Supplementary data

Determination of the absolute configurations and anti-angiogenic activities of new diarylheptanoid glucosides from *Curcuma phaeocaulis*

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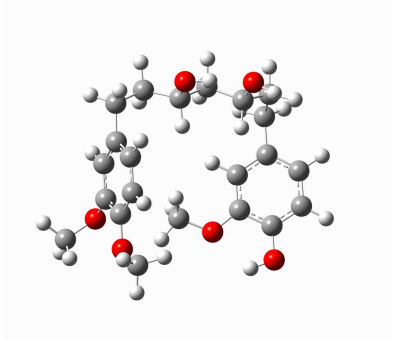
ECD calculation of compounds 1a, 4a-7a.

ECD calculation of compound 1a. Conformation searches based on molecular mechanics with MMFF94s force field were performed for (3*R*,5*S*)-**1a** within 10 kcal/mol and gave 521 conformers. In this case, 17 conformers were selected for the calculations (Boltzmann distribution ⩾ 1%, Figure S1) [1]. The selected conformers were optimized using DFT at the B3LYP/6-31G (d) level in vacuum, and the solve for more states (N=50) was set. This was carried out using the Gaussian 16 program (Table S1), while memory limit was 10 GB [2]. The B3LYP/6-31G (d)-optimized conformers were then reoptimized at the *ω*B97XD/DGDZVP level in acetonitrile. ECD computations for the *ω*B97XD/DGDZVP-optimized conformers (Fig. S1) were carried out at the CAM-B3LYP/DGDZVP level in acetonitrile [3]. The model of solvation in acetonitrile was IEFPCM. According to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG), the ECD spectrum for (3*R*,5*S*)-**1a** was generated using SpecDis 1.71 with σ = 0.25 eV [4]. The corresponding theoretical ECD spectrum of (3*S*,5*R*)-**1a** was depicted by inverting that of (3*R*,5*S*)-**1a**.

Table S1. Energy analysis for the conformers of (3*R*,5*S*)-**1a**.

Conf.	MMFF energy	B3LYP/6-31G (d) Gibbs free energy (298.15 K)			*ω*B97XD/DGDZVP Gibbs free energy (298.15 K)		
	ΔE (kcal/mol)	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution
1a-1	0	-1307.269769	0.0650	0.179	-1307.021966	1.2590	0.063
1a-2	0.23766	-1307.267745	1.3350	0.021	-1307.020001	2.4920	0.008

1a-3	0.41412	-1307.268213	1.0410	0.034	-1307.020192	2.3720	0.01
1a-4	0.5267	-1307.269333	0.3390	0.113	-1307.022242	1.0860	0.084
1a-5	0.8877	-1307.269044	0.5200	0.083	-1307.022835	0.7140	0.158
1a-6	1.01408	-1307.268867	0.6310	0.069	-1307.019608	2.7390	0.005
1a-7	1.19945	-1307.269872	0.0000	0.199	-1307.021494	1.5550	0.038
1a-8	1.22704	-1307.269316	0.3490	0.111	-1307.023973	0.0000	0.528
1a-9	1.39302	-1307.267945	1.2100	0.026	-1307.019959	2.5180	0.008
1a-10	1.43303	-1307.26703	1.7840	0.01	-1307.020146	2.4010	0.009
1a-11	1.43447	-1307.268224	1.0350	0.035	-1307.020703	2.0520	0.017
1a-12	1.49673	-1307.268244	1.0220	0.036	-1307.019331	2.9120	0.004
1a-13	1.52988	-1307.26511	2.9890	0.001	-1307.019663	2.7040	0.005
1a-14	1.61391	-1307.268413	0.9160	0.042	-1307.021059	1.8280	0.024
1a-15	1.62922	-1307.266112	2.3600	0.004	-1307.020763	2.0140	0.018
1a-16	1.63068	-1307.26824	1.0240	0.035	-1307.019339	2.9070	0.004
1a-17	1.70283	-1307.265999	2.4310	0.003	-1307.020792	1.9960	0.018



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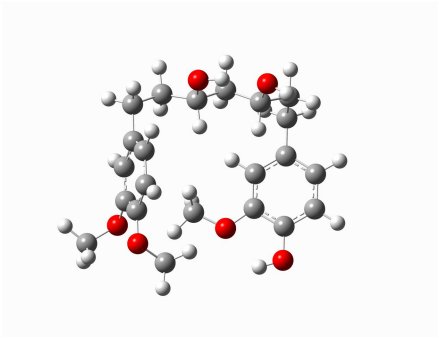

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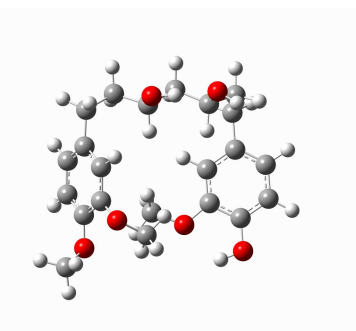

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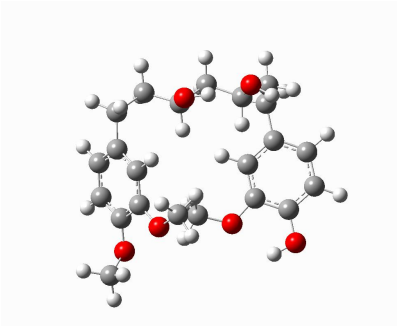

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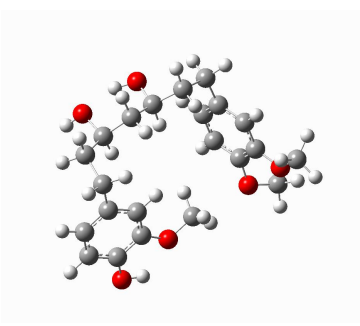

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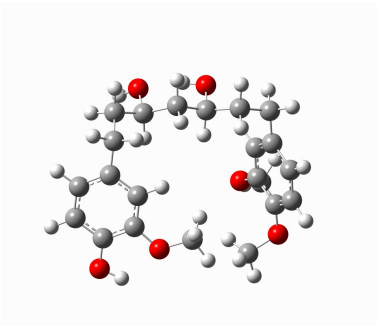

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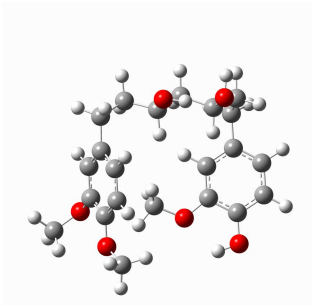

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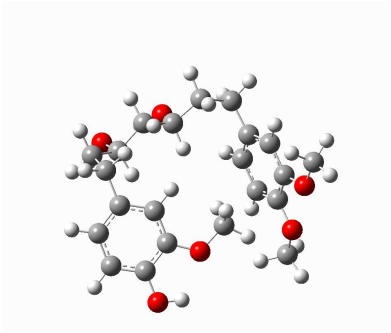

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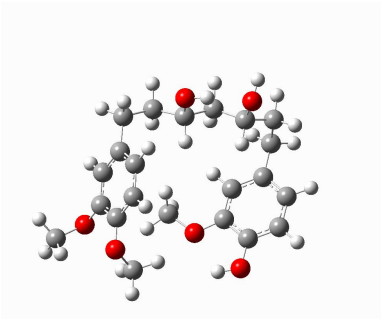

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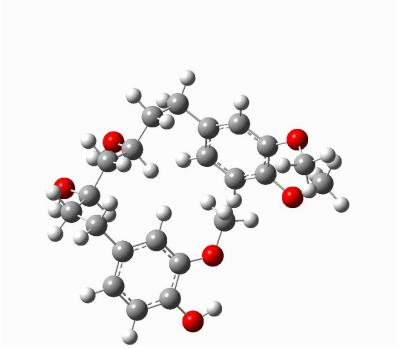

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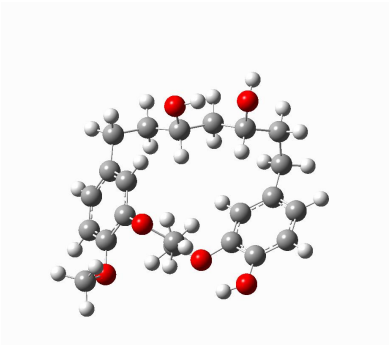

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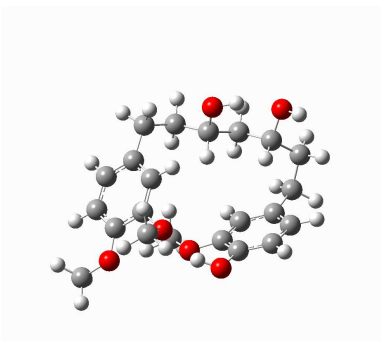

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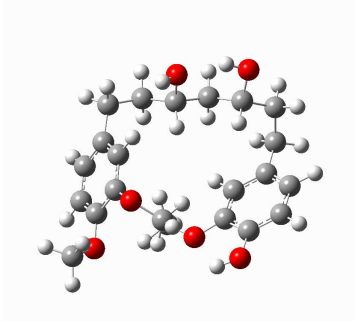

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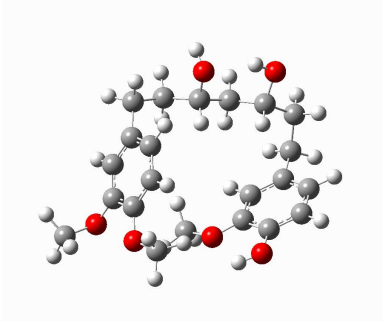

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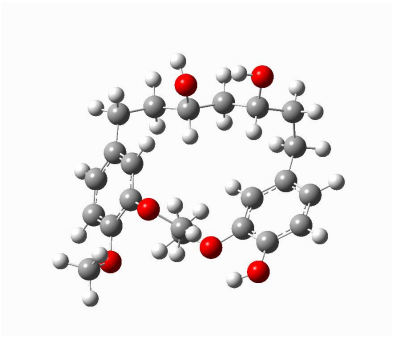

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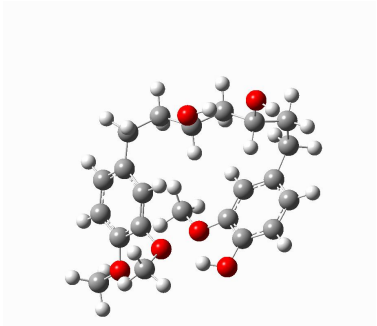

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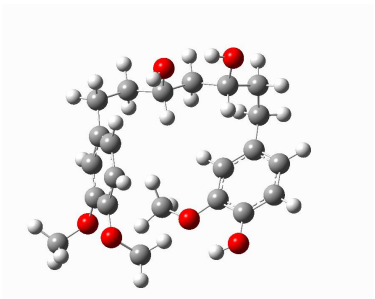


1a-17

Figure S1. ωB97XD/DGDZVP-optimized 17 conformers of (3*R*,5*S*)-**1a**.

ECD calculation of compound 4a. Conformation searches based on molecular mechanics with MMFF94s force field were performed for (3*R*,5*S*,6*R*)-**4a** and (3*S*,5*R*,6*R*)-**4a**. As a result, 954 and 5475 conformers were generated for (3*R*,5*S*,6*R*)-**4a** and (3*S*,5*R*,6*R*)-**4a** within 10 kcal/mol**,** among them, 13 and 21 conformers were selected for calculations (Boltzmann distribution≥1%, Figure S2 and S3) [1]. The selected conformers were optimized using DFT at the B3LYP/6-31G (d) level in vacuum, and the solve for more states (N=50) was set. This was carried out using the Gaussian 16 program (Table S2 and S3), while memory limit was 10 GB [2]. ECD computations for the B3LYP/6-31G (d)-optimized conformers (Fig. S2 and S3) were carried out at the CAM-B3LYP/DGDZVP level in acetonitrile [3]. The model of solvation in acetonitrile was IEFPCM. According to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG), the ECD spectra for (3*R*,5*S*,6*R*)-**4a** and (3*S*,5*R*,6*R*)-**4a** were generated using SpecDis 1.71 with σ = 0.25 eV and a UV shift of +10 nm [4].

Table S2. Energy analysis for the conformers of (3*R*,5*S*,6*R*)-**4a**.

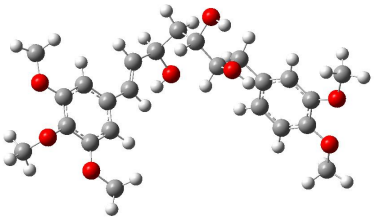
Conf.	**MMFF energy**	**B3LYP/6-31G(d) Gibbs free energy (298.15 K)**		
	ΔE (kcal/ mol)	**G (Hartree)**	**ΔG (kcal/mol)**	**Boltzmann Distribution**
(3*R*,5*S*,6*R*)-**4a-1**	0	-1535.034582	4.0740	0
(3*R*,5*S*,6*R*)-**4a-2**	0.03	-1535.035399	3.5610	0.001
(3*R*,5*S*,6*R*)-**4a-3**	0.66	-1535.034592	4.0680	0
(3*R*,5*S*,6*R*)-**4a-4**	0.76	-1535.035395	3.5640	0.001
(3*R*,5*S*,6*R*)-**4a-5**	0.91	-1535.041074	0.0000	0.472
(3*R*,5*S*,6*R*)-**4a-6**	0.96	-1535.03475	3.9690	0.001

(3*R*,5*S*,6*R*)-**4a-7**	1.08	-1535.034587	4.0710	0
(3*R*,5*S*,6*R*)-**4a-8**	1.48	-1535.038344	1.7130	0.026
(3*R*,5*S*,6*R*)-**4a-9**	1.65	-1535.039866	0.7580	0.131
(3*R*,5*S*,6*R*)-**4a-10**	1.74	-1535.040145	0.5830	0.176
(3*R*,5*S*,6*R*)-**4a-11**	1.91	-1535.039436	1.0280	0.083
(3*R*,5*S*,6*R*)-**4a-12**	1.94	-1535.035346	3.5950	0.001
(3*R*,5*S*,6*R*)-**4a-13**	1.94	-1535.039656	0.8900	0.105

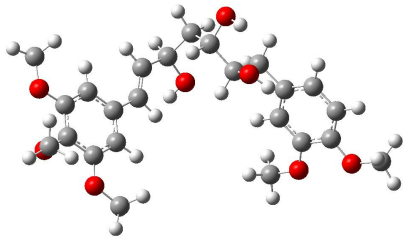
Table S3. Energy analysis for the conformers of (3*S*,5*R*,6*R*)-**4a**.

Conf.	**MMFF energy**	**B3LYP/6-31G(d) Gibbs free energy (298.15 K)**		
	ΔE (kcal/ mol)	**G (Hartree)**	**ΔG (kcal/mol)**	**Boltzmann Distribution**
(3*S*,5*R*,6*R*)-**4a-1**	0	-1535.030116	0.9050	0.026
(3*S*,5*R*,6*R*)-**4a-2**	0.0154	-1535.031201	0.2240	0.082
(3*S*,5*R*,6*R*)-**4a-3**	0.217	-1535.030113	0.9070	0.026
(3*S*,5*R*,6*R*)-**4a-4**	0.2812	-1535.029482	1.3030	0.013
(3*S*,5*R*,6*R*)-**4a-5**	0.2926	-1535.028295	2.0480	0.004
(3*S*,5*R*,6*R*)-**4a-6**	0.3042	-1535.031552	0.0040	0.119
(3*S*,5*R*,6*R*)-**4a-7**	0.3371	-1535.031232	0.2050	0.084
(3*S*,5*R*,6*R*)-**4a-8**	0.339	-1535.031555	0.0020	0.119
(3*S*,5*R*,6*R*)-**4a-9**	0.3541	-1535.029377	1.3690	0.012
(3*S*,5*R*,6*R*)-**4a-10**	0.3739	-1535.030115	0.9060	0.026
(3*S*,5*R*,6*R*)-**4a-11**	0.3974	-1535.031264	0.1850	0.087
(3*S*,5*R*,6*R*)-**4a-12**	0.4262	-1535.031558	0.0000	0.119
(3*S*,5*R*,6*R*)-**4a-13**	0.4609	-1535.029377	1.3690	0.012
(3*S*,5*R*,6*R*)-**4a-14**	0.4847	-1535.028306	2.0410	0.004
(3*S*,5*R*,6*R*)-**4a-15**	0.4852	-1535.031334	0.1410	0.094
(3*S*,5*R*,6*R*)-**4a-16**	0.5339	-1535.030857	0.4400	0.057
(3*S*,5*R*,6*R*)-**4a-17**	0.5394	-1535.028301	2.0440	0.004
(3*S*,5*R*,6*R*)-**4a-18**	0.5442	-1535.030089	0.9220	0.025

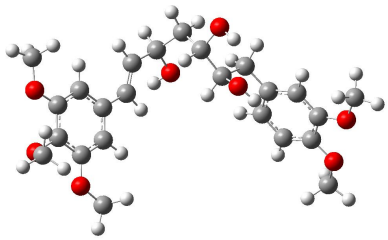
(3*S*,5*R*,6*R*)-**4a-19**	0.5501	-1535.030085	0.9240	0.025
(3*S*,5*R*,6*R*)-**4a-20**	0.5515	-1535.029622	1.2150	0.015
(3*S*,5*R*,6*R*)-**4a-21**	0.5731	-1535.030688	0.5460	0.047



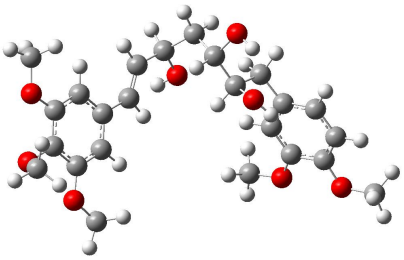
(3*R*,5*S*,6*R*)-**4a-1**



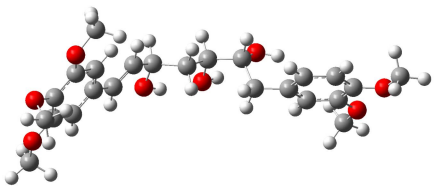
(3*R*,5*S*,6*R*)-**4a-2**



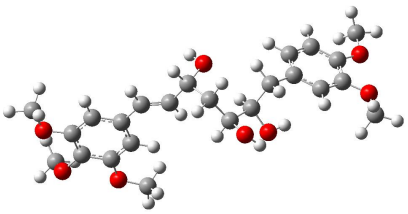
(3*R*,5*S*,6*R*)-**4a-3**



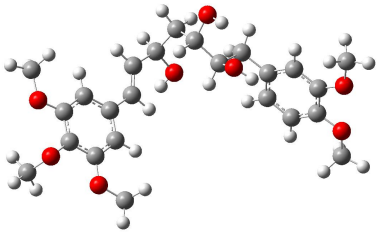
(3*R*,5*S*,6*R*)-**4a-4**



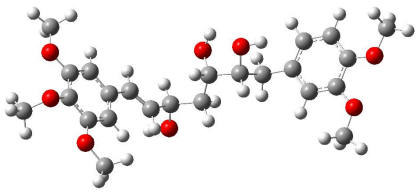
(3*R*,5*S*,6*R*)-**4a-5**



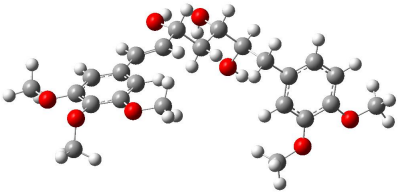
(3*R*,5*S*,6*R*)-**4a-6**



(3*R*,5*S*,6*R*)-**4a-7**



(3*R*,5*S*,6*R*)-**4a-8**



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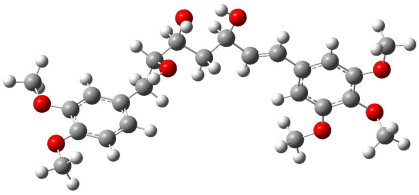
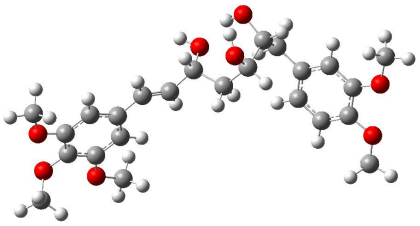
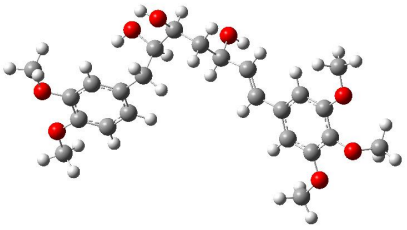


(3*R*,5*S*,6*R*)-**4a-10**



(3*R*,5*S*,6*R*)-**4a-11**



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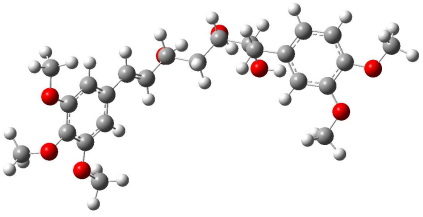
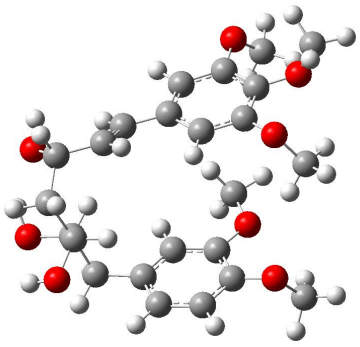
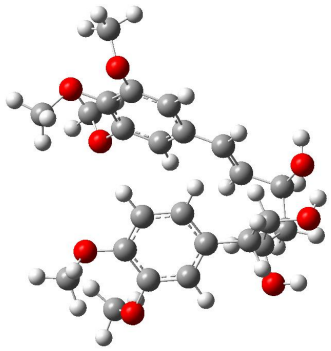


(3*R*,5*S*,6*R*)-**4a-13**

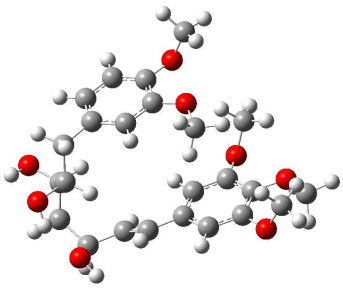
Figure S2. B3LYP/6-31G (d)-optimized 13 conformers of (3*R*,5*S*,6*R*)-**4a**.



(3*S*,5*R*,6*R*)-**4a-1**



(3*S*,5*R*,6*R*)-**4a-2**



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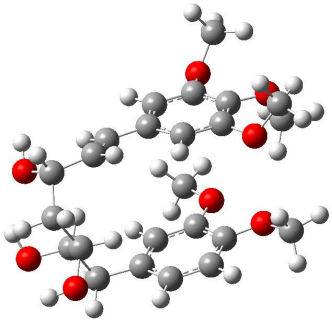
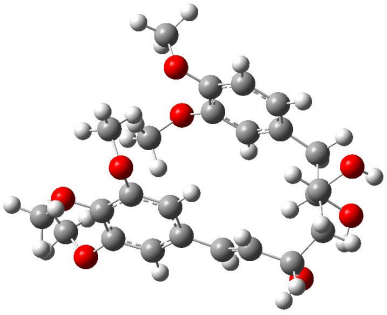
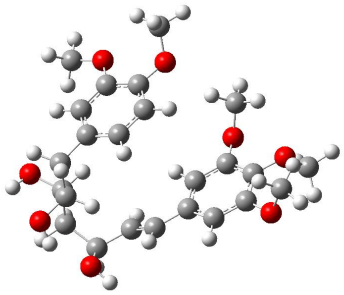


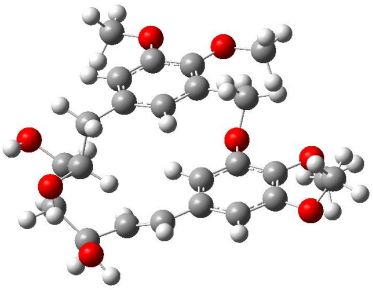
(3*S*,5*R*,6*R*)-**4a-4**



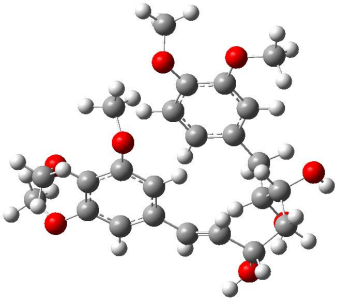
(3*S*,5*R*,6*R*)-**4a-5**



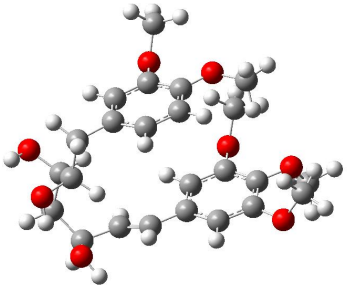
(3*S*,5*R*,6*R*)-**4a-6**



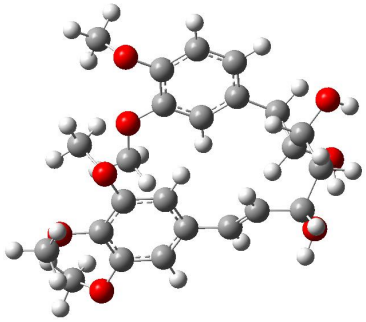
(3*S*,5*R*,6*R*)-**4a-7**



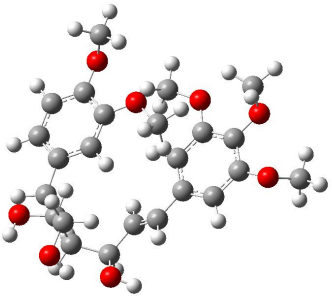
(3*S*,5*R*,6*R*)-**4a-8**



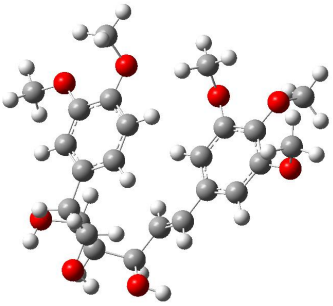
(3*S*,5*R*,6*R*)-**4a-9**



(3*S*,5*R*,6*R*)-**4a-10**



(3*S*,5*R*,6*R*)-**4a-11**



(3*S*,5*R*,6*R*)-**4a-12**

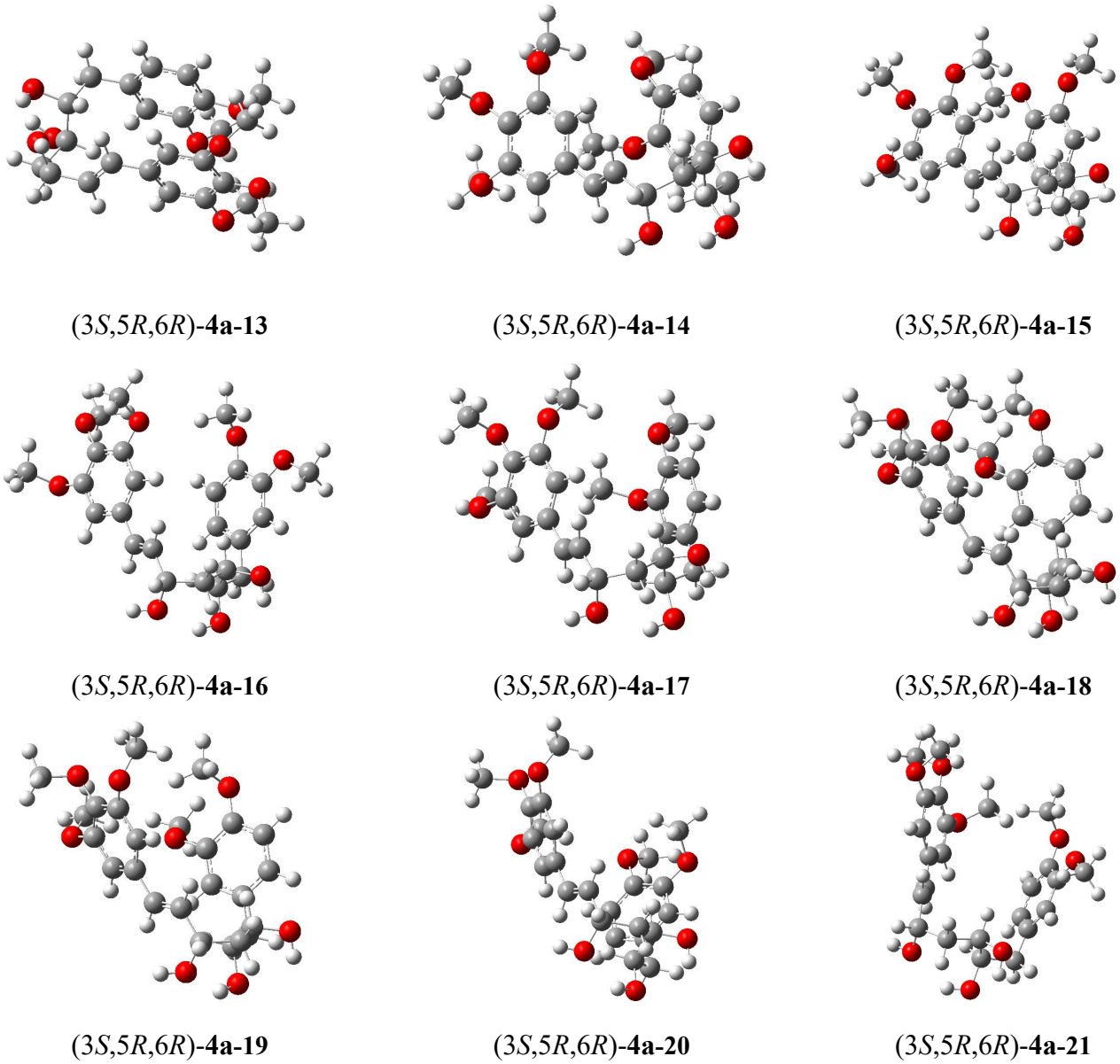


Figure S3. B3LYP/6-31G (d)-optimized 21 conformers of (3*S*,5*R*,6*R*)-**4a**.

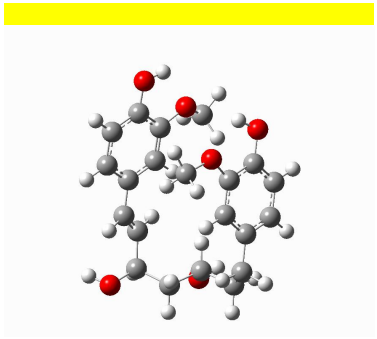
ECD calculation of Compound 5a Conformation searches based on molecular mechanics with MMFF94s force field were performed for (3*R*,5*R*)-**5a** within 10 kcal/mol and gave 4042 conformers. Among them, 16 conformers were selected for the calculations (Boltzmann distribution≥1%, Figure S4). [1]. The selected conformers were optimized using DFT at B3LYP/6-31G (d) level in vacuum, and the solve for more states (N=50) was set. This was carried out using the Gaussian 16 program (Table S4), while memory limit was 10 GB [2]. The B3LYP/6-31G (d)-optimized conformers were

then reoptimized at the ωB97XD/DGDZVP level in acetonitrile. ECD computations for the ω B97XD/DGDZVP-optimized conformers except for the repetitive ones (Fig. S4) were carried out at the CAM-B3LYP/DGDZVP level in acetonitrile [3]. The model of solvation in acetonitrile was IEFPCM. According to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG), the ECD spectrum for (3*R*,5*R*)-**5a** was generated using SpecDis 1.71 with σ = 0.30 eV and a UV shift of +20 nm [4]. The corresponding theoretical ECD spectrum of (3*S*,5*S*)-**5a** was depicted by inverting that of (3*R*,5*R*)-**5a**.

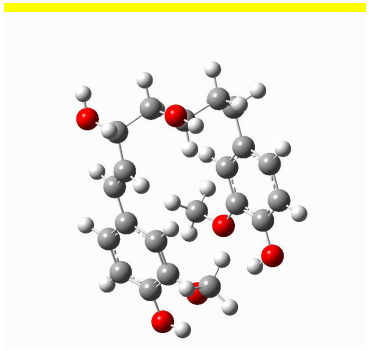
Table S4. Energy analysis for the conformers of (3*R*,5*R*)-**5a**.

Conf.	MMFF energy	B3LYP/6-31G (d) Gibbs free energy (298.15 K)			ωB97XD/DGDZVP Gibbs free energy (298.15 K)		
	ΔE (kcal/mol)	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution
5a-1	0	-1266.789441	5.8920	0	-1266.550546	1.0830	0.028
5a-2	0.4044	-1266.788465	6.5040	0	-1266.550014	1.4170	0.016
5a-3	0.4338	-1266.792895	3.7250	0.001	-1266.552043	0.1440	0.135
5a-4	0.438	-1266.789752	5.6970	0	-1266.550088	1.3700	0.017
5a-5	0.7565	-1266.788651	6.3880	0	-1266.550126	1.3470	0.018
5a-6	0.8028	-1266.787586	7.0560	0	-1266.552272	0.0000	0.172
5a-7	0.8238	-1266.786473	7.7540	0	-1266.551757	0.3230	0.1
5a-8	0.8427	-1266.788638	6.3960	0	-1266.549428	1.7850	0.008
5a-9	0.9976	-1266.790322	5.3390	0	-1266.550534	1.0910	0.027
5a-10	1.1128	-1266.788266	6.6290	0	-1266.551806	0.2920	0.105
5a-11	1.3137	-1266.79883	0.0000	0.499	-1266.551694	0.3630	0.093
5a-12	1.3254	-1266.79883	0.0000	0.499	-1266.551694	0.3630	0.093
5a-13	1.3397	-1266.790548	5.1970	0	-1266.549395	1.8050	0.008

5a-14	1.3798	-1266.787844	6.8940	0	-1266.550008	1.4210	0.016
5a-15	1.3966	-1266.790865	4.9980	0	-1266.551954	0.1990	0.123
5a-16	1.4189	-1266.787925	6.8430	0	-1266.550952	0.8280	0.042



5a-1



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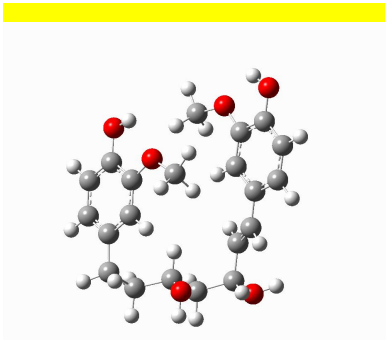

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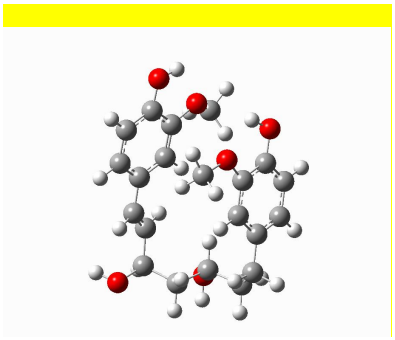

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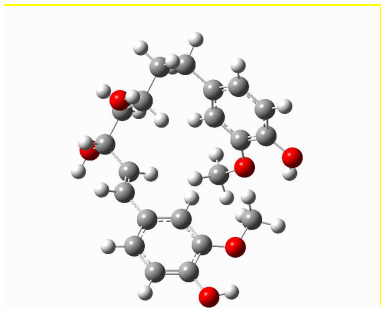

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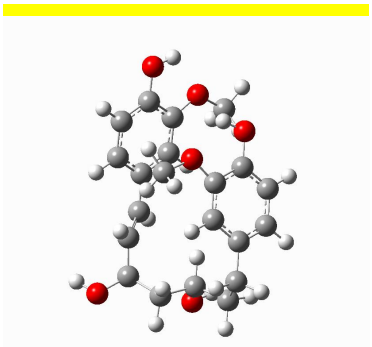
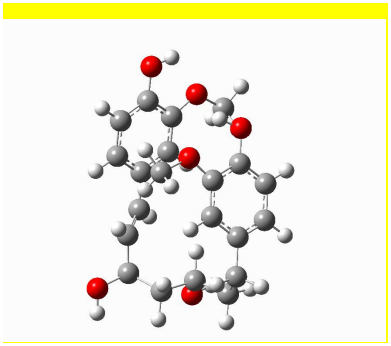
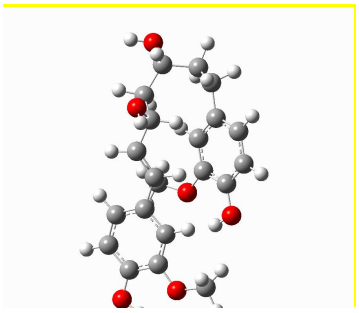


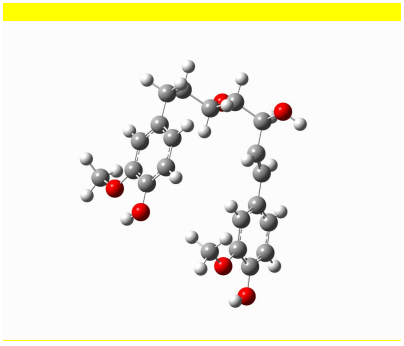
5a-6



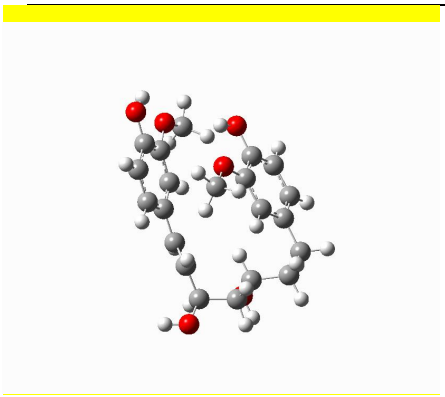
5a-7



5a-8



5a-9



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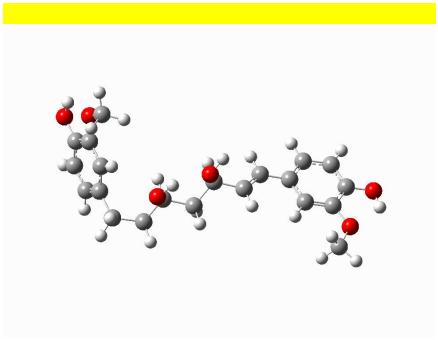

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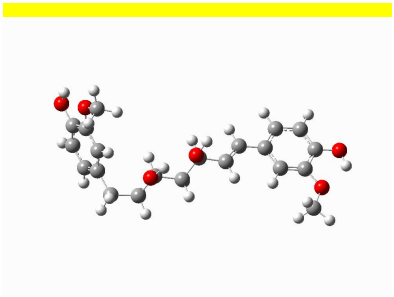

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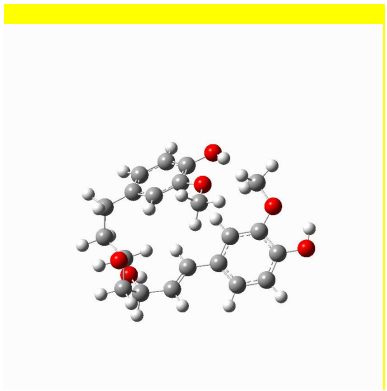

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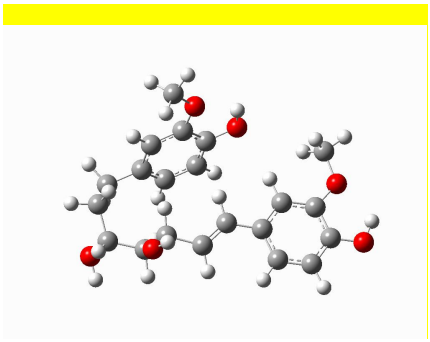

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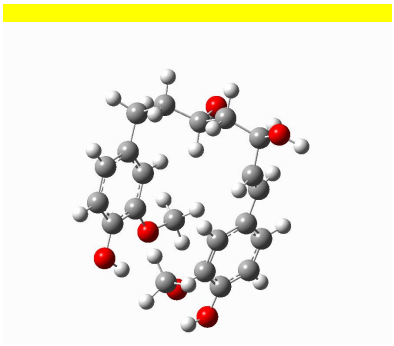
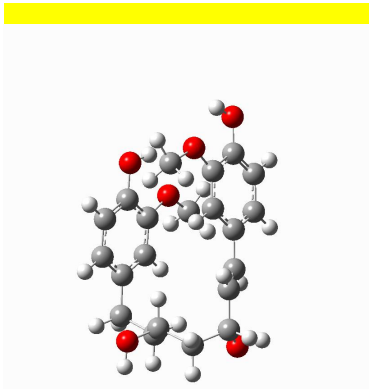


5a-15



5a-16

Figure S4. ωB97XD/DGDZVP optimized 16 conformers of (3*R*,5*R*)-**5a**

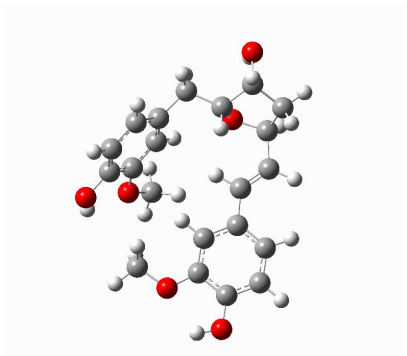
ECD calculation of compound 6a. Conformation searches based on molecular mechanics with MMFF94s force field were performed for (3*S*,5*R*,6*R*)-**6a** within 10 kcal/mol and gave 619 conformers. Among them, 27 conformers were selected for the calculations (Boltzmann distribution

≥1%, Figure S5). [1]. The selected conformers were optimized using DFT at the B3LYP/6-31G (d) level in vacuum, and the solve for more states (N=50) was set. This was carried out using the Gaussian 16 program (Table S5), while memory limit was 10 GB [2]. The B3LYP/6-31G (d)-optimized conformers were then reoptimized at the *ω*B97XD/DGDZVP level in acetonitrile. ECD computations for the *ω*B97XD/DGDZVP-optimized conformers (Fig. S5) were carried out at the CAM-B3LYP/DGDZVP level in acetonitrile [3]. The model of solvation in acetonitrile was IEFPCM. According to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG), the ECD spectrum for (3*S*,5*R*,6*R*)-**6a** was generated using SpecDis 1.71 with σ = 0.25 eV [4]. The corresponding theoretical ECD spectrum of (3*R*,5*S*,6*S*)-**6a** was depicted by inverting that of (3*S*,5*R*,6*R*)-**6a**.

Table S5. Energy analysis for the conformers of (3*S*,5*R*,6*R*)-**6a**.

Conf.	MMFF energy	B3LYP/6-31G (d) Gibbs free energy (298.15 K)			*ω*B97XD/DGDZVP Gibbs free energy (298.15 K)		
	ΔE (kcal/mol)	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution
6a-1	0	-1265.605411	0.7580	0.04	-1265.355677	1.2860	0.031
6a-2	0.5782	-1265.6053	0.8280	0.035	-1265.355532	1.3770	0.026
6a-3	0.5826	-1265.606029	0.3700	0.076	-1265.355117	1.6370	0.017
6a-4	0.803	-1265.605983	0.3990	0.072	-1265.355723	1.2570	0.032
6a-5	0.8364	-1265.605984	0.3980	0.073	-1265.355721	1.2580	0.032
6a-6	0.9299	-1265.603029	2.2530	0.003	-1265.355227	1.5680	0.019
6a-7	1.018	-1265.604136	1.5580	0.01	-1265.353819	2.4520	0.004
6a-8	1.2395	-1265.604513	1.3220	0.015	-1265.355895	1.1490	0.039
6a-9	1.2808	-1265.604314	1.4460	0.012	-1265.354228	2.1950	0.007

6a-10	1.3143	-1265.606619	0.0000	0.142	-1265.356235	0.9360	0.056
6a-11	1.3535	-1265.604819	1.1290	0.021	-1265.35533	1.5040	0.021
6a-12	1.4011	-1265.606131	0.3060	0.085	-1265.356692	0.6490	0.09
6a-13	1.4089	-1265.604014	1.6350	0.009	-1265.353506	2.6480	0.003
6a-14	1.4246	-1265.605311	0.8210	0.036	-1265.355567	1.3550	0.027
6a-15	1.4845	-1265.605311	0.8210	0.036	-1265.355561	1.3590	0.027
6a-16	1.4907	-1265.60466	1.2290	0.018	-1265.354746	1.8700	0.011
6a-17	1.5134	-1265.604747	1.1750	0.02	-1265.35471	1.8930	0.011
6a-18	1.5744	-1265.604392	1.3970	0.013	-1265.357727	0.0000	0.27
6a-19	1.5748	-1265.606295	0.2030	0.101	-1265.355966	1.1050	0.042
6a-20	1.5755	-1265.602338	2.6860	0.002	-1265.354349	2.1190	0.008
6a-21	1.6013	-1265.604817	1.1310	0.021	-1265.355581	1.3460	0.028
6a-22	1.6047	-1265.606294	0.2040	0.101	-1265.355966	1.1050	0.042
6a-23	1.6111	-1265.60418	1.5300	0.011	-1265.354706	1.8950	0.011
6a-24	1.6186	-1265.604394	1.3960	0.013	-1265.356938	0.4950	0.117
6a-25	1.6338	-1265.603939	1.6820	0.008	-1265.353388	2.7220	0.003
6a-26	1.6408	-1265.604372	1.4100	0.013	-1265.354754	1.8650	0.012
6a-27	1.6493	-1265.604465	1.3520	0.015	-1265.354951	1.7420	0.014



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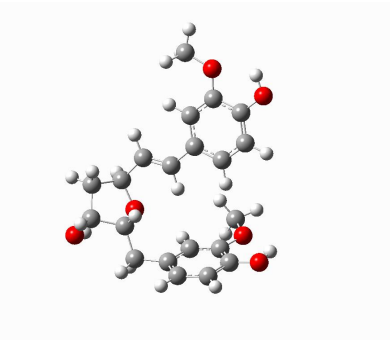
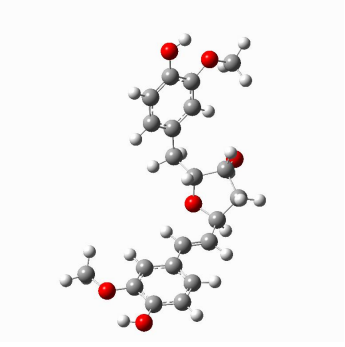


6a-2



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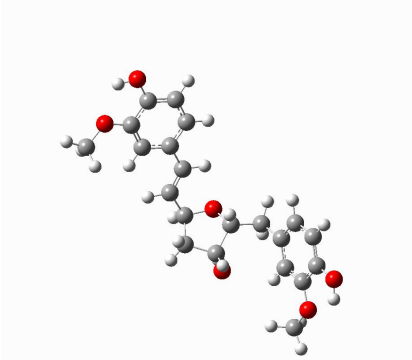
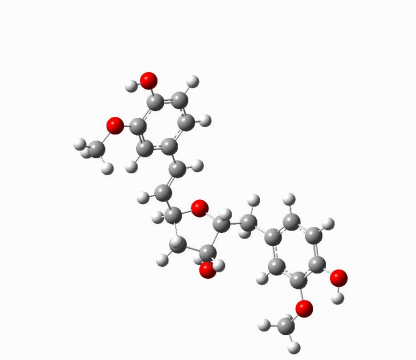
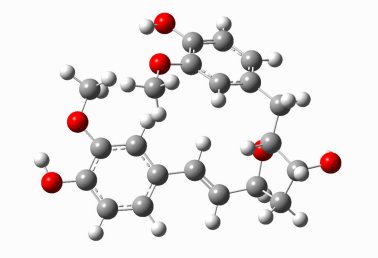


6a-4



6a-5



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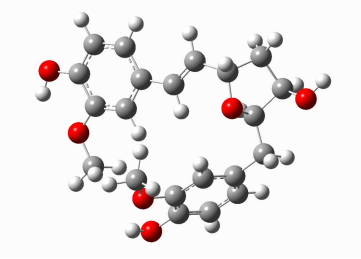

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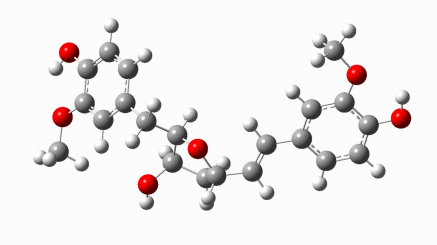

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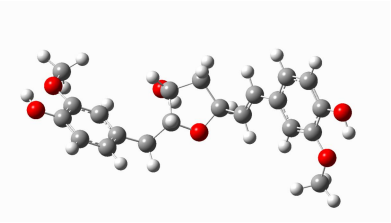
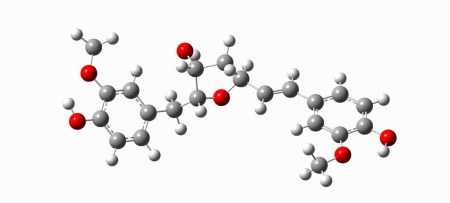


6a-9



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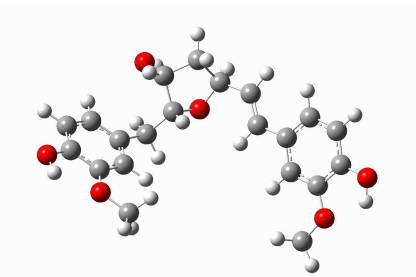

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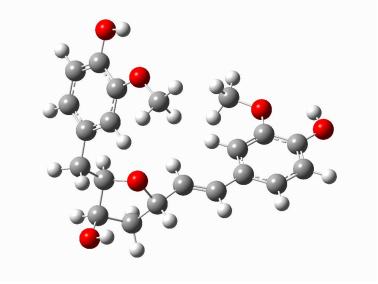

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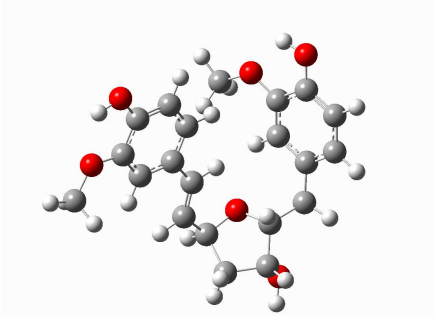

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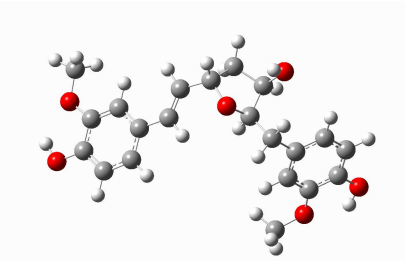

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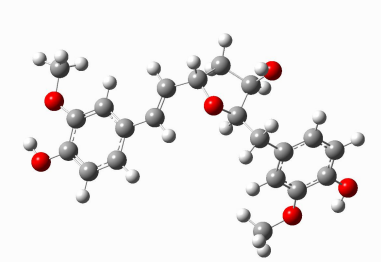

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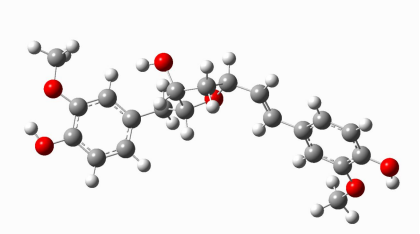

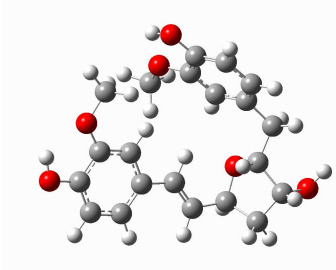

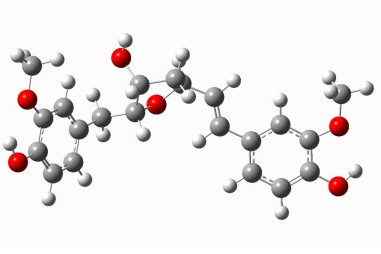

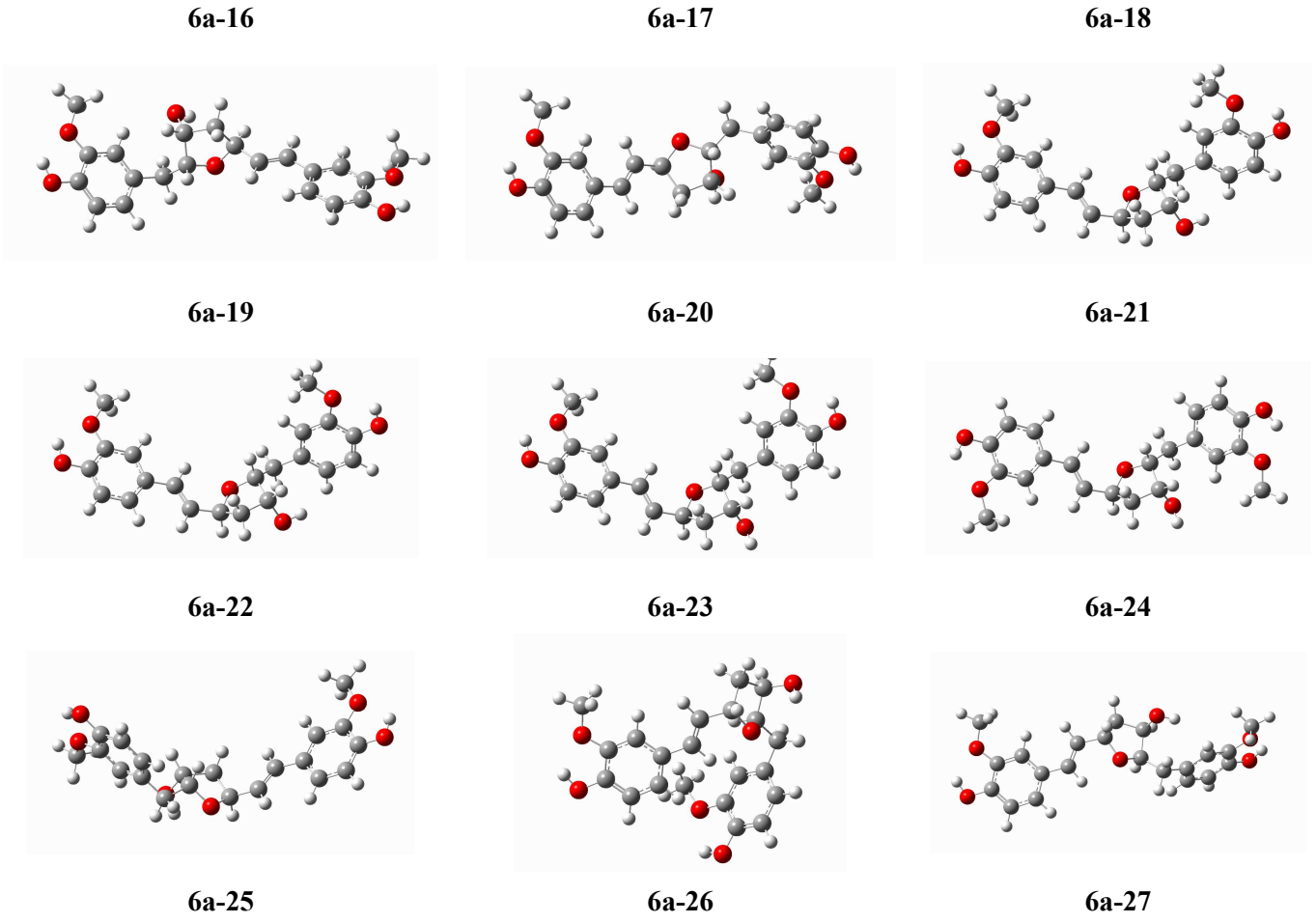

Figure S5. *ω*B97XD/DGDZVP-optimized 27 conformers of (3*S*,5*R*,6*R*)-**6a**.

ECD calculation of compound 7a. Conformation searches based on molecular mechanics with MMFF94s force field were performed for (1*R*,2*S*,3*S*,5*S*)-**7a** within 10 kcal/mol and gave 254 conformers. Among them, 10 conformers were selected for the calculations (Boltzmann distribution ≥1%, Figure S6) [1]. The selected conformers were optimized using DFT at the B3LYP/6-31G (d) level in vacuum, and the solve for more states (N=50) was set. This was carried out using the Gaussian 16 program (Table S6), while memory limit was 10 GB [2]. The B3LYP/6-31G (d)-optimized conformers were then reoptimized at the *ω*B97XD/DGDZVP level in acetonitrile. ECD computations for the *ω*B97XD/DGDZVP-optimized conformers (Fig. S6) were carried out at

the CAM-B3LYP/DGDZVP level in acetonitrile [3]. The model of solvation in acetonitrile was IEFPCM. According to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG), the ECD spectrum for (1*R*,2*S*,3*S*,5*S*)-**7a** was generated using SpecDis 1.71 with σ = 0.25 eV [4]. The corresponding theoretical ECD spectrum of (1*S*,2*R*,3*R*,5*R*)-**7a** was depicted by inverting that of (1*R*,2*S*,3*S*,5*S*)-**7a**.

Table S6. Energy analysis for the conformers of (1*R*,2*S*,3*S*,5*S*)-**7a**.

Conf.	MMFF energy	B3LYP/6-31G (d) Gibbs free energy (298.15 K)			ωB97XD/DGDZVP Gibbs free energy (298.15 K)		
	ΔE (kcal/ mol)	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution	G (Hartree)	ΔG (kcal/mol)	Boltzmann Distribution
7a-1	0	-1342.021021	1.8690	0.016	-1341.781389	0.0000	0.403
7a-2	0.34907	-1342.022861	0.7140	0.116	-1341.780735	0.4100	0.202
7a-3	0.7028	-1342.021375	1.6470	0.024	-1341.77976	1.0220	0.072
7a-4	1.54516	-1342.022804	0.7500	0.109	-1341.779725	1.0440	0.069
7a-5	1.71868	-1342.02193	1.2990	0.043	-1341.780534	0.5370	0.163
7a-6	1.86335	-1342.020825	1.9920	0.013	-1341.777119	2.6790	0.004
7a-7	1.91997	-1342.024	0.0000	0.386	-1341.778706	1.6840	0.023
7a-8	1.92395	-1342.016572	4.6610	0	-1341.776879	2.8300	0.003
7a-9	1.99913	-1342.023737	0.1650	0.292	-1341.779378	1.2620	0.048
7a-10	2.02204	-1342.016969	4.4120	0	-1341.778065	2.0860	0.012

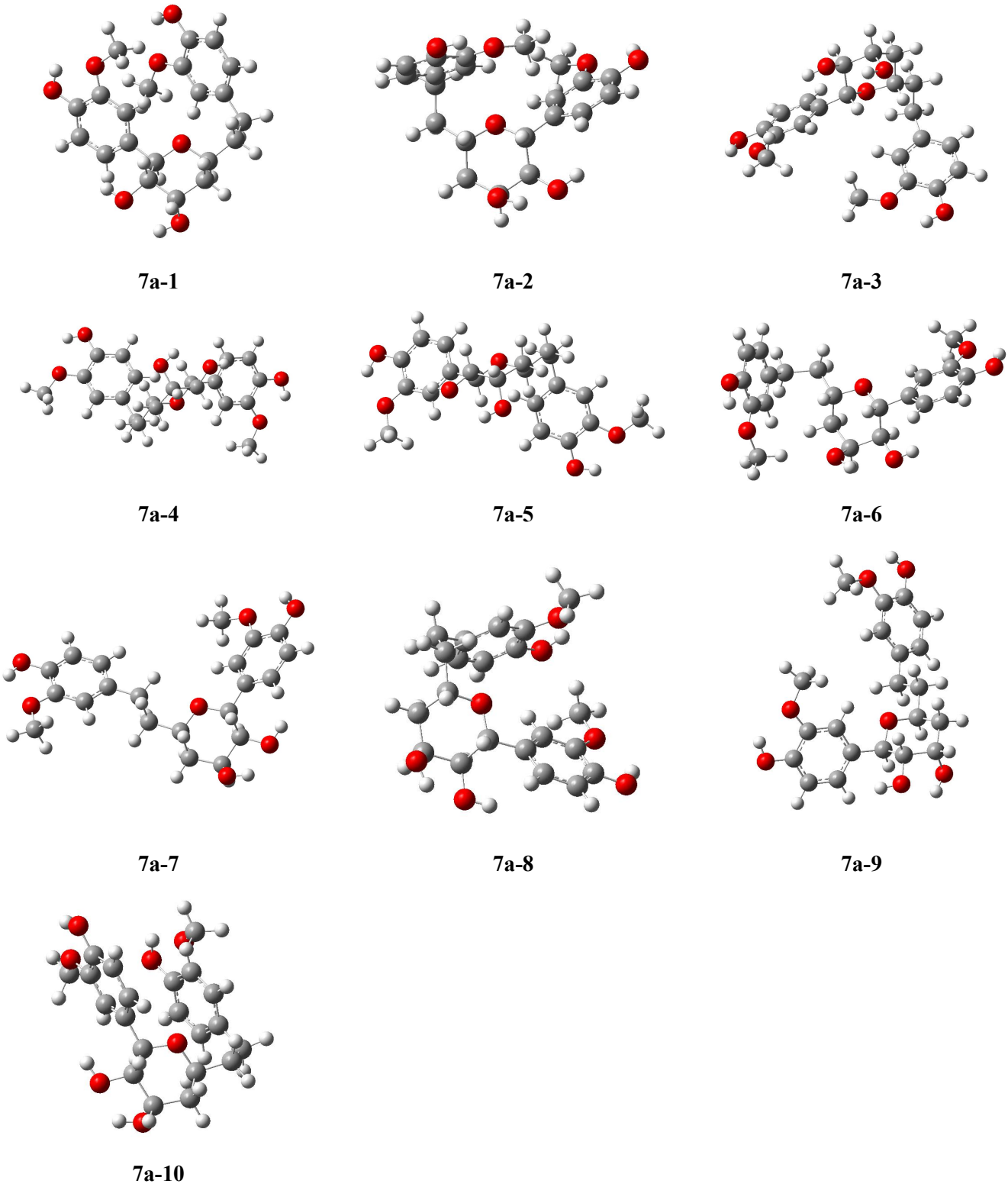

Figure S6. ωB97XD/DGDZVP-optimized 10 conformers of (1*R*,2*S*,3*S*,5*S*)-**7a**.

UV/ECD experiment of compound 1a-7a. Compounds **1a** (1.15 mmol/L), **2a** (1.24 mmol/L), **3a** (1.04 mmol/L), **4a** (0.94 mmol/L), **5a** (1.07 mmol/L), **6a** (1.16 mmol/L), and **7a** (1.18 mmol/L) were putted into the Spectrophotometer Cell (path length:1 cm). Baseline corrections of compounds **1a** and **4a-7a** were with acetonitrile as blank solvent, while compounds **2a** and **3a** were with methanol as blank solvent. The data was recorded by Applied Chirascan-plus Circular Dichroism Spectrometer, and the scans were repeated twice and averaged.

References

[1] (a) Goto, H., and Osawa, E. (1989). Corner flapping: a simple and fast algorithm for exhaustive generation of ring conformations. *J. Am. Chem. Soc.* 111, 8950-8951. (b) Goto, H., and Osawa, E. (1993). An efficient algorithm for searching low-energy conformers of cyclic and acyclic molecules. *J. Chem. Soc., Perkin. Trans.* 2, 187-198.

[2] Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., Scalmani, G., Barone, V., Petersson, G. A., Nakatsuji, H., Li, X., Caricato, M., Marenich, A. V., Bloino, J., Janesko, B. G., Gomperts, R., Mennucci, B., Hratchian, H. P., Ortiz, J. V., Izmaylov, A. F., Sonnenberg, J. L., Williams-Young, D., Ding, F., Lipparini, F., Egidi, F., Goings, J., Peng, B., Petrone, A., Henderson, T., Ranasinghe, D., Zakrzewski, V. G., Gao, J., Rega, N., Zheng, G>, Liang, W., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Throssell, K., Montgomery, J. A., Peralta, J. E., Ogliaro, F., Bearpark, M. J., Heyd, J. J., Brothers, E. N., Kudin, K. N., Staroverov, V. N., Keith, T. A., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A. P., Burant, J. C.,

Iyengar, S. S., Tomasi, J., Cossi, M., Millam, J. M., Klene, M., Adamo, C., Cammi, R., Ochterski, J. W., Martin, R. L., Morokuma, K., Farkas, O., Foresman, J. B., Fox, D. J. Gaussian 16, Revision B.01, Gaussian, Inc., Wallingford CT, 2016.

[3]. Liu, Y.; Liu, F.; Qiao M.M.; Guo, L.; Chen, M.H.; Peng, C.; Xiong, L. Curcumanes A and B, Two Bicyclic Sesquiterpenoids with Significant Vasorelaxant Activity from *Curcuma longa*. *Org. Lett*. 2019, 21(4), 1197−1201.

[4]. Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. Spec Dis, version 1.71, University of Würzburg, Germany, 2017

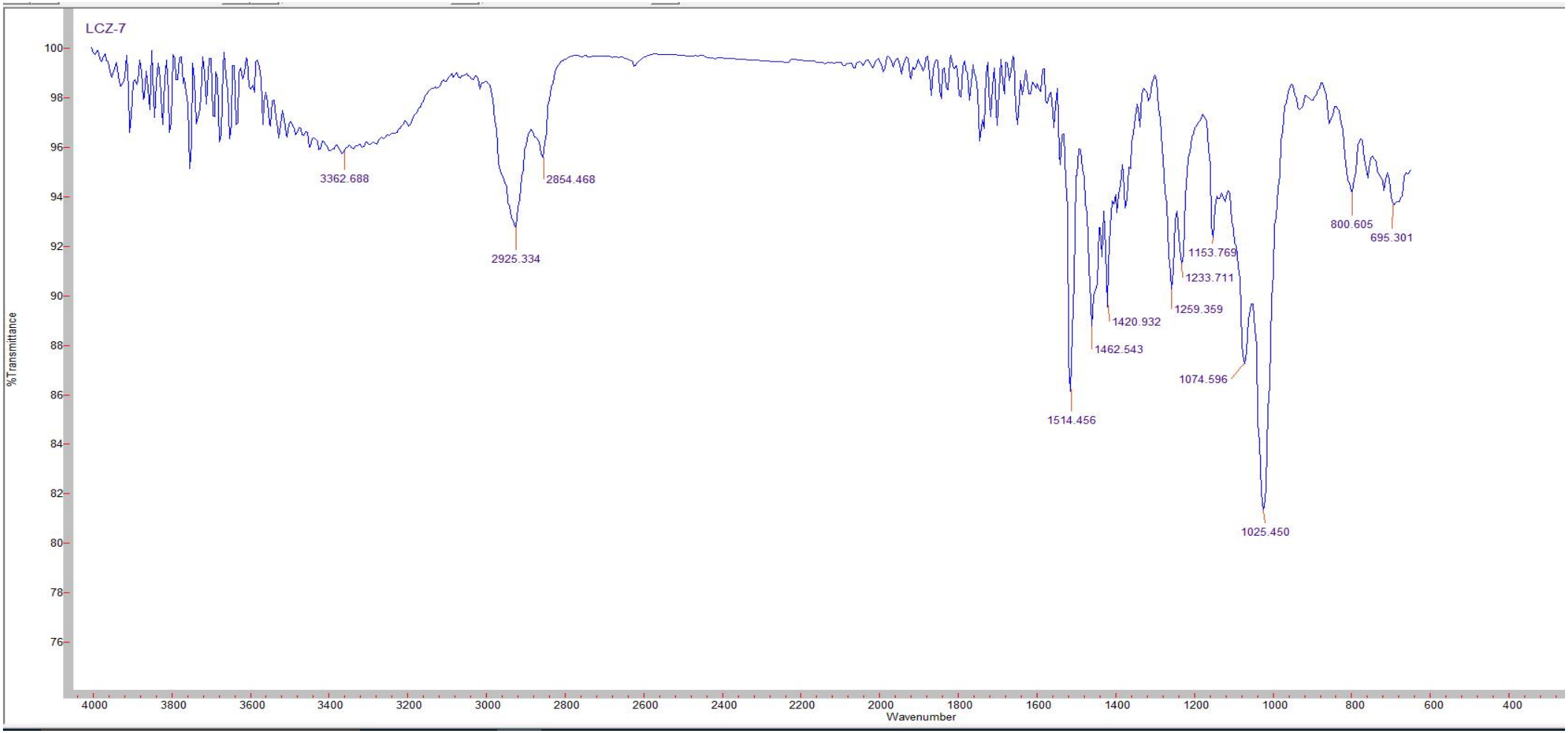

Figure S7. The IR spectrum of compound **1**.

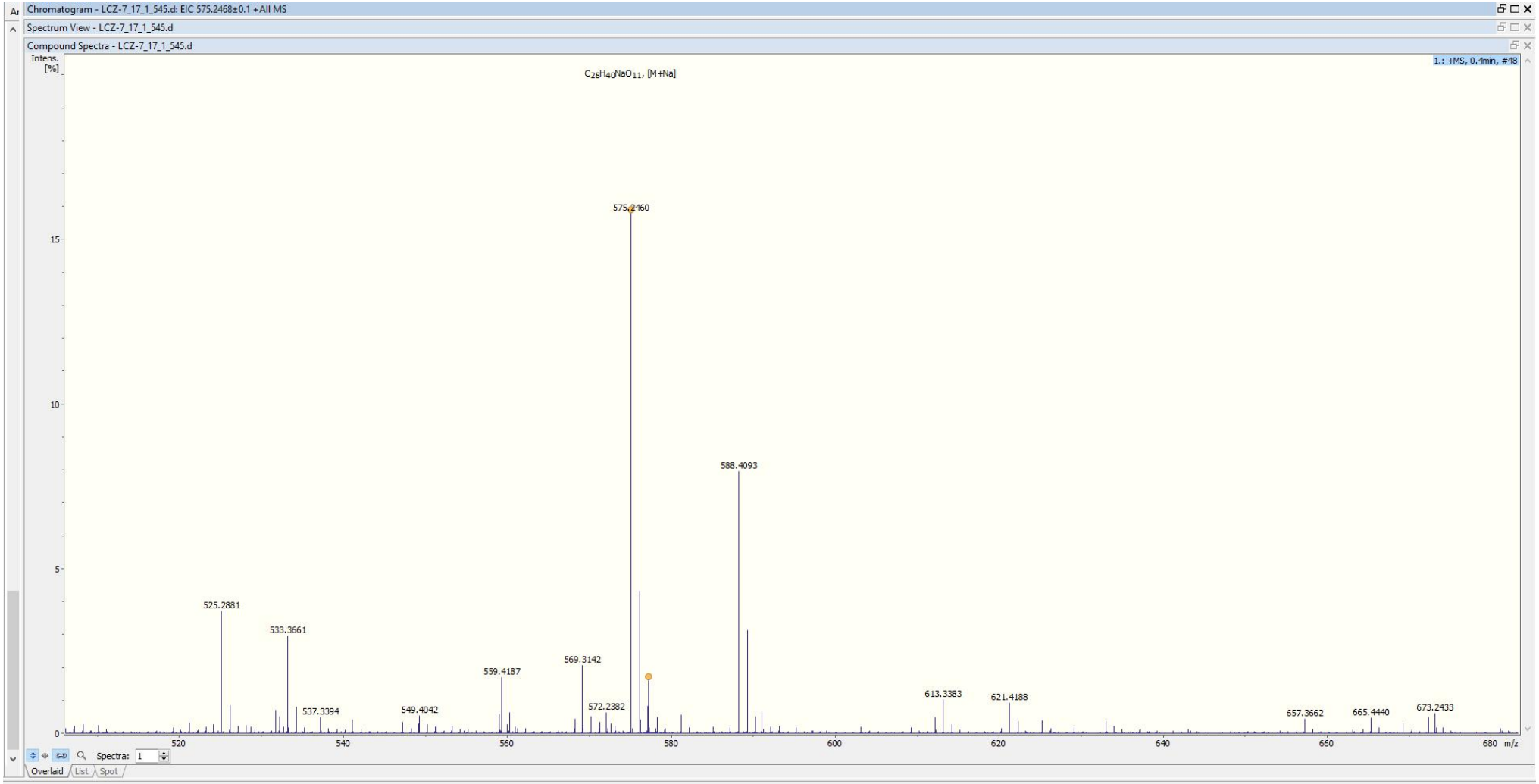

Figure S8. The (+)-HRESIMS spectroscopic data of compound **1**.

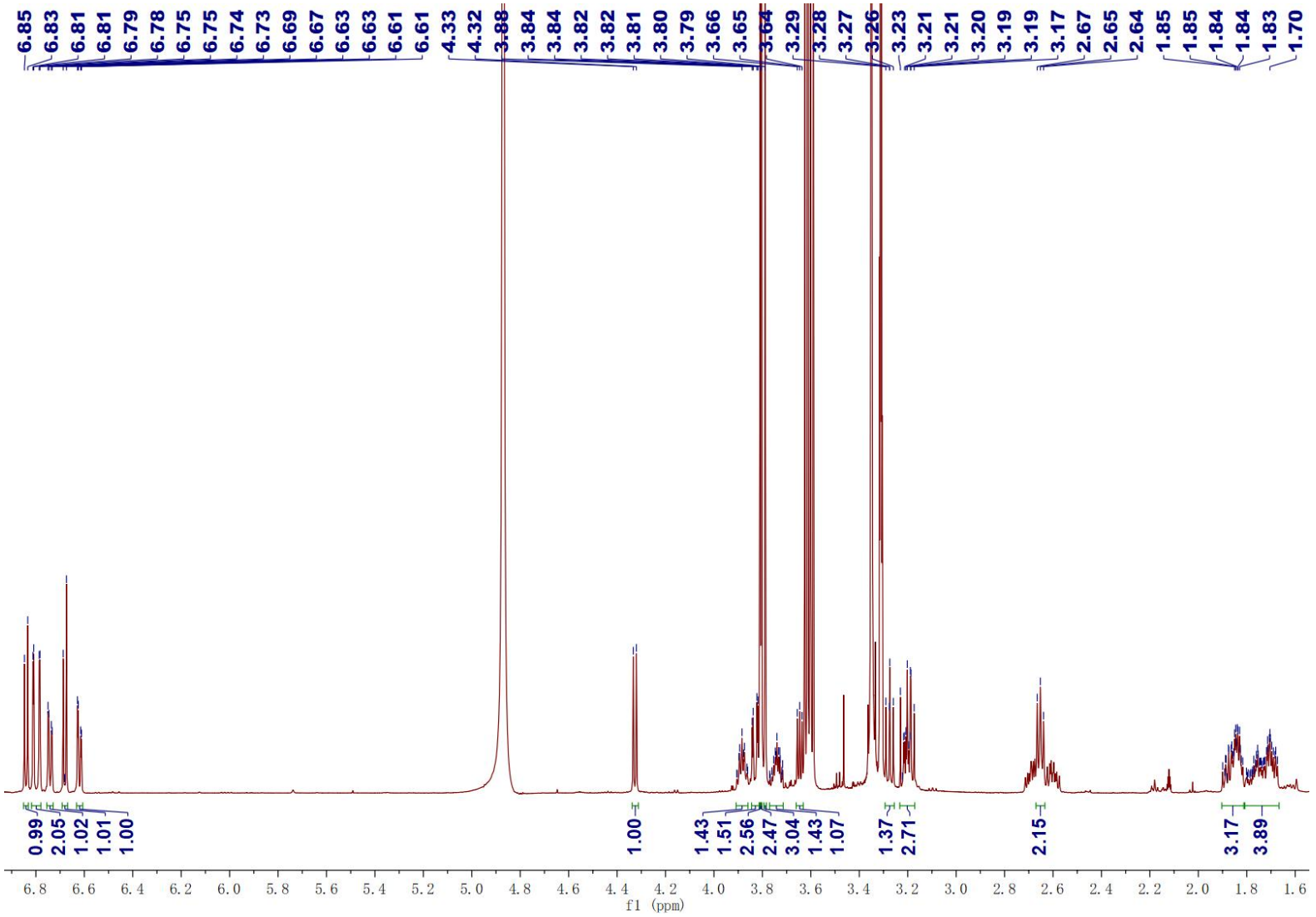

Figure S9. The ^{1}H NMR spectrum of compound **1** in CD_3OD.

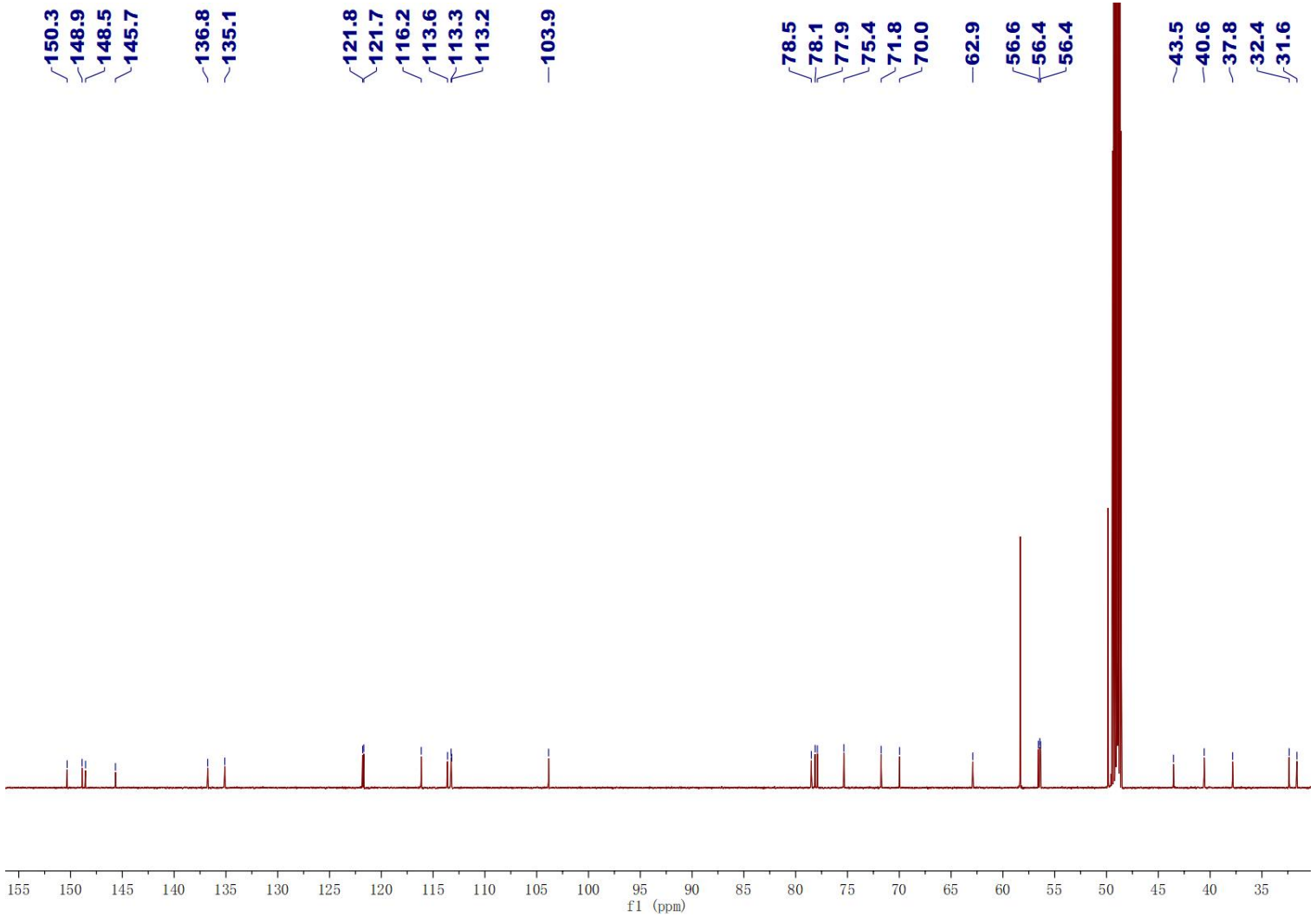

Figure S10. The ^{13}C NMR spectrum of compound **1** in CD_3OD.

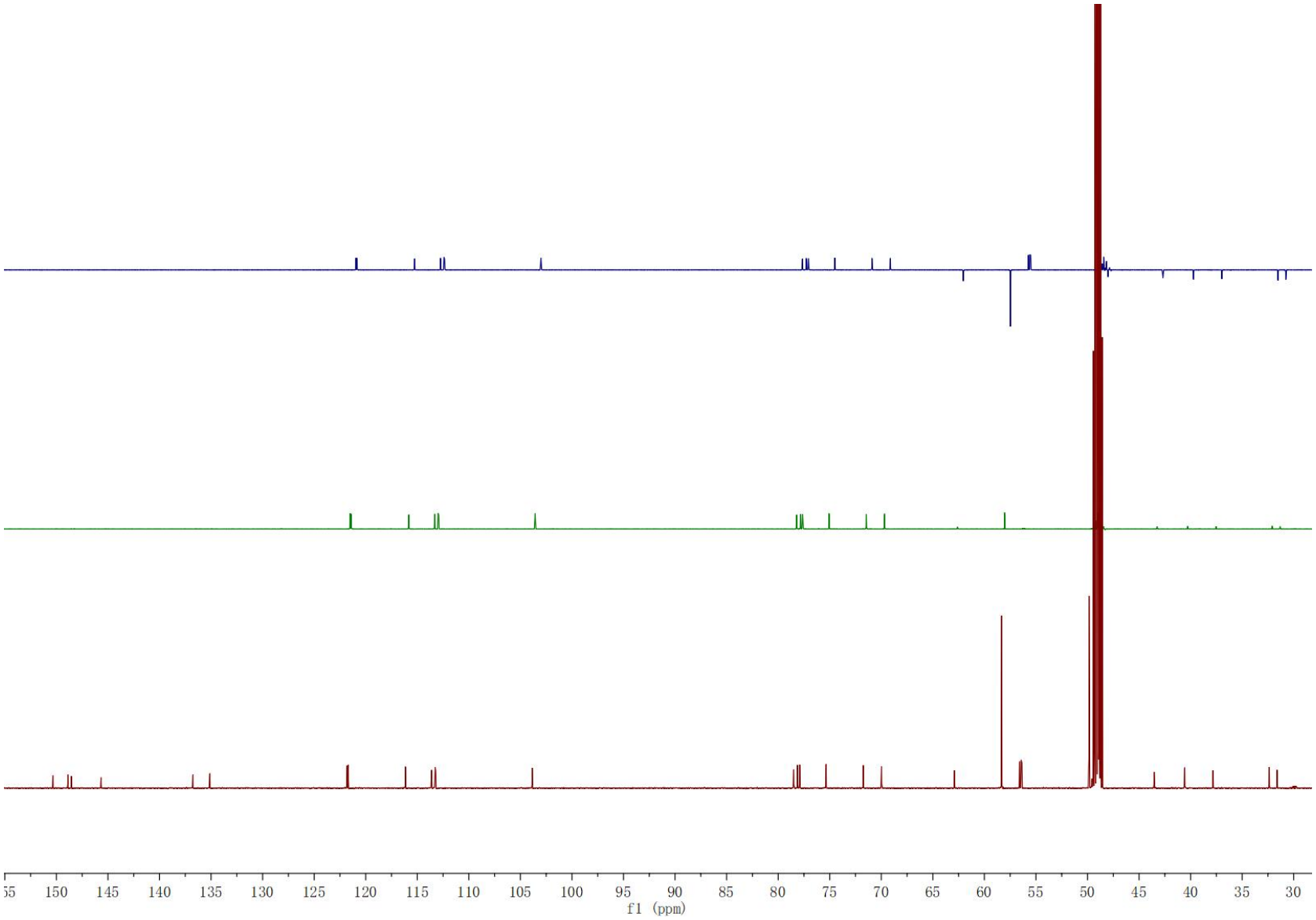

Figure S11. The DEPT spectrum of compound **1** in CD_3OD.

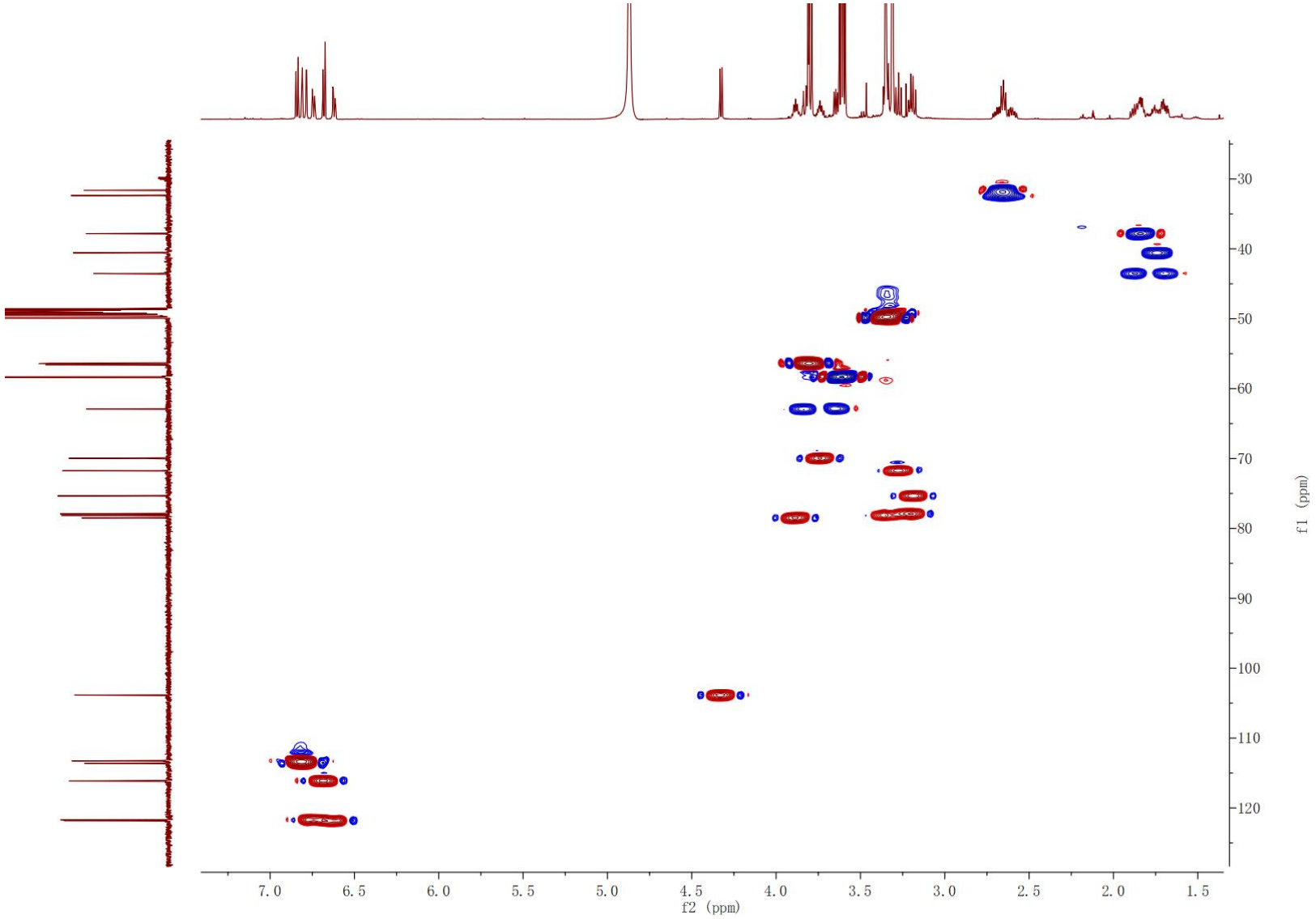

Figure S12. The HSQC spectrum of compound **1** in CD_3OD.

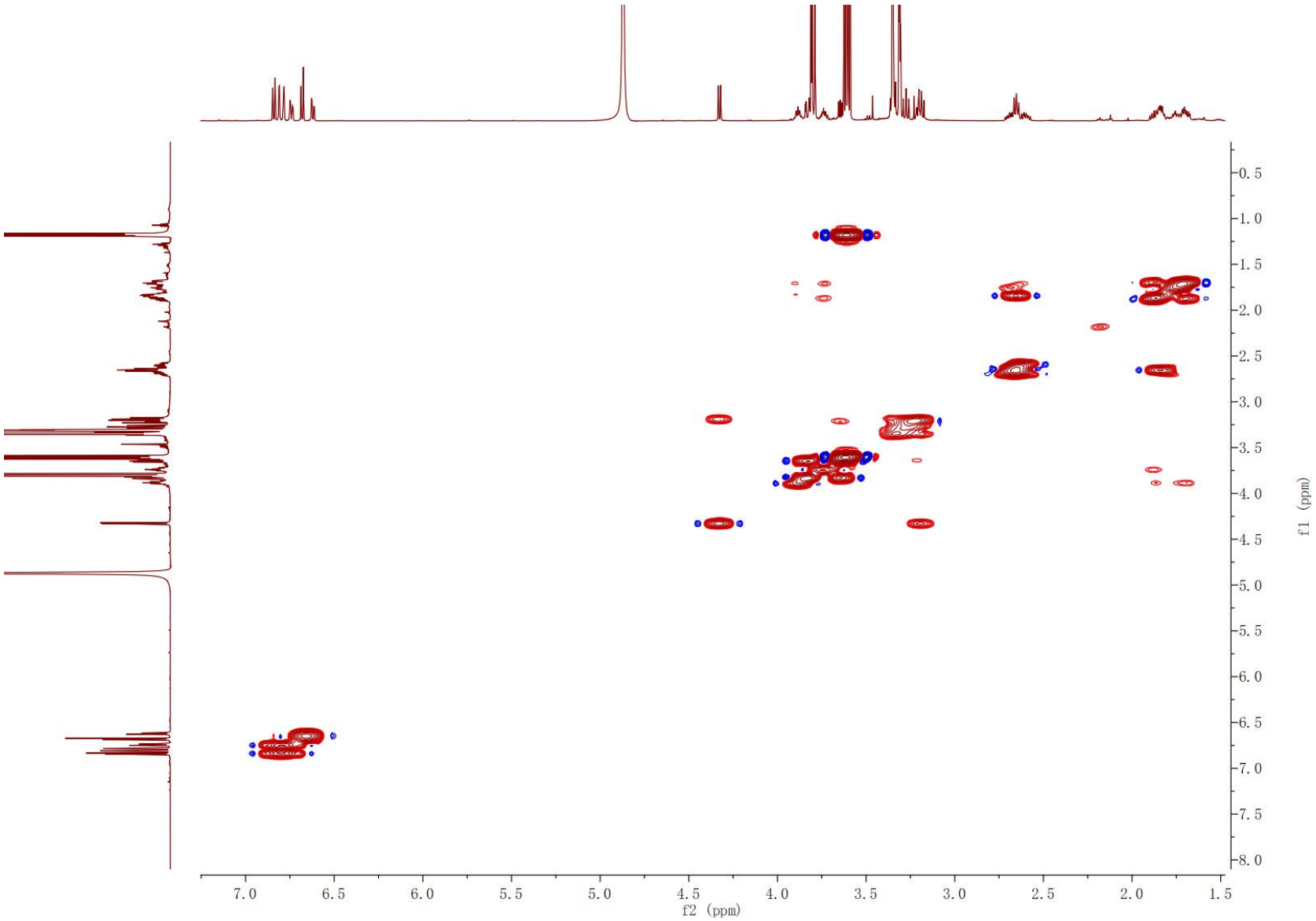

Figure S13. The ^{1}H-^{1}H COSY spectrum of compound **1** in CD_3OD.

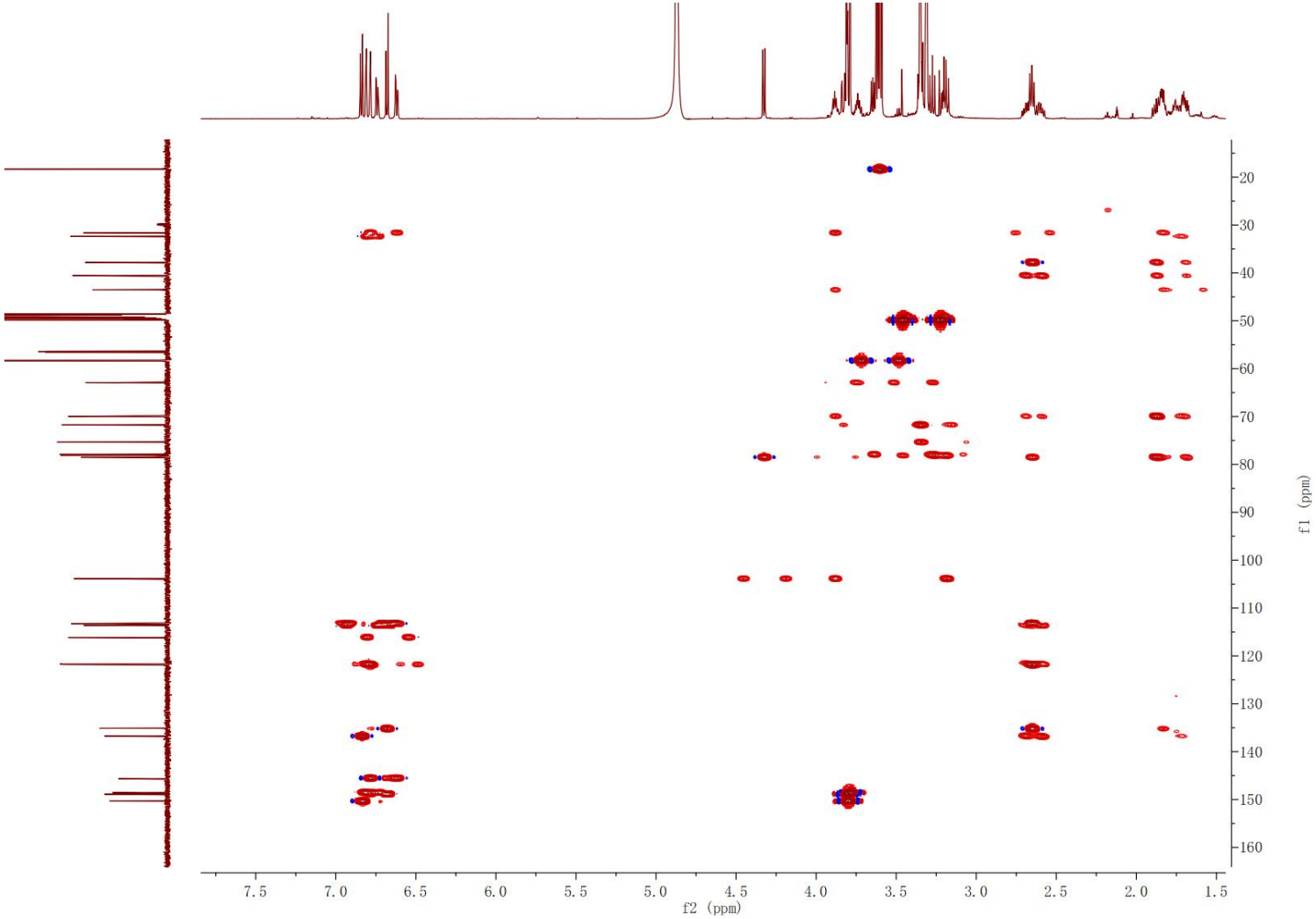

Figure S14. The HMBC spectrum of compound **1** in CD_3OD.

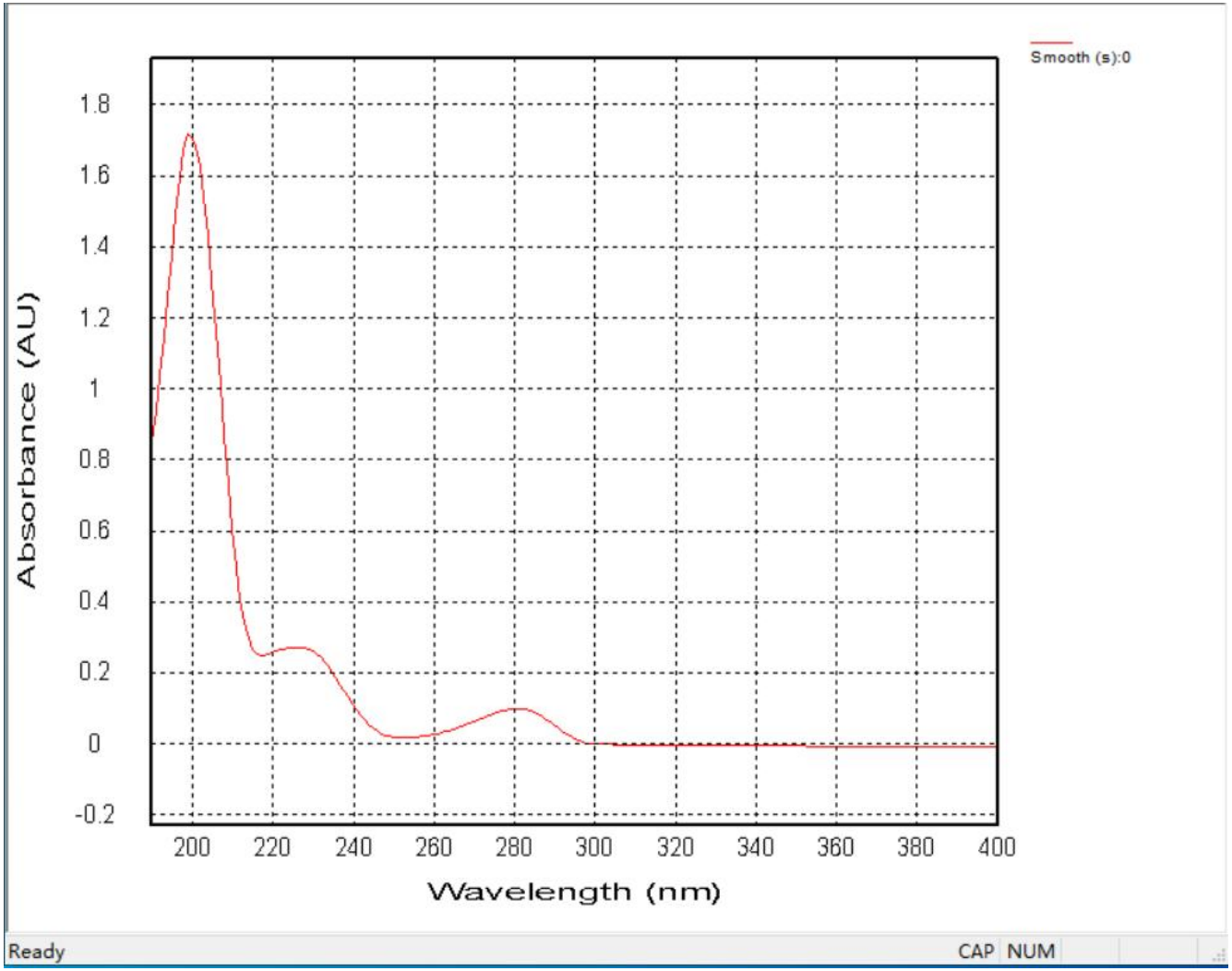

Figure S15. The UV spectrum of compound **1a**

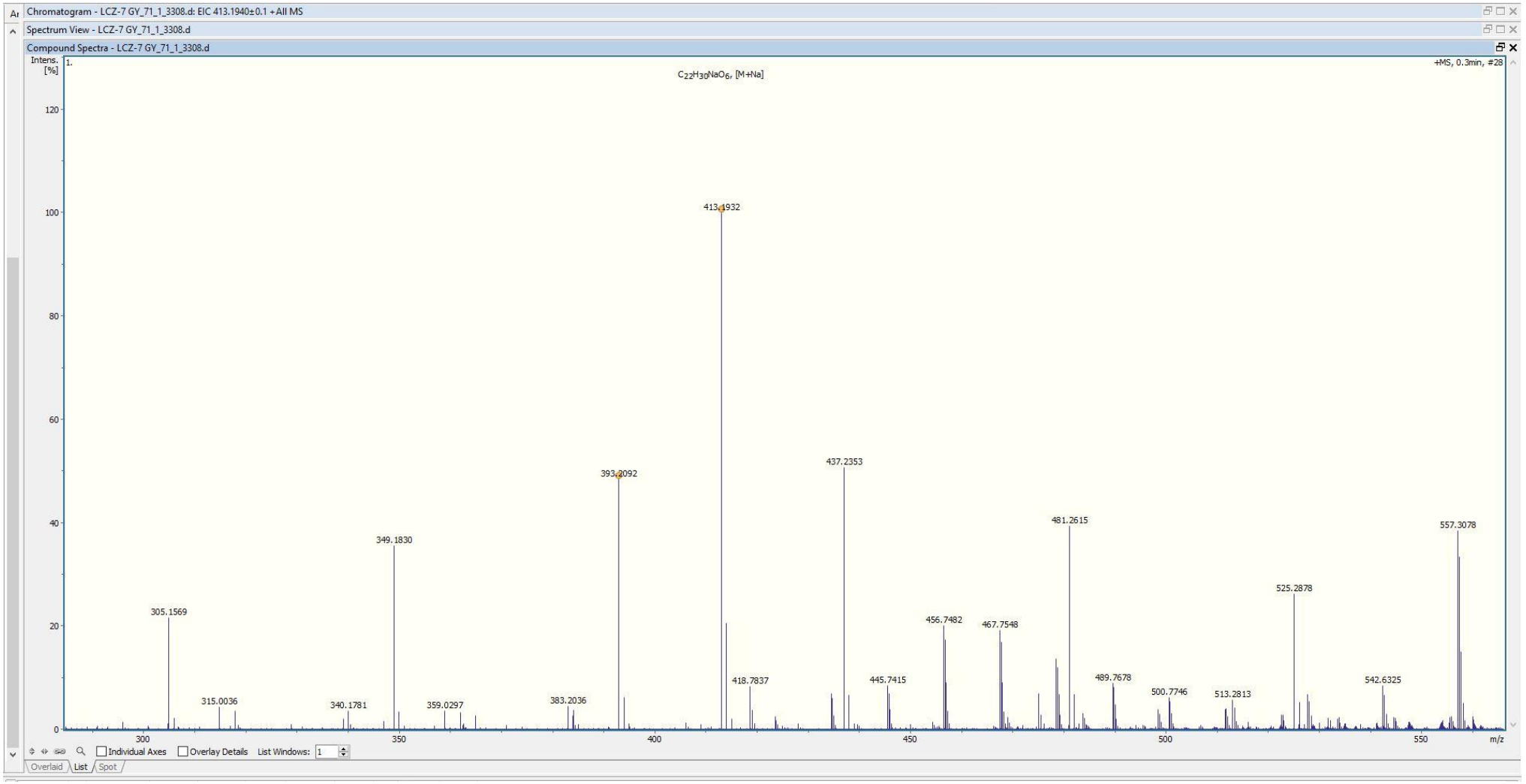

Figure S16. The (+)-HRESIMS spectroscopic data of compound **1a**.

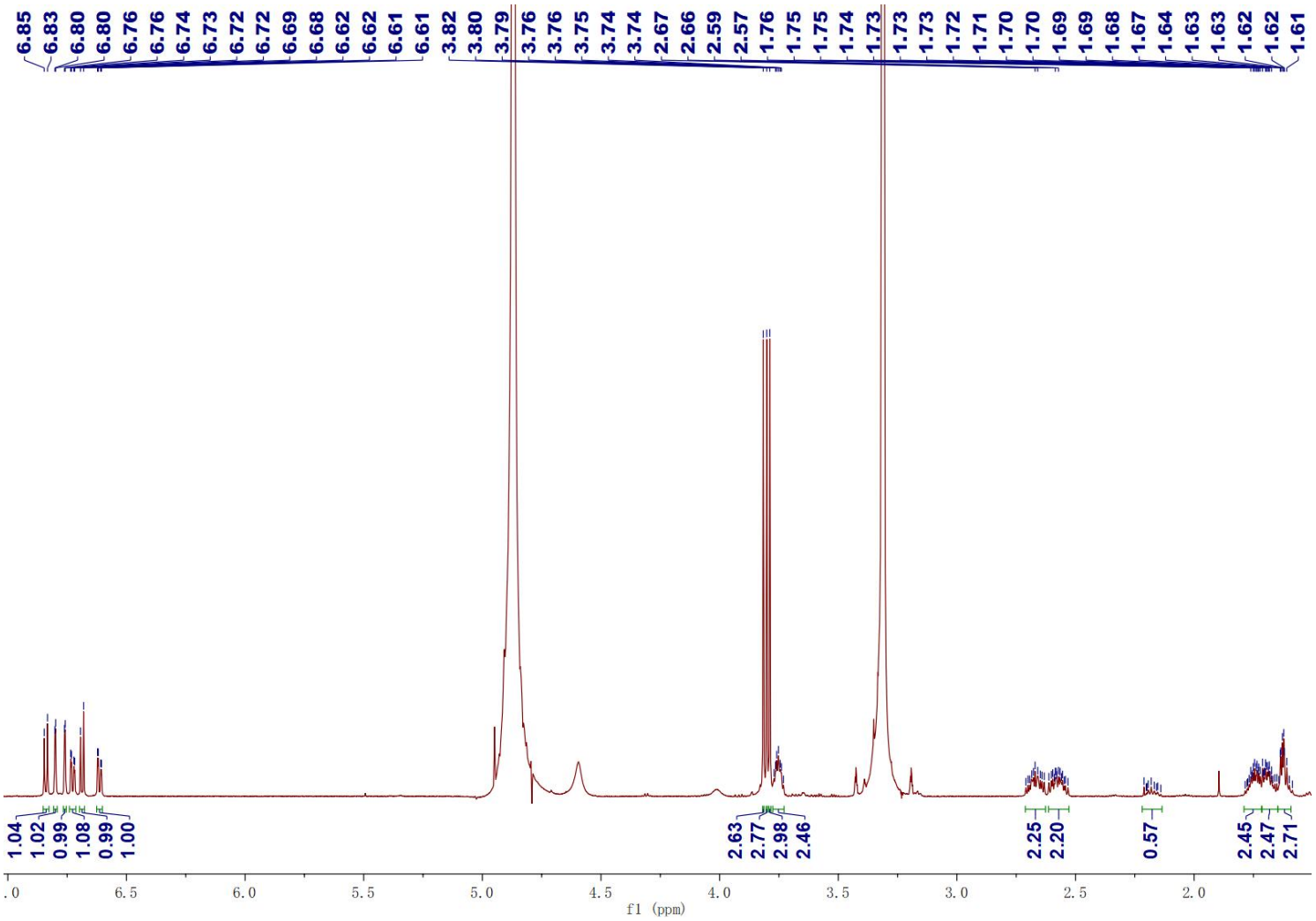

Figure S17. The ^{1}H NMR spectrum of compound **1a** in CD_3OD.

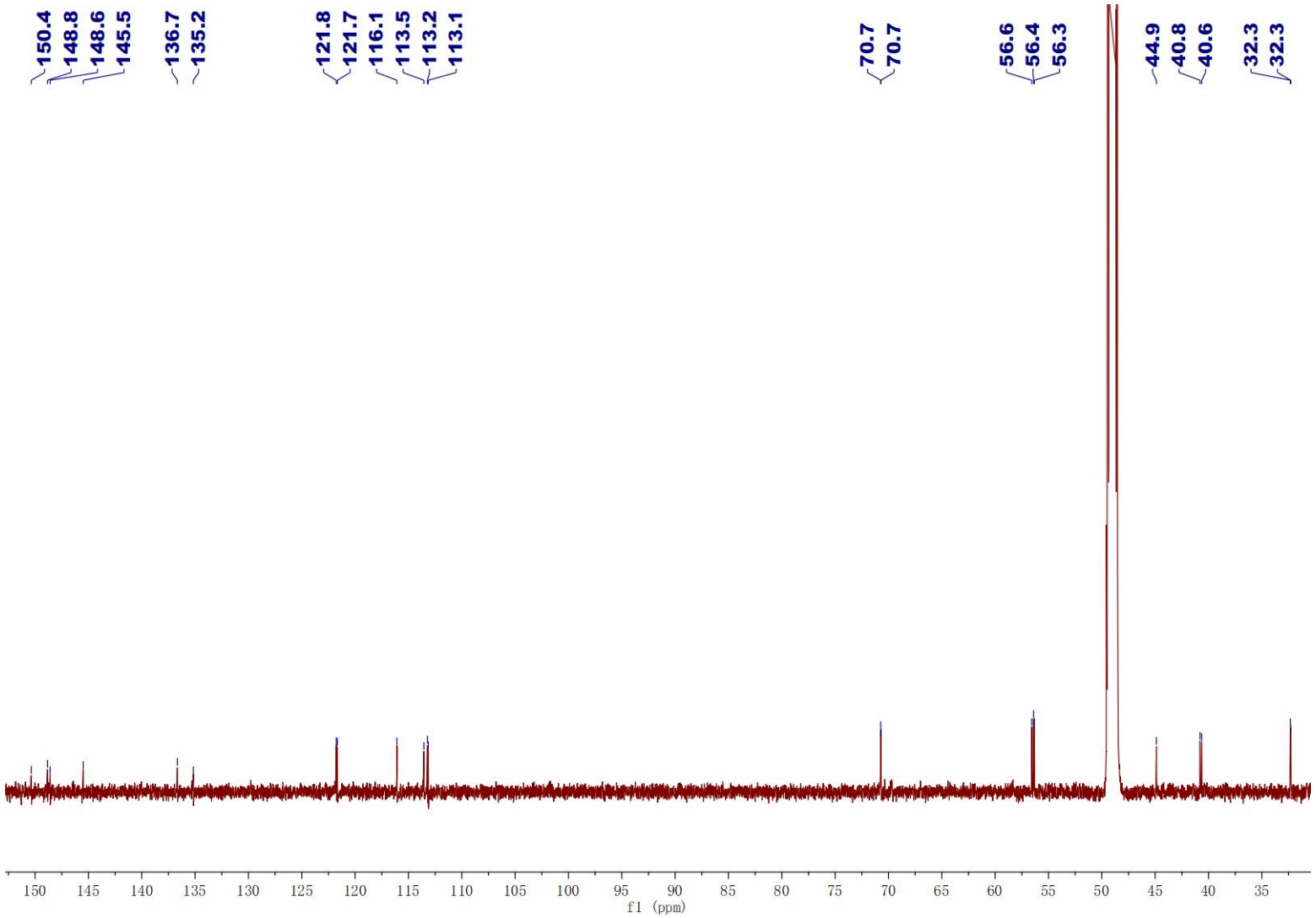

Figure S18. The ^{13}C NMR spectrum of compound **1a** in CD_3OD.

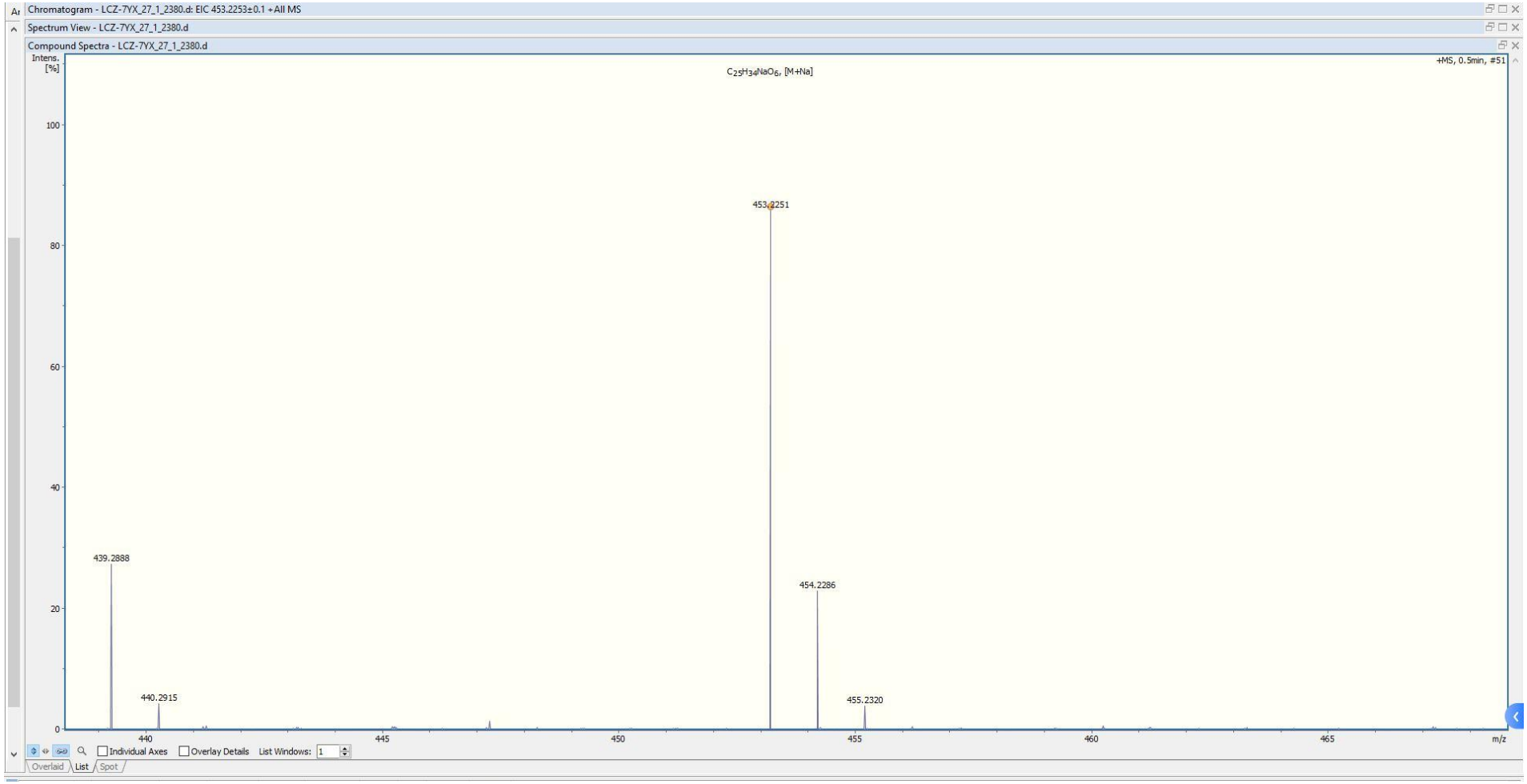

Figure S19. The (+)-HRESIMS spectroscopic data of compound **1b**.

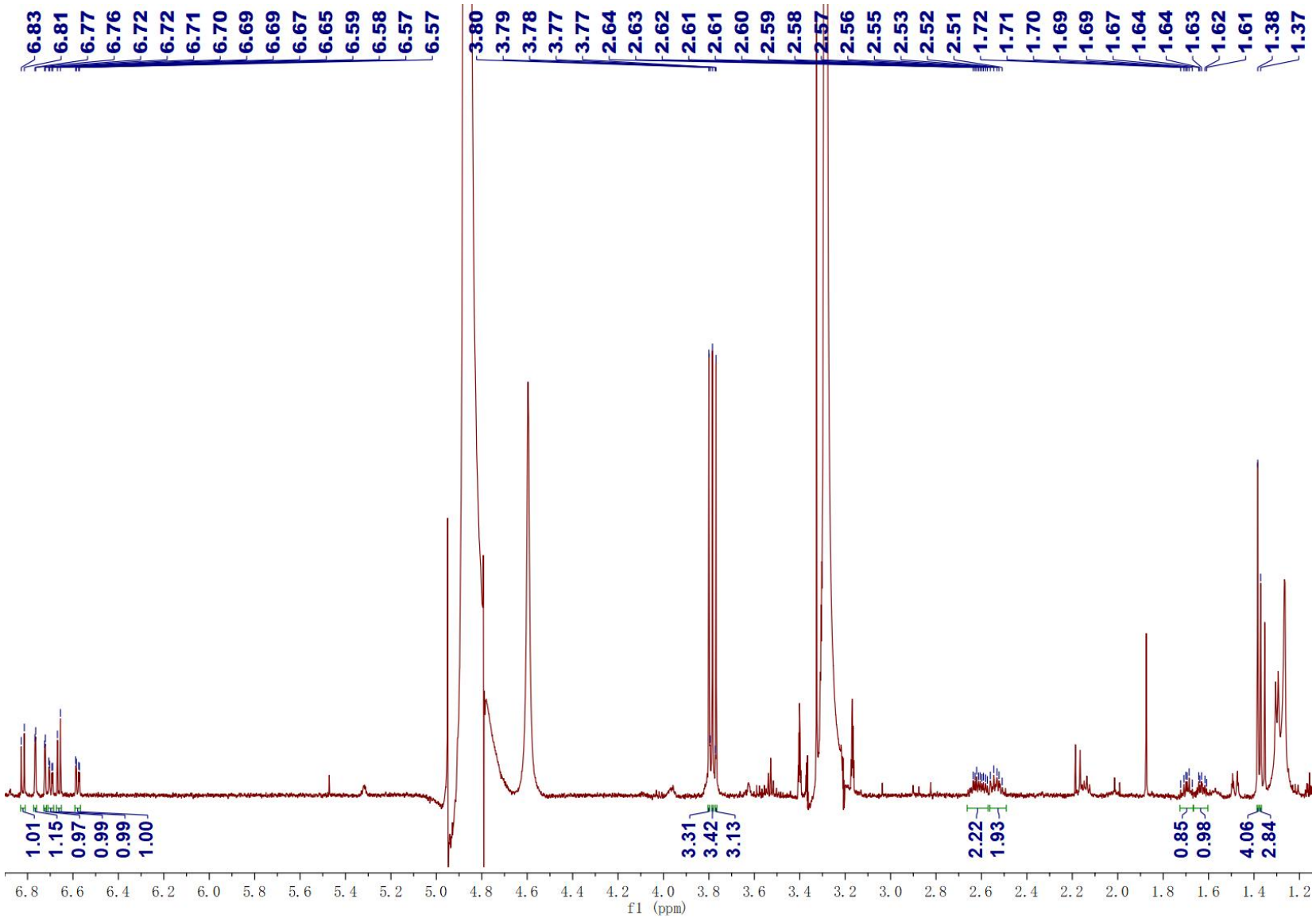

Figure S20. The ^{1}H NMR spectrum of compound **1b** in CD_3OD.

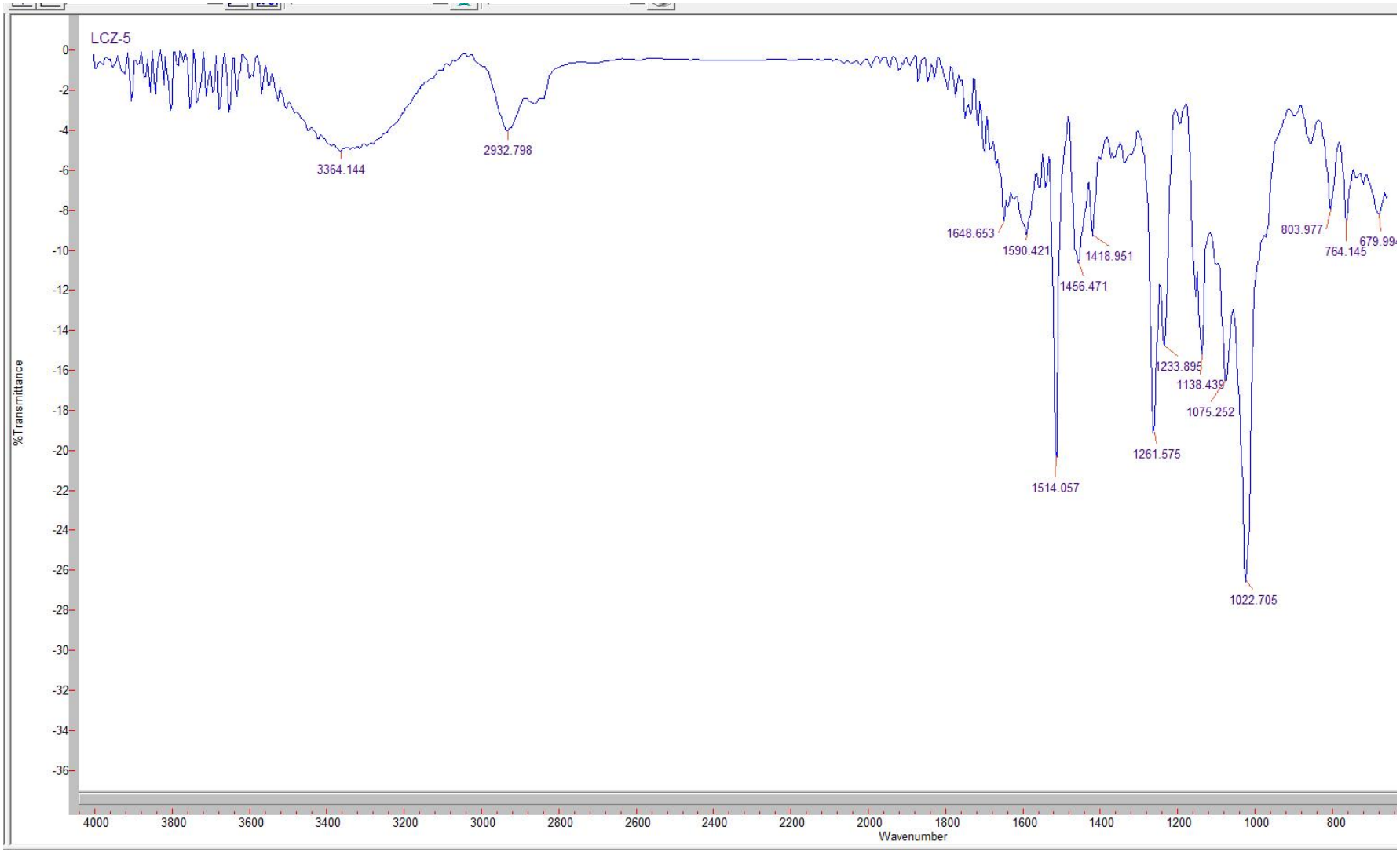

Figure S21. The IR spectrum of compound **2**.

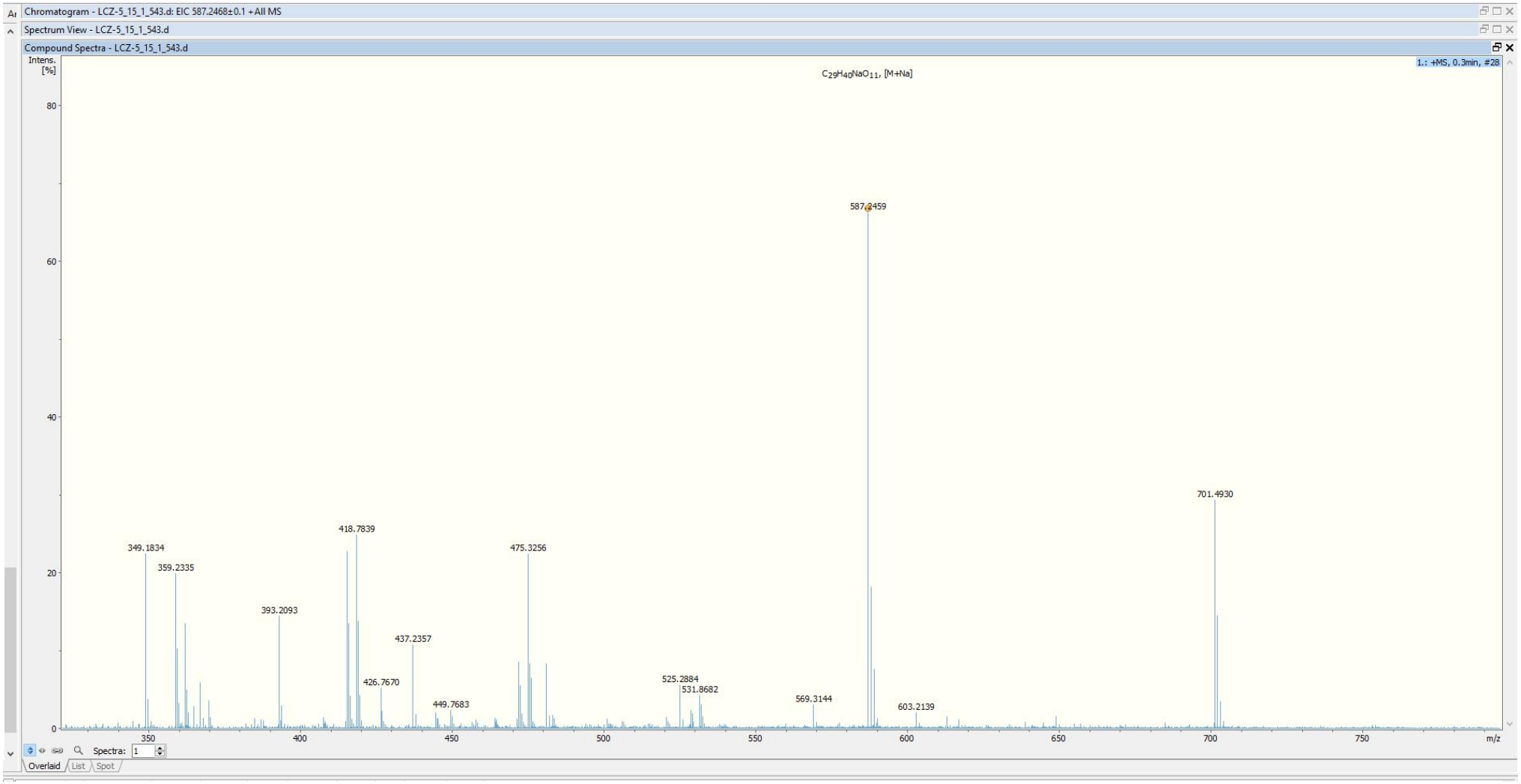

Figure S22. The (+)-HRESIMS spectroscopic data of compound **2**.

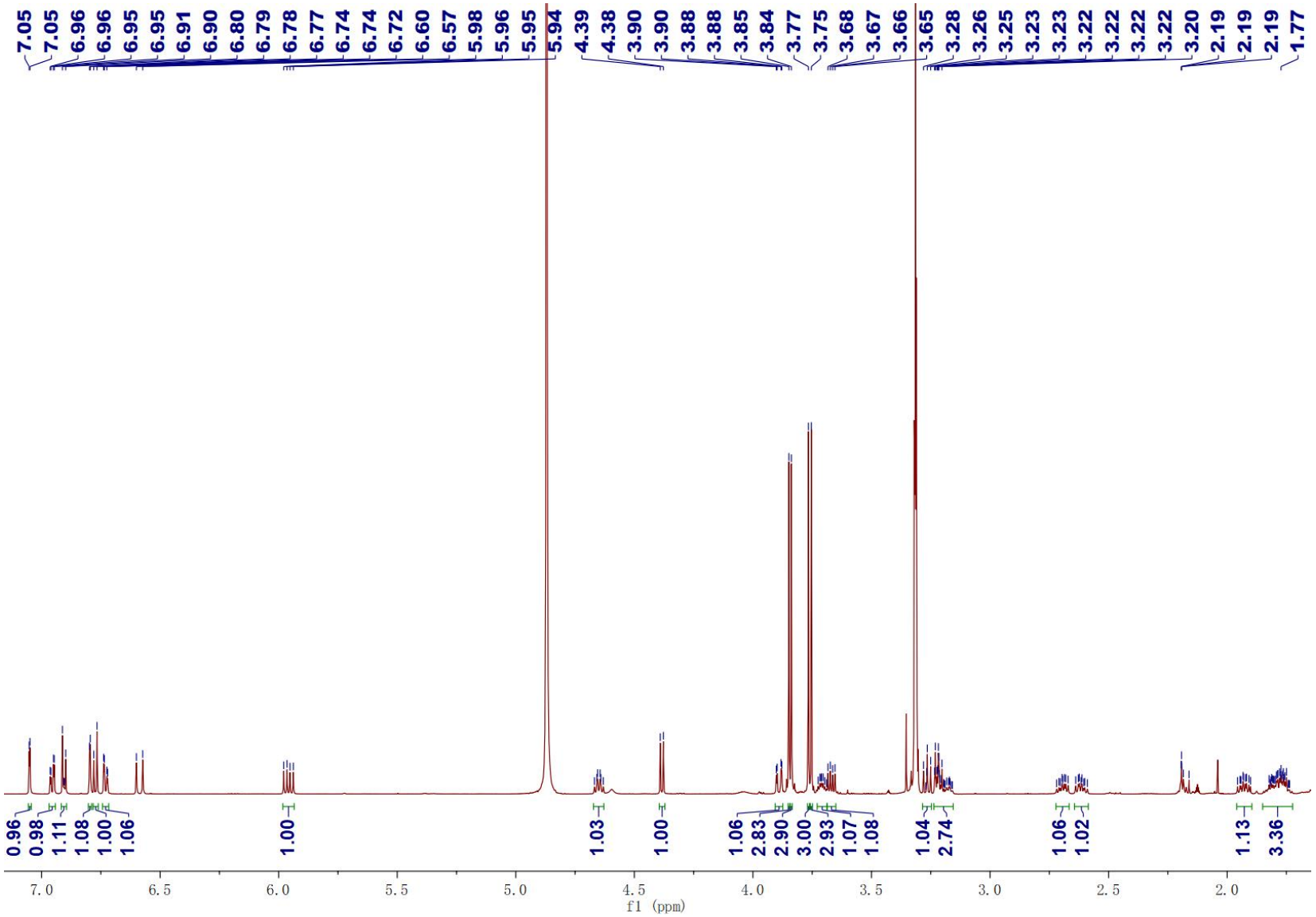

Figure S23. The ^{1}H NMR spectrum of compound **2** in CD_3OD.

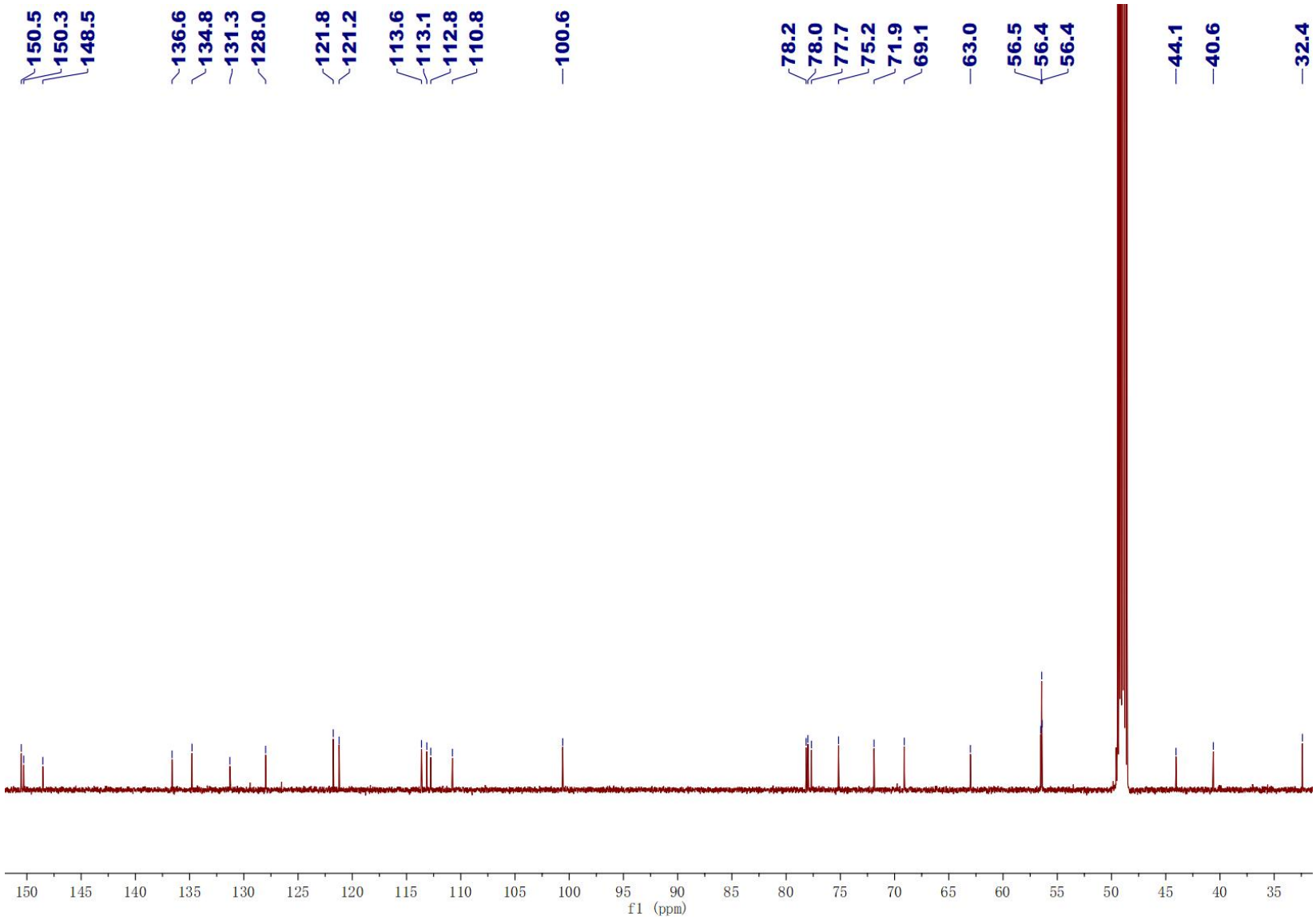

Figure S24. The ^{13}C NMR spectrum of compound **2** in CD_3OD.

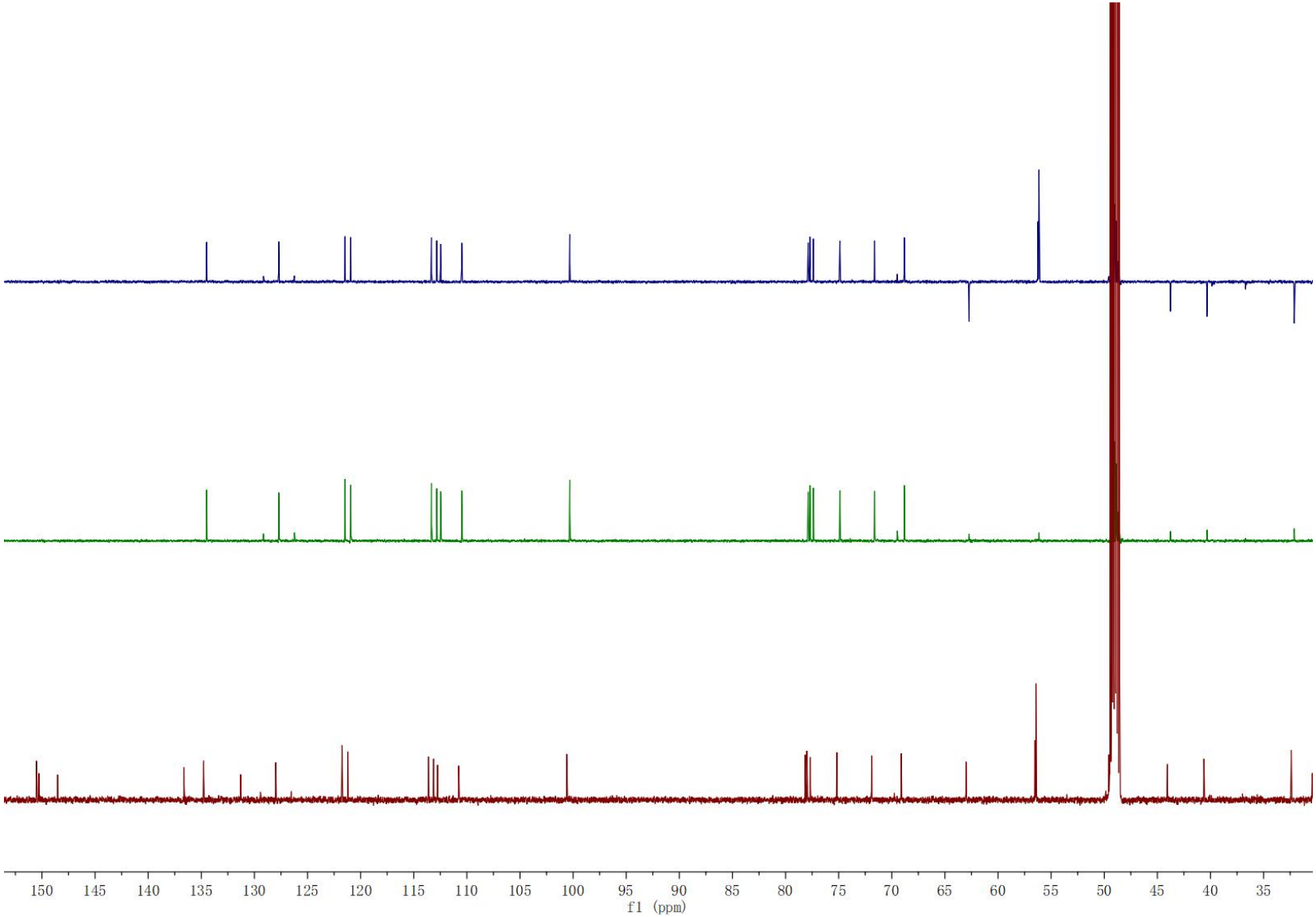

Figure S25. The DEPT spectrum of compound **2** in CD_3OD.

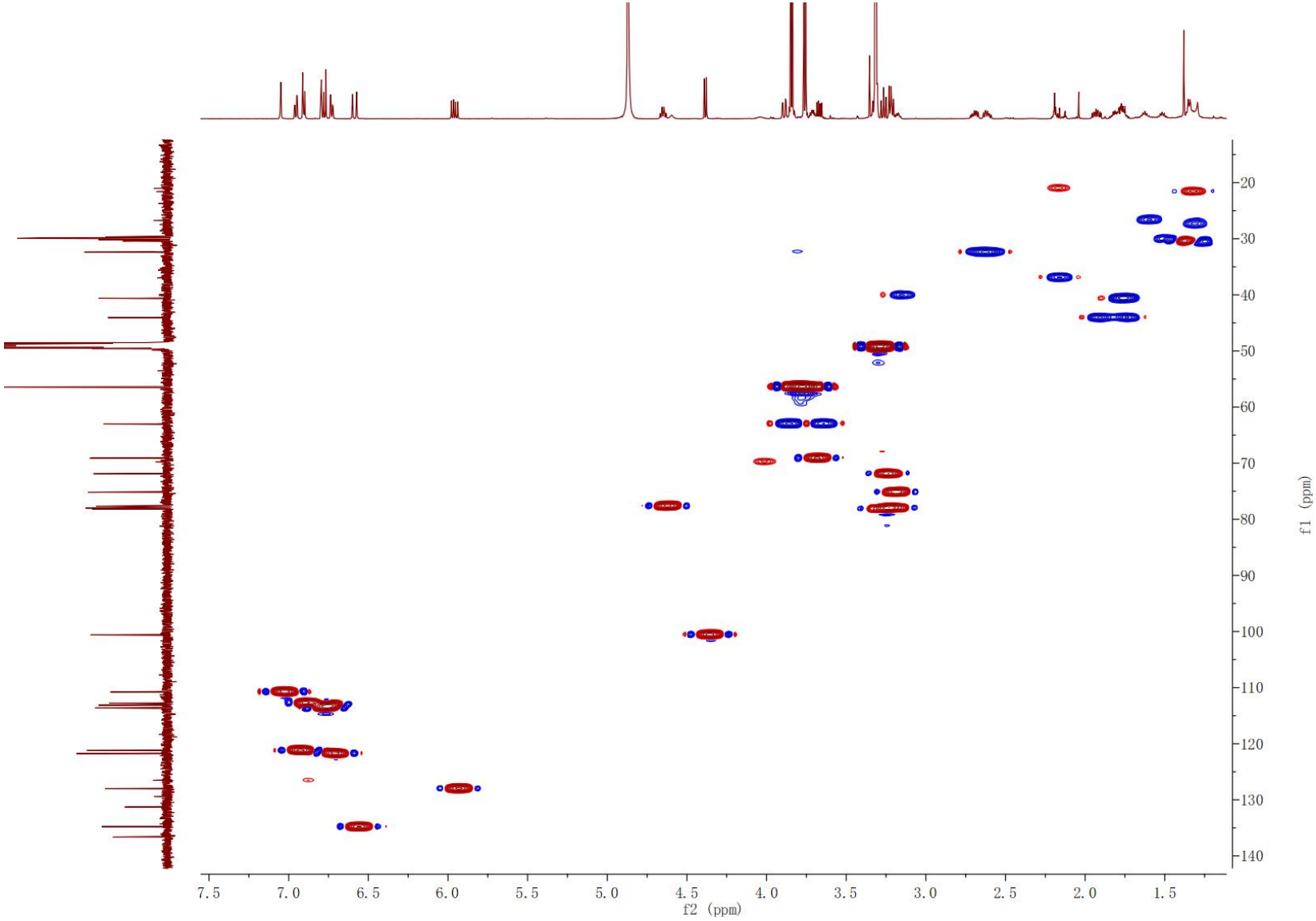

Figure S26. The HSQC spectrum of compound **2** in CD_3OD.

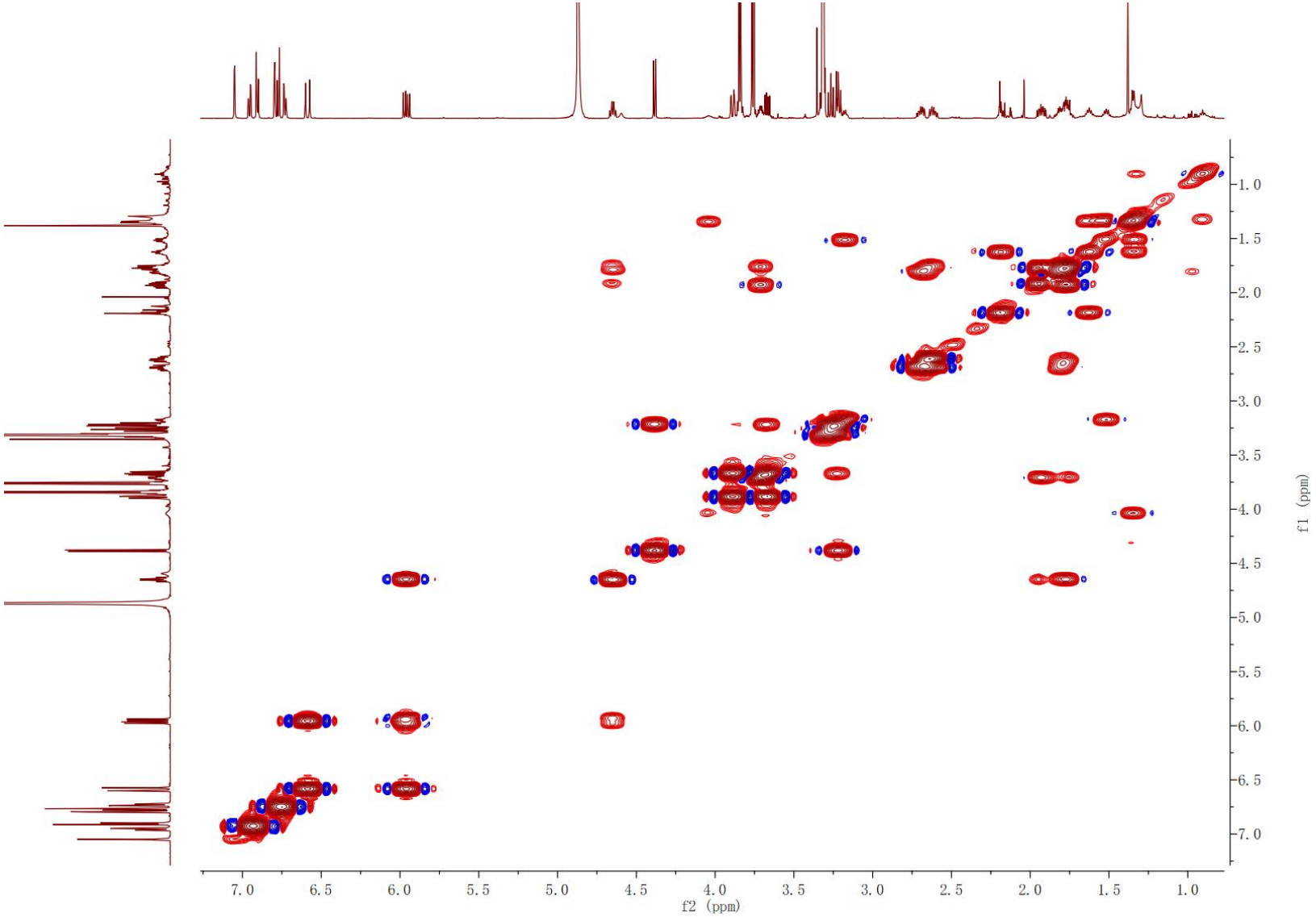

Figure S27. The ^{1}H-^{1}H COSY spectrum of compound **2** in CD_3OD.

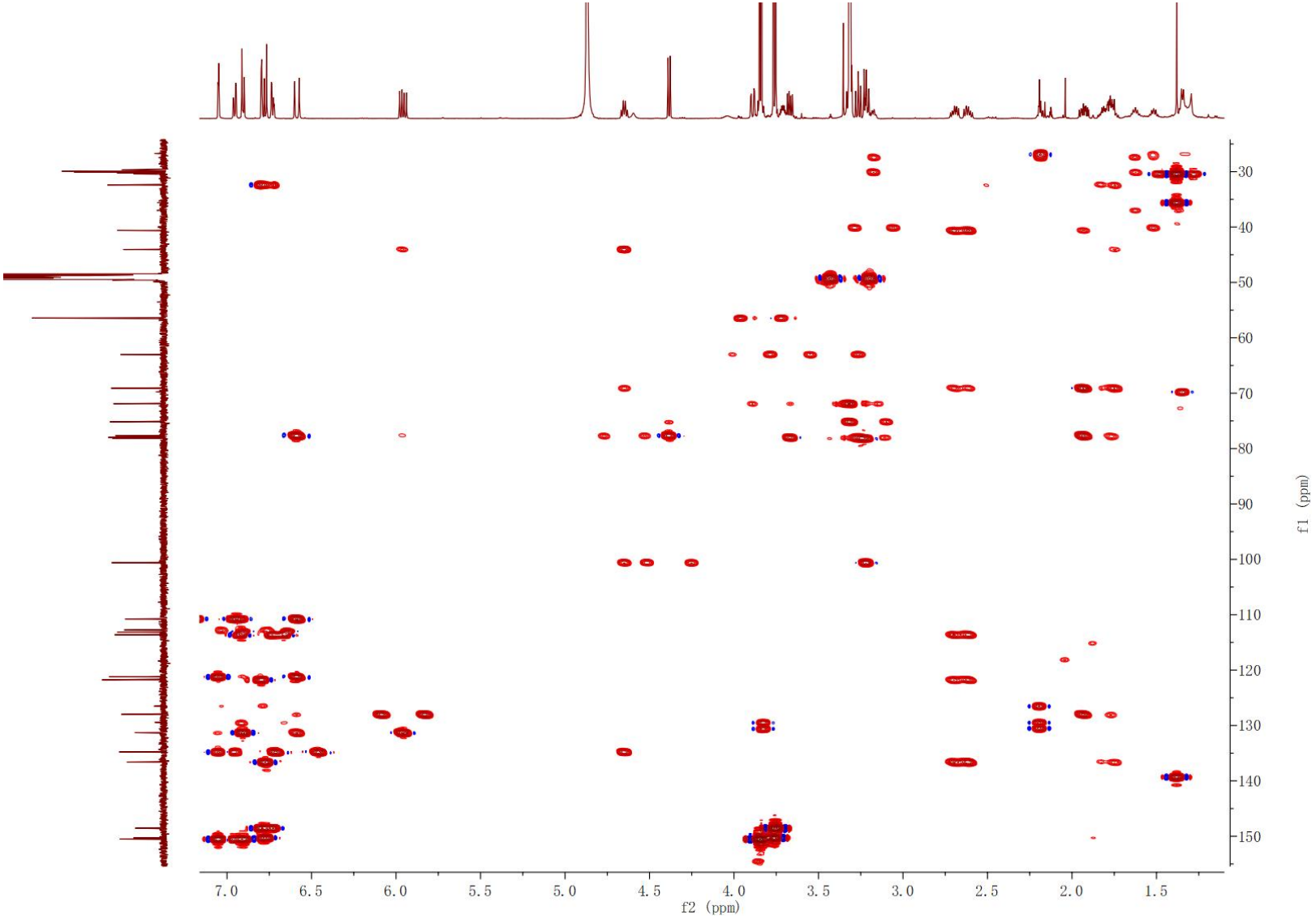

Figure S28. The HMBC spectrum of compound **2** in CD_3OD.

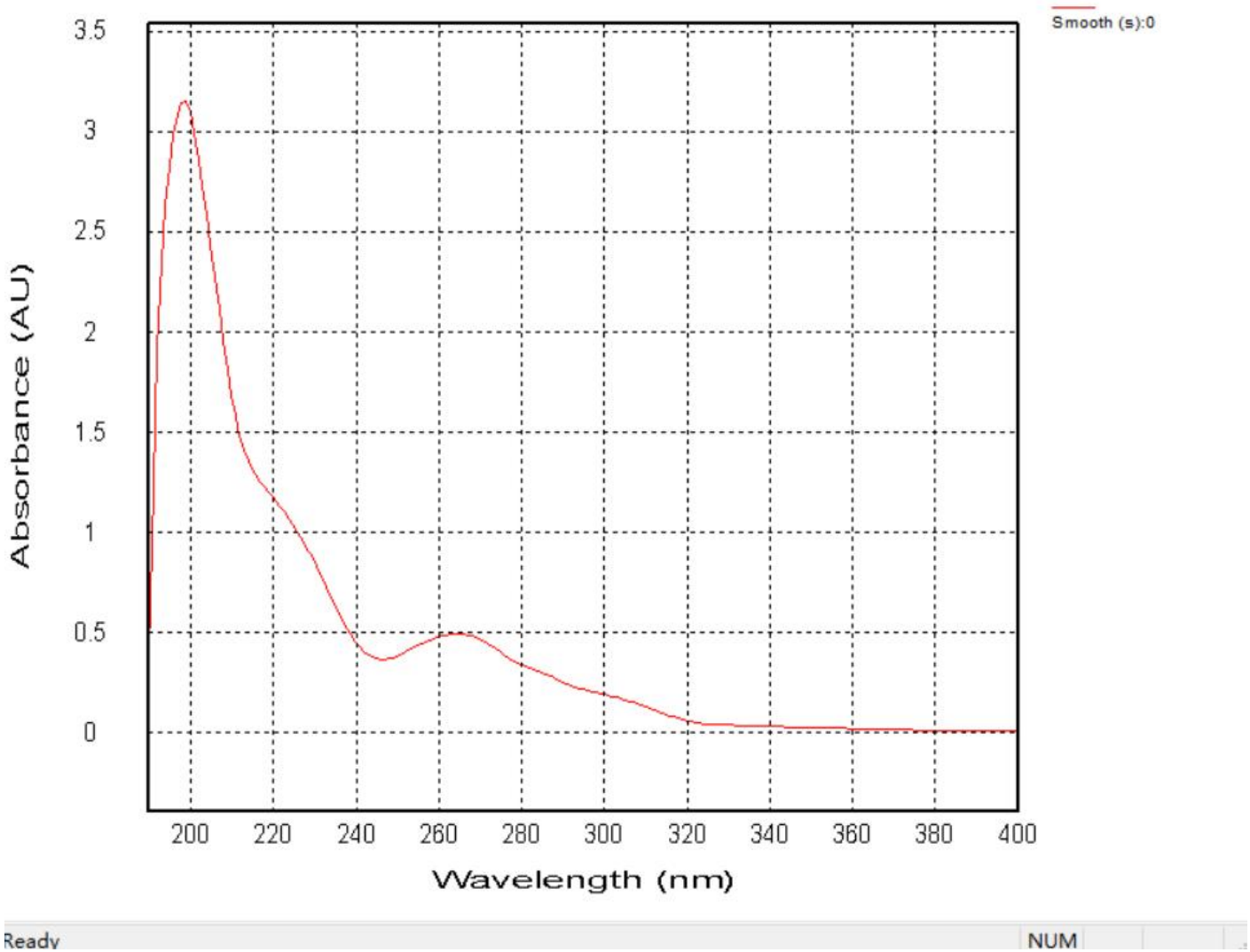

Figure S29. The UV spectrum of compound **2a**.

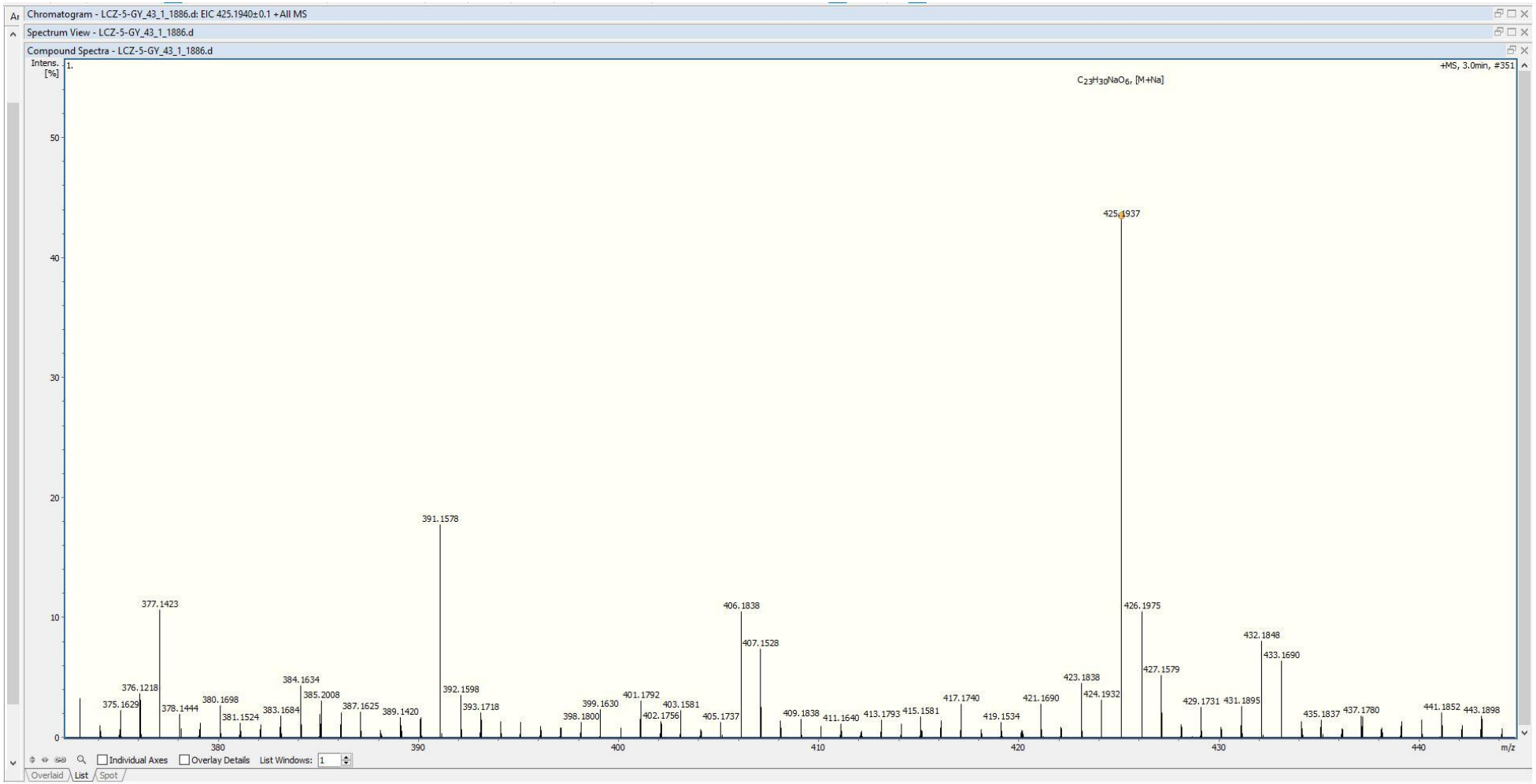

Figure S30. The (+)-HRESIMS spectroscopic data of compound **2a**.

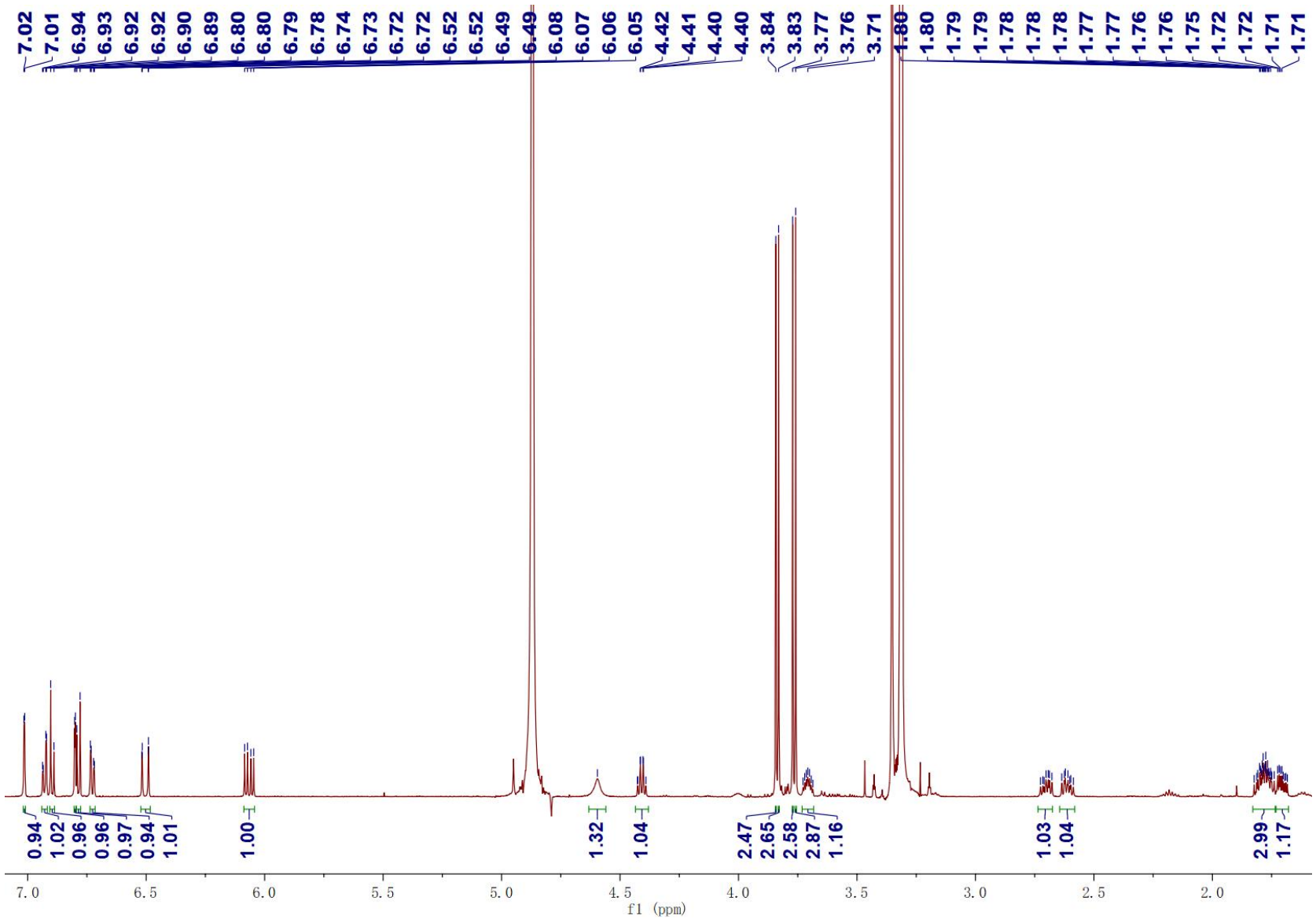

Figure S31. The ^{1}H NMR spectrum of compound **2a** in CD_3OD.

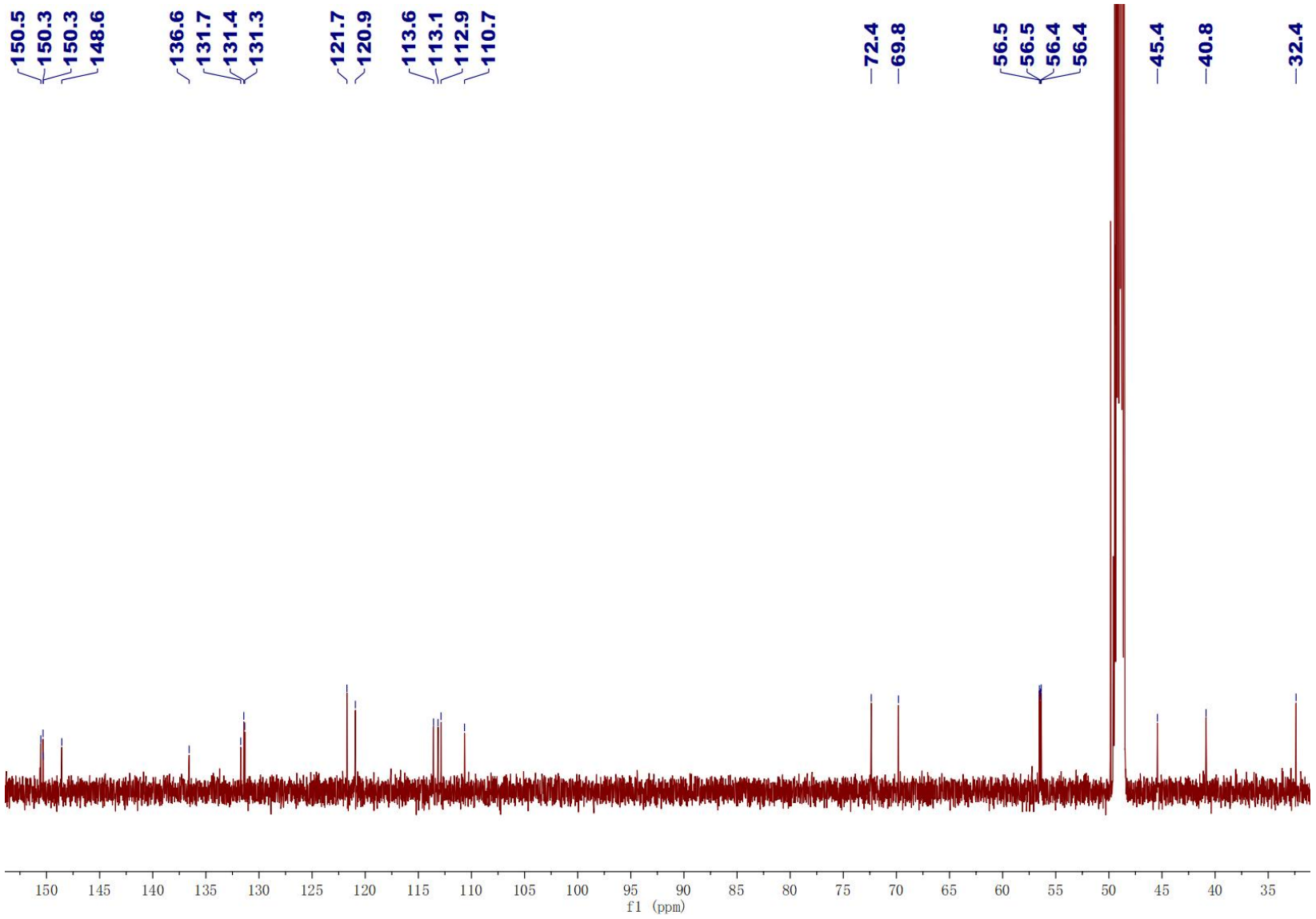

Figure S32. The ^{13}C NMR spectrum of compound **2a** in CD_3OD.

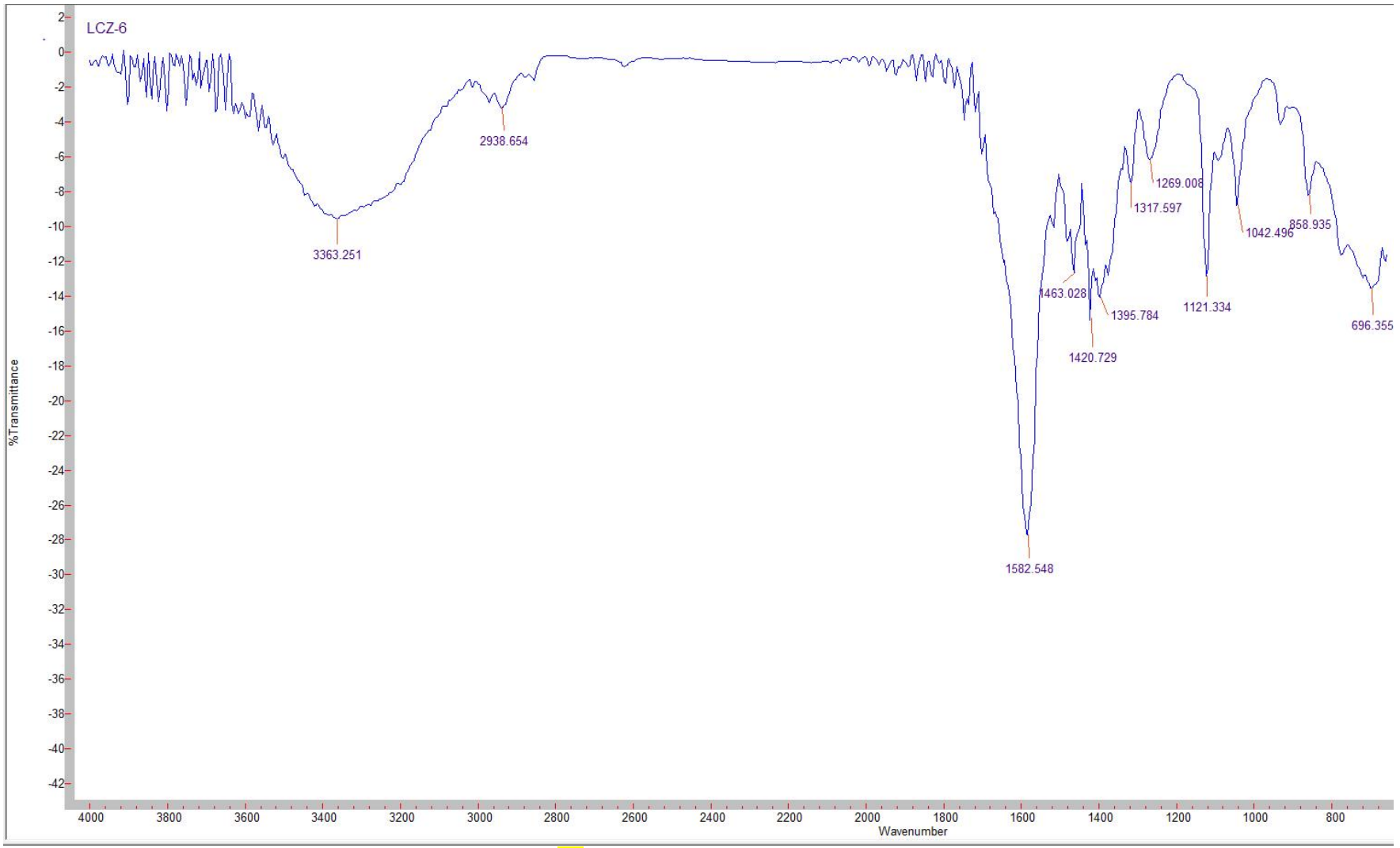

Figure S33. The IR spectrum of compound **3**.

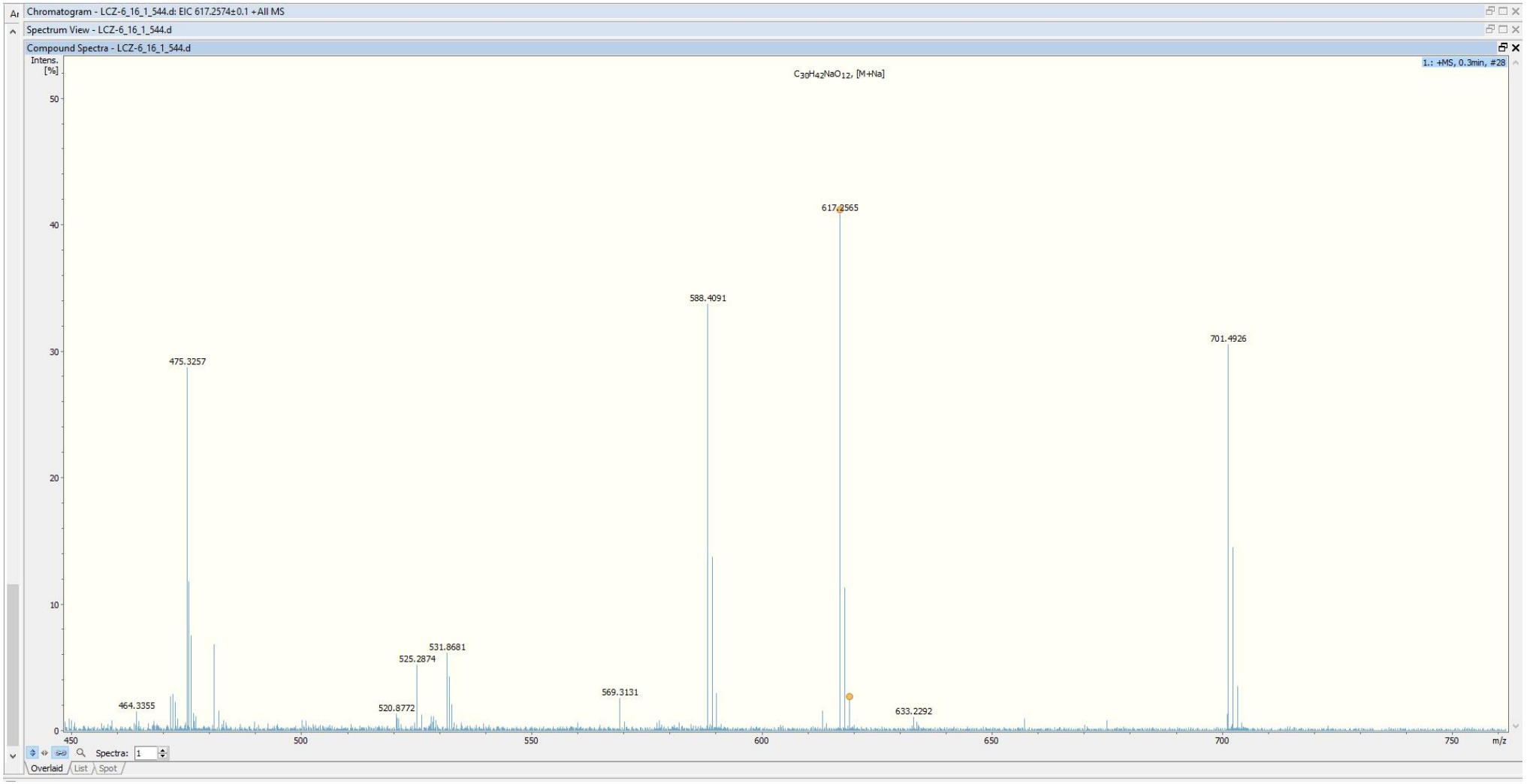

Figure S34. The (+)-HRESIMS spectroscopic data of compound **3**.

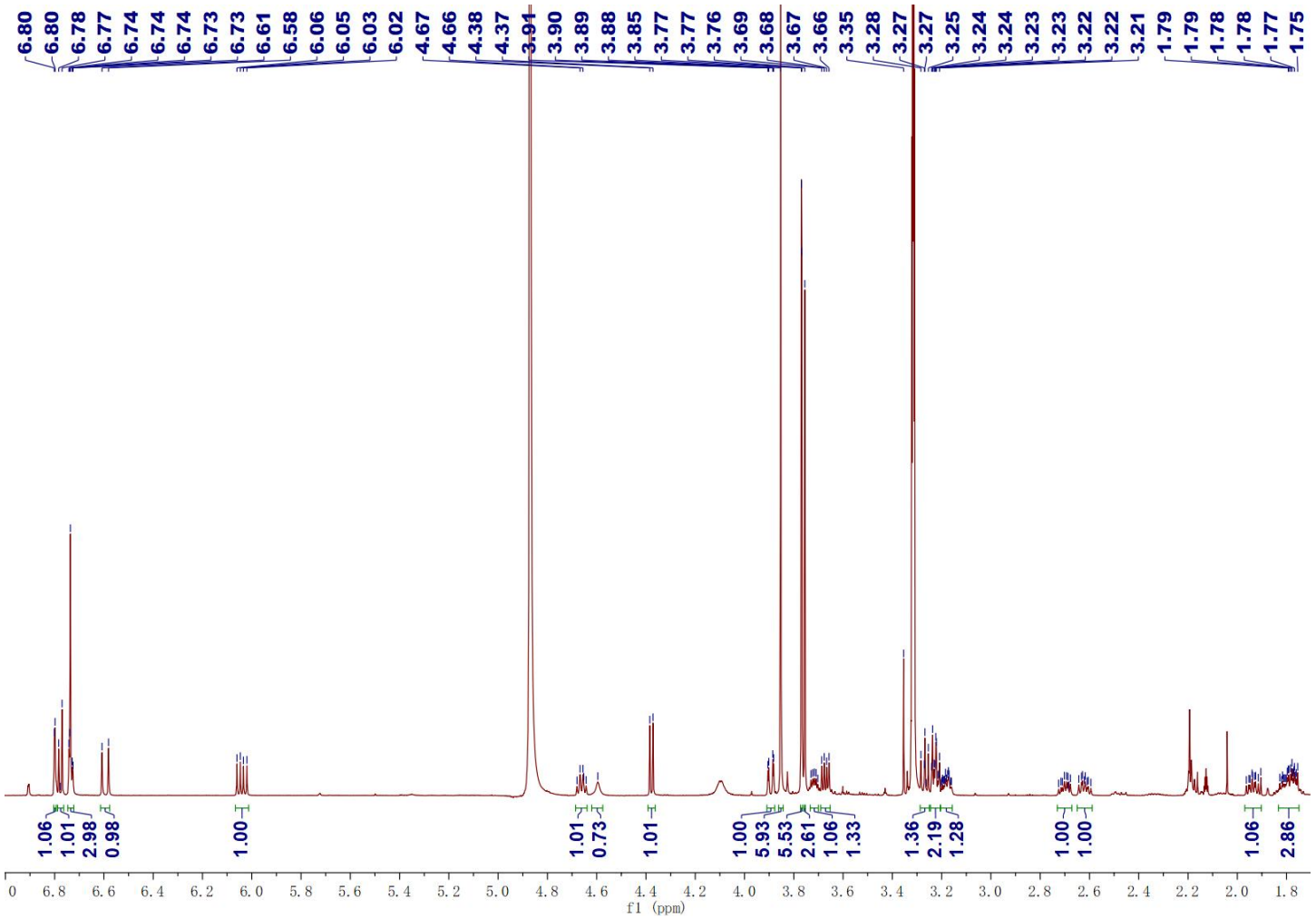

Figure S35. The ^{1}H NMR spectrum of compound **3** in CD_3OD.

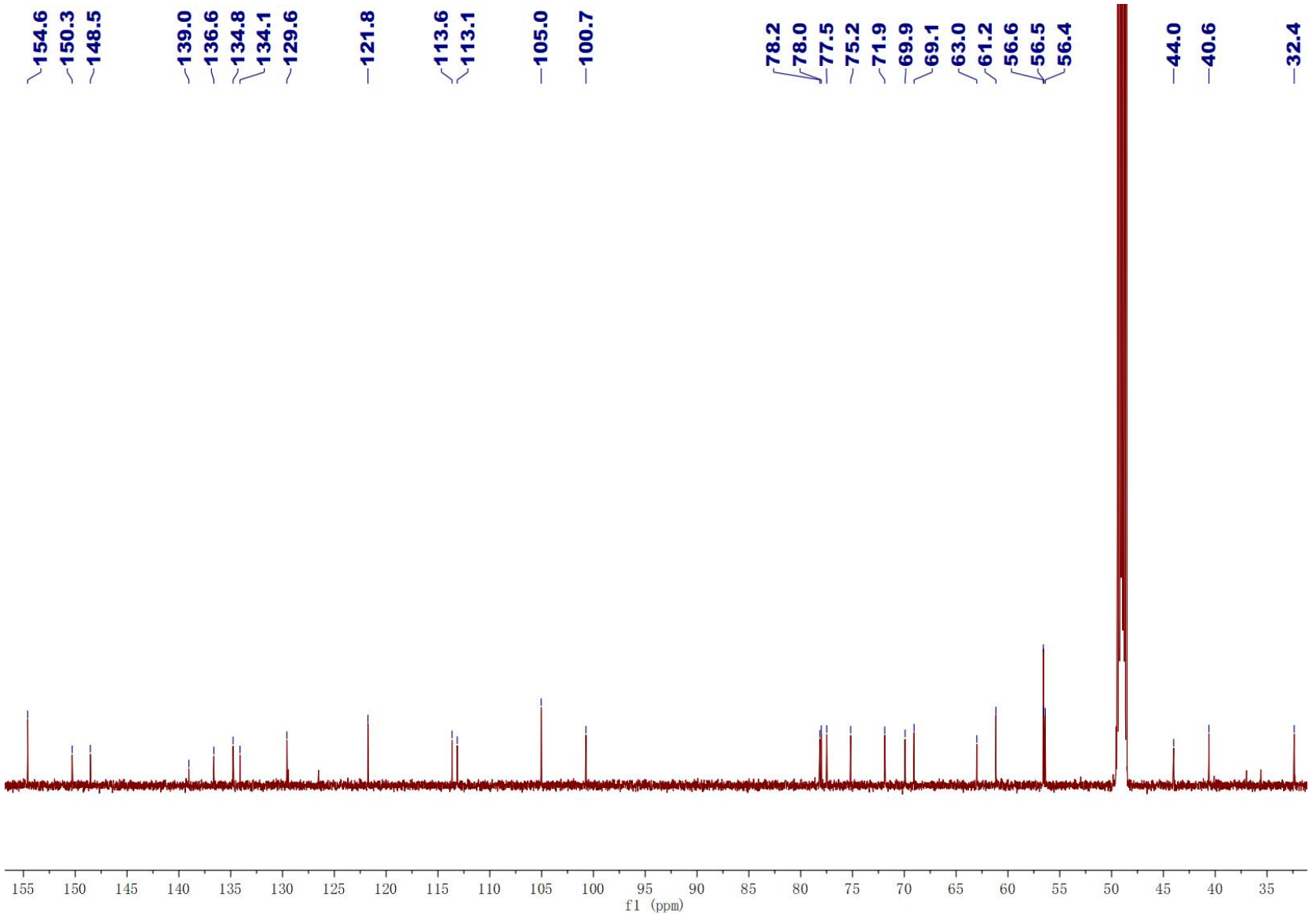

Figure S36. The ^{13}C NMR spectrum of compound **3** in CD_3OD.

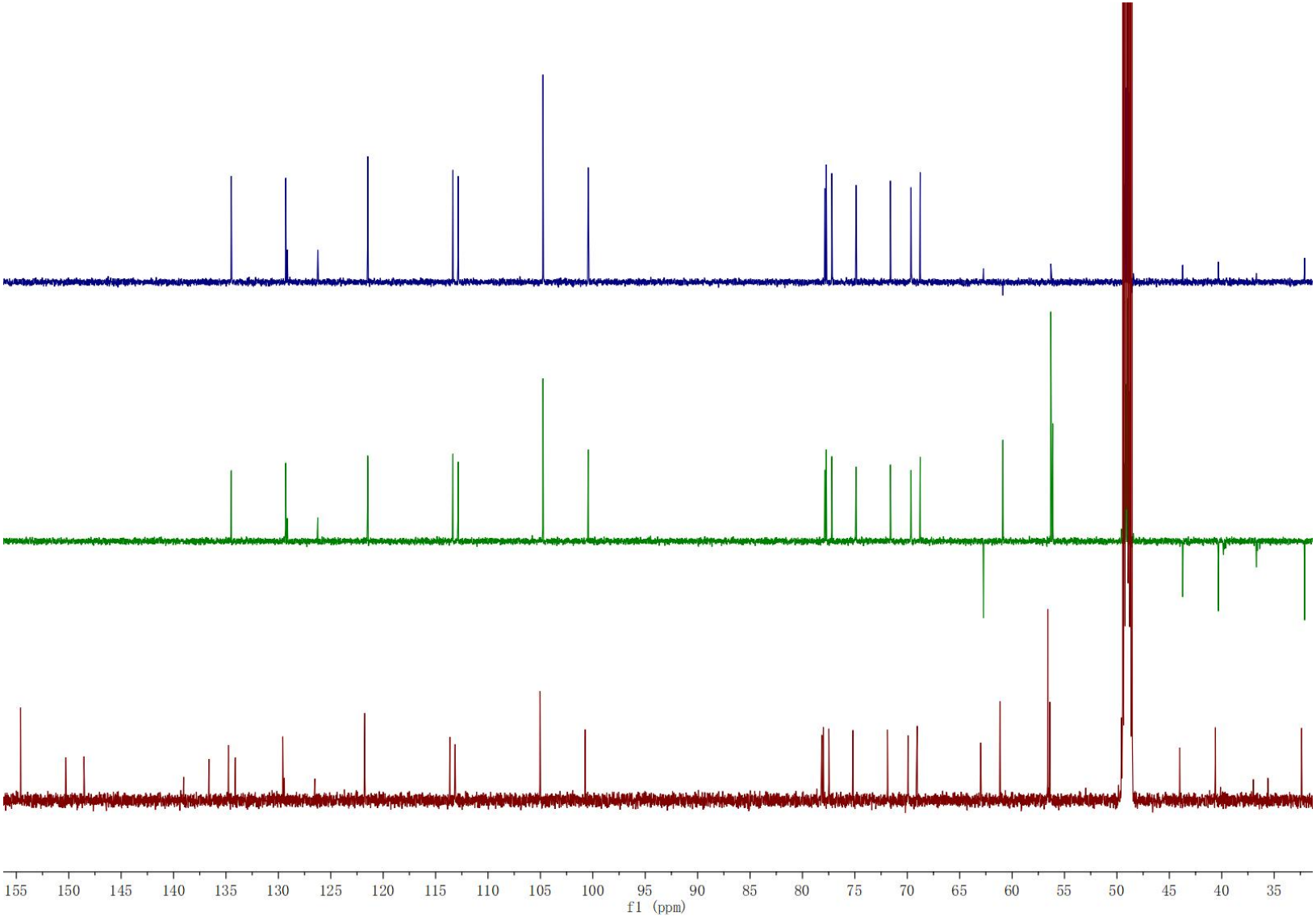

Figure S37. The DEPT spectrum of compound **3** in CD_3OD.

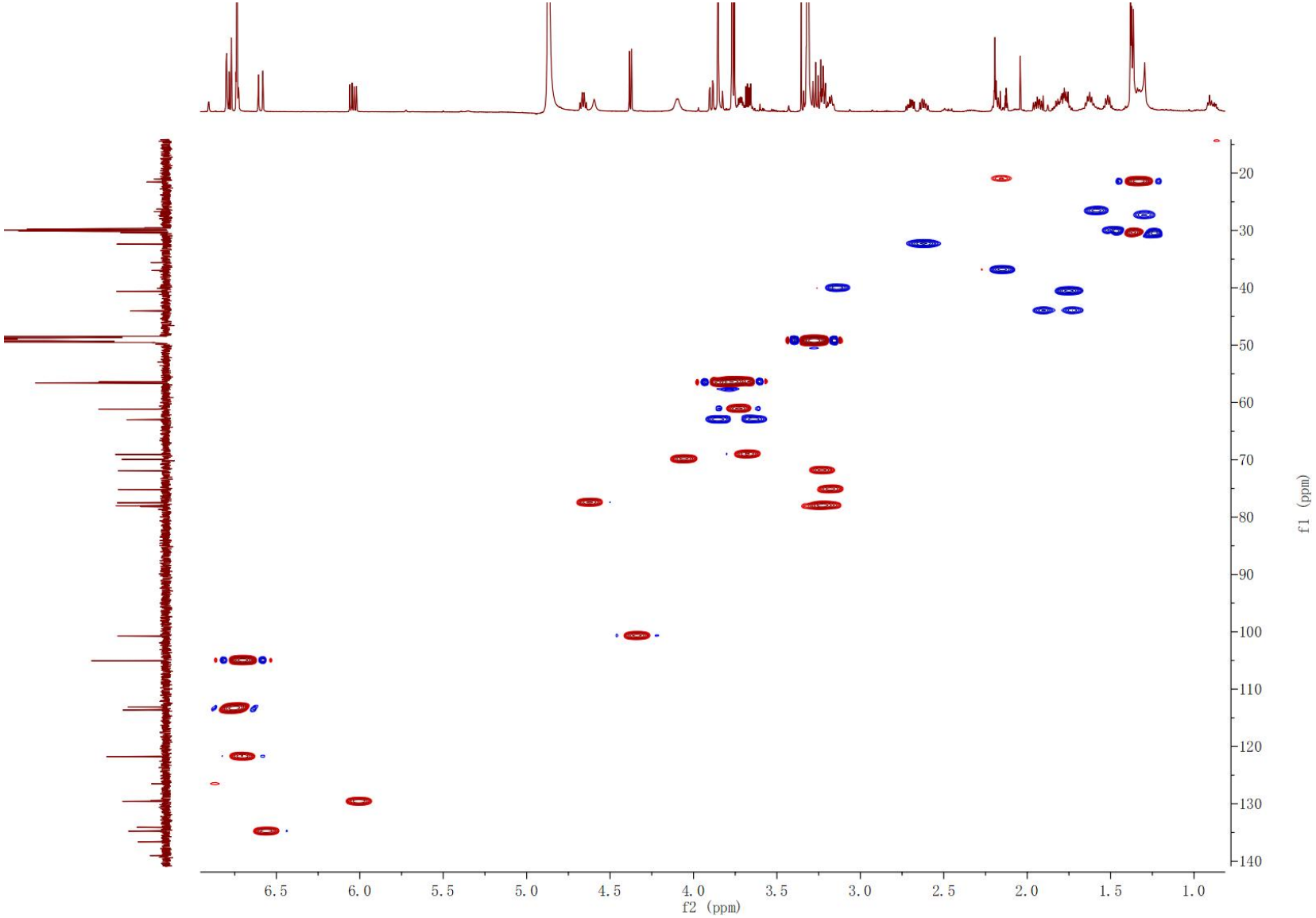

Figure S38. The HSQC spectrum of compound **3** in CD_3OD.

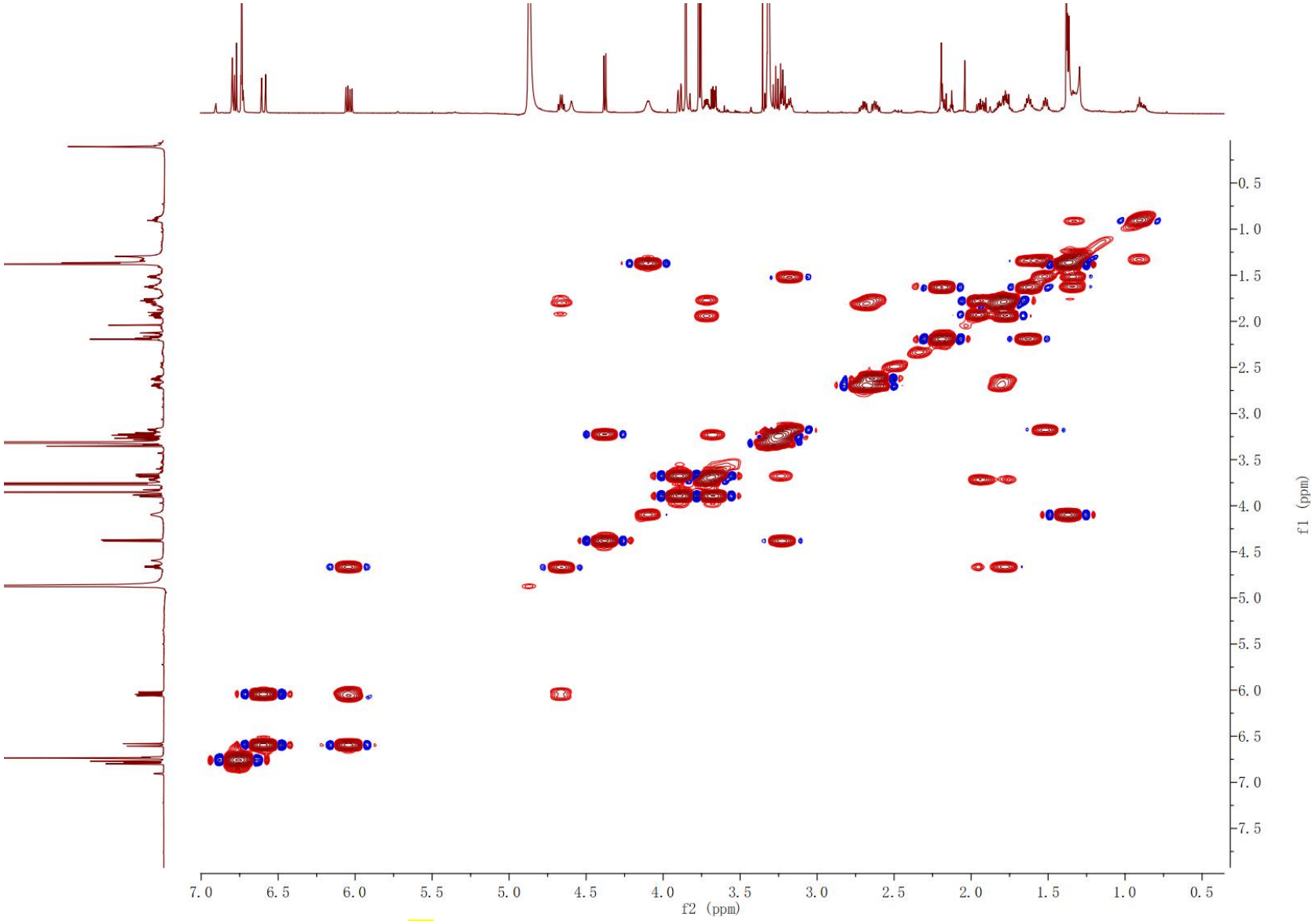

Figure S39. The ^{1}H-^{1}H COSY spectrum of compound **3** in CD_3OD.

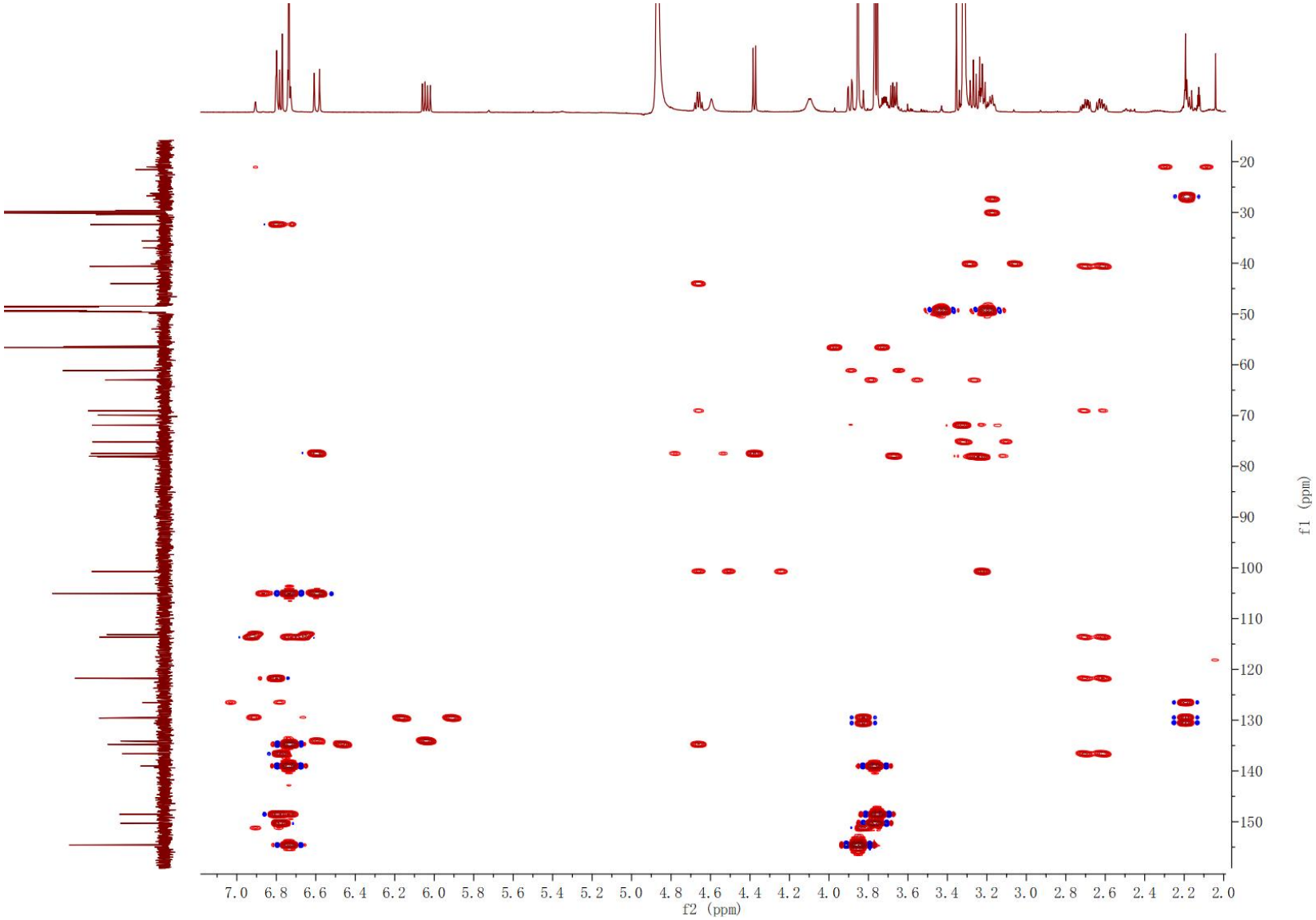

Figure S40. The HMBC spectrum of compound **3** in CD_3OD.

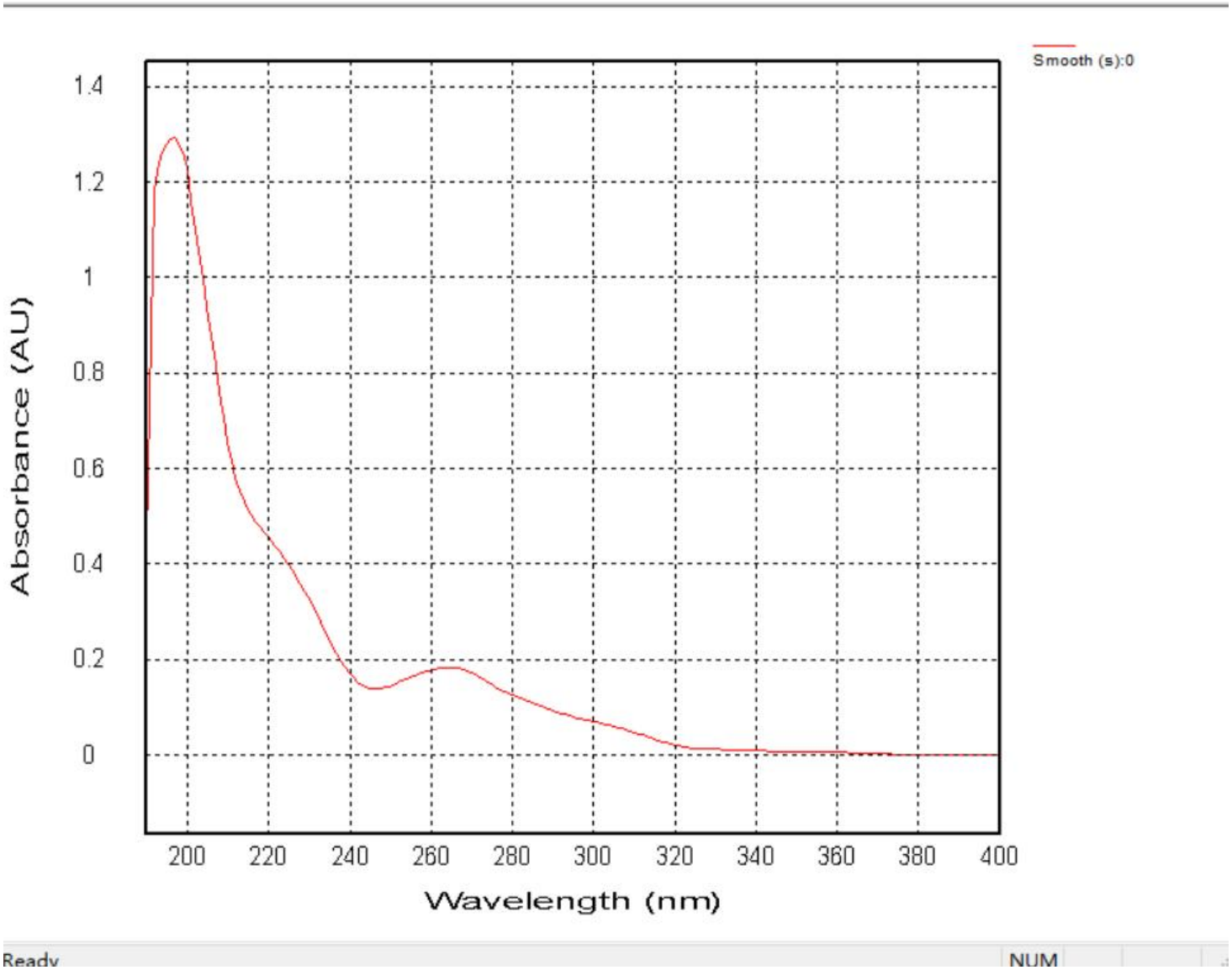

Figure S41. The UV spectrum of compound **3a**.

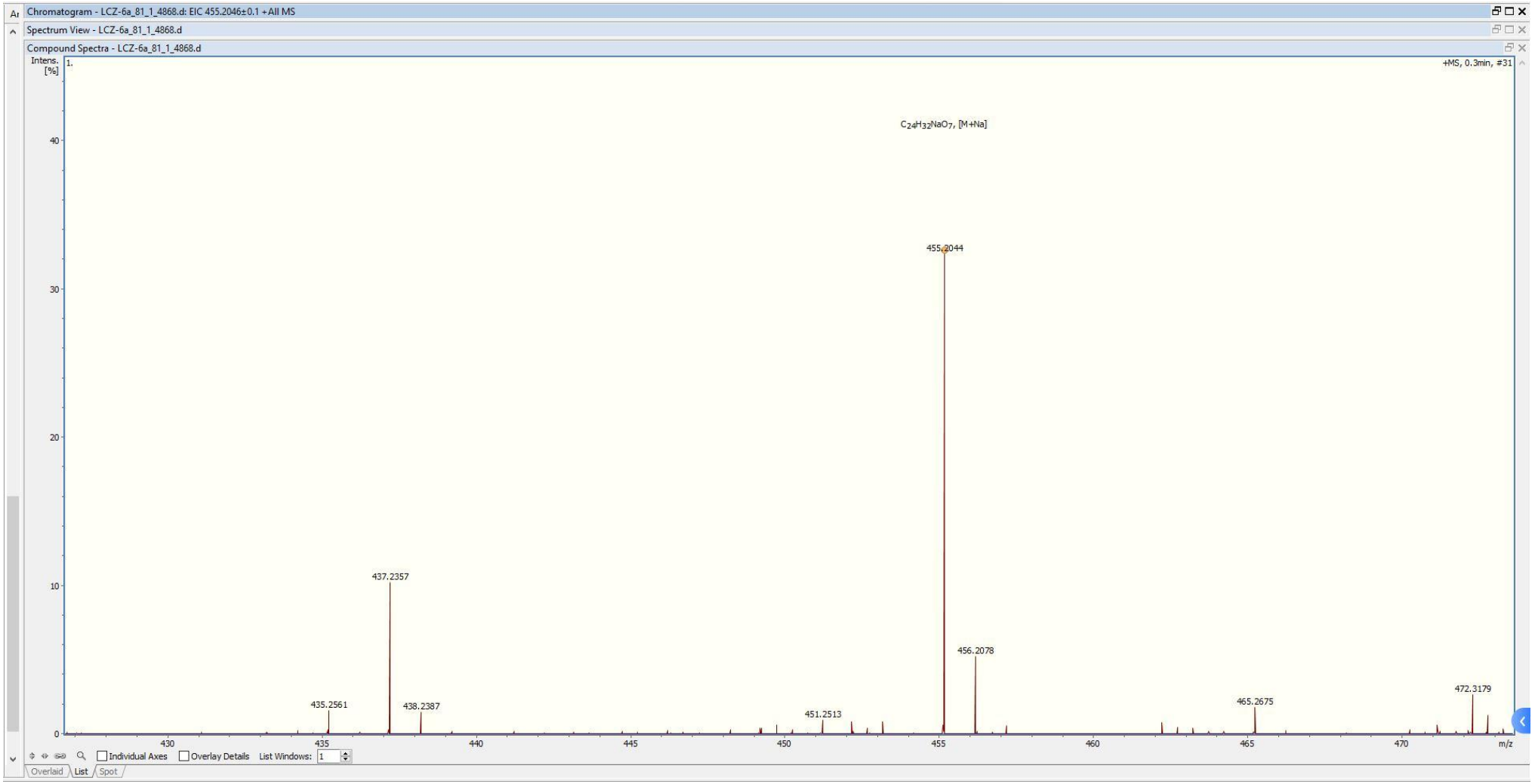

Figure S42. The (+)-HRESIMS spectroscopic data of compound **3a**.

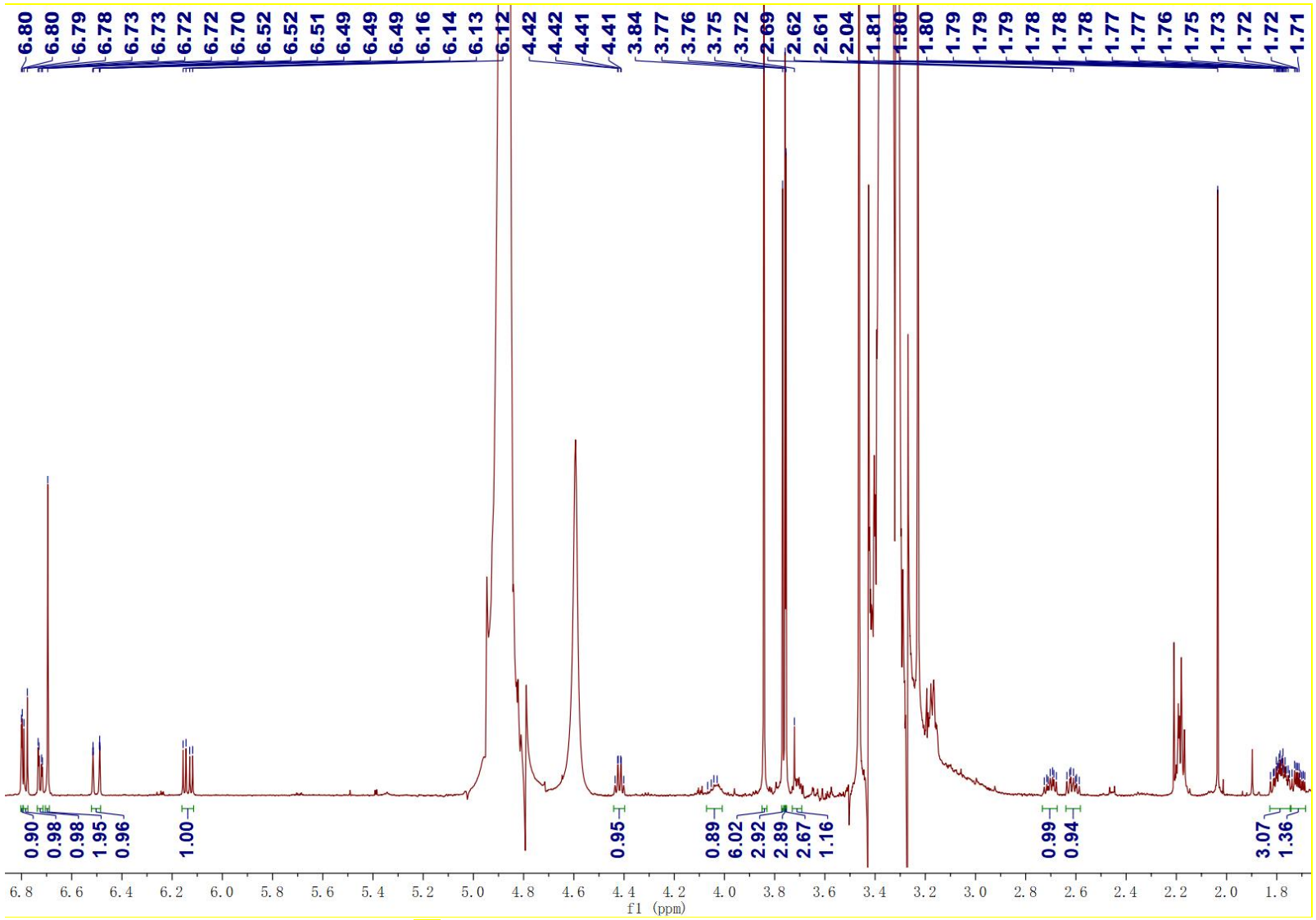

Figure S43. The ^{1}H NMR spectrum of compound **3a** in CD_3OD.

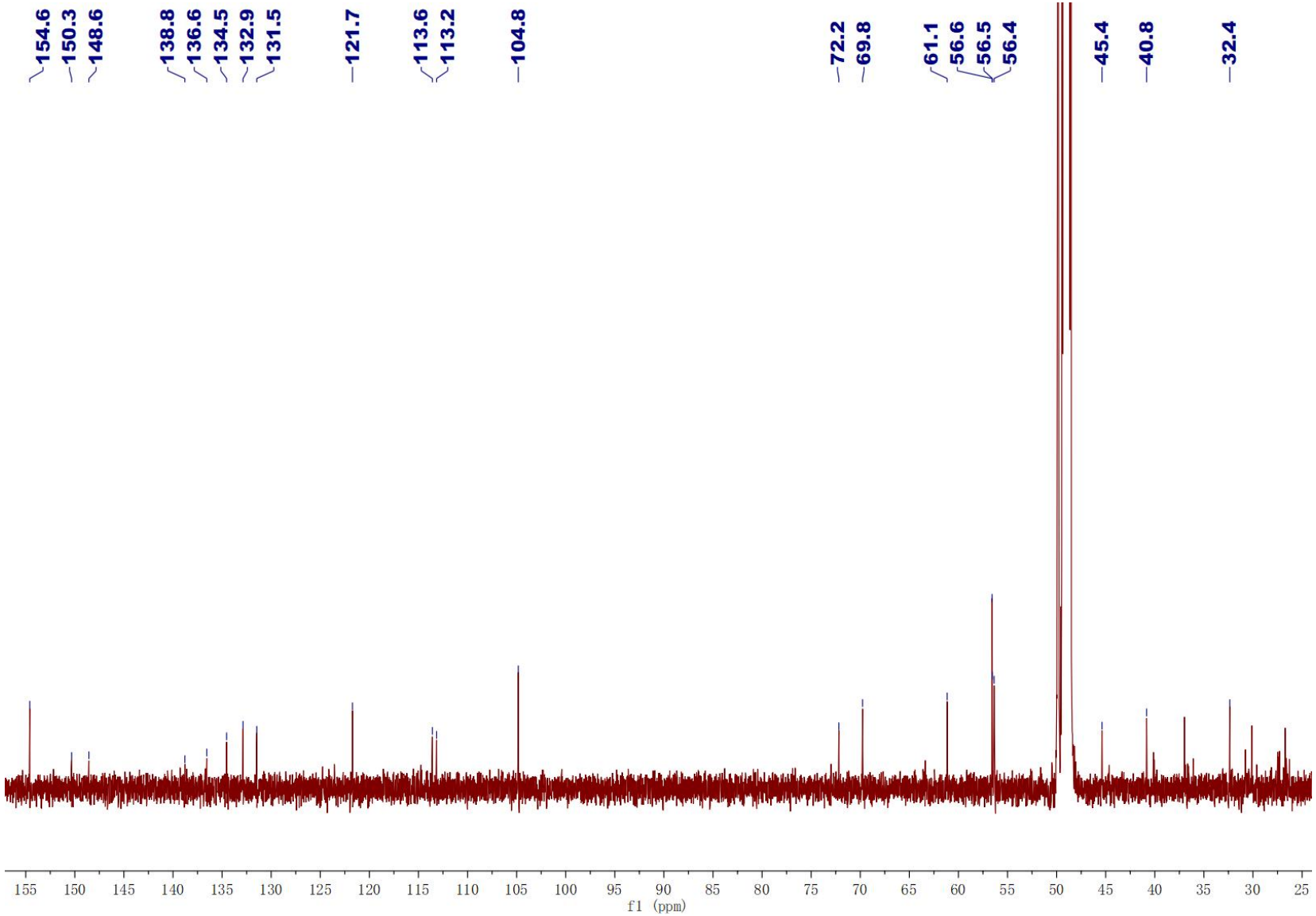

Figure S44. The ^{13}C NMR spectrum of compound **3a** in CD_3OD.

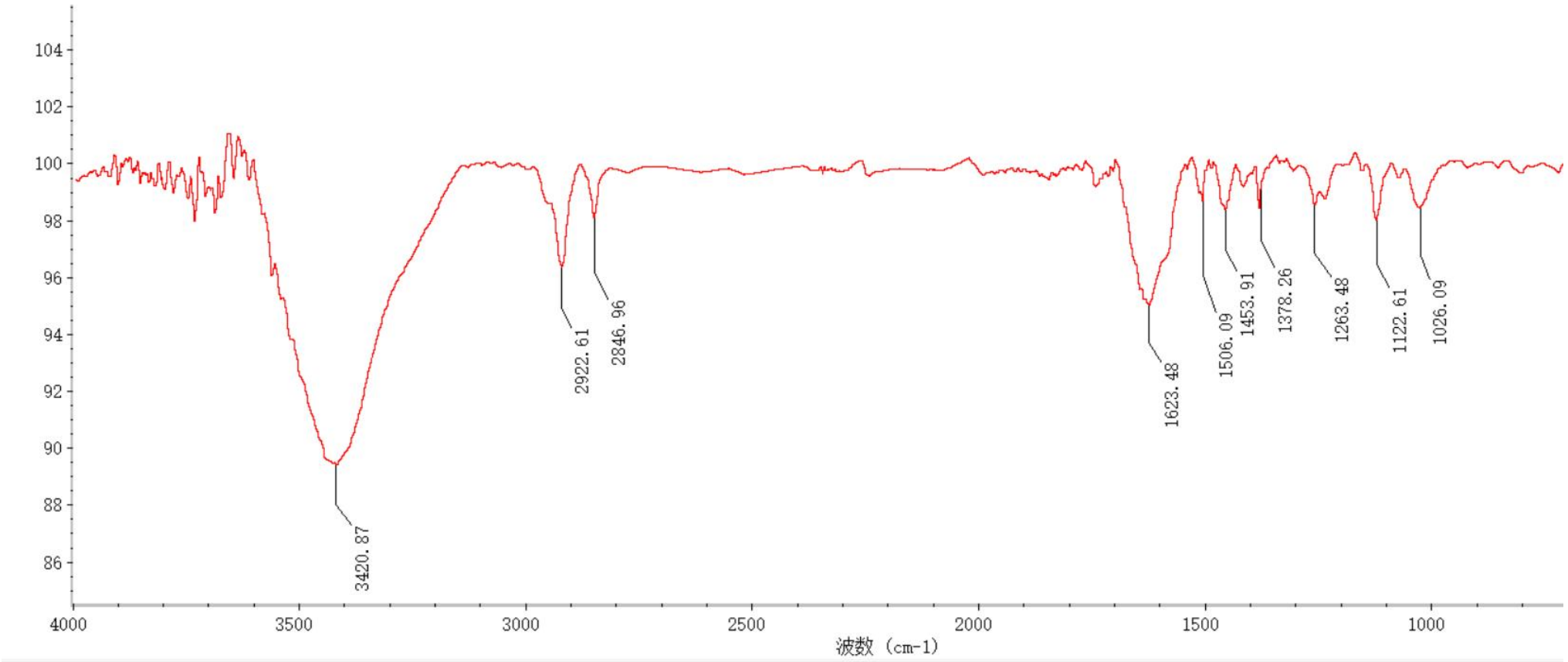

Figure S45. The IR spectrum of compound **4**.

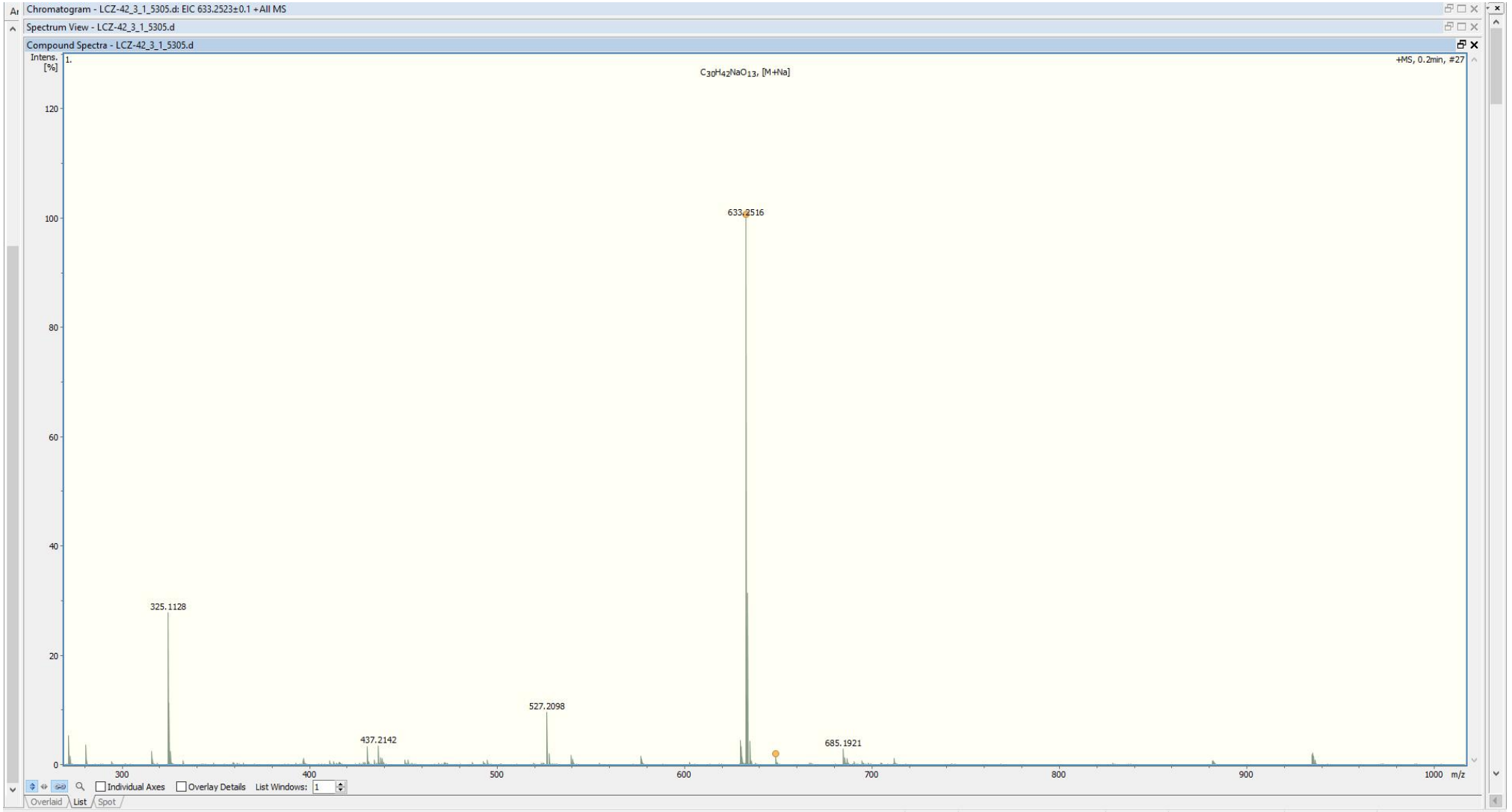

Figure S46. The (+)-HRESIMS spectroscopic data of compound **4**.

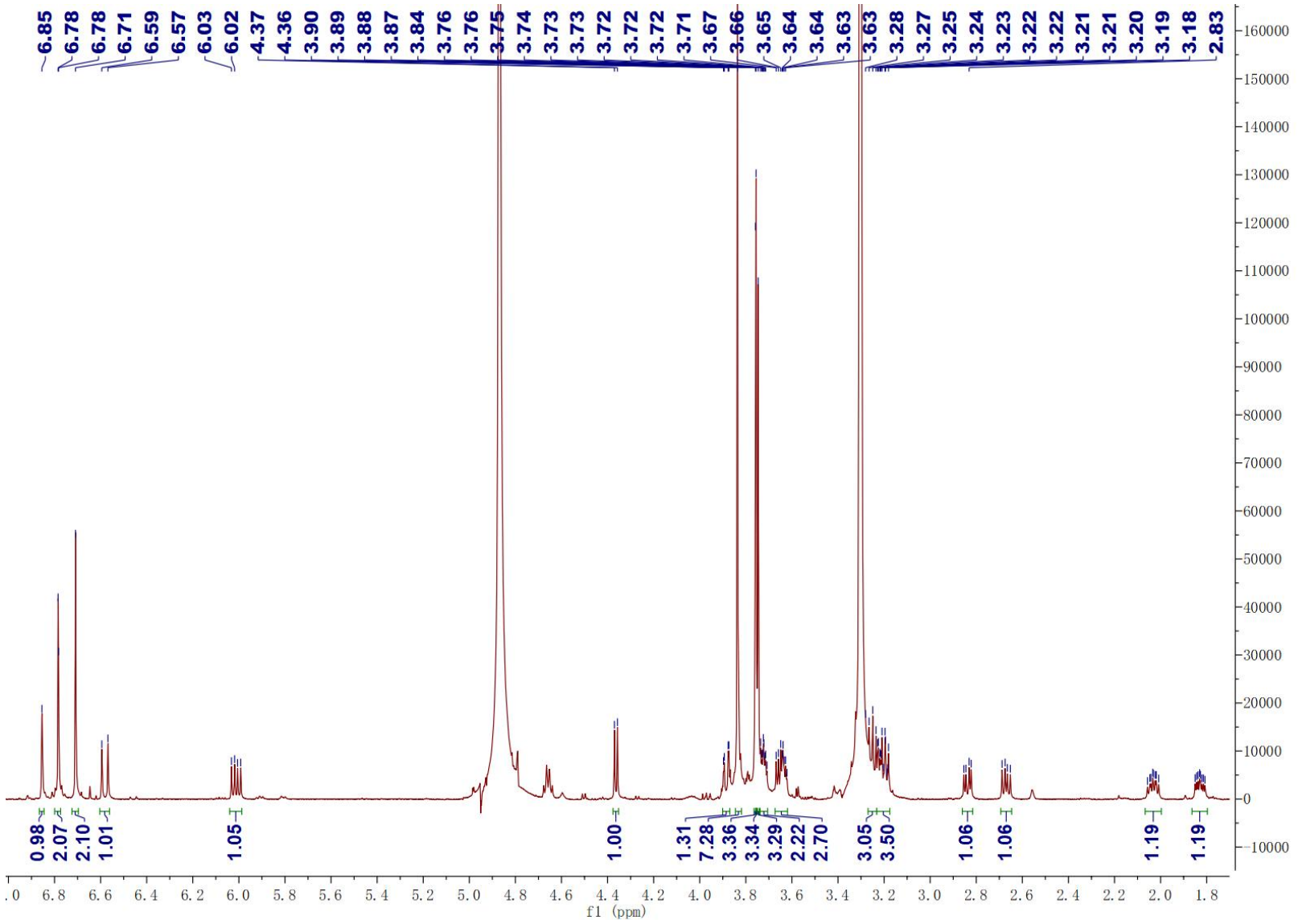

Figure S47. The ^{1}H NMR spectrum of compound **4** in CD_3OD.

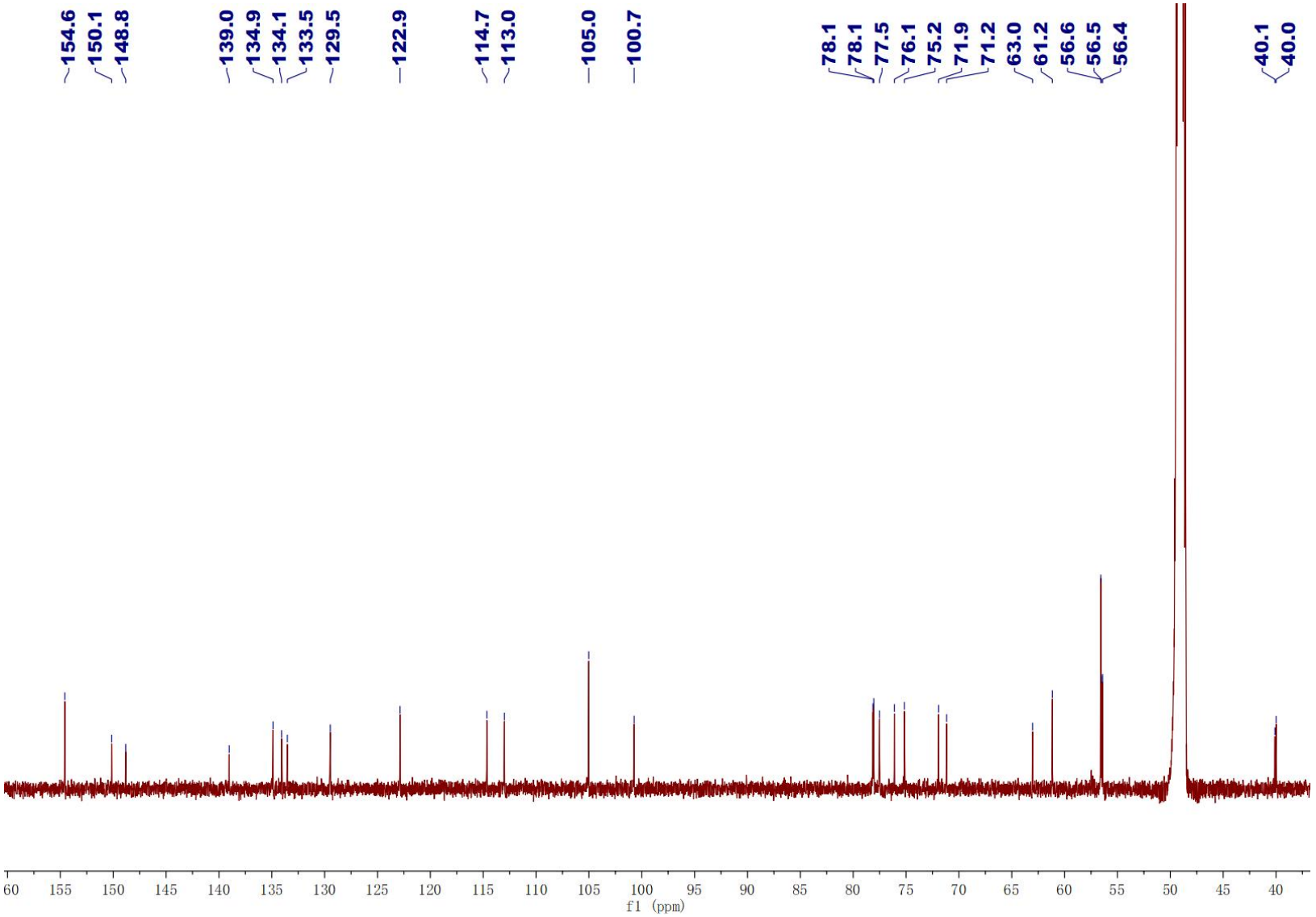

Figure S48. The ^{13}C NMR spectrum of compound **4** in CD_3OD.

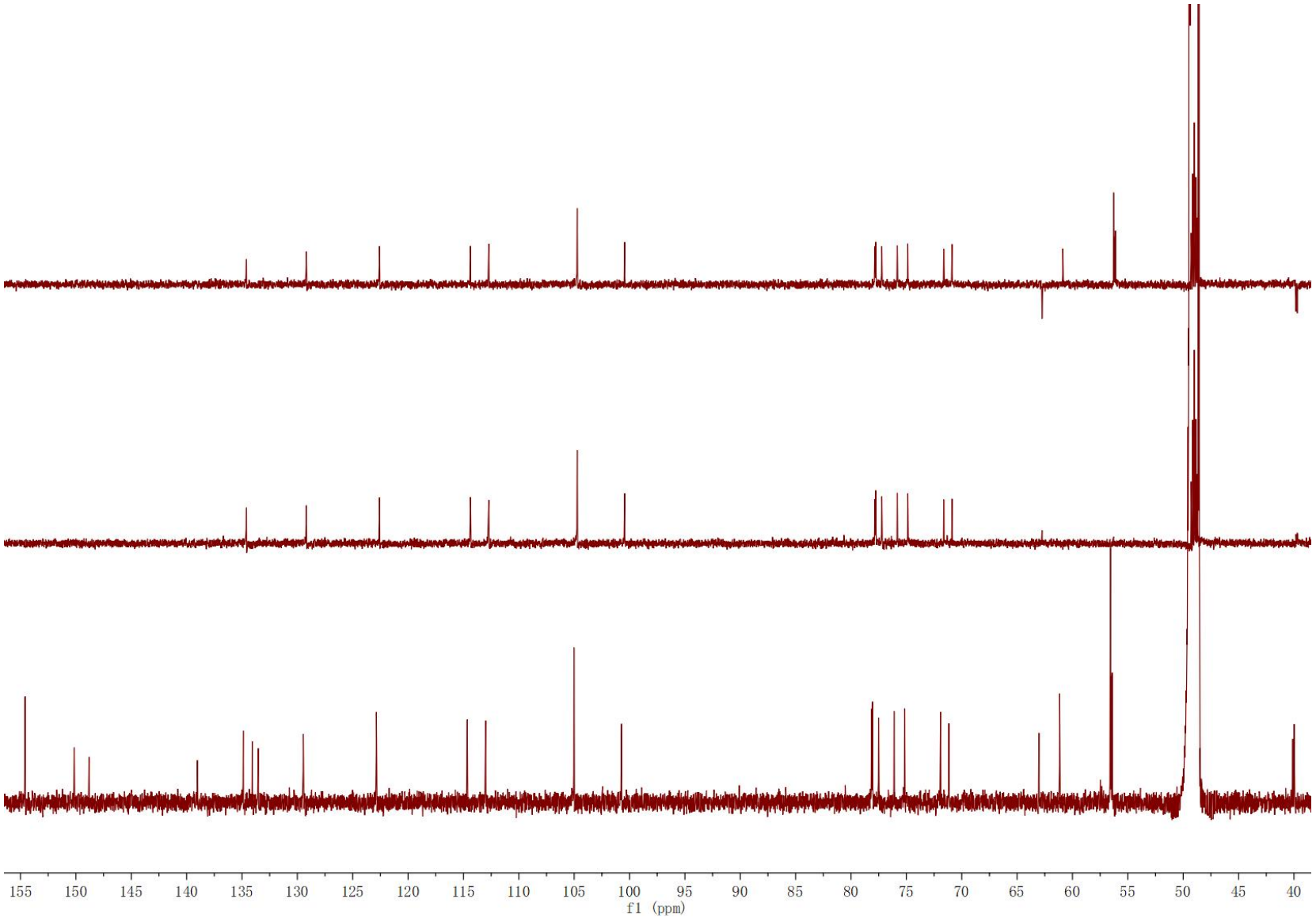

Figure S49. The DEPT spectrum of compound **4** in CD_3OD.

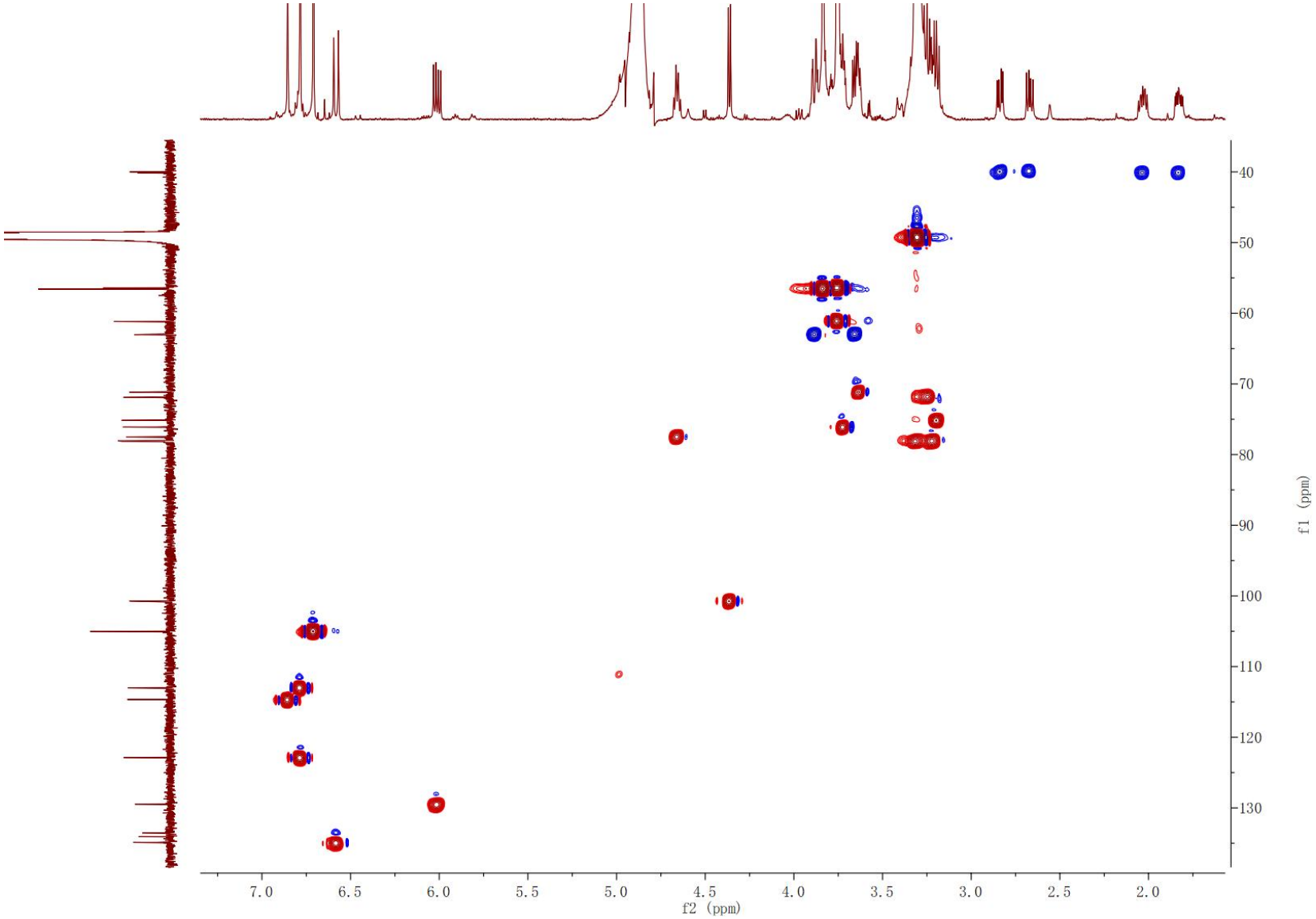

Figure S50. The HSQC spectrum of compound **4** in CD_3OD.

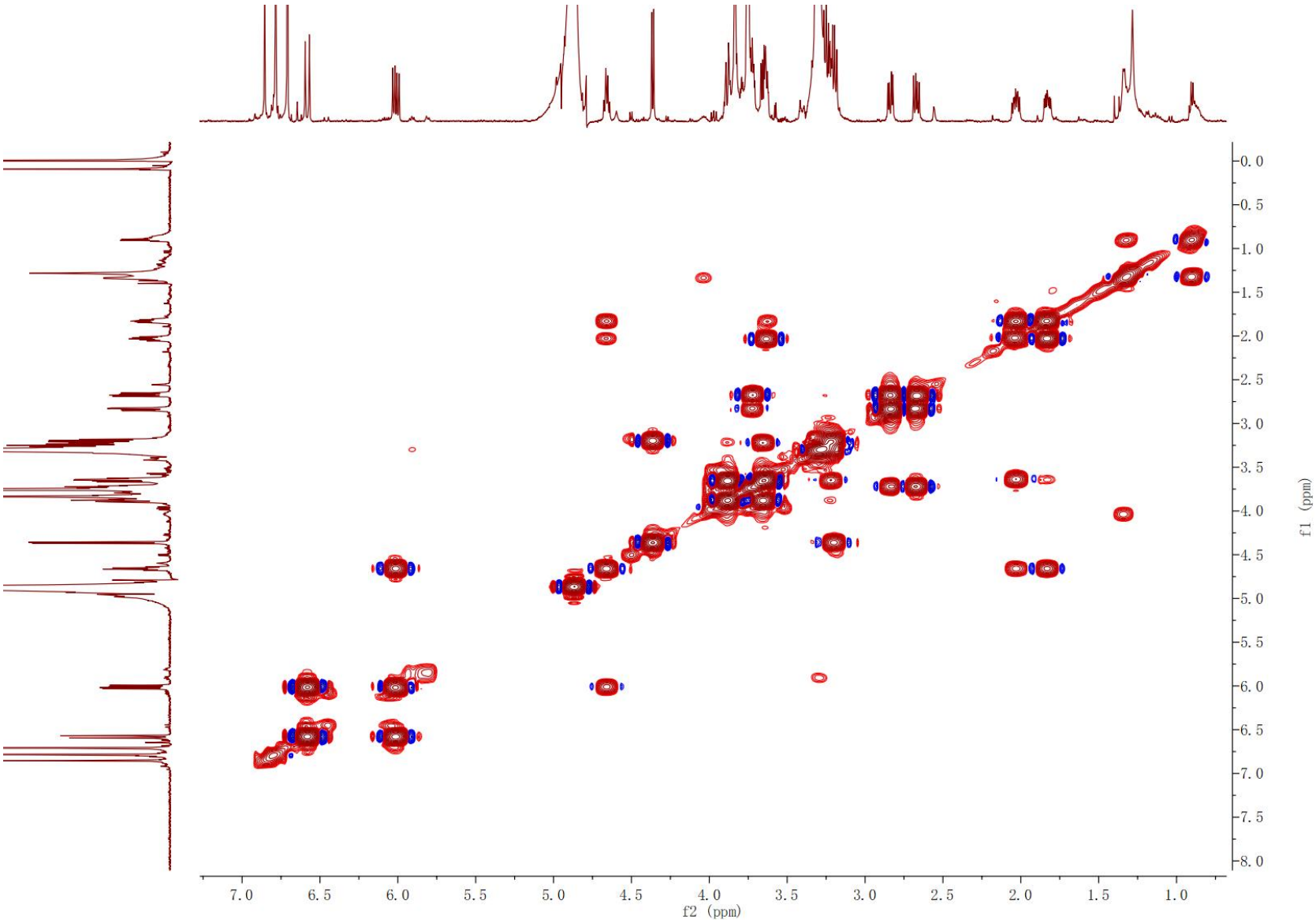

Figure S51. The ^{1}H-^{1}H COSY spectrum of compound **4** in CD_3OD.

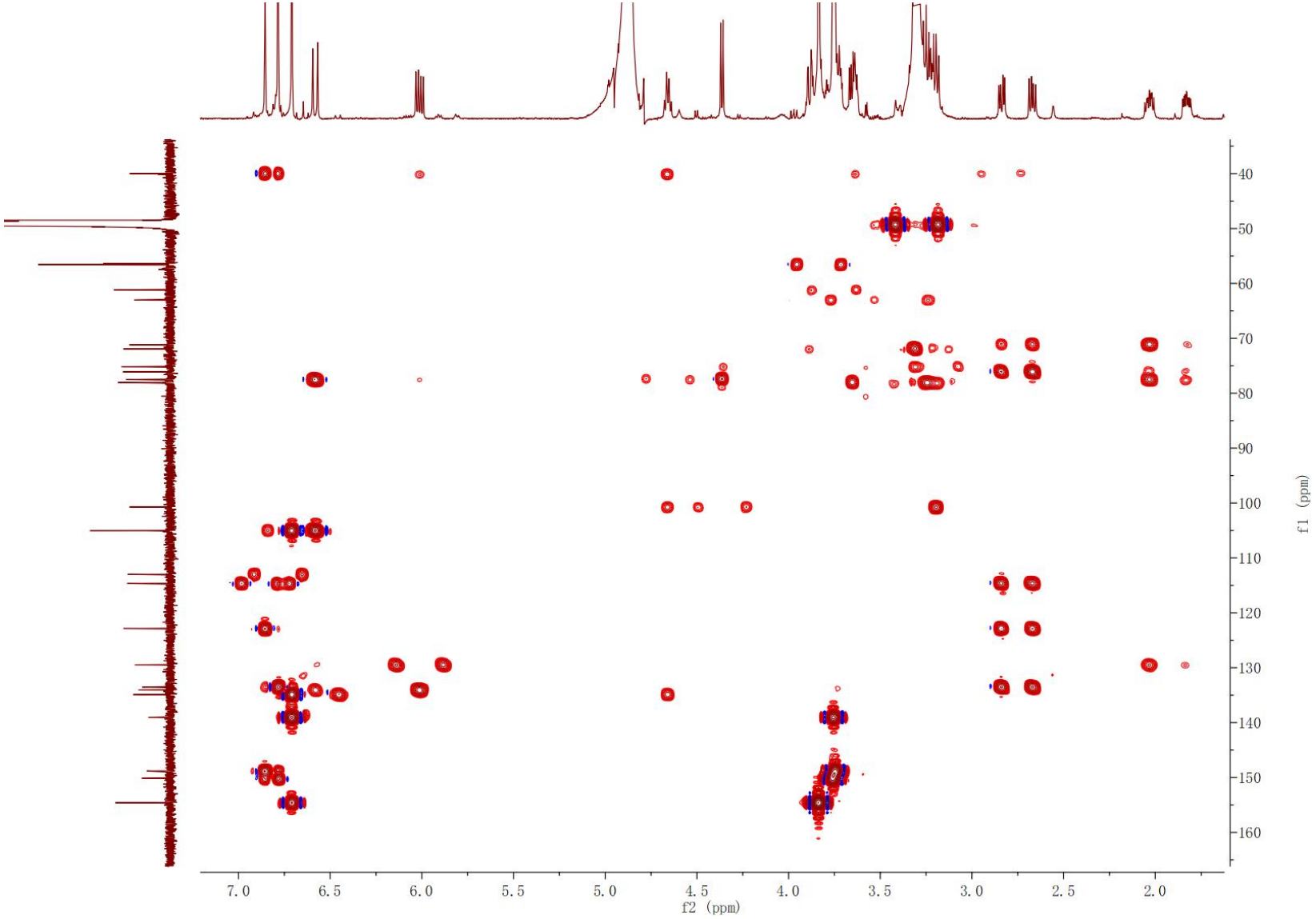

Figure S52. The HMBC spectrum of compound **4** in CD_3OD.

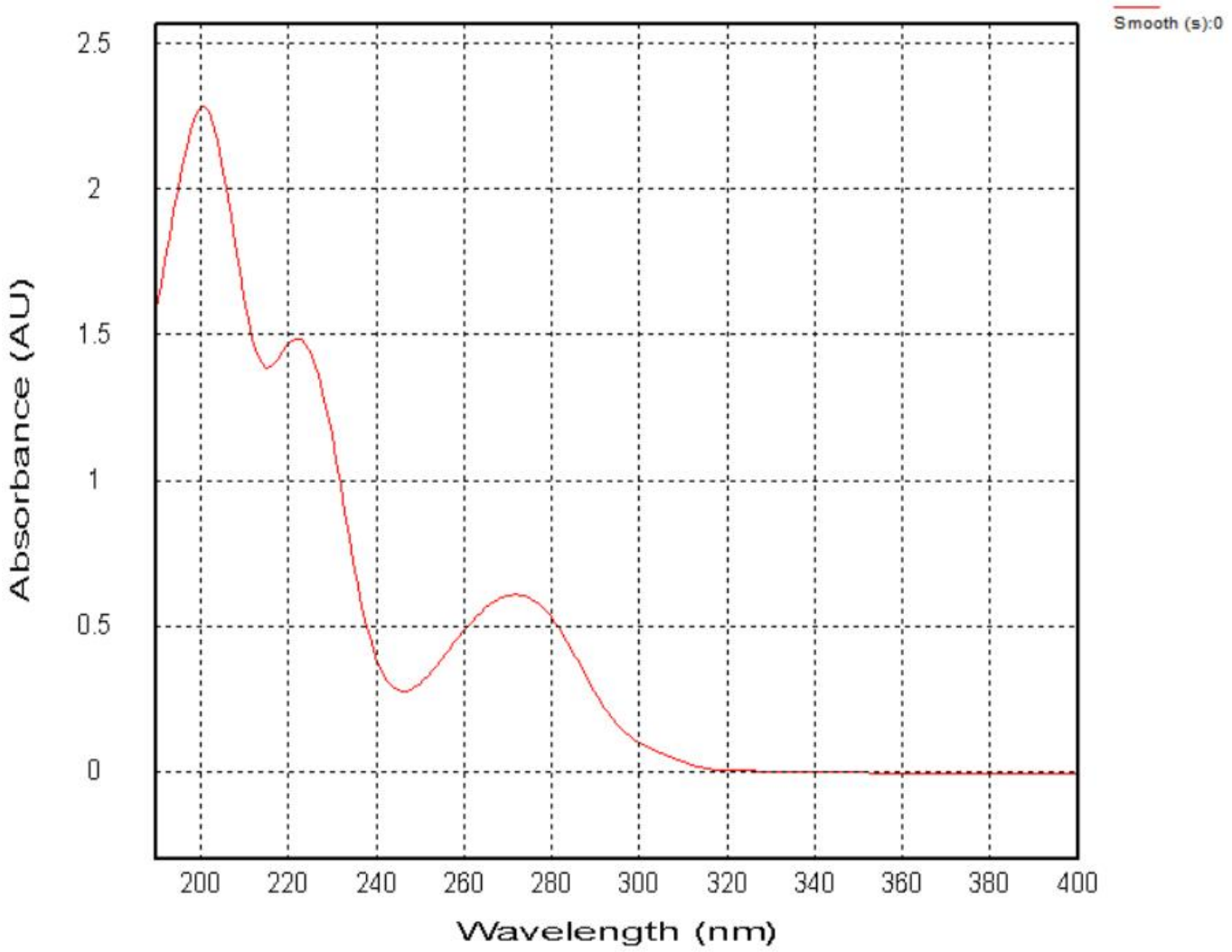

Figure S53. The UV spectrum of compound **4a**.

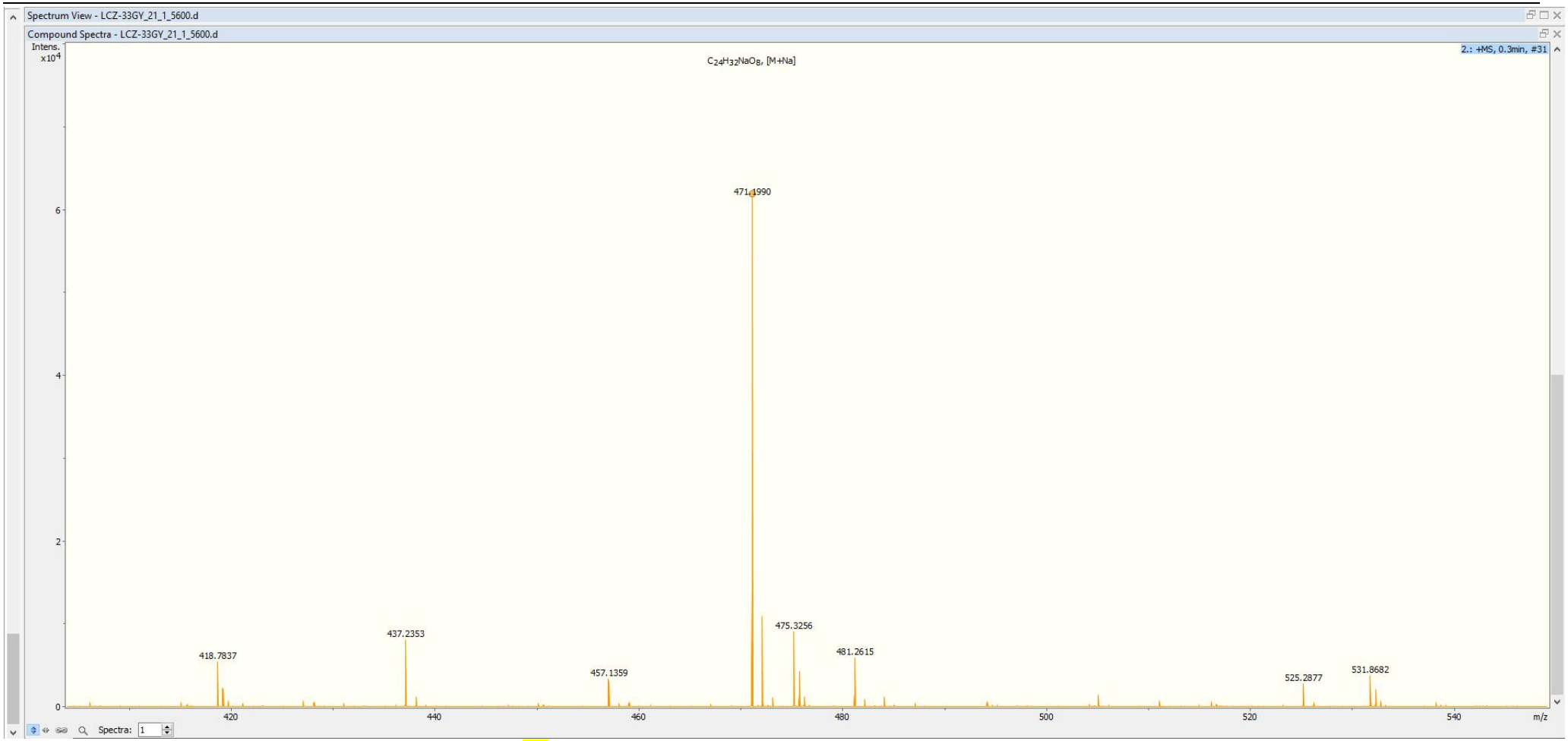

Figure S54. The (+)-HRESIMS spectroscopic data of compound **4a**.

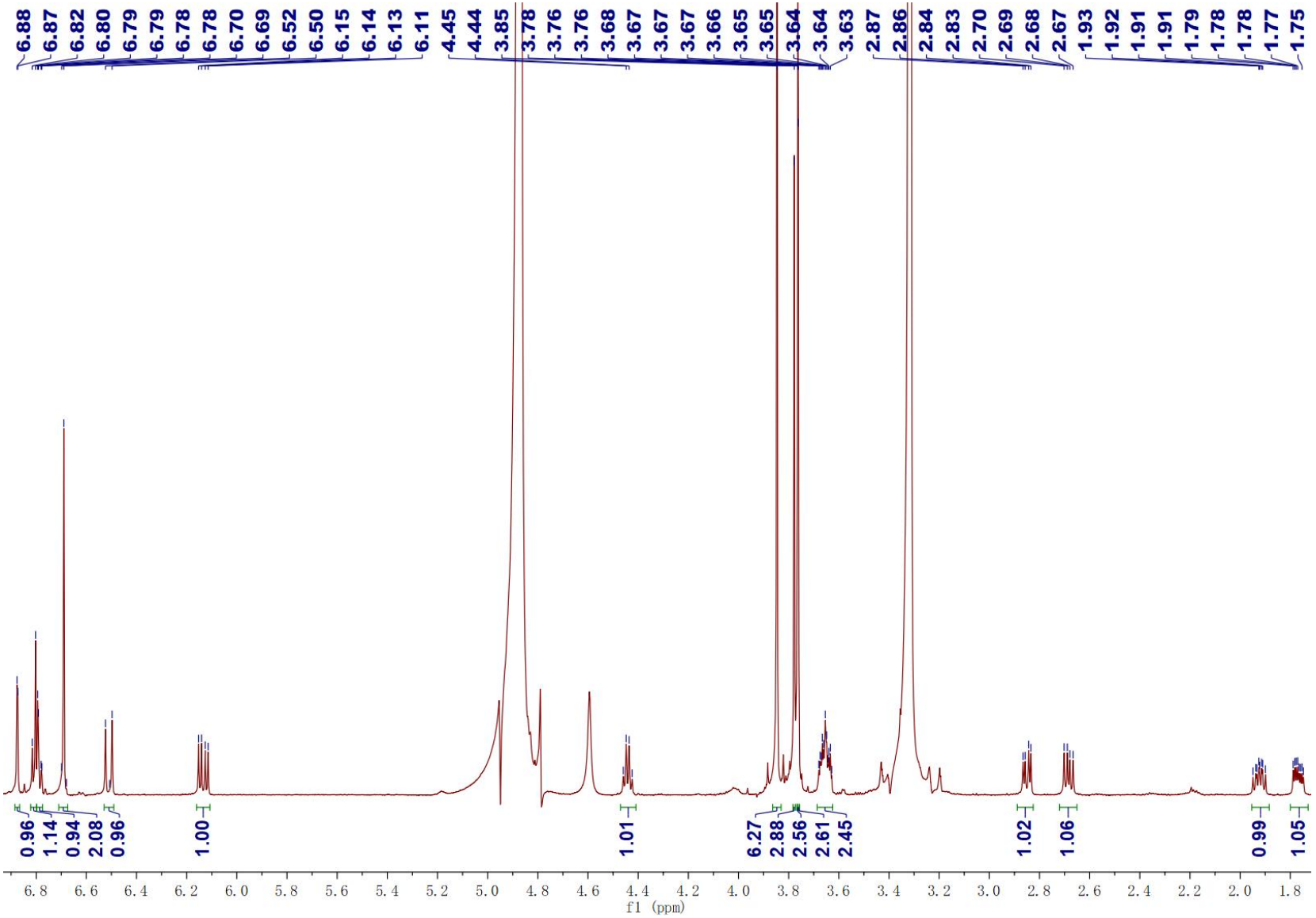

Figure S55. The ^{1}H NMR spectrum of compound **4a** in CD_3OD.

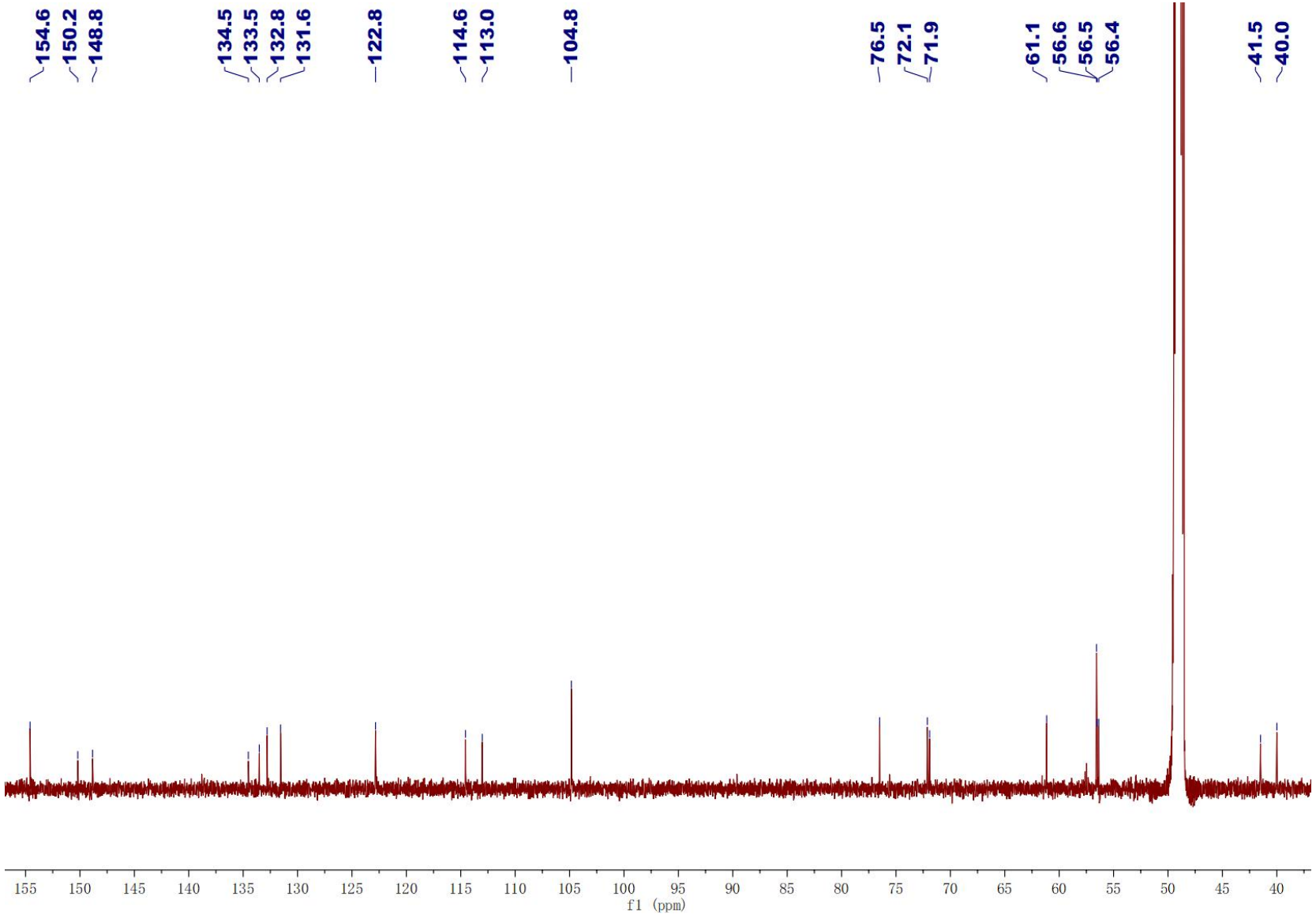

Figure S56. The ^{13}C NMR spectrum of compound **4a** in CD_3OD.

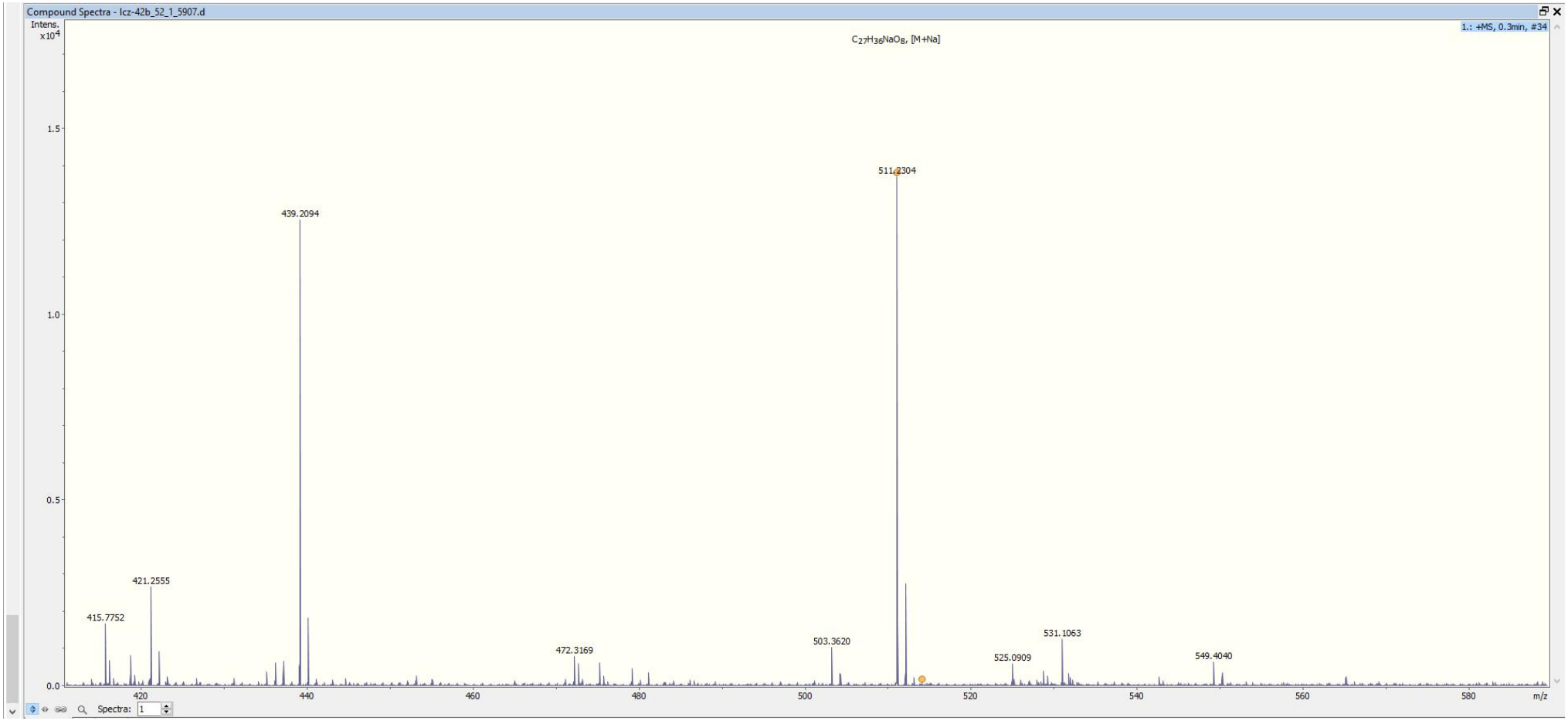

Figure S57. The (+)-HRESIMS spectroscopic data of compound **4b**.

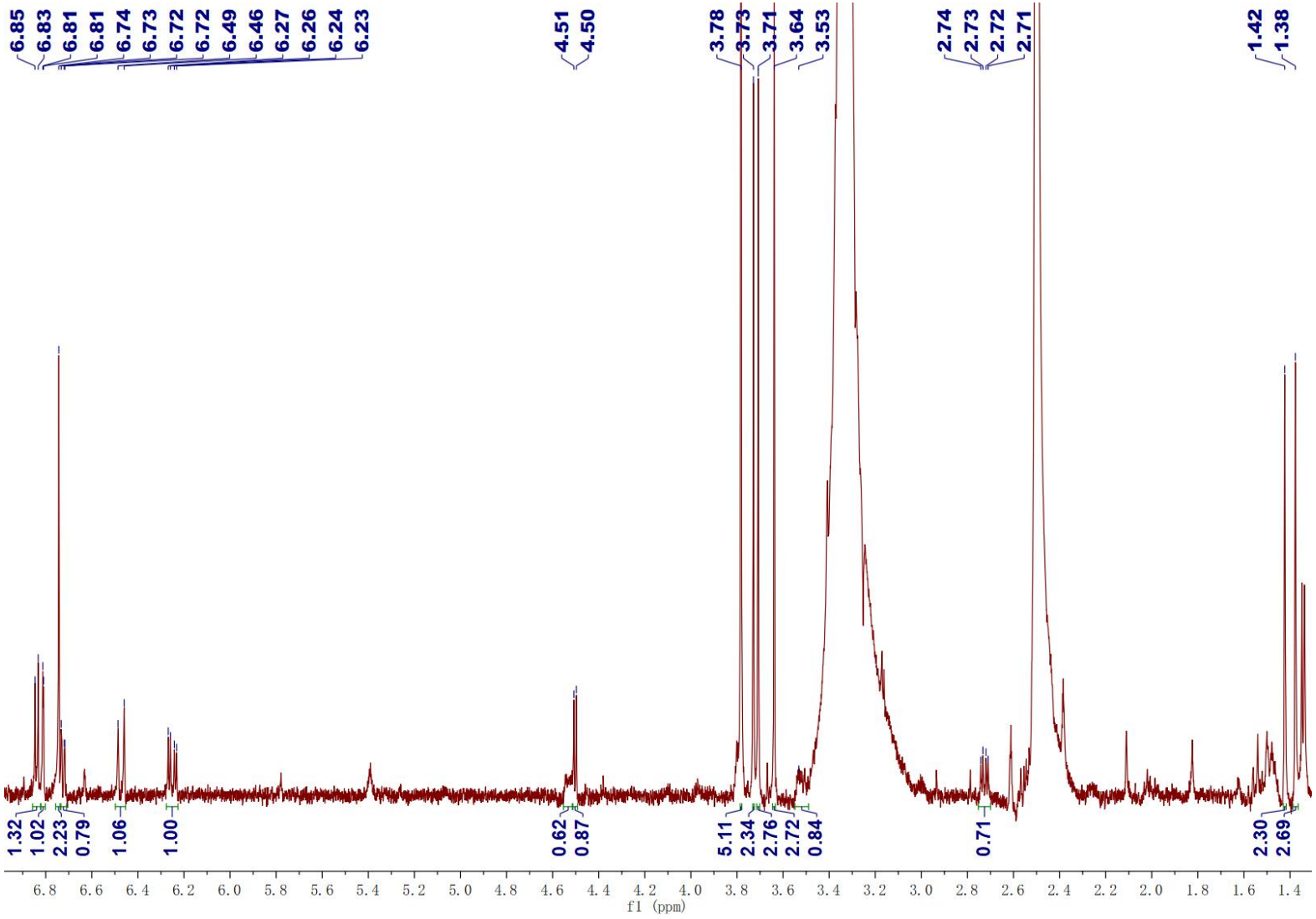

Figure S58. The ^{1}H NMR spectrum of compound **4b** in DMSO-d_6.

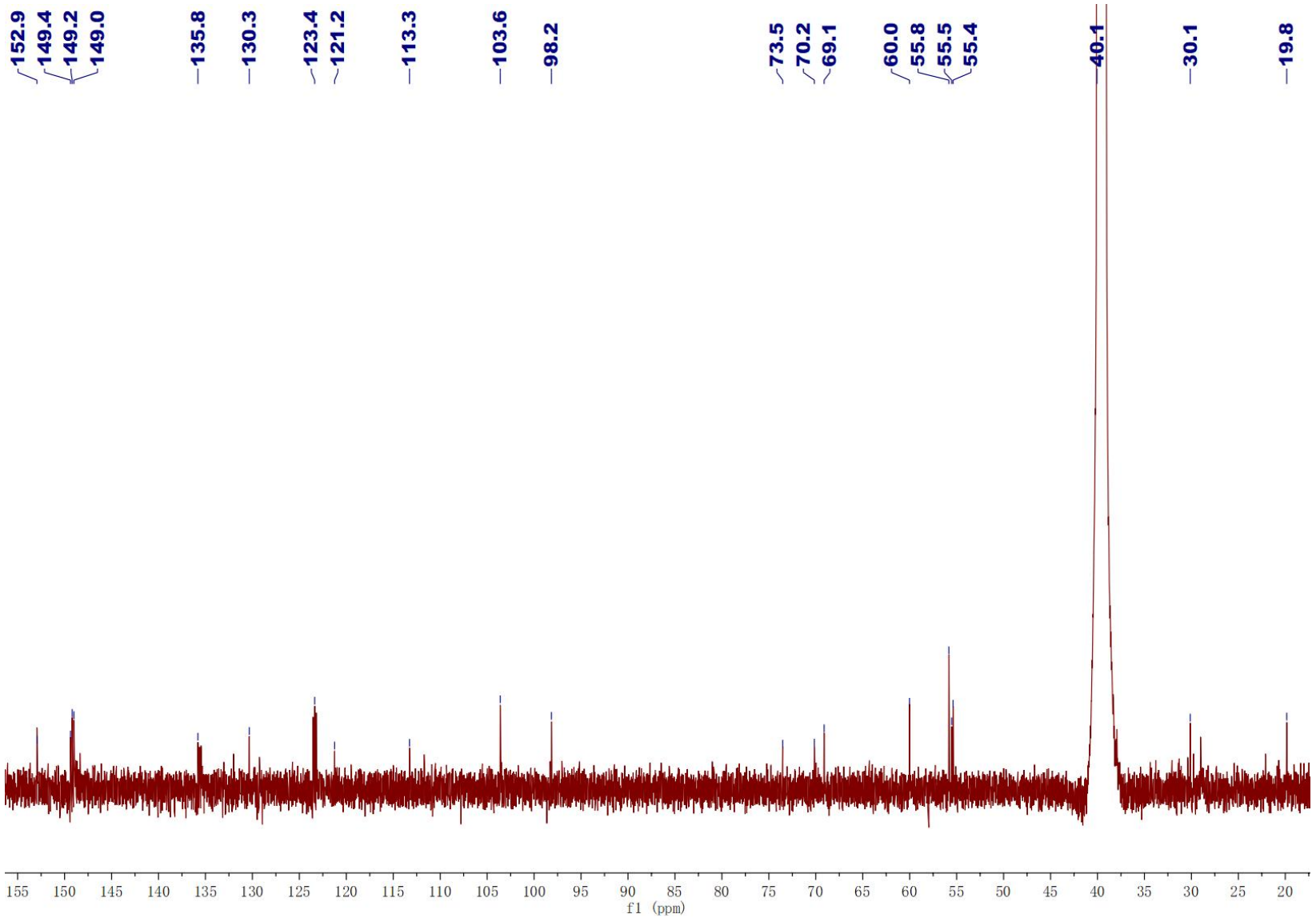

Figure S59. The ^{13}C NMR spectrum of compound **4b** in DMSO-d_6.

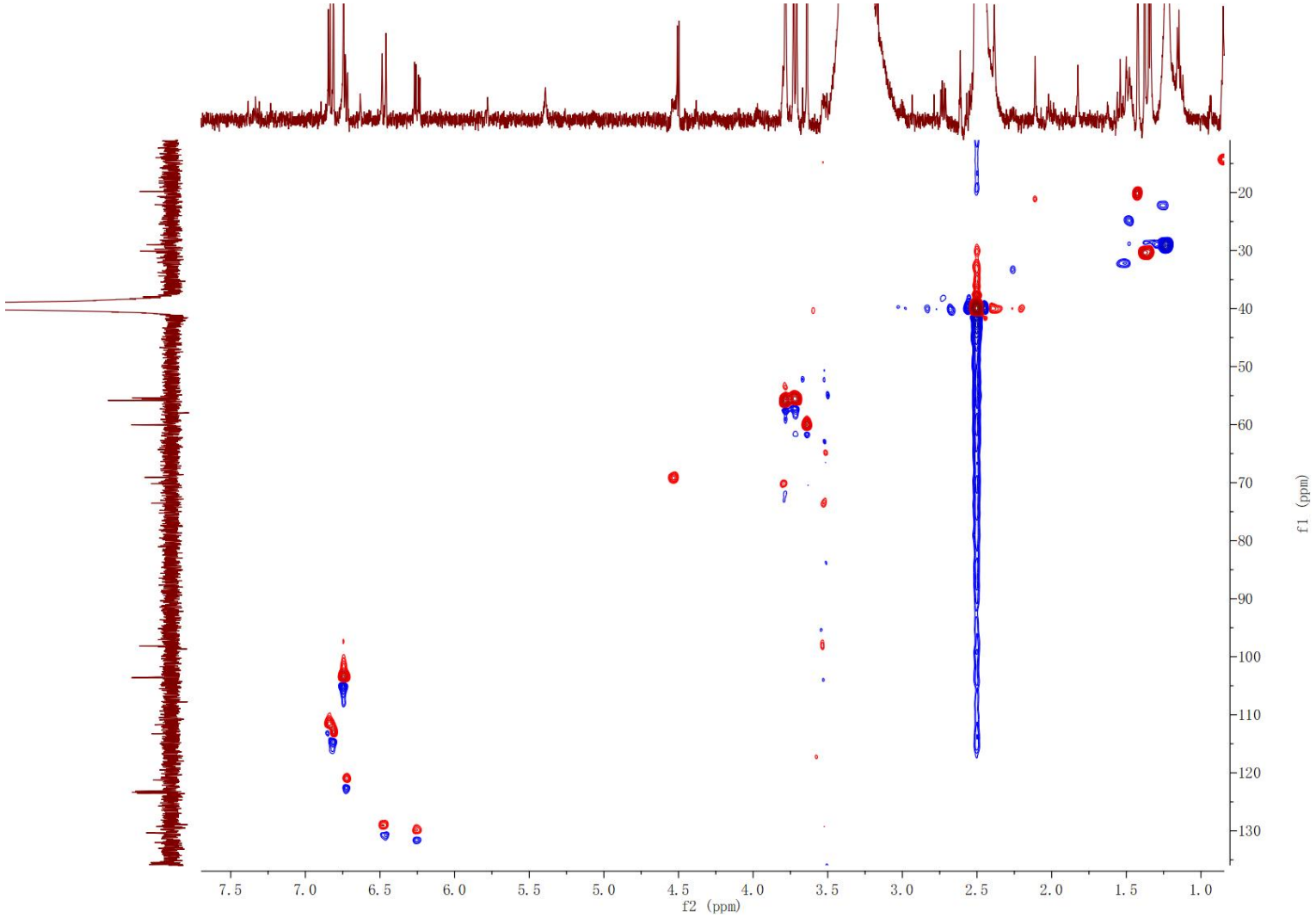

Figure S60. The HSQC spectrum of compound **4b** in DMSO-d_6.

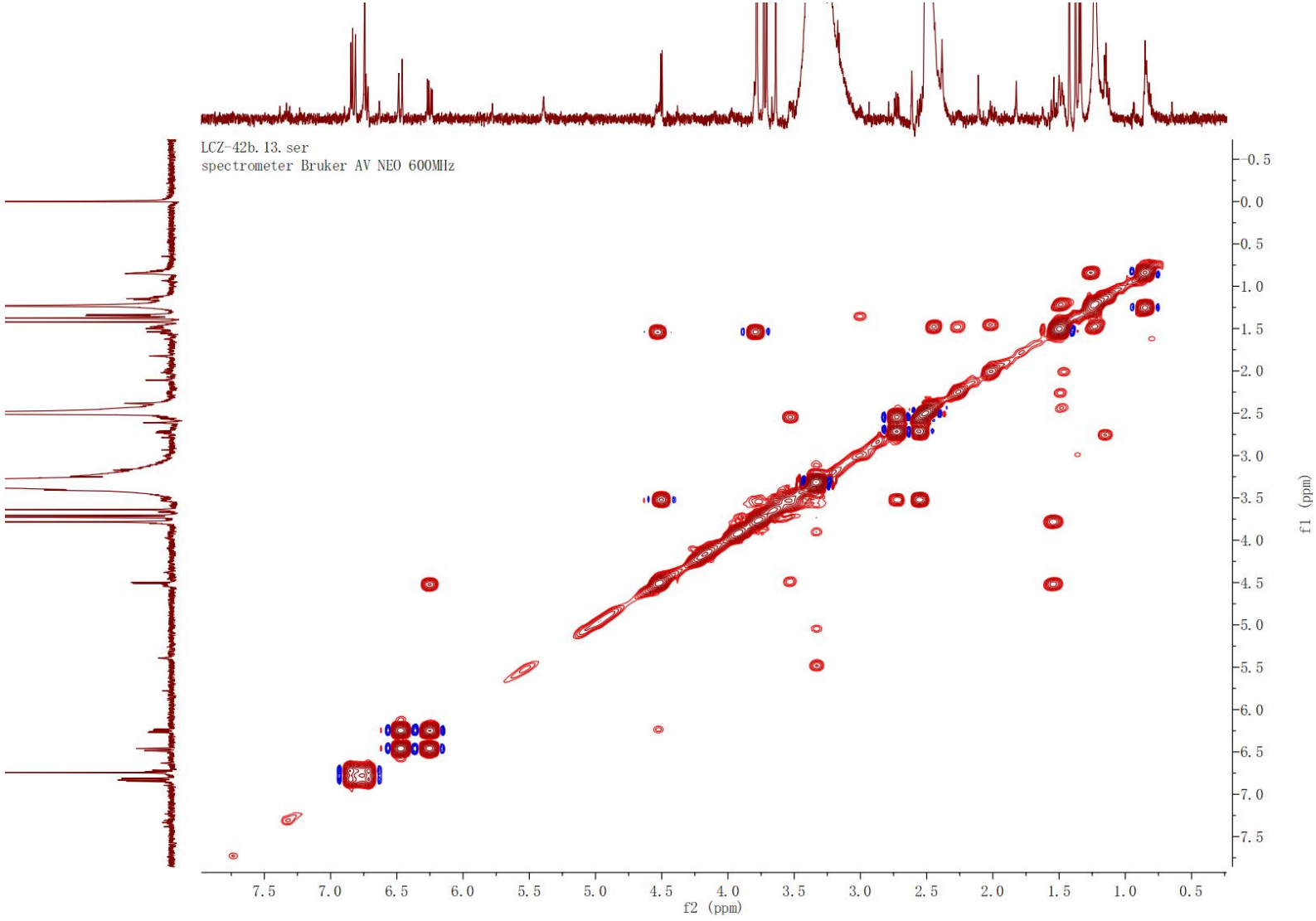

Figure S61. The ^{1}H-^{1}H COSY spectrum of compound **4b** in DMSO-d_6.

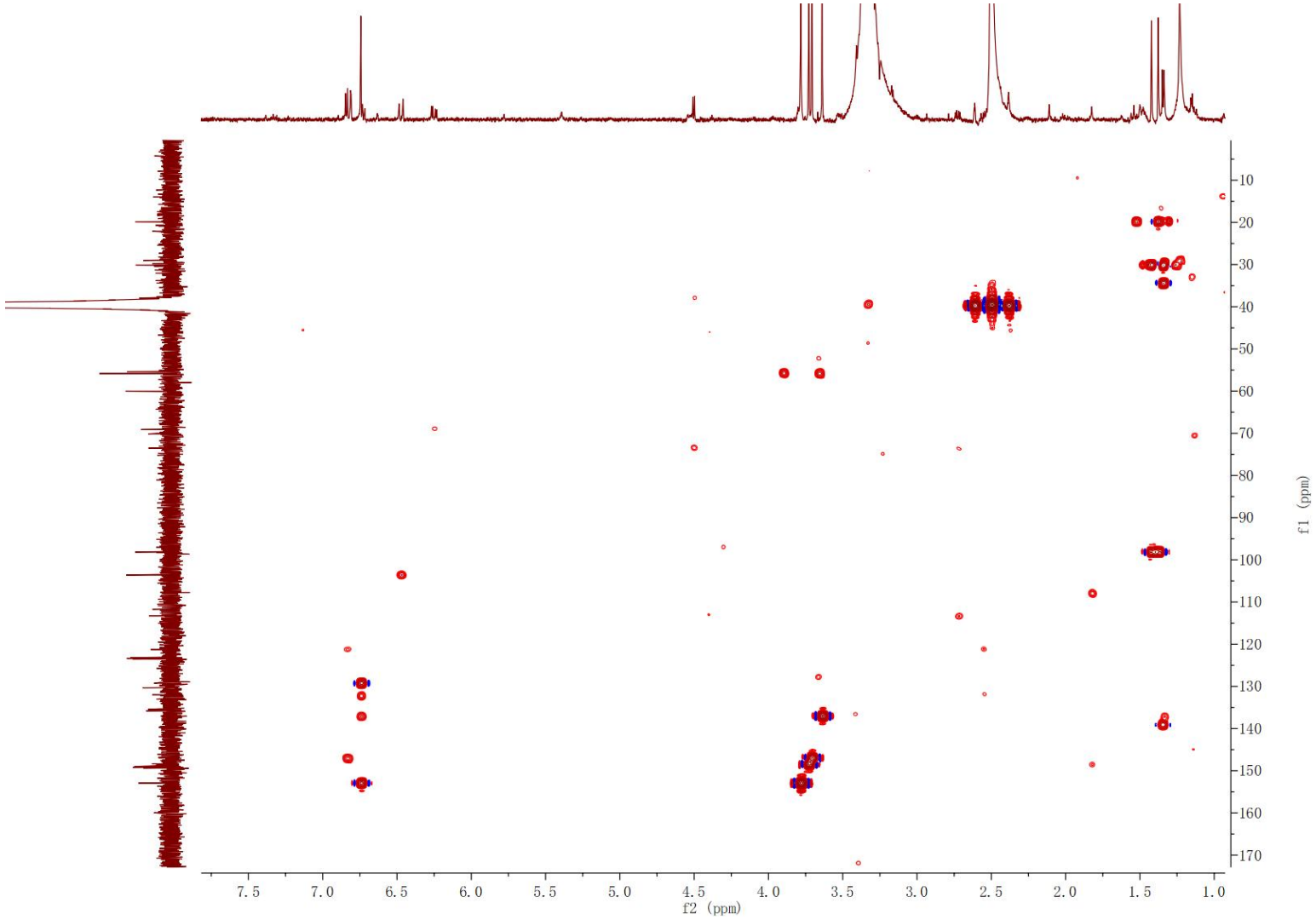

Figure S62. The HMBC spectrum of compound **4b** in DMSO-d_6.

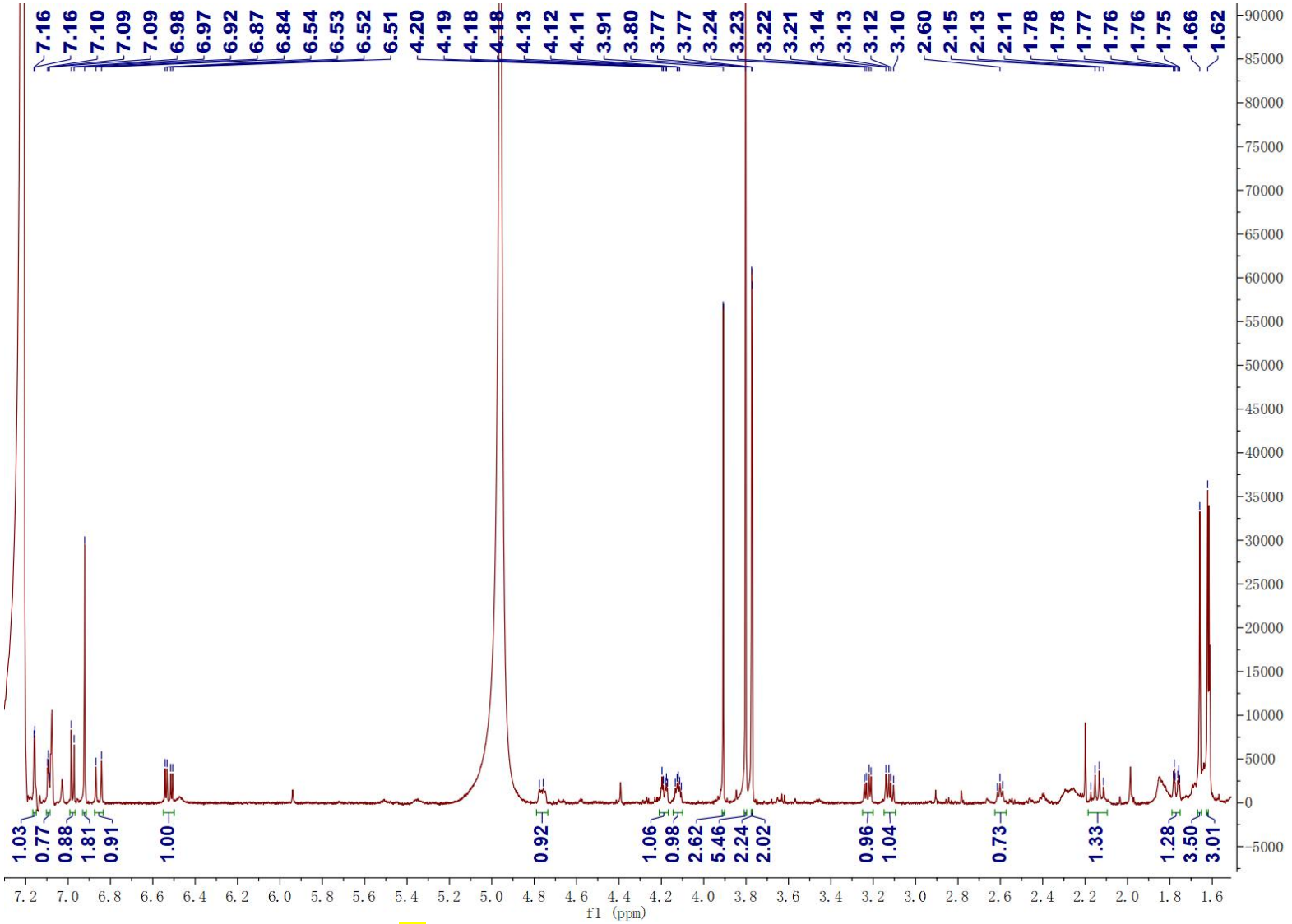

Figure S63. The ^{1}H NMR spectrum of compound **4b** in pyridine-d_5.

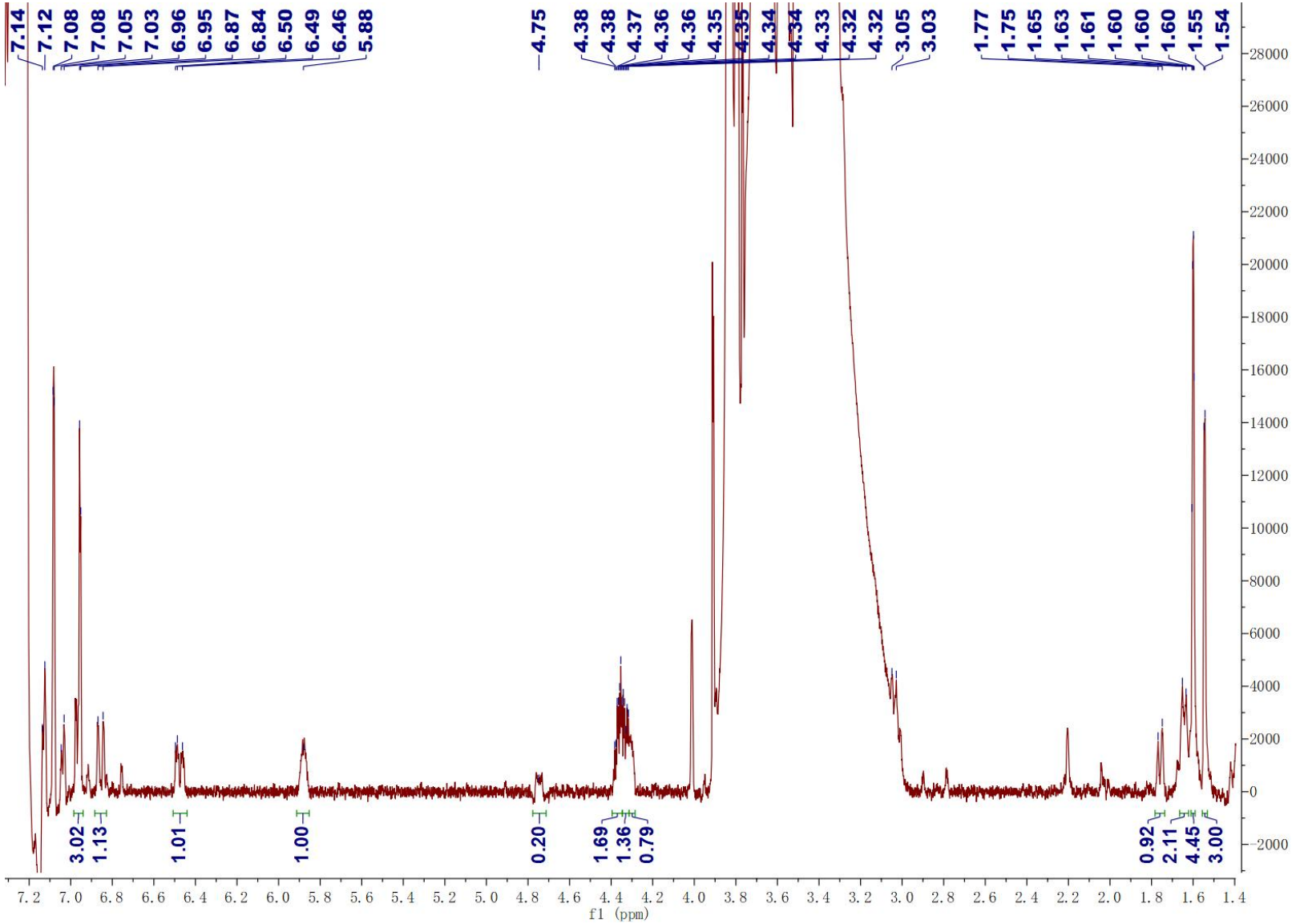

Figure S64. The ^{1}H NMR spectrum of compound **4c** in pyridine-d_5.

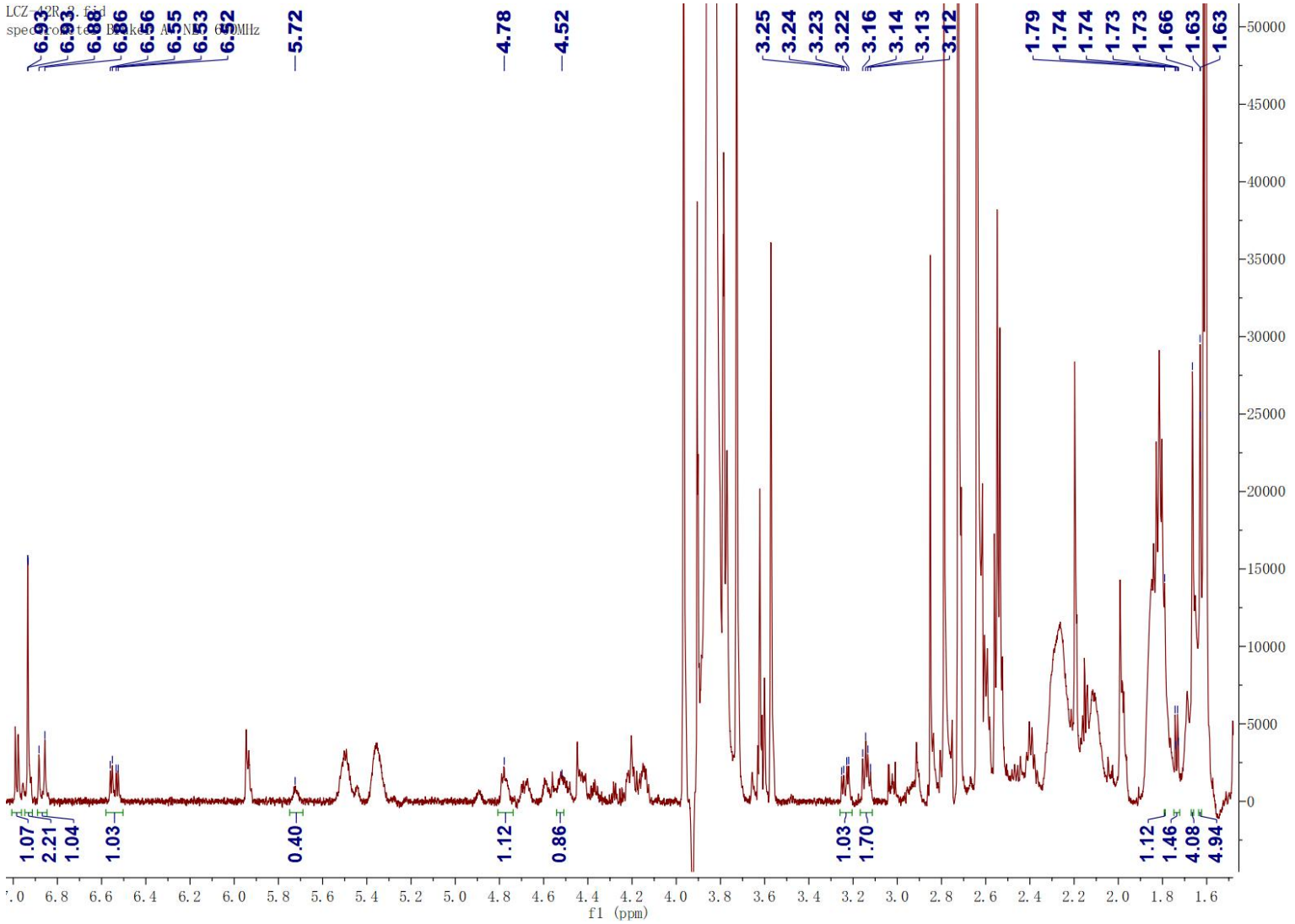

Figure S65. The ^{1}H NMR spectrum of compound **4d** in pyridine-d_5.

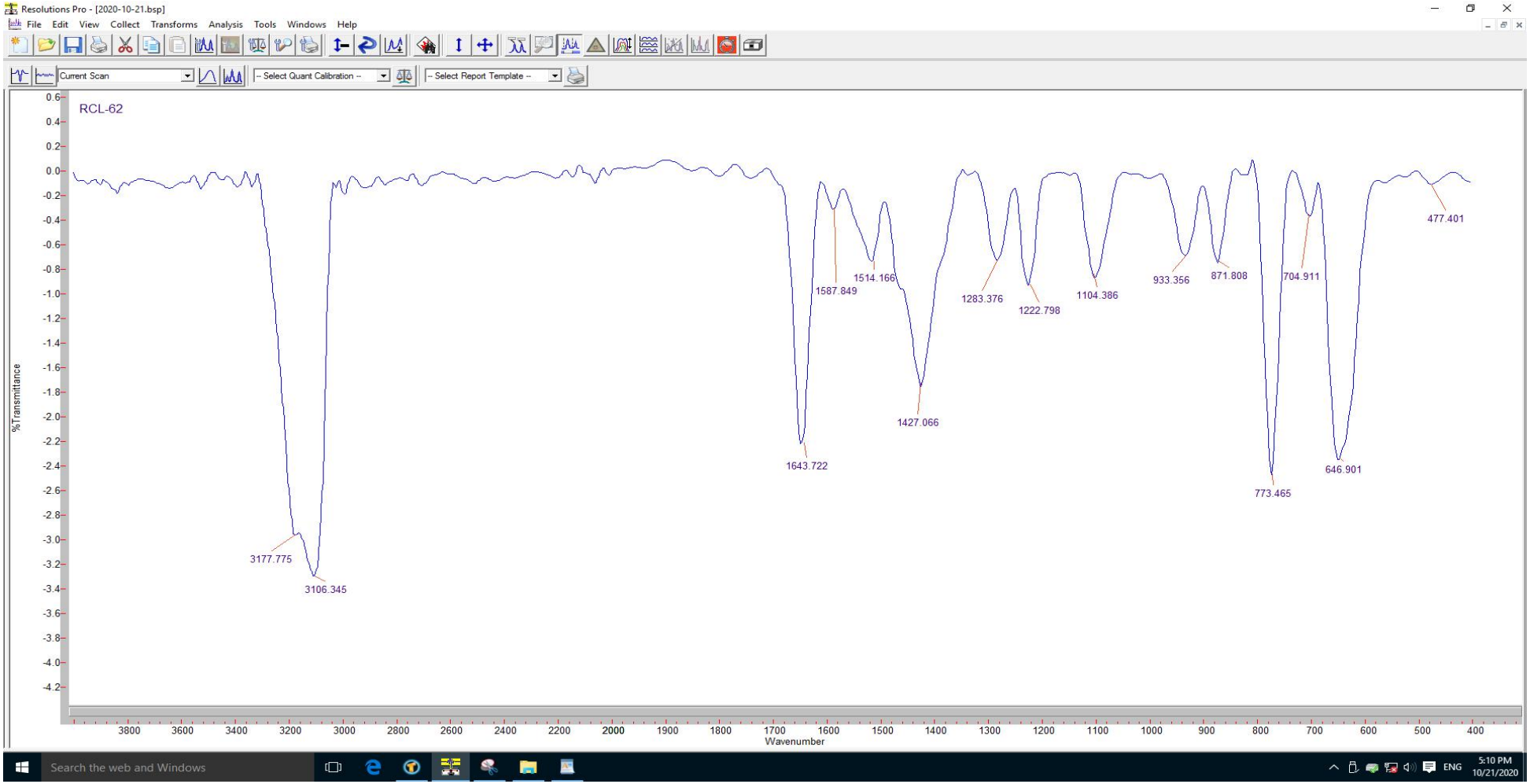

Figure S66. The IR spectrum of compound **5**.

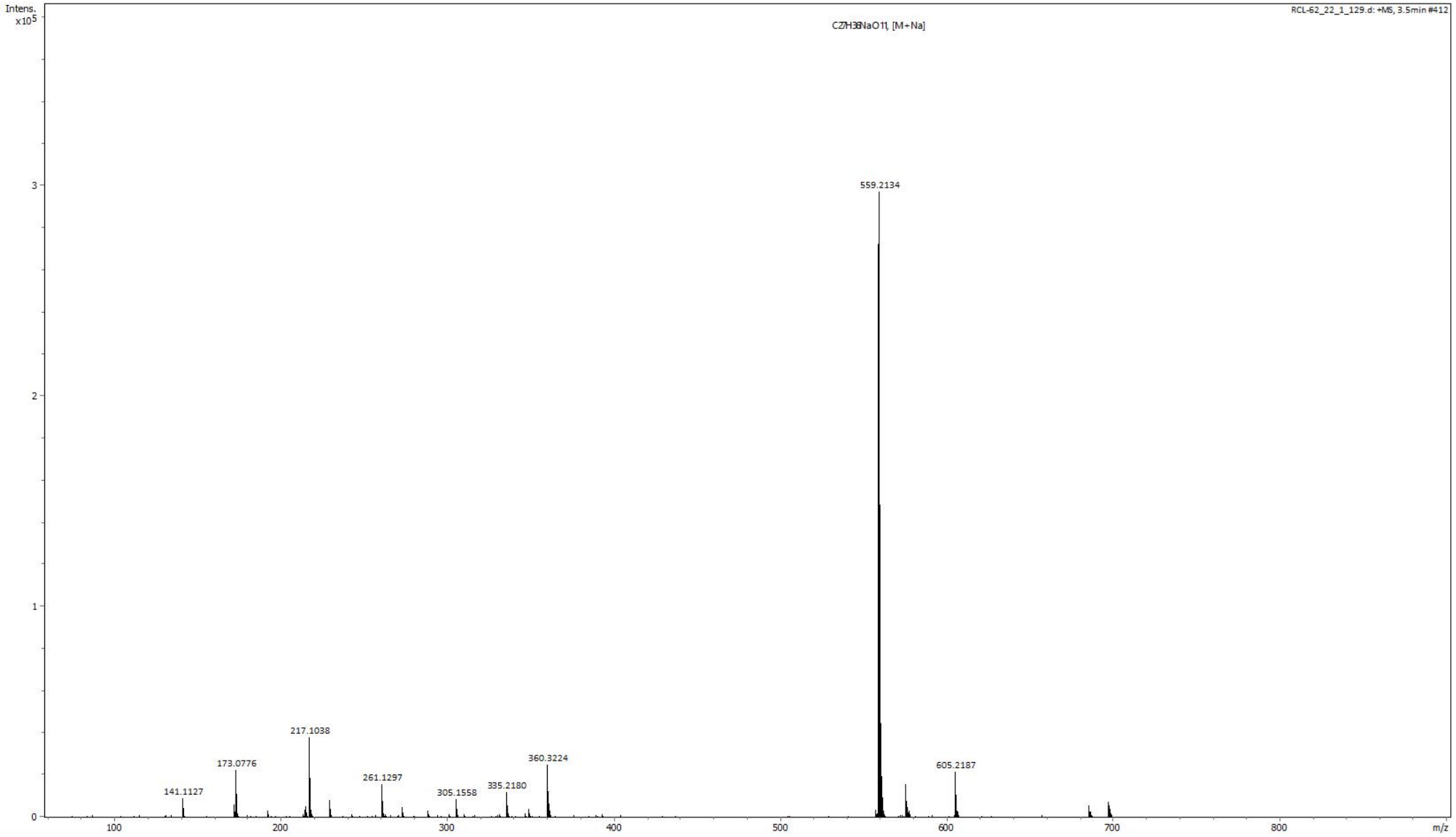

Figure S67. The (+)-HRESIMS spectroscopic data of compound **5**.

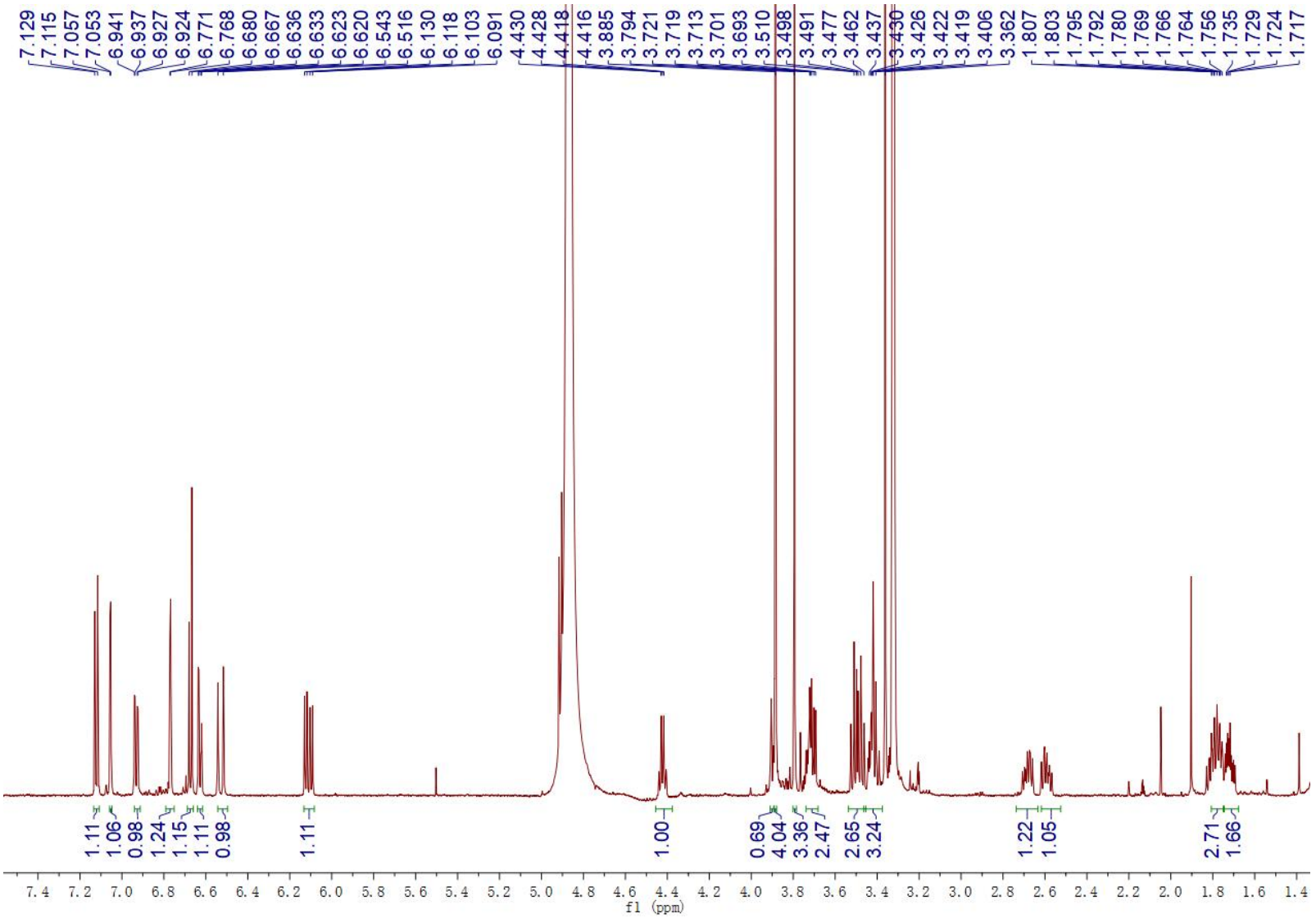

Figure S68. The ^{1}H NMR spectrum of compound **5** in CD_3OD.

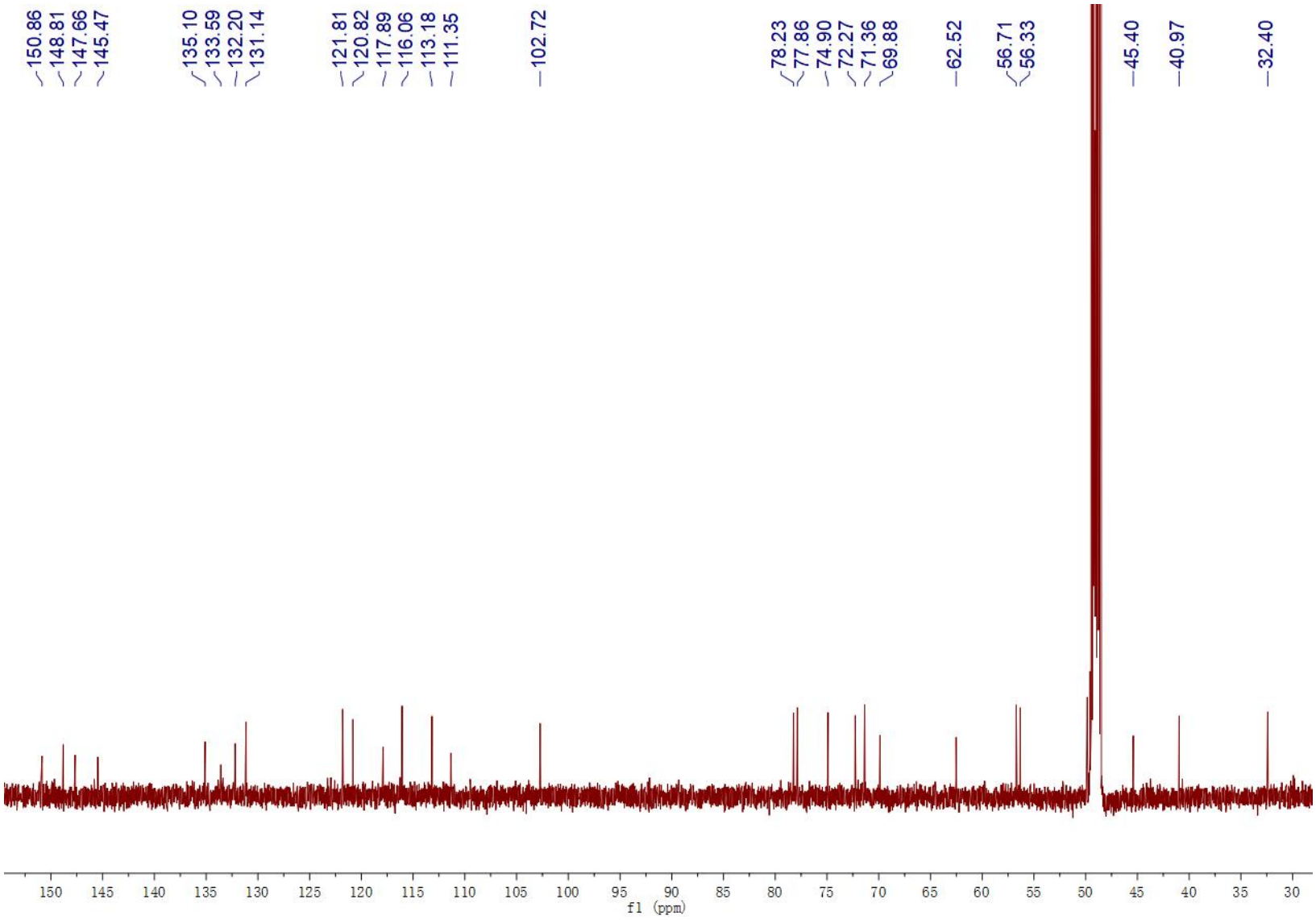

Figure S69. The ^{13}C NMR spectrum of compound **5** in CD_3OD.

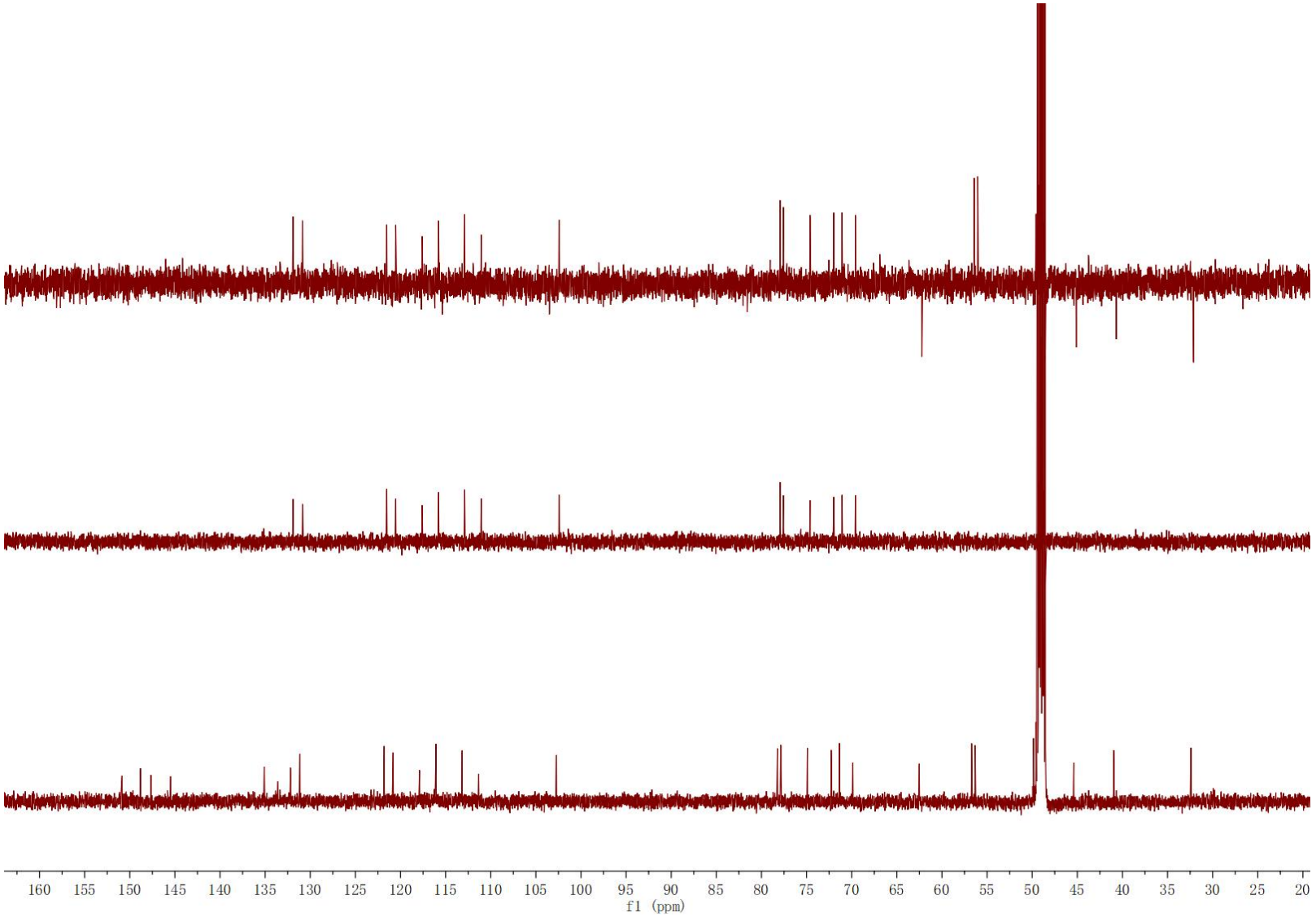

Figure S70. The DEPT spectrum of compound **5** in CD_3OD.

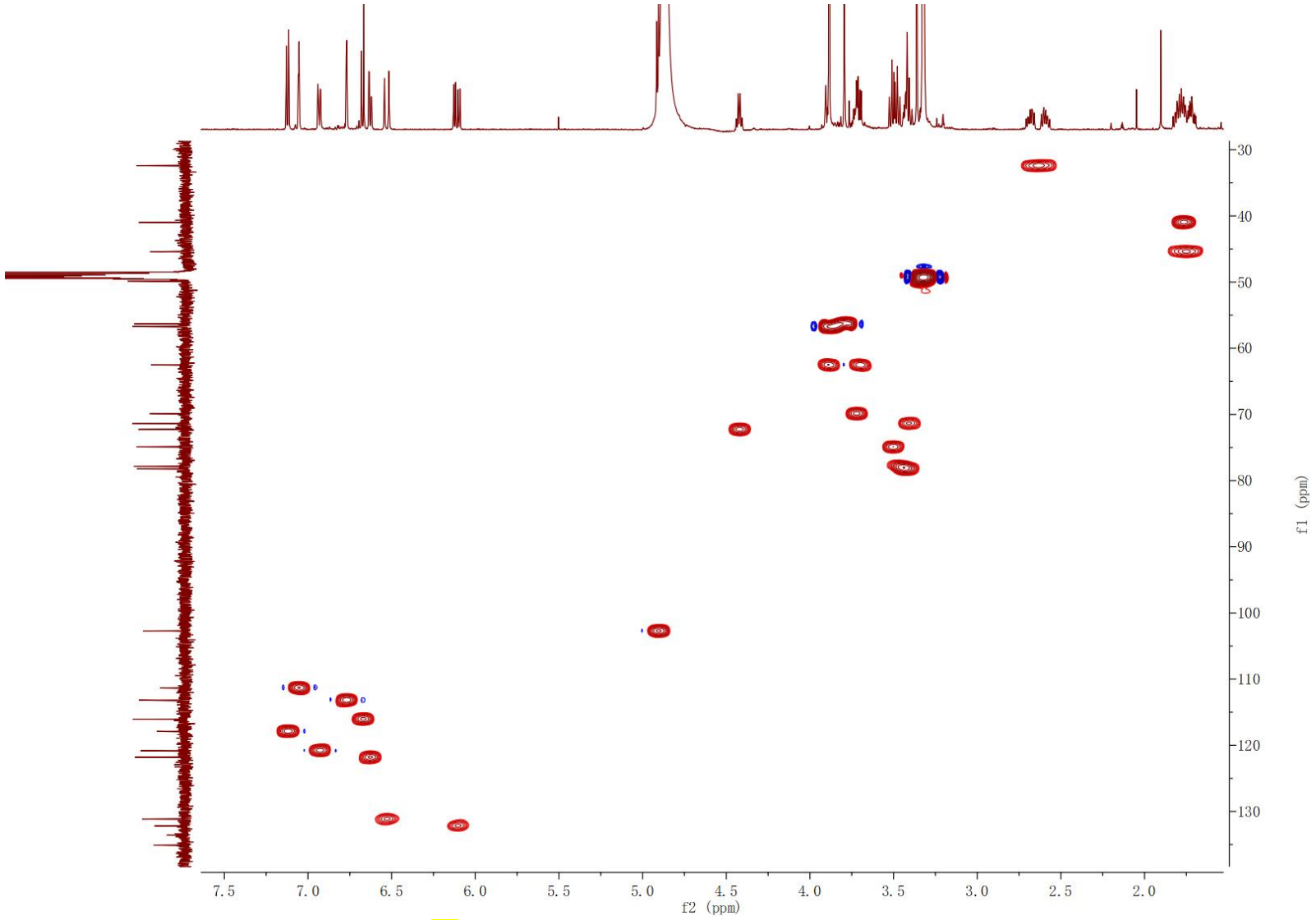

Figure S71. The HSQC spectrum of compound **5** in CD_3OD.

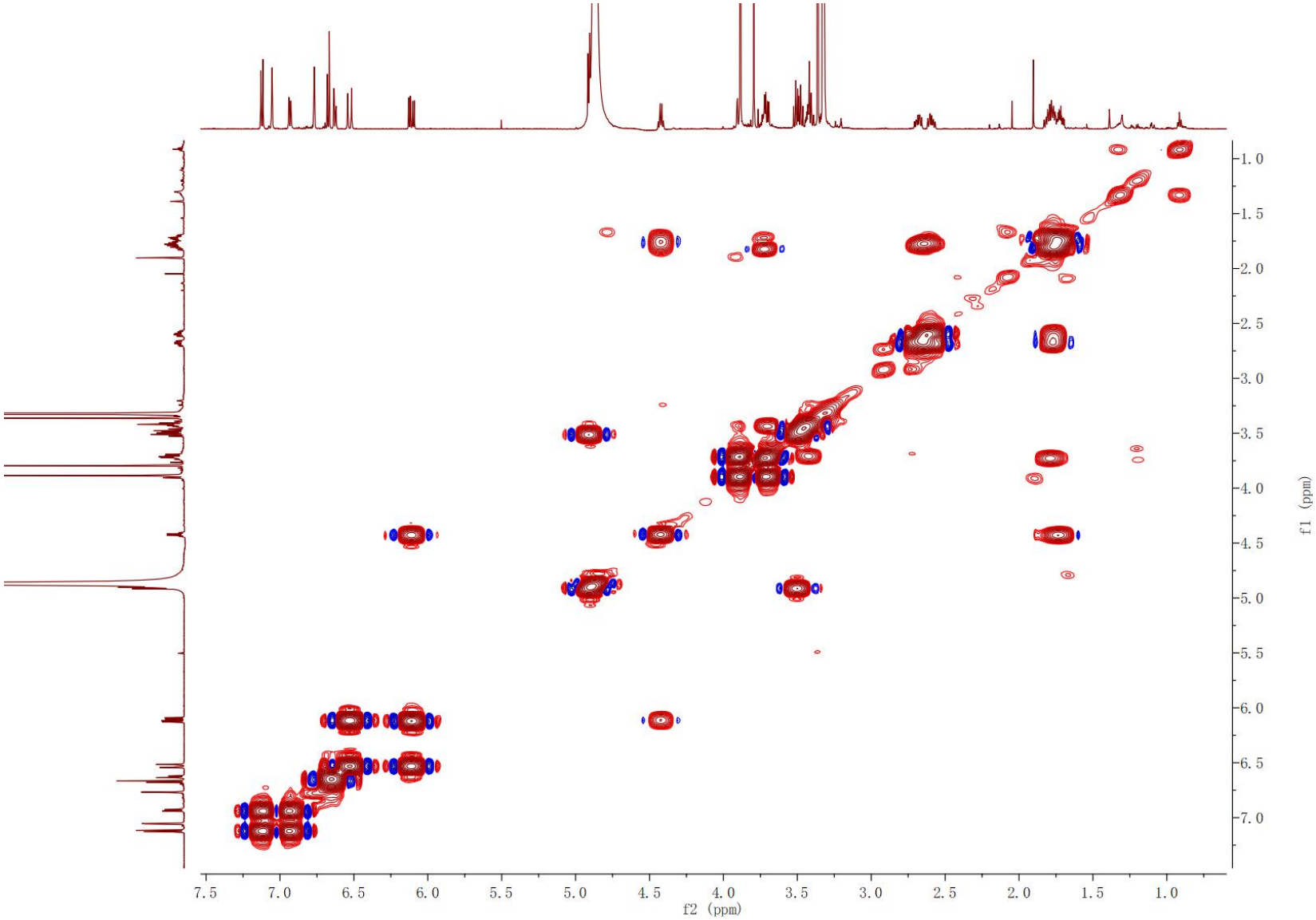

Figure S72. The ^{1}H-^{1}H COSY spectrum of compound **5** in CD_3OD.

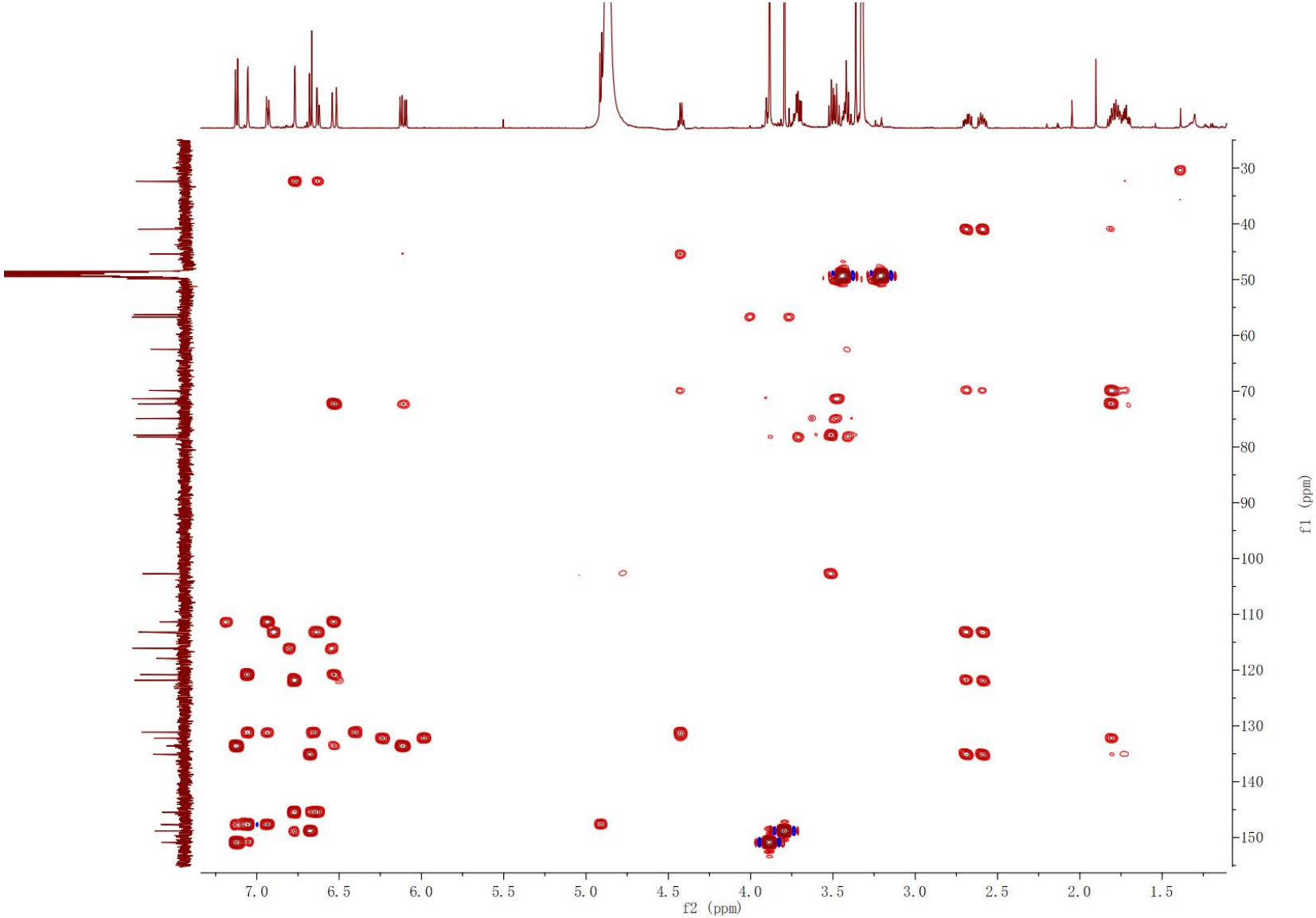

Figure S73. The HMBC spectrum of compound **5** in CD_3OD.

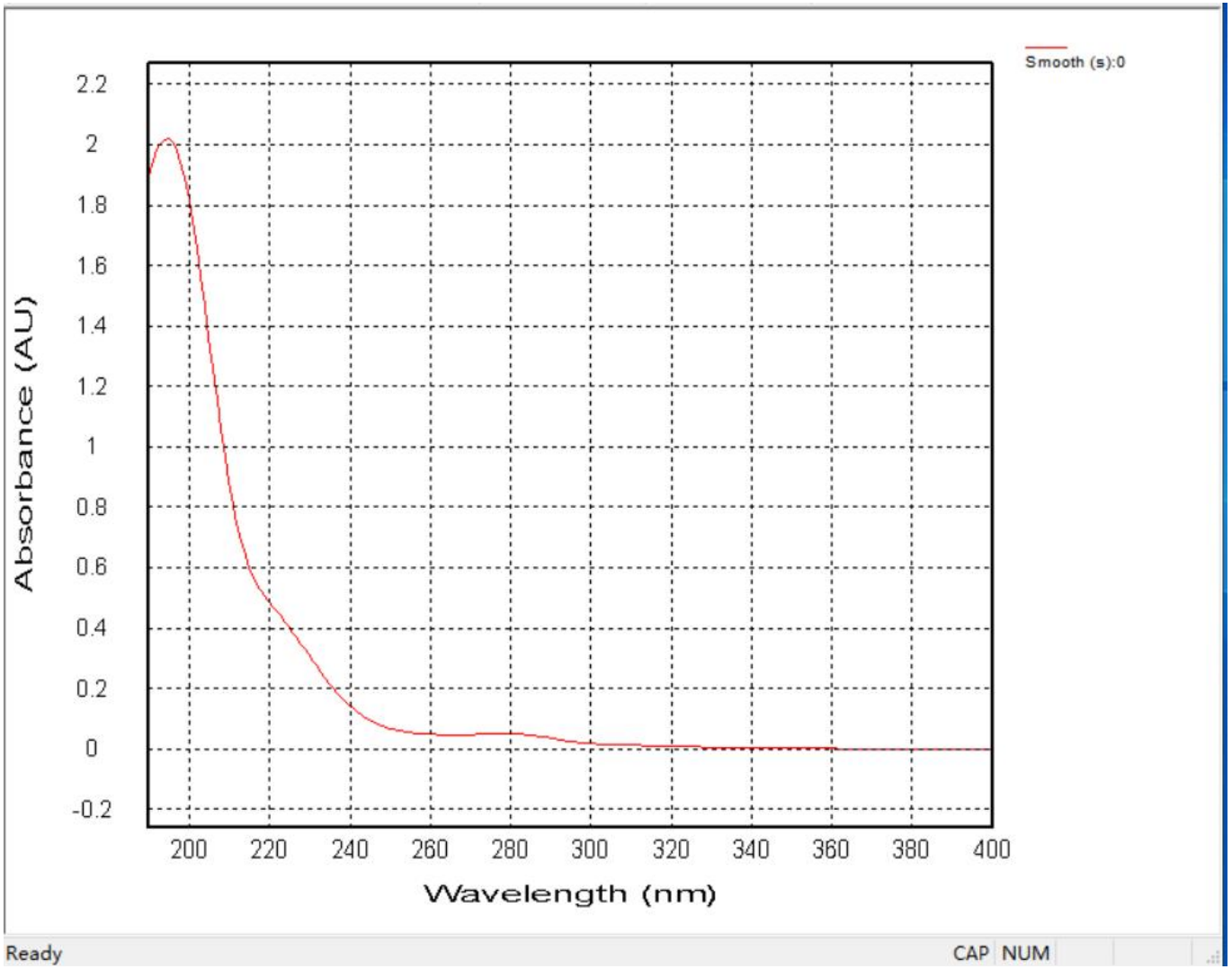

Figure S74. The UV spectrum of compound **5a**.

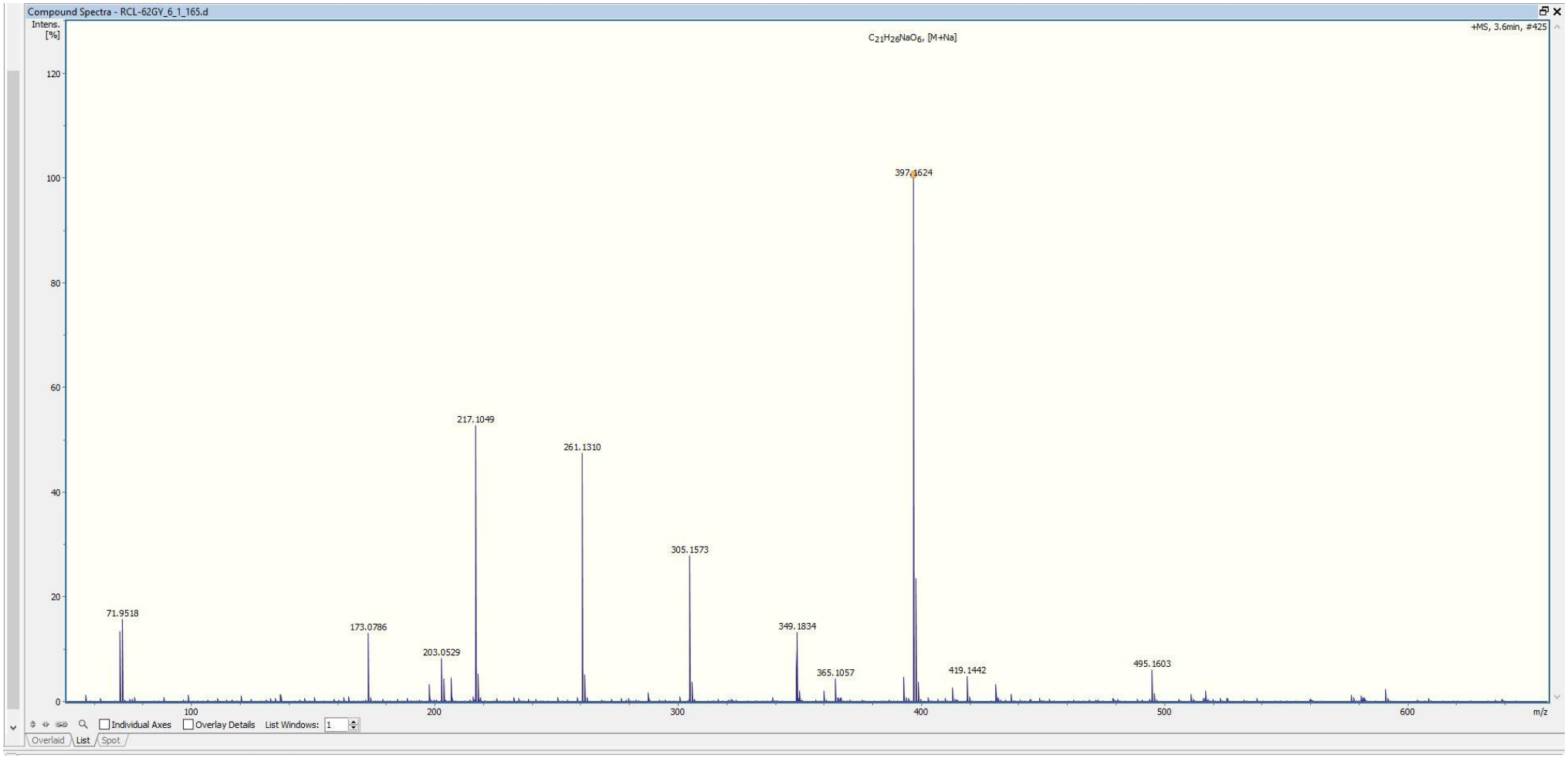

Figure S75. The (+)-HRESIMS spectroscopic data of compound **5a**.

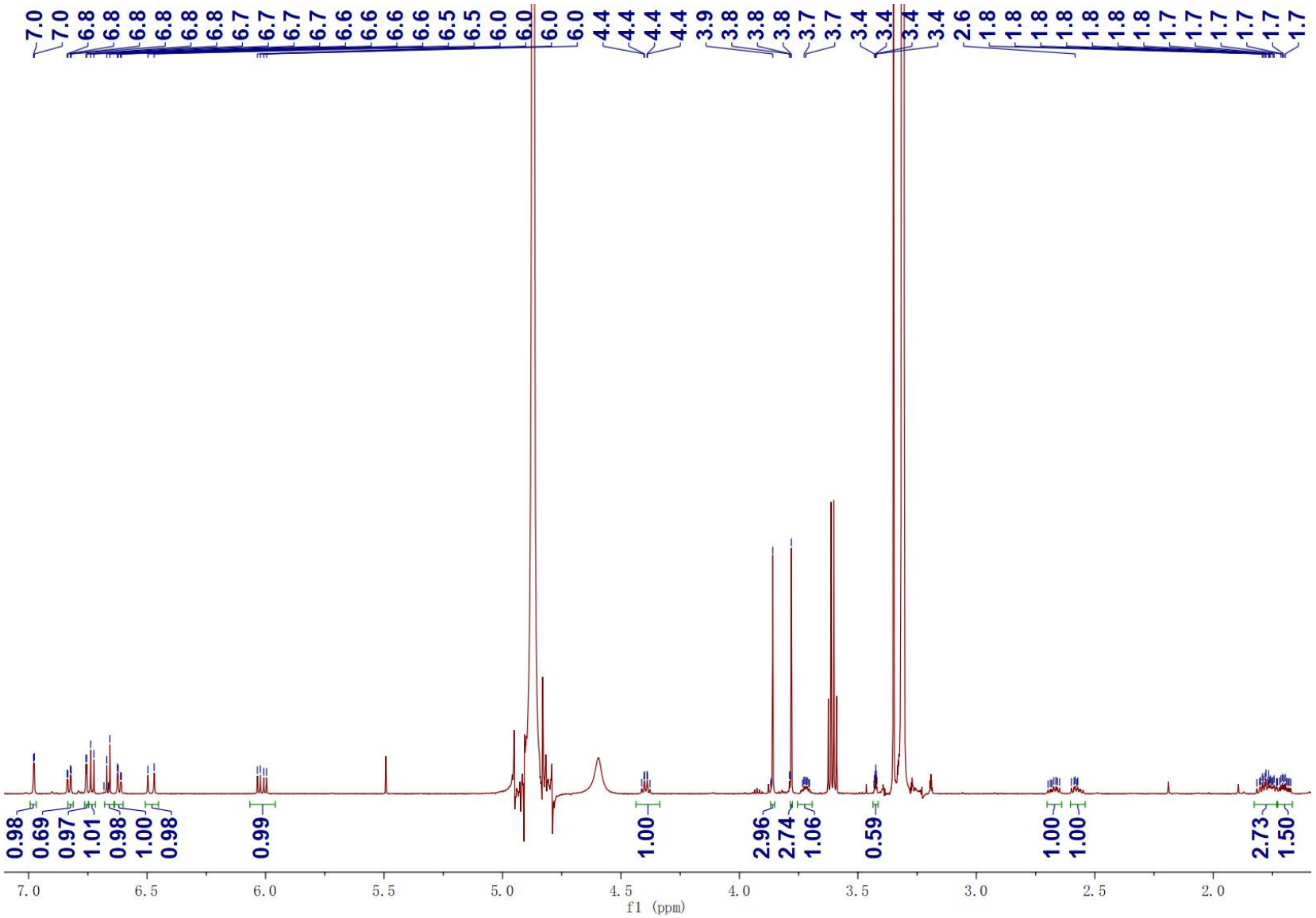

Figure S76. The ^{1}H NMR spectrum of compound **5a** in CD_3OD.

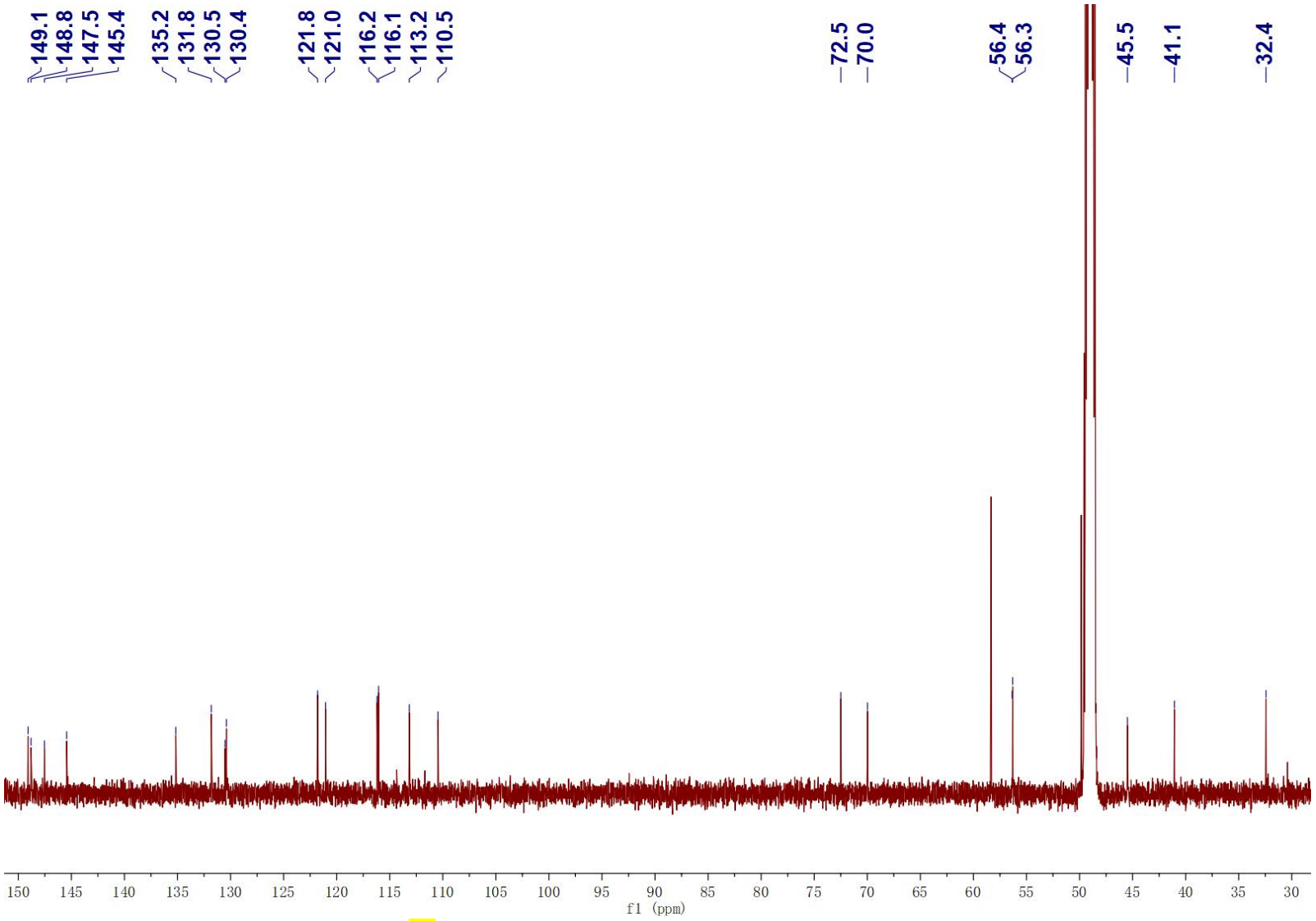

Figure S77. The ^{13}C NMR spectrum of compound **5a** in CD_3OD.

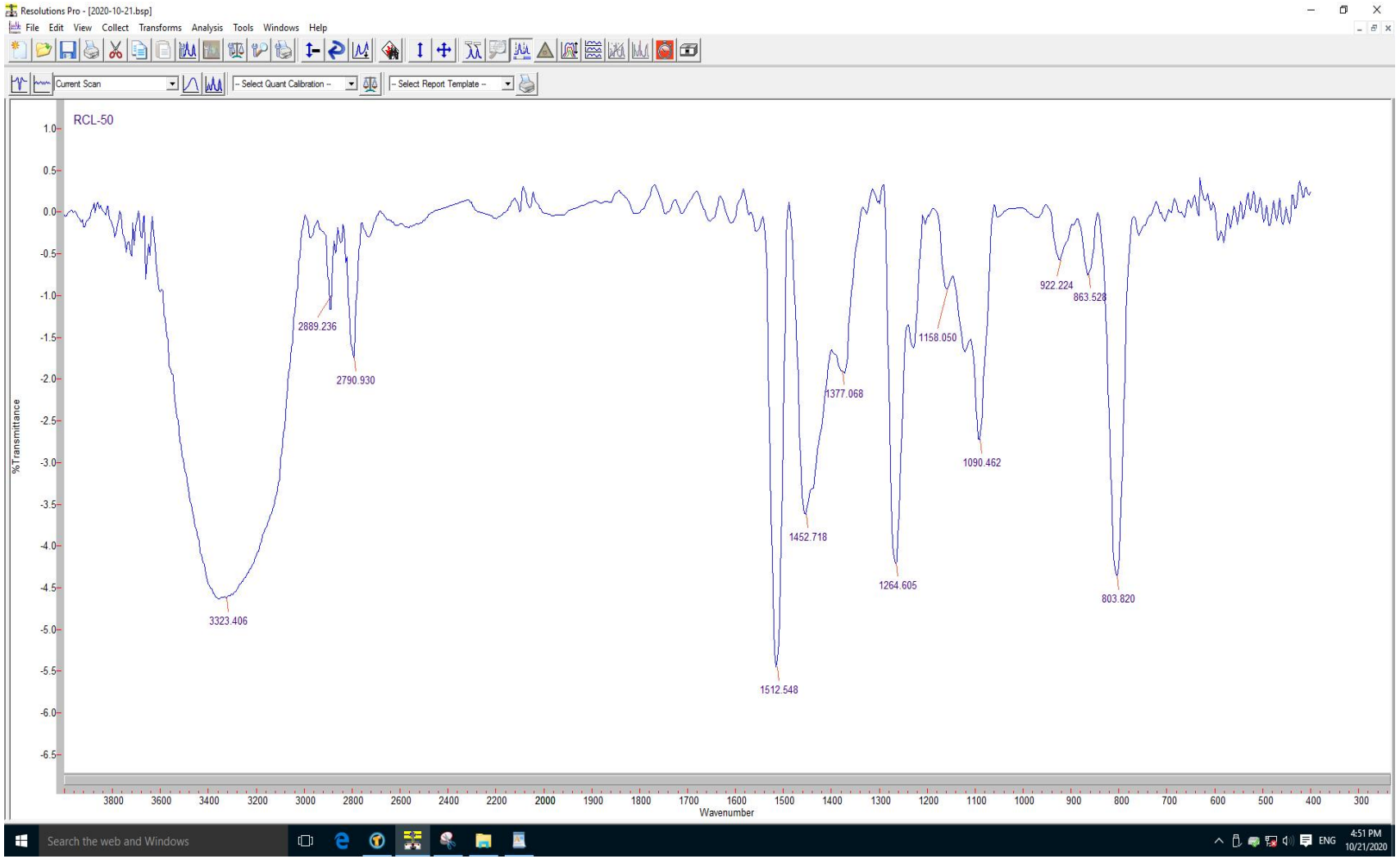

Figure S78. The IR spectrum of compound **6**.

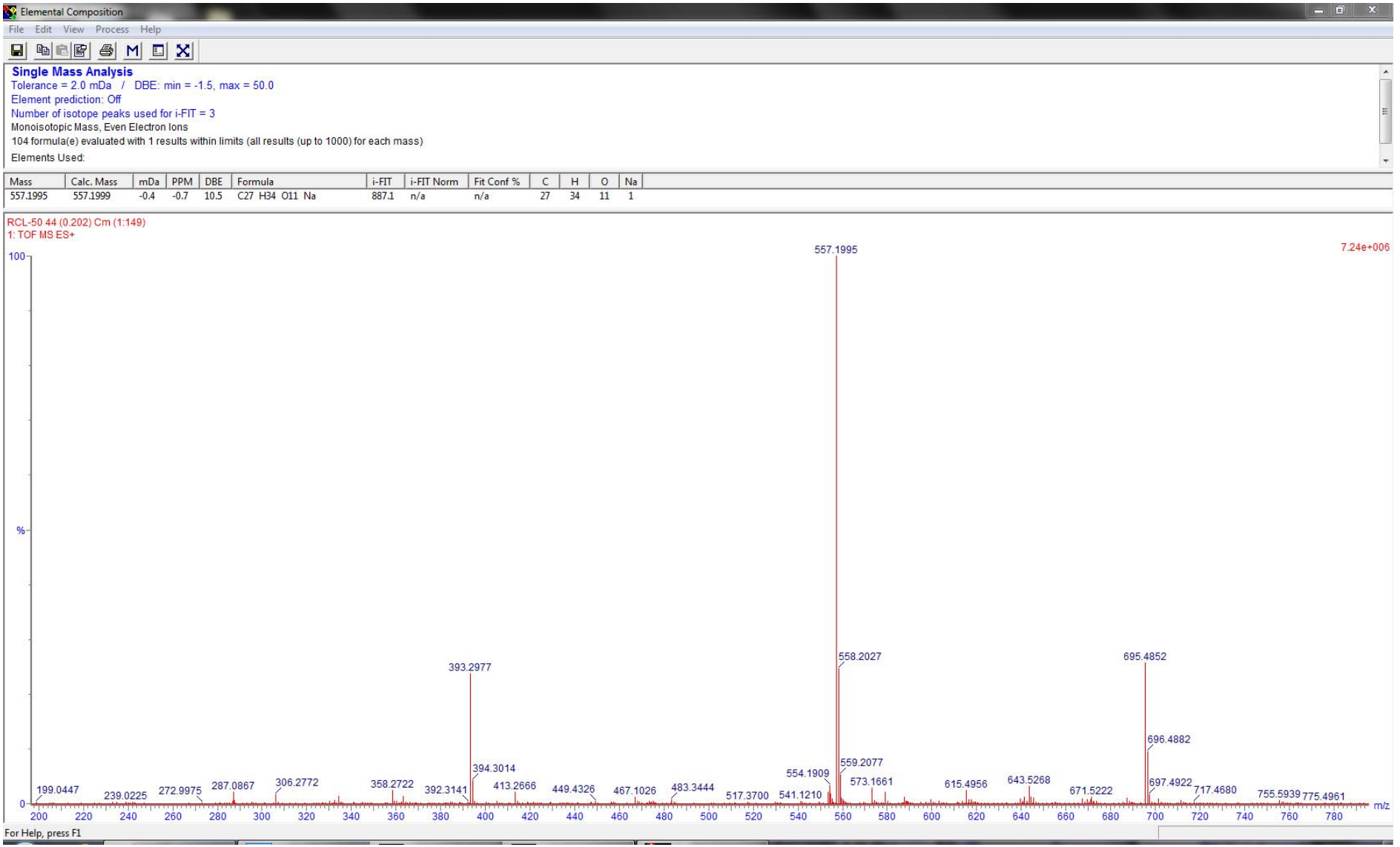

Figure S79. The (+)-HRESIMS spectroscopic data of compound **6**.

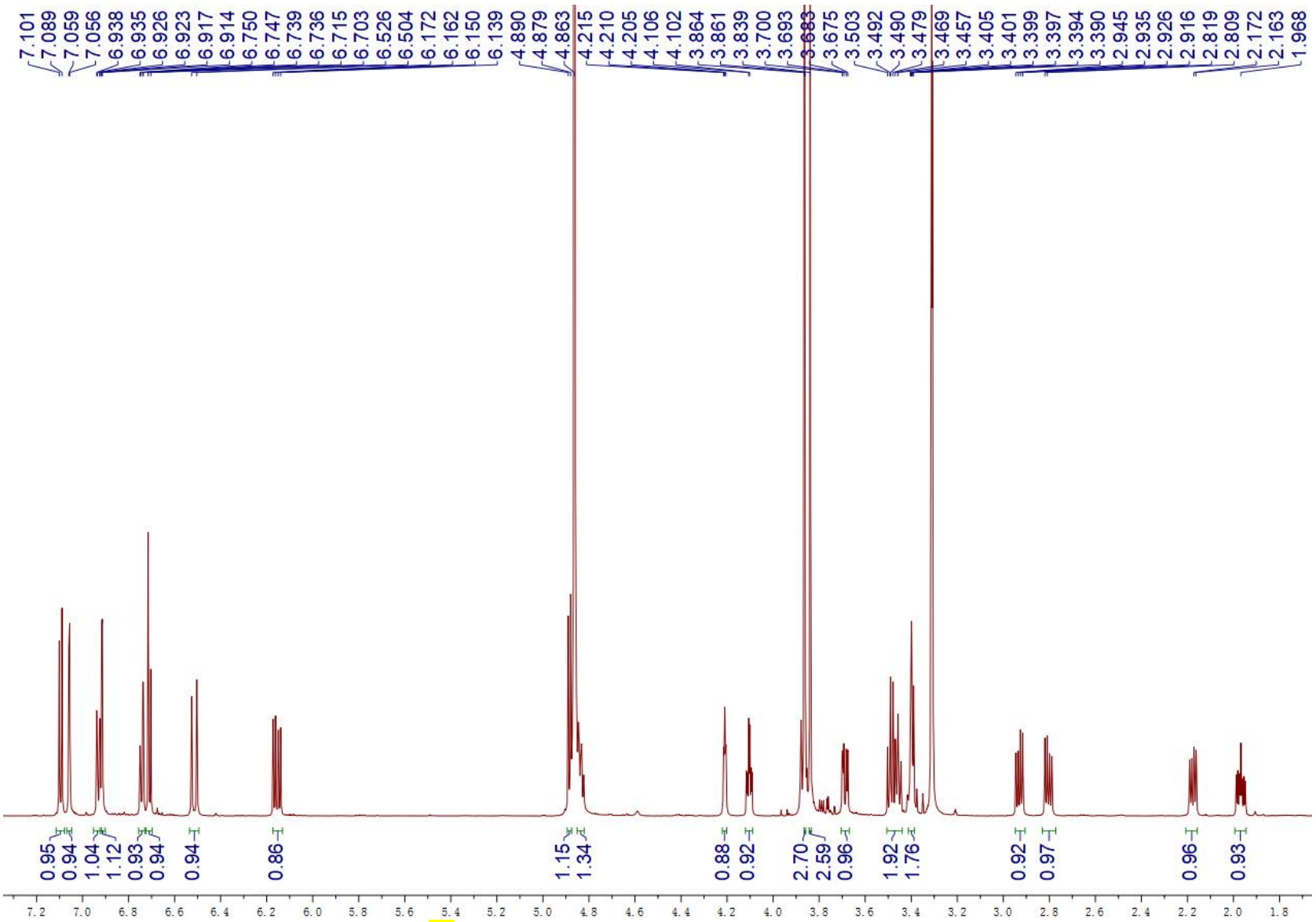

Figure S80. The ^{1}H NMR spectrum of compound **6** in CD_3OD.

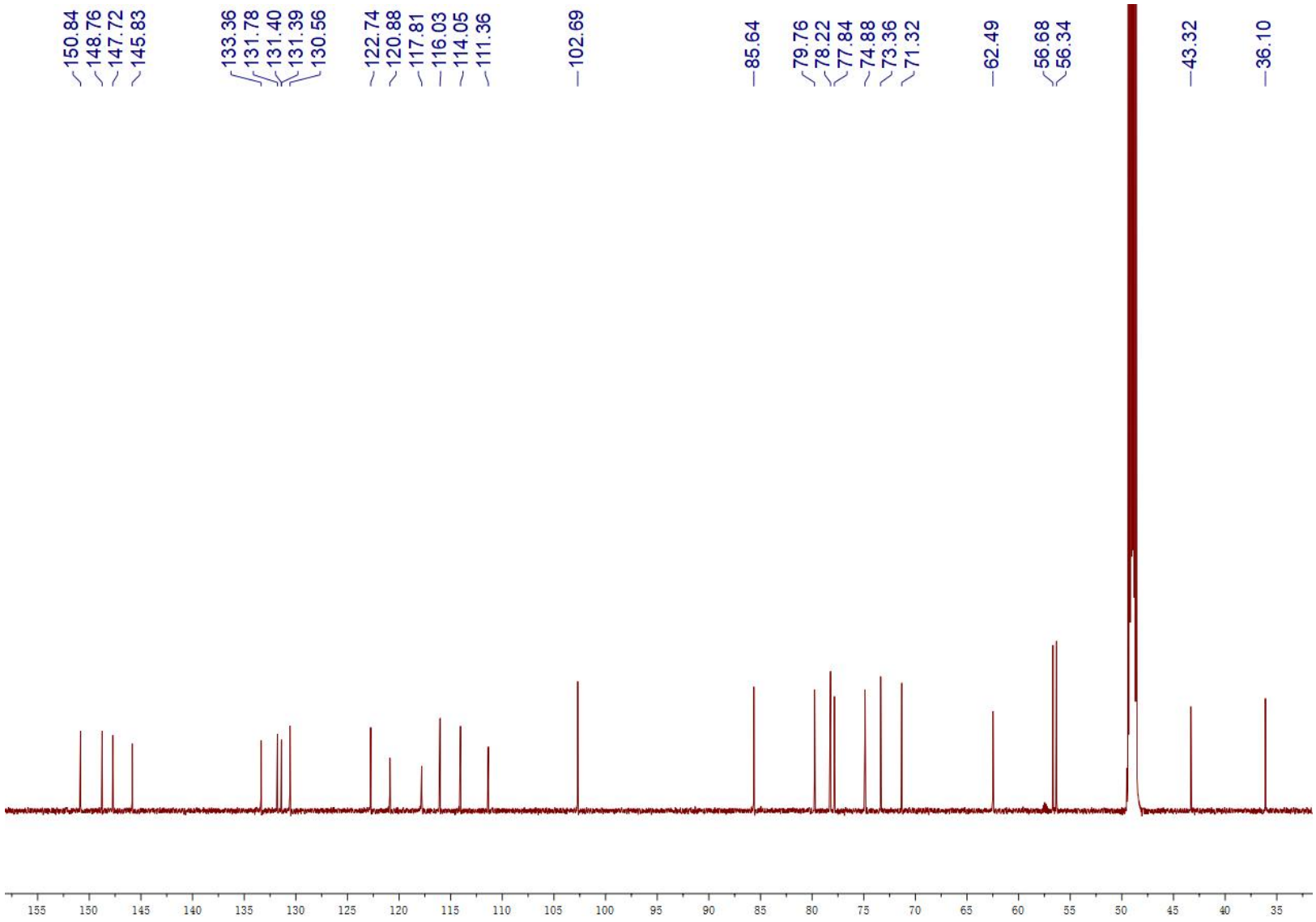

Figure S81. The ^{13}C NMR spectrum of compound **6** in CD_3OD.

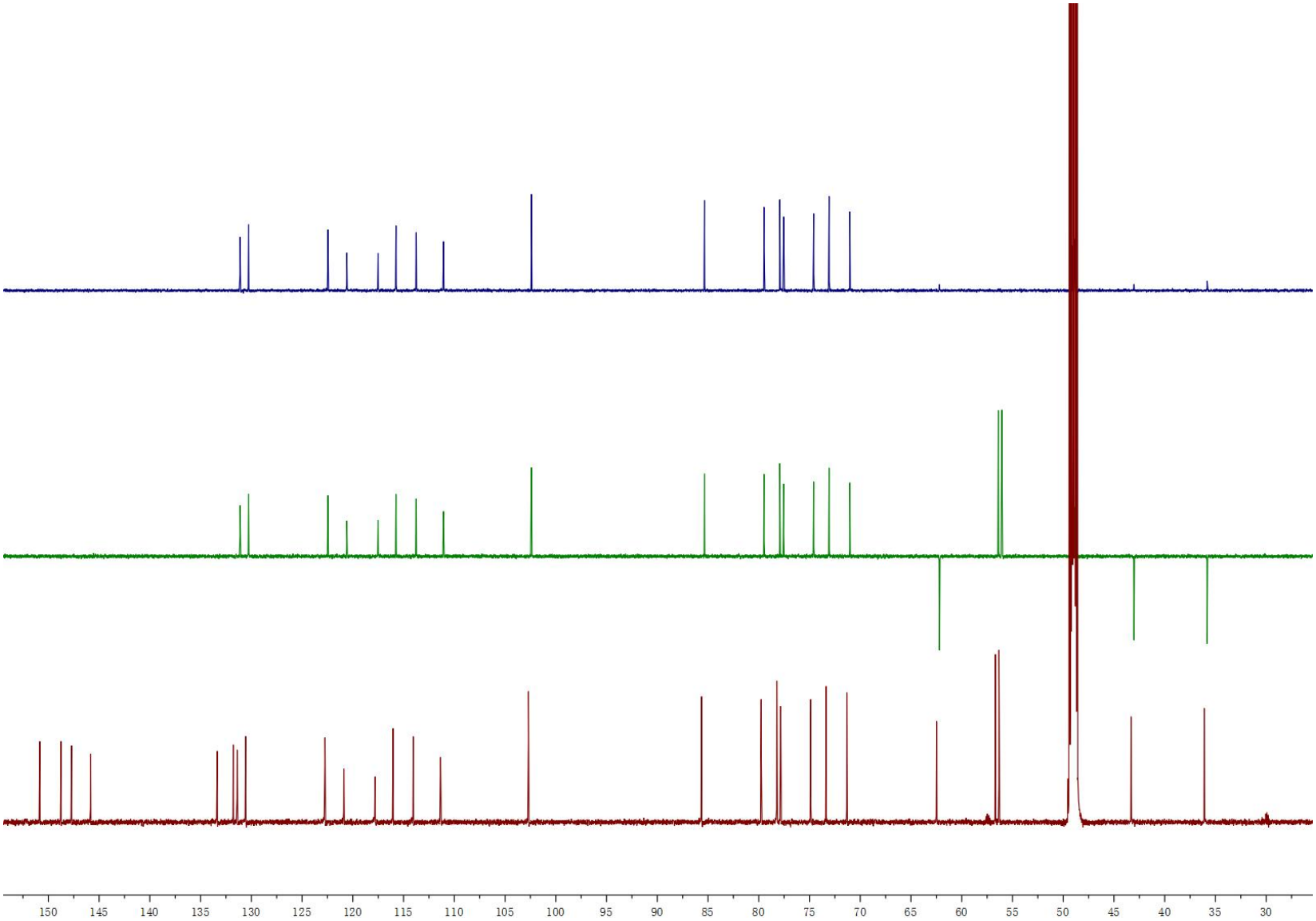

Figure S82. The DEPT spectrum of compound **6** in CD_3OD.

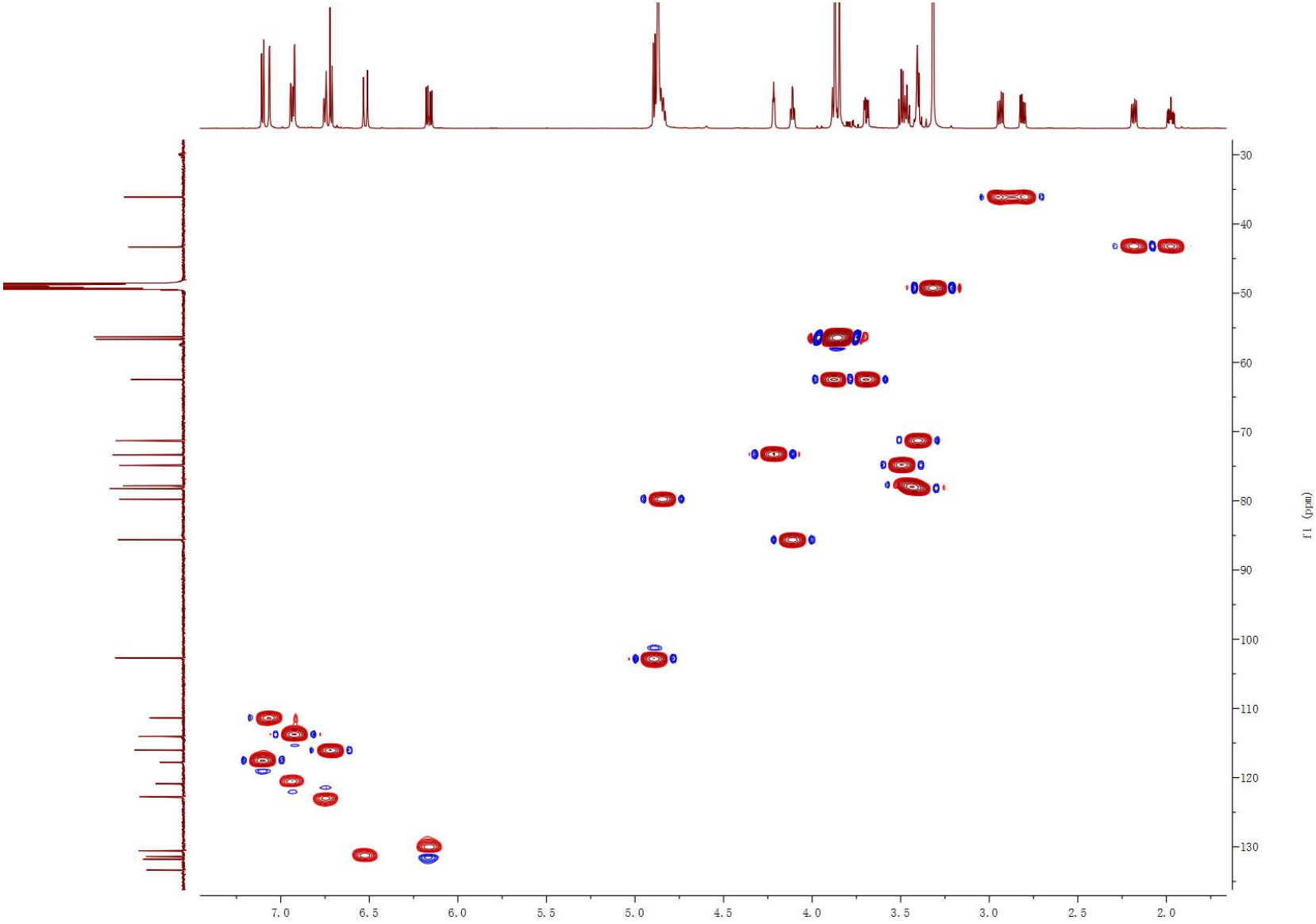

Figure S83. The HSQC spectrum of compound **6** in CD_3OD.

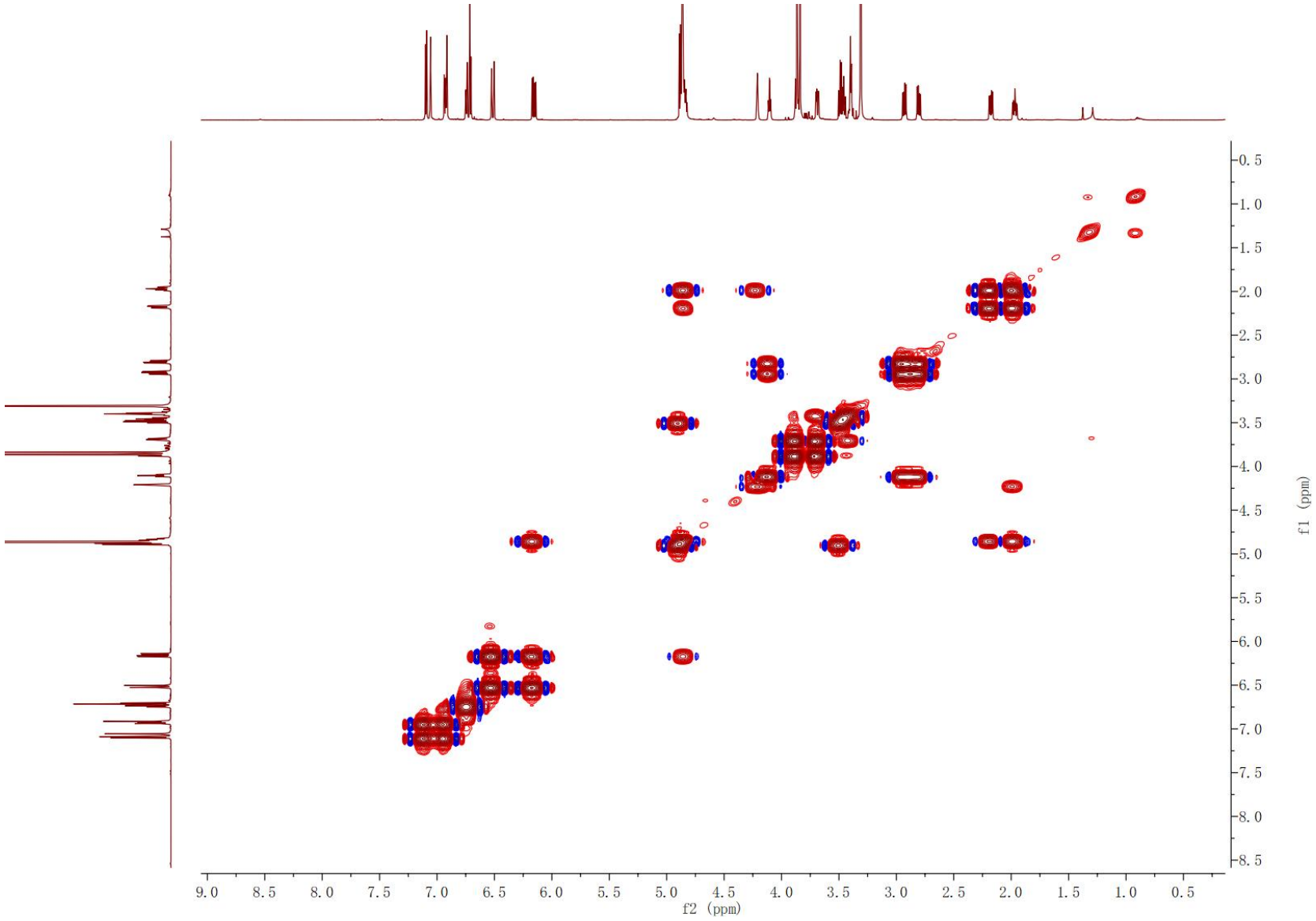

Figure S84. The ^{1}H-^{1}H COSY spectrum of compound **6** in CD_3OD.

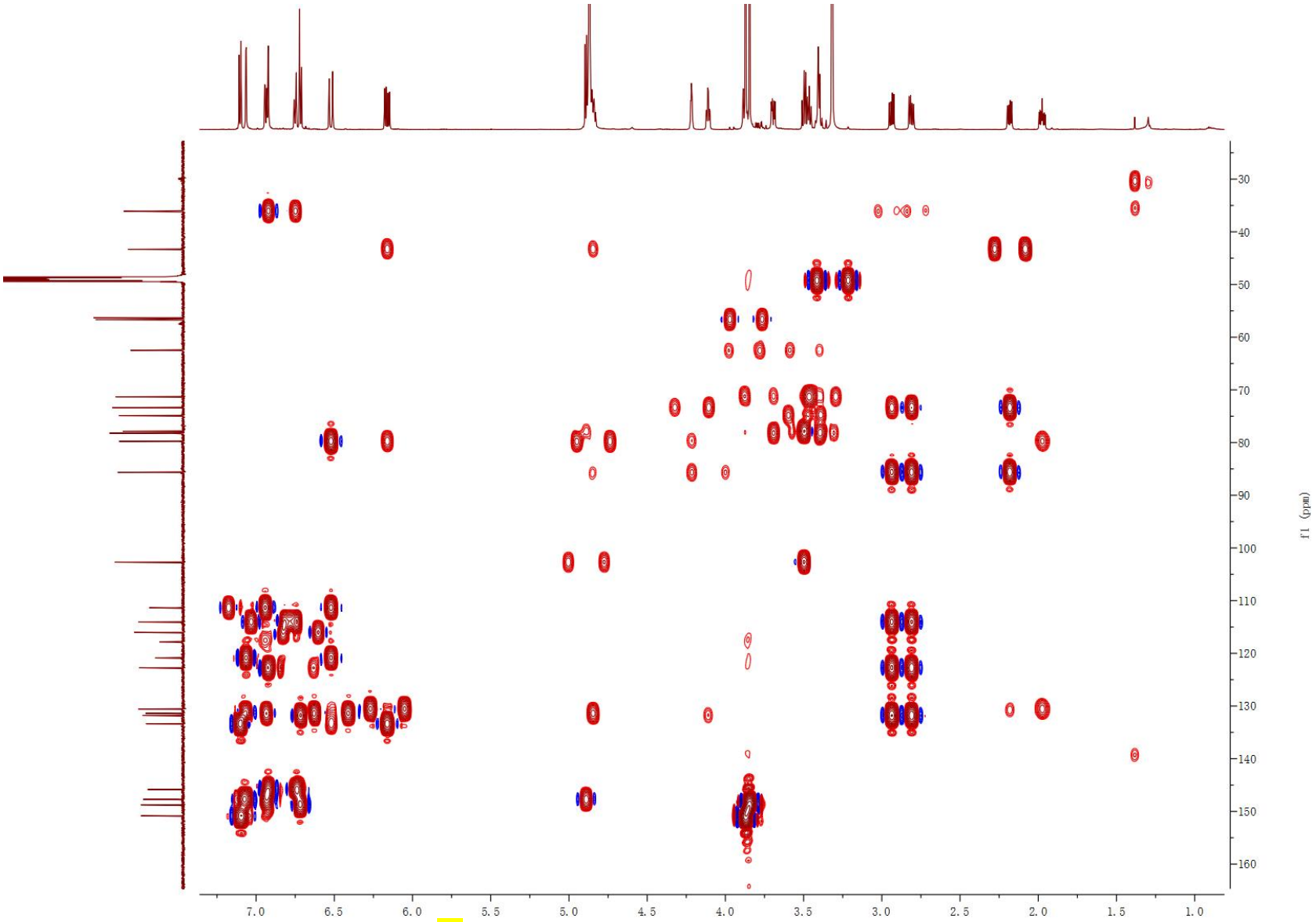

Figure S85. The HMBC spectrum of compound **6** in CD_3OD.

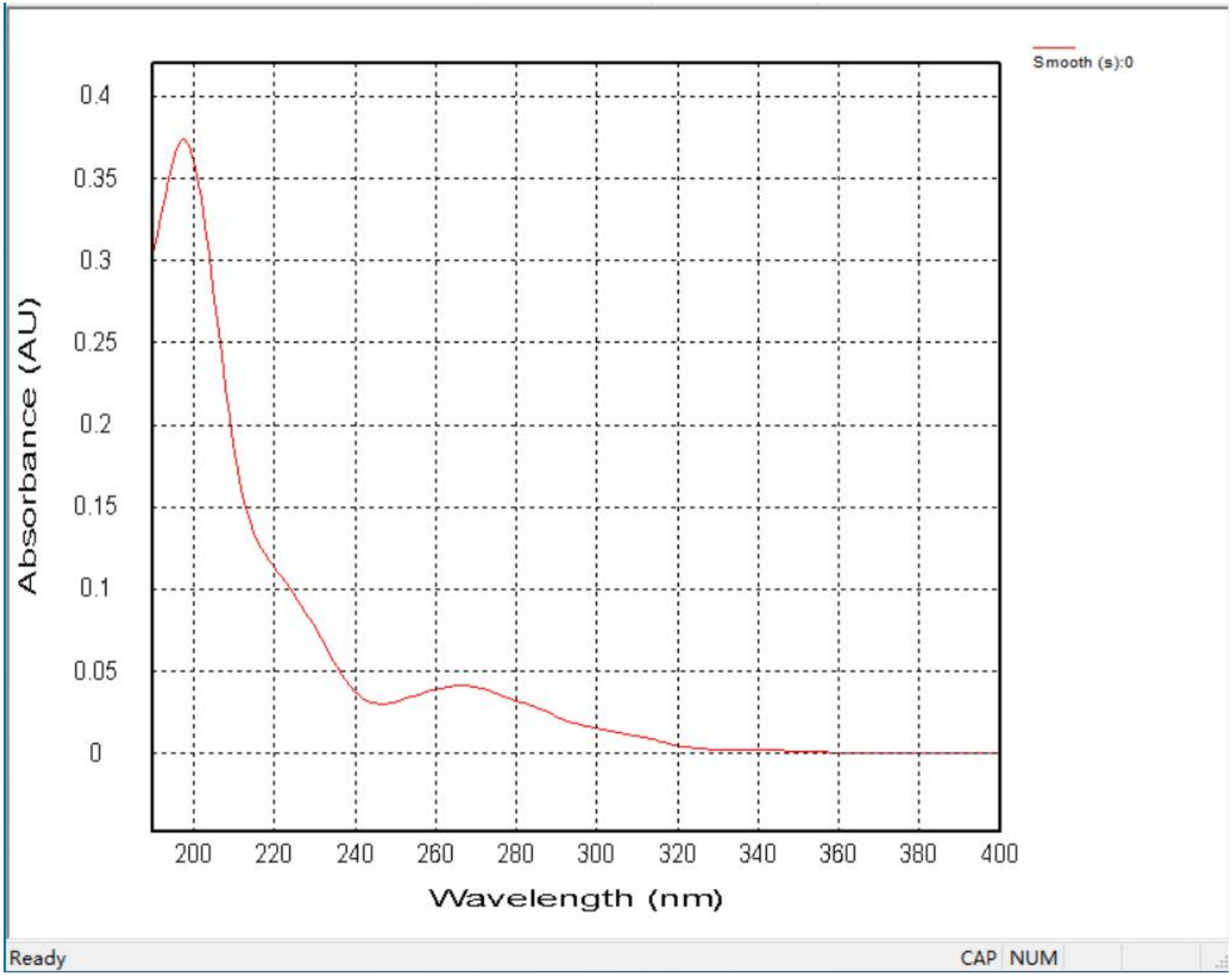

Figure S86. The UV spectrum of compound **6a**.

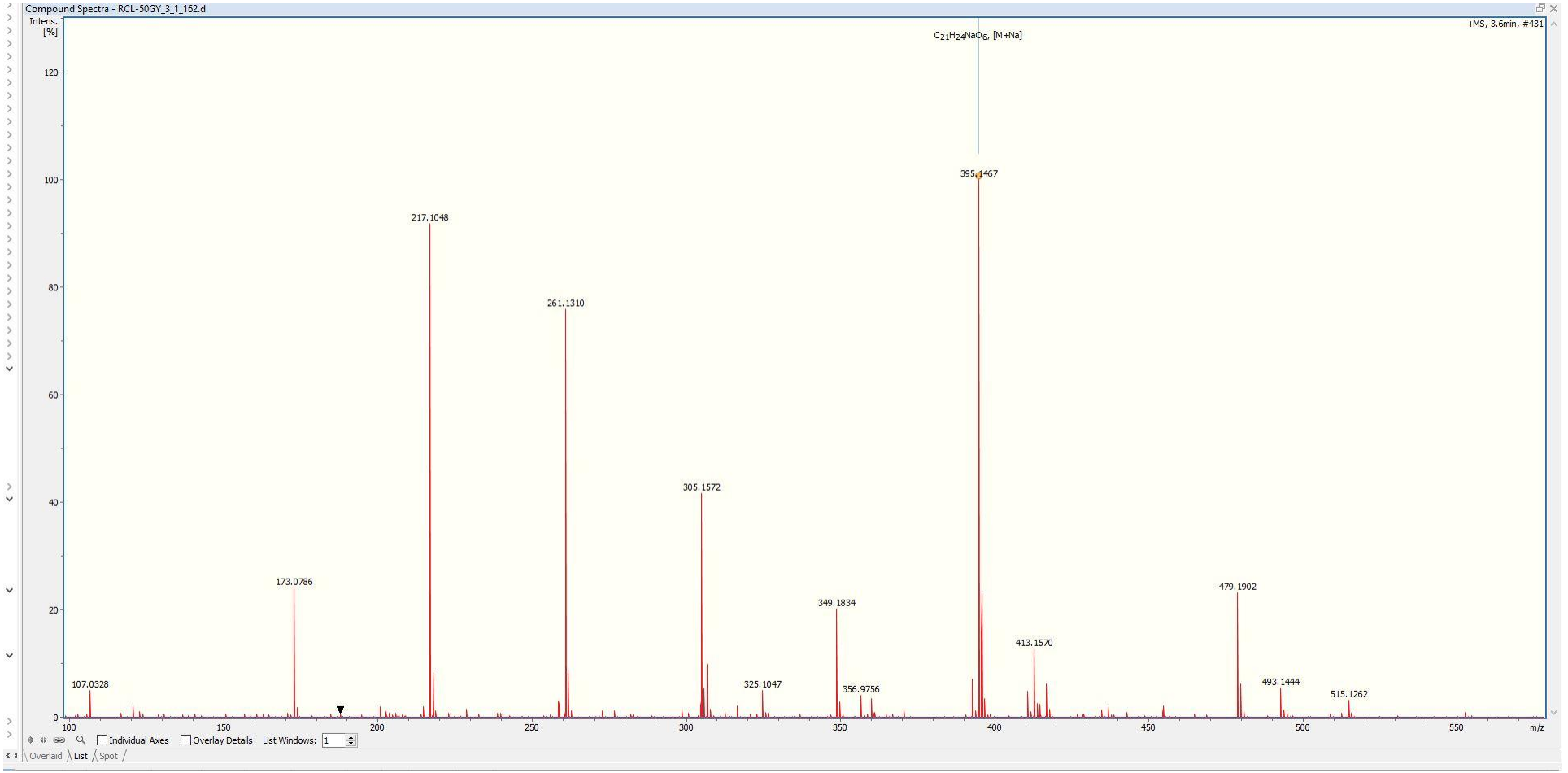

Figure S87. The (+)-HRESIMS spectroscopic data of compound **6a**.

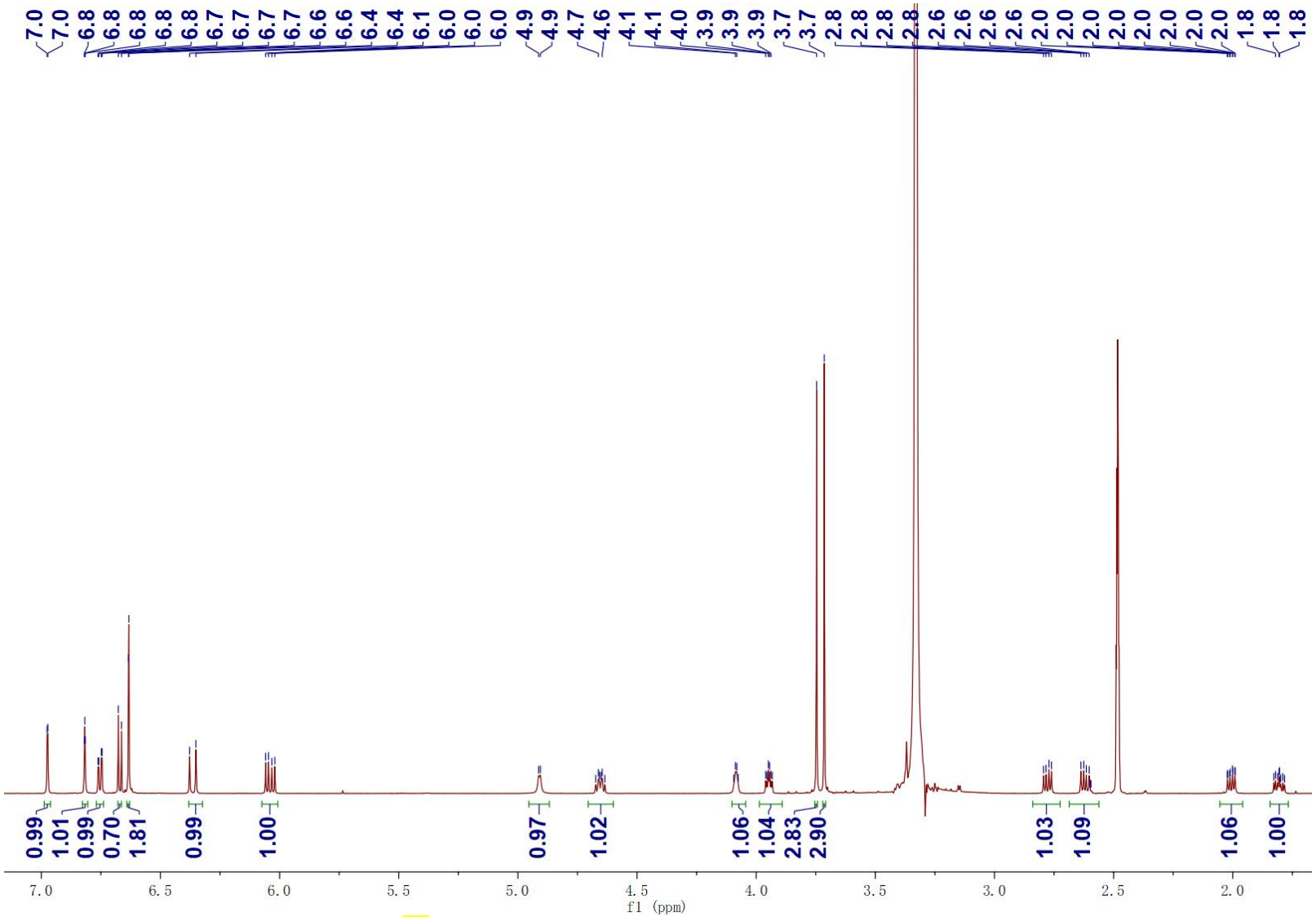

Figure S88. The ^{1}H NMR spectrum of compound **6a** in DMSO-d_6.

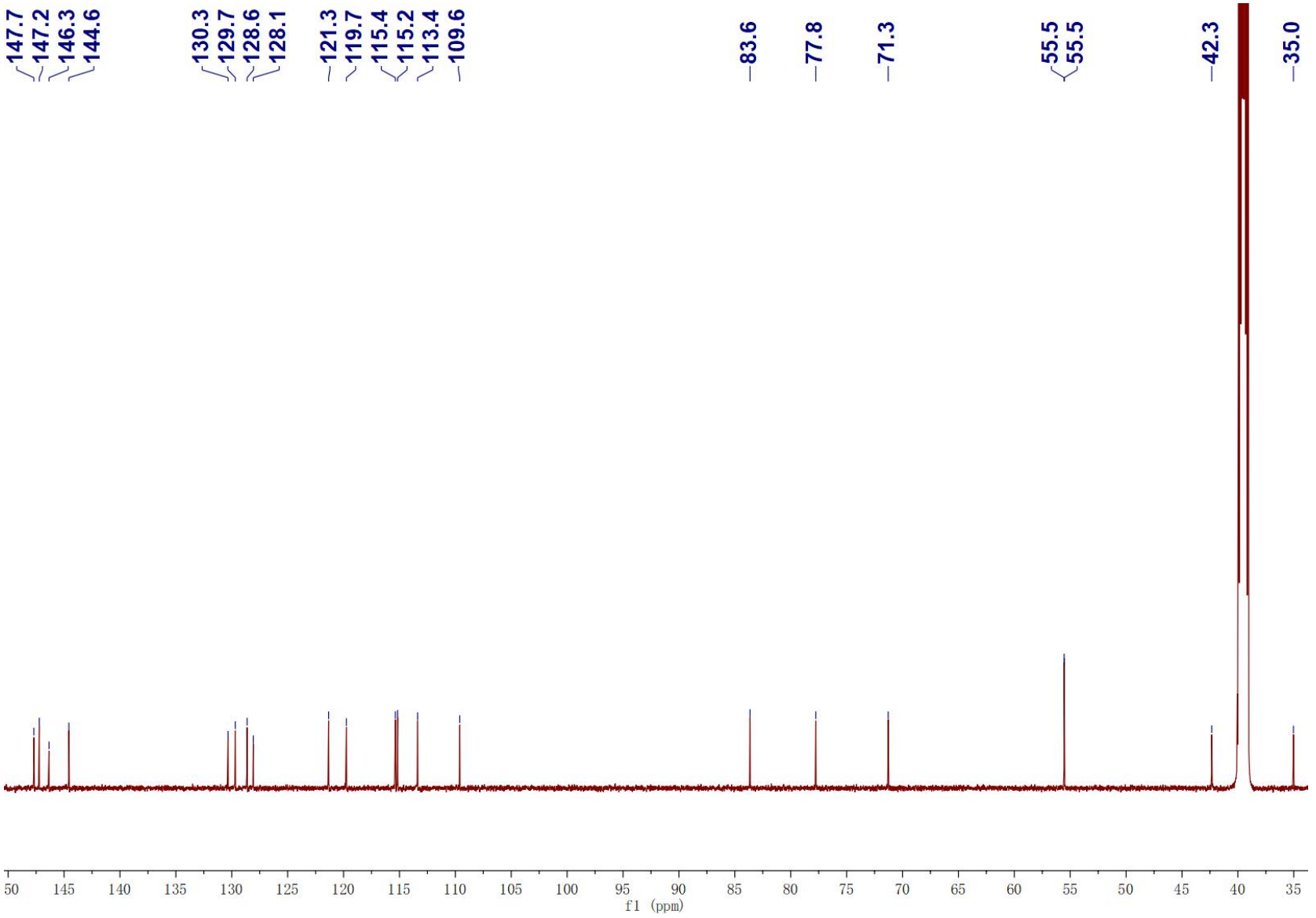

Figure S89. The ^{13}C NMR spectrum of compound **6a** in DMSO-d_6.

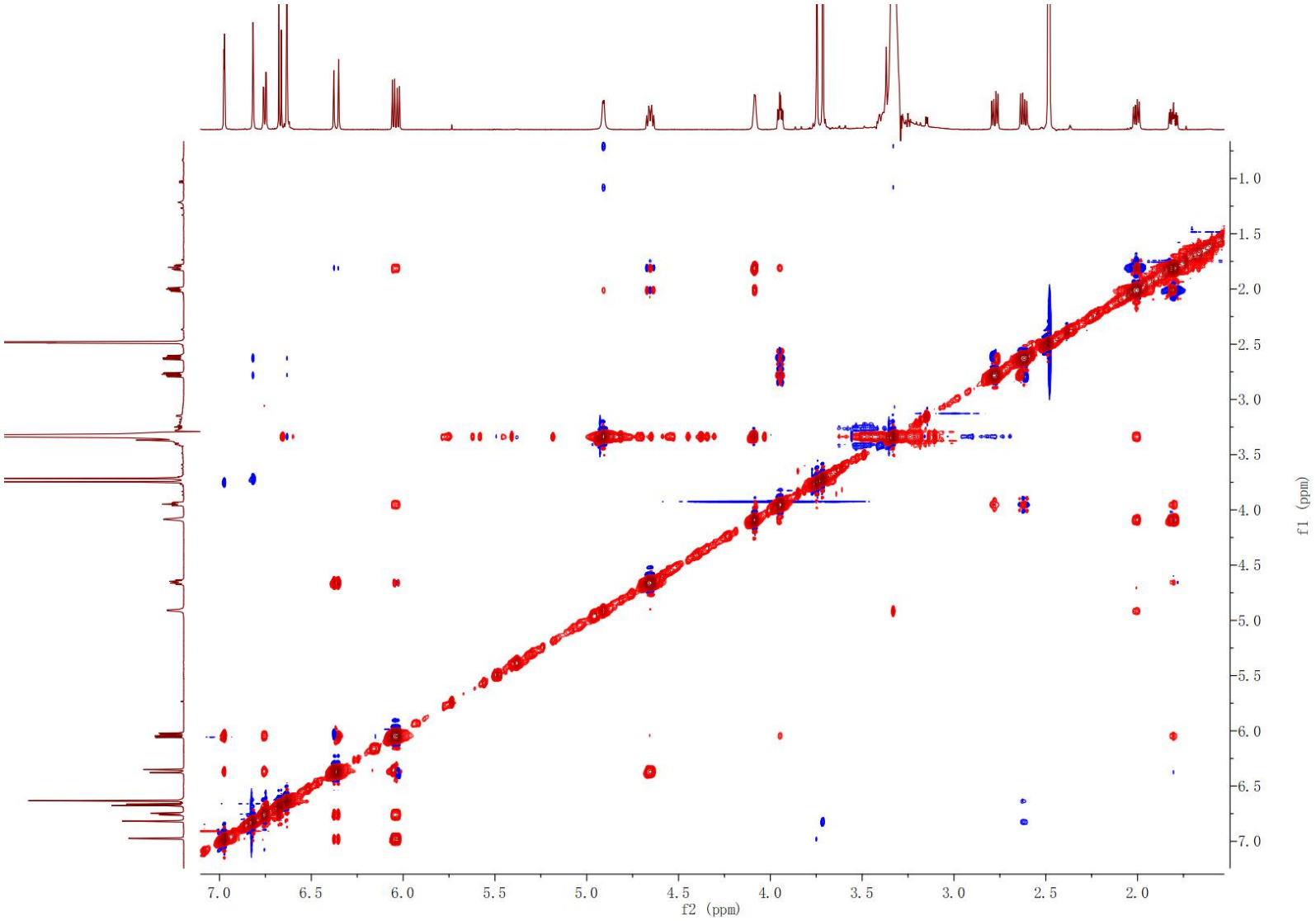

Figure S90. The NOESY spectrum of compound **6a** in DMSO-d_6.

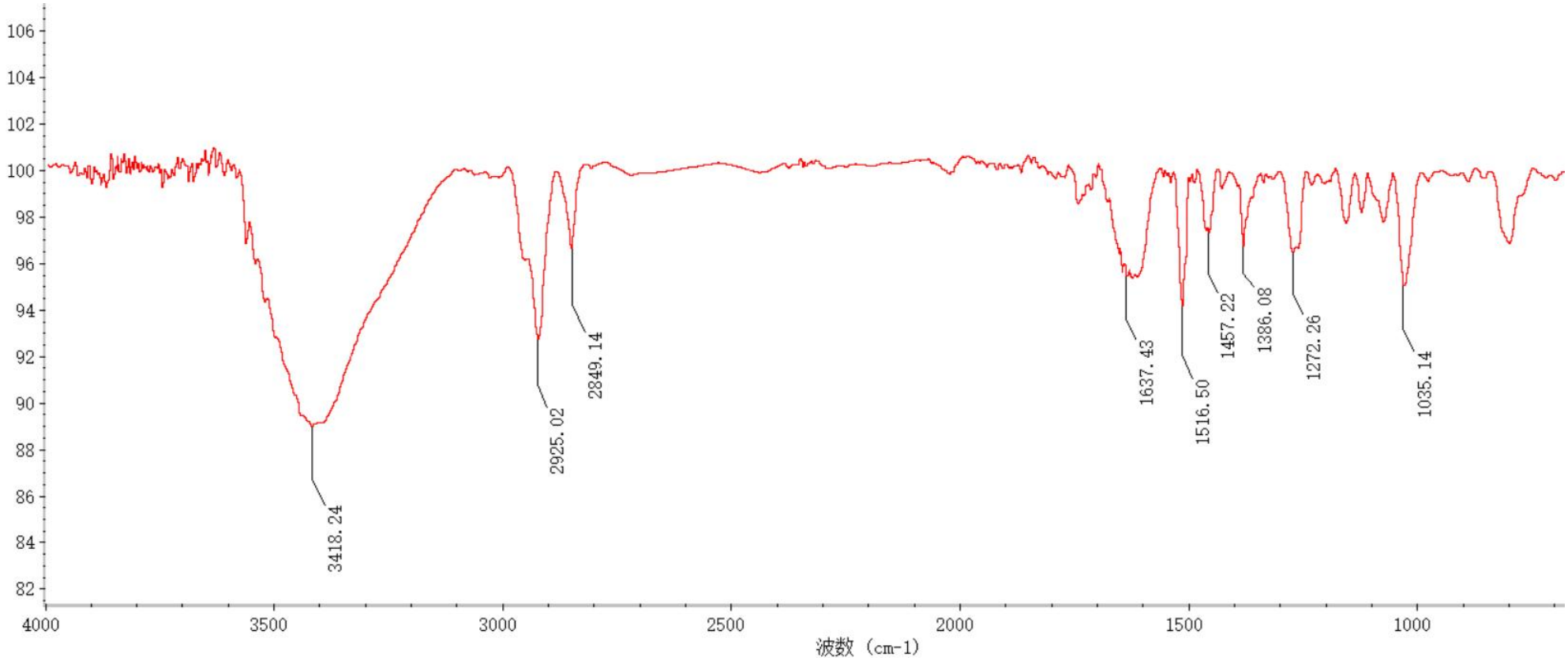

Figure S91. The IR spectrum of compound **7**.

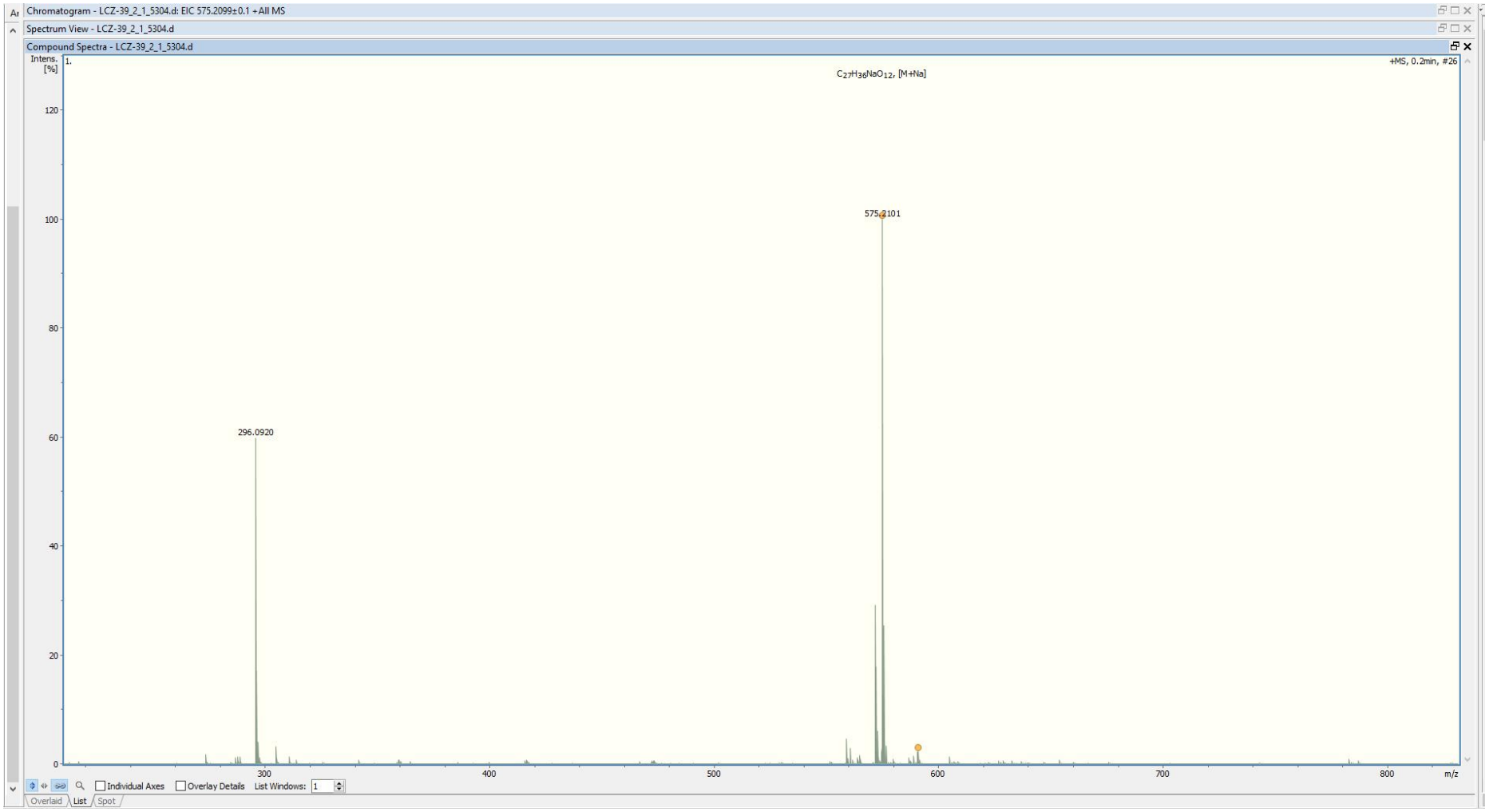

Figure S92. The (+)-HRESIMS spectroscopic data of compound **7**.

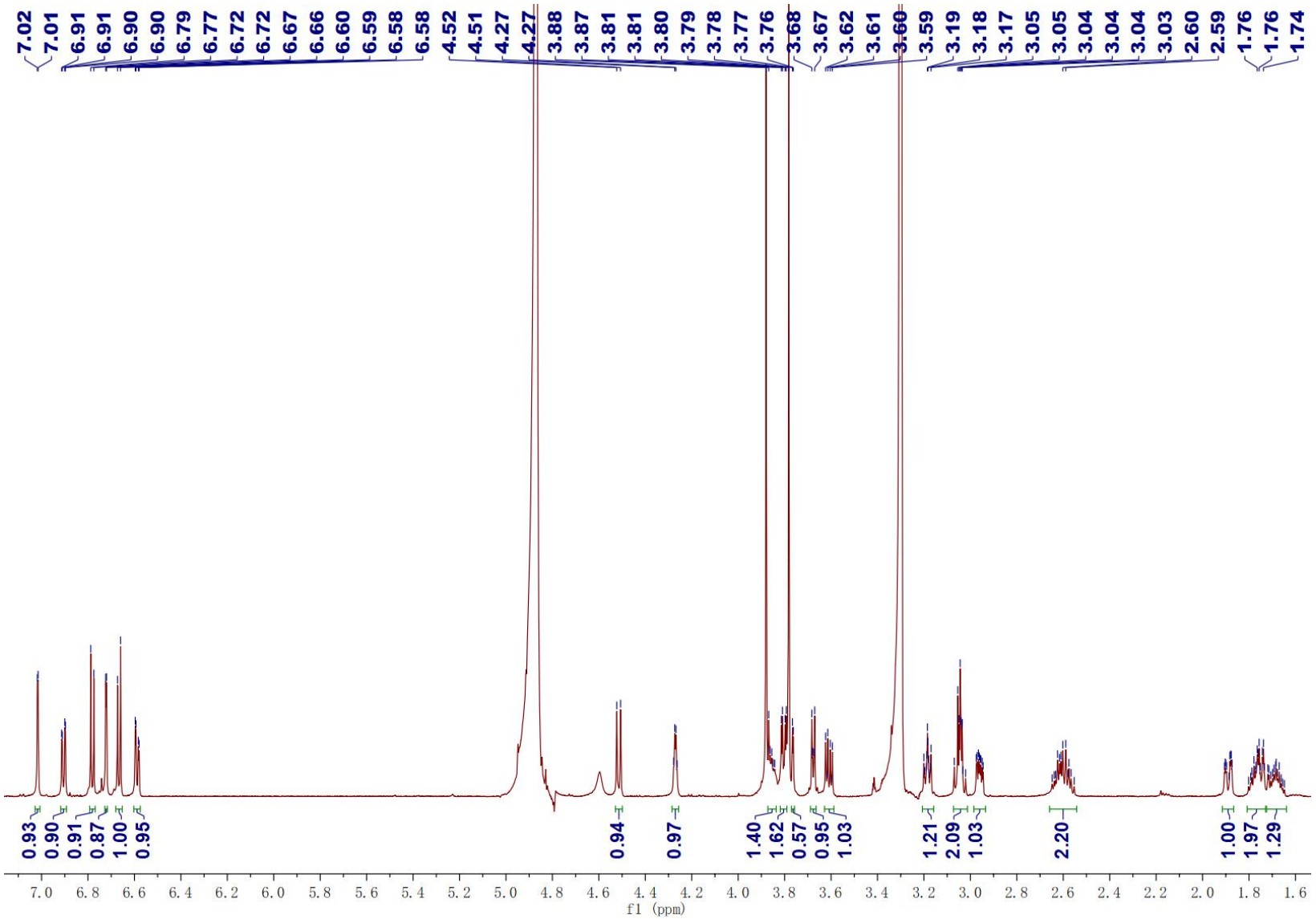

Figure S93. The ^{1}H NMR spectrum of compound **7** in CD_3OD.

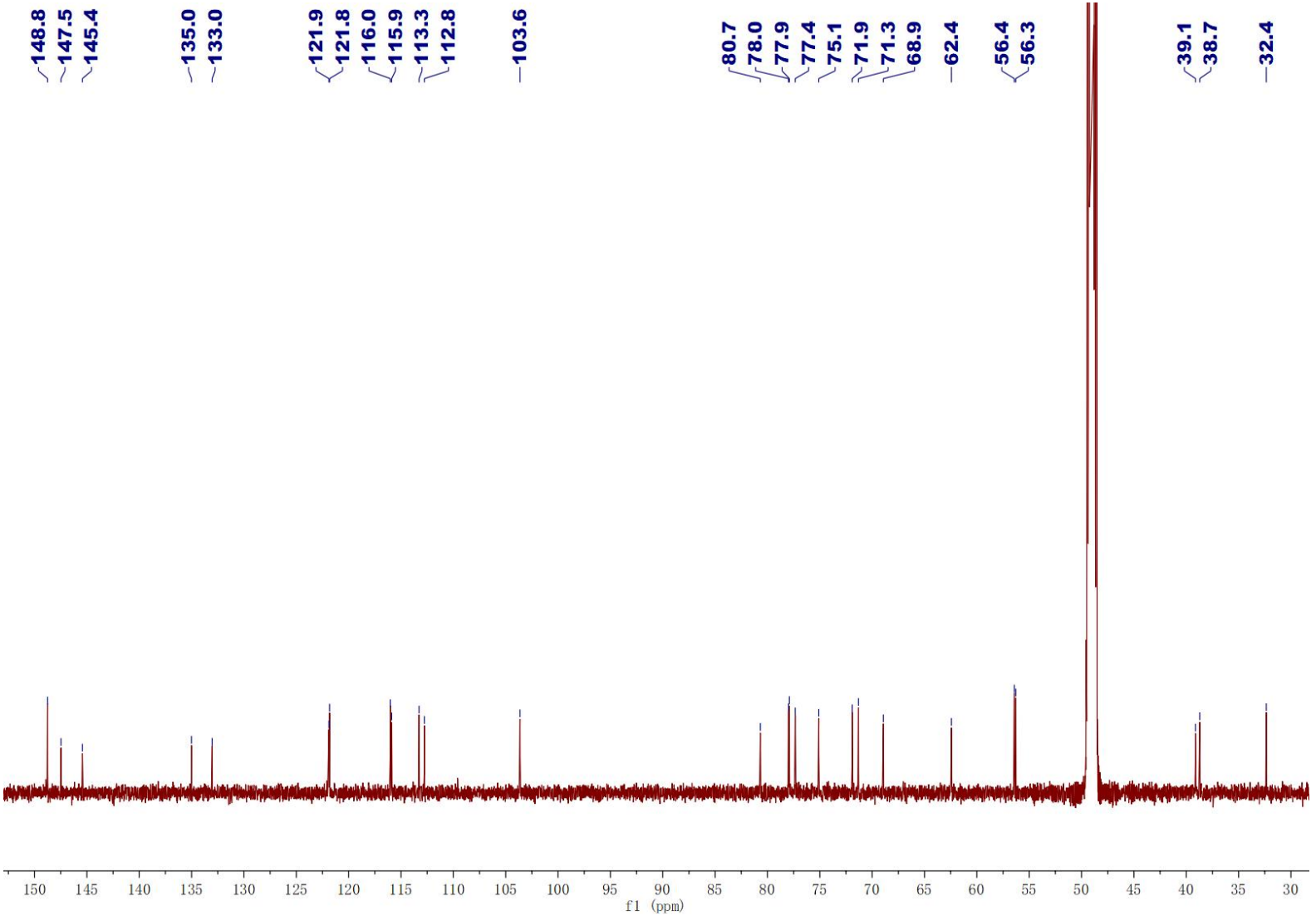

Figure S94. The ^{13}C NMR spectrum of compound **7** in CD_3OD.

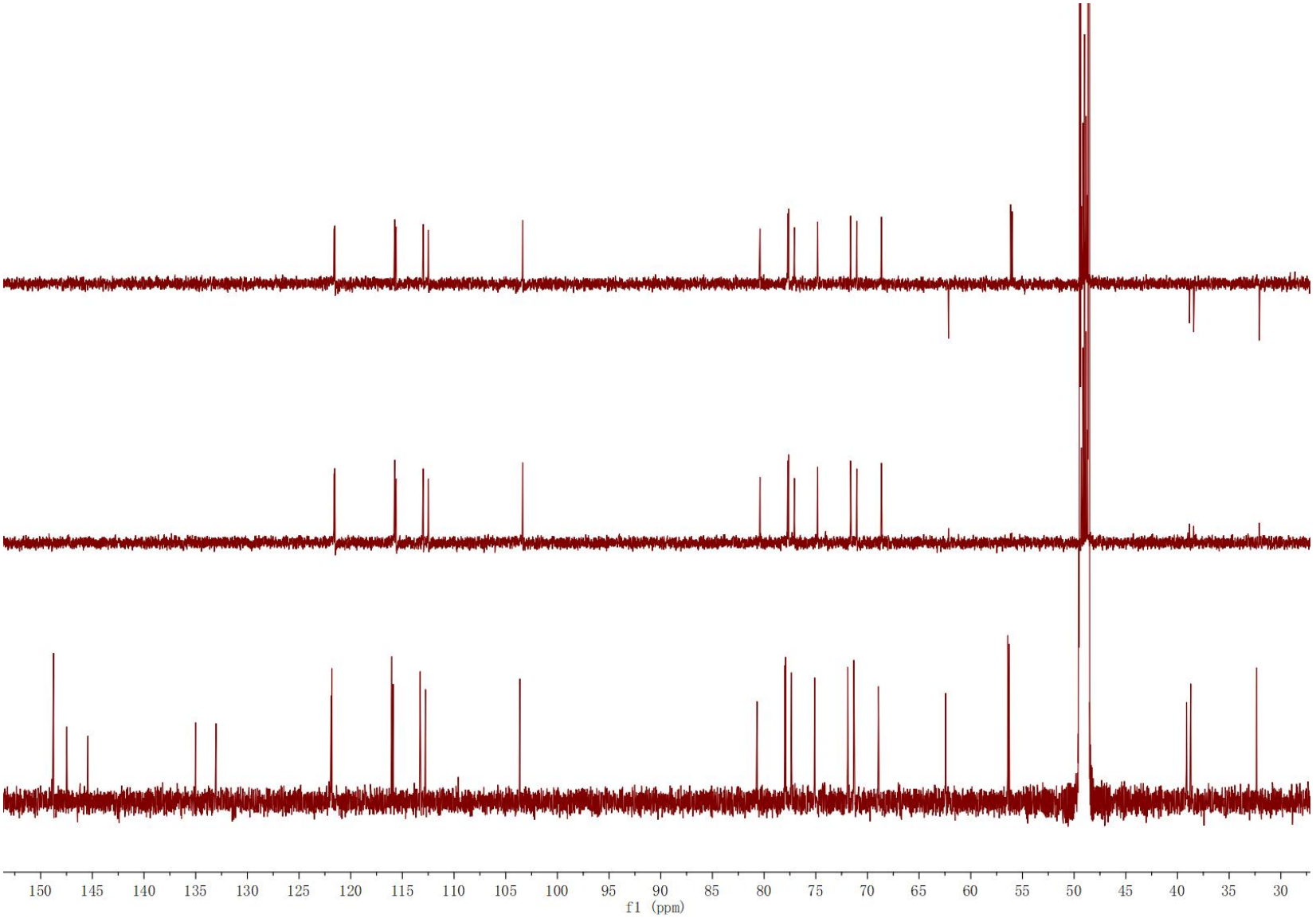

Figure S95. The DEPT spectrum of compound **7** in CD_3OD.

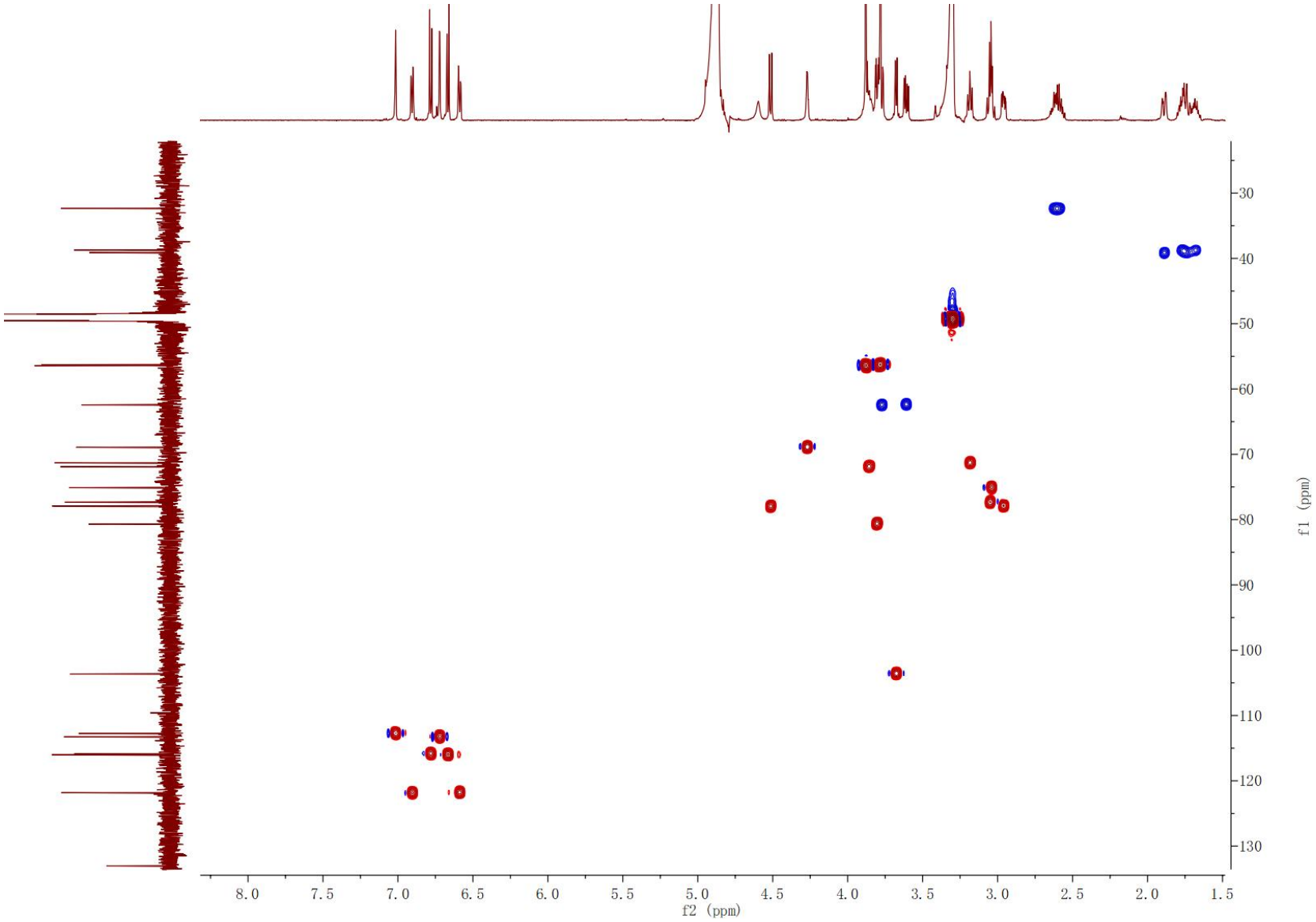

Figure S96. The HSQC spectrum of compound **7** in CD_3OD.

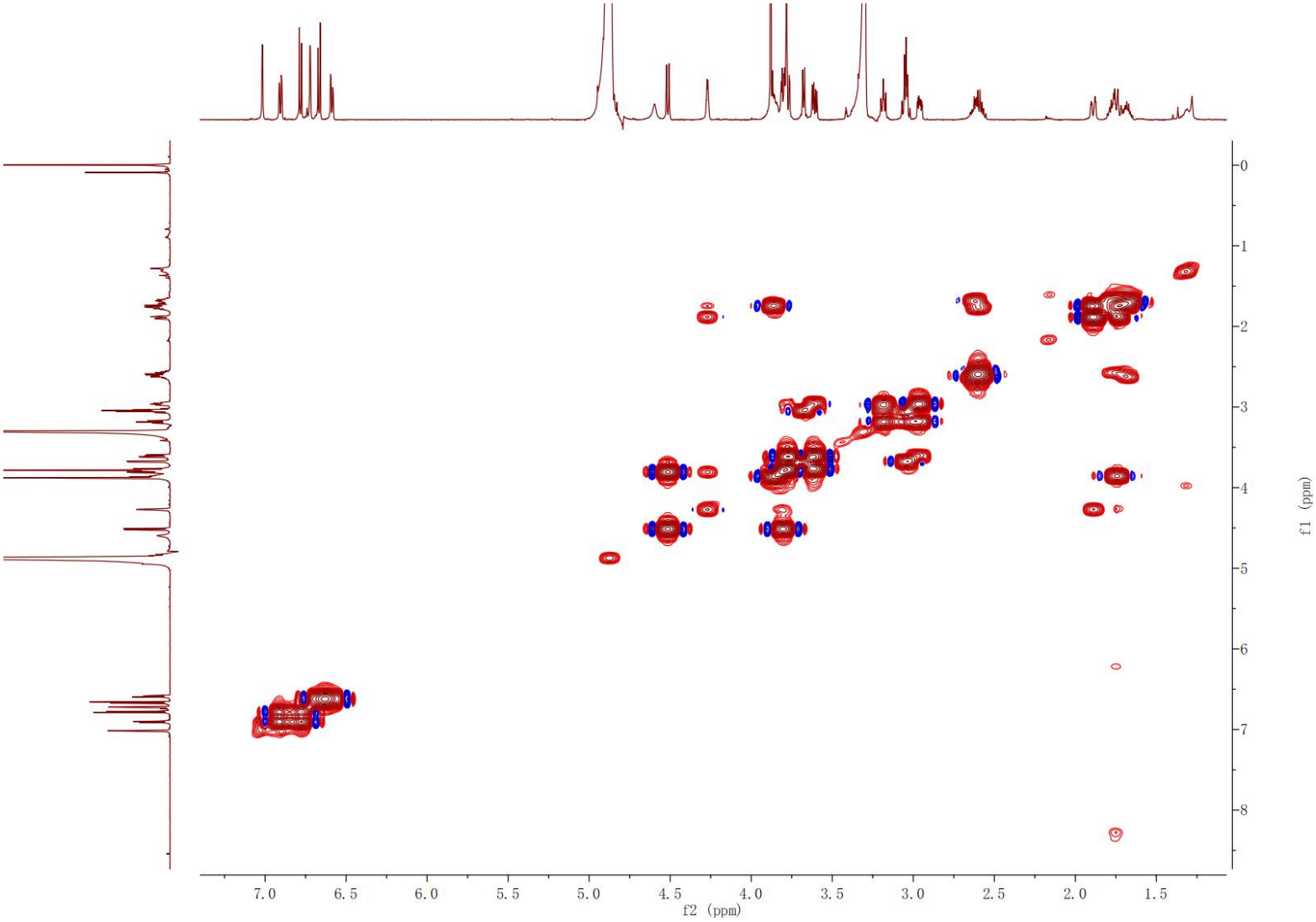

Figure S97. The ^{1}H-^{1}H COSY spectrum of compound **7** in CD_3OD.

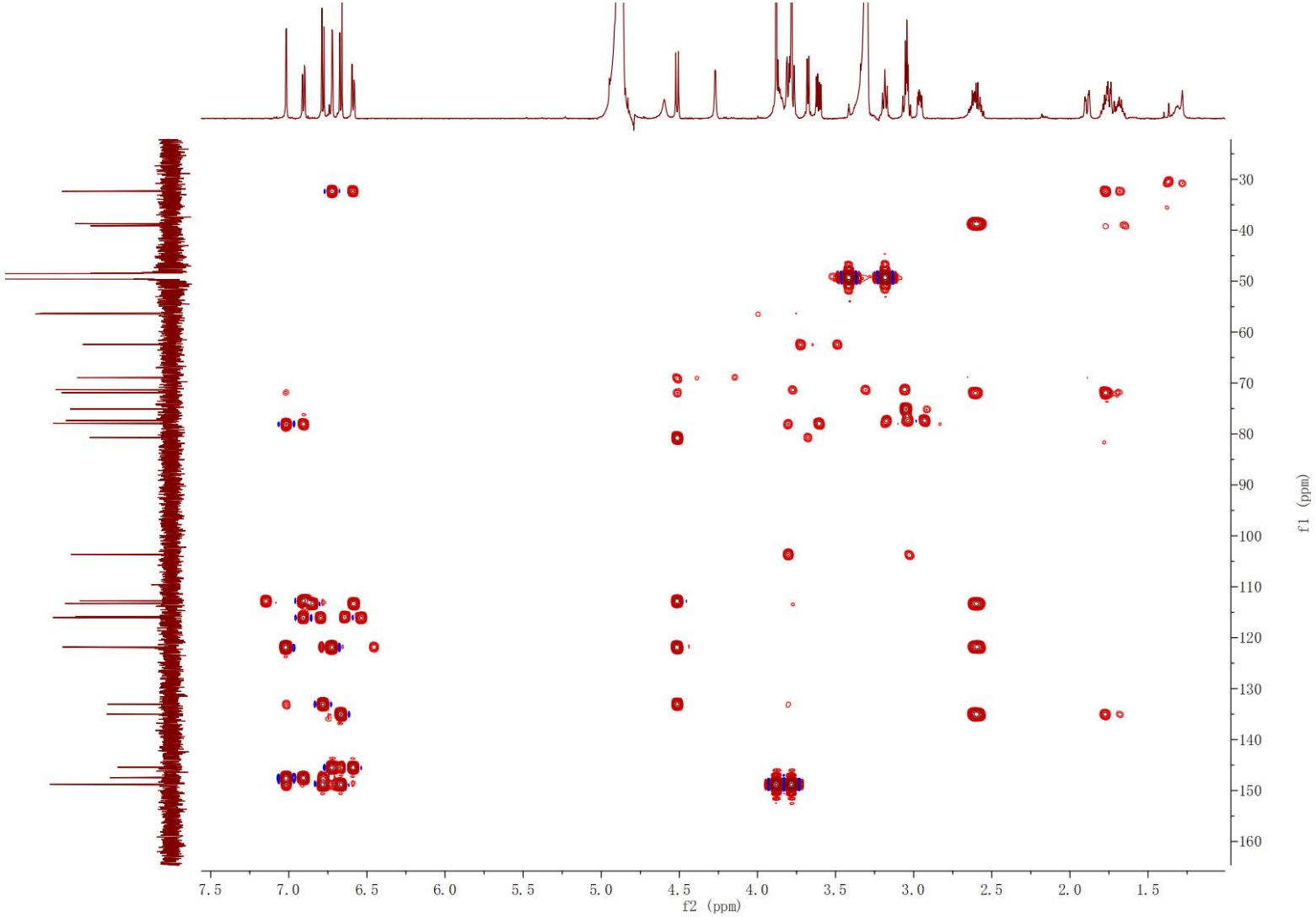

Figure S98. The HMBC spectrum of compound **7** in CD_3OD.

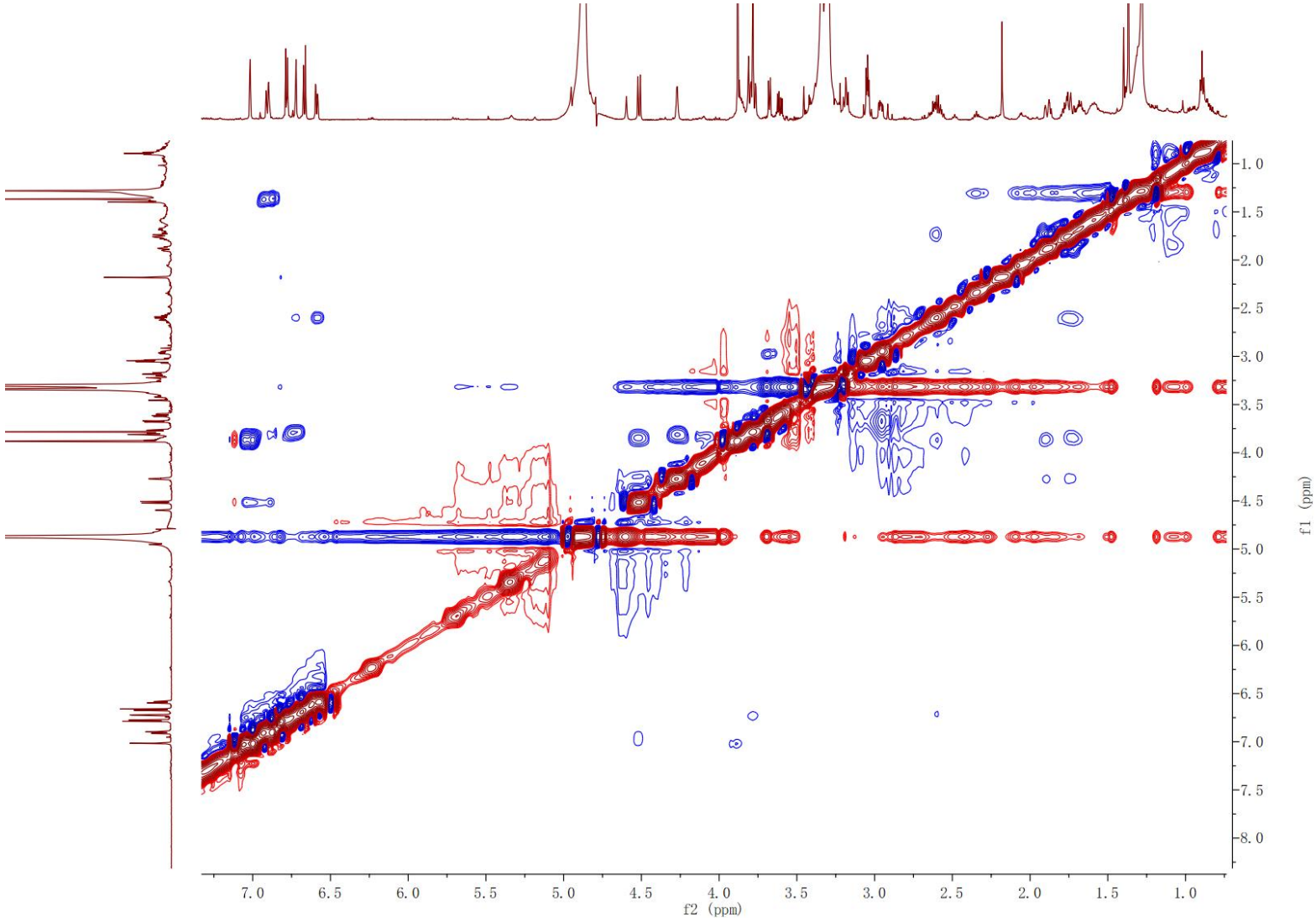

Figure S99. The NOESY spectrum of compound **7** in CD_3OD.

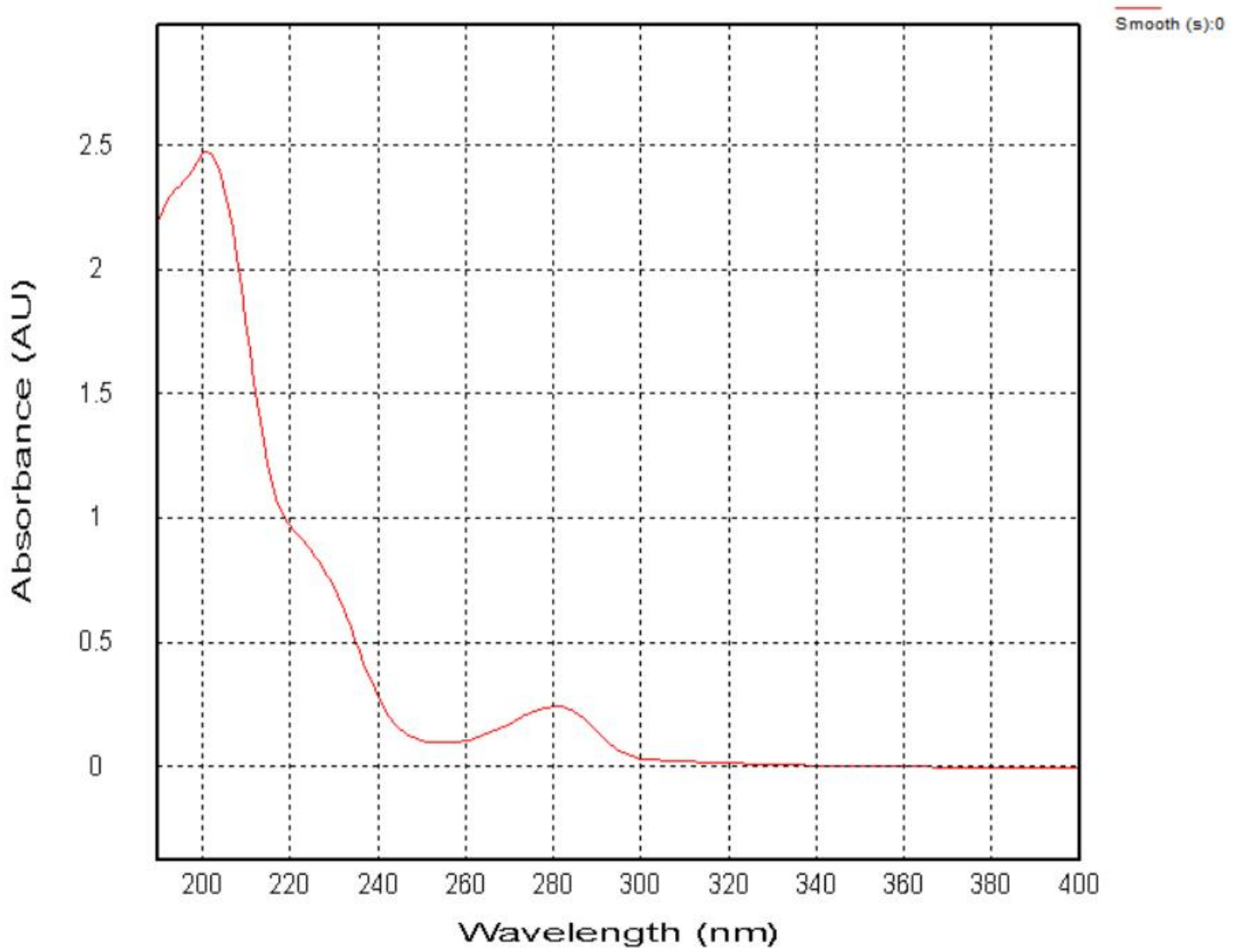

Figure S100. The UV spectrum of compound **7a**.

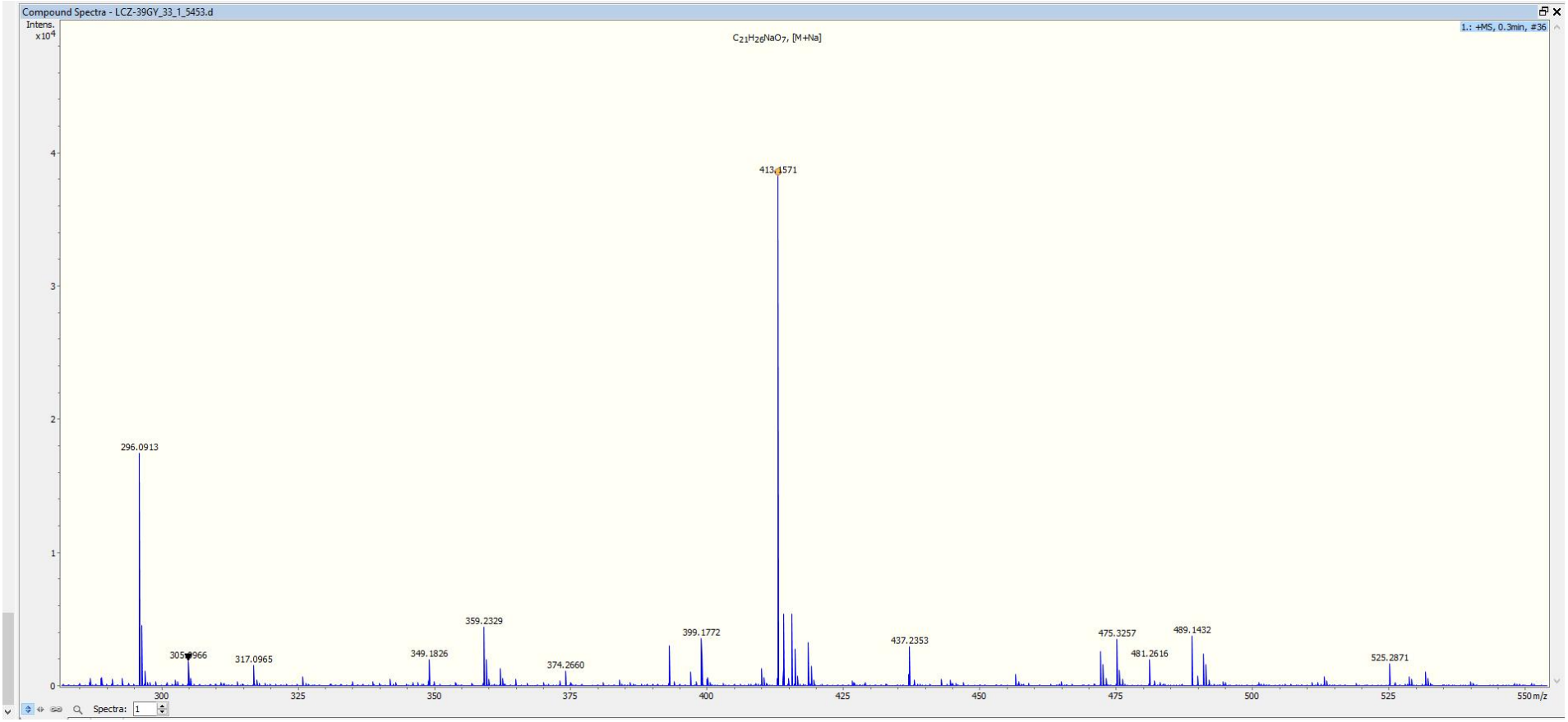

Figure S101. The (+)-HRESIMS spectroscopic data of compound **7a**.

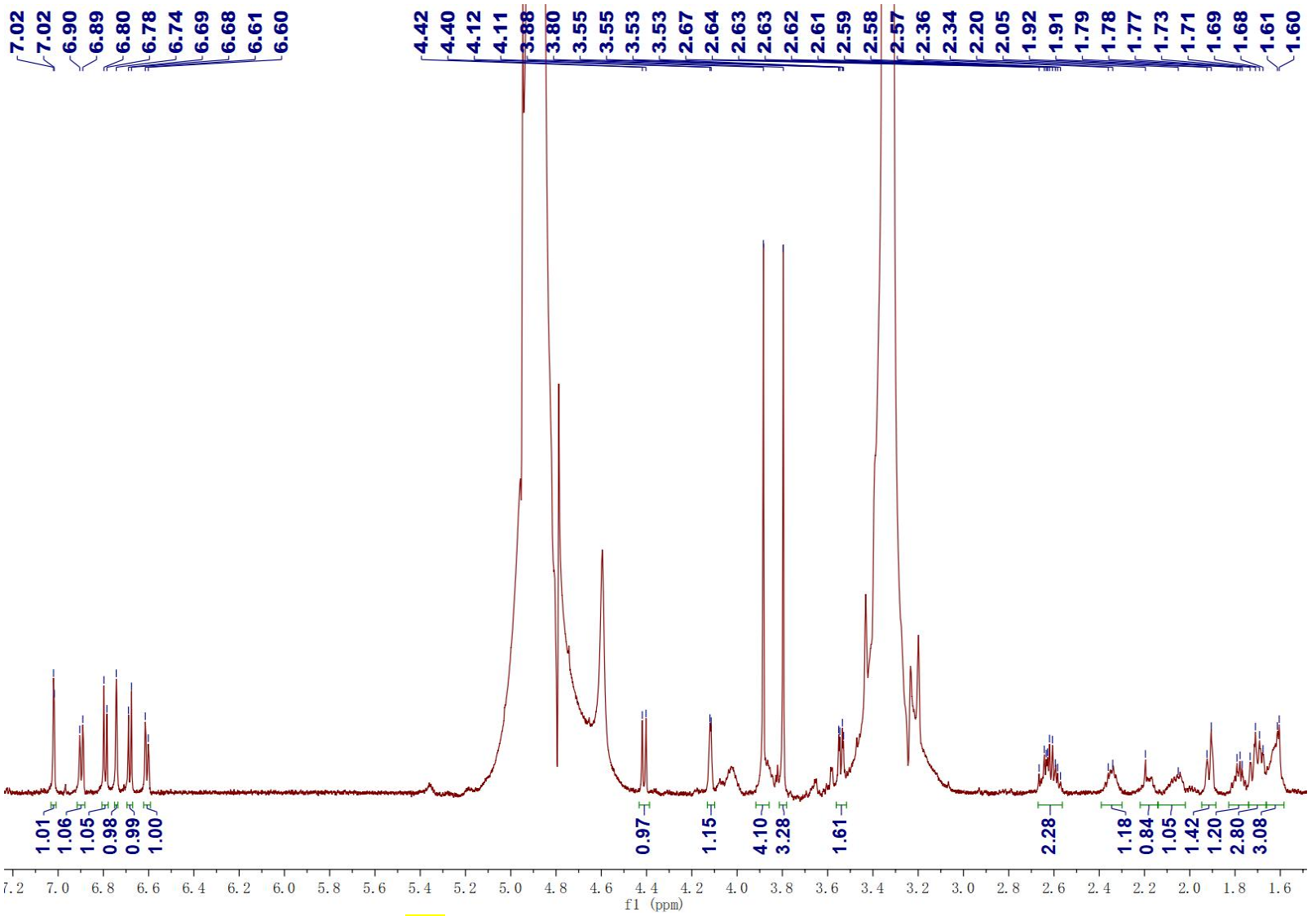

Figure S102. The ^{1}H NMR spectrum of compound **7a** in CD_3OD.

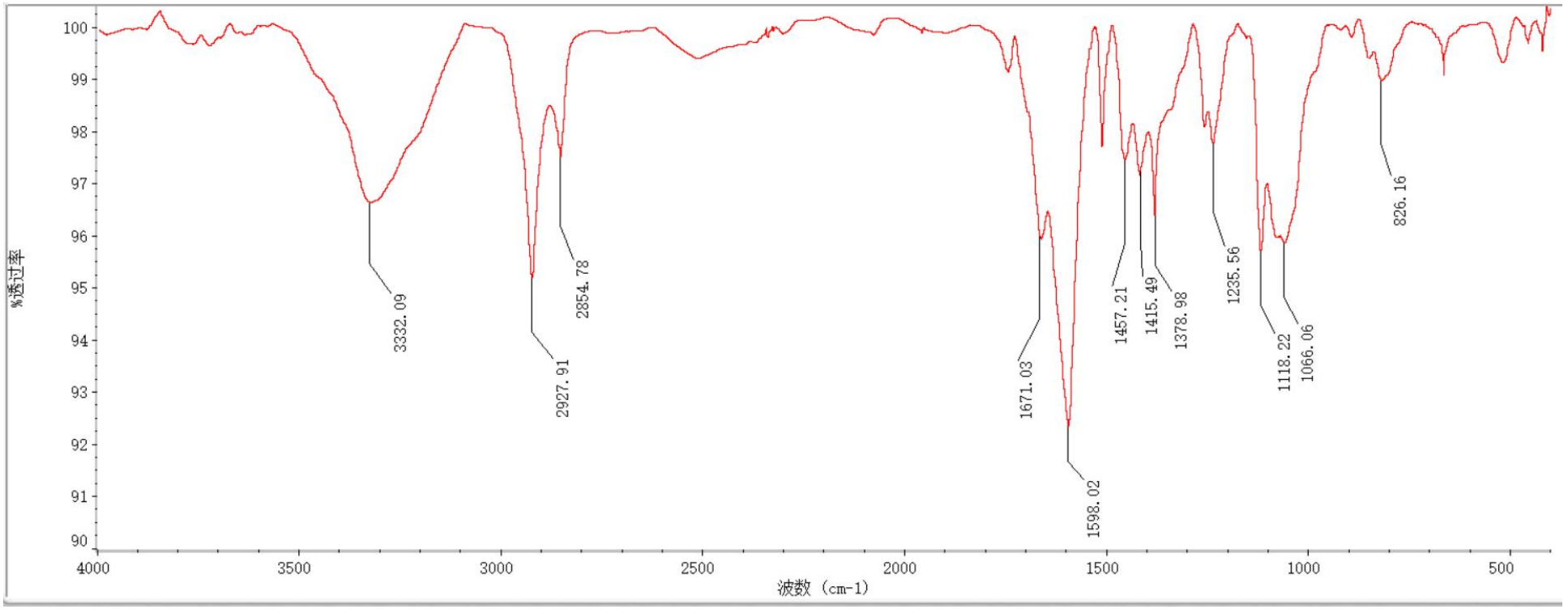

Figure S103. The IR spectrum of compound **8**.

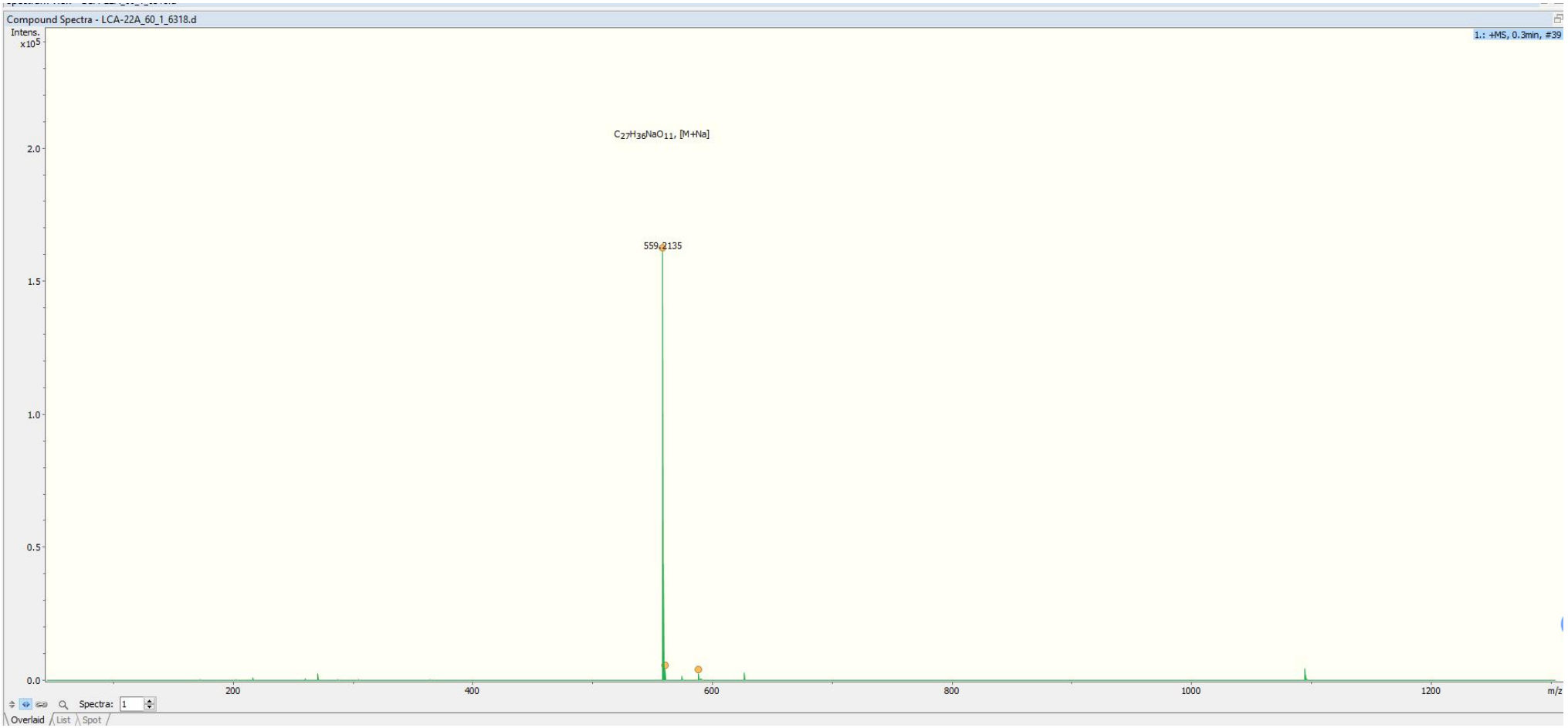

Figure S104. The (+)-HRESIMS spectroscopic data of compound **8**.

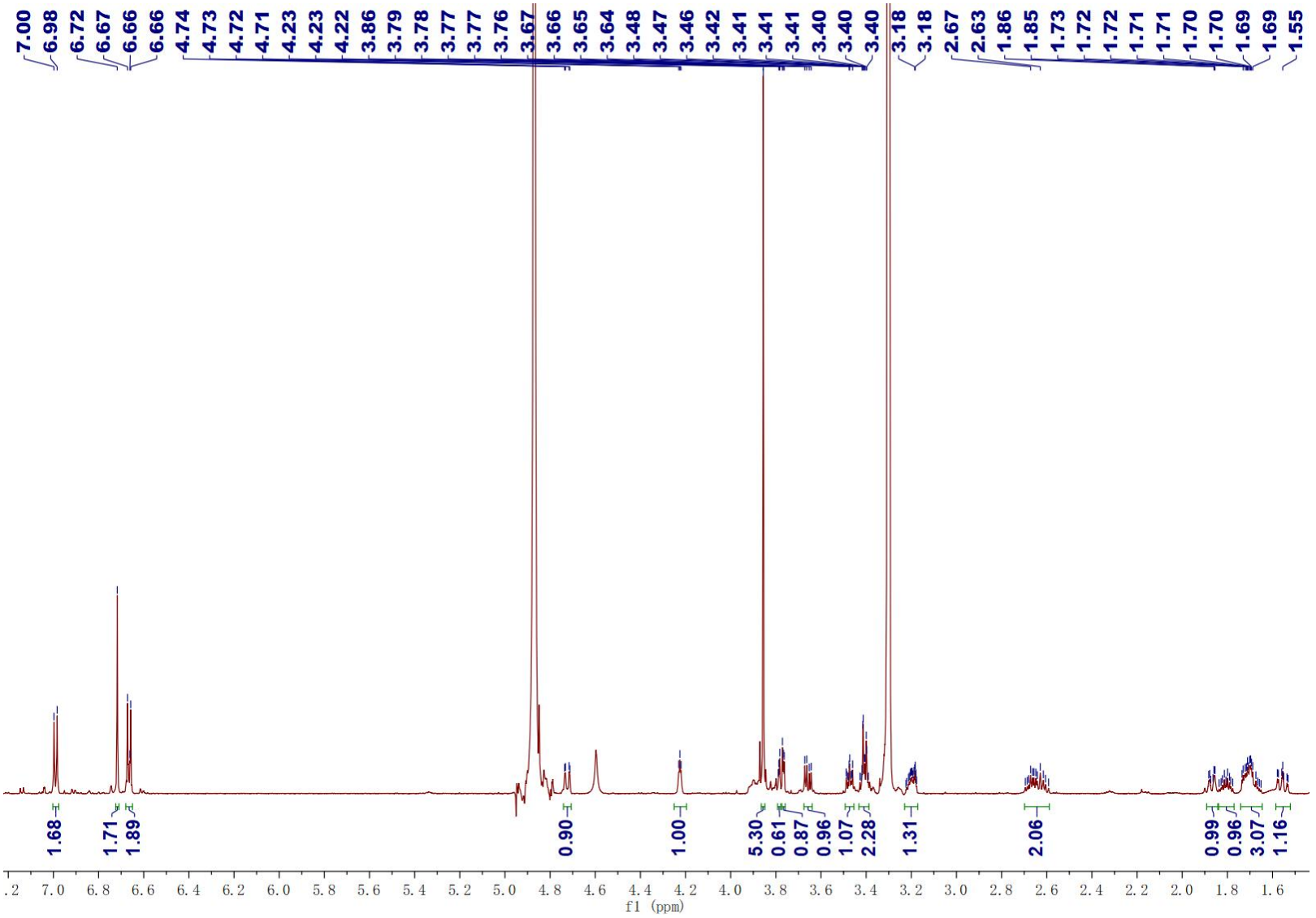

Figure S105. The ^{1}H NMR spectrum of compound **8** in CD_3OD.

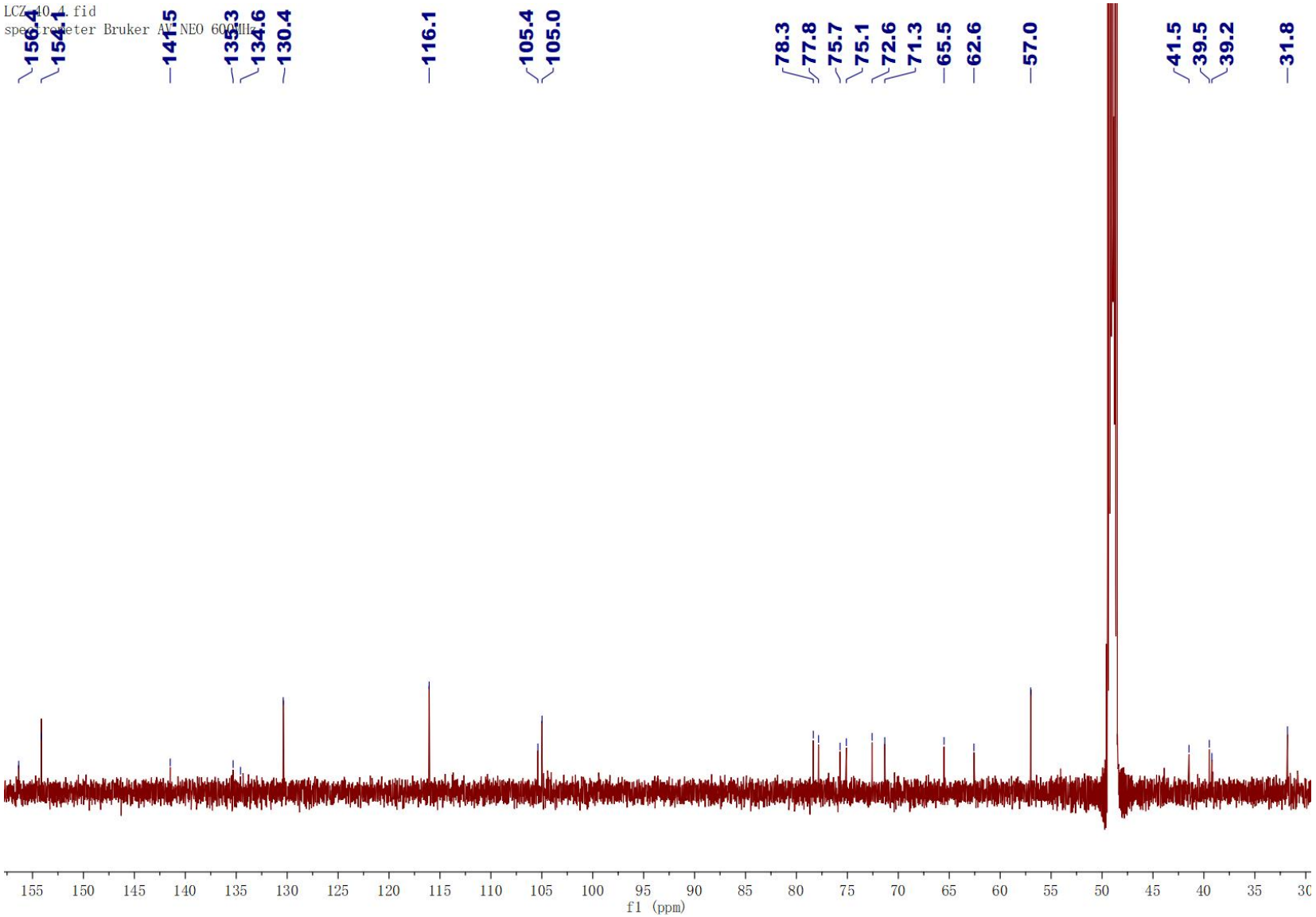

Figure S106. The ^{13}C NMR spectrum of compound **8** in CD_3OD.

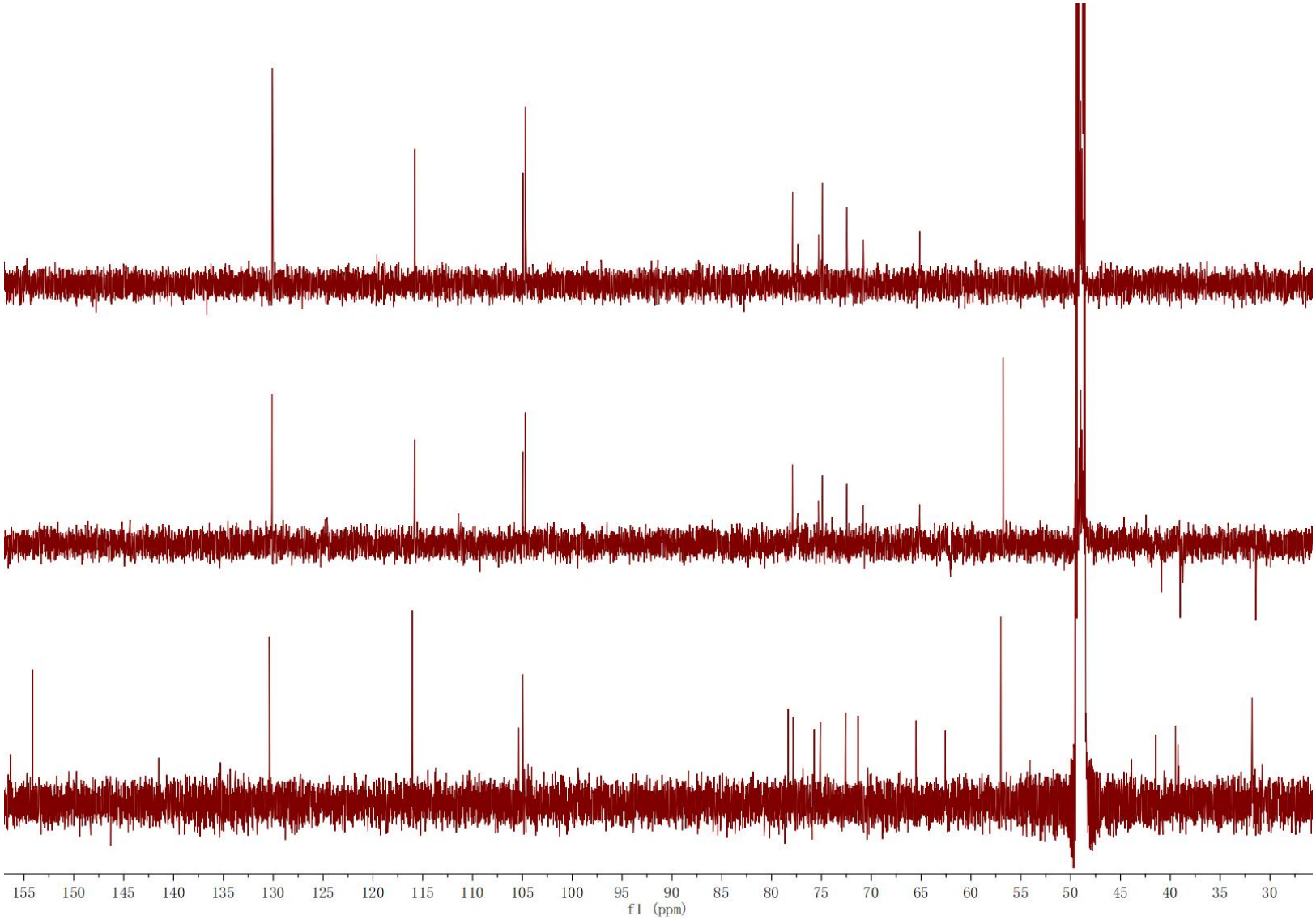

Figure S107. The DEPT spectrum of compound **8** in CD_3OD.

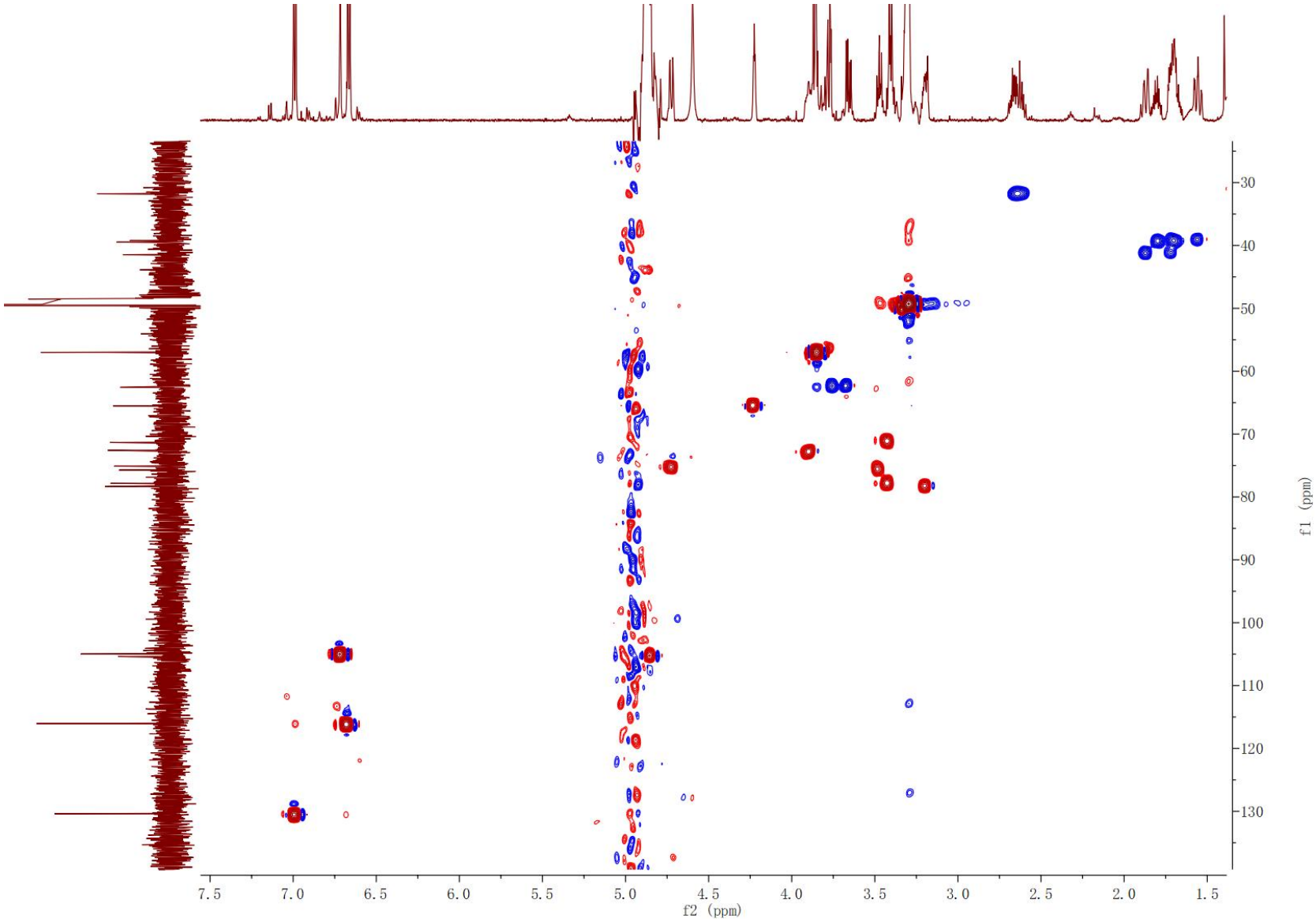

Figure S108. The HSQC spectrum of compound **8** in CD_3OD.

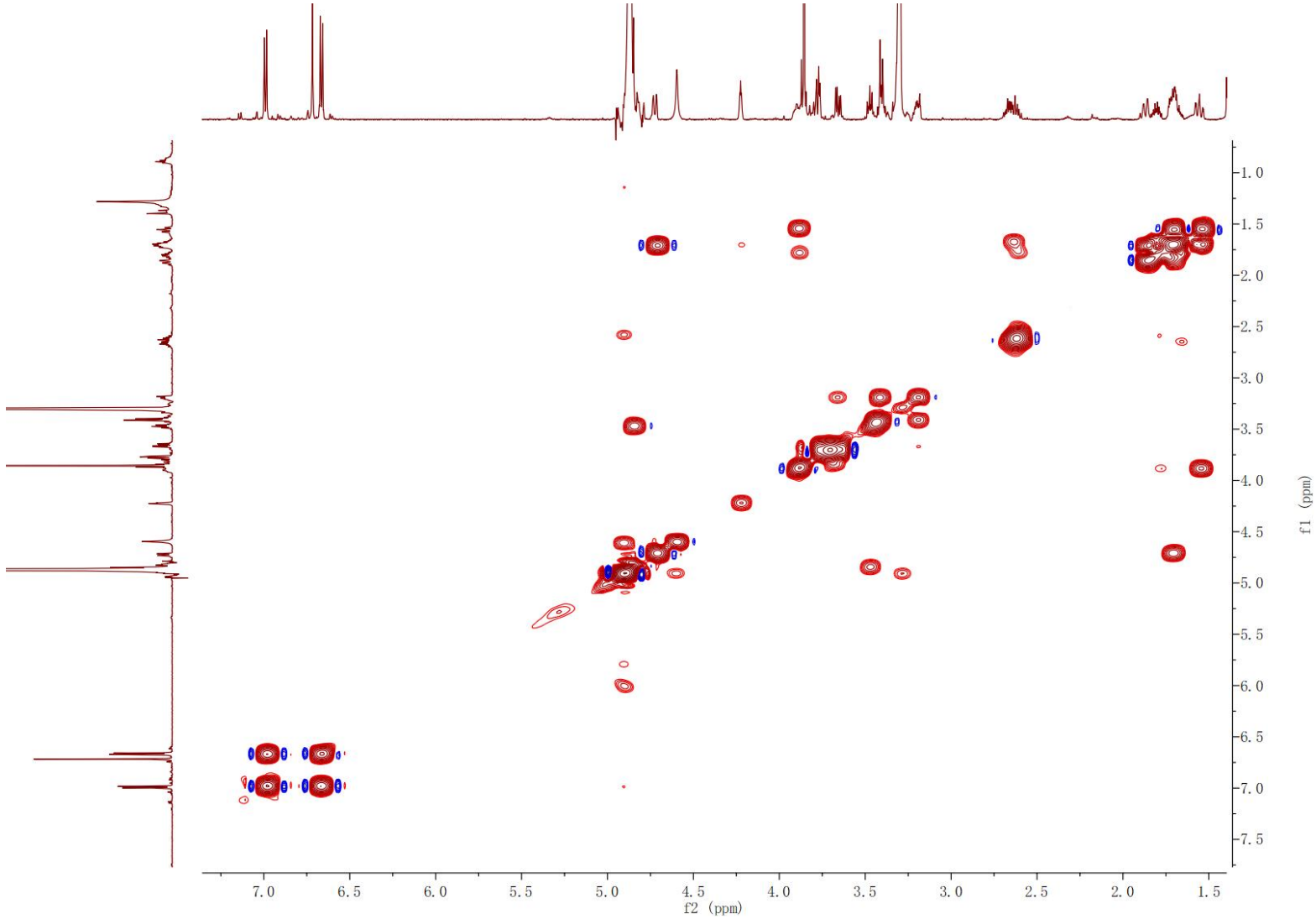

Figure S109. The ^{1}H-^{1}H COSY spectrum of compound **8** in CD_3OD.

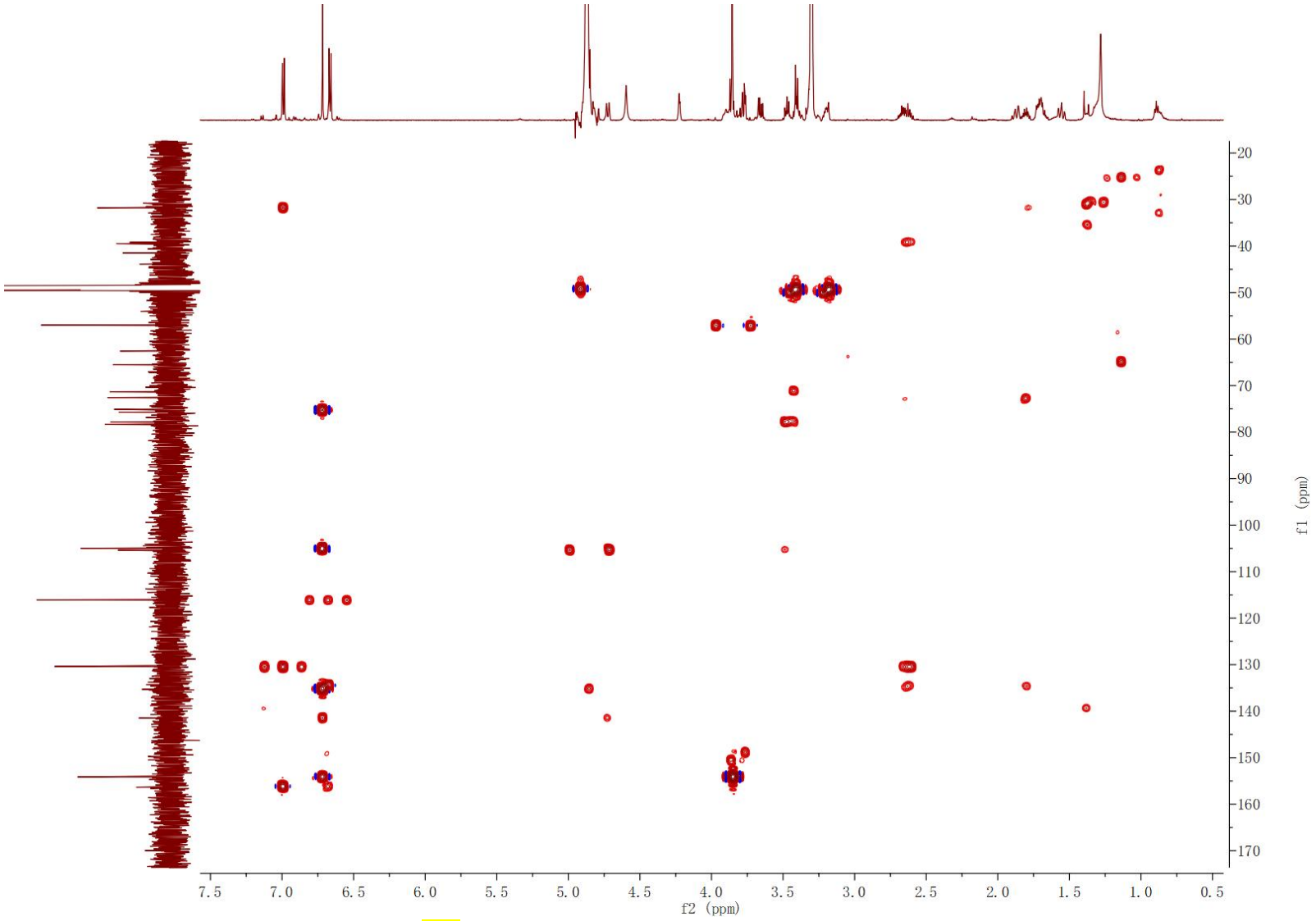

Figure S110. The HMBC spectrum of compound **8** in CD_3OD.

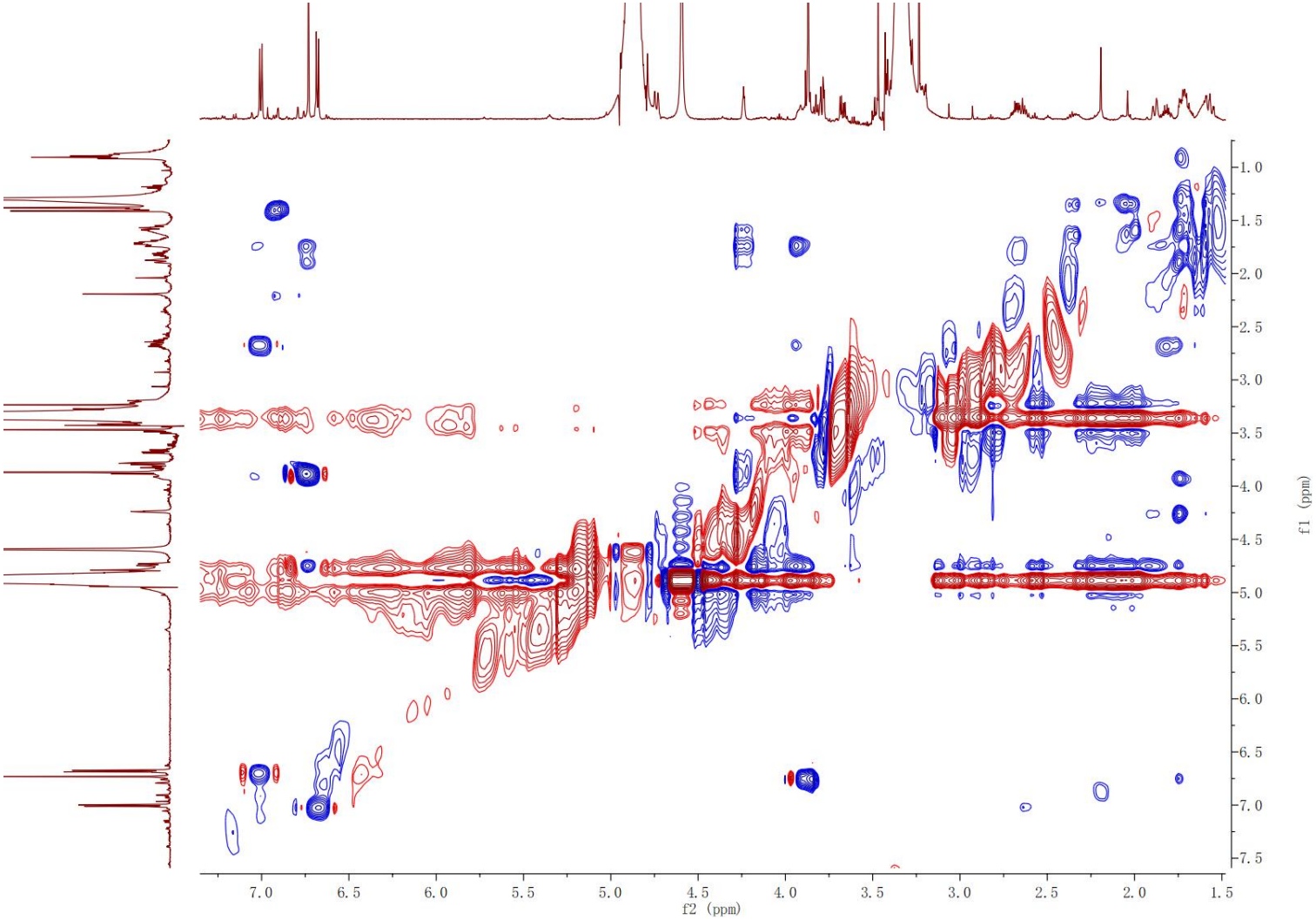

Figure S111. The NOESY spectrum of compound **8** in CD_3OD.

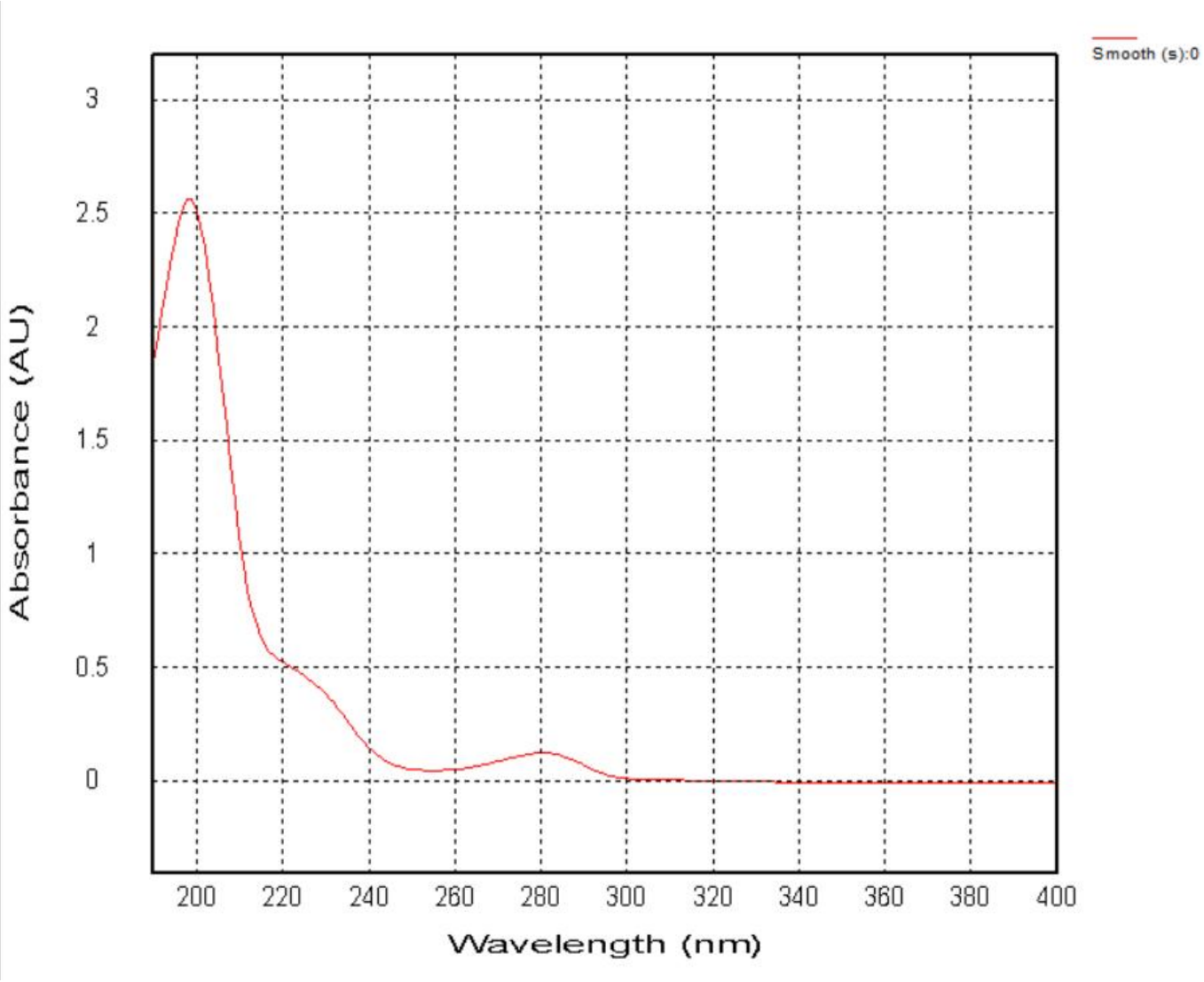

Figure S112. The UV spectrum of compound **8a**.

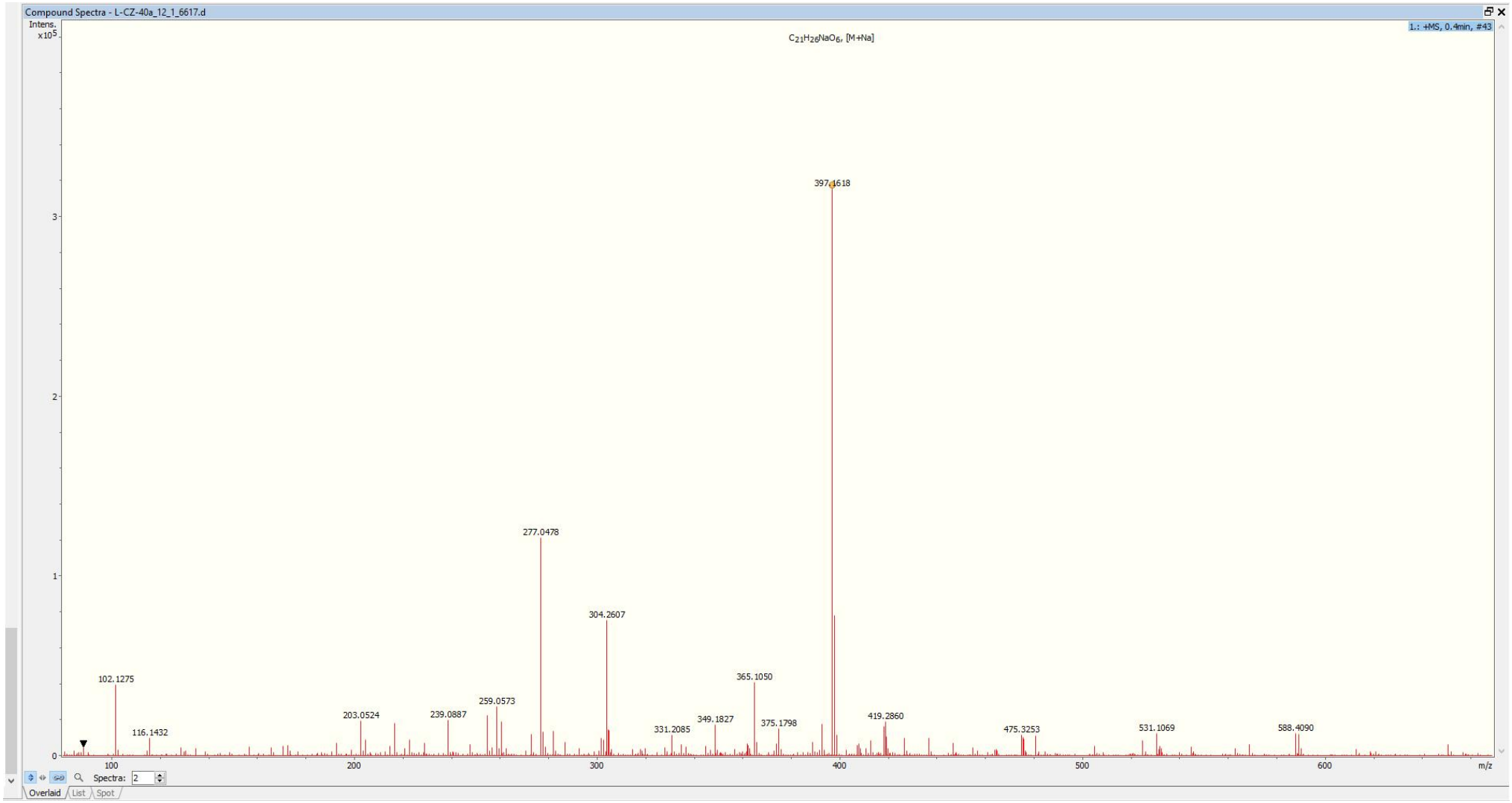

Figure S113. The (+)-HRESIMS spectroscopic data of compound **8a**.

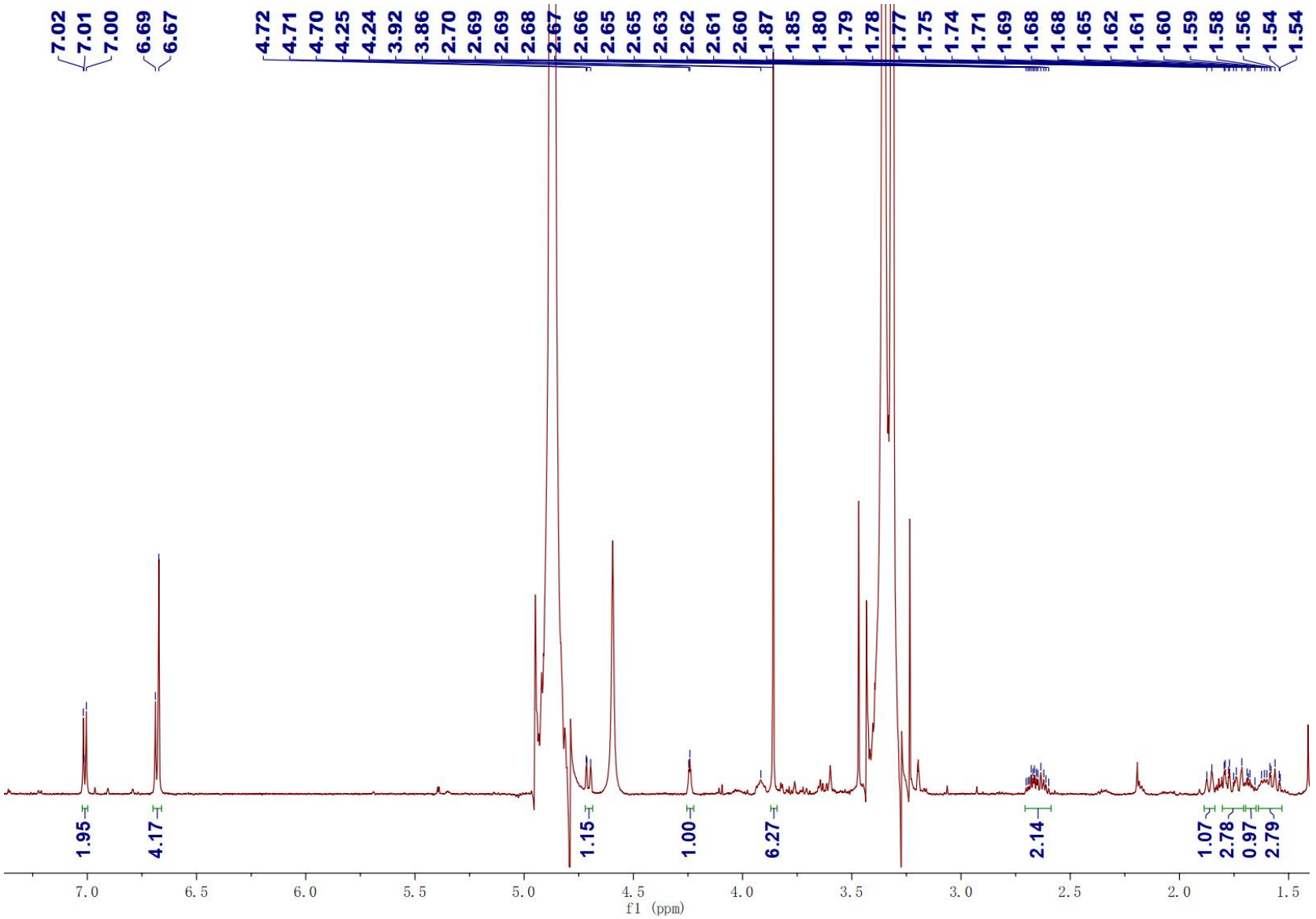

Figure S114. The ^{1}H NMR spectrum of compound **8a** in CD_3OD.

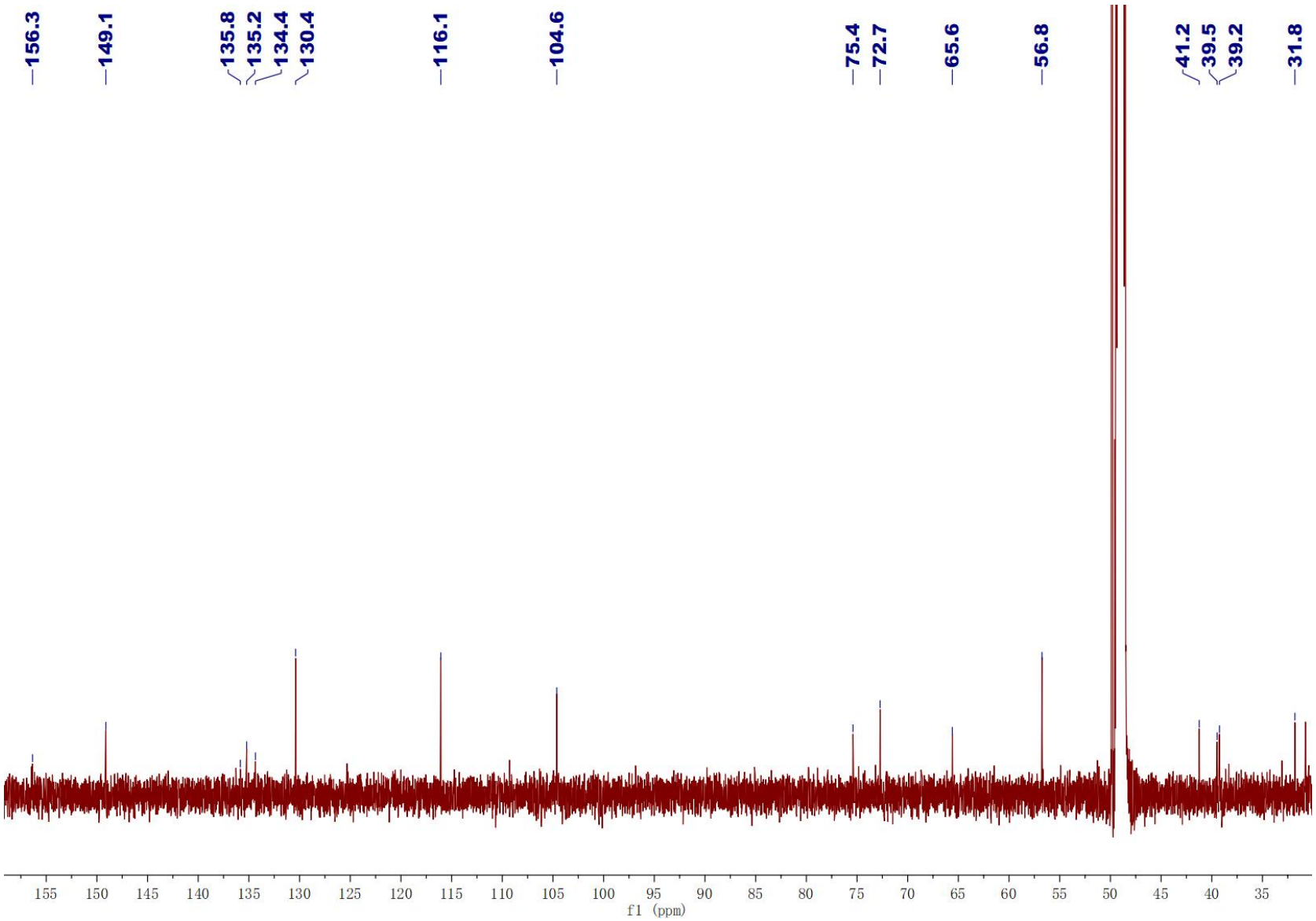

Figure S115. The ^{13}C NMR spectrum of compound **8a** in CD_3OD.

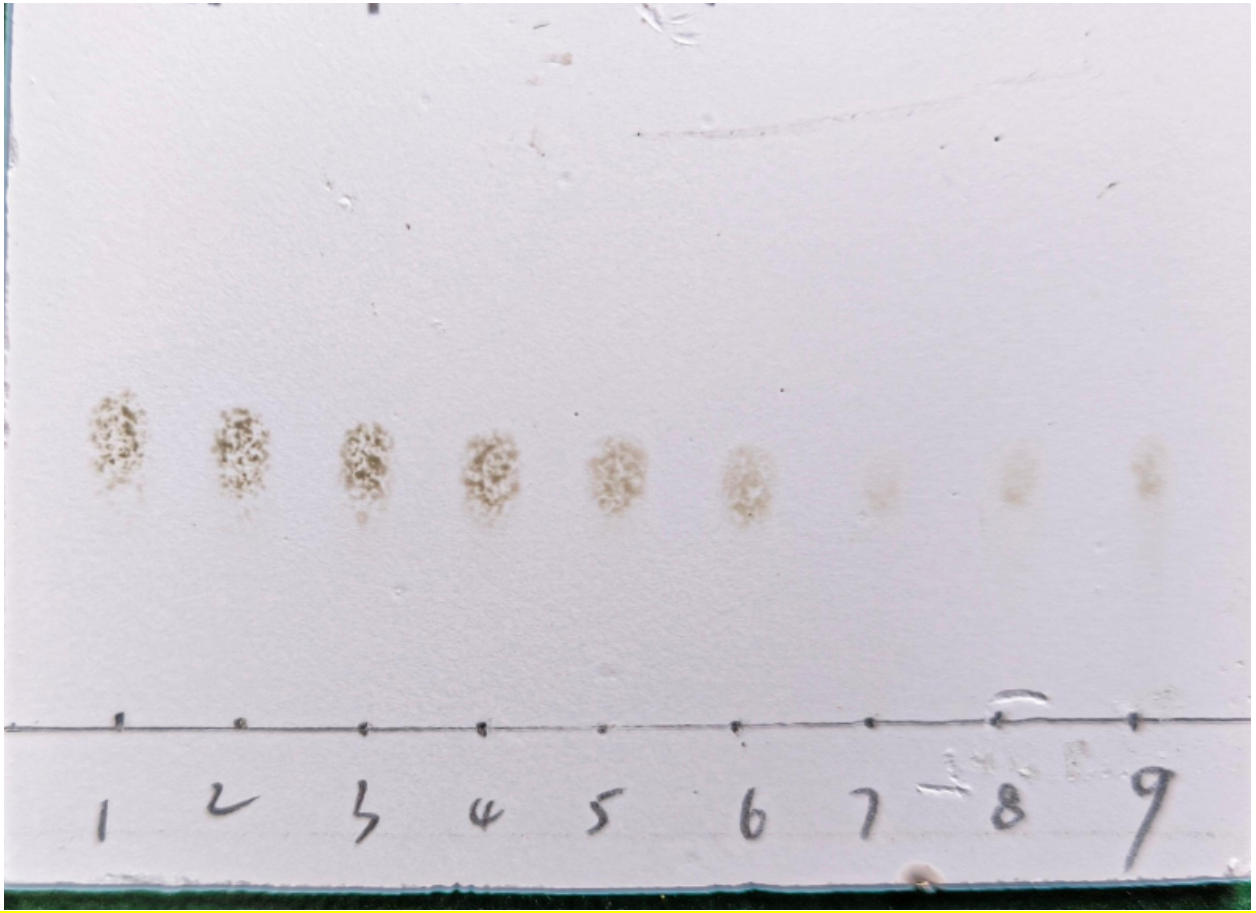

Figure S116. The TLC picture of the glucose in the compounds with the authentic sugar sample ($CHCl_3$/MeOH/H_2O, 7:3:0.1; R_f = 0.2; 1: D-glucose; 2-9: the glucose in the compounds **1-8**)