Supporting information

On the role of the vinylsulfoxide side chain of dirchromone towards its biological activities

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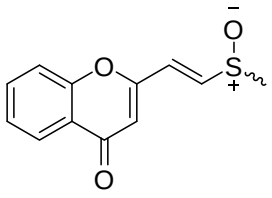
I. General experimental procedures

All starting materials and reagents were purchased from commercial sources (Sigma-Aldrich, Toronto Research Chemicals, TCI America, Alfa Aesar and Oakwood Chemicals) and used as received without further purification. Unless noted otherwise, reactions were conducted using anhydrous commercial solvents under argon atmosphere, introducing reagents with dry disposable syringes and needles. Anhydrous solvents, supplied over molecular sieves, were used as received. Reactions were monitored by thin-layer chromatography (TLC) with silica gel 60 F_{254} 0.25 mm pre-coated aluminum foil plates (MilliPore) and visualised under UV_{254}. All flash chromatographic purifications were performed using a low-pressure liquid chromatographic system (Büchi) and silica gel 60 (15-40 µm) columns packed on-site. NMR spectra were recorded with a Bruker Avance 400 spectrometer at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei, using deuterated chloroform ($CDCl_3$) or pyridine (C_6D_5N) as the solvent. Chemical shifts were reported in ppm relative to the solvent residual peak (δ = 7.26 ppm for ^{1}H and 77.1 ppm for ^{13}C) in chloroform, and to TMS in pyridine, and coupling constants *J* were expressed in Hertz (Hz). Multiplicities were reported using the following abbreviations: s, singlet; d, doublet, t, triplet; q, quartet; m, multiplet. HRMS were recorded on an Agilent 6210 TOF-MS mass spectrometer equipped with an electrospray source. Purities were measured by injecting the compounds dissolved at about 1 mg/mL in acetonitrile on an Agilent 1100 HPLC system equipped with a DAD detector, and monitoring the chromatogram at 250 nm with a 100 nm bw (reference 375 nm, 5 nm bw), except where noted otherwise; a blank run was substracted. The column used was a Kinetex C_{18} 250 x 4.6 mm column (5 µm particle size, Phenomenex), maintained at 25 °C, with a gradient from 10 to 100% acetonitrile (0.1% formic acid) in water (0.1% formic acid) in 12 minutes, with pure acetonitrile maintained for 3 further minutes, at 1 mL/min.

The DLD-1 human colorectal adenocarcinoma, A549 human lung carcinoma and WS-1 human skin fibroblast cell lines were obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA). Cell lines were grown in minimum essential medium containing Earle's salt (Mediatech Cellgro, Herndon, VA, USA), supplemented with 10% fetal calf serum (Hyclone, Logan, UT, USA), 1 × solution of vitamins, 1 × sodium pyruvate, 1 × non-essential amino acids, 100 I.U. of penicillin and 100 µg/mL of streptomycin (Mediatech Cellgro). Cells were cultured at 37 °C in a humidified atmosphere containing 5% CO_2. Exponentially growing cells were plated at a density of 5 × 103 cells per well in 96-well microplates (BD Falcon) in culture medium (100 µL) and were allowed to adhere for 16 h before treatment. Then, cells were were incubated for 48 h in the presence or absence of 100 µL of increasing concentrations of compounds dissolved in culture medium and DMSO. The final concentration of DMSO in the culture medium was maintained at 0.5% (v/v) to avoid toxicity. Cytotoxicity was assessed using Hoechst (bis-benzimide)[1]. It was expressed as the concentration of drug inhibiting cell growth by 50% (IC_{50}). For fluorescent visualization, a A-549 cells monolayer was incubated with 10 µM dirchromone (**1**) in phosphate buffer (PBS) for 4 h. The PBS was then removed, replaced with fresh PBS, and the cells were observed using a Cytation 3 imaging system (BioTek, Winooski, VT, USA) using a DAPI filter (exc. 377 nm, em. 447 nm).

II. Experimental procedures and characterization

Dichromone (**1**)



1

This compound was prepared according to the published procedure[2]. Its HPLC purity was 99.7%.

Enantiomeric separation

rac-Dirchromone was suspended in denatured reagent alcohol, HPLC grade, at a concentration of 33 mg/mL (almost saturated). This solution was injected by preparative HPLC (Shimadzu) in 250 µL portions onto a Lux® 5µm *i*-Amylose 1 semi-preparative column, 250 x 10.0 mm (Phenomenex, CA), eluting isocratically with 15% denatured reagent alcohol (HPLC) in hexanes (HPLC) at a rate of 12 mL/min. The (−) enantiomer eluted first and collected separately; the (+) enantiomer was partly contaminated with tailing (−), and had to be repurified. The process was repeated until enough (+)-dirchromone was obtained. Enantiomeric excesses (figure S1) were measured at 251 nm (100 nm bw) onto the same column, eluting isocratically with 20% denatured reagent alcohol in hexanes, by injecting 10 µL of each enantiomer at a concentration of 5 mg/mL

(−)-Dirchromone (**(−)-1**). $[\alpha]_D^{20}$: -164.1 (c = 0.2, Acetone); *ee* (HPLC-UV) 92%; HPLC purity 99.2%.

(+)-Dirchromone (**(+)-1**). $[\alpha]_D^{20}$: +161.8 (c = 0.6, Acetone); *ee* (HPLC-UV) 98%; HPLC purity 99.7%.

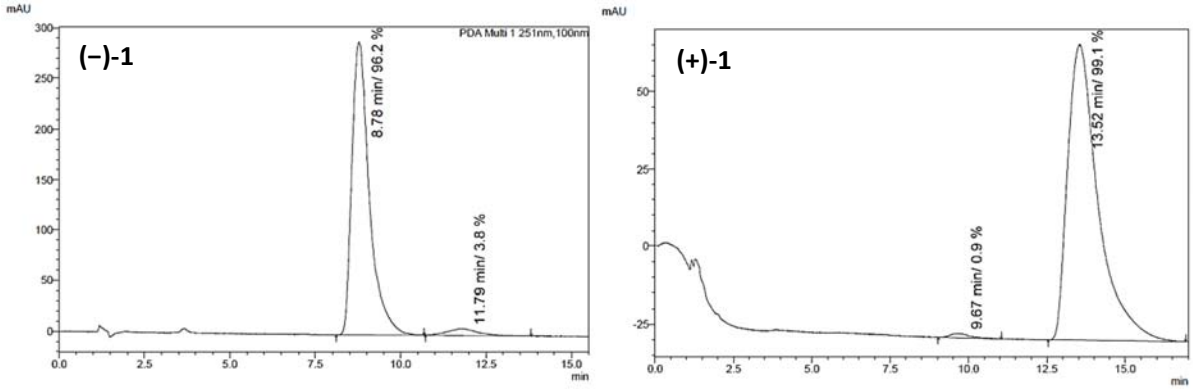
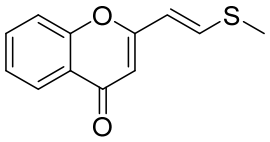


Figure S1. Enantiomeric excesses measured by chiral HPLC-UV for enantiomers of compound **1**.

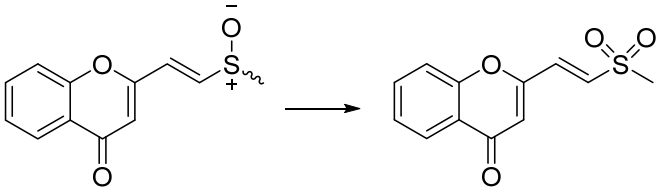
Deoxydirchromone (**2a**)



2a

Deoxydirchromone (**2a**) was prepared according to the published procedure[2] as a red solid. The latter was repeatedly recrystallized from methanol to afford straw-coloured needles. Its HPLC purity was 99.8%; contrarily to the other compounds, purity was evaluated at 275 nm (150 nm bw) from a solution at 2 mg/mL, owing to a significantly different UV absorption spectrum of **2** compared to the other analogs.

S-Oxodirchromone (**3**)

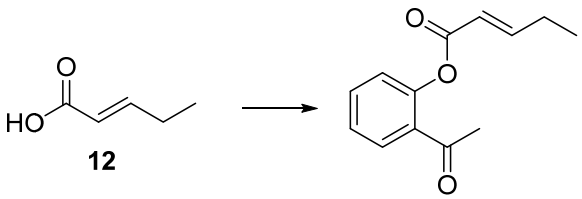


1 **3**

Dirchromone **1** (234 mg, 1.0 mmol) was stirred at room temperature in 2 mL acetic acid. Hydrogen peroxide 30% (1.02 mL, 10 mmol) was added. After 18 h, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with 3 × ethyl acetate. The combined organic phases were dried over Na_2SO_4 and evaporated to dryness. The residue was purified by flash chromatography with 10-50% acetone in hexanes to afford compound **3** (201 mg, 80% yield) as a white solid.

R_f = 0.46 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (dd, *J* = 7.9, 1.6, 1H), 7.72 (ddd, *J* = 8.6, 7.3, 1.6, 1H), 7.47 (d, *J* = 8.4, 1H), 7.42 (ddd, *J* = 8.0, 7.2, 0,7, 1H), 7.41 (d, *J* = 15.1, 1H), 7.30 (d, *J* = 15.1 , 1H), 6.49 (s, 1H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.9, 156.7, 155.8, 135.3, 134.9, 133.8, 126.0, 125.9, 124.1, 118.1, 116.1, 43.0; HRMS (ESI) *m/z* calcd for $C_{12}H_{11}O_4S$ $[M+H]^+$ 251.0373, found 251.0374; HPLC purity 99.8%.

2-Acetylphenyl (*E*)-pent-2-enoate (**13**)



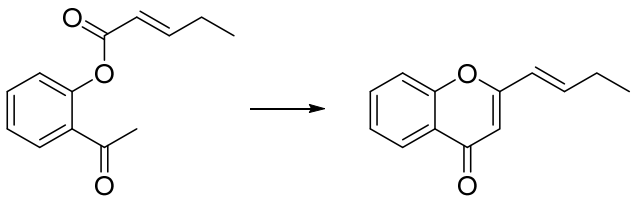
12 **13**

(2*E*)-Pentenoic acid **12** (2.65 g, 26.4 mmol) was dissolved in 10 mL anhydrous dichloromethane under argon atmosphere. After addition of 5 drops of dimethylformamide, oxalyl chloride (3.40 mL, 39.7 mmol) was added slowly, and the resulting mixture was stirred until no more gas evolved.

In a separate flask, 2'-hydroxyacetophenone (6.46 mL, 52.8 mmol) was suspended in 25 mL methanol and potassium hydroxide (2.96 g, 52.8 mmol) was added. When all of the base had dissolved, the solution was dried under reduced vacuum, and resuspended in 30 mL anhydrous dimethylformamide. The (2*E*)-pentenoyl chloride solution was then poured slowly into this solution, stirring vigorously. After 5 minutes stirring, saturated aqueous NH_4Cl was added, alongside 50 mL of ethyl acetate/toluene 1:1. The organic layer was decanted, washed with a further portion of NH_4Cl then brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography with 0-15% ethyl acetate in hexanes to afford compound **13** (3.70 g, 64% yield) as a yellow oil.

R_f = 0.59 (Hex/AcOEt 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (dd, *J* = 7.7, 1.3, 1H), 7.49 (td, *J* = 8.1, 1.5, 1H), 7.30 – 7.19 (m, 2H), 7.10 (d, *J* = 8.1, 1H), 6.04 (dt, *J* = 15.8, 1.6, 1H), 2.50 (s, 3H), 2.34 – 2.25 (m, 2H), 1.10 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.7, 164.8, 154.0, 149.1, 133.3, 131.3, 130.0, 125.9, 123.7, 119.3, 29.7, 25.5, 11.9; HRMS (ESI) *m/z* calcd for $C_{13}H_{14}O_3Na$ $[M+Na]^+$ 241.0835, found 241.0836.

(*E*)-2-(but-1-en-1-yl)-4*H*-chromen-4-one (**14**)

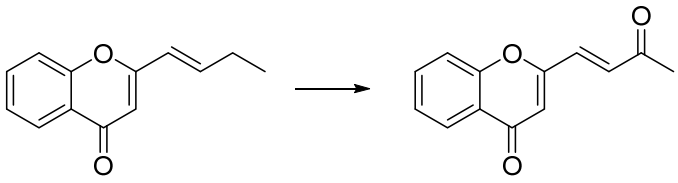


13 **14**

Ester **13** (3.7 g, 17.0 mmol) was stirred into 25 mL dichloromethane open to air. Magnesium bromide diethyl etherate (5.47 g, 21.2 mmol) was added, then diisopropylethylamine (4.4 mL, 25.4 mmol) was added slowly. The reaction was stirred overnight, then quenched by pouring 50 mL of 10% HCl into the reaction vessel. Ethyl acetate (50 mL) was added, and the organic phase was decanted. The aqueous phase was extracted twice more with 10 mL ethyl acetate. The combined organic phases were dried over Na_2SO_4 and dried under reduced pressure. The residue was redissolved in 25 mL methanol, to which was added 6 mL of HCl 37%. The reaction was stirred overnight, then quenched by pouring 50 mL of saturated $NaHCO_3$. The reaction mixture was then extracted with 3 × ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography with 0-50% ethyl acetate in hexanes to afford compound **14** (930 mg, 27%) as a yellow oil. It was noticed that another portion of the product has undergone addition of a methoxy residue to the double bond, lowering overall yield, and this byproduct was discarded.

R_f = 0.42 (Hex/AcOEt 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 7.9, 1H), 7.30 (ddd, *J* = 8.4, 7.2, 1.4, 1H), 7.08 (d, *J* = 8.4, 1H), 7.02 (t, *J* = 7.5, 1H), 6.53 (dt, *J* = 15.7, 6.4, 1H), 5.83 (s, 1H), 5.78 (d, *J* = 15.7, 1H), 2.03 – 1.91 (m, 2H), 0.82 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.7, 161.2, 155.3, 142.2, 133.0, 124.8, 124.2, 123.3, 121.3, 117.3, 108.5, 25.4, 12.1; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}O_2$ $[M+H]^+$ 201.0910, found 201.0908.

(*E*)-2-(3-oxobut-1-en-1-yl)-4*H*-chromen-4-one (**4**)

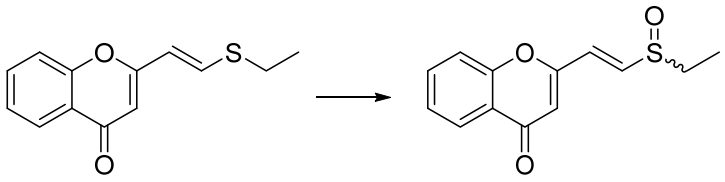


14 **4**

Inspired by a published procedure[3], compound **14** (479 mg, 2.4 mmol) was mixed with 169 mg 10% coal-supported palladium hydroxide (0.12 mmol) and 83 mg (0.6 mmol) potassium carbonate, and vigorously stirred at room temperature in 7.5 mL dichloromethane, open to air. *Tert*-Butyl hydrogen peroxide 70% (1.65 mL, 12.0 mmol) was added. After 48 h, a further portion of 1.65 mL of *tert*-butyl hydrogen peroxide 70% (12.0 mmol) was again added. After 72 h, the reaction mixture was filtered over celite and dried. The residue was purified by flash chromatography with 20-55% ethyl acetate in hexanes to afford compound **4** (137 mg, 27% yield) as a white solid.

R_f = 0.19 (Hex/AcOEt 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 7.9, 1H), 7.63 (t, *J* = 7.7, 1H), 7.41 (d, *J* = 8.4, 1H), 7.33 (t, *J* = 7.5, 1H), 7.03 (q, *J* = 15.9, 2H), 6.39 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.0, 178.0, 158.9, 155.8, 134.4, 133.8, 132.5, 125.6, 125.5, 123.9, 118.0, 114.8, 28.4; HRMS (ESI) *m/z* calcd for $C_{13}H_{11}O_3$ $[M+H]^+$ 215.0703, found 215.0699; HPLC purity 93.7%.

Homodirchromone (**5**)

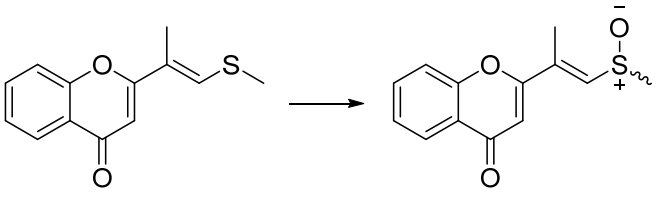


2b **5**

To (*E*)-2-(2-(ethylthio)vinyl)-4H-chromen-4-one **2b** (90 mg, 0.39 mmol) prepared according to the published procedure[2] and dissolved in 5 mL dichloromethane open to air was added *meta*-chloroperbenzoic acid 75% (89 mg, 0.39 mmol). The reaction was stirred overnight. The dried residue was purified by flash chromatography with 0-35% acetone in dichloromethane to afford compound **5** (64 mg, 67%) as an off-white solid.

R_f = 0.34 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 7.9, 1H), 7.64 (t, *J* = 7.8, 1H), 7.48 – 7.39 (m, 2H), 7.35 (t, *J* = 7.5, 1H), 6.94 (d, *J* = 14.9, 1H), 6.32 (s, 1H), 3.01 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.76 (dq, *J* = 14.3, 7.4, 1H), 1.32 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.3, 158.1, 155.8, 139.7, 134.3, 128.1, 125.7, 125.4, 123.9, 117.9, 112.9, 46.4, 5.8; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}O_3S$ $[M+H]^+$ 249.0580, found 249.0575; HPLC purity 99.7%.

11-Methyldirchromone (**6**)

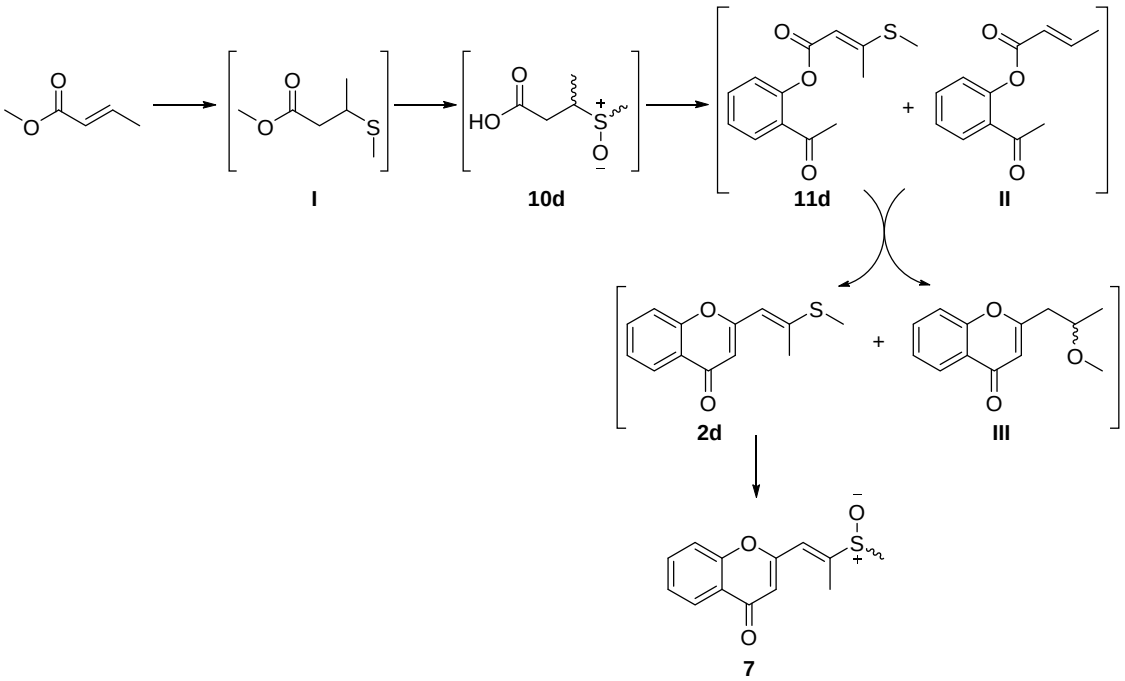


2c **6**

11-methyldeoxydirchromone **2c** (165 mg, 0.71 mmol), prepared as described previously[2], was dissolved in 10 mL dichloromethane open to air. To this solution was added *meta*-chloroperbenzoic acid 75% (163 mg, 0.71 mmol), and the resulting solution was stirred overnight. The dried residue was purified by flash chromatography with 5-50% acetone in dichloromethane to afford compound **6** (124 mg, 70%) as a beige solid.

R_f = 0.18 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, *J* = 7.9, 1.3, 1H), 7.60 (ddd, *J* = 8.6, 7.3, 1.3, 1H), 7.37 (d, *J* = 8.6, 1H), 7.30 (t, *J* = 7.5, 1H), 7.24 (s, 1H), 6.41 (s, 1H), 2.71 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.2, 159.8, 155.6, 139.2, 137.0, 134.4, 125.5, 125.4, 123.4, 117.9, 110.3, 40.2, 14.6; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}O_3S$ $[M+H]^+$ 249.0580, found 249.0575; HPLC purity 98.1%.

12-Methyldirchromone (**7**)



I **10d** **11d** **II** **2d** **III** **7**

To a solution of methyl crotonate (479 µL, 4.5 mmol) in 50 mL water was added *S*-methylthiourea (1.26 g, 4.5 mmol) and sodium hydroxide (452 mg, 11.3 mmol). The reaction was stirred 30 min, then more sodium hydroxide (542 mg, 13.5 mmol) was added and the reaction was heated at 60 °C for 30 min. The reaction was quenched with an excess of 37% aqueous HCl, and the reaction was extracted with 2 × ethyl acetate. The combined organic phases were dried over Na_2SO_4 and

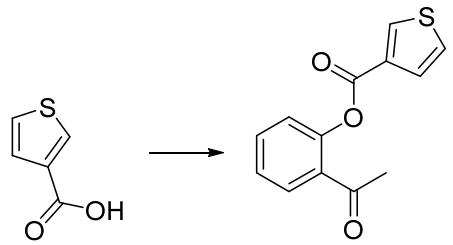
evaporated to dryness to afford 623 mg of a yellow oil of the intermediate sulfide **I**, which was used as is for the next step.

A) The residue was resuspended in 20 mL water + 5 mL methanol, and 508 µL 30% aqueous hydrogen peroxide (5.0 mmol) was added. The reaction was stirred overnight and evaporated to dryness to afford intermediate sulfoxide **10d** (626 mg) as a colorless oil, which was used as is for the ensuing steps.
B) To a solution of sulfoxide **10d** (626 mg, 4.2 mmol) in dry dichloromethane (15 mL) containing a drop of dry dimethylformamide was slowly added oxalyl chloride (714 µL, 8.3 mmol) under argon atmosphere. The solution was stirred at room temperature for approximately 1h30, or until no more gas was evolving.
C) In a separate flask, 2'-hydroxyacetophenone (2.1 mL, 16.7 mmol) was mixed to ACS grade methanol (15 mL). To this solution was added potassium hydroxide (934 mg, 16.7 mmol), and the resulting solution was sonicated until all the base was dissolved. This solution was then thoroughly evaporated under reduced pressure and dried at 10 mbar. The resulting solid was then dissolved in 5 mL of dry dimethylformamide under argon atmosphere.
D) Solution A) was transferred dropwise to solution B) with vigorous stirring. After 10 minutes, the reaction was quenched with NH_4Cl, and extracted with ethyl acetate/toluene 1:1. The organic phase was washed with 3 × NH_4Cl, 1 × brine, dried with Na_2SO_4, and evaporated. The residue was purified by flash chromatography with 0-15% ethyl acetate in hexanes to afford 401 mg of a mixture of two intermediate esters **11d** and **II** in an approximate 6:4 proportion which could not be readily separated. These were thus engaged together in the ensuing step.
E) Esters **11d** and **II** were suspended in 15 mL ACS grade dichloromethane open to air, and 1.03 g (4.0 mmol) magnesium bromide diethyl etherate was added. The resulting suspension was stirred for 2 minutes, and diisopropylethylamine (832 µL, 4.8 mmol) was added. The reaction was stirred overnight with a stopper to prevent excessive evaporation of the solvent. The reaction was quenched by pouring 15 mL of HCl 10% into the reaction vessel and was extracted with 3 × dichloromethane. The combined organic phases were washed with brine, dried with Na_2SO_4, and evaporated. The dried residue was then dissolved in 25 mL of ACS grade methanol. Concentrated HCl (3.0 mL) was then added, and the solution was stirred overnight. The reaction was quenched by pouring 30 mL of saturated NaHCO3 into the reaction vessel and was extracted with 3 × dichloromethane. The combined organic phases were washed with brine, dried with Na2SO4, and evaporated. The crude product was purified by flash chromatography with 15-25% ethyl acetate in hexanes to 147 mg of an unresolved mixture of chromones **2d** and **III** in an approximate 4:6 ratio which could not be readily separated. These were thus engaged together in the ensuing step.
F) Chromones **2d** and **III** were suspended in 10 mL ACS grade dichloromethane open to air, and 64 mg of *meta*-chloroperbenzoic acid 75% (0.28 mmol) was added. The reaction was stirred overnight and evaporated to dryness. The residue was purified by flash chromatography with 0-65% acetonitrile in dichloromethane to afford 12-methyldirchromone **7** (71 mg, 6.3% overall yield from methyl crotonate) as an off-white solid.

R_f = 0.21 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (dd, *J* = 7.9, 1.5, 1H), 7.68 (ddd, *J* = 8.4, 7.1, 1.5, 1H), 7.44 (d, *J* = 8.4, 1H), 7.40 (t, *J* = 7.6, 1H), 6.84 (s, 1H), 6.38 (s, 1H), 2.67 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.3, 160.5, 156.0, 152.3, 134.2, 125.9, 125.6, 124.0, 120.9,

118.0, 113.7, 39.1, 13.8; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}O_3S$ $[M+H]^+$ 249.0580, found 249.0580; HPLC purity 98.8%.

2-Acetylphenyl thiophene-3-carboxylate (**16**)



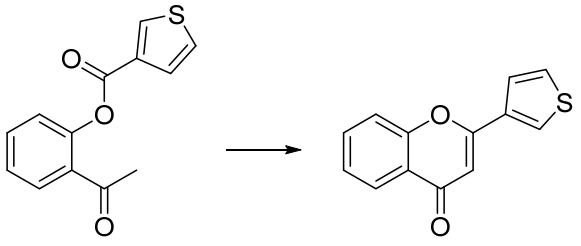
15 **16**

Thiophene-3-carboxylic acid **15** (254 mg, 2.0 mmol) was dissolved in 8 mL anhydrous dichloromethane under argon atmosphere. After addition of 2 drops of dimethylformamide, oxalyl chloride (340 µL, 4.0 mmol) was added slowly, and the resulting mixture was stirred until no more gas evolved.

In a separate flask, 2'-hydroxyacetophenone (969 µL, 7.9 mmol) was suspended in 5 mL methanol and potassium hydroxide (444 mg, 7.9 mmol) was added. When all the base had dissolved, the solution was dried under reduced vacuum, and resuspended in 8 mL anhydrous dimethylformamide. The thiophene-3-carboxyloyl chloride solution was then poured slowly into this solution, stirring vigorously. After 5 minutes stirring, saturated aqueous NH_4Cl was added, alongside 20 mL of ethyl acetate/toluene 1:1. The organic layer was decanted, washed with a further portion of NH_4Cl then brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography with 0-15% ethyl acetate in hexanes to afford compound **16** (402 mg, 82% yield) as a white solid.

R_f = 0.71 (Hex/AcOEt 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 (dd, *J* = 2.9, 1.0, 1H), 7.85 (dd, *J* = 7.8, 1.3, 1H), 7.67 (dd, *J* = 5.1, 0.9, 1H), 7.57 (td, *J* = 7.9, 1.5, 1H), 7.39 (dd, *J* = 5.0, 3.1, 1H), 7.35 (t, *J* = 7.6, 1H), 7.23 (d, *J* = 8.1, 1H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.7, 160.9, 149.1, 134.6, 133.5, 132.5, 131.4, 130.3, 128.3, 126.7, 126.3, 124.0, 29.9; HRMS (ESI) *m/z* calcd for $C_{26}H_{20}NaO_6S_2$ $[2M+Na]^+$ 515.0594, found 515.0595.

2-(Thiophen-3-yl)-4H-chromen-4-one (**8**)



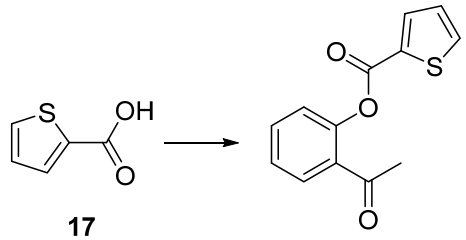
16 **8**

Ester **16** (390 mg, 1.6 mmol) was stirred into 10 mL dichloromethane open to air. Magnesium bromide diethyl etherate (1020 mg, 4.0 mmol) was added, then diisopropylethylamine (822 µL,

4.8 mmol) was added slowly. The reaction was stirred overnight, then quenched by pouring 20 mL of 10% HCl into the reaction vessel. Ethyl acetate (20 mL) was added, and the organic phase was decanted. The aqueous phase was extracted twice more with 10 mL ethyl acetate. The combined organic phases were dried over Na_2SO_4 and dried under reduced pressure. The residue was redissolved in 10 mL methanol, to which was added 2 mL of HCl 37%. The reaction was stirred overnight, then quenched by pouring 30 mL of saturated $NaHCO_3$. The reaction mixture was then extracted with 3 × ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography with 10-30% ethyl acetate in hexanes to afford compound **8** (286 mg, 79%) as an off-white solid.

R_f = 0.45 (Hex/AcOEt 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (dd, *J* = 7.9, 1.5, 1H), 7.97 (dd, *J* = 2.8, 1.2, 1H), 7.63 (ddd, *J* = 8.6, 7.4, 1.6, 1H), 7.47 (d, *J* = 8.3, 1H), 7.44 – 7.38 (m, 2H), 7.35 (t, *J* = 7.5, 1H), 6.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.4, 159.5, 156.0, 134.1, 133.7, 127.4, 126.9, 125.6, 125.2, 125.0, 123.9, 118.0, 107.1; HRMS (ESI) *m/z* calcd for $C_{13}H_9O_2S$ $[M+H]^+$ 229.0318, found 229.0316.

2-Acetylphenyl thiophene-2-carboxylate (**18**)



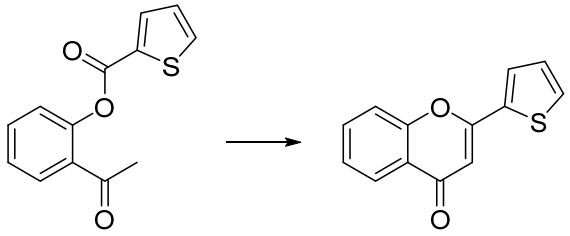
Thiophene-2-carboxylic acid **17** (263 mg, 2.1 mmol) was dissolved in 8 mL anhydrous dichloromethane under argon atmosphere. After addition of 2 drops of dimethylformamide, oxalyl chloride (352 µL, 4.1 mmol) was added slowly, and the resulting mixture was stirred until no more gas evolved.

In a separate flask, 2'-hydroxyacetophenone (1005 µL, 8.2 mmol) was suspended in 5 mL methanol and potassium hydroxide (461 mg, 8.2 mmol) was added. When all the base had dissolved, the solution was dried under reduced vacuum, and resuspended in 8 mL anhydrous dimethylformamide. The thiophene-2-carboxyloyl chloride solution was then poured slowly into this solution, stirring vigorously. After 5 minutes stirring, saturated aqueous NH_4Cl was added, alongside 20 mL of ethyl acetate/toluene 1:1. The organic layer was decanted, washed with a further portion of NH_4Cl then brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography with 0-15% ethyl acetate in hexanes to afford compound **18** (407 mg, 81% yield) as a white solid.

R_f = 0.41 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (dd, *J* = 3.7, 1.1, 1H), 7.85 (dd, *J* = 7.8, 1.3, 1H), 7.69 (dd, *J* = 5.0, 1.0, 1H), 7.57 (td, *J* = 8.1, 1.5, 1H), 7.36 (td, *J* = 7.7, 0.9, 1H), 7.25 (d, *J* = 7.4, 1H), 7.19 (dd, *J* = 4.9, 3.9, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.7, 160.5, 149.0,

135.3, 134.1, 133.5, 132.5, 131.4, 130.4, 128.3, 126.4, 124.0, 30.1; HRMS (ESI) *m/z* calcd for $C_{26}H_{20}NaO_6S_2$ $[2M+Na]^+$ 515.0594, found 515.0597.

2-(Thiophen-2-yl)-4H-chromen-4-one (**9**)



18 **9**

Ester **18** (387 mg, 1.6 mmol) was stirred into 10 mL dichloromethane open to air. Magnesium bromide diethyl etherate (1015 mg, 3.9 mmol) was added, then diisopropylethylamine (816 µL, 4.7 mmol) was added slowly. The reaction was stirred overnight, then quenched by pouring 20 mL of 10% HCl into the reaction vessel. Ethyl acetate (20 mL) was added, and the organic phase was decanted. The aqueous phase was extracted twice more with 10 mL ethyl acetate. The combined organic phases were dried over Na_2SO_4 and dried under reduced pressure. The residue was redissolved in 10 mL methanol, to which was added 2 mL of HCl 37%. The reaction was stirred overnight, then quenched by pouring 30 mL of saturated $NaHCO_3$. The reaction mixture was then extracted with 3 × ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography with 10-30% ethyl acetate in hexanes to afford compound **9** (311 mg, 87%) as a yellow solid.

R_f = 0.40 (Hex/Act 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (dd, *J* = 7.9, 1.3, 1H), 7.69 – 7.58 (m, 2H), 7.51 (d, *J* = 5.0, 1H), 7.45 (d, *J* = 8.4, 1H), 7.35 (t, *J* = 7.5, 1H), 7.12 (dd, *J* = 4.9, 3.9, 1H), 6.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.8, 159.0, 155.8, 135.0, 133.7, 130.3, 128.50, 128.46, 125.6, 125.2, 123.9, 117.9, 106.1; HRMS (ESI) *m/z* calcd for $C_{13}H_9O_2S$ $[M+H]^+$ 229.0318, found 229.0318.

Reaction products of dirchromone and cysteamine

A chromatographic profile (figure S2) was established by dissolving 5 mg of dirchromone in 1 mL dimethylsulfoxide and adding 7 mg of cysteamine. After a few minutes, the reaction mixture was directly injected on the HPLC system described in the general experimental procedures for purity determinations, using the same column and gradient.

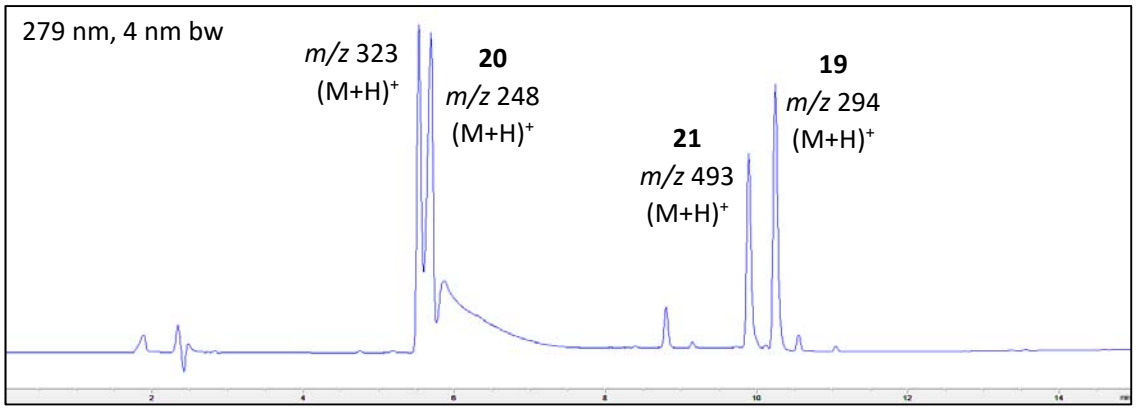
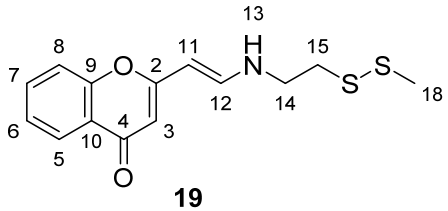


Figure S2. Chromatographic profile of the fresh reaction of dirchromone with 4 eq. cysteamine in dimethylsulfoxide.

To dirchromone (150 mg, 0.64 mmol) suspended in dimethylsulfoxide (2 mL) was added cysteamine (198 mg, 2.6 mmol). The solution was sonicated until all cysteamine was dissolved, which was accompanied by evolution of a mercaptan-like odour and a brownish colour. The reaction mixture was diluted with 25 mL ethyl acetate and washed with 2 × brine and evaporated to dryness. The residue was purified by column chromatography with 15-100% isopropanol in toluene to afford compounds **19-21**. Given partial peak overlaps and tailing of some compounds, the peaks were not fully recovered, and efforts were chiefly made to characterize compounds rather than to establish yields.

(E)-2-(2-((2-(Methyldisulfaneyl)ethyl)amino)vinyl)-4H-chromen-4-one (**19**)



19

R_f = 0.54 (Tol/iPA 4:1; blue fluorescence under 365 nm); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (dd, *J* = 7.9, 1.5, H-5), 7.55 (ddd, *J* = 8.6, 7.2, 1.7, H-7), 7.48 (dd, *J* = 13.4, 8.0, H-12), 7.33 (d, *J* = 8.3, H-8), 7.30 (ddd, *J* = 8.0, 7.1, 0.9, H-6), 5.92 (s, H-3), 5.14 (d, *J* = 13.5, H-11), 3.52 (dd, *J* = 12.3, 6.1, H-14), 2.91 (t, *J* = 6.3, H-15), 2.43 (s, H-18); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.7 (C-4), 166.0 (C-2), 155.8 (C-9), 142.5 (C-12), 132.7 (C-7), 125.6 (C-5), 124.4 (C-6), 124.2 (C-10), 117.2 (CC-8), 103.7 (C-3), 90.2 (C-11), 42.6 (C-14), 36.0 (C-15), 23.2 (C-18); HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO_2S_2$ $[M+H]^+$ 294.0617, found 294.0621.

Compound **19** was isolated as a yellow film, and found to correspond to the formula $C_{14}H_{15}NO_2S_2$ based on the LC-MS-APCI peak $[M+H]^+$ pseudomolecular ion peak at *m/z* = 294. The 2-substituted chromone moiety could readily be assigned on the basis of the analogous structures, with the characteristic olefinic H-3 methine being more shielded than in dirchromone analogs. The latter predictably correlated in HMBC with C-4, C-2 and C-11, which was also quite upfield compared to dirchromones. H-11 and H-12 were part of a spin system, with H-12 showing as a doubled doublet whose coupling constants indicated a (*E*) olefin and further interaction with another proton (concluded to be from the amine). Additionally, H-12 featured a HMBC correlation with the shielded signals of methylene C-14 (showing as a weak peak in 1D experiments, but clearly legible from 2D cross-couplings). H-14 and H-15 are part of a separate spin system. At this point, a strongly shielded methyl (C-18) was left, with no correlation to any other signal of the NMR experiments, alongside the two sulfur atoms: it was therefore concluded that this likely arose from a disulfide bridge, which was consistent with observed chemical shifts. The key correlations are depicted in figure S3.

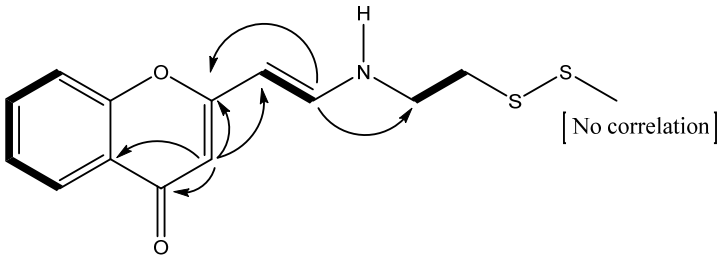
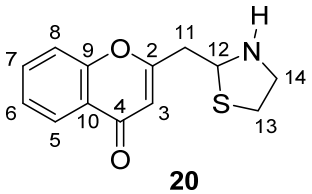


Figure S3. DQF-COSY correlations (in bold) and key HMBC correlations (arrows, H→C) used to elucidate the structure of compound **19**.

2-(Thiazolidin-2-ylmethyl)-4*H*-chromen-4-one (**20**)



20

R_f = 0.37 (Tol/iPA 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (dd, *J* = 8.0, 1.4, H-5), 7.65 (ddd, *J* = 8.6, 7.2, 1.7, H-7), 7.43 (d, *J* = 8.5, H-8), 7.39 (ddd, *J* = 8.0, 7.2, 0.9, H-6), 6.28 (s, H-3), 4.95 (t, *J* = 6.9 Hz, H-12), 3.41 (dt, *J* = 12.4, 5.8, H-14a), 3.16 (dd, *J* = 12.7, 6.5, H-14b), 3.08 (d, *J* = 7.4, H-11a), 3.04 (d, *J* = 6.4, H-11b), 3.02 – 2.97 (m, H-13); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 178.3 (C-4), 165.7 (C-2), 156.6 (C-9), 133.7 (C-7), 125.9 (C-5), 125.3 (C-6), 124.0 (C-10), 118.1 (C-8), 111.5 (C-3), 67.8 (C-12), 51.9 (C-14), 41.9 (C-11), 36.1 (C-13); HRMS (ESI) *m/z* calcd for $C_{13}H_{14}NO_2S$ $[M+H]^+$ 248.0740, found 248.0736.

Compound **20** was isolated as a white solid and found to correspond to the formula $C_{13}H_{13}NO_2S$ based on the LC-MS-APCI peak $[M+H]^+$ pseudomolecular ion peak at *m/z* = 248. As for compound **19**, the chromone moiety was easily assigned by analogy with other derivatives. Olefinic H-3 showed HMBC correlations with C-4, C-10, C-2 and C-11, the latter corresponding to a methylene and therefore saturated compared to the parent structure. H-11 was part of a spin system with

the methine H-12, and the latter was likely chiral given the differentiation in signals associated to the two protons H-11. Two other vicinal methylenes, H-13 and H-14, both exhibited HMBC correlation with C-11. Based on the structure of compound **19**, it was envisioned that compound **20** could arise from the Michael addition of the terminal thiol of cysteamine on the lateral chain alkene instead of its reduction with another thiol in the reaction media, suggesting a structure that was consistent with observed correlations. Methylenes H-13 and H-14 were respectively assigned based on their shielding, with the proximity of the amine leading to downfield signals for position 14. The key correlations are depicted in figure S4.

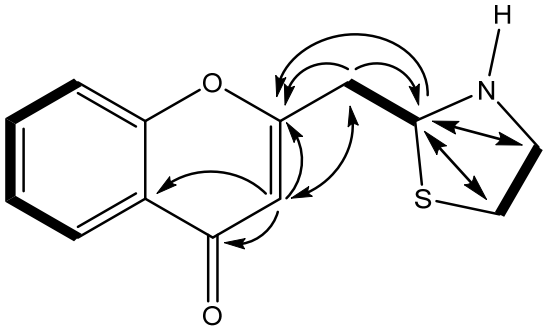
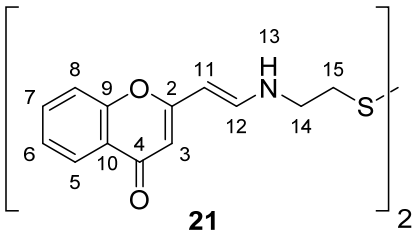


Figure S4. DQF-COSY correlations (in bold) and key HMBC correlations (arrows, H→C) used to elucidate the structure of compound **20**.

2,2'-((1*E*,1'*E*)-((disulfanediylbis(ethane-2,1-diyl))bis(azanediyl))bis(ethene-2,1-diyl))bis(4*H*-chromen-4-one) (**21**)



21

R_f = 0.28 (Tol/iPA 4:1; blue fluorescence under 365 nm); ^{1}H NMR (400 MHz, C_6D_5N) δ: 8.48 (dd, *J* = 8.0, 2.0, H-5), 7.88 (dd, *J* = 13.5, 8.0, H-12), 7.51 (ddd, *J* = 8.3, 7.1, 1.9, H-7), 7.35 (dd, *J* = 8.2, 1.9, H-8), 7.29 (ddd, *J* = 8.0, 7.1, 1.4, H-6), 6.30 (s, H-3), 5.39 (d, *J* = 13.5, H-11), 3.52 (m, H-14), 3.07 (t, *J* = 6.5, H-15); ^{13}C NMR (100 MHz, C_6D_5N) δ: 176.7 (C-4), 167.1 (C-2), 156.1 (C-9), 144.1* (C-12), 132.7 (C-7), 125.6 (C-5), 124.9 (C-10), 124.5 (C-6), 117.6 (C-8), 102.7 (C-3), 88.3 (C-11), 43.0* (C-14), 37.2* (C-15); HRMS (ESI) *m/z* calcd for $C_{26}H_{25}N_2O_4S_2$ $[M+H]^+$ 493.1250, found 493.1262.

**Not visible in DEPT135 owing to peak broadening; visible in 2D experiments*

Compound **21** was isolated as a yellow solid and found to correspond to the formula $C_{26}H_{24}N_2O_4S_2$ based on the LC-MS-APCI peak $[M+H]^+$ pseudomolecular ion peak at *m/z* = 493. As for compounds **19-20**, the chromone moiety was easily assigned by analogy with other derivatives. The compound was only poorly soluble in both deuterated DMSO and pyridine, and the side-chain carbon signals did not relax well. Nevertheless, 2D NMR experiments cross peaks allowed to situate them satisfactorily. Examination of the correlations pointed toward a similar structure to

19, without the lone methyl group at the end of the sidechain. Based on the molecular mass, it was concluded that **21** was a symmetrical dimer assembled by a central disulfide bridge, which was consistent with the other structures. The key correlations are depicted in figure S5.

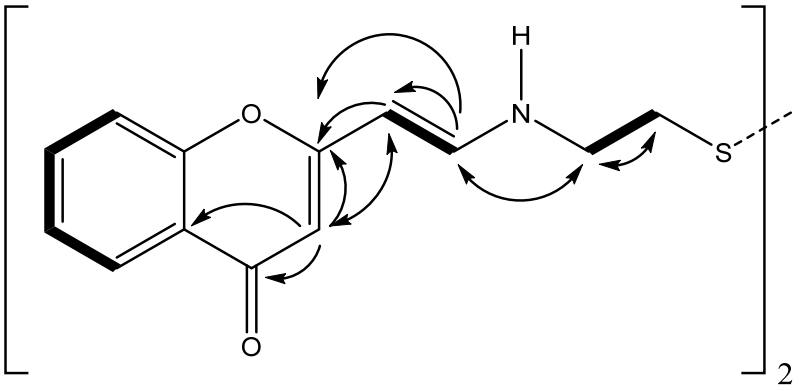


Figure S5. DQF-COSY correlations (in bold) and key HMBC correlations (arrows, H→C) used to elucidate the structure of compound **21**.

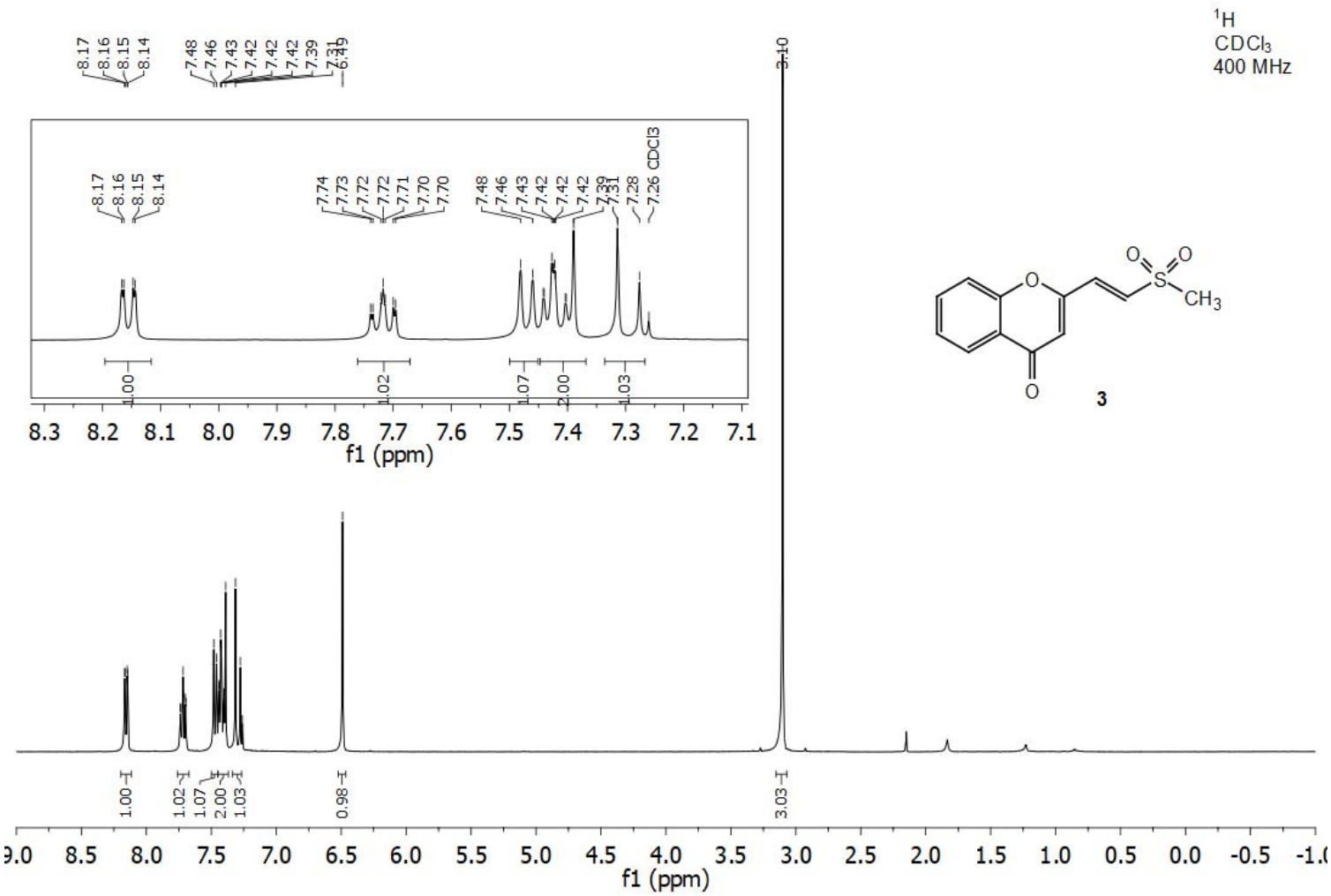
III. References

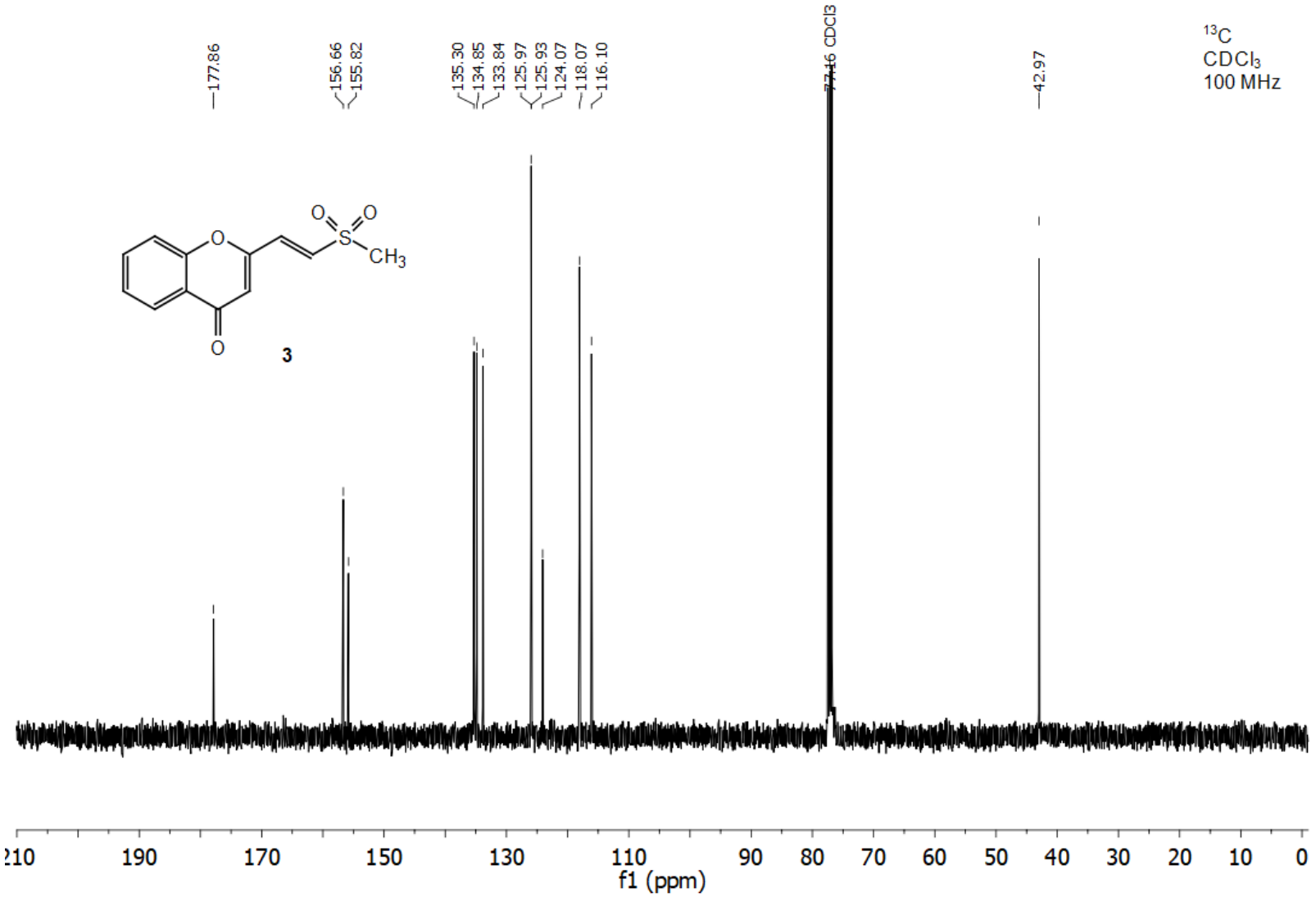
(1) Rago, R.; Mitchen, J.; Wilding, G. DNA Fluorometric Assay in 96-Well Tissue Culture Plates Using Hoechst 33258 after Cell Lysis by Freezing in Distilled Water. *Anal. Biochem.* **1990**, *191* (1), 31–34.

(2) St-Gelais, A.; Alsarraf, J.; Legault, J.; Gauthier, C.; Pichette, A. Soft-Enolization Baker-Venkataraman Rearrangement Enabled Total Synthesis of Dirchromones and Related 2-Substituted Chromones. *Org. Lett.* **2018**, *20* (23), 7424–7428.

(3) Yu, J.-Q.; Corey, E. J. A Mild, Catalytic, and Highly Selective Method for the Oxidation of α,β-Enones to 1,4-Enediones. *J. Am. Chem. Soc.* **2003**, *125* (11), 3232–3233.

IV. NRM spectra

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CDCl3
100 MHz
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O
O
S
CH3
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20
10
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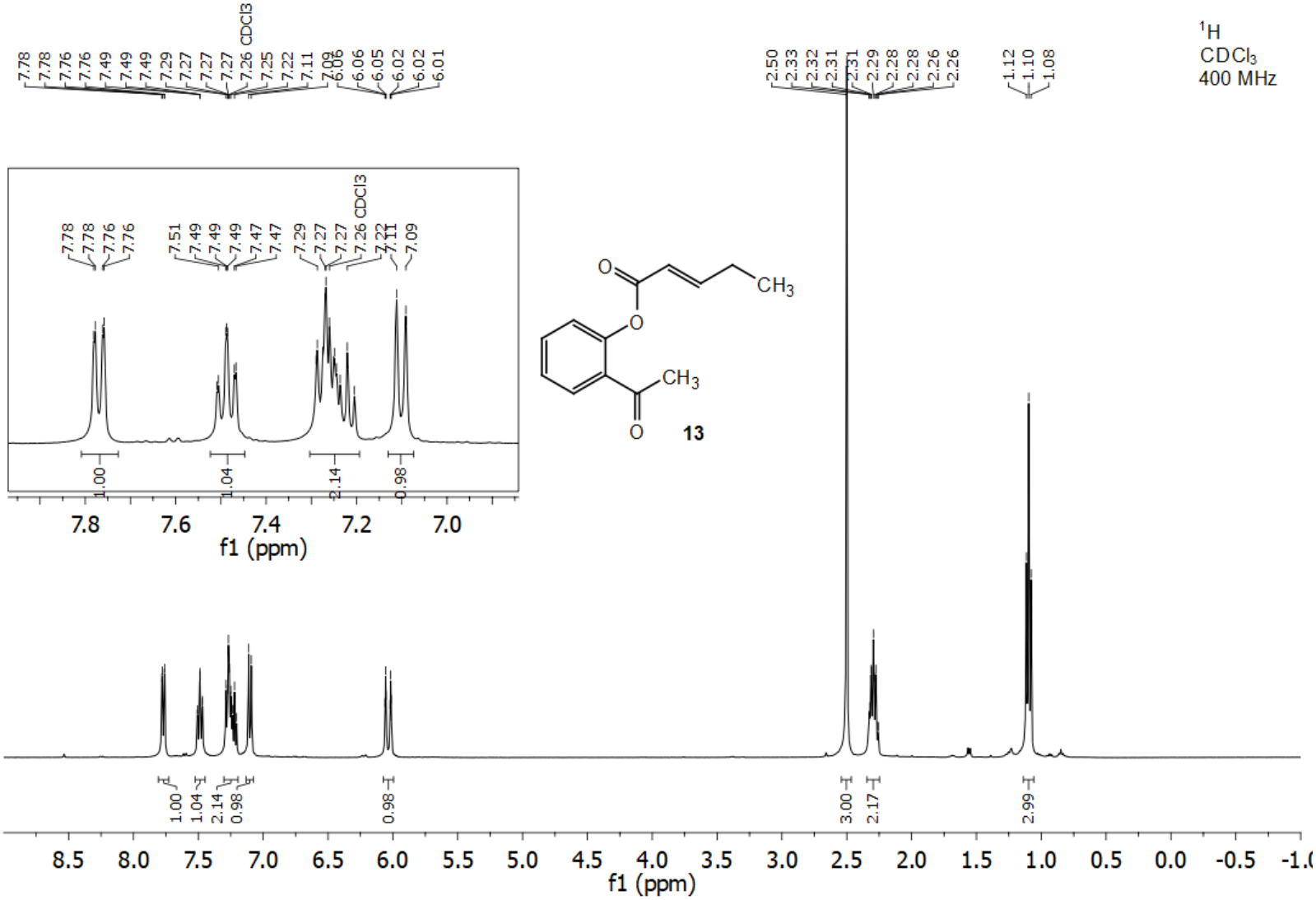
f1 (ppm)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13
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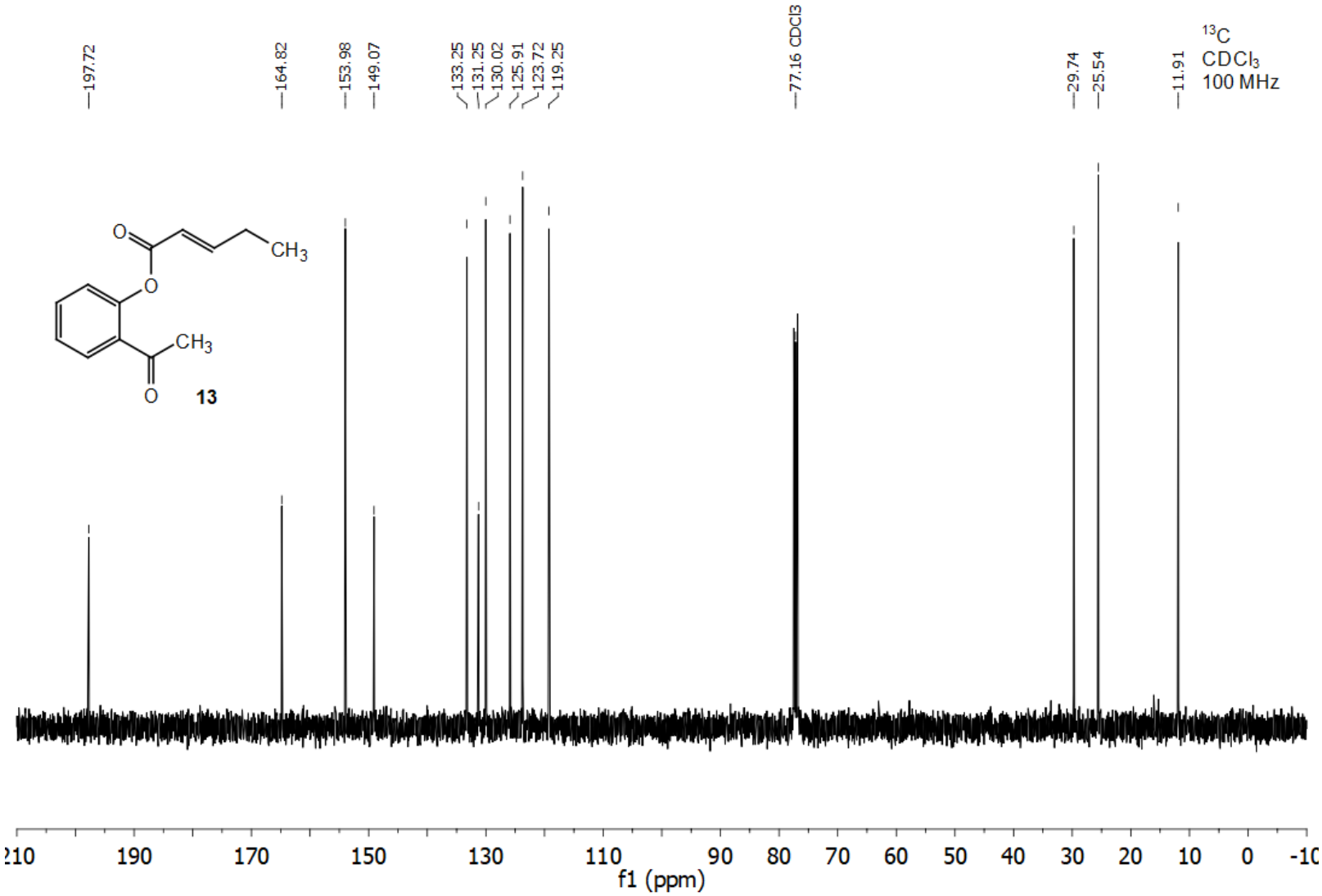
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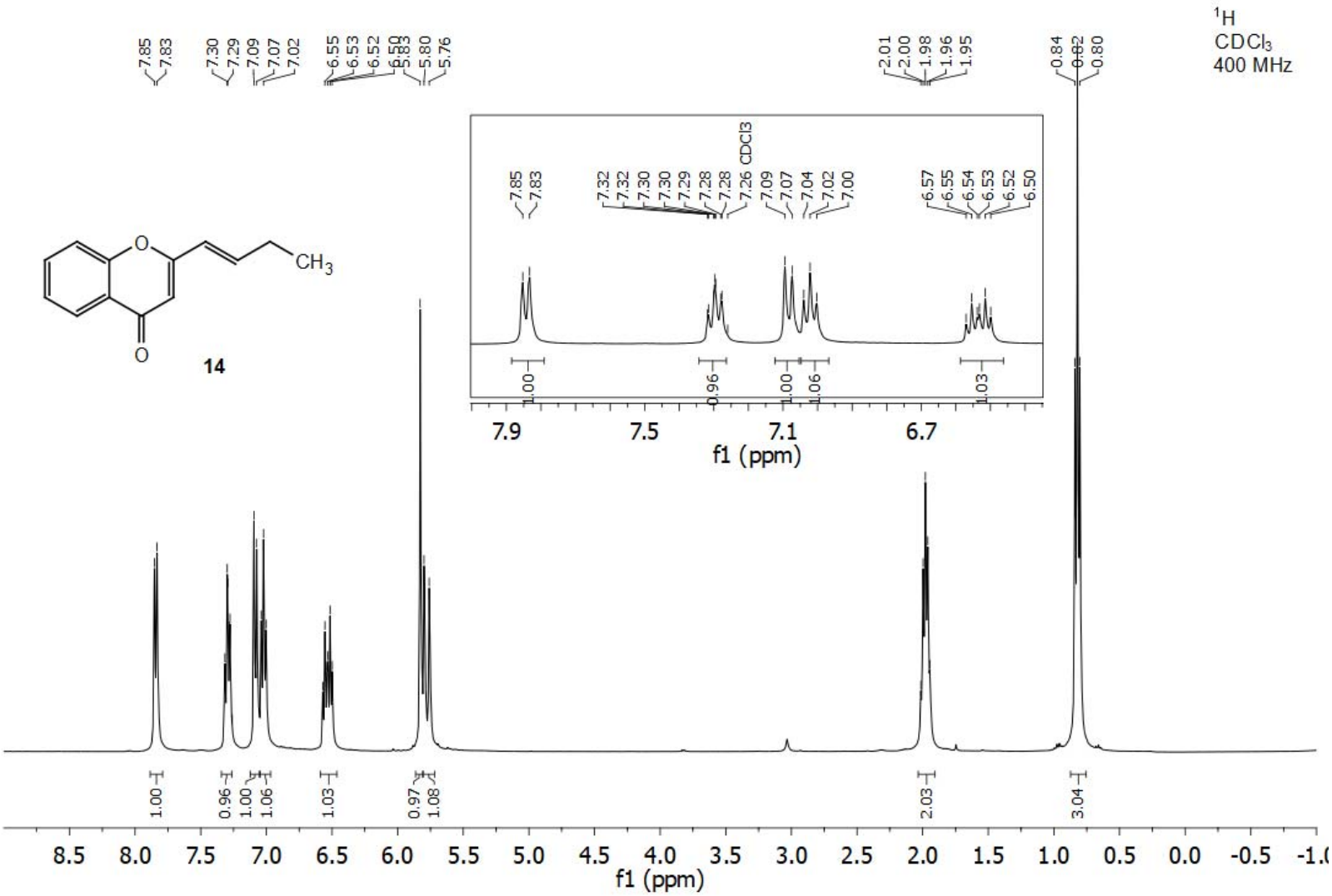
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f1 (ppm)
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CH_3
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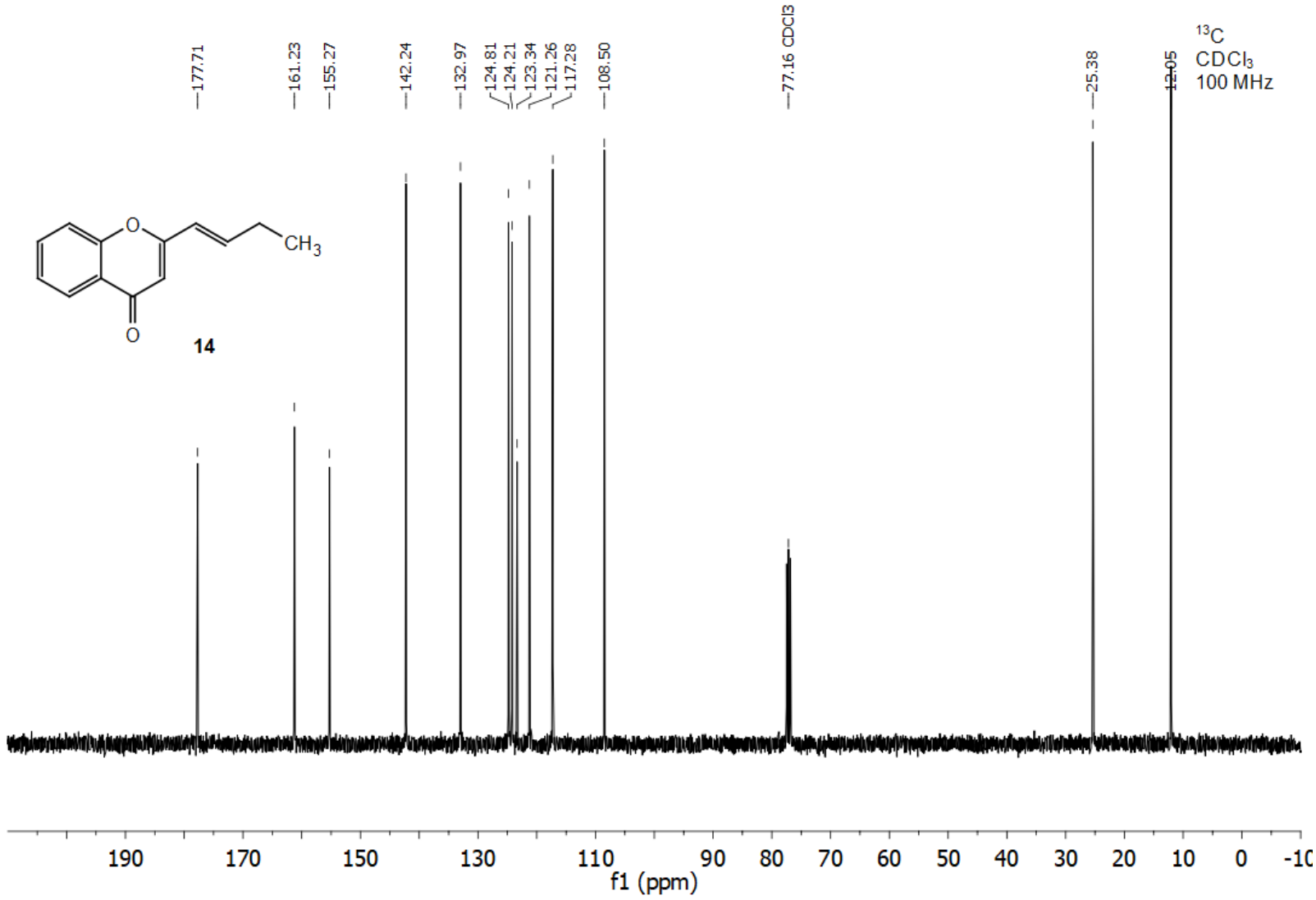
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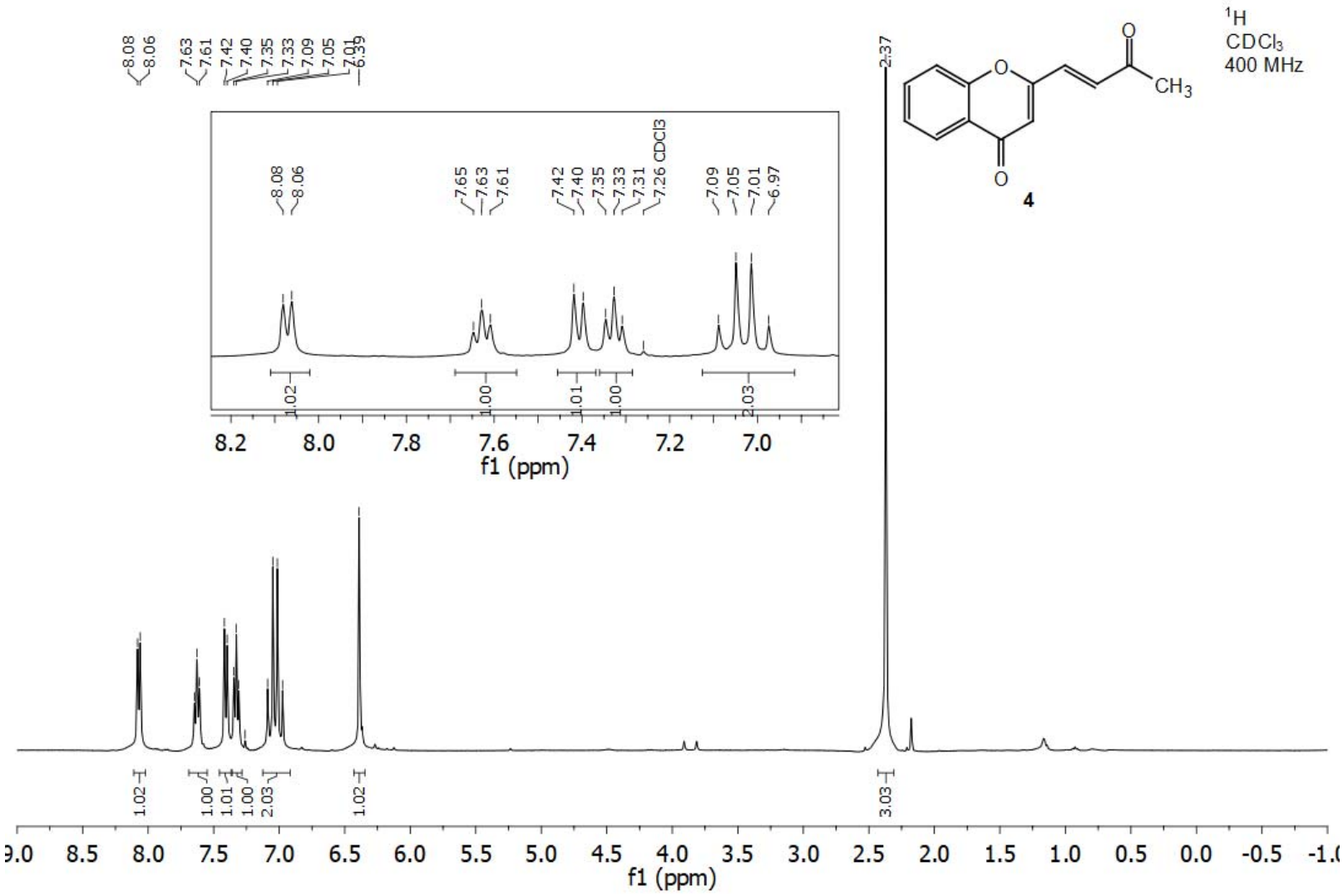
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2.03
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3.03
f1 (ppm)
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7.61
7.42
7.40
7.35
7.33
7.31
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7.05
7.01
6.97
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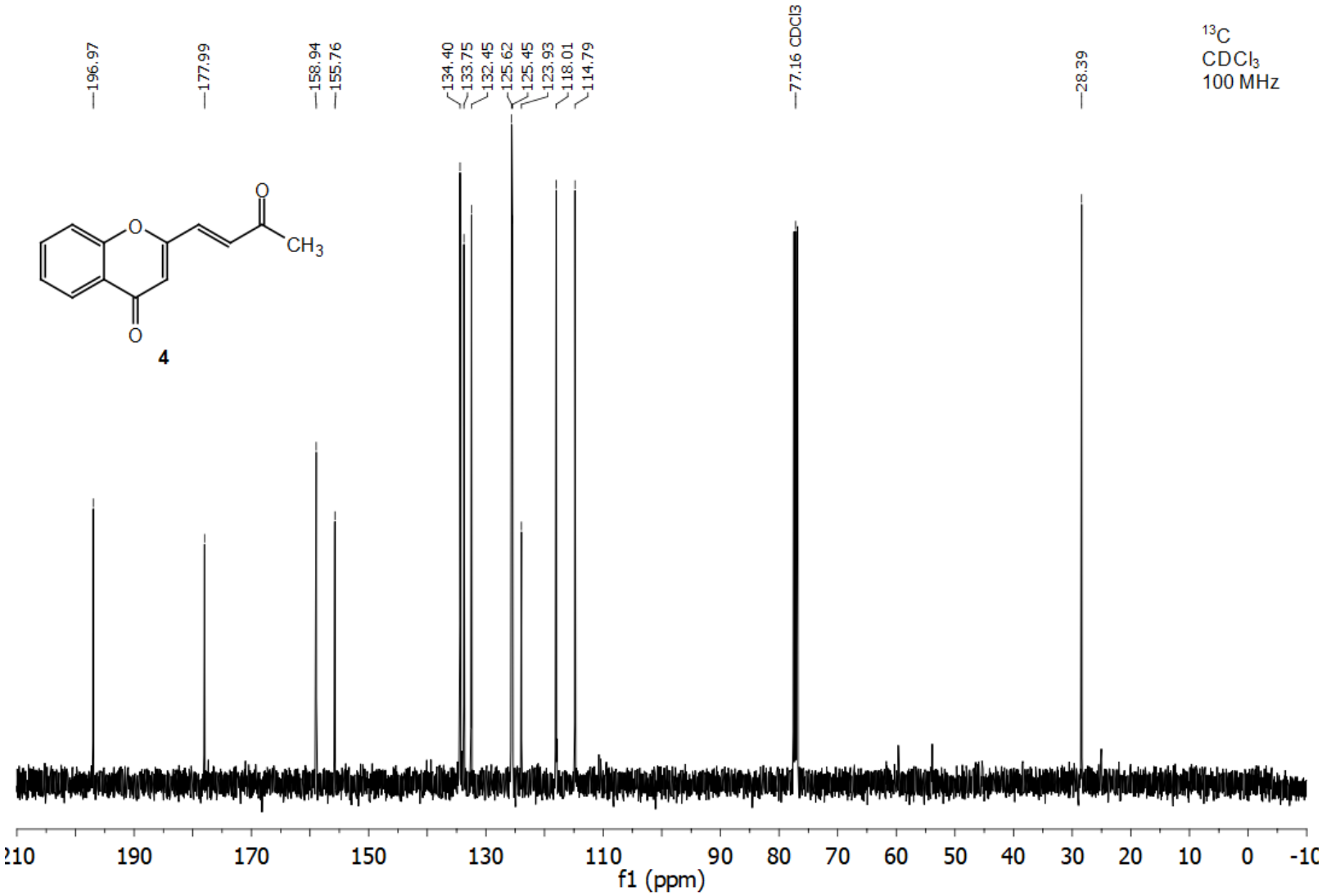
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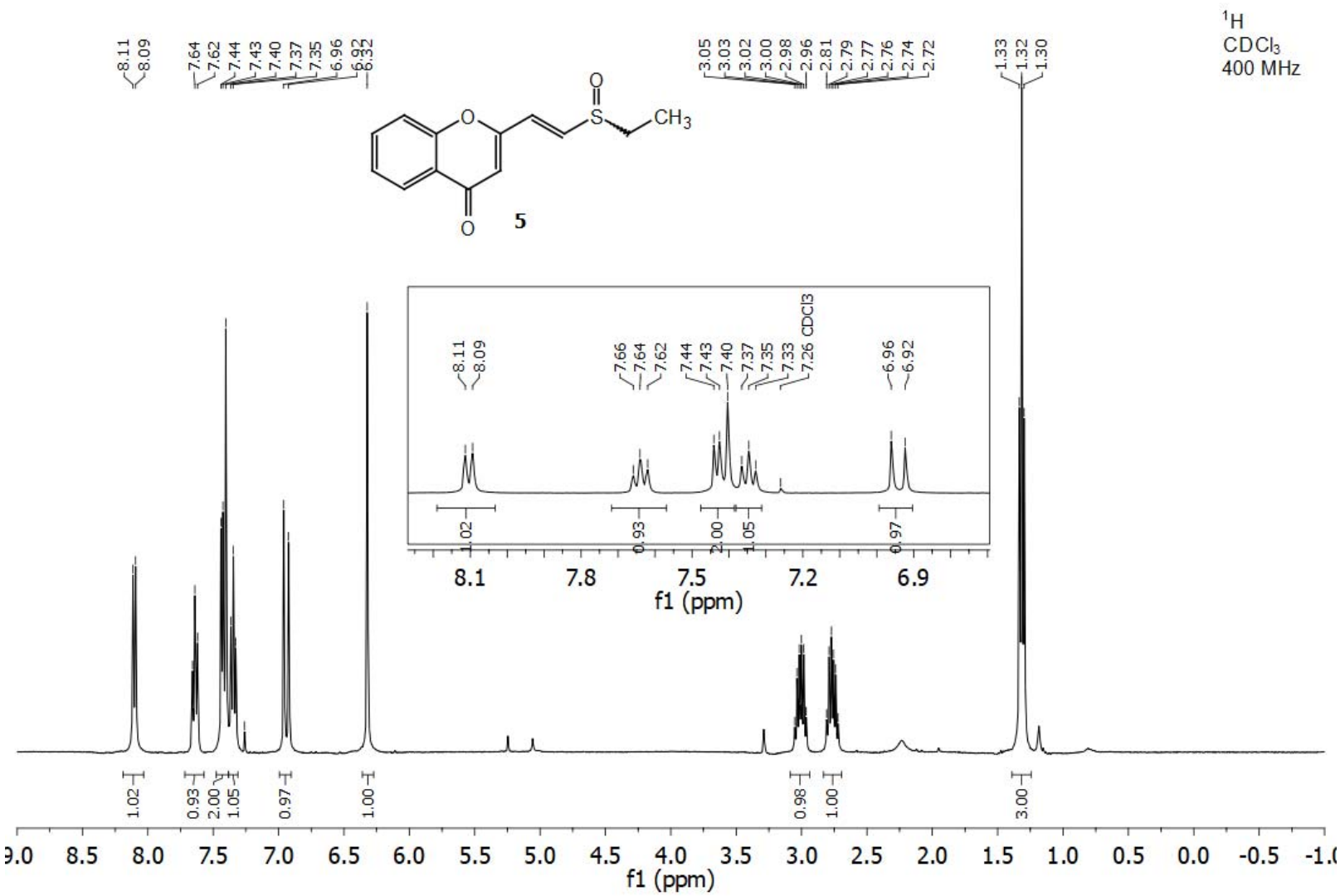
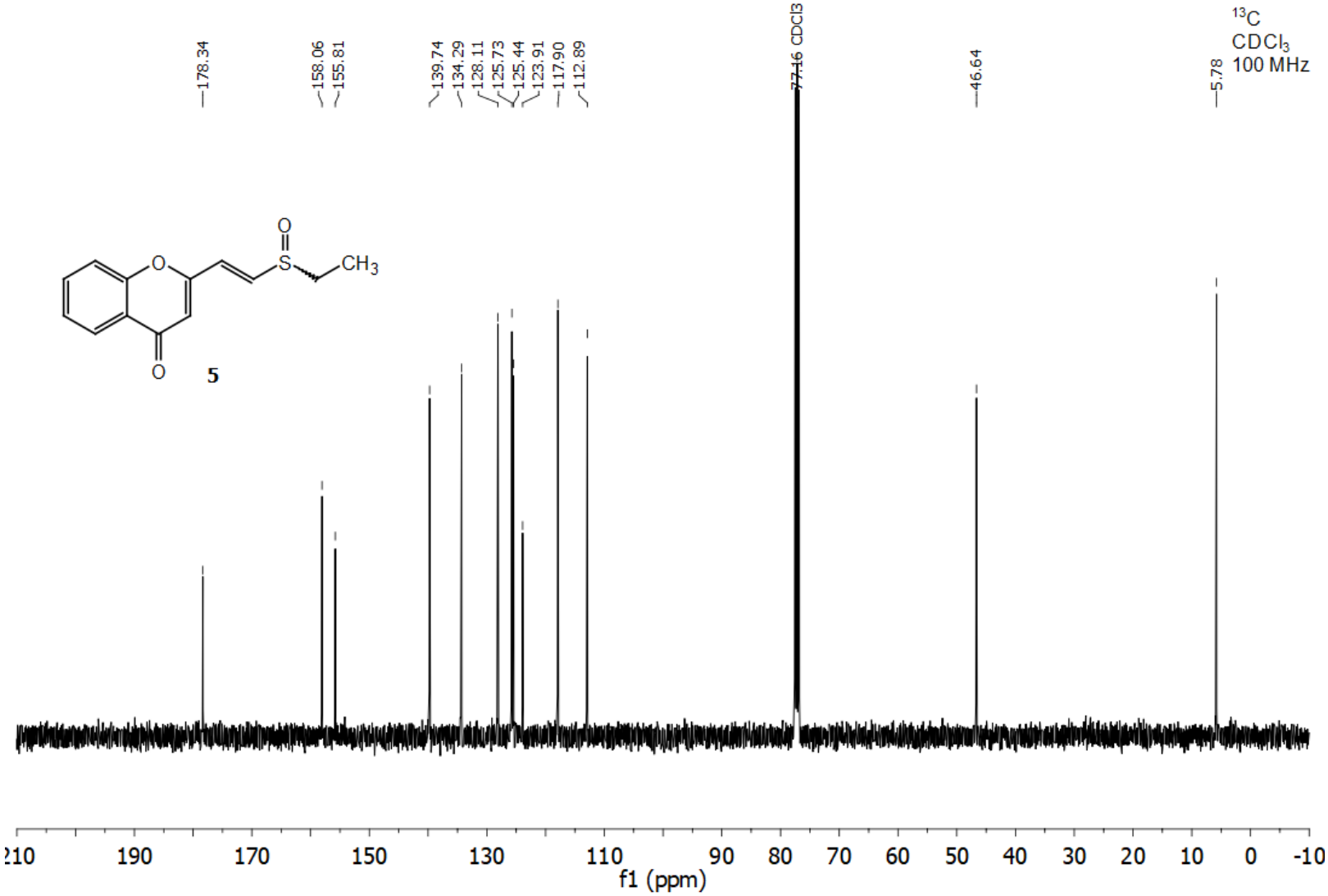
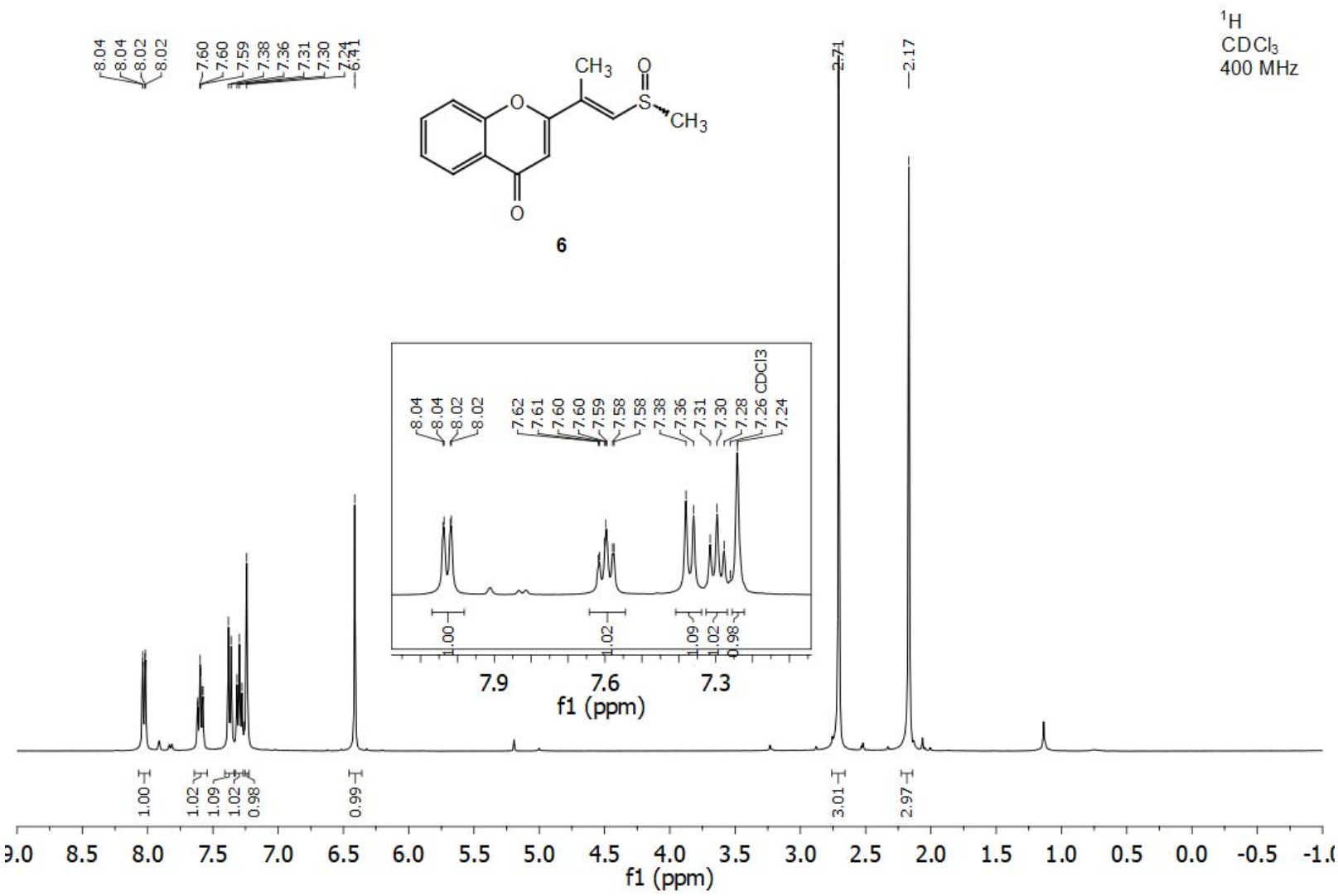
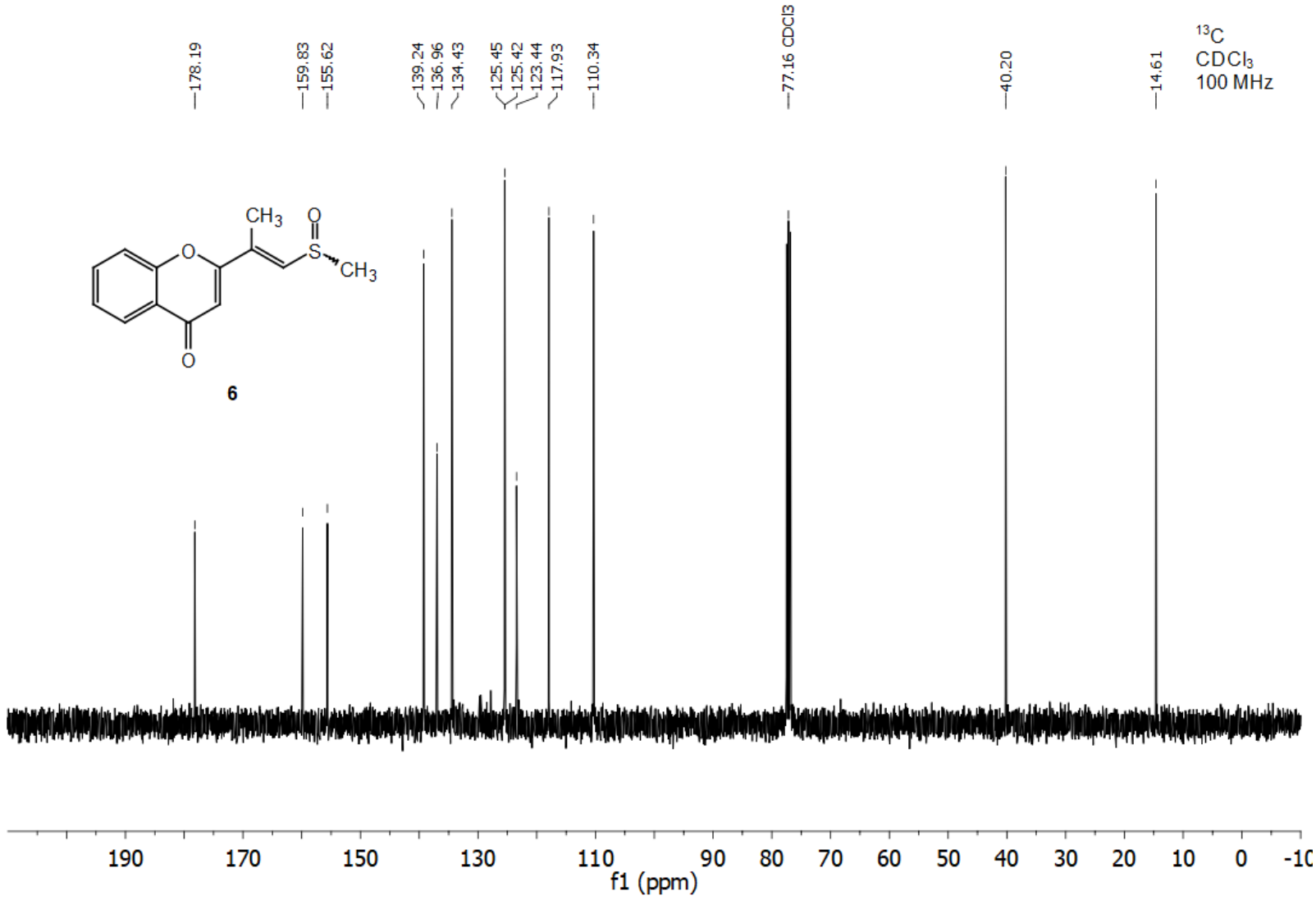
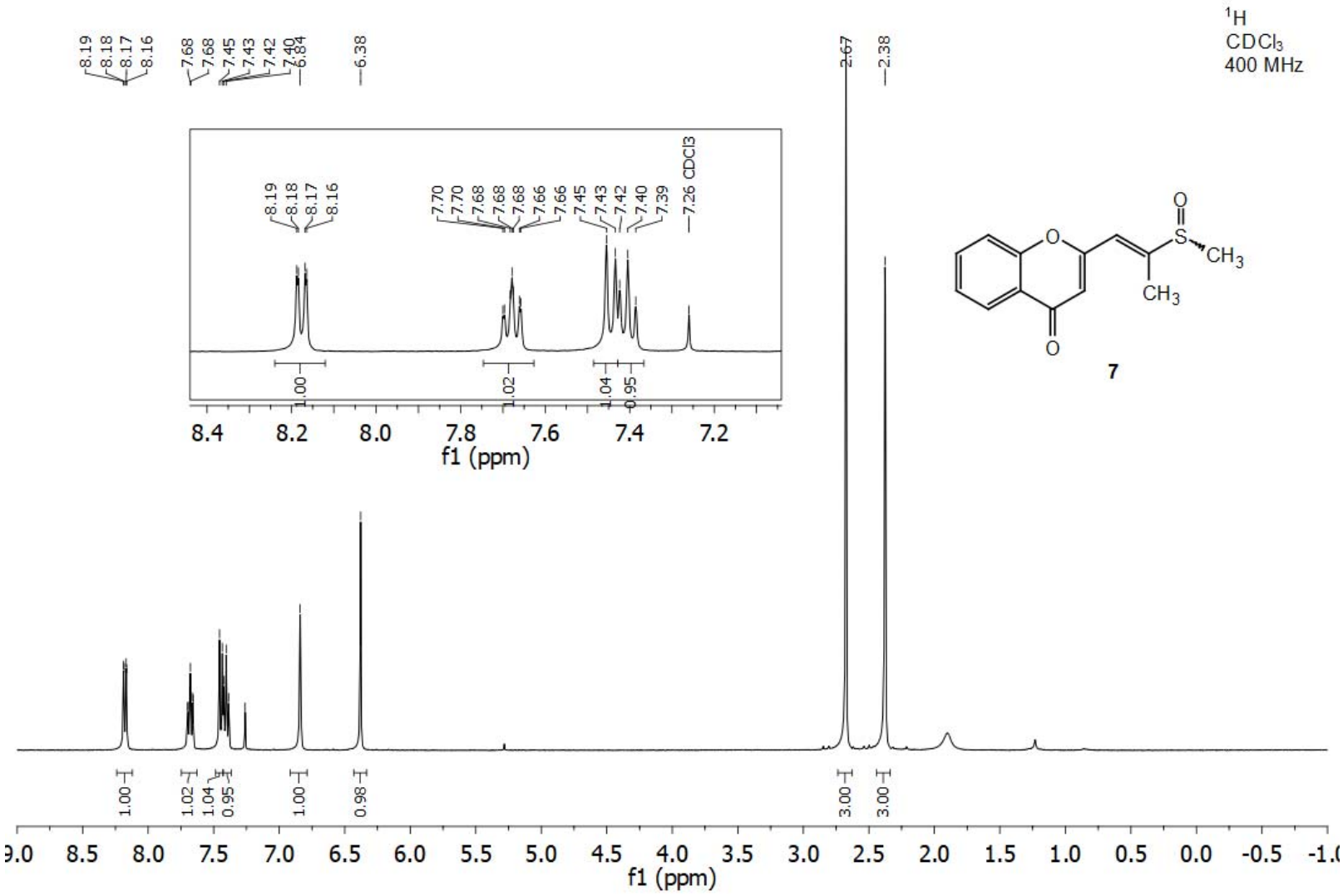
-10
f1 (ppm)

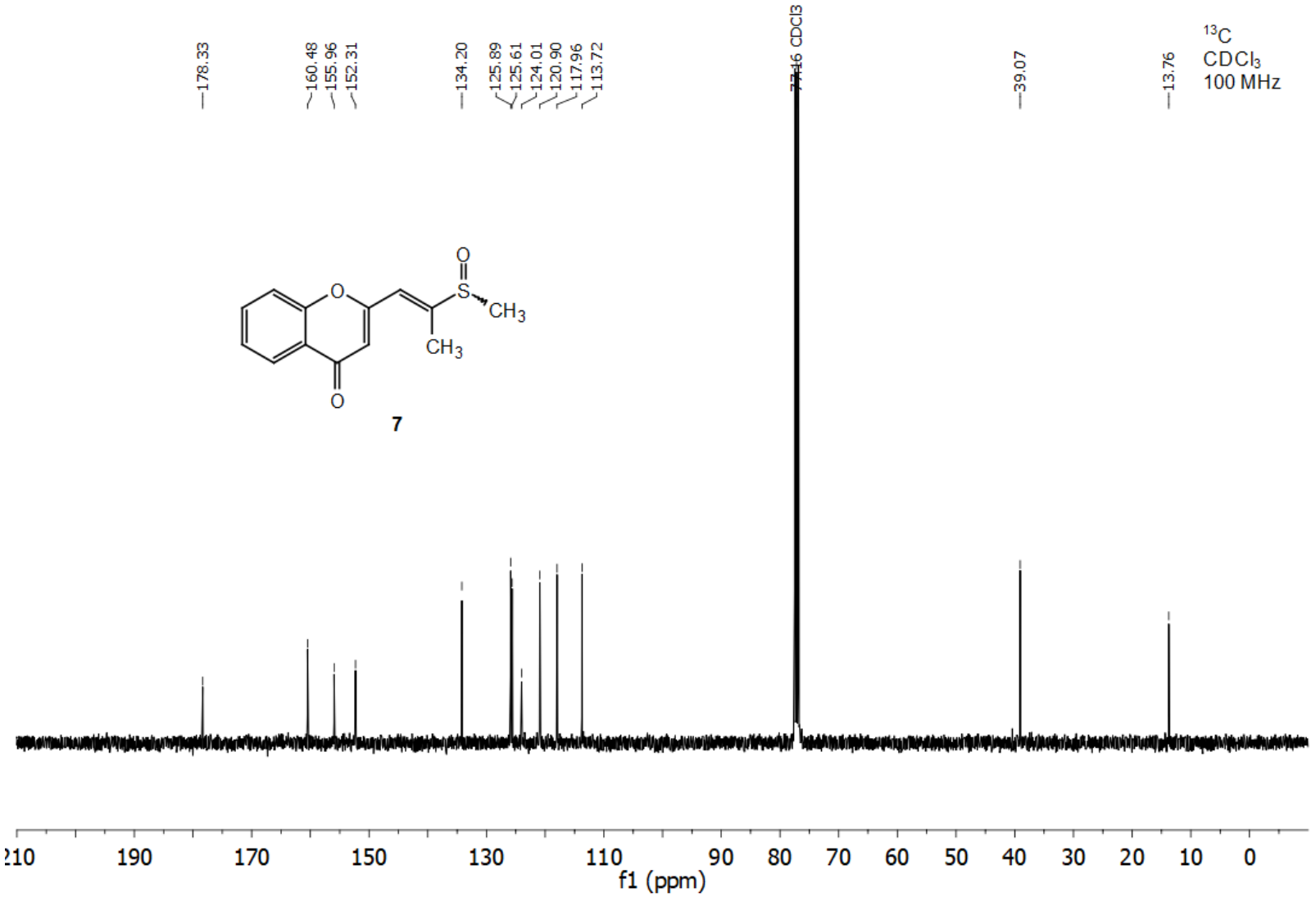

1H
CDCl3
400 MHz
8.11
8.09
7.64
7.62
7.44
7.43
7.40
7.37
7.35
6.96
6.92
6.32
3.05
3.03
3.02
3.00
2.98
2.96
2.81
2.79
2.77
2.76
2.74
2.72
1.33
1.32
1.30
O
S
CH3
O
O
5
7.66
7.33
7.26 CDCl3
1.02
0.93
2.00
1.05
0.97
0.98
1.00
3.00
f1 (ppm)

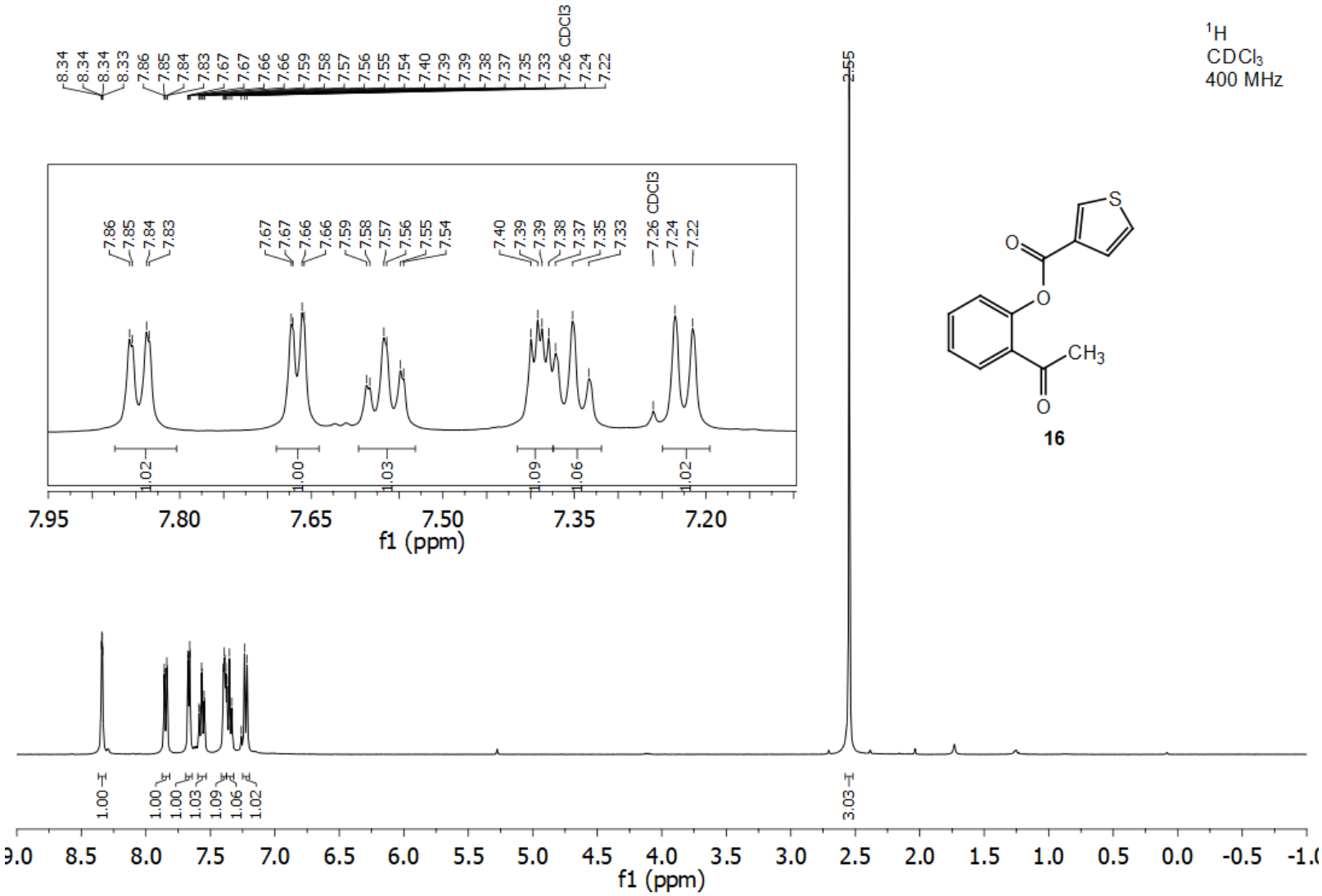

178.34
158.06
155.81
139.74
134.29
128.11
125.73
125.44
123.91
117.90
112.89
77.16 CDCl3
46.64
5.78
13C
CDCl3
100 MHz
O
S
CH3
O
O
5
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

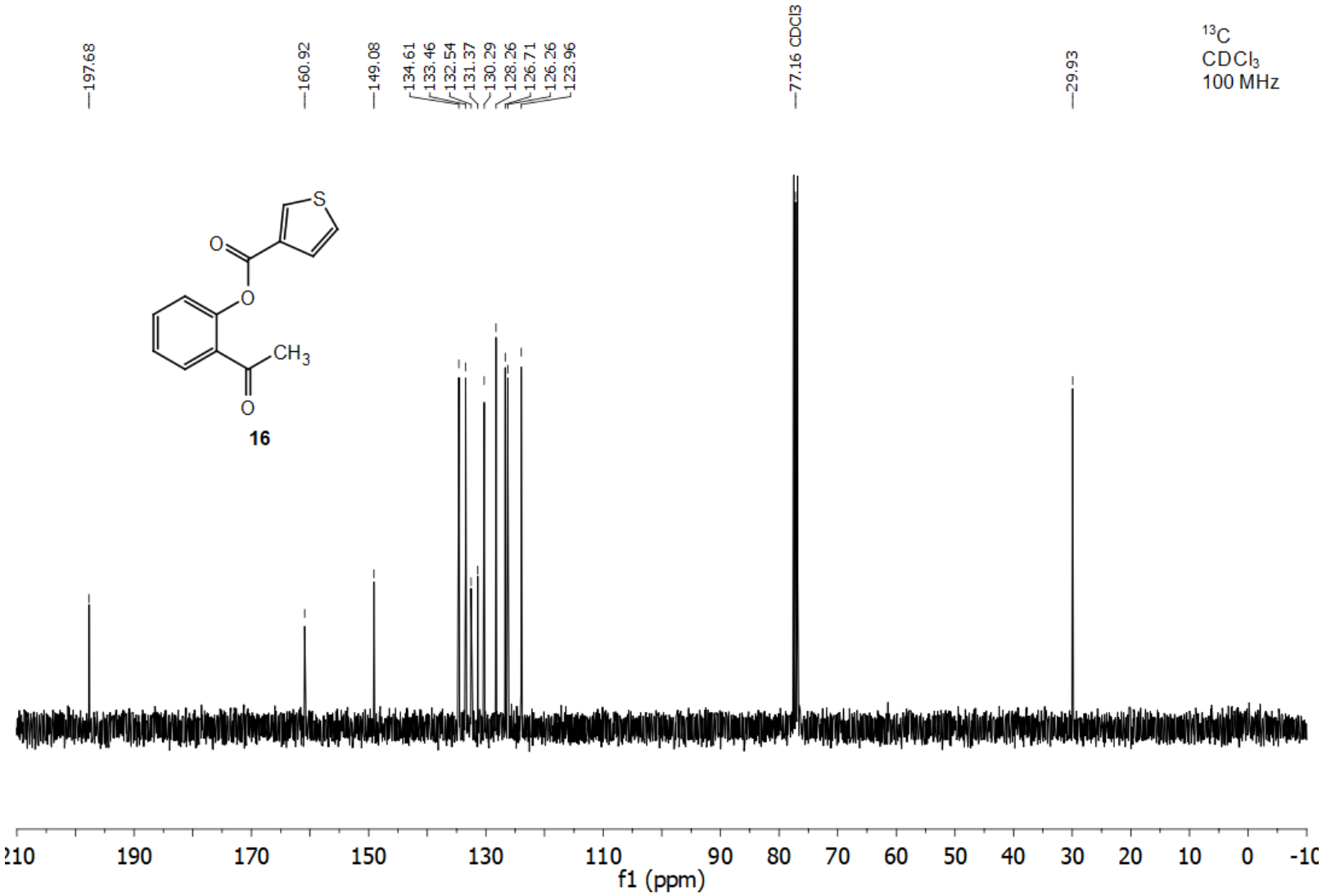

1H
CDCl3
400 MHz
6
f1 (ppm)

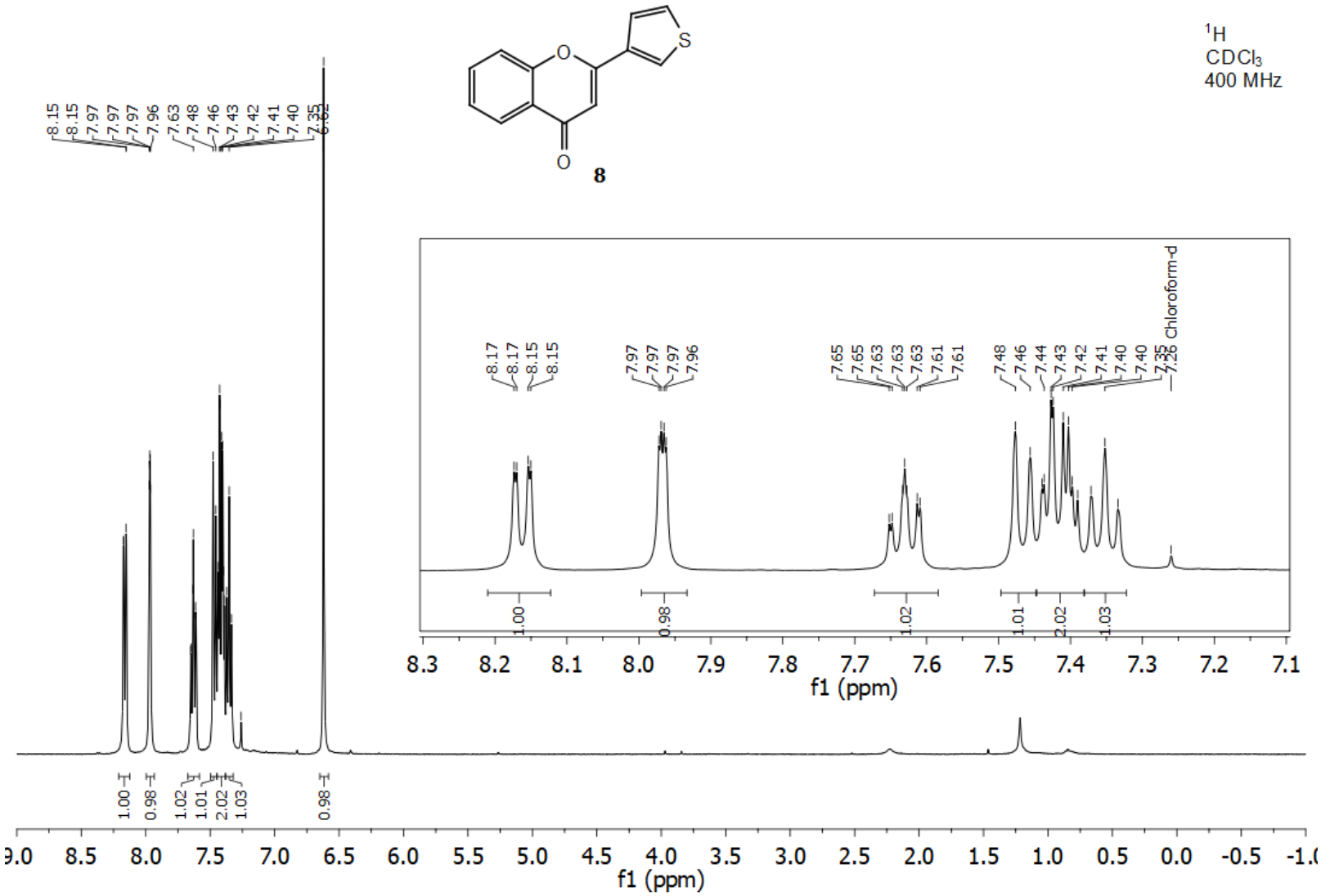

178.19
159.83
155.62
139.24
136.96
134.43
125.45
125.42
123.44
117.93
110.34
77.16 CDCl3
40.20
14.61
13C
CDCl3
100 MHz
CH3
O
S
CH3
O
O
6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

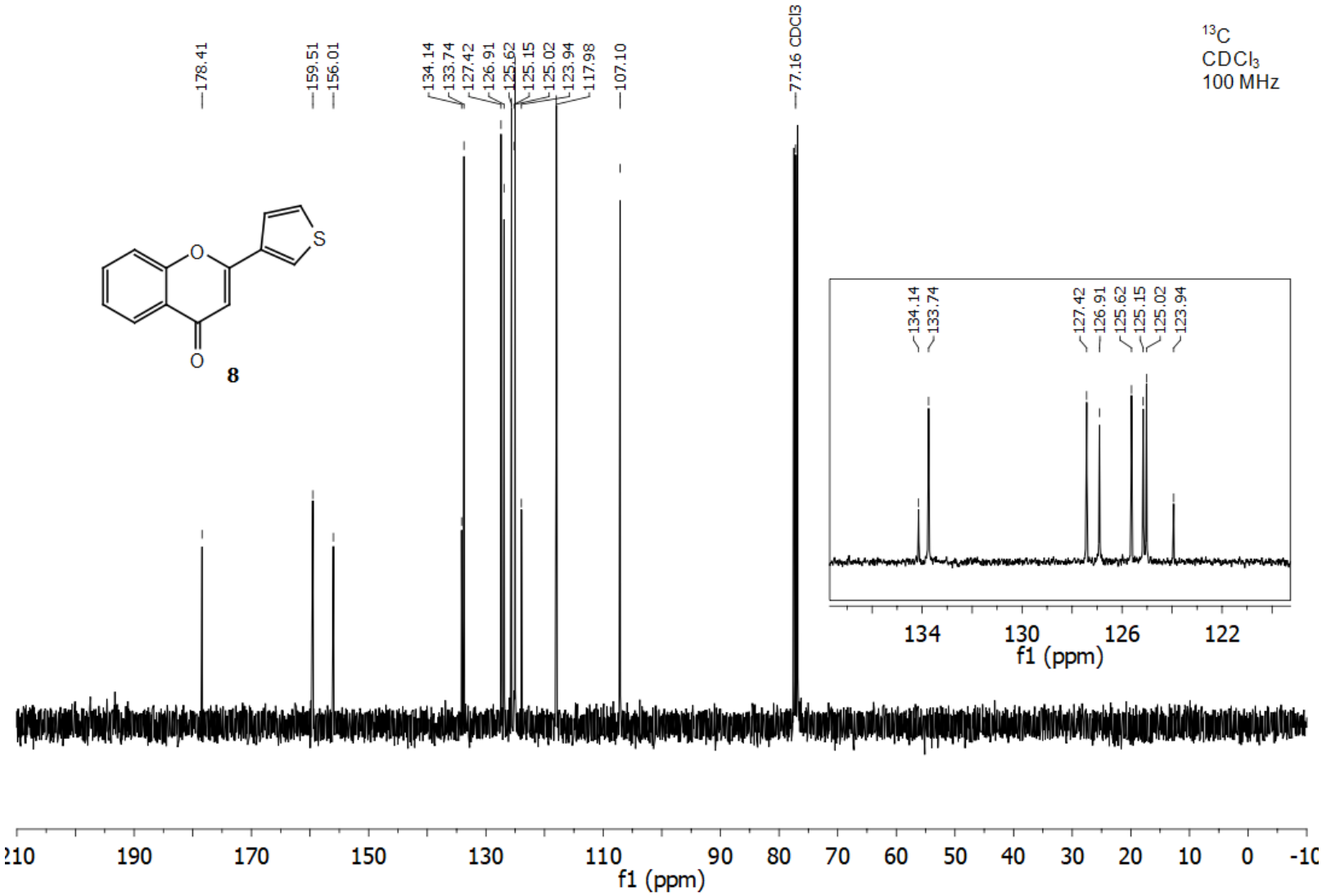

1H
CDCl3
400 MHz
8.19
8.18
8.17
8.16
7.68
7.68
7.45
7.43
7.42
7.40
6.84
6.38
2.67
2.38
7.70
7.70
7.68
7.68
7.68
7.66
7.45
7.43
7.42
7.40
7.39
7.26 CDCl3
1.00
1.02
1.04
0.95
f1 (ppm)
1.00
1.02
1.04
0.95
1.00
0.98
3.00
3.00
f1 (ppm)
O
S
CH3
CH3
O
O
7

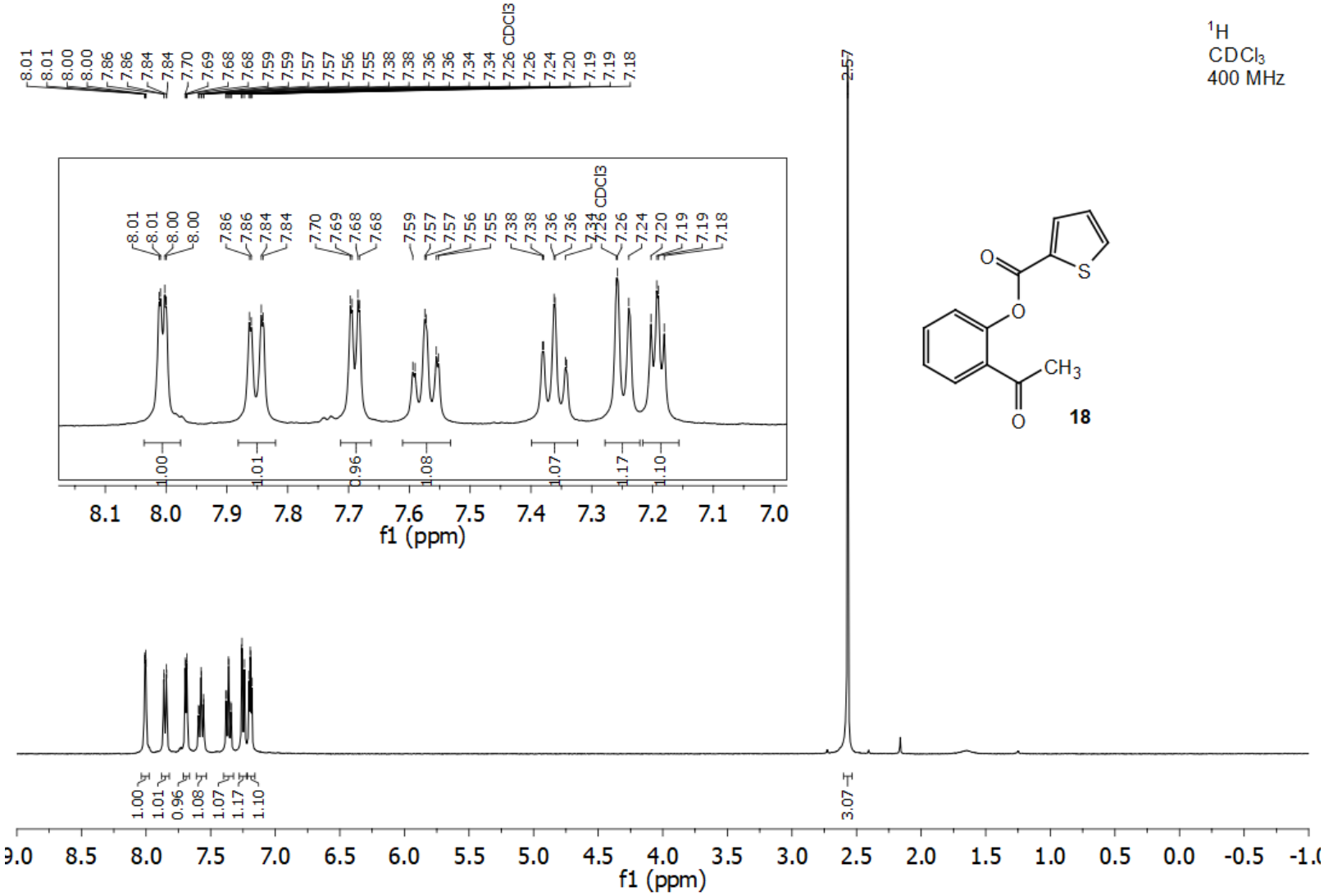

178.33
160.48
155.96
152.31
134.20
125.89
125.61
124.01
120.90
117.96
113.72
77.46 CDCl3
39.07
13.76
13C
CDCl3
100 MHz
O
S
CH3
CH3
O
O
7
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

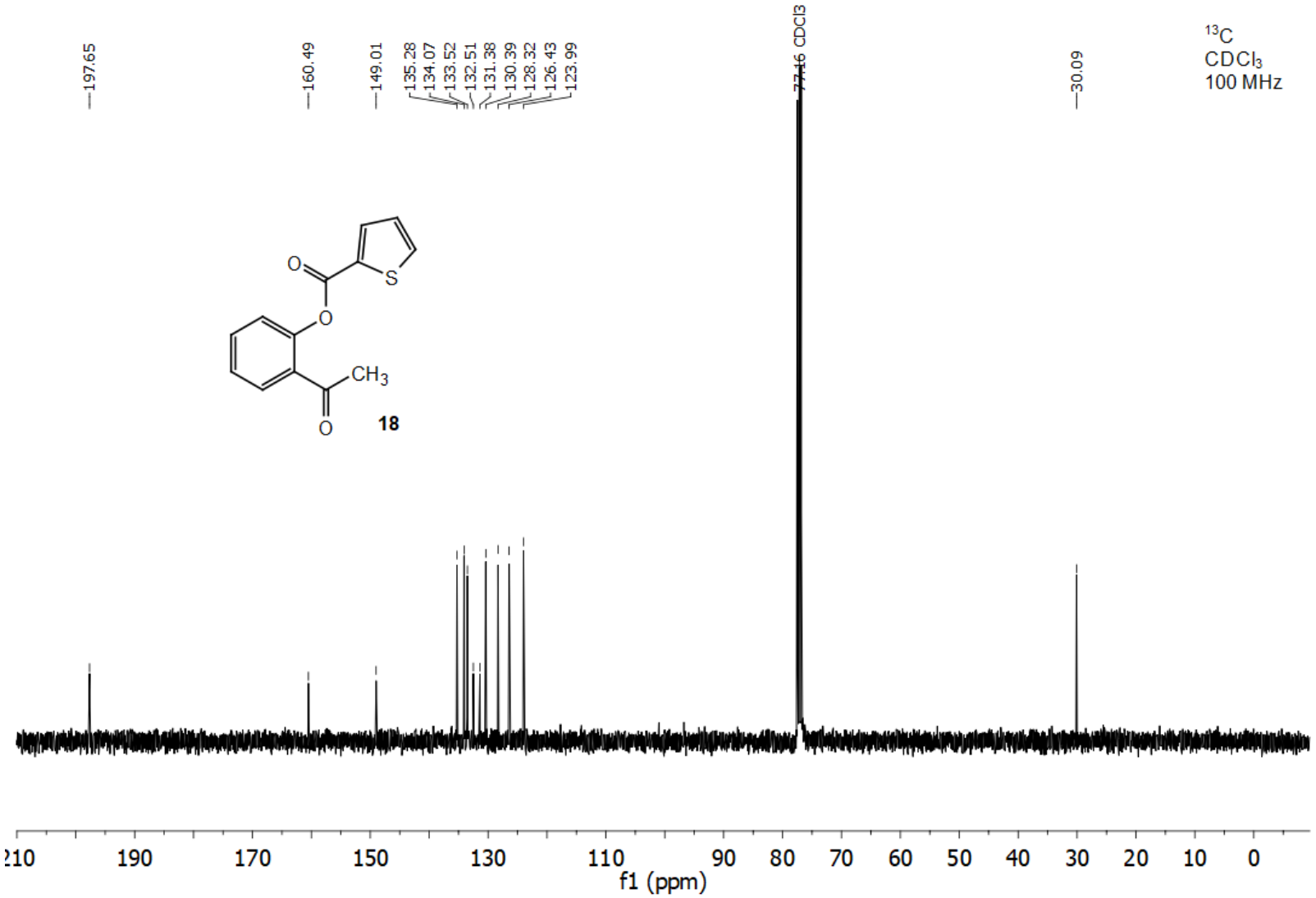

^{1}H
$CDCl_3$
400 MHz
16
f1 (ppm)

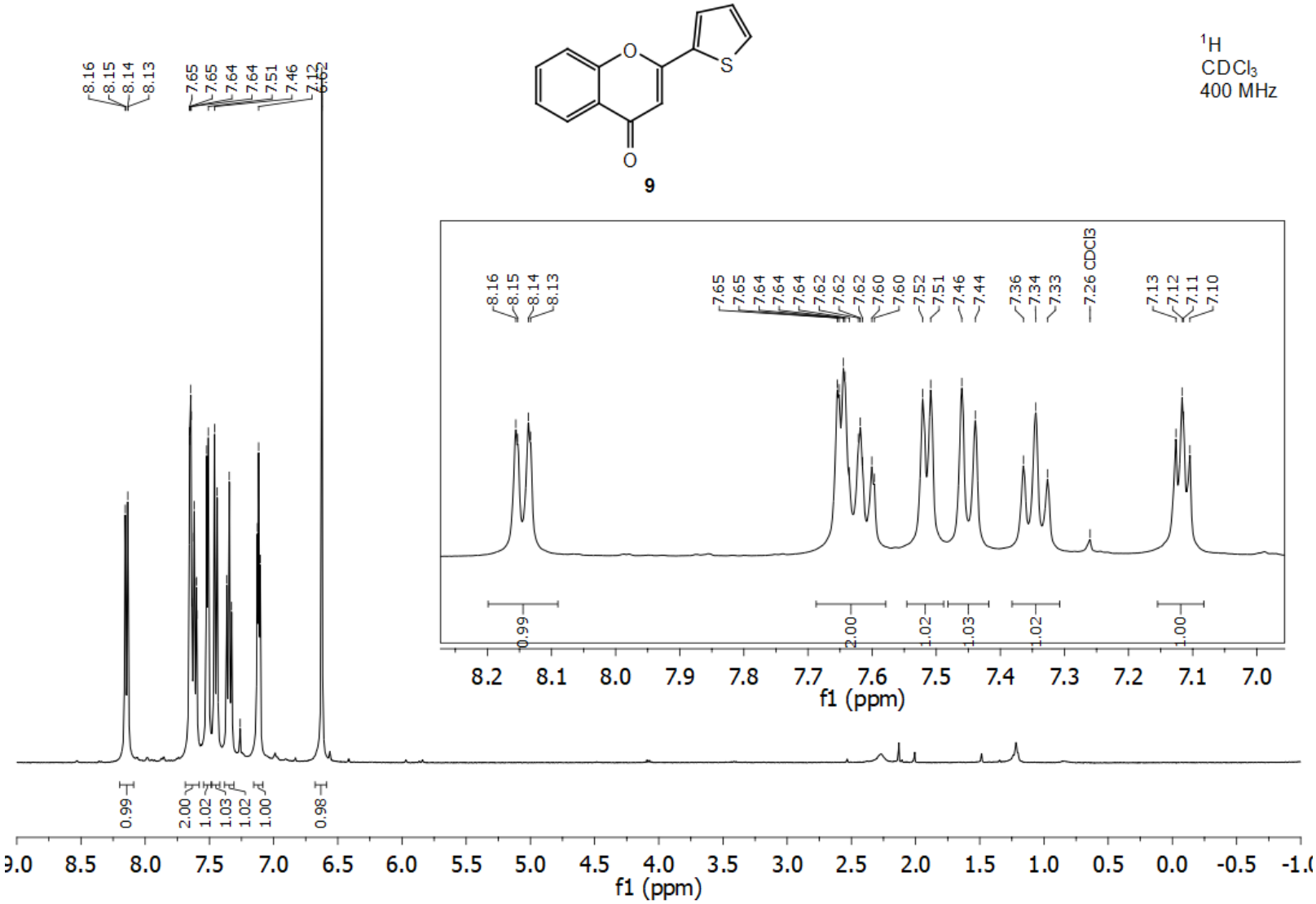

197.68
160.92
149.08
134.61
133.46
132.54
131.37
130.29
128.26
126.71
126.26
123.96
77.16 CDCl3
29.93
13C
CDCl3
100 MHz
S
O
O
CH3
O
16
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

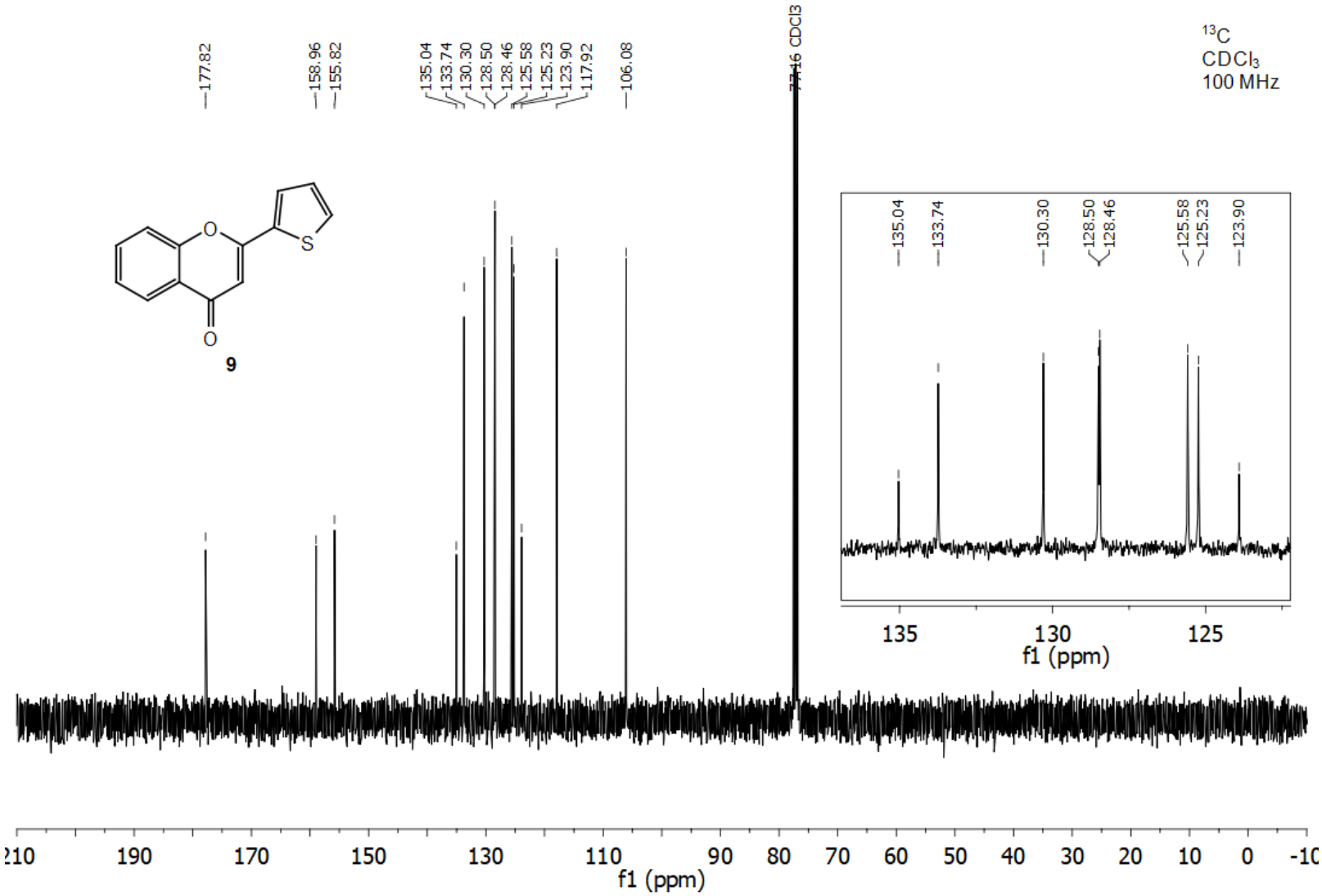

8
^{1}H
$CDCl_3$
400 MHz
Chloroform-d
f1 (ppm)

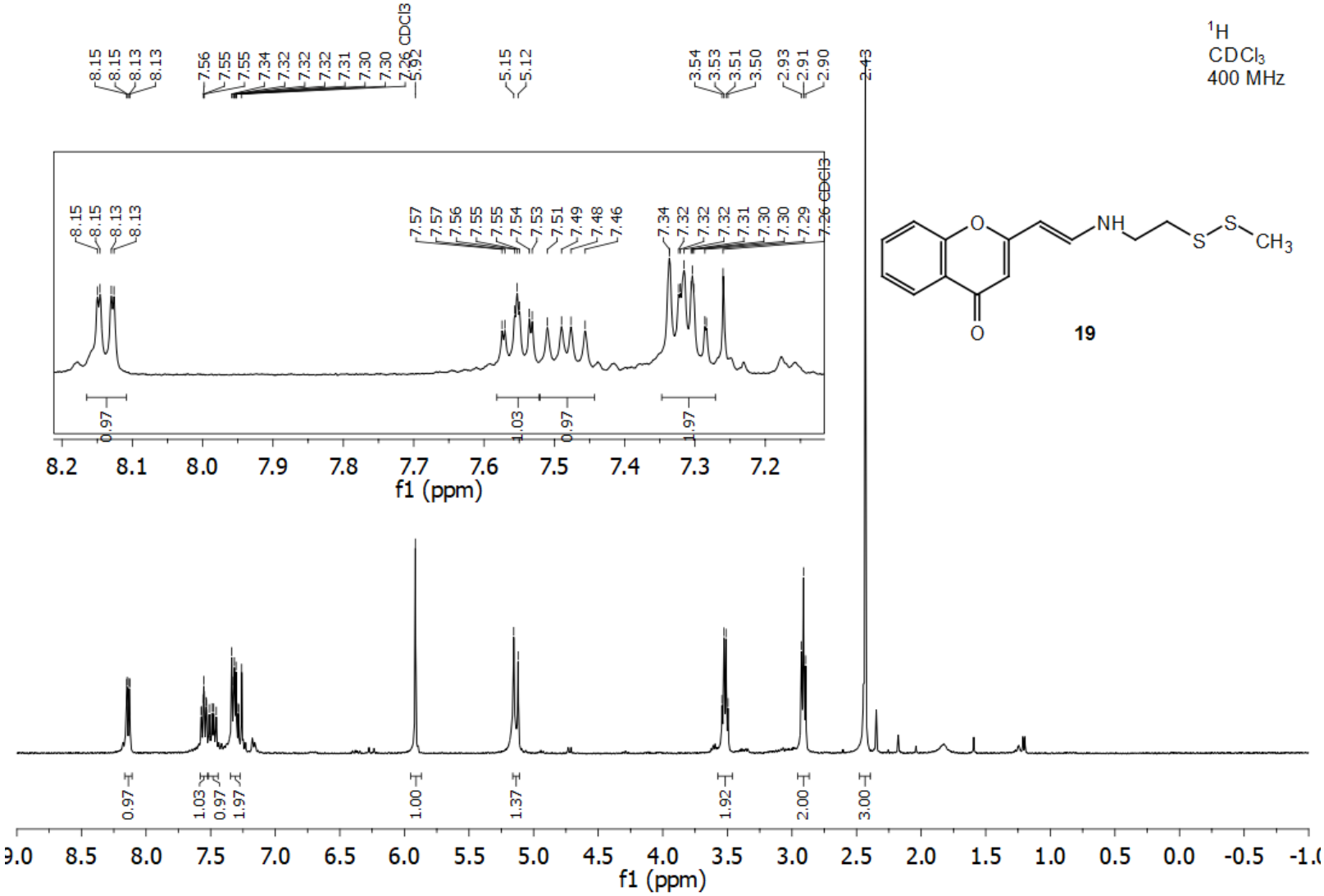

178.41
159.51
156.01
134.14
133.74
127.42
126.91
125.62
125.15
125.02
123.94
117.98
107.10
77.16 CDCl3
^{13}C
CDCl$_3$
100 MHz
O
S
O
8
f1 (ppm)
f1 (ppm)

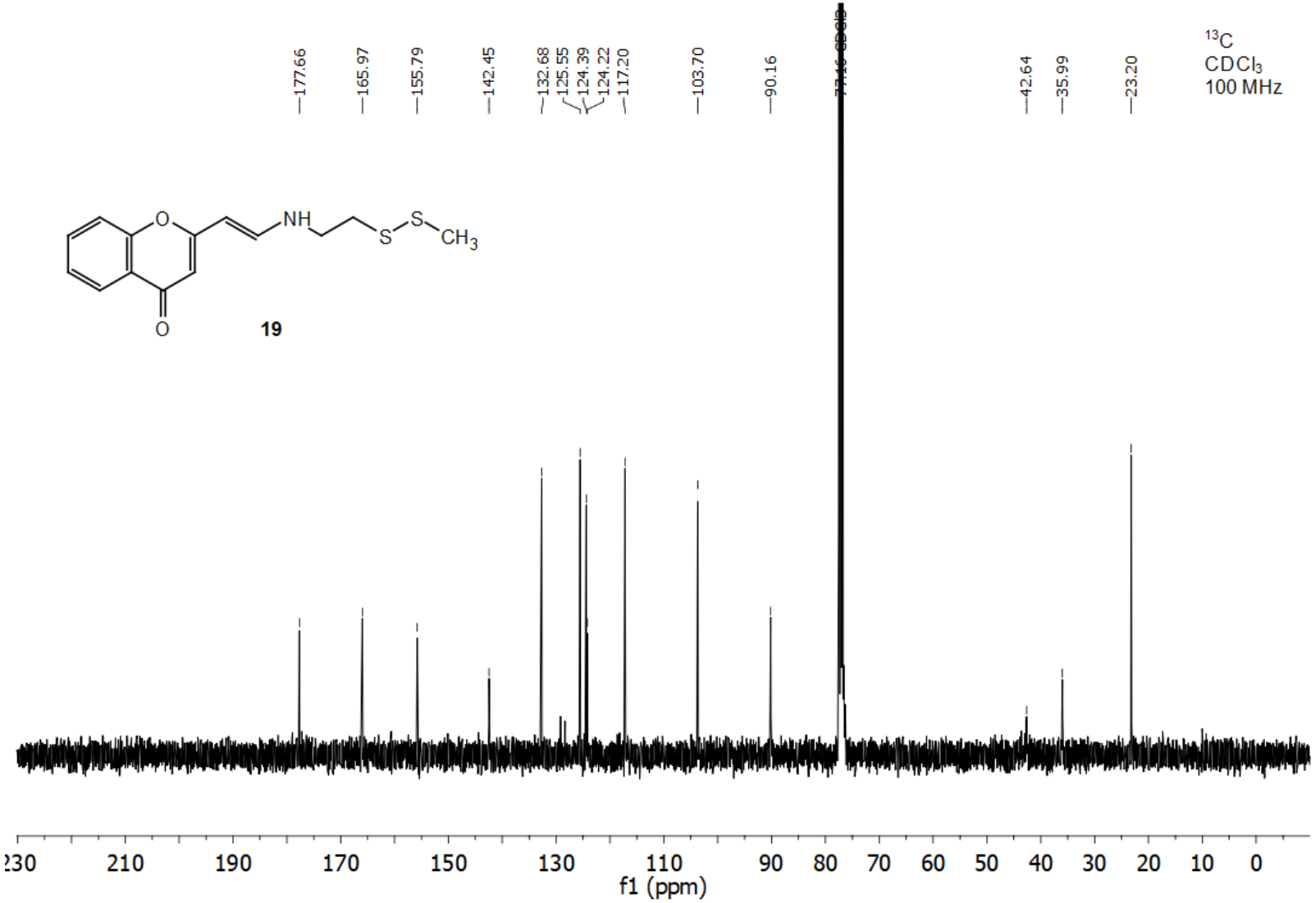

^{1}H
$CDCl_3$
400 MHz
CDCl3
2.57
O
S
O
CH_3
O
18
f1 (ppm)
f1 (ppm)

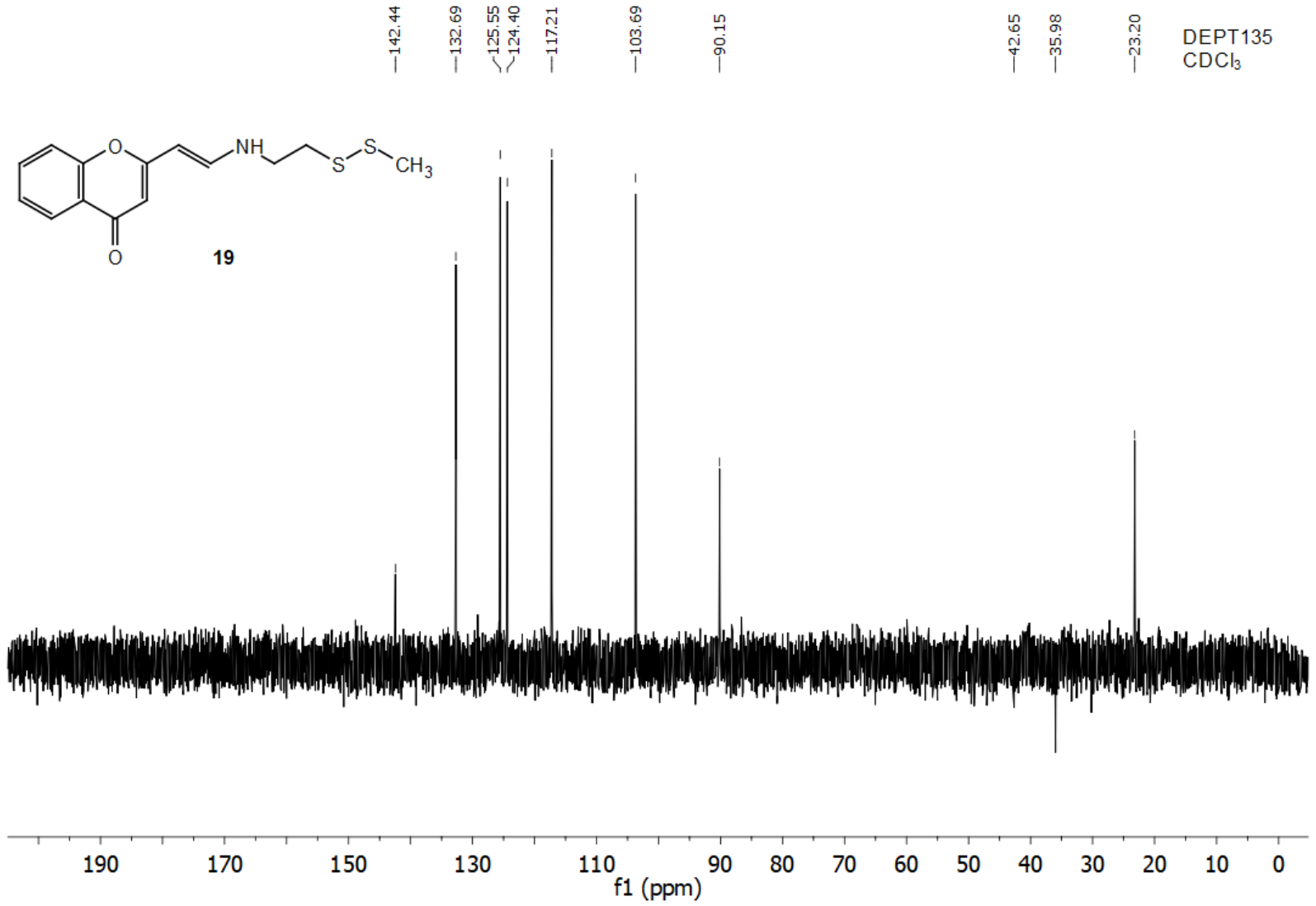

197.65
160.49
149.01
135.28
134.07
133.52
132.51
131.38
130.39
128.32
126.43
123.99
77.46 CDCl3
30.09
13C
CDCl3
100 MHz
O
S
O
CH3
O
18
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

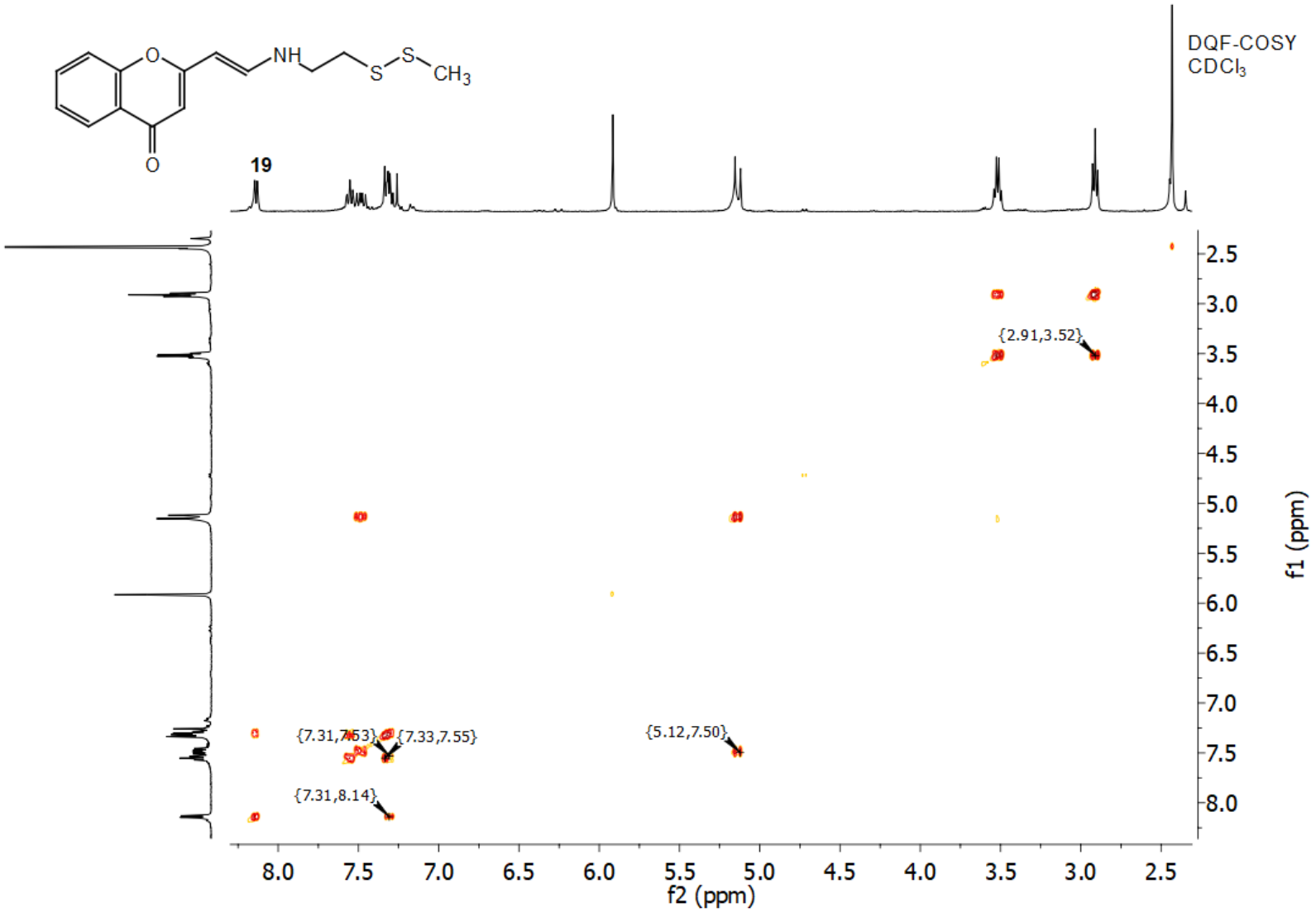

9
^{1}H
$CDCl_3$
400 MHz
8.16
8.15
8.14
8.13
7.65
7.65
7.64
7.64
7.51
7.46
7.12
6.62
7.26 CDCl3
f1 (ppm)

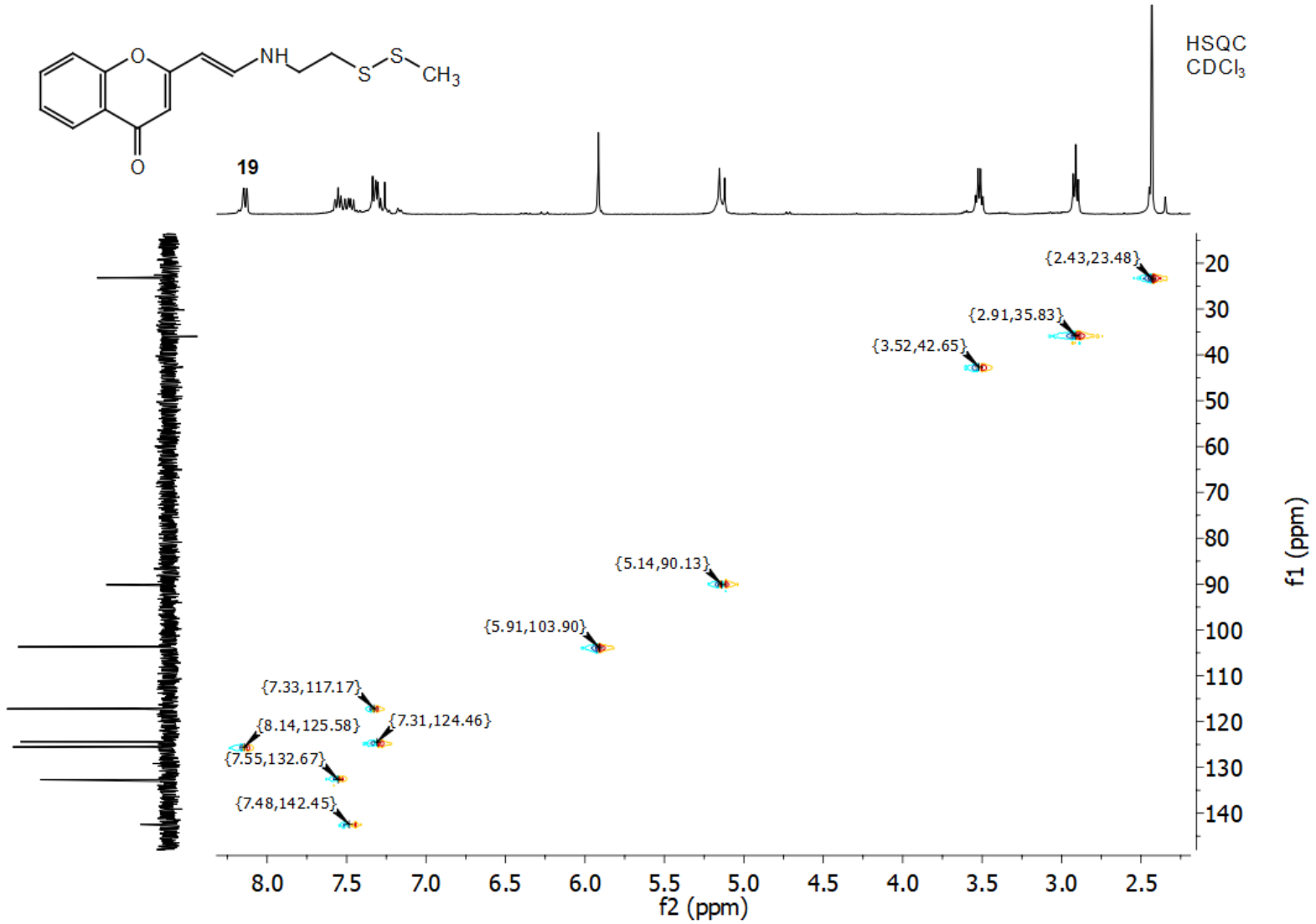

177.82
158.96
155.82
135.04
133.74
130.30
128.50
128.46
125.58
125.23
123.90
117.92
106.08
77.16 CDCl3
13C
CDCl3
100 MHz
O
S
O
9
135.04
133.74
130.30
128.50
128.46
125.58
125.23
123.90
135
130
125
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

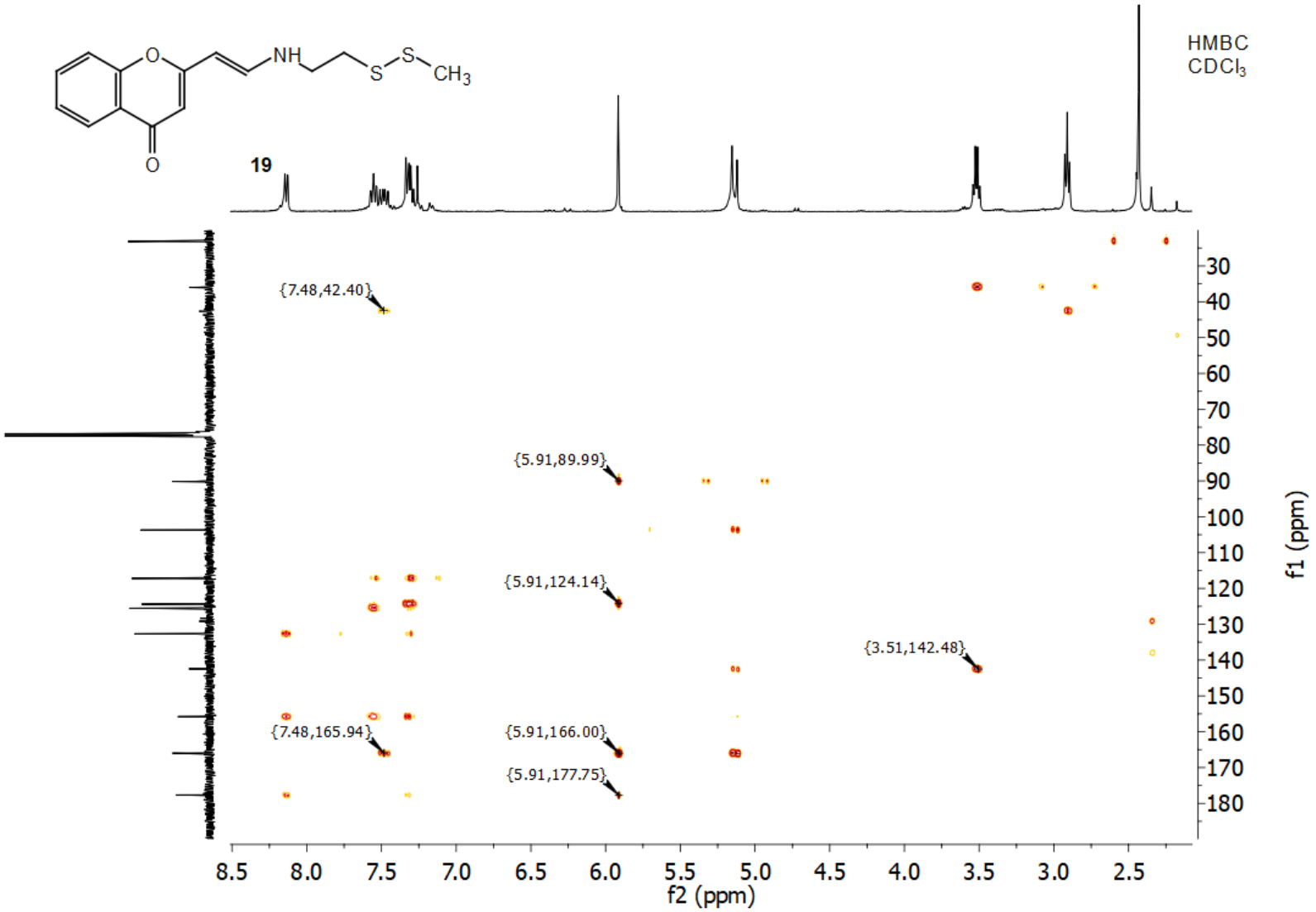

1H
CDCl3
400 MHz
19
f1 (ppm)

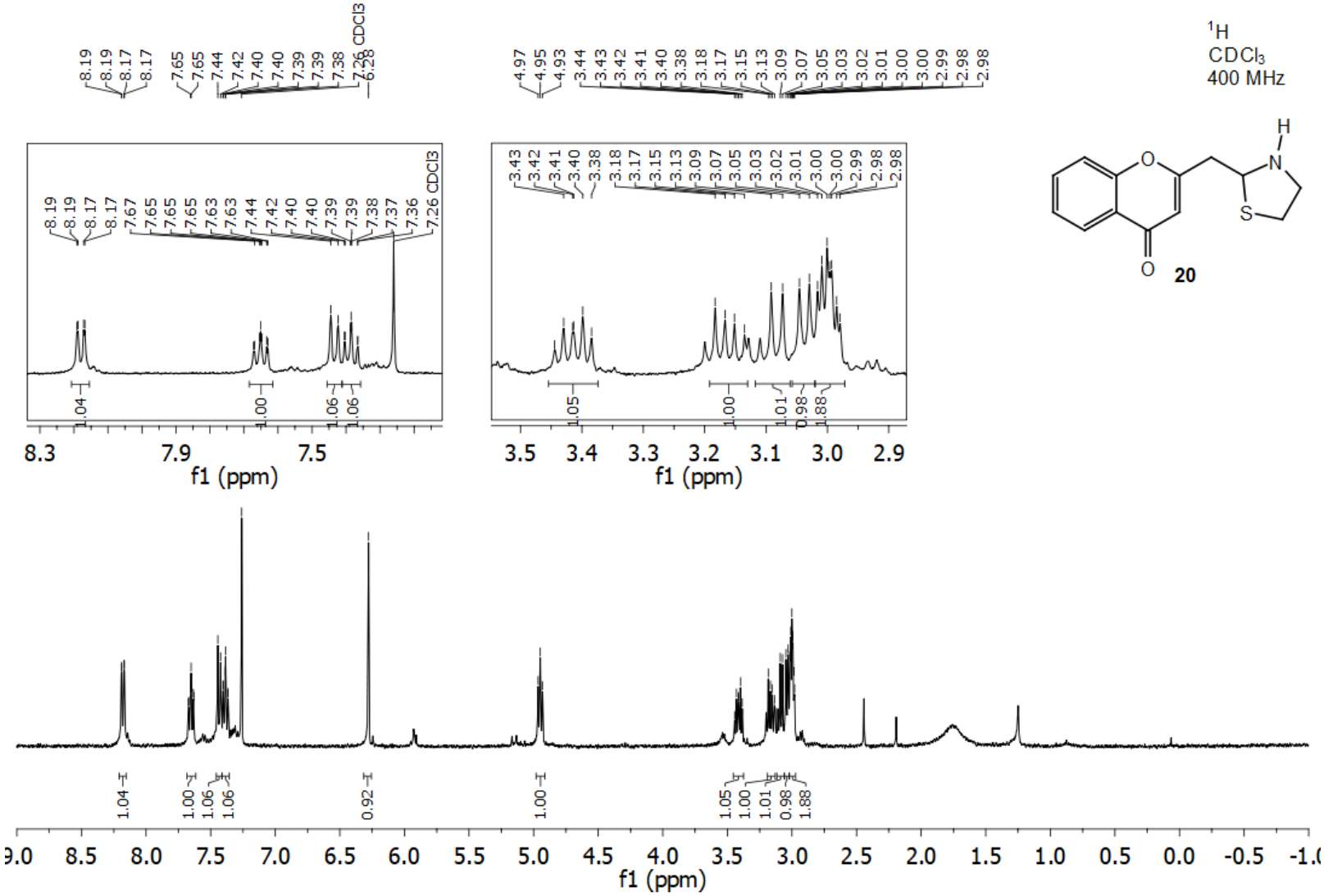

177.66
165.97
155.79
142.45
132.68
125.55
124.39
124.22
117.20
103.70
90.16
42.64
35.99
23.20
13C
CDCl3
100 MHz
O
NH
S
S
CH3
O
19
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

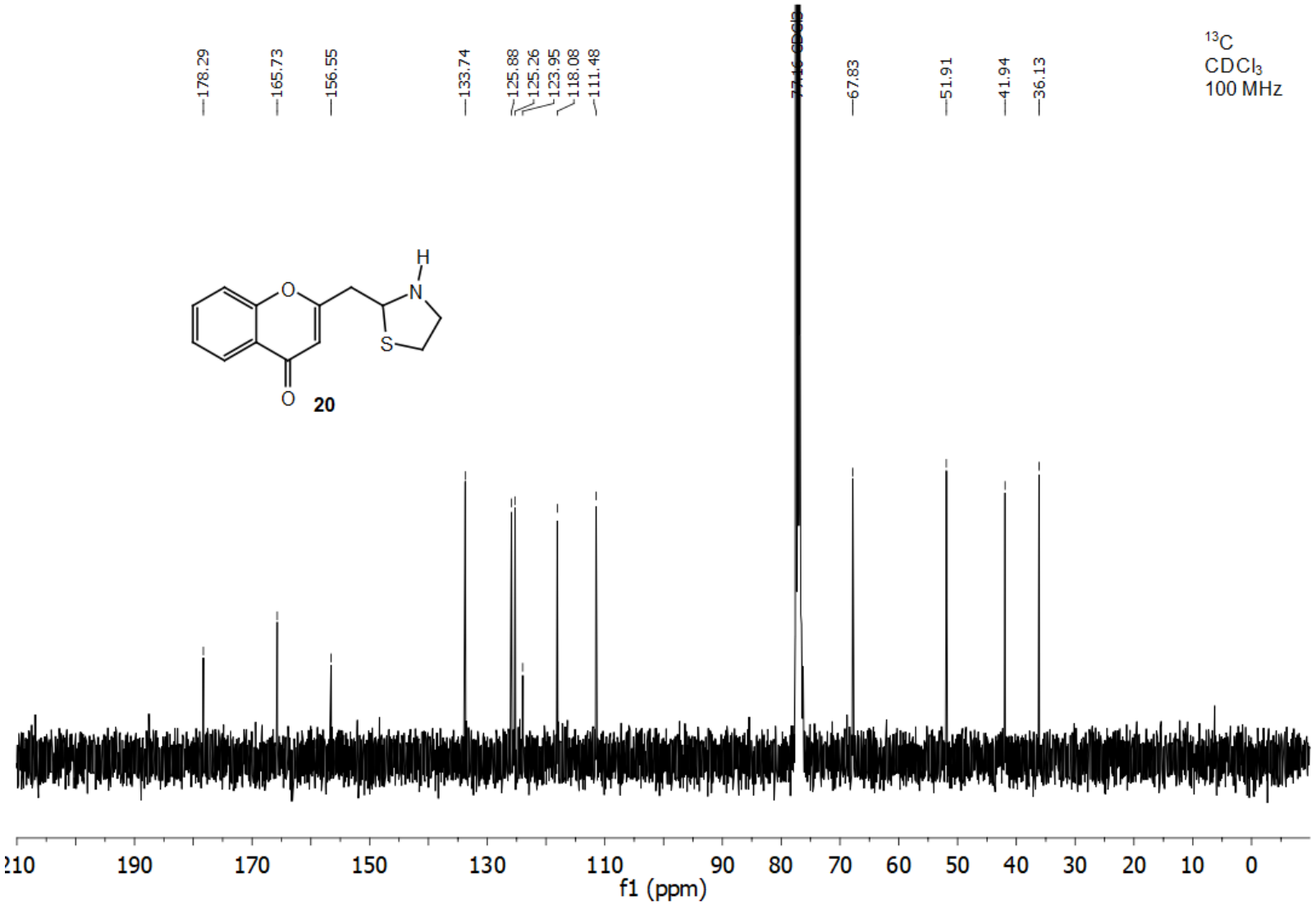

142.44
132.69
125.55
124.40
117.21
103.69
90.15
42.65
35.98
23.20
DEPT135
CDCl3
O
NH
S
S
CH3
O
19
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

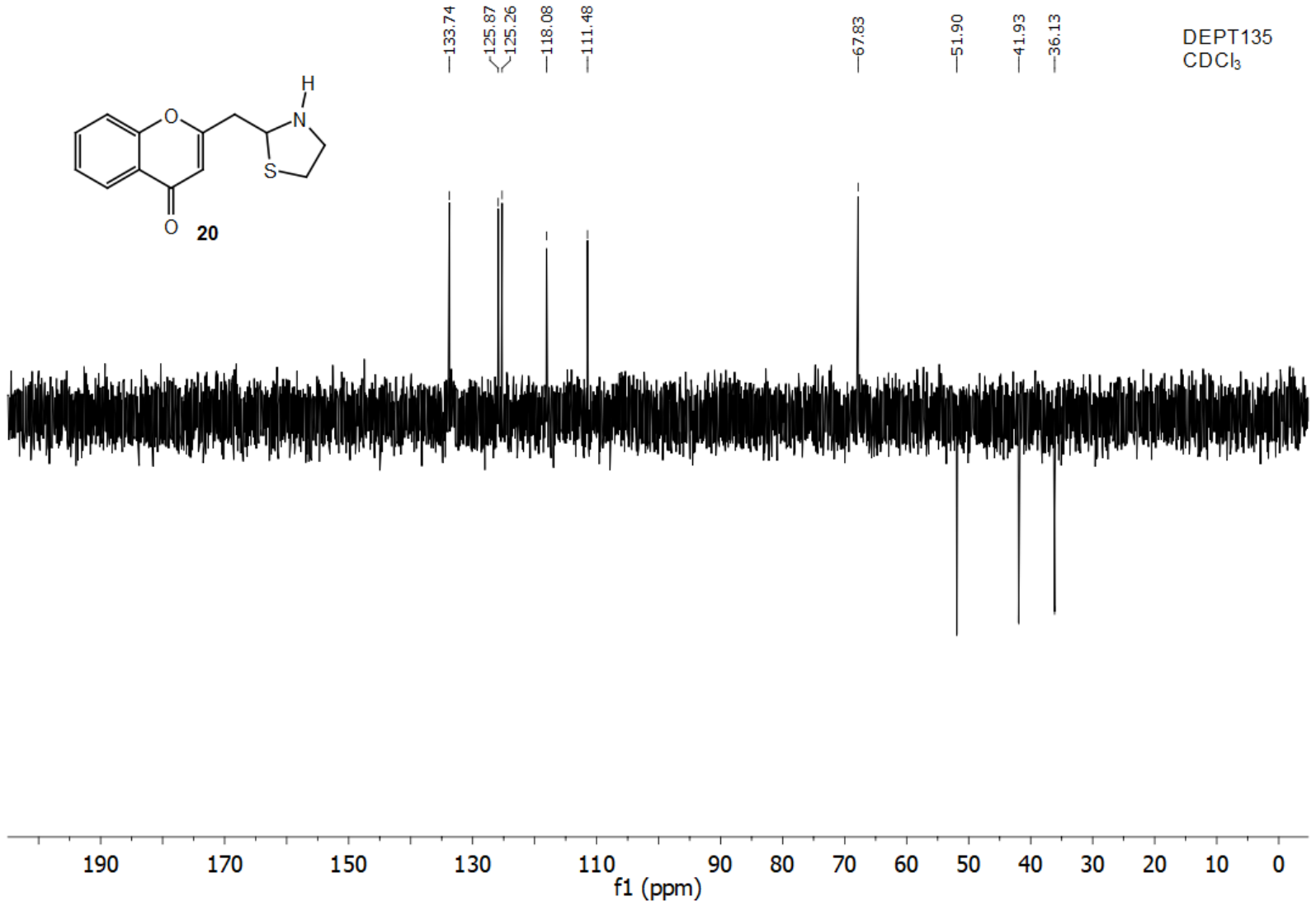

DQF-COSY
CDCl3
19
{2.91,3.52}
{7.31,7.53}
{7.33,7.55}
{5.12,7.50}
{7.31,8.14}
f1 (ppm)
f2 (ppm)

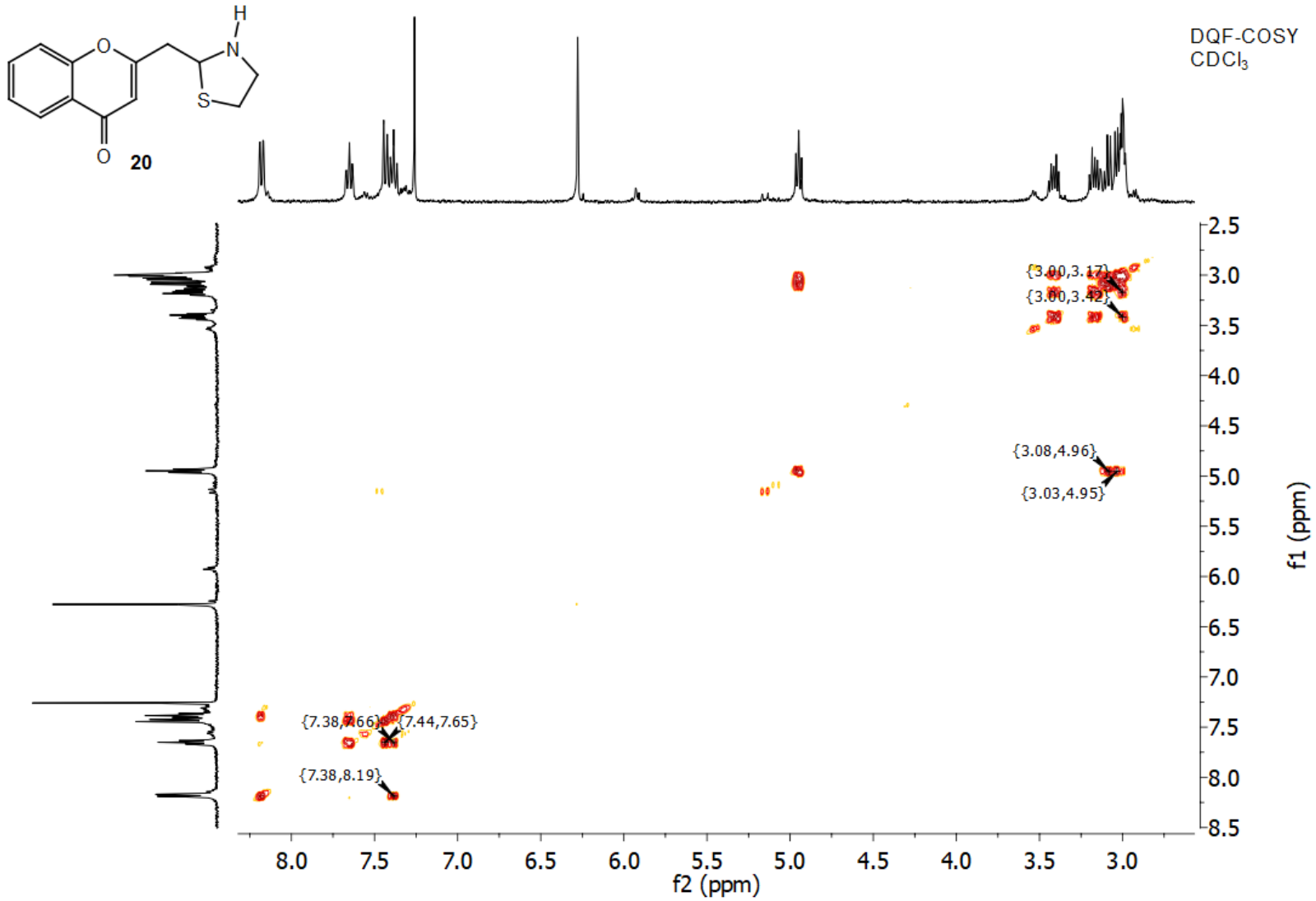

HSQC
CDCl3
19
{2.43,23.48}
{2.91,35.83}
{3.52,42.65}
{5.14,90.13}
{5.91,103.90}
{7.33,117.17}
{8.14,125.58}
{7.31,124.46}
{7.55,132.67}
{7.48,142.45}
f1 (ppm)
f2 (ppm)

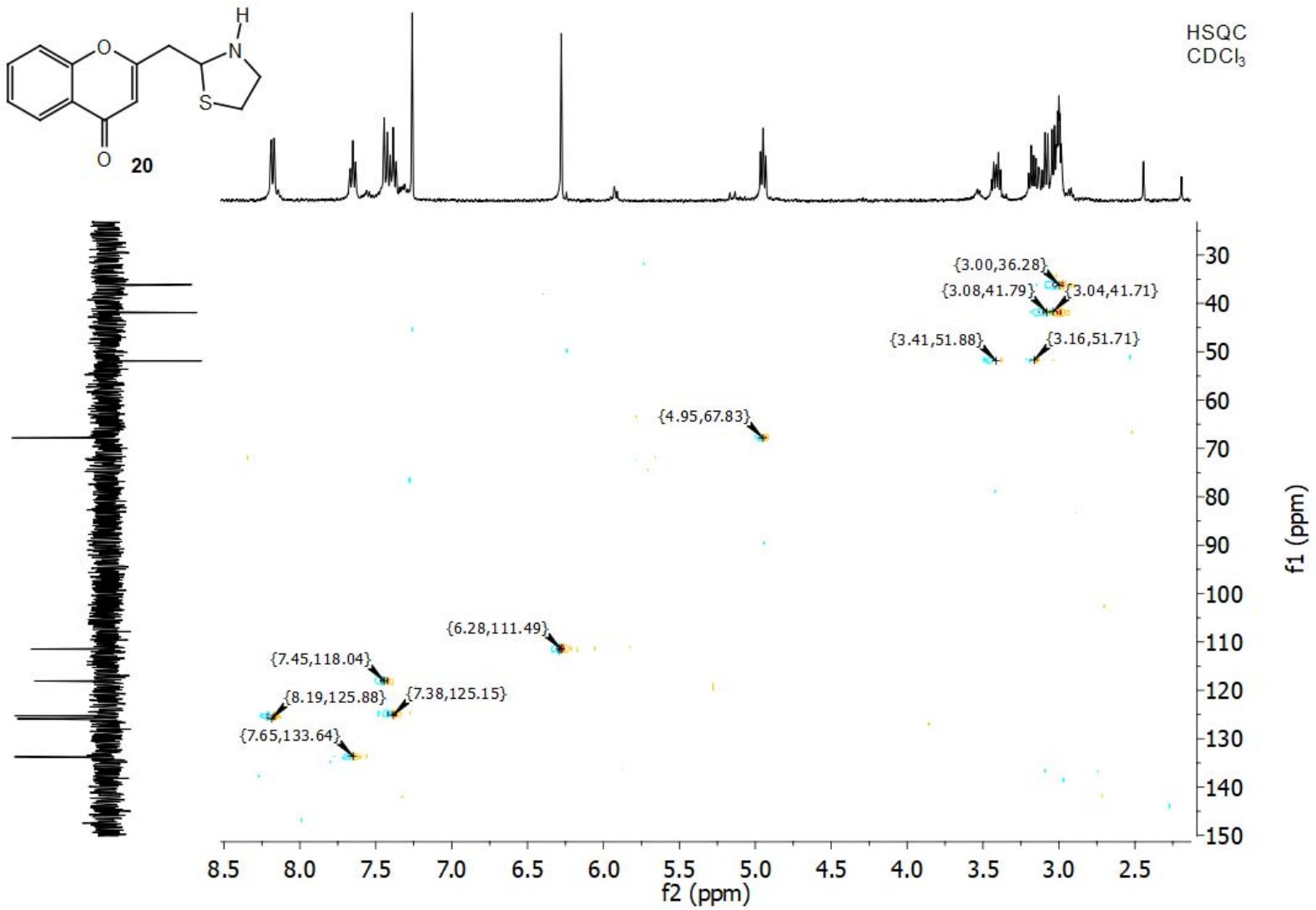

HMBC
CDCl3
19
{7.48,42.40}
{5.91,89.99}
{5.91,124.14}
{3.51,142.48}
{7.48,165.94}
{5.91,166.00}
{5.91,177.75}
f1 (ppm)
f2 (ppm)

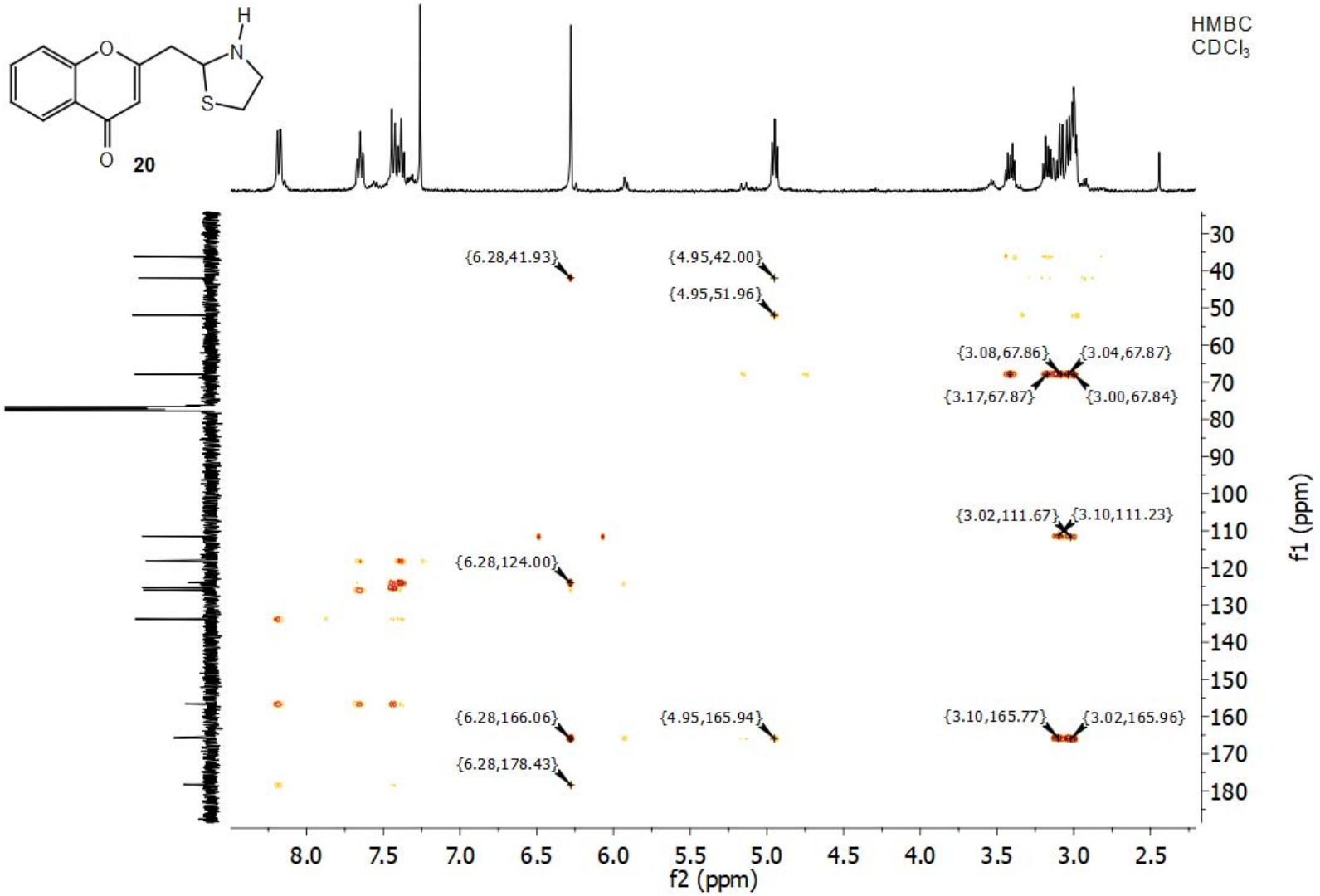

1H
CDCl3
400 MHz
20
f1 (ppm)

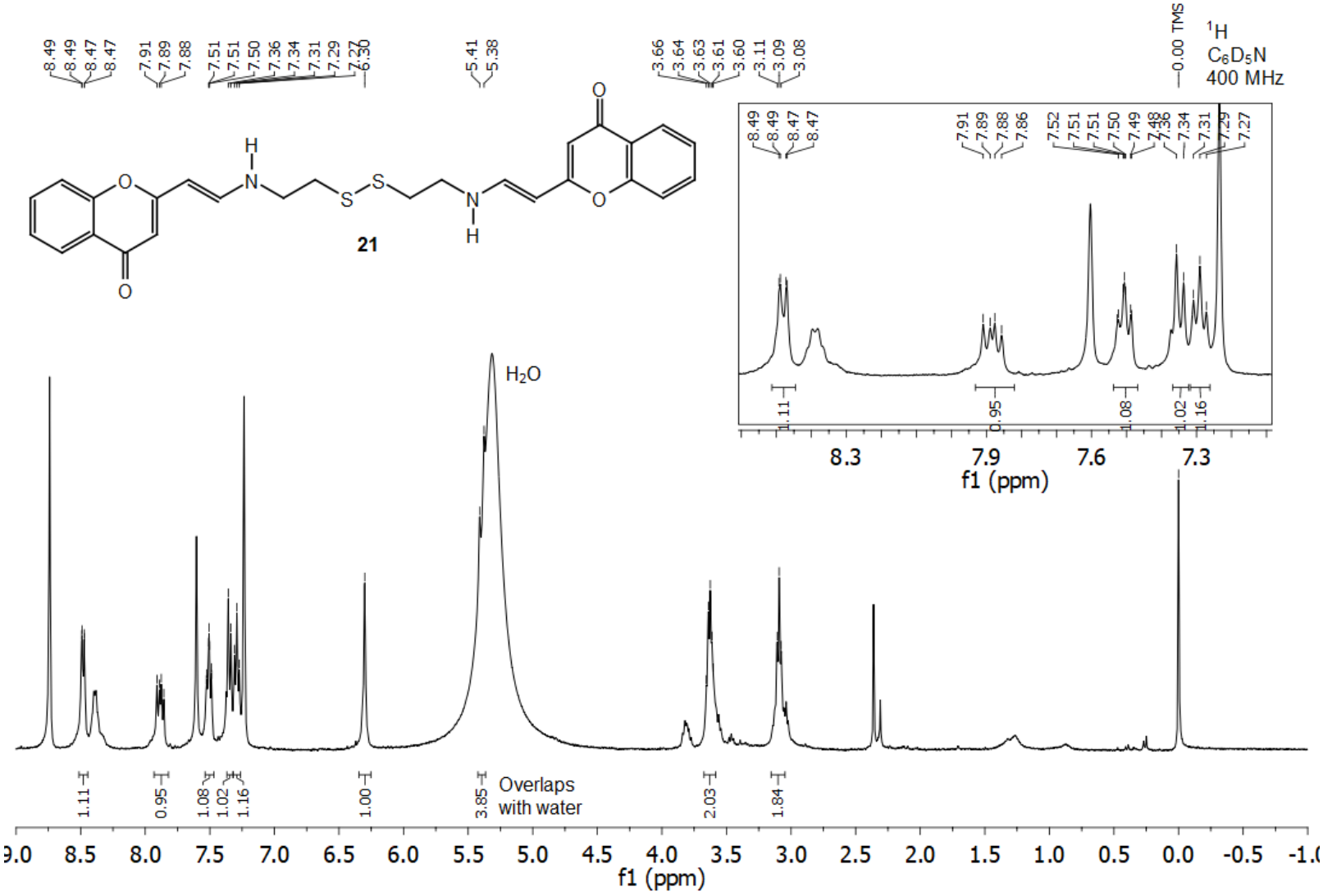

178.29
165.73
156.55
133.74
125.88
125.26
123.95
118.08
111.48
77.16 CDCl3
67.83
51.91
41.94
36.13
13C
CDCl3
100 MHz
H
N
O
S
O
O
20
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

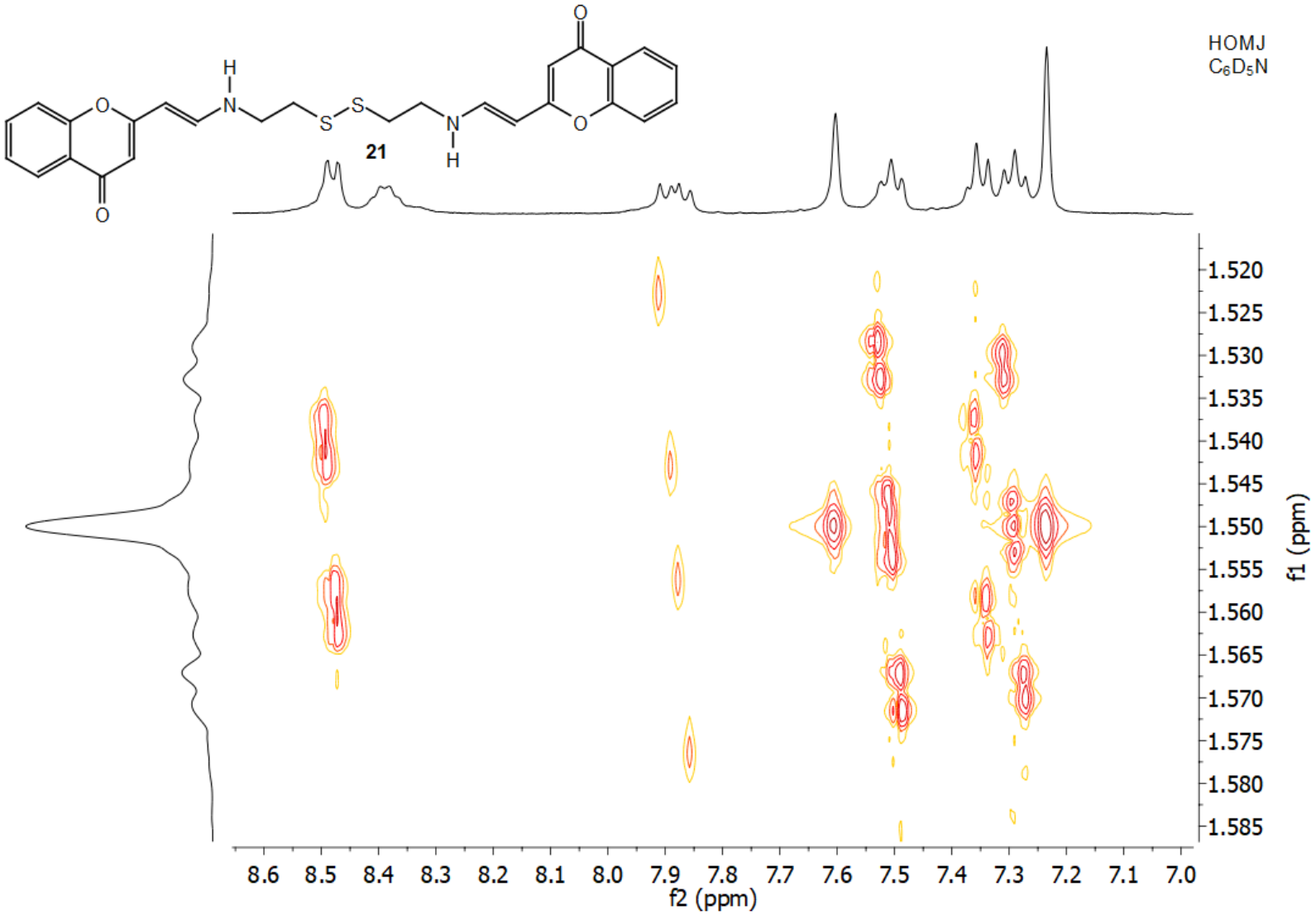

133.74
125.87
125.26
118.08
111.48
67.83
51.90
41.93
36.13
DEPT135
CDCl3
H
N
O
S
O
20
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

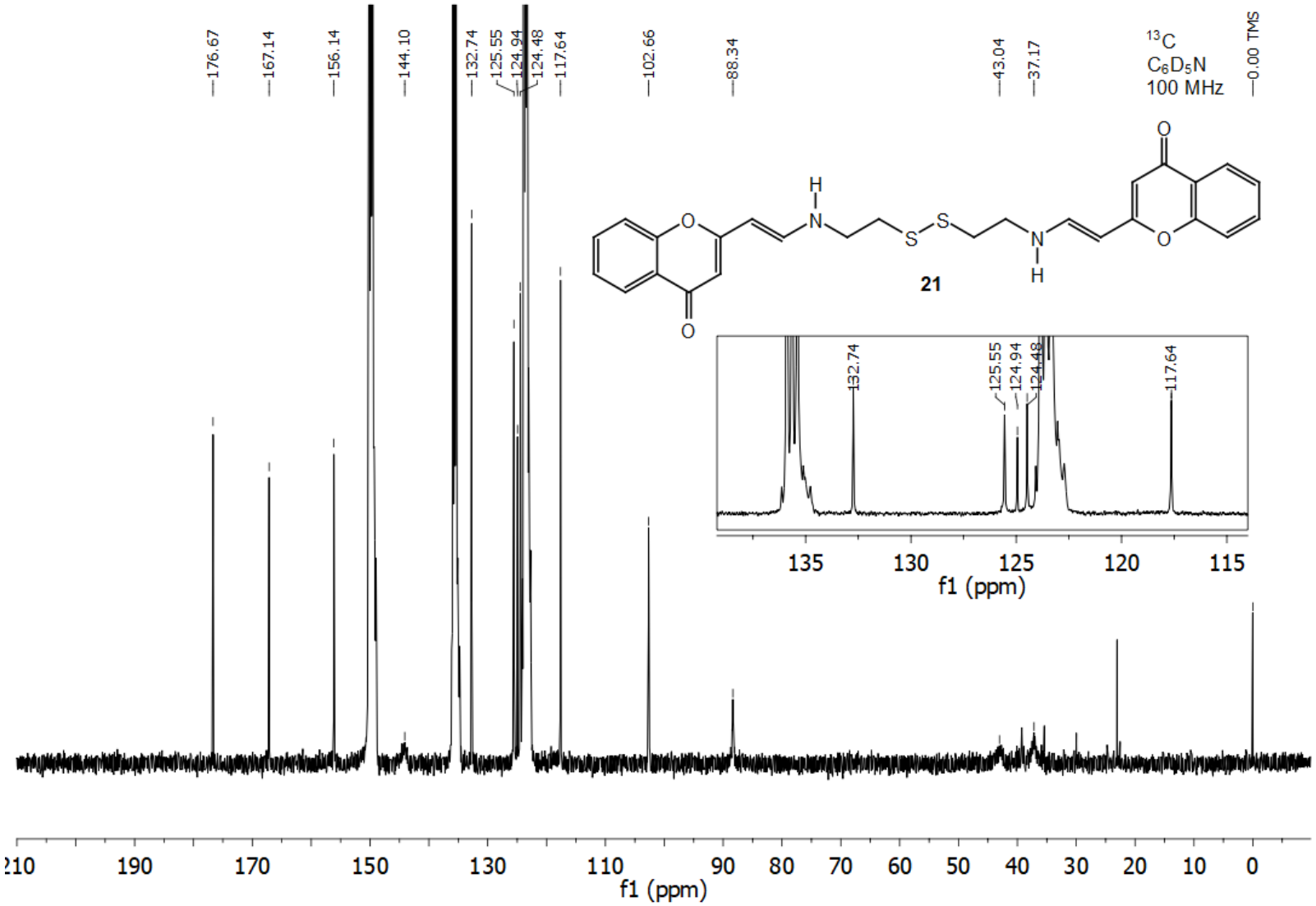

H
N
O
S
O
20
DQF-COSY
CDCl3
{3.00,3.17}
{3.00,3.42}
{3.08,4.96}
{3.03,4.95}
{7.38,7.66}
{7.44,7.65}
{7.38,8.19}
f1 (ppm)
f2 (ppm)

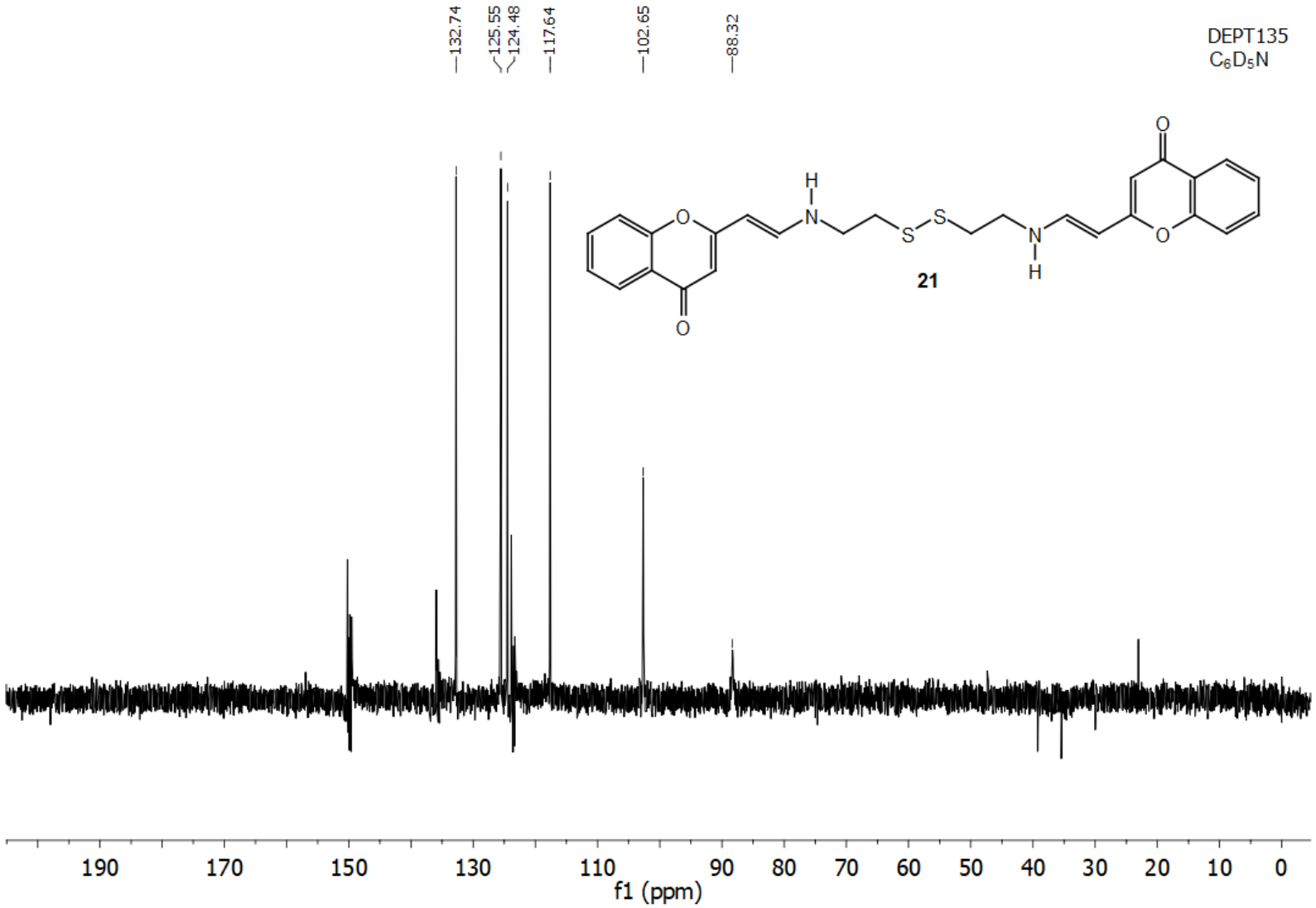

H
N
O
S
O
20
HSQC
CDCl3
{3.00,36.28}
{3.08,41.79}
{3.04,41.71}
{3.41,51.88}
{3.16,51.71}
{4.95,67.83}
{6.28,111.49}
{7.45,118.04}
{8.19,125.88}
{7.38,125.15}
{7.65,133.64}
f2 (ppm)
f1 (ppm)

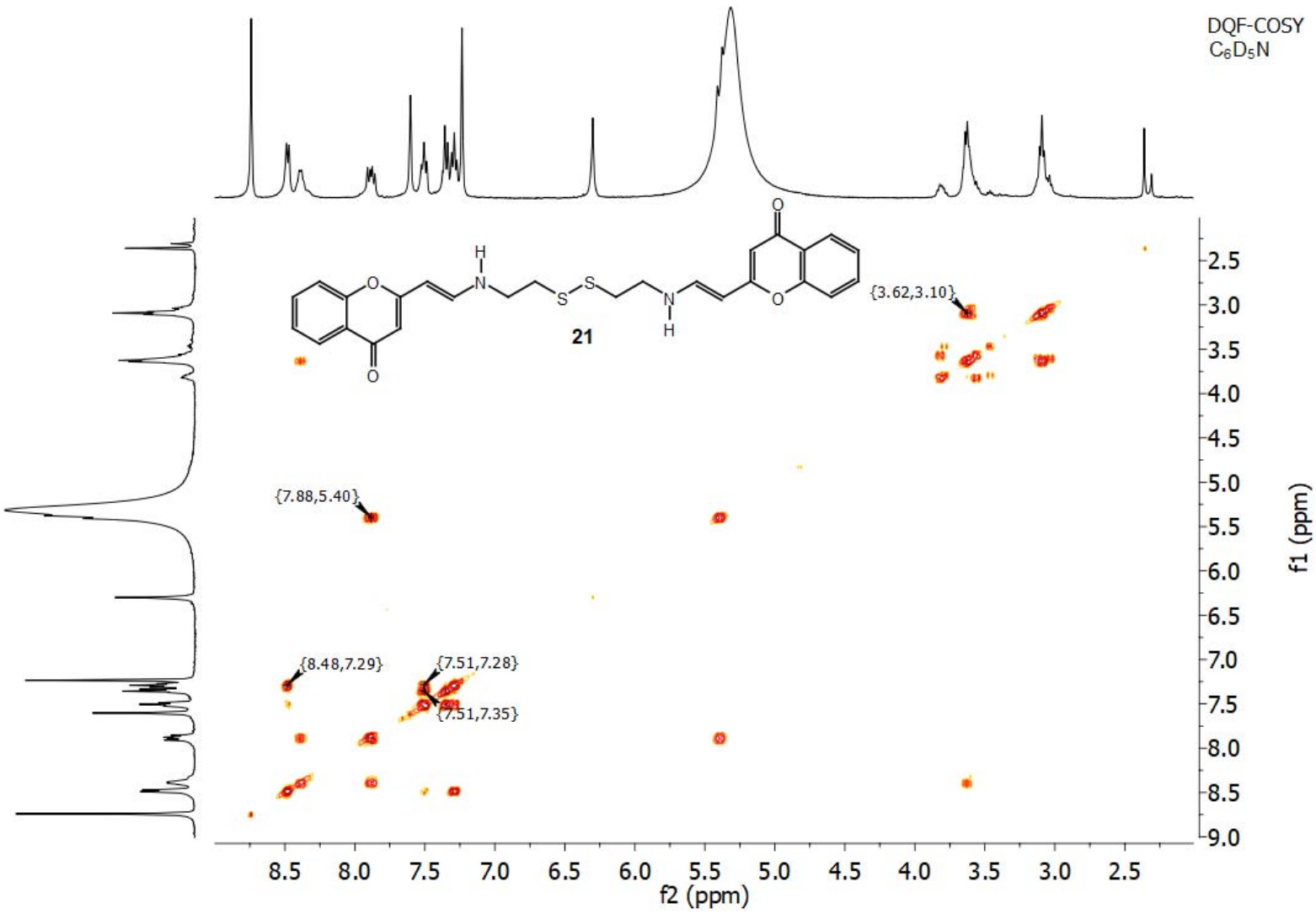

HMBC
CDCl3
20
{6.28,41.93}
{4.95,42.00}
{4.95,51.96}
{3.08,67.86}
{3.04,67.87}
{3.17,67.87}
{3.00,67.84}
{3.02,111.67}
{3.10,111.23}
{6.28,124.00}
{6.28,166.06}
{4.95,165.94}
{3.10,165.77}
{3.02,165.96}
{6.28,178.43}
f2 (ppm)
f1 (ppm)

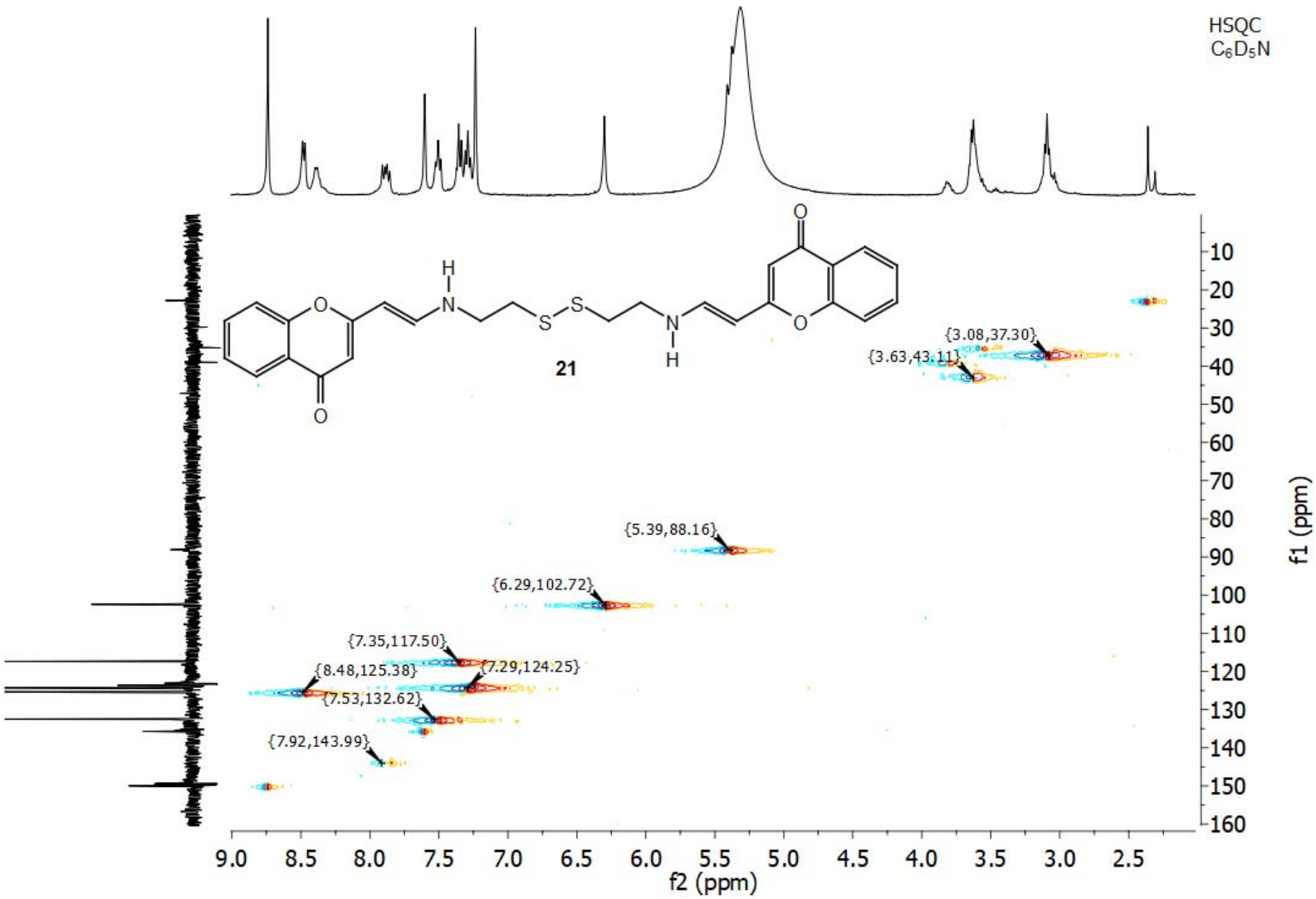

21
^{1}H
C_6D_5N
400 MHz
0.00 TMS
H_2O
Overlaps
with water
f1 (ppm)

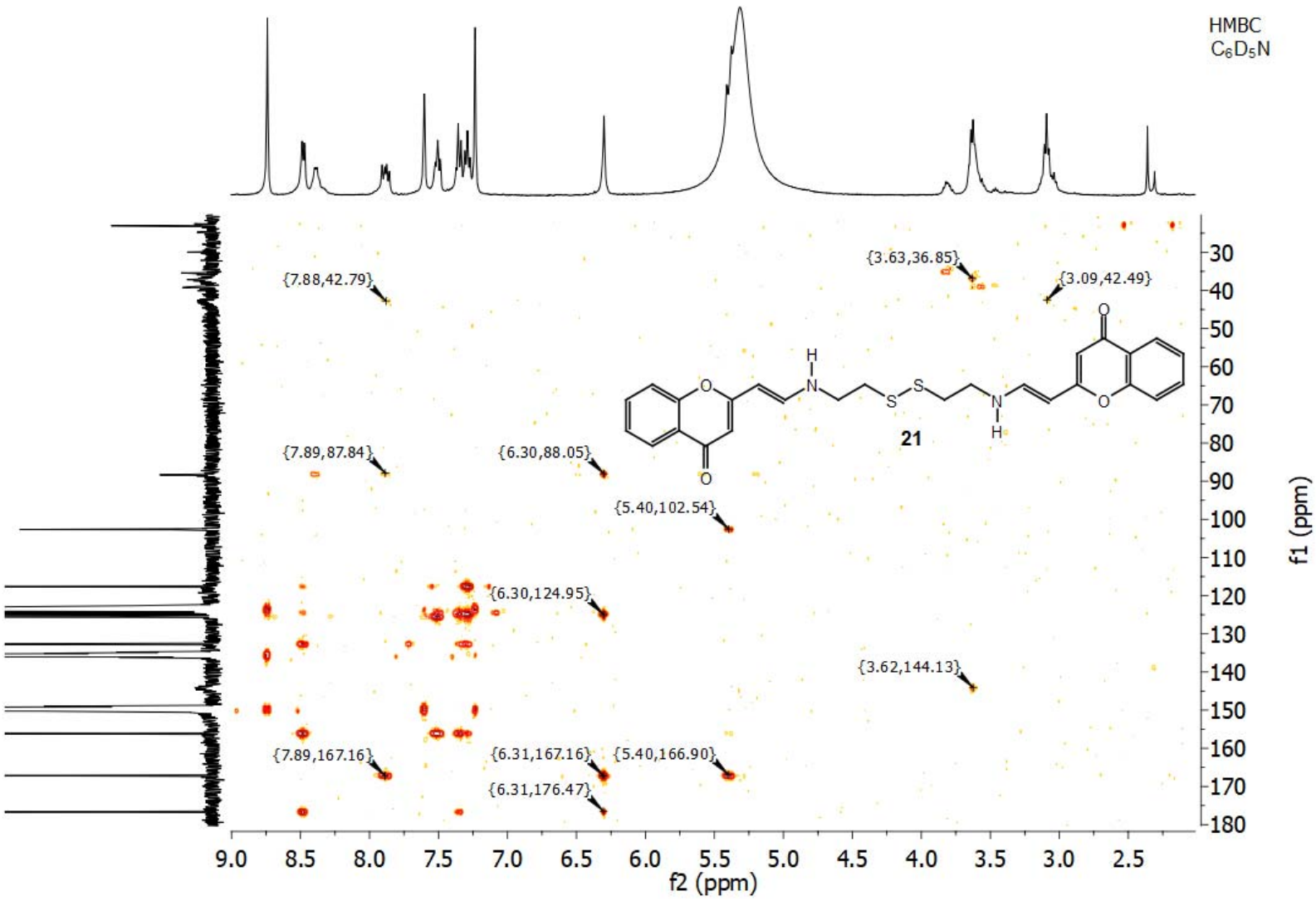

HOMJ
C6D5N
21
f2 (ppm)
f1 (ppm)


176.67
167.14
156.14
144.10
132.74
125.55
124.94
124.48
117.64
102.66
88.34
43.04
37.17
0.00 TMS
^{13}C
C_6D_5N
100 MHz
21
f1 (ppm)
f1 (ppm)

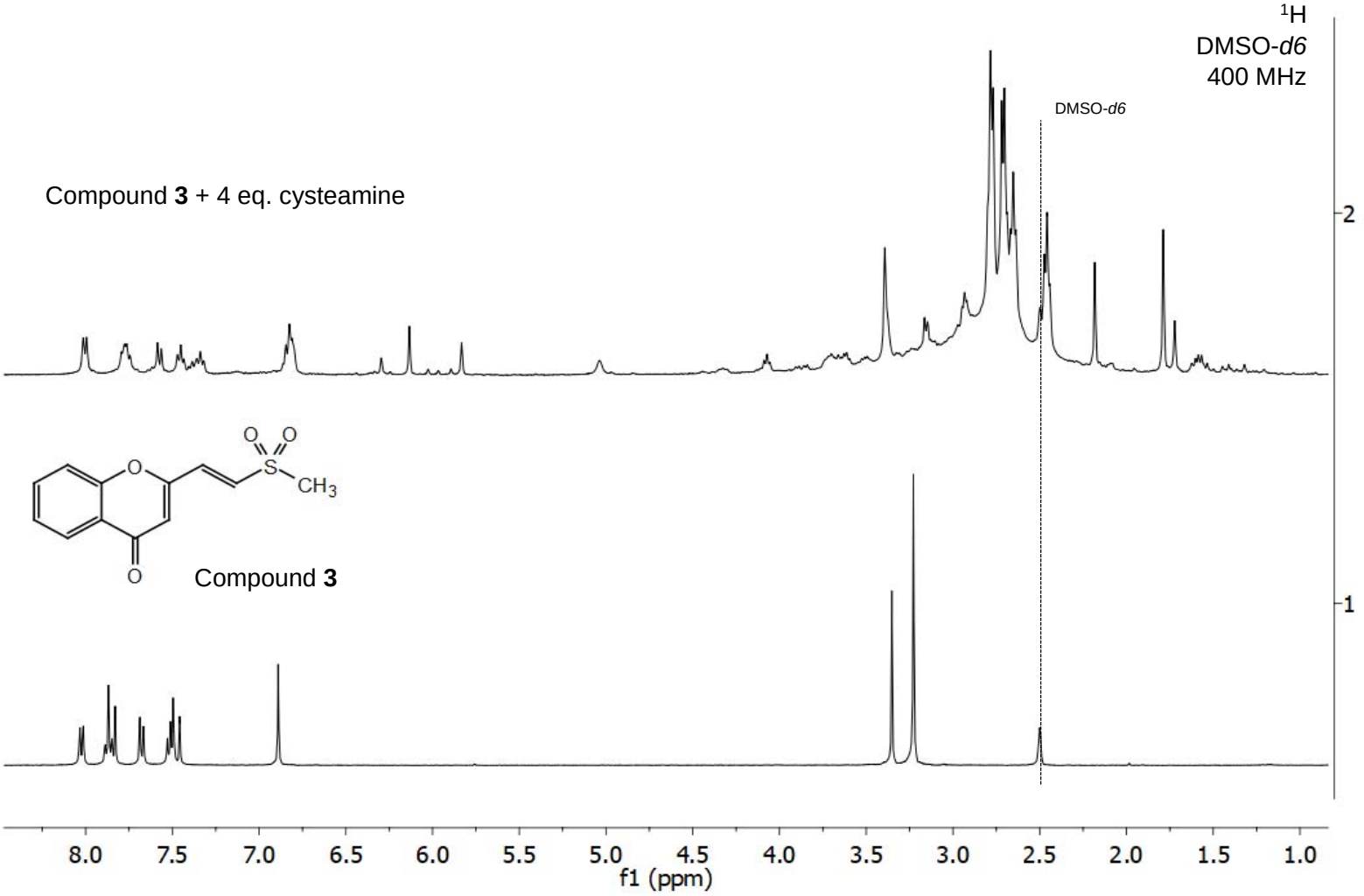

132.74
125.55
124.48
117.64
102.65
88.32
DEPT135
C6D5N
21
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

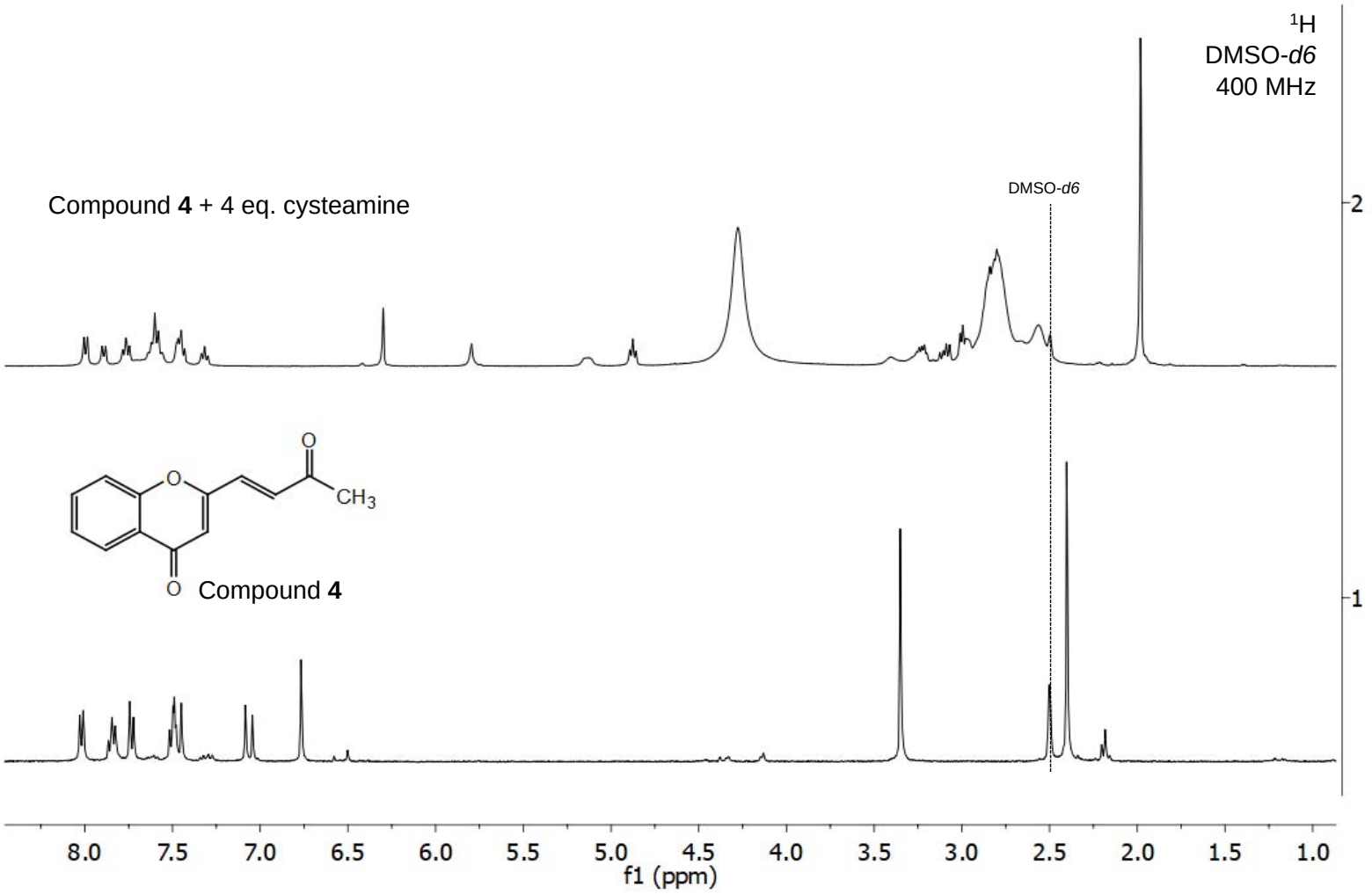

DQF-COSY
C6D5N
21
{3.62,3.10}
{7.88,5.40}
{8.48,7.29}
{7.51,7.28}
{7.51,7.35}
f2 (ppm)
f1 (ppm)


HSQC
C6D5N
21
{3.08,37.30}
{3.63,43.11}
{5.39,88.16}
{6.29,102.72}
{7.35,117.50}
{8.48,125.38}
{7.29,124.25}
{7.53,132.62}
{7.92,143.99}
f1 (ppm)
f2 (ppm)


HMBC
C6D5N
{7.88,42.79}
{3.63,36.85}
{3.09,42.49}
{7.89,87.84}
{6.30,88.05}
{5.40,102.54}
{6.30,124.95}
{3.62,144.13}
{7.89,167.16}
{6.31,167.16}
{5.40,166.90}
{6.31,176.47}
21
f2 (ppm)
f1 (ppm)

V. NRM spectra of Michael addition NMR assays




^{1}H
DMSO-*d6*
400 MHz
Compound **4** + 4 eq. cysteamine
DMSO-*d6*
2
1
O
O
CH3
O
Compound **4**
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)