SUPPORTING INFORMATION

An Iridoid Glucoside and the Related Aglycones from *Cornus florida*

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Table of Contents:

Extraction and Purification Procedures.

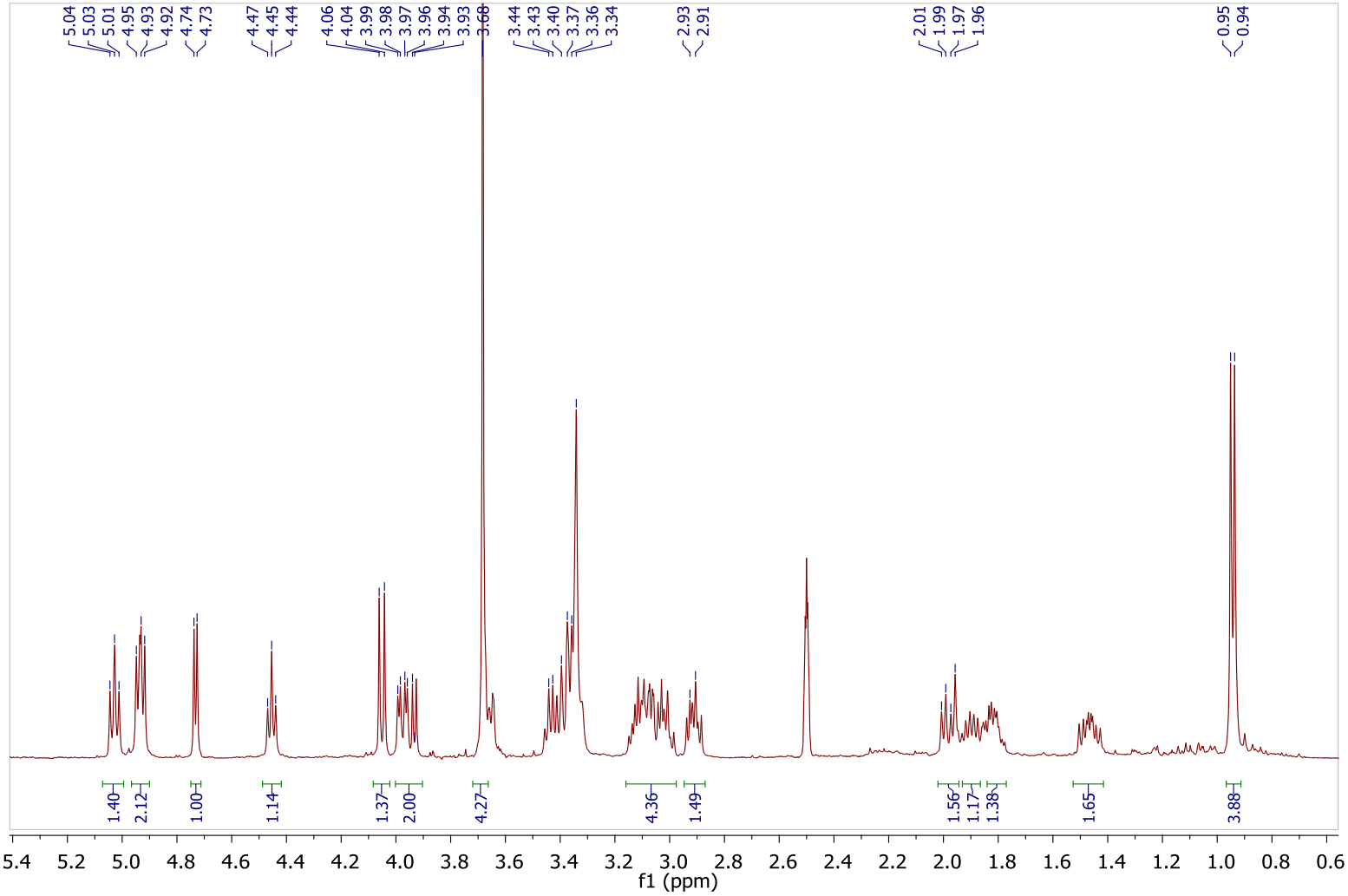
The leaves of *C. florida* (15.0 kg, dry weight) were extracted with 90% ethanol, and dried in *vacuo* to give a crude extract (900 g). A portion if this crude extract (400 g) was separated on a silica gel column (20 x 70 cm) using a stepwise gradient of hexanes/EtOAc (100:0, 80:20, 50:50 and 100:0, v/v, each 3 L) and EtOAc/CH_3OH mixtures (80:20, 60:40, 50:50 and 0:100, v/v, each 3 L) to afford eight fractions (Fr. A – Fr. H). Fraction E (220 g) was then chromatographed on an HP-20 column (8 x 50 cm) using a stepwise gradient of acetone/water (10:90, 20:80, 50:50, 60:40, 80:20 and 100:0, v/v, each 2 L) to give six sub-fractions (Fr. E_1– E_6). Fraction E_2 (40 g) was chromatographed on a preparative C_{18} reversed-phase MPLC column (20 x 250 mm; 20–35% CH_3OH/H_2O over 40 min, 35–65% CH_3OH/H_2O over 20 min; flow rate: 12 mL/min) to afford eight sub-fractions (Fr. E_{2a}–E_{2h}). Fraction E_{2d} (4.0 g) was further chromatographed on a preparative C_{18} reversed-phase HPLC (Shim-park RP-C_{18} column; 5 μm; 20 x 250 mm; 8–45% CH_3CN/H_2O over 120 min, 7 mL/min) to yield eight sub-fractions (Fr. E_{2d-1} to Fr. E_{2d-8}). Fraction F_{2d-1} and Fraction E_{2d-2} were combined and chromatographed on a preparative C_{18} reversed-phase HPLC (Shim-park RP-C_{18} column; 5 μm; 20 x 250 mm; 5–35% CH_3CN/H_2O over 50 min, 35–100% CH_3OH/H_2O over 10 min, 7 mL/min) to give cornin (9.7 mg, t_R 31.6 min), dihydrocornin (2.0 mg, t_R 34.4 min). Fraction E_{2d-3} (30.0 mg) was chromatographed by preparative C_{18} reversed-phase HPLC (Shim-park RP-C_{18} column; 5 μm; 20 x 250 mm; 15–45% CH_3OH/H_2O over 50 min, 7 mL/min) to give hastatoside (3.5 mg, t_R 34.3 min). Sub-fraction E_{2d-4} (50 mg) was purified by C_8 reversed phase HPLC (Polar-C_8; 5 μm; 20 x 250 mm; 15–45% CH_3OH/H_2O over 130 min, 5 mL/min) to yield cornusoside A (**1**, 5.0 mg, t_R 76.2 min) and cornalternoside (10.2 mg, t_R 80.4 min). Then, Fraction E_{2d-6} (832 mg) was subjected to silica gel column (6 × 70 cm) chromatography using CH_2Cl_2-MeOH (90:10 to 0:100, v/v, each 500 mL) to

afford nine fractions (Fr. $E_{2d\text{-}6\text{-}a}$ to Fr. $E_{2d\text{-}6\text{-}h}$). Fraction $F_{2d\text{-}6\text{-}a}$ (320 mg) was purified by C_8 reversed-phase HPLC (Polar-C_8; 5 μm; 20 x 250 mm; 20–65% CH_3OH/H_2O over 70 min, 5 mL/min) to yield two fractions. The first fraction (60 mg) was purified was purified on a polymeric HPLC column (Hamilton PRP-1; 5 μm; 20 x 250 mm; 10–40% CH_3CN/H_2O over 50 min, 7 mL/min) to yield cornolactone C (**4**, 8.0 mg, t_R 41.5 min). The second fraction (40 mg) was purified on a polymeric HPLC column (Hamilton PRP-1; 5 μm; 20 x 250 mm; 15–45% CH_3CN in H_2O for 70 min, 7 mL/min) to yield cornolactone B (**3**, 4.0 mg, t_R 37.9 min).

The remaining crude extract (500 g) was loaded on to a silica gel column (20 x 70 cm) and eluted using a stepwise gradient of hexanes/EtOAc (100:0, 80:20, 50:50 and 0:100, v/v, each 4 L) and EtOAc/CH_3OH mixtures (80:20, 60:40, 50:50 and 0:100, v/v, each 4 L) to afford eight fractions. Fraction E (320 g) was then fractionated on a HP-20 column (20 x 70 cm) with a stepwise gradient of acetone/water (5:95, 10:90, 15:85, 20:80, 30:70, 40:60, 50:50, 60:40, 80:20 and 100:0, v/v, each 3 L) to give ten sub-fractions (Fr. E_1 to Fr. E_{10}). Fraction E_2 and Fraction E_3 were combined (50 g) and chromatographed on a polymeric HP-20SS column (10 × 60 cm) using a stepwise gradient elution of acetone/water (5:95, 10:90, 15:85, 20:80, 25:75, 30:70, 40:60, 60:40, 80:20 and 100:0, v/v, each 1 L) to give ten sub-fractions (Fr. E_{3a} to Fr. E_{3j}). Fraction E_{3e} (120 mg) was then chromatographed on a silica gel column (6 x 60 cm) using a stepwise gradient from 10% MeOH in CH_2Cl_2 to 100% MeOH to yield 3,3′-dimethyl-4-*O*-β-D-glucopyranosyl ellagic acid (3.0 mg) and 3,4,3′-trimethyl-4-*O*-β-D-glucopyranosyl ellagic acid (2.5 mg). Fraction E_{3b} (9.9 g) was fractionated on a reversed phase C_{18} column (4 × 60 cm) using a stepwise gradient of MeOH/H_2O (5:95, 10:90, 15:85, 20:80, 30:70, 40:60, 50:50, 60:40, 80:20 and 100:0, v/v, each 500 mL) to afford ten fractions (Fr. $E_{3b\text{-}A}$ to Fr. $E_{3b\text{-}I}$). The first two fractions were combined (Fr. $E_{3b\text{-}A+B}$, 1.2 g) and chromatographed on a Sephadex LH-20 column (4 x 60

cm) using methanol to afford four sub-fractions (Fr. $E_{3b\text{-}A+B\text{-}1}$ to Fr. $E_{3b\text{-}A+B\text{-}4}$). Fraction $E_{3b\text{-}A+B\text{-}2}$ (960 mg) was separated by preparative reversed-phase C_{18} HPLC (Shim-park RP-C_{18} column; 5 μm; 20 x 250 mm; 5–50% CH_3CN/H_2O over 50 min, 50–100% over 10 min, 7 mL/min) to yield five fractions (Fr. $E_{3b\text{-}A+B\text{-}2\text{-}a}$ to Fr. $E_{3b\text{-}A+B\text{-}2\text{-}e}$) with t_R at 33.9, 36.0, 36.8, 38.7 and 39.6 min, respectively. Fraction $E_{3b\text{-}A+B\text{-}2\text{-}a}$ (97.5 mg) was separated on reversed-phase C_{18} HPLC (Shim-park RP-C_{18} column; 5 μm; 20 x 250 mm; 5–40% CH_3CN/H_2O over 70 min, 50–100% CH_3CN/H_2O over 10 min, 7 mL/min) to yield cornolactone D (**5**, 12 mg, t_R 51.5 min). Fraction $E_{3b\text{-}A+B\text{-}2\text{-}b}$ (71.4 mg) was purified on reversed-phase C_8 HPLC column (Polar-C_8, 5 μm; 20 x 250 mm; 10–40% CH_3CN/H_2O over 70 min, 50–100% over 10 min, 7 mL/min) to yield alternoside **A** (5.0 mg, t_R 11.8 min). Fraction $E_{3b\text{-}A+B\text{-}2\text{-}c}$ (51.0 mg) was also purified using reversed-phase C_8 HPLC (Polar-C_8, 5 μm; 20 x 250 mm; 20–60% CH_3OH/H_2O over 70 min, 7 mL/min) to yield cornolactone A (**2**, 15.0 mg, t_R 51.1 min) and lauroside A (5.6 mg, t_R 63.8 min). Additionally, Fraction $E_{3b\text{-}A+B\text{-}2\text{-}d}$ (632 mg) was also purified using reversed-phase C_8 HPLC (Polar-C_8, 5 μm; 20 x 250 mm; 10–20% CH_3OH/H_2O over 70 min, 5 mL/min) to obtain cornusoside A (**1**, 60.0 mg, t_R 44.0 min) and (5*S**,6*R**)-9-hydroxymegastigm-7-en-3-one (20.0 mg, t_R 55.1 min). Finally Fraction E_3 (20 g) was fractionated on a silica gel column (5 × 60 cm) and eluted using a stepwise gradient of CH_2Cl_2/MeOH (90:10 to 0:100, v/v, each 500 mL) to afford nine fractions (Fr. $E_{3\text{-}a}$ to Fr. $E_{3\text{-}h}$). The sub-fraction $E_{3\text{-}b}$ (30 mg) was further purified by reversed-phase C_8 HPLC (Polar-C_8; 5 μm; 10 x 250 mm; 10–65% CH_3CN/H_2O over 70 min, 5 mL/min) to yield isoquercitrin (5.2 mg, t_R 60.6 min).

^{1}H NMR Spectrum of Cornusoside A (**1**) (DMSO-d_6, 400 MHz)



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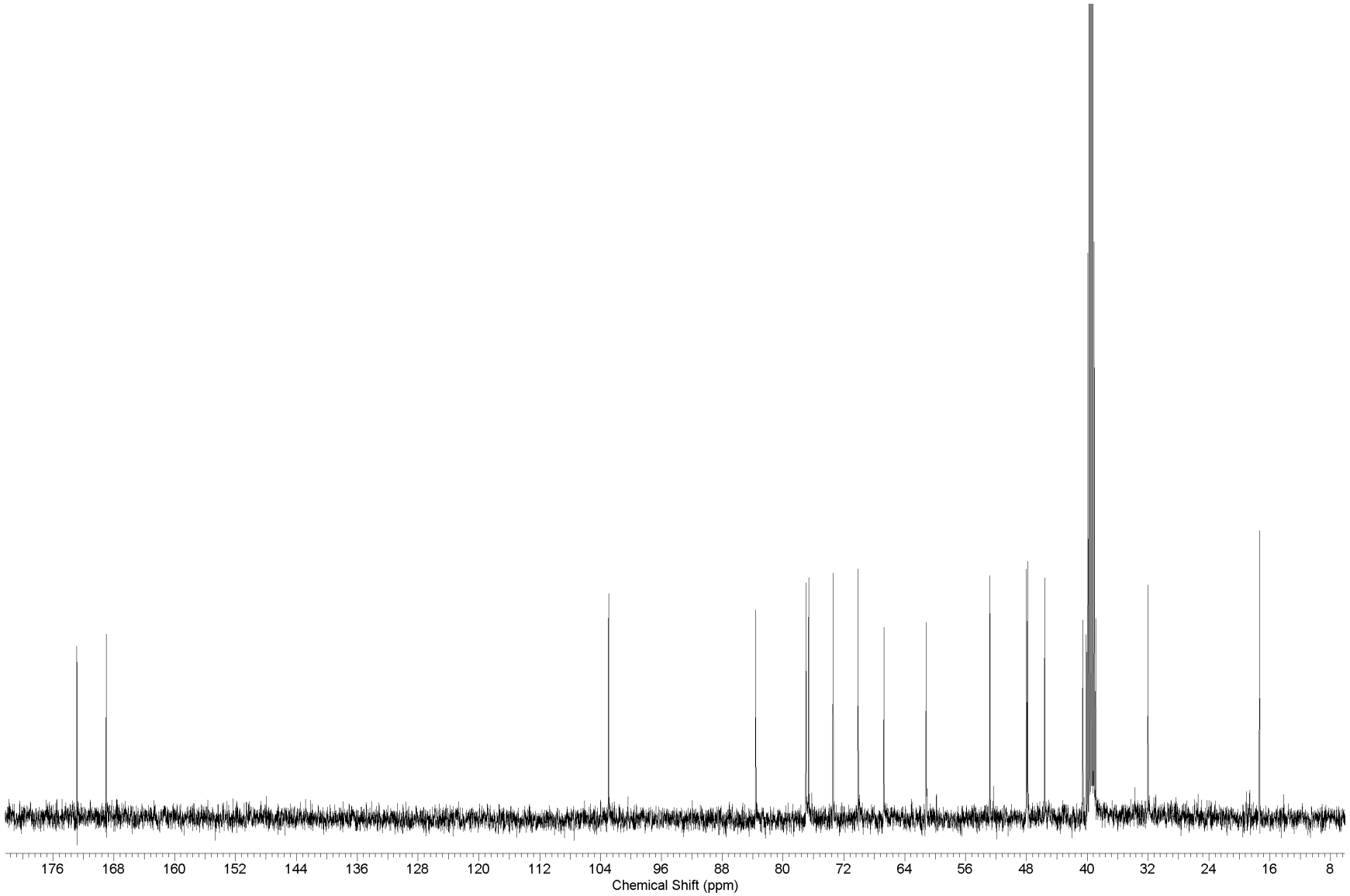

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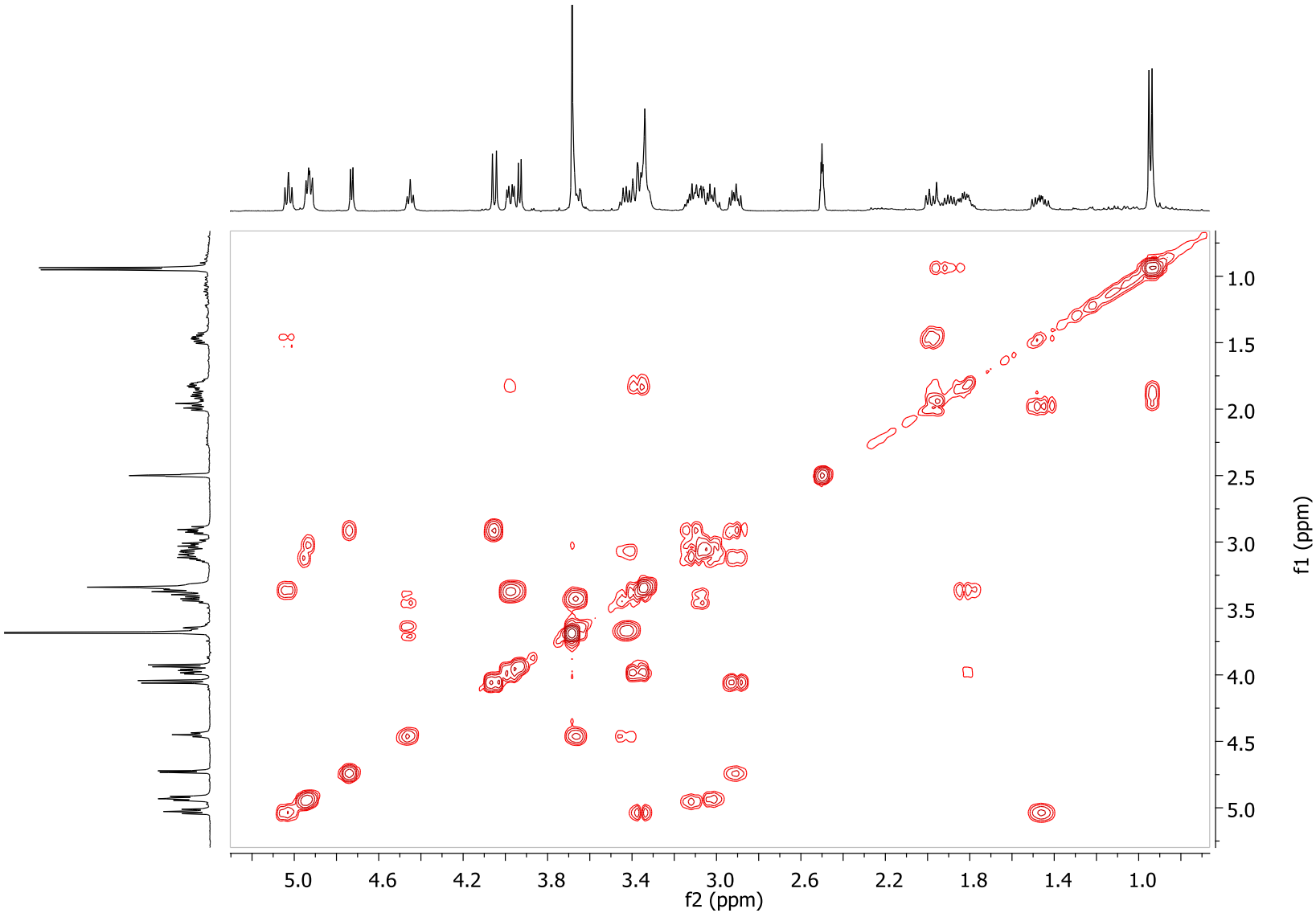
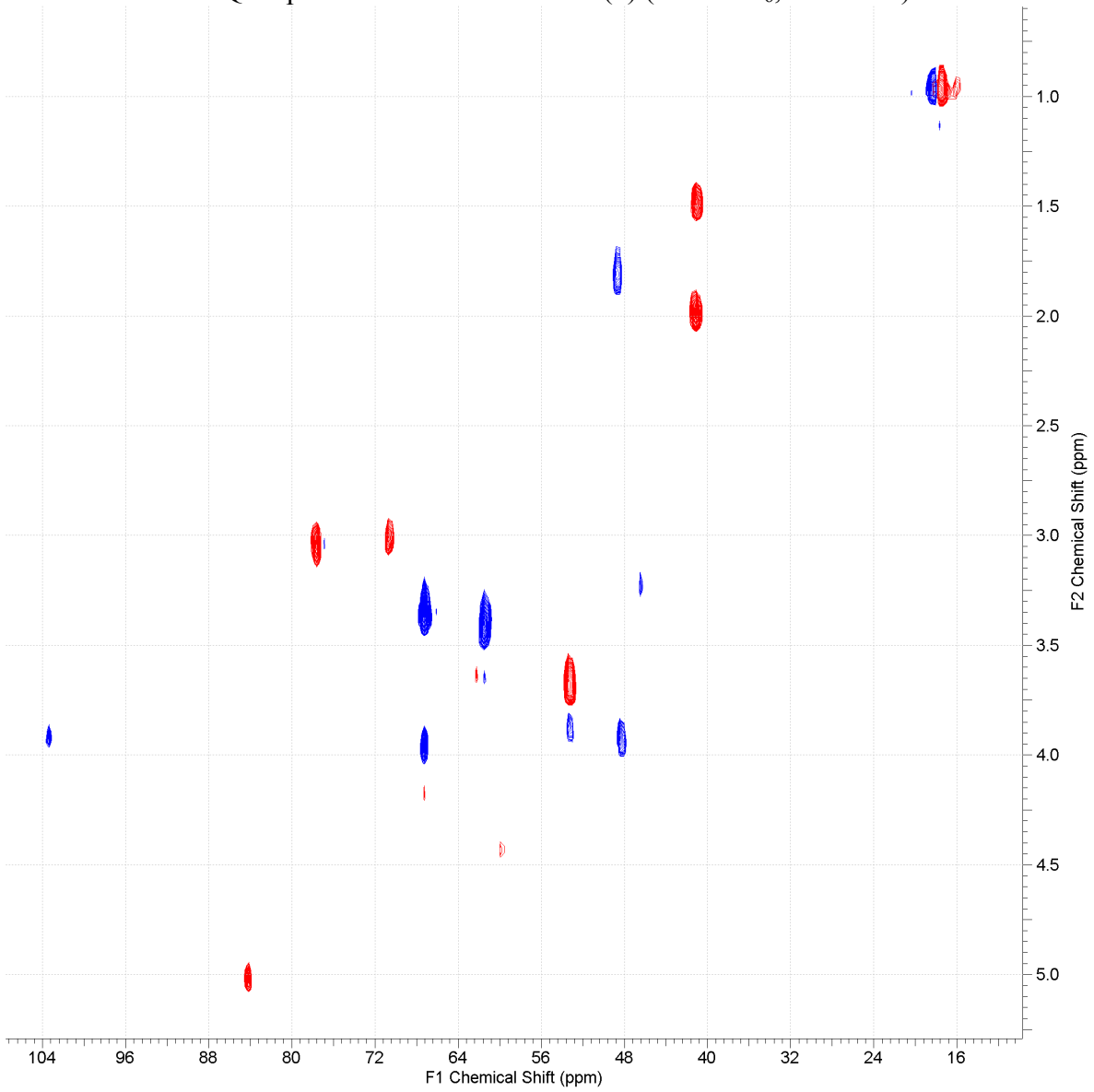
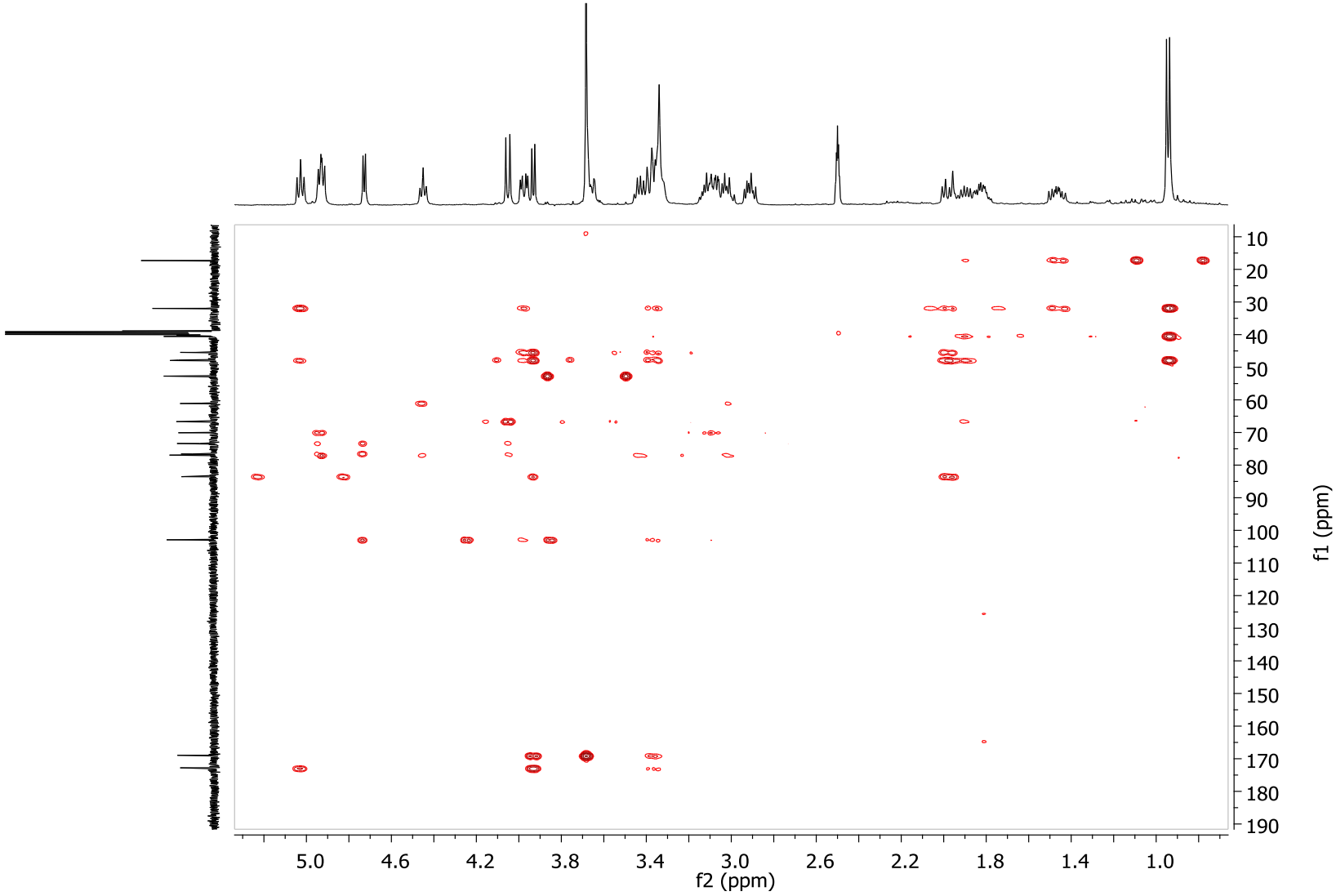


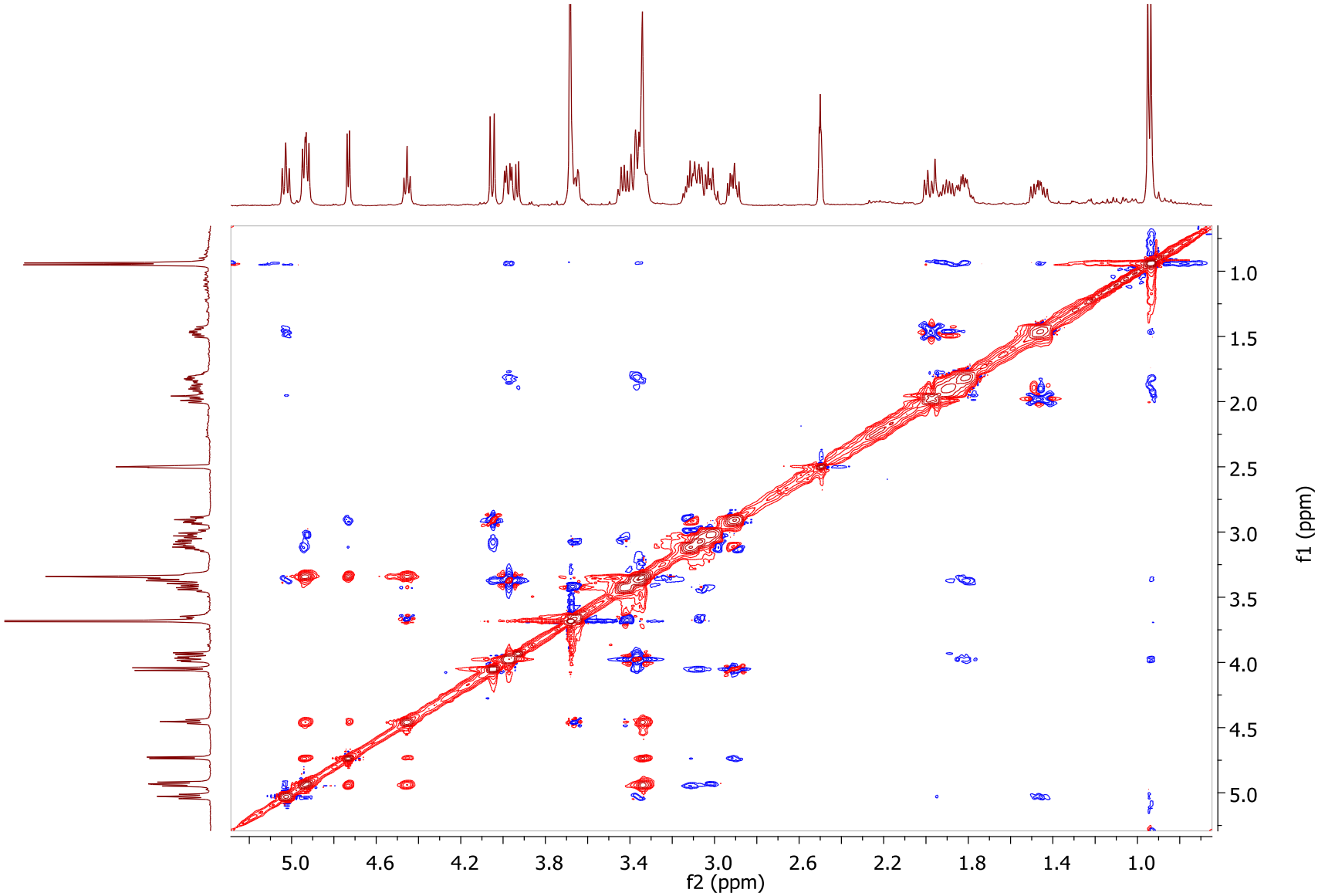
HSQC Spectrum of Cornusoside A (**1**) (DMSO-d_6, 400 MHz)



HMBC spectrum of Cornusoside A (**1**) (DMSO-d_6, 400 MHz)



NOESY Spectrum of Cornusoside A (**1**) (DMSO-d_6, 400 MHz)



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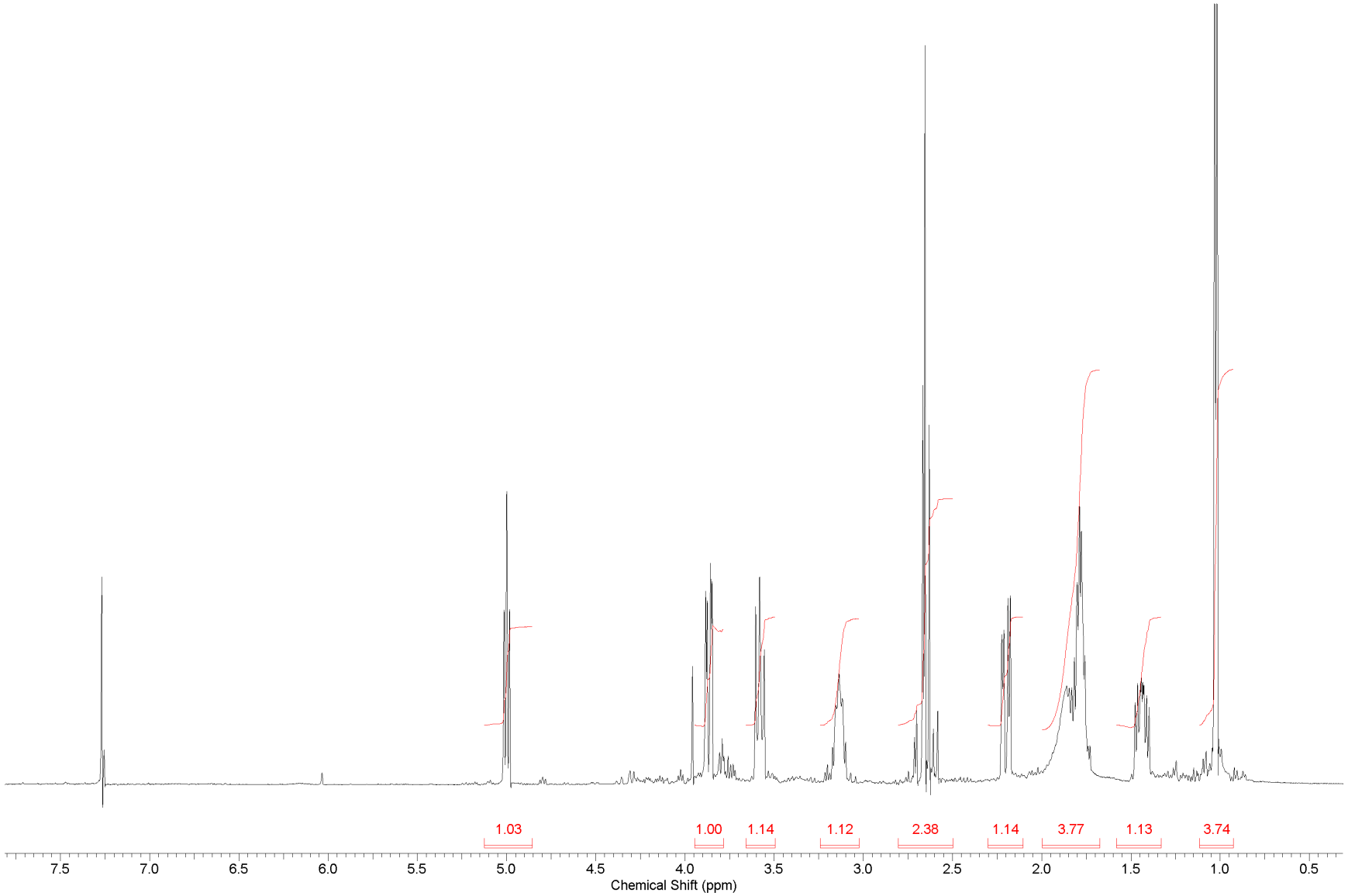

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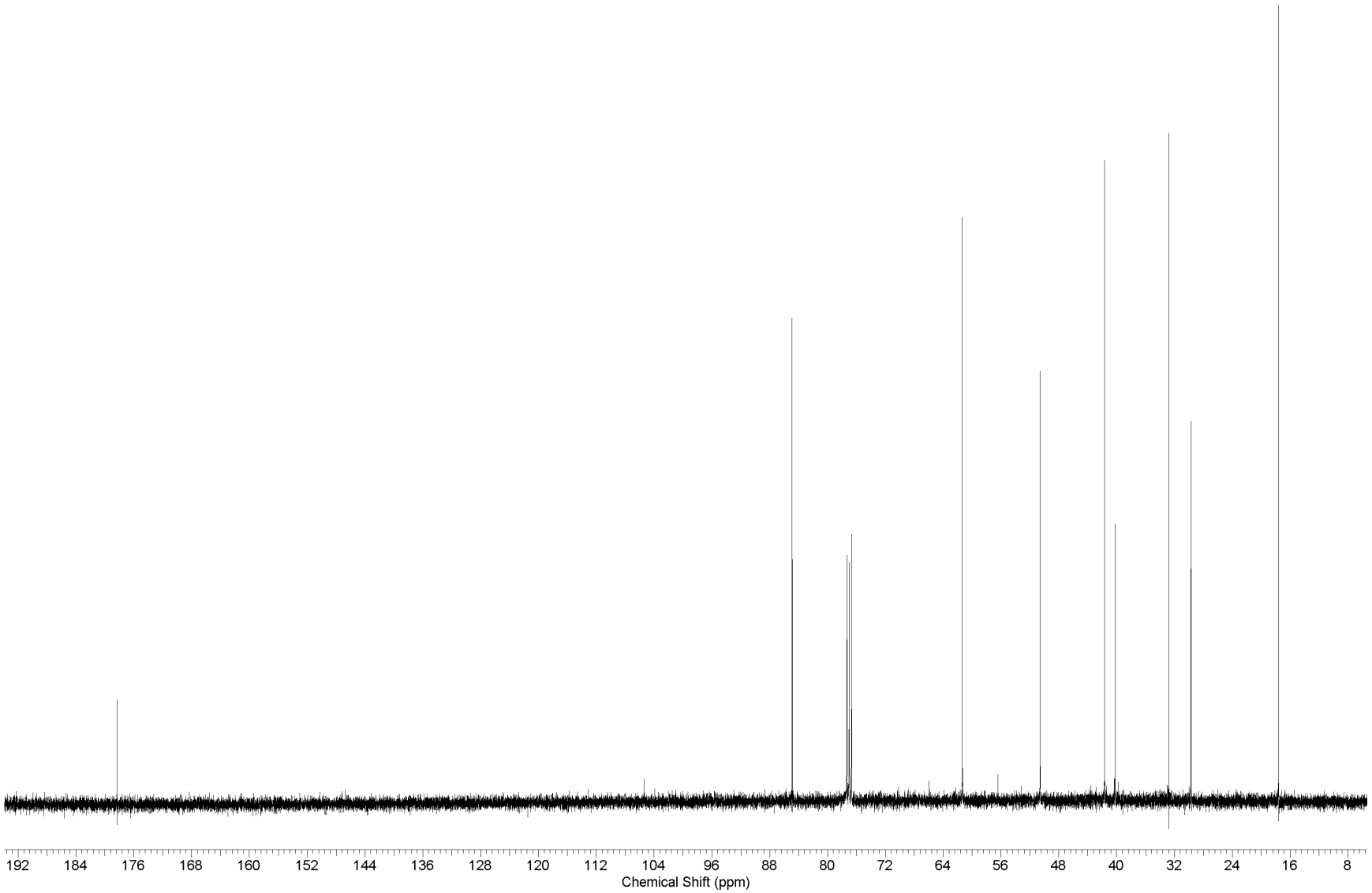

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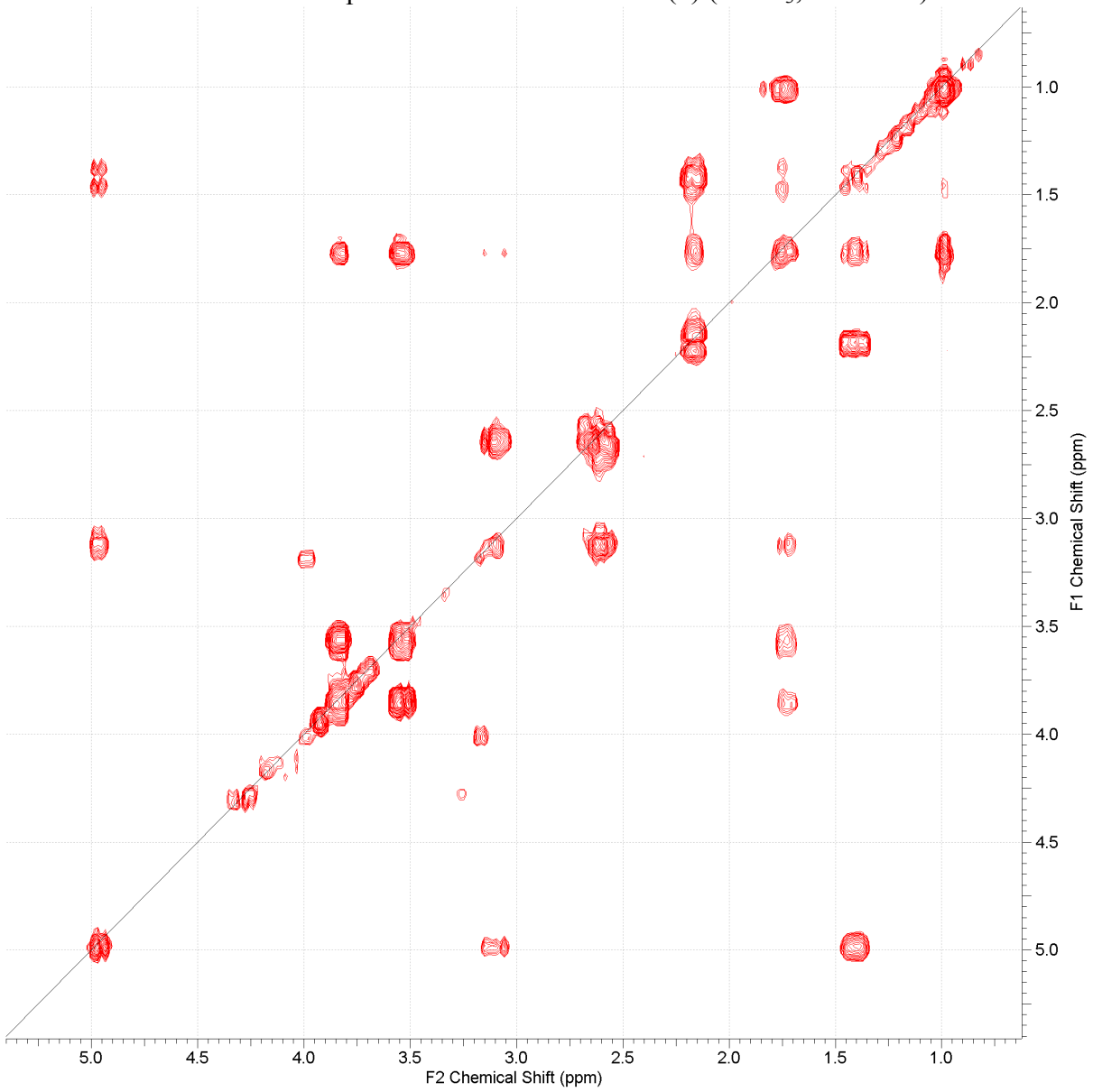

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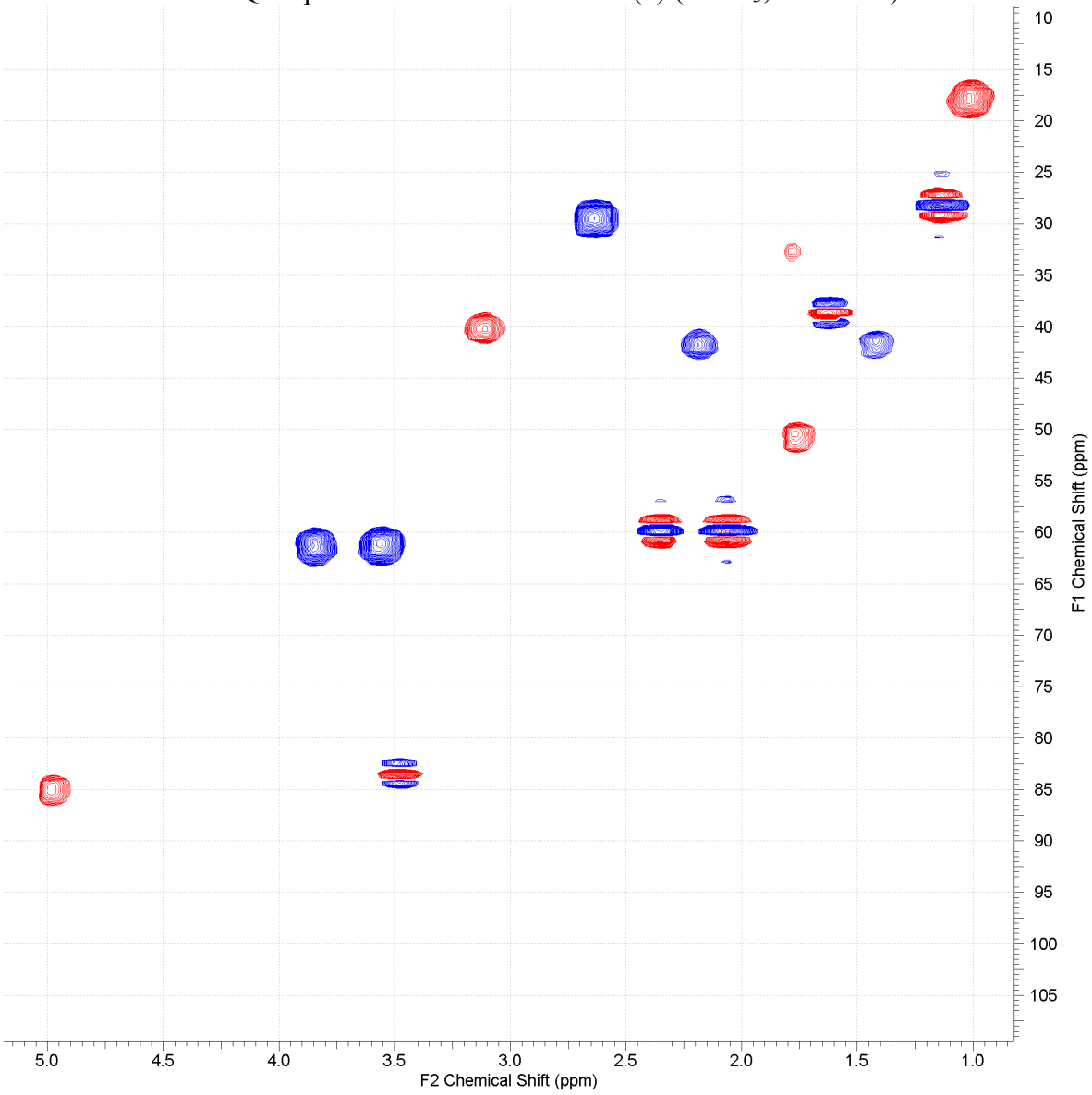

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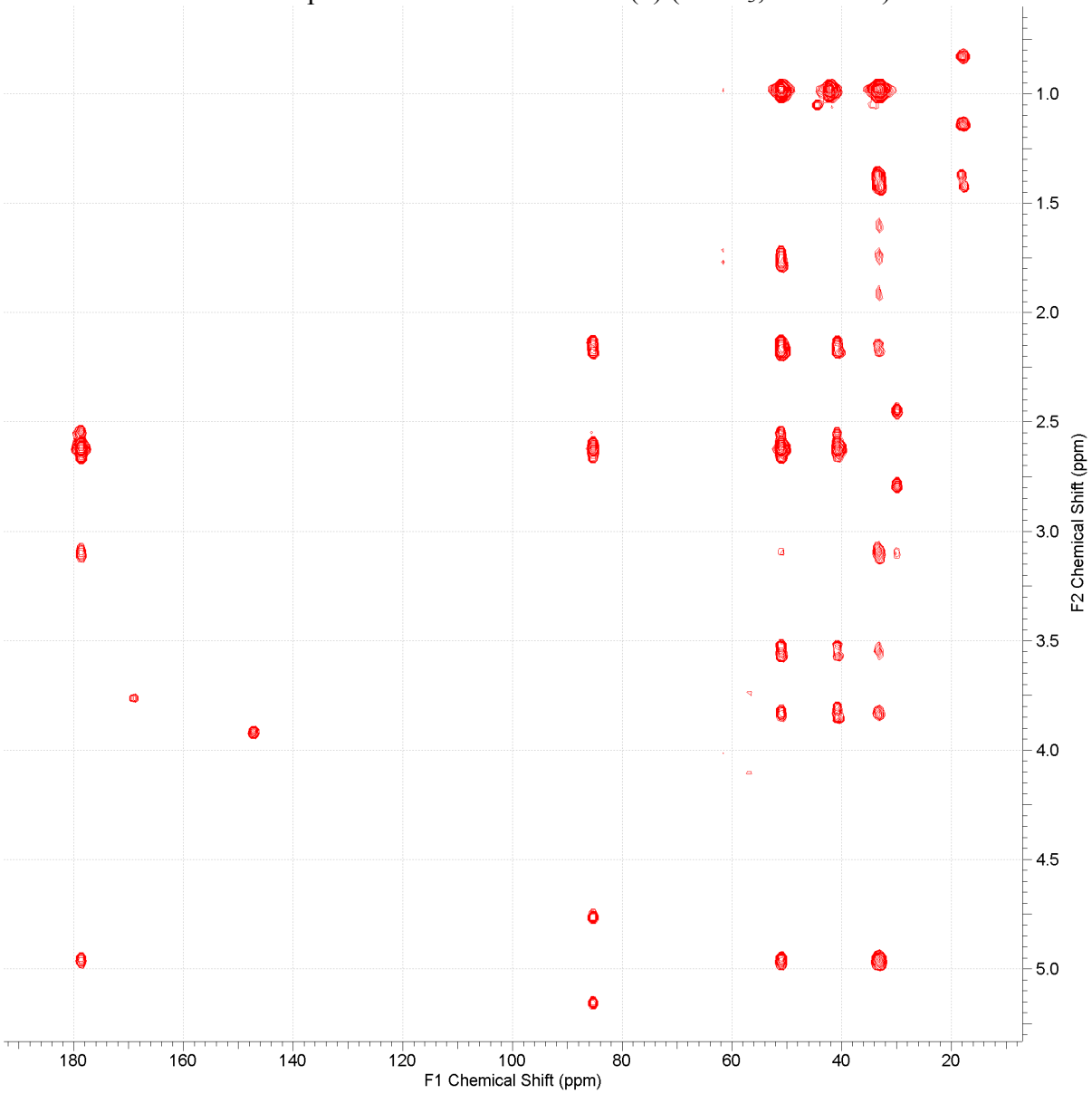

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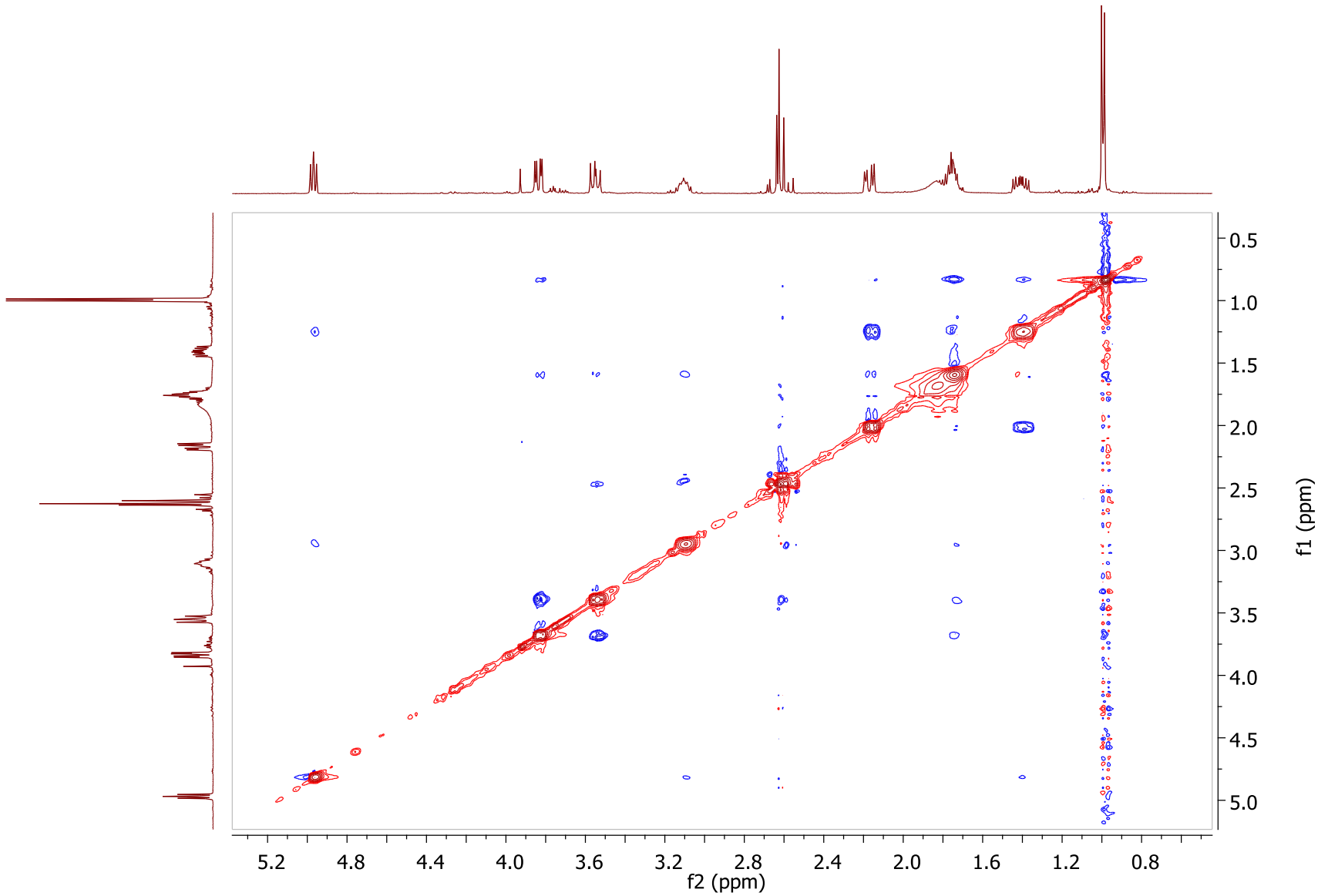

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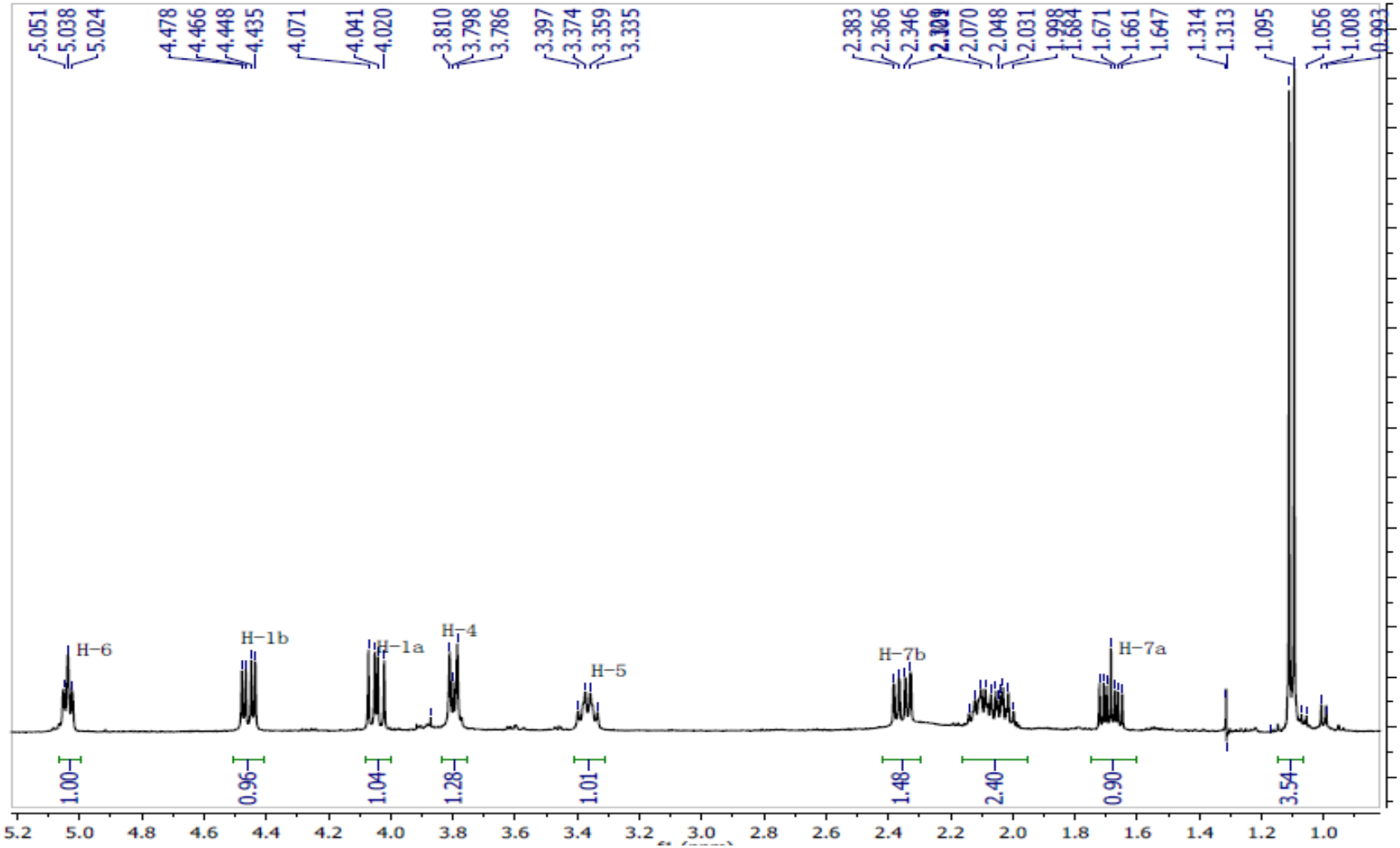

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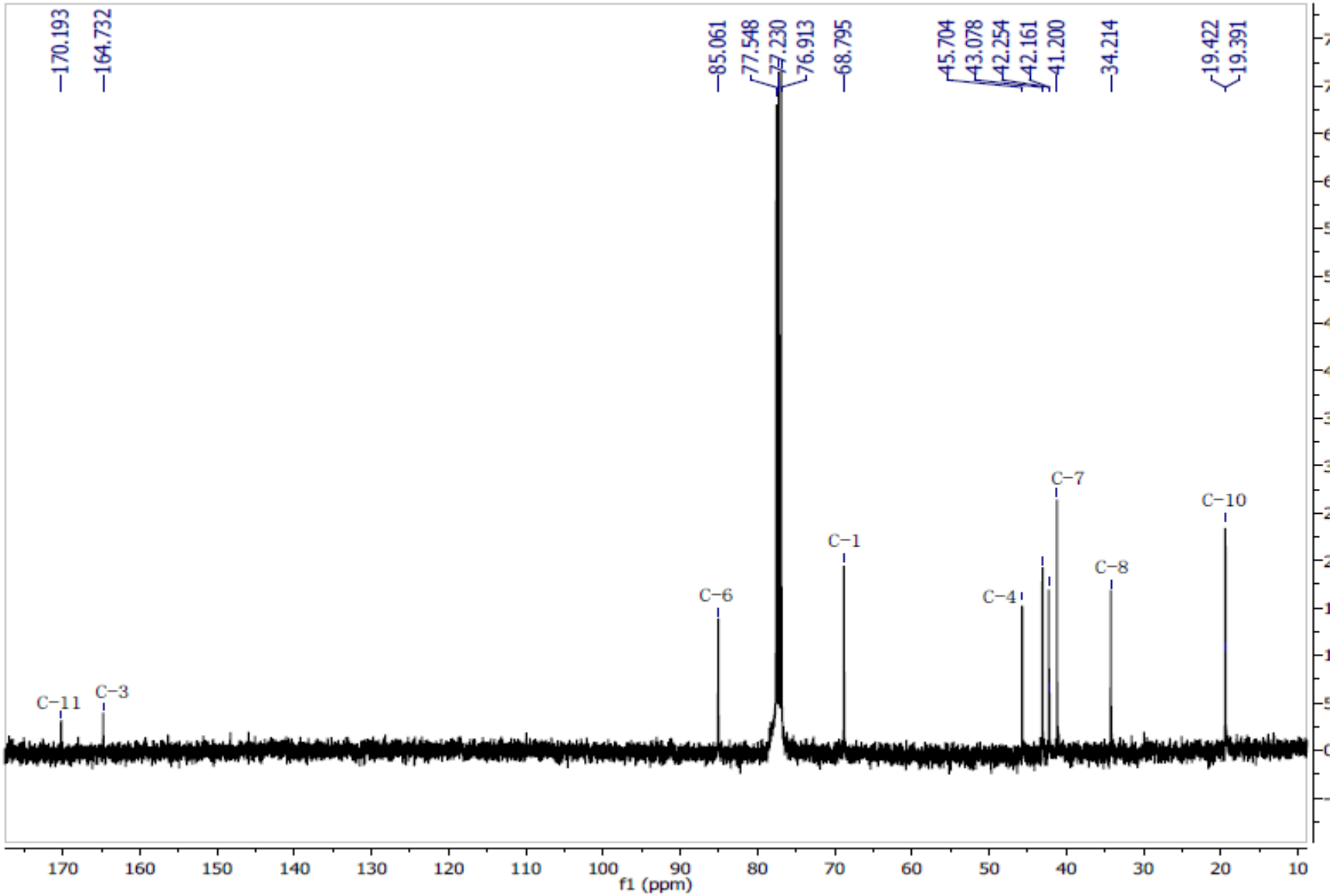

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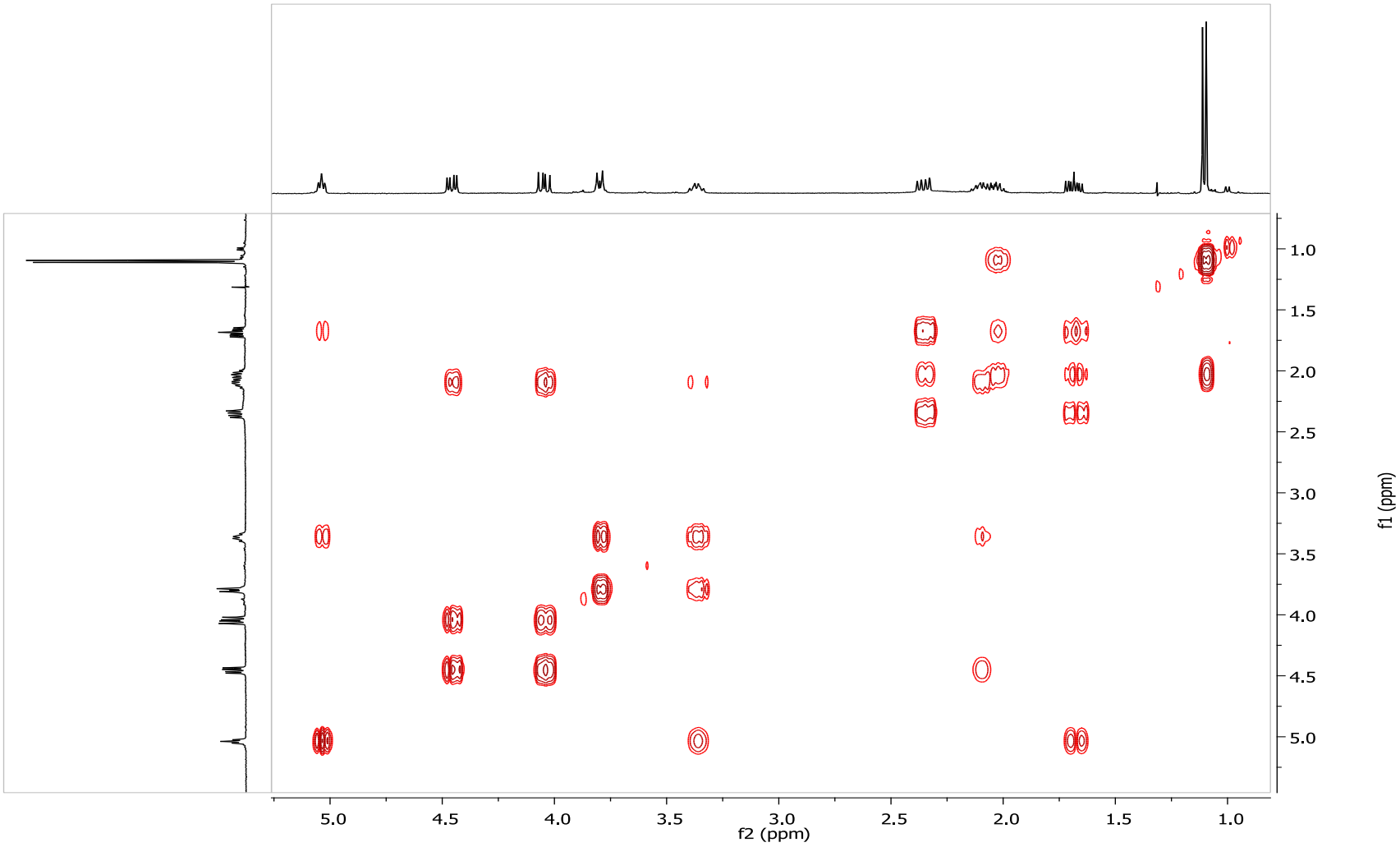

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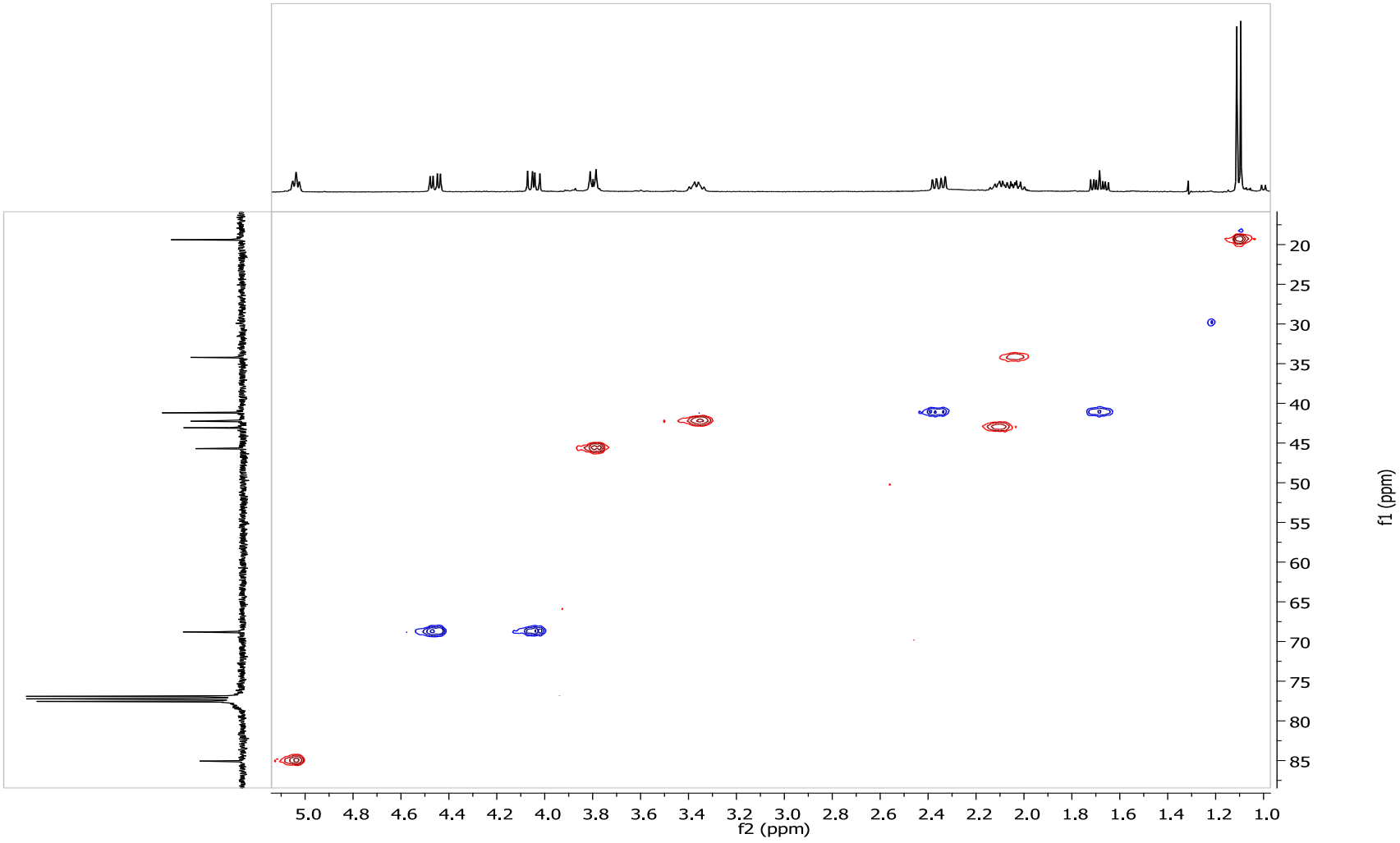

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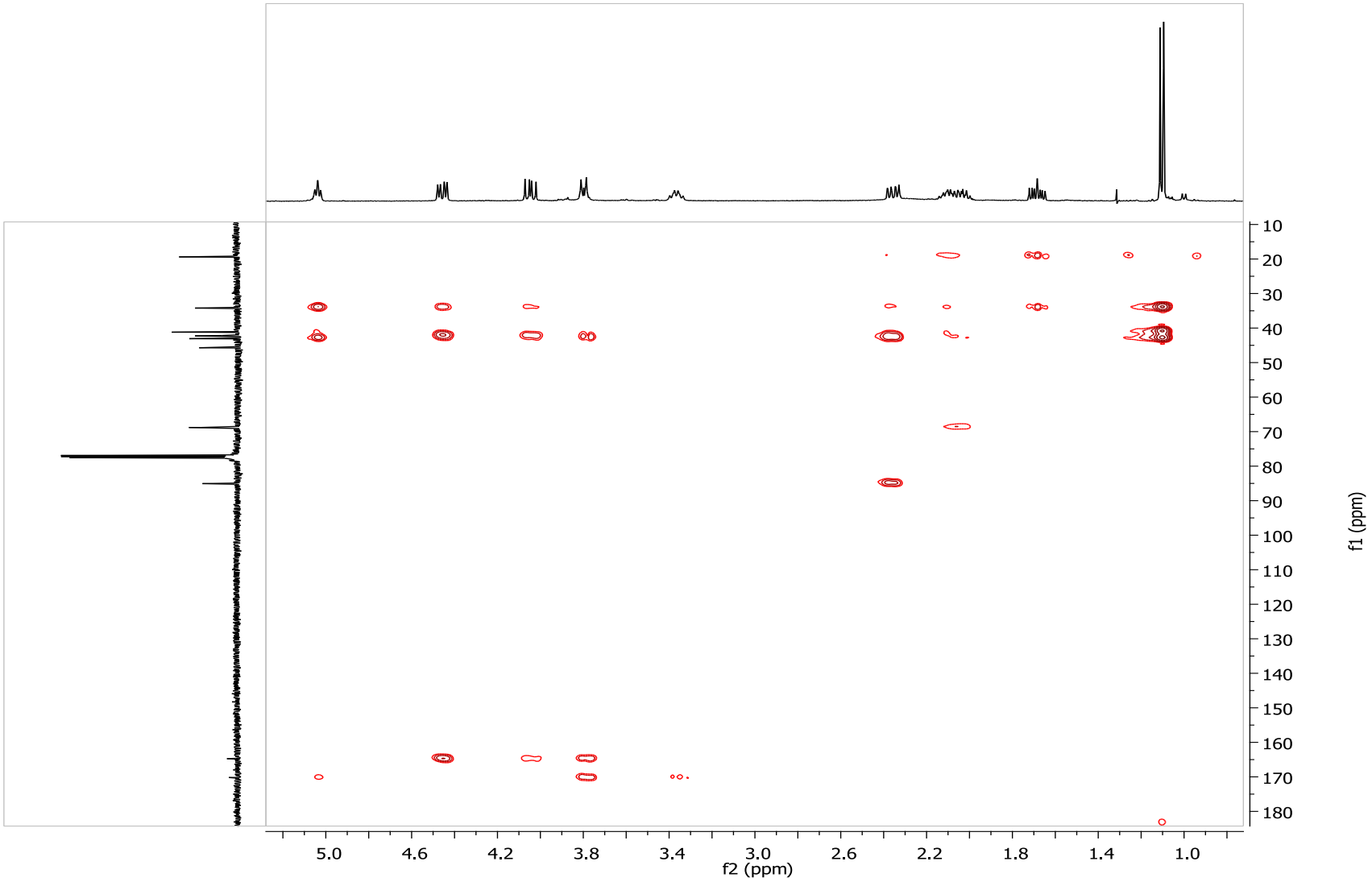

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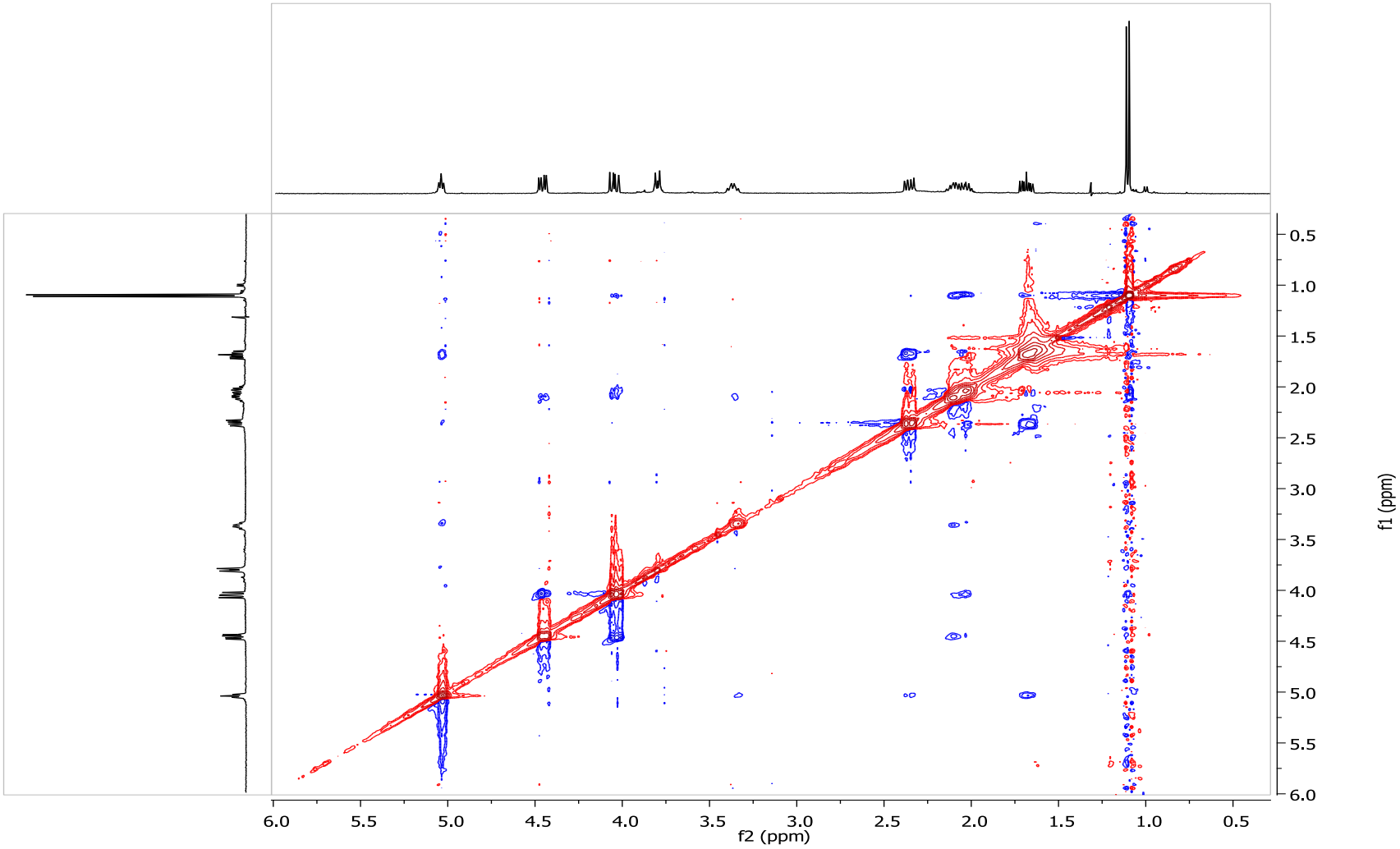
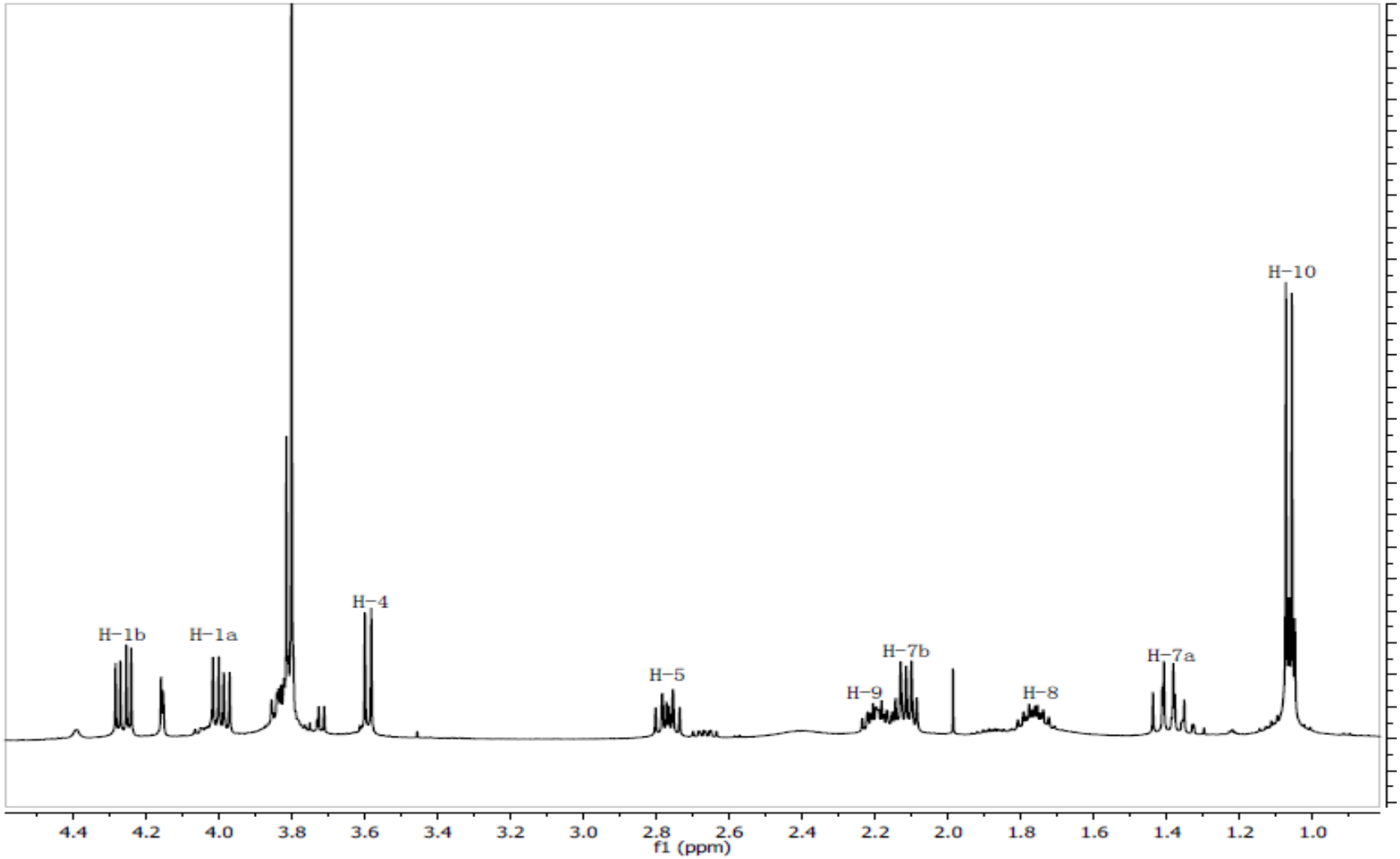


^{1}H NMR Spectrum of Cornolactone C (**4**) ($CDCl_3$, 400 MHz)



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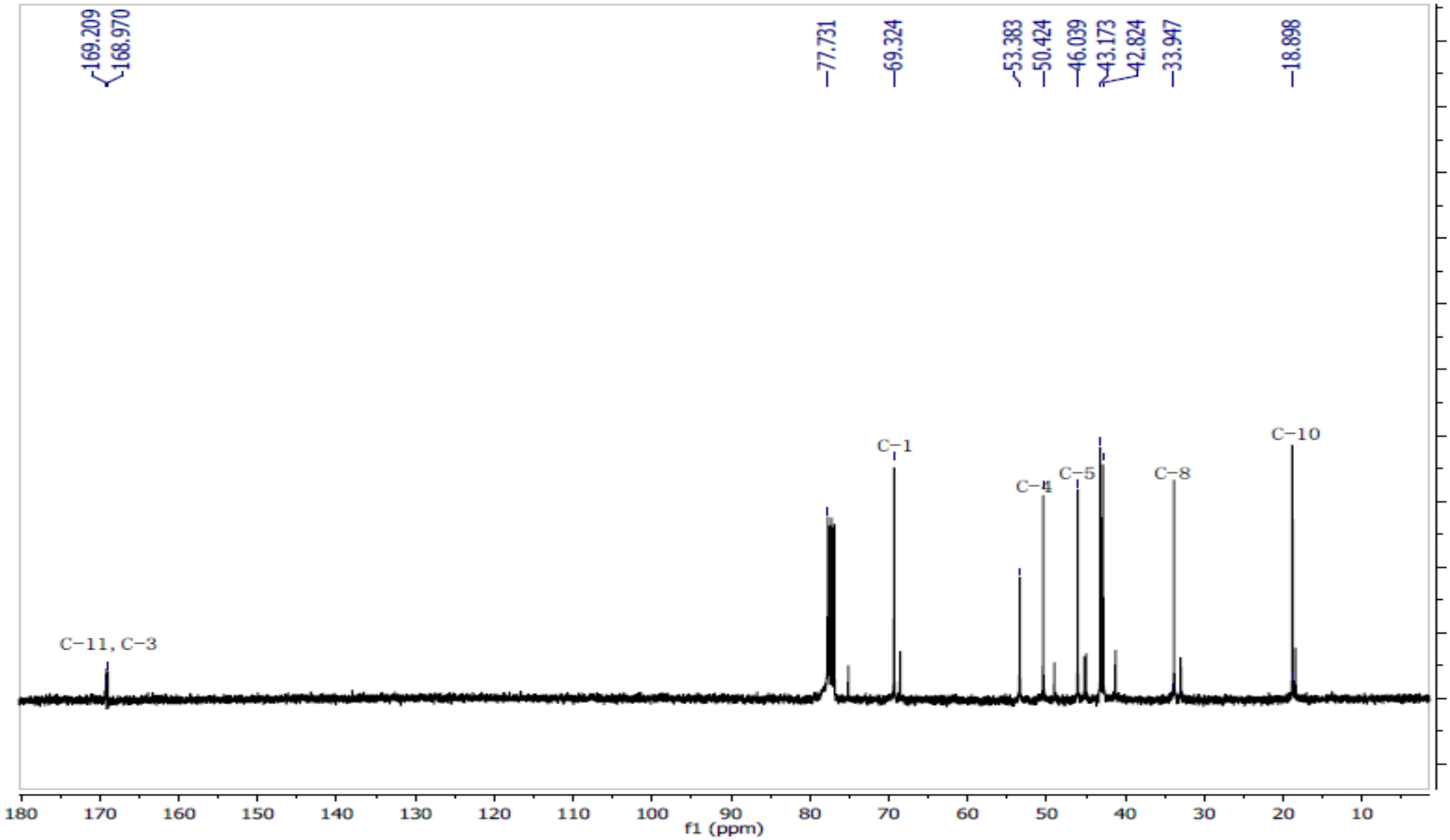
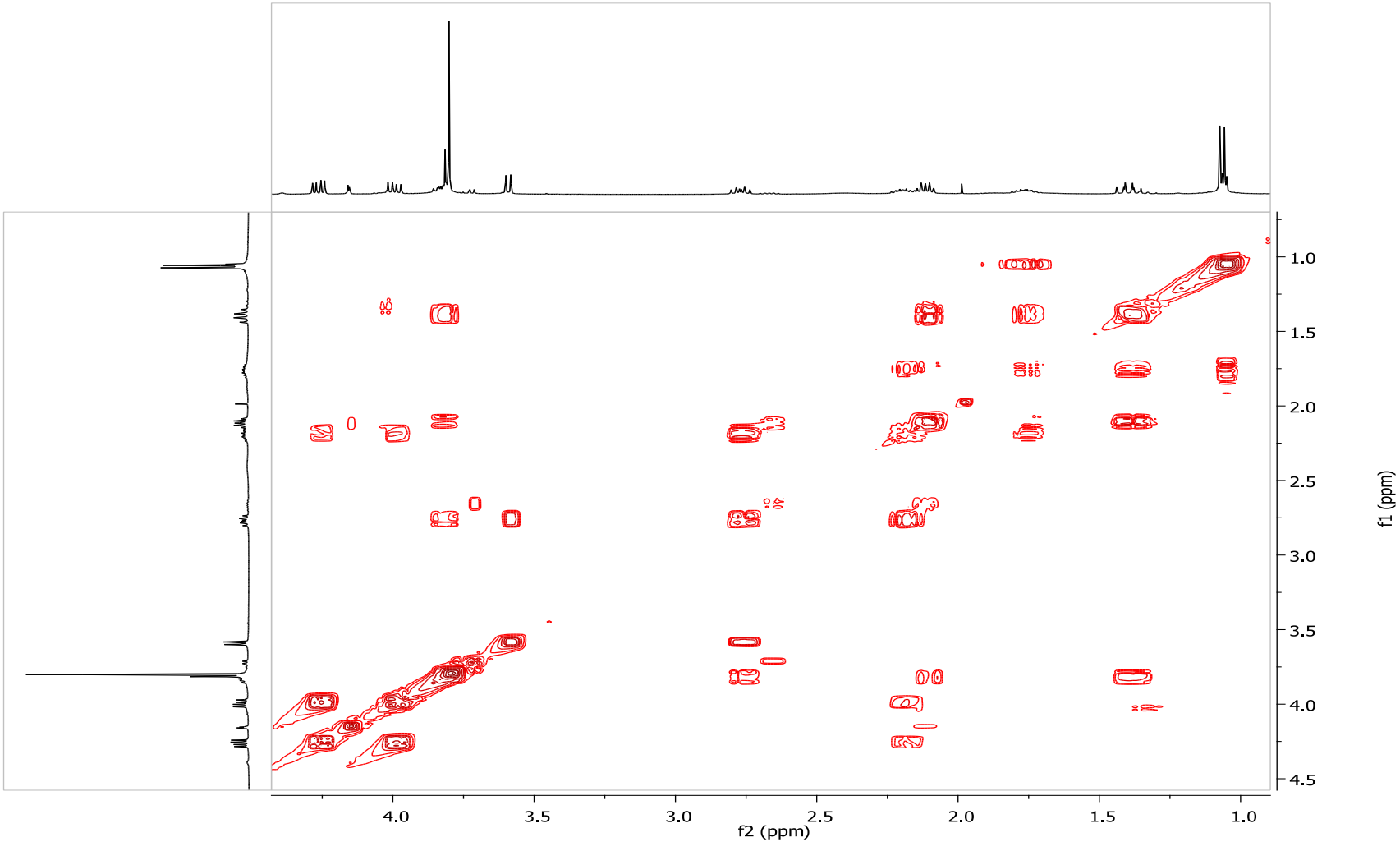


$^{1}H–^{1}H$ COSY Spectrum of Cornolactone C (**4**) ($CDCl_3$, 400 MHz)



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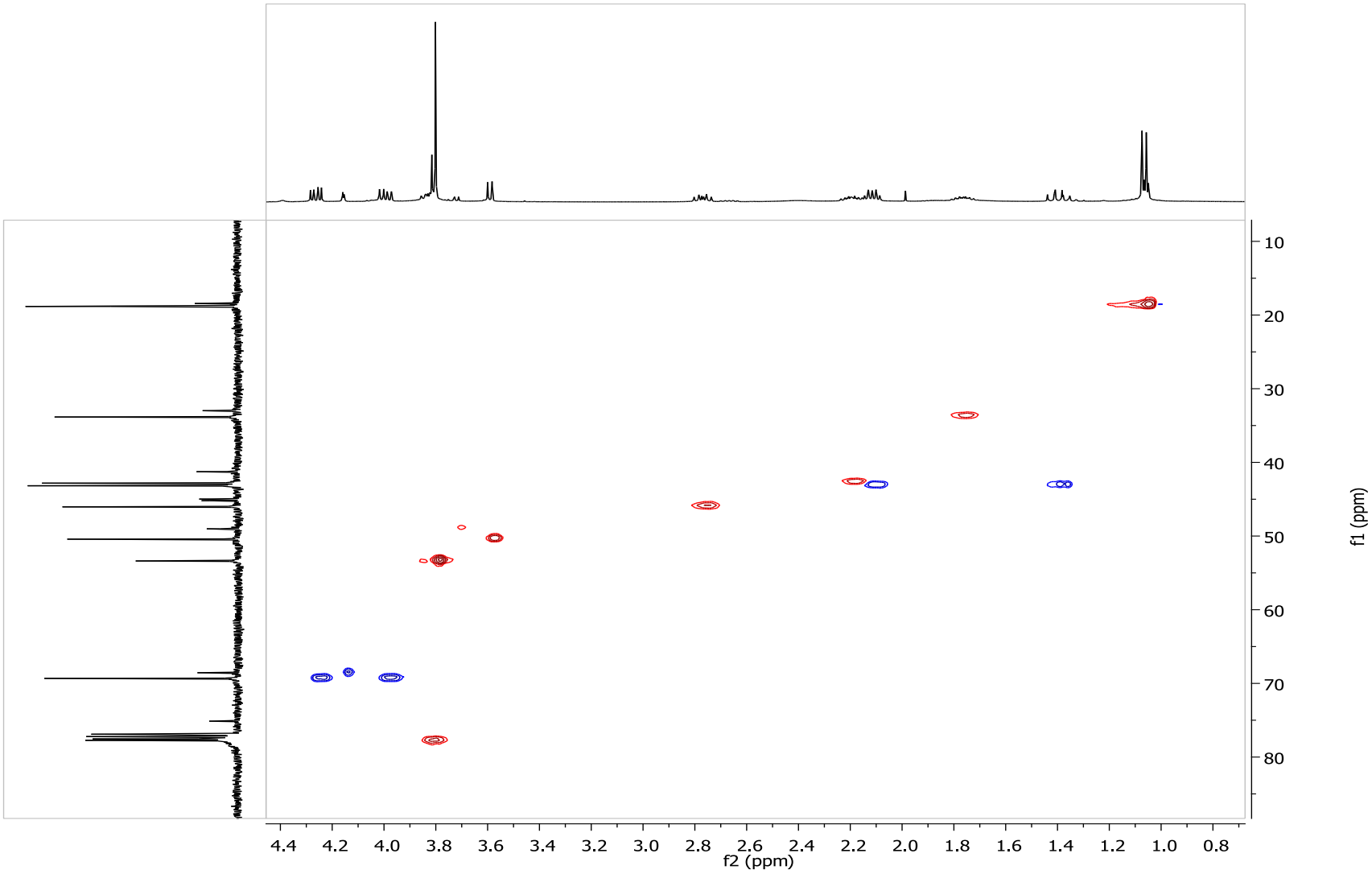
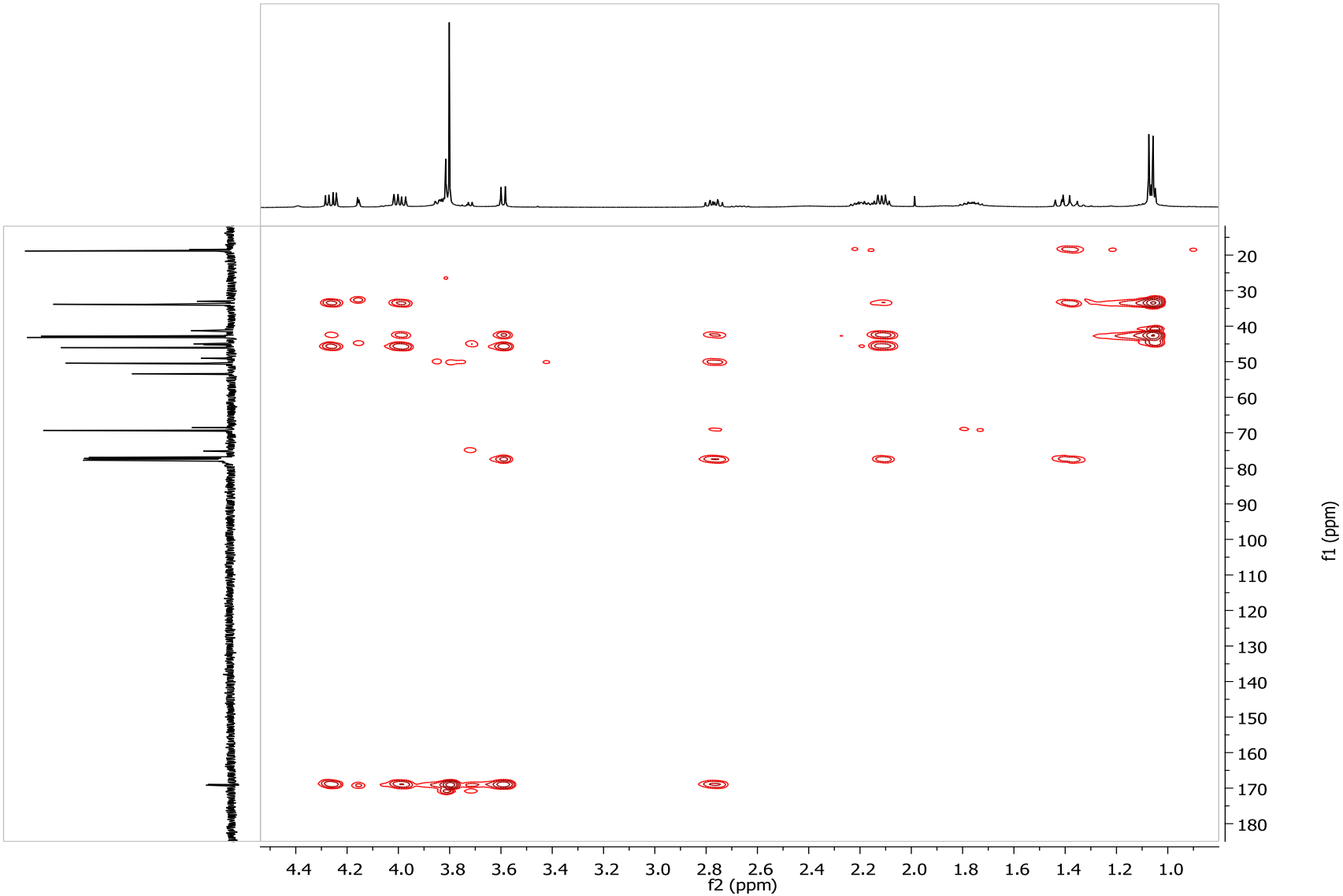


HMBC Spectrum of Cornolactone C (**4**) ($CDCl_3$, 400 MHz)



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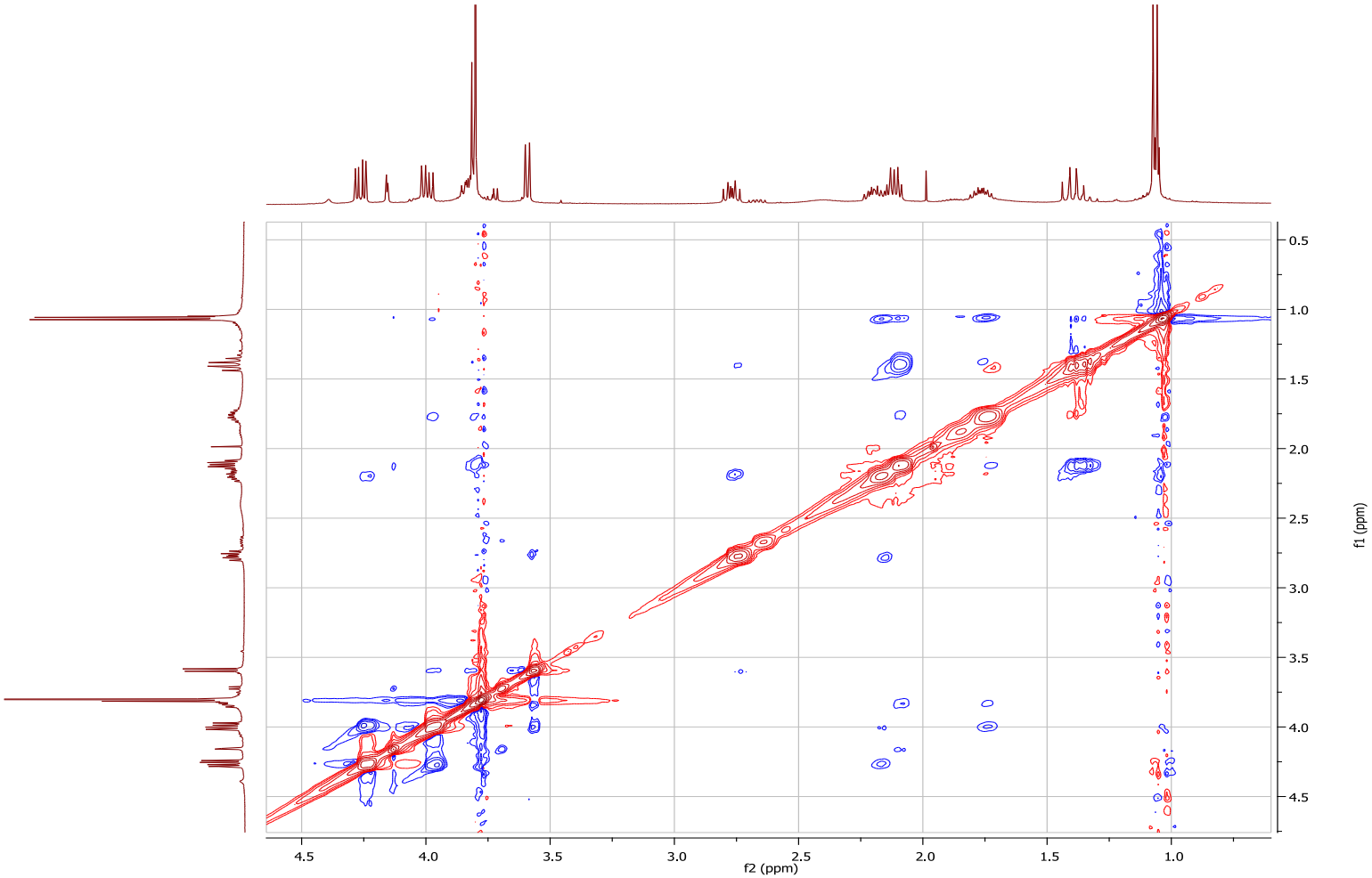

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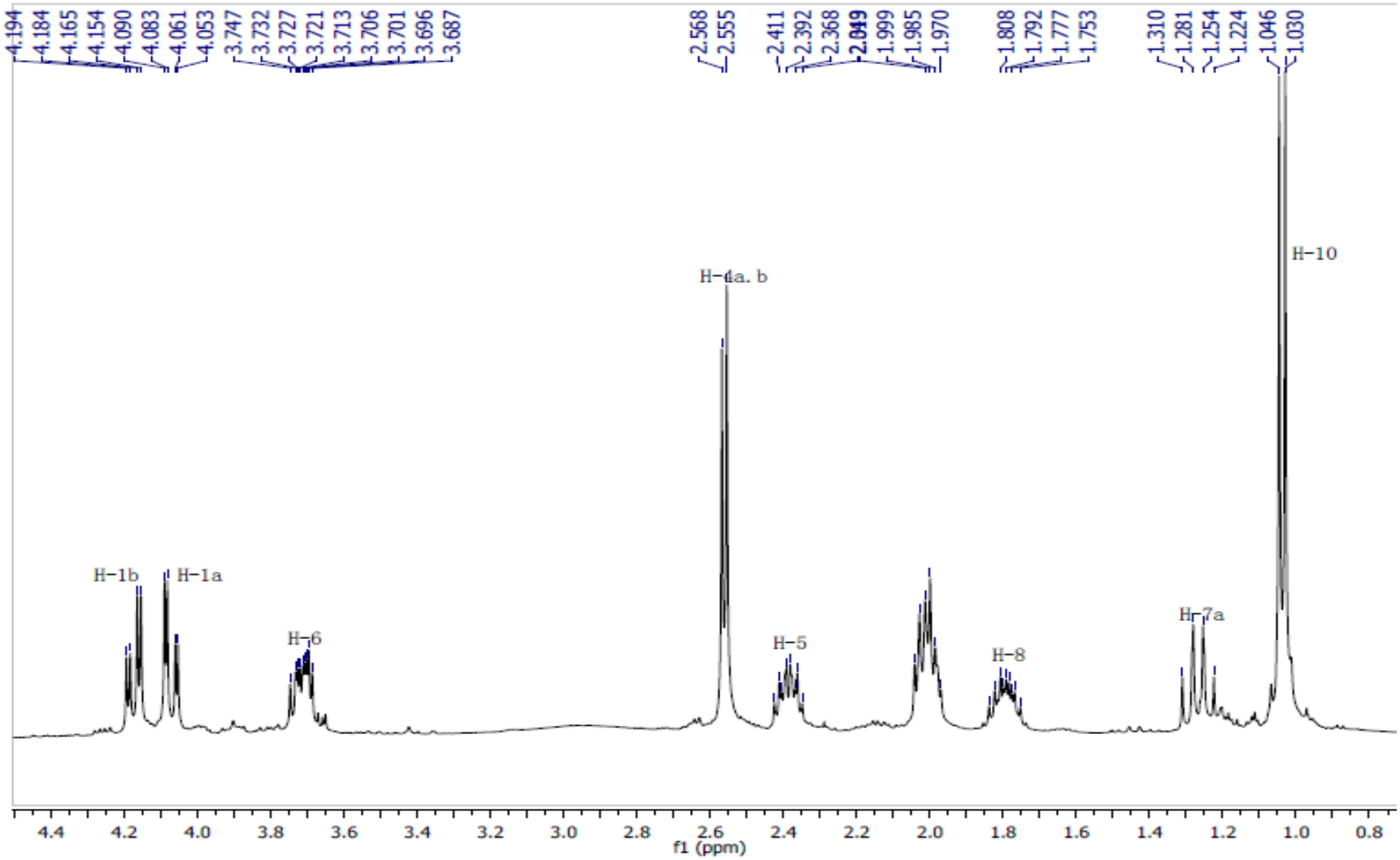

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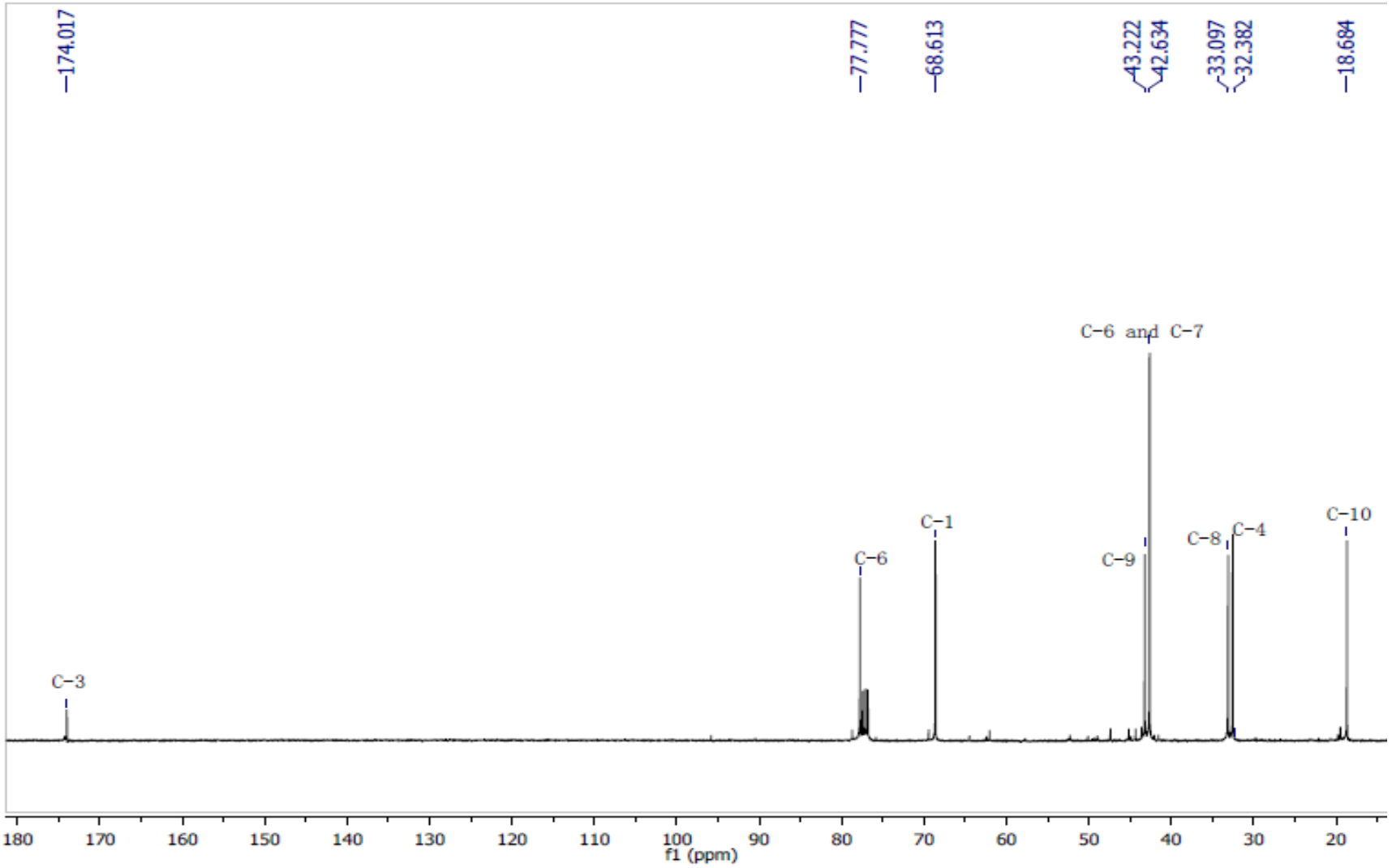
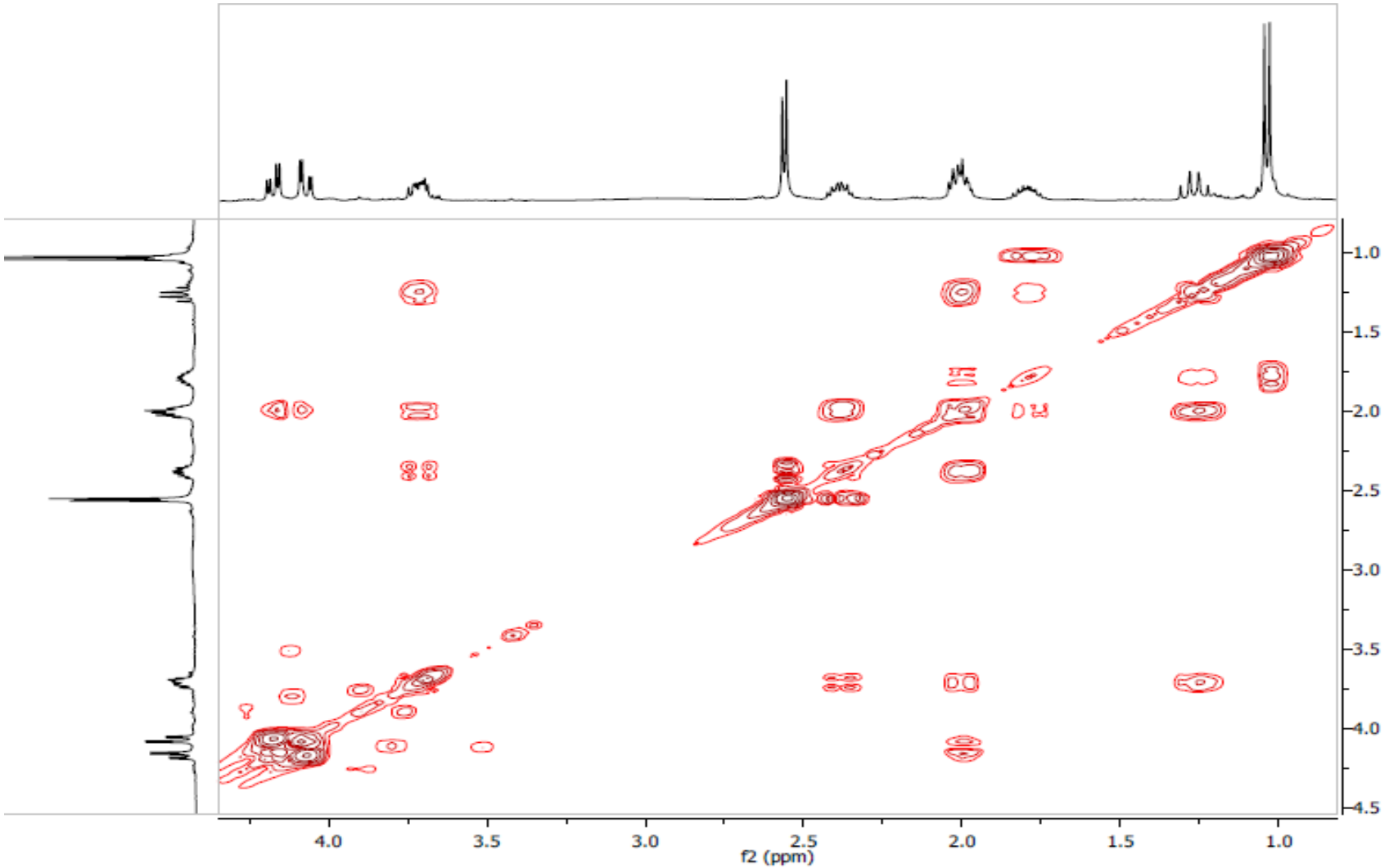


^{1}H–^{1}H COSY Spectrum of Cornolactone D (**5**) ($CDCl_3$, 400 MHz)



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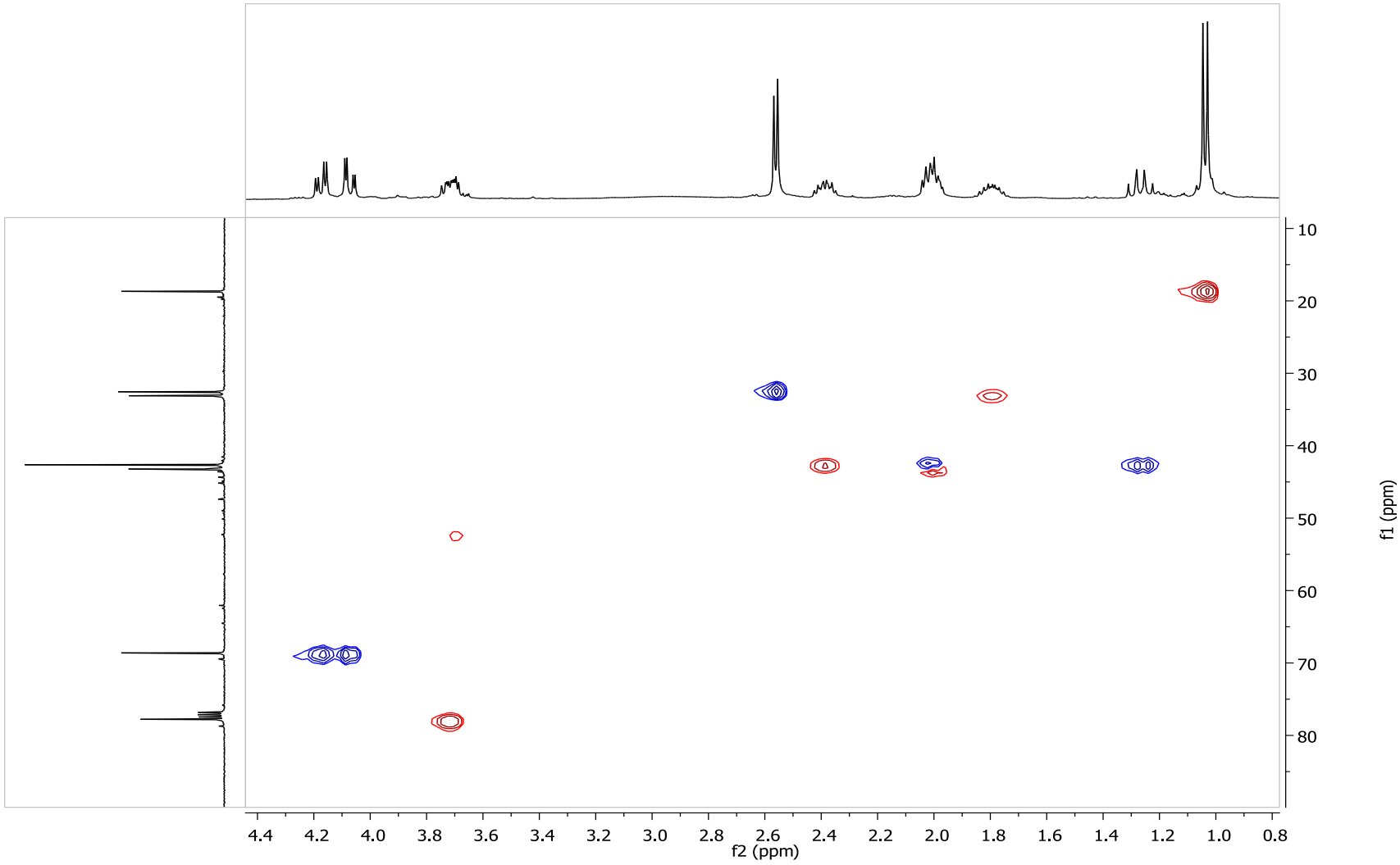
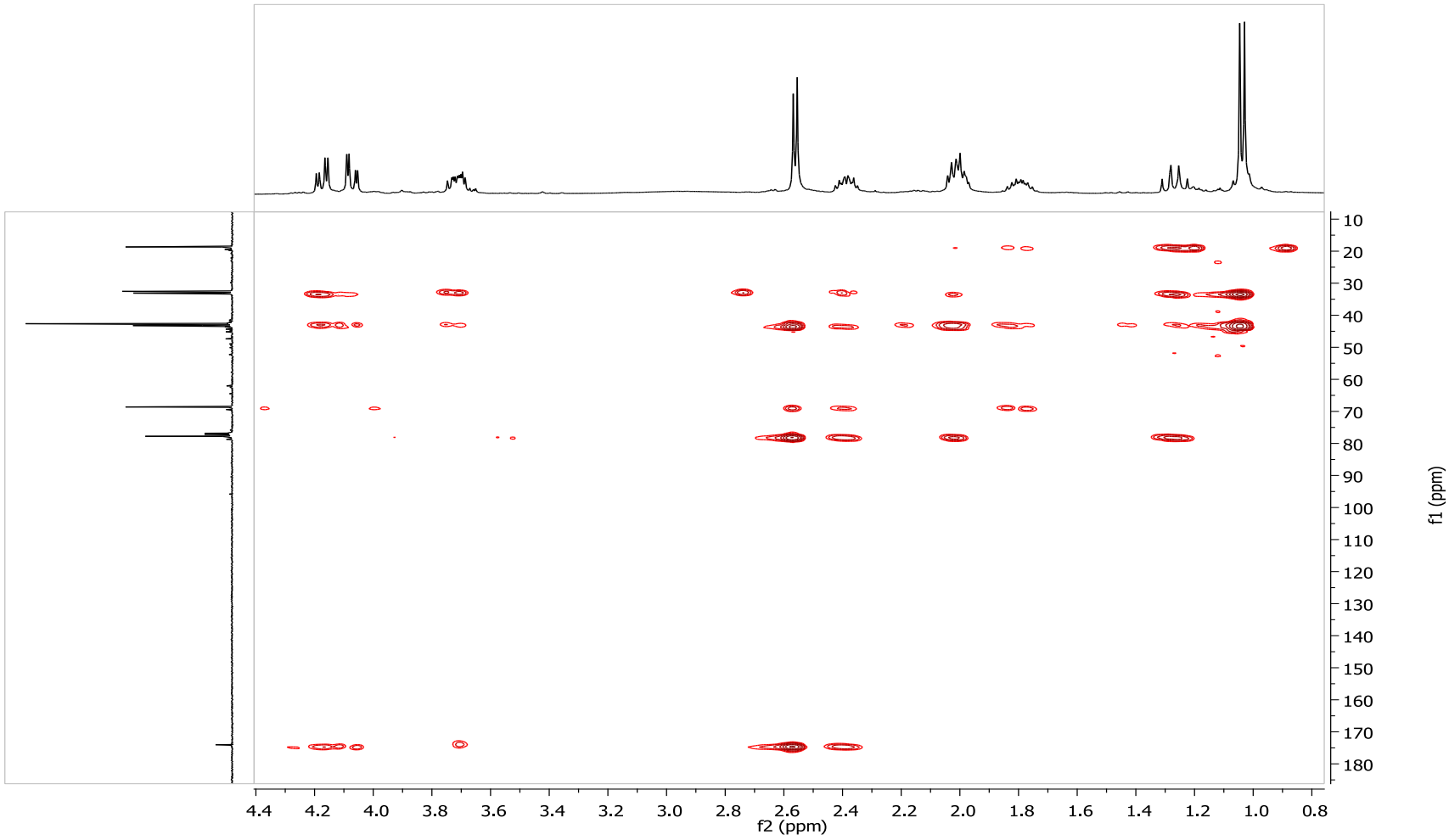


HMBC Spectrum of Cornolactone D (**5**) ($CDCl_3$, 400 MHz)



NOESY Spectrum of Cornolactone D (**5**) ($CDCl_3$, 400 MHz)