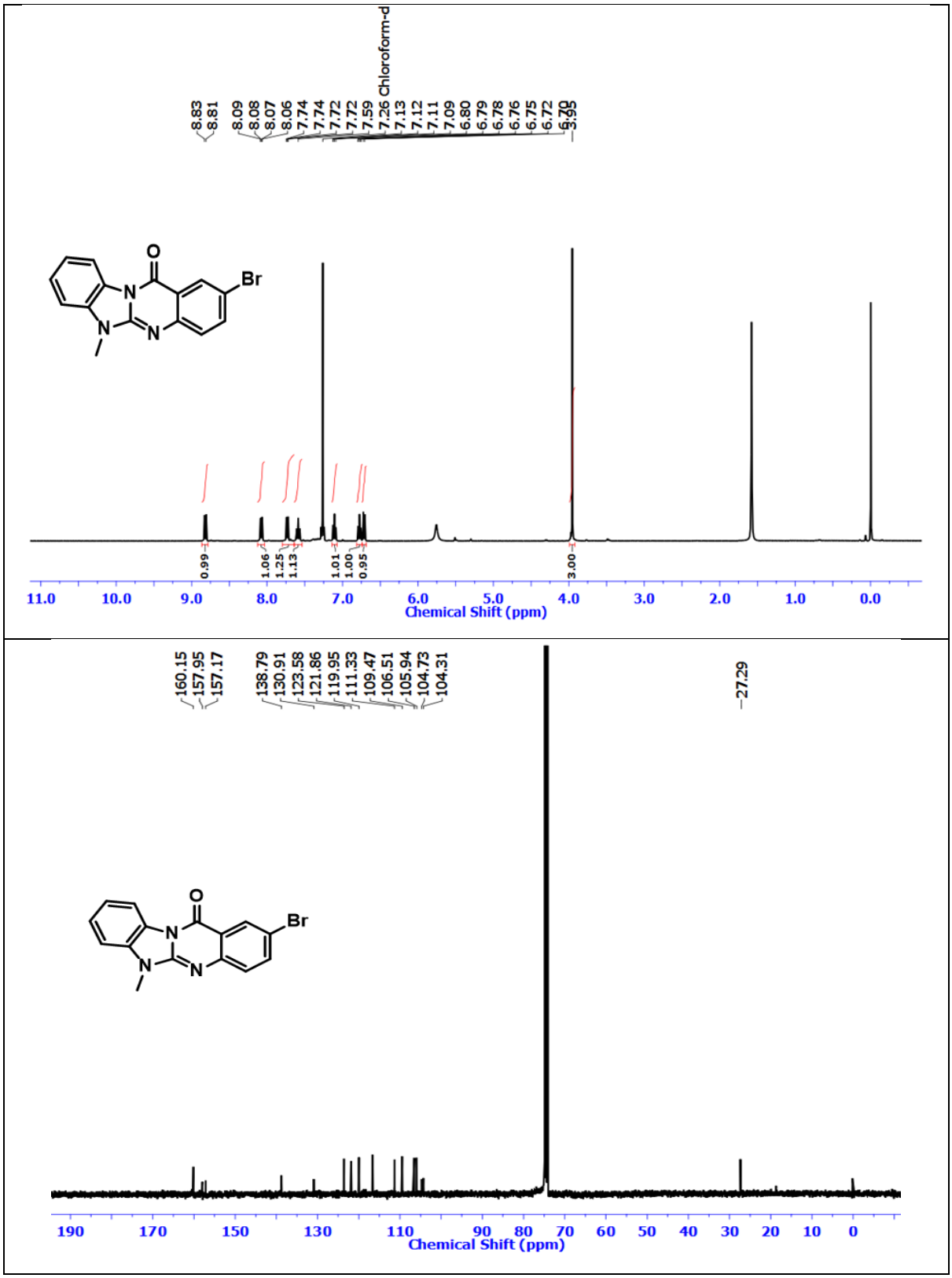


Figure S80: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32b** in $CDCl_3$.*d*.

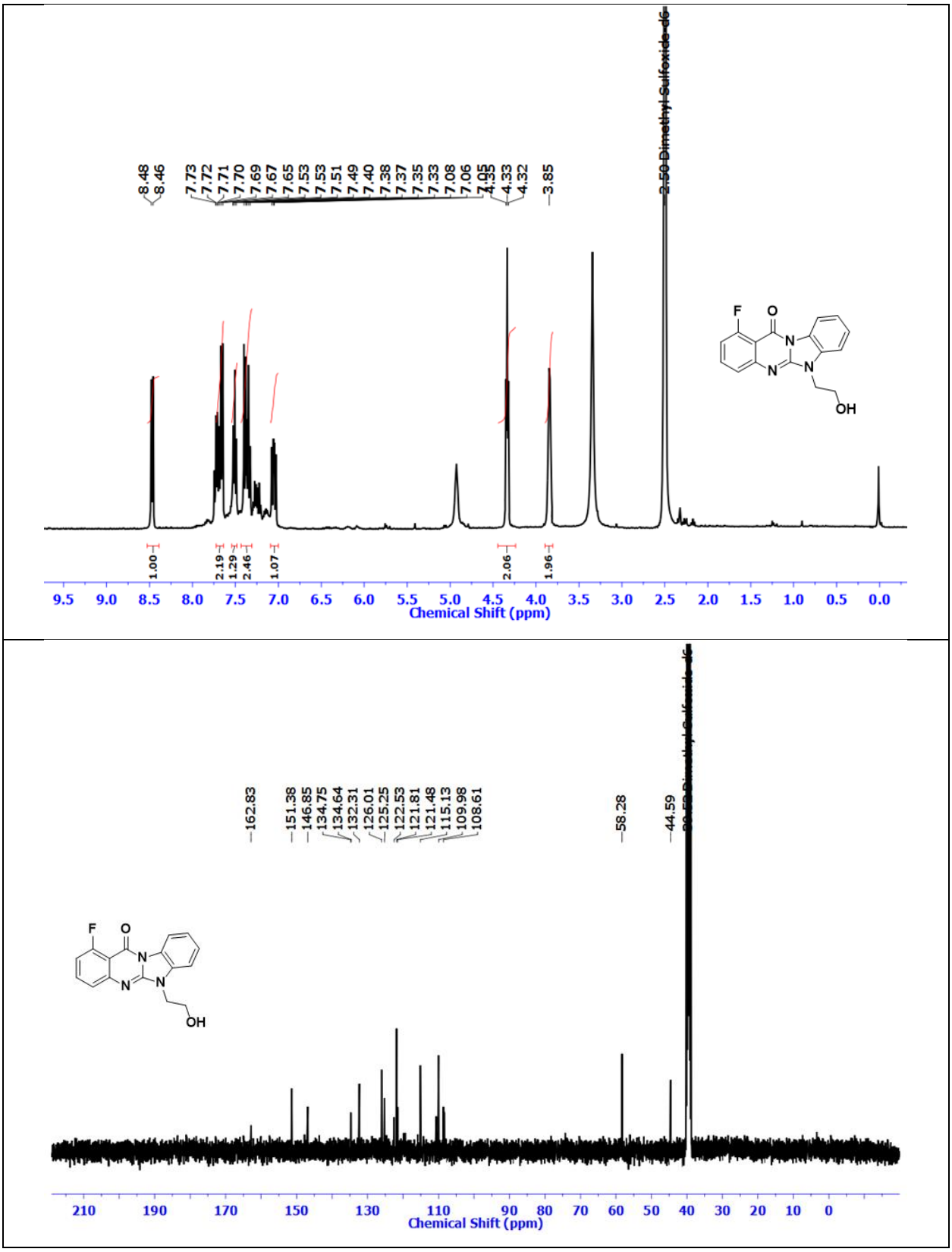


Figure S81: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32g** in DMSO-d_6.

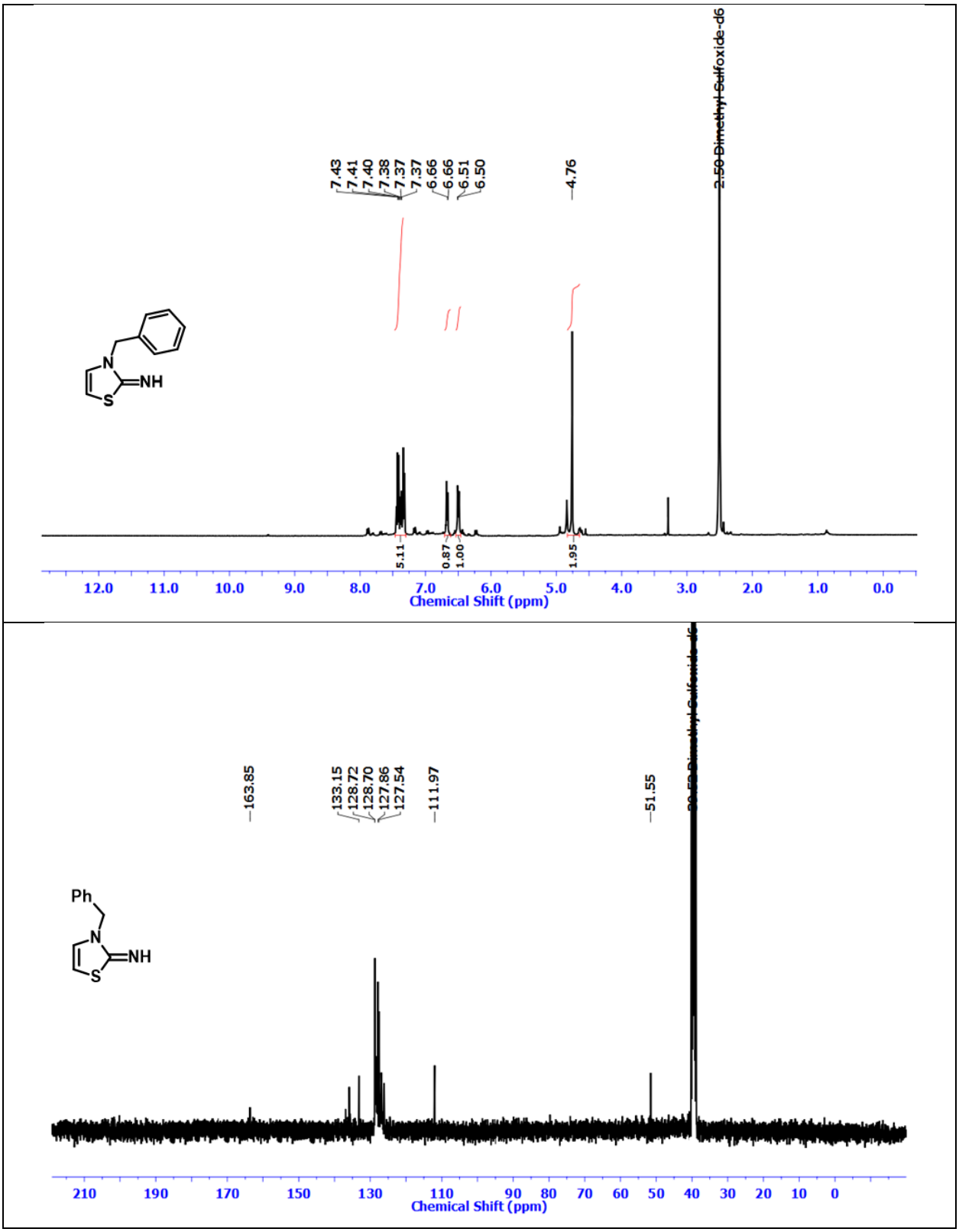


Figure S82: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **19b** in DMSO-d_6.

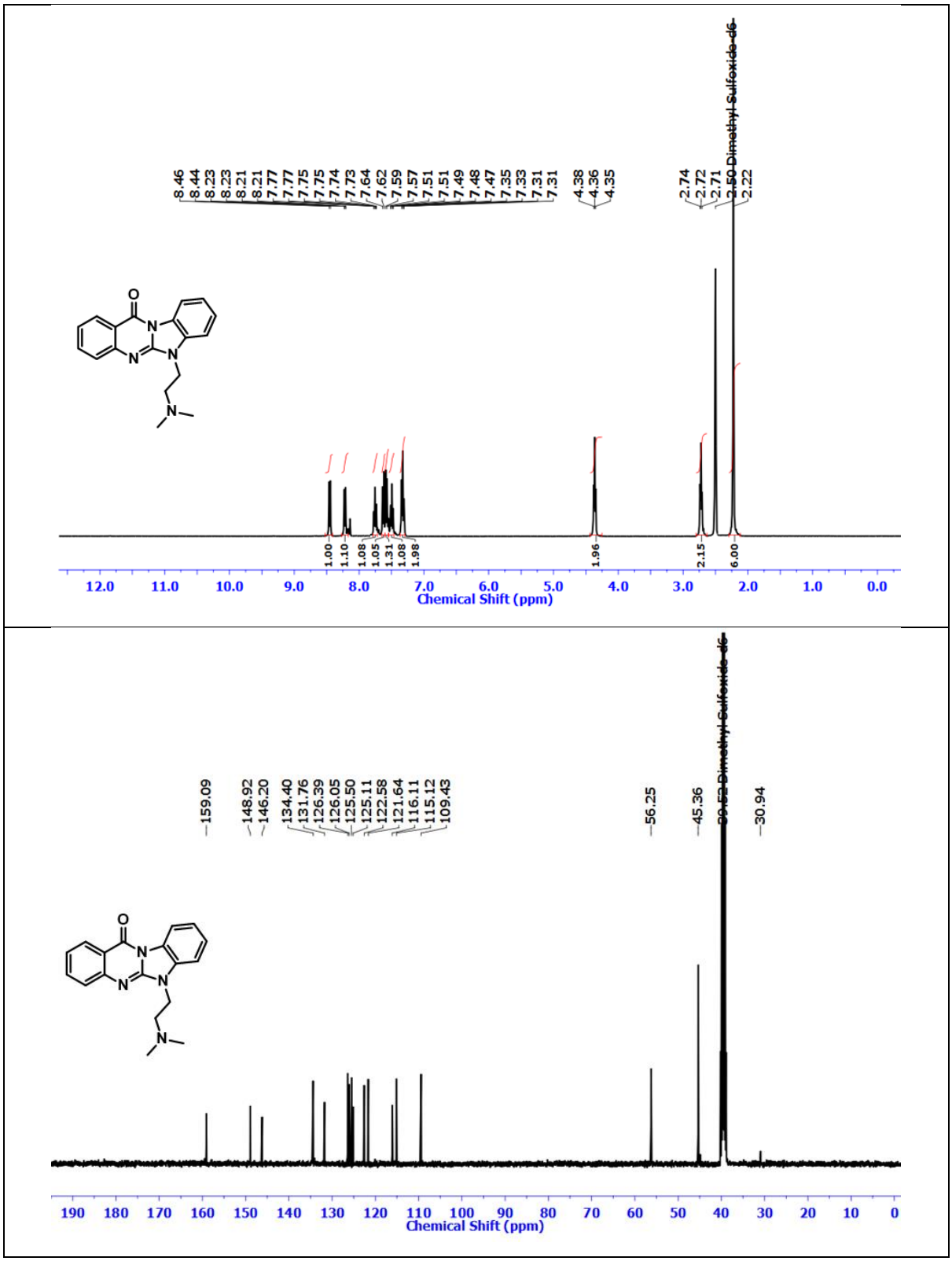


Figure S83: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32e** in DMSO-d_6.

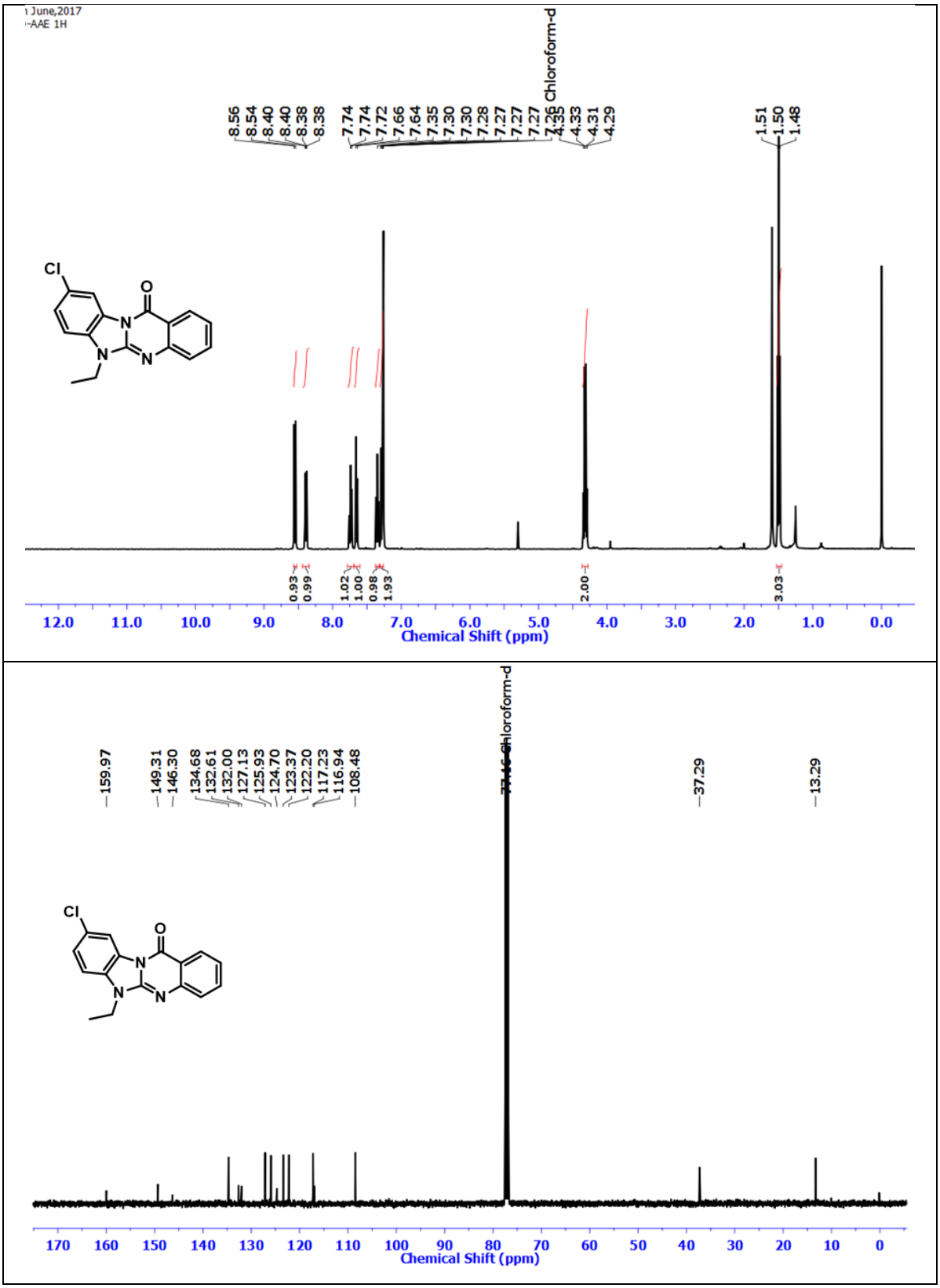


Figure S84: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32c** in $CDCl_3$-*d*.

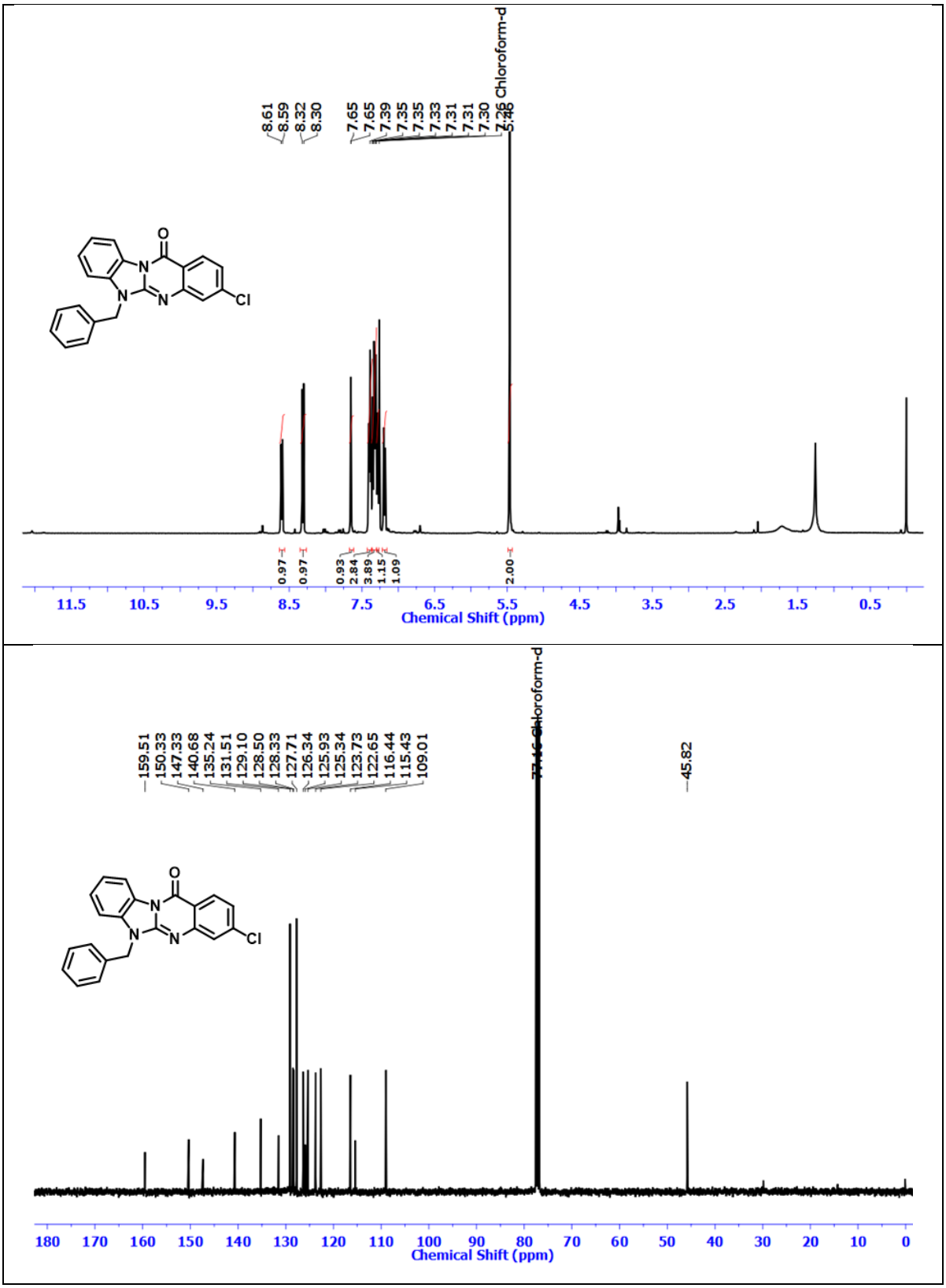


Figure S85: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32h** in $CDCl_3$-*d*.

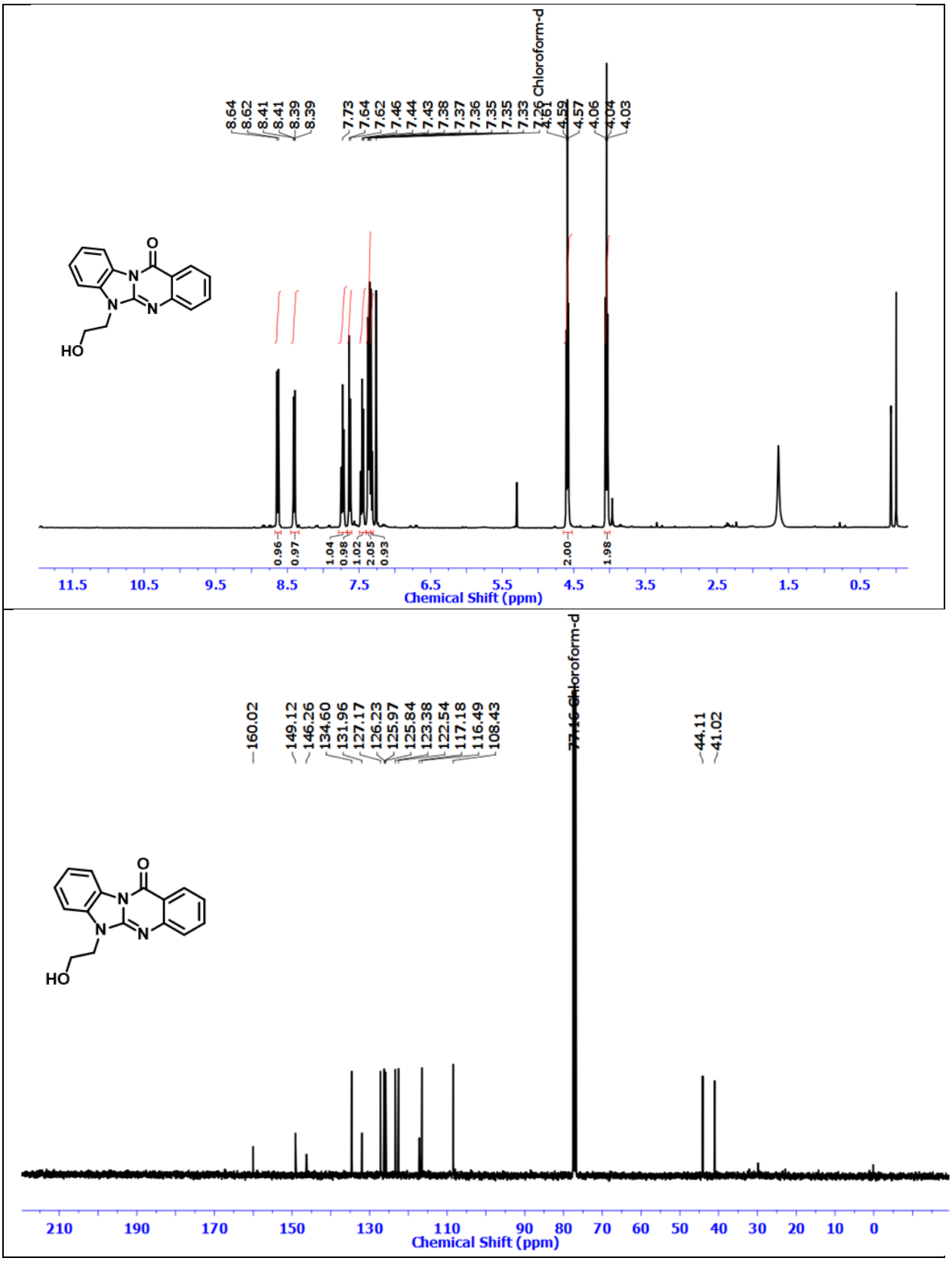


Figure S86: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **32f** in $CDCl_3$-*d*.

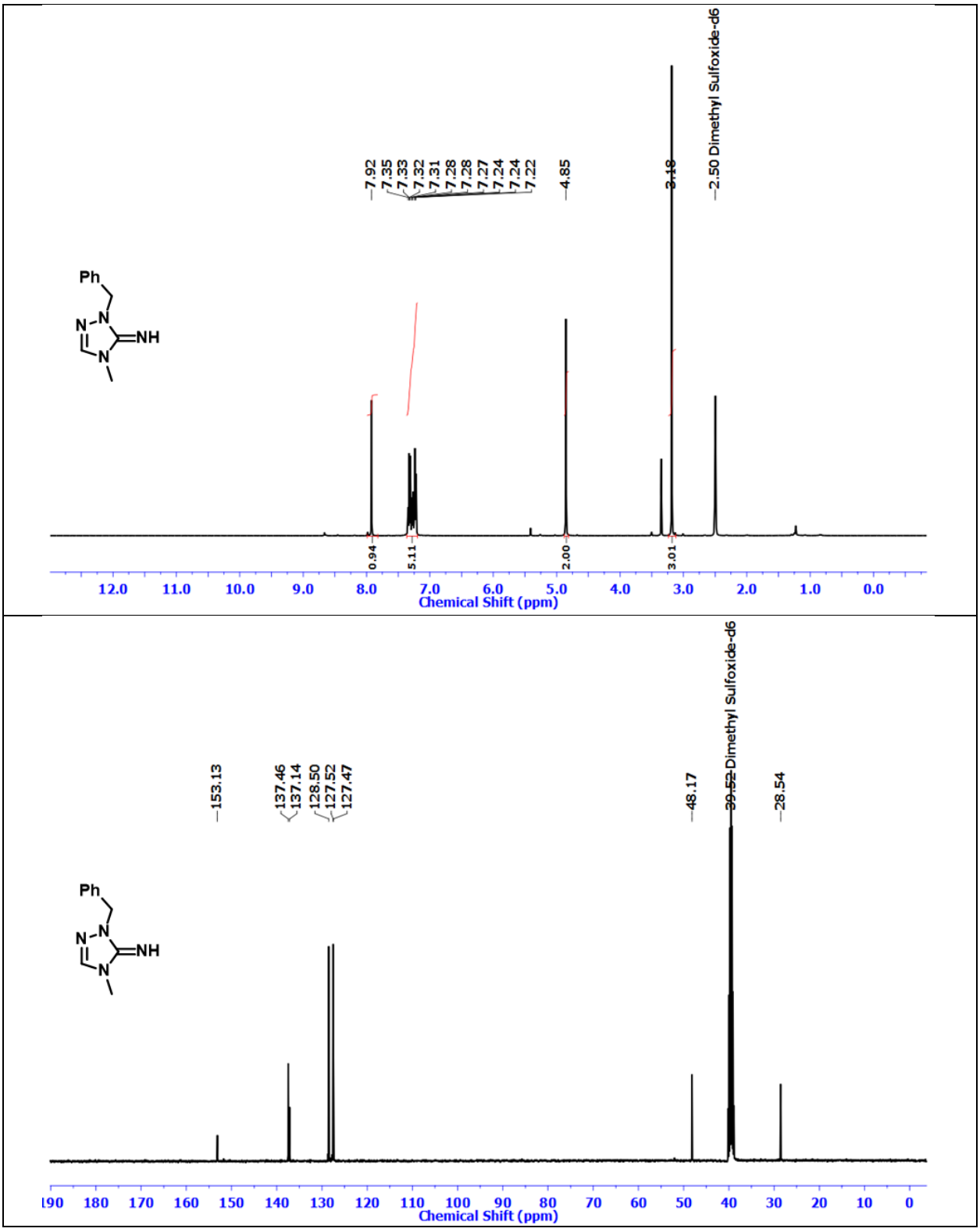


Figure S87: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **21** in DMSO-d_6.

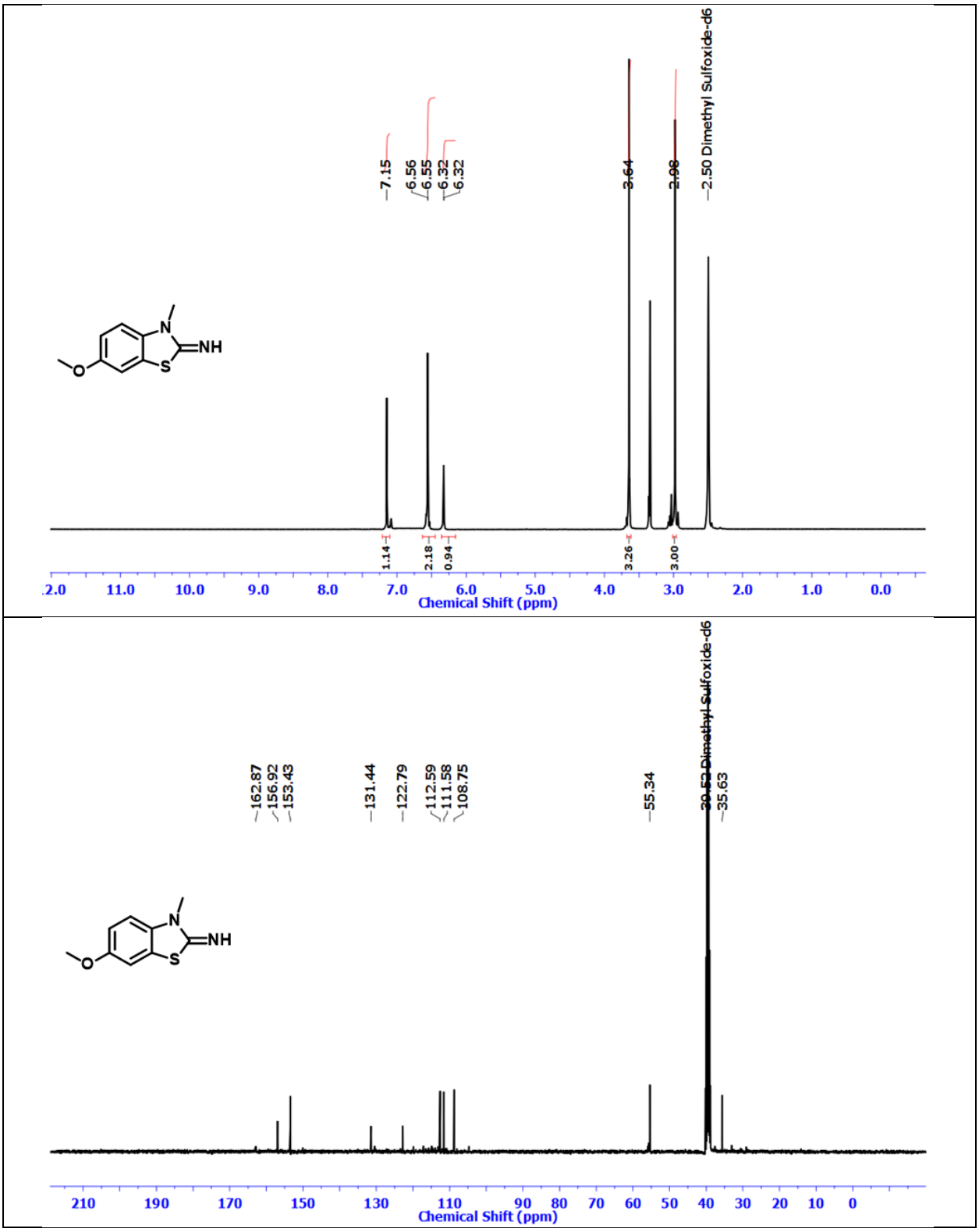


Figure S88: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **17d** in DMSO-d_6.

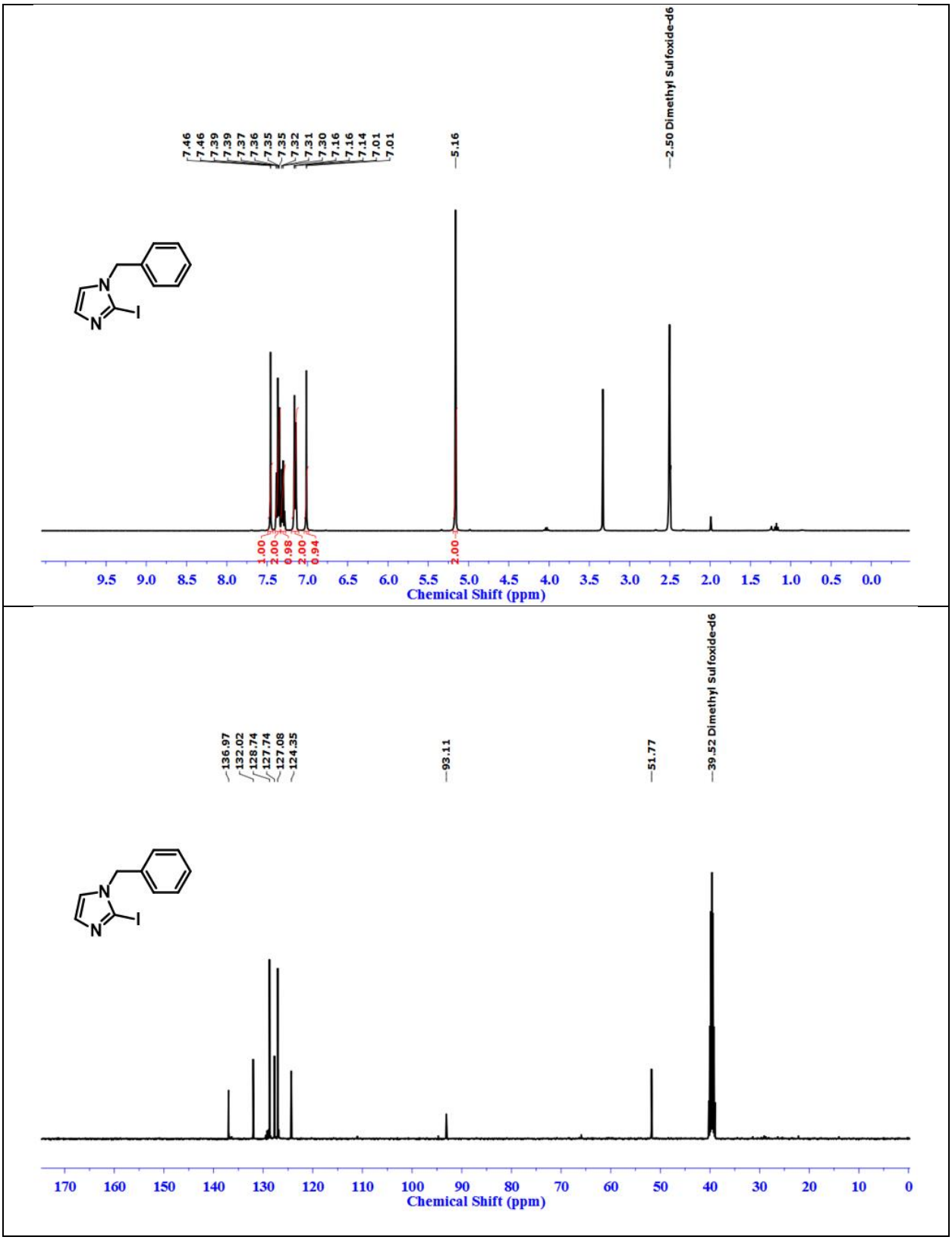


Figure S89: ^{1}H NMR spectrum and ^{13}C NMR spectrum of **15c** in DMSO-d_6

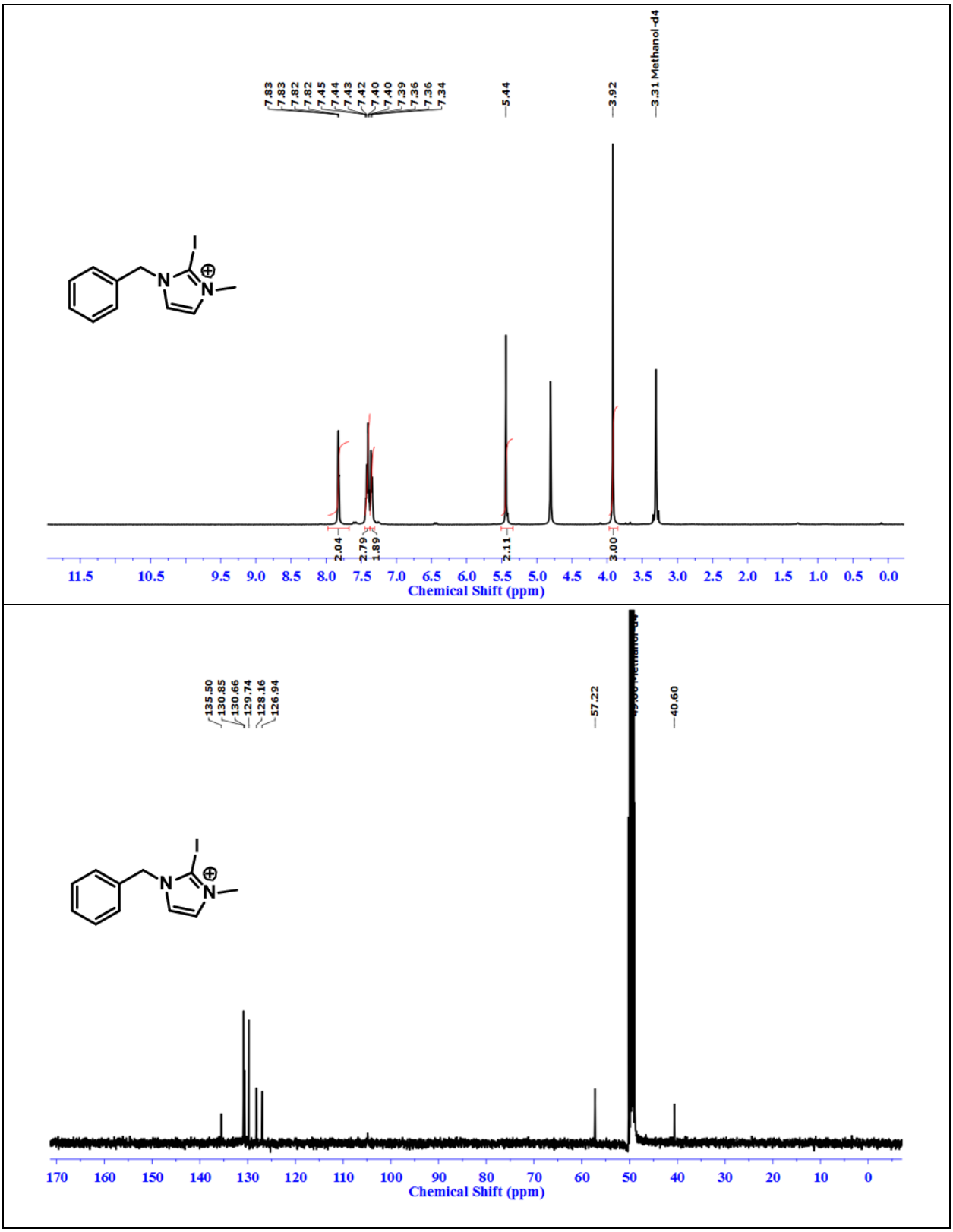


Figure S90: ^{1}H NMR spectrum in DMSO-d_6 and ^{13}C NMR spectrum in MeOH-d_4 of **15a.**