# Two highly oxygenated *nor*-clerodane diterpenoids from *Croton caudatus*

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## 1. ECD calculations for compounds 1 and 2

## 2. NMR, HRESIMS, and IR spectra for compounds 1 and 2:



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**1. ECD calculations for compounds 1 and 2:**

In general, conformational analyses were carried out via random searching in the Sybyl-X 2.0 using the MMFF94S force field with an energy cutoff of 3.0 kcal/mol.[1] The results showed three lowest energy conformers for both **1** and **2**. Subsequently, the conformers were re-optimized using TDDFT at the b3lyp/6-31+g(d) level in MeCN by the GAUSSIAN 09 program.[2] The energies, oscillator strengths, and rotational strengths (velocity) of the first 30 electronic excitations were calculated using the TDDFT methodology at the rcam-b3lyp/6-31+g(d,p) level in MeCN. The ECD spectra were simulated by the overlapping Gaussian function (half the bandwidth at 1/e peak height, $\sigma$ = 0.35 for ycyl-15 and 0.30 for ycyl-17).[3] To get the final spectra, the simulated spectra of the conformers were averaged according to the Boltzmann distribution theory and their relative Gibbs free energy ($\Delta G$), theoretical ECD spectrum of the corresponding enantiomer was obtained by directly inverse of the ECD spectrum of the calculated model molecule, respectively. By comparing the experiment spectrum with the calculated ECD spectra, the absolute configurations of **1** and **2** were resolved.

1. Sybyl Software, version X 2.0; Tripos Associates Inc.: St. Louis, MO, 2013.

2. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J.Gaussian 09, Rev. C 01; Gaussian, Inc., Wallingford CT, 2009.

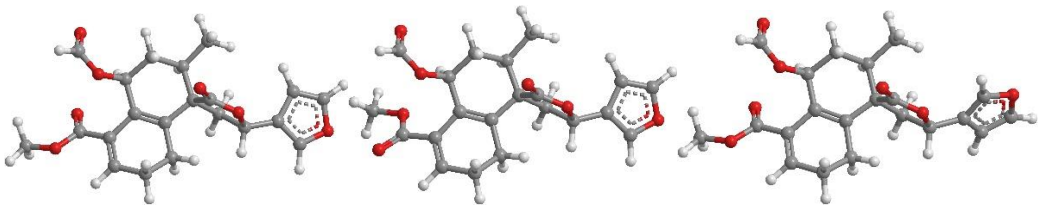
3. Stephens, P. J.; Harada, N. ECD cotton effect approximated by the Gaussian curve and other methods. *Chirality* **2010**, *22*, 229–233.

**Table S1.** Energy analysis for (6*S*,8*R*,9*R*,12*S*)-**1**.

| conformer | Gibbs free energy (298.15 K) | | |
|---|---|---|---|
| | G (Hartree) | ΔE (kcal/mol) | Population (%) |
| C1 | -1340.1218685 | 0.00 | 54.69 |
| C2 | -1340.1211677 | 0.0007008 | 26.02 |
| C3 | -1340.1208856 | 0.0009829 | 19.29 |

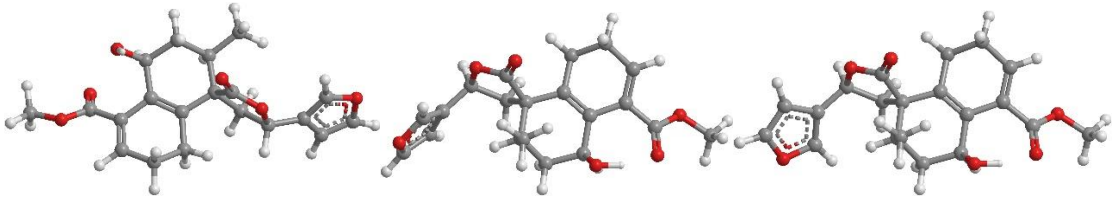
**Table S2.** Energy analysis for (6*S*,8*R*,9*R*,12*S*)-**2**.

| conformer | Gibbs free energy (298.15 K) | | |
|---|---|---|---|
| | G (Hartree) | ΔE (kcal/mol) | Population (%) |
| C1 | -1226.7779116 | 0.00 | 85.27 |
| C2 | -1226.7759487 | 0.0019629 | 10.64 |
| C3 | -1226.7750467 | 0.0028649 | 4.09 |



C1 C2 C3

**Figure S1.** B3LYP-SCRF (PCM, MeCN)/6-31G(d) optimized lowest energy conformers for (6*S*,8*R*,9*R*,12*S*)-**1**.



C1 C2 C3

**Figure S2.** B3LYP-SCRF (PCM, MeCN)/6-31G(d) optimized lowest energy conformers for (6*S*,8*R*,9*R*,12*S*)-**2**.

**Table S3.** Calculated ECD data for (6*S*,8*R*,9*R*,12*S*)-**1**.

| State | C1 | | C2 | | C3 | |
|---|---|---|---|---|---|---|
| | Excitation energies(ev) | Rotatory strengths* | Excitation energies(ev) | Rotatory strengths* | Excitation energies(ev) | Rotatory strengths* |
| 1 | 4.1784 | 31.2275 | 4.1796 | 18.7551 | 4.1783 | 25.3637 |
| 2 | 4.6442 | -1.5957 | 4.6464 | -1.7571 | 4.5252 | 0.9508 |
| 3 | 4.9173 | 58.1523 | 4.9178 | 48.8351 | 4.9122 | 59.8234 |
| 4 | 5.0206 | -5.2007 | 5.0392 | 29.2438 | 5.0183 | -4.7386 |
| 5 | 5.2745 | -8.0657 | 5.2328 | -6.1288 | 5.2810 | -7.9756 |
| 6 | 5.3667 | -27.9777 | 5.3665 | -24.7529 | 5.3042 | -1.6116 |
| 7 | 5.4326 | -17.2675 | 5.4245 | 0.1058 | 5.4009 | -48.8494 |
| 8 | 5.5031 | -5.1078 | 5.4994 | -1.7958 | 5.4969 | 11.8946 |
| 9 | 5.6689 | -1.3035 | 5.6669 | 0.8841 | 5.6451 | 0.2976 |
| 10 | 5.7100 | -6.3394 | 5.7107 | -1.1823 | 5.6841 | -2.8214 |
| 11 | 5.7218 | -34.4986 | 5.7488 | -38.5601 | 5.7166 | -35.8454 |
| 12 | 5.7856 | 11.4007 | 5.7911 | 1.4566 | 5.7787 | -0.5208 |
| 13 | 5.8314 | 35.1104 | 5.8524 | 28.4431 | 5.8141 | -12.9314 |
| 14 | 5.8818 | 36.4937 | 5.8839 | 22.1338 | 5.8207 | -1.7423 |
| 15 | 5.9396 | 3.0501 | 5.9058 | 14.6782 | 5.8277 | 26.5488 |
| 16 | 5.9603 | -53.4437 | 5.9625 | -50.9973 | 5.8850 | 47.3549 |
| 17 | 5.9984 | -7.6055 | 5.9985 | -14.3185 | 5.8927 | 58.6604 |
| 18 | 6.0256 | 33.7344 | 6.0242 | 29.9339 | 5.9340 | -42.3238 |
| 19 | 6.0552 | 26.6709 | 6.0301 | 7.3269 | 6.0244 | 30.3298 |
| 20 | 6.0625 | 5.1972 | 6.0552 | 21.6879 | 6.0782 | 20.7103 |
| 21 | 6.0943 | 19.9034 | 6.1331 | 1.4477 | 6.0819 | 15.9297 |
| 22 | 6.1231 | 0.3692 | 6.1454 | -10.8371 | 6.1005 | 0.6230 |
| 23 | 6.1826 | -8.6717 | 6.1656 | -25.5607 | 6.1784 | -11.9417 |
| 24 | 6.2228 | -9.9982 | 6.2345 | -18.3671 | 6.2015 | -8.9853 |
| 25 | 6.2540 | -30.4429 | 6.2876 | 4.6709 | 6.2219 | 0.2977 |
| 26 | 6.2998 | 8.2072 | 6.3020 | 11.4168 | 6.2568 | -24.9891 |
| 27 | 6.3423 | -16.5879 | 6.3405 | -24.2197 | 6.3336 | -2.1332 |
| 28 | 6.4314 | 0.3110 | 6.4395 | -0.5321 | 6.3871 | 0.7896 |
| 29 | 6.4466 | -5.4349 | 6.4598 | -7.8019 | 6.4310 | -1.6854 |
| 30 | 6.4979 | 0.6658 | 6.4805 | 3.6720 | 6.4528 | 11.4470 |

* R(velocity) 10**-40 erg-esu-cm

**Table S4.** Calculated ECD data for (6*S*,8*R*,9*R*,12*S*)-**2**.

| State | C1 | | C2 | | C3 | |
|---|---|---|---|---|---|---|
| | Excitation energies(ev) | Rotatory strengths* | Excitation energies(ev) | Rotatory strengths* | Excitation energies(ev) | Rotatory strengths* |
| 1 | 4.2351 | 17.2805 | 4.0165 | -3.3996 | 4.0278 | -0.4484 |
| 2 | 4.6681 | 0.8515 | 4.4731 | 1.6894 | 4.5344 | -0.7066 |
| 3 | 4.8758 | 49.7985 | 4.8436 | 6.8879 | 4.8428 | 6.8533 |
| 4 | 5.1225 | 7.5664 | 4.9491 | 15.2783 | 4.9994 | 14.2350 |
| 5 | 5.3225 | -7.7712 | 5.1846 | 12.6089 | 5.1860 | 10.6316 |
| 6 | 5.3527 | -29.0102 | 5.2291 | -52.2170 | 5.2347 | -56.4271 |
| 7 | 5.3731 | -2.2000 | 5.3920 | -6.1362 | 5.4232 | -1.4461 |
| 8 | 5.5241 | 8.9806 | 5.4459 | 0.2995 | 5.4477 | 3.8346 |
| 9 | 5.5669 | 5.2884 | 5.4970 | -4.1757 | 5.4984 | 7.8221 |
| 10 | 5.6677 | -2.8325 | 5.5753 | -0.0479 | 5.5780 | -3.3397 |
| 11 | 5.7748 | 1.9316 | 5.5962 | -0.0618 | 5.6746 | -2.7836 |
| 12 | 5.8484 | -1.4267 | 5.6667 | 8.5626 | 5.6955 | -6.2925 |
| 13 | 5.8650 | 23.8989 | 5.7946 | 7.2942 | 5.8138 | -19.2079 |
| 14 | 5.9248 | -7.9254 | 5.8075 | 16.8195 | 5.8236 | 1.5474 |
| 15 | 5.9456 | 53.7688 | 5.8262 | -1.0035 | 5.8547 | -2.1463 |
| 16 | 5.9755 | -25.0412 | 5.8703 | -0.3259 | 5.9096 | -23.9265 |
| 17 | 5.9977 | -3.1041 | 5.9211 | -4.5303 | 5.9338 | -10.9567 |
| 18 | 6.0380 | 46.4177 | 5.9469 | 17.4375 | 5.9529 | 4.2734 |
| 19 | 6.0539 | 3.9464 | 6.0525 | 17.2141 | 6.0461 | -4.3016 |
| 20 | 6.1576 | 5.2702 | 6.0598 | 1.0618 | 6.0817 | -11.8900 |
| 21 | 6.1899 | -20.5166 | 6.0980 | 12.6872 | 6.1040 | 11.8840 |
| 22 | 6.2252 | -28.6400 | 6.2010 | -18.3630 | 6.2581 | 14.5561 |
| 23 | 6.3016 | -5.6931 | 6.2680 | 1.2436 | 6.2861 | 6.3621 |
| 24 | 6.3082 | -5.9766 | 6.3126 | 4.1212 | 6.3013 | 1.4364 |
| 25 | 6.3395 | 7.9714 | 6.3490 | -4.7717 | 6.3281 | -7.7233 |
| 26 | 6.3535 | 2.5935 | 6.3500 | 0.0907 | 6.3665 | 5.8013 |
| 27 | 6.3767 | -14.8897 | 6.3552 | 6.8222 | 6.3804 | 2.8258 |
| 28 | 6.3827 | 2.2025 | 6.3703 | 3.5258 | 6.3914 | -2.2033 |
| 29 | 6.4841 | 20.6991 | 6.3851 | -5.9174 | 6.4544 | 15.6929 |
| 30 | 6.5167 | 8.2010 | 6.4457 | 15.4708 | 6.4639 | 0.1261 |

* R(velocity) 10**-40 erg-esu-cm

**Figure S3.** $^{1}$H NMR spectrum (500 MHz) of **1** in $CDCl_3$.

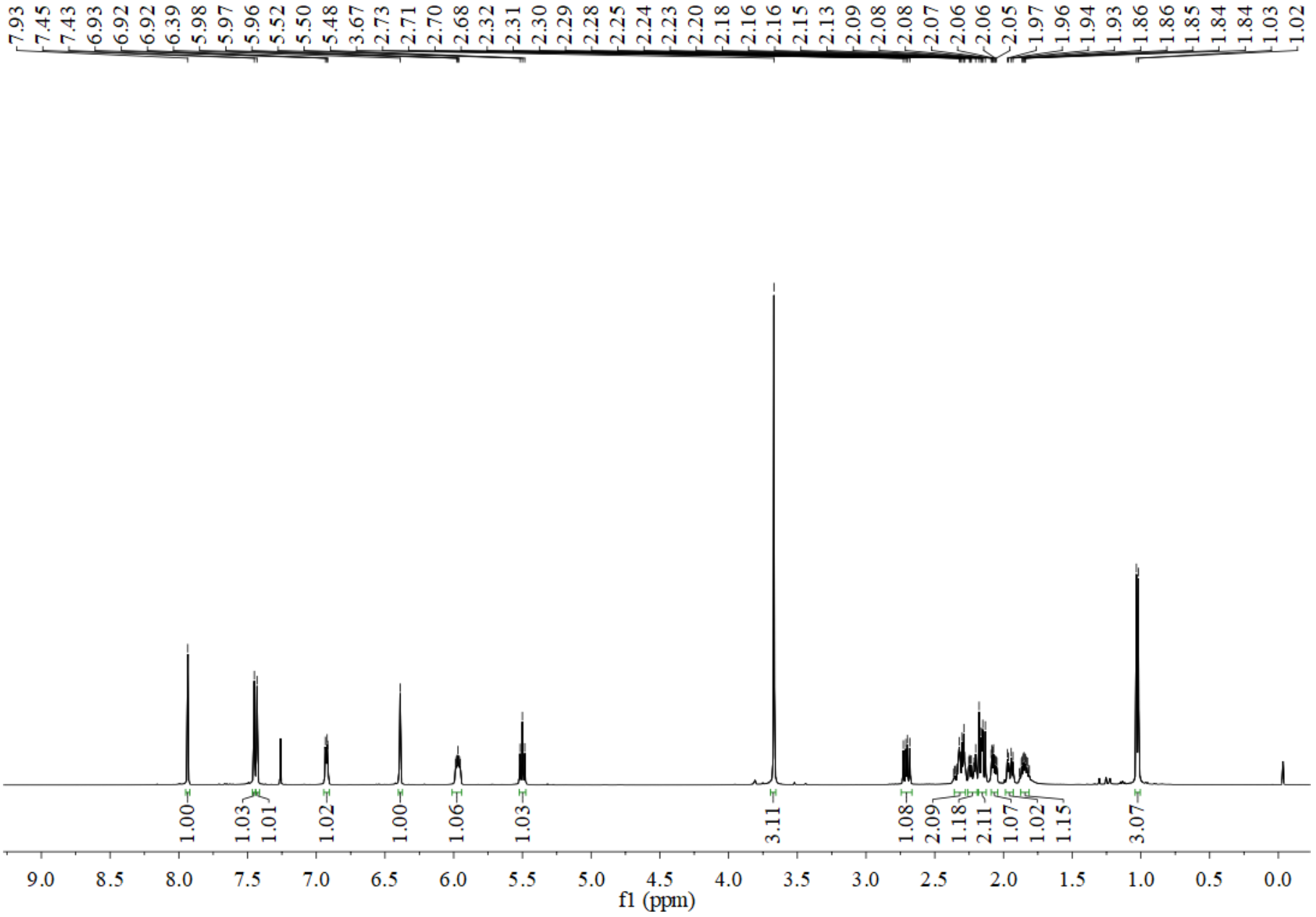


**Figure S4.** $^{13}C$ NMR spectrum (125 MHz) of **1** in $CDCl_3$.

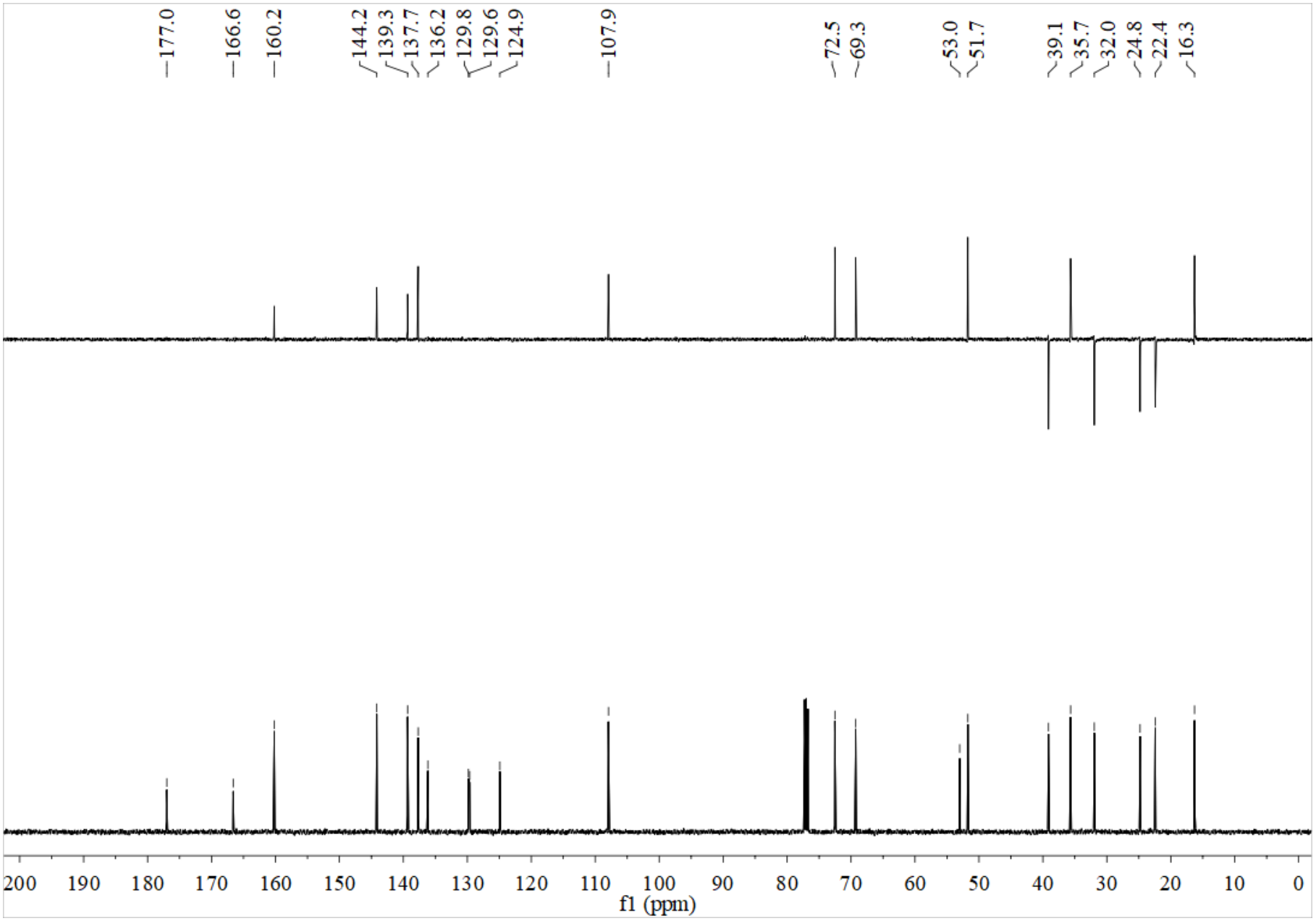


**Figure S5.** HSQC spectrum (500 MHz) of **1** in $CDCl_3$.

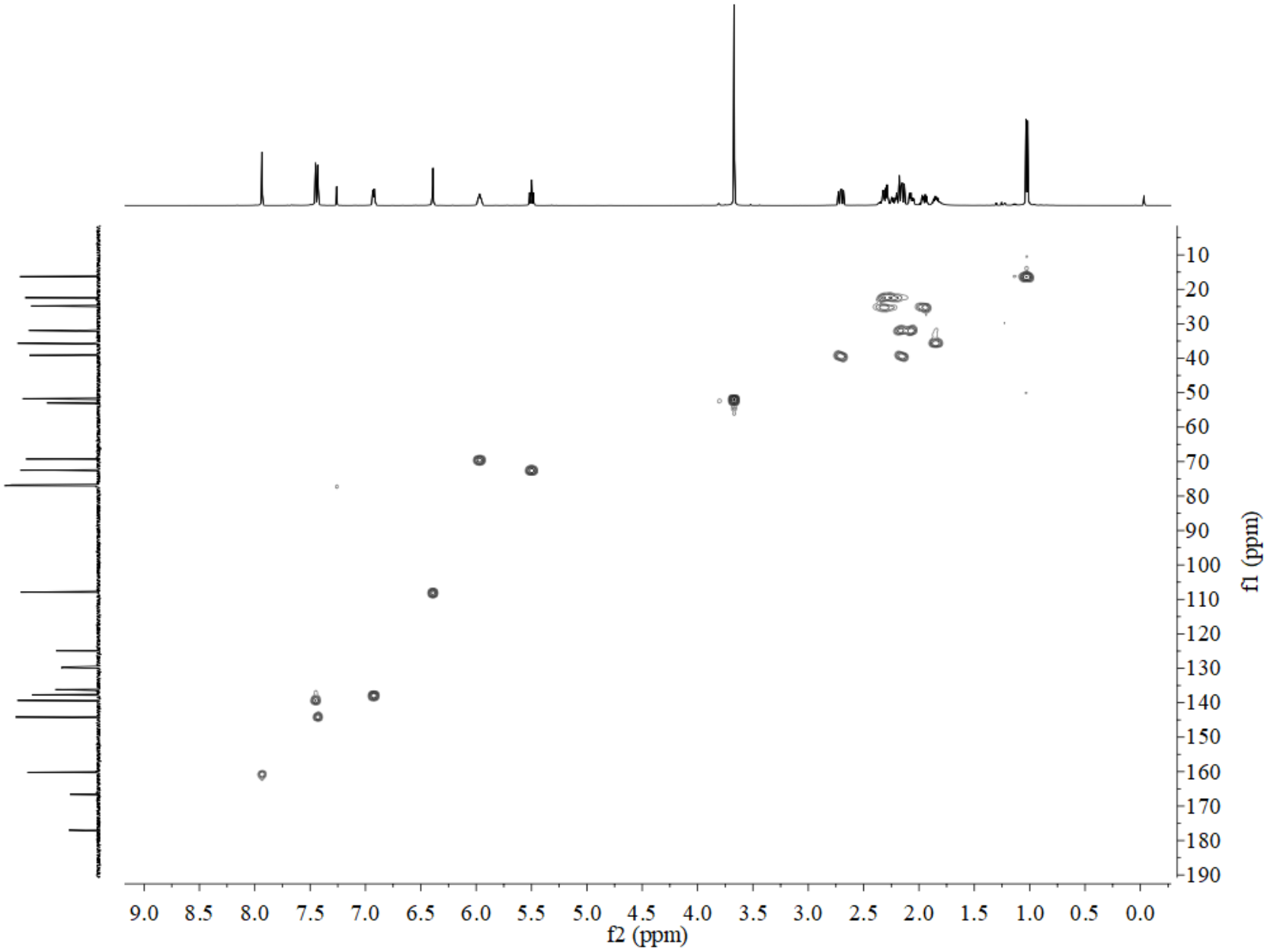


**Figure S6.** HMBC spectrum (500 MHz) of **1** in $CDCl_3$.

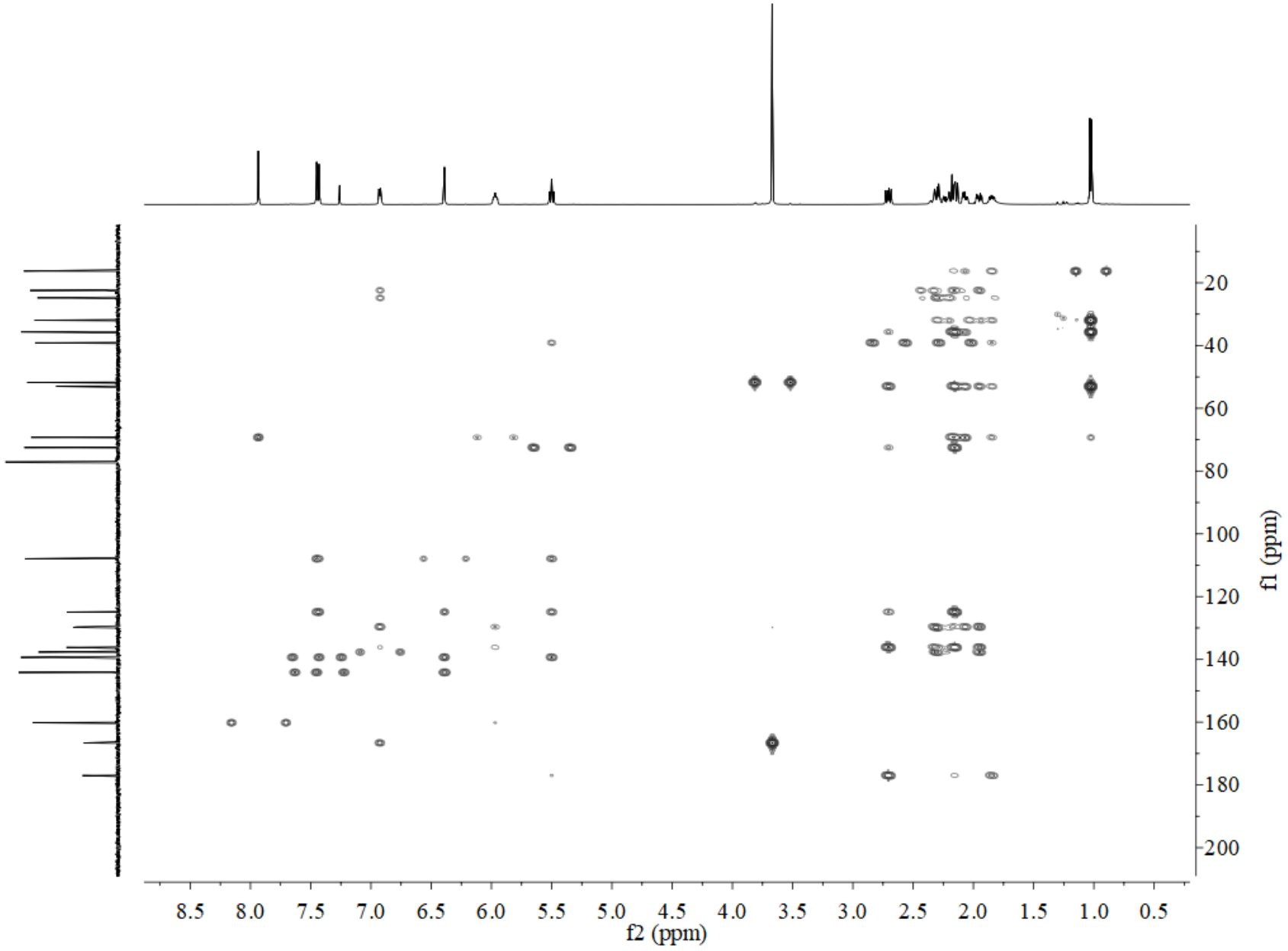


**Figure S7.** $^{1}H–^{1}H$ COSY spectrum (500 MHz) of **1** in $CDCl_3$.

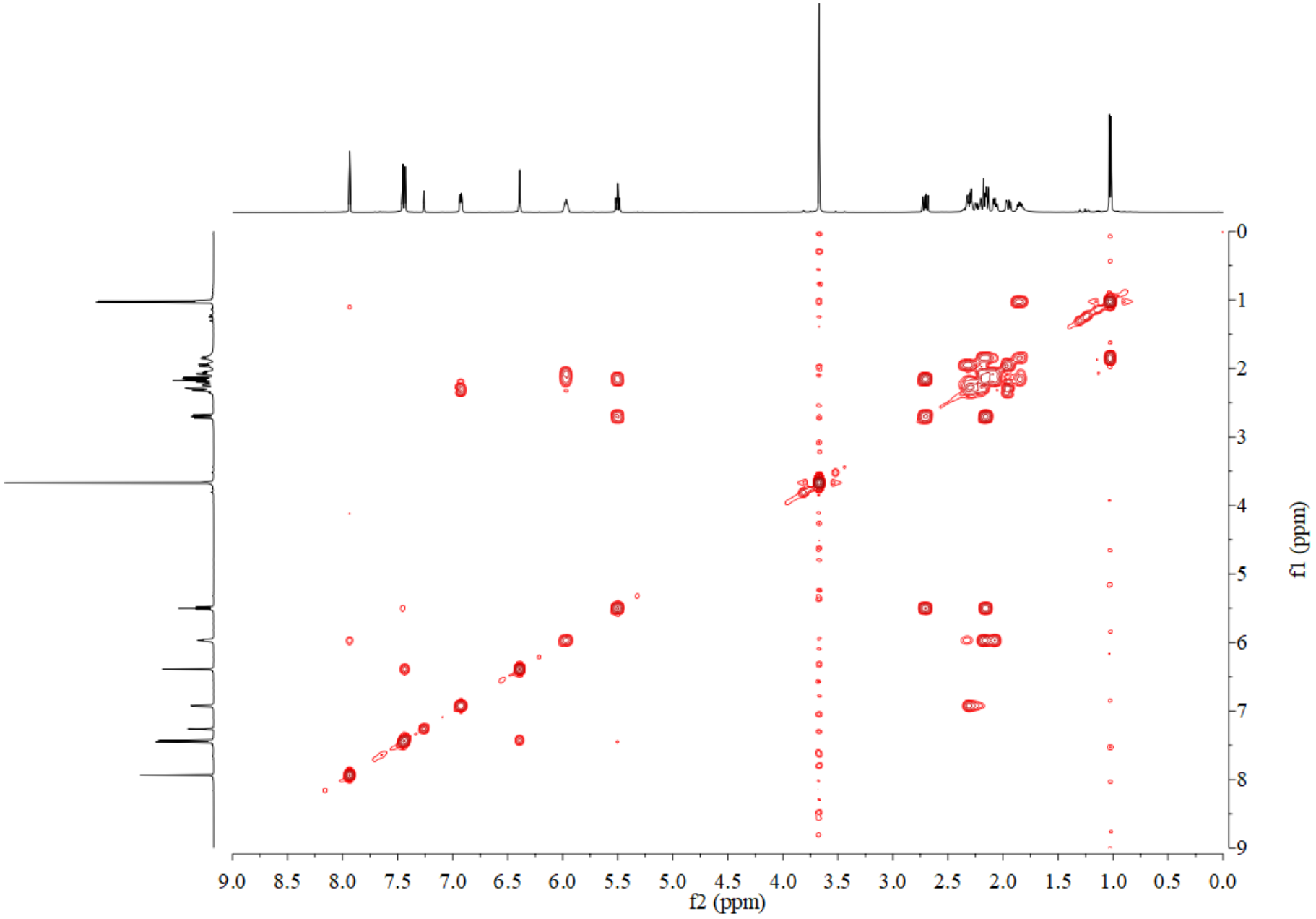


**Figure S8.** NOESY spectrum (500 MHz) of **1** in $CDCl_3$.

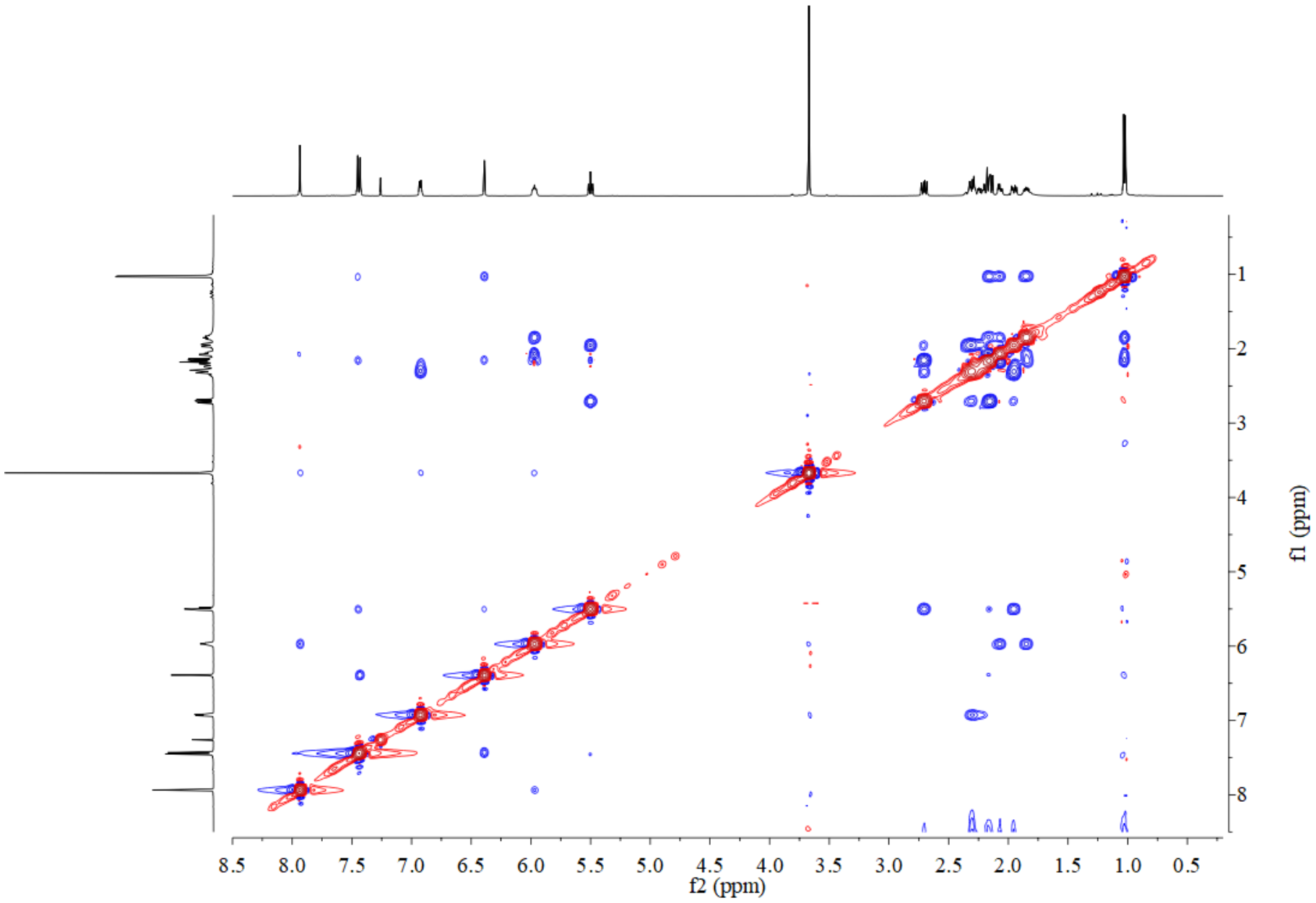
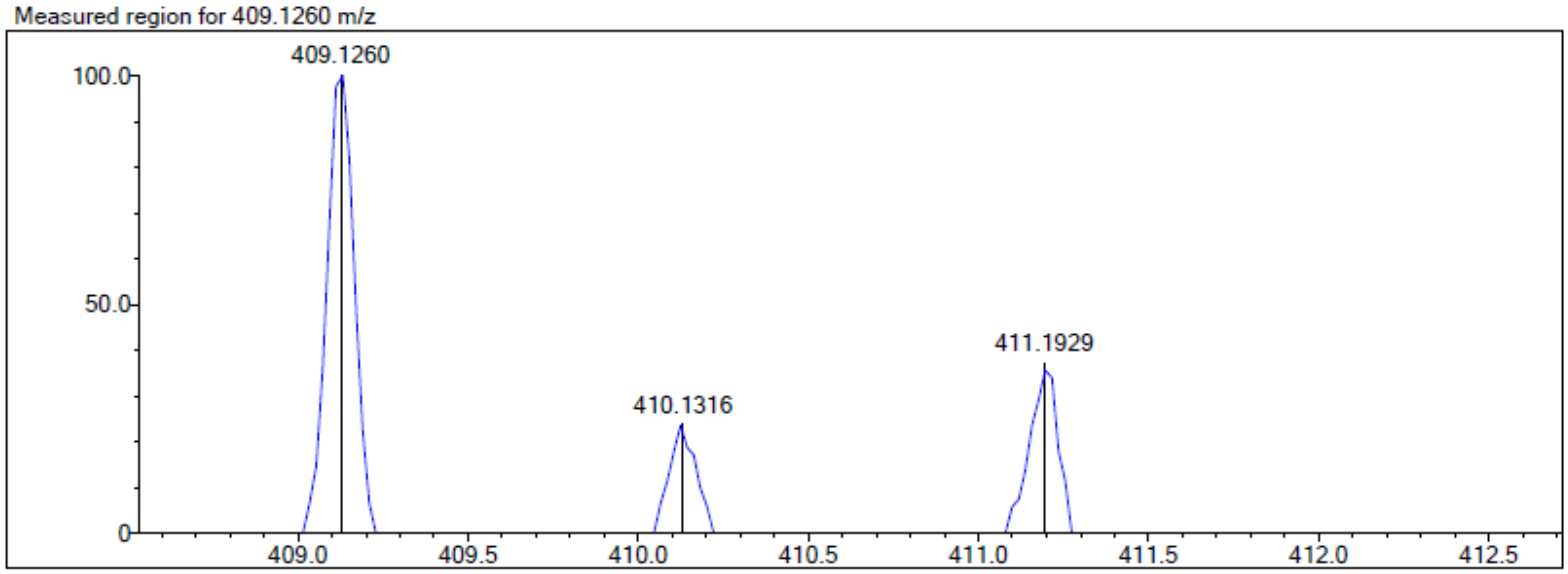
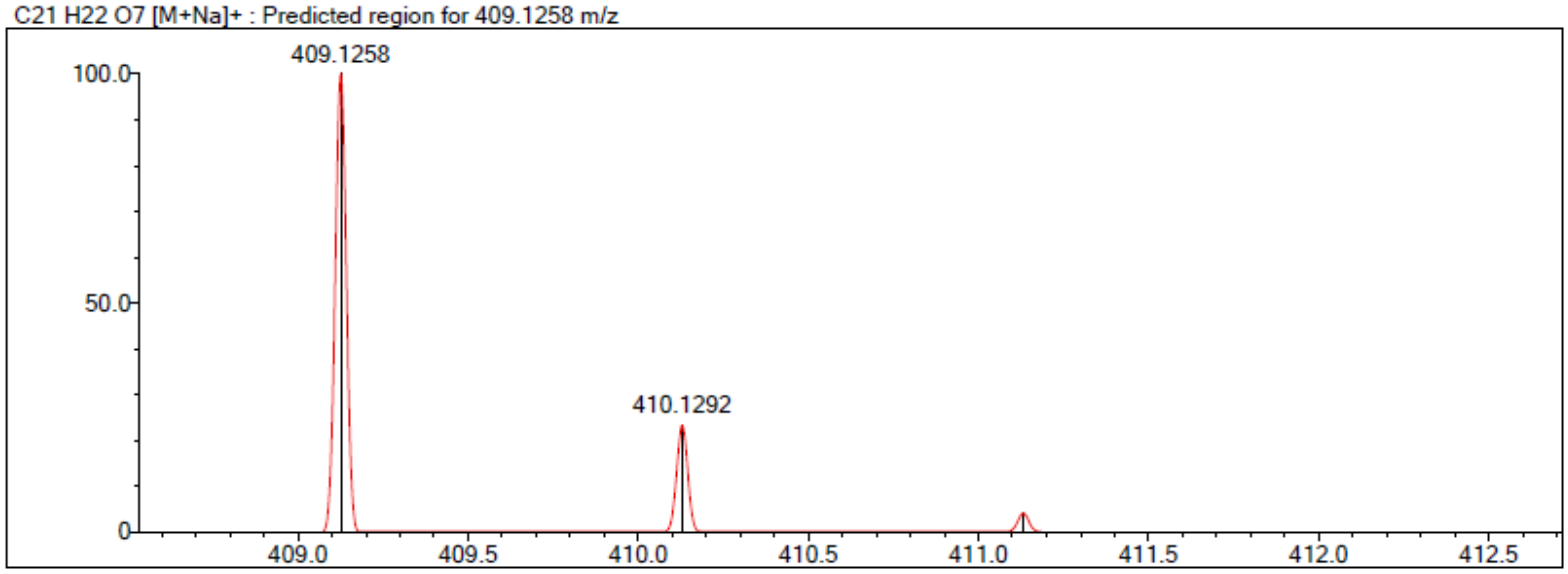


**Figure S9.** HRESIMS spectrum of **1**.




| Rank | Score | Formula (M) | Ion | Meas. m/z | Pred. m/z | Df. (mDa) | Df. (ppm) | Iso | DBE |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 28.32 | C21 H22 O7 | [M+Na]+ | 409.1260 | 409.1258 | 0.2 | 0.49 | 28.32 | 11.0 |

**Figure S10.** IR (KBr disc) spectrum of **1**.

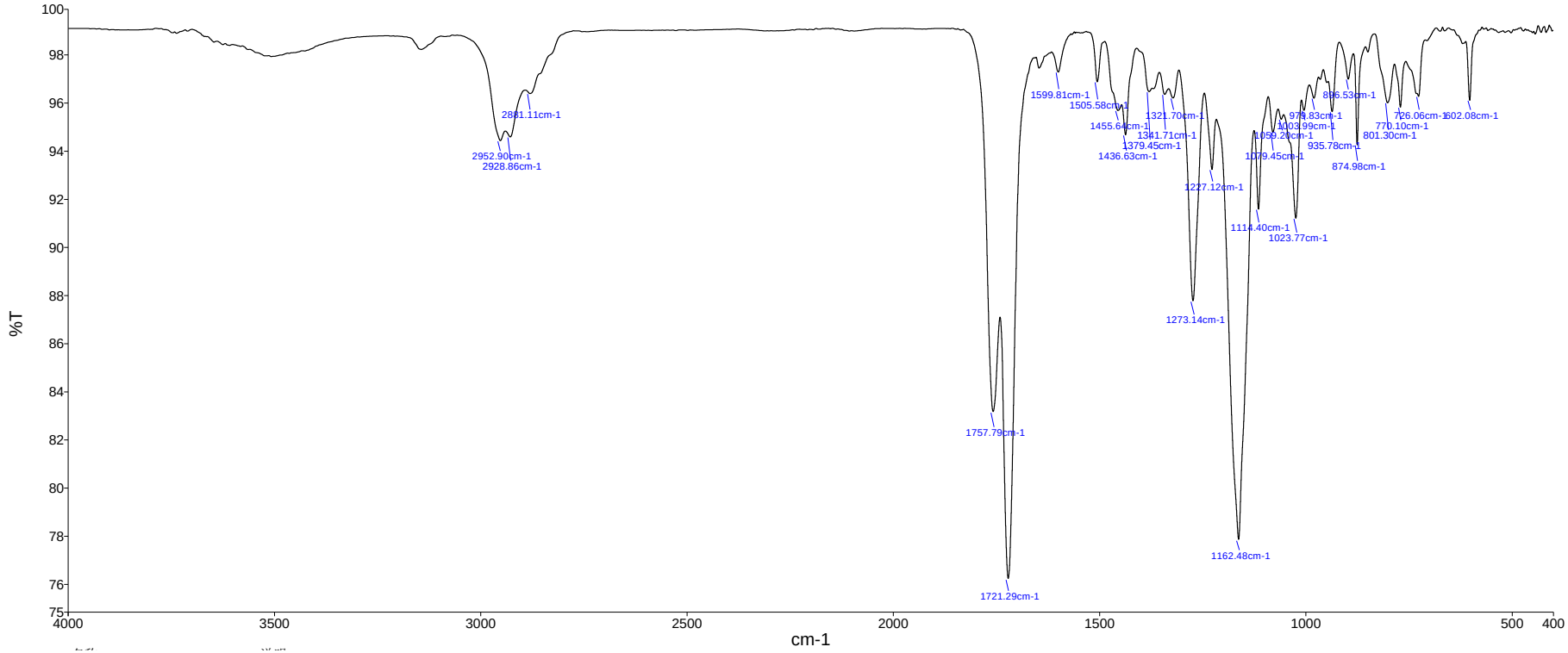


**Figure S11.** CD spectrum of **1**.

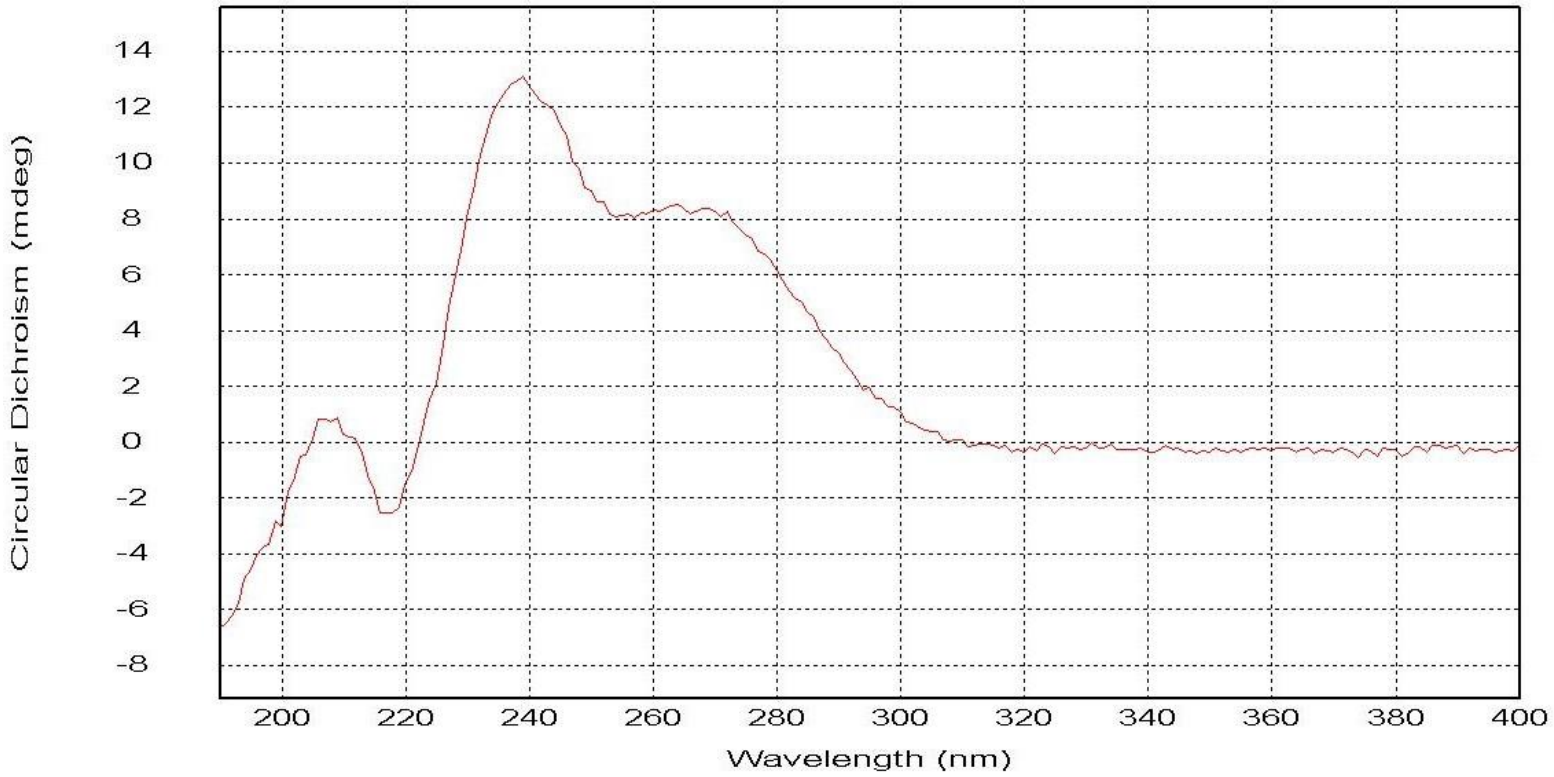


**Figure S12.** UV spectrum of **1**.

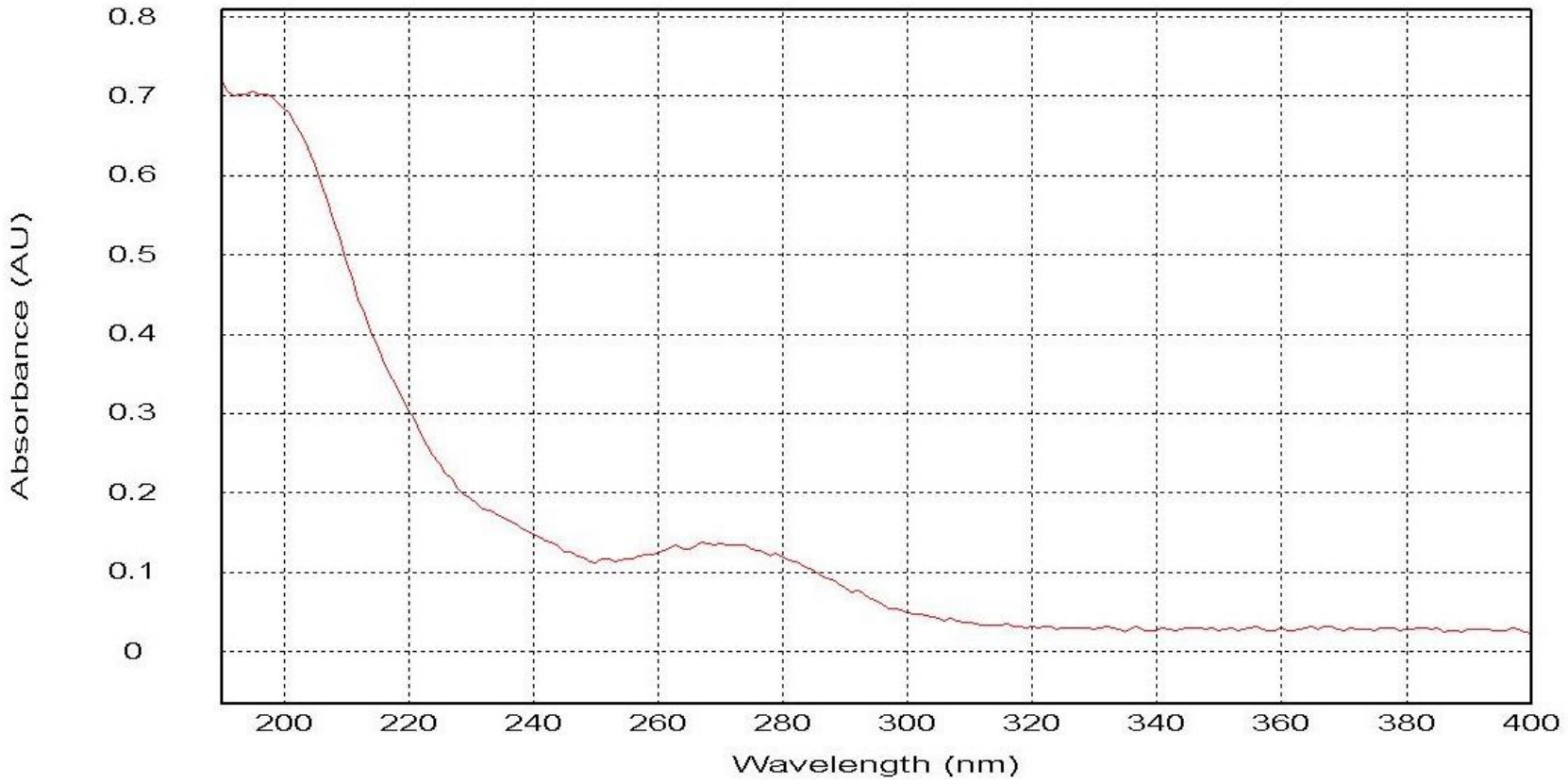


**Figure S13.** $^{1}$H NMR spectrum (500 MHz) of **2** in $CDCl_3$.

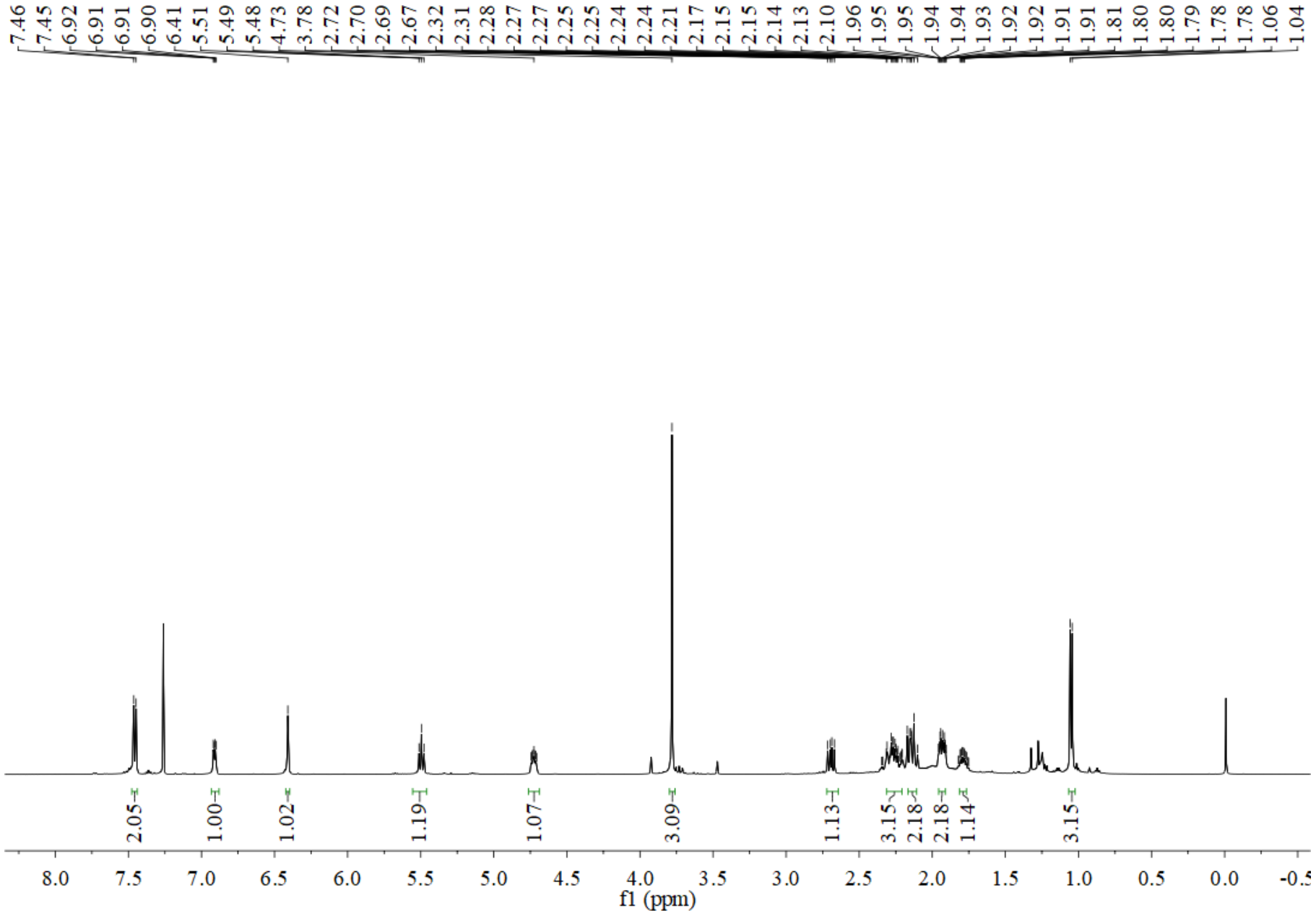


**Figure S14.** $^{13}C$ NMR spectrum (125 MHz) of **2** in $CDCl_3$.

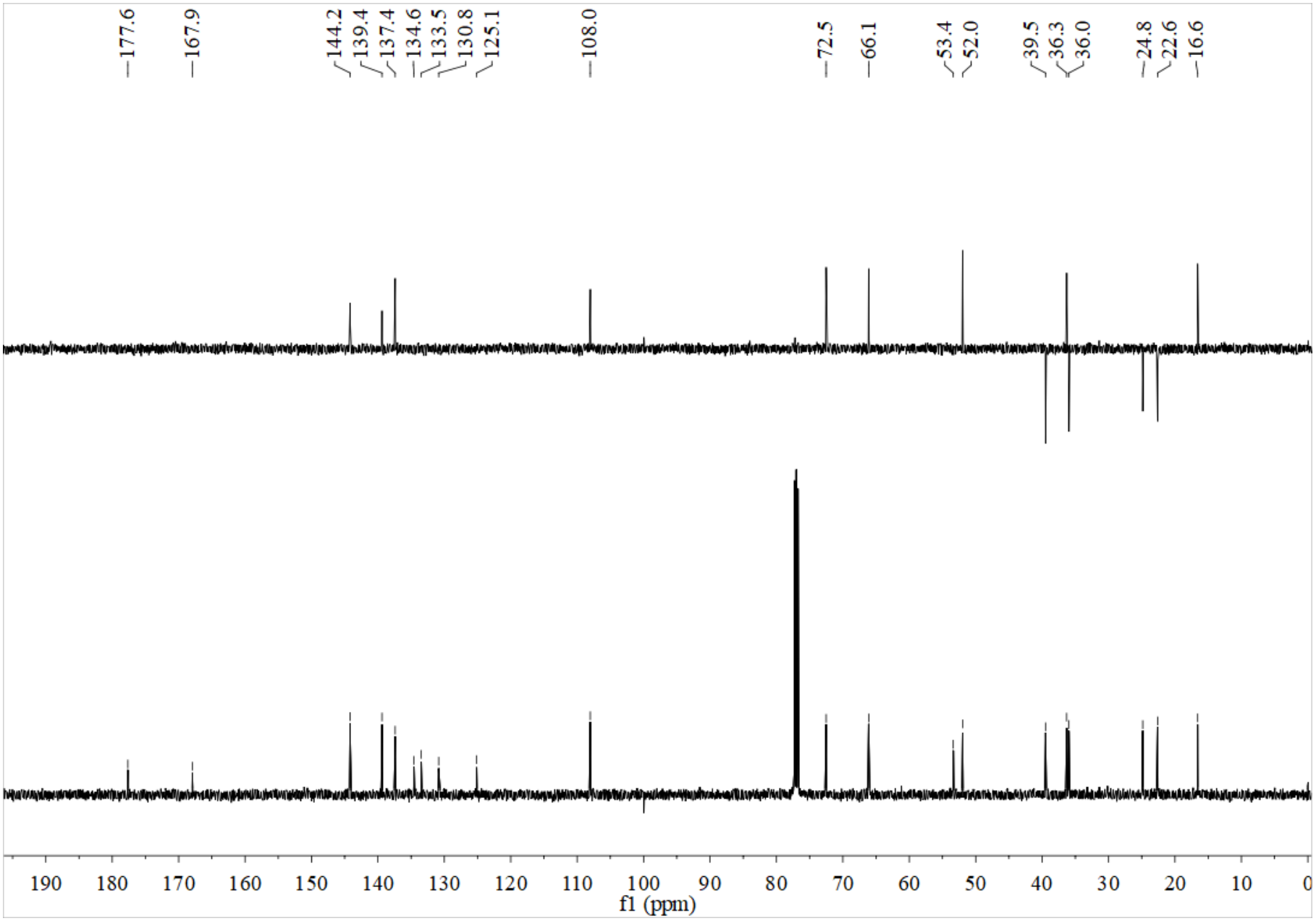


**Figure S15.** HSQC spectrum (500 MHz) of **2** in $CDCl_3$.

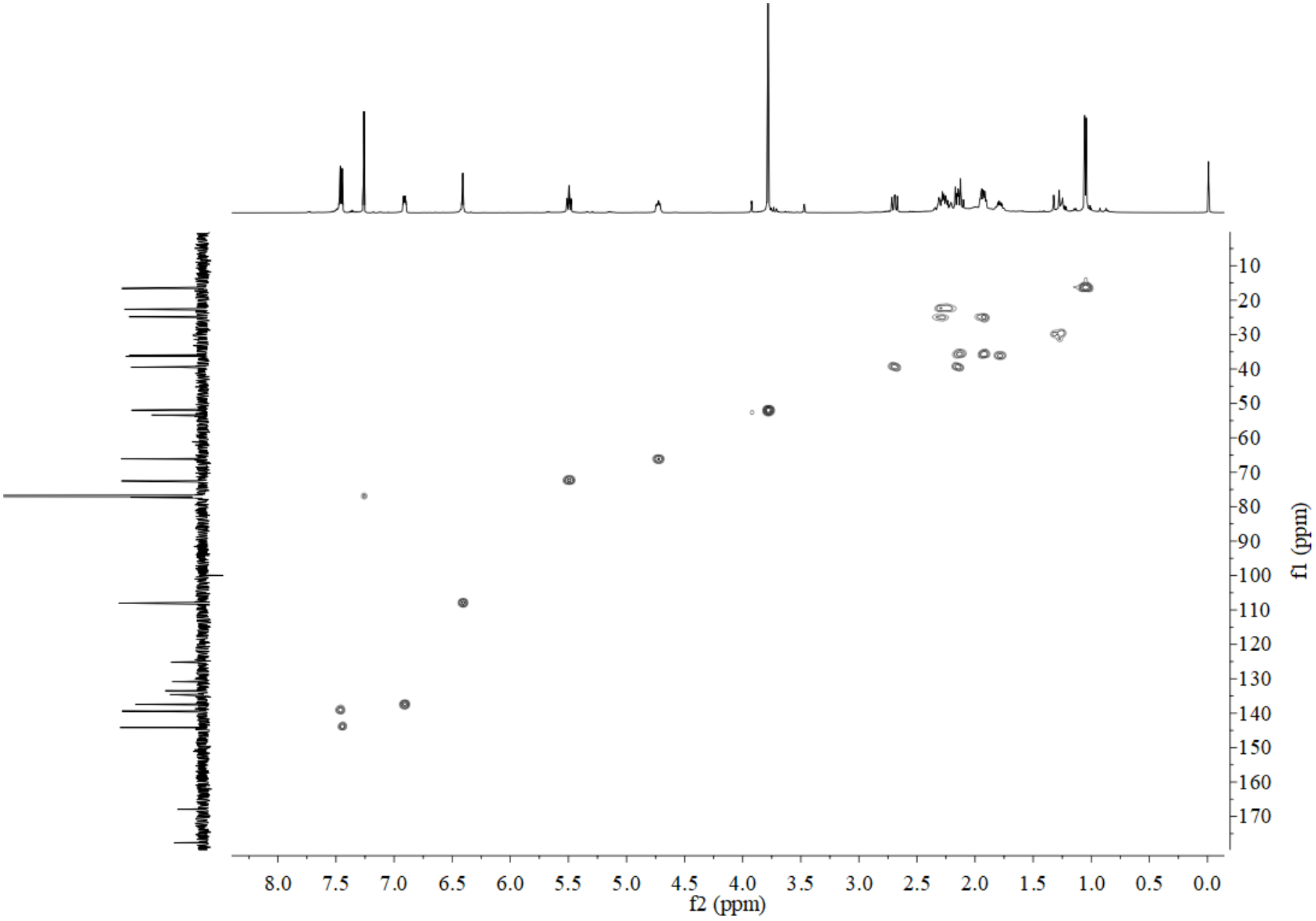


**Figure S16.** HMBC spectrum (500 MHz) of **2** in $CDCl_3$.

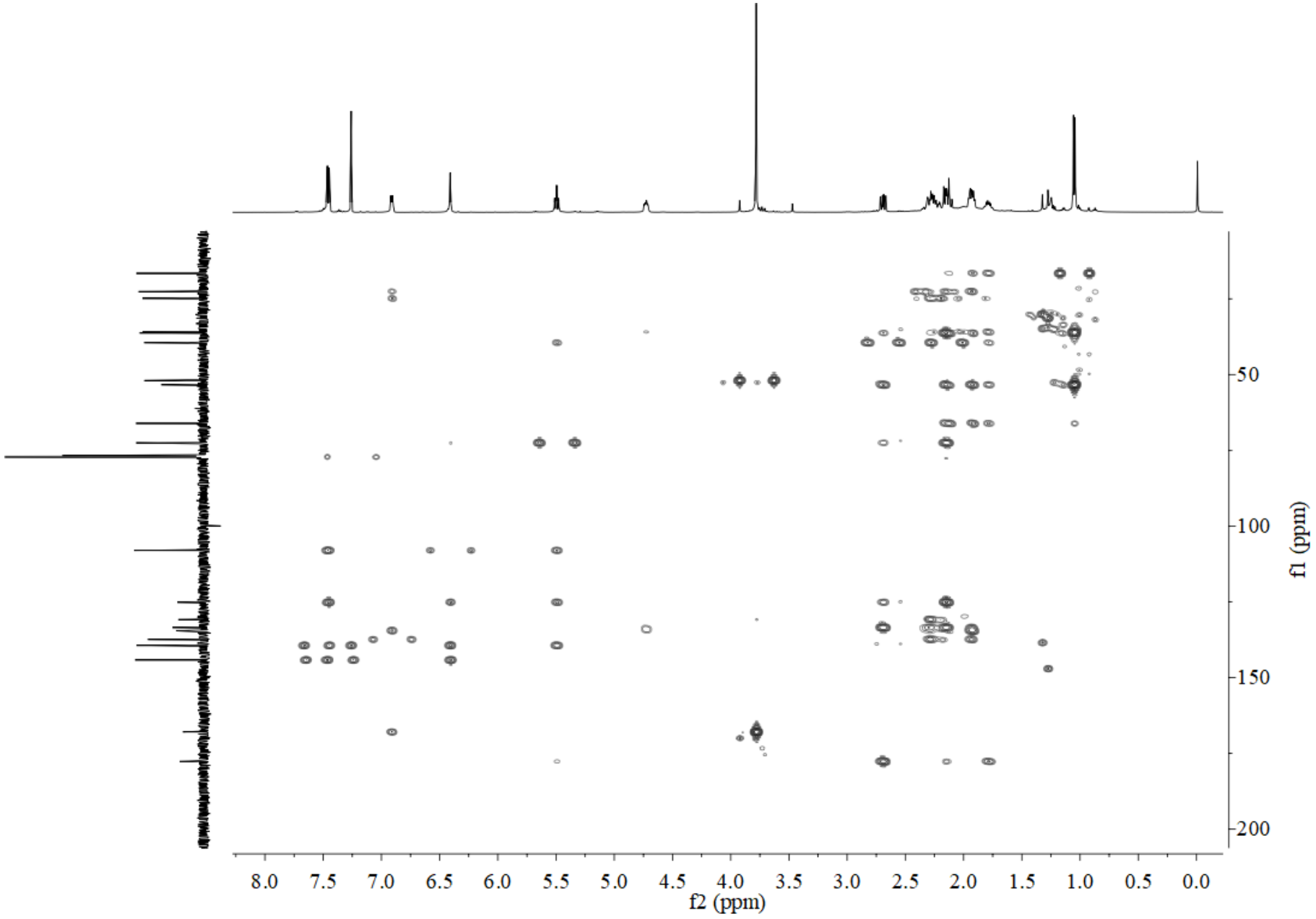


**Figure S17.** $^{1}H–^{1}H$ COSY spectrum (500 MHz) of **2** in $CDCl_3$.

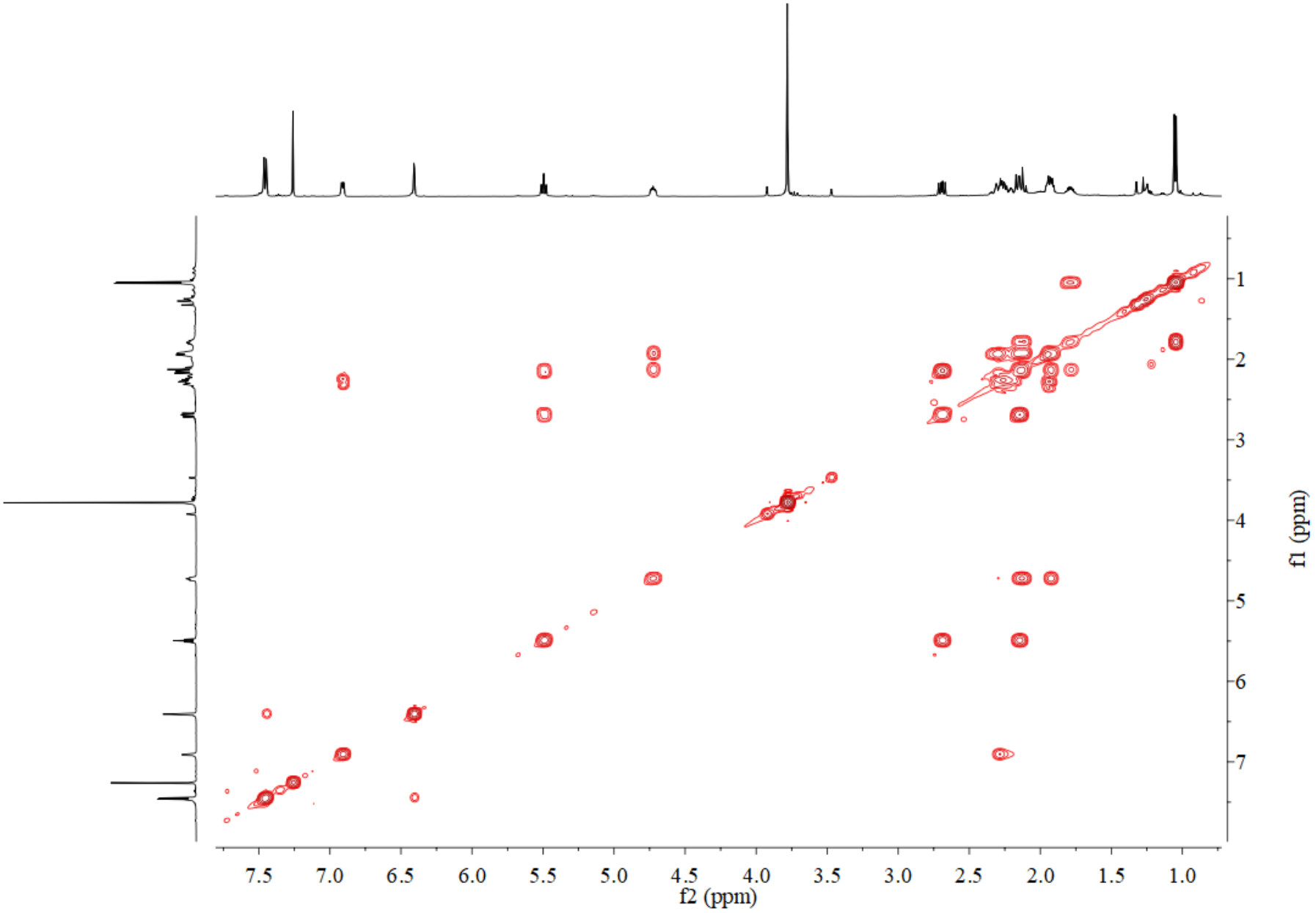


**Figure S18.** NOESY spectrum (500 MHz) of **2** in $CDCl_3$.

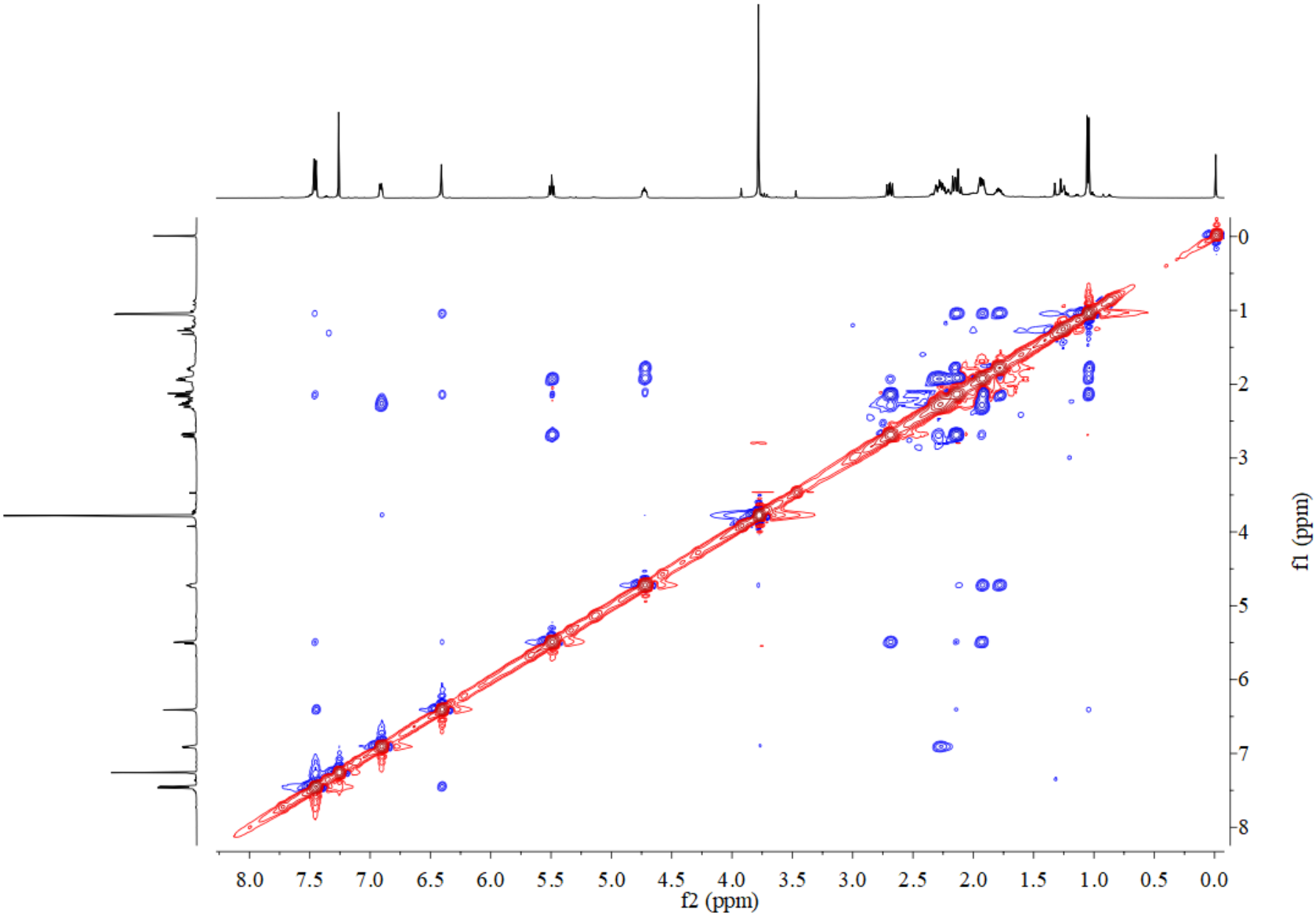
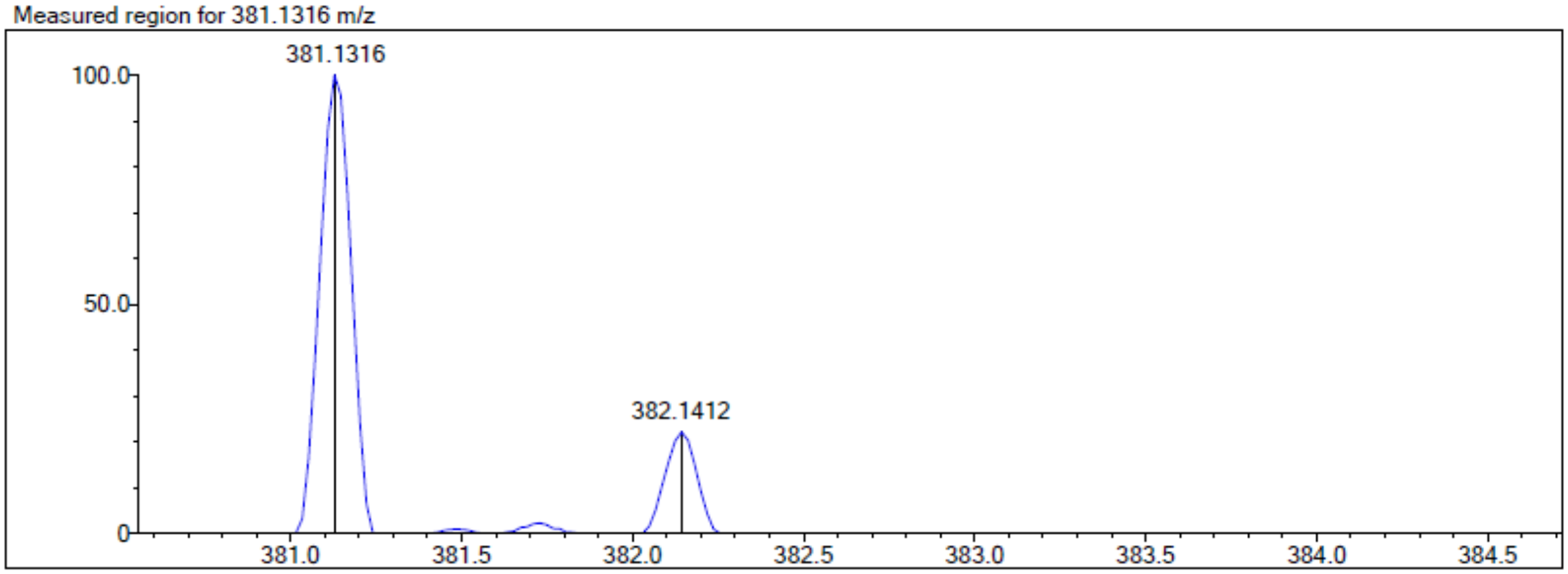
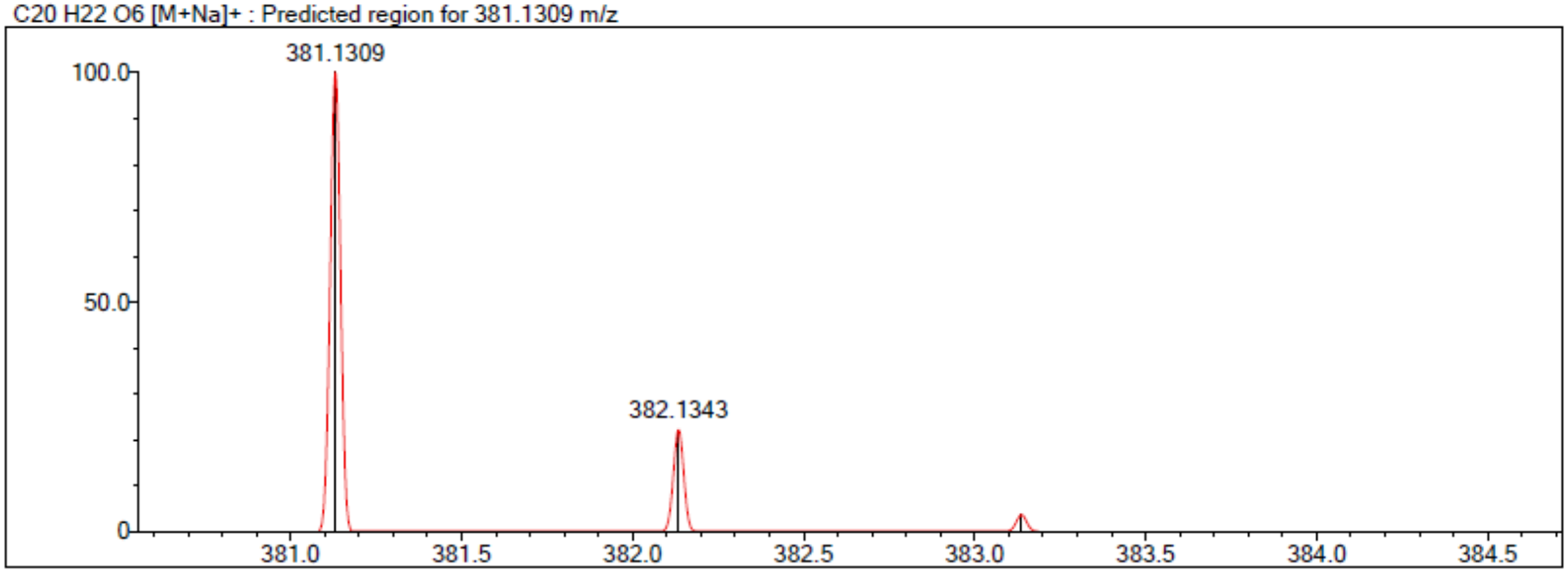


**Figure S19.** HRESIMS spectrum of **2**.




| Rank | Score | Formula (M) | Ion | Meas. m/z | Pred. m/z | Df. (mDa) | Df. (ppm) | Iso | DBE |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 80.22 | C20 H22 O6 | [M+Na]+ | 381.1316 | 381.1309 | 0.7 | 1.84 | 81.94 | 10.0 |

**Figure S20.** IR (KBr disc) spectrum of **2**.

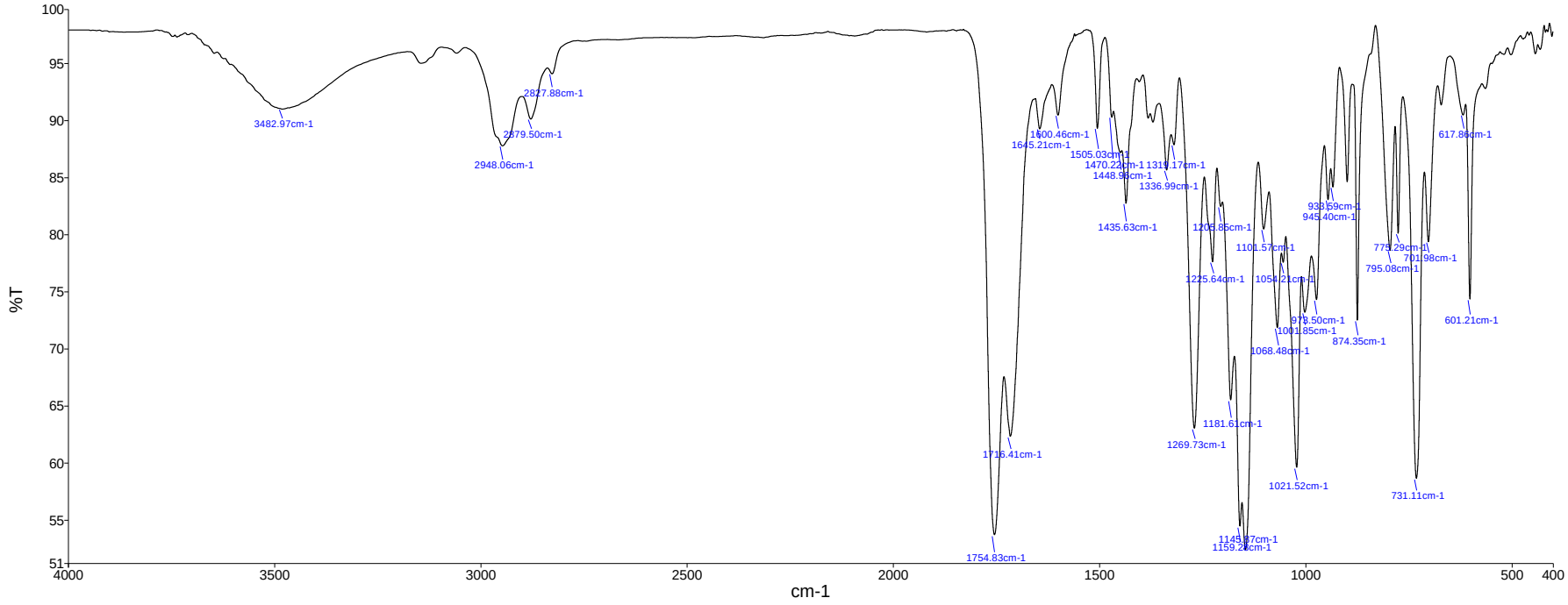


**Figure S21.** CD spectrum of **2**.

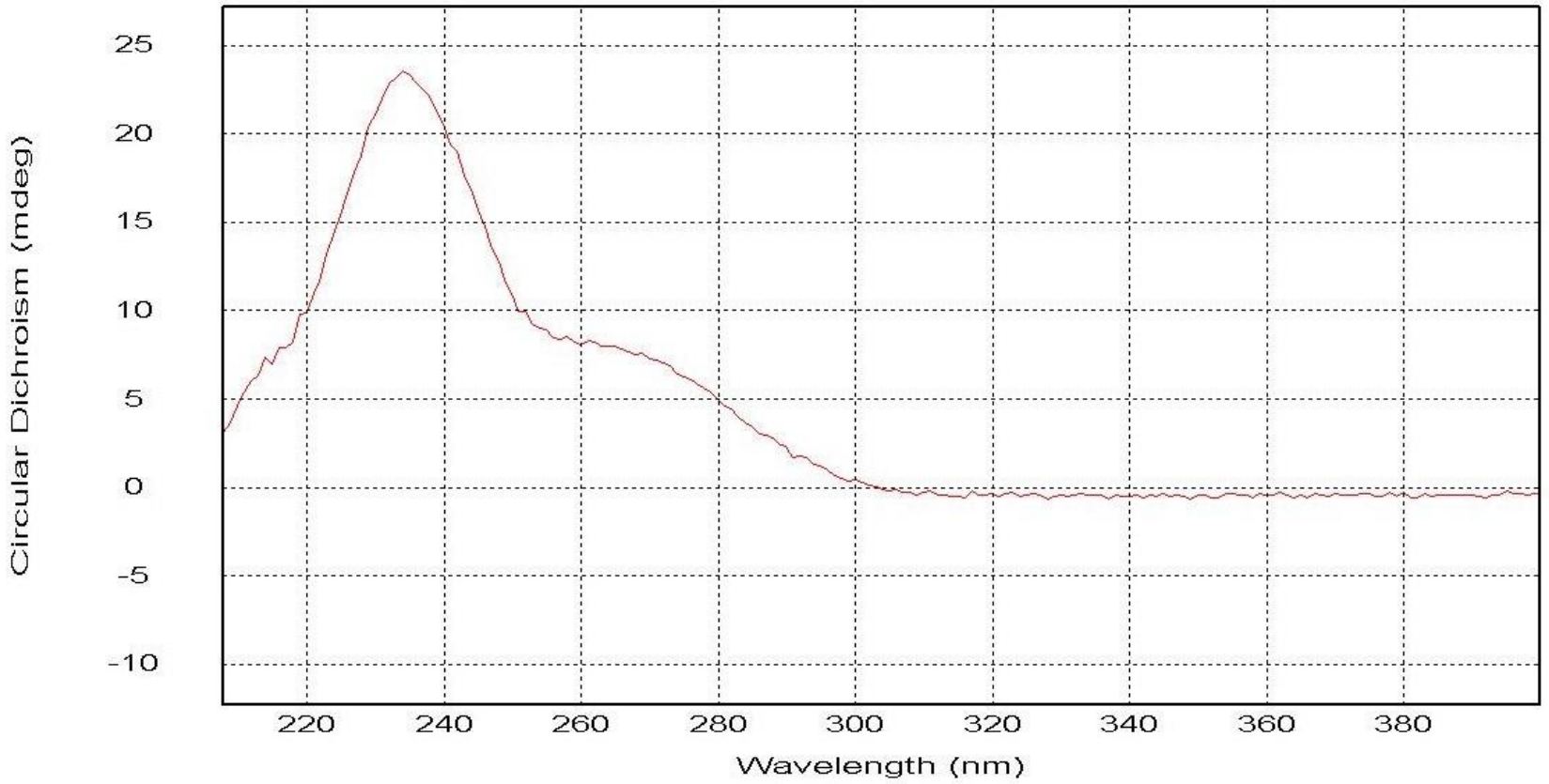


**Figure S22.** UV spectrum of **2**.