

# Molecular Diversity from Longipinenes of *Santolina viscosa* Lag. through Acid Catalysis: Biocidal Activity

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## EXPERIMENTAL SECTION

### General Remarks

NMR spectra were recorded on Bruker Nanobay Avance III HD 600 MHz spectrometer (magnetic field: 14.09 Tesla; probes: QCI-P CryoProbe™ (5mm quad probe with reverse sensing)  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ,  $^{15}\text{N}$ ; gradients in the Z axis; thermostatted automatic changer). Proton-decoupled  $^{13}\text{C}$  NMR and DEPT-135 were measured in all cases. HMBC, edited HSQC, COSY, TOCSY and NOESY experiments were used for the complete signal assignment. Chemical shifts ( $\delta$ ) are expressed in ppm and coupling constants ( $J$ ) in hertz (Hz). Chemical shifts are reported using  $\text{CDCl}_3$  as internal reference. IR Spectra were recorded on a Bruker Alpha spectrometer. Mass spectra were recorded on a Waters Xevo by LC-QToF-MS by electrospray ionization. X-ray structure analyses were performed on a Bruker AXS Smart APEX diffractometer. Using Olex2 [23], the structure was solved with the SHELXT [24] structure solution program using Intrinsic Phasing and refined with the SHELXL [25] refinement package using Least Squares minimization. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2 mm DC-Fertigfolien Alugram® XtraSil G/UV254 silica gel plates. The TLC plates were visualized with UV light and 7% phosphomolybdic acid/heat. Flash chromatography was performed on silica gel 60 (0.04–0.06 mm) using different eluents depending on the compound to be separated. Commercially available chemicals such as silicotungstic acid hydrate, indium chloride and fluorosulfonic acid were obtained from Aldrich Chemical Co., Alfa Aesar used as received. Zeolite Y-CBV720 was supplied by the “Instituto Universitario Mixto de Tecnología Química (ITQ), Universidad de Valencia”. Reactions were performed under nitrogen atmosphere, using oven-dried glassware in all cases. Additionally, anhydrous  $\text{CH}_2\text{Cl}_2$  was distilled from  $\text{CaH}_2$  under a nitrogen atmosphere.

### Computational Chemistry Calculations

Computational calculations were performed with Spartan'20 (Wavefunction Inc., Irvine, CA, USA). To obtain the  $^{13}\text{C}$  NMR data by computational calculation, the automated protocol implemented in Spartan'20 has been followed [26]. This protocol consists of five steps: (1) systematic conformational search using MMFF molecular mechanics, eliminating duplicate conformers and those with energy 40 kJ/mol above the global minimum, (2) geometric calculation using HF/3-21G, also eliminating duplicate conformers and those with energy higher than 40 kJ/mol above the global minimum; (3) energy calculation with the  $\omega\text{B97X-D/6-31G}^*$  model and removal of conformers above 15 kJ/mol with respect to the global minimum, (4) geometric calculation with the  $\omega\text{B97X-D/6-31G}^*$  model and removal of conformers with energies higher than 10 kJ/mol from that of the global minimum, (5) energy calculation with the  $\omega\text{B97X-V/6-311+G(2df,2p)[6-311G}^*]$ , and finally (6) the NMR calculation (following calculation of Boltzmann weights for conformationally flexible molecules) using the  $\omega\text{B97X-D/6-31G}^*$  method that has been corrected empirically based on the comparison of calculated and experimental  $^{13}\text{C}$  shifts for ~2000 rigid molecules. These corrections are on the order of 1–3 ppm.

### Biocidal Activity

*S. littoralis*, *M. persicae* and *R. padi* colonies were maintained at ICA-CSIC, reared on an artificial diet, bell pepper (*Capsicum annuum*) and barley (*Hordeum vulgare*) plants, respectively, and kept at  $22 \pm 1^\circ\text{C}$  and  $>70\%$  RH, with a photoperiod of 16:8 h (L:D) in a custom-made walk-in growth chamber. The bioassays were conducted as described [27]. The upper surface of *C. annuum* and *H. vulgare* leaf disks or fragments (1.0  $\text{cm}^2$ ) were treated with 10  $\mu\text{L}$  of the test substance. The products were tested at dose of 5 and 2.5  $\text{mg/mL}$ . A total of 5 to 7 Petri dishes or 20 ventilated square plastic boxes (2  $\times$  2 cm) with 2 sixth-instar *S. littoralis* larvae ( $>24$  h after molting) or 10 apterous aphid adults (24–48 h old) each were allowed to feed in a growth chamber (until 75% larval consumption of control disks or 24 h for aphids, environmental conditions as above). Each experiment was repeated 2–3 times. Feeding inhibition or aphid settling was calculated by measuring the disk surface consumption (digitalized with <https://imagej.nih.gov/ij/>) [28] or by counting the number of aphids on each leaf fragment. Feeding/settling inhibition (%FI or %SI) was calculated as  $\% \text{FI/SI} = [1 - (T/C) \times 100]$ , where T and C represent feeding/settling on treated and control leaf disks, respectively. The antifeedant effects (%FI/SI) were analyzed for significance by the nonparametric Wilcoxon paired signed-rank test comparing the consumption/settling between the treatment and control leaf disks. Compounds with an FI/SI  $>60\%$  were further tested in a dose-response experiment (1:2 serial dilutions to cover a range of activities between 100 and  $<50\%$  feeding inhibition with a minimum

of 3 doses) to calculate their effective dose LC<sub>50</sub> (dose to give a 50% settling reduction) from linear regression analysis (% FI/SI on Log-dose, STATGRAPHICS Centurion XVI, version 16.1.02).

Experiments for phytotoxic evaluation were conducted with *Lactuca sativa*, and *Lolium perenne* seeds (40 seeds/test) in 12-well microplates, as described previously [29]. The compounds were tested at concentrations of 5 mg/mL. Juglone (97%; Sigma) was included as positive control (0.1 mg/mL), resulting in 100% germination inhibition. Germination was monitored for six (*L. sativa*) or seven days (*L. perenne*), and the root length (25 plants randomly selected and digitalized) was measured (ImageJ, <http://rsb.info.nih.gov/ij/>) at the end of the experiment. A nonparametric analysis of variance (ANOVA) was performed on root/leaf length data.

*Hyalomma lusitanicum* engorged female ticks were collected in central Spain (Finca La Garganta, Ciudad Real) from their host (deer) and *Rhipicephalus bursa* adults were collected from the vegetation. Adults of *R. bursa* were fed in vitro to obtain engorged females [30]. Both engorged females were maintained at 22–24 °C and 70% RH until oviposition and egg hatching. Resulting larvae (4–6 weeks old) were used for the bioassays. Briefly, 50 µL of test solution were added to 25 mg of powdered cellulose at different concentrations (initial concentration of 10 mg/mL) and the solvent was evaporated. For each test, three replicates with 20 larvae each were used. Dead ticks were counted after 24 h of contact with the treated cellulose at the environmental conditions described, using a binocular magnifying glass. The larvicidal activity data are presented as percent mortality corrected according to Schneider–Orelli’s formula. Effective lethal doses (LD<sub>50</sub>) were calculated by Probit Analysis (5 serial dilutions, STATGRAPHICS Centurion XVI, version 16.1.02, Statgraphics Technologies, Inc., P.O. Box 134, The Plains, Virginia 20198, USA).

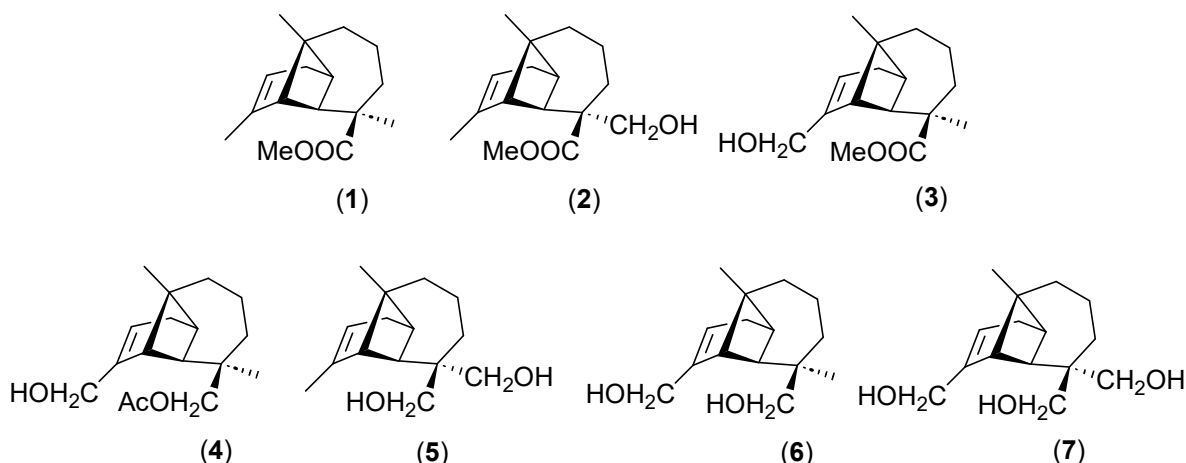
A *Meloidogyne javanica* population maintained on *Lycopersicon esculentum* plants (var. Marmande) in pot cultures at 25 ± 1 °C with 70% relative humidity was used in this work. Egg masses of *M. javanica* were hand-picked from infected tomato roots. Second stage juveniles (J2) were obtained from hatched eggs by incubating egg masses in a water suspension at 25 °C for 24 h. Bioassays were performed in 96-well plates (BD Falcon, Plants 2022, 11, 418 8 of 9 San Jose, CA, USA) as described by Andrés *et al.* [31]. Compounds were dissolved in water with a 5% DMSO-Tween solution (0.5% Tween 20 in DMSO), and 5 µL of this solution was added to 95 µL of water containing 90–100 nematodes to obtain an initial concentration of 1 mg/mL per well. Treatments were replicated 4 times. As a control, 4 wells were filled with 95 µL of solvent. The plates were covered to prevent evaporation and were maintained in the dark at 25 °C. After 72 h, the dead J2 were counted under a binocular microscope. The nematocidal activity data were presented as percent dead J2s and corrected according to Schneider–Orelli’s formula [32].

## Plant Material

*Santolina viscosa* Lag. (Compositae) was collected in Los Yesares (Tabernas), Almería, Spain, in July 2020. It was identified in “Departamento de Biología Vegetal, Universidad de Almería”.

## Extraction and Isolation

The air-dried material (658 g) was extracted by immersion in Et<sub>2</sub>O for 24h, yielding in 70 g of extract. The ethereal extract was dissolved in 175 mL of hot chloroform and 875 mL of boiling methanol was slowly added. The solution was allowed to cool to room temperature and then further cooled to -4 °C for 4 days. Vacuum filtration produced 2 g of solid residue (waxes) and 60 g of dewaxed extract. A portion of 34 g was defatted, dissolved in Et<sub>2</sub>O, and extracted with 1N NaOH solution to yield 22 g of a neutral fraction. The aqueous phase was acidified with 2N HCl (pH 2) and extracted with Et<sub>2</sub>O (x3), obtaining 11 g of dewaxed acidic extract. **Acidic fraction:** a portion of 5 g of the acidic extract was esterified with CsCO<sub>3</sub> (13 g) and CH<sub>3</sub>I (3 mL) in DMF (60 mL), resulting in 4g of esterified acidic extract. The acid-esterified fraction underwent column chromatography on silica gel using a hexane/AcOEt mixture. Three main compounds (1–3) were obtained. Fraction 1 [hexane/AcOEt, (7:3)] consisted in 500 mg of 1 and fraction 2, a mixture of 1 g of 2 and 3. F2 was rechromatographed [hexane/AcOEt, (8:2)] to obtain 500 mg of 2 and 300 mg of a mixture 2 and 3 (2:1). **Neutral fraction:** a portion of 3 g of the neutral fraction underwent column chromatography on silica gel using hexane/AcOEt/MeOH mixtures of increasing polarity as eluents. Four main compounds (4–7) with longipin-9-ene structure were isolated. Fraction 1 [hexane/AcOEt, (7:3)] consisted in 402 mg of 4. Fraction 2 [hexane/AcOEt, (6:4)] consisted in 907 mg of 5. Fraction 3 [hexane/AcOEt, (6:4)] consisted in 460 mg of 6. The most polar compound in the extract (7) was obtained using MeOH as eluent (503 mg). The isolated longipinenes 1–7 match those described by Barrero *et al.* [20,21].



**Figure 1.** Seven main compounds with  $\Delta^9$ -longipinene structures (1–7) of which longipinene acids were isolated as methyl esters (1–3).

## Experimental procedures

### General procedure for treatment of longipinenes 1, 2 and 5 with zeolite Y-CBV720

Under  $N_2$  atmosphere, zeolite Y-CBV720 (50% by weight of the starting material) was added to a solution of longipinene (1 eq.) in anhydrous  $CH_2Cl_2$  (10 mL/mmol). The mixture was stirred overnight at reflux. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a short plug of silica gel and celite (4:1), which was washed with  $CH_2Cl_2$ . Finally, the resulting crude from each reaction was concentrated under reduced pressure and purified through flash silica gel column chromatography (hexane/EtOAc mixtures) to yield pure products 9, 10, 12, 16 and 17. Yields are reported in Table 1.

### General procedure for treatment of longipinenes 1, 2 and 5 with silicotungstic acid hydrate ( $H_6SiW_{12}O_{41}$ )

Under  $N_2$  atmosphere,  $H_6SiW_{12}O_{41}$  (0.05 eq.) was added to a solution of longipinene (1 eq.) in anhydrous  $CH_2Cl_2$  (10 mL/mmol). The mixture was stirred overnight at room temperature. A solution of  $Et_3N$  (0.25 mL/mmol) in ethyl acetate (0.06 mL/mmol) was added, and the mixture was diluted with water. The aqueous phase was extracted with ethyl acetate (x3). The combined organic layer was dried over anhydrous  $MgSO_4$  and the solvent was removed. In this manner, products 10, 12 and 13 were obtained after purification through flash silica gel column chromatography (hexane/EtOAc mixtures) from their respective processes. Yields are reported in Table 1.

### General procedure for treatment of natural longipinenes 1, 2 and 5 with indium chloride ( $InCl_3$ )

Under  $N_2$  atmosphere,  $InCl_3$  (0.2 eq.) was added to a solution of longipinene (1 eq.) in anhydrous  $CH_2Cl_2$  (0.03 mM) was added. The mixture was stirred overnight at reflux. The solvent was removed under reduced pressure and crude reaction mixture was passed through a short plug of silica gel and celite (4:1), which was washed with  $CH_2Cl_2$ . Finally, the resulting crude from each reaction was concentrated under reduced pressure and purified through flash silica gel column chromatography. Products 9, 11 and 13–18 were obtained and their yields are reported in Table 1.

### General procedure for treatment of natural longipinenes 1, 2 and 5 with fluorosulfonic acid ( $HSO_3F$ )

Under  $N_2$  atmosphere,  $HSO_3F$  (1 eq.) was added to a solution of longipinene (1 eq.) in anhydrous nitropropano: $CH_2Cl_2$  (12:1) (10 mL/mmol) at  $-78^\circ C$ . The mixture was stirred at  $-78^\circ C$  for 30 min. A solution of  $Et_3N$  (0.25 mL/mmol) in ethyl acetate (0.06 mL/mmol) was added, and the mixture was diluted with water. The aqueous phase was extracted with ethyl acetate (x3). The combined organic layer was dried over anhydrous  $MgSO_4$  and the solvent was removed. Products 9, 12, 13, 17 and 18 were obtained from each reaction and purified through flash silica gel column (hexane/EtOAc mixtures). Yields are reported in Table 1.



### Protection of hydroxyl groups with MOM from longipinene 5

Under N<sub>2</sub> atmosphere, DIPEA (0.62 g, 4.8 mmol, 4 eq.) and MOMBr (0.40 g, 2.88 mmol, 2.4 eq) was added to a solution of **5** (0.29 g, 1.20 mmol, 1 eq.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (6 mL) at 0°C. The mixture was stirred at room temperature for 3h. The reaction mixture was diluted with water and extracted with ethyl acetate (x3). The combined organic layer was washed with brine and dried over anhydrous MgSO<sub>4</sub>. The resulting crude was concentrated under reduced pressure and purified through flash silica gel column chromatography using a hexane/AcOEt mixture (8:2) as the solvent. An isomeric mixture with partially protected hydroxyl groups (**19a/19b**) (0.06 g, 0.24 mmol, 20%) and compound **5** with fully protected hydroxyl groups (0.23 g, 0.72 mmol, 60%) were obtained as colorless syrup.

### Treatment of the isomeric mixture 19a/19b with indium chloride (InCl<sub>3</sub>)

Under N<sub>2</sub> atmosphere, InCl<sub>3</sub> (0.01 g, 0.04 mmol, 0.2 eq.) was added to a solution of **19a/19b** (0.06 g, 0.21 mmol, 1 eq.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (9 mL). The mixture was stirred overnight at reflux. The solvent was removed under reduced pressure, and the crude reaction mixture was passed through a short plug of silica gel and celite (4:1), which was washed with CH<sub>2</sub>Cl<sub>2</sub>. Finally, the resulting crude was concentrated under reduced pressure and purified through flash silica gel column chromatography using a hexane/AcOEt mixture (8:2) as the solvent. Compound **20** was obtained as a colorless syrup (0.04 g, 0.16 mmol, 76%).

### Epoxidation reaction of longipinenes 2 and 5

Under N<sub>2</sub> atmosphere, *m*CPBA (2 eq.) was added to a solution of longipinene (1 eq.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (20 mL/mmol). The mixture was stirred at 0°C for 2h. To the reaction mixture, 10% Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, saturated NaHCO<sub>3</sub>, and ethyl acetate were added and stirred for 30 min. The organic layer was washed with saturated NaHCO<sub>3</sub> and brine and dried over anhydrous MgSO<sub>4</sub>. From longipinene **2**, epoxide **21** was obtained as colorless syrup (0.17g, 0.61 mmol, 82%). From longipinene **5**, epoxide **22** was obtained as colorless syrup (1.02 g, 4.04 mmol, 84%).

### Treatment of epoxides 21 and 22 with indium chloride (InCl<sub>3</sub>)

Under N<sub>2</sub> atmosphere, InCl<sub>3</sub> (0.2 eq.) was added to a solution of epoxide (1 eq.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (0.03 mM) at 0°C. The mixture was stirred for 1h. The solvent was removed under reduced pressure, and the crude reaction mixture was passed through a short plug of silica gel and celite (4:1), which was washed with CH<sub>2</sub>Cl<sub>2</sub>. Finally, the resulting crude was concentrated under reduced pressure and purified through flash silica gel column chromatography using a hexane/AcOEt mixture as the solvent. From epoxide **21**, *secolongibornene* aldehyde **23** was obtained (0.12g, 0.44 mmol, 53%). From epoxide **22**, *secolongibornene* aldehyde **24** was obtained (0.21g, 0.83 mmol, 51%).

### Treatment of epoxides with zeolite Y-CBV720

Under N<sub>2</sub> atmosphere, zeolite Y-CBV-720 (50% by weight of the starting material) was added to a solution of longipinene (1 eq.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (10 mL/mmol). The mixture was stirred for 5h at room temperature. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a short plug of silica gel and celite (4:1), which was washed with CH<sub>2</sub>Cl<sub>2</sub>. Finally, the resulting crude from each reaction was concentrated under reduced pressure and purified through flash silica gel column chromatography (hexane/EtOAc mixtures). From epoxide **21**, *secolongibornene* aldehyde **23** was obtained (0.13g, 0.49 mmol, 57%). From epoxide **22**, *secolongibornene* aldehyde **24** was obtained (0.22g, 0.88 mmol, 54%).

## Characterization of molecules 9-24

**Methyl 14-hydroxylongipin-9(12)-en-15-oate (9).** From longipinene **2**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3494, 2938, 1707, 1436, 1195, 1059, 889, 840. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 4.72 (1H, s, H-12a), 4.49 (1H, s, H-12b), 3.68 (2H, m, H-14), 3.64 (3H, s, COOCH<sub>3</sub>), 2.35 (1H, d, *J* = 4.8 Hz, H-8), 2.09 (1H, d, *J* = 13.2 Hz, H-5a), 2.05 (1H, m, H-1), 1.80 (1H, s, H-7), 1.70 (1H, m, H-10a), 1.67 (1H, m, H-3a), 1.64 (1H, m, H-11a), 1.58 (1H, m, H-3b), 1.56 (1H, d, *J* = 14.4 Hz, H-5b), 1.52 (1H, m, H-4a), 1.44 (1H, m, H-4b), 1.38 (1H, m, H-11b), 1.10 (1H, ddd, *J* = 12.0, 9.0, 5.8 Hz, H-10b), 0.95 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 177.1 (C, C-15), 166.5 (C, C-9), 100.0 (CH<sub>2</sub>, C-12), 66.6 (CH<sub>2</sub>, C-14), 53.4 (CH, C-7), 52.0 (C, C-6), 51.7 (CH<sub>3</sub>, COOCH<sub>3</sub>), 49.3 (CH, C-8), 45.4 (CH, C-1), 44.2 (C, C-2), 42.8 (CH<sub>2</sub>, C-3), 29.8 (CH<sub>3</sub>, C-13), 29.1 (CH<sub>2</sub>, C-10), 25.2 (CH<sub>2</sub>, C-11), 24.9 (CH<sub>2</sub>, C-5), 20.0 (CH<sub>2</sub>, C-4). HRESIMS *m/z* 265.1797 [M + H]<sup>+</sup> calcd for [C<sub>16</sub>H<sub>24</sub>O<sub>3</sub> + H]<sup>+</sup> 265.1804.

**Longipin-9(12)-ene-14,15-diol (10).** From longipinene **5**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3333, 2924, 1454, 1376, 1032, 951, 872, 817. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 4.73 (1H, s, H-12a), 4.46 (1H, s, H-12b), 3.58 (2H, m, H-14), 3.55 (2H, s, H-15), 2.56 (1H, d,  $J$  = 4.8 Hz, H-8), 2.06 (1H, d,  $J$  = 3.6 Hz, H-1), 1.72 (1H, m, H-10a), 1.65 (1H, m, H-11a), 1.59 (1H, s, H-7), 1.56 (1H, m, H-3b), 1.45 (1H, m, H-4a), 1.43 (1H, m, H-4b), 1.39 (1H, m, H-11b), 1.32 (1H, m, H-5b), 1.14 (1H, ddd,  $J$  = 12.0, 9.0, 5.8 Hz, H-10b), 0.97 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 167.1 (C, C-9), 99.6 (CH<sub>2</sub>, C-12), 70.6 (CH<sub>2</sub>, C-15), 69.8 (CH<sub>2</sub>, C-14), 52.5 (CH, C-7), 47.2 (CH, C-8), 45.5 (CH, C-1), 44.4 (C, C-2), 42.9 (CH<sub>2</sub>, C-3), 41.4 (C, C-6), 29.9 (CH<sub>3</sub>, C-13), 29.6 (CH<sub>2</sub>, C-10), 27.0 (CH<sub>2</sub>, C-5), 25.2 (CH<sub>2</sub>, C-11), 20.1 (CH<sub>2</sub>, C-4).

**Methyl 14-hydroxylongiborn-7(8)-en-15-oate (11).** From longipinene **2**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3465, 1720, 1435, 1263, 1197, 1056. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.18 (1H, m, H-8), 3.74 (1H, d,  $J$  = 11.4 Hz, H-14a), 3.67 (1H, d,  $J$  = 11.4 Hz, H-14b), 3.60 (3H, s, COOCH<sub>3</sub>), 2.22 (1H, m, H-10a), 1.99 (1H, m, H-10b), 1.79 (1H, m, H-5a), 1.74 (1H, br s, H-1), 1.72 (1H, m, H-4a), 1.66 (1H, m, H-3a), 1.53 (1H, m, H-11a), 1.50 (1H, m, H-11b), 1.44 (1H, m, H-3b), 1.33 (1H, ddd,  $J$  = 13.2, 10.8, 6.6 Hz, H-5b), 1.11 (1H, m, H-4b), 0.99 (3H, s, H-12), 0.90 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 176.4 (C, C-15), 154.0 (C, C-7), 112.2 (CH, C-8), 67.9 (CH<sub>2</sub>, C-14), 51.8 (C, C-6), 51.3 (CH<sub>3</sub>, COOCH<sub>3</sub>), 49.9 (C, C-9), 46.5 (CH, C-1), 41.3 (C, C-2), 40.3 (CH<sub>2</sub>, C-11), 29.3 (CH<sub>2</sub>, C-4), 29.1 (CH<sub>3</sub>, C-13), 25.5 (CH<sub>2</sub>, C-5), 25.4 (CH<sub>3</sub>, C-12), 24.2 (CH<sub>2</sub>, C-3), 23.2 (CH<sub>2</sub>, C-10).

**Longibornan-15,8-olide (12).** From longipinene **1**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2926, 1748, 1449, 1376, 1102, 1009, 732, 556. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 4.24 (1H, d,  $J$  = 7.8 Hz, H-8), 2.19 (1H, d,  $J$  = 7.8 Hz, H-7), 2.01 (1H, ddd,  $J$  = 16.2, 11.4, 4.8 Hz, H-5a), 1.94 (1H, d,  $J$  = 4.8 Hz, H-1), 1.80 (1H, ddd,  $J$  = 16.9, 13.2, 4.2 Hz, H-3a), 1.71 (1H, m, H-11a), 1.66 (1H, m, H-5b), 1.63 (2H, m, H-4), 1.46 (1H, m, H-10a), 1.14 (3H, s, H-14), 1.00 (1H, m, H-10b), 1.00 (1H, m, H-11b), 0.97 (3H, s, H-12), 0.92 (1H, dt,  $J$  = 16.9, 4.2 Hz, H-3b), 0.80 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 185.3 (C, C-15), 88.6 (CH, C-8), 54.9 (CH, C-7), 49.9 (C, C-9), 49.4 (C, C-2), 44.1 (C, C-6), 44.0 (CH, C-1), 33.4 (CH<sub>2</sub>, C-5), 32.7 (CH<sub>2</sub>, C-10), 29.7 (CH<sub>3</sub>, C-14), 27.9 (CH<sub>2</sub>, C-3), 27.1 (CH<sub>2</sub>, C-11), 21.1 (CH<sub>3</sub>, C-13), 20.0 (CH<sub>2</sub>, C-4), 11.0 (CH<sub>3</sub>, C-12).

**14-Hydroxylongibornan-15,8-olide (13).** From longipinene **2**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3399, 2958, 1730, 1451, 1377, 1323, 1196, 1072, 1031, 972, 561, 449. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 4.24 (1H, d,  $J$  = 8.4 Hz, H-8), 3.55 (1H, d,  $J$  = 8.4 Hz, H-14a), 3.33 (1H, d,  $J$  = 10.2 Hz, H-14b), 2.45 (1H, d,  $J$  = 8.4 Hz, H-7), 1.98 (1H, m, H-5a), 1.91 (1H, d,  $J$  = 4.2 Hz, H-1), 1.77 (1H, m, H-3a), 1.71 (1H, m, H-11a), 1.65 (1H, m, H-4a), 1.58 (1H, m, H-5b), 1.47 (1H, dt,  $J$  = 11.4, 3.0 Hz, H-10a), 1.07 (1H, m, H-11b), 1.02 (1H, m, H-10b), 0.96 (3H, s, H-12), 0.93 (1H, m, H-3b), 0.80 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 184.2 (C, C-15), 89.8 (CH, C-8), 69.8 (CH<sub>2</sub>, C-14), 50.8 (C, C-6), 50.2 (CH, C-7), 50.2 (C, C-2), 49.3 (C, C-9), 43.7 (CH, C-1), 32.7 (CH<sub>2</sub>, C-10), 28.1 (CH<sub>2</sub>, C-3), 27.7 (CH<sub>2</sub>, C-5), 27.0 (CH<sub>2</sub>, C-11), 21.0 (CH<sub>3</sub>, C-13), 19.4 (CH<sub>2</sub>, C-4), 11.0 (CH<sub>3</sub>, C-12). HRESIMS  $m/z$  251.1648 [M + H]<sup>+</sup> calcd for [C<sub>15</sub>H<sub>22</sub>O<sub>3</sub> + H]<sup>+</sup> 251.1647. Crystal Data for C<sub>15</sub>H<sub>22</sub>O<sub>3</sub> (M = 250.32 g/mol): orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> (no. 19),  $a$  = 8.1459(2) Å,  $b$  = 12.0831(4) Å,  $c$  = 13.4903(4) Å,  $V$  = 1327.82(7) Å<sup>3</sup>,  $Z$  = 4,  $T$  = 155.70 K,  $\mu$ (CuK $\alpha$ ) = 0.685 mm<sup>-1</sup>,  $D_{\text{calc}}$  = 1.252 g/cm<sup>3</sup>, 16026 reflections measured (12.694° ≤  $2\theta$  ≤ 143.86°), 2585 unique ( $R_{\text{int}}$  = 0.0402,  $R_{\text{sigma}}$  = 0.0282) which were used in all calculations. The final  $R_1$  was 0.0341 ( $I > 2\sigma(I)$ ) and  $wR_2$  was 0.0927.

**Methyl 8,15-bisepoxylongibornan-14-oate (14).** From longipinene **2**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2950, 2879, 1729, 1451, 1218, 1087, 1010. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 3.75 (1H, d,  $J$  = 1.2 Hz, H-8), 3.73 (2H, m, H-14), 3.61 (3H, s, COOCH<sub>3</sub>), 2.38 (1H, d,  $J$  = 8.4 Hz, H-7), 1.94 (1H, d,  $J$  = 4.2 Hz, H-1), 1.83 (1H, m, H-4a), 1.74 (2H, m, H-5), 1.70 (1H, m, H-11a), 1.59 (1H, ddd,  $J$  = 15.0, 5.4, 1.8 Hz, H-3a), 1.47 (1H, m, H-4b), 1.39 (1H, m, H-10a), 1.36 (1H, m, H-3b), 1.00 (1H, ddd,  $J$  = 13.2, 9.6, 4.2 Hz, H-11b), 0.94 (1H, ddd,  $J$  = 12.6, 9.0, 3.6 Hz, H-10b), 0.91 (3H, s, H-12), 0.78 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 176.7 (C, C-15), 91.7 (CH, C-8), 74.5 (CH<sub>2</sub>, C-14), 55.1 (CH, C-7), 55.0 (C, C-6), 52.0 (CH<sub>3</sub>, COOCH<sub>3</sub>), 51.3 (C, C-2), 48.6 (C, C-9), 44.2 (CH, C-1), 35.2 (CH<sub>2</sub>, C-3), 33.7 (CH<sub>2</sub>, C-10), 32.7 (CH<sub>2</sub>, C-5), 28.5 (CH<sub>2</sub>, C-11), 23.8 (CH<sub>3</sub>, C-13), 22.7 (CH<sub>2</sub>, C-4), 10.9 (CH<sub>3</sub>, C-12). HRESIMS  $m/z$  265.1790 [M + H]<sup>+</sup> calcd for [C<sub>16</sub>H<sub>24</sub>O<sub>3</sub> + H]<sup>+</sup> 265.1804.

**8,15-Bisepoxylongibornan-14-ol (15).** From longipinene **5**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3373, 2927, 2866, 1450, 1226, 1043, 1001, 967, 624. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 3.71 (1H, d,  $J$  = 8.8 Hz, H-8), 3.61 (1H, d,  $J$  = 8.8 Hz, H-15a), 3.44 (1H, d,  $J$  = 10.6 Hz, H-14a), 3.39 (1H, d,  $J$  = 10.6 Hz, H-14b), 3.36 (1H, dd,  $J$  = 8.8, 2.3 Hz, H-15b), 1.87 (1H, d,  $J$  = 8.8 Hz, H-7), 1.81 (1H, m, H-4a), 1.76 (1H, d,  $J$  = 4.2 Hz, H-1), 1.69 (1H, m, H-11a), 1.65 (1H, m, H-3a), 1.54 (1H, m, H-5a), 1.48 (1H, m, H-4b), 1.40 (1H, dt,  $J$  = 13.1, 2.3 Hz, H-5b), 1.36 (1H, m, H-10a), 1.30 (1H, ddd,  $J$  = 15.2, 10.5, 5.9 Hz, H-3b), 0.94 (1H, m, H-11b), 0.91 (3H, s, H-12), 0.89 (1H, m, H-10b), 0.76 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 92.1 (CH, C-8), 75.9

(CH<sub>2</sub>, C-15), 70.3 (CH<sub>2</sub>, C-14), 55.0 (CH, C-7), 50.9 (C, C-2), 50.0 (C, C-9), 48.5 (C, C-6), 44.1 (CH, C-1), 34.9 (CH<sub>2</sub>, C-3), 33.8 (CH<sub>2</sub>, C-10), 31.3 (CH<sub>2</sub>, C-5), 28.6 (CH<sub>2</sub>, C-11), 23.7 (CH<sub>3</sub>, C-13), 22.5 (CH<sub>2</sub>, C-4), 11.1 (CH<sub>3</sub>, C-12).

**Himachal-8(9)-en-15,1-olide (16).** From longipinene **1**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2921, 1760, 1452, 1377, 1210, 1183, 1113, 948. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.15 (1H, br s, H-8), 2.79 (1H, br s, H-7), 2.30 (1H, ddd,  $J$  = 13.9, 4.6, 2.2 Hz, H-11a), 2.01 (1H, br t,  $J$  = 15.3 Hz, H-10a), 1.87 (1H, m, H-5a), 1.72 (1H, m, H-2), 1.71 (1H, m, H-3a), 1.69 (1H, m, H-10b), 1.65 (3H, br s, H-12), 1.58 (2H, m, H-4), 1.57 (1H, m, H-5b), 1.40 (1H, quin,  $J$  = 8.3 Hz, H-3b), 1.32 (1H, dt,  $J$  = 13.1, 5.0 Hz, H-11b), 1.09 (3H, s, H-14), 1.02 (3H, d,  $J$  = 7.2 Hz, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 183.4 (C, C-15), 135.7 (C, C-9), 119.6 (CH, C-8), 85.4 (C, C-1), 48.4 (C, C-6), 45.2 (CH, C-7), 42.4 (CH, C-2), 41.7 (CH<sub>2</sub>, C-5), 32.4 (CH<sub>2</sub>, C-3), 31.8 (CH<sub>2</sub>, C-11), 24.7 (CH<sub>2</sub>, C-10), 23.8 (CH<sub>3</sub>, C-12), 22.5 (CH<sub>3</sub>, C-14), 22.0 (CH<sub>2</sub>, C-4), 16.2 (CH<sub>3</sub>, C-13).

**Himachal-8(9)-en-15,2-olide (17).** From longipinene **1**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2932, 1733, 1453, 1378, 1274, 1210, 1164, 1086, 965. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.37 (1H, s, H-8), 2.33 (1H, d,  $J$  = 12.0 Hz, H-7), 2.24 (1H, dt,  $J$  = 12.0, 6.6 Hz, H-1), 1.96 (1H, dt,  $J$  = 15.6, 3.6 Hz, H-10a), 1.88 (1H, m, H-10b), 1.83 (1H, m, H-3a), 1.77 (1H, m, H-4a), 1.73 (3H, s, H-12), 1.71 (1H, m, H-3b), 1.68 (1H, m, H-11a), 1.64 (1H, m, H-5a), 1.48 (1H, m, H-5b), 1.40 (1H, m, H-4b), 1.37 (3H, s, H-13), 1.28 (1H, dd,  $J$  = 12.0, 4.8 Hz, H-11b), 1.23 (3H, s, H-14). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 178.5 (C, C-15), 138.2 (C, C-9), 119.1 (CH, C-8), 83.8 (C, C-2), 44.4 (C, C-6), 41.3 (CH, C-1), 39.0 (CH, C-7), 34.6 (CH<sub>2</sub>, C-3), 31.7 (CH<sub>2</sub>, C-5), 29.6 (CH<sub>3</sub>, C-13), 29.0 (CH<sub>2</sub>, C-10), 24.4 (CH<sub>3</sub>, C-14), 24.2 (CH<sub>3</sub>, C-12), 23.7 (CH<sub>2</sub>, C-11), 20.5 (CH<sub>2</sub>, C-4).

**Methyl 2,14-bisepoxyhimachal-8(9)-en-15-oate (18).** From longipinene **2**. IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2927, 2876, 1726, 1439, 1372, 1217, 1037, 835. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.25 (1H, br s, H-8), 3.95 (1H, dd,  $J$  = 10.2, 1.8 Hz, H-14a), 3.81 (1H, d,  $J$  = 10.2 Hz, H-14b), 3.62 (3H, s, COOCH<sub>3</sub>), 2.85 (1H, d,  $J$  = 10.8 Hz, H-1), 2.17 (1H, dd,  $J$  = 10.8, 4.5 Hz, H-7), 2.13 (1H, m, H-5a), 1.88 (1H, m, H-5b), 1.87 (1H, m, H-10a), 1.83 (1H, m, H-10b), 1.76 (1H, m, H-3a), 1.66 (3H, s, H-12), 1.63 (1H, m, H-4a), 1.56 (1H, m, H-3b), 1.50 (1H, m, H-4b), 1.22 (2H, m, H-11), 1.14 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 175.9 (C, C-15), 136.8 (C, C-9), 121.6 (CH, C-8), 76.5 (C, C-2), 71.0 (CH<sub>2</sub>, C-14), 52.2 (CH<sub>3</sub>, COOCH<sub>3</sub>), 48.9 (C, C-6), 40.5 (CH, C-7), 37.5 (CH<sub>2</sub>, C-3), 36.8 (CH, C-1), 31.2 (CH<sub>2</sub>, C-5), 30.4 (CH<sub>3</sub>, C-13), 28.9 (CH<sub>2</sub>, C-10), 24.1 (CH<sub>2</sub>, C-11), 24.0 (CH<sub>3</sub>, C-12), 19.4 (CH<sub>2</sub>, C-4). HRESIMS  $m/z$  265.1795 [M + H]<sup>+</sup> calcd for [C<sub>16</sub>H<sub>24</sub>O<sub>3</sub> + H]<sup>+</sup> 265.1804.

**15-(Methoxymethoxy)longinin-9(10)-en-14-ol (19a) / 14-(methoxymethoxy)longinin-9(10)-en-15-ol (19b).** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3448, 2915, 2837, 1738, 1442, 1373, 1213, 1147, 1108, 1038. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.21 (2H, s, H-10), 4.62 (2H, s, OCH<sub>2</sub>O), 4.60 (2H, s, OCH<sub>2</sub>O), 3.48 (4H, m, CH<sub>2</sub>O), 3.52 (4H, m, CH<sub>2</sub>OH), 3.37 (3H, s, OCH<sub>3</sub>), 3.36 (3H, s, OCH<sub>3</sub>), 2.25 (4H, m), 2.14 (2H, m), 2.03 (2H, m), 1.80 (2H, br s), 1.67 (14H, m), 1.43 (4H, m), 0.86 (6H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 147.3–147.1 (C, C9), 117.6–117.3 (CH, C10), 96.8–96.7 (CH<sub>2</sub>, OCH<sub>2</sub>O), 72.9–72.8 (CH<sub>2</sub>, CH<sub>2</sub>O), 67.6 (CH<sub>2</sub>, CH<sub>2</sub>OH), 55.4–55.3 (CH<sub>3</sub>, OCH<sub>3</sub>), 49.5 (CH), 45.7 (CH), 40.7 (CH<sub>2</sub>), 40.7 (C), 40.3 (C), 39.4 (CH), 34.0 (CH<sub>2</sub>), 29.0 (CH<sub>2</sub>), 23.4 (CH<sub>3</sub>, C13), 22.9–22.8 (CH<sub>3</sub>, C12), 20.9 (CH<sub>2</sub>).

**Compound 20.** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 2918, 1454, 1174, 1155, 1036, 928. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 5.16 (1H, br s, H-10), 4.75 (1H, d,  $J$  = 6.6 Hz, H-16a), 4.69 (1H, d,  $J$  = 6.6 Hz, H-16b), 3.56 (2H, dd,  $J$  = 33.6, 10.8 Hz, H14\*), 3.46 (2H, dd,  $J$  = 33.6, 10.8 Hz, H15\*), 2.21 (2H, m, H-11), 2.07 (1H, m, H-8), 1.94 (1H, d,  $J$  = 6.6 Hz, H-7), 1.87 (1H, br s, H-1), 1.61 (3H, d,  $J$  = 1.8 Hz, H-12), 1.58 (2H, m, H-3), 1.53 (2H, m, H-4), 1.52 (1H, m, H-5a), 1.42 (1H, m, H-5b), 0.80 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 147.0 (C, C-9), 117.6 (CH, C-10), 94.3 (CH<sub>2</sub>, C-16), 74.3 (CH<sub>2</sub>, C-14/15), 50.2 (CH, C-1), 45.5 (CH, C-7), 40.7 (CH<sub>2</sub>, C-3), 39.2 (CH, C-8), 35.3 (C, C-6), 34.0 (CH<sub>2</sub>, C-11), 31.2 (CH<sub>2</sub>, C-5), 23.4 (CH<sub>3</sub>, C-13), 22.9 (CH<sub>3</sub>, C-12), 20.8 (CH<sub>2</sub>, C-4). \*Interchangeable signals.

**Methyl 9,10 bisepoxy-14-hydroxylongipinan-15-oate (21).** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3433, 2920, 1723, 1438, 1204, 1043, 837. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 3.61 (3H, s, COOCH<sub>3</sub>), 3.48 (1H, d,  $J$  = 11.1 Hz, H-14a), 3.41 (1H, d,  $J$  = 11.1 Hz, H-14b), 3.00 (1H, da,  $J$  = 3.0 Hz, H-10), 2.38 (1H, s), 2.11 (1H, d,  $J$  = 5.7 Hz), 1.79 (5H, m), 1.48 (4H, m), 1.29 (3H, s, H-12), 0.86 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 176.7 (C, COOCH<sub>3</sub>), 66.5 (CH<sub>2</sub>, C-14), 61.9 (C), 56.9 (CH, C-10), 51.8 (CH<sub>3</sub>, COOCH<sub>3</sub>), 51.1 (C), 44.1 (CH), 40.5 (CH<sub>2</sub>), 43.0 (C), 40.9 (CH), 39.1 (CH), 29.8 (CH<sub>2</sub>), 29.2 (CH<sub>2</sub>), 22.2 (CH<sub>3</sub>, C-12), 21.7 (CH<sub>2</sub>), 21.6 (CH<sub>3</sub>, C-13).

**9,10-Bisepoxylongipinano-14,15-diol (22).** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3376, 2919, 2817, 1455, 1437, 1378, 1278. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 3.53 (4H, m, H-14, H-15), 3.11 (1H, da,  $J$  = 3.9 Hz, H-10), 2.14 (1H, s), 2.03–1.91 (4H, m), 1.63 (4H, br s), 1.40 (3H, s, H-12), 1.44 (2H, br s), 0.96 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 67.8 (CH<sub>2</sub>, C-15\*), 67.5

(CH<sub>2</sub>, C-14\*), 62.2 (C), 57.7 (CH, C-10), 43.3 (C), 43.2 (CH), 40.9 (CH<sub>2</sub>), 40.3 (C), 40.0 (CH), 38.4 (CH), 29.3 (CH<sub>2</sub>), 28.9 (CH<sub>2</sub>), 22.3 (CH<sub>3</sub>, C-12), 21.8 (CH<sub>3</sub>, C-13), 20.9 (CH<sub>2</sub>). \*Interchangeable signals.

**Methyl 10-oxo-14-hydroxysecolongifol-8(9)-en-15-oate (23).** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3444, 2945, 2912, 1717, 1439, 1216, 1058, 914, 842, 731. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.68 (1H, s, H-10), 5.11 (1H, br t, H-8), 3.61 (3H, s, COOCH<sub>3</sub>), 3.67 (1H, d,  $J$  = 11.2 Hz, H-14a), 3.49 (1H, d,  $J$  = 11.2 Hz, H-14b), 2.49 (2H, m, H-11), 2.39 (1H, m, H-1), 2.39 (1H, m, H-7), 2.08 (1H, m, H-5a), 1.53 (1H, m, H-5b), 1.51 (1H, m, H-3a), 1.51 (1H, m, H-4a), 1.47 (1H, m, H-4b), 1.42 (3H, s, H-12), 1.29 (1H, m, H-3b), 0.88 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 204.4 (CH, C-10), 175.9 (C, C-15), 144.9 (C, C-9), 125.4 (CH, C-8), 70.1 (CH<sub>2</sub>, C-14), 54.2 (C, C-6), 52.0 (CH, C-7), 51.5 (CH<sub>3</sub>, COOCH<sub>3</sub>), 51.2 (C, C-2), 47.1 (CH<sub>2</sub>, C-11), 42.5 (CH<sub>2</sub>, C-3), 42.4 (CH, C-1), 30.7 (CH<sub>2</sub>, C-5), 21.2 (CH<sub>2</sub>, C-4), 21.1 (CH<sub>3</sub>, C-13), 12.4 (CH<sub>3</sub>, C-12).

**14,15-Dihydroxysecolongifol-8(9)-en-10-al (24).** IR (ATR)  $\nu$  (cm<sup>-1</sup>) 3333, 2916, 1715, 1438, 1375, 1019, 914, 836. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.73 (1H, br s, H-10), 5.44 (1H, br s, H-8), 3.70 (1H, dd,  $J$  = 11.4, 1.8 Hz, H-14a), 3.55 (1H, dd,  $J$  = 10.8, 1.8 Hz, H-15a), 3.44 (1H, d,  $J$  = 10.8 Hz, H-15b), 3.41 (1H, d,  $J$  = 11.4 Hz, H-14b), 2.55 (1H, dd,  $J$  = 18.0, 3.6 Hz, H-11a), 2.50 (1H, ddd,  $J$  = 18.6, 10.8, 1.8 Hz, H-11b), 2.23 (1H, dd,  $J$  = 10.8, 3.6 Hz, H-1), 2.40 (1H, s, H-7), 1.52 (1H, dt,  $J$  = 13.8, 4.2 Hz, H-3a), 1.47 (3H, br s, H-12), 1.33 (2H, m, H-4), 1.25 (1H, ddd,  $J$  = 13.8, 11.4, 3.6 Hz, H-3b), 1.19 (1H, m, H-5a), 0.97 (1H, ddd,  $J$  = 13.8, 11.4, 1.2 Hz, H-5b), 0.90 (3H, s, H-13). <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 205.0 (CH, C-10), 143.8 (C, C-9), 125.8 (CH, C-8), 71.2 (CH<sub>2</sub>, C-14), 69.2 (CH<sub>2</sub>, C-15), 50.7 (C, C-2), 48.1 (CH, C-7), 47.1 (CH<sub>2</sub>, C-11), 44.0 (C, C-6), 42.5 (CH<sub>2</sub>, C-3), 42.1 (CH, C-1), 31.3 (CH<sub>2</sub>, C-5), 21.3 (CH<sub>3</sub>, C-13), 20.4 (CH<sub>2</sub>, C-4), 12.5 (CH<sub>3</sub>, C-12). HRESIMS  $m/z$  253.1795 [M + H]<sup>+</sup> calcd for [C<sub>15</sub>H<sub>24</sub>O<sub>3</sub> + H]<sup>+</sup> 253.1804.

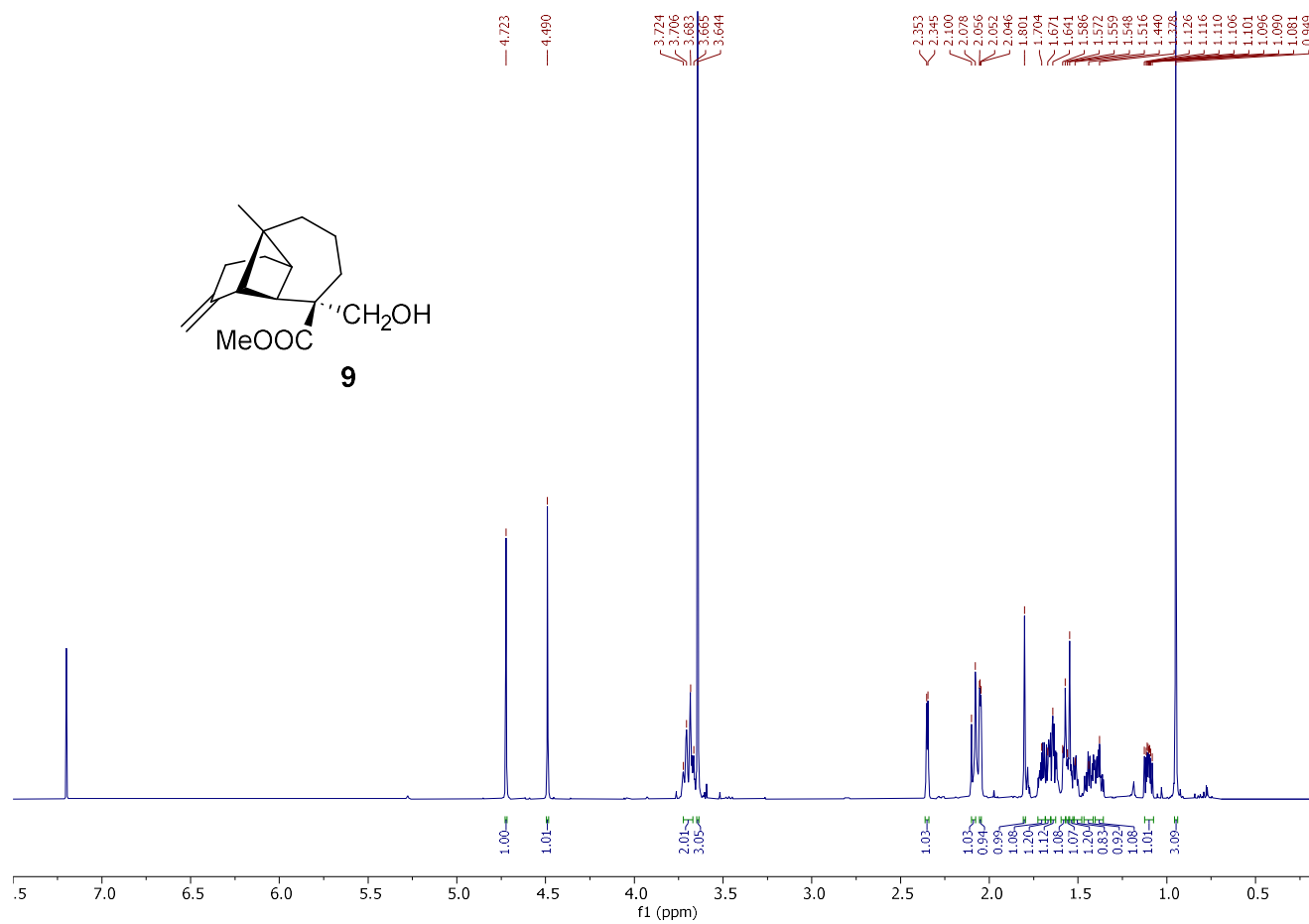
## References

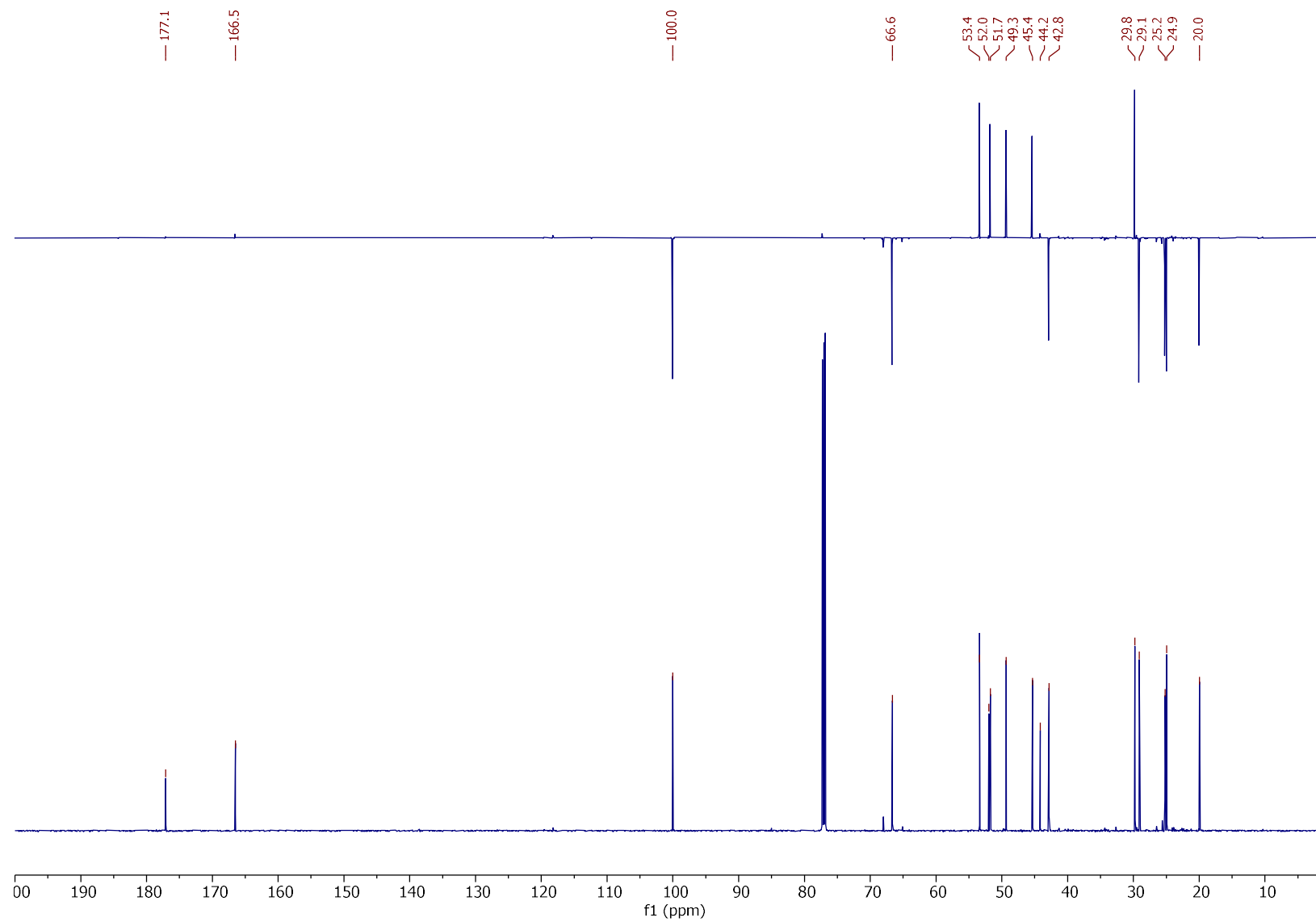
1. European Commission. Pacto Verde: Propuestas Pioneras para Restaurar la Naturaleza en Europa de Aquí a 2050 y Reducir a la Mitad el uso de Plaguicidas de Aquí a 2030. Available online: [https://ec.europa.eu/commission/presscorner/detail/es/ip\\_22\\_3746](https://ec.europa.eu/commission/presscorner/detail/es/ip_22_3746) (accessed on 12 July 2023).
2. European Commission. Glyphosate. Available online: [https://food.ec.europa.eu/plants/pesticides/approval-active-substances/renewal-approval/glyphosate\\_en](https://food.ec.europa.eu/plants/pesticides/approval-active-substances/renewal-approval/glyphosate_en) (accessed on 27 January 2024).
3. Roman, L.U.; Hernandez, J.D.; Del Rio, R.E.; Bucio, M.A.; Cerda-Garcia-Rojas, C.M.; Joseph-Nathan, P. Wagner-Meerwein Rearrangements of Longipinane Derivatives. *J. Org. Chem.* **1991**, *56*, 1938. <https://doi.org/10.1021/jo00005a050>.
4. Borgo, J.; Laurella, L.C.; Martini, F.; Catalán, C.A.N.; Sülsen, V.P. *Stevia* Genus: Phytochemistry and Biological Activities Update *Molecules* **2021**, *26*, 2733. <https://doi.org/10.3390/molecules26092733>.
5. Román, L.U.; Zepeda, L.G.; Morales, N.R.; Hernández, J.D.; Cerda-García-Rojas, C.M.; Joseph-Nathan, P. Molecular Rearrangement of Rastevione Mesylate into Arteagane Derivatives. *J. Nat. Prod.* **1995**, *58*, 1808. <https://doi.org/10.1021/np50126a002>.
6. Román, L.U.; Zepeda, L.G.; Morales, N.R.; Flores, S.; Hernández, J.D.; Cerda-García-Rojas, C.M.; Joseph-Nathan, P. Mechanistic Studies of the Longipinane to Arteagane Rearrangement. *J. Nat. Prod.* **1996**, *59*, 391. <https://doi.org/10.1021/np960072x>.
7. Cerda-García-Rojas, C.M.; Flores-Sandoval, C.A.; Román, L.U.; Hernández, J.D.; Joseph-Nathan, P. A Regioselective Wagner-Meerwein Rearrangement Directed towards the Six-Membered Ring of the Longipinane Skeleton. *Tetrahedron* **2002**, *58*, 1061. [https://doi.org/10.1016/S0040-4020\(01\)01205-4](https://doi.org/10.1016/S0040-4020(01)01205-4).
8. Román, L.U.; Cerda-García-Rojas, C.M.; Guzmán, R.; Armenta, C.; Hernández, J.D.; Joseph-Nathan, P. Jiquilpane Hydrocarbon Skeleton Generated by Two Successive Wagner-Meerwein Rearrangements of Longipinane Derivatives. *J. Nat. Prod.* **2002**, *65*, 1540. <https://doi.org/10.1021/np0201570>.
9. Chacón-Morales, P.A.; Amaro-Luis, J.M. Meridane and Uladane, Two Unprecedented Sesquiterpene Skeletons Obtained by Wagner-Meerwein Rearrangements of Longipinane Derivatives. *Tetrahedron Lett.* **2016**, *57*, 2713. <https://doi.org/10.1016/j.tetlet.2016.04.116>.
10. Reddy, D.S.; Kutateladze, A.G. Computational Structure Revision of a Longipinane Derivative Meridane. *Tetrahedron Lett.* **2016**, *57*, 4727. <https://doi.org/10.1016/j.tetlet.2016.09.030>.
11. Román, L.U.; Rebeca Morales, N.; Hernández, J.D.; Cerda-García-Rojas, C.M.; Gerardo Zepeda, L.; Flores-Sandoval, C.A.; Joseph-Nathan, P. Generation of the New Quirogane Skeleton by a Vinylogous retro-Michael Type Rearrangement of Longipinane Derivatives. *Tetrahedron* **2001**, *57*, 7269. [https://doi.org/10.1016/S0040-4020\(01\)00718-9](https://doi.org/10.1016/S0040-4020(01)00718-9).
12. Joseph-Nathan, P.; Meléndez-Rodríguez, M.; Cerda-García-Rojas, C.M.; Catalan, C.A.N. Photochemical Rearrangements of Highly Functionalized Longipinane Derivatives. *Tetrahedron Lett.* **1996**, *37*, 8093. [https://doi.org/10.1016/0040-4039\(96\)01848-5](https://doi.org/10.1016/0040-4039(96)01848-5).
13. Meléndez-Rodríguez, M.; Cerda-García-Rojas, C.M.; Joseph-Nathan, P. Quirogane, Prenopsane, and Patzcuarane Skeletons Obtained by Photochemically Induced Molecular Rearrangements of Longipinane Derivatives. *J. Nat. Prod.* **2002**, *65*, 1398. <https://doi.org/10.1021/np020158s>.

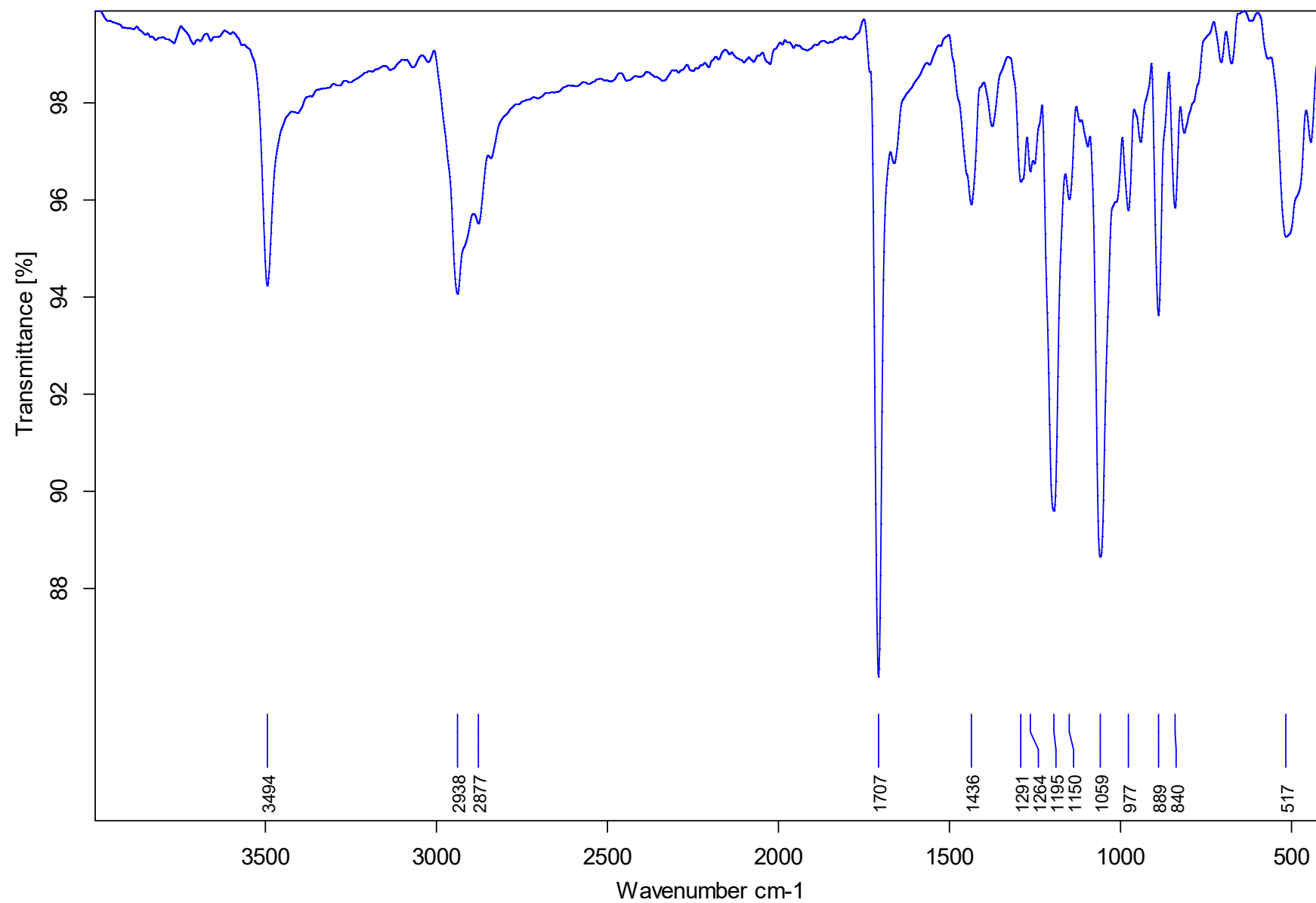
14. Román, L.U.; Hernández, J.D.; Cerda-García-Rojas, C.M.; Domínguez-López, R.M.; Joseph-Nathan, P. Molecular Rearrangements in the Longipinene Series. *J. Nat. Prod.* **1992**, *55*, 577. <https://doi.org/10.1021/np50083a004>.
15. Joseph-Nathan, P.; Cerda-García-Rojas, C.M. Molecular Rearrangements in Longipinane Derivatives. *Pure & Appl. Chem.* **1994**, *66*, 2361. <https://doi.org/10.1351/pac199466102361>.
16. Chacón-Morales, P.A.; Amaro-Luis, J.M.; Kutateladze, A.G. Structure Determination and Mechanism of Formation of a *seco*-Moreliane Derivative Supported by Computational Analysis. *J. Nat. Prod.* **2017**, *80*, 1214. <https://doi.org/10.1021/acs.jnatprod.7b00041>.
17. Armenta-Salinas, C.; Guzmán-Mejía, R.; García-Gutiérrez, H.A.; Román-Marín, L.U.; Hernández-Hernández, J.D.; Cerda-García-Rojas, C.M.; Joseph-Nathan, P. Novel Sesquiterpene Skeletons by Multiple Wagner–Meerwein Rearrangements of a Longipinane-1,9-diol Derivative. *J. Nat. Prod.* **2019**, *82*, 3410. <https://doi.org/10.1021/acs.jnatprod.9b00784>.
18. Ruiz-Ferrer, C.; Román-Marín, L.U.; Hernández-Hernández, J.D.; Cerda-García-Rojas, C.M.; Joseph-Nathan, P. Novel Sesquiterpenoid Skeletons by Wagner–Meerwein Rearrangements of Longipinane-9,13-diol-1-one Derivatives. *J. Nat. Prod.* **2021**, *84*, 1087. <https://doi.org/10.1021/acs.jnatprod.0c01160>.
19. Meléndez-Rodríguez, M.; Cerda-García-Rojas, C.M.; Catalán, C.A.N.; Joseph-Nathan, P. Mechanistic Studies of the Photochemical Rearrangement of 1-Oxolongipin-2-ene Derivatives. *Tetrahedron* **2002**, *58*, 2331. [https://doi.org/10.1016/S0040-4020\(02\)00121-7](https://doi.org/10.1016/S0040-4020(02)00121-7).
20. Barrero, A.F.; Herrador, M.M.; Molina, J.M.; Quílez, J.F.; Quirós, M.  $\alpha$ -Longipinene Derivatives from *Santolina viscosa*. A Conformational Analysis of the Cycloheptane Ring. *J. Nat. Prod.* **1994**, *57*, 873. <https://doi.org/10.1021/np50109a001>.
21. Barrero, A.F.; Herrador, M.M.; Álvarez-Manzaneda, R.J.; Quirós, M.; Lara, A.; Quílez del Moral, J. Longipinene Derivatives from *Santolina viscosa*. *J. Nat. Prod.* **2000**, *63*, 587. <https://doi.org/10.1021/np9904206>.
22. Shastri, M.H.; Dev, S. Studies in Sesquiterpenes-LX<sup>a,b</sup> Reversion of Longipinane to Himachalane System: Revision of Structure of Isocentdarol. *Tetrahedron* **1992**, *48*, 4905.
23. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr.* **2009**, *42*, 339. <https://doi.org/10.1107/S0021889808042726>.
24. Sheldrick, G. M. SHELXT—Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr. Sect A Foundations and Advances* **2015**, *71*, 3. <https://doi.org/10.1107/S2053273314026370>.
25. Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr. Sect C Structural Chemistry* **2015**, *71*, 3. <https://doi.org/10.1107/S2053229614024218>.
26. Hehre, W.; Klunzinger, P.; Deppmeier, B.; Driessen, A.; Uchida, N.; Hashimoto, M.; Fukushi, E.; Takata, Y., Efficient Protocol for Accurately Calculating <sup>13</sup>C Chemical Shifts of Conformationally Flexible Natural Products: Scope, Assessment, and Limitations. *J. Nat. Prod.* **2019**, *82*, 2299. <https://doi.org/10.1021/acs.jnatprod.9b00603>.
27. Navarro-Rocha, J.; Andrés, M. F.; Díaz, C. E.; Burillo, J.; González-Coloma, A. Composition and Biocidal Properties of Essential Oil from pre-Domesticated Spanish *Satureja Montana*. *Industrial Crops and Products* **2020**, *145*, 111958. <https://doi.org/https://doi.org/10.1016/j.indcrop.2019.111958>.
28. Rueden, C. T.; Schindelin, J.; Hiner, M. C.; DeZonia, B. E.; Walter, A. E.; Arena, E. T.; Eliceiri, K. W. ImageJ2: ImageJ for the Next Generation of Scientific Image Data. *BMC Bioinformatics* **2017**, *18*, 529. <https://doi.org/10.1186/s12859-017-1934-z>.
29. Santana, O.; Andrés, M. F.; Sanz, J.; Errahmani, N.; Abdeslam, L.; González-Coloma, A. Valorization of Essential Oils from Moroccan Aromatic Plants. *Nat. Prod. Commun.* **2014**, *9*, 1109. <https://doi.org/10.1177/1934578X1400900812>.
30. González, J.; Valcárcel, F.; Aguilar, A.; Olmeda, A. S. In vitro Feeding of *Hyalomma lusitanicum* Ticks on Artificial Membranes. *Exp. Appl. Acarol.* **2017**, *72*, 449. <https://doi.org/10.1007/s10493-017-0167-1>.
31. Andrés, M. F.; González-Coloma, A.; Muñoz, R.; De la Peña, F.; Julio, L. F.; Burillo, J. Nematicidal Potential of Hydrolates from the semi-Industrial Vapor-Pressure Extraction of Spanish Aromatic Plants. *Environ. Sci. Pollut. Res.* **2018**, *25*, 29834. <https://doi.org/10.1007/s11356-017-9429-z>.
32. Püntener, W. Manual for Field Trials in Plant Protection. *Ciba-Geigy Limited: Basel, Switzerland* **1981**, 205.

## NMR AND IR SPECTRA

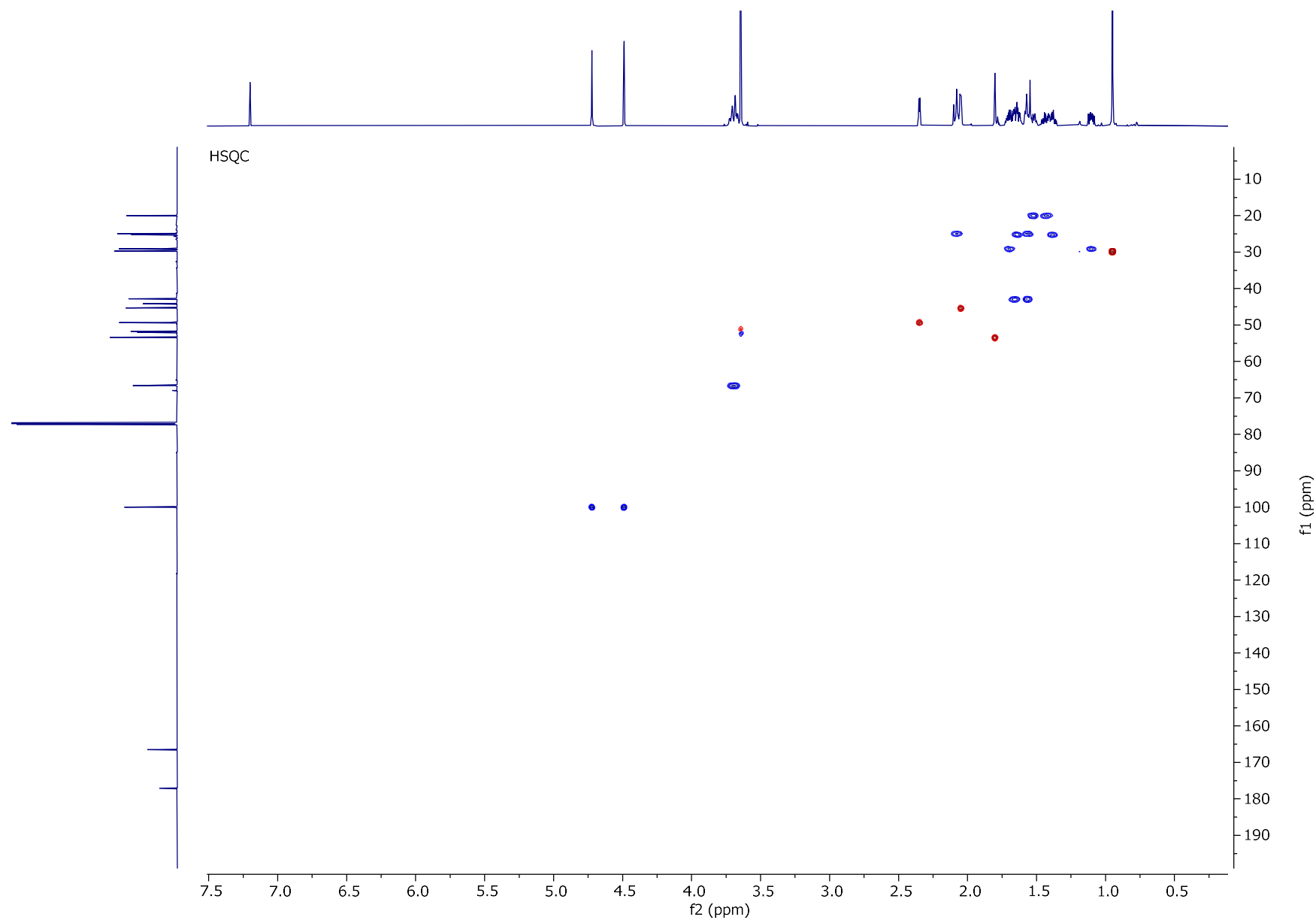
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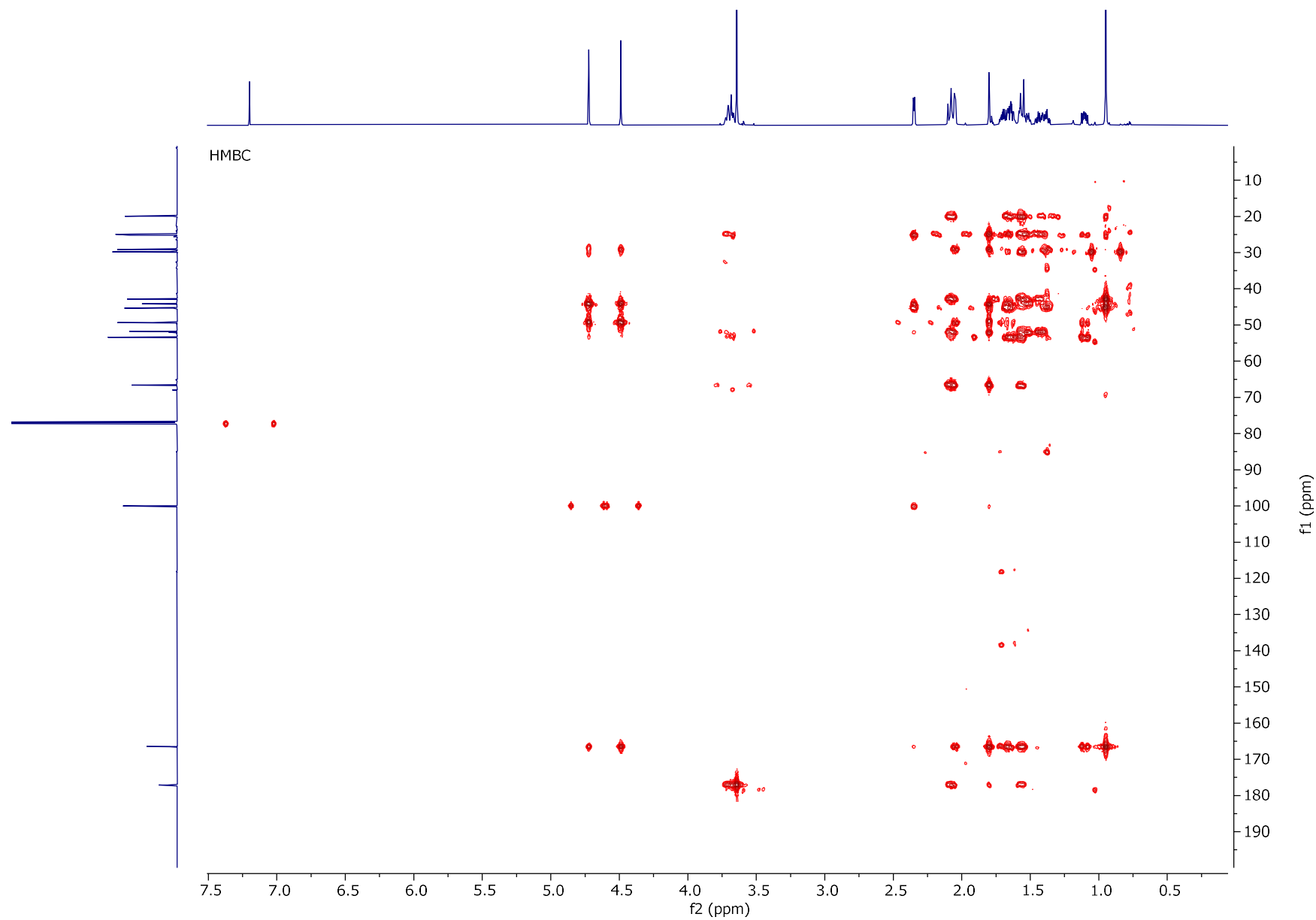


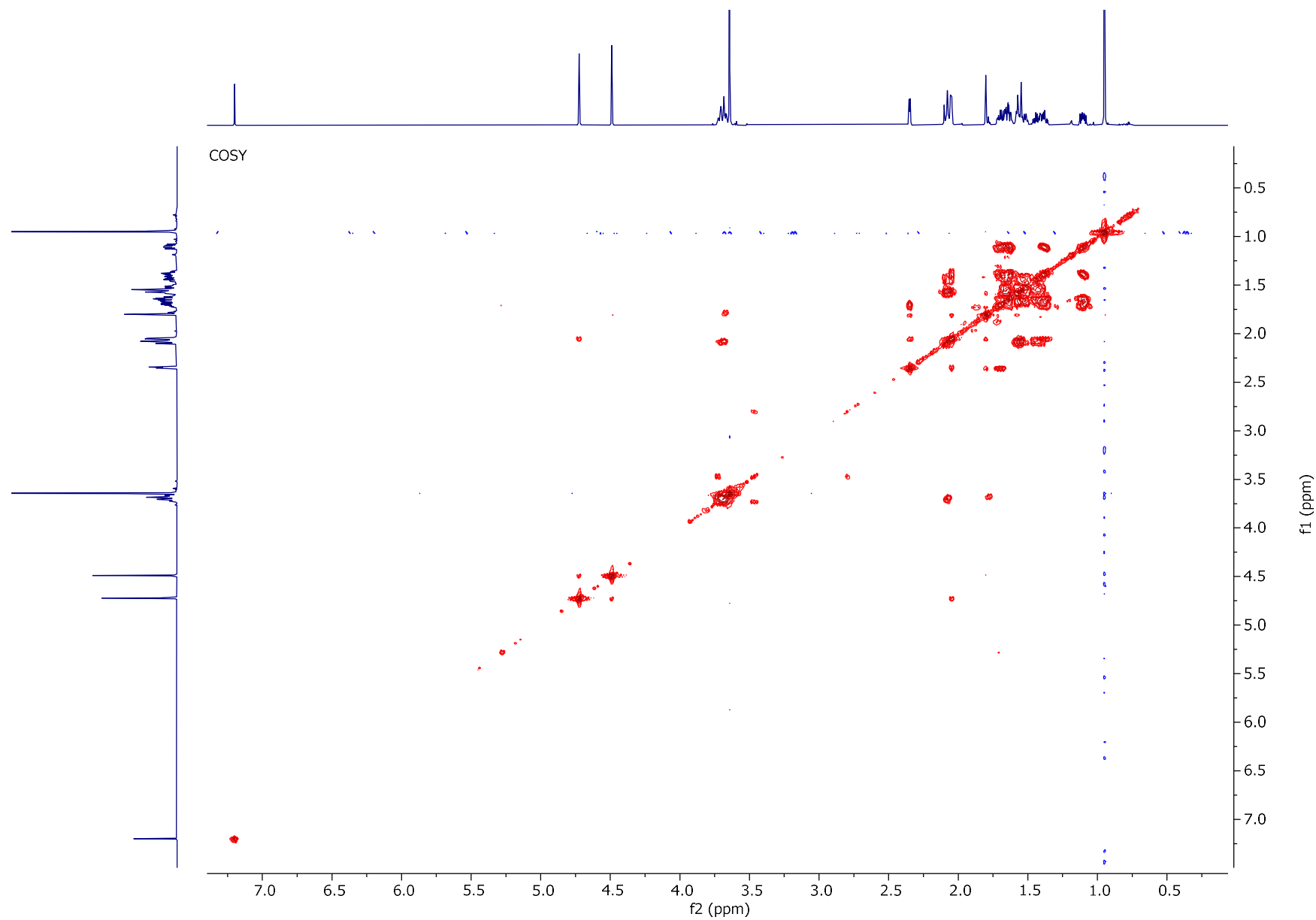


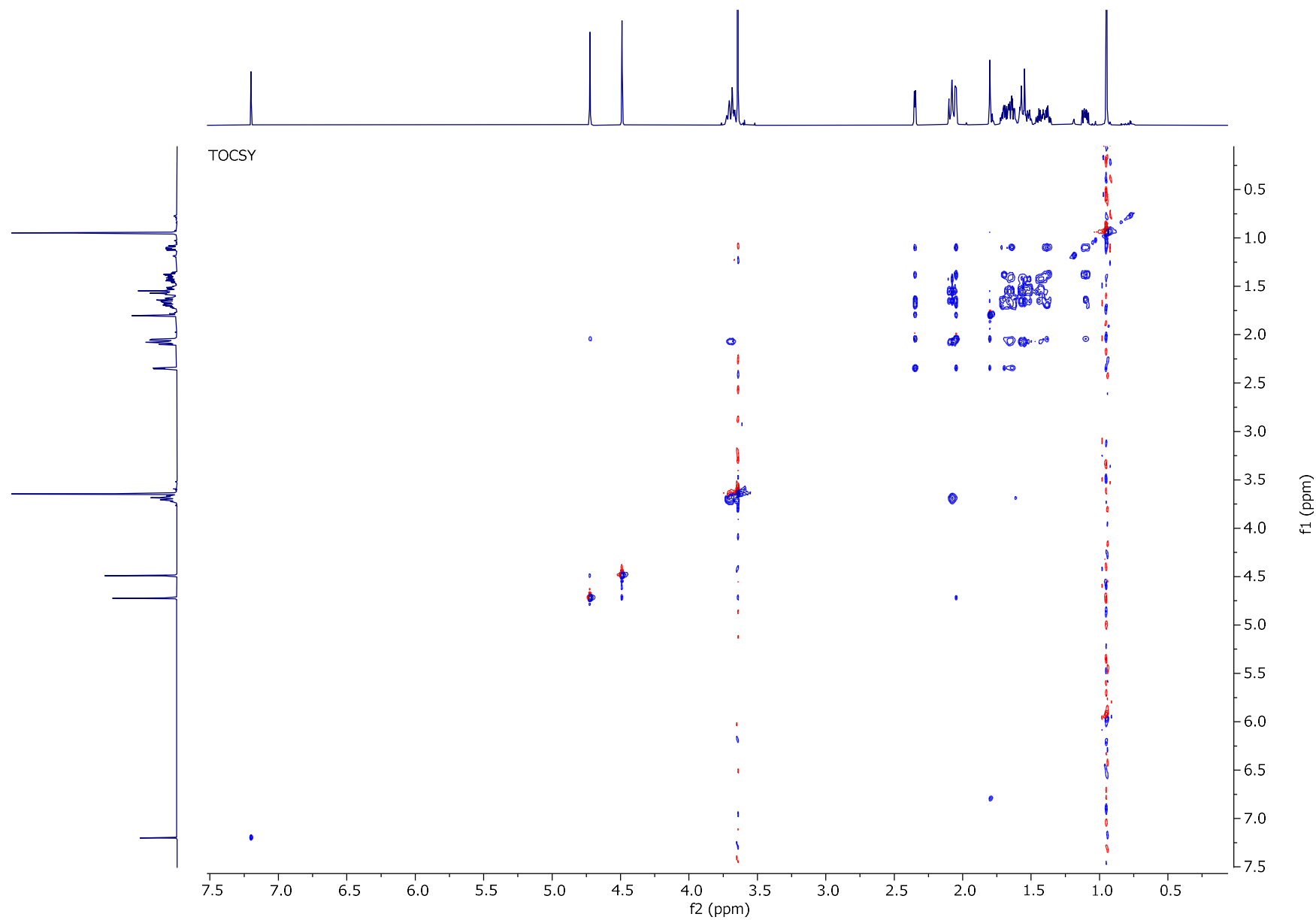


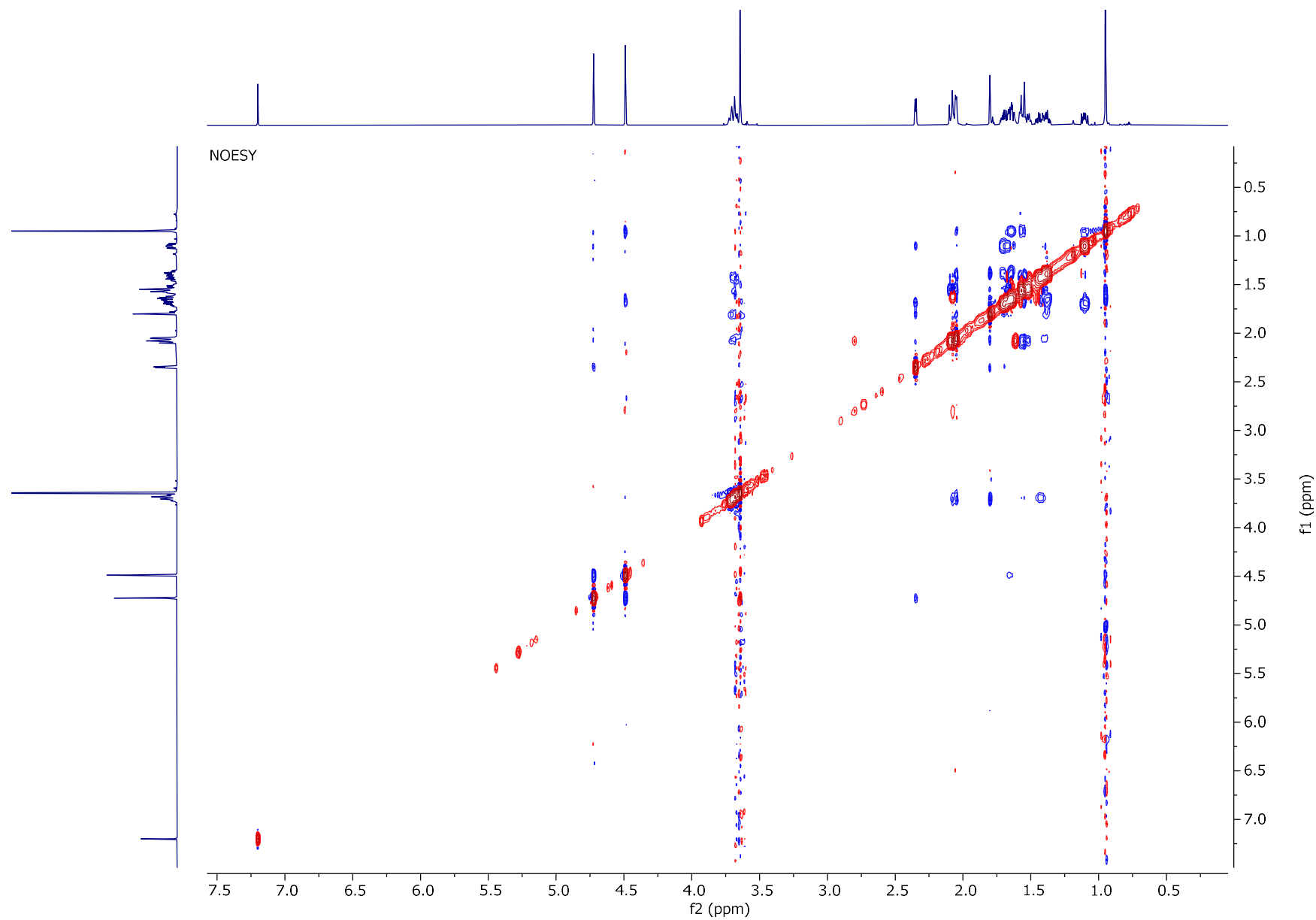


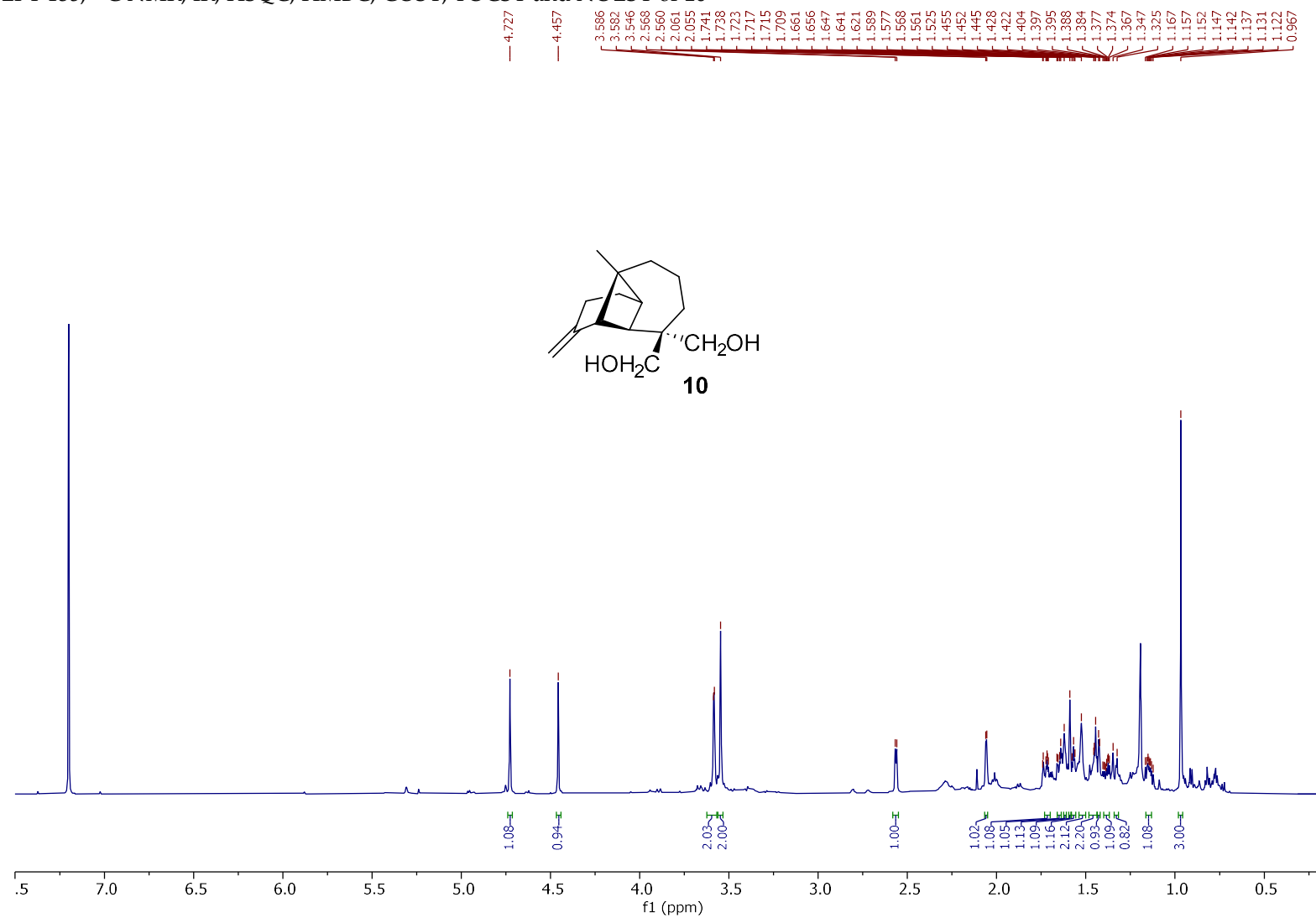


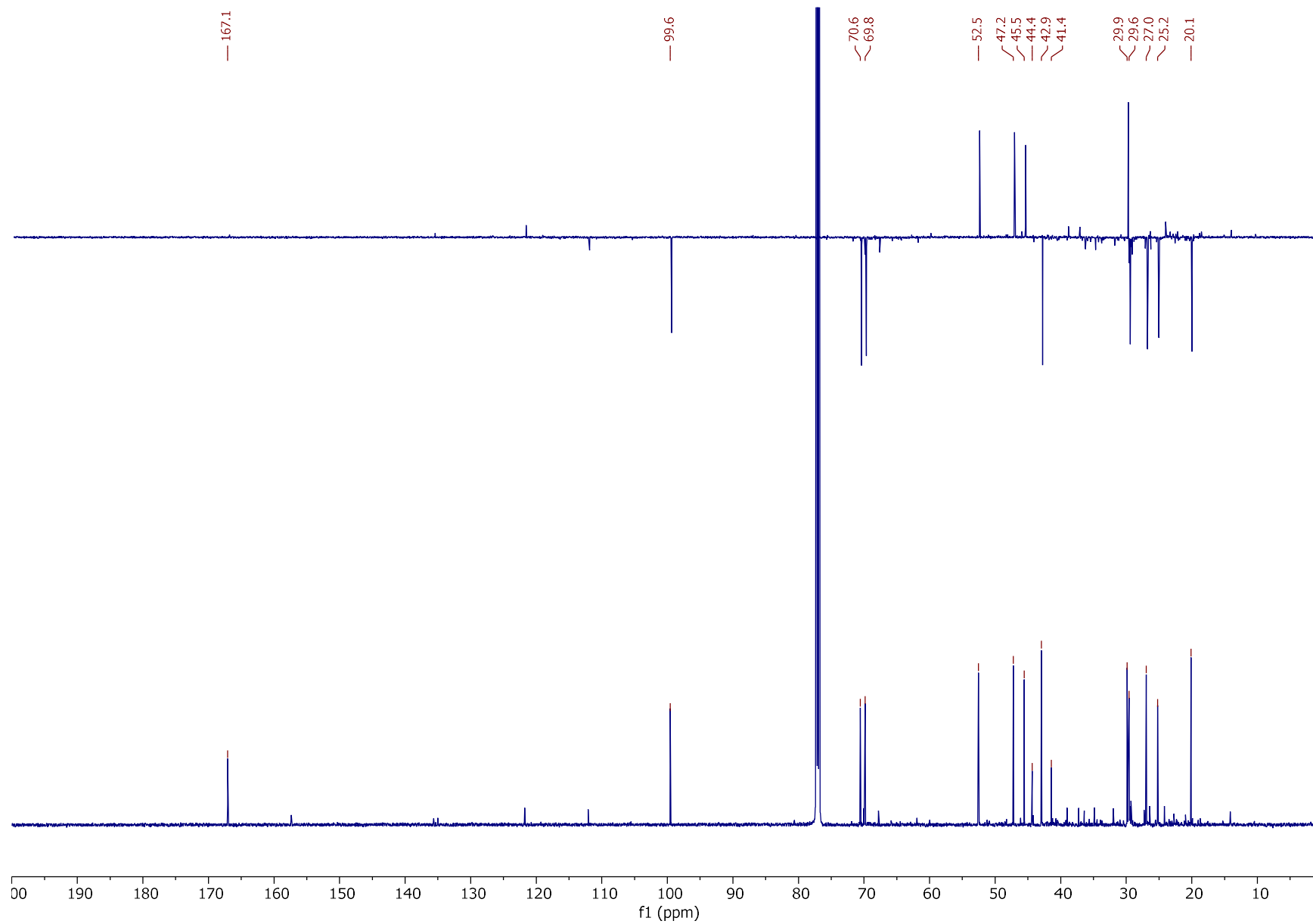


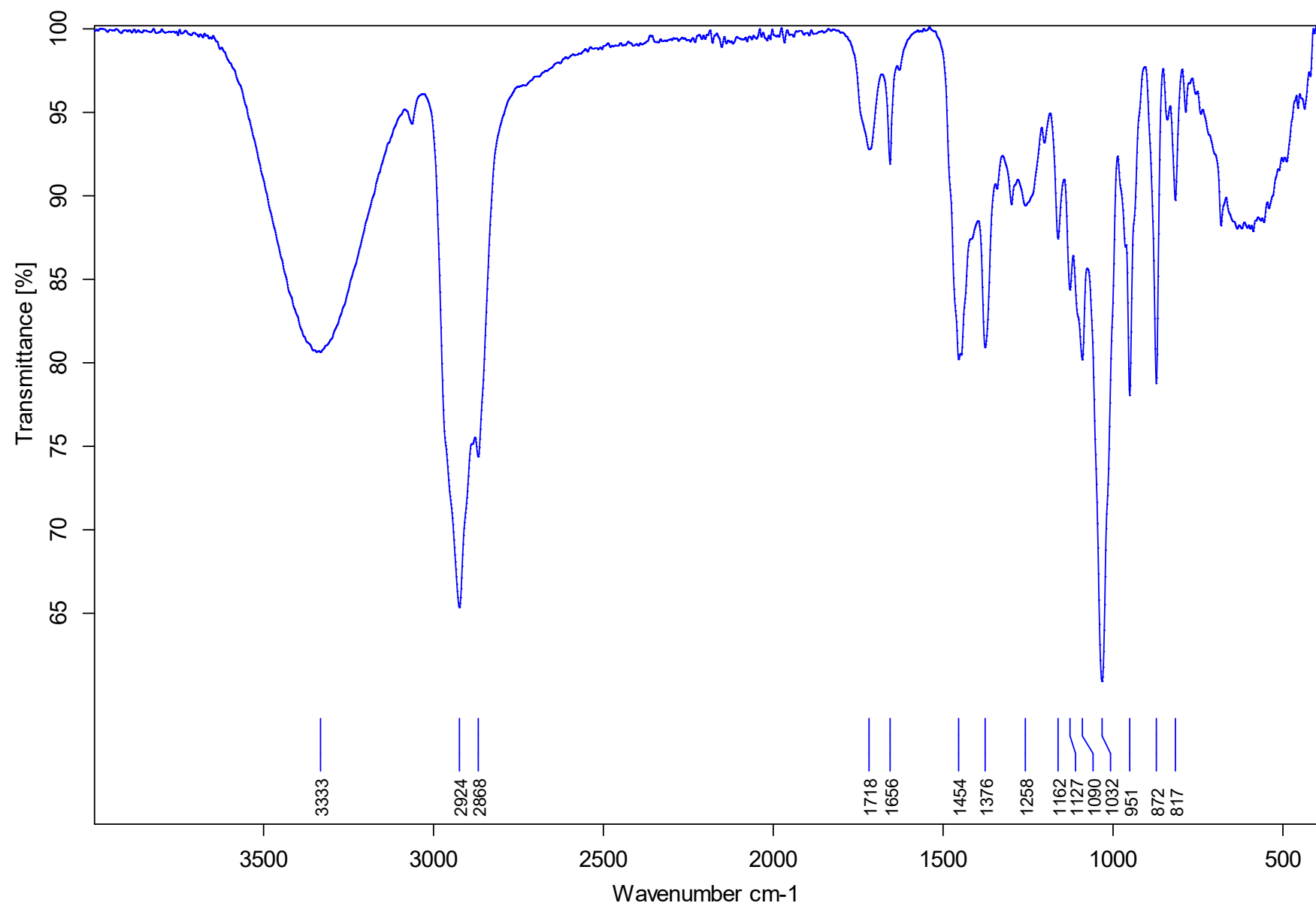




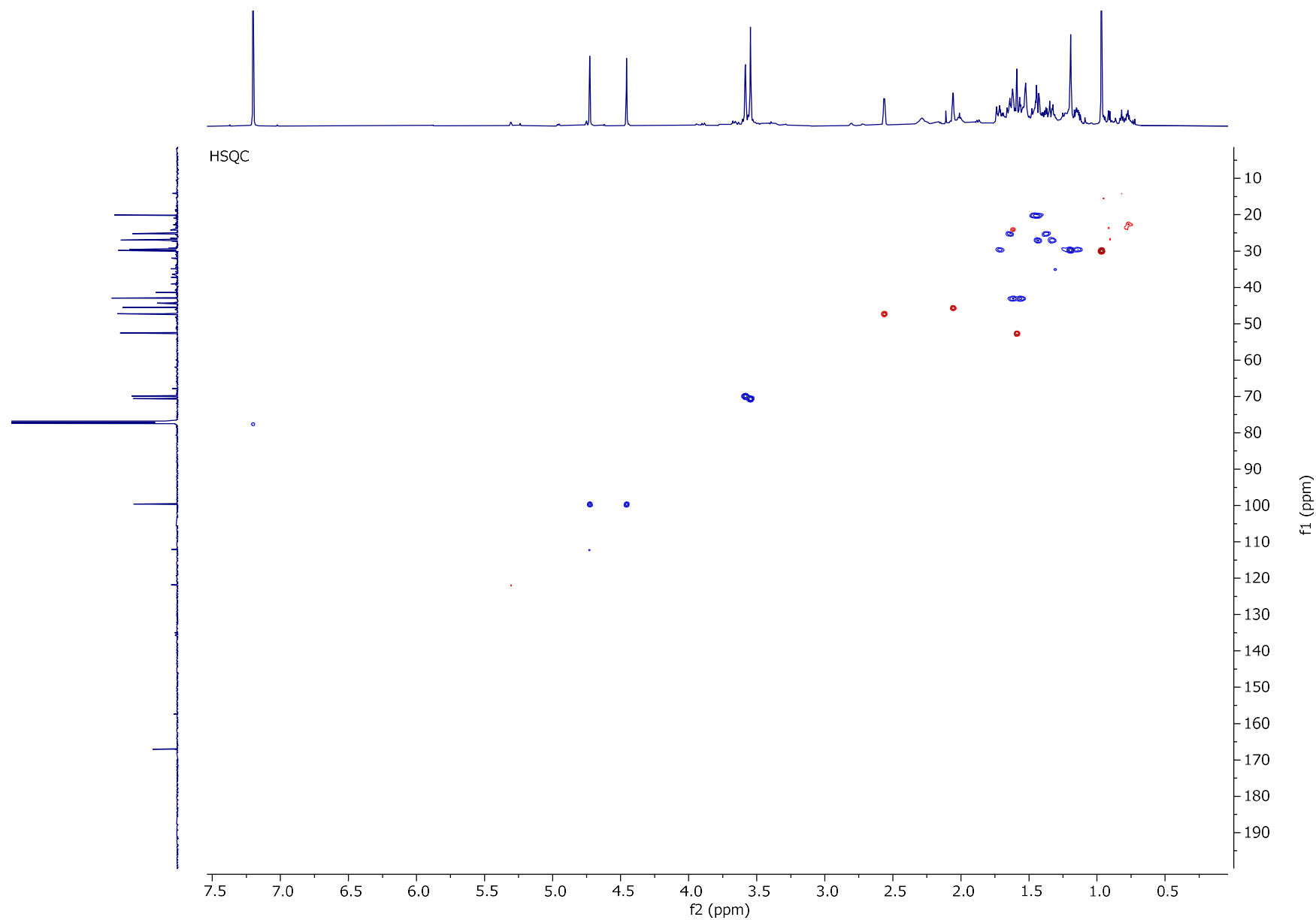


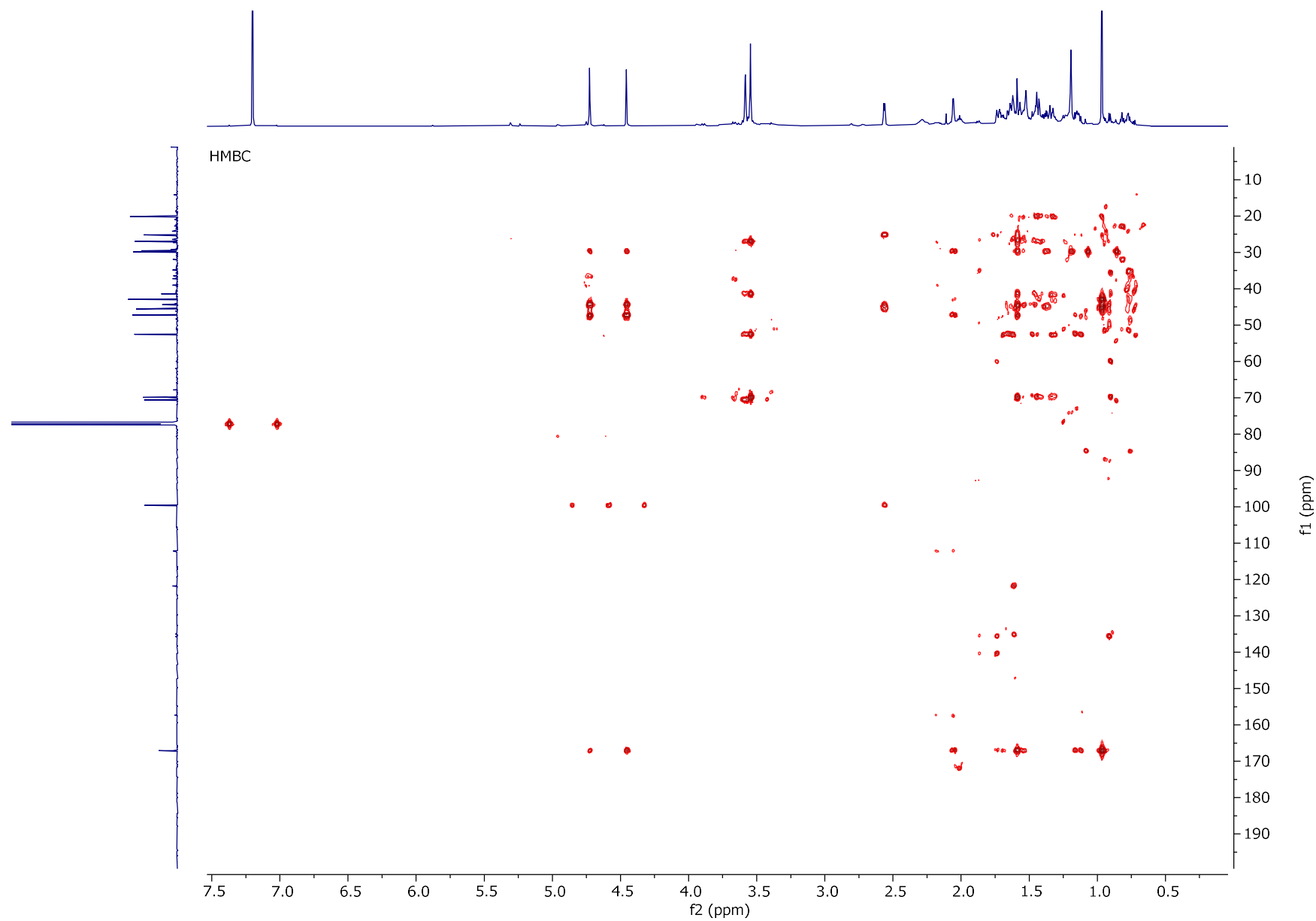
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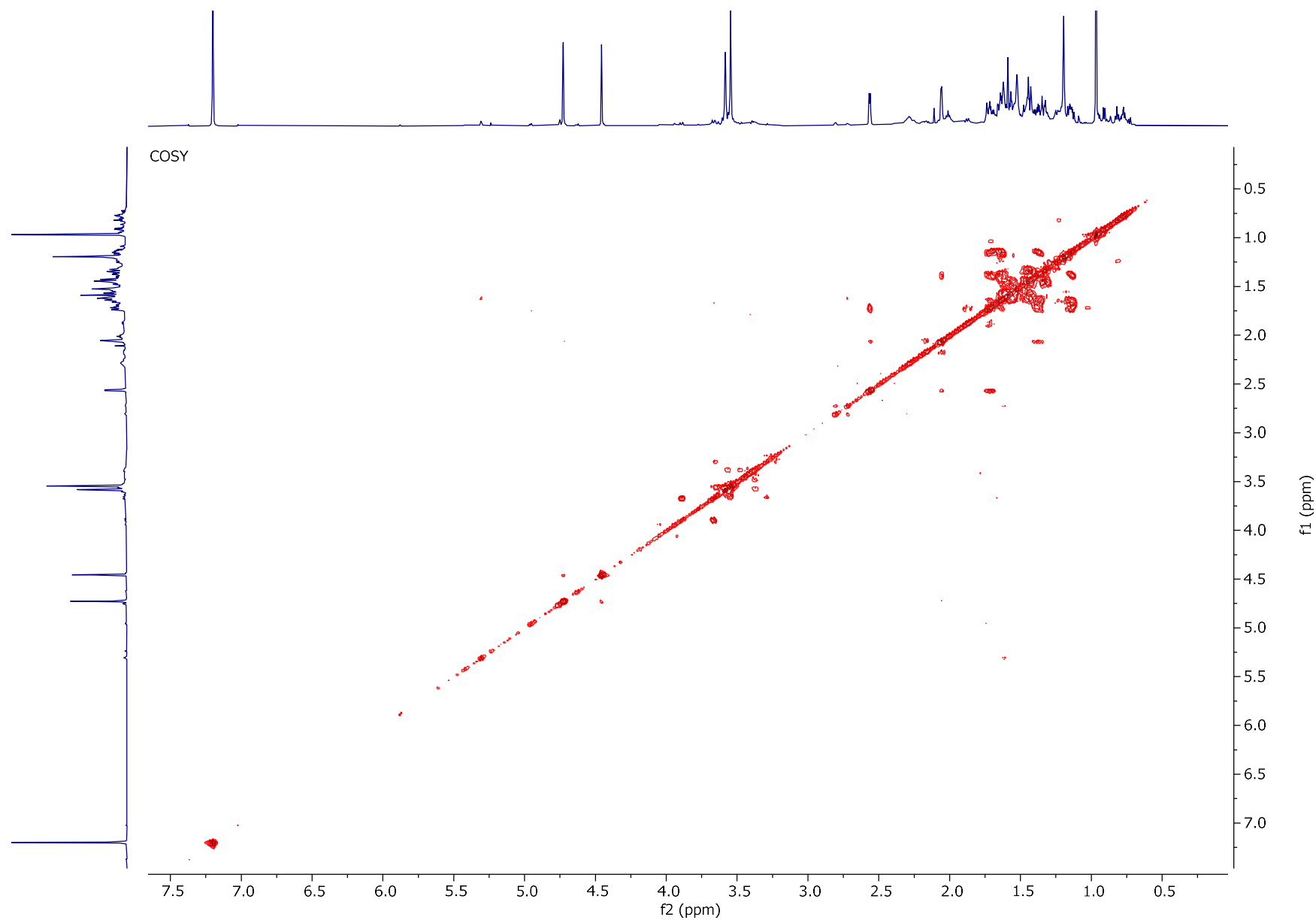


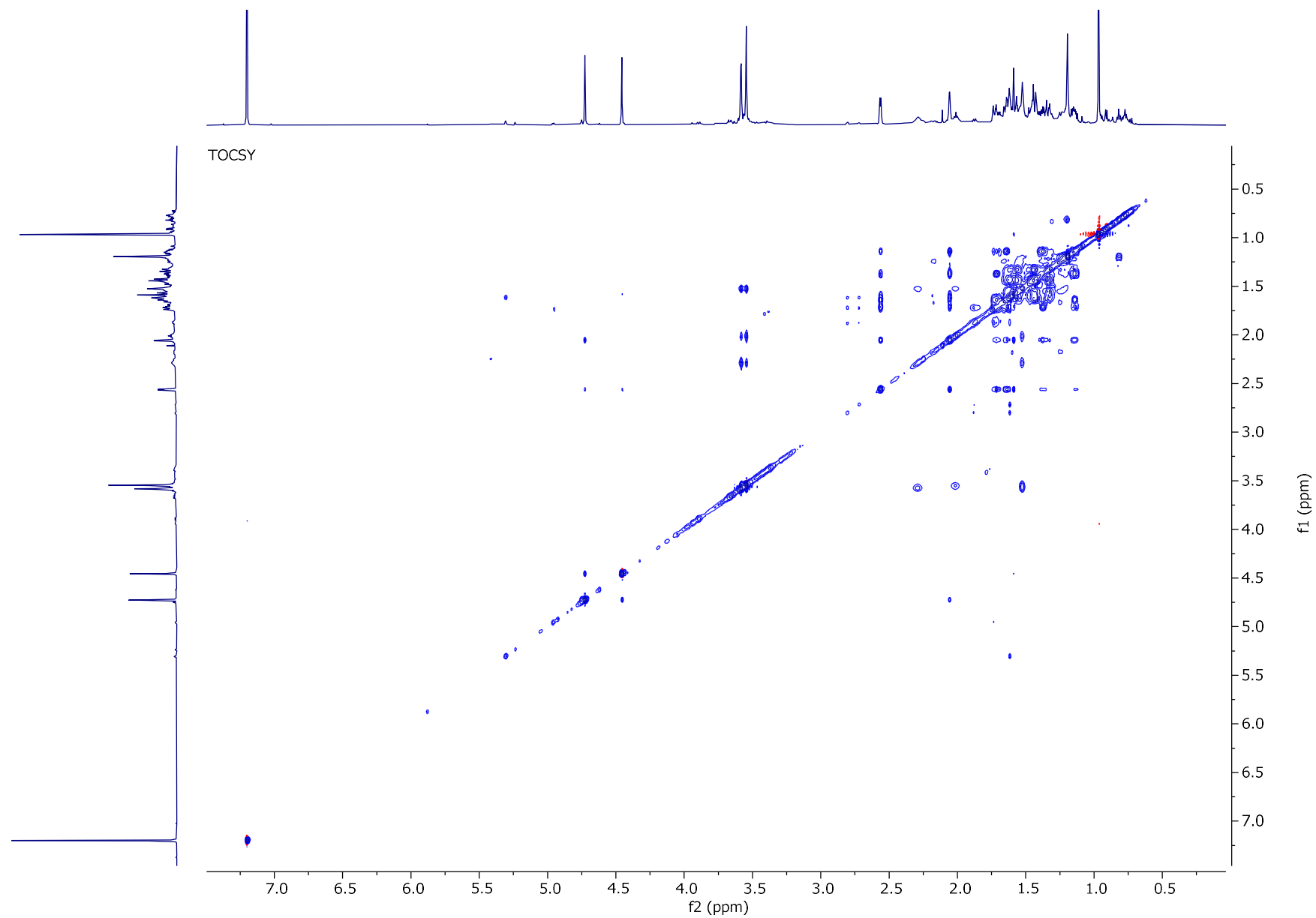


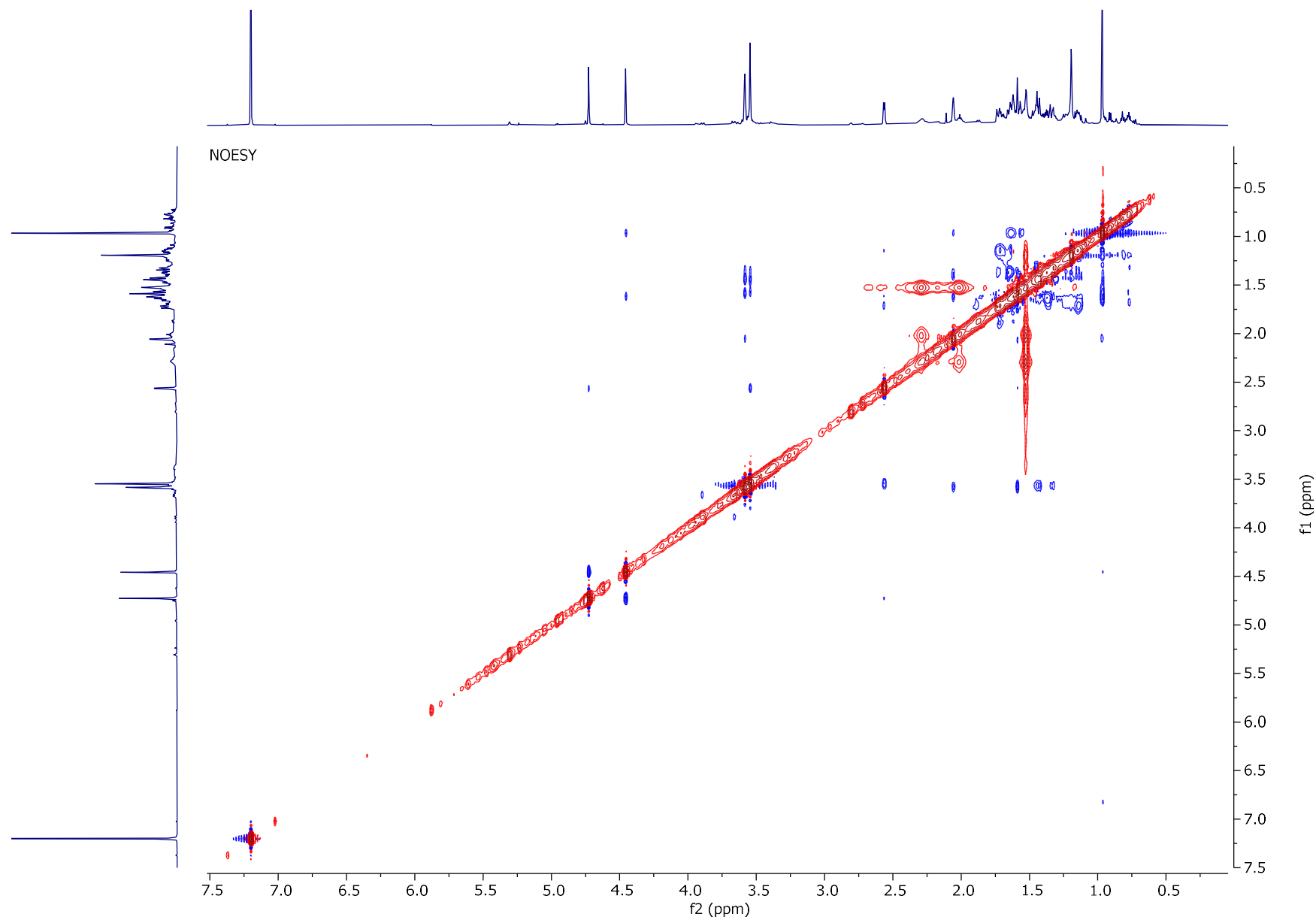




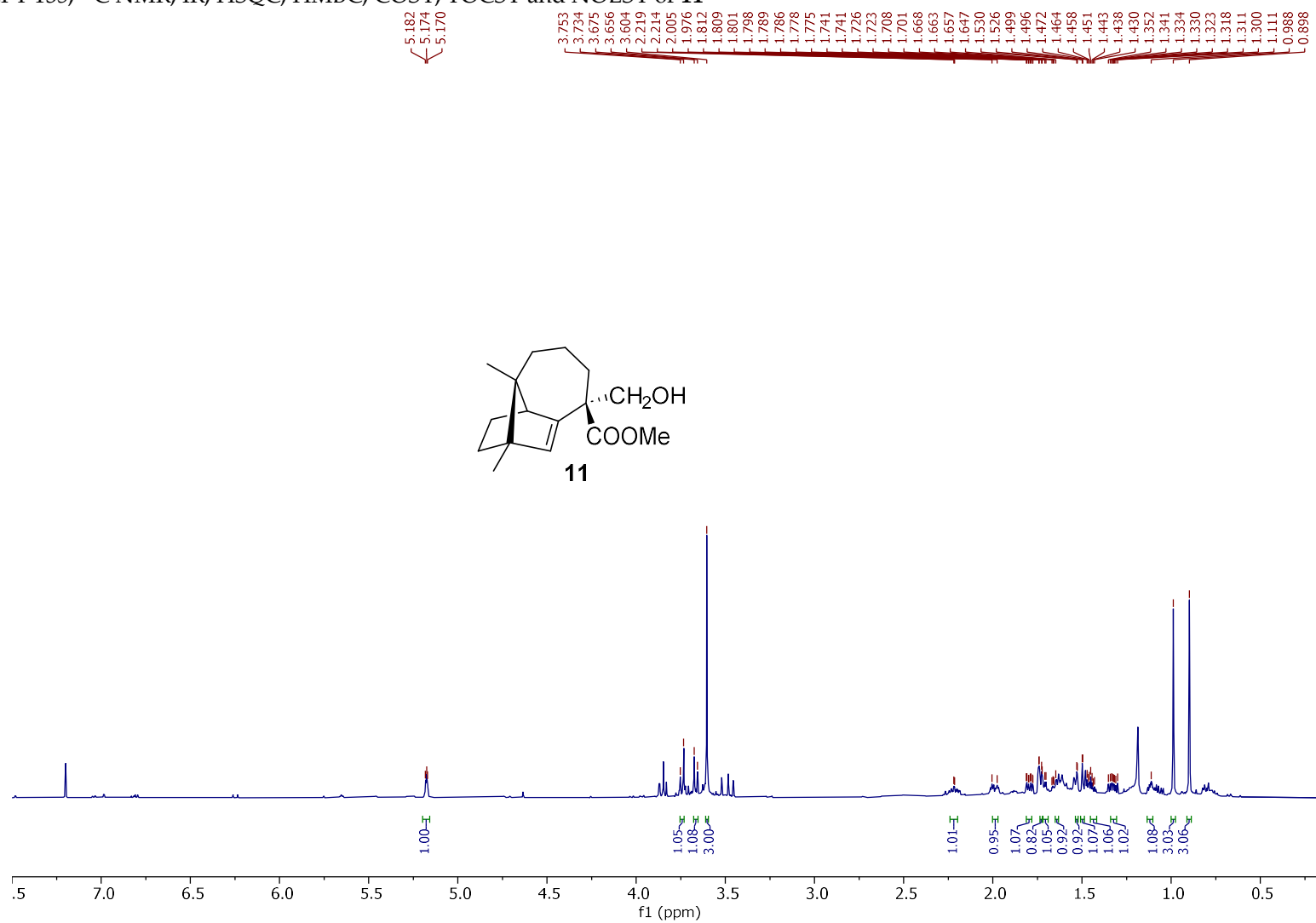


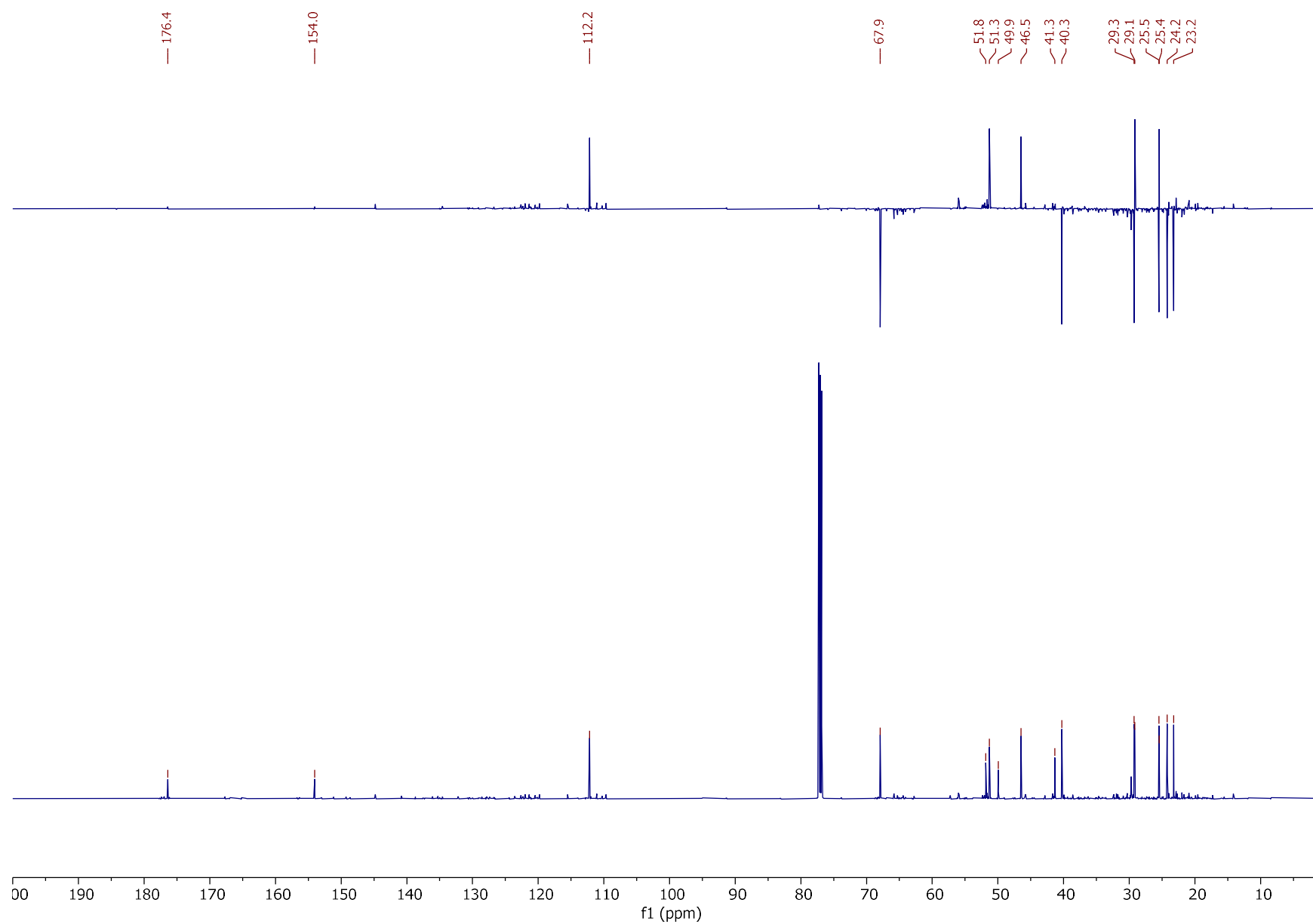


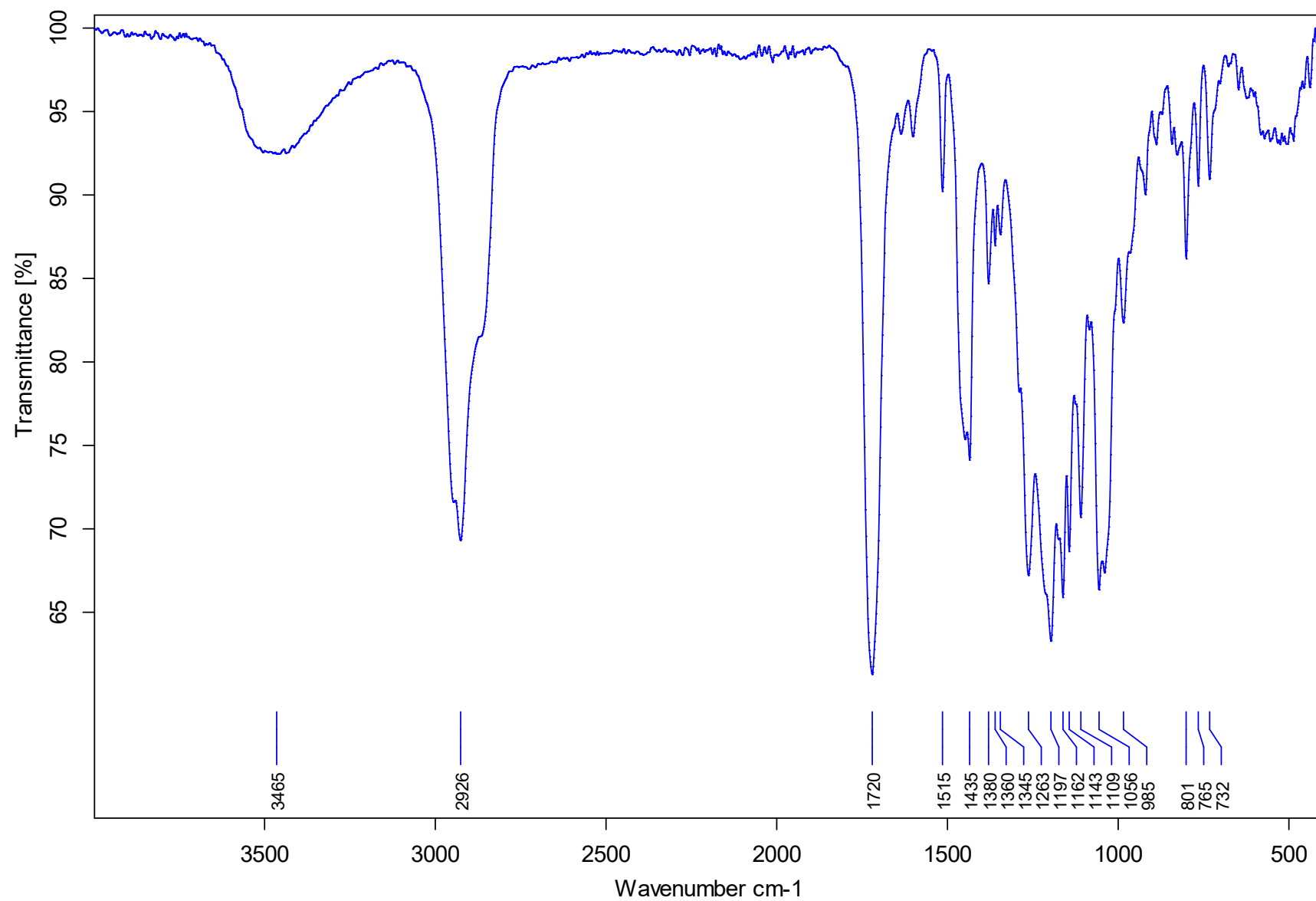




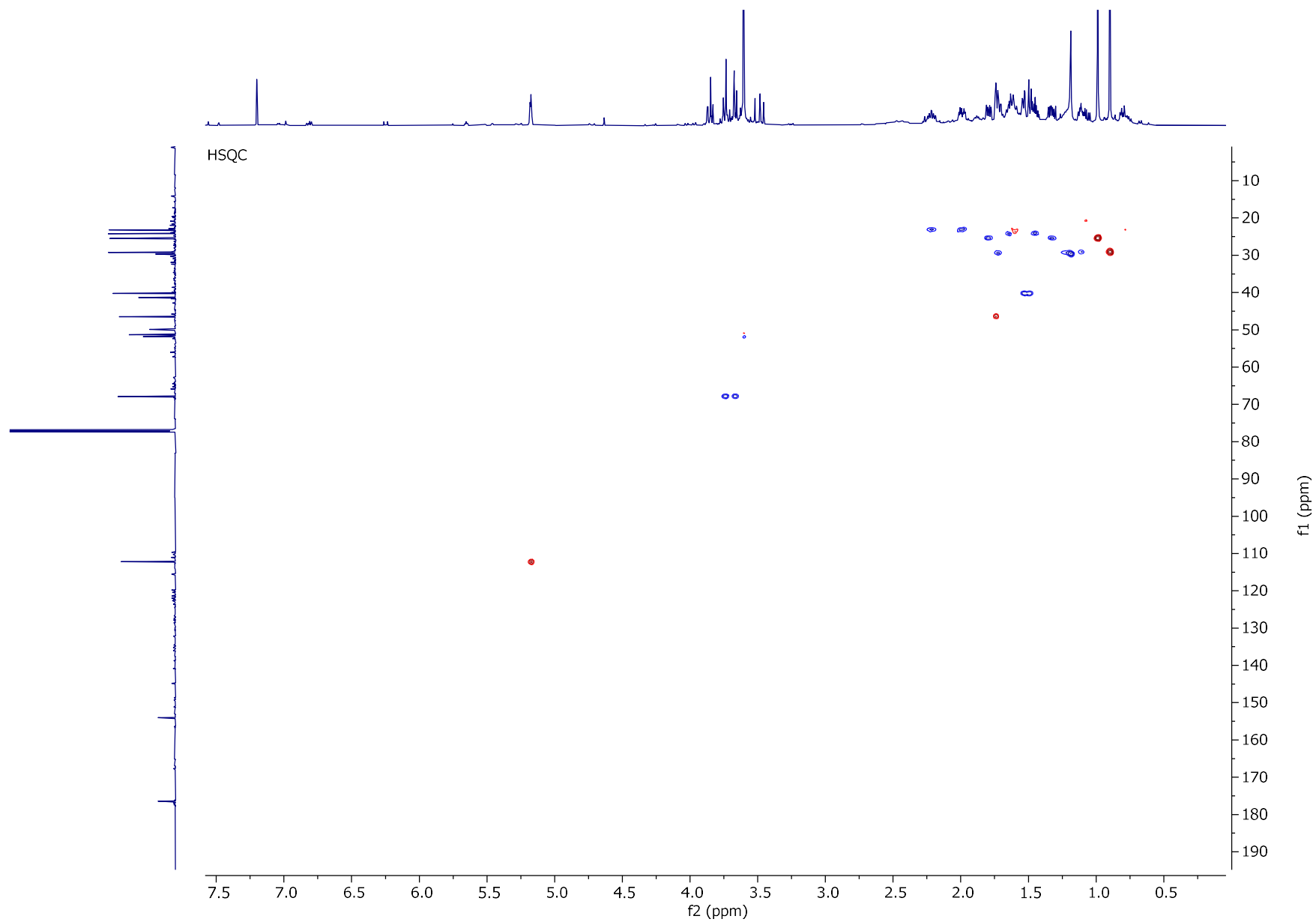
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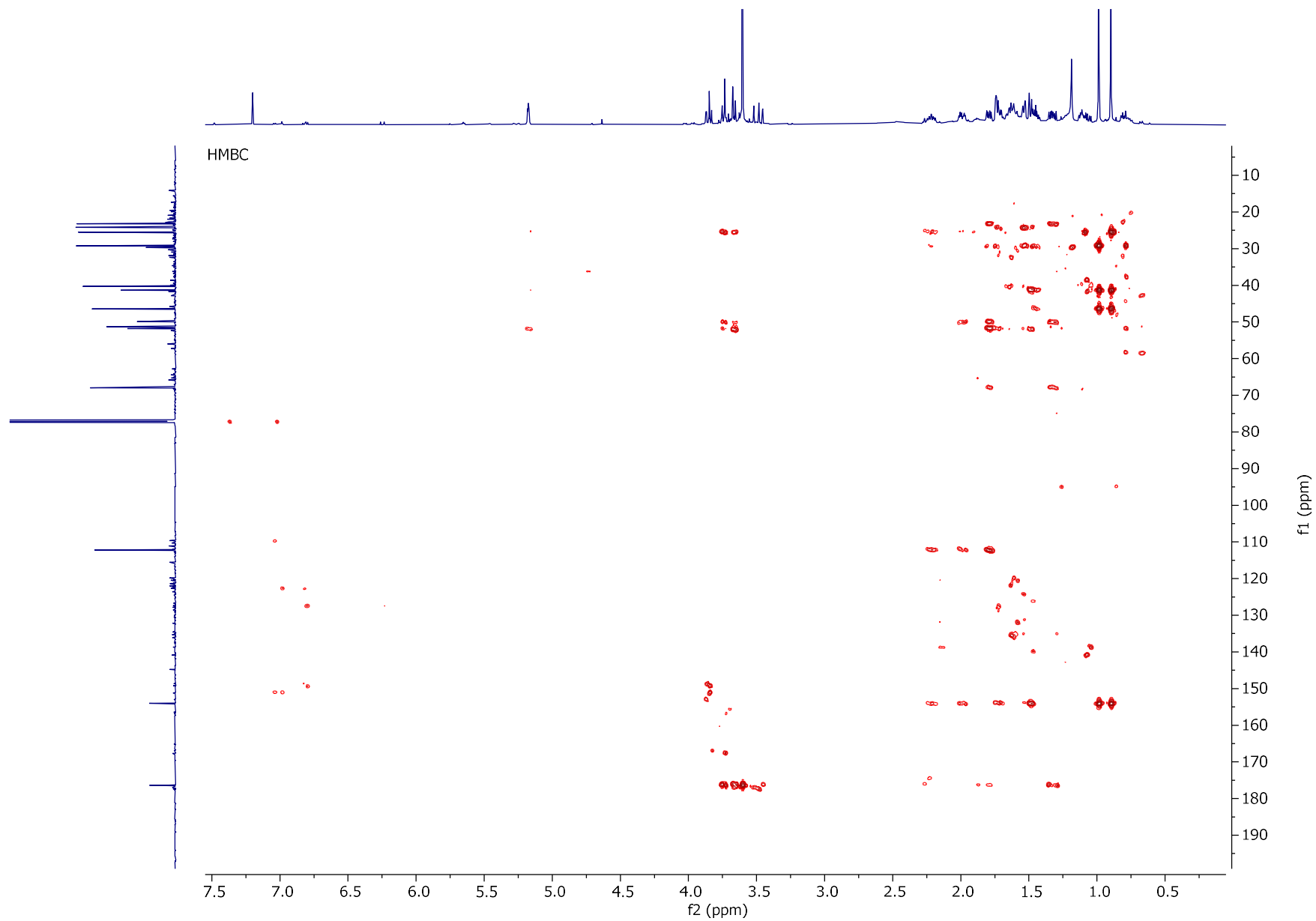


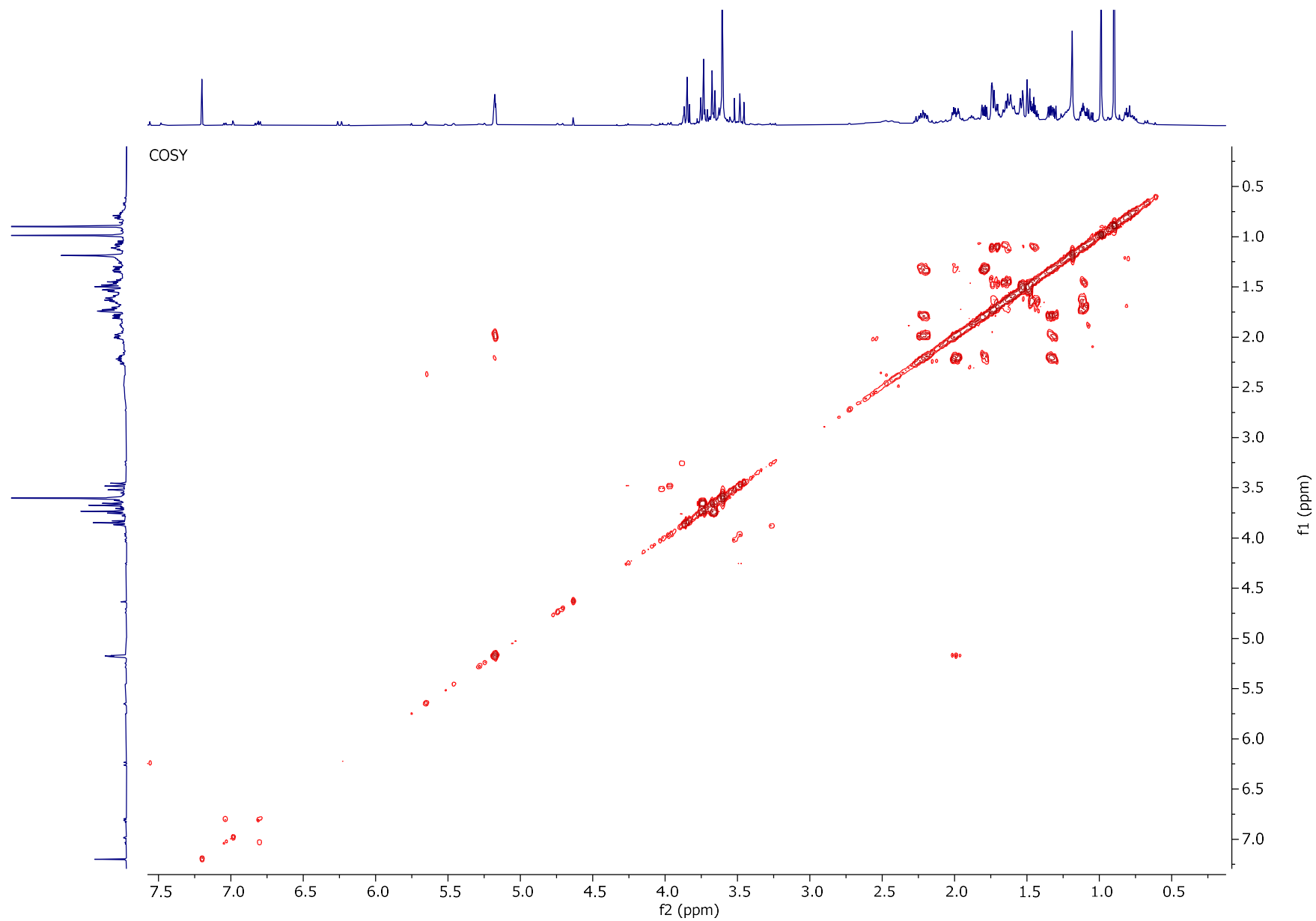


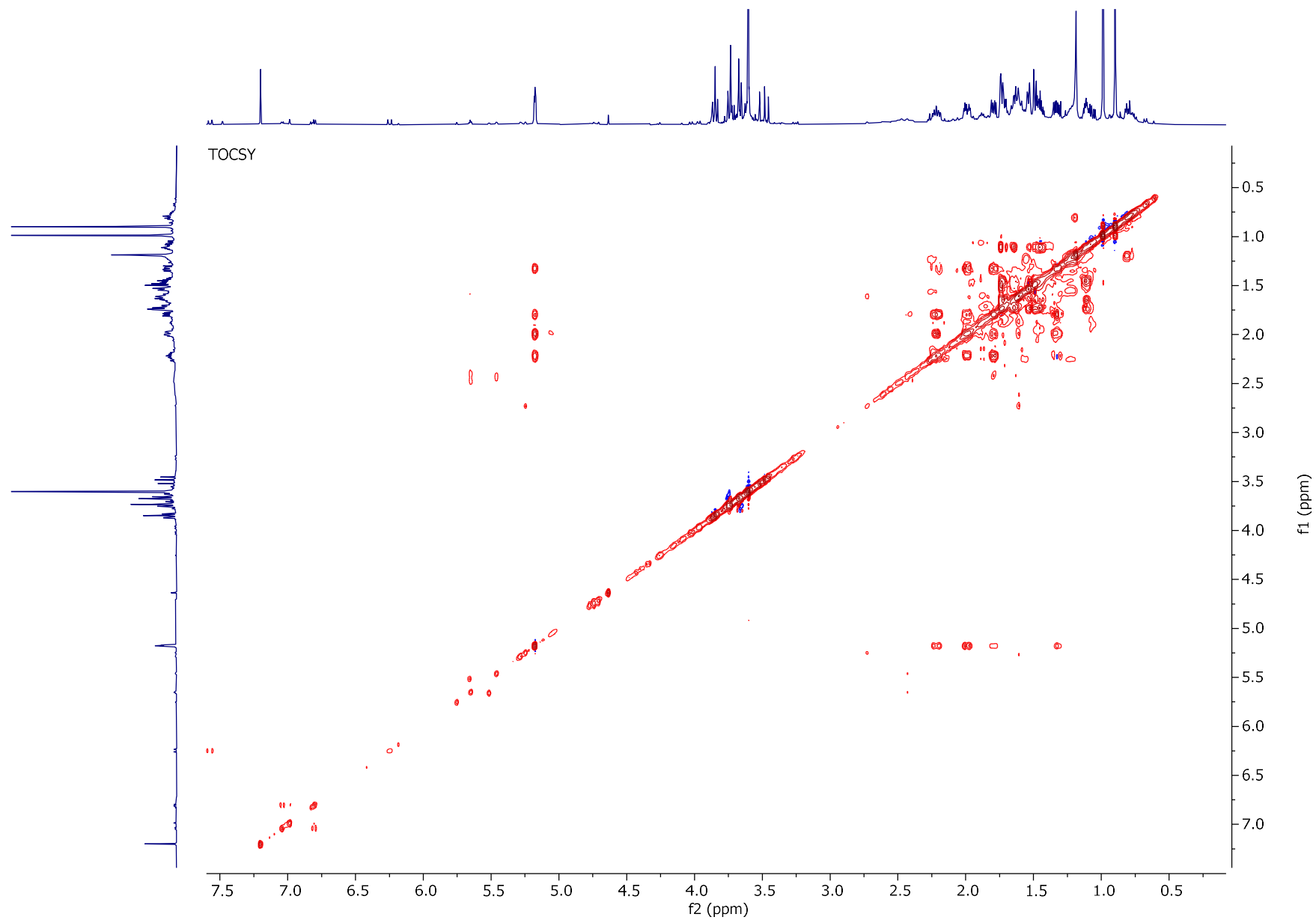


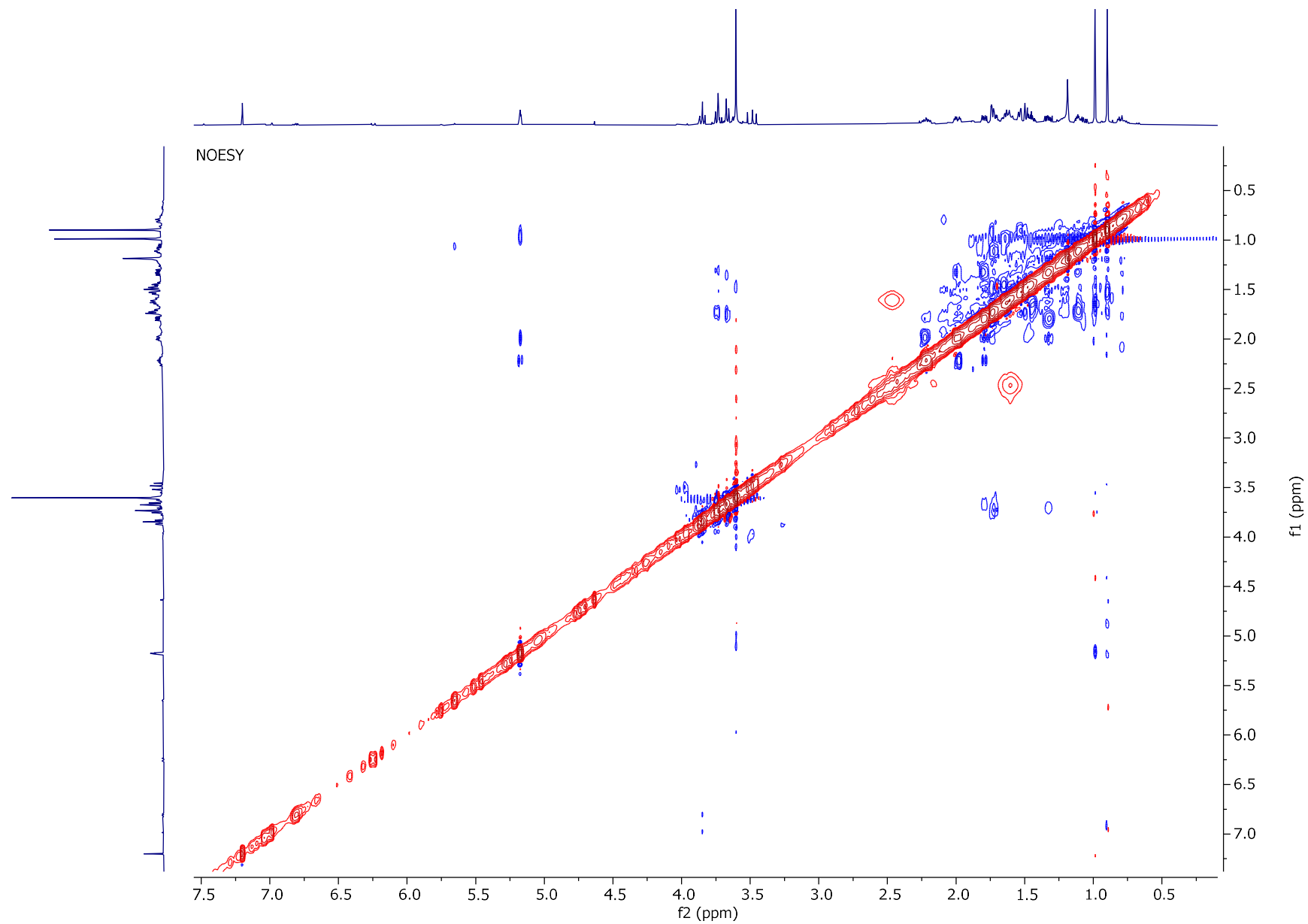




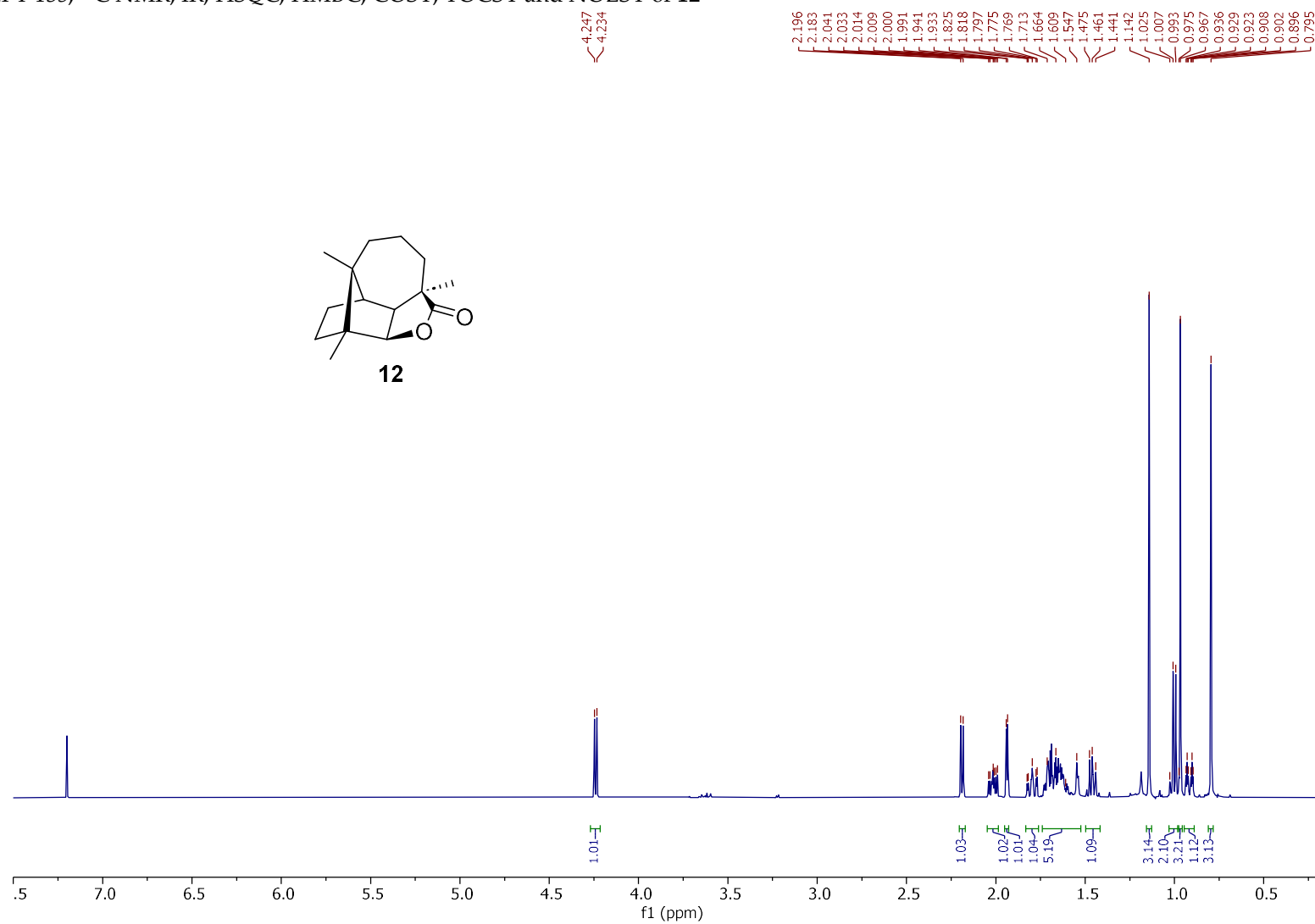


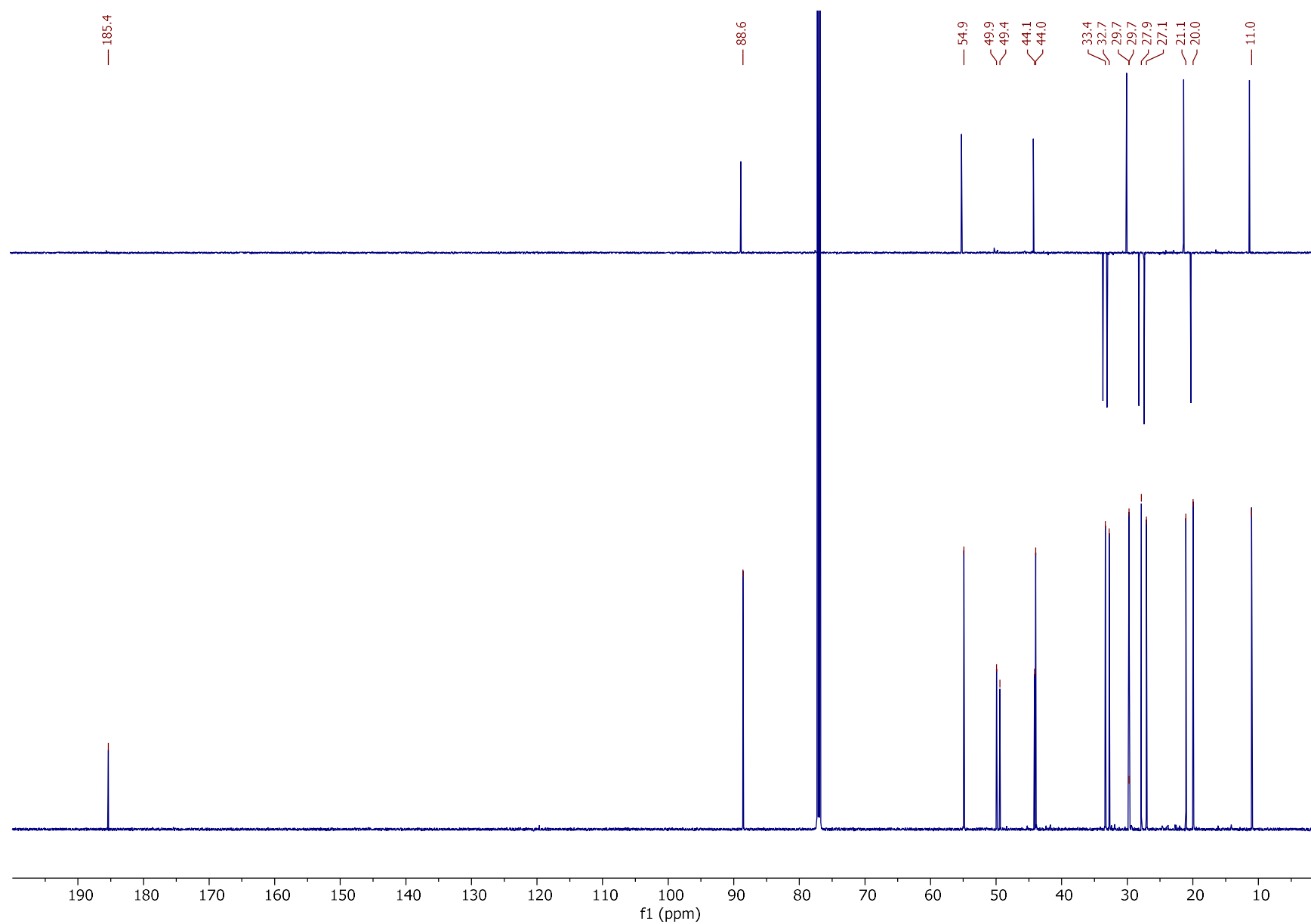


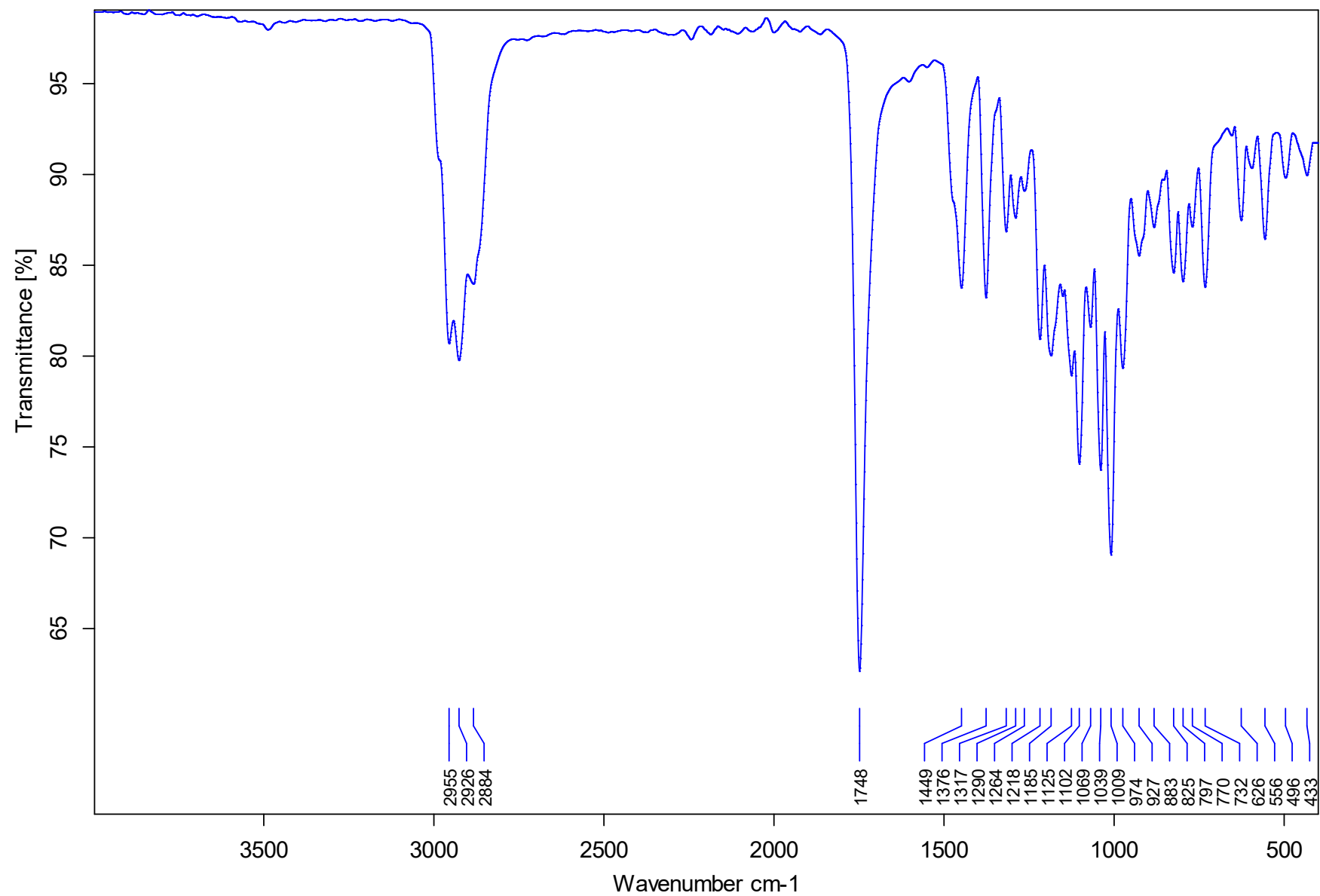




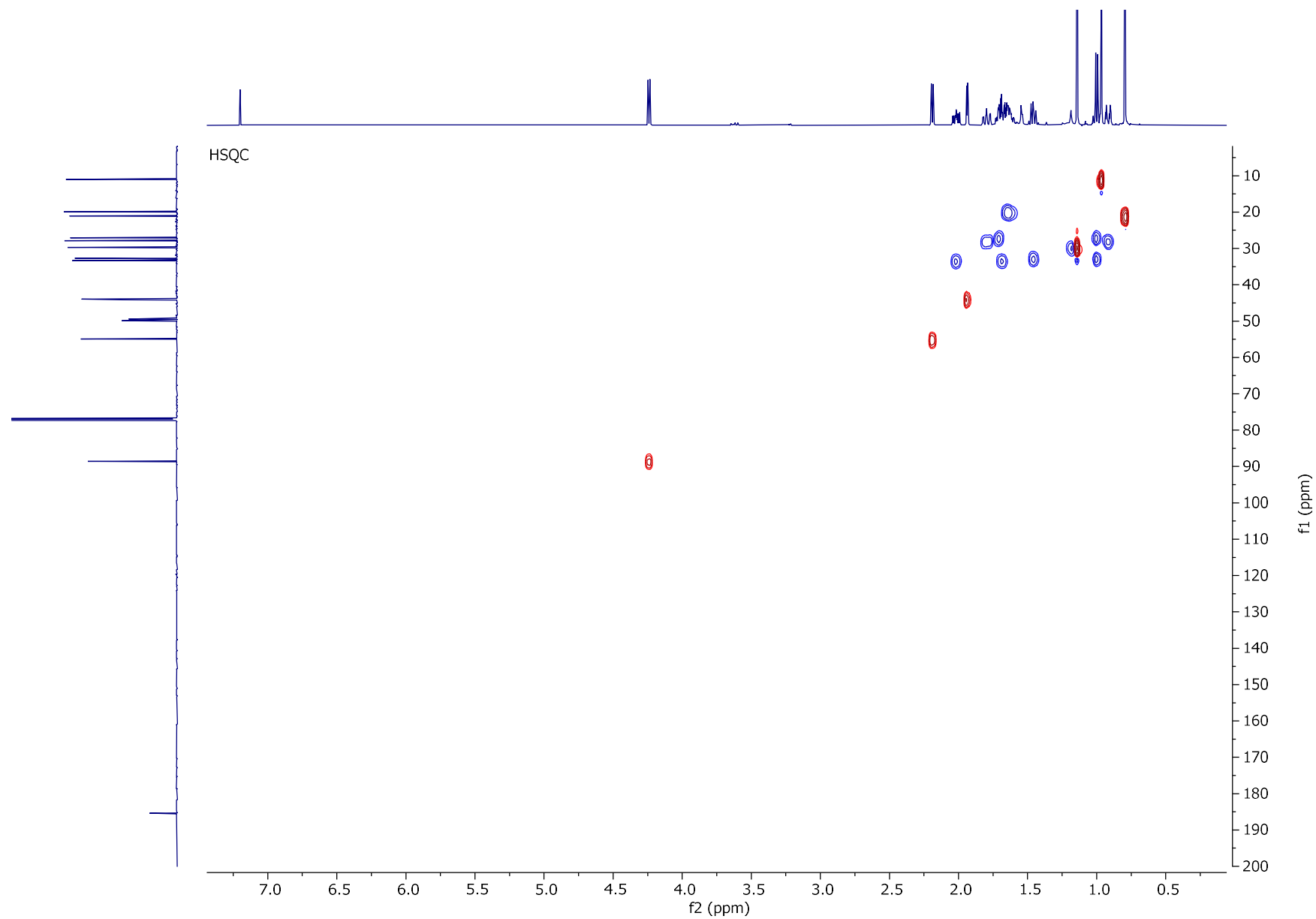
$^1\text{H}$  NMR DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **12**

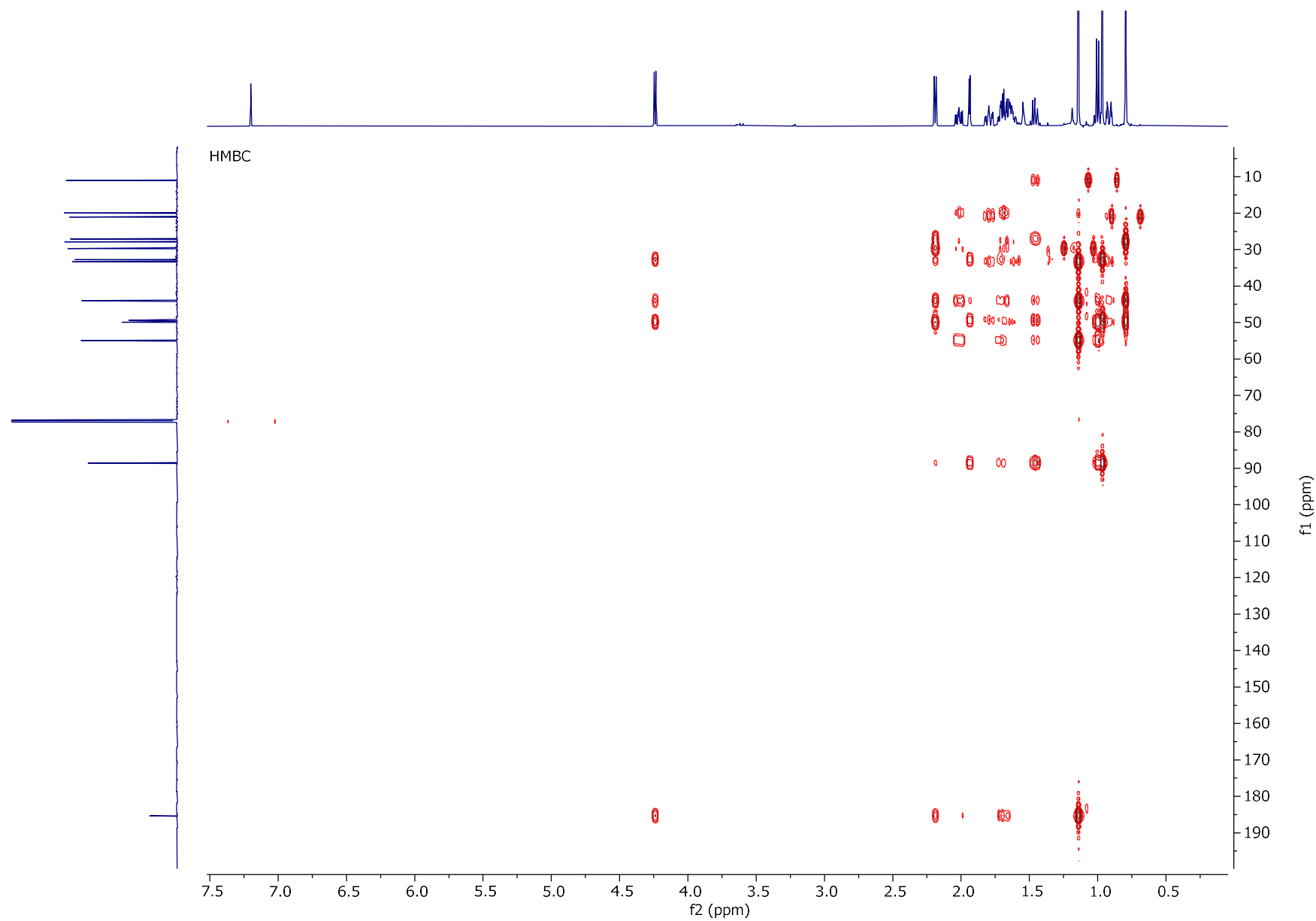


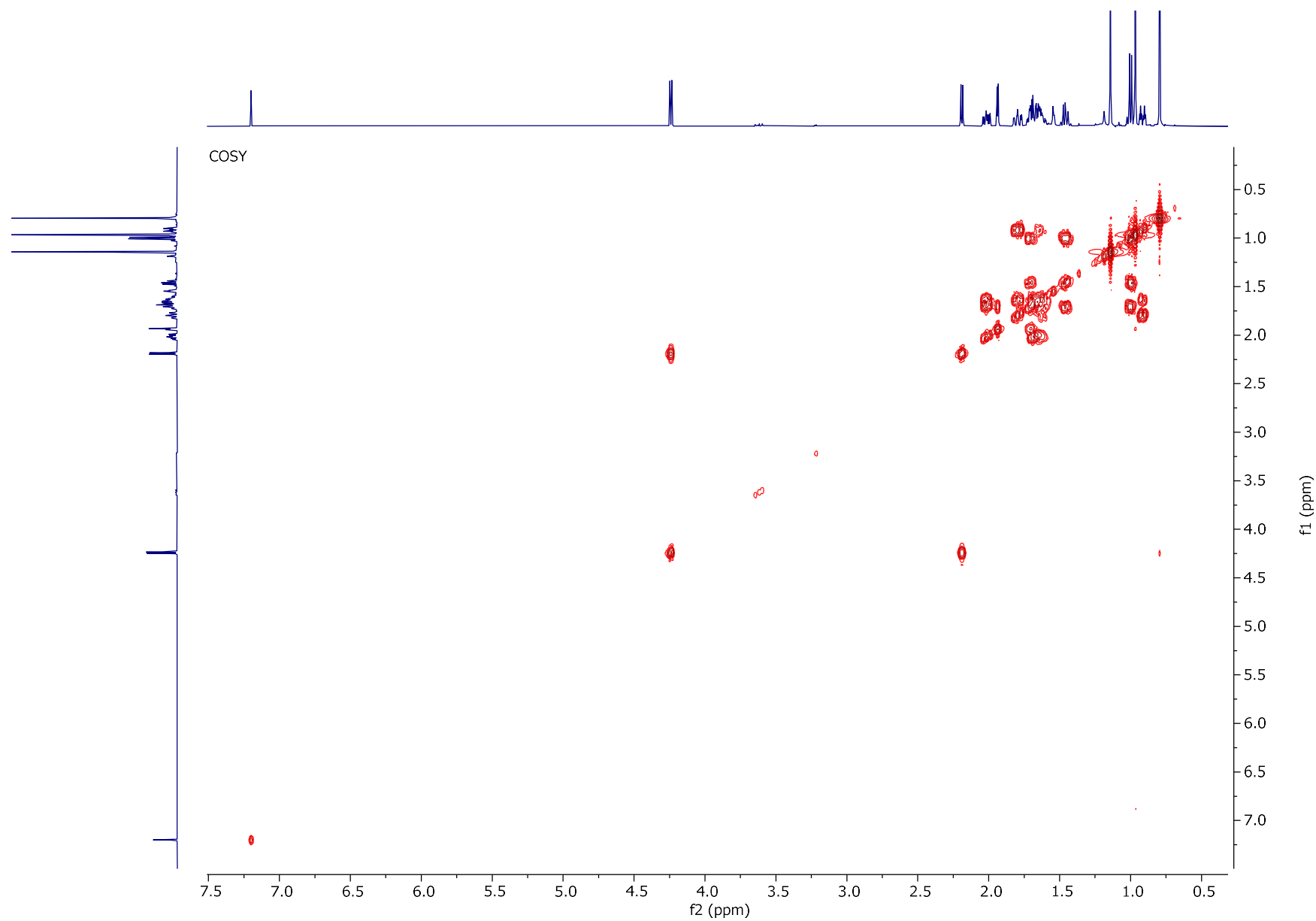


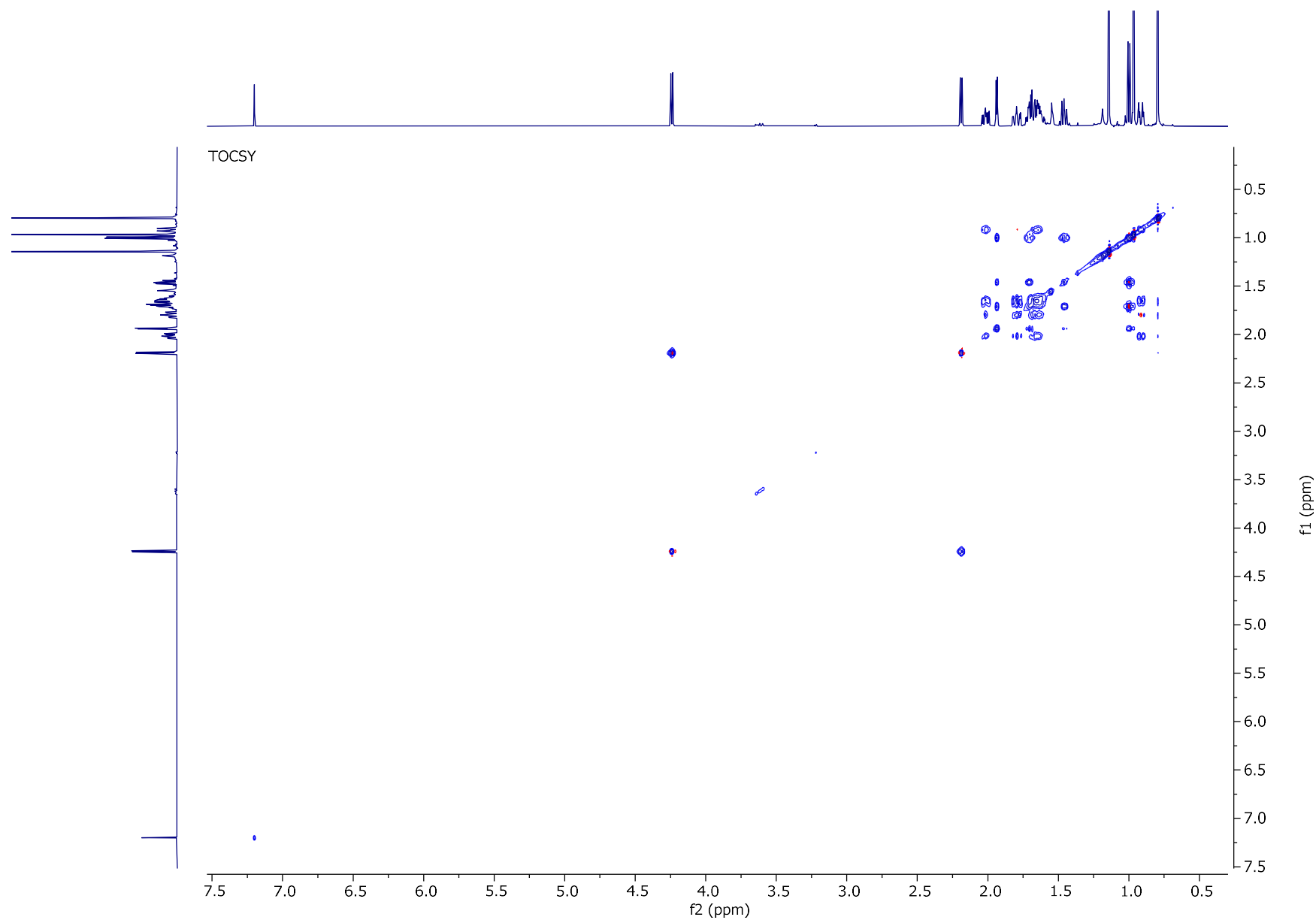


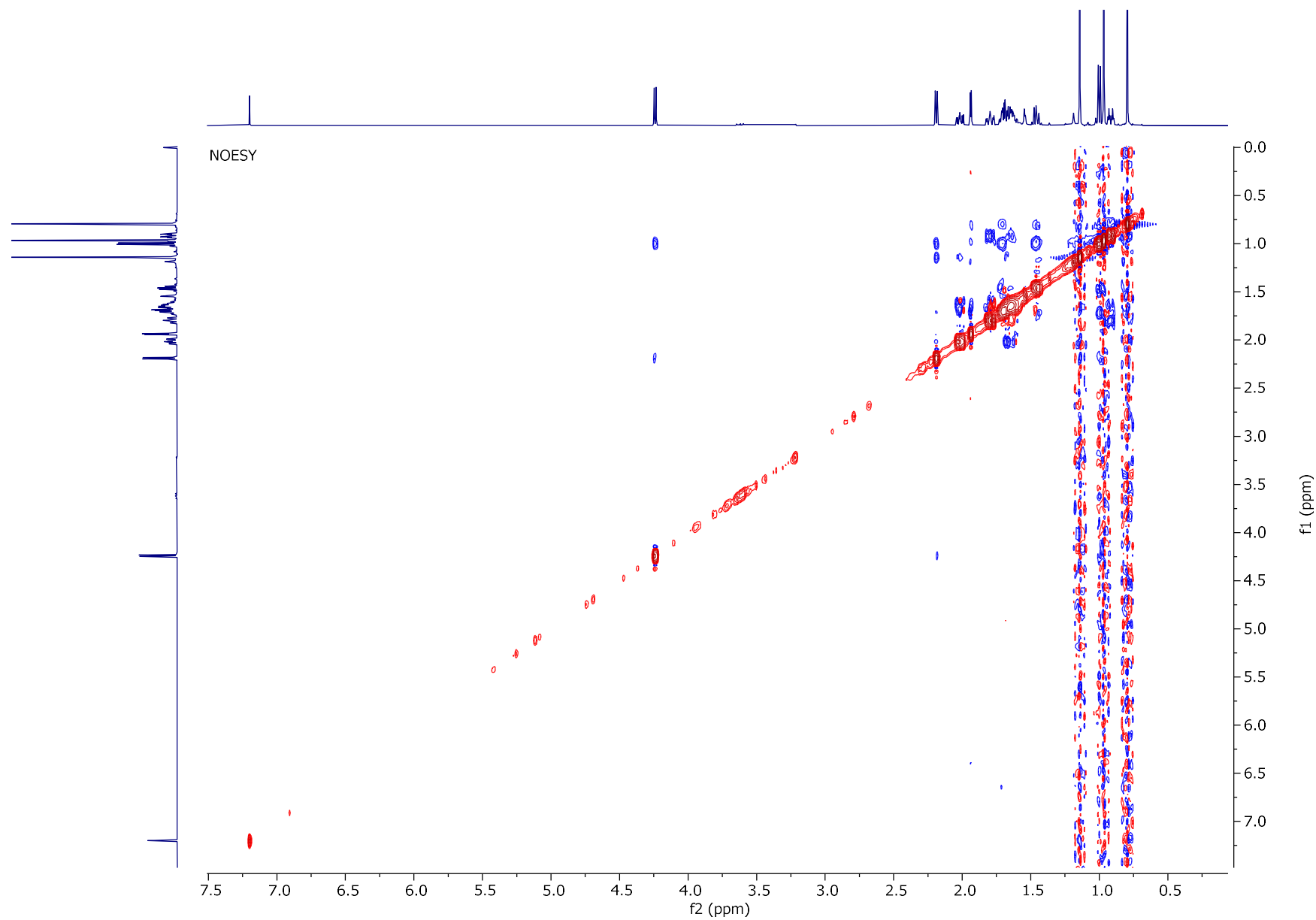




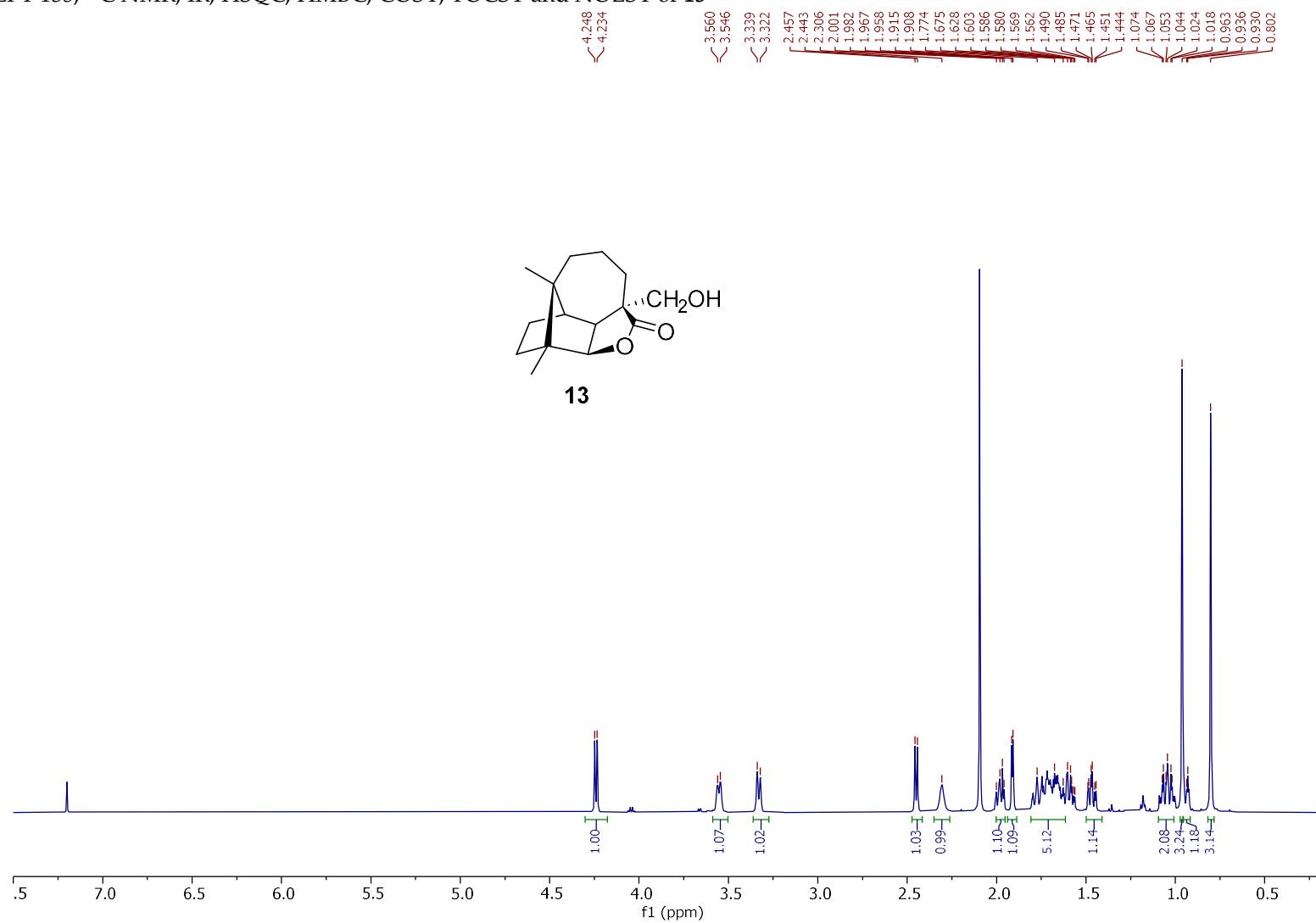


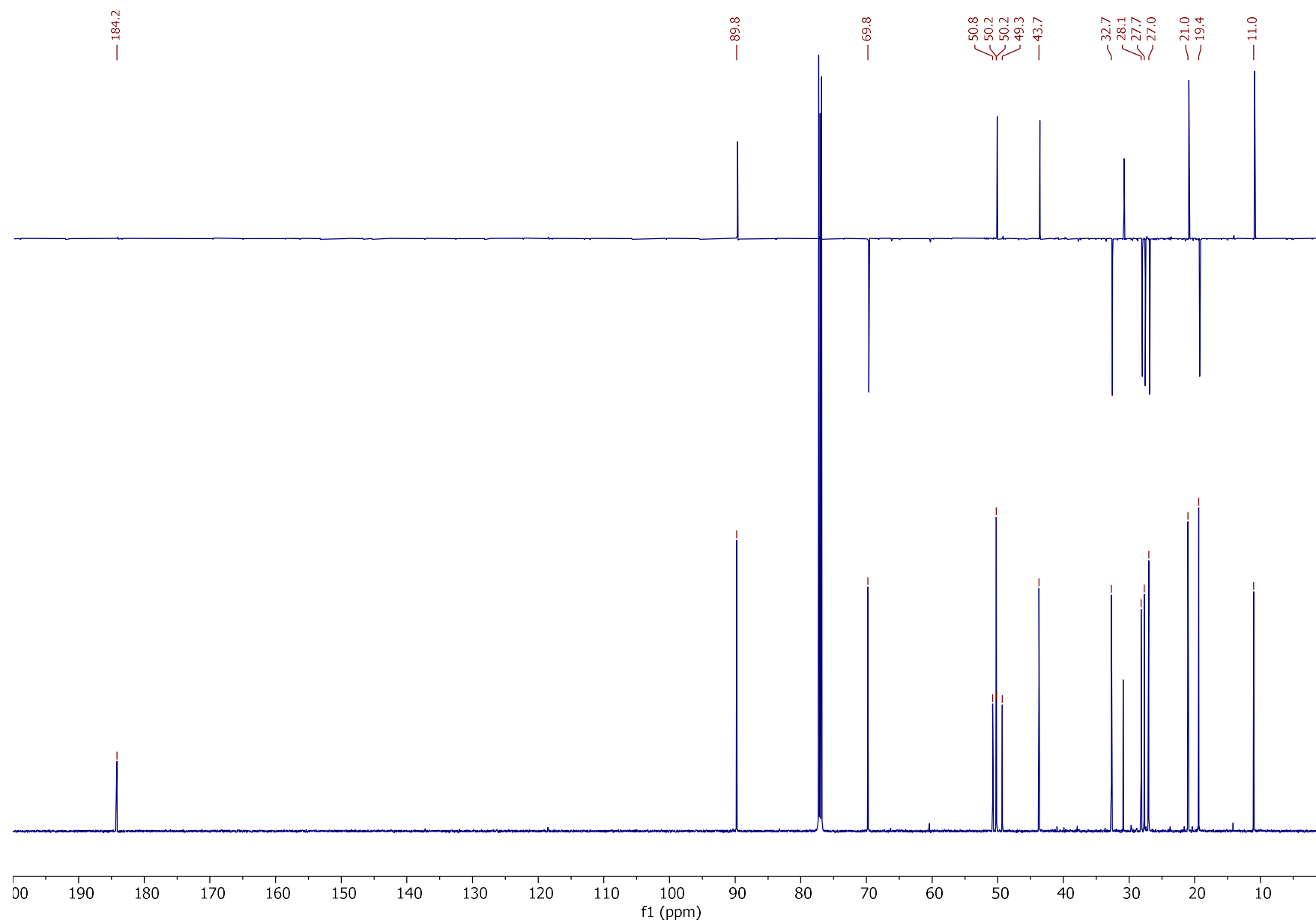


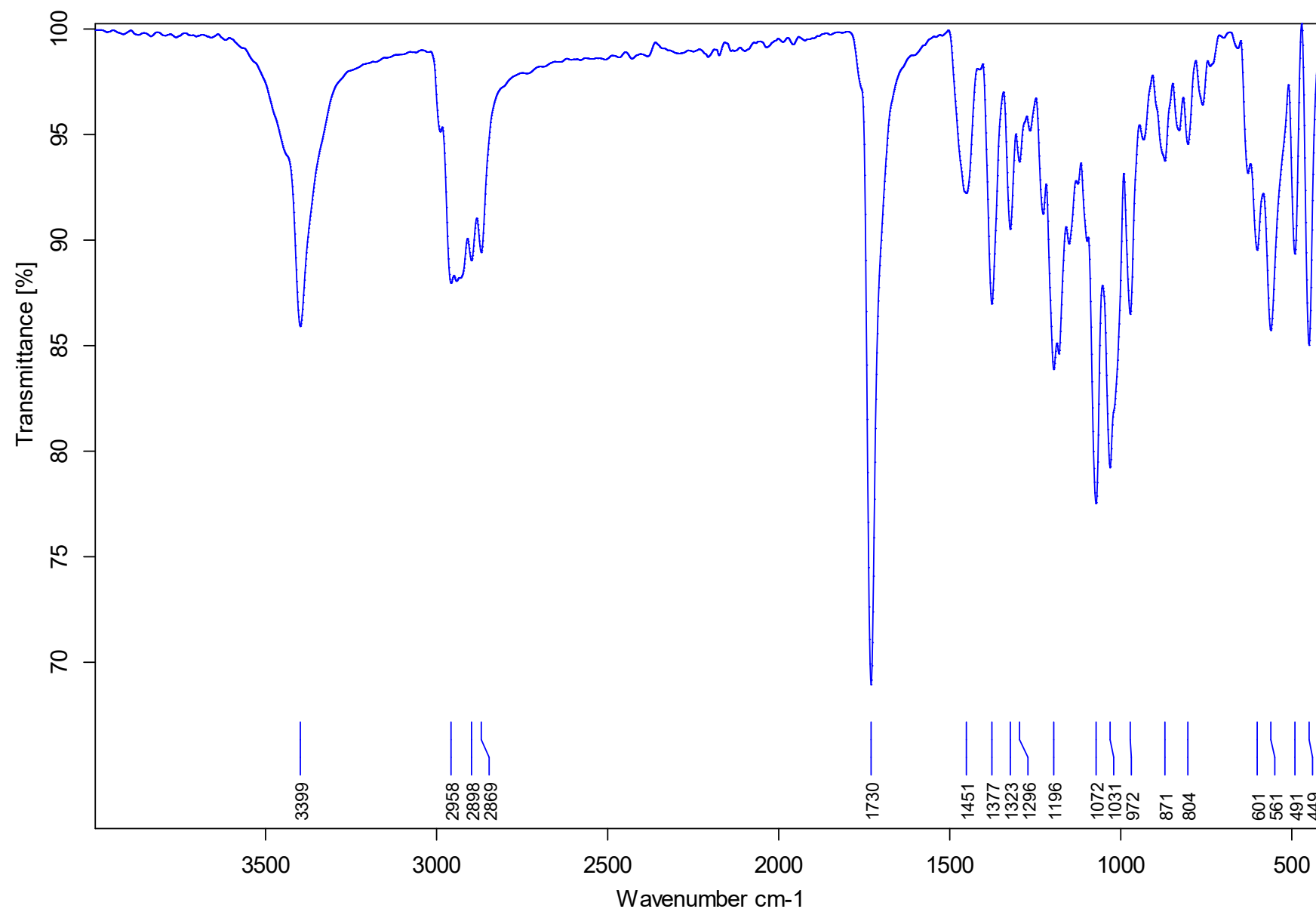




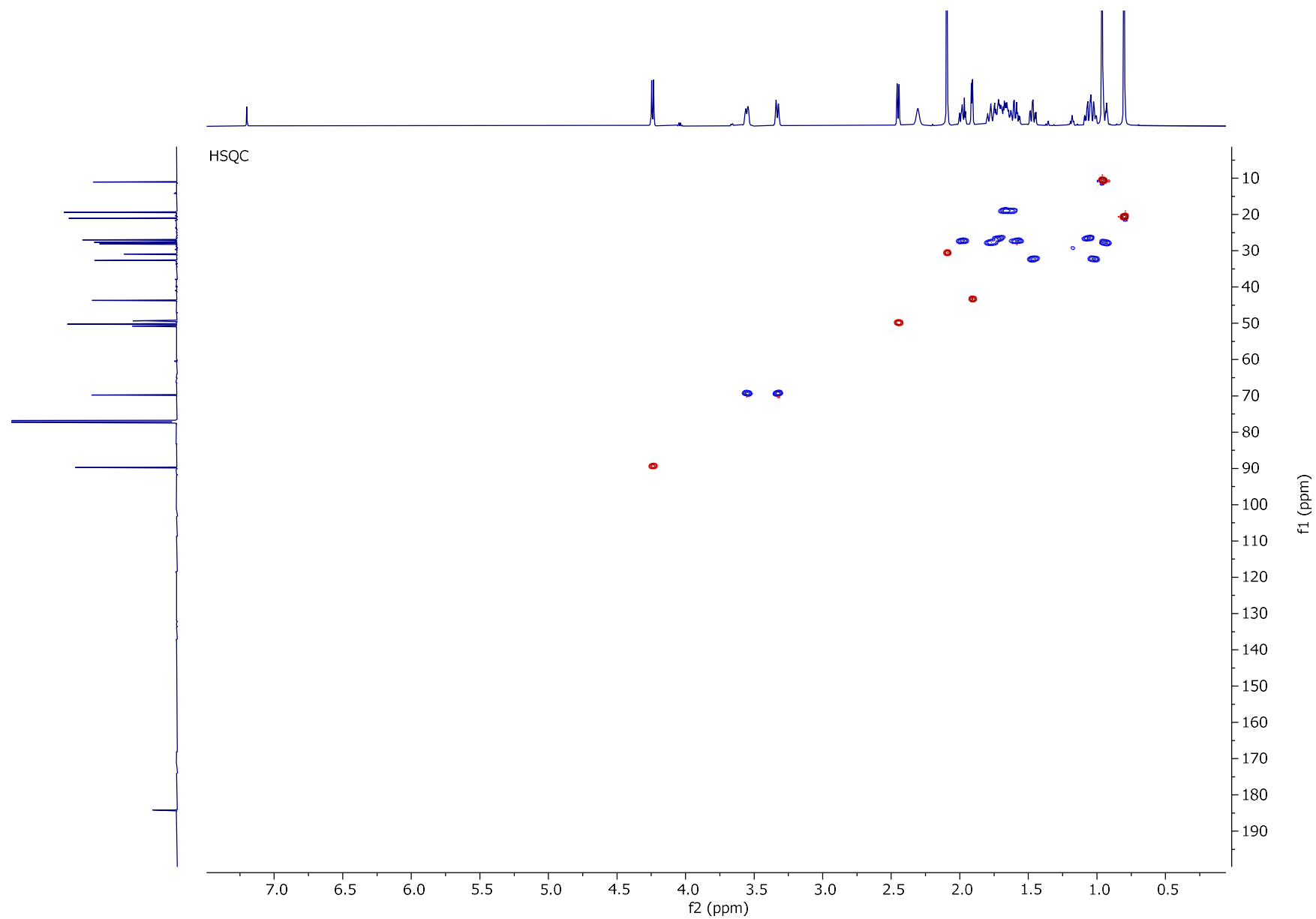
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **13**

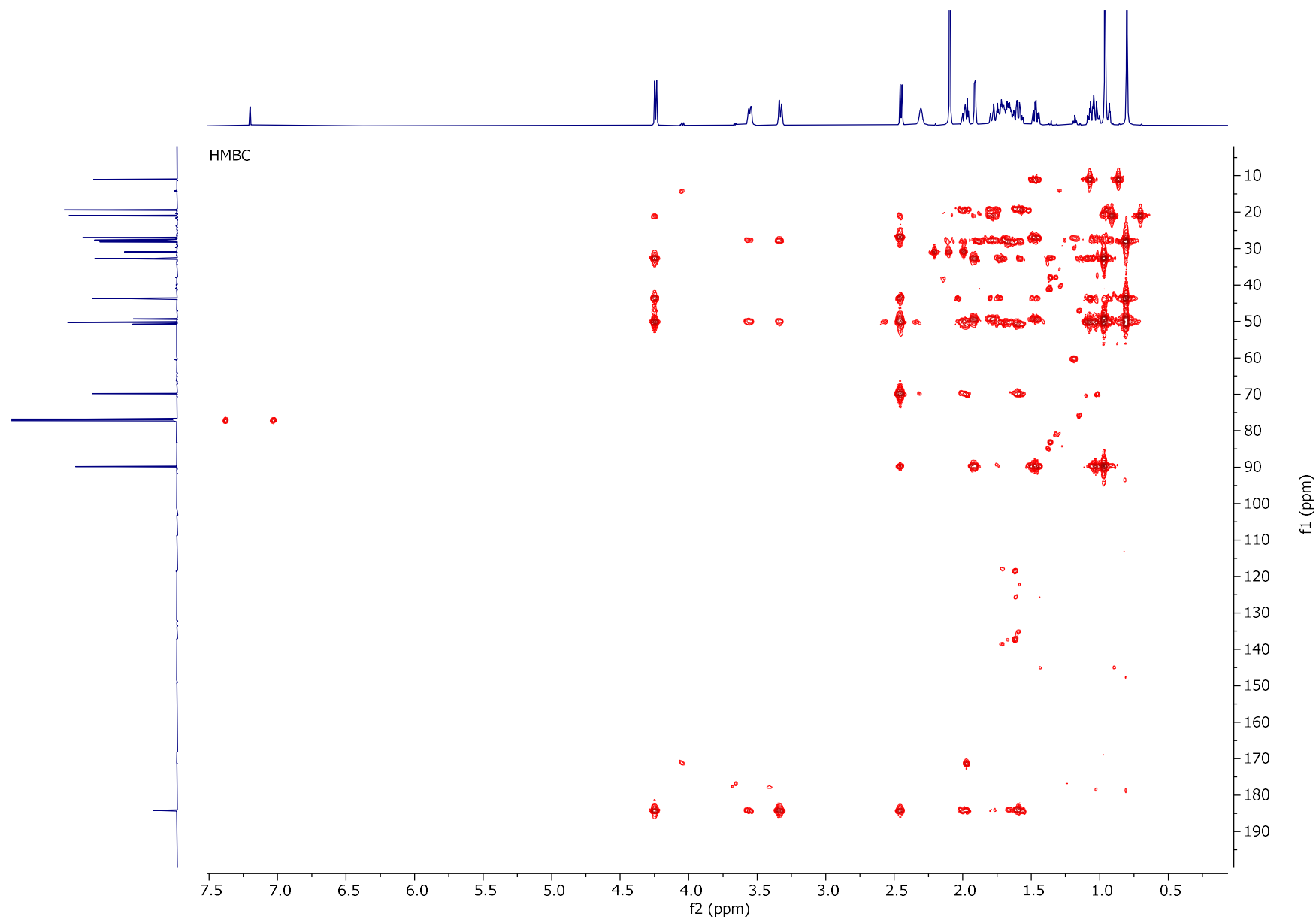


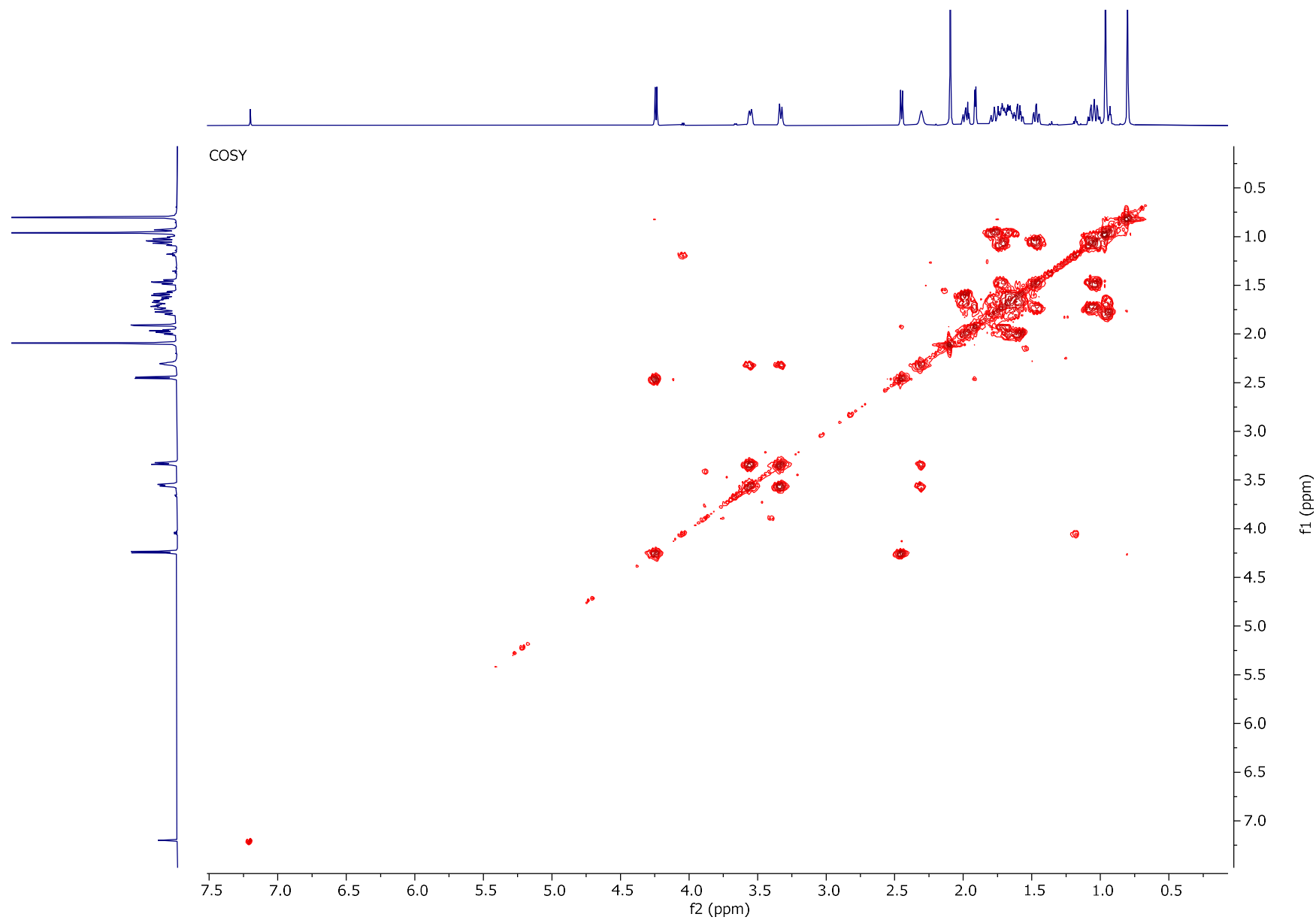


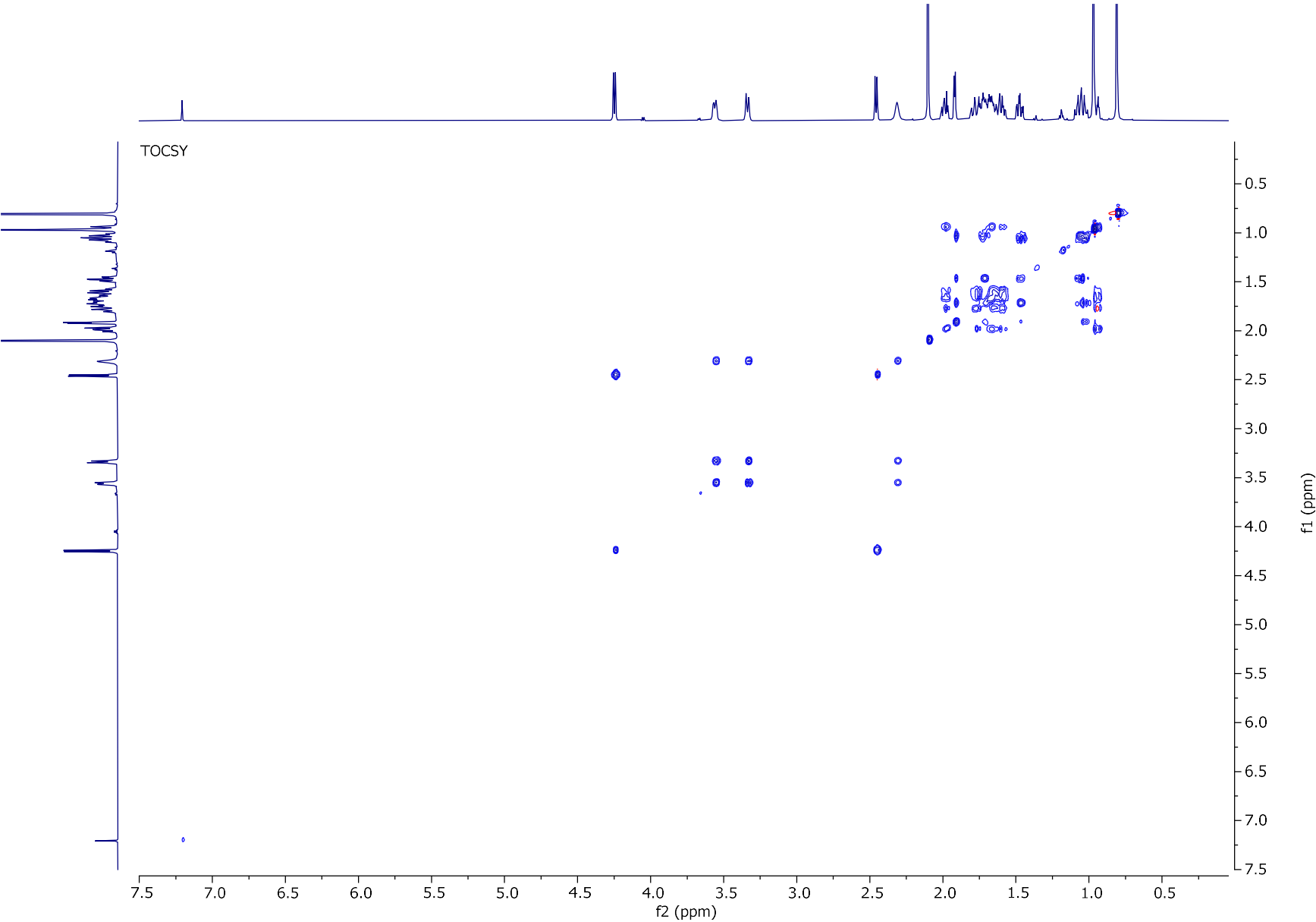


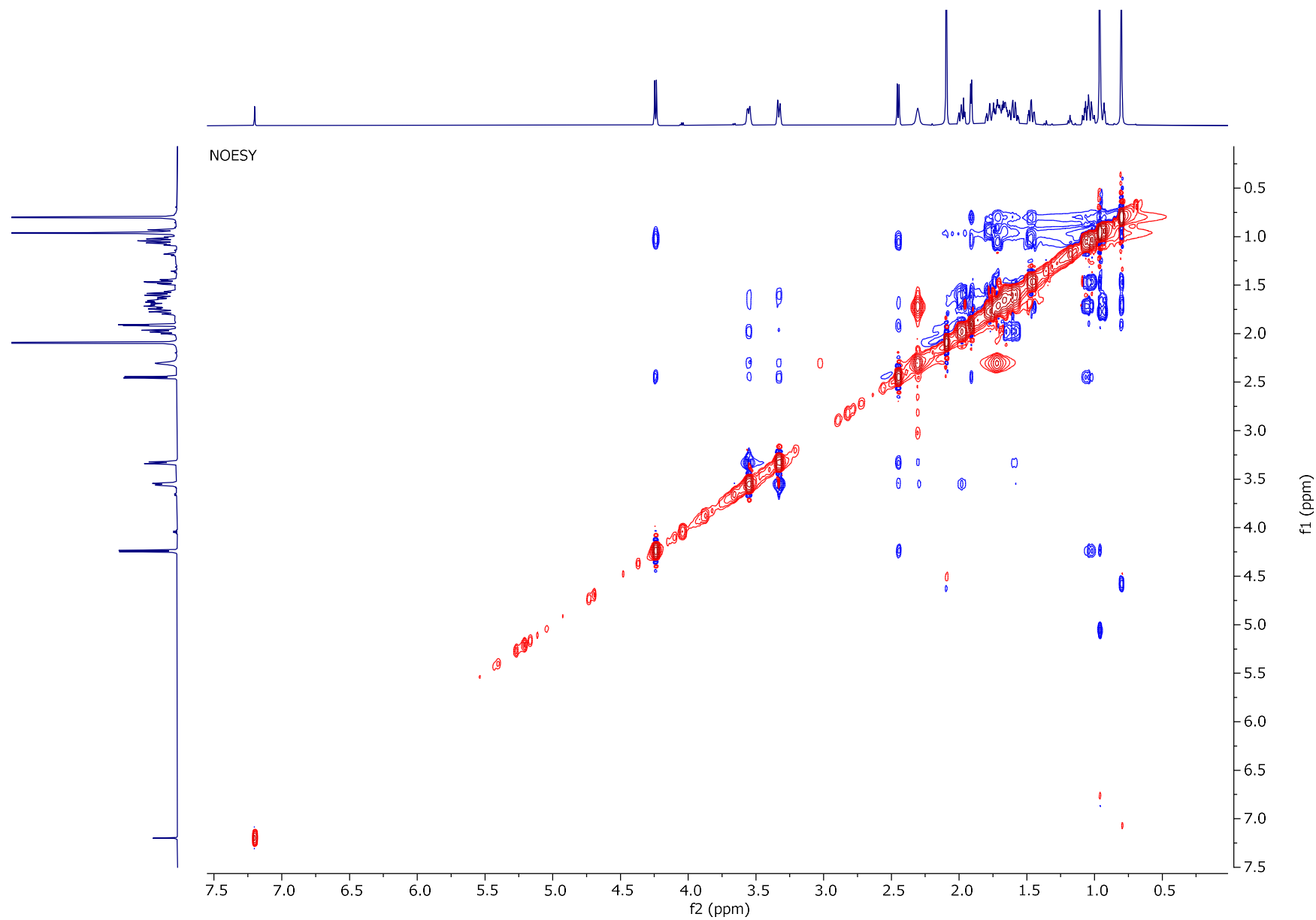


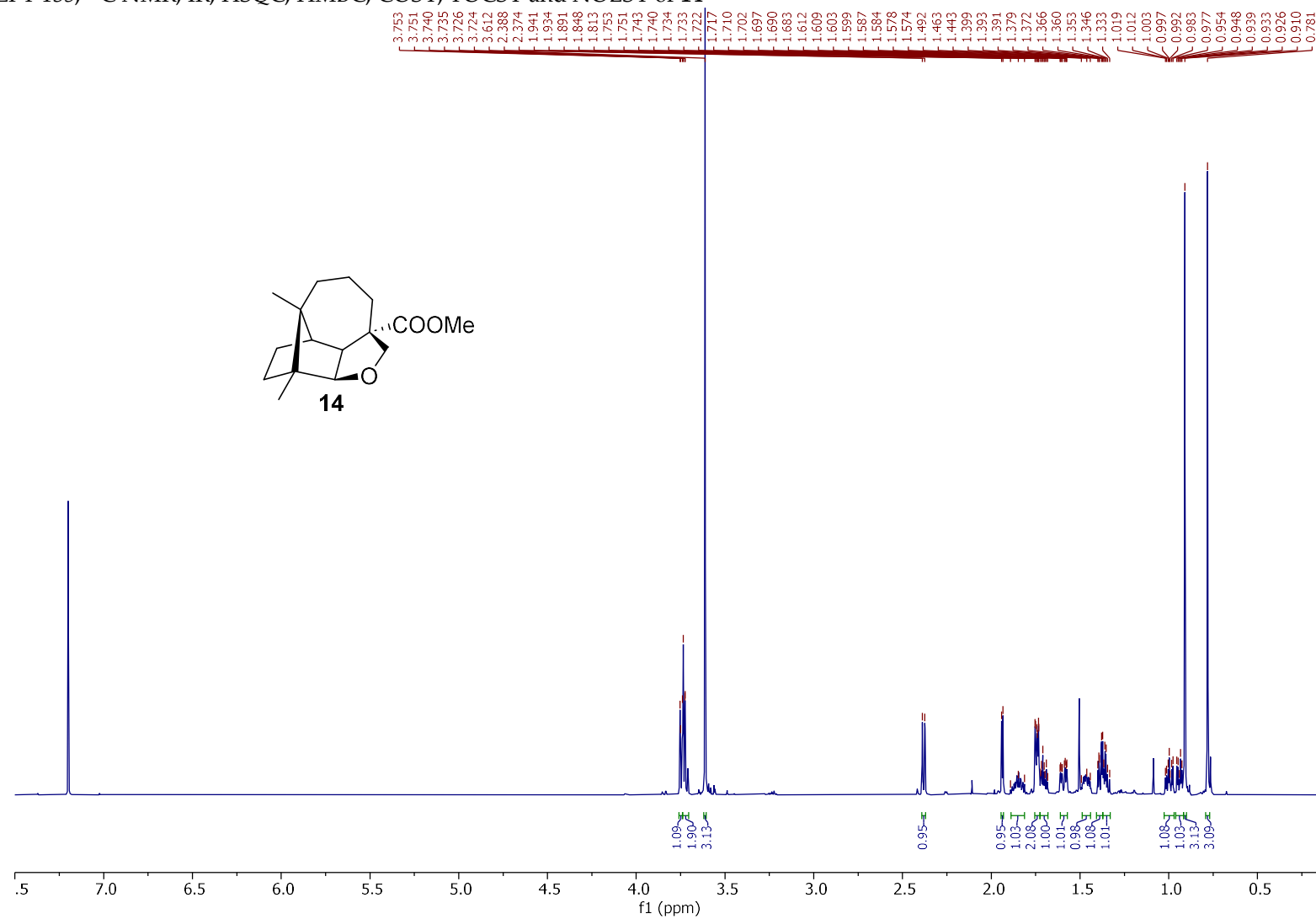


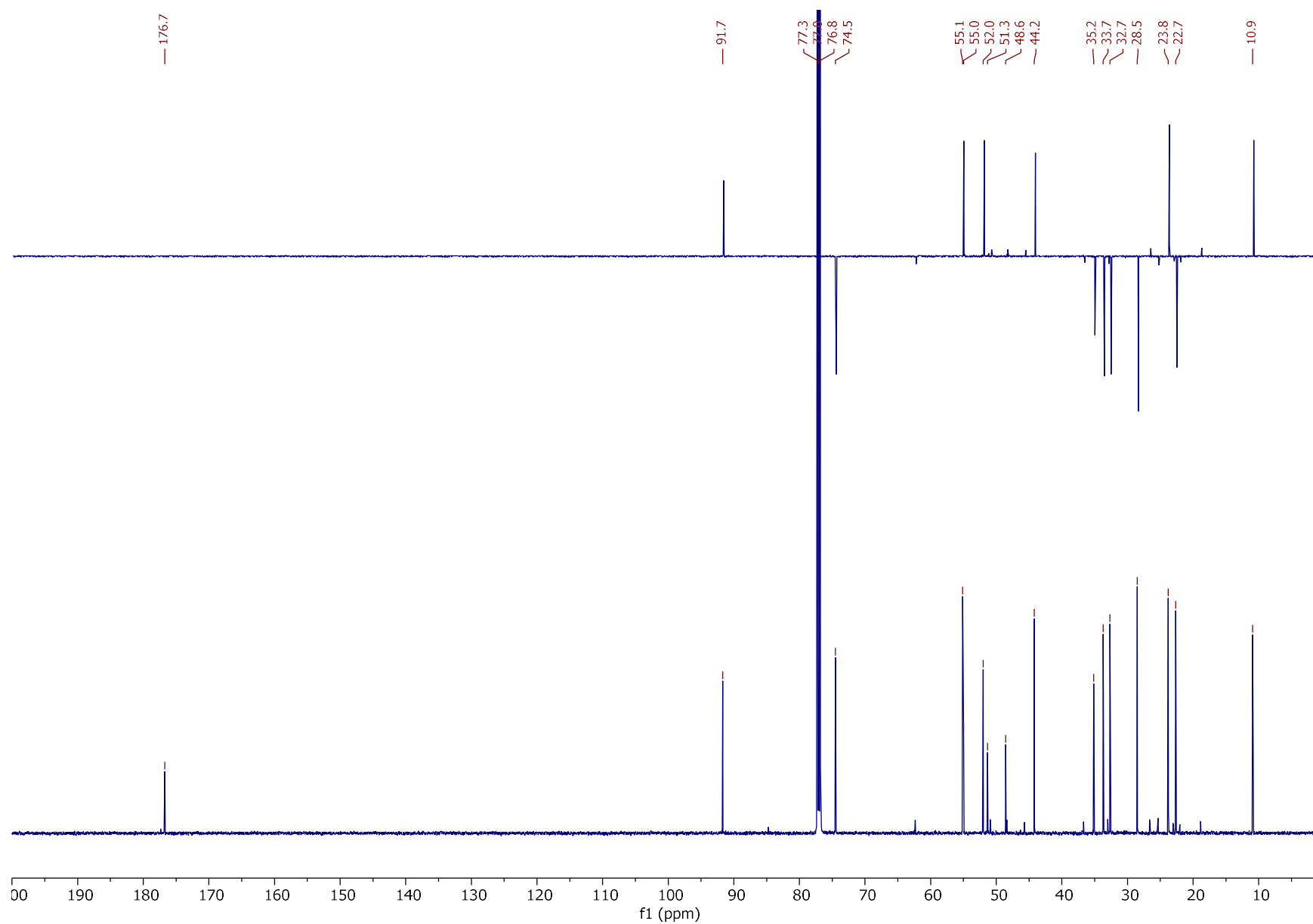


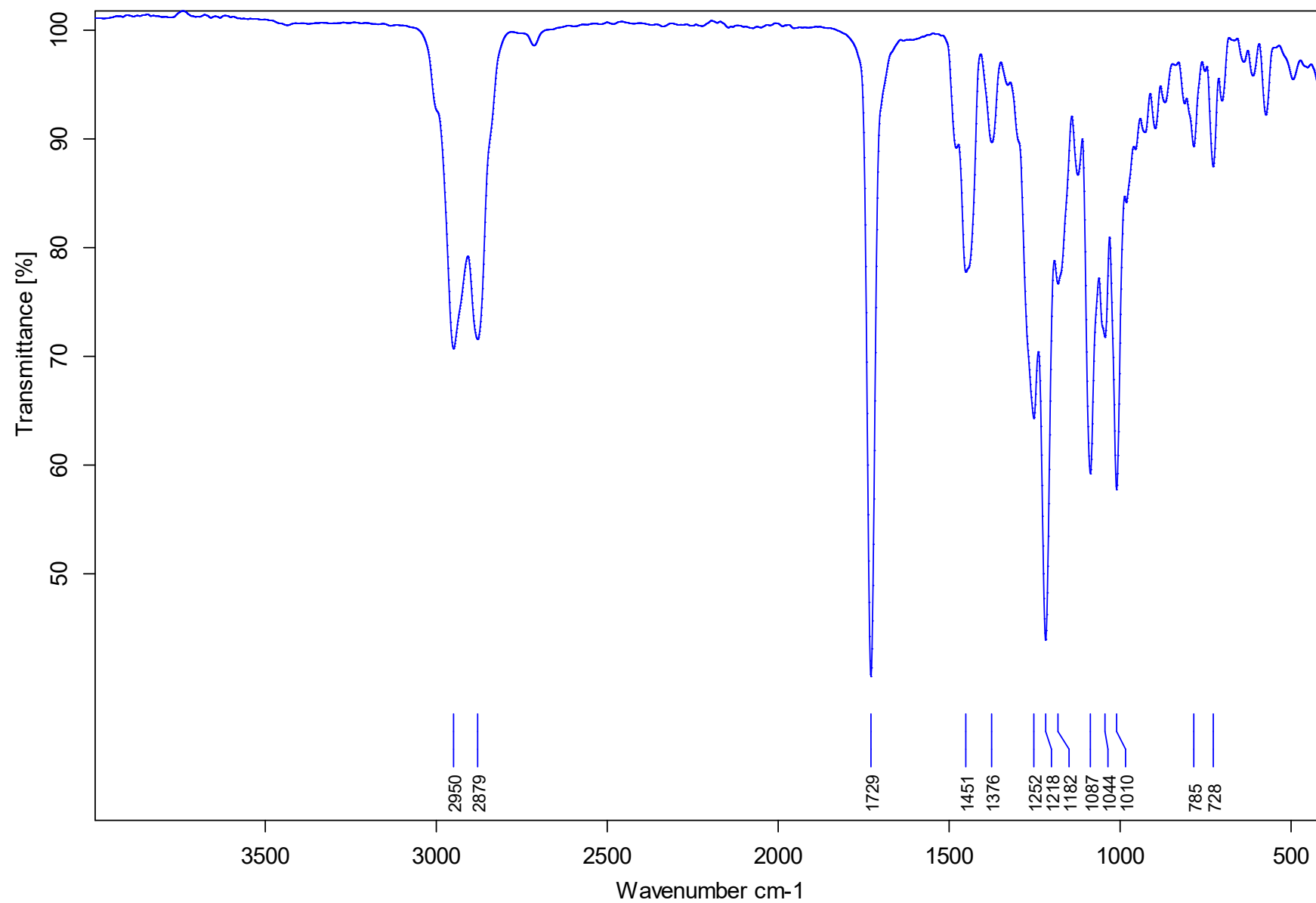




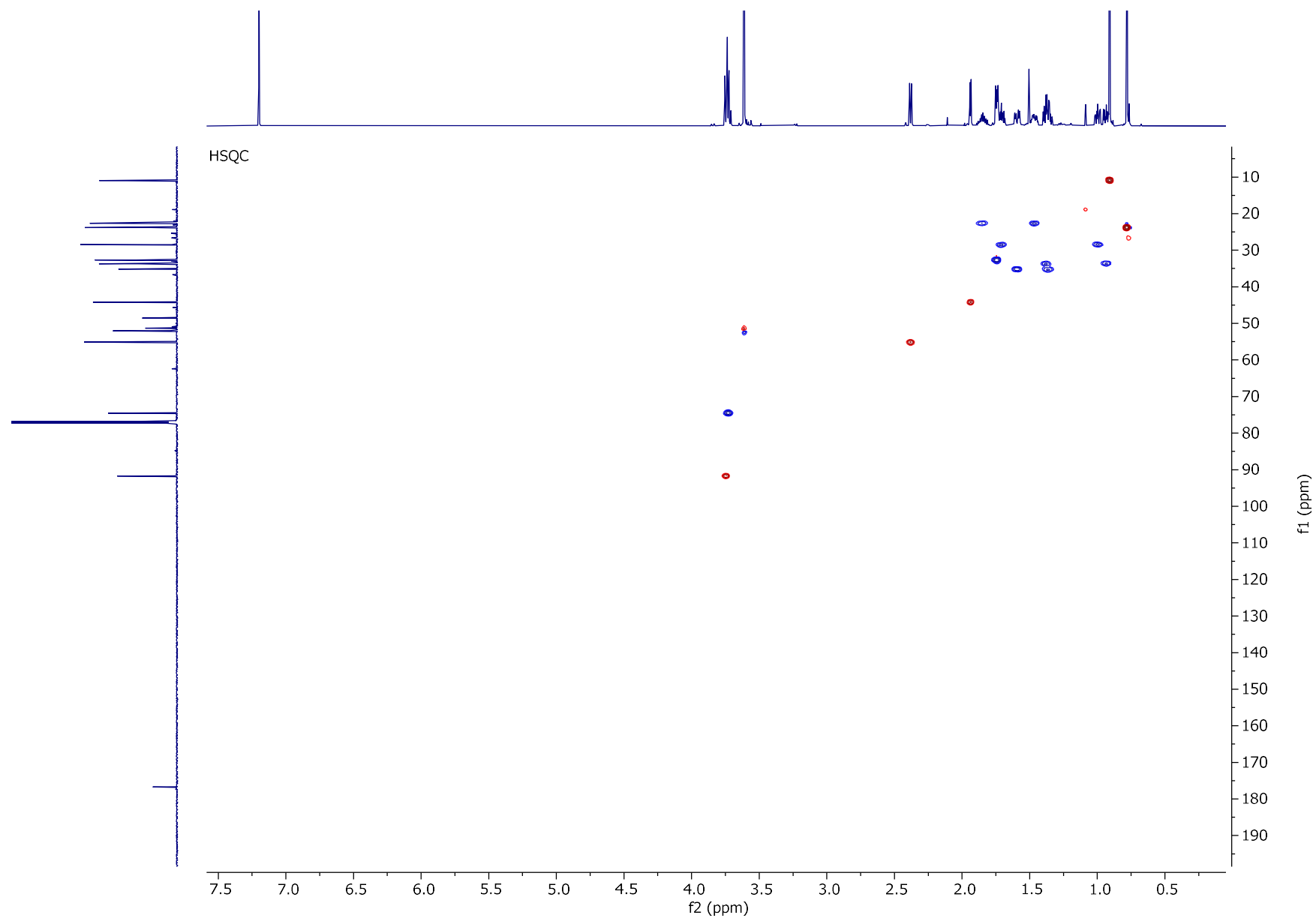


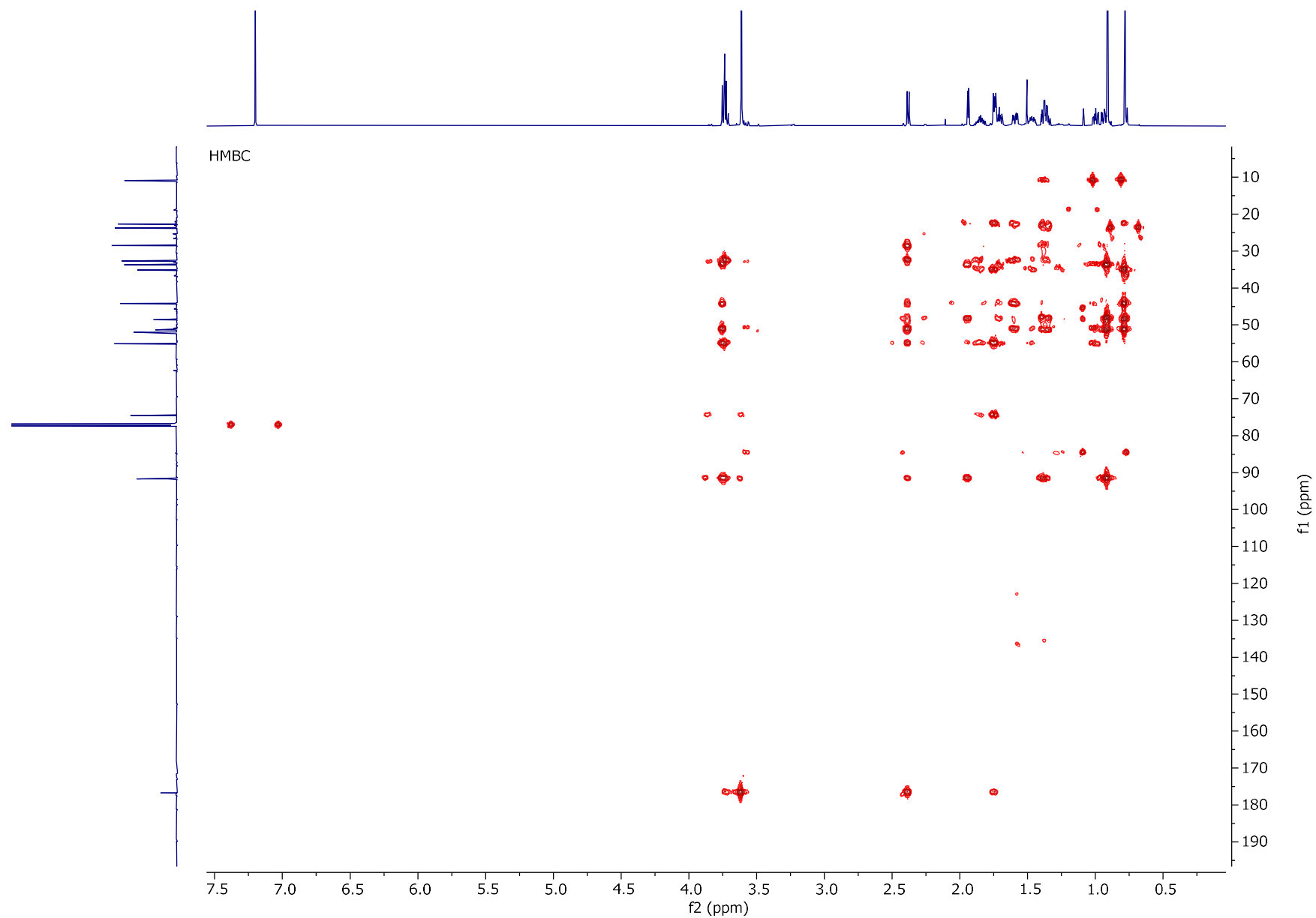
<sup>1</sup>H NMR, DEPT 135, <sup>13</sup>C NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **14**

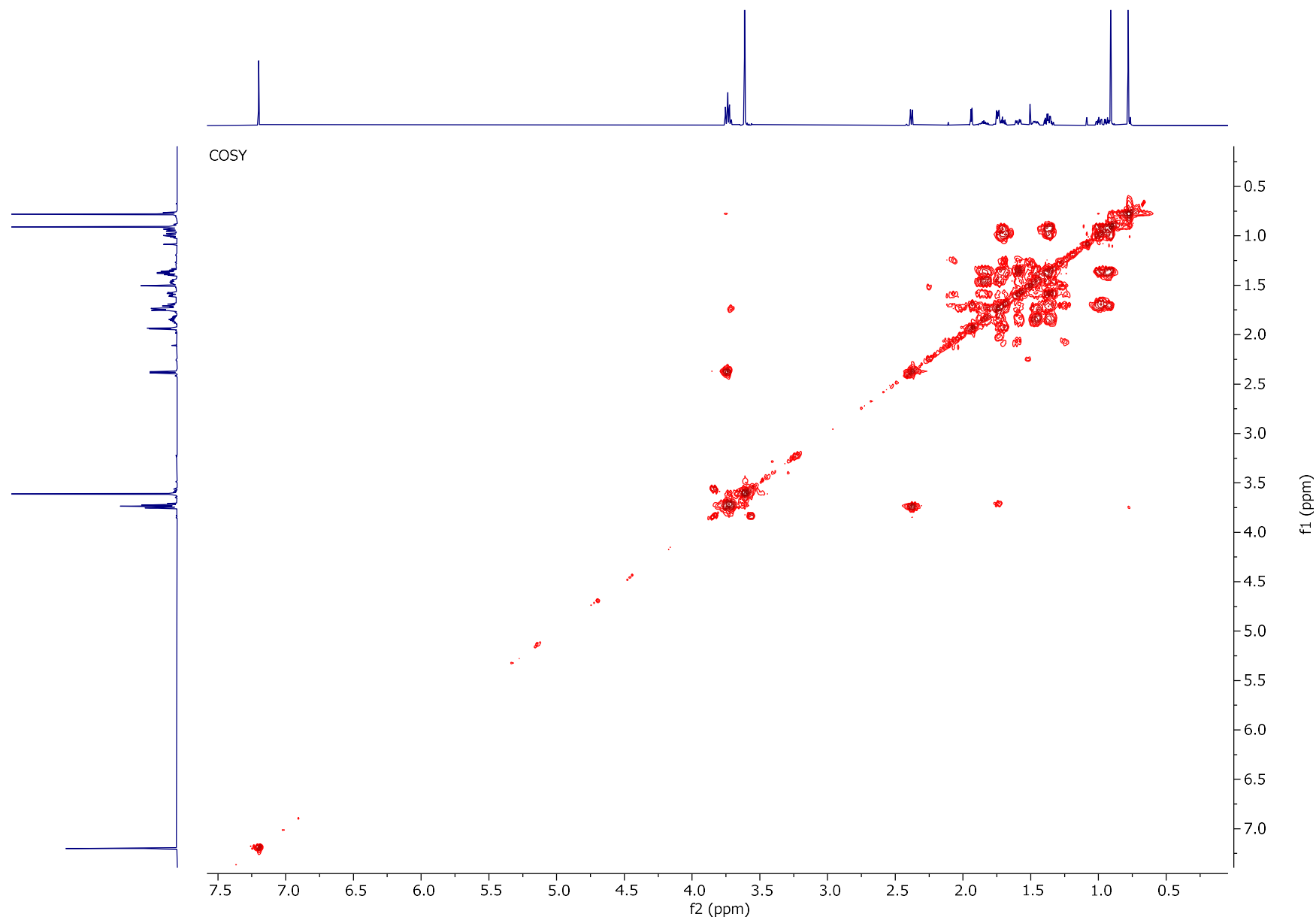


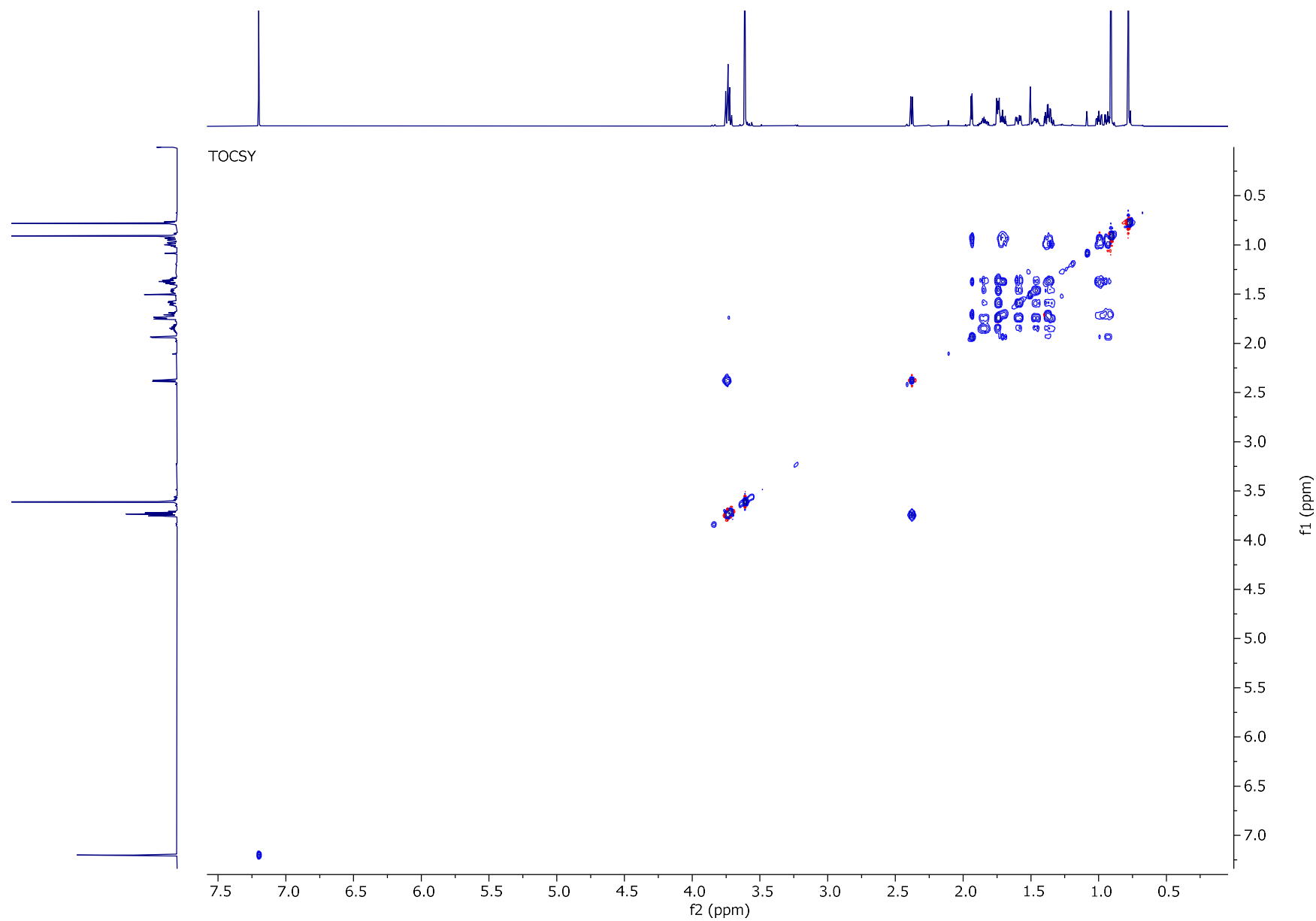


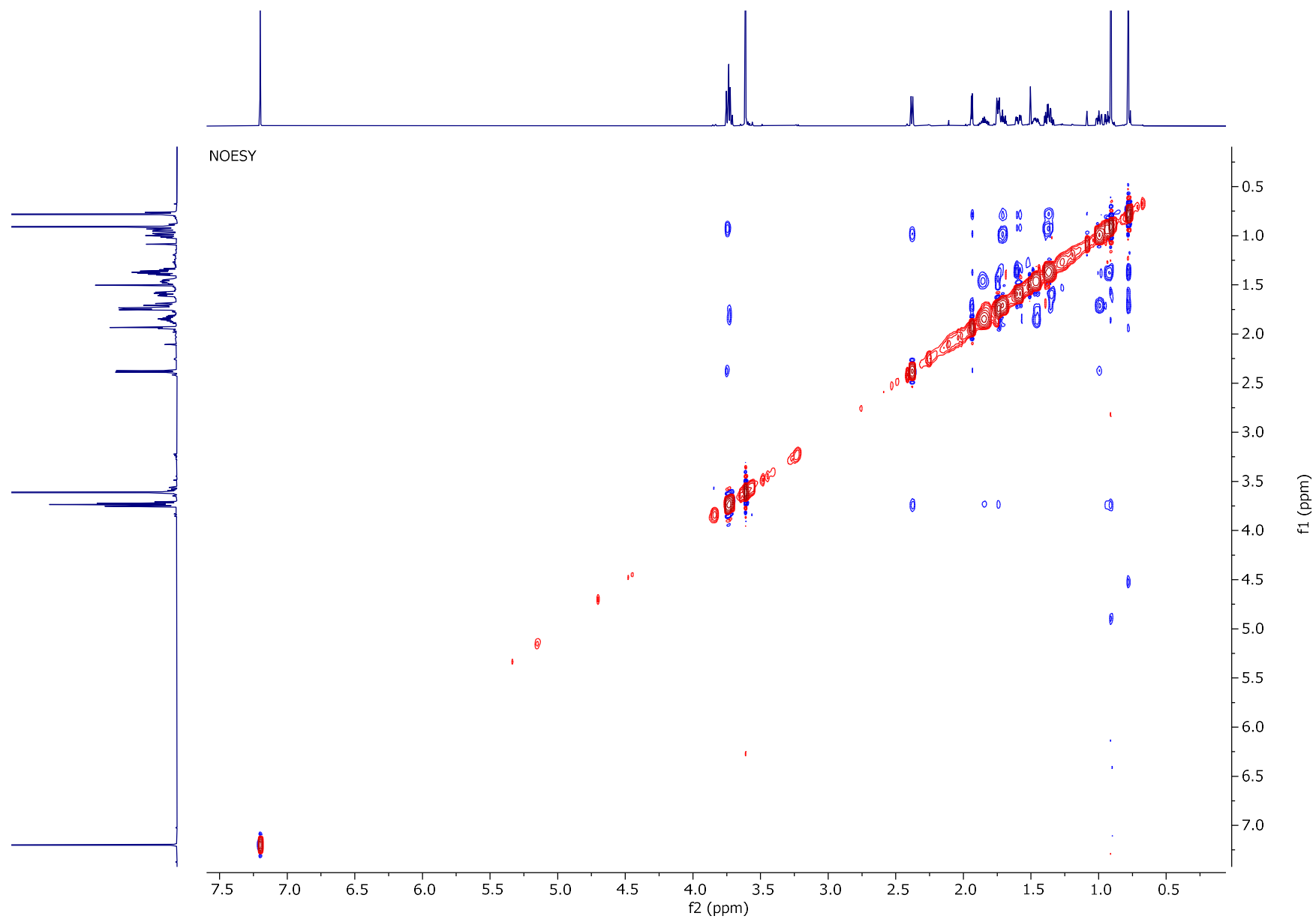


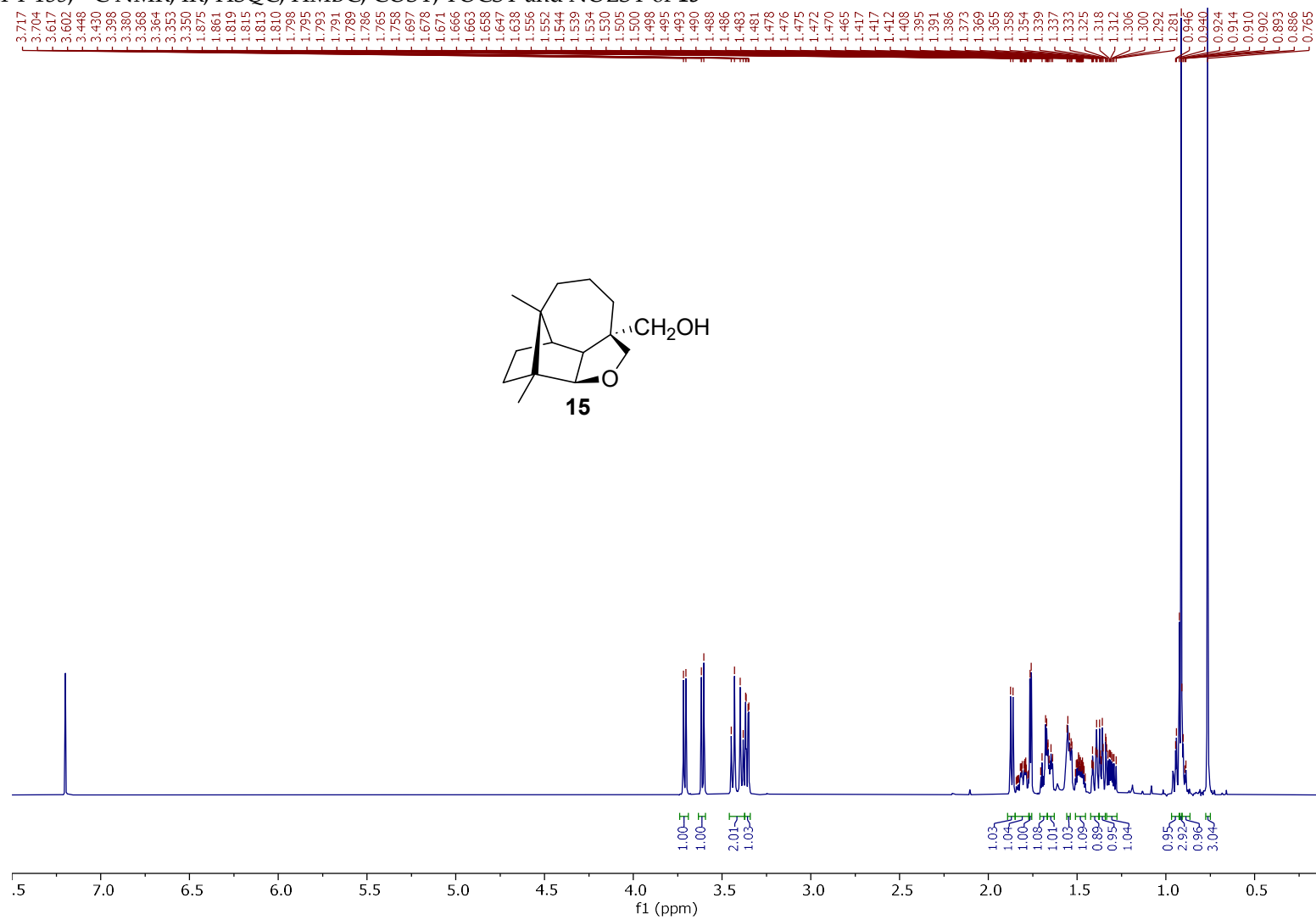


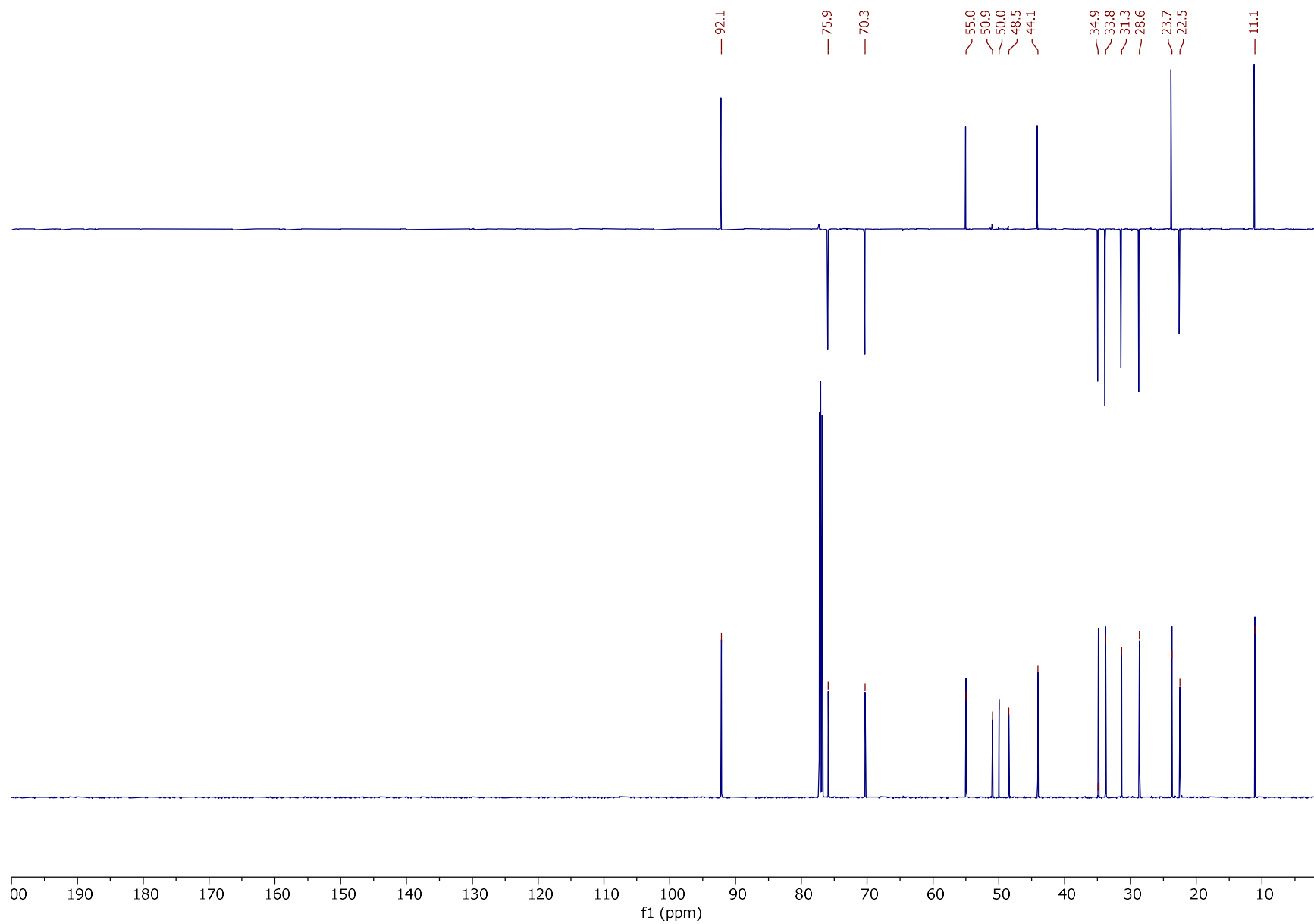


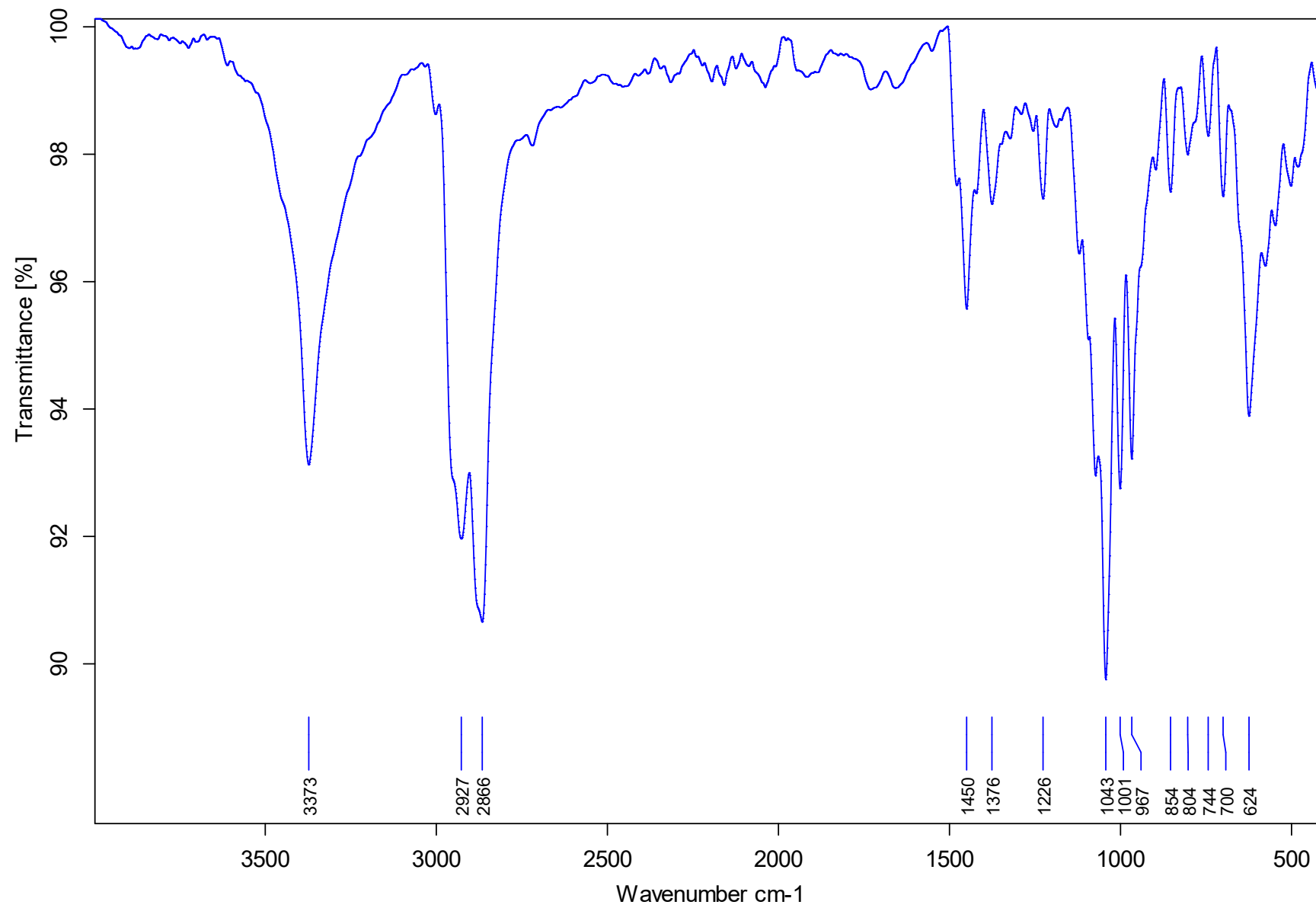




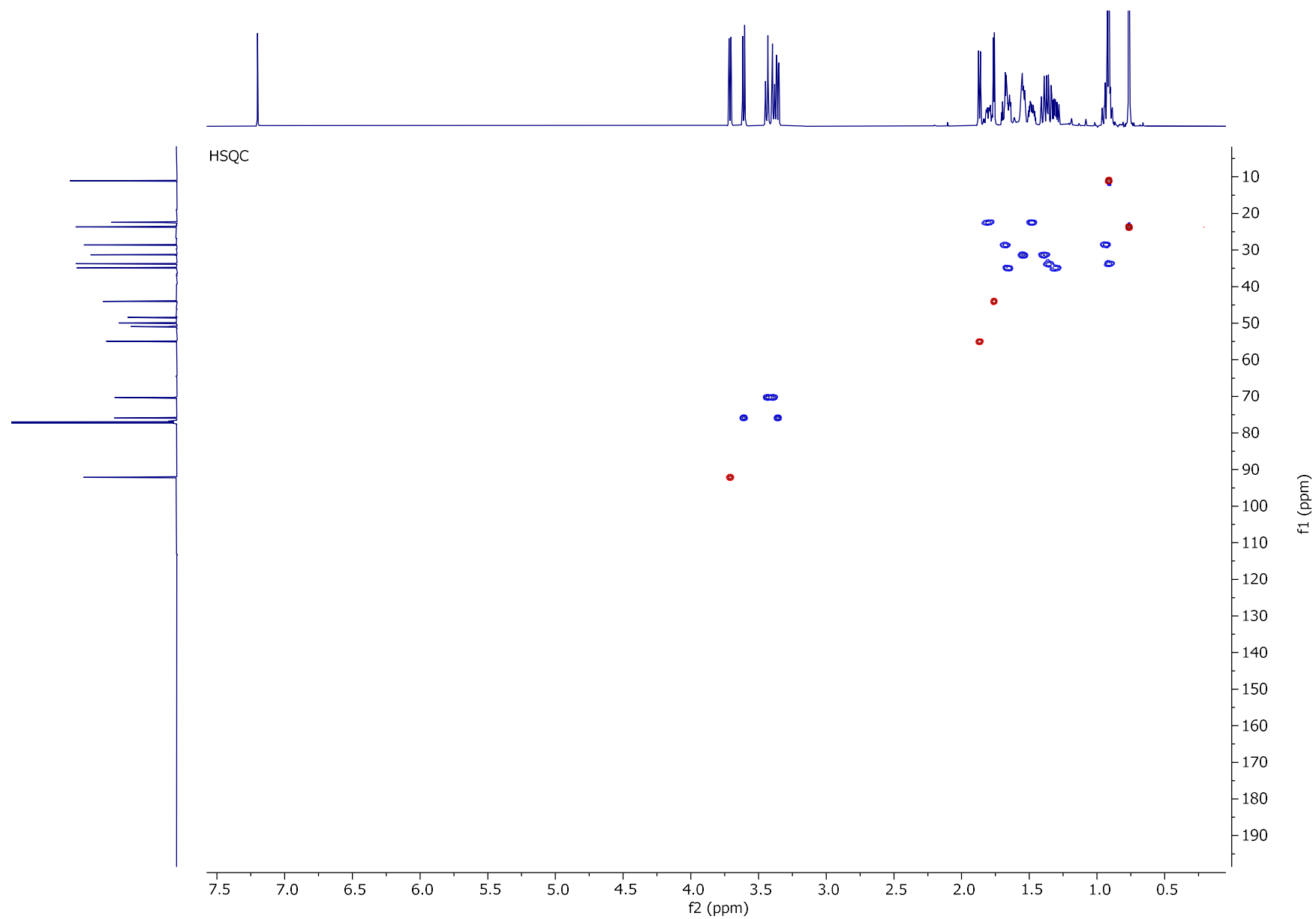


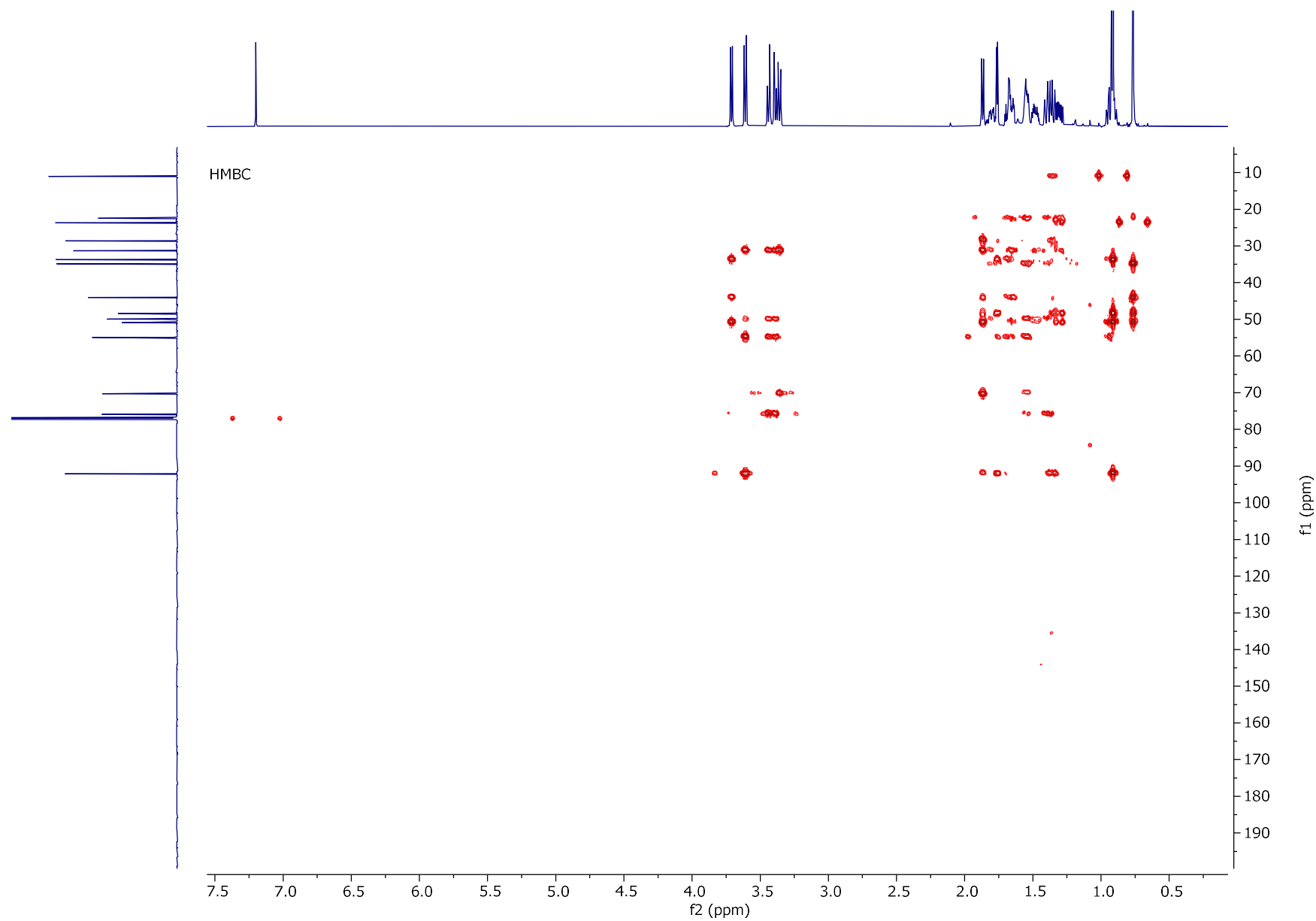
<sup>1</sup>H NMR, DEPT 135, <sup>13</sup>C NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **15**

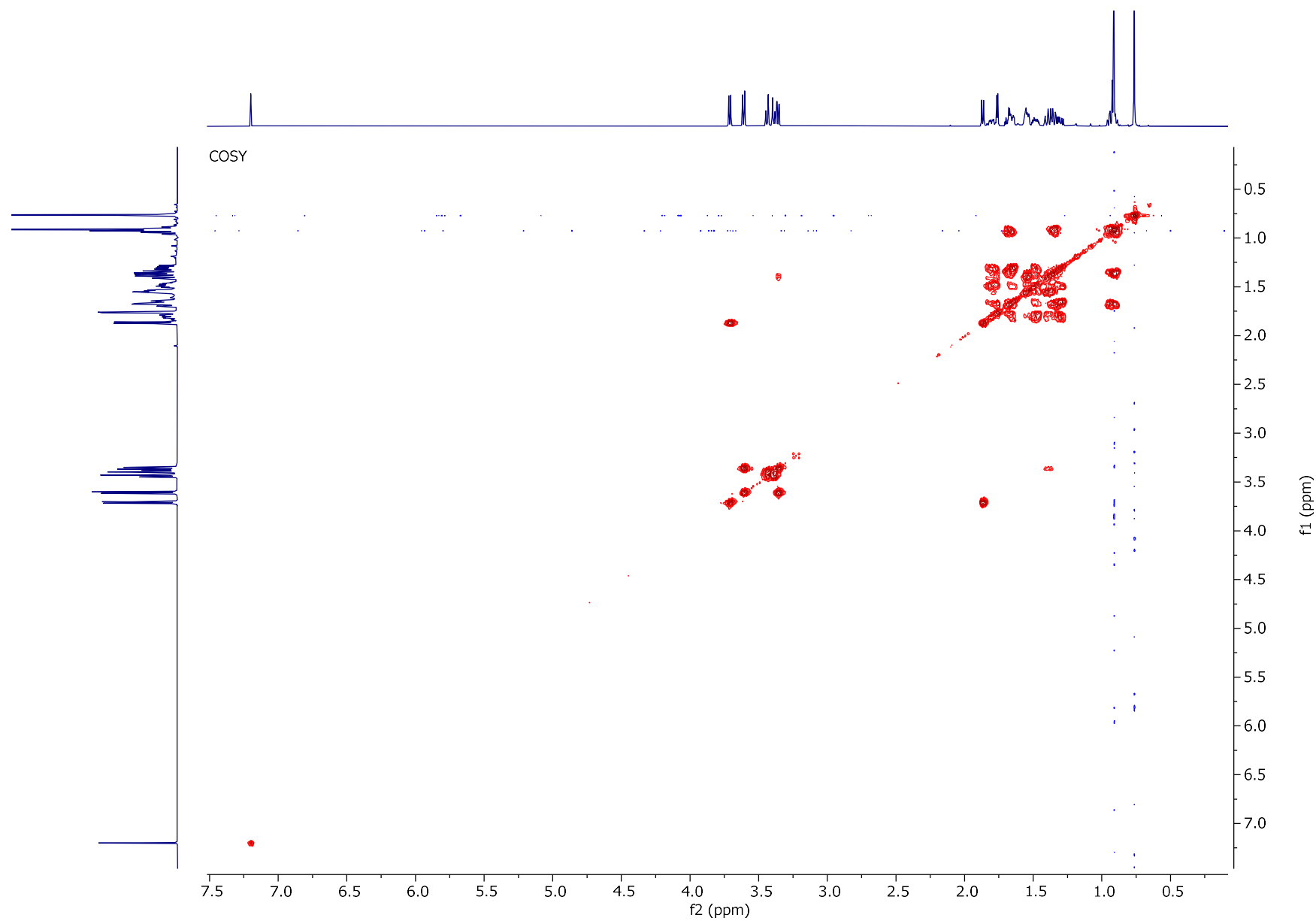


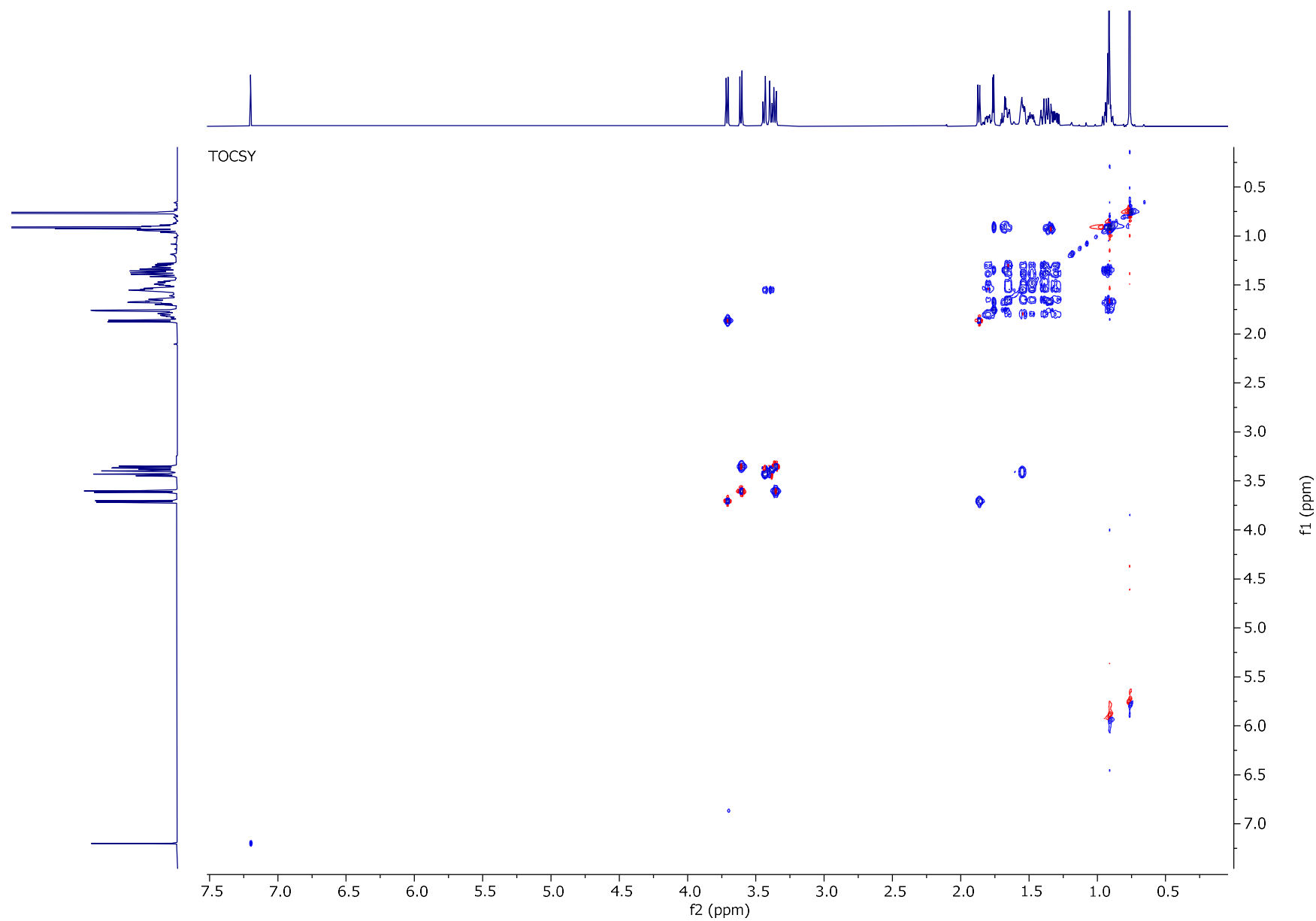


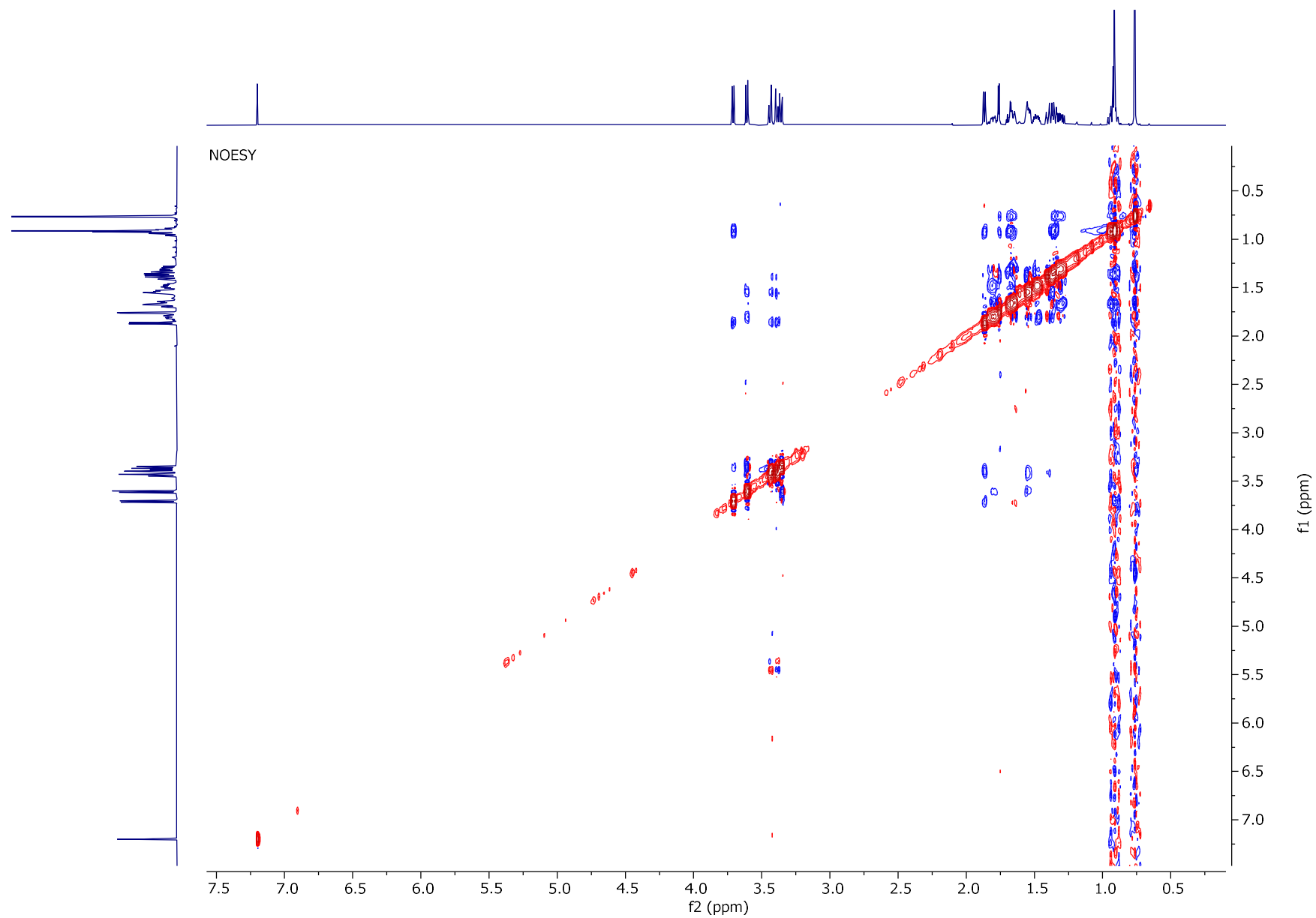




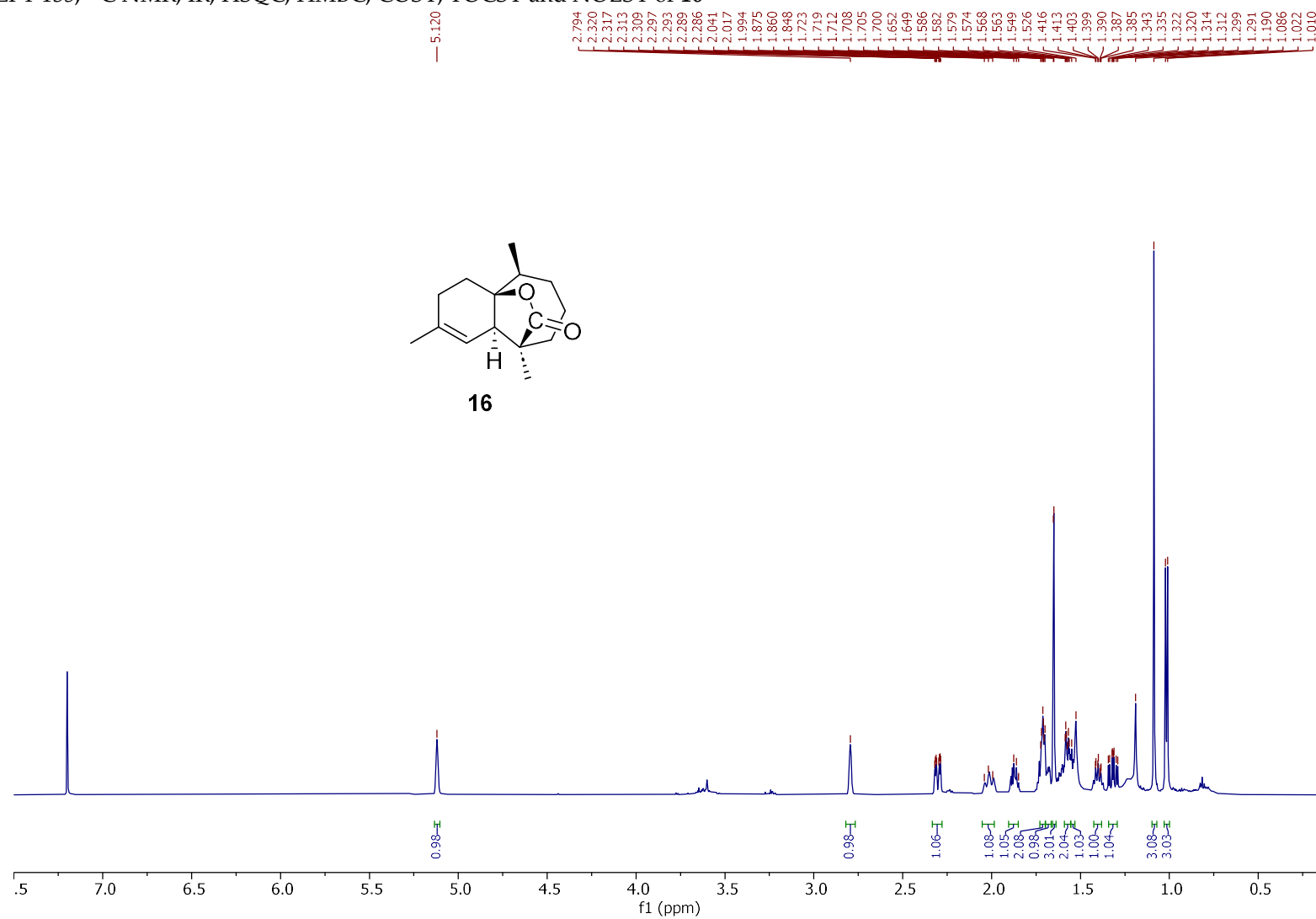


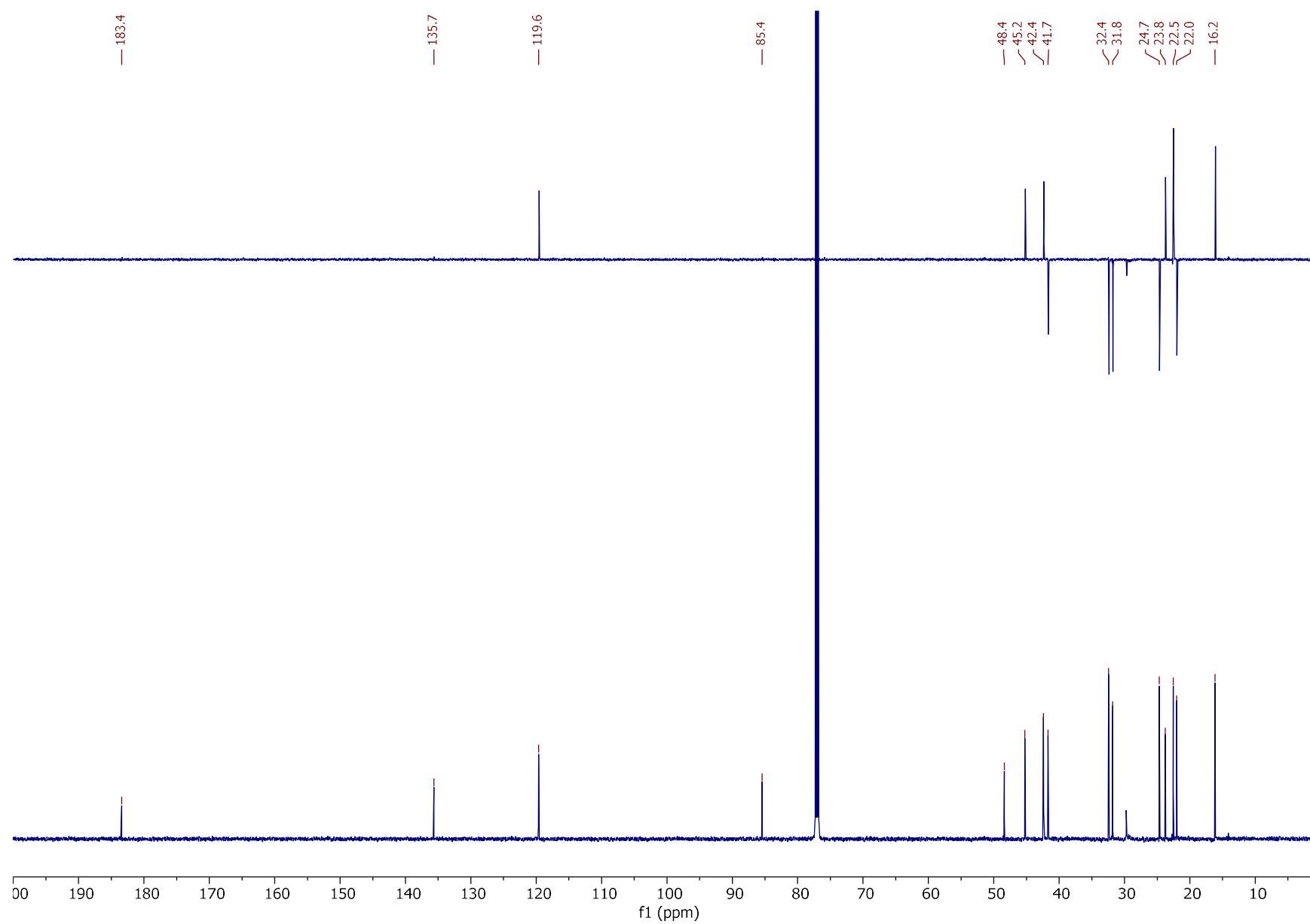


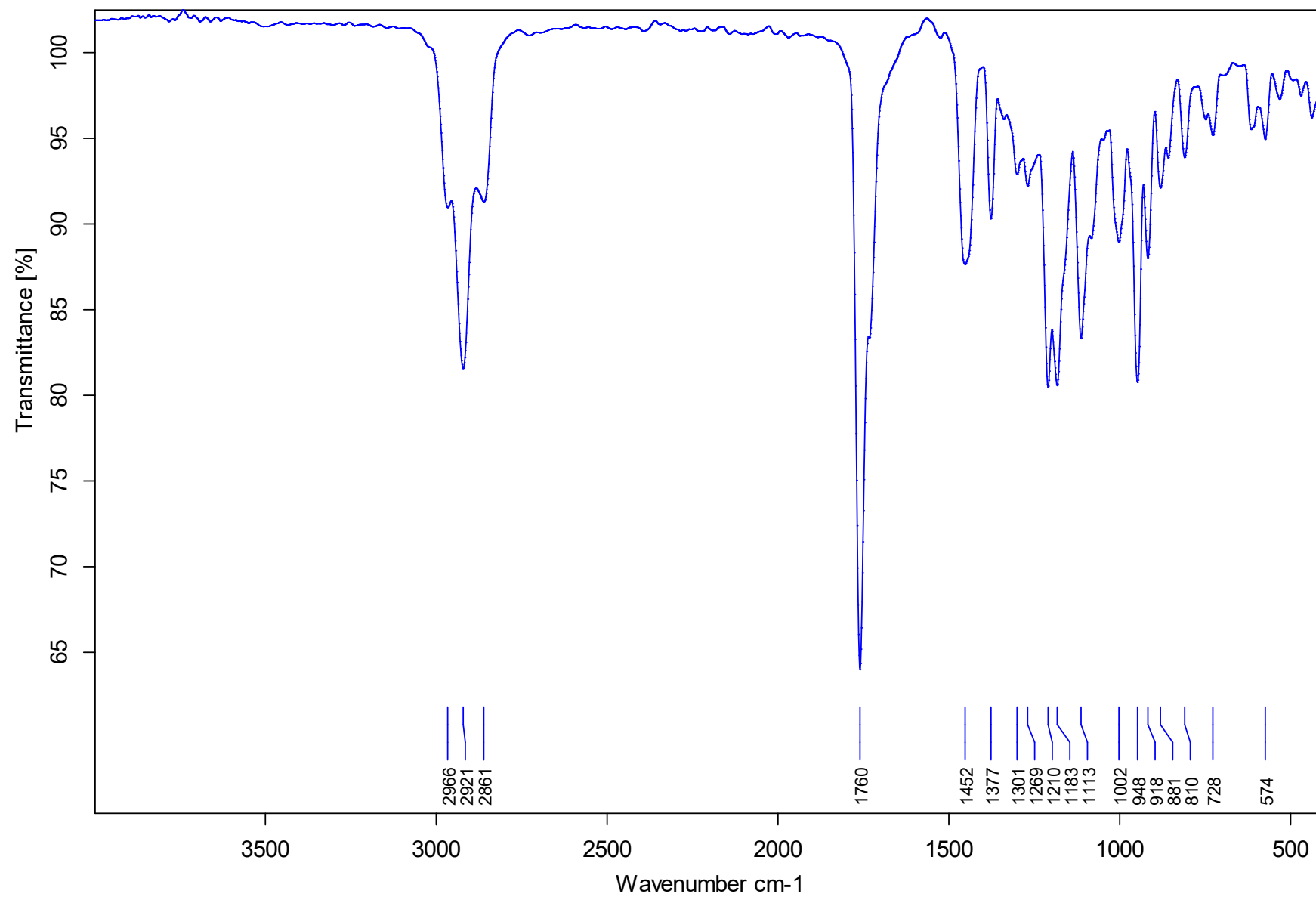




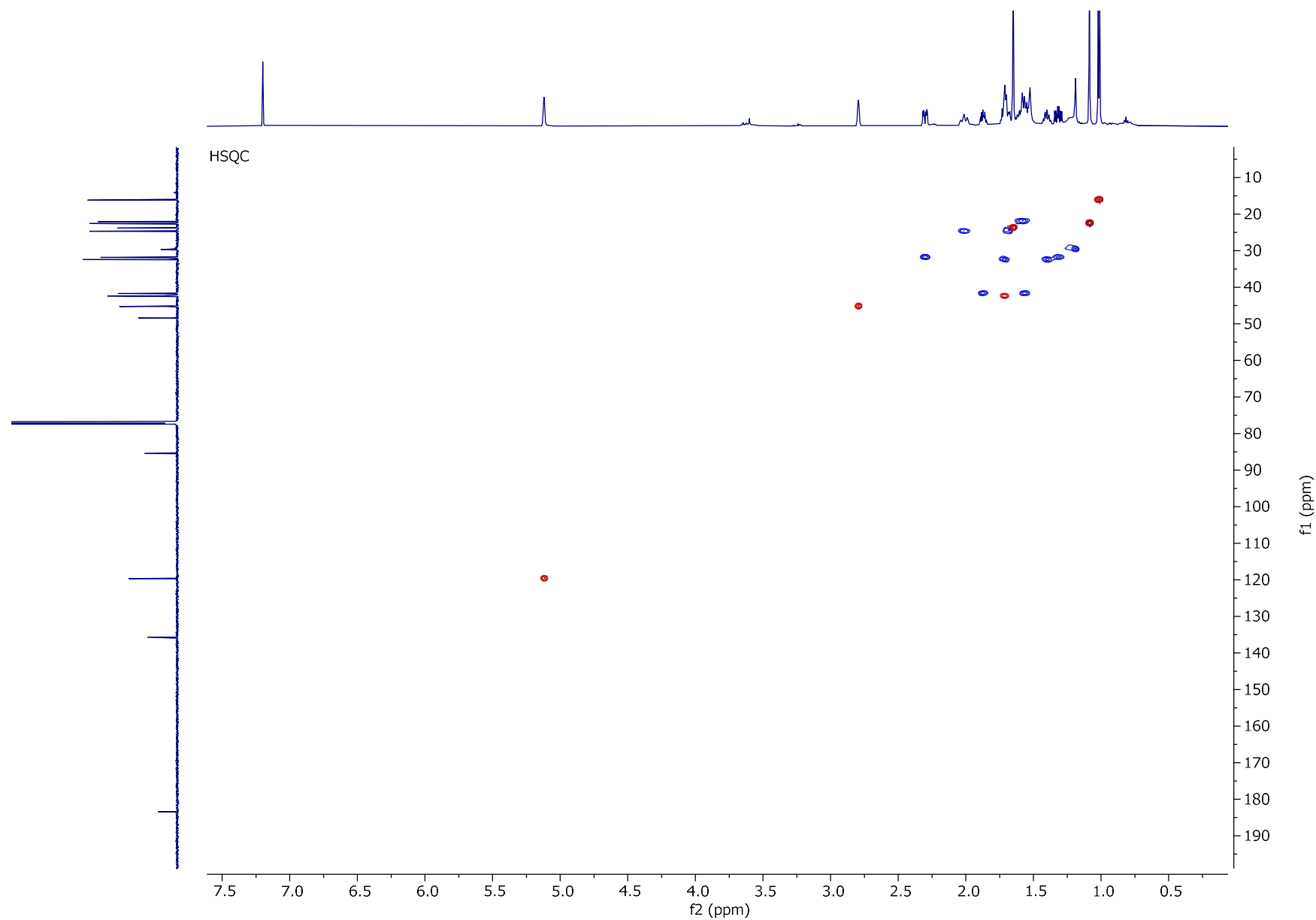
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **16**

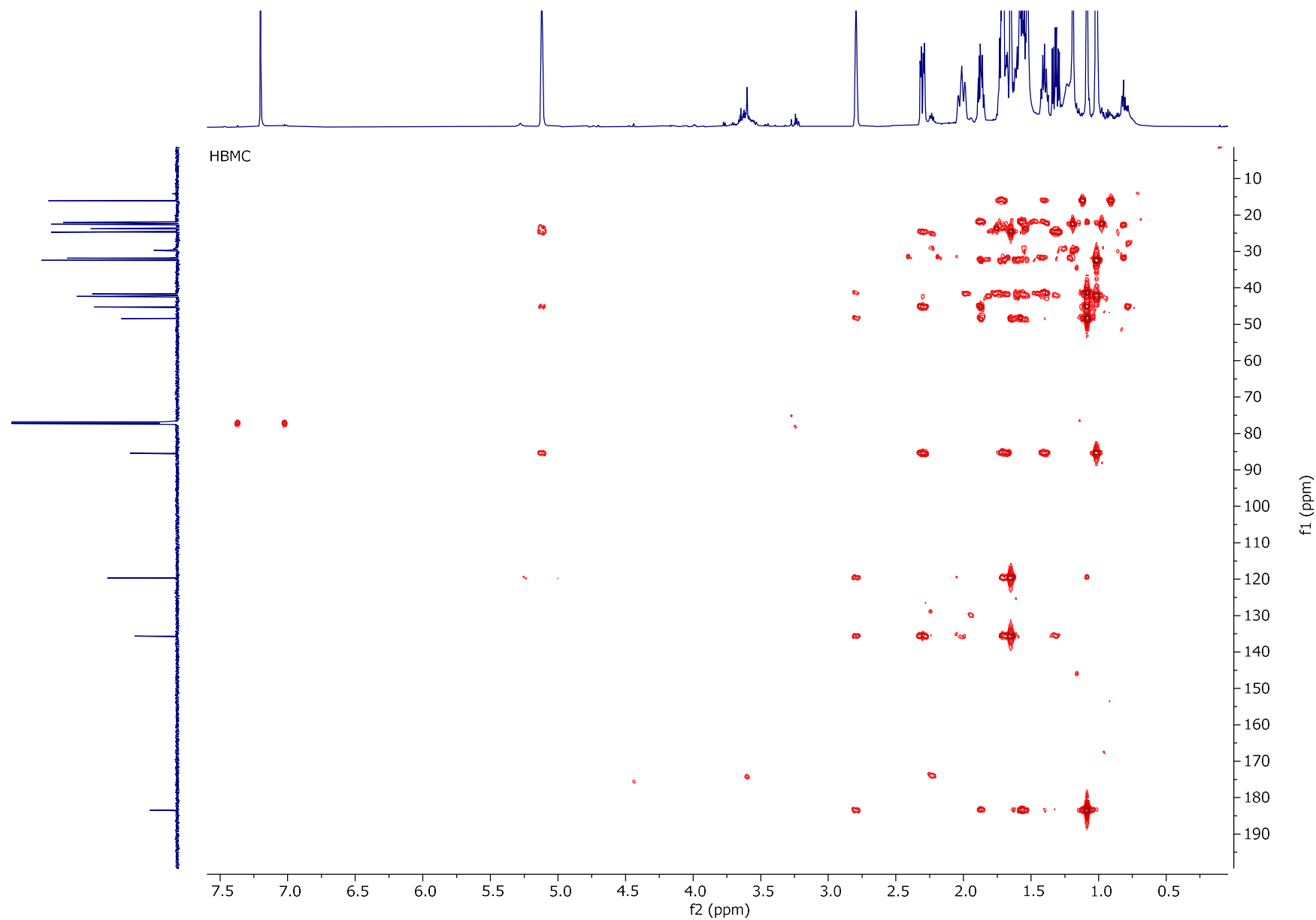


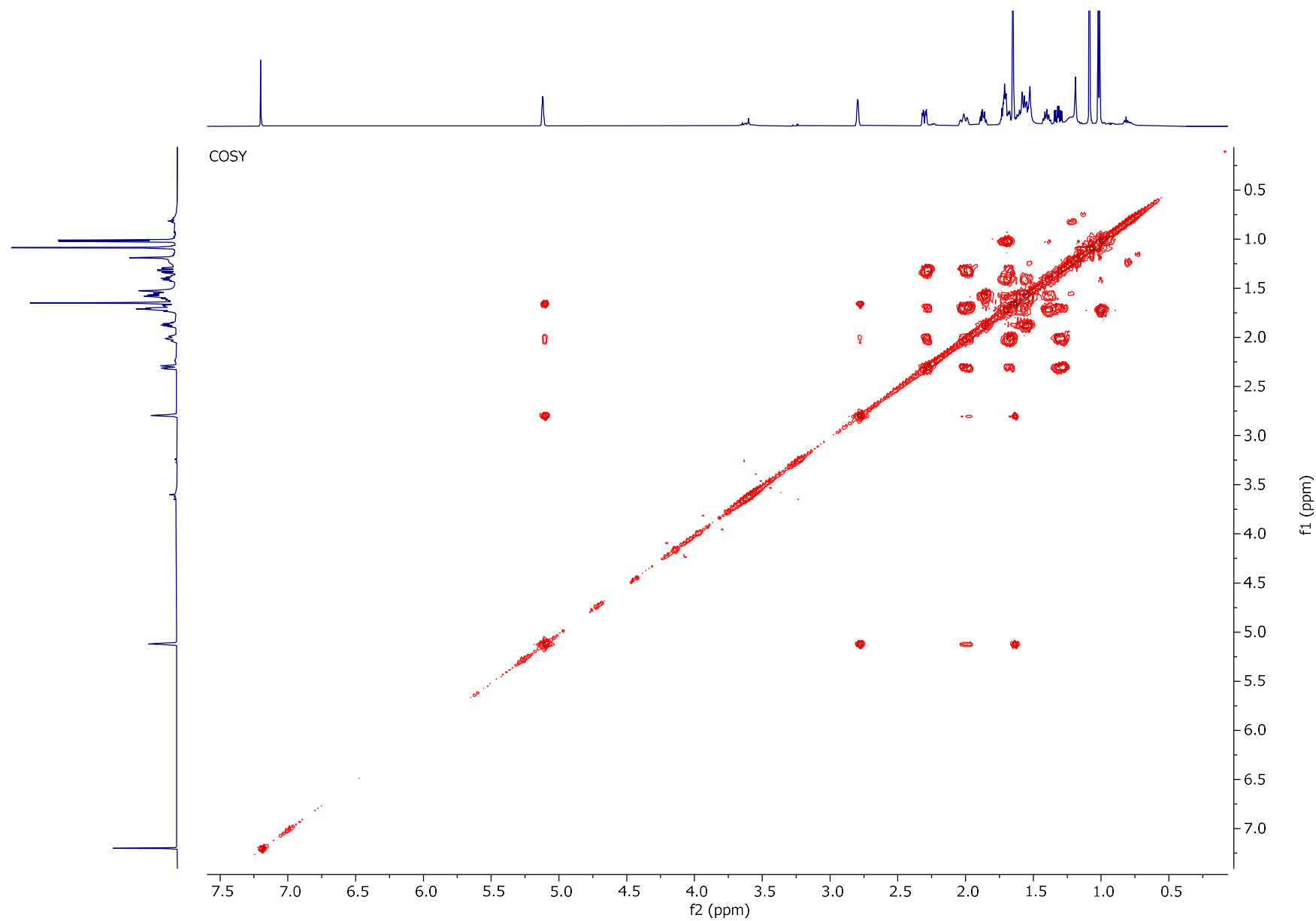


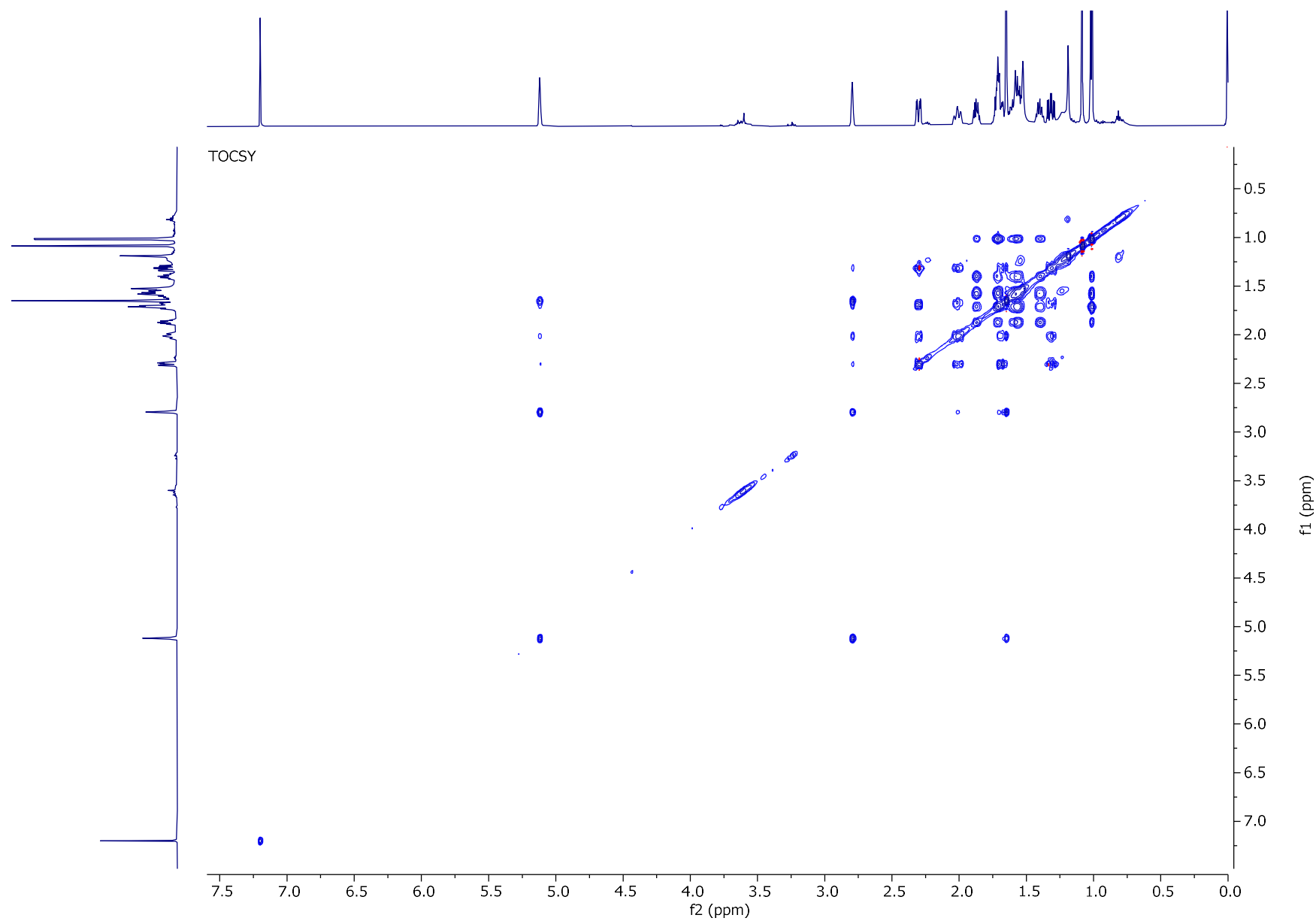


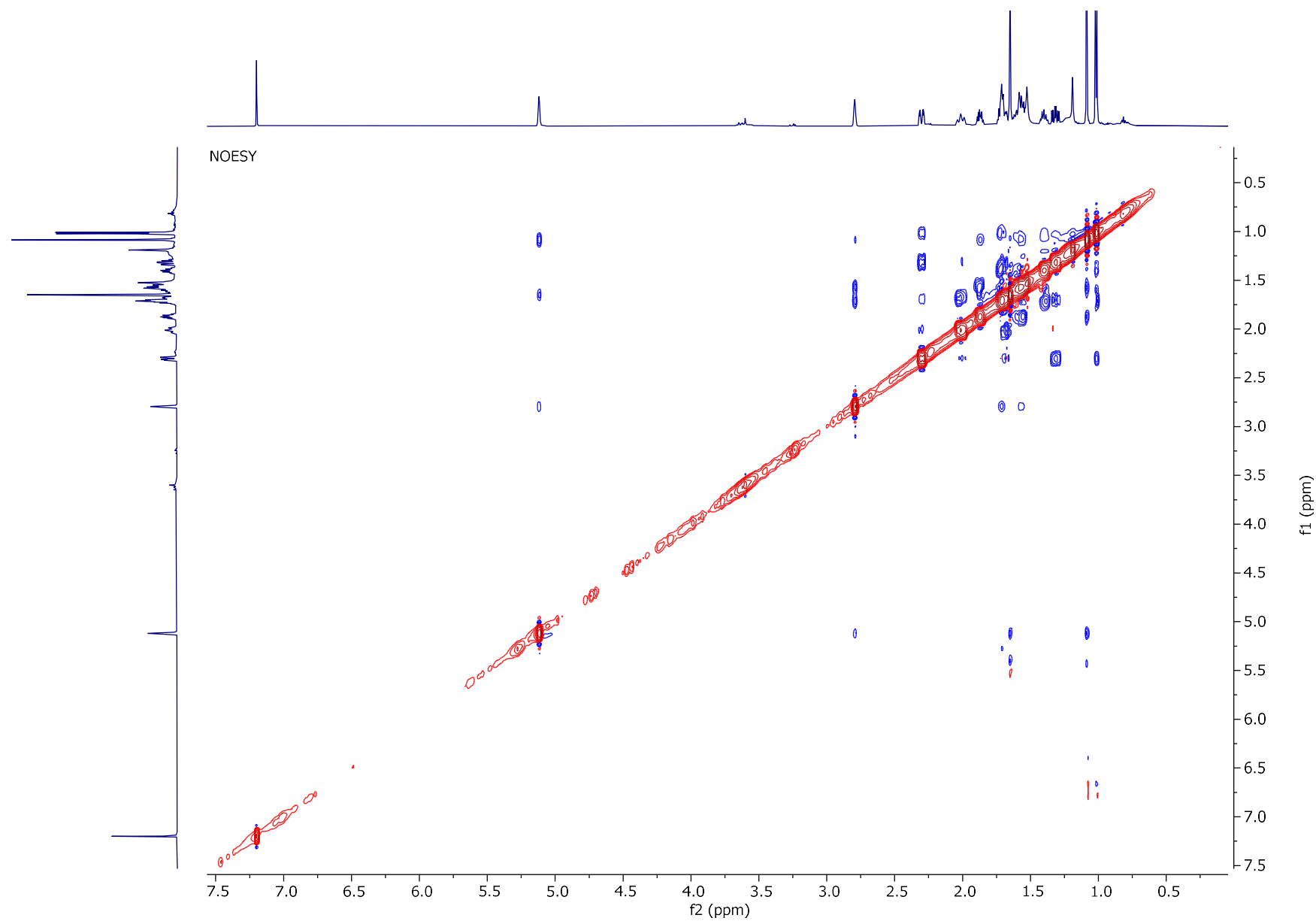




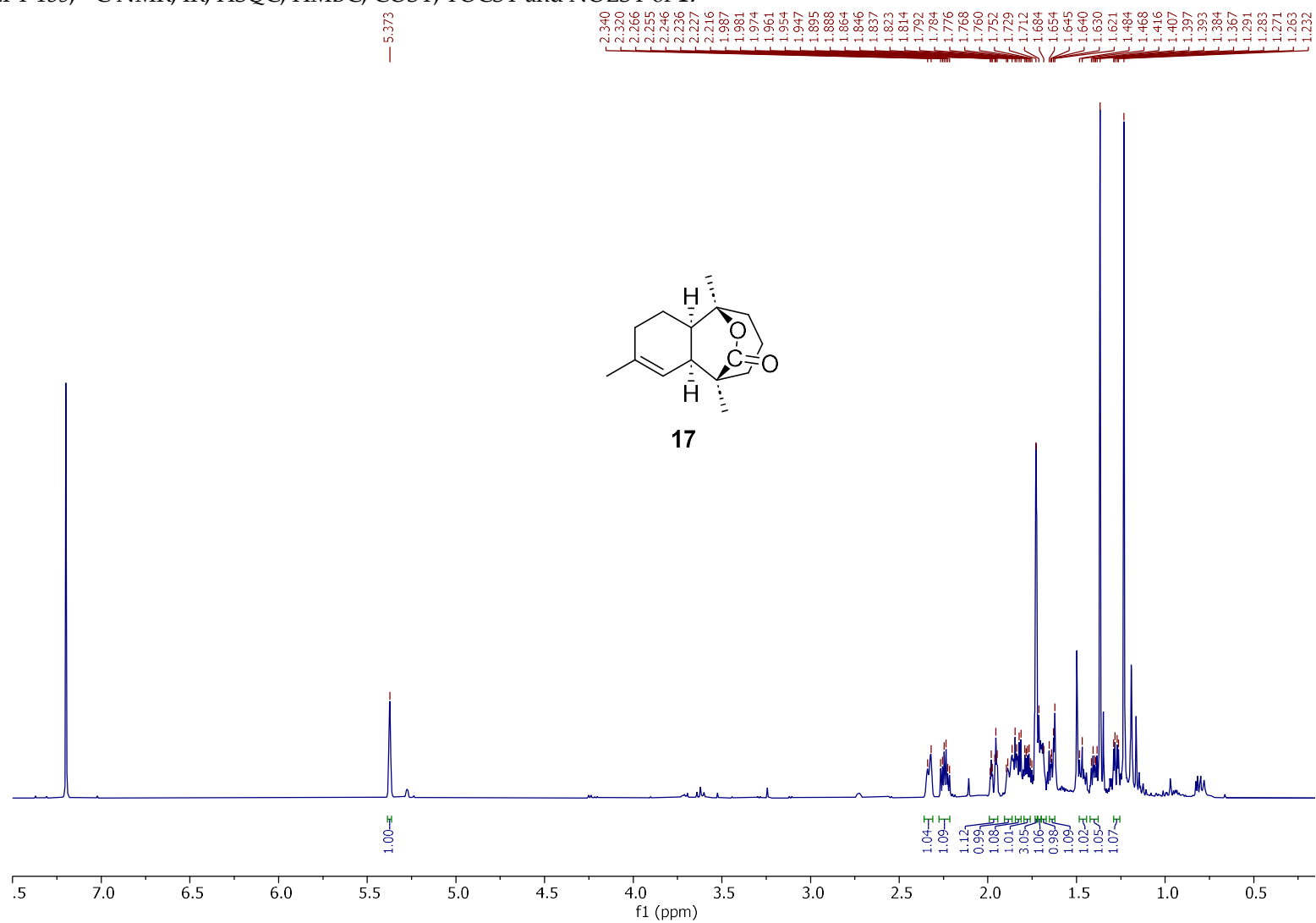


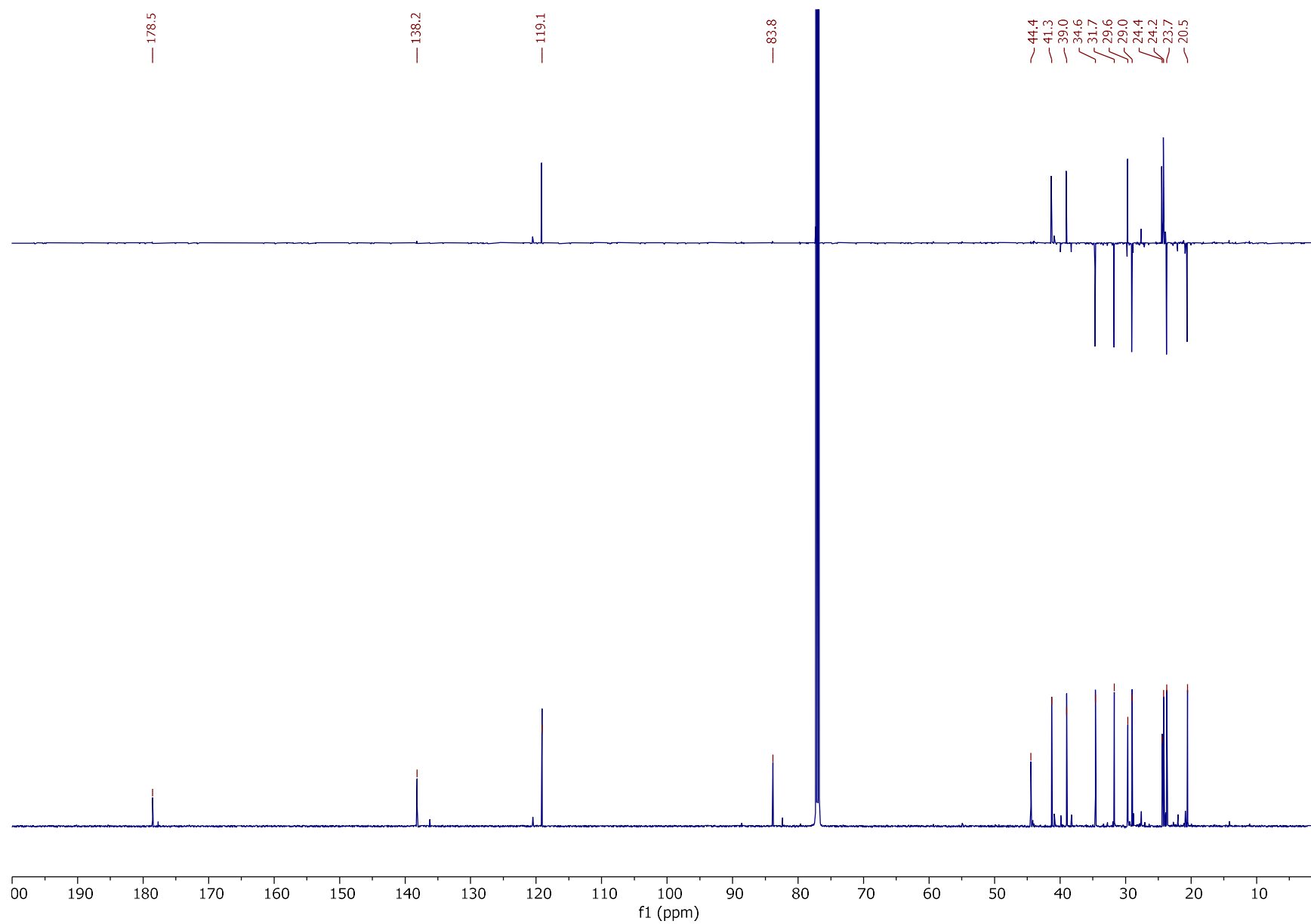


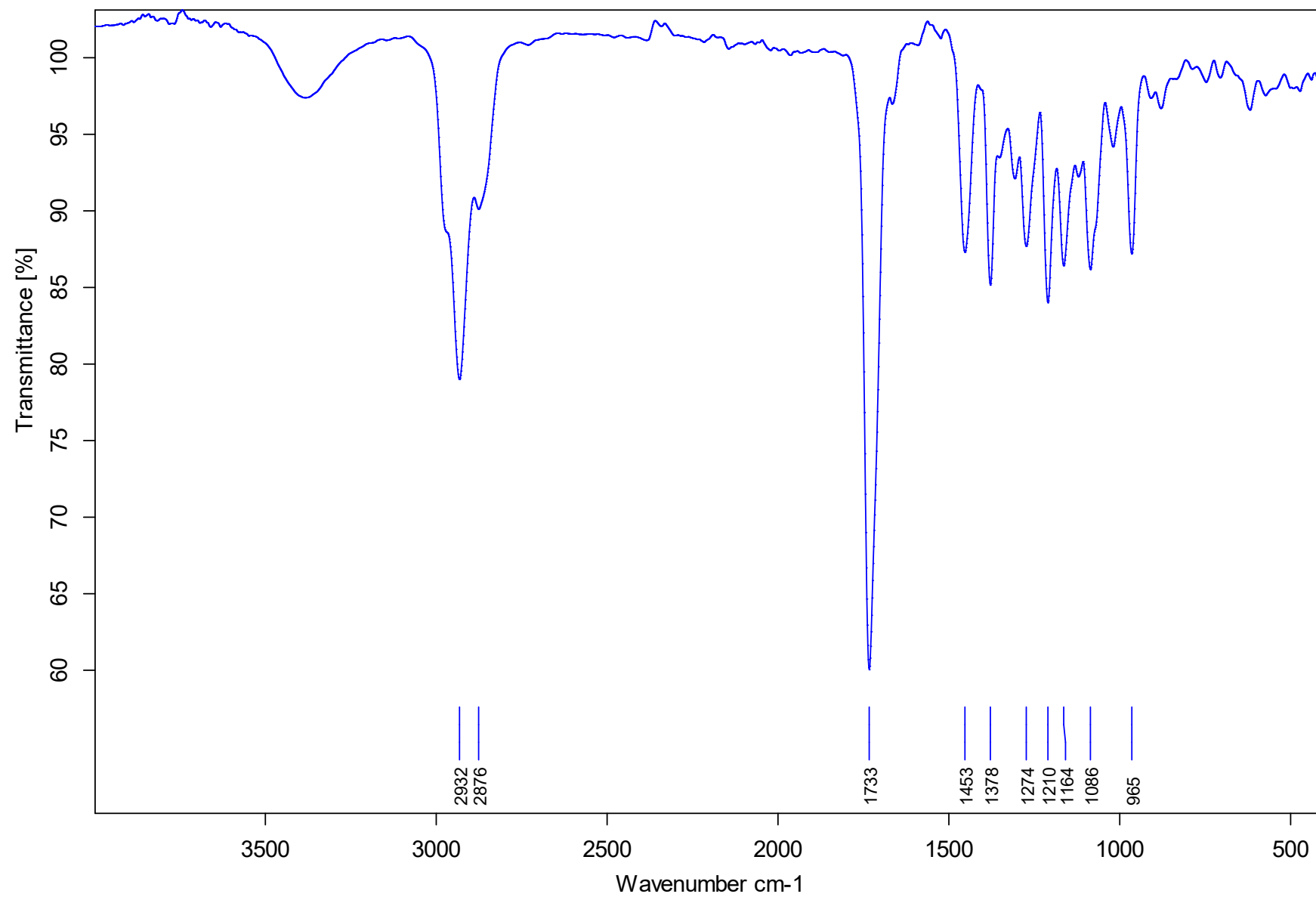




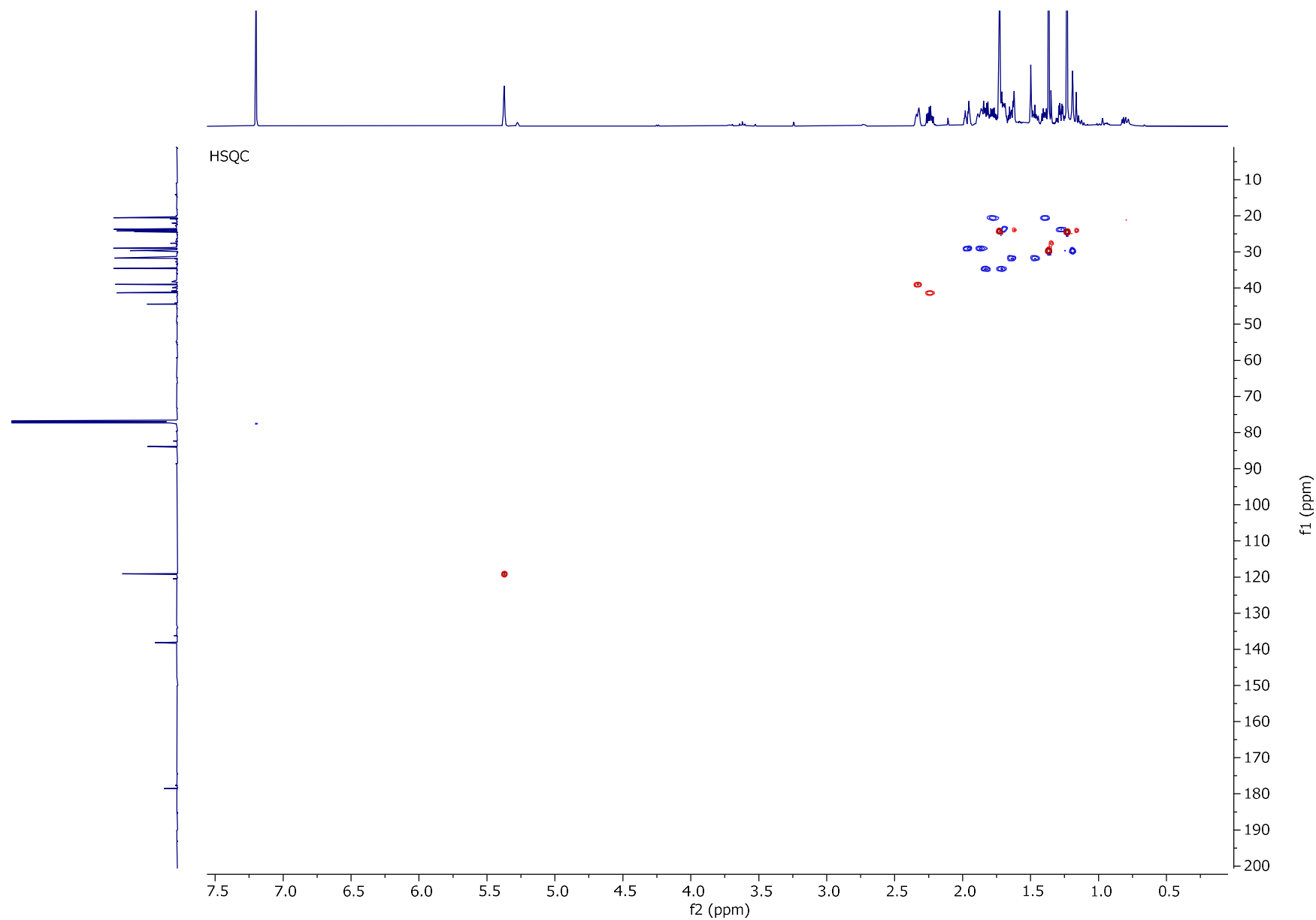
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **17**

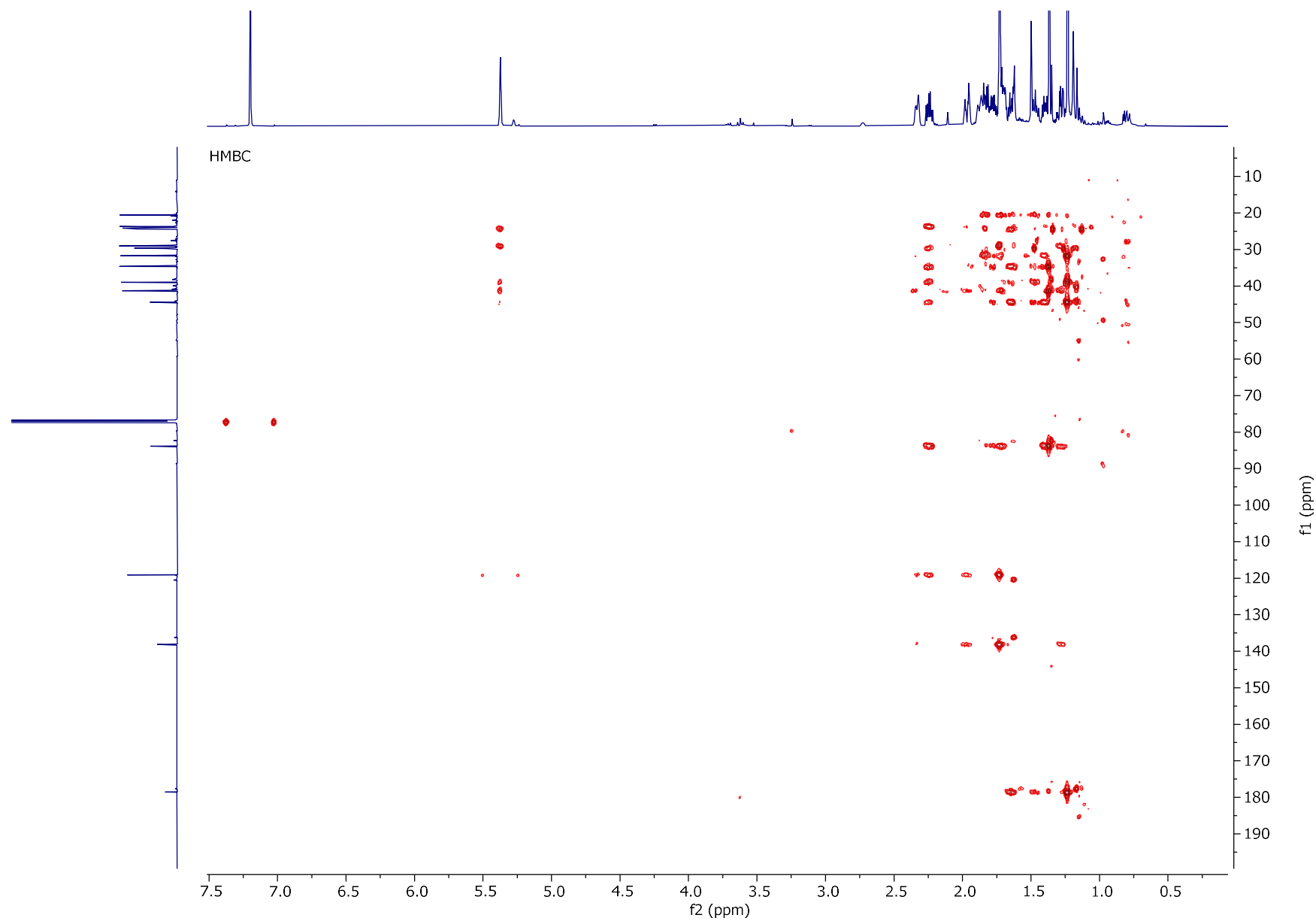


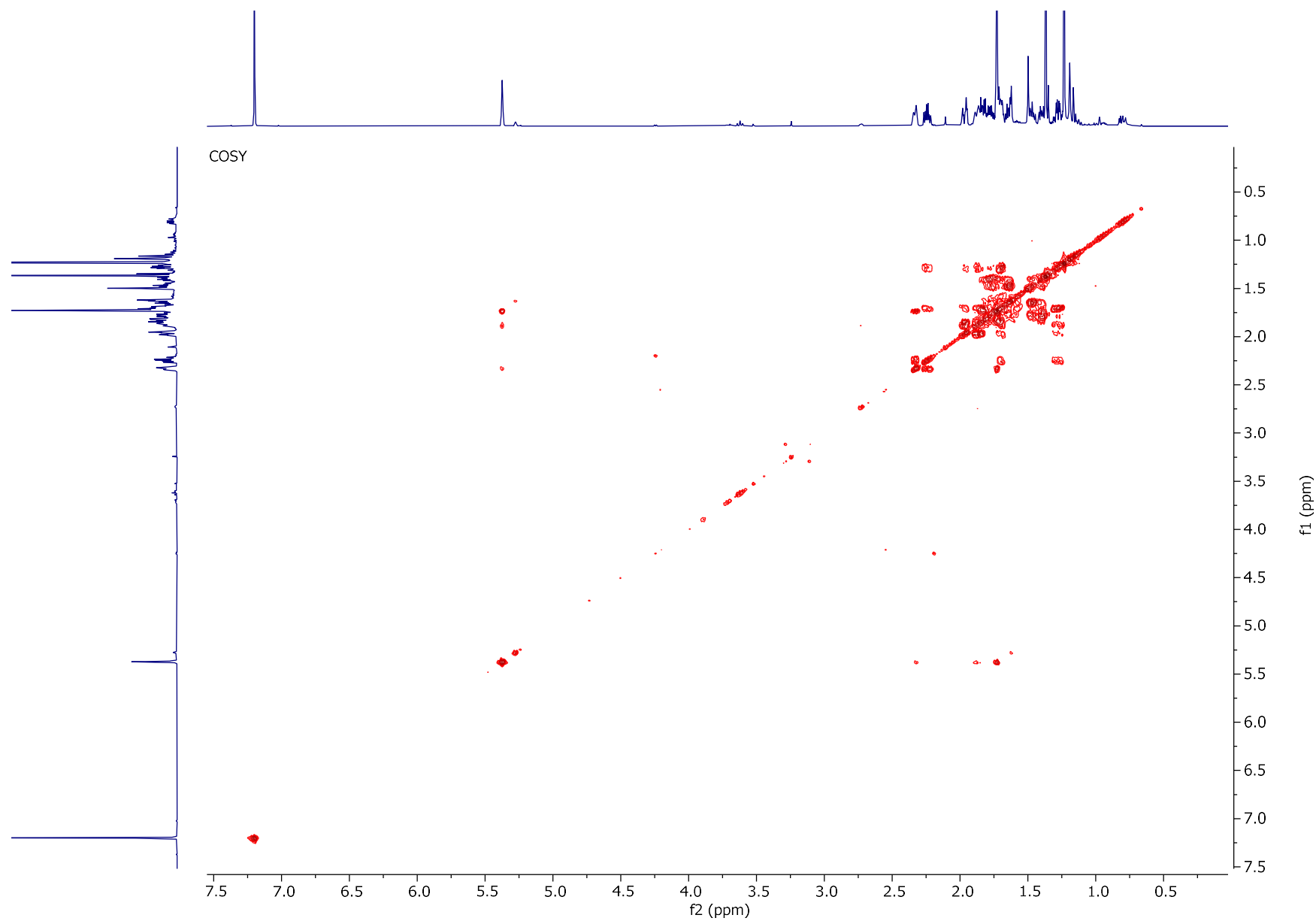


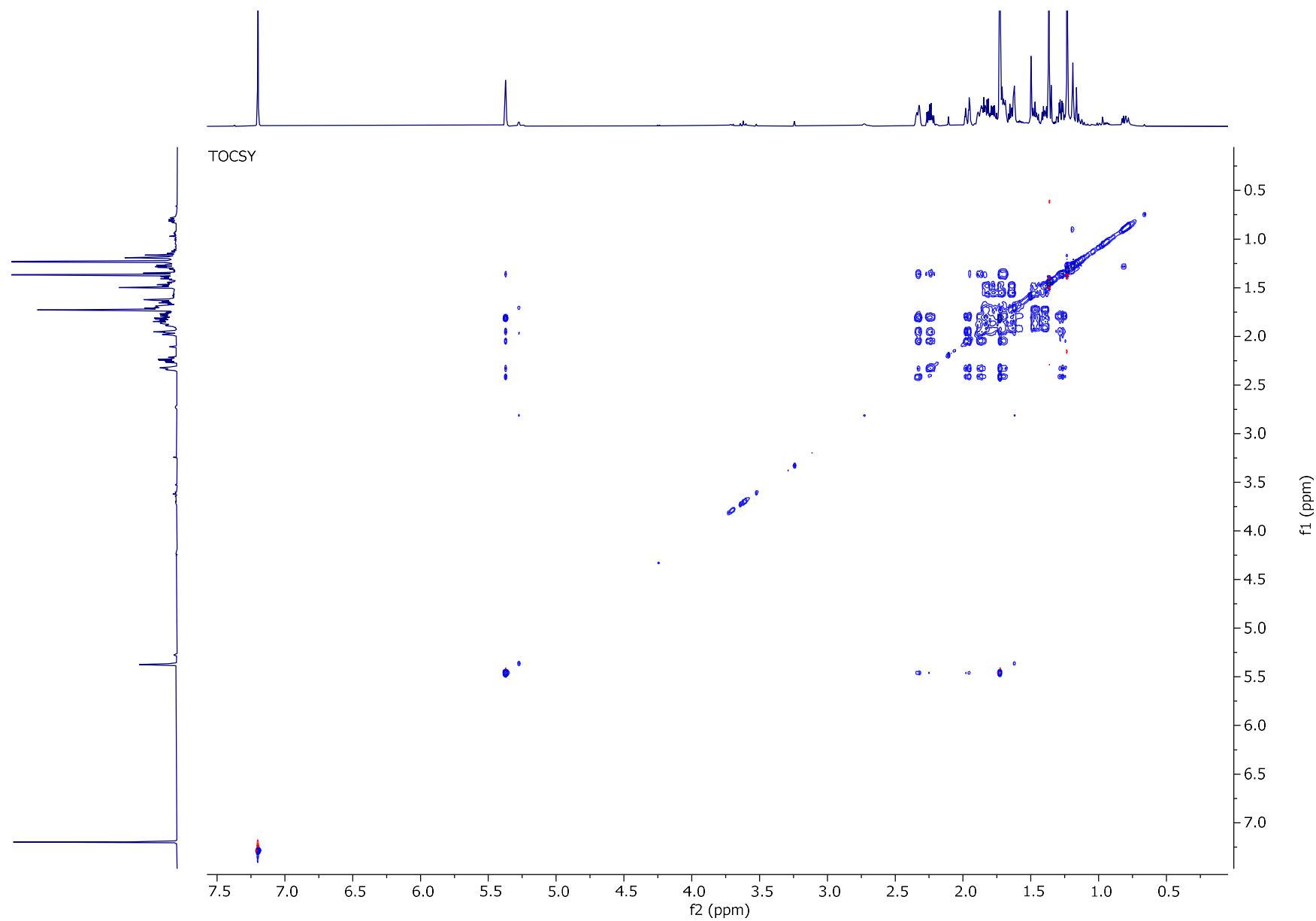


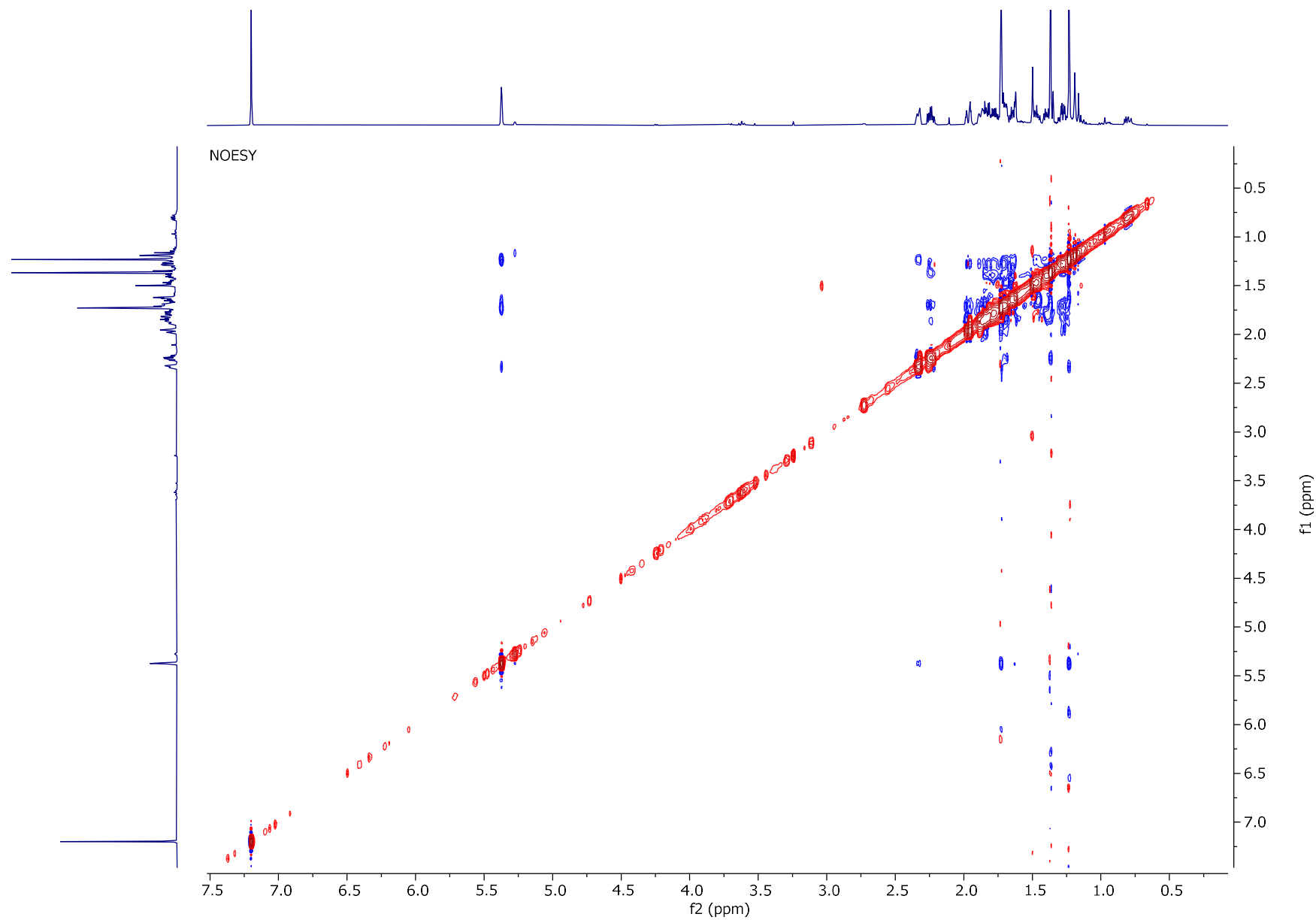




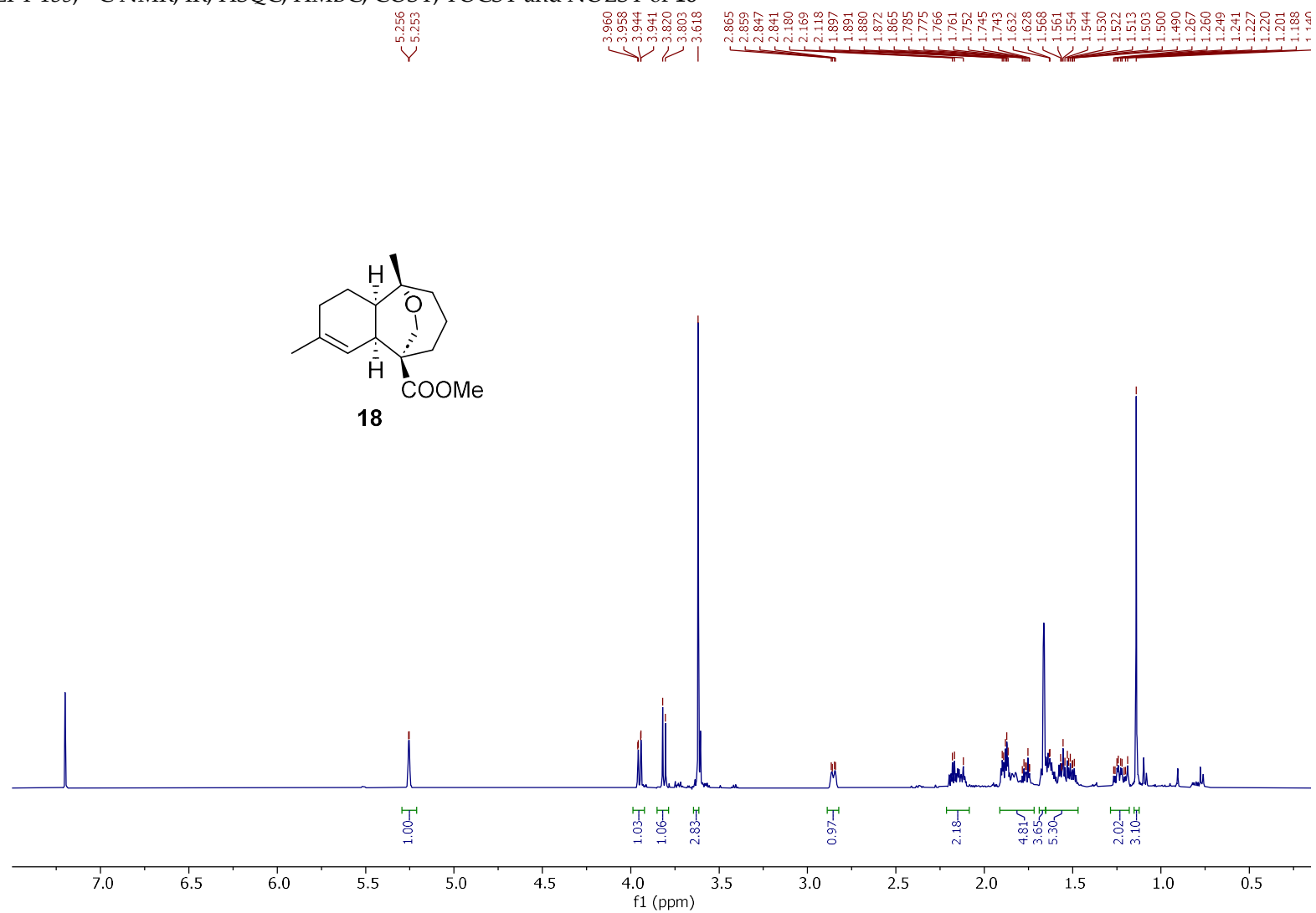


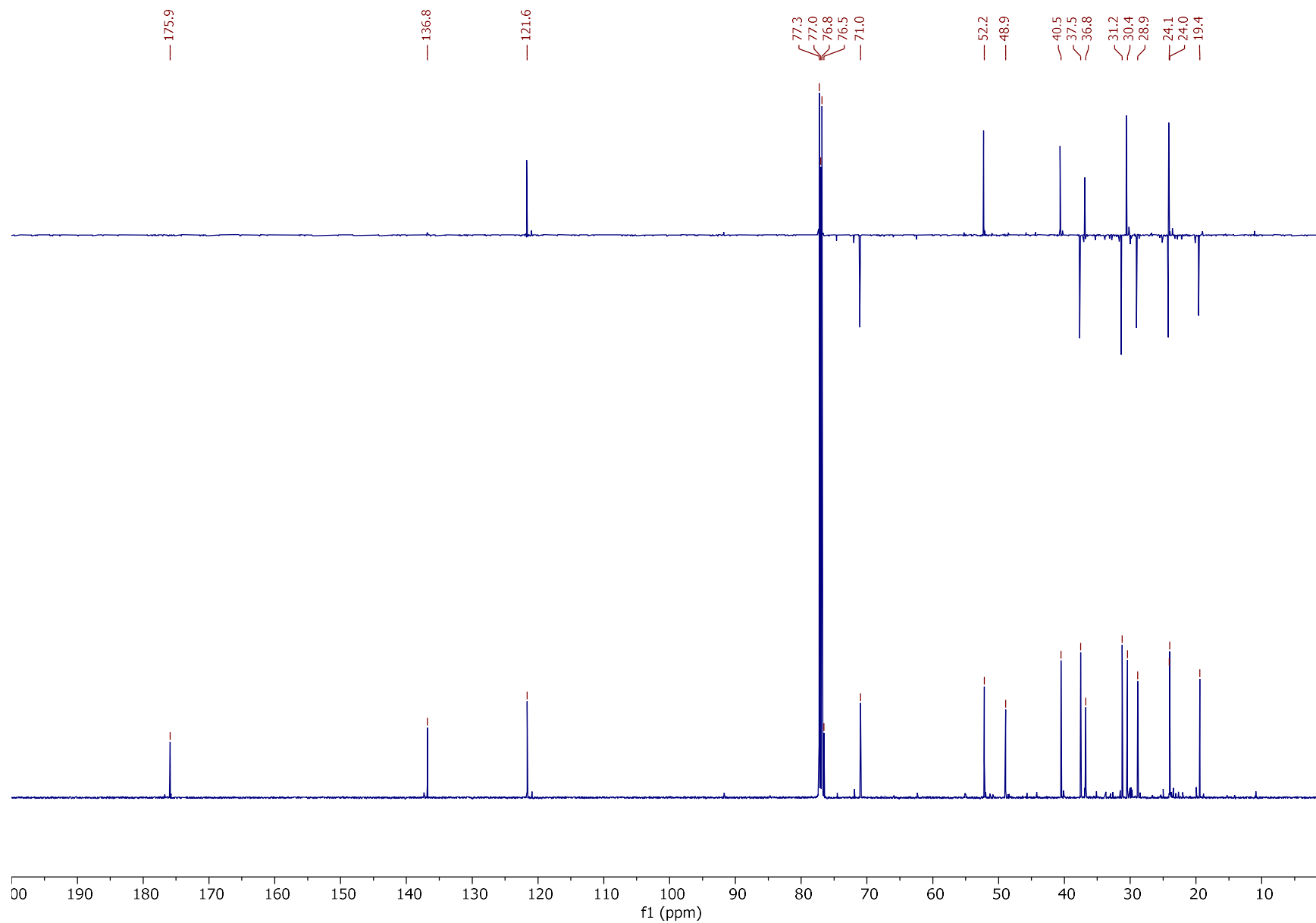


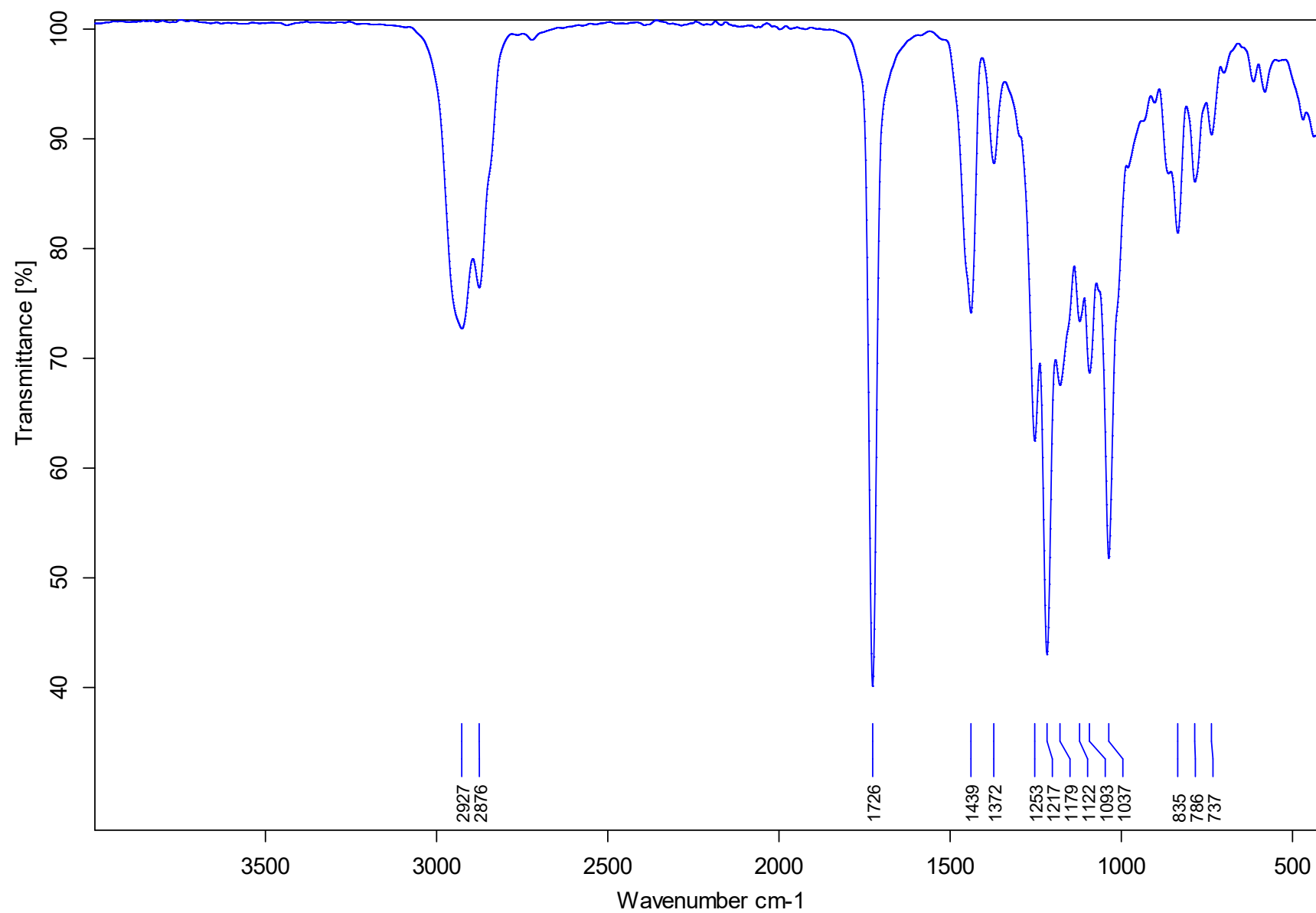




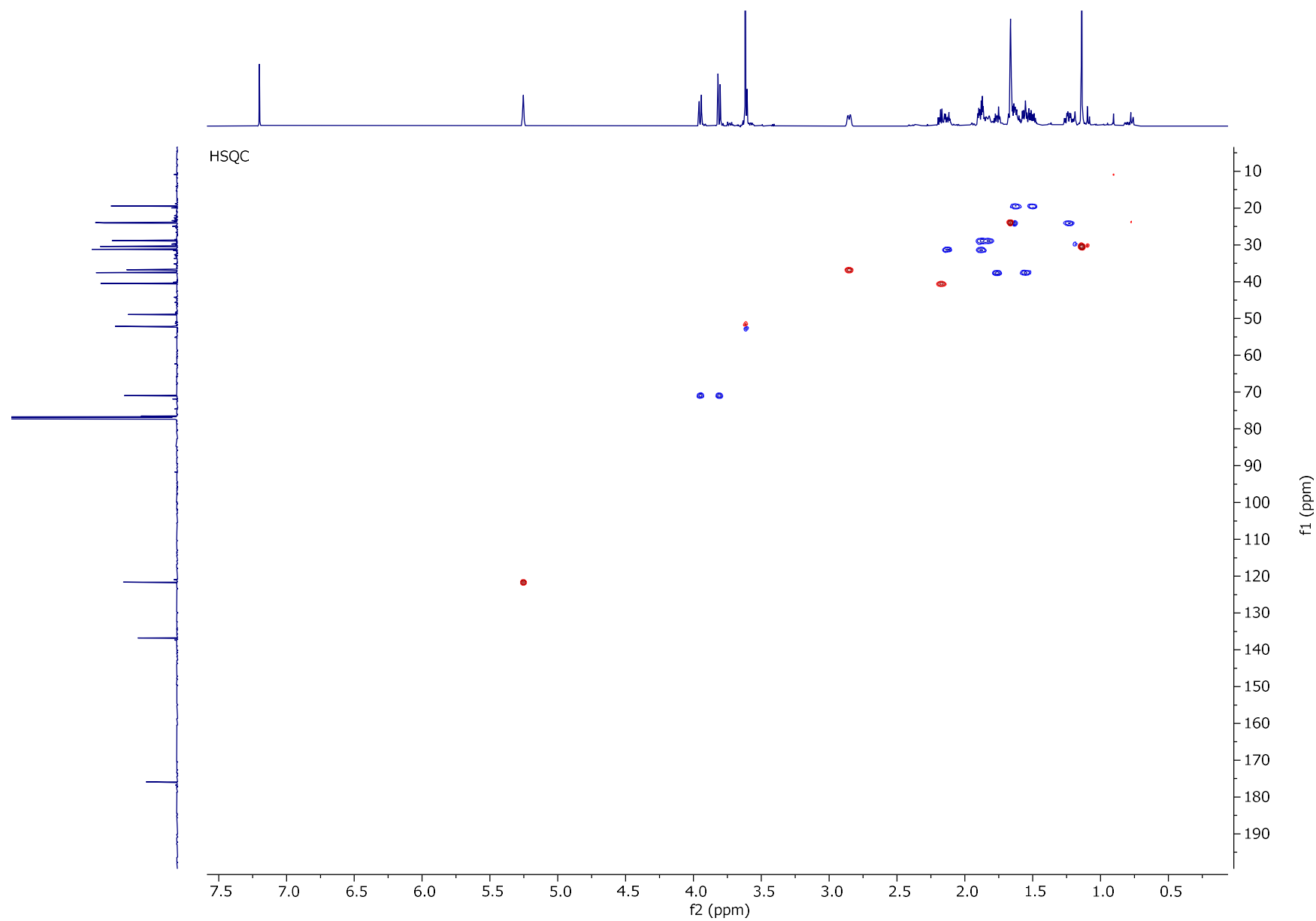
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **18**

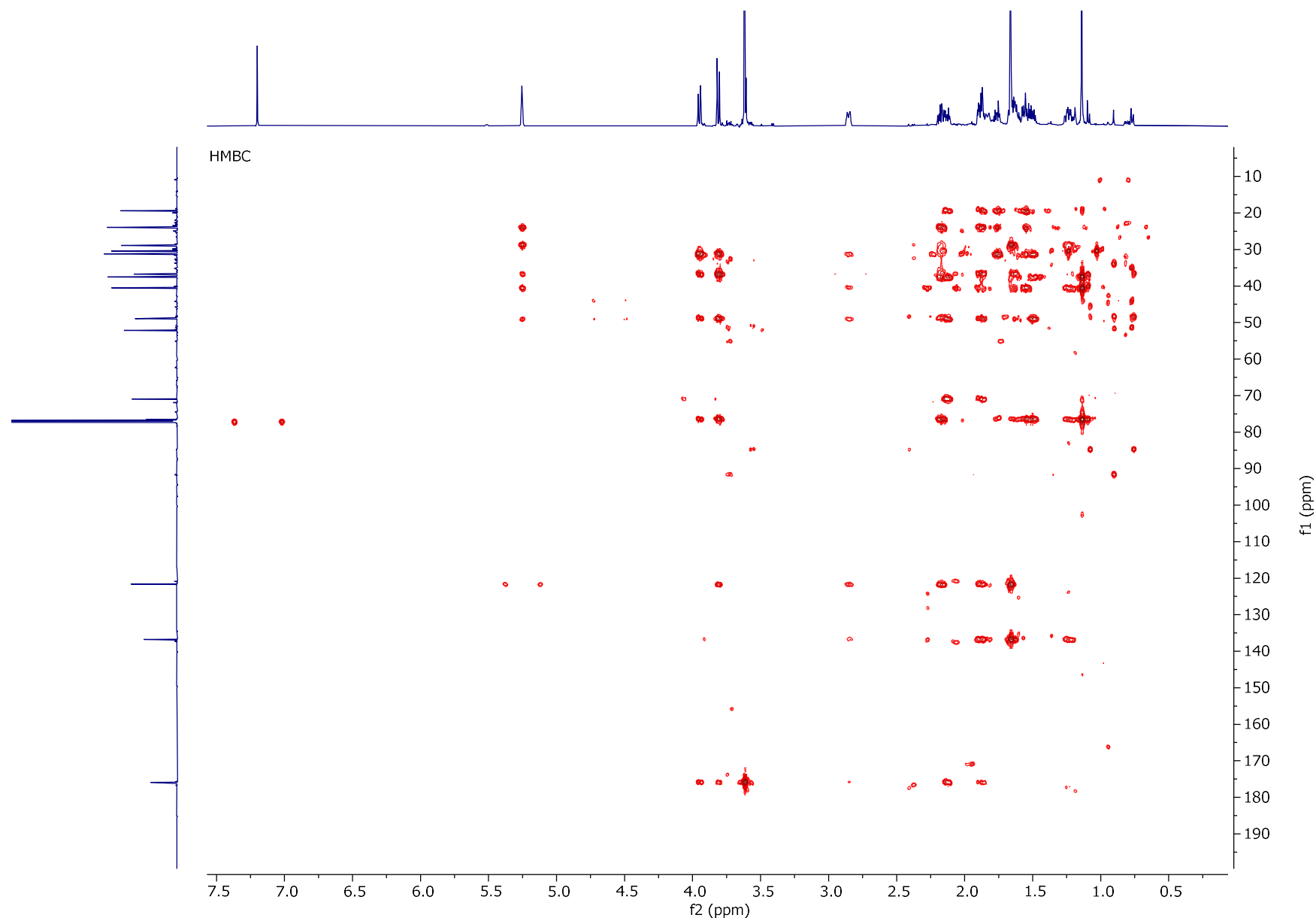


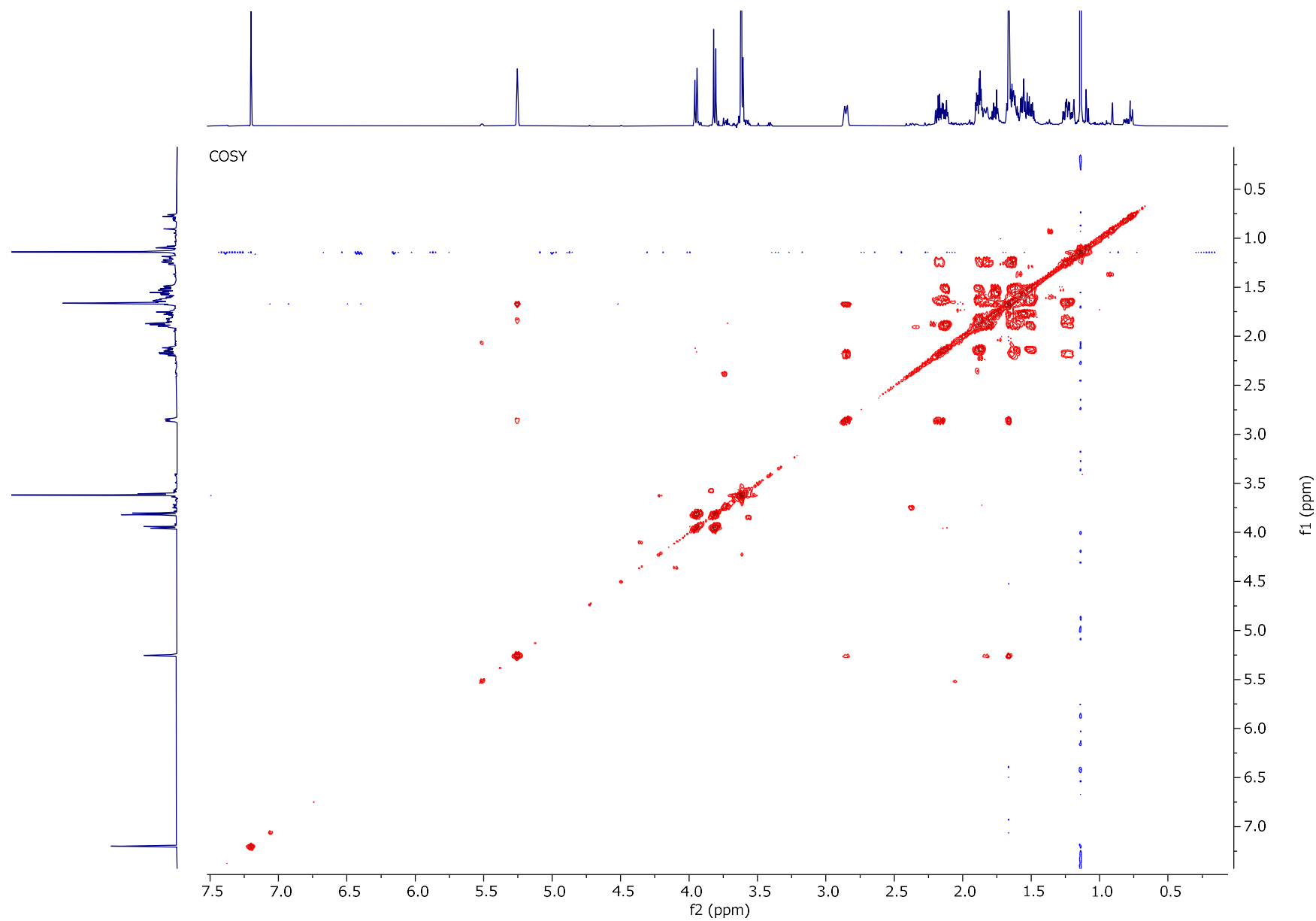


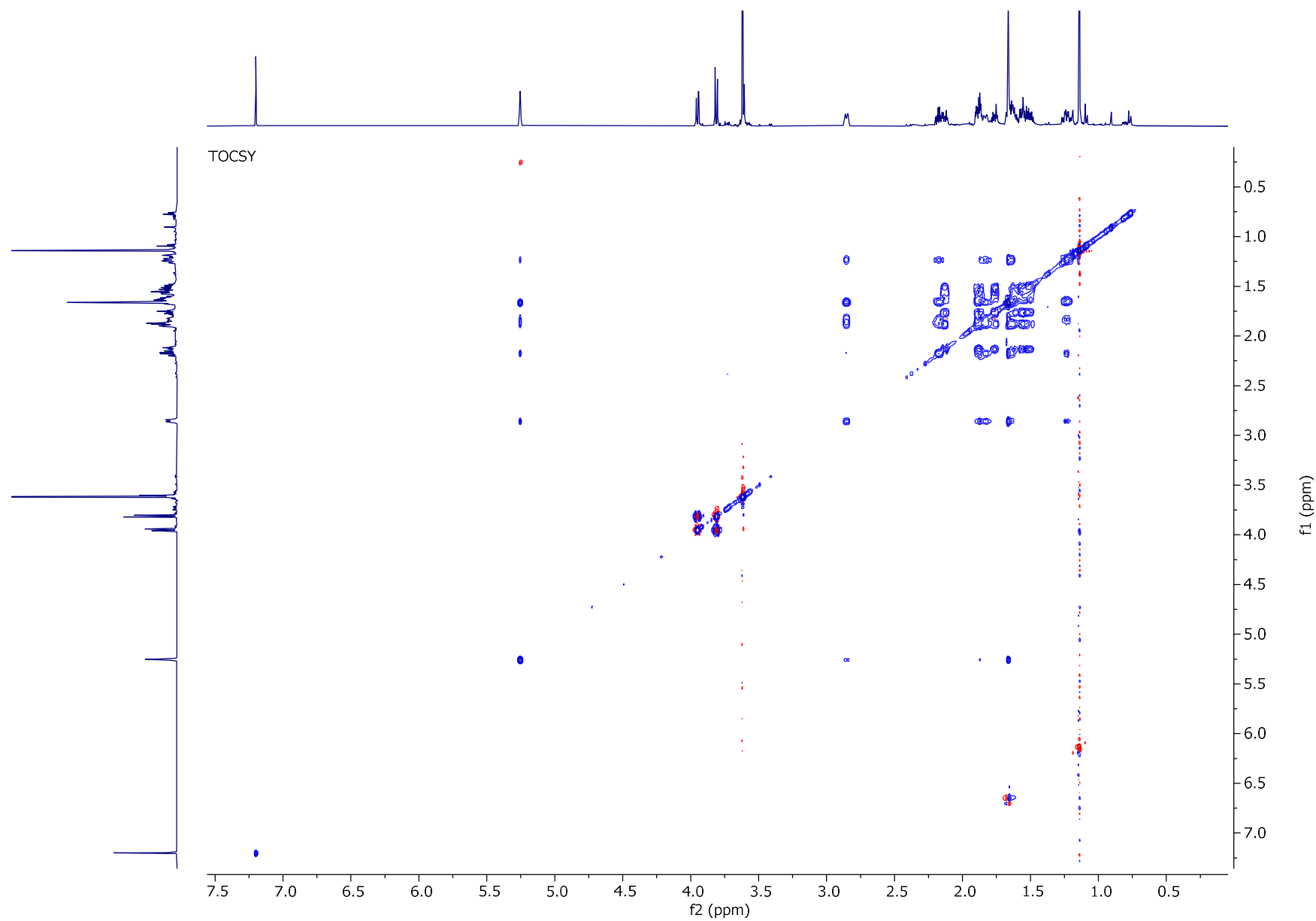


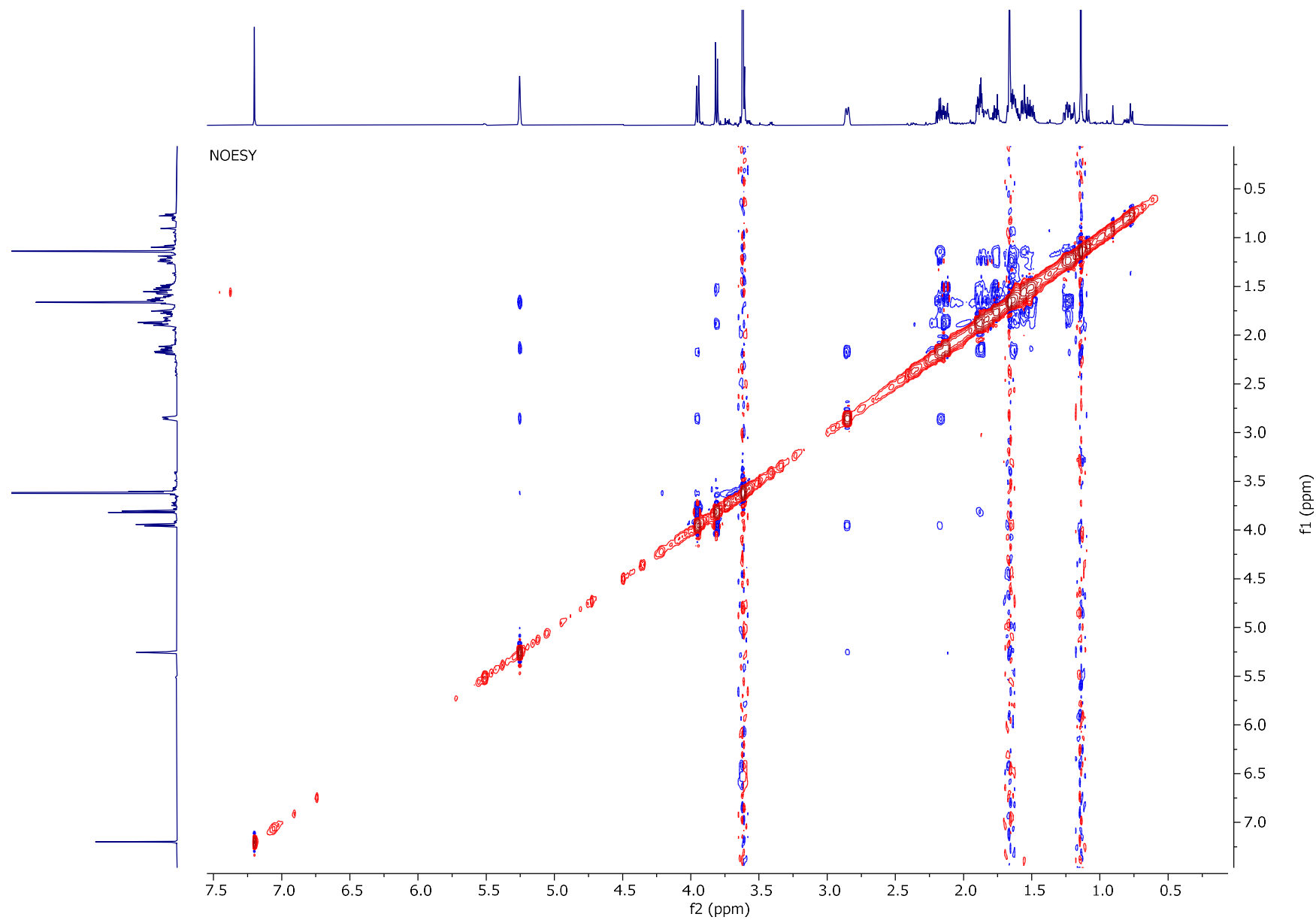


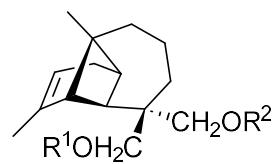






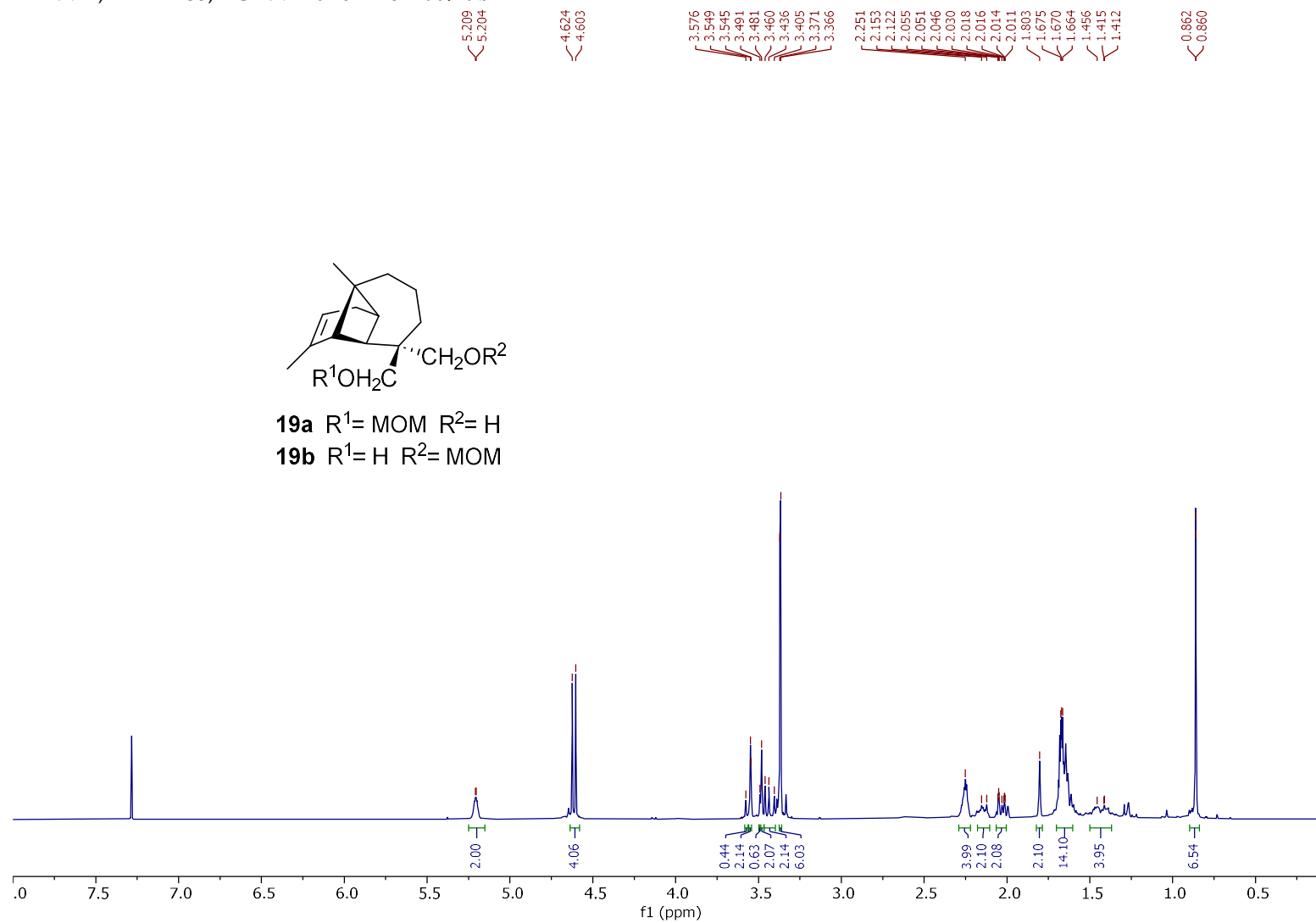


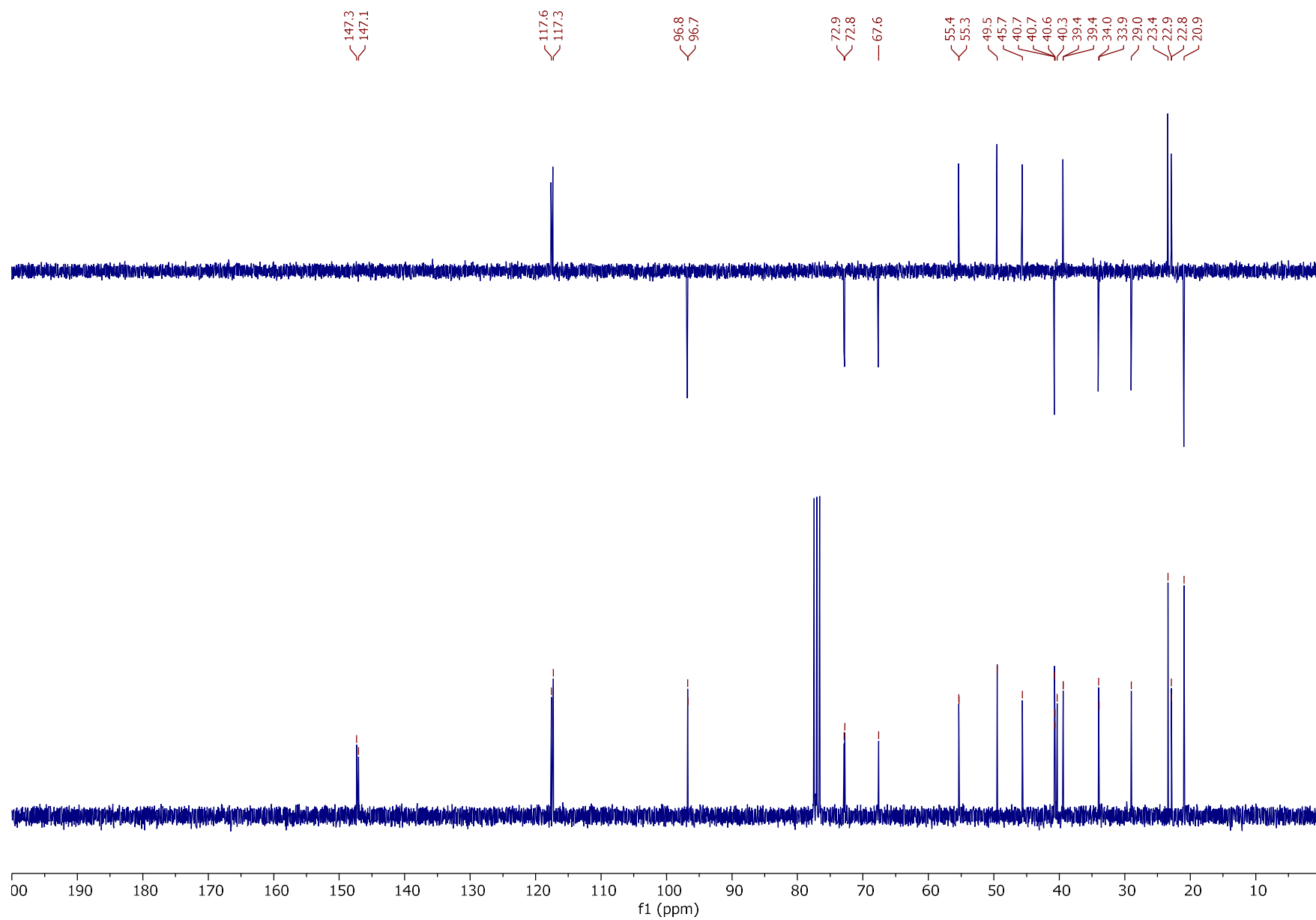


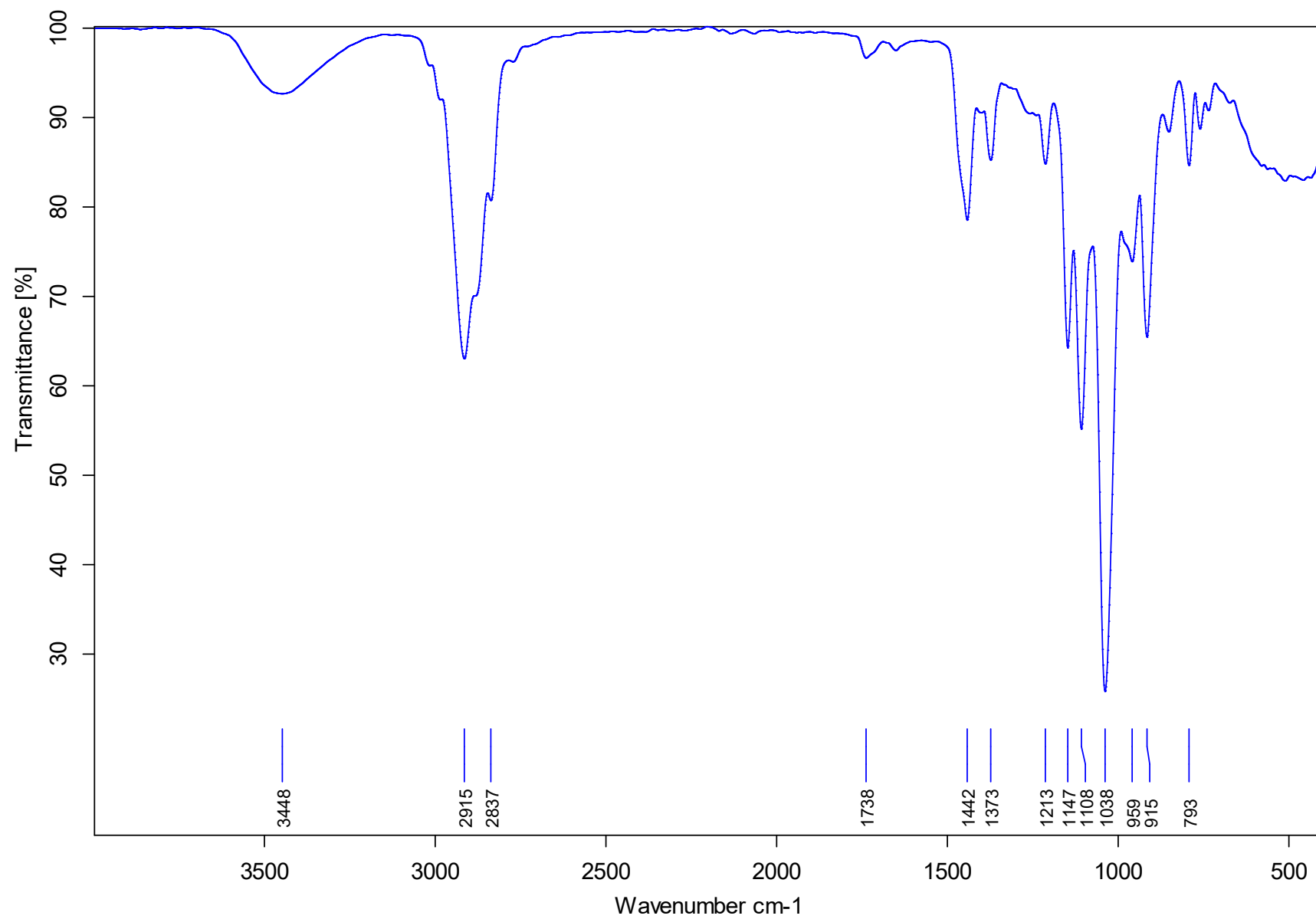
<sup>1</sup>H NMR, DEPT 135, <sup>13</sup>C NMR and IR of **19a/19b**

**19a**  $R^1 = MOM$   $R^2 = H$

**19b**  $R^1 = H$   $R^2 = MOM$

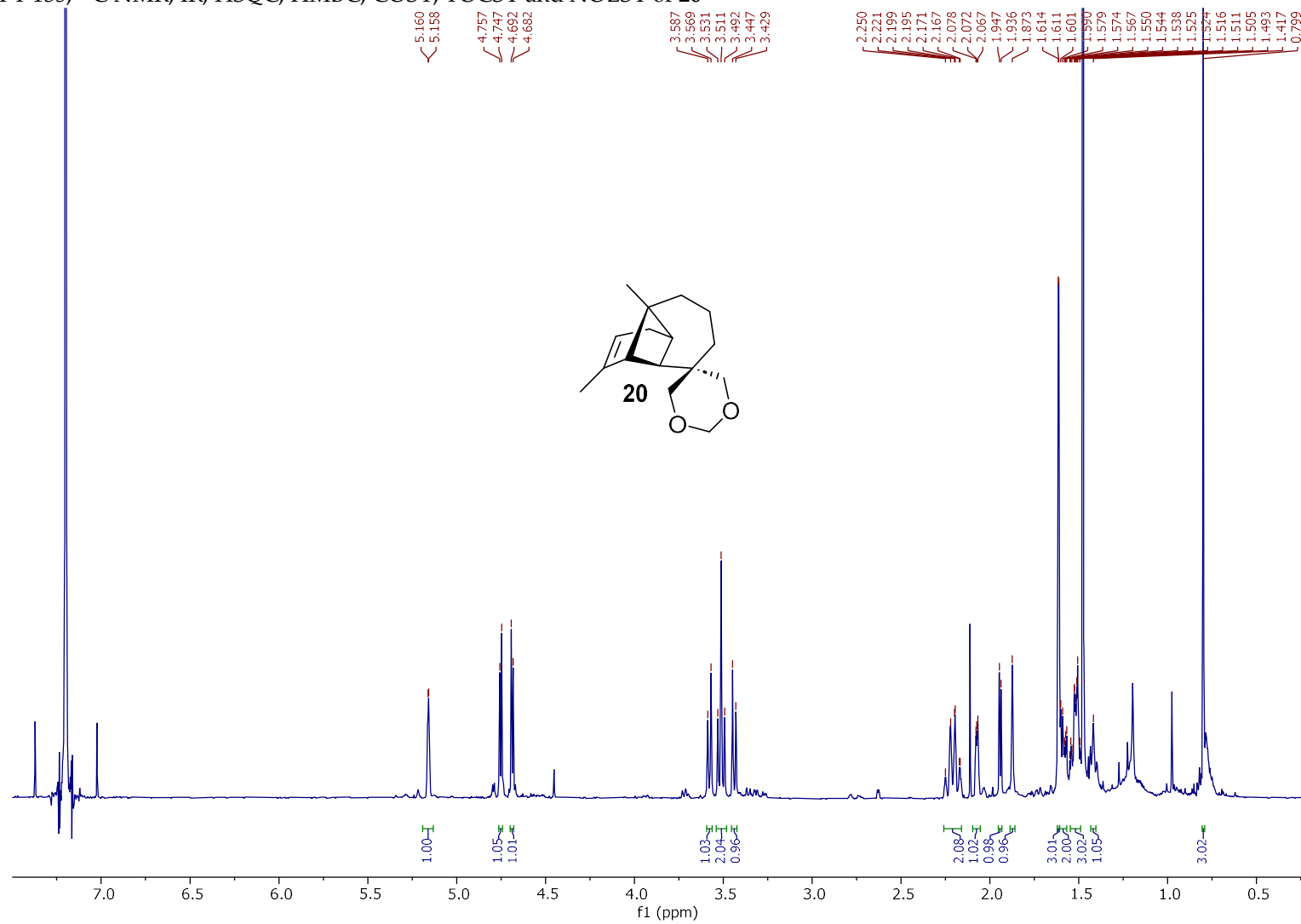


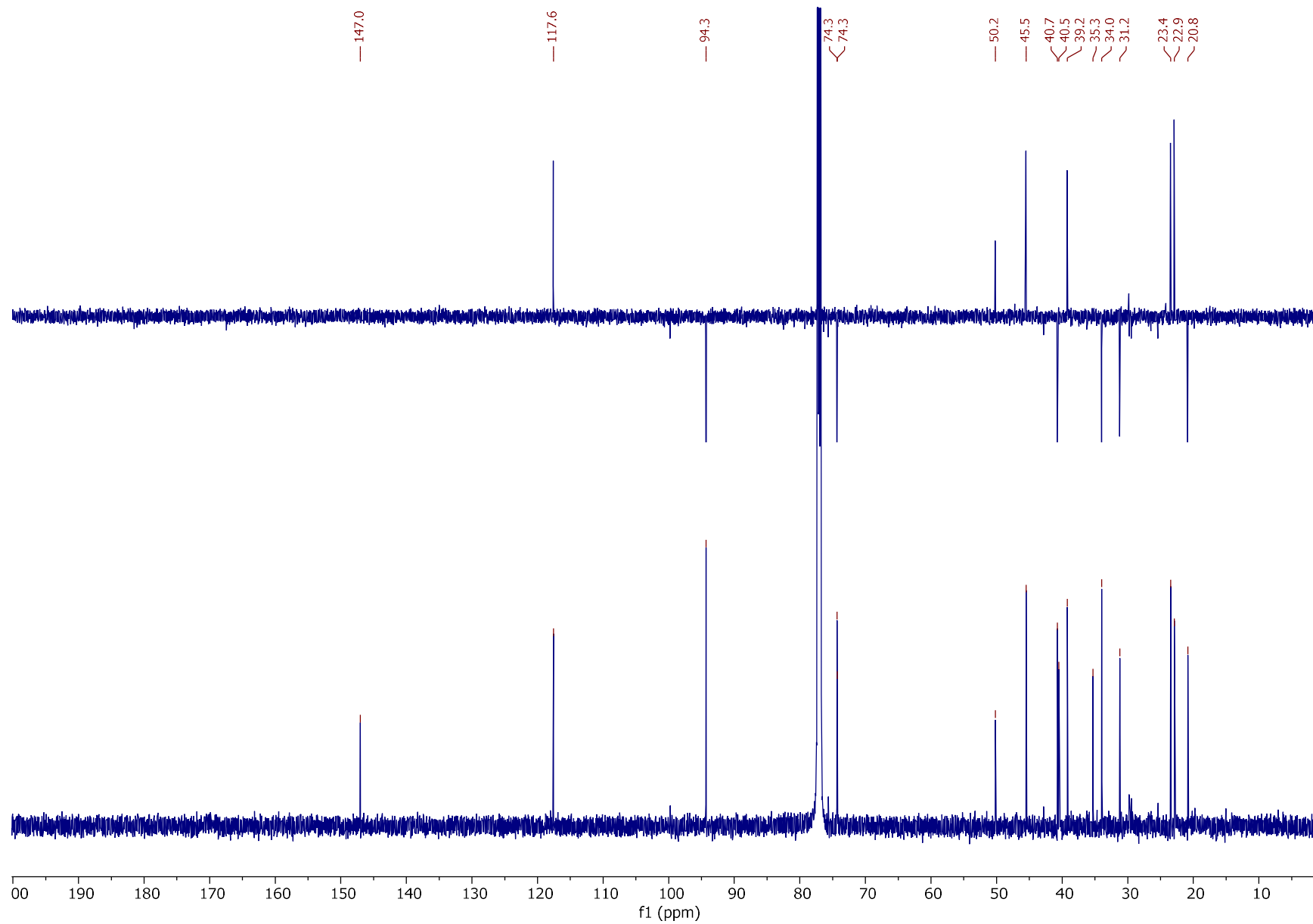


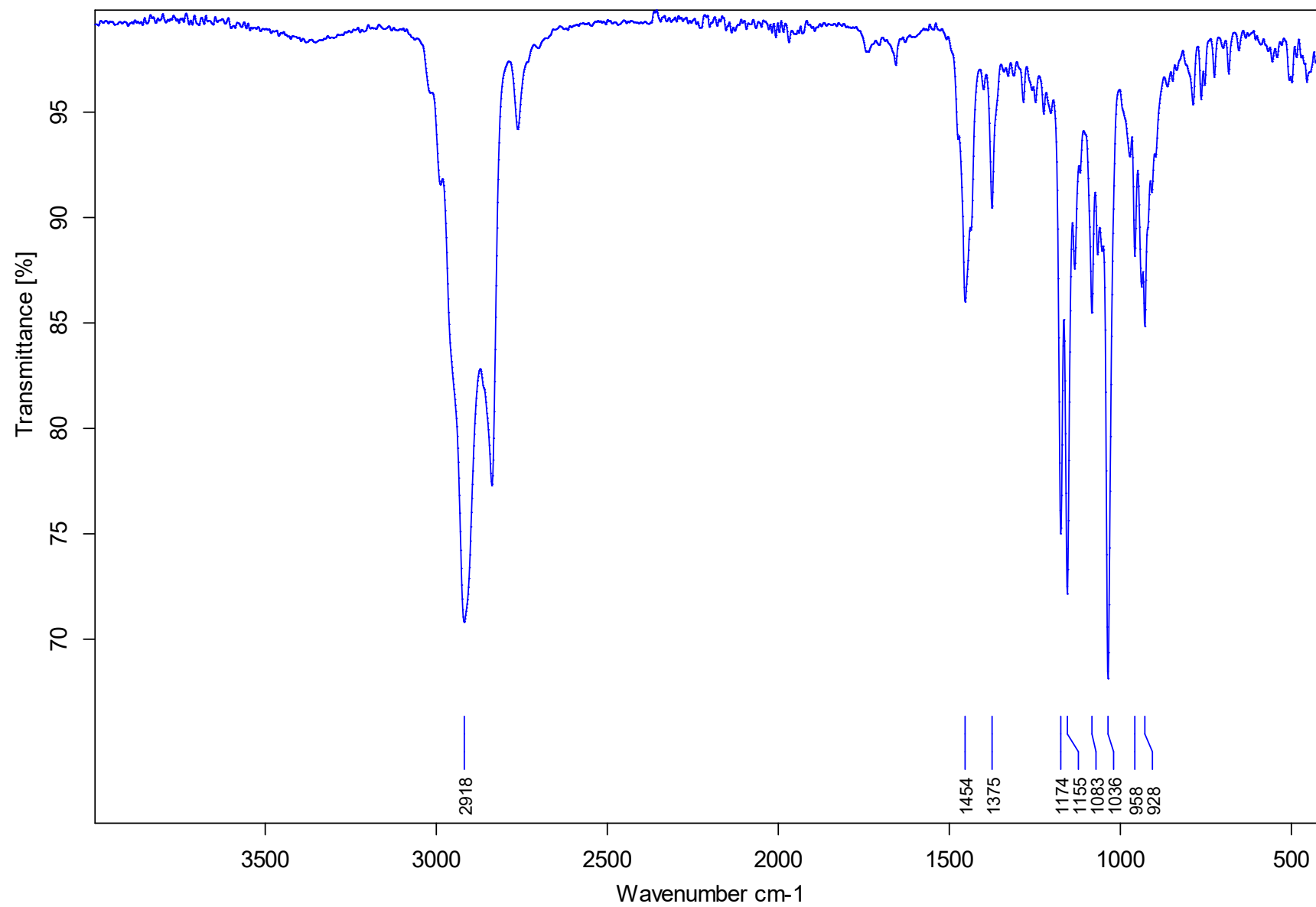


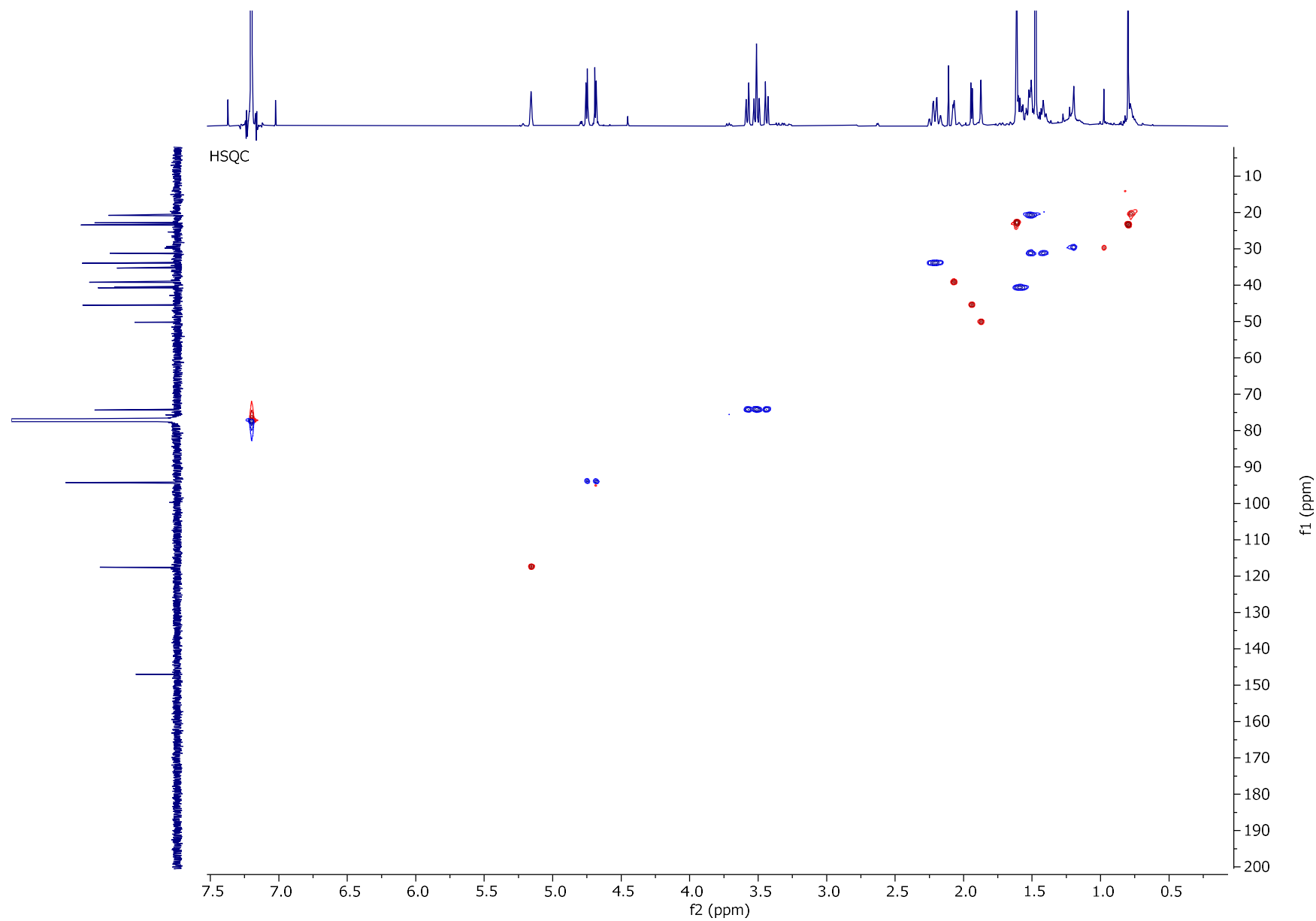


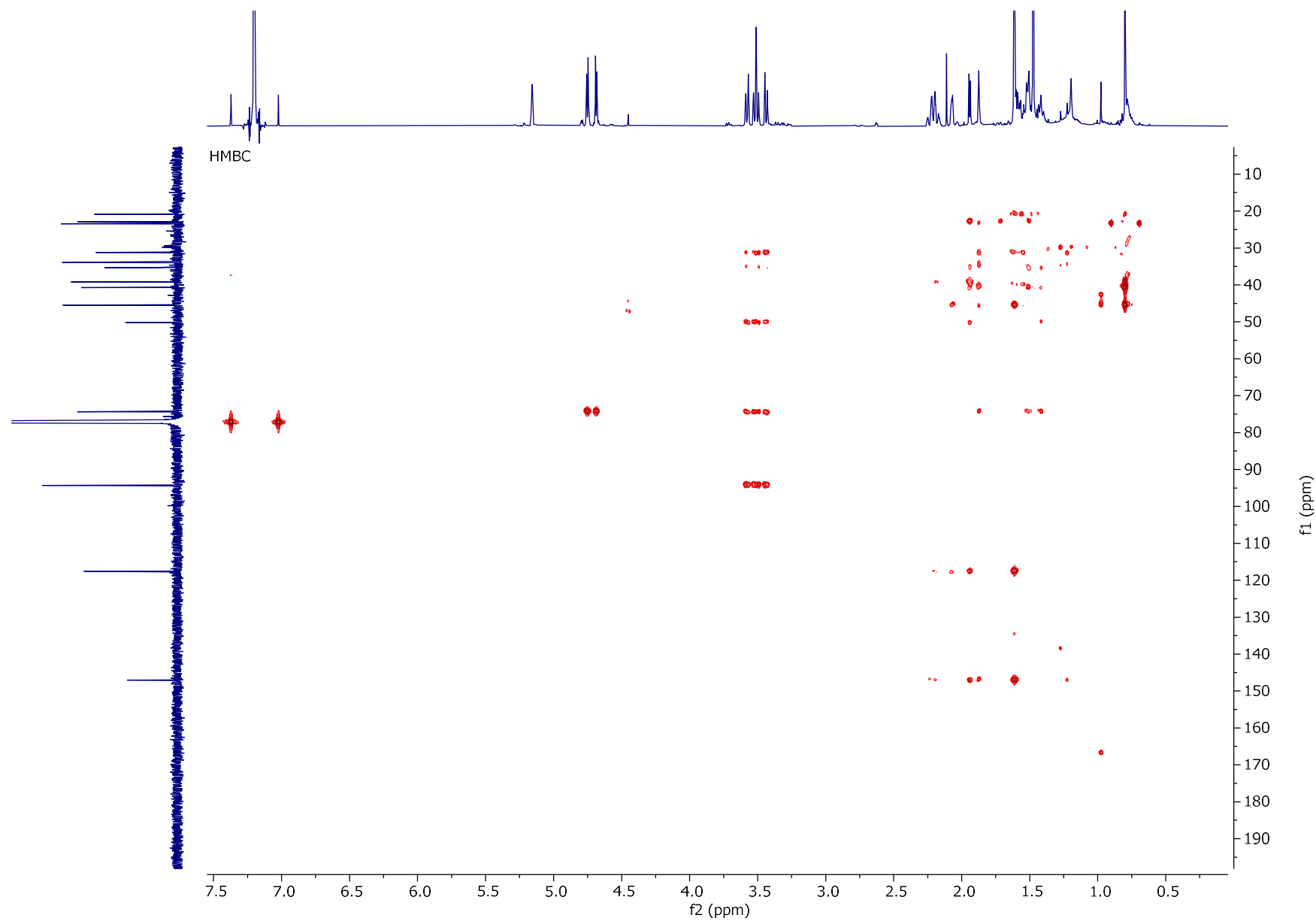
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **20**

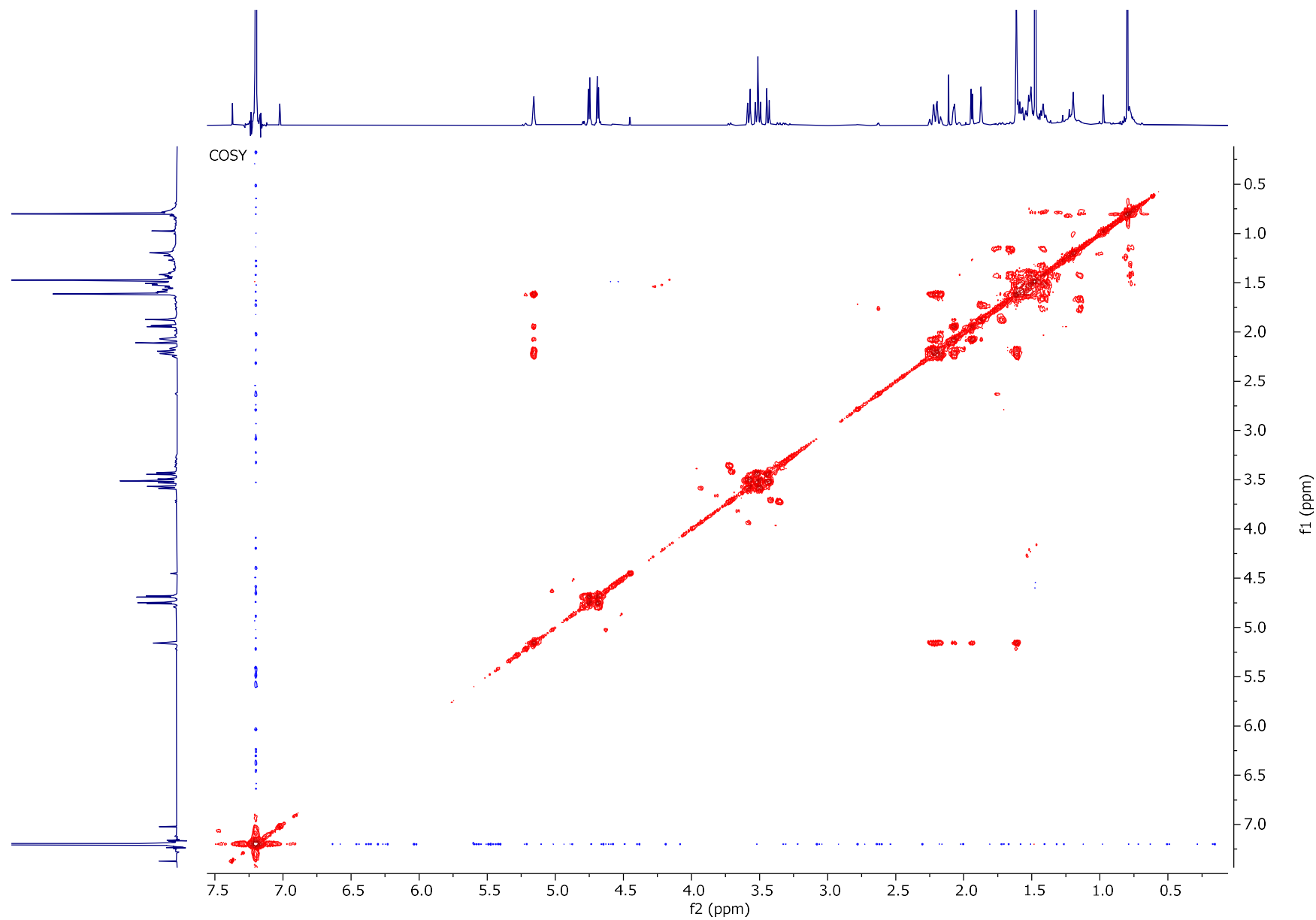


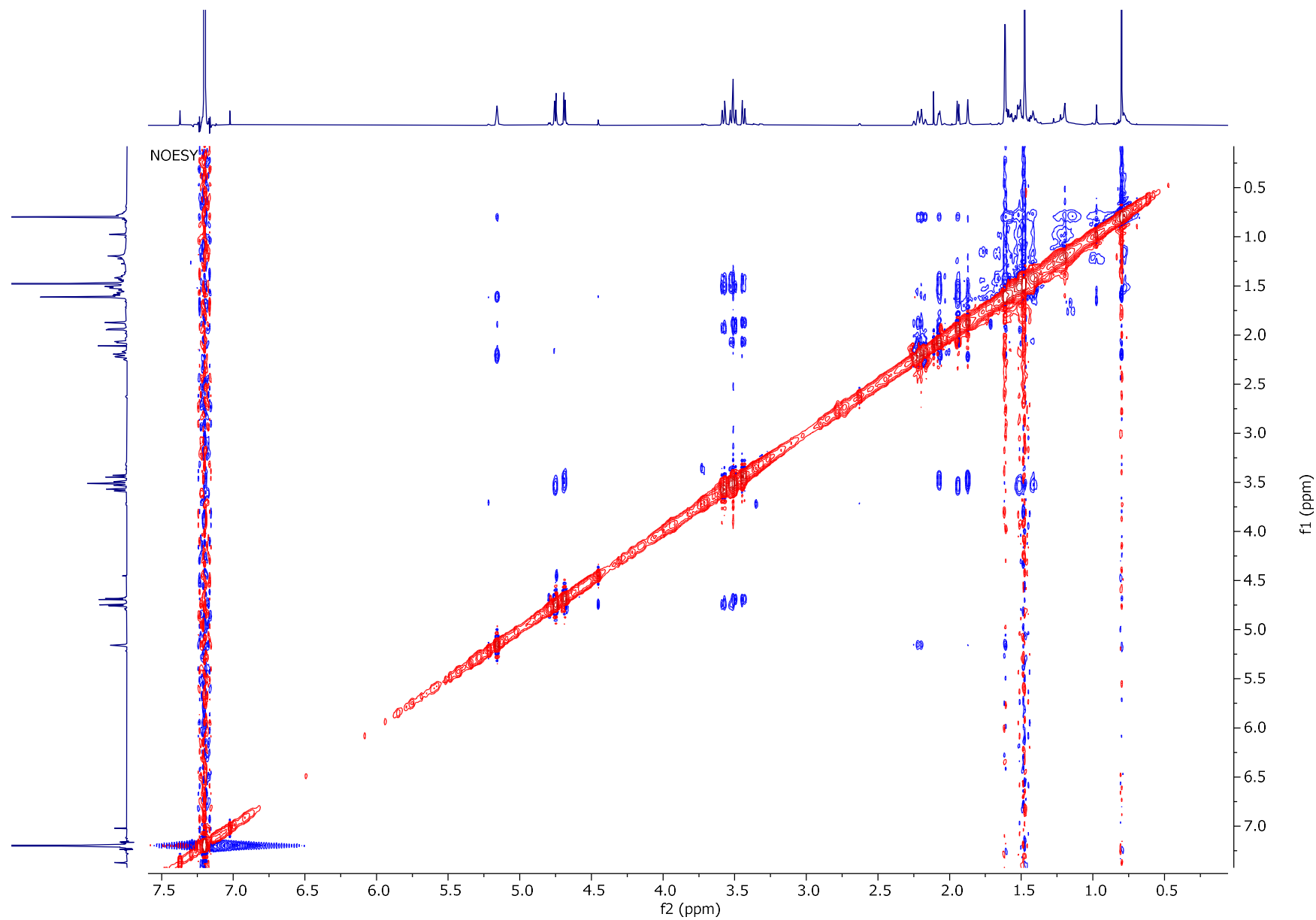


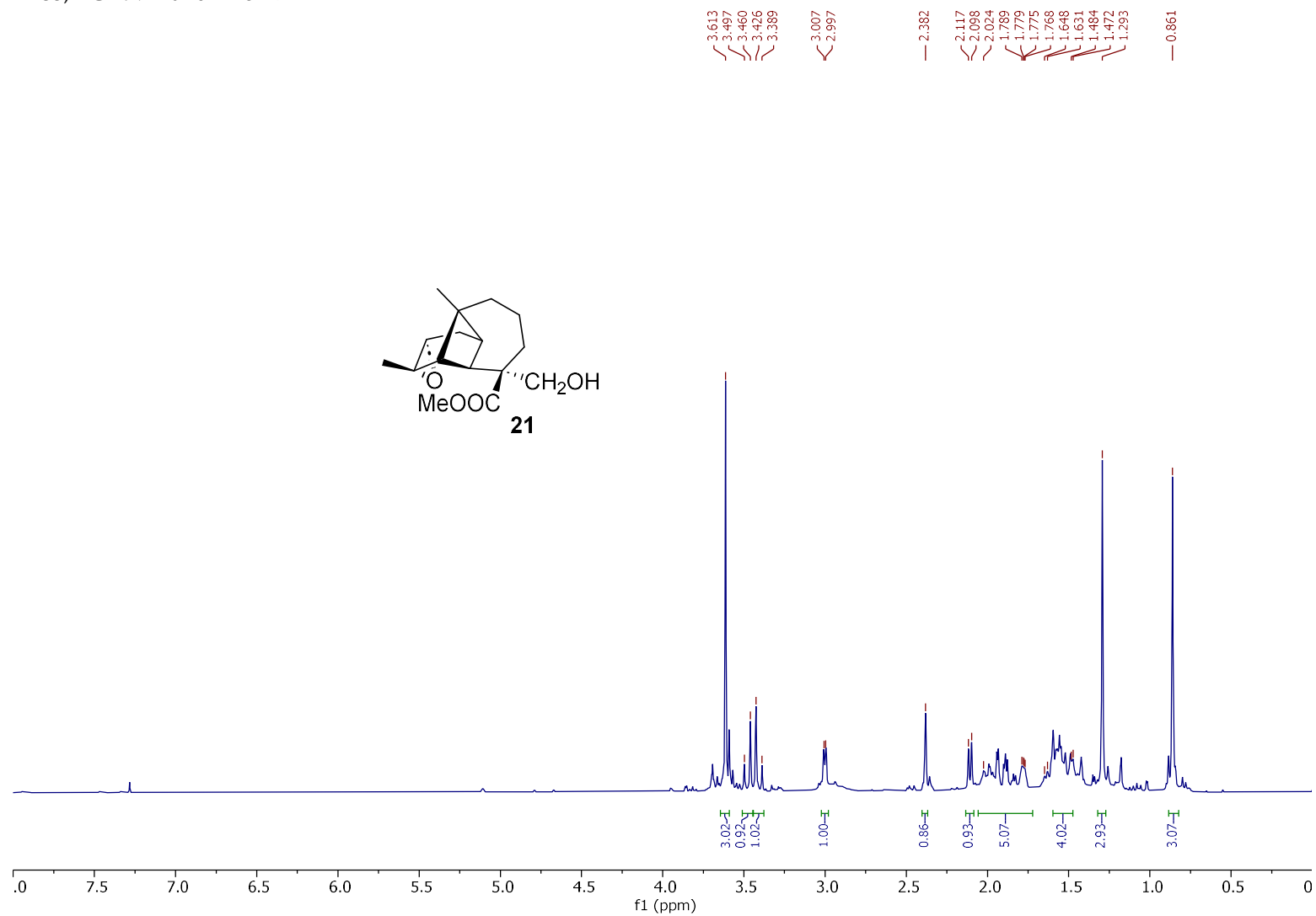




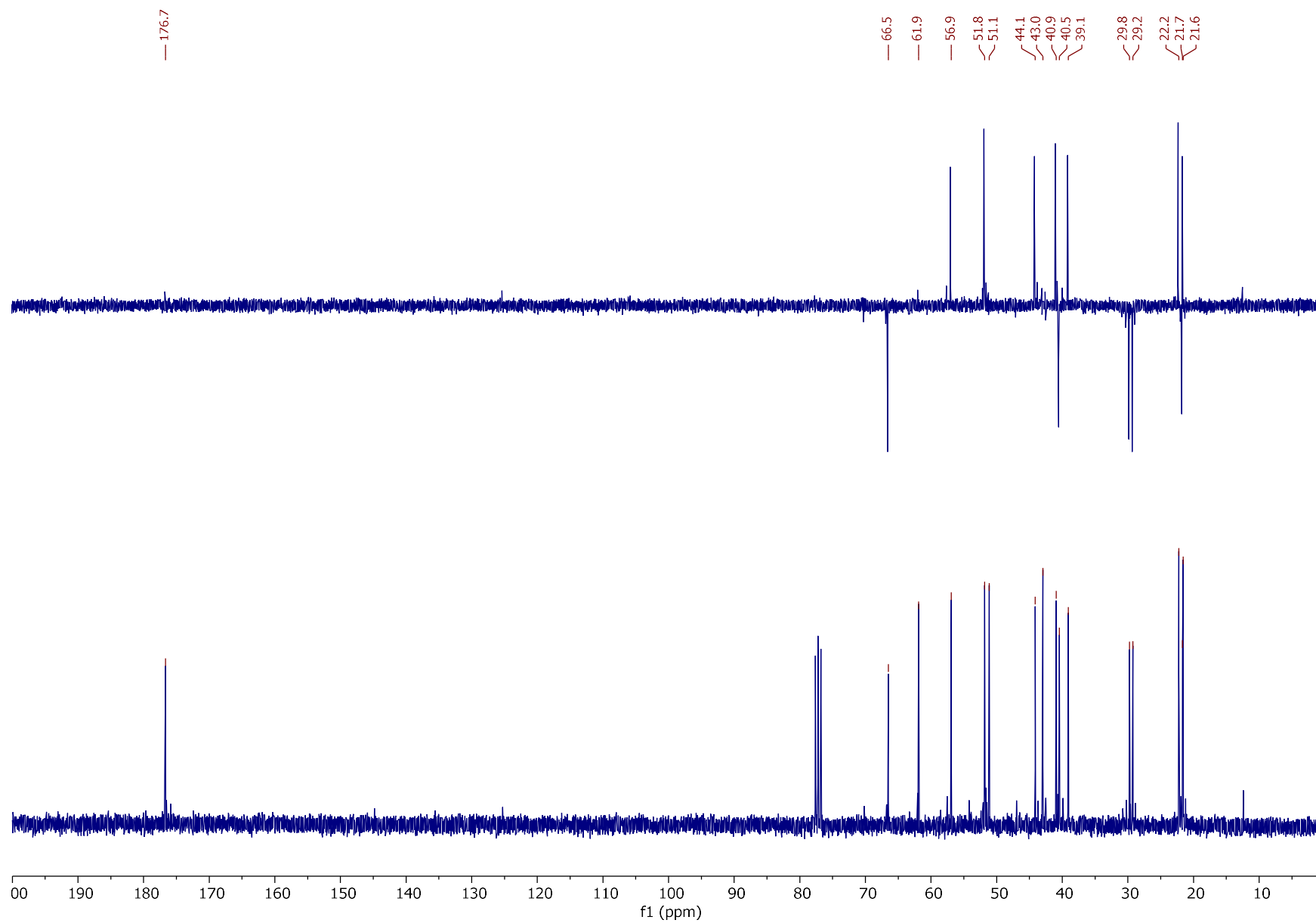


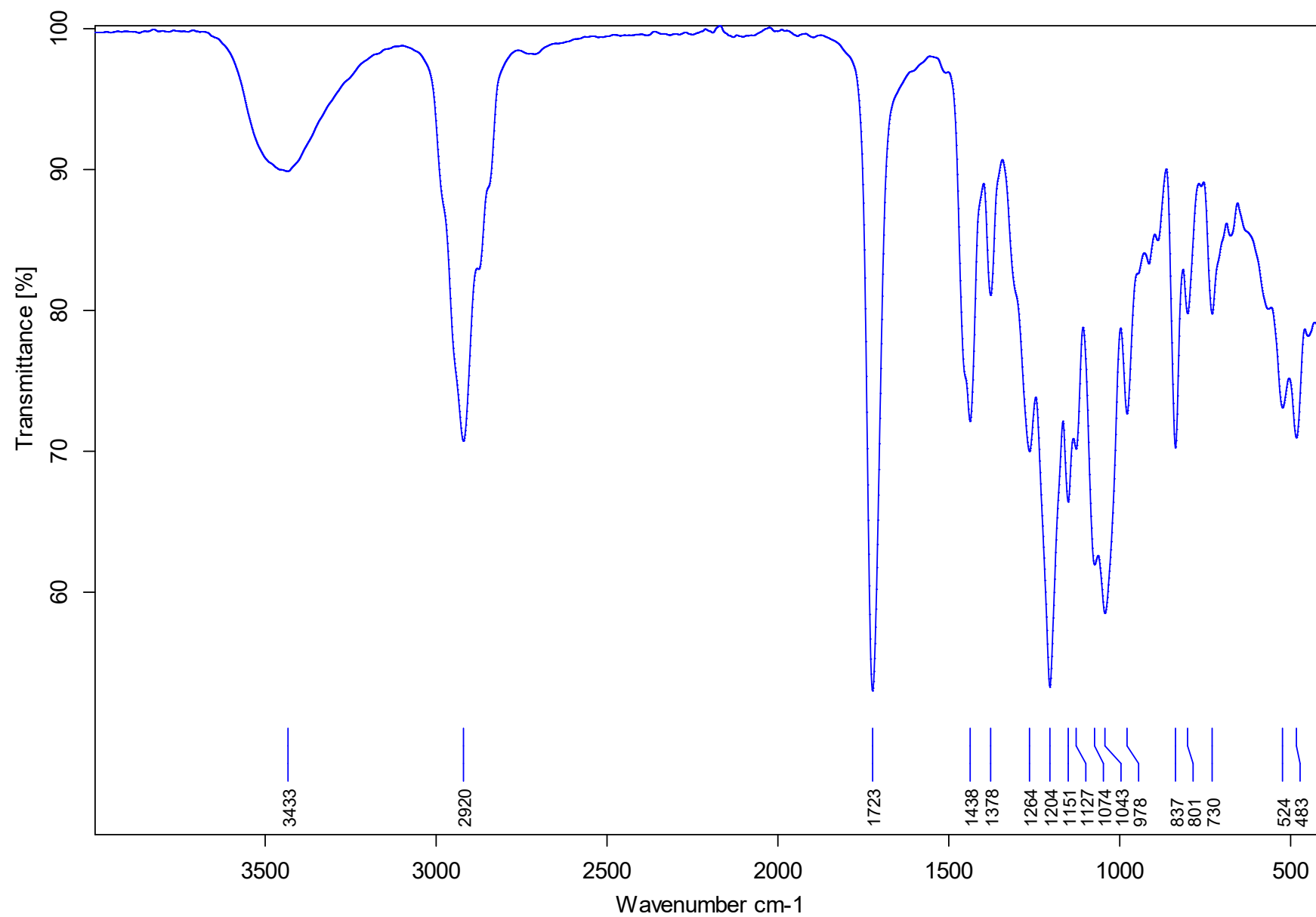




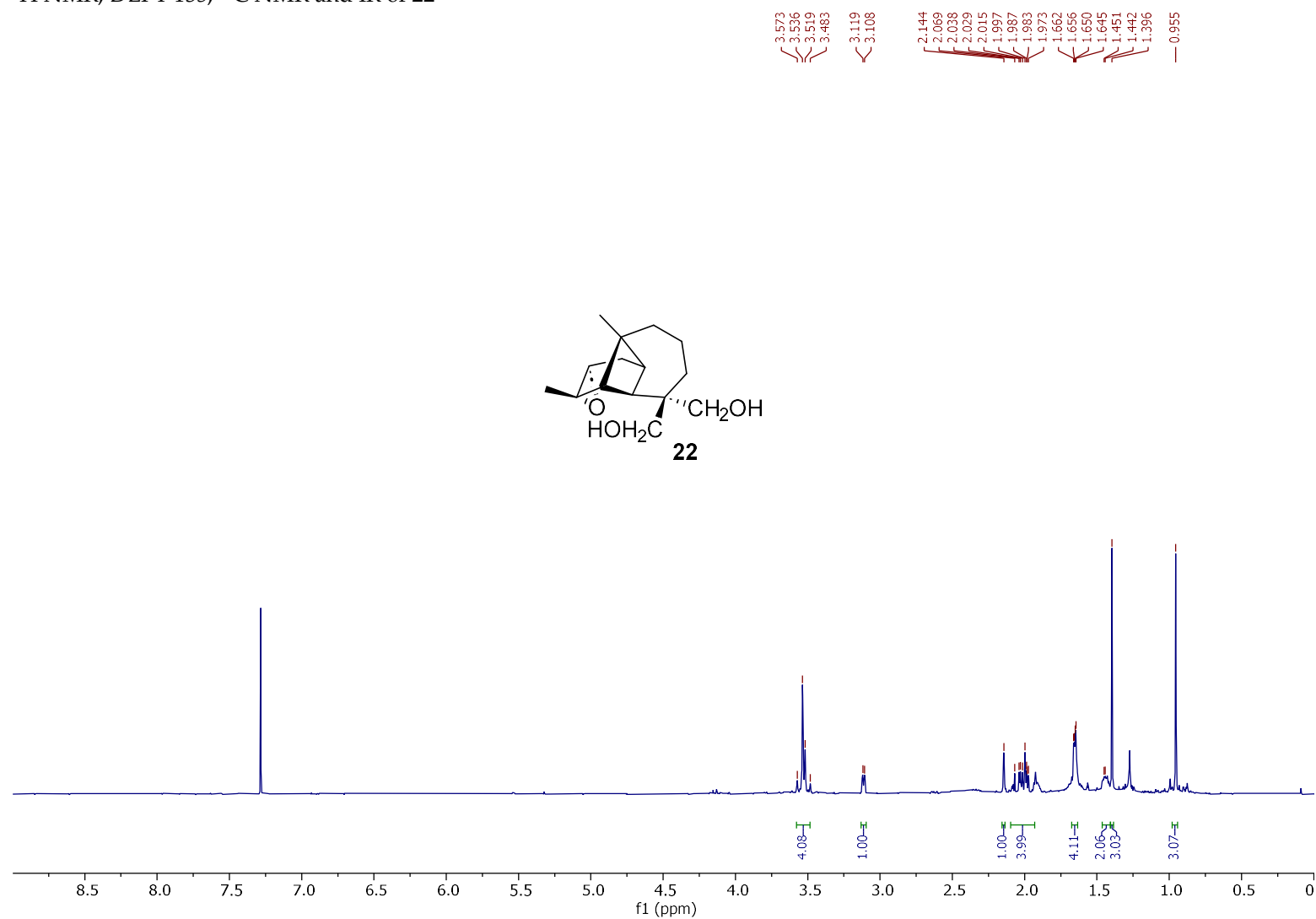
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR and IR of **21**

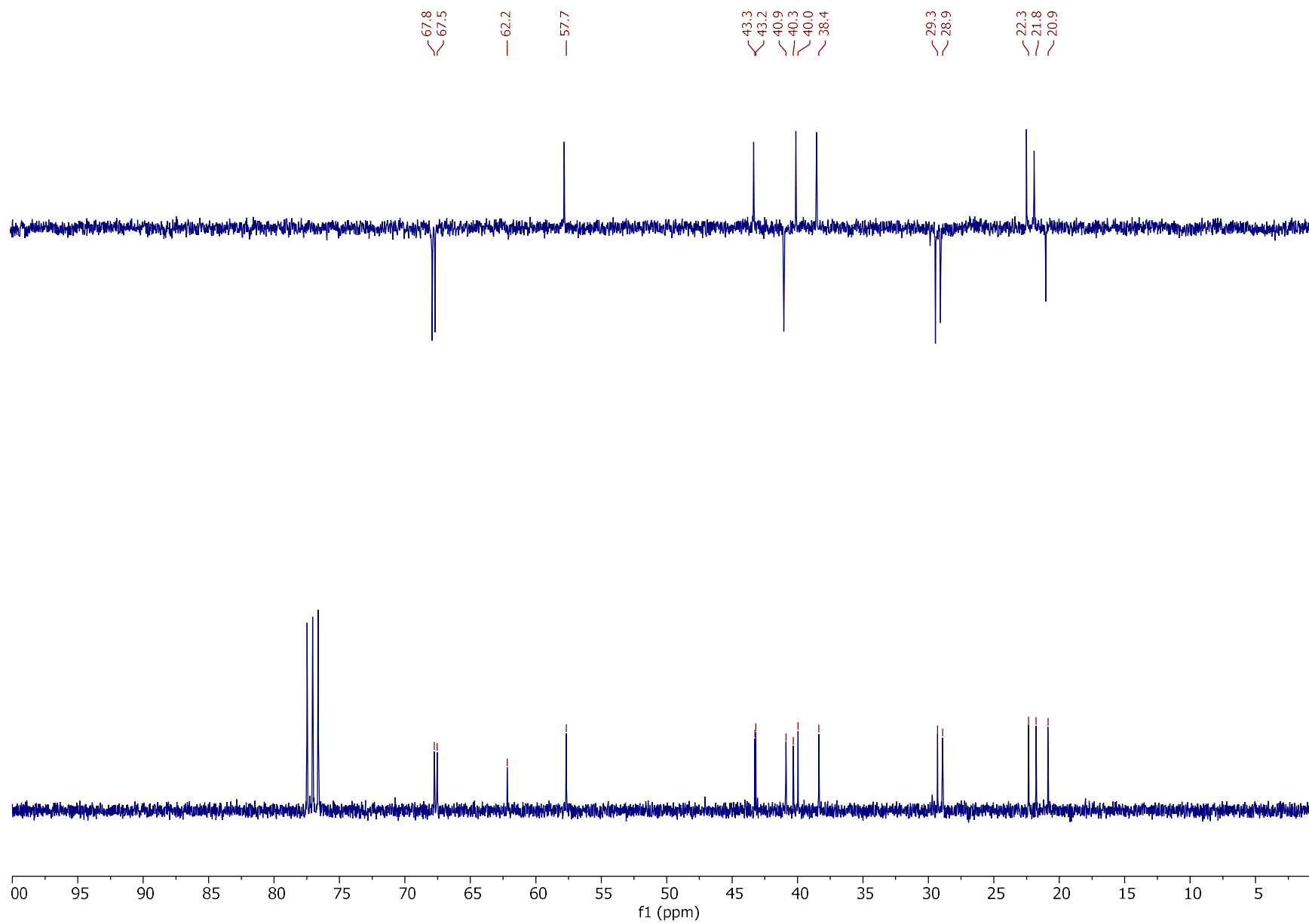


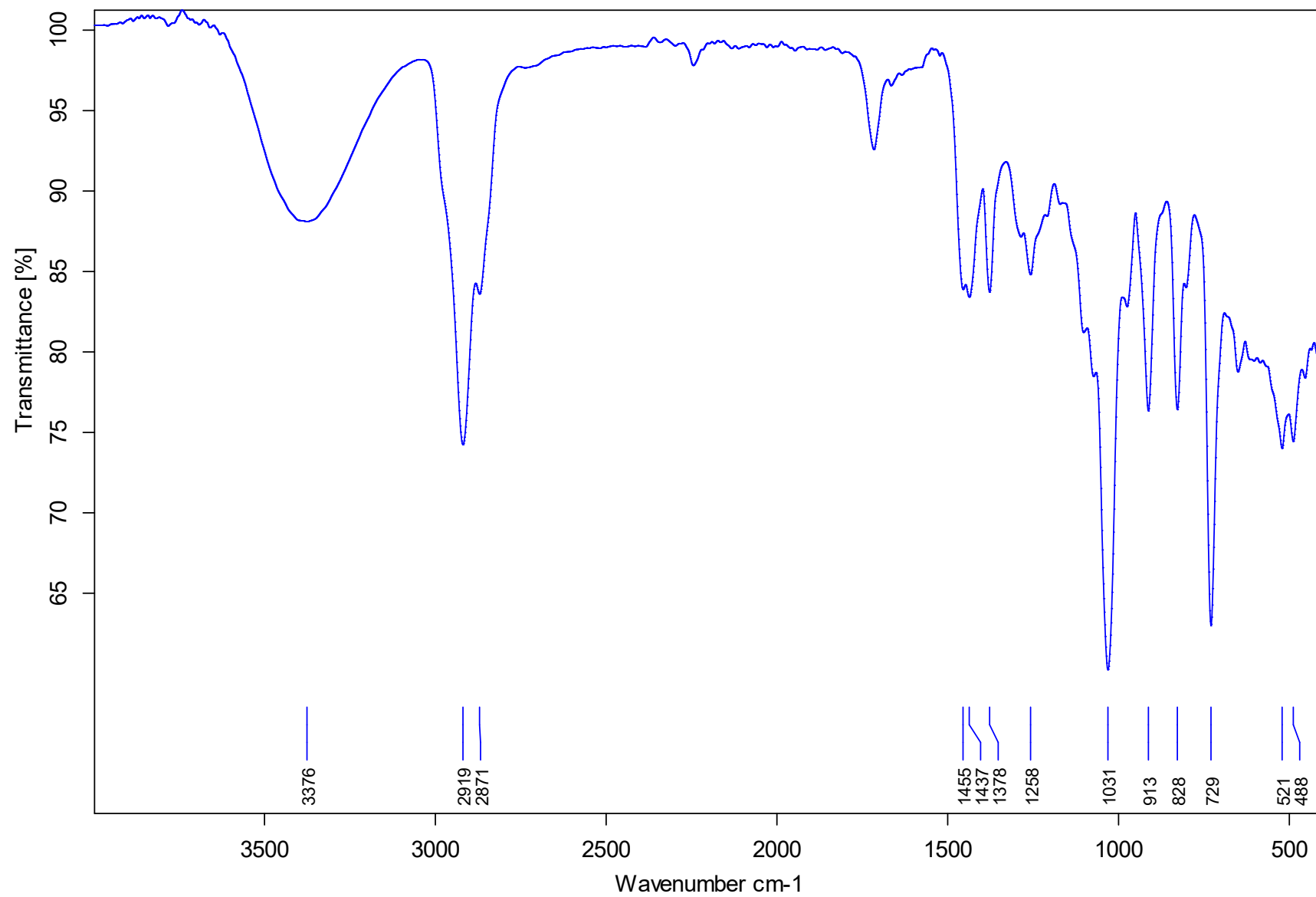




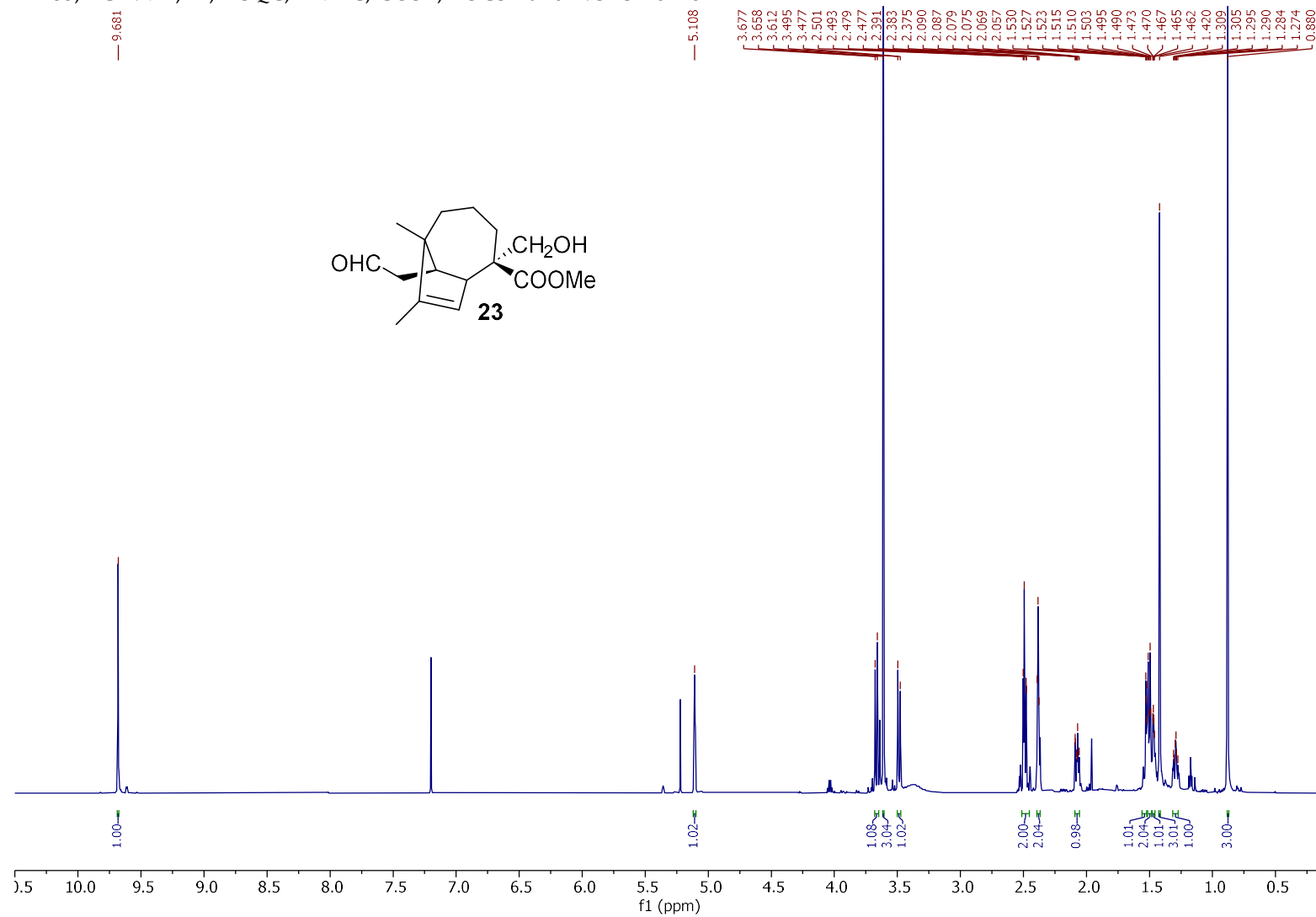
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR and IR of **22**

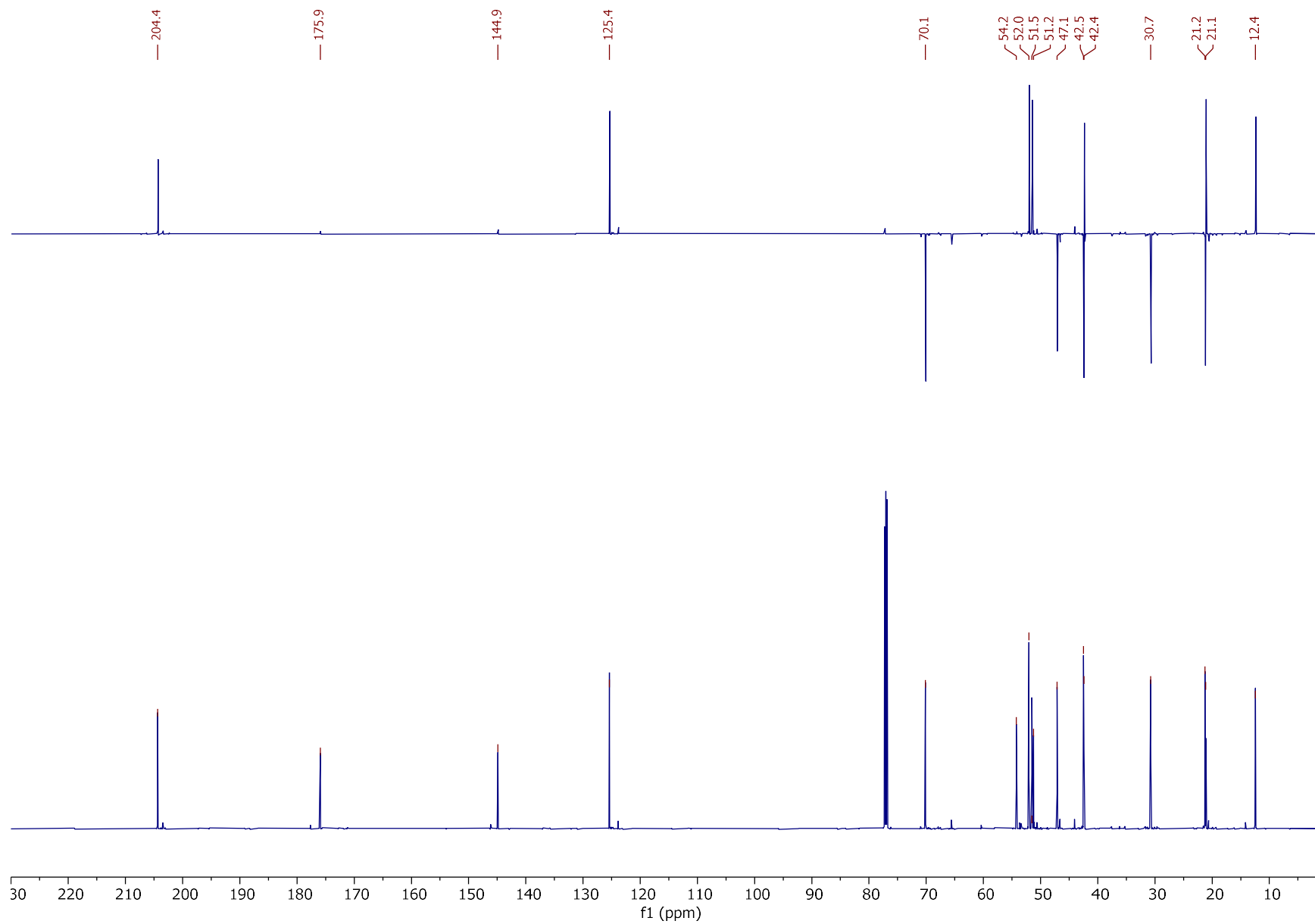


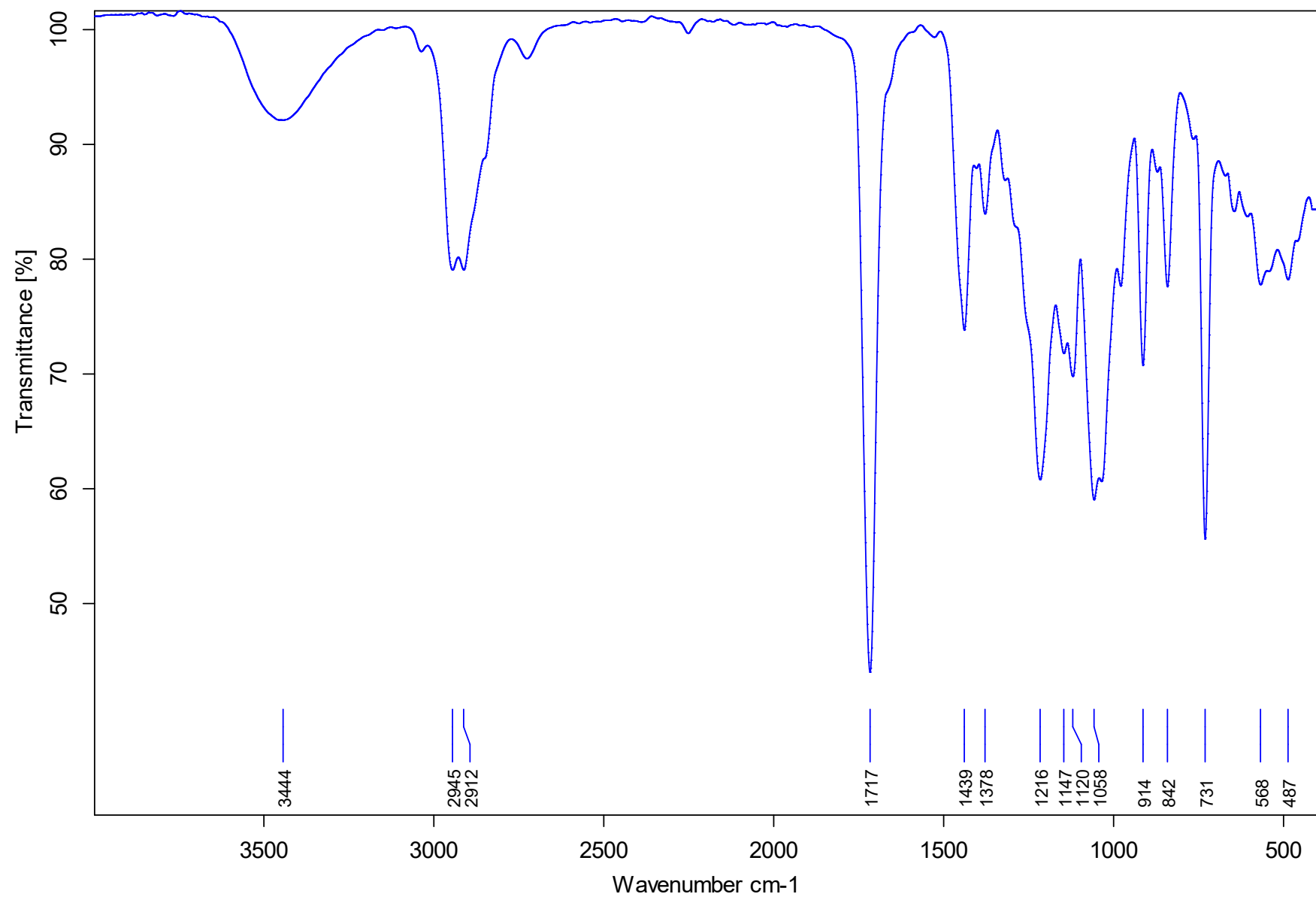




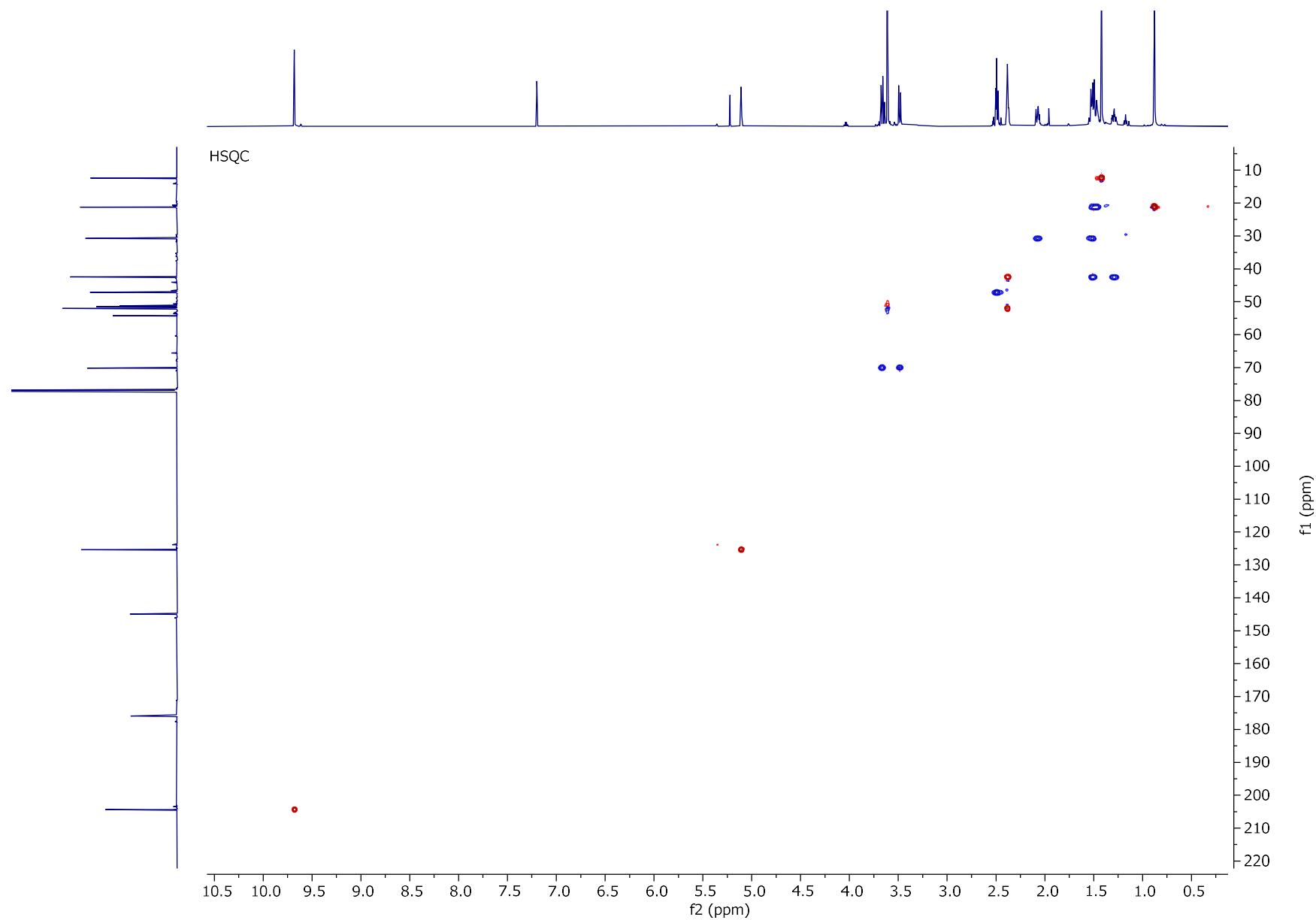
$^1\text{H}$  NMR, DEPT 135,  $^{13}\text{C}$  NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **23**

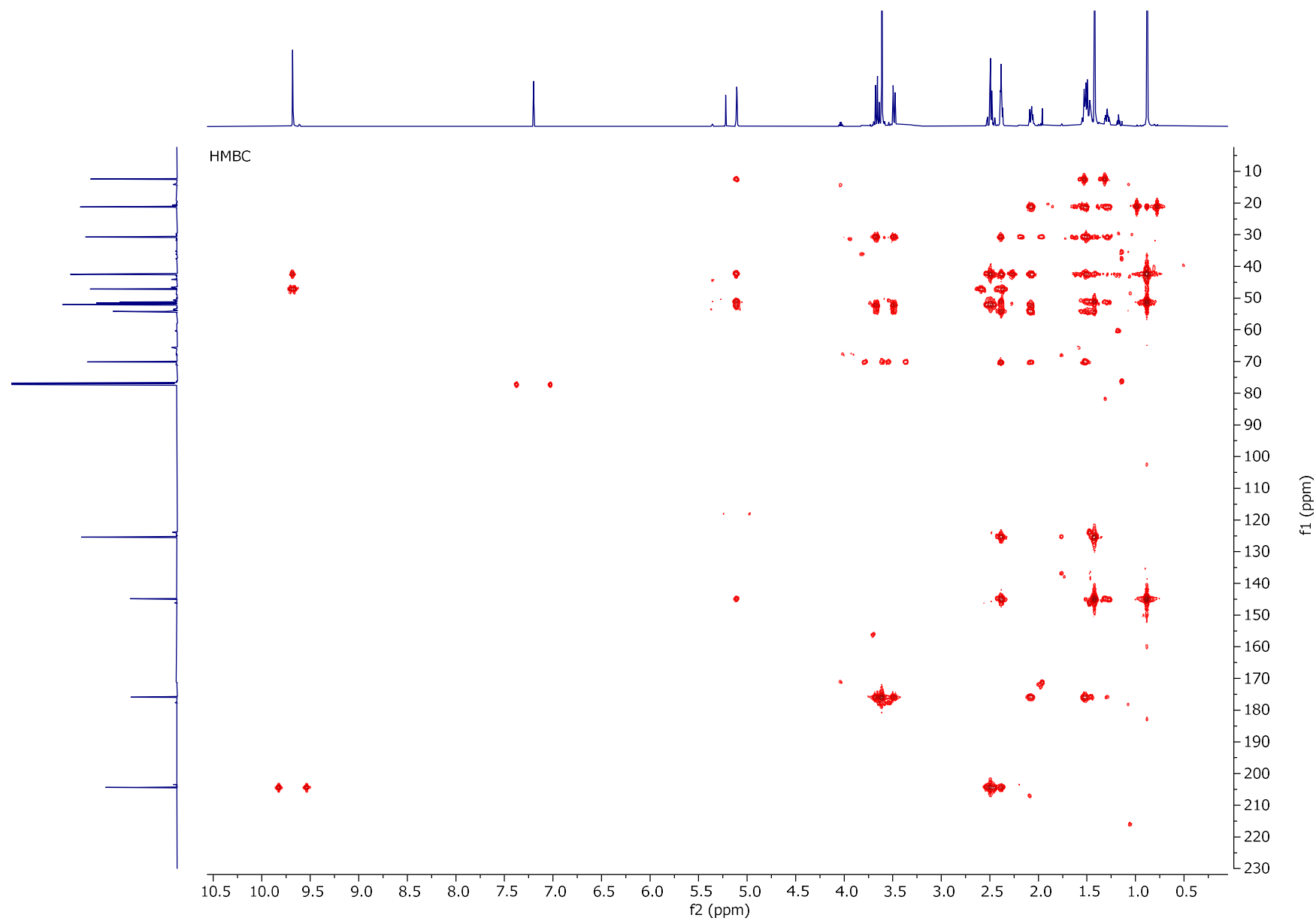


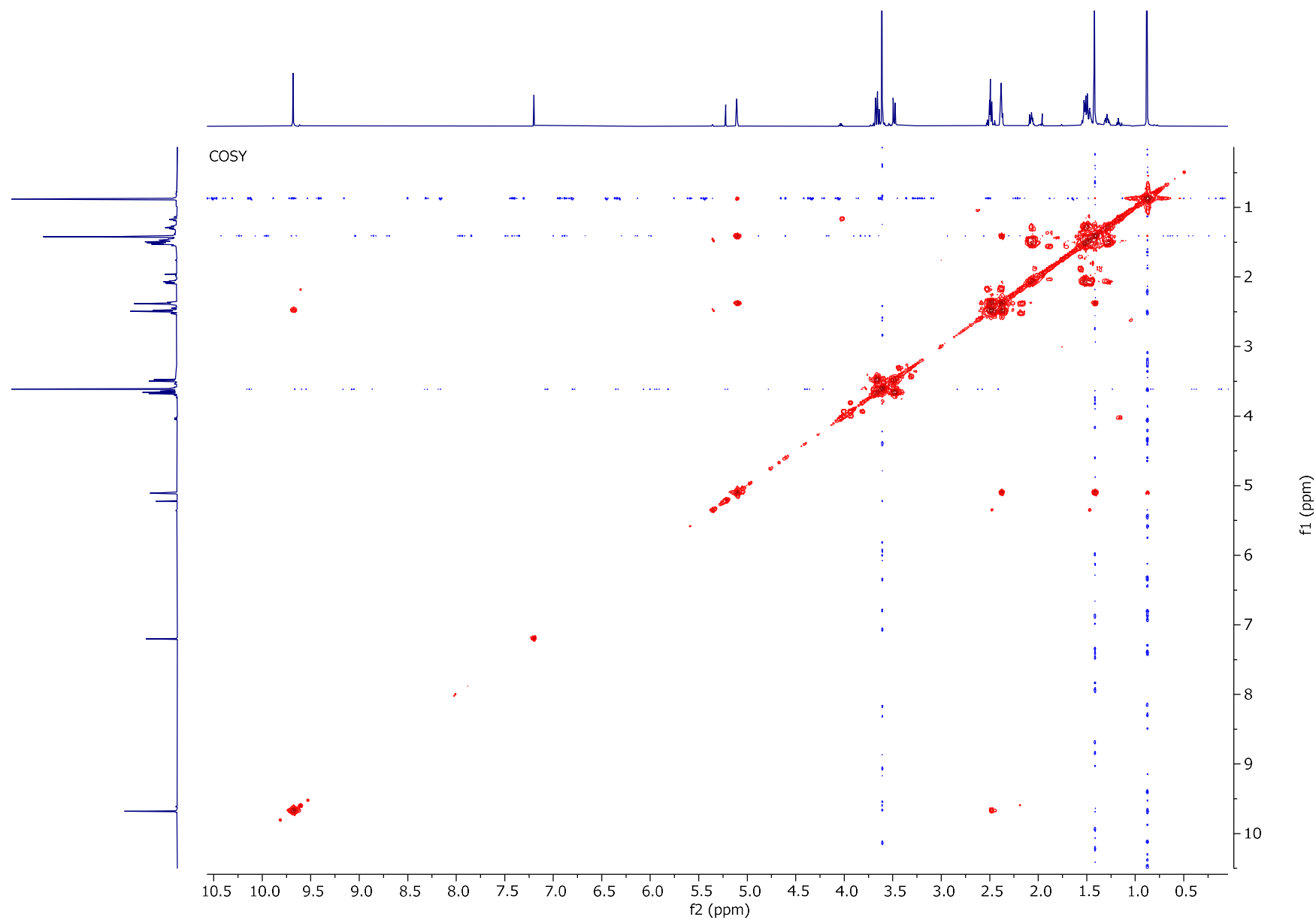


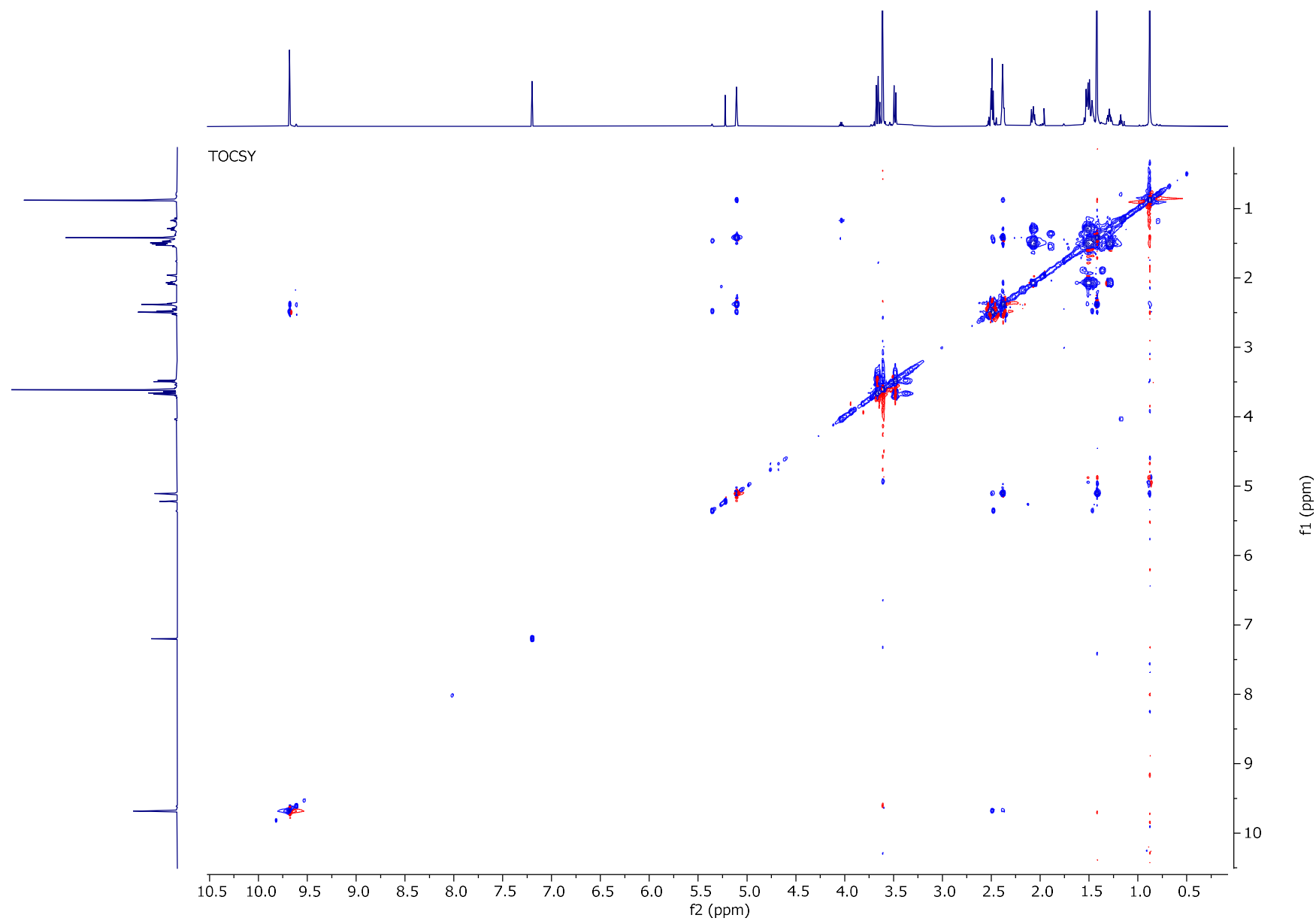


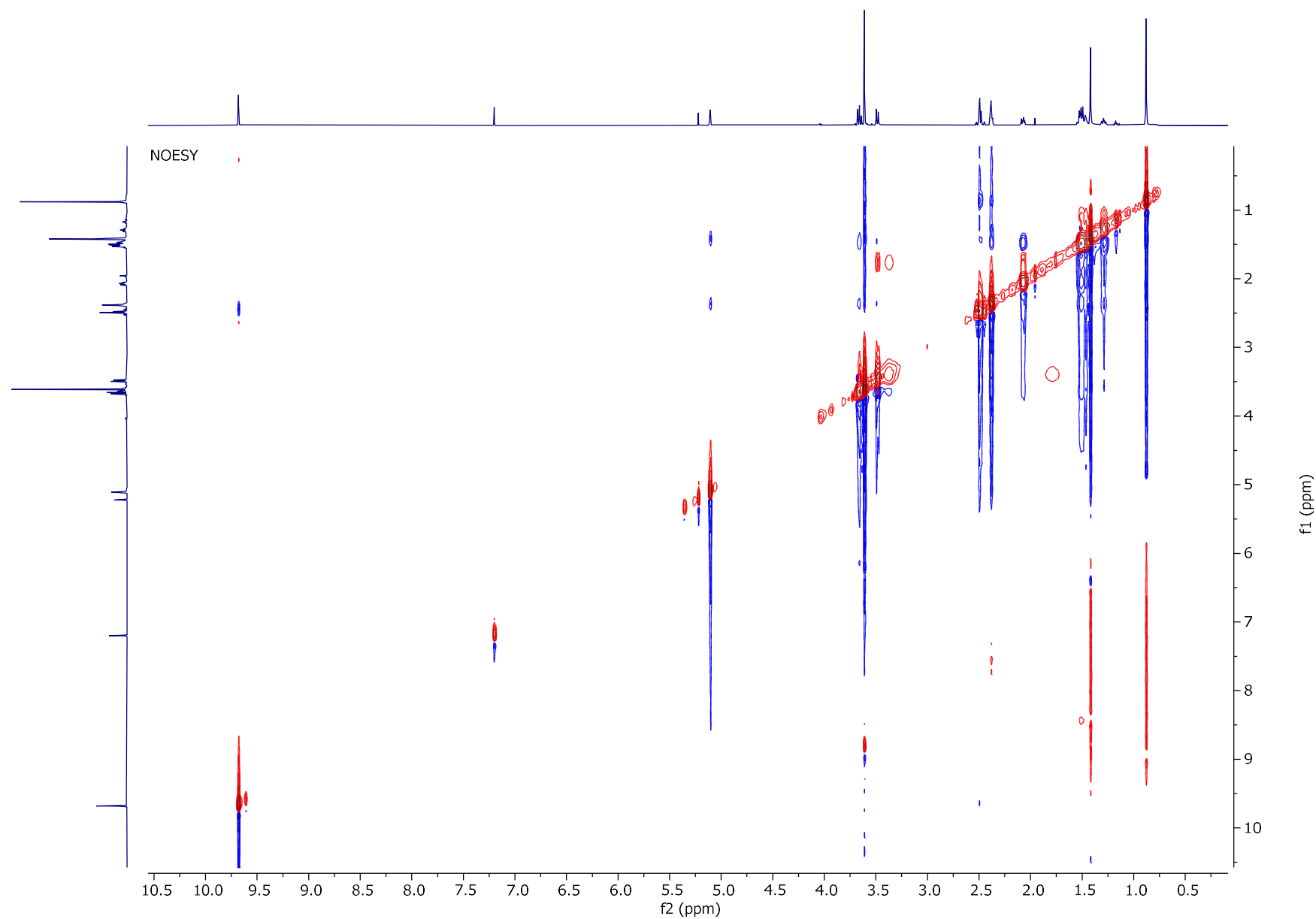


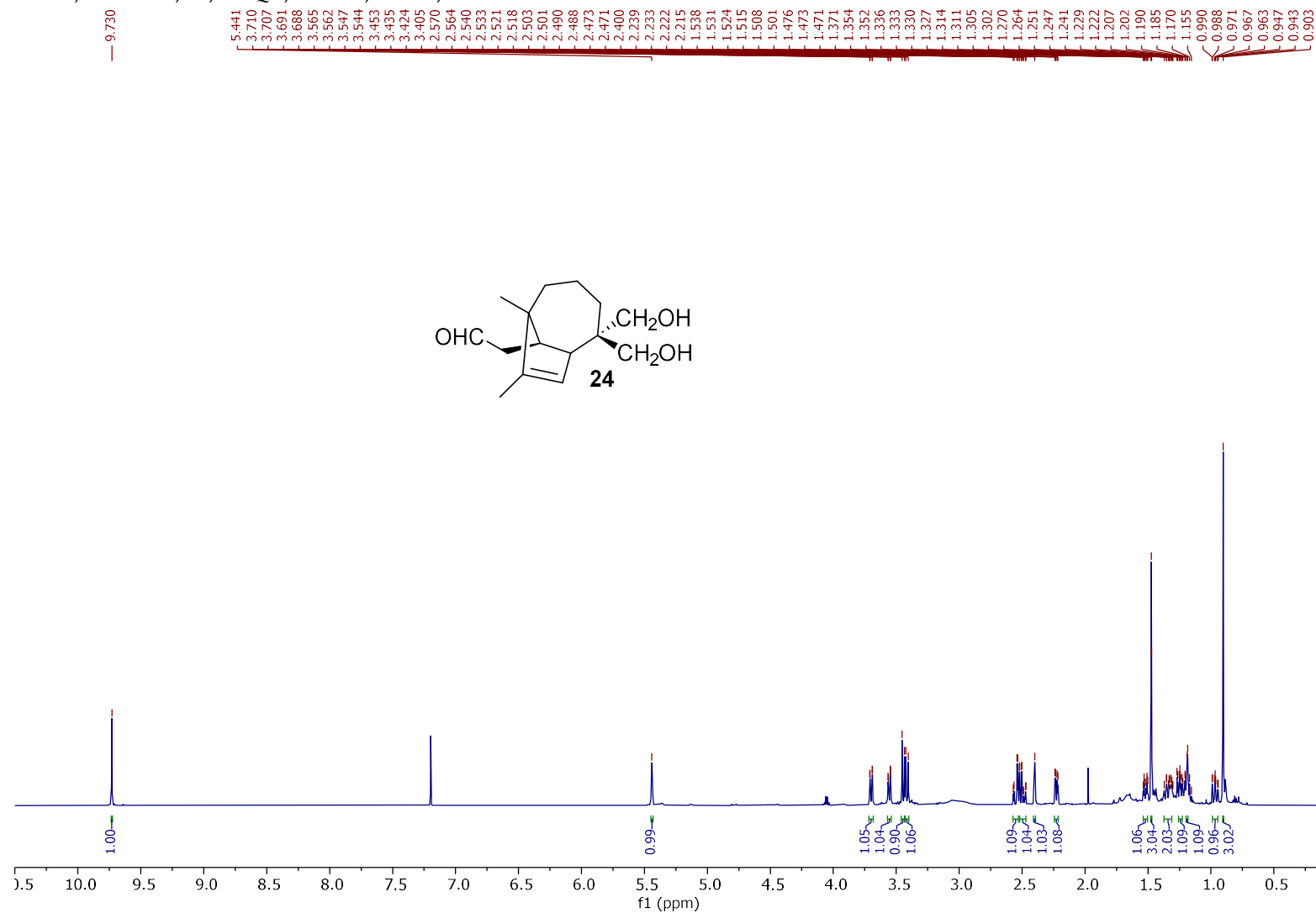


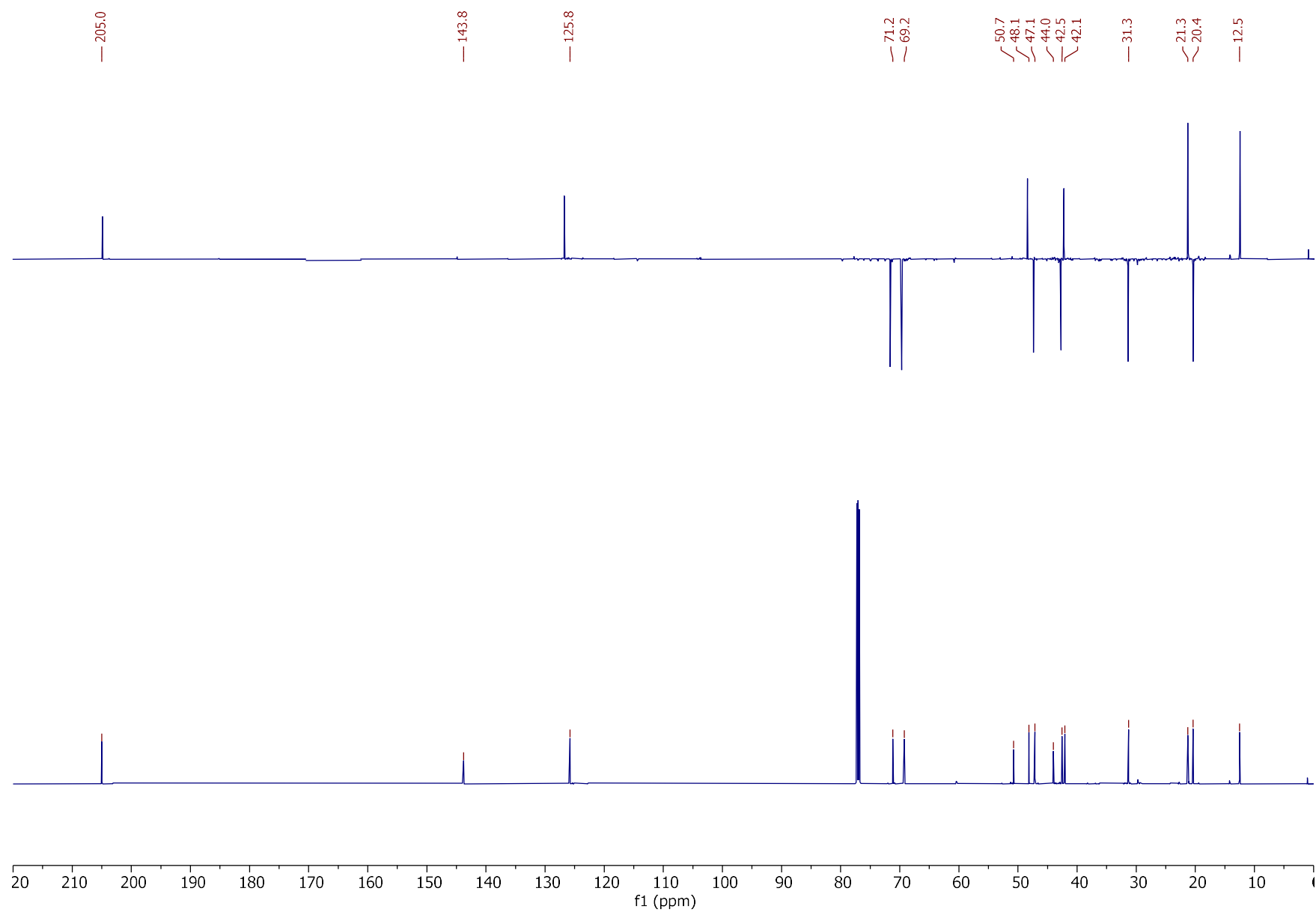


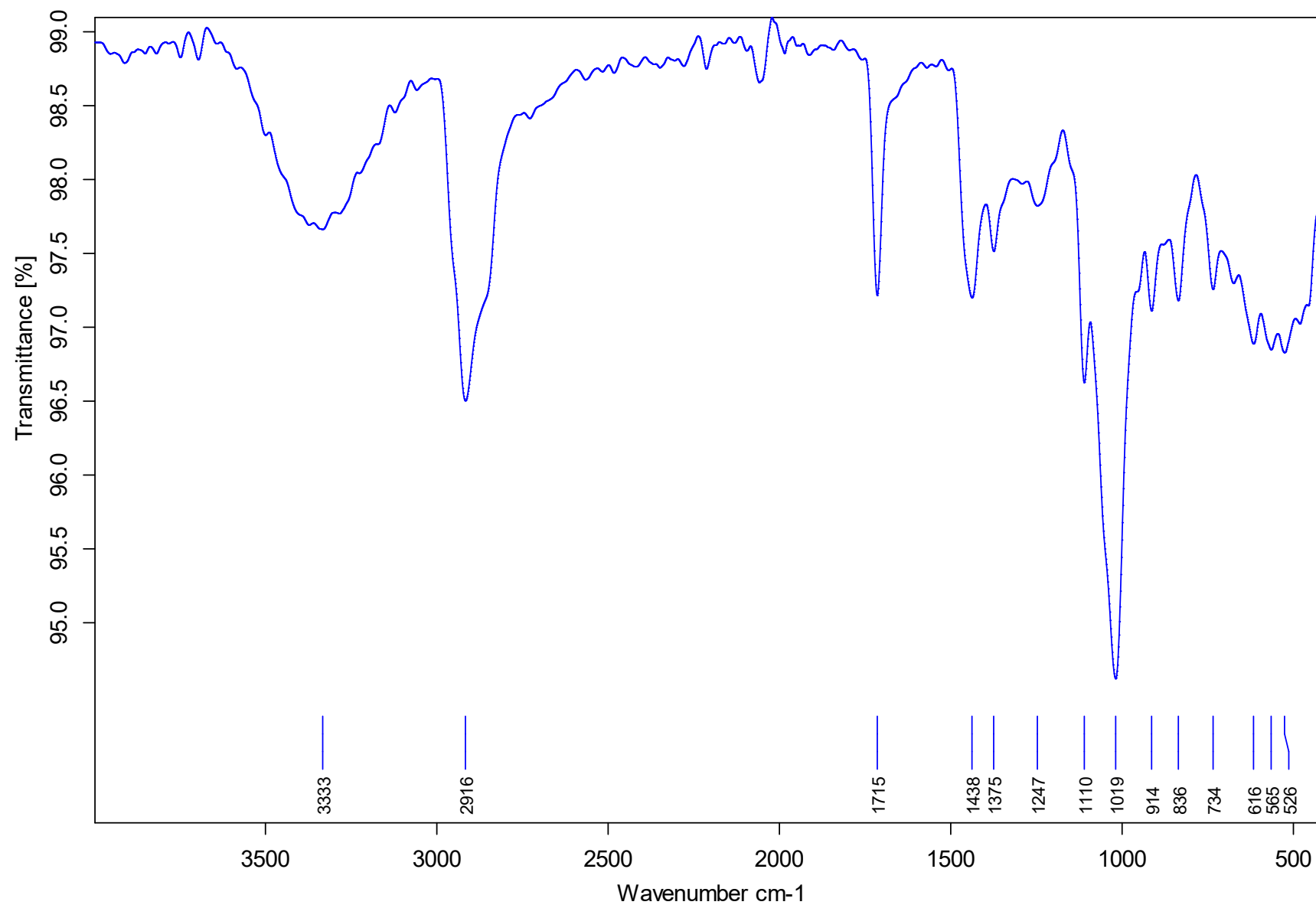




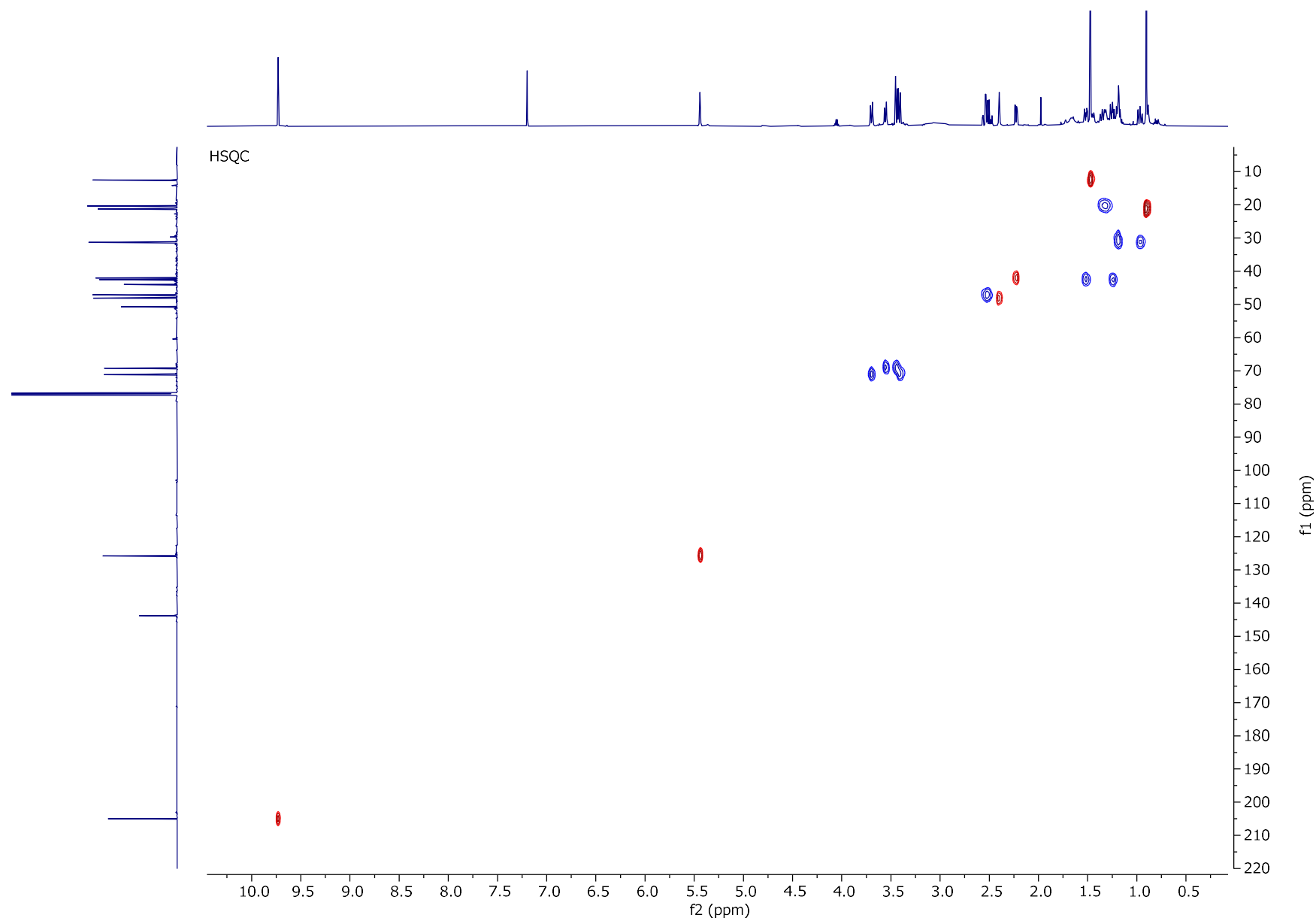


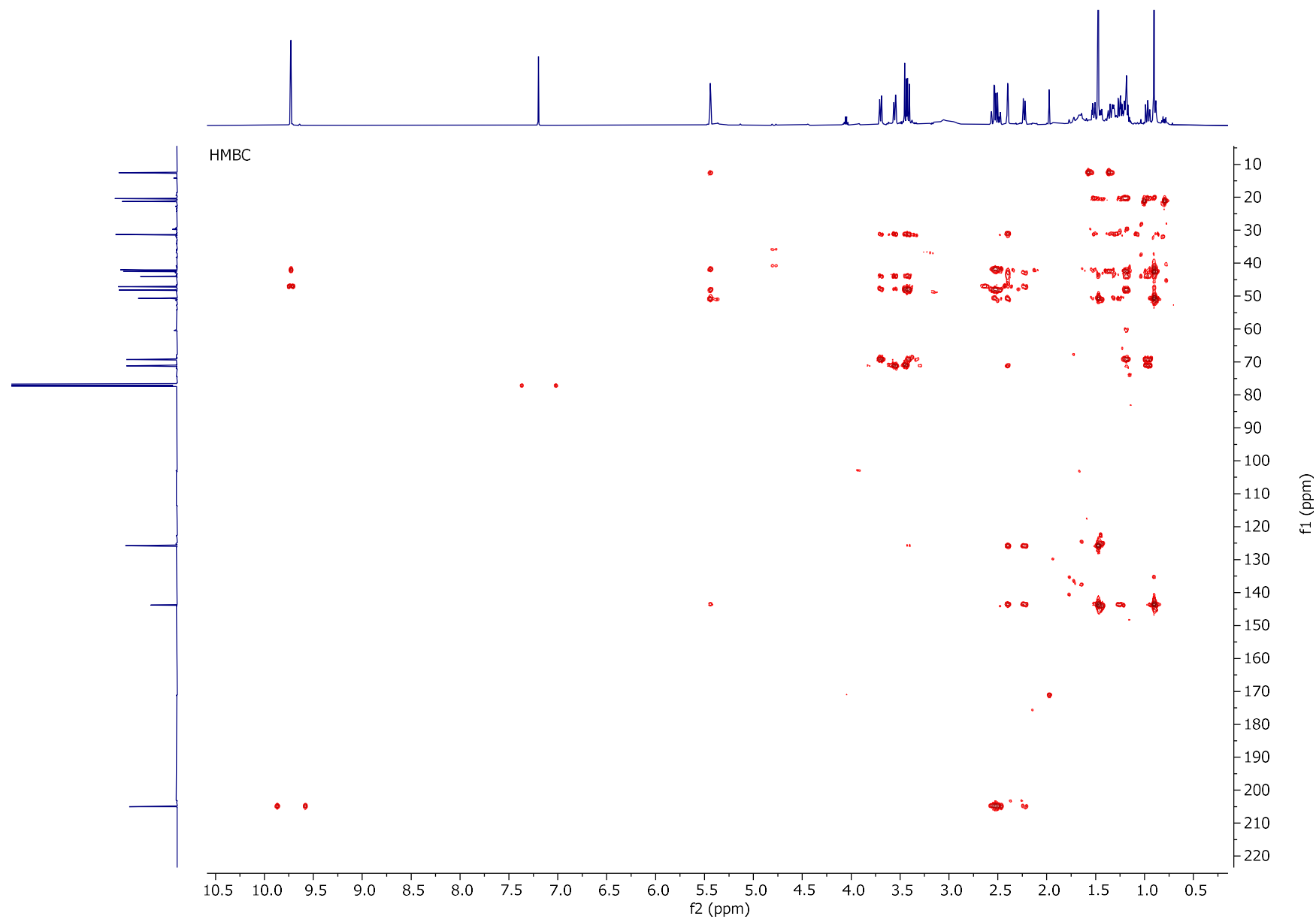
<sup>1</sup>H NMR, DEPT 135, <sup>13</sup>C NMR, IR, HSQC, HMBC, COSY, TOCSY and NOESY of **24**

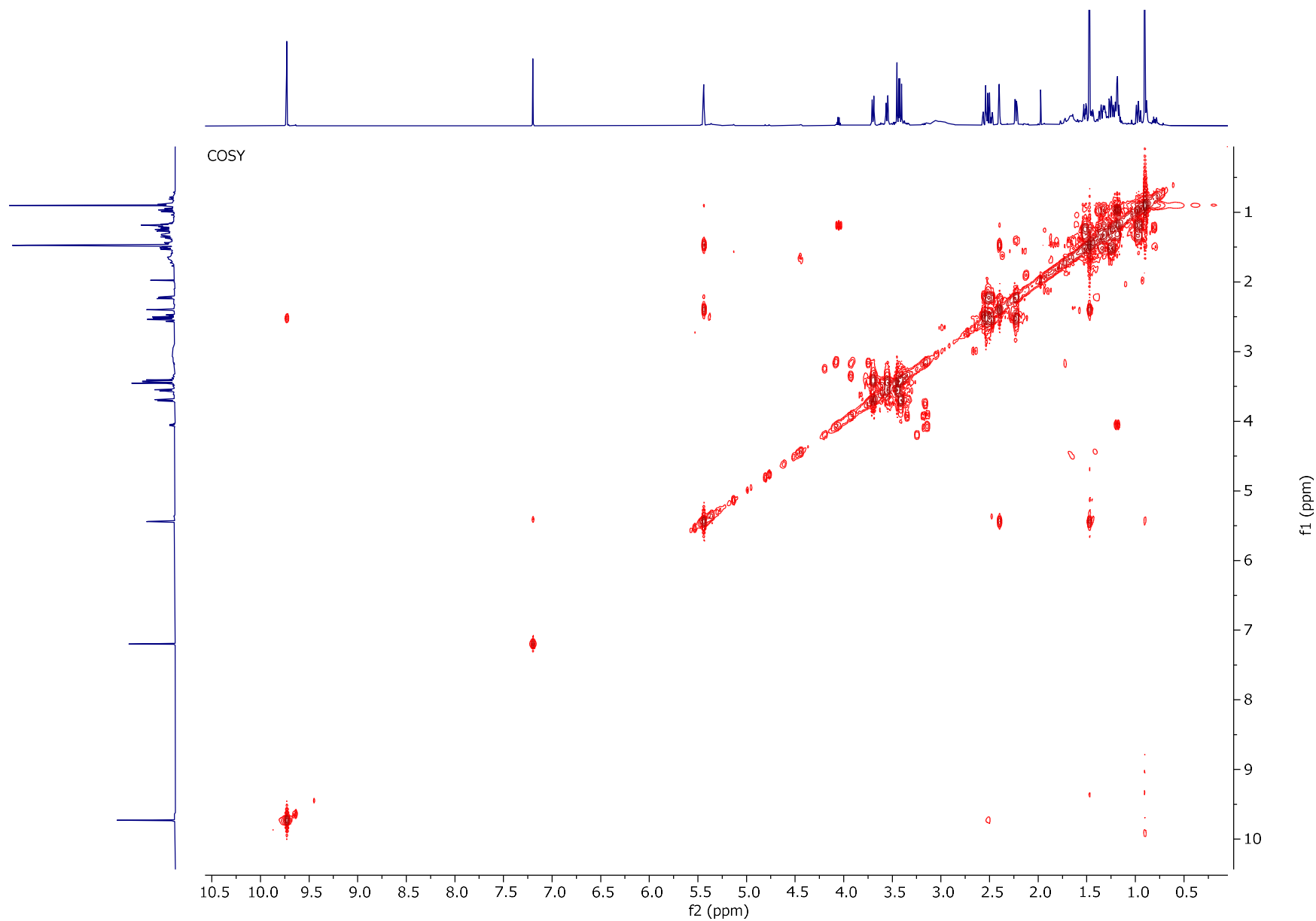


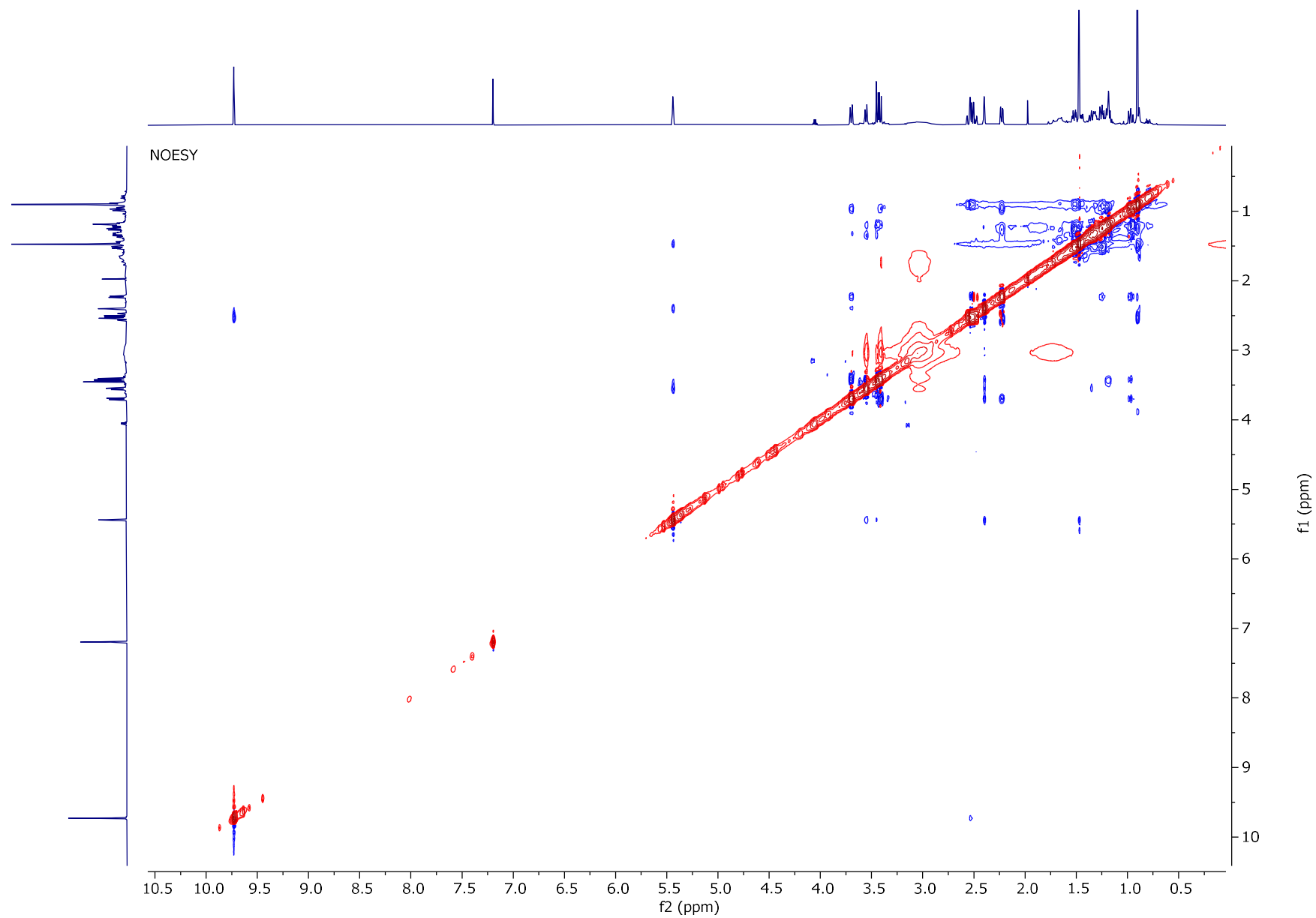












## CRYSTAL DATA AND STRUCTURE REFINEMENT FOR 13

**Table 1.** Crystal data and structure refinement for 13.

	<b>longibornane 13</b>
empirical formula	C <sub>15</sub> H <sub>22</sub> O <sub>3</sub>
molecular weight	250.32
temperatura (K)	155.70
crystal size (mm <sup>3</sup> )	0.372 × 0.231 × 0.07
crystal system	orthorhombic
space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
<i>a</i> (Å)	8.1459 (2)
<i>b</i> (Å)	12.0831 (4)
<i>c</i> (Å)	13.4903 (4)
$\alpha$ (deg)	90
$\beta$ (deg)	90
$\gamma$ (deg)	90
volume (Å <sup>3</sup> )	1327.82 (7)
<i>Z</i> , $\rho$ calculated (g/cm <sup>3</sup> )	4, 1.252
$\mu$ (mm <sup>−1</sup> )	0.685
<i>F</i> (000)	544.0
radiation	CuK $\alpha$ ( $\lambda$ = 1.54178)
2 $\Theta$ range for data collection (deg)	12.694 to 143.86
index ranges	−10 ≤ <i>h</i> ≤ 9, −14 ≤ <i>k</i> ≤ 14, −16 ≤ <i>l</i> ≤ 16
collected reflections	16026
independent reflections	2585 [ <i>R</i> <sub>int</sub> = 0.0402, <i>R</i> <sub>sigma</sub> = 0.0282]
data/restraints/parameters	2585/0/168
goodness-of-fit on <i>F</i> <sup>2</sup>	1.067
final <i>R</i> indexes [ <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0341, <i>wR</i> <sub>2</sub> = 0.0917
final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0349, <i>wR</i> <sub>2</sub> = 0.0927
largest diff. peak/hole (e Å <sup>−3</sup> )	0.17/−0.15
Flack parameters	0.09 (5)

**Table 2.** Fractional atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **13**.  $U_{eq}$  is defined as 1/3 of the trace of the orthogonalised  $U_{ij}$  tensor.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{eq}$
O3	7852(2)	7807.7(13)	4941.0(13)	60.0(4)
O1	7757.0(17)	5096.9(12)	4684.3(9)	42.7(3)
O2	10314.4(18)	5701.4(14)	4760.8(12)	55.9(4)
C13	6077(3)	3130.4(18)	7444.4(19)	59.1(6)
C2	6651(2)	4037.1(14)	6729.9(13)	37.6(4)
C1	6025(2)	5204.0(14)	7016.4(12)	34.3(4)
C7	6546(2)	5926.3(12)	6136.5(12)	31.9(3)
C6	8367(2)	6257.6(13)	6052.1(13)	34.0(4)
C14	8551(3)	7511.8(16)	5859.3(17)	47.6(5)
C8	6236(2)	5150.6(15)	5247.7(12)	35.4(4)
C15	8952(2)	5676.2(15)	5115.6(14)	38.5(4)
C9	5730(2)	4036.6(14)	5715.4(13)	38.7(4)
C12	5940(3)	3045.0(18)	5038(2)	60.9(6)
C3	8549(2)	3930.3(15)	6650.2(15)	42.6(4)
C4	9503(3)	4752.6(19)	7281.6(16)	50.4(5)
C5	9456(2)	5967.4(18)	6944.6(15)	45.8(4)
C11	4145(2)	5078.2(17)	6929.5(16)	45.7(4)
C10	3942(2)	4262.3(17)	6051.9(17)	48.1(5)

**Table 3.** Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **13**. The anisotropic displacement factor exponent takes the form:  
 $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$ .

Atom	U <sub>11</sub>	U <sub>22</sub>	U <sub>33</sub>	U <sub>23</sub>	U <sub>13</sub>	U <sub>12</sub>
O3	62.9(9)	48.5(9)	68.6(10)	17.9(8)	5.9(8)	7.1(7)
O1	46.5(7)	50.5(7)	31.0(6)	-5.2(6)	4.0(5)	-5.9(6)
O2	42.4(8)	66.6(9)	58.5(9)	-2.0(8)	16.4(6)	-3.2(7)
C13	73.5(15)	45.1(10)	58.7(12)	16.5(9)	10.7(12)	-4.2(11)
C2	44.2(9)	31.6(8)	37.1(9)	2.8(7)	3.7(8)	1.5(7)
C1	35.1(8)	35.9(8)	32.0(7)	-3.4(6)	4.5(6)	-2.0(7)
C7	32.1(8)	28.1(7)	35.4(8)	-1.7(6)	-0.3(7)	1.4(6)
C6	32.3(8)	32.9(8)	36.8(8)	-1.5(6)	-0.5(7)	-1.2(6)
C14	44.8(10)	35.6(9)	62.4(12)	-0.7(8)	3.3(9)	-7.2(8)
C8	34.8(8)	39.1(8)	32.4(8)	-0.7(7)	-3.6(6)	-1.4(7)
C15	37.7(9)	40.1(8)	37.6(8)	4.6(7)	5.2(7)	0.4(7)
C9	43.0(9)	32.5(8)	40.5(9)	-6.9(7)	0.4(8)	-4.2(7)
C12	73.0(14)	45.2(10)	64.5(13)	-23.5(10)	3.3(12)	-9.2(10)
C3	45.9(10)	37.9(8)	44.1(9)	6.9(7)	1.0(9)	12.6(8)
C4	41.4(10)	65.2(13)	44.7(10)	9.7(9)	-10.8(8)	7.1(9)
C5	38.3(9)	55.4(11)	43.8(10)	-3.2(8)	-8.1(8)	-3.9(8)
C11	34.9(9)	44.3(9)	57.8(11)	-7.2(8)	10.4(8)	-4.8(8)
C10	37.0(9)	45.8(10)	61.6(12)	-6.9(9)	0.0(9)	-9.9(8)

**Table 4.** Bond lengths for **13**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O3	C14	1.410(3)	C7	C8	1.543(2)
O1	C8	1.455(2)	C6	C14	1.545(2)
O1	C15	1.332(2)	C6	C15	1.522(2)
O2	C15	1.209(2)	C6	C5	1.536(3)
C13	C2	1.532(3)	C8	C9	1.543(2)
C2	C1	1.548(2)	C9	C12	1.516(3)
C2	C9	1.560(3)	C9	C10	1.550(3)
C2	C3	1.556(3)	C3	C4	1.522(3)
C1	C7	1.533(2)	C4	C5	1.537(3)
C1	C11	1.544(2)	C11	C10	1.550(3)
C7	C6	1.540(2)			

**Table 5.** Bond angles for **13**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C15	O1	C8	111.73(13)	O3	C14	C6	110.95(16)
C13	C2	C1	113.19(16)	O1	C8	C7	107.09(13)
C13	C2	C9	113.90(17)	O1	C8	C9	113.72(15)
C13	C2	C3	106.70(16)	C7	C8	C9	104.83(13)
C1	C2	C9	93.50(13)	O1	C15	C6	112.10(14)
C1	C2	C3	114.83(15)	O2	C15	O1	120.72(17)
C3	C2	C9	114.64(15)	O2	C15	C6	127.18(18)
C7	C1	C2	103.53(13)	C8	C9	C2	103.30(13)
C7	C1	C11	105.79(15)	C8	C9	C10	102.56(15)
C11	C1	C2	102.59(14)	C12	C9	C2	118.32(18)
C1	C7	C6	118.16(14)	C12	C9	C8	114.40(17)
C1	C7	C8	102.16(12)	C12	C9	C10	114.90(17)
C6	C7	C8	104.95(13)	C10	C9	C2	101.23(15)
C7	C6	C14	111.16(14)	C4	C3	C2	114.50(16)
C15	C6	C7	104.05(14)	C3	C4	C5	116.44(16)
C15	C6	C14	106.41(15)	C6	C5	C4	117.65(16)
C15	C6	C5	111.36(15)	C1	C11	C10	103.10(15)
C5	C6	C7	116.04(15)	C11	C10	C9	103.60(15)
C5	C6	C14	107.43(15)				



**Table 6.** Torsion angles for **13**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C8	C9	C2	87.22(16)	C7	C8	C9	C10	75.50(16)
O1	C8	C9	C12	-42.8(2)	C6	C7	C8	O1	-2.43(17)
O1	C8	C9	C10	-167.86(14)	C6	C7	C8	C9	118.68(14)
C13	C2	C1	C7	-172.64(17)	C14	C6	C15	O1	-117.21(17)
C13	C2	C1	C11	-62.7(2)	C14	C6	C15	O2	62.6(2)
C13	C2	C9	C8	167.74(16)	C14	C6	C5	C4	-179.36(18)
C13	C2	C9	C12	-64.7(2)	C8	O1	C15	O2	178.19(17)
C13	C2	C9	C10	61.79(19)	C8	O1	C15	C6	-1.9(2)
C13	C2	C3	C4	-99.99(19)	C8	C7	C6	C14	115.50(16)
C2	C1	C7	C6	-75.89(17)	C8	C7	C6	C15	1.34(16)
C2	C1	C7	C8	38.61(16)	C8	C7	C6	C5	-121.36(16)
C2	C1	C11	C10	-34.40(19)	C8	C9	C10	C11	-70.14(18)
C2	C9	C10	C11	36.39(19)	C15	O1	C8	C7	2.78(19)
C2	C3	C4	C5	-70.8(2)	C15	O1	C8	C9	-112.53(16)
C1	C2	C9	C8	50.44(15)	C15	C6	C14	O3	49.1(2)
C1	C2	C9	C12	178.01(18)	C15	C6	C5	C4	-63.2(2)
C1	C2	C9	C10	-55.51(15)	C9	C2	C1	C7	-54.75(15)
C1	C2	C3	C4	26.3(2)	C9	C2	C1	C11	55.16(16)
C1	C7	C6	C14	-131.54(16)	C9	C2	C3	C4	132.93(17)
C1	C7	C6	C15	114.31(16)	C12	C9	C10	C11	165.10(18)
C1	C7	C6	C5	-8.4(2)	C3	C2	C1	C7	64.50(18)
C1	C7	C8	O1	-126.29(14)	C3	C2	C1	C11	174.41(15)
C1	C7	C8	C9	-5.18(17)	C3	C2	C9	C8	-68.97(18)
C1	C11	C10	C9	-1.5(2)	C3	C2	C9	C12	58.6(2)
C7	C1	C11	C10	73.80(18)	C3	C2	C9	C10	-174.91(14)
C7	C6	C14	O3	-63.6(2)	C3	C4	C5	C6	4.1(3)
C7	C6	C15	O1	0.28(19)	C5	C6	C14	O3	168.43(17)
C7	C6	C15	O2	-179.87(19)	C5	C6	C15	O1	126.00(16)
C7	C6	C5	C4	55.6(2)	C5	C6	C15	O2	-54.1(3)
C7	C8	C9	C2	-29.42(17)	C11	C1	C7	C6	176.60(14)
C7	C8	C9	C12	-159.41(18)	C11	C1	C7	C8	-68.91(16)

**Table 7.** Hydrogen atom coordinates ( $\text{\AA} \times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **13**.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
H3	7050(50)	8260(30)	5020(30)	90
H13A	4894.6	3205.67	7559.79	89
H13B	6664.12	3203.2	8075.14	89
H13C	6305.84	2402.55	7155.25	89
H1	6415.2	5474.37	7676.18	41
H7	5829.39	6596.01	6090.08	38
H14A	8003.75	7929.53	6397.19	57
H14B	9729.74	7711.64	5862.02	57
H8	5328.62	5446.3	4824.77	43
H12A	5290.3	3154.09	4434.9	91
H12B	5563.87	2375.82	5380.44	91
H12C	7100.98	2964.05	4862.55	91
H3A	8868.63	3171.31	6848.24	51
H3B	8871.49	4030.96	5948.44	51
H4A	10664.39	4512.29	7302.19	61
H4B	9073.36	4714.55	7967.27	61
H5A	9089.9	6421.5	7513.94	55
H5B	10593.47	6195.88	6785.72	55
H11A	3615.5	5797.59	6784.12	55
H11B	3670.37	4769.69	7546.08	55
H10A	3291.54	4599.6	5510.38	58
H10B	3397.21	3570.86	6268.69	58

## Refinement model description

Number of restraints - 0, number of constraints - unknown.

## Details:

## 1. Fixed Uiso

At 1.2 times of:

All C(H) groups, All C(H,H) groups

At 1.5 times of:

All C(H,H,H) groups, All O(H) groups

## 2.a Ternary CH refined with riding coordinates:

C3(H3), C4(H4), C7(H7)

## 2.b Secondary CH2 refined with riding coordinates:

C6(H6A,H6B), C11(H11A,H11B), C12(H12A,H12B), C13(H13A,H13B), C14(H14A,H14B),  
C15(H15A,H15B)

## 2.c Idealised Me refined as rotating group:

C1(H1A,H1B,H1C), C10(H10A,H10B,H10C)

