Electronic Supplementary Material (ESI) for RSC Advances.

Cytotoxic Metabolites from the Endophytic Fungus *Chaetomium globosum* 7951

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Supporting Information

List of Content

EXPERIMENTAL SECTION

General experimental procedures

Optical rotations were measured using a Rudolph Research Autopol III automatic polarimeter. UV, CD, and IR spectra were recorded using a Cary 300 spectrometer, a JASCO J-815 CD spectrometer, and a Nicolet 5700 FT-IR spectrometer (FT-IR microscope transmission), respectively. ^{1}H and ^{13}C NMR spectra were obtained at 600 MHz and 150 MHz, respectively, using a Bruker-AVIIIHD-600 spectrometer with solvent peaks used as references. HR-ESIMS data were measured using an AB SCIEX QTOF MS (QSTAR Elite). ESIMS data were measured using an Agilent 1100 series LC/MSD mass spectrometer. Column chromatography was performed using silica gel (200–300 mesh, Qingdao Marine Chemical Inc., China). HPLC separation was performed using an Agilent 1200 series (quaternary pump, autosampler, diode array detector) with a Shiseido Capcell-Pak C_{18} MGII, 5 μm, 250 × 10 mm column. TLC was performed using glass precoated silica gel GF_{254} plates (Qingdao Marine Chemical Inc., Qingdao, China).

NMR chemical shifts and ORs calculation of compound 3.

Conformational analysis of the (3*S*,6*S*)-**3** and (3*R*,6*S*)-**3** (Fig. S1) were carried out via Monte Carlo searching with the MMFF94s molecular mechanics force field using the spartan 14 software.[1] 16 of (3*S*,6*S*)-**3** and 30 of (3*R*,6*S*)-**3** geometries having relative energies within 4 kcal/mol were optimized using DFT at the B3LYP/6-31+G (d, p) level in vacuum with the Gaussian 09 program, respectively.[2] NMR chemical shifts calculation for those B3LYP/6-31+G (d, p)-optimized conformers with their Boltzmann distribution (>1%) [(3*S*,6*S*)-**3**: Table S1; (3*R*,6*S*)-**3**: Table S2] were carried out at PCM/mPW1PW91/6-311+G (d, p) level in DMSO with GIAO method. After Boltzmann weighing of the calculated chemical shift of each isomers, the DP4+ parameters were calculated using the excel file, which was provided by Ariel M. Sarotti.[3]

In addition, those stable conformers of (3*S*,6*S*)-**3** with their Boltzmann distribution (>1%) also were carried out at the B3LYP/DGDZVP level in the methanol for OR computation. The final OR values of (3*S*,6*S*)-**3** was obtained according to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG). The theoretically calculated OR value of (3*S*,6*S*)-**3** (+56.1, Table S8) was in good agreement with the experimental OR value of **3** (+80.0) in methanol.

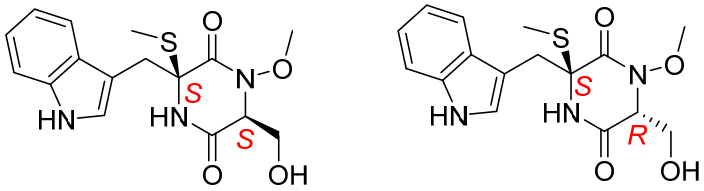

Figure S1. Proposed the calculated structure of **3**

Table S1. Free energies (Δ*G*), and Boltzmann distribution abundances of conformers of (3*S*,6S)-**3**

Conf.	B3LYP/6-31+G(d, p) Gibbs free energy (298.15 K)		
	G (Hartree)	ΔG (Kcal/mol)	Boltzmann Distribution
C1	-1484.221198	2.196	0.01
C2	-1484.221255	2.161	0.01
C3	-1484.221693	1.886	0.017
C4	-1484.223411	0.808	0.102
C5	-1484.224698	0.000	0.398
C6	-1484.219509	3.256	0
C7	-1484.217677	4.406	0
C8	-1484.219121	3.500	0
C9	-1484.221061	2.282	0
C10	-1484.223898	0.502	0.171
C11	-1484.224244	0.285	0.246
C12	-1484.221052	2.288	0
C13	-1484.216574	5.098	0
C14	-1484.222356	1.470	0.033
C15	-1484.215629	5.691	0
C16	-1484.221444	2.042	0.013

Table S2. Free energies (Δ*G*), and Boltzmann distribution abundances of conformers of (3*R*,6S)-**3**

Conf.	B3LYP/6-31+G(d, p) Gibbs free energy (298.15 K)		
	G (Hartree)	ΔG (Kcal/mol)	Boltzmann Distribution
C1	-1484.221999	2.541	0
C2	-1484.222998	1.914	0.012
C3	-1484.225876	0.108	0.244
C4	-1484.224187	1.168	0.041
C5	-1484.223606	1.532	0.022
C6	-1484.222573	2.181	0
C7	-1484.226048	0.000	0.293
C8	-1484.222847	2.009	0
C9	-1484.223604	1.534	0.022
C10	-1484.223367	1.682	0.017
C11	-1484.224831	0.764	0.081
C12	-1484.221535	2.832	0
C13	-1484.21958	4.059	0
C14	-1484.220119	3.721	0
C15	-1484.222324	2.337	0
C16	-1484.222789	2.045	0
C17	-1484.223119	1.838	0.013
C18	-1484.221549	2.823	0
C19	-1484.218496	4.739	0
C20	-1484.219996	3.798	0
C21	-1484.222914	1.967	0.011
C22	-1484.222121	2.465	0
C23	-1484.22588	0.105	0.245
C24	-1484.222788	2.046	0
C25	-1484.219455	4.137	0

C26	-1484.221537	2.831	0
C27	-1484.218916	4.475	0
C28	-1484.222793	2.043	0
C29	-1484.220681	3.368	0
C30	-1484.221459	2.880	0

Table S3. Experimental ^{13}C-NMR chemical shifts and GIAO isotropic magnetic shielding values calculated for PCM/mPW1PW91/6-311+G (d, p) geometries of (3*S*,6*S*)-**3**

No.	Exptl.	C1	C2	C3	C4	C5	C10	C11	C14	C16	Averaged[a]
6	66.5	114.9769	108.5195	112.6983	108.2301	107.0752	113.6604	114.6748	111.7805	110.0783	110.5719385
4	165.1	17.2399	15.5522	19.0163	14.4098	16.2886	10.6846	11.2553	12.5185	17.5556	13.8410642
3	63.5	118.1173	118.449	117.6364	119.4394	118.9974	118.9879	120.0416	120.3384	116.7889	119.2758532
1	162.7	9.181	9.951	11.441	10.6678	10.2735	15.8025	16.2642	12.8586	12.2494	12.8495823
15	58.5	120.4052	120.749	120.0163	126.5321	126.1491	122.4193	123.2764	121.8845	124.6944	124.4683455
7	33.7	148.7233	146.8503	151.0603	146.9839	148.6909	156.0894	156.5694	150.3688	149.1325	151.8033498
8	107.2	74.5763	74.2694	73.0246	74.1121	72.463	77.3486	77.468	75.0897	74.9347	74.8654332
6-S-Me	12.5	166.0234	169.7367	165.1926	169.6971	169.6896	165.014	165.6566	169.2876	169.2606	167.7672364
14a	127.9	55.1147	55.1217	53.1597	55.0671	53.8879	52.9216	53.0721	52.7329	52.5964	53.5995764
10a	135.6	45.4893	45.8449	45.7037	45.6756	45.8288	46.145	46.0396	45.6696	45.6181	45.9057472
9	125.0	52.9579	53.4567	55.6852	53.6282	54.4794	53.8233	53.3351	54.8142	54.9407	54.0109886
14	118.9	62.2748	62.28565	63.5936	62.3569	63.3496	63.8801	63.9698	62.7984	62.5747	63.4461265
13	118.3	62.661	62.28565	62.4239	62.233	62.2991	62.4452	62.2279	62.7408	62.7535	62.3259151
12	120.7	60.1627	59.6795	59.9805	59.6875	60.0888	59.8721	59.7651	59.8413	59.8439	59.9146352
11	111.1	71.3716	70.7568	70.7858	70.7689	71.0967	70.9053	70.9334	71.0854	71.0384	70.9832971
2-N-OMe	61.0	123.2211	122.5034	123.3515	122.766	122.7156	121.629	122.2561	122.5498	122.6367	122.4291414

[a]Averaged according to the Boltzmann-calculated contribution at B3LYP/6-31+G(d, p) level.

Table S4. Experimental ^{1}H-NMR chemical shifts and GIAO isotropic magnetic shielding values calculated for PCM/mPW1PW91/6-311+G (d, p) geometries of (3*S*,6*S*)-**3**

No.	Exptl.	C1	C2	C3	C4	C5	C10	C11	C14	C16	Averaged[a]
NH-5	8.58	26.3143	26.2467	26.279	26.0045	25.9702	26.5209	26.187	25.9608	25.8974	26.1314001
3	4.36	28.6966	29.0586	28.051	29.223	28.6864	27.5191	28.4515	27.5102	27.49105	28.42240755
15a	3.58	27.9071	27.9837	27.7878	28.01385	27.8708	27.8794	27.8028	27.74785	27.49105	27.8612206
15b	3.58	27.7024	27.7443	27.679	28.1427	27.9263	27.7518	27.932	27.74785	27.7527	27.90352675
OH-15	4.93	29.6377	29.7663	29.4184	30.2036	30.1397	28.42665	30.4264	27.9754	30.005	29.82962535
7a	3.58	28.7484	28.7227	28.5773	28.7781	28.4798	28.195	28.6641	27.8717	27.8099	28.4848601
7b	3.20	27.5317	27.8808	27.6114	27.9198	27.99965	28.42665	27.6508	28.5801	28.5456	27.99248915
6-S-Me	2.13	29.7779	29.7663	29.6495	29.7377	29.7122	29.6591	29.5833	29.7794	29.831	29.6779056
	2.13	28.4576	29.4213	28.7322	29.4547	29.4421	29.2286	28.6641	29.8349	29.56935	29.20798405
	2.13	29.0214	29.6238	29.0641	29.6303	29.5519	29.1662	29.045	29.5984	29.56935	29.35812745
NH-10	10.9	23.6911	23.5529	23.4988	23.5468	23.6348	23.411	23.7124	23.4066	23.4474	23.594109
9	7.19	24.29305	24.3795	24.3363	24.3831	24.3838	24.0588	24.3572	24.2304	24.216	24.3126084
14	7.58	23.6911	23.7242	23.8237	23.753	23.7878	23.8776	23.8274	23.6641	23.6192	23.8020812
13	6.93	24.29305	24.19715	24.2629	24.2734	24.25455	24.26	24.25745	24.2304	24.216	24.2567729
12	7.02	24.2253	24.19715	24.1772	24.2142	24.25455	24.1263	24.25745	24.1042	24.1422	24.2206134
11	7.28	24.0485	23.9878	23.9332	23.998	24.0872	23.8776	24.1067	23.9056	23.9361	24.0351009
2-N-OMe	3.65	28.124	27.3306	28.051	28.01385	27.4838	28.1349	28.001	28.2035	27.95735	27.82085305
	3.65	28.124	28.11495	28.051	28.1427	27.99965	27.9522	28.0796	27.9754	27.95735	28.02771415
	3.65	27.4181	28.11495	27.3575	27.567	28.0637	27.1572	27.5429	27.3438	27.2407	27.6775037

[a]Averaged according to the Boltzmann-calculated contribution at B3LYP/6-31+G(d, p) level.

Table S5. Experimental ^{13}C-NMR chemical shifts and GIAO isotropic magnetic shielding values calculated for PCM/mPW1PW91/6-311+G (d, p) geometries of (3*R*,6*S*)-**3**

No.	Exptl.	C2	C3	C4	C5	C7	C9	C10	C11	C17	C21	C23	Averaged[a]
6	66.5	112.8483	113.7624	112.6728	114.1085	112.5674	114.1114	108.156	115.6793	111.5711	110.7772	113.7599	113.4837003
4	165.1	14.9664	13.3129	18.145	16.137	13.0001	16.1352	15.7609	9.0513	15.5916	15.3116	13.3065	13.3232086
3	63.5	118.1098	118.5297	118.4707	117.5335	119.1282	117.5343	118.586	122.6546	116.0892	116.8086	118.5223	119.0549196
1	162.7	15.7676	15.017	16.7659	10.4404	15.4848	10.4364	14.055	15.477	8.4998	8.7246	15.0075	14.9129746
15	58.5	122.4278	126.6138	114.0812	122.0075	126.8891	122.0037	125.4283	123.0315	121.3896	121.9001	126.6103	125.6233047
7	33.7	152.9946	157.4656	151.2107	153.9985	153.1007	153.9983	150.6077	150.0272	150.5279	148.5678	157.4686	154.9750646
8	107.2	72.8309	77.5978	72.5823	76.7678	73.2046	76.7682	73.3723	73.8316	75.8622	74.5752	77.6029	75.6573831
6-S-Me	12.5	166.6235	166.6891	165.2002	164.8754	166.5171	164.8783	169.8742	166.4041	169.2325	169.7236	166.6946	166.7626749
14a	127.9	53.5618	53.0822	53.6759	52.8181	53.273	52.8172	53.614	55.3135	53.3263	52.7822	53.0869	53.400444
10a	135.6	46.084	45.962	46.3975	46.3343	46.0244	46.3338	46.0605	45.6917	45.8738	45.9422	45.9586	46.0395177
9	125.0	55.6617	53.5723	54.6347	54.0193	55.6879	54.0181	54.0392	54.1218	52.9208	55.2956	53.5739	54.3973415
14	118.9	64.6095	64.2944	64.0504	63.5752	64.8907	63.575	64.5556	61.5326	63.2426	62.744	64.2938	64.2453981
13	118.3	62.1319	62.1358	62.3181	62.3031	62.0547	62.3026	62.366	62.9751	62.1795	62.4938	62.1346	62.26506
12	120.7	59.9997	59.7928	60.118	60.0395	59.8875	60.04	60.0307	60.2534	60.0165	60.0468	59.7935	59.9542482
11	111.1	70.7159	70.6326	71.0841	70.9321	70.6799	70.9317	70.9314	71.4435	70.925	71.1776	70.6311	70.829963
2-N-OMe	61.0	121.1694	121.9413	125.1641	124.4422	121.8903	124.4442	122.3856	122.1906	124.2887	123.9521	121.9425	122.3619293

[a]Averaged according to the Boltzmann-calculated contribution at B3LYP/6-31+G(d, p) level.

Table S6. Experimental ^{1}H-NMR chemical shifts and GIAO isotropic magnetic shielding values calculated for PCM/mPW1PW91/6-311+G (d, p) geometries of (3*R*,6*S*)-**3**

No.	Exptl.	C2	C3	C4	C5	C7	C9	C10	C11	C17	C21	C23	Averaged[a]
NH-5	8.58	26.0861	26.2479	26.2536	26.7747	25.9137	26.7746	25.9412	26.0921	26.7235	26.1217	23.3622	25.4776608
3	4.36	27.3588	27.56985	27.3888	27.6387	27.5282	27.6386	27.65715	27.6059	27.6235	27.584	23.758	26.64964195
15a	3.58	27.9159	27.56985	28.8629	27.8787	27.6498	27.8786	27.65715	27.90925	27.8798	27.8571	23.846	26.8154214
15b	3.58	27.5981	27.56985	28.4655	27.2811	27.6498	27.281	27.8917	28.13065	27.1957	27.2184	23.9815	26.80821925
OH-15	4.93	29.3531	29.8928	29.3036	30.471	30.1667	30.4709	31.2535	28.13065	30.5064	30.5921	24.1597	28.48920785
7a	3.58	28.4694	28.1409	28.5208	28.1075	28.4682	28.1077	28.5058	28.7212	28.1936	27.9687	24.1597	27.35959663
7b	3.20	27.5981	28.3369	27.6732	28.2413	27.5282	28.2411	27.7965	27.4572	28.1936	28.3388	26.2469	27.4936652
6-S-Me	2.13	29.7236	29.8357	29.7121	29.6668	29.7422	29.6668	29.6795	29.7272	29.77815	29.901	27.4798	29.23562655
	2.13	29.2888	29.3886	28.7284	28.8515	29.3635	28.8519	29.5183	29.0394	29.77815	29.6956	27.5702	28.89559163
	2.13	29.2272	29.3202	29.07	29.1494	29.2529	29.1496	29.6282	29.2187	29.4951	29.5451	27.5702	28.88392228
NH-10	10.9	23.5306	23.3622	23.6052	23.3012	23.5222	23.3013	23.7752	23.6826	23.3508	23.3905	27.5702	24.50583458
9	7.19	24.3204	23.9798	24.2447	24.1047	24.3019	24.1046	24.2617	24.28665	24.1109	24.2688	27.5702	25.03276893
14	7.58	23.7873	23.758	23.7893	23.7118	23.7582	23.7116	23.8353	23.4728	23.7487	23.5282	28.0015	24.796636
13	6.93	24.2125	24.15975	24.2447	24.2697	24.1673	24.2696	24.2002	24.3706	24.2646	24.19715	28.142	25.19026565
12	7.02	24.2125	24.15975	24.2447	24.172	24.1673	24.1719	24.1278	24.28665	24.1741	24.19715	28.3371	25.2245591
11	7.28	24.0071	23.846	24.0735	23.942	23.989	23.942	23.9356	24.0782	23.9322	23.9645	29.3204	25.2912132
2-N-OMe	3.65	27.9159	28.0017	27.9819	27.5494	28.0636	28.0469	27.2626	28.2753	27.4575	27.96867	29.3883	28.37891673
	3.65	28.019	27.56985	28.1398	27.986	27.7269	27.5491	28.0657	28.8352	27.994	27.4178	29.8358	28.350814
	3.65	27.1602	27.4799	27.6732	28.0468	27.5282	27.9861	28.0657	27.90925	27.994	27.96867	29.8948	28.19767508

[a]Averaged according to the Boltzmann-calculated contribution at B3LYP/6-31+G(d, p) level.

Table S7. Experimental chemical shifts, the calculated shielding tensors for (3*S*,6*S*)-**3** (isomer 1) and (3*R*,6*S*)-**3** (isomer 2), and the DP4+ probability of (3*S*,6*S*)-**3** and (3*R*,6*S*)-**3**

	A	B	C	D	E	F	G	H
1	Functional		Solvent?		Basis Set		Type of Data	
2	mPW1PW91		PCM		6-311+G(d,p)		Shielding Tensors	
3								
12			DP4+	100.00%	0.00%	–	–	–
14	Nuclei	sp2?	xperimenta	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
15	C		66.5	110.6	113.5			
16	C	x	165.1	13.8	13.3			
17	C		63.5	119.3	119.1			
18	C	x	162.7	12.8	14.9			
19	C		58.5	124.5	125.6			
20	C		33.7	151.8	155.0			
21	C	x	107.2	74.9	75.7			
22	C		12.5	167.8	166.8			
23	C	x	127.9	53.6	53.4			
24	C	x	135.6	45.9	46.0			
25	C	x	125	54.0	54.4			
26	C	x	118.9	63.45	64.25			
27	C	x	118.3	62.33	62.27			
28	C	x	120.7	59.91	59.95			
29	C	x	111.1	70.98	70.83			
30	C		61	122.43	122.36			
31								
32	H		8.58	26.13	25.48			
33	H		4.36	28.42	26.65			
34	H		3.58	27.86	26.82			
35	H		3.58	27.90	26.81			
36	H		4.93	29.83	28.49			
37	H		3.58	28.48	27.49			
38	H		3.2	27.99	27.36			
39	H		2.13	29.68	29.24			
40	H		2.13	29.2079841	28.8955916			
41	H		2.13	29.3581275	28.8839223			
42	H		10.9	23.594109	24.5058346			
43	H	x	7.19	24.3126084	25.0327689			
44	H	x	7.58	23.8020812	24.796636			
45	H	x	6.93	24.2567729	25.1902657			
46	H	x	7.02	24.2206134	25.2245591			
47	H	x	7.28	24.0351009	25.2912132			
48	H		3.65	27.8208531	28.3789167			
49	H		3.65	28.0277142	28.350814			
50	H		3.65	27.6775037	28.1976751			
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Table S8. Calculated OR Values of the Lowest Energy Conformers of (3*S*,6*S*)-**3**.

Conf.	Boltzmann Distribution	Calculated OR Value
C1	0.01	-44.18
C2	0.01	-168.98
C3	0.017	132.13
C4	0.102	-173.55
C5	0.398	71.65
C10	0.171	35.11
C11	0.246	130.96
C14	0.033	158.73
C16	0.013	133.83
	Averaged[a]	56.1

[a]Averaged according to the Boltzmann-calculated contribution at B3LYP/DGDZVP level.

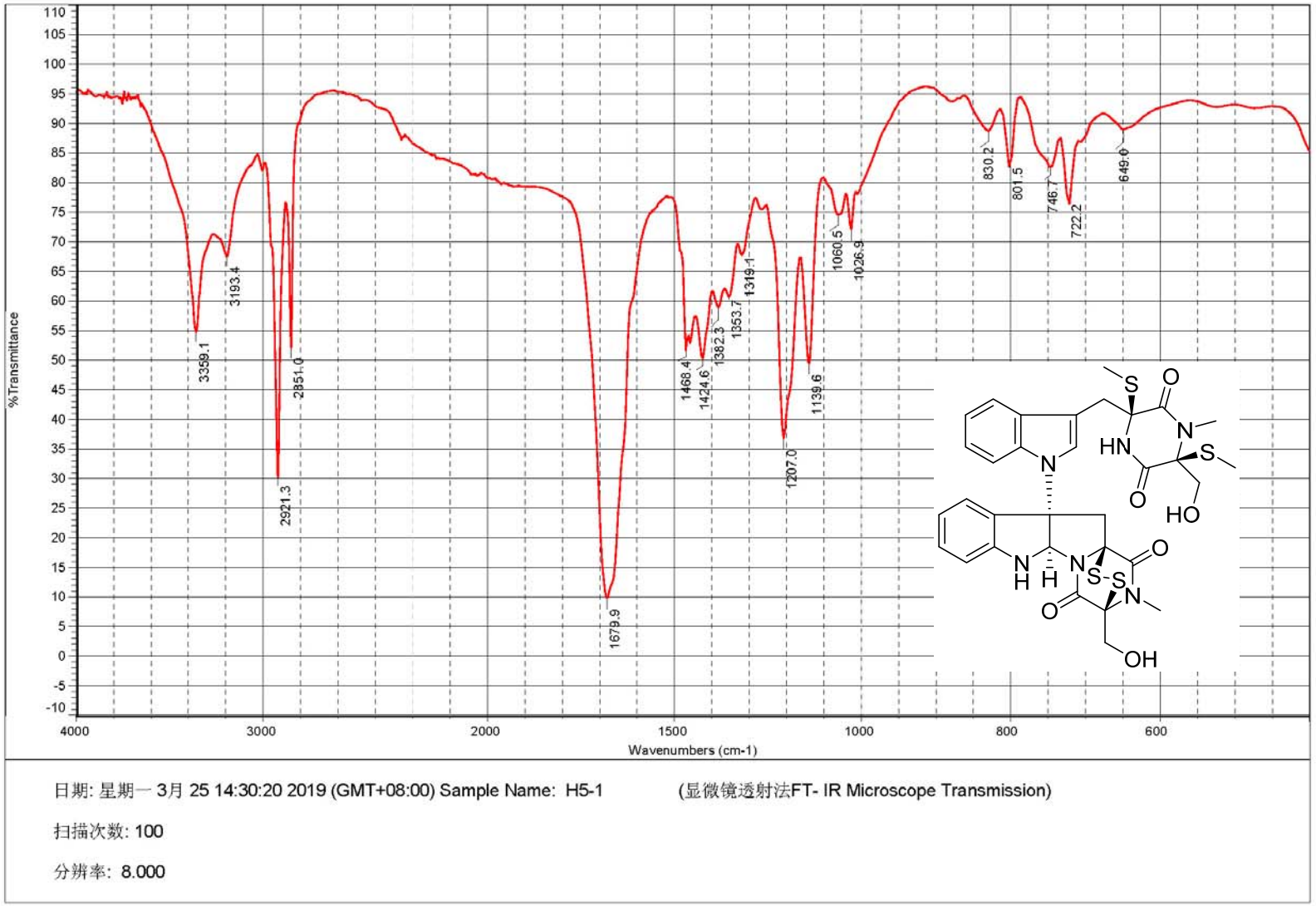

Figure S2. The IR Spectrum of Compound **1**

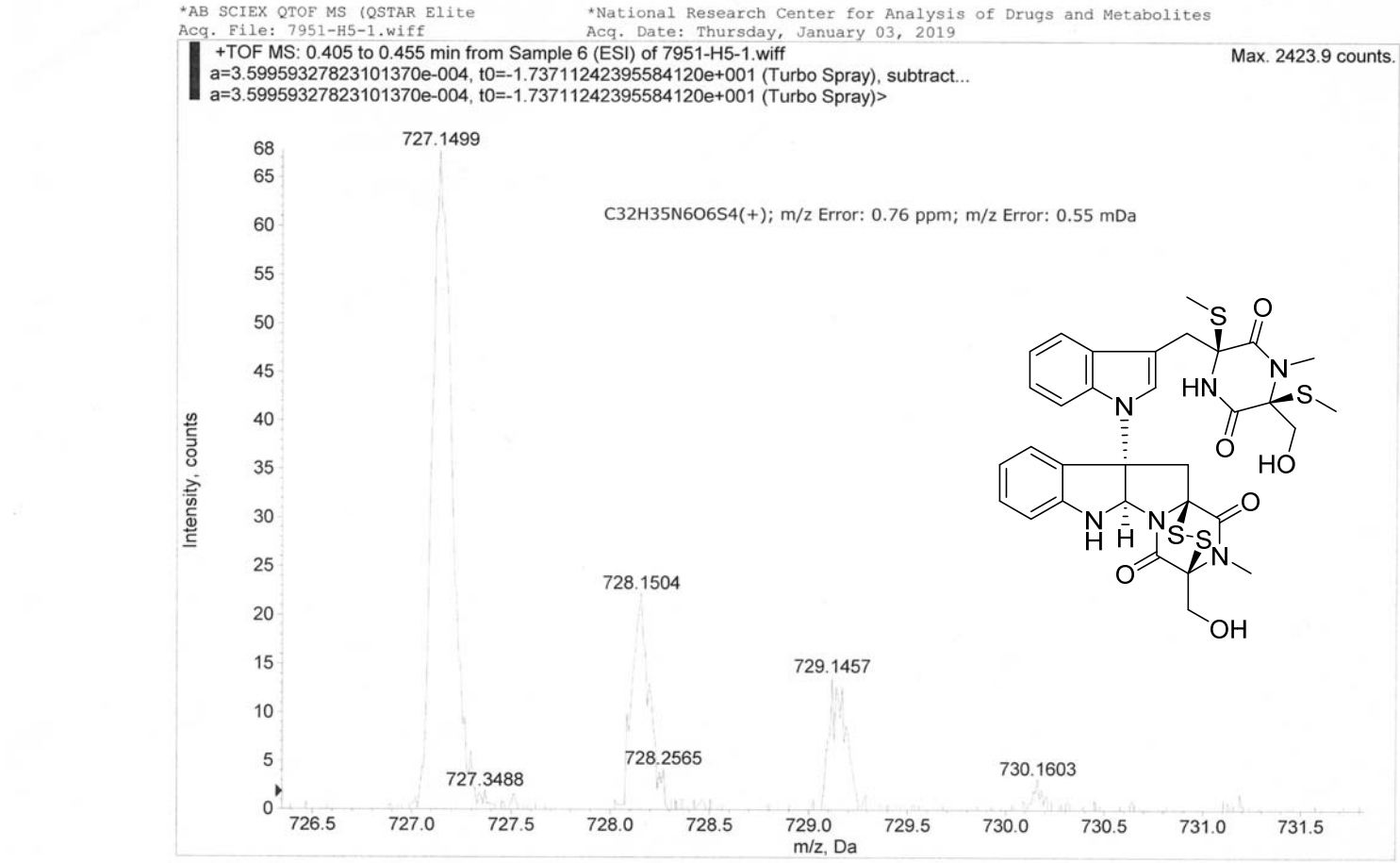

Figure S3. The (+)-HRESIMS Spectroscopic Data of Compound **1**

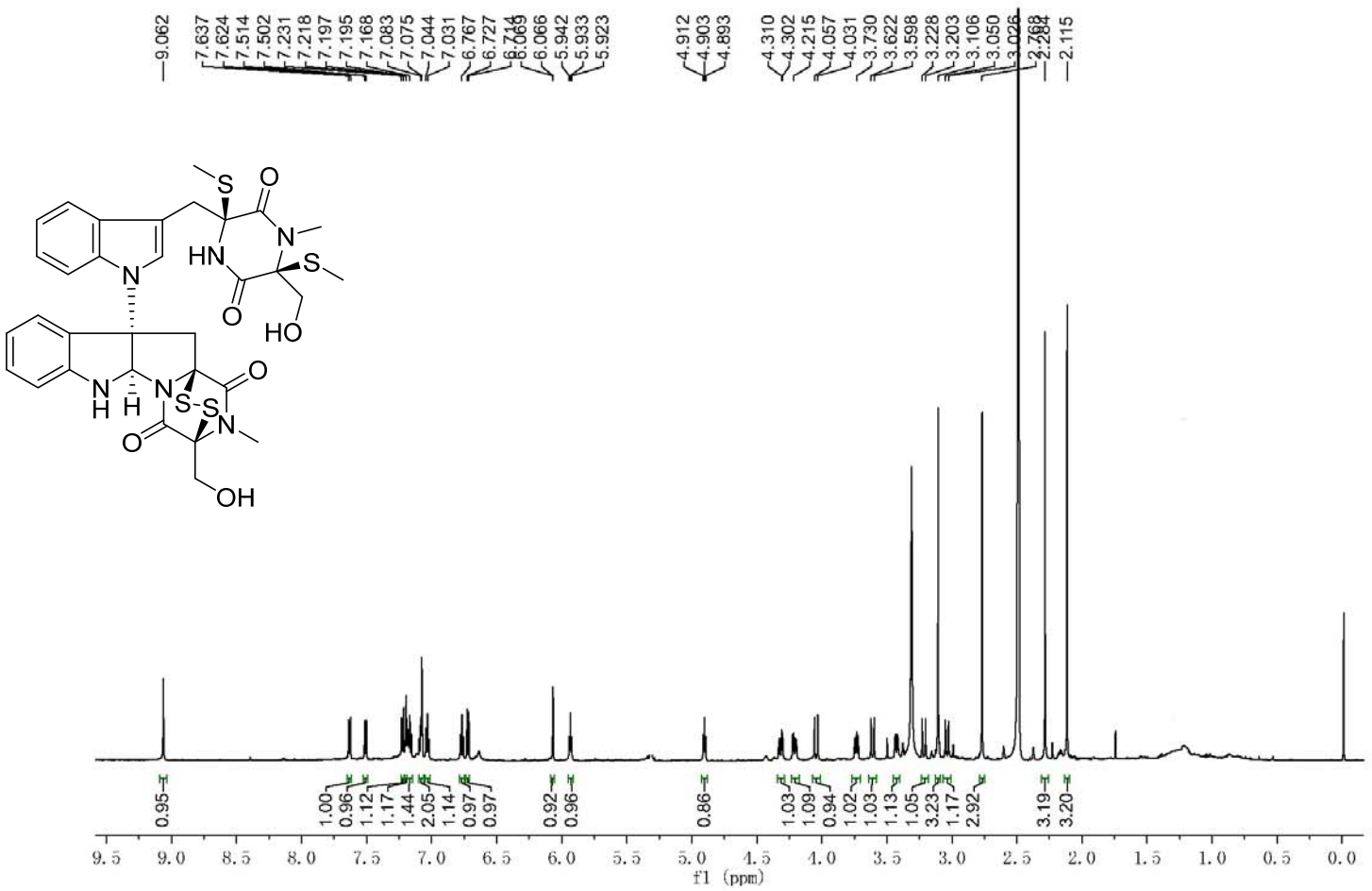

Figure S4. The ^{1}H NMR Spectrum of Compound **1** in DMSO−d_6

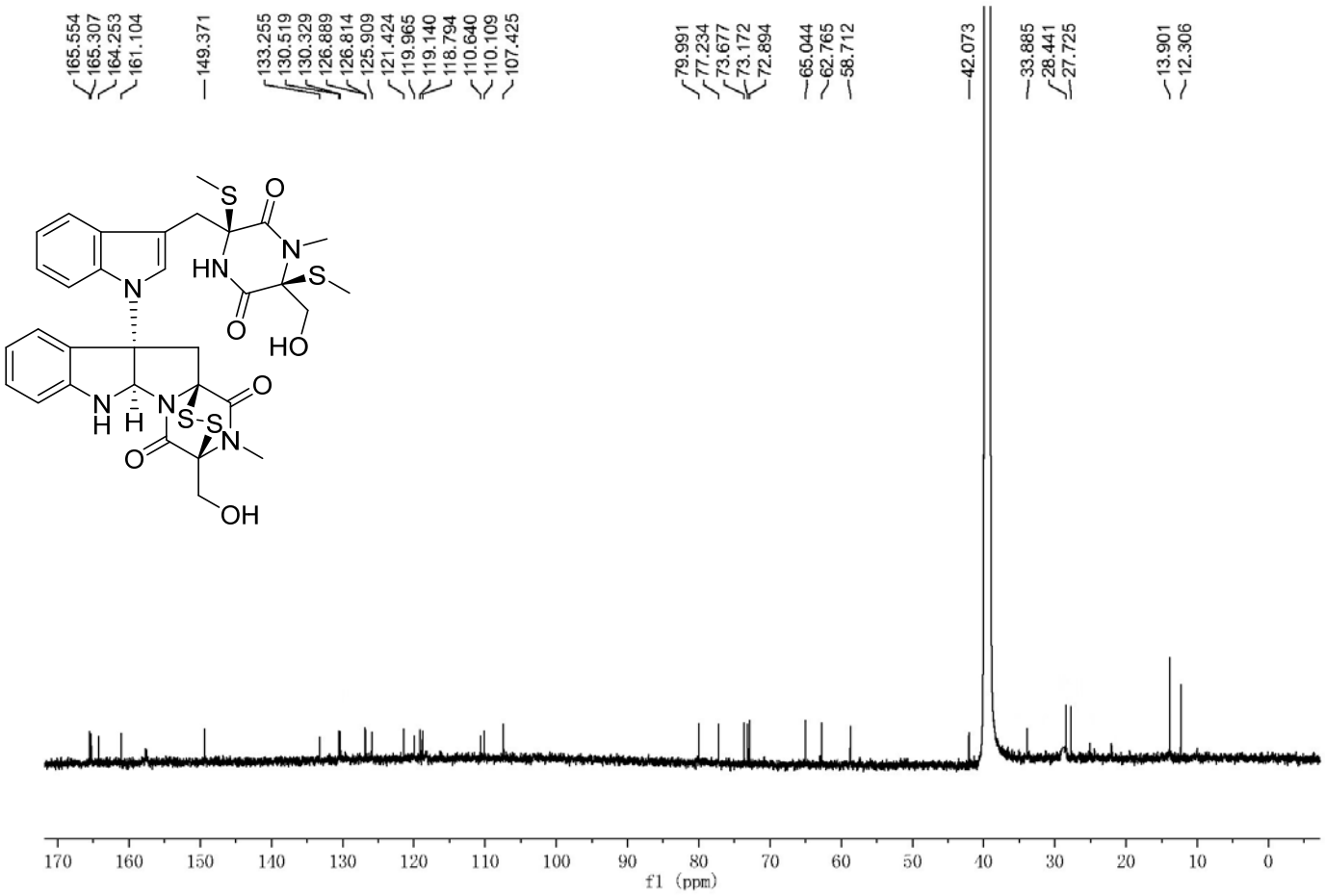

Figure S5. The ^{13}C NMR Spectrum of Compound **1** in DMSO–d_6

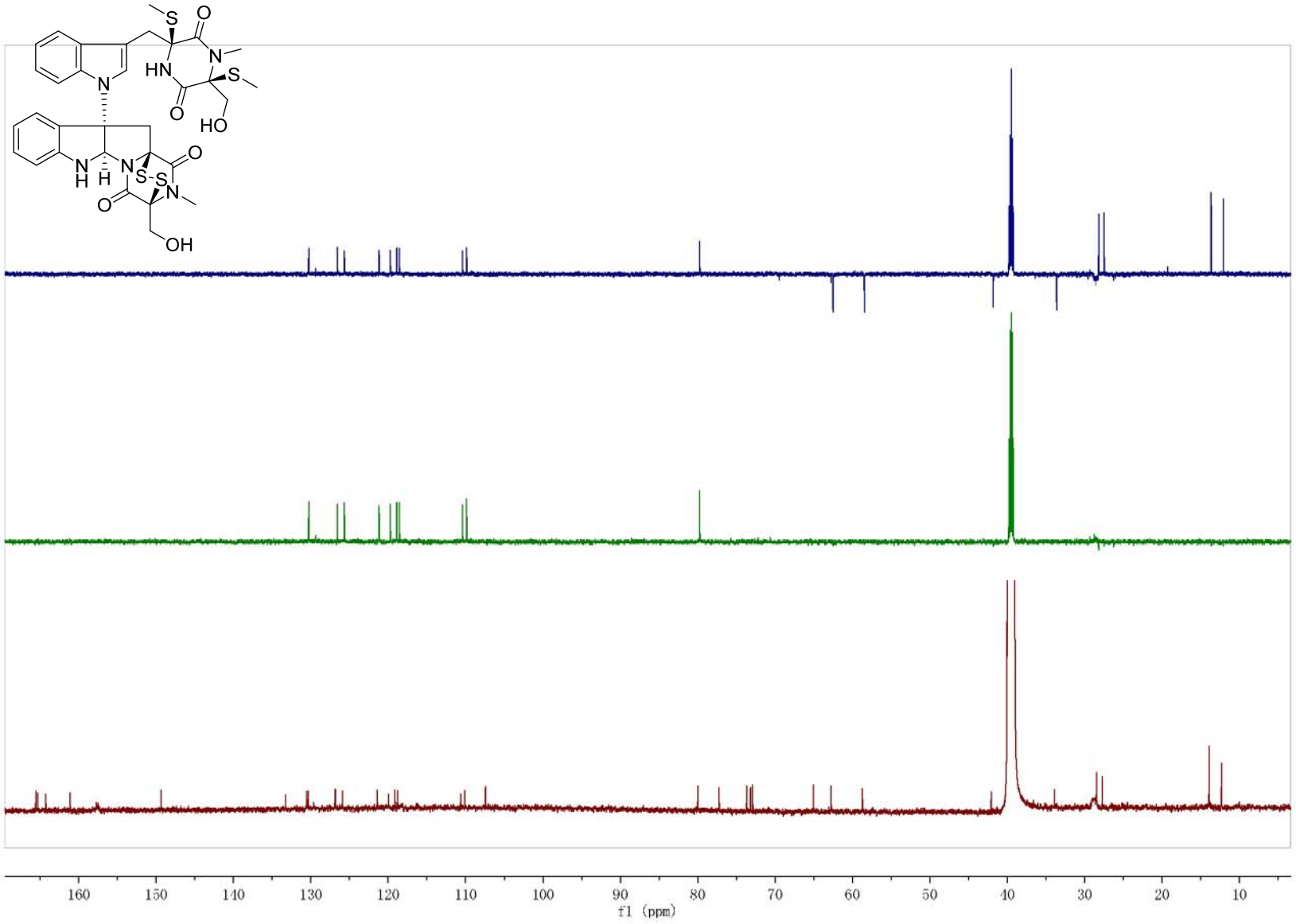

Figure S6. The DEPT Spectrum of Compound **1** in DMSO–d_6

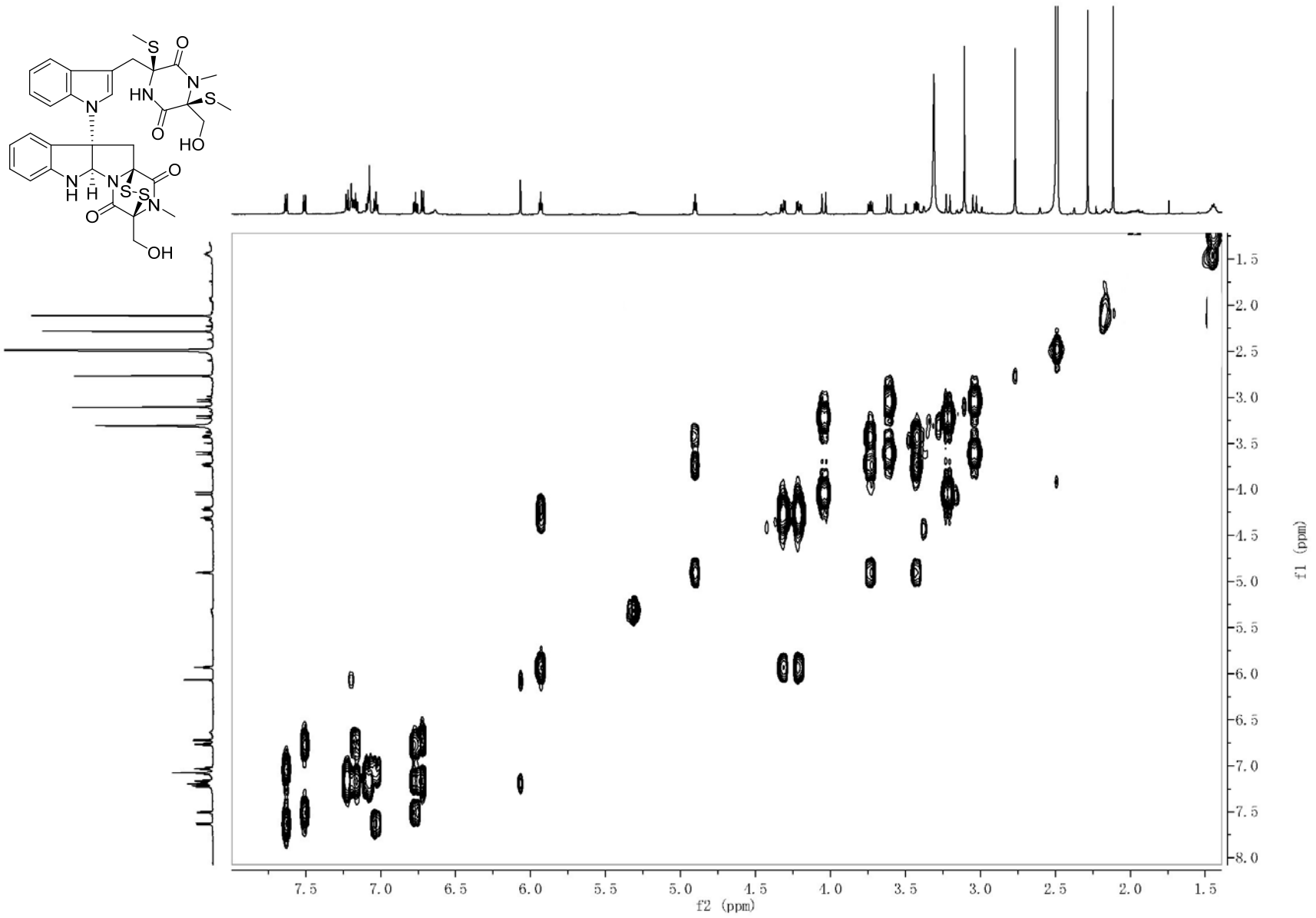

Figure S7. The ^{1}H-^{1}HCOSY Spectrum of Compound **1** in DMSO−d_6

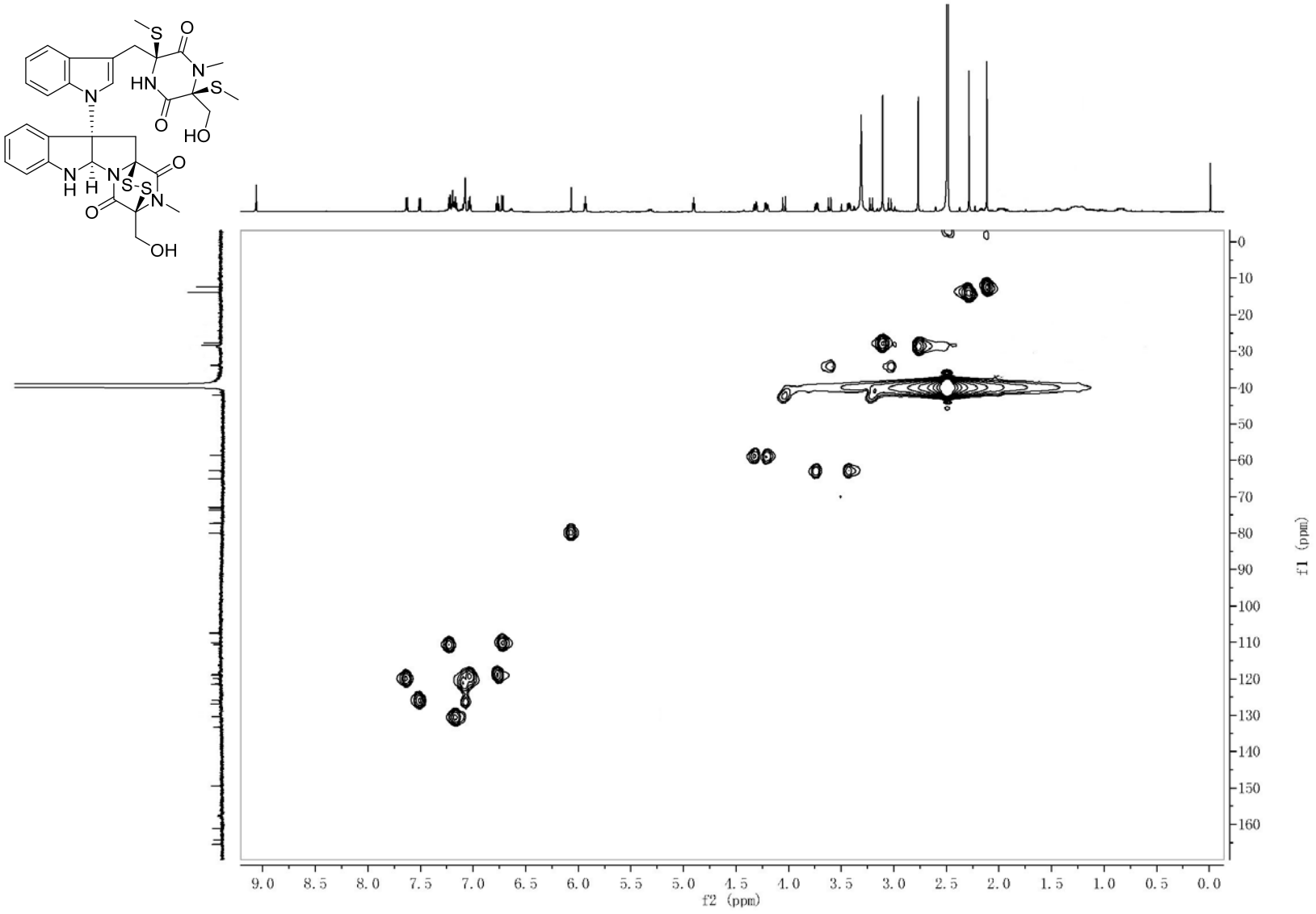

Figure S8. The HSQC Spectrum of Compound **1** in DMSO–d_6

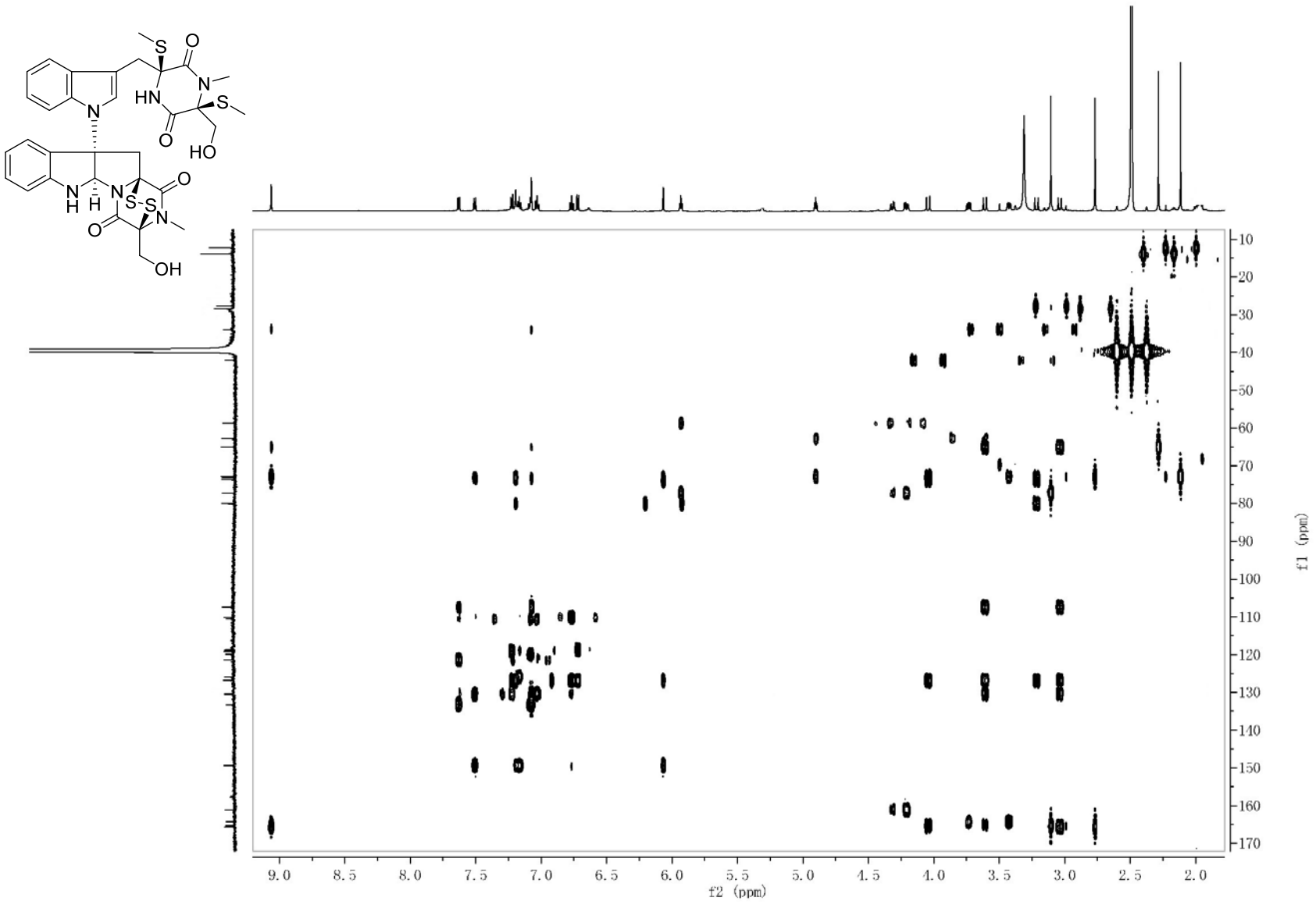

Figure S9. The HMBC Spectrum of Compound **1** in DMSO–d_6

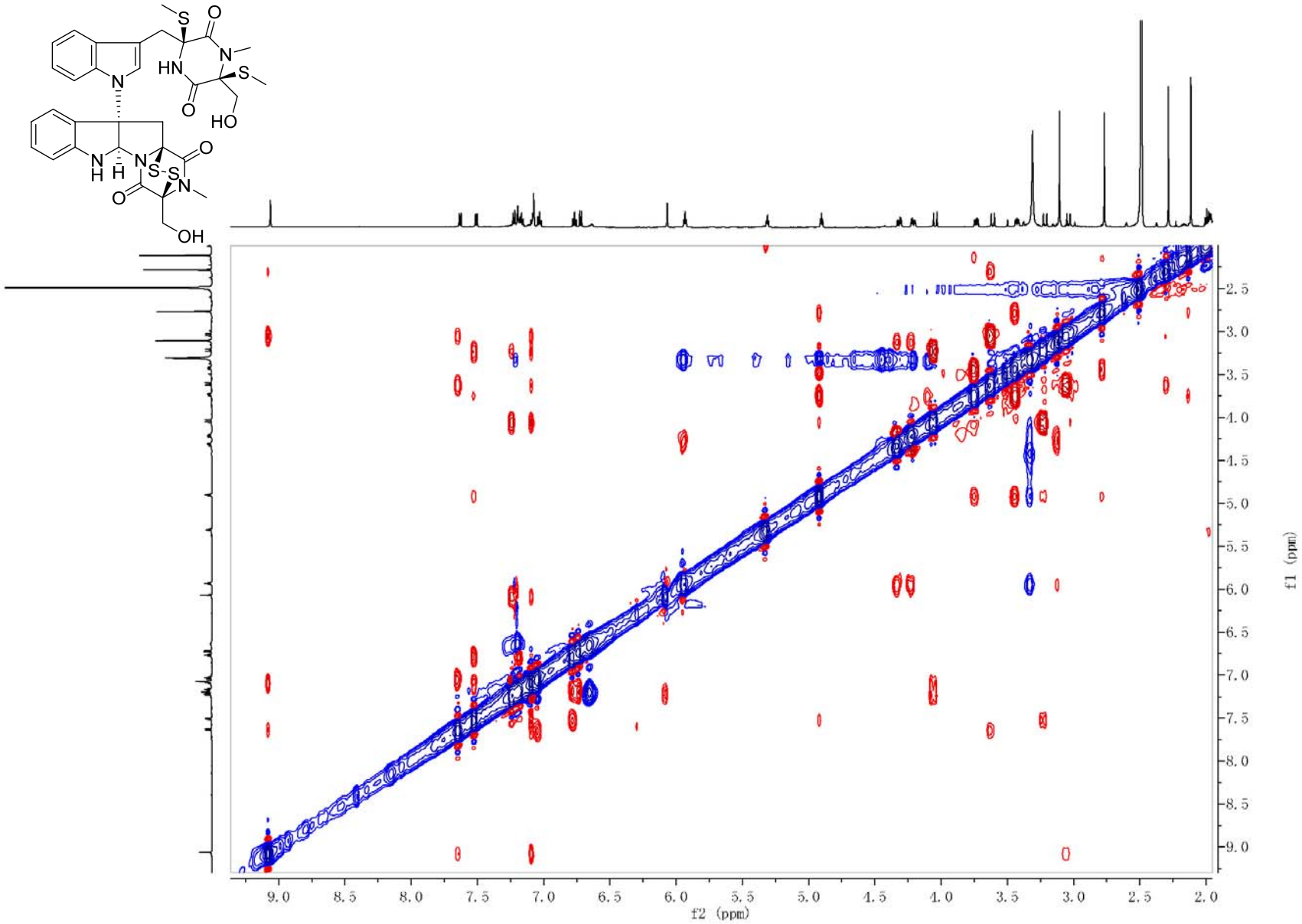

Figure S10. The ROESY Spectrum of Compound **1** in DMSO–d_6

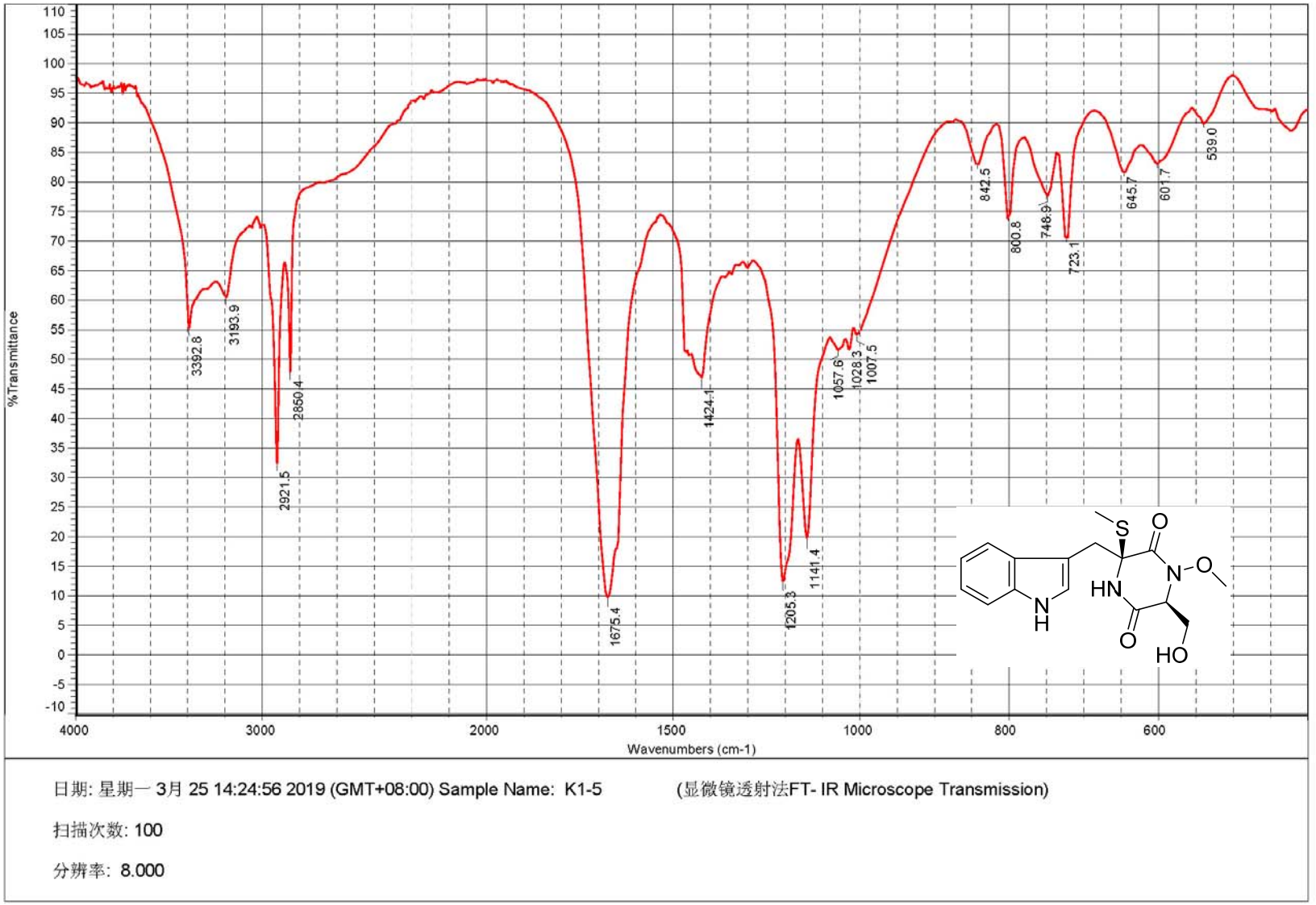

Figure S11. The IR Spectrum of Compound **3**

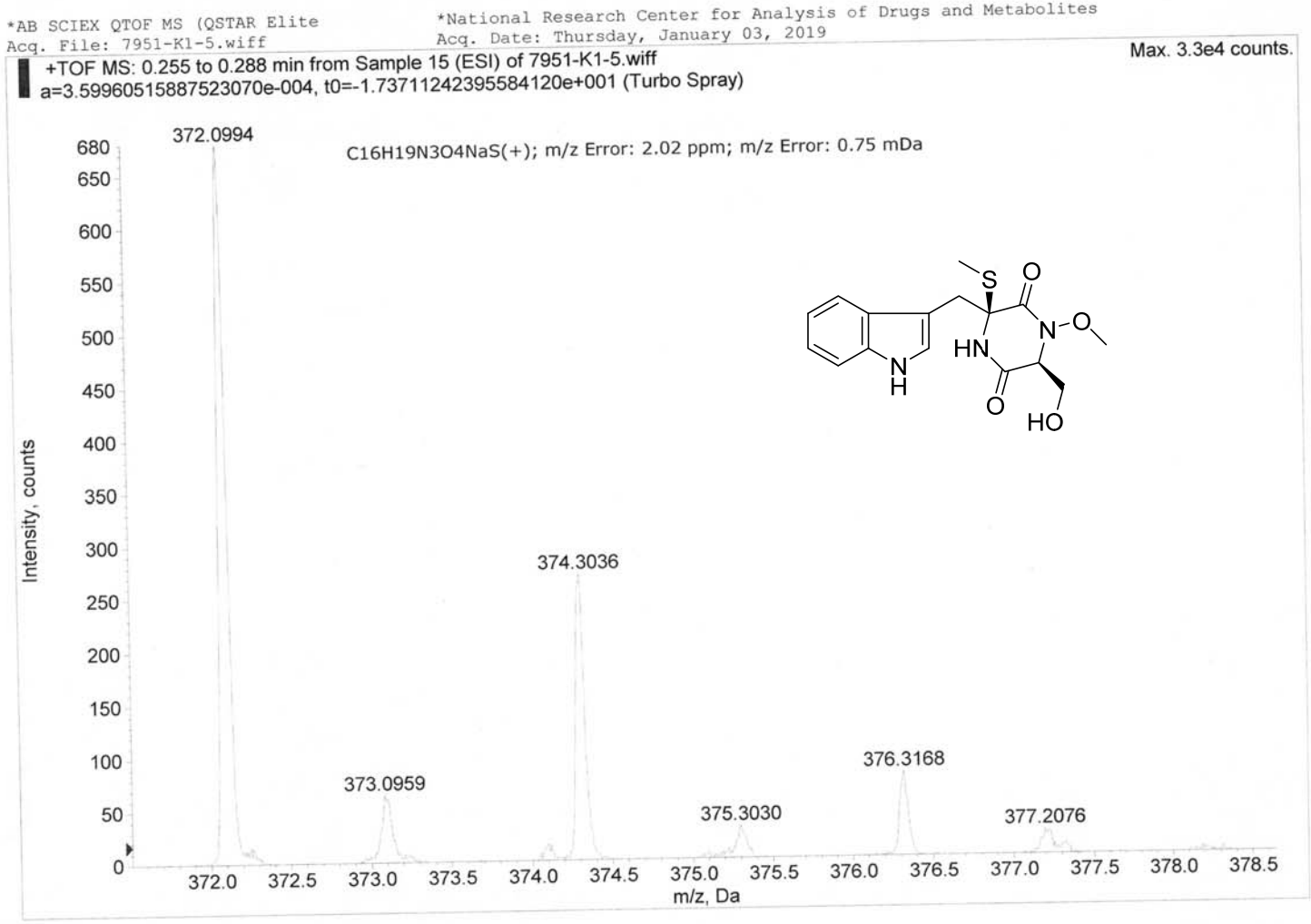

Figure S12. The (+)-HRESIMS Spectroscopic of Compound **3**

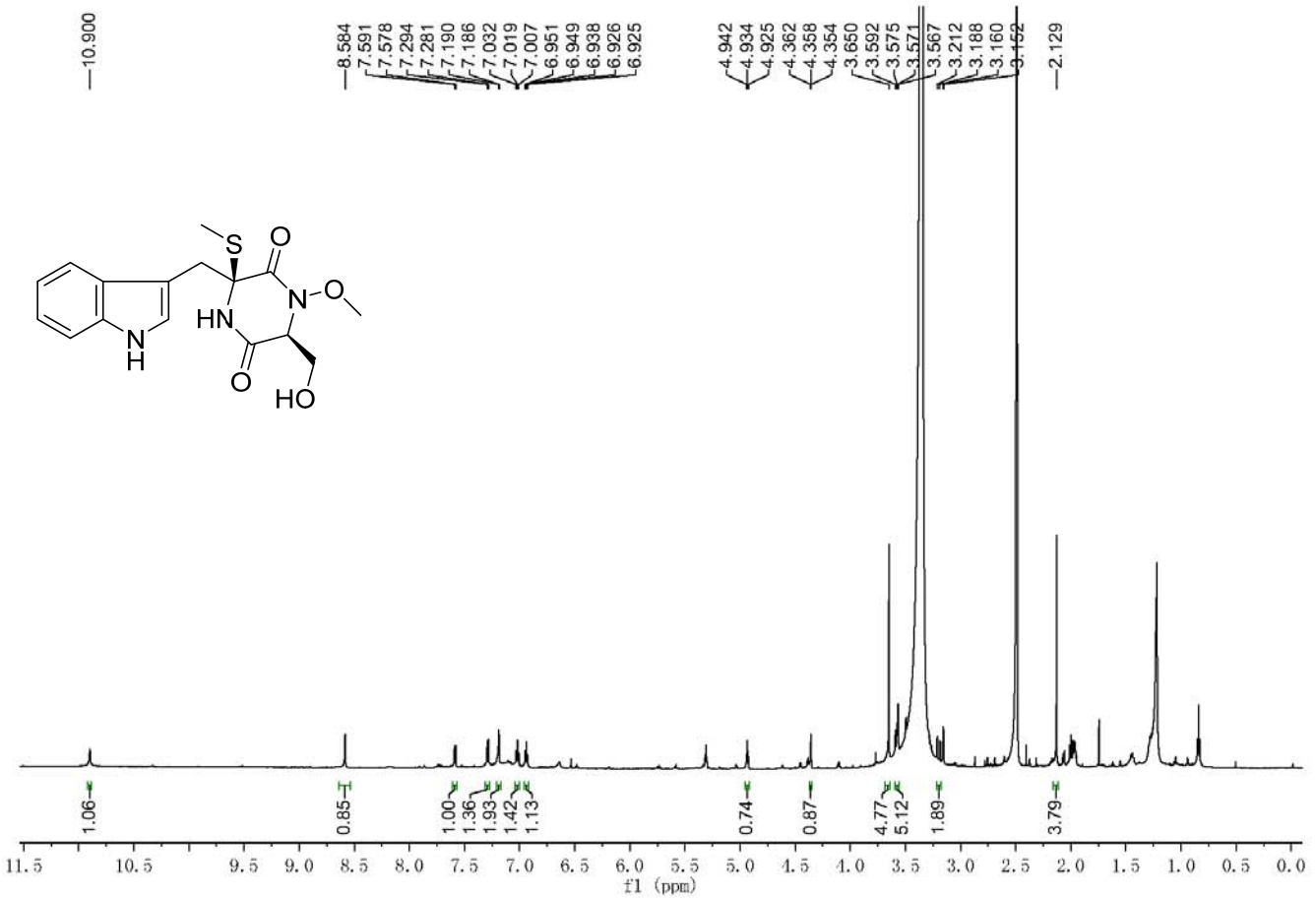

Figure S13. The ^{1}H NMR Spectrum of Compound **3** in DMSO–d_6

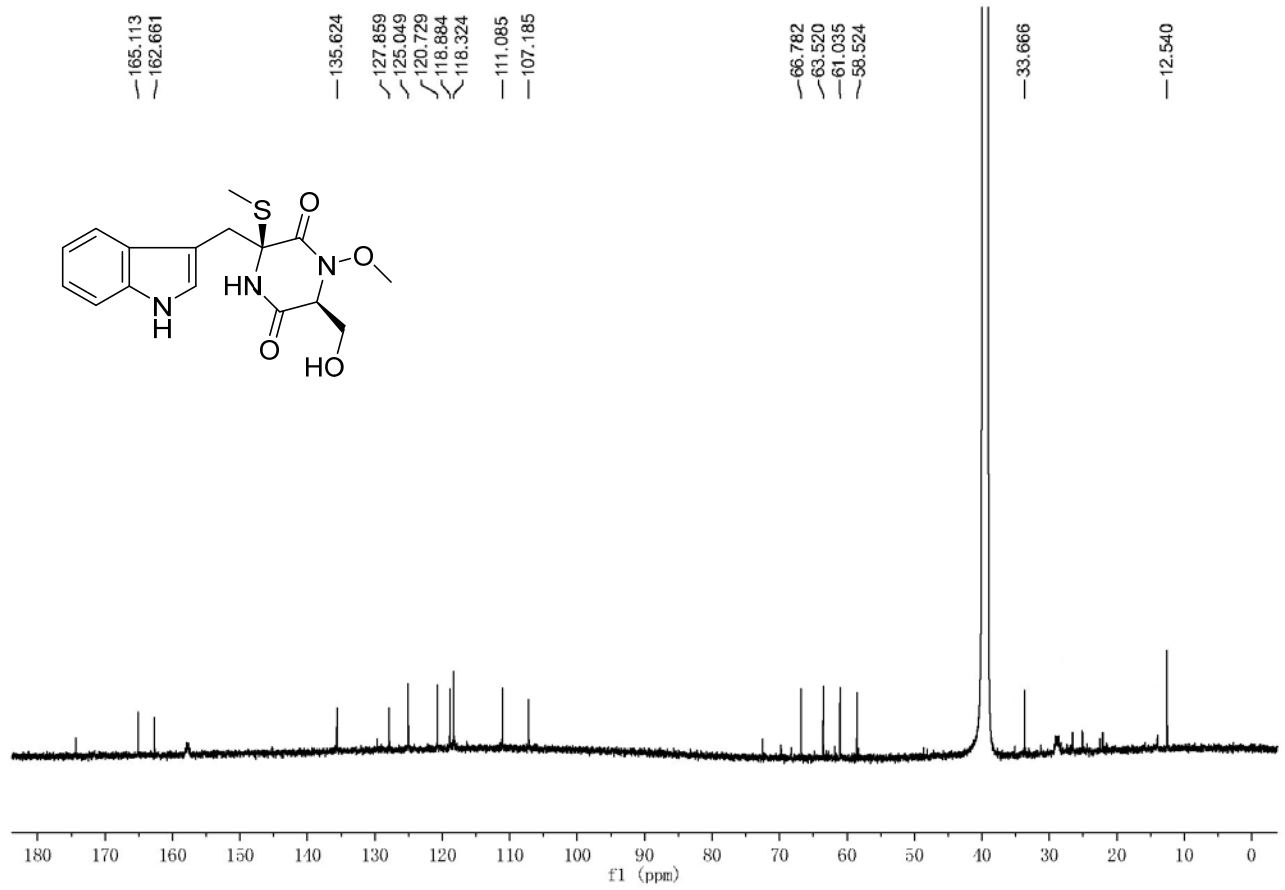

Figure S14. The ^{13}C NMR Spectrum of Compound **3** in DMSO−d_6

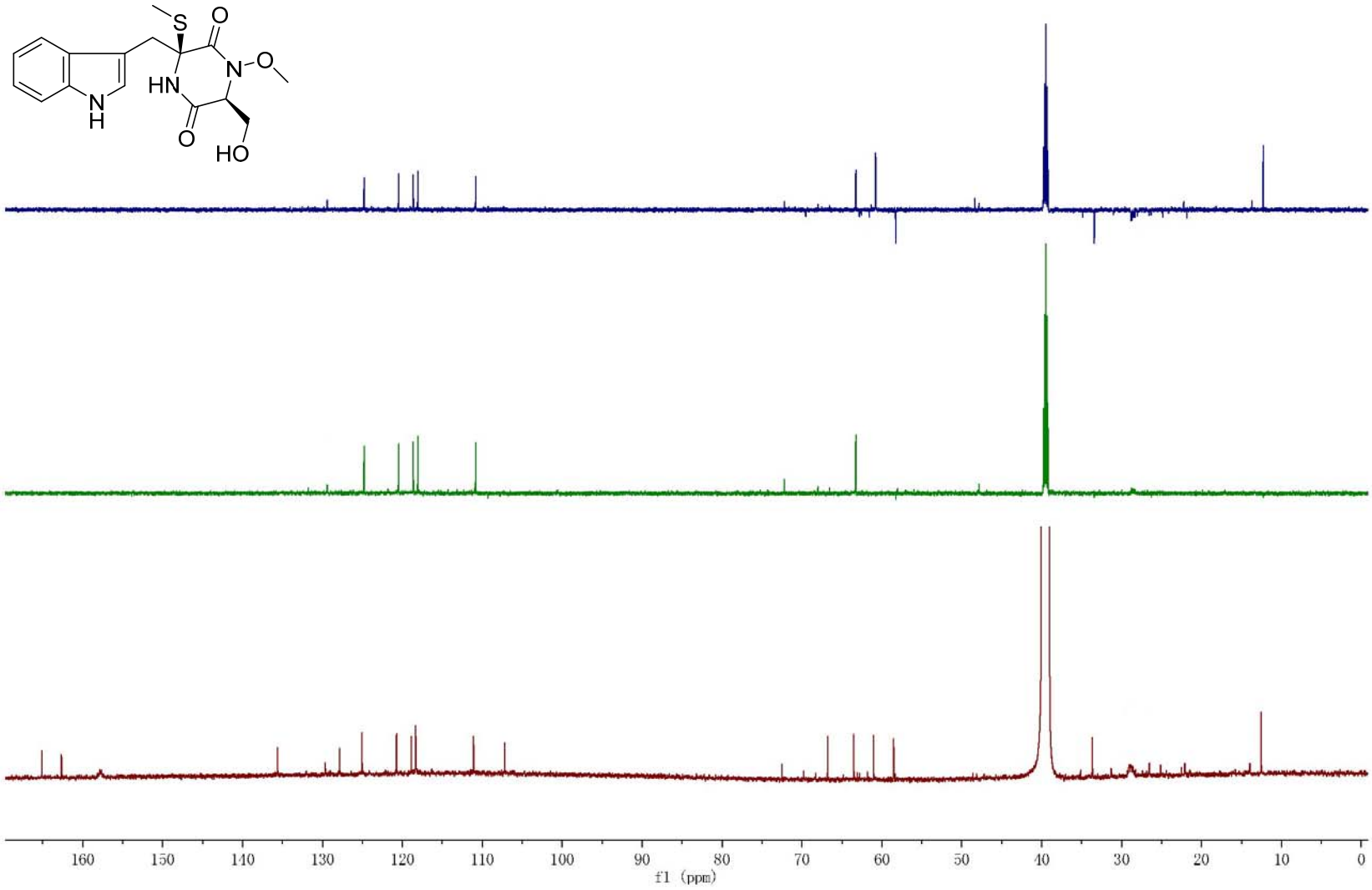

Figure S15. The DEPT Spectrum of Compound **3** in DMSO–d_6

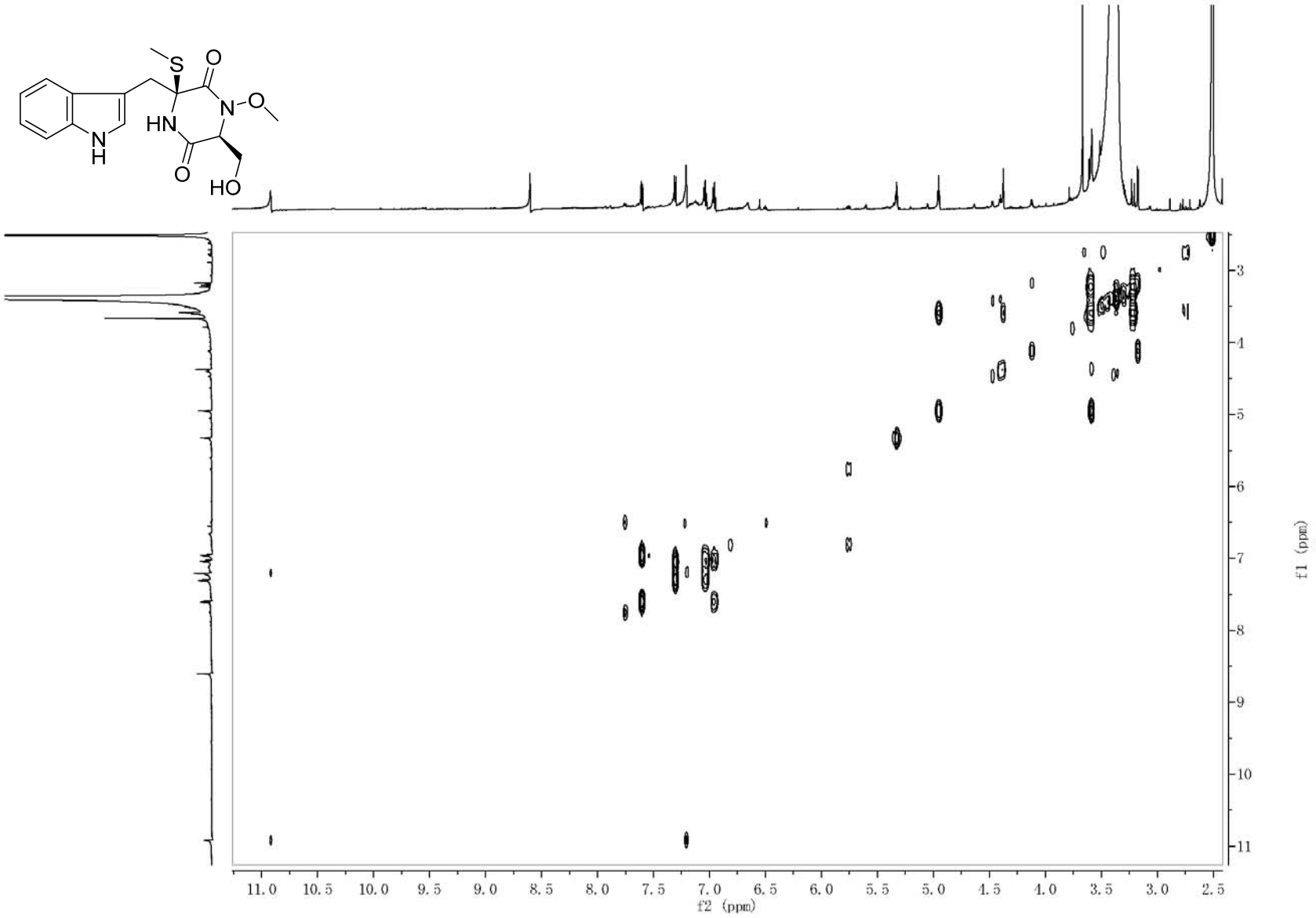

Figure S16. The ^{1}H-^{1}H COSY Spectrum of Compound **3** in DMSO–d_6

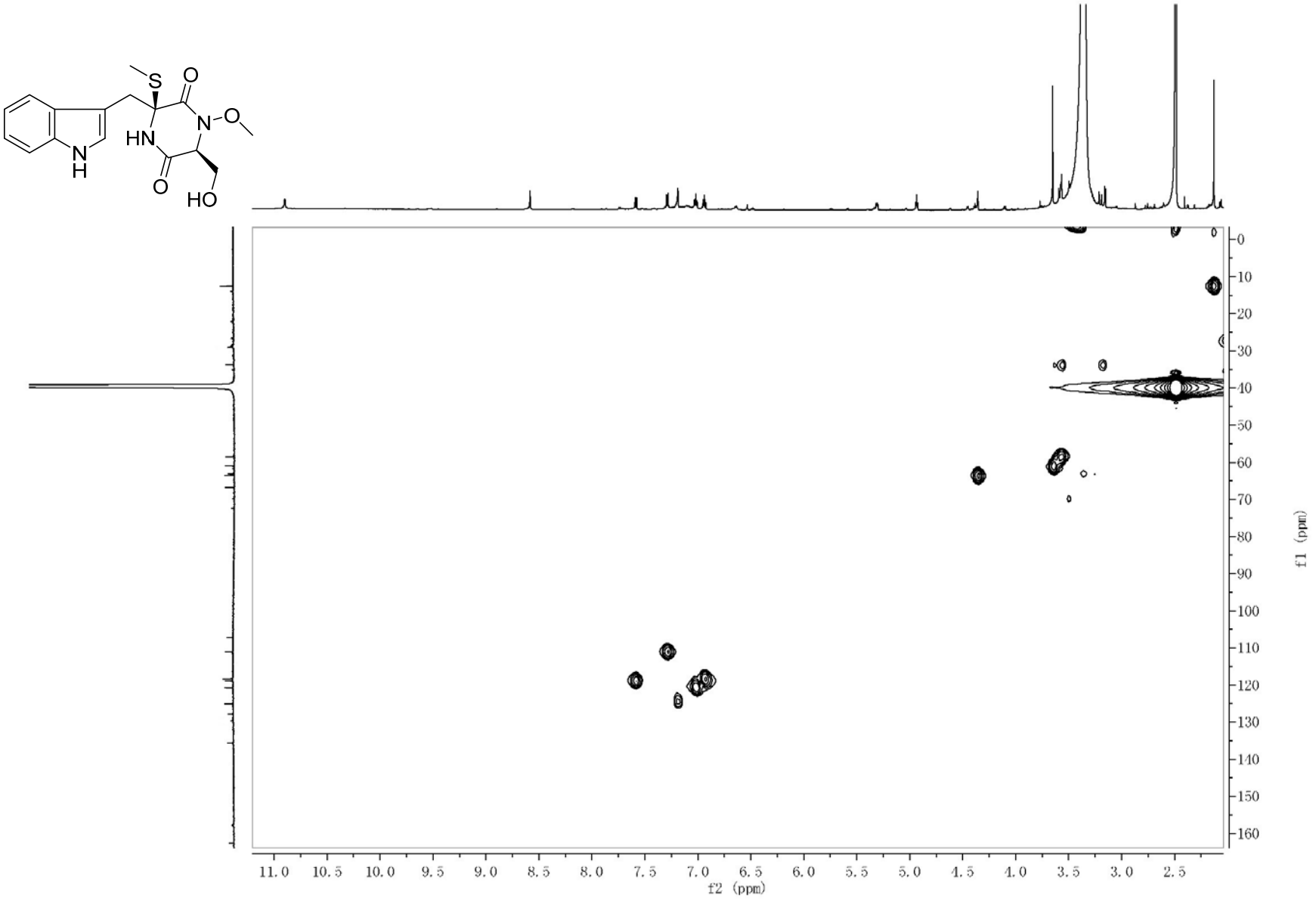

Figure S17. The HSQC Spectrum of Compound **3** in DMSO–d_6

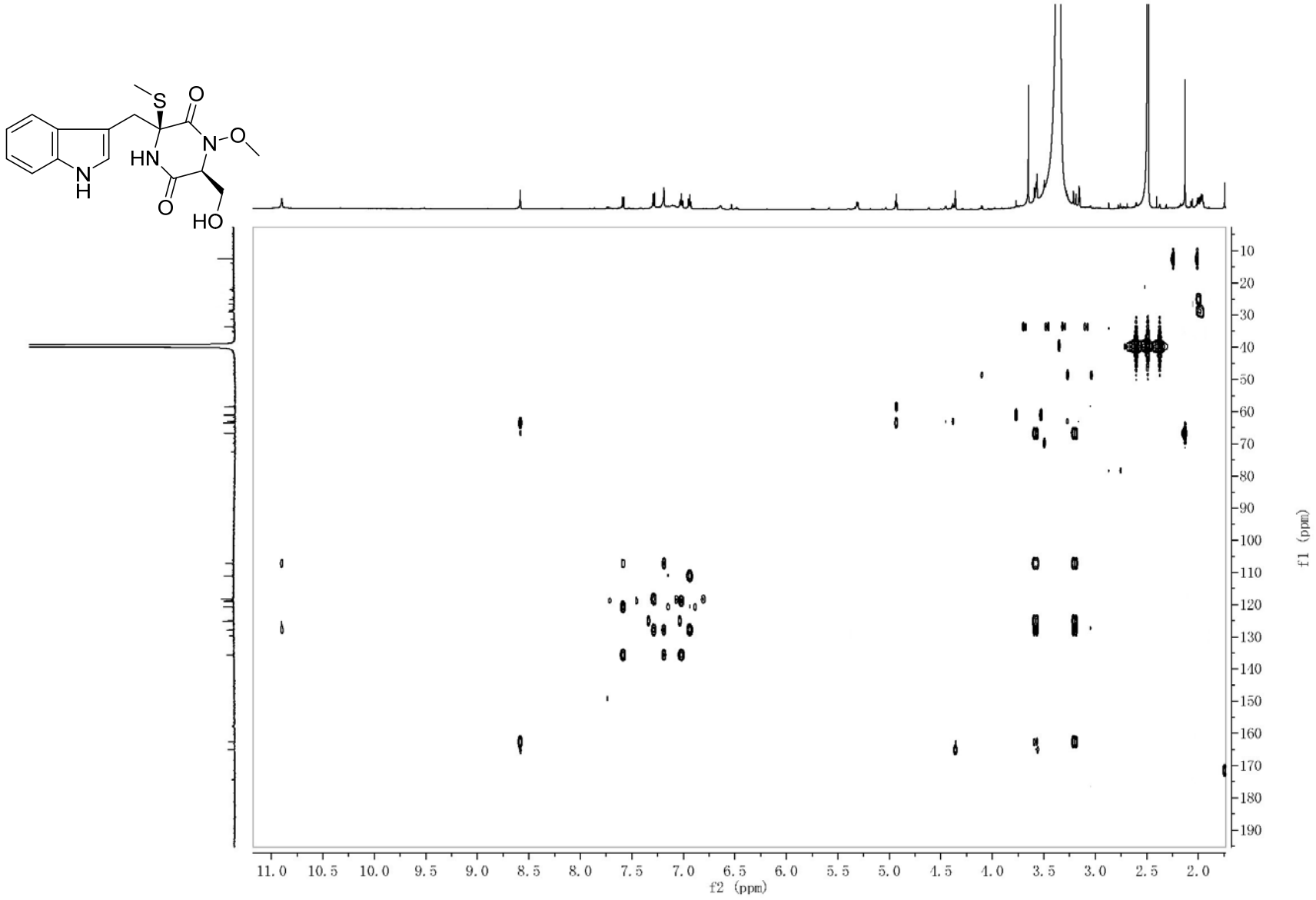

Figure S18. The HMBC Spectrum of Compound **3** in DMSO–d_6

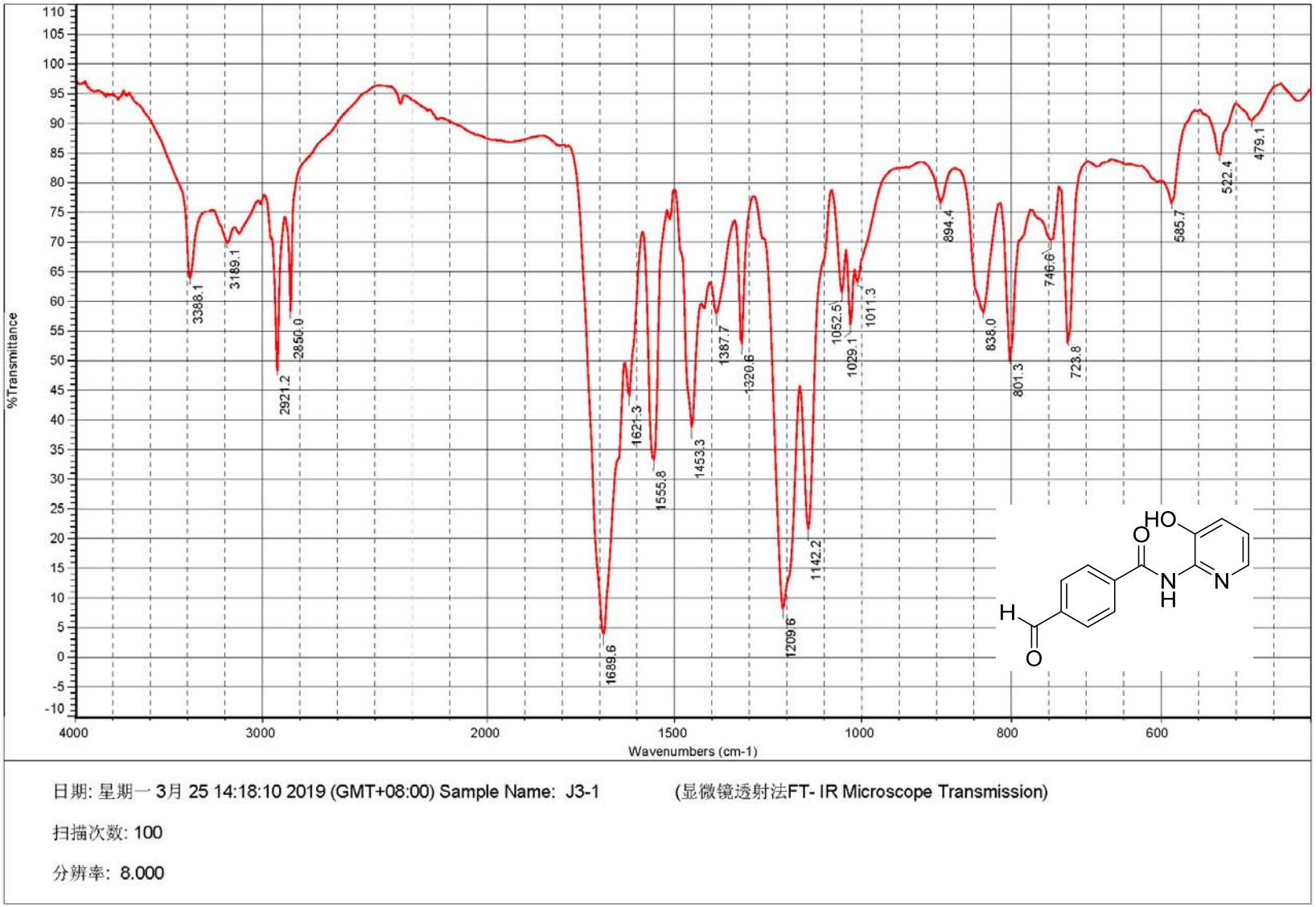

Figure S19. The IR Spectrum of Compound **6**

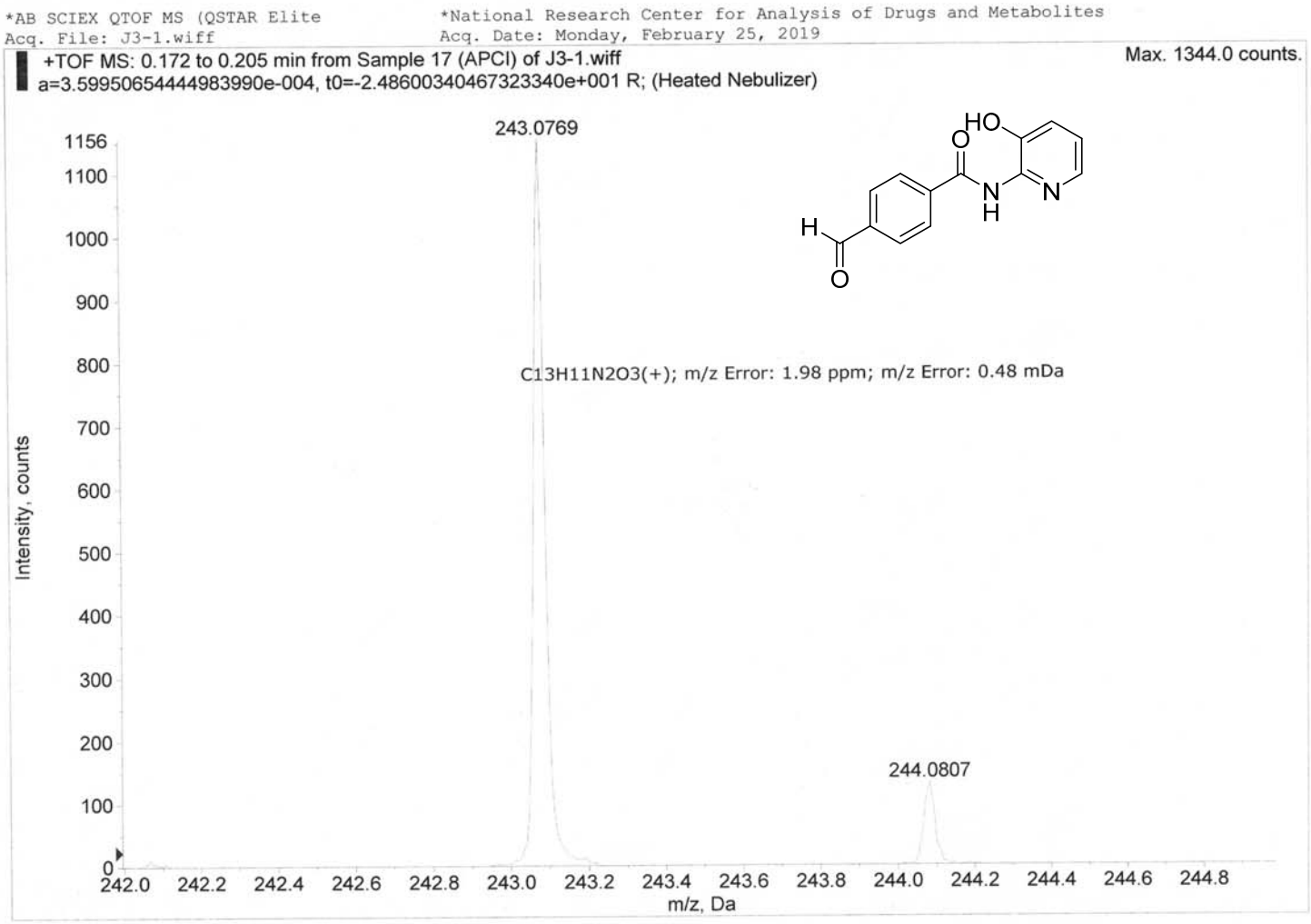

Figure S20. The (+)-HRESIMS Spectroscopic Data of Compound **6**

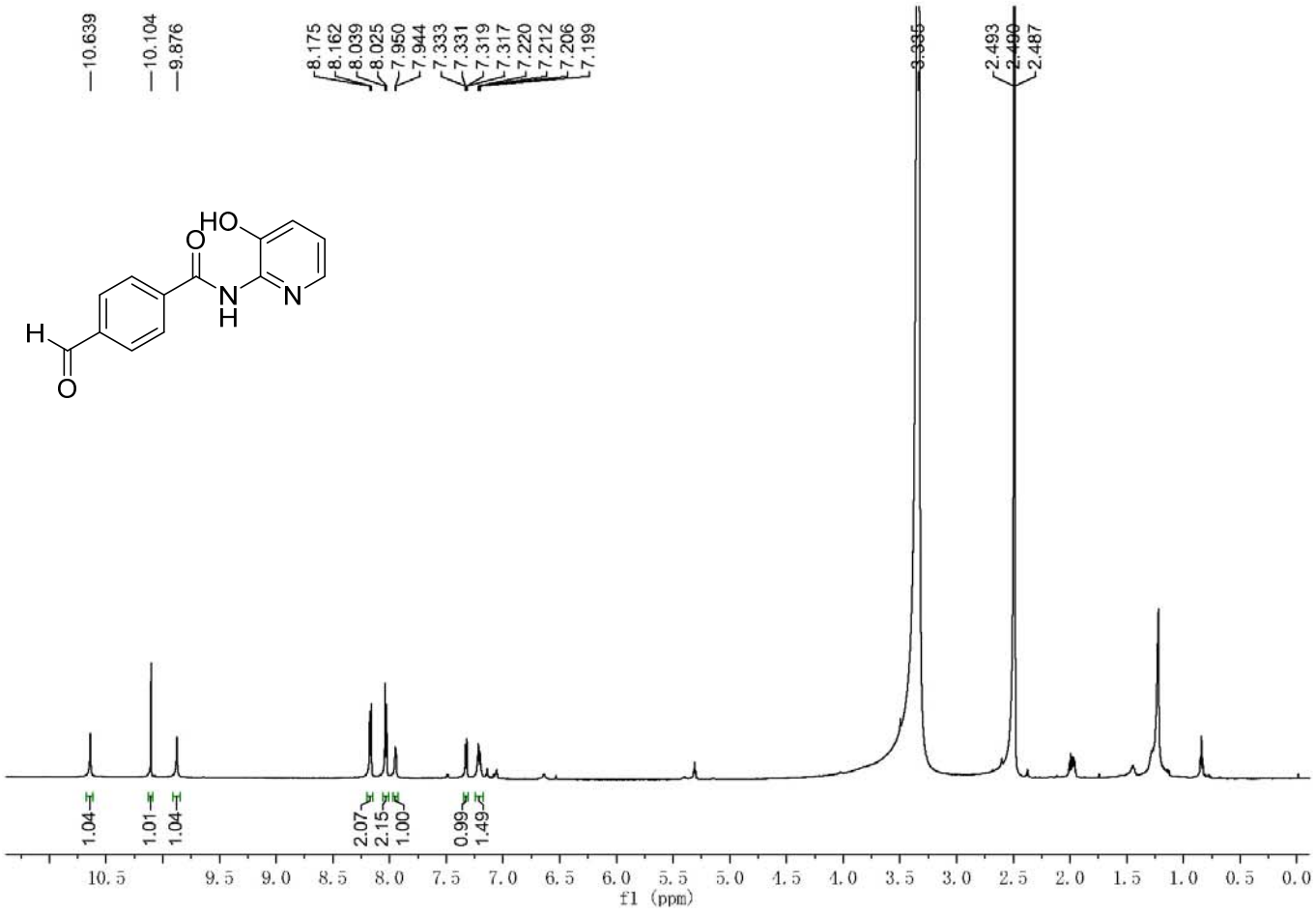

Figure S21. The ^{1}H NMR Spectrum of Compound **6** in DMSO–d_6

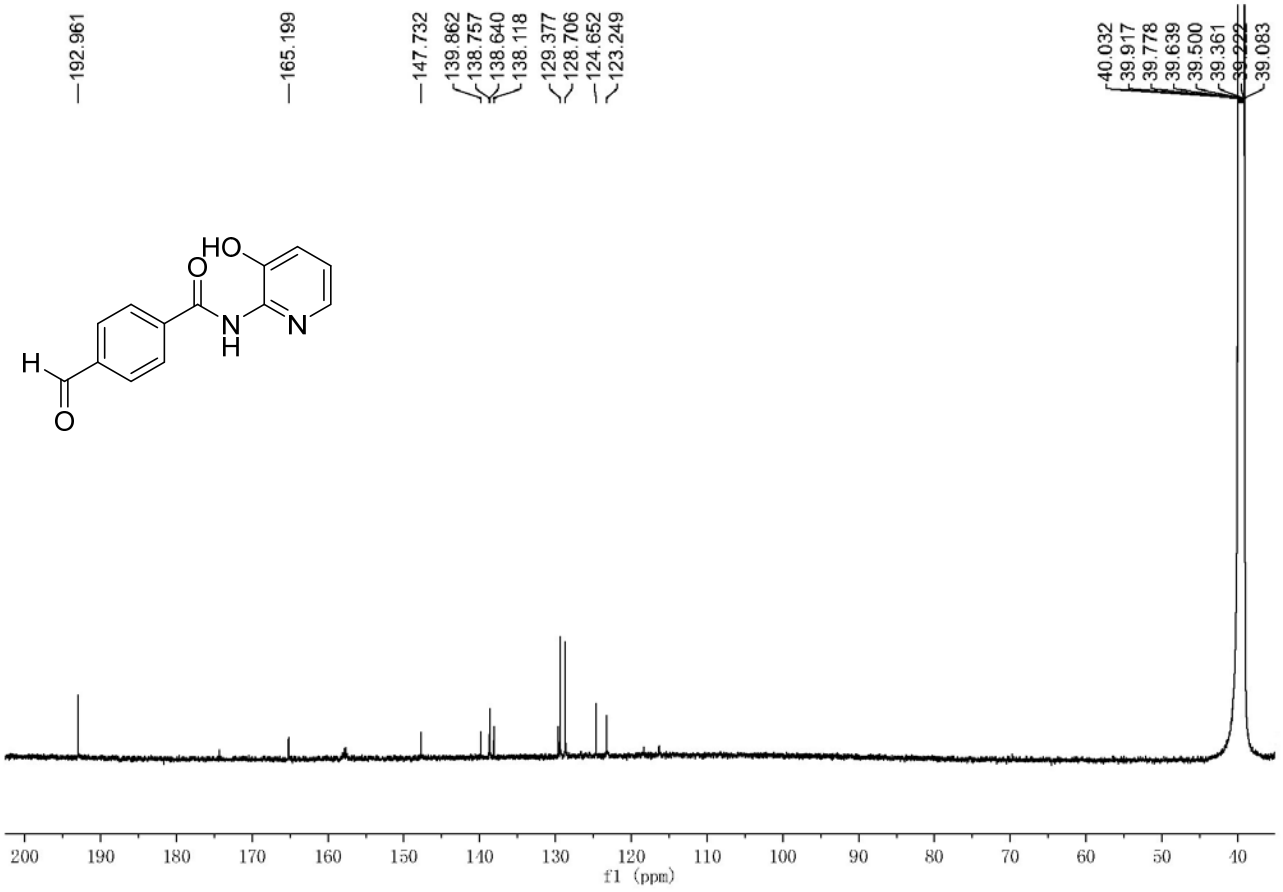

Figure S22. The ^{13}C NMR Spectrum of Compound **6** in DMSO−d_6

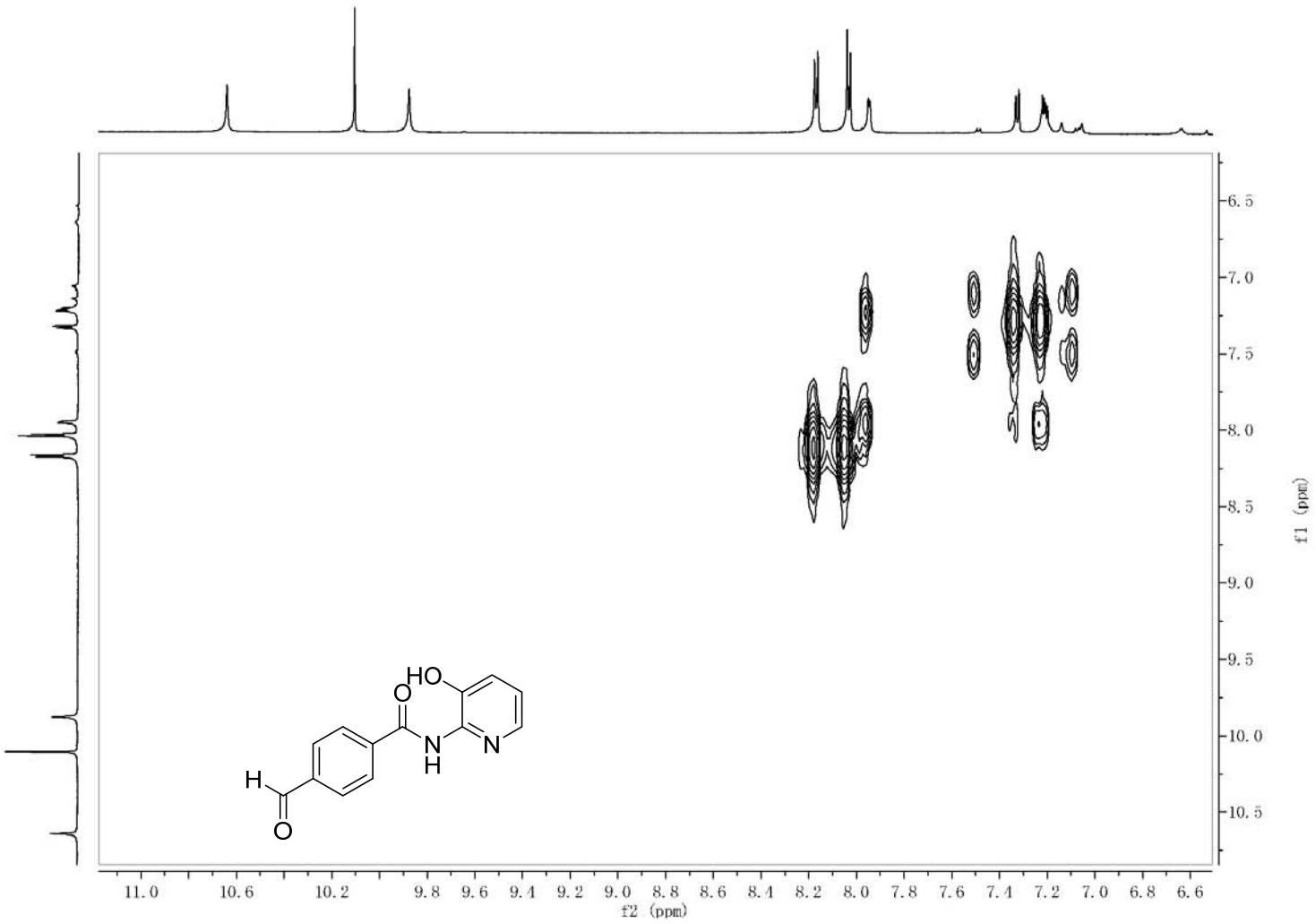

Figure S23. The ^{1}H-^{1}H COSY Spectrum of Compound **6** in DMSO–d_6

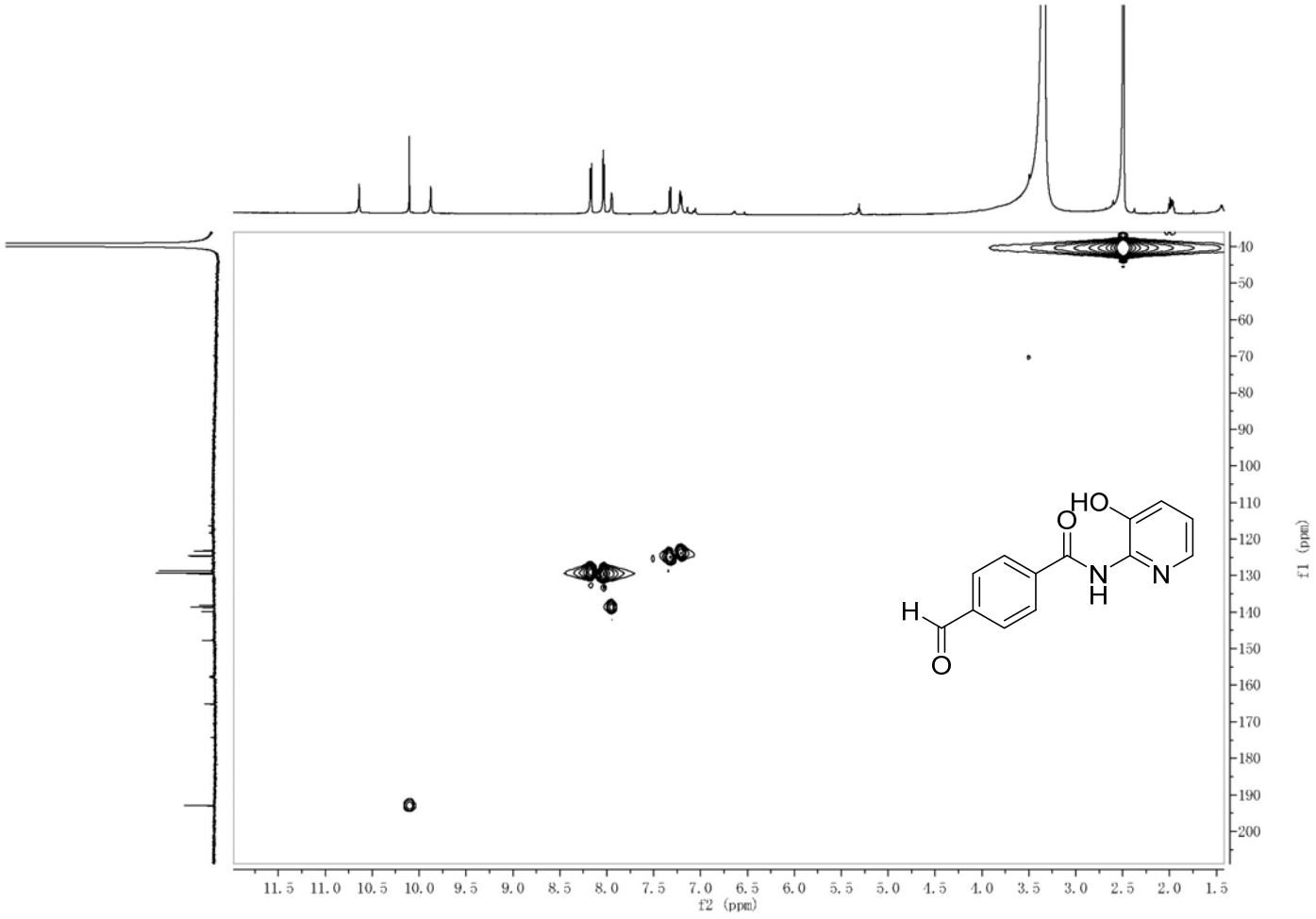

Figure S24. The HSQC Spectrum of Compound **6** in DMSO–d_6

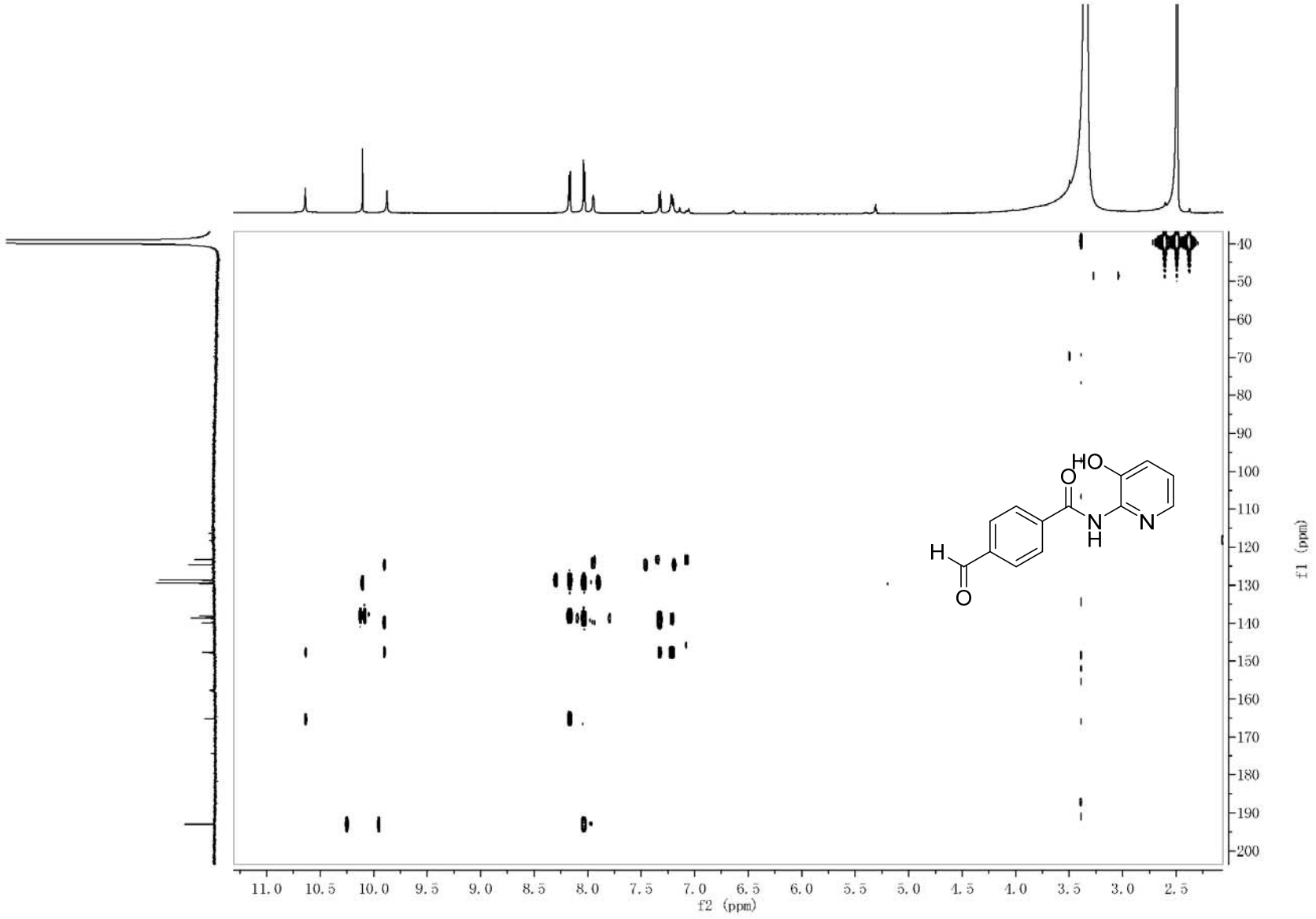

Figure S25. The HMBC Spectrum of Compound **6** in DMSO−d_6