

Supporting Information

Divergent Access to Fused *N*-Heterocycle-Thiazolines by Solvent-dependent Reaction of Isoquinolinium Thiolates with Silylketene Acetals

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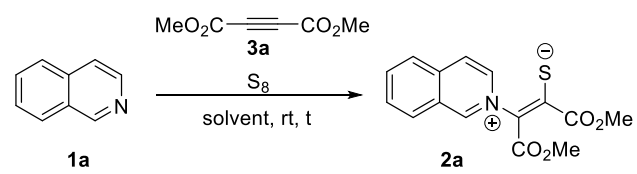
1. General Information and Materials

¹H, ¹³C and ¹⁹F-NMR spectra were recorded in CDCl₃ (reference signals: ¹H = 7.26 ppm, ¹³C = 77.16 ppm), CD₂Cl₂ (reference signals: ¹H = 5.32 ppm, ¹³C = 53.84 ppm) or DMSO-*d*₆ (reference signals: ¹H = 2.50 ppm, ¹³C = 39.52) on a Bruker Avance II 300, Bruker Avance II 400, an Agilent DD2 500 or an Agilent DD2 600. ¹H-NMR chemical shifts are given relative to TMS and are referenced to the solvent signal. Chemical shifts (δ) are given in ppm and spin-spin coupling constants (*J*) are given in Hz. Analytical thin layer chromatography was performed using silica gel 60 F254. Column chromatography was performed on silica gel 60 (0.040-0.063 mm). ESI accurate masses were measured on a MicroTof (Bruker Daltronics, Bremen) with loop injection or on an LTQ Orbitap LTQ XL (Thermo-Fisher Scientific, Bremen) with nanospray (alternatively HPLC, loop injection, syringe pump). Mass calibration on the MicroTof device was performed by using sodium formate cluster ions, immediately followed by the sample in a quasi-internal calibration. APCI mass spectra were recorded on an LTQ Orbitap LTQ XL (Thermo-Fisher Scientific, Bremen) with loop injection. The diastereomeric ratios of the isoquinuclidine derivatives were determined by ¹H-NMR spectroscopy. The employed silyl ketene acetals were synthesized following the described procedures reported in the literature.¹ Commercially available reagents were used without further purification. The employed solvents were purchased dry or distilled in a solvent purification system and stored over 3 or 4 Å molecular sieves.

2. Synthesis and Analytical Data of Isoquinolinium Zwitterions 1

Initially, the reported conditions by Bazgir *et al.* for the synthesis of the pyridinium derivatives with activated alkynes and elemental sulfur were tested.² However, only minimal formation of desired product **1a** was observed when stoichiometric amounts of dimethyl but-2-ynedioate and S₈ were reacted with isoquinoline in DCM, followed by subsequent precipitation with diethyl ether. A short optimization of the reaction conditions (Table S1) revealed that the best result was obtained in a 10:1 mixture of Et₂O and CH₂Cl₂, in which the product precipitated out of the solution, affording **1a** in 55% yield (entry 8).

Table S1. Optimization of the reaction conditions for the synthesis of **1a**

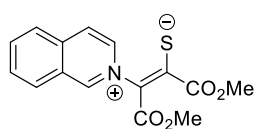


Entry	Solvent	t (h)	Yield 1a (%) ^[b]
1	DCM	24	7
2	DCM	1	<5
3	DCM	0.5	<5
4	Et ₂ O	24	10
5	Et ₂ O	0.5	<5
6	Et ₂ O	72	0
7	Et ₂ O/DCM (5:1)	24	41
8	Et ₂ O/DCM (10:1)	24	55
9	Et ₂ O/DCM (20:1)	24	36

^[a] Reaction conditions: Isoquinoline (1.0 equiv), sulfur (1.0 equiv), dimethyl 2-butynedioate (1.0 equiv) solvent (5 mL/mmol), air, 25 °C.

General procedure for the synthesis of the N,S-zwitterions 1: Dialkyl 2-butynedioate (3.0 mmol, 1.0 equiv.) was added to a suspension of the corresponding isoquinoline (3.0 mmol, 1.0 equiv.) and elemental sulfur (3.0 mmol, 1.0 equiv.) in a 1:10 solvent mixture of CH₂Cl₂ and Et₂O (16.5 mL). The mixture was stirred for 18 h at room temperature. The precipitate was filtered off, washed with Et₂O and dried *in vacuo*.

3-(Isoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (**1a**)

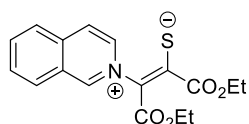


Following the general procedure, the reaction between isoquinoline (355 μ L, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedioate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1a** (496 mg, 1.64 mmol, 55%) as an orange solid. **M.p.:** 140 °C (decomposition).

¹H NMR (400 MHz, DMSO-d₆) δ = 10.03 (br s, 1H), 8.59 – 8.49 (m, 3H), 8.36 (d, *J* = 8.4 Hz, 1H), 8.27 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 8.04 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 3.75 (s, 3H), 3.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.3, 169.0, 160.3, 154.1, 138.4, 137.2, 137.1, 130.8, 130.5, 127.5, 127.2, 125.4, 124.7, 51.9, 51.5;

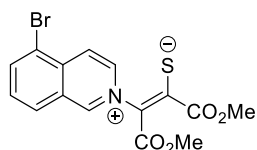
HRMS (ESI): *m/z* calcd. for [C₁₅H₁₃NO₄SNa]⁺: 326.0455, found: 326.0457.

1,4-Diethoxy-3-(isoquinolin-2-ium-2-yl)-1,4-dioxobut-2-ene-2-thiolate (**1b**)



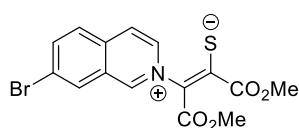
Following the general procedure, the reaction between isoquinoline (365 μ L, 3.0 mmol, 1.0 equiv.) and diethyl 2-butynedionate (481 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1b** (248 mg, 0.75 mmol, 25%) as an orange solid. **M.p.:** 139 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 10.05 (s, 1H), 8.56 – 8.49 (m, 3H), 8.35 (d, J = 7.4 Hz, 1H), 8.26 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 8.03 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 4.08 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 178.0, 168.5, 159.9, 154.1, 138.5, 137.1, 137.1, 130.7, 130.5, 127.5, 127.2, 125.2, 124.9, 60.6, 60.1, 14.2, 14.0; **HRMS (ESI):** m/z calcd. for $[C_{17}H_{17}NO_4SNa]^+$: 354.0771, found: 354.0769.

3-(5-Bromoisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (**1c**)



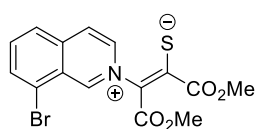
Following the general procedure, the reaction between 5-bromo isoquinoline (624 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1c** (343 mg, 0.90 mmol, 30%) as a red solid. **M.p.:** 141 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 10.12 (s, 1H), 8.62 (dd, J = 11.6, 8.1 Hz, 2H), 8.53 (dd, J = 14.9, 7.7 Hz, 2H), 7.95 (t, J = 7.9 Hz, 1H), 3.75 (s, 3H), 3.60 (s, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 177.0, 168.8, 160.1, 153.2, 140.6, 139.9, 135.6, 131.7, 130.7, 128.7, 124.7, 123.8, 120.8, 52.0, 51.6; **HRMS (ESI):** m/z calcd. for $[C_{15}H_{12}NO_4SBrNa]^+$: 405.9543, found: 405.9541.

3-(7-Bromoisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (**1d**)



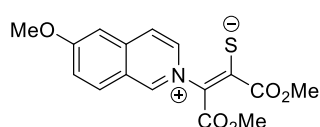
Following the general procedure, the reaction between 7-bromo isoquinoline (624 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1d** (661 mg, 1.73 mmol, 58%) as an orange solid. **M.p.:** 153 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 9.95 (s, 1H), 8.78 (d, J = 2.1 Hz, 1H), 8.62 – 8.58 (m, 2H), 8.40 (dd, J = 8.9, 2.0 Hz, 1H), 8.31 (d, J = 8.9 Hz, 1H), 3.75 (s, 3H), 3.59 (s, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 177.9, 168.9, 160.1, 152.7, 139.9, 139.0, 135.9, 132.0, 129.4, 128.6, 125.5, 123.8, 52.0, 51.6; **HRMS (ESI):** m/z calcd. for $[C_{15}H_{12}NO_4SBrNa]^+$: 405.9543, found: 405.9541.

3-(8-Bromoisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (**1e**)



Following the general procedure, the reaction between 8-bromo isoquinoline (624 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1e** (676 mg, 1.77 mmol, 59%) as a red solid. **M.p.:** 156 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 9.80 (s, 1H), 8.68 (dd, J = 6.8, 1.4 Hz, 1H), 8.62 (d, J = 6.4 Hz, 1H), 8.40 – 8.32 (m, 2H), 8.13 (dd, J = 8.4, 7.4 Hz, 1H), 3.75 (s, 3H), 3.60 (s, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 177.2, 169.0, 160.0, 152.4, 139.3, 139.2, 137.7, 134.9, 127.3, 126.0, 125.9, 125.2, 123.5, 52.0, 51.6; **HRMS (ESI):** m/z calcd. for $[C_{15}H_{12}NO_4SBrNa]^+$: 405.9543, found: 405.9540.

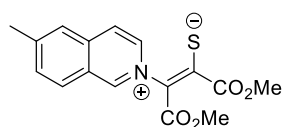
3-(6-Methoxyisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (**1f**)



Following the general procedure, the reaction between 6-methoxy isoquinoline (478 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1f** (380 mg, 1.14 mmol, 38%) as an orange solid. **M.p.:**

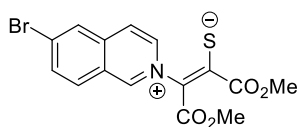
142 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆) δ = 9.73 (s, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.36 (dd, *J* = 6.8, 1.4 Hz, 1H), 8.29 (d, *J* = 6.9 Hz, 1H), 7.75 (d, *J* = 2.6 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.5 Hz, 1H), 4.06 (s, 3H), 3.73 (s, 3H), 3.57 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.3, 169.1, 165.8, 160.6, 152.2, 140.1, 138.7, 132.5, 124.3, 123.5, 123.4, 122.9, 105.9, 56.6, 51.9, 51.5; **HRMS (ESI)**: *m/z* calcd. for [C₁₆H₁₅NO₅SNa]⁺: 356.0563, found: 356.0559).

3-(6-Methylisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (1g)



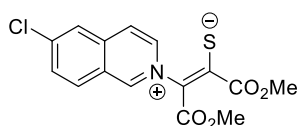
Following the general procedure, the reaction between 6-methyl isoquinoline (430 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μL, 3.0 mmol, 1.0 equiv.) led to the product **1g** (142 mg, 0.45 mmol, 15%) as a brown solid. **M.p.**: 153 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆) δ = 9.91 (s, 1H), 8.49 – 8.33 (m, 3H), 8.13 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 3.74 (s, 3H), 3.57 (s, 3H), 2.66 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.8, 169.5, 160.9, 153.9, 149.4, 139.0, 137.8, 133.4, 130.7, 126.5, 126.3, 125.0, 124.9, 52.4, 52.0, 22.8; **HRMS (ESI)**: *m/z* calcd. for [C₁₆H₁₅NO₄SNa]⁺: 340.0614, found: 340.0614.

3-(6-Bromoisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (1h)



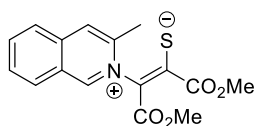
Following the general procedure, the reaction between 6-bromo isoquinoline (624 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μL, 3.0 mmol, 1.0 equiv.) led to the product **1h** (453 mg, 1.19 mmol, 40%) as a brown solid. **M.p.**: 153 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆) δ = 10.04 (s, 1H), 8.69 (s, 1H), 8.60z (d, *J* = 6.8 Hz, 1H), 8.45 (t, *J* = 7.9 Hz, 2H), 8.20 (dd, *J* = 8.8, 1.9 Hz, 1H), 3.74 (s, 3H), 3.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.0, 168.9, 160.2, 154.0, 139.6, 137.9, 134.1, 132.3, 132.0, 129.6, 126.2, 124.7, 124.4, 52.0, 52.0; **HRMS (ESI)**: *m/z* calcd. for [C₁₅H₁₂NO₄SBrNa]⁺: 405.9543, found: 405.9540.

3-(6-Chloroisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (1i)



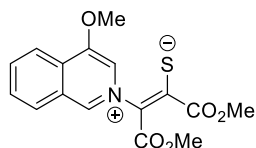
Following the general procedure, the reaction between 6-chloro isoquinoline (491 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (368 μL, 3.0 mmol, 1.0 equiv.) led to the product **1i** (361 mg, 1.07 mmol, 36%) as a brown solid. **M.p.**: 149 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆) δ = 10.06 (s, 1H), 8.59 (dd, *J* = 6.8, 1.4 Hz, 1H), 8.55 (d, *J* = 8.9 Hz, 1H), 8.52 (d, *J* = 2.0 Hz, 1H), 8.48 (d, *J* = 6.9 Hz, 1H), 8.08 (dd, *J* = 8.8, 2.1 Hz, 1H), 3.74 (s, 3H), 3.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.1, 169.0, 160.2, 153.9, 142.4, 139.6, 137.9, 132.6, 131.6, 126.4, 126.0, 124.7, 124.6, 52.0, 51.6; **HRMS (ESI)**: *m/z* calcd. for [C₁₅H₁₂NO₄SClNa]⁺: 360.0068, found: 360.0067.

1,4-Dimethoxy-3-(3-methylisoquinolin-2-ium-2-yl)-1,4-dioxobut-2-ene-2-thiolate (1j)



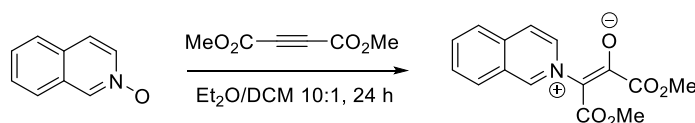
Following the general procedure, the reaction between 3-methyl isoquinoline (286 mg, 2.0 mmol, 1.0 equiv.) and dimethyl 2-butynedionate (245 μL, 2.0 mmol, 1.0 equiv.) led to the product **1j** (83 mg, 0.26 mmol, 13%) as a brown solid. **M.p.**: 169 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆) δ = 9.94 (br s, 1H), 8.54 (br s, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 8.28 – 8.17 (m, 1H), 7.99 – 7.94 (m, 1H), 3.75 (s, 3H), 3.57 (s, 3H), 2.58 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ = 178.3, 169.0, 160.3, 154.1, 138.4, 137.2, 137.1, 130.8, 130.5, 127.5, 127.2, 125.4, 124.7, 51.9, 51.5; **HRMS (ESI)**: *m/z* calcd. for [C₁₆H₁₅NO₄SNa]⁺: 340.0611, found: 340.0614.

3-(4-Methoxyisoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-ene-2-thiolate (1k)



Following the general procedure, the reaction between 4-methoxy isoquinoline (478 mg, 3.0 mmol, 1.0 equiv.) and dimethyl 2-butynedioate (368 μ L, 3.0 mmol, 1.0 equiv.) led to the product **1k** (170 mg, 0.51 mmol, 17%) as an orange solid. **M.p.:** 141 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 9.69 (s, 1H), 8.51 (d, J = 8.1 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 8.30 – 8.20 (m, 2H), 8.06 (t, J = 7.6 Hz, 1H), 4.13 (s, 3H), 3.75 (s, 3H), 3.59 (s, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 178.0, 169.0, 160.3, 153.7, 147.7, 136.5, 131.2, 130.3, 129.3, 127.5, 125.5, 121.3, 120.1, 58.1, 51.9, 51.4; **HRMS (ESI):** m/z calcd. for $[C_{16}H_{15}NO_5SNa]^+$: 356.0563, found: 356.0561.

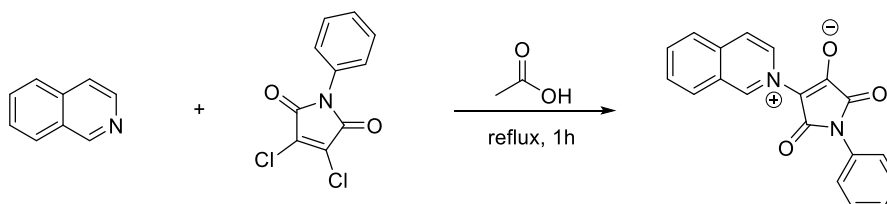
3-(Isoquinolin-2-ium-2-yl)-1,4-dimethoxy-1,4-dioxobut-2-en-2-olate (1l)



Isoquinolinium *N*-oxide (145 mg, 1.0 mmol, 1.0 equiv.) was dissolved in a solvent mixture of Et₂O/DCM (5.5 ml, 10:1) and dimethyl 2-butynedioate (122 μ L, 1.0 mmol, 1.0 equiv.) added to the mixture. The mixture was stirred for 24 h at room temperature. The precipitate was filtered off, washed with Et₂O and dried *in vacuo* leading to the product **1l** (201 mg, 0.7 mmol, 70%) as a yellow solid. **M.p.:** 156 °C (decomposition). **¹H NMR** (400 MHz, DMSO- d_6) δ = 9.85 (s, 1H), 8.51 – 8.39 (m, 3H), 8.30 (d, J = 8.3 Hz, 1H), 8.20 (t, J = 7.6 Hz, 1H), 8.00 (t, J = 7.6 Hz, 1H), 3.74 (s, 3H), 3.53 (s, 3H); **¹³C NMR** (100 MHz, DMSO- d_6) δ = 171.1, 168.0, 163.5, 153.4, 139.5, 136.6, 136.3, 130.6, 130.2, 127.3, 127.1, 124.6, 51.4, 50.3; **HRMS (ESI):** m/z calcd. for $[C_{15}H_{13}NO_5Na]^+$: 310.0686, found: 310.0683.

Note: highly unstable product. Due to fast partial decomposition, it was not enrolled in the reaction with silyl ketene acetals.

4-(Isoquinolin-2-ium-2-yl)-2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-olate (1m)



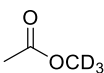
This compound was synthesized according to a procedure reported in the literature:³ Dichloro maleimide (484 mg, 2.0 mmol, 2.0 equiv.) was suspended in acetic acid (3 mL) and heated to 110 °C. After dropwise addition of isoquinoline (118 μ L, 1.0 mmol, 1.0 equiv.), the mixture was stirred for 1 h. After cooling to room temperature, the formed precipitate was filtered off, washed with Et₂O and dried *in vacuo* leading to the product **1m** (284 mg, 0.9 mmol, 90%) as yellow solid. **M.p.:** 166 °C (decomposition). **¹H NMR** (400 MHz, CD₂Cl₂) δ = 10.63 (s, 1H), 9.76 (s, 1H), 8.36 – 7.73 (m, 5H), 7.60 – 7.28 (m, 5H); **HRMS (ESI):** m/z calcd. for $[C_{19}H_{12}N_2O_3Na]^+$: 339.0740, found: 339.0737. The analytical data is in accordance to the one reported in the literature.³

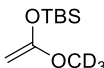
3. Synthesis and Analytical Data of Enolates 2

General procedure for the synthesis of enolates:

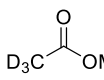
In a flame dried Schlenk-tube under argon atmosphere, diisopropylamine (1.1 equiv.) was dissolved in dry THF (2 mL/mmol). The reaction mixture was cooled down to -78 °C and subsequently, a solution of *n*BuLi (1,6 M in hexane, 1.1 equiv.) was added dropwise to the reaction. After 30 min of stirring, DMPU (1.2 equiv.) was added dropwise to the reaction at -78 °C and stirring was continued for 30 min. Afterwards, the corresponding *in situ* ester (1.0 equiv.) was added dropwise at -78 °C and the reaction was stirred for 30 min observing a slightly yellow colour. Then TBSCl (1.1 equiv.) was added in one portion and the reaction was stirred for 2 h reaching ambient temperature. After the reaction was concluded, pentane (25 mL) was added and the organic layer was washed two times with cold water, followed by drying over MgSO₄. After filtration, the crude product was concentrated under reduced pressure removing all volatile compounds. The residue was purified by bulb-to-bulb distillation to provide the desired enolate.

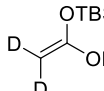
tert-Butyl((1-(methoxy-*d*₃)vinyl)oxy)dimethylsilane (2b-D)

 Al₂O₃ (407.8 mg, 4.00 mmol, 10 mol%) was added to methanol-*d*₄ (1.62 mL, 40.00 mmol, 1.0 equiv.) and the resulting suspension was cooled down to 0 °C. Acetyl chloride (3.14 mL, 44.00 mmol, 1.1 equiv.) was added dropwise and the reaction was stirred at 0 °C for 15 min. Subsequently the reaction was stirred for 12 h, reaching room temperature. The mixture was neutralized with NaHCO₃ (sat., aq., ~5mL), diluted with water (10 mL) and extracted with minimal amount of hexane (3 x 2 mL). The obtained solution was used directly for the next step without further purification.

 Following the general procedure, the *in situ* methyl-*d*₃ acetate (1.00 g, 13.00 mmol, 1.0 equiv) gave the corresponding enolate (621.9 mg, 3.25 mmol, 25%) as a colourless liquid with an observed boiling point of 76 °C at 32 mbar. ¹H NMR (600 MHz, CDCl₃) δ = 3.23 (d, *J* = 2.7 Hz, 1H), 3.10 (d, *J* = 2.7 Hz, 1H), 0.94 (s, 9H), 0.18 (s, 6H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ = 162.5, 64.5, 60.2, 25.8, 18.1, -3.4 ppm; HRMS (ESI): *m/z* calcd. for [C₉H₁₇O₂D₃Si]⁺: 191.1415, found: 191.1415.

tert-Butyl((1-methoxyvinyl-2,2-*d*₂)oxy)dimethylsilane (2b-D')

 In a flame dried Schlenk tube under argon atmosphere, a solution of acetic acid *d*₄ (1.14 mL, 20.00 mmol, 1.0 equiv.), dimethyl sulfate (1.90 mL, 20.00 mmol, 1.0 equiv.) and DMF (1.56 mL, 20.00 mmol, 1.0 equiv.) was prepared. The resulting mixture was stirred at 150 °C for 16 h. The colourless organic layer was isolated (803.35 mg, 10.42 mmol, 52%) and used directly for the next step without further purification. ¹H NMR (400 MHz, CDCl₃) δ = 3.66 (s, 3H).

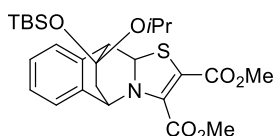
 Following the general procedure, the *in situ* methyl acetate-*d*₃ (771.6 mg, 10.00 mmol, 1.0 equiv.) gave the corresponding enolate (557.7 mg, 2.93 mmol, 29%) as a colourless liquid with an observed boiling point of 76 °C at 32 mbar. ¹H NMR (600 MHz, CDCl₃) δ = 3.53 (s, 3H), 0.93 (s, 9H), 0.17 (s, 6H) ppm; ¹³C NMR (150 MHz, CDCl₃) δ = 162.5, 60.2 (t, *J* = 25.0 Hz), 55.1, 25.8, 18.3, -4.6 ppm. HRMS (EI): *m/z* calcd. for [C₉H₁₈D₂O₂Si]⁺: 190.1358, found: 190.1355.

4. Synthesis and Analytical Data of Isoquinuclidines 3

General procedure for the synthesis of isoquinuclidines:

The corresponding isoquinolinium zwitterion **1** (0.2 mmol, 1.0 equiv.) was added to a reaction vessel under argon atmosphere. After addition of DCE (1 mL) the corresponding nucleophile **2** (0.4 mmol, 2.0 equiv.) was added dropwise. The mixture was stirred for 18 h at room temperature. The solvent was evaporated, the residual dark slur taken up in dichloromethane and dry loaded onto silica. The product was purified *via* flash column chromatography (pentane/EtOAc) and dried *in vacuo*.

Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-isopropoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (**3a**)

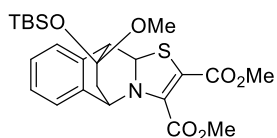


Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2a** (102.0 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the

product **3a** (73.0 mg, 0.14 mmol, 70%, 7:1 d.r.) as a yellow solid. **M.p.:** 117-125 °C. **R_f**(pentane/EtOAc 8:1) = 0.83.

Major product (11*S,10*aS**)-endo:** ¹H NMR (500 MHz, DMSO-*d*₆) δ = 7.35 – 7.22 (m, 4H), 7.20 (d, *J* = 6.6 Hz, 1H), 6.16 (d, *J* = 1.5 Hz, 1H), 4.41 (t, *J* = 3.1 Hz, 1H), 4.24 (p, *J* = 6.1 Hz, 1H), 3.79 (s, 3H), 3.68 (br s, 1H), 3.49 (s, 3H), 2.19 (dd, *J* = 14.4, 2.7 Hz, 1H) 1.93 (dd, *J* = 14.4, 3.9 Hz, 1H), 1.19 (d, *J* = 6.1 Hz, 3H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.61 (s, 9H), -0.03 (s, 3H), -0.71 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ = 161.8, 161.5, 143.6, 139.9, 135.4, 128.8, 127.5, 126.6, 123.7, 108.0, 100.2, 66.5, 63.3, 55.1, 52.9, 51.9, 50.7, 43.3, 25.5, 24.8, 24.0, 17.8, -3.0, -4.3; **Minor product (11*R**,10*aS**)-endo:** ¹H NMR (500 MHz, DMSO-*d*₆) δ = 7.35 – 7.22 (m, 4H), 7.20 (d, *J* = 6.6 Hz, 1H), 6.22 (d, *J* = 1.7 Hz, 1H), 4.39 (t, *J* = 3.1 Hz, 1H), 4.05 – 4.00 (m, 1H), 3.78 (s, 3H), 3.77 (br s, 1H), 3.33 (s, 3H), 2.33 (dd, *J* = 14.2, 3.1 Hz, 1H), 1.81 (dd, *J* = 14.1, 3.1 Hz, 1H), 1.18 (d, *J* = 6.1 Hz, 3H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.96 (s, 9H), 0.26 (s, 3H), 0.19 (s, 3H); **HRMS (ESI):** *m/z* calcd. for [C₂₆H₃₇NO₆SSiNa]⁺: 542.2003, found: 542.2003.

Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (**3b**)

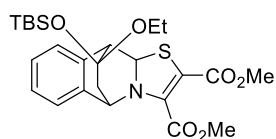


Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the

product **3b** (69.0 mg, 0.14 mmol, 70%, 7:1 d.r.) as a yellow solid. In the up-scaling reaction, **1a** (364.0 mg, 1.20 mmol, 1.0 equiv.) was reacted with silyl ketene acetal **2b** (525.6 μ L, 2.40 mmol, 2.0 equiv.) to afford **3b** (400 mg, 0.81 mmol, 68%, 7:1 d.r.). **M.p.:** 57-65 °C. **R_f**(pentane/EtOAc 8:1) = 0.8; **Major product (11*S**,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.35 – 7.33 (m, 1H), 7.30 – 7.26 (m, 2H), 7.17 (d, *J* = 6.9 Hz, 1H), 6.16 (d, *J* = 1.5 Hz, 1H), 4.29 (t, *J* = 3.2 Hz, 1H), 3.83 (s, 3H), 3.56 (br s, 1H), 3.55 (s, 3H), 3.35 (s, 3H), 2.38 (dd, *J* = 14.0, 2.9 Hz, 1H), 1.84 (ddd, *J* = 14.0, 3.3, 0.9 Hz, 1H), 0.57 (s, 9H), 0.03 (s, 3H), -0.27 (s, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 162.9, 162.4, 143.5, 140.7, 135.7, 129.3, 128.2, 127.2, 123.7, 111.2, 101.0, 67.3, 56.7, 53.2, 52.3, 50.3, 50.2, 44.0, 26.1, 25.6, 18.2, -3.0, -3.5; **Minor product (11*R**,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.40 – 7.36 (m, 2H), 7.34 (d, *J* = 1.3 Hz, 1H), 7.21 – 7.19 (m, 1H), 6.26 (d, *J* = 1.6 Hz, 1H), 4.33 (t, *J* = 3.1 Hz, 1H), 3.82 (s,

3H), 3.54 (s, 3H), 3.53 (br s, 1H), 3.15 (s, 3H), 2.37 (dd, $J = 13.8, 2.7$ Hz, 1H), 1.89 (ddd, $J = 13.8, 3.3, 0.9$ Hz, 1H), 0.98 (s, 9H), 0.22 (s, 3H), 0.17 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[C_{24}H_{33}NO_6SSiNa]^+$: 514.1691, found: 514.1690.

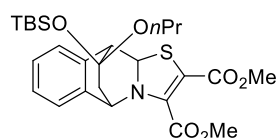
Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-ethoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (3c)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2c** (95.2 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3c** (71.0 mg, 0.14 mmol, 70%, 7:1 d.r.) as a yellow solid. **M.p.**: 53-59 °C. **R_f**(pentane/EtOAc 10:1) = 0.6.

Major product (11S*,10aS*)-endo: 1H NMR (600 MHz, CD_2Cl_2) $\delta = 7.37 - 7.32$ (m, 1H), 7.30 - 7.24 (m, 2H), 7.19 - 7.15 (m, 1H), 6.19 (d, $J = 1.7$ Hz, 1H), 3.83 (s, 3H), 3.75 (dq, $J = 8.9, 7.1$ Hz, 1H), 3.55 (br s, 1H), 3.55 (s, 3H), 3.54 (dq, $J = 8.9, 7.1$ Hz, 1H), 2.39 (dd, $J = 14.0, 2.9$ Hz, 1H), 1.86 (ddd, $J = 14.0, 3.3, 0.9$ Hz, 1H), 1.23 (t, $J = 7.1$ Hz, 3H), 0.56 (s, 9H), 0.01 (s, 3H), -0.29 (s, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2) $\delta = 162.9, 162.5, 143.5, 140.7, 135.9, 129.3, 128.2, 127.2, 123.7, 111.1, 100.6, 67.4$ (d, $J = 4.5$ Hz), 57.6, 56.6, 53.2 (d, $J = 3.8$ Hz), 52.3 (d, $J = 3.3$ Hz), 50.7 (d, $J = 3.1$ Hz), 44.5, 25.6, 18.2, 15.5, -3.0, -3.5 (d, $J = 1.9$ Hz); **Minor product (11R*,10aS*)-endo**: 1H NMR (600 MHz, CD_2Cl_2) $\delta = 7.39 - 7.36$ (m, 1H), 7.35 - 7.30 (m, 2H), 7.21 - 7.19 (m, 1H), 6.27 (d, $J = 1.7$ Hz, 1H), 4.33 (t, $J = 3.0$ Hz, 1H), 3.82 (s, 3H), 3.65 - 3.58 (m, 1H), 3.56 (br s, 1H), 3.54 (s, 3H), 3.51 - 3.46 (m, 1H), 2.38 (d, $J = 14.0, 2.9$ Hz, 1H), 1.88 (ddd, $J = 14.0, 3.2, 0.8$ Hz, 1H), 1.23 (t, $J = 7.1$ Hz, 3H), 0.97 (s, 9H), 0.23 (s, 3H), 0.16 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[C_{25}H_{35}NO_6SSiNa]^+$: 528.1847, found: 528.1848.

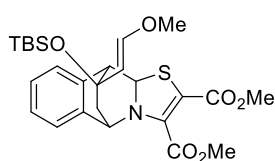
Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-propoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (3d)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2d** (100.7 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3d** (61.0 mg, 0.12 mmol, 60%, 7:1 d.r.) as a yellow solid. **M.p.**: 48-58 °C. **R_f**(pentane/EtOAc 8:1) = 0.41.

Major product (11S*,10aS*)-endo: 1H NMR (500 MHz, CD_2Cl_2) $\delta = 7.35$ (td, $J = 7.4, 1.3$ Hz, 1H), 7.30 - 7.25 (m, 2H), 7.18 (d, $J = 7.9$ Hz, 1H), 6.18 (d, $J = 1.6$ Hz, 1H), 4.29 (t, $J = 3.1$ Hz, 1H), 3.83 (s, 3H), 3.65 (dt, $J = 8.8, 6.8$ Hz, 1H), 3.57 (br s, 1H), 3.55 (s, 3H), 3.42 (dt, $J = 8.9, 6.9$ Hz, 1H), 2.40 (dd, $J = 14.0, 2.9$ Hz, 1H), 1.87 (ddd, $J = 14.0, 3.3, 0.9$ Hz, 1H), 1.63 (ddd, $J = 13.7, 7.3, 3.1$ Hz, 2H), 0.98 (t, $J = 7.4$ Hz, 3H), 0.57 (s, 9H), 0.01 (s, 3H), -0.32 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) $\delta = 163.0, 162.5, 143.5, 140.7, 135.9, 129.3, 128.2, 127.2, 123.7, 111.1, 100.5, 67.3, 63.7, 56.7, 54.2, 53.2, 52.3, 25.6, 23.6, 18.2, 10.9, -3.0, -3.6$; **Minor product (11R*,10aS*)-endo**: 1H NMR (500 MHz, CD_2Cl_2) $\delta = 7.38 - 7.35$ (m, 1H), 7.33 - 7.30 (m, 2H), 7.20 (d, $J = 7.9$ Hz, 1H), 6.27 (d, $J = 1.6$ Hz, 1H), 4.33 (t, $J = 3.1$ Hz, 1H), 3.82 (s, 3H), 3.56 (br s, 1H), 3.54 (s, 3H), 3.52 - 3.47 (m, 1H), 3.36 (dt, $J = 8.6, 7.1$ Hz, 1H), 2.38 (dd, $J = 13.8, 2.8$ Hz, 1H), 1.90 (ddd, $J = 13.8, 3.4, 0.9$ Hz, 1H), 1.64 - 1.56 (m, 2H), 0.97 (s, 9H), 0.66 (t, $J = 7.4$ Hz, 3H), 0.23 (s, 3H), 0.16 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[C_{26}H_{37}NO_6SSiNa]^+$: 542.2003, found: 542.2005.

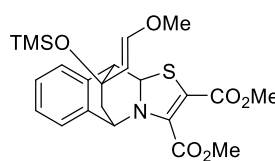
Dimethyl (E)-11-((tert-butyldimethylsilyl)oxy)-11-(2-methoxyvinyl)-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3e)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and Danishefsky's diene **2e** (95.3 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3e** (31.0 mg, 0.06 mmol, 30%, 8:1 d.r.) as a yellow solid. **M.p.**: 53-63 °C.

R_f(pentane/EtOAc 8:1) = 0.59. **Major product (11S*,10aS*)-endo**: ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.34 (td, *J* = 7.6, 1.3 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.18 – 7.16 (m, 1H), 6.72 (d, *J* = 13.0 Hz, 1H), 6.05 (d, *J* = 1.5 Hz, 1H), 5.00 (d, *J* = 13.0 Hz, 1H), 4.29 (t, *J* = 3.0 Hz, 1H), 3.83 (s, 3H), 3.62 (s, 3H), 3.54 (s, 3H), 3.20 (t, *J* = 1.1 Hz, 1H), 2.46 (dd, *J* = 14.3, 2.9 Hz, 1H), 1.66 (ddd, *J* = 14.3, 3.4, 1.1 Hz, 1H), 0.47 (s, 9H), -0.03 (s, 3H), -0.23 (s, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 163.0, 162.5, 150.6, 143.6, 140.2, 136.7, 129.6, 128.0, 126.8, 123.5, 111.0, 108.6, 74.0, 67.8, 56.7, 56.2, 55.8, 53.2, 52.3, 41.9, 25.4, 17.9, -1.9, -2.7; **Minor product (11R*,10aS*)-endo**: ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.32 (td, *J* = 7.4, 1.3 Hz, 1H), 7.26 – 7.24 (m, 2H), 7.19 – 7.17 (m, 1H), 6.54 (d, *J* = 1.5 Hz, 1H), 5.80 (d, *J* = 13.0 Hz, 1H), 4.62 (d, *J* = 13.0 Hz, 1H), 4.27 (t, *J* = 3.0 Hz, 1H), 3.83 (s, 3H), 3.54 (s, 3H), 3.29 (s, 3H), 3.17 (t, *J* = 1.1 Hz, 1H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 (s, 9H); **HRMS (ESI)**: *m/z* calcd. for [C₂₆H₃₅NO₆SSiNa]⁺: 540.1847, found: 540.1854.

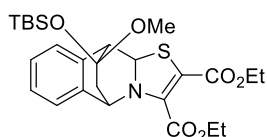
Dimethyl (E)-11-(2-methoxyvinyl)-11-((trimethylsilyl)oxy)-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3f)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1 equiv.) and Danishefsky's diene **2f** (77.4 μ L, 0.40 mmol, 2 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3f** (31.0 mg, 0.067 mmol, 33%, 7:1 d.r.) as a yellow solid. **M.p.**: 143-150 °C.

R_f(pentane/EtOAc 8:1) = 0.5. **Major product (11S*,10aS*)-endo**: ¹H NMR (500 MHz, CD₂Cl₂) δ = 7.36 (td, *J* = 7.5, 1.4 Hz, 1H), 7.29 (td, *J* = 7.5, 1.4 Hz, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 12.9 Hz, 1H), 6.08 (d, *J* = 1.6 Hz, 1H), 5.06 (d, *J* = 12.8 Hz, 1H), 4.28 (t, *J* = 3.1 Hz, 1H), 3.83 (s, 3H), 3.62 (s, 3H), 3.54 (s, 3H), 3.22 (br s, 1H), 2.44 (dd, *J* = 14.3, 2.8 Hz, 1H), 1.73 (dd, *J* = 14.3, 4.4 Hz, 1H), -0.18 (s, 9H); ¹³C NMR (125 MHz, CD₂Cl₂) δ = 163.0, 162.5, 150.7, 143.5, 140.1, 136.8, 129.3, 128.0, 126.8, 123.6, 111.3, 108.6, 74.4, 67.9, 56.7, 56.1, 55.6, 53.2, 52.3, 42.7, 2.0; **Minor product (11R*,10aS*)-endo**: ¹H NMR (500 MHz, CD₂Cl₂) δ = 7.45 – 7.40 (m, 1H), 7.34 – 7.31 (m, 2H), 7.14 (d, *J* = 1.5 Hz, 1H), 5.90 (d, *J* = 12.9 Hz, 1H), 4.55 (d, *J* = 12.9 Hz, 1H), 4.27 (t, *J* = 3.1 Hz, 1H), 3.82 (s, 3H), 3.54 (s, 3H), 3.29 (s, 3H), 3.14 (br s, 1H), 2.27 (dd, *J* = 14.2, 2.7 Hz, 1H), 1.97 (dd, *J* = 14.2, 3.5 Hz, 1H), 0.16 (s, 9H); **HRMS (ESI)**: *m/z* calcd. for [C₂₃H₂₉NO₆SSiNa]⁺: 498.1377, found: 498.1379.

Diethyl 11-((tert-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3g)

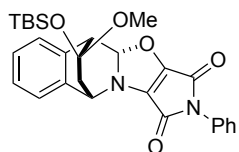


Following the general procedure, the reaction between isoquinolinium **1b** (66.3 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 20:1) the product **3g**

(77.0 mg, 0.148 mmol, 74%, 7:1 d.r.) as an orange solid. **M.p.**: 61-68°C. **R_f**(pentane/EtOAc 20:1) = 0.75. **Major product (11S*,10aS*)-endo**: ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.37 – 7.34 (m, 1H), 7.31 – 7.26 (m, 2H), 7.19 – 7.17 (m, 1H), 6.16 (d, *J* = 1.6 Hz, 1H), 5.33 (s, 1H), 4.34 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.29 (t, *J* = 3.1 Hz, 1H), 4.24 (dq, 10.8, 7.1 Hz,

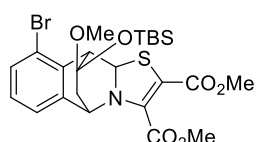
1H), 4.06 – 3.94 (m, 2H), 3.56 (d, $J = 1.9$ Hz, 1H), 3.36 (s, 3H), 2.38 (dd, $J = 14.0, 2.9$ Hz, 1H), 1.84 (ddd, $J = 14.0, 3.4, 0.9$ Hz, 1H), 1.35 (t, $J = 7.2$ Hz, 3H), 1.14 (t, $J = 7.1$ Hz, 3H), 0.57 (s, 9H), 0.03 (s, 3H), -0.27 (s, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2) $\delta = 162.5, 162.0, 143.4, 140.7, 135.8, 129.3, 128.2, 127.2, 123.8, 111.0, 101.0, 67.0, 62.6, 61.4, 56.6, 50.3, 50.1, 25.6, 18.2, 14.2, -3.0, -3.5$; **Minor product (11R*,10aS*)-endo**: ^1H NMR (600 MHz, CD_2Cl_2) $\delta = 7.41 - 7.38$ (m, 1H), 7.35 – 7.32 (m, 2H), 7.21 – 7.19 (m, 1H), 6.26 (d, $J = 1.6$ Hz, 1H), 4.33 – 4.20 (m, 3H), 3.54 (d, $J = 1.6$ Hz, 1H), 3.15 (s, 3H), 2.37 (dd, $J = 13.8, 2.8$ Hz, 1H), 1.88 (dd, $J = 13.8, 3.5, 0.9$ Hz, 1H), 1.34 (t, $J = 7.2$ Hz, 3H), 1.13 (t, $J = 7.1$ Hz, 3H), 0.98 (s, 9H), 0.22 (s, 3H), 0.17 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{26}\text{H}_{37}\text{NO}_6\text{SiNa}]^+$: 542.2003, found: 542.2003.

(4aS*,5R*,10S*,13R*)-13-((tert-Butyldimethylsilyl)oxy)-13-methoxy-2-phenyl-4a,5-dihydro-1H,10H-5,10-ethanopyrrolo[3',4':4,5]oxa-zolo[3,2-b]isoquinoline-1,3(2H)-dione (3h)



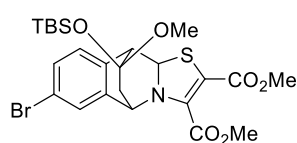
Following the general procedure, the reaction between isoquinolinium **1m** (73.2 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 10:1) the product **3h** (53.0 mg, 0.105 mmol, 53%, single isomer) as a red solid. **M.p.**: 75–83 $^\circ\text{C}$. **R_f**(pentane/EtOAc 60:1) = 0.8. ^1H NMR (500 MHz, CD_2Cl_2) $\delta = 7.50 - 7.43$ (m, 2H), 7.40 – 7.31 (m, 3H), 7.23 (td, $J = 7.4, 1.6$ Hz, 1H), 7.15 (td, $J = 7.3, 1.3$ Hz, 1H), 7.13 – 7.11 (m, 1H), 7.08 (dd, $J = 7.7, 1.3$ Hz, 1H), 6.05 (td, $J = 7.3, 1.3$ Hz, 1H), 5.90 (d, $J = 7.8$ Hz, 1H), 3.56 (s, 3H), 2.88 (dd, $J = 14.8, 6.9$ Hz, 1H), 2.65 (dd, $J = 14.8, 7.1$ Hz, 1H), 1.00 (s, 9H), 0.33 (s, 3H), 0.29 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) $\delta = 171.1, 166.6, 166.1, 133.4, 131.8, 131.0, 130.6, 129.3, 129.1, 128.5, 127.9, 126.8, 126.6, 126.3, 124.6, 123.1, 106.3, 55.6, 52.0, 39.6, 30.1, 25.8, 18.9, -3.9, -4.1$; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_5\text{SiNa}]^+$: 527.1973, found: 527.1974.

Dimethyl 9-bromo-11-((tert-butyl dimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3i)



Following the general procedure, the reaction between 5-bromo isoquinolinium **1c** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3i** (71.0 mg, 0.12 mmol, 60%, 3:1 d.r.) an orange solid. **M.p.**: 148–156 $^\circ\text{C}$. **R_f**(pentane/EtOAc, 8:1) = 0.77. **Major product (11S*,10aS*)-endo**: ^1H NMR (500 MHz, CD_2Cl_2) $\delta = 7.57$ (dd, $J = 6.3, 2.9$ Hz, 1H), 7.18 – 7.15 (m, 2H), 6.13 (d, $J = 1.7$ Hz, 1H), 4.30 (t, $J = 3.1$ Hz, 1H), 3.83 (s, 3H), 3.56 (s, 3H), 3.39 (s, 3H), 3.24 (s, 1H), 2.34 (dd, $J = 14.1, 2.8$ Hz, 1H), 1.88 (ddd, $J = 14.1, 3.4, 0.9$ Hz, 1H), 0.62 (s, 9H), 0.05 (s, 3H), -0.28 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) $\delta = 162.8, 162.4, 142.9, 142.9, 135.9, 131.8, 128.5, 124.8, 123.1, 112.0, 101.0, 67.0$ (d, $J = 3.0$ Hz), 56.8, 52.4 (d, $J = 2.6$ Hz), 50.2 (d, $J = 1.9$ Hz), 48.6 (d, $J = 1.0$ Hz), 44.2, 25.6, 18.1, -3.2, -3.3; **Minor product (11R*,10aS*)-endo**: ^1H NMR (500 MHz, CD_2Cl_2) $\delta = 7.59$ (dd, $J = 7.9, 1.3$ Hz, 1H), 7.23 – 7.19 (m, 2H), 6.28 (d, $J = 1.7$ Hz, 1H), 4.33 (t, $J = 3.1$ Hz, 1H), 3.82 (s, 3H), 3.56 (s, 3H), 3.24 (s, 3H), 2.38 (dd, $J = 13.8, 2.8$ Hz, 1H), 1.91 (ddd, $J = 13.8, 3.6, 0.9$ Hz, 1H), 0.98 (s, 9H), 0.23 (s, 3H), 0.19 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{24}\text{H}_{32}\text{NO}_6\text{SBrSiNa}]^+$: 592.0795, found: 592.0780.

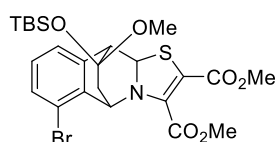
Dimethyl 7-bromo-11-((tert-butyl dimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3j)



Following the general procedure, the reaction between 7-bromo isoquinolinium **1d** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography

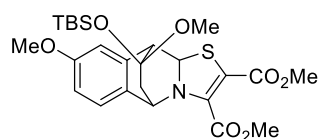
(pentane/EtOAc 8:1) the product **3j** (55.0 mg, 0.096 mmol, 48%, 7:1 d.r.) as an orange solid. **M.p.:** 59-67 °C. **Major product (11S*,10aS*)-endo:** R_f (pentane/EtOAc, 8:1) = 0.43; $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.50 (dd, J = 7.9, 2.0 Hz, 1H), 7.36 (d, J = 2.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 6.14 (d, J = 1.6 Hz, 1H), 4.27 (t, J = 3.1 Hz, 1H), 3.84 (s, 3H), 3.57 (s, 3H), 3.55 (s, 1H), 3.34 (s, 3H), 2.38 (dd, J = 14.0, 2.9 Hz, 1H), 1.82 (ddd, J = 14.0, 3.4, 0.9 Hz, 1H), 0.59 (s, 9H), 0.04 (s, 3H), -0.23 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 162.8, 162.3, 142.9, 142.7, 135.0, 131.1, 130.8, 126.9, 120.9, 111.8, 100.7, 67.0, 56.2, 52.4, 50.2, 50.0, 43.7, 25.6, 18.2, -3.0, -3.4; **Minor product (11R*,10aS*)-endo:** R_f (pentane/EtOAc, 8:1) = 0.52; $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.52 (dd, J = 7.9, 2.0 Hz, 1H), 7.36 (d, J = 2.0 Hz, 1H), 7.22 (d, J = 7.9 Hz, 1H), 6.24 (d, J = 1.6 Hz, 1H), 4.31 (t, J = 3.2 Hz, 1H), 3.83 (s, 3H), 3.57 (s, 3H), 3.53 (s, 1H), 3.13 (s, 3H), 2.36 (dd, J = 13.9, 2.8 Hz, 1H), 1.87 (ddd, J = 13.8, 3.6, 0.9 Hz, 1H), 0.97 (s, 9H), 0.21 (s, 3H), 0.17 (s, 3H); **HRMS (ESI):** m/z calcd. for $[\text{C}_{24}\text{H}_{32}\text{NO}_6\text{SBrSiNa}]^+$: 592.0795, found: 592.0801.

Dimethyl 6-bromo-11-((tert-butyldimethylsilyloxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3k)



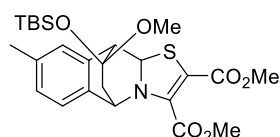
Following the general procedure, the reaction between 8-bromo isoquinolinium **1e** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3k** (88.0 mg, 0.15 mmol, 75%, 5:1 d.r.) as an orange solid. **M.p.:** 125-133 °C. R_f (pentane/EtOAc, 8:1) = 0.56. **Major product (11S*,10aS*)-endo:** $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.47 (dd, J = 7.2, 2.0 Hz, 1H), 7.25 – 7.22 (m, 2H), 6.14 (d, J = 1.5 Hz, 1H), 4.76 (t, J = 3.1 Hz, 1H), 3.82 (s, 3H), 3.57 (s, 3H), 3.56 (s, 1H), 3.34 (s, 3H), 2.39 (dd, J = 14.1, 2.9 Hz, 1H), 1.87 (ddd, J = 14.1, 3.5, 0.9 Hz, 1H), 0.58 (s, 9H), 0.04 (s, 3H), -0.26 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CD_2Cl_2) δ = 162.5, 162.0, 142.3, 140.5, 138.5, 130.8, 129.6, 128.7, 118.9, 112.9, 100.7, 66.6, 55.5, 53.2, 52.4, 50.8, 50.2, 43.1, 25.6, 18.2, -3.1, -3.5; **Minor product (11R*,10aS*)-endo:** $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.50 (dd, J = 8.0, 1.2 Hz, 1H), 7.32 – 7.26 (m, 2H), 6.25 (d, J = 1.5 Hz, 1H), 4.79 (t, J = 3.2 Hz, 1H), 3.81 (s, 3H), 3.56 (s, 3H), 3.55 (s, 1H), 3.12 (s, 3H), 2.36 (d, J = 2.8 Hz, 1H), 1.90 (ddd, J = 13.9, 3.6, 0.9 Hz, 1H), 0.97 (s, 9H), 0.22 (s, 3H), 0.17 (s, 3H); **HRMS (ESI):** m/z calcd. for $[\text{C}_{24}\text{H}_{32}\text{NO}_6\text{SBrSiNa}]^+$: 592.0795, found: 592.0799.

Dimethyl 11-((tert-butyldimethylsilyloxy)-8,11-dimethoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3l)



Following the general procedure, the reaction between 6-methoxy isoquinolinium **1f** (66.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3l** (26.0 mg, 0.05 mmol, 25%, 50:1 d.r.) as a brown solid. **M.p.:** 60-70 °C. R_f (pentane/EtOAc, 10:1) = 0.33. **Major product (11S*,10aS*)-endo:** $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.08 (d, J = 8.1 Hz, 1H), 6.85 (d, J = 2.5 Hz, 1H), 6.80 (dd, J = 8.1, 2.5 Hz, 1H), 6.12 (d, J = 1.6 Hz, 1H), 4.26 (t, J = 3.1 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.56 (s, 3H), 3.50 (s, 1H), 3.34 (s, 3H), 2.35 (dd, J = 13.9, 2.9 Hz, 1H), 1.82 (ddd, J = 13.8, 3.4, 0.9 Hz, 1H), 0.60 (s, 9H), 0.04 (s, 3H), -0.26 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CD_2Cl_2) δ = 163.0, 162.5, 160.1, 143.6, 137.0, 132.8, 124.7, 115.1, 112.5, 111.0, 101.0, 67.1, 56.3, 55.7, 53.2, 52.3, 50.7, 50.1, 44.4, 25.6, 18.2, -3.0, -3.5; **HRMS (ESI):** m/z calcd. for $\text{C}_{25}\text{H}_{35}\text{NO}_7\text{SSiNa}^+$: 544.1796, found: 544.17955.

Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-8-methyl-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (3m)

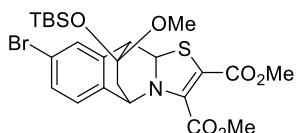


Following the general procedure, the reaction between 6-methyl isoquinolinium **1g** (63.5 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3m** (35.0 mg, 0.069 mmol, 35%, 7:1 d.r.) as a brown solid. **M.p.:** 66-71 °C. **R_f** (pentane/EtOAc, 8:1) = 0.63.

Major product (11*S,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.11 – 7.03 (m, 3H), 6.14 (d, *J* = 1.5 Hz, 1H), 4.25 (t, *J* = 3.1 Hz, 1H), 3.82 (s, 3H), 3.55 (s, 3H), 3.48 (s, 1H), 3.34 (s, 3H), 2.37 (s, 3H), 2.37 – 2.34 (m, 1H), 1.81 (ddd, *J* = 14.0, 3.4, 0.9 Hz, 1H), 0.57 (s, 9H), 0.03 (s, 3H), -0.27 (s, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 163.0, 162.5, 143.7, 138.0, 137.7, 135.5, 130.1, 127.6, 123.5, 110.8, 101.1, 67.2, 56.5, 53.2, 52.3, 50.4, 50.1, 44.1, 25.5, 21.5, 18.2, -3.0, -3.5;

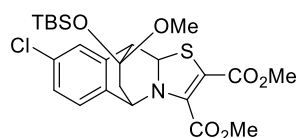
Minor product (11*R,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.16 – 7.13 (m, 3H), 7.07 (d, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 1.6 Hz, 1H), 4.29 (t, *J* = 3.1 Hz, 1H), 3.82 (s, 3H), 3.55 (s, 3H), 3.48 (s, 1H), 3.15 (s, 3H), 2.41 (s, 3H), 2.35 (dd, *J* = 13.7, 2.8 Hz, 1H), 1.85 (ddd, *J* = 13.7, 3.6, 0.9 Hz, 1H), 0.97 (s, 9H), 0.21 (s, 3H), 0.17 (s, 3H); **HRMS (ESI):** *m/z* calcd. for [C₂₅H₃₅NO₆SSiNa]⁺: 528.1847, found: 528.1849.

Dimethyl 8-bromo-11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (3n)



Following the general procedure, the reaction between 6-bromo isoquinolinium **1h** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 6:1) the product **3n** (39.0 mg, 0.068 mmol, 34%, 7:1 d.r.) as an orange solid. **M.p.:** 69-77 °C. **R_f** (pentane/EtOAc, 6:1) = 0.73. **Major product (11*S**,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.45 – 7.42 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.12 (d, *J* = 1.5 Hz, 1H), 4.30 (t, *J* = 3.1 Hz, 1H), 3.82 (s, 3H), 3.57 (s, 3H), 3.52 (s, 1H), 3.34 (s, 3H), 2.38 (ddd, *J* = 14.1, 2.8, 0.9 Hz, 1H), 1.82 (ddd, *J* = 14.0, 3.5, 0.9 Hz, 1H), 0.60 (s, 9H), 0.05 (s, 3H), -0.23 (s, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 162.9, 162.3, 143.1, 139.7, 138.2, 132.2, 130.2, 125.5, 122.0, 111.5, 100.8, 66.8, 56.1, 53.3, 52.4, 50.5, 50.3, 43.7, 25.5, 18.2, -3.0, -3.4; **Minor product (11*R**,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.49 – 7.46 (m, 2H), 7.11 – 7.09 (m, 1H), 6.23 (d, *J* = 1.5 Hz, 1H), 4.33 (t, *J* = 3.1 Hz, 1H), 3.82 (s, 3H), 3.56 (s, 3H), 3.51 (s, 1H), 3.15 (s, 3H), 2.34 (dd, *J* = 13.3, 2.7 Hz, 1H), 1.88 (ddd, 13.9, 3.7, 0.8 Hz, 1H), 0.97 (s, 9H), 0.21 (s, 3H), 0.17 (s, 3H); **HRMS (ESI):** *m/z* calcd. for [C₂₄H₃₂NO₆SBrSiNa]⁺: 592.0795, found: 592.0799.

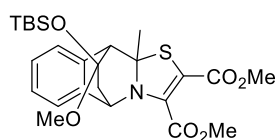
Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-8-chloro-11-methoxy-10,10a-dihydro-5*H*-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (3o)



Following the general procedure, the reaction between 6-chloro isoquinolinium **1i** (67.5 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3o** (49.0 mg, 0.093 mmol, 47%, 7:1 d.r.) as an orange solid. **M.p.:** 70-78 °C. **R_f** (pentane/EtOAc, 8:1) = 0.47. **Major product (11*S**,10*aS**)-endo:** ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.29 – 7.27 (m, 2H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.13 (d, *J* = 1.6 Hz, 1H), 4.31 (t, *J* = 3.1 Hz, 1H), 3.83 (s, 3H), 3.56 (s, 3H), 3.53 (br s, 1H), 3.35 (s, 3H), 2.39 (dd, *J* = 14.1, 2.8 Hz, 1H), 1.83 (ddd, *J* = 14.1, 3.5, 0.9 Hz, 1H), 0.60 (s, 9H), 0.06 (s, 3H), -0.22 (s, 3H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 162.9, 162.3, 143.1, 139.2, 137.8, 133.9, 129.3, 127.2, 125.2, 111.5, 100.8,

66.8, 56.1, 53.3, 52.4, 50.5, 50.3, 43.8, 25.5, 18.2, -3.0, -3.4; **Minor product (11R*,10aS*)-endo**: $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.34 – 7.30 (m, 2H), 7.16 (d, J = 7.8 Hz, 1H), 6.23 (d, J = 1.6 Hz, 1H), 4.34 (t, J = 3.1 Hz, 1H), 3.82 (s, 3H), 3.56 (s, 3H), 3.52 (br s, 1H), 3.15 (s, 3H), 2.36 (dd, J = 13.8, 2.8 Hz, 1H), 1.88 (ddd, J = 13.8, 3.5, 0.9 Hz, 1H), 0.97 (s, 9H), 0.22 (s, 3H), 0.17 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{24}\text{H}_{32}\text{NO}_6\text{SiNa}]^+$: 548.1300, found: 548.1302.

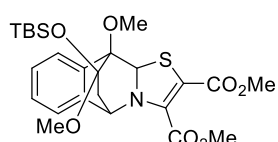
Dimethyl 11-((tert-butyldimethylsilyl)oxy)-11-methoxy-10a-methyl-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3p)



Following the general procedure, the reaction between 3-methyl isoquinolinium **1j** (31.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (43.8 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 10:1) the product **3p** (52.0 mg, 0.097 mmol, 33%, 3:1 d.r.) as a brown solid. **M.p.**: 57-65 $^\circ\text{C}$.

R_f(pentane/EtOAc 10:1) = 0.46. **Major product (11S*,10aS*)-endo**: $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.27 (td, J = 7.0, 2.0 Hz, 1H), 7.24 – 7.13 (m, 2H), 7.08 (dd, J = 7.3, 1.3 Hz, 1H), 4.29 (dd, J = 3.9, 2.3 Hz, 1H), 3.82 (s, 3H), 3.64 (br s, 1H), 3.56 (s, 3H), 3.36 (s, 3H), 2.41 (dd, J = 14.1, 2.4 Hz, 1H), 2.14 (s, 3H), 1.98 (ddd, J = 14.1, 3.8, 1.1 Hz, 1H), 0.55 (s, 9H), 0.01 (s, 3H), -0.39 (s, 3H); $^{13}\text{C NMR}$ (101 MHz, CD_2Cl_2) δ = 163.0, 162.9, 140.9, 139.3, 139.2, 127.9, 127.9, 126.2, 124.3, 114.1, 101.7, 81.6, 56.7, 53.1, 52.4, 52.1, 49.2, 44.0, 32.7, 25.7, 18.2, -3.1, -3.4; **Minor product (11R*,10aS*)-endo**: $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.26 – 7.20 (m, 4H), 4.47 (t, J = 2.8 Hz, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.42 (br s, 1H), 3.30 (s, 3H), 2.43 (dd, J = 13.9, 2.7 Hz, 1H), 2.12 (s, 3H), 1.98 (ddd, J = 13.9, 2.7, 0.9 Hz, 1H), 0.55 (s, 9H), 0.03 (s, 3H), -0.32 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{25}\text{H}_{35}\text{NO}_6\text{SSiNa}]^+$: 528.1847, found: 528.1846.

Dimethyl 11-((tert-butyldimethylsilyl)oxy)-10,11-dimethoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (3q)

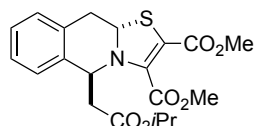


Following the general procedure, the reaction between 4-methoxy isoquinolinium **1k** (66.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) afforded after purification *via* flash column chromatography (pentane/EtOAc 8:1) the product **3q** (10.0 mg, 0.02 mmol, 10%, 10:1 d.r.) as a brown solid. **M.p.**: 54-62 $^\circ\text{C}$. **R_f** (pentane/EtOAc, 8:1) = 0.58. **Major product (11S*,10aS*)-endo**: $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.57 – 7.52 (m, 1H), 7.39 (td, J = 7.5, 1.3 Hz, 1H), 7.28 (td, J = 7.6, 1.3 Hz, 1H), 7.16 (d, J = 7.3 Hz, 1H), 6.54 (s, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.55 (s, 3H), 3.35 (s, 3H), 2.60 (dd, J = 13.6, 3.2 Hz, 1H), 1.72 (dd, J = 13.6, 3.2 Hz, 1H), 0.69 (s, 9H), 0.01 (s, 3H), -0.36 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CD_2Cl_2) δ = 162.7, 162.5, 142.8, 138.6, 137.3, 127.9, 127.2, 126.5, 123.2, 113.1, 102.6, 81.8, 70.2, 55.7, 55.5, 53.2, 52.4, 49.9, 41.9, 25.8, 18.7, -2.1, -4.3; **Minor product (11R*,10aS*)-endo**: $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.62 (d, J = 6.9 Hz, 1H), 7.42 (td, J = 7.5, 1.3 Hz, 1H), 7.32 (td, J = 7.6, 1.3 Hz, 1H), 6.46 (s, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.55 (s, 3H), 3.32 (s, 3H), 2.40 – 2.36 (m, 1H), 2.01 – 1.97 (m, 1H), 1.00 (s, 9H), 0.24 (s, 3H), 0.07 (s, 3H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{25}\text{H}_{35}\text{NO}_7\text{SSiNa}]^+$: 544.1796, found: 544.1792.

5. Synthesis and Analytical Data of Tetrahydrothiazoloisoquinolines 4

General procedure for the synthesis of tetrahydrothiazoloisoquinolines: The isoquinolinium zwitterion **1** (0.2 mmol, 1.0 equiv.) was added to a reaction vessel under argon atmosphere. After addition of DMF (1 mL), the nucleophile **2** (0.4 mmol, 2.0 equiv.) was added dropwise. The mixture was stirred for 18 h at r.t.; then quenched with H₂O (1 mL) and extracted with CH₂Cl₂ (3 x 1 mL). The solvent was evaporated, the residual dark slur taken up in CH₂Cl₂ and dry loaded onto silica. The product was purified *via* flash column chromatography (pentane/EtOAc) and dried *in vacuo*.

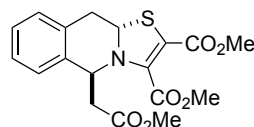
Dimethyl (5S*,10aS*)-5-(2-isopropoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (**4a**)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2a** (102.0 μ L, 0.40 mmol, 2.0 equiv.) in DMF

afforded after purification *via* flash column chromatography (pentane/EtOAc 4:1) the product **4a** (52.0 mg, 0.13 mmol, 64%) as a yellow oil. R_f (pentane/EtOAc 8:1) = 0.37. $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ = 7.23 – 7.19 (m, 3H), 7.14 – 7.11 (m, 1H), 5.76 (dd, J = 10.7, 4.1 Hz, 1H), 4.93 (p, J = 6.2 Hz, 1H), 4.88 (dd, J = 9.3, 4.4 Hz, 1H), 3.79 (s, 3H), 3.60 (s, 3H), 3.34 (dd, J = 16.1, 10.7 Hz, 1H), 2.95 (dd, J = 15.4, 9.3 Hz, 1H), 2.82 (dd, J = 15.4, 4.4 Hz, 1H), 2.79 (dd, J = 16.1, 4.1 Hz, 1H), 1.20 (d, J = 6.2 Hz, 6H); $^{13}\text{C NMR}$ (125 MHz, DMSO- d_6) δ = 169.4, 162.5, 161.6, 144.1, 135.1, 132.7, 129.1, 127.3, 126.7, 126.3, 94.9, 67.9, 62.4, 54.3, 53.2, 51.6, 41.9, 36.0, 21.4; **HRMS (ESI):** m/z calcd. for [C₂₀H₂₃NO₆SNa]⁺: 428.1144, found: 428.1126.

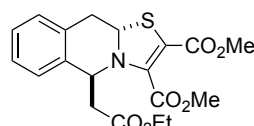
Dimethyl (5S*,10aS*)-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (**4b**)



Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF

afforded after purification *via* flash column chromatography (pentane/EtOAc 3:1) the product **4b** (46.0 mg, 0.122 mmol, 61%) as a yellow oil. R_f (pentane/EtOAc 3:1) = 0.5. $^1\text{H NMR}$ (500 MHz, CD₂Cl₂) δ = 7.23 – 7.19 (m, 2H), 7.13 – 7.08 (m, 1H), 7.09 – 7.06 (m, 1H), 5.52 (dd, J = 11.0, 3.8 Hz, 1H), 4.98 (dd, J = 8.5, 4.8 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.53 (ddt, J = 16.1, 10.8, 0.9 Hz, 1H), 2.94 (dd, J = 15.6, 8.7 Hz, 1H), 2.82 (dd, J = 15.5, 4.7 Hz, 1H), 2.79 (dd, J = 16.1, 3.9 Hz, 1H); $^{13}\text{C NMR}$ (125 MHz, CD₂Cl₂) δ = 170.7, 163.4, 162.6, 144.1, 135.4, 133.2, 129.7, 128.0, 127.4, 126.5, 97.4, 63.4, 54.9, 53.6, 52.4, 52.0, 42.7, 37.3; **HRMS (ESI):** m/z calcd. for [C₁₈H₁₉NO₆SNa]⁺: 400.0825, found: 400.0822.

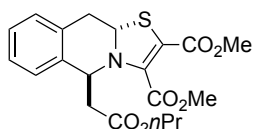
Dimethyl (5S*,10aS*)-5-(2-ethoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (**4c**)



Following the general procedure, the reaction between isoquinolinium **1a** (60.6 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2c** (95.2 μ L, 0.40 mmol, 2.0 equiv.) in DMF

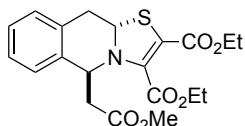
afforded after purification *via* flash column chromatography (pentane/EtOAc 4:1) the product **4c** (46.0 mg, 0.118 mmol, 59%) as a yellow oil. R_f (pentane/EtOAc 4:1) = 0.5. $^1\text{H NMR}$ (400 MHz, CD₂Cl₂) δ = 7.23 – 7.19 (m, 2H), 7.12 – 7.06 (m, 2H), 5.54 (dd, J = 10.9, 4.0 Hz, 1H), 4.98 (dd, J = 8.4, 4.9 Hz, 1H), 4.23 – 4.11 (m, 2H), 3.86 (s, 3H), 3.67 (s, 3H), 3.54 (dd, J = 16.1, 10.8 Hz, 1H), 2.92 (dd, J = 15.5, 8.5 Hz, 1H), 2.80 (dd, J = 15.6, 4.8 Hz, 1H), 2.80 (dd, J = 16.1, 4.8 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CD₂Cl₂) δ = 170.3, 163.4, 162.5, 144.2, 135.5, 129.7, 127.9, 127.3, 126.5, 97.3, 63.4, 61.5, 54.9, 53.6, 52.0, 42.9, 37.3, 14.3; **HRMS (ESI):** m/z calcd. for [C₁₉H₂₁NO₆SNa]⁺: 414.0982, found: 414.0988.

Dimethyl (5S*,10aS*)-5-(2-oxo-2-propoxyethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4d)



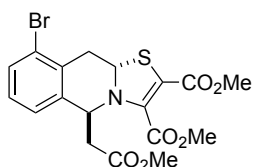
Following the general procedure, the reaction between isoquinolinium **1a** (60.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2d** (100.7 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 2:1) the product **4d** (34.0 mg, 0.084 mmol, 42%) as a yellow oil. R_f (pentane/EtOAc 2:1) = 0.67. $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.23 – 7.19 (m, 2H), 7.12 – 7.07 (m, 2H), 5.54 (dd, J = 10.8, 4.0 Hz, 1H), 4.98 (dd, J = 8.3, 5.0 Hz, 1H), 4.14 – 4.03 (m, 2H), 3.86 (s, 3H), 3.67 (s, 3H), 3.53 (dd, J = 16.1, 10.8 Hz, 1H), 2.94 (dd, J = 15.6, 8.3 Hz, 1H), 2.84 – 2.77 (m, 2H), 1.70 – 1.64 (m, 2H), 0.94 (t, J = 7.4 Hz, 2H); $^{13}\text{C NMR}$ (100 MHz CD_2Cl_2) δ = 170.9, 163.0, 144.6, 136.0, 133.5, 130.1, 128.4, 127.8, 126.9, 67.5, 63.9, 55.3, 54.0, 52.5, 43.3, 37.8, 22.7, 11.0; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{20}\text{H}_{23}\text{NO}_6\text{SNa}]^+$: 428.1138, found: 428.1133.

Diethyl (5S*,10aS*)-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4e)



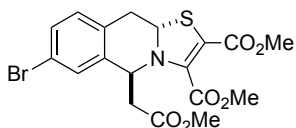
Following the general procedure, the reaction between isoquinolinium **1b** (66.3 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 4:1) the product **4e** (57.0 mg, 0.14 mmol, 70%) as a yellow oil. R_f (pentane/EtOAc 4:1) = 0.8. $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.25 – 7.18 (m, 2H), 7.14 – 7.05 (m, 2H), 5.51 (dd, J = 10.8, 4.1 Hz, 1H), 4.99 (dd, J = 8.4, 5.0 Hz, 1H), 4.33 (qd, J = 7.2, 1.6 Hz, 1H), 4.13 (q, J = 7.1 Hz, 1H), 3.72 (s, 3H), 3.53 (dd, J = 15.9, 10.7 Hz, 1H), 2.95 (dd, J = 15.6, 8.4 Hz, 1H), 2.82 (dd, J = 15.6, 5.0 Hz, 1H), 2.80 (dd, J = 16.2, 4.1 Hz, 1H), 1.34 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.8, 162.9, 162.1, 144.1, 135.5, 133.2, 129.7, 127.9, 127.3, 126.4, 97.6, 63.2, 63.1, 60.9, 54.8, 52.3, 42.6, 37.2, 14.5, 14.0; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{20}\text{H}_{23}\text{NO}_6\text{SNa}]^+$: 428.1138, found: 428.1136.

Dimethyl (5S*,10aS*)-9-bromo-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4f)



Following the general procedure, the reaction between 5-bromo isoquinolinium **1c** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 1:1) the product **4f** (58.0 mg, 0.13 mmol, 65%) as an orange oil. R_f (pentane/EtOAc 1:1) = 0.65; $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.51 (dd, J = 7.6, 1.5 Hz, 1H), 7.13 – 7.06 (m, 2H), 5.50 (dd, J = 10.6, 4.4 Hz, 1H), 4.98 (dd, J = 8.8, 4.8 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.68 (s, 3H), 3.33 (dd, J = 16.9, 10.6 Hz, 1H), 3.03 (dd, J = 16.9, 4.4 Hz, 1H), 2.94 (ddd, J = 15.8, 8.8, 0.8 Hz, 1H), 2.81 (dd, J = 15.7, 4.7 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.7, 163.4, 162.5, 143.9, 138.1, 133.1, 132.3, 128.6, 126.0, 125.6, 98.5, 63.4, 54.8, 53.8, 52.6, 52.3, 42.5, 37.9; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{18}\text{H}_{18}\text{NO}_6\text{SBrNa}]^+$: 479.9911, found: 479.9909.

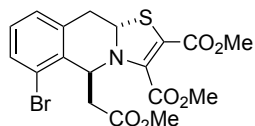
Dimethyl (5S*,10aS*)-7-bromo-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4g)



Following the general procedure, the reaction between 7-bromo isoquinolinium **1d** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 2:1) the product **4g** (42.0 mg, 0.092 mmol, 46%) as an orange oil. R_f (pentane/EtOAc 2:1) = 0.62.

$^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.35 (dd, J = 8.3, 2.1 Hz, 1H), 7.25 (d, J = 2.1 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 5.47 (dd, J = 10.8, 4.0 Hz, 1H), 4.95 (dd, J = 8.7, 4.6 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.45 (dd, J = 16.2, 10.7 Hz, 1H), 2.93 (dd, J = 15.7, 8.8 Hz, 1H), 2.80 (dd, J = 15.8, 4.7 Hz, 1H), 2.75 (dd, J = 16.3, 4.0 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.7, 163.4, 162.6, 144.0, 137.6, 132.5, 131.5, 131.2, 129.6, 120.8, 98.2, 63.2, 54.5, 53.8, 52.6, 52.2, 42.6, 36.8; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{18}\text{H}_{18}\text{NO}_6\text{SBrNa}]^+$: 479.9911, found: 479.9908.

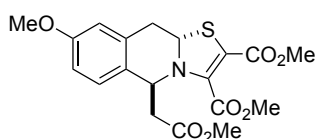
Dimethyl (5S*,10aS*)-6-bromo-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4h)



Following the general procedure, the reaction between 8-bromo isoquinolinium **1e** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 2:1)

the product **4h** (49.0 mg, 0.11 mmol, 55%) as a red oil. R_f (pentane/EtOAc 2:1) = 0.64. $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.44 (dt, J = 7.7, 1.2 Hz, 1H), 7.15 – 7.06 (m, 2H), 5.60 (ddd, J = 10.3, 5.0, 1.3 Hz, 1H), 5.09 (dd, J = 10.9, 2.7 Hz, 1H), 3.88 (s, 3H), 3.74 (s, 3H), 3.66 (s, 3H), 3.54 (dd, J = 16.6, 10.1 Hz, 1H), 3.00 (ddd, J = 15.9, 3.0, 1.2 Hz, 1H), 2.84 (dd, J = 16.7, 5.0 Hz, 1H), 2.75 (ddd, J = 16.0, 10.9, 1.2 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.3, 163.5, 162.3, 144.1, 136.1, 135.2, 132.0, 129.7, 129.2, 122.2, 62.9, 55.5, 53.7, 52.5, 52.2, 39.4, 36.7; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{18}\text{H}_{18}\text{NO}_6\text{SBrNa}]^+$: 479.9911, found: 479.9908.

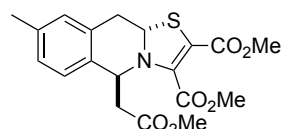
Dimethyl (5S*,10aS*)-8-methoxy-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4i)



Following the general procedure, the reaction between 6-methoxy isoquinolinium **1f** (66.7 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography

(pentane/EtOAc 1:2) the product **4i** (47.0 mg, 0.12 mmol, 60%) as a red oil. R_f (pentane/EtOAc 1:2) = 0.9; $^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 6.98 (d, J = 8.6 Hz, 1H), 6.79 – 6.75 (m, 1H), 6.61 (d, J = 2.7 Hz, 1H), 5.49 (dd, J = 10.9, 3.9 Hz, 1H), 4.92 (dd, J = 8.6, 4.8 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H), 3.71 (s, 3H), 3.67 (s, 3H), 3.51 (dd, J = 16.1, 10.8 Hz, 1H), 2.90 (dd, J = 15.5, 8.6 Hz, 1H), 2.78 (dd, J = 15.5, 4.8 Hz, 1H), 2.74 (dd, J = 16.3, 4.2 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.9, 163.5, 162.7, 159.4, 144.4, 134.6, 127.8, 127.6, 114.1, 114.0, 63.4, 55.8, 54.7, 52.5, 52.2, 42.9, 37.8, 26.0; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{19}\text{H}_{21}\text{NO}_7\text{SNa}]^+$: 430.0931, found: 430.0935.

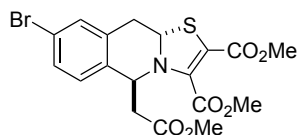
Dimethyl (5S*,10aS*)-5-(2-methoxy-2-oxoethyl)-8-methyl-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4j)



Following the general procedure, the reaction between 6-methyl isoquinolinium **1g** (63.5 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μL , 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography

(pentane/EtOAc 1:1) the product **4j** (22.0 mg, 0.056 mmol, 28%) as a red oil. R_f (pentane/EtOAc 1:1) = 0.78. $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.03 (d, J = 8.0 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 6.92 (s, 1H), 5.50 (dd, J = 10.9, 4.0 Hz, 1H), 4.94 (dd, J = 8.7, 4.7 Hz, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.67 (s, 3H), 3.49 (dd, J = 15.9, 10.9 Hz, 1H), 2.91 (dd, J = 15.6, 8.7 Hz, 1H), 2.79 (dd, J = 15.6, 4.7 Hz, 1H), 2.73 (dd, J = 16.1, 4.0 Hz, 1H), 2.29 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CD_2Cl_2) δ = 170.9, 163.6, 162.7, 144.4, 138.1, 133.1, 132.5, 130.3, 128.4, 126.5, 63.6, 54.9, 53.7, 52.5, 52.2, 42.9, 37.5, 26.0, 21.2; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{19}\text{H}_{21}\text{NO}_6\text{SCINa}]^+$: 414.0982, found: 414.0979.

Dimethyl (5S*,10aS*)-8-bromo-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4k)

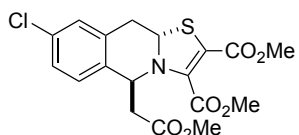


Following the general procedure, the reaction between 6-bromo isoquinolinium **1h** (76.4 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography

(pentane/EtOAc 1:1) the product **4k** (50.0 mg, 0.11 mmol, 55%) as an orange oil. R_f (pentane/EtOAc 1:1) = 0.79.

$^1\text{H NMR}$ (400 MHz, CD_2Cl_2) δ = 7.35 (dd, J = 8.3, 2.2 Hz, 1H), 7.29 – 7.26 (m, 1H), 6.98 (d, J = 8.3 Hz, 1H), 5.48 (dd, J = 10.7, 3.9 Hz, 1H), 4.94 (dd, J = 8.6, 4.7 Hz, 1H), 3.87 (s, 3H), 3.71 (s, 3H), 3.67 (s, 3H), 3.51 (dd, J = 16.2, 10.7 Hz, 1H), 2.92 (dd, J = 15.8, 8.5 Hz, 1H), 2.79 (dd, J = 15.8, 4.7 Hz, 1H), 2.76 (dd, J = 16.3, 4.8 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.7, 163.4, 162.6, 144.0, 135.7, 134.7, 132.6, 130.6, 128.4, 121.8, 98.1, 63.1, 54.6, 53.8, 52.6, 52.3, 42.6, 37.0; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{18}\text{H}_{18}\text{NO}_6\text{SBrNa}]^+$: 479.9911, found: 479.9908.

Dimethyl (5S*,10aS*)-8-chloro-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4l)

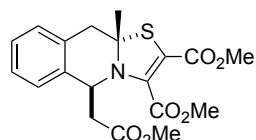


Following the general procedure, the reaction between 6-chloro isoquinolinium **1i** (67.6 mg, 0.20 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (87.6 μ L, 0.40 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography

(pentane/EtOAc 1:1) the product **4l** (62.0 mg, 0.15 mmol, 75%) as a red oil. R_f (pentane/EtOAc 1:1) = 0.76. $^1\text{H NMR}$

(400 MHz, CD_2Cl_2) δ = 7.19 (ddd, J = 8.4, 2.3, 0.9 Hz, 1H), 7.11 (t, J = 1.6 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 5.47 (dd, J = 10.8, 4.0 Hz, 1H), 4.95 (dd, J = 8.6, 4.8 Hz, 1H), 3.85 (s, 3H), 3.70 (s, 3H), 3.66 (s, 3H), 3.49 (dd, J = 16.2, 10.8 Hz, 1H), 2.91 (dd, J = 15.7, 8.6 Hz, 1H), 2.78 (dd, J = 15.7, 4.8 Hz, 1H), 2.75 (dd, J = 16.3, 4.0 Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_2Cl_2) δ = 170.7, 163.4, 162.6, 144.0, 135.4, 134.2, 133.7, 129.6, 128.2, 127.7, 98.0, 63.1, 54.6, 53.8, 52.6, 52.3, 42.6, 37.1; **HRMS (ESI)**: m/z calcd. for $[\text{C}_{18}\text{H}_{18}\text{NO}_6\text{SClNa}]^+$: 434.0436, found: 434.0435.

Dimethyl (5S*,10aS*)-5-(2-methoxy-2-oxoethyl)-10a-methyl-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4m)

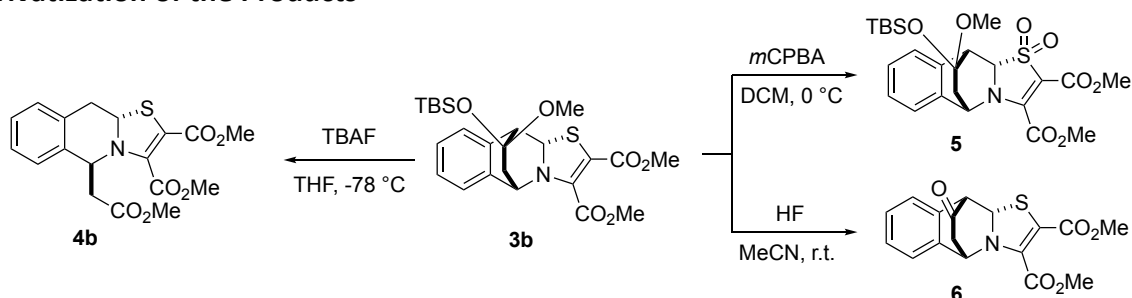


Following the general procedure, the reaction between 3-methyl isoquinolinium **1j** (29.3 mg, 0.09 mmol, 1.0 equiv.) and silyl ketene acetal **2b** (39.4 μ L, 0.18 mmol, 2.0 equiv.) in DMF afforded after purification *via* flash column chromatography

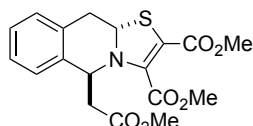
(pentane/EtOAc 1:1) the product **4m** (14.0 mg, 0.036 mmol, 39%, 2.5:1 d.r.) as a yellow oil. R_f (pentane/EtOAc

1:1) = 0.77. **Major product (5S*,10aS*)**: $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.30 – 7.18 (m, 2H), 7.17 – 7.10 (m, 2H), 4.93 (t, J = 7.1 Hz, 1H), 3.87 (s, 3H), 3.71 (s, 3H), 3.63 (s, 3H), 3.48 (d, J = 16.2 Hz, 1H), 3.02 (d, J = 16.2 Hz, 1H), 2.91 (dd, J = 15.7, 7.8 Hz, 1H), 2.70 (dd, J = 15.6, 6.5 Hz, 1H), 1.83 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CD_2Cl_2) δ = 171.4, 163.4, 163.3, 143.5, 137.2, 133.1, 129.7, 128.5, 127.6, 126.8, 102.4, 77.0, 55.9, 53.8, 52.5, 52.3, 43.1, 41.3, 31.9; **Minor product (5R*,10aS*)**: $^1\text{H NMR}$ (600 MHz, CD_2Cl_2) δ = 7.26 – 7.24 (m, 2H), 7.15 (dd, J = 4.6, 3.1 Hz, 2H), 4.98 (dd, J = 10.6, 3.2 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.58 (s, 3H), 3.13 (d, J = 14.7 Hz, 1H), 3.07 (dd, J = 15.2, 3.2 Hz, 1H), 2.68 – 2.64 (m, 1H); **HRMS (ESI)**: m/z calcd. for $[\text{C}_{19}\text{H}_{21}\text{NO}_6\text{SNa}]^+$: 414.0982, found: 414.0978.

6. Derivatization of the Products

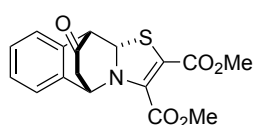


Dimethyl (5S*,10aS*)-5-(2-methoxy-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4b)



Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (**3b**) (49.2 mg, 0.10 mmol, 1.0 equiv.) was dissolved in THF (1 mL) and cooled to -78 °C. A 1.0 M solution of tetrabutylammonium fluoride (TBAF, 150 μ L, 0.15 mmol, 1.5 equiv.) was added dropwise and stirred for 8 h at 0 °C. The reaction was quenched with water (5 mL), extracted with Et₂O (3 x 5 mL), the organic layer washed with brine (5 mL) and dried over MgSO₄. After removal of the solvent under reduced pressure, the product was purified by flash column chromatography (pentane/EtOAc 4:1) to afford **4b** (19.0 mg, 0.051 mmol, 51%).

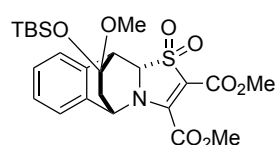
Dimethyl 11-oxo-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (5)



Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (**3b**) (97.0 mg, 0.198 mmol) was dissolved

in a HF-MeCN solution (1:19, 2 mL) and stirred for 1.5 h at room temperature. The reaction was cooled to 0 °C and quenched with aq. sat. NaHCO₃ (10 mL). The mixture was extracted with EtOAc (3 x 6 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄ and concentrated under reduced pressure. The product **5** was isolated by flash column chromatography (CH₂Cl₂/EtOAc 40:1 \rightarrow 20:1) as a yellow solid (33.2 mg, 0.096 mmol, 49%, 2.5:1 d.r.). **M.p.:** 57-62 °C. **R_f**(CH₂Cl₂/EtOAc 20:1) = 0.50. **Major product:** ¹H NMR (400 MHz, CD₂Cl₂) δ = 7.46 – 7.38 (m, 2H), 7.34 – 7.30 (m, 2H), 6.26 (d, *J* = 1.5 Hz, 1H), 4.68 (t, *J* = 2.8 Hz, 1H), 3.91 – 3.88 (m, 1H), 3.85 (s, 3H), 3.56 (s, 3H), 2.79 (dd, *J* = 18.6, 2.7 Hz, 1H), 2.30 (dd, *J* = 18.6, 3.0 Hz, 1H); ¹³C NMR (100 MHz, CD₂Cl₂) δ = 203.8, 162.5, 162.0, 140.8, 133.9, 131.1, 129.3, 128.7, 128.6, 124.6, 112.9, 68.9, 58.4, 58.0, 53.4, 52.5, 41.2. **Minor product:** ¹H NMR (400 MHz, CD₂Cl₂) δ = 7.57 – 7.17 (m, 4H), 5.72 (d, *J* = 1.8 Hz, 1H), 4.79 (t, *J* = 2.4 Hz, 1H), 3.88 (s, 3H), 3.86 (br s, 1H), 3.71 (s, 3H), 3.01 (dd, *J* = 18.6, 2.9 Hz, 1H), 2.44 (dd, *J* = 18.6, 1.8 Hz, 1H); ¹³C NMR (100 MHz, CD₂Cl₂) δ = 204.0, 162.5, 162.0, 142.5, 139.4, 135.4, 129.5, 129.0, 126.5, 124.5, 114.0, 69.8, 58.7, 57.4, 53.6, 52.7, 42.3. **HRMS (ESI):** *m/z* calcd. for [C₁₇H₁₅NO₅SN_a]⁺: 368.0563, found: 368.0564.

Dimethyl 11-((tert-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-b]isoquinoline-2,3-dicarboxylate 1,1-dioxide (6)



Dimethyl 11-((*tert*-butyldimethylsilyl)oxy)-11-methoxy-10,10a-dihydro-5H-5,10-ethanothiazolo[3,2-*b*]isoquinoline-2,3-dicarboxylate (**3b**) (49.2 mg, 0.10 mmol, 1.0 equiv.) was dissolved in DCM and cooled to 0 °C. To the mixture was added *m*CPBA (51.8 mg,

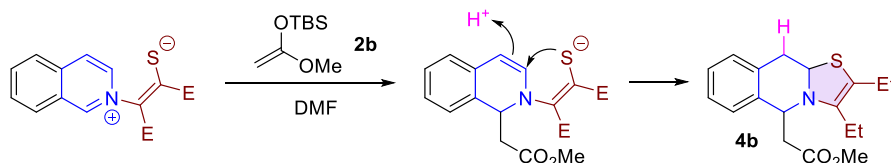
0.30 mmol, 3.0 equiv.) and the mixture was stirred for 16 h while warming to room temperature. The reaction was quenched with aq. 5% Na₂SO₃ (5 mL), sat. aq. NaHCO₃ (2x5 mL) and brine (5 mL) and the organic phase dried over

Na₂SO₄. The solvent was removed under reduced pressure to obtain the desired product **6** as a yellow solid upon drying *in vacuo* (47.0 mg, 0.09 mmol, 90%, 3:1:1: d.r.). **M.p.**: 131-136 °C (decomposition). **R_f**(pentane/EtOAc 3:1) = 0.65. **Major product (11S*,10aS*)-endo**: ¹H NMR (500 MHz, CD₂Cl₂) δ = 7.43 – 7.40 (m, 1H), 7.35 (td, *J* = 7.5, 1.4 Hz, 1H), 7.30 (td, *J* = 7.5, 1.4 Hz, 1H), 7.09 – 7.07 (m, 1H), 5.02 (d, *J* = 1.4 Hz, 1H), 4.63 (t, *J* = 3.2 Hz, 1H), 4.11 (br s, 1H), 3.96 (s, 3H), 3.67 (s, 3H), 3.42 (s, 3H), 2.52 (dd, *J* = 14.3, 2.8 Hz, 1H), 1.98 (ddd, *J* = 14.3, 3.3, 0.8 Hz, 1H), 0.57 (s, 9H), 0.06 (s, 3H), -0.26 (s, 3H); ¹³C NMR (125 MHz, CD₂Cl₂) δ = 161.1, 160.0, 155.5, 137.4, 133.1, 130.0, 129.0, 129.0, 128.1, 122.6, 112.3, 100.5, 73.8, 58.1, 52.5, 50.3, 44.3, 43.6, 25.5, 18.2, -3.1, -3.5; **HRMS (ESI)**: *m/z* calcd. for [C₂₄H₃₃NO₈SSiK]⁺: 562.1328, found: 562.1344.

7. Mechanistic Studies

7.1. Deuterium incorporation studies

The proposed mechanism for the reaction carried out in DMF suggests the formation of the anionic intermediate. Arguing from the final structure of product **4b**, the subsequent cyclization step creates a negative charge in the 4-position of the original isoquinoline moiety, resulting in a proton abstraction from an external source.



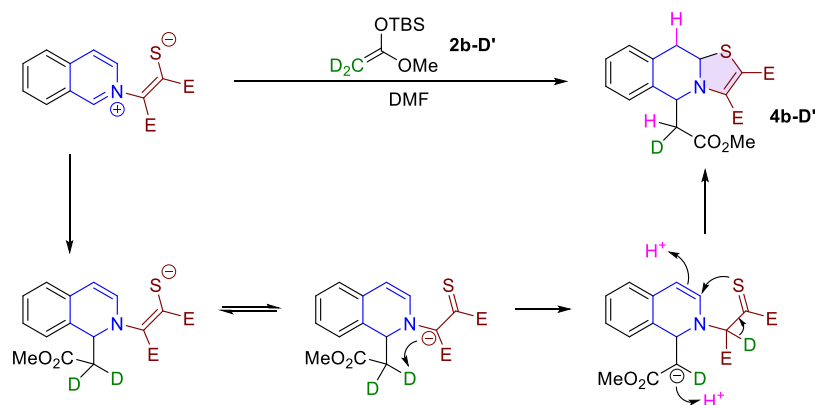
For a better understanding of the reaction, it was desirable to determine the mentioned proton source. In this regard, several deuteration experiments were carried out. The first reactions excluded that the protonation is based on either the aqueous workup, the reaction solvent or the water traces in the dry solvent (Table S2, entries 1-3).

Table S2. Deuteration experiments aimed at determining the external proton source in the reaction

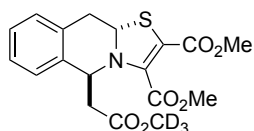
Entry	Nucleophile	Conditions	Product
1	2b	Aqueous workup with D ₂ O instead of H ₂ O	4b
2	2b	Reaction carried out in DMF-d ₇ as solvent	4b
3	2b	Addition of 5% D ₂ O to dry solvent (0.1 ppm H ₂ O)	4b
4	2b-D	Employment of methoxy-deuterated nucleophile	4b-D
5	2b-D'	Employment of α-deuterated nucleophile	4b-D'
6	2b-D'	Crude product from reaction in DMF-d ₇ without workup directly applied to NMR analysis	4b-D'

Thus, the focus was put on the applied nucleophile. While nucleophiles **2b-D** and **2b-D'** were easily obtained, all approaches to prepare the D-TMS or D₃-TMS ketene acetal derivatives of **2b** were unsuccessful. Nevertheless, the two deuterated derivatives **2b-D** and **2b-D'** were employed under otherwise regular conditions (entries 4 and 5). Analysis of the respective products **4b-D** and **4b-D'** showed that neither incorporated a deuterium atom in the corresponding 4-position. An additional reaction employing **2b-D'** was further carried out in deuterated solvent (entry 6). The resulting crude mixture was analyzed by NMR without workup, but no difference to the previous attempt was observed regarding the deuterium incorporation.

Judging from NMR-analysis and mass spectrometry, the employment of nucleophile **2b-D'** leads to the cyclization product **4b-D'**, which only incorporates one deuterium atom. Computational studies revealed that tautomerization of the thiolate moiety within the zwitterionic compound is energetically favored. This enables the abstraction of one deuterium atom at the alpha-position of the ester, which before or during the final cyclization step the resulting carbanion is re-protonated. Since the corresponding CD₂-group in the zwitterionic species is symmetric, both deuterium atoms are exchanged to the same extent, which was supported by NMR-experiments.



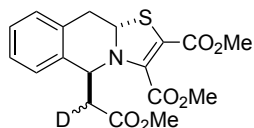
Dimethyl (5S*,10aS*)-5-(2-(methoxy-*d*₃)-2-oxoethyl)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4b-D**)**



Following the general procedure, the reaction between 3-methyl isoquinolinium **1a** (60.7 mg, 0.2 mmol, 1.0 equiv.) and silyl ketene acetal **2g** (190 μ L, 1.0 mmol, 5.0 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 4:1)

the product **4b-D** (38.7 mg, 0.10 mmol, 51%) as a yellow oil. R_f (pentane/EtOAc 3:1) = 0.5. ¹H NMR (400 MHz, CD₂Cl₂) δ = 7.26 – 7.17 (m, 2H), 7.13 – 7.05 (m, 2H), 5.52 (dd, J = 10.8, 4.0 Hz, 1H), 4.98 (dd, J = 8.6, 4.7 Hz, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 3.54 (ddt, J = 16.2, 10.8, 0.8 Hz, 1H), 2.94 (dd, J = 15.6, 8.6 Hz, 1H), 2.85 – 2.76 (m, 2H).

Dimethyl 5-(2-methoxy-2-oxoethyl-1-*d*)-10,10a-dihydro-5H-thiazolo[3,2-b]isoquinoline-2,3-dicarboxylate (4b-D'**)**



Following the general procedure, the reaction between 3-methyl isoquinolinium **1a** (60.7 mg, 0.2 mmol, 1.0 equiv.) and silyl ketene acetal **2h** (188 μ L, 0.89 mmol, 4.5 equiv.) in DMF afforded after purification *via* flash column chromatography (pentane/EtOAc 4:1)

the product **4b-D'** (41.6 mg, 0.11 mmol, 55%) as a yellow oil. R_f (pentane/EtOAc 3:1) = 0.5. ¹H NMR (600 MHz, CD₂Cl₂) δ = 7.25 – 7.19 (m, 2H), 7.14 – 7.08 (m, 1H), 7.09 – 7.06 (m, 1H), 5.52 (dd, J = 10.8, 4.2 Hz, 1H), 5.00 – 4.96 (m, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.53 (dd, J = 16.2, 10.8 Hz, 1H), 2.97 – 2.76 (m, 2H); ¹³C NMR (150 MHz, CD₂Cl₂) δ = 170.3, 162.9, 162.1, 143.7, 134.9, 132.7, 129.3, 127.5, 126.9, 126.1, 96.9, 62.9, 54.4, 53.1, 51.9, 51.6, 42.2, 36.8; HRMS (ESI): m/z calcd. for [C₁₈H₁₈DNO₆Na]⁺: 401.0888, found: 401.0890.

7.2. Computational studies on the formation of 3

DFT Calculations - Methods: All calculations were performed with TURBOMOLE 7.5.1.⁴ The structures were optimized without any geometry constraints using the TPSS meta-GGA functional⁵ and an atom-pairwise dispersion correction (D3).⁶ A flexible triple zeta basis set (def2-TZVP)⁷ was used in all calculations. Harmonic force constants and vibrational frequencies were calculated proving the nature of the stationary points as either minima (no negative frequency) or transition structures (one negative frequency). Thermostatistical contributions from translation, rotation and internal vibrations (G_{rrho}) were calculated with these frequencies for $T = 298$ K. Single point energy DFT calculations were performed using the hybrid functional PW6B95(-D3)⁸ and the def2-TZVP basis set. Free energies of solvation G_{solv} were obtained with the COSMO-RS model implemented in the COSMOtherm program⁹ at 298 K using 1,2-dichloroethane (DCE) as solvent.

Relative values of free enthalpy in solution (ΔG^s_{298}), as shown in Scheme 3 of the manuscript were obtained using the sum of the differences in PW6B95-D3 electronic energies, $G^{RRHO}(298K)$, and G_{solv} as

$$\Delta G^s_{298} = \Delta E(\text{PW6B95-D3}) + \Delta G^{rrho}(298K) + \Delta G_{solv} \quad (1)$$

Results:

Table S2: Electronic energies, free energy contributions of translation, rotation and harmonic vibration (G^{rrho}) after optimization (TPSS-D3/def2-TZVP) of structures shown in Scheme 3a. Electronic single point energies of these structures with PW6B95-D3/def2-TZVP. Solvation free energies G_{solv} as obtained with COSMO-RS (solvent: DCE). ΔG^s_{298} calculated from Eq. (1).

Structure	E_{el} (TPSS-D3) [E _h]	$G^{rrho}(298K)$ (TPSS-D3) [kcal/mol]	E_{el} (PW6B95-D3) [kcal/mol]	$G_{solv}(\text{DCE}, 298K)$ (COSMO-RS) [kcal/mol]	ΔG^s_{298} [kcal/mol]
1a	-1333.837345	128.569	-1335.105042	-20.621	
2	-677.333032	93.786	-677.964331	-2.061	
(S*)- TS4	-2011.129189	237.850	-2013.018845	-16.482	53.40
(R*)- TS3	-2011.140750	238.731	-2013.033867	-16.374	44.96
TS1	-2011.179213	239.051	-2013.072598	-21.114	16.24
7	-2011.191568	239.193	-2013.087903	-21.078	6.81
TS2	-2011.180077	240.402	-2013.076044	-24.621	11.92
(11R*,10aS*)-endo- 3a	-2011.222372	242.281	-2013.129461	-17.576	-12.67
(11S*,10aS*)-endo- 3a	-2011.226859	242.015	-2013.134009	-18.132	-16.35

Figure S1: Optimized structures (TPSS-D3/def2-TZVP) of intermediates reported in Scheme 3a. Element colors: gray (C), red (O), blue (N), yellow (S), white (H).

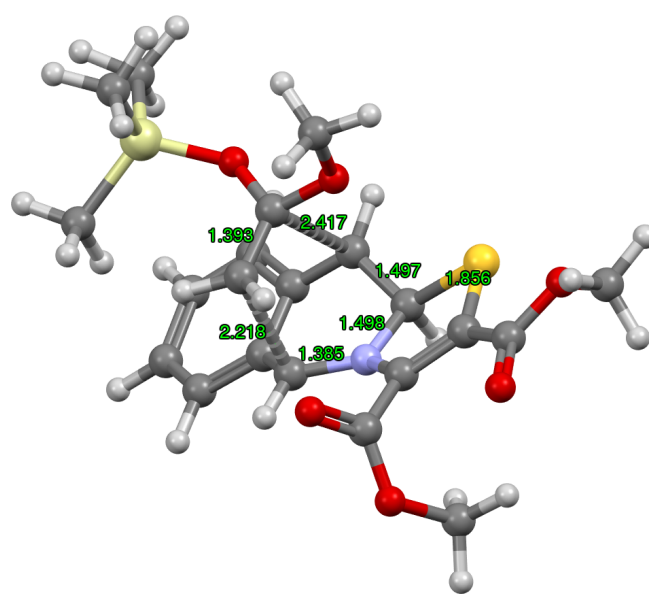
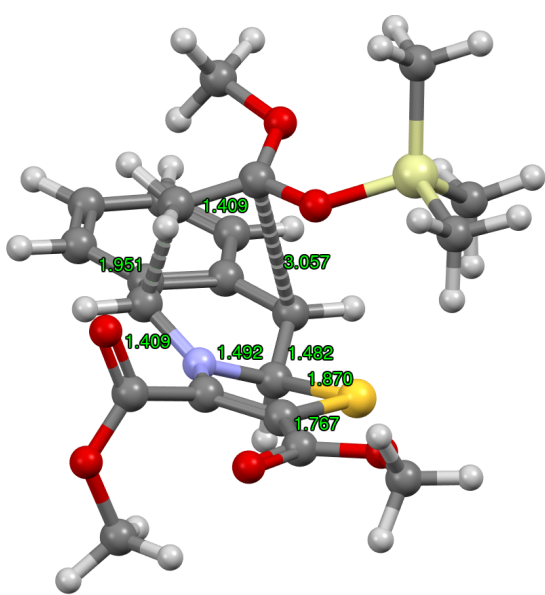
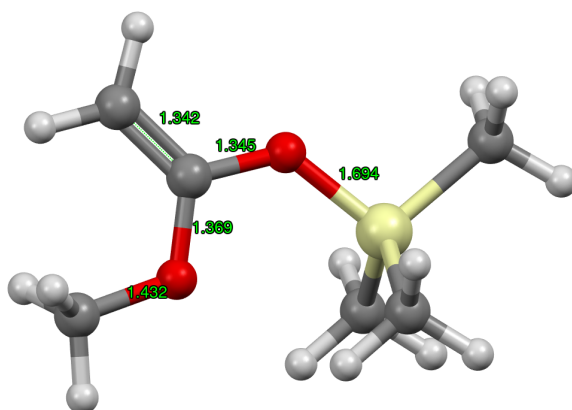
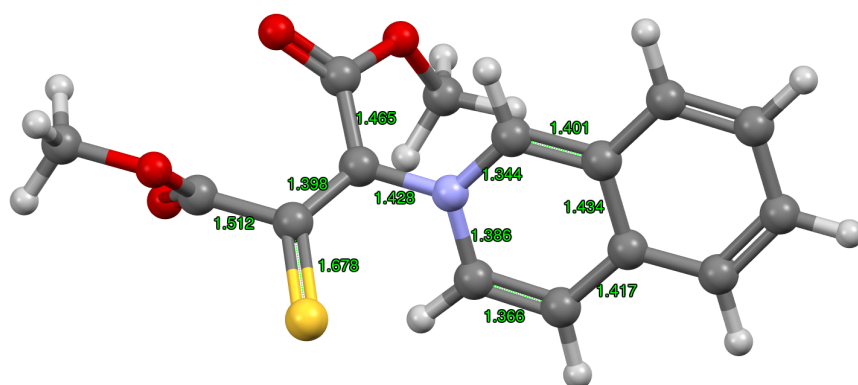
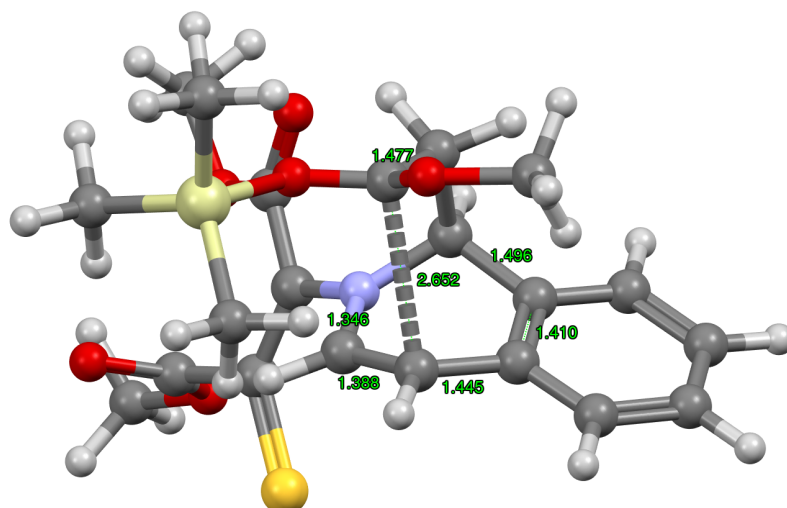
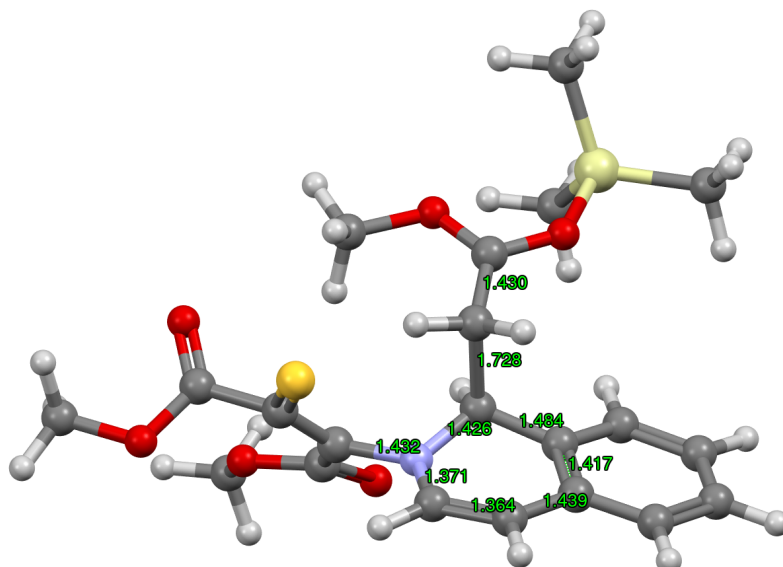
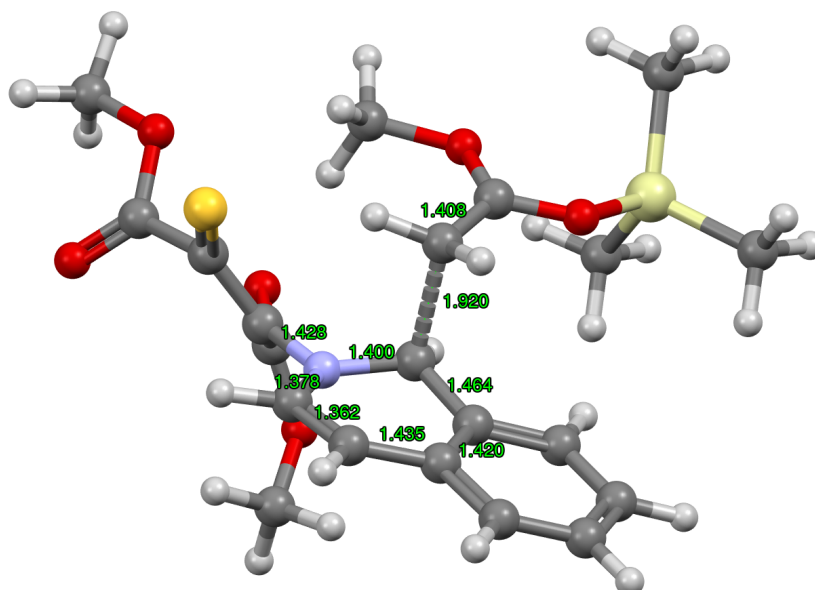
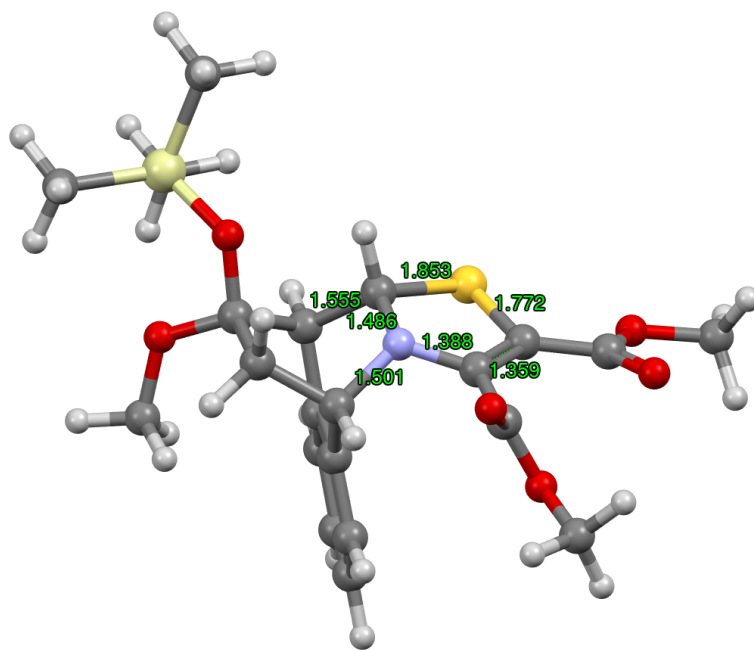


Figure S1 (continued): Optimized structures (TPSS-D3/def2-TZVP) of intermediates reported in Scheme 3a. Element colors: gray (C), red (O), blue (N), yellow (S), white (H).

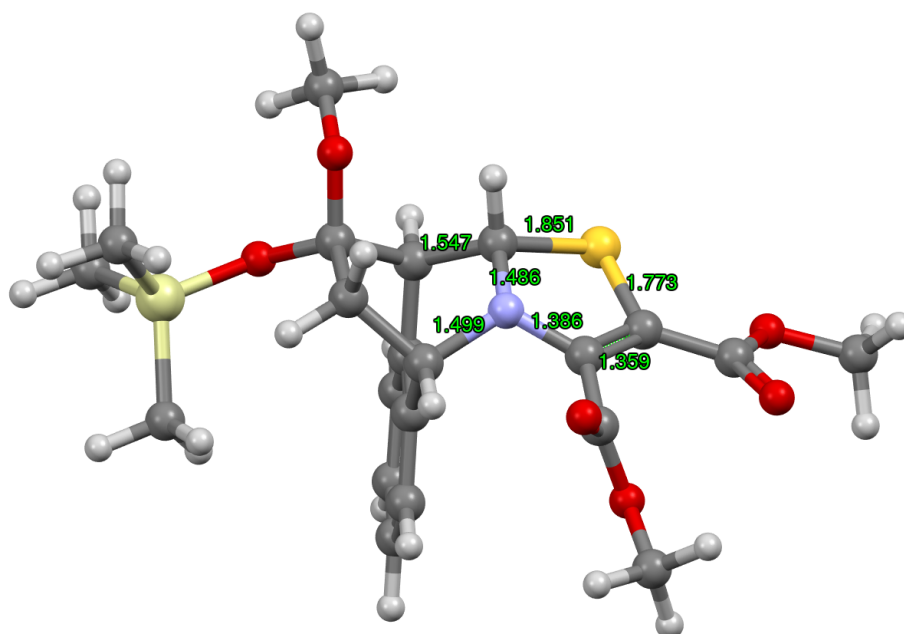


S23

Figure S1 (continued): Optimized structures (TPSS-D3/def2-TZVP) of intermediates reported in Scheme 3a. Element colors: gray (C), red (O), blue (N), yellow (S), white (H).



(11*R**,10*aS**)-endo-3a



(11*S**,10*aS**)-endo-3a

DFT optimized (TPSS-D3/def2-TZVP) cartesian coordinates

1a

E(TPSS-D3/def2-TZVP) = -1333.837345358 (conv) Lowest Freq. = 26.08 cm⁻¹

34, 1a (001c1/opt)

C	-4.2994960	-0.1482331	0.7923647	O	3.7698915	-1.7575095	-1.2349767
C	-4.8609045	1.0323929	1.2331625	H	-4.9069731	-1.0415788	0.6785678
C	-4.0741397	2.2000445	1.3815590	H	-5.9201467	1.0714041	1.4689581
C	-2.7295033	2.1755966	1.0903292	H	-4.5387414	3.1180251	1.7275027
C	-2.1264140	0.9735754	0.6357016	H	-2.1175611	3.0661414	1.2015606
C	-2.9223987	-0.2089512	0.4804786	H	-2.8230768	-2.3094300	-0.0750278
C	-2.2684266	-1.3831008	0.0320934	H	-0.1169154	1.7808219	0.3696511
C	-0.7656006	0.9155618	0.3071510	H	-0.3683957	-2.2528996	-0.5428916
N	-0.1817145	-0.2258752	-0.0971703	H	5.2195202	-1.2612974	-3.3848486
C	-0.9319747	-1.3807672	-0.2519685	H	5.1766429	0.4768420	-3.8495418
C	1.2115101	-0.2569658	-0.4096463	H	5.5222345	-0.0048002	-2.1496406
C	1.6072678	-0.8146319	-1.6293268	O	1.7965144	0.5647847	1.8137269
C	2.1343507	0.4609672	0.4723583	C	1.1401988	-0.5434859	2.4634913
C	3.0982557	-0.9468600	-1.8418422	O	3.1624467	0.9886461	0.0972009
S	0.6282384	-1.4549161	-2.8328985	H	0.0700337	-0.3424337	2.5870079
O	3.5485643	-0.1395709	-2.8149272	H	1.6072270	-0.6361158	3.4458505
C	4.9722590	-0.2472853	-3.0618203	H	1.2872271	-1.4680951	1.8978109

2

E(TPSS-D3/def2-TZVP) = -677.3330317722 (conv) Lowest Freq. = 22.75 cm⁻¹

23, 2 (002c2/opt)

C	1.1994616	-0.8014901	-2.5424927	H	3.0246024	-1.8302106	-0.6958305
C	0.7486617	-0.5365924	-1.3064207	H	1.7004965	-3.0175585	-0.9237277
O	1.1236893	-1.1688538	-0.1516203	H	-2.5032108	-1.0135211	0.4493641
O	-0.1608221	0.4204893	-1.0496786	H	-2.3463581	-0.2939673	2.0599827
H	1.9323249	-1.5721361	-2.7320344	H	-1.1055590	-1.4143531	1.4646652
H	0.8185666	-0.2251735	-3.3742129	H	-2.7699954	1.8611943	-0.7604965
C	2.0882202	-2.2196360	-0.2799814	H	-1.4812867	3.0503483	-0.5081898
Si	-0.8464932	0.8415324	0.4408487	H	-2.5511748	2.6055955	0.8329477
C	-1.7846550	-0.6080571	1.1711479	H	1.1559847	0.6745834	1.9120308
C	-2.0204467	2.2166118	-0.0444990	H	0.0054748	1.8767620	2.5293318
C	0.4673347	1.4730785	1.6194855	H	1.0536283	2.2767464	1.1589539
H	2.2515562	-2.5953925	0.7304264				

(S*)-TS4

E(TPSS-D3/def2-TZVP) = -2011.129189276 (conv) Lowest Freq. = -438.17 cm⁻¹

57, (S*)-TS4 (004TSc1/opt)

C	-2.8208865	-0.8955406	1.9799394	C	0.8453164	-1.4933031	1.4471238
C	-3.5796111	0.0507569	2.6333793	C	2.5878741	0.0599087	0.8577205
C	-3.0169835	1.2905359	3.0253926	C	3.1288644	-1.0900876	0.3611009
C	-1.6997892	1.5751370	2.7255229	C	3.1778786	1.4454413	0.7783356
C	-0.8874748	0.6101830	2.0901613	C	4.4460714	-1.1393918	-0.2495757
C	-1.4372696	-0.6741841	1.7346788	S	2.0323036	-2.4716164	0.4086313
C	-0.5924354	-1.5448386	1.0335569	O	4.6809167	-2.3417666	-0.8394423
C	0.3803004	0.9281776	1.5246815	C	5.9697940	-2.4512736	-1.4869516
N	1.3257621	-0.0751084	1.3896713	O	5.2556918	-0.2190742	-0.2428100

H	-3.2572376	-1.8437653	1.6783679	O	0.1268776	-1.0996488	-1.6083733
H	-4.6243322	-0.1532493	2.8526485	O	-2.0376023	-0.4995380	-1.1629788
H	-3.6284948	2.0205035	3.5469957	C	0.2767593	-0.8691247	-3.0246262
H	-1.2736563	2.5426103	2.9807405	H	-0.6712343	-1.0413284	-3.5461644
H	-0.9652057	-2.4623413	0.5926515	H	1.0242208	-1.5891919	-3.3600951
H	0.7813619	1.9343088	1.5762889	H	0.6268837	0.1538561	-3.2096728
H	0.9877130	-1.8268663	2.4873893	Si	-3.3398702	0.4459472	-1.6674140
H	6.7696828	-2.3155513	-0.7549187	C	-3.0671247	0.9155687	-3.4645690
H	5.9904107	-3.4558222	-1.9078992	H	-2.1479656	1.5015464	-3.5831450
H	6.0622383	-1.6940077	-2.2691468	H	-3.8986159	1.5285163	-3.8343441
O	4.0293062	1.8346827	1.7435199	H	-2.9914153	0.0317119	-4.1079890
C	4.5192395	0.8568769	2.6974124	C	-3.5854217	1.9941415	-0.6395823
O	2.8115324	2.2306174	-0.0700168	H	-4.6032444	2.3717010	-0.8045129
H	3.6902895	0.3096979	3.1539466	H	-2.8940477	2.7980200	-0.9142022
H	5.0424390	1.4442711	3.4512526	H	-3.4741652	1.7915189	0.4301633
H	5.2061960	0.1760214	2.1921396	C	-4.7929887	-0.7134547	-1.4669550
C	-0.7189377	-0.2172963	-0.9822717	H	-4.6294315	-1.6489396	-2.0133261
C	-0.2576412	1.0393662	-0.5972096	H	-5.7156451	-0.2568359	-1.8448037
H	0.7483599	1.3257823	-0.8831157	H	-4.9464091	-0.9596637	-0.4105916
H	-0.9691470	1.8354035	-0.4267091				

(R*)-TS3

E(TPSS-D3/def2-TZVP) = -2011.140750452 (conv) Lowest Freq. = -476.60 cm⁻¹

57, (R*)-TS3 (004TSc2/opt)

C	-3.1527945	-0.3479041	2.6298191	H	5.9943364	-1.6092840	-1.4100104
C	-3.9267873	0.6598336	3.1561155	H	5.0536341	-2.7434666	-2.4423801
C	-3.4330805	1.9846769	3.2737529	H	5.0505914	-0.9767541	-2.7847104
C	-2.1509920	2.2692034	2.8323687	O	3.5647922	2.5009525	1.5004605
C	-1.3274291	1.2591292	2.3084706	C	4.1370228	1.5281045	2.4123893
C	-1.8047590	-0.1005188	2.2075624	O	2.1810130	2.8986745	-0.1862914
C	-0.9688162	-1.0620185	1.6523139	H	3.3523720	1.0085090	2.9684172
C	-0.1597637	1.5767953	1.5271804	H	4.7529462	2.1162535	3.0919541
N	0.8446207	0.5908834	1.4541126	H	4.7501402	0.8229153	1.8487616
C	0.4945021	-0.8357643	1.7124297	C	-1.3176790	0.6107859	-0.8822083
C	2.0383843	0.7278464	0.7797549	C	-0.8173669	1.7905771	-0.2967603
C	2.5434416	-0.4259098	0.2522029	H	0.1167742	2.1274340	-0.7384889
C	2.6192717	2.1122648	0.6264984	H	-1.5413809	2.5761847	-0.1107406
C	3.7665372	-0.4636904	-0.5302818	O	-2.6123140	0.2563084	-0.9398501
S	1.4828291	-1.8221123	0.4681700	O	-0.5137878	-0.1748342	-1.5746247
O	3.9190092	-1.6584826	-1.1645817	C	-3.6074409	1.1904717	-0.4529885
C	5.0903666	-1.7447758	-2.0086177	H	-3.4182554	1.4615536	0.5866168
O	4.5663093	0.4591967	-0.6269995	H	-4.5519619	0.6542954	-0.5312845
H	-3.5475979	-1.3573523	2.5432624	H	-3.6160382	2.0765059	-1.0967684
H	-4.9375871	0.4385825	3.4904558	Si	-0.8992592	-1.5349949	-2.5429746
H	-4.0538648	2.7624247	3.7068115	C	-2.0939891	-0.9799832	-3.8777541
H	-1.7722570	3.2891670	2.8739599	H	-3.0734410	-0.7221563	-3.4636911
H	-1.3119765	-2.0809829	1.5074470	H	-2.2375986	-1.7835770	-4.6111636
H	0.2451052	2.5829990	1.6049191	H	-1.7075879	-0.1065012	-4.4156593
H	0.9443786	-1.0868467	2.6886833	C	-1.6344239	-2.9063062	-1.5077169

H	-1.9162720	-3.7474878	-2.1540580	H	1.1776380	-1.1377952	-3.8325999
H	-2.5309992	-2.5653235	-0.9807710	H	0.6447241	-2.8213959	-3.9839666
H	-0.9161685	-3.2722067	-0.7684388	H	1.4686301	-2.2784579	-2.5065575
C	0.7542996	-1.9856455	-3.2819518				

TS1

E(TPSS-D3/def2-TZVP) = -2011.179213307 (conv) Lowest Freq. = -331.65 cm⁻¹

57, TS1 (004TSc5/opt)

C	-1.6774330	-2.3692543	3.8294172	C	2.8370083	0.4608916	2.7096884
C	-2.6777259	-1.4674135	4.1583992	O	3.0044563	1.3151840	-0.6777953
C	-2.7692955	-0.2306046	3.4999756	H	1.8878056	0.1803612	3.1753511
C	-1.8633355	0.0817129	2.4951148	H	3.3996513	1.1164058	3.3775624
C	-0.8583137	-0.8268803	2.1404946	H	3.4239892	-0.4333773	2.4846943
C	-0.7395039	-2.0675407	2.8201042	C	-1.2841602	-0.1244454	-1.2695733
C	0.3635920	-2.9227241	2.4864714	C	-0.8091846	-1.2438540	-0.5600936
C	0.0460140	-0.5642991	1.0191270	H	-1.5949633	-1.8434268	-0.1138656
N	1.2694476	-1.2438012	1.0512314	H	-0.0011706	-1.8245898	-1.0067163
C	1.3433072	-2.4828663	1.6493187	O	-0.6418147	0.5395931	-2.2139299
C	2.2947116	-0.7839908	0.1694265	O	-2.4087472	0.4519501	-0.8953449
C	2.7492553	-1.5960857	-0.8631191	C	0.6435393	0.0587460	-2.7356414
C	2.6830484	0.6223603	0.2792630	H	1.4417870	0.4212832	-2.0859079
C	3.9585700	-1.1108345	-1.6234444	H	0.7157482	0.5085531	-3.7242551
S	2.1719137	-3.1248282	-1.3072539	H	0.6488204	-1.0307899	-2.7973230
O	3.6621595	-0.8141380	-2.9113295	Si	-2.9564667	2.0465277	-1.2847938
C	4.7981605	-0.3623085	-3.6852404	C	-3.3095251	2.1542533	-3.1155659
O	5.0759870	-1.0586842	-1.1524756	H	-2.3914031	2.0965768	-3.7074469
H	-1.5988316	-3.3168105	4.3559346	H	-3.8042249	3.1057792	-3.3467905
H	-3.3904959	-1.7150084	4.9399388	H	-3.9774547	1.3468127	-3.4363075
H	-3.5449794	0.4773508	3.7755226	C	-1.6550684	3.2609480	-0.7146385
H	-1.9281121	1.0325721	1.9735300	H	-2.0089957	4.2880572	-0.8678231
H	0.4679903	-3.8901006	2.9645439	H	-0.7168883	3.1440040	-1.2654829
H	0.1768809	0.4813517	0.7555066	H	-1.4392046	3.1456168	0.3538009
H	2.2497136	-3.0337323	1.4411035	C	-4.5161861	2.1500459	-0.2647693
H	5.5600287	-1.1444519	-3.7232348	H	-5.2427274	1.3909810	-0.5752007
H	4.4009640	-0.1556364	-4.6790388	H	-4.9882349	3.1331617	-0.3777086
H	5.2189056	0.5391349	-3.2332872	H	-4.3055609	1.9980779	0.7995565
O	2.6065525	1.2341843	1.5103204				

7

E(TPSS-D3/def2-TZVP) = -2011.191567949 (conv) Lowest Freq. = 15.94 cm⁻¹

57, 7 (010c3/opt)

C	-2.9022727	-3.2434803	2.0812694	C	0.4938785	-3.1682928	0.5535072
C	-3.7789115	-2.3507317	2.6827929	C	2.0559615	-1.3078336	0.2718057
C	-3.5065515	-0.9757665	2.6836319	C	2.6245037	-1.6050350	-0.9599570
C	-2.3619159	-0.5031349	2.0476691	C	2.6006398	-0.4125137	1.2860981
C	-1.4883580	-1.3888833	1.4156139	C	3.9107939	-0.9501266	-1.3856598
C	-1.7307609	-2.7849621	1.4450185	S	1.9606323	-2.5462467	-2.2097246
C	-0.7322738	-3.6611137	0.8928043	O	4.9828595	-1.7434429	-1.1941610
C	-0.3306896	-0.9126398	0.6178767	C	6.2265359	-1.1972755	-1.6911858
N	0.7643850	-1.8254502	0.6108014	O	3.9560654	0.1408707	-1.9300184

H	-3.1031353	-4.3114599	2.1117108	O	-0.3690709	1.4985562	-1.7335313
H	-4.6751749	-2.7231641	3.1713061	O	-2.3851846	0.9953947	-0.9820003
H	-4.1825533	-0.2848111	3.1786411	C	1.0163080	1.1408340	-2.0821848
H	-2.1375042	0.5604834	2.0424730	H	1.5509416	0.8512076	-1.1790286
H	-0.9016838	-4.7313172	0.8621353	H	1.4305176	2.0495888	-2.5105673
H	0.0256611	0.0683571	0.9239450	H	1.0224893	0.3196136	-2.8006479
H	1.3296854	-3.7939302	0.2696784	Si	-2.9582858	2.6269103	-0.8273336
H	6.4461566	-0.2501653	-1.1915678	C	-2.9847940	3.4024982	-2.5253097
H	6.9799303	-1.9485227	-1.4559529	H	-1.9740977	3.5254282	-2.9265882
H	6.1587870	-1.0332067	-2.7694427	H	-3.4539146	4.3930647	-2.4799129
O	3.9021080	-0.0702340	1.0553393	H	-3.5630284	2.7932769	-3.2290163
C	4.4418831	0.9005673	1.9738840	C	-1.8403017	3.5268077	0.3687426
O	1.9745011	0.0213463	2.2500968	H	-2.2463957	4.5247150	0.5760701
H	4.4287769	0.5066269	2.9931493	H	-0.8308468	3.6522176	-0.0340532
H	3.8588074	1.8248457	1.9379223	H	-1.7648897	2.9972279	1.3248262
H	5.4635159	1.0733366	1.6351668	C	-4.6645069	2.3396327	-0.1355437
C	-1.1952031	0.5646831	-1.3068472	H	-5.2831605	1.7667800	-0.8349837
C	-0.8282016	-0.7894278	-1.0325057	H	-5.1709724	3.2919102	0.0608816
H	-1.6742861	-1.4676582	-1.1153531	H	-4.6151080	1.7799330	0.8049935
H	0.0277090	-1.1558878	-1.6067739				

TS2

E(TPSS-D3/def2-TZVP) = -2011.180076589 (conv) Lowest Freq. = -37.53 cm⁻¹
57, TS2 (O19TSc1/opt)

C	-3.1210063	0.0094058	2.9540361	H	6.6616424	0.3859694	2.8953605
C	-3.4730806	1.0913885	3.7545852	H	6.4785871	-1.2725423	2.2227703
C	-2.7699354	2.3001353	3.6720301	O	3.7241600	1.4040161	-0.2453612
C	-1.7175849	2.4299336	2.7644984	C	4.2932392	2.1967526	-1.3033863
C	-1.3739068	1.3567691	1.9466456	O	1.6940237	1.8102754	-1.1734774
C	-2.0582271	0.1274197	2.0397946	H	3.8815975	3.2094072	-1.2858573
C	-1.5528916	-0.9477063	1.2173216	H	4.0872665	1.7400162	-2.2752831
C	-0.3940206	1.4389288	0.8197099	H	5.3645796	2.2090527	-1.1022288
N	0.4422162	0.2503487	0.7554899	C	-1.7614452	0.3080282	-1.1091609
C	-0.2148582	-0.9204170	0.8498842	C	-1.2121167	1.5619183	-0.5536223
C	1.8631398	0.2933569	0.6565496	H	-0.4609176	1.9133702	-1.2671583
C	2.6076762	-0.5518377	1.4818423	H	-1.9969483	2.3029137	-0.4013550
C	2.3767846	1.2122045	-0.3315151	O	-3.0568500	0.0712136	-1.3280196
C	4.0914720	-0.6890323	1.2618831	O	-0.9555217	-0.4107610	-1.8385396
S	2.0283232	-1.6029727	2.6712340	C	-4.0502161	0.8551100	-0.6122941
O	4.8073474	-0.0185287	2.1928435	H	-3.8008288	0.8991214	0.4479926
C	6.2347132	-0.2150659	2.0925029	H	-4.9866725	0.3210366	-0.7657878
O	4.5814782	-1.3921249	0.3991973	H	-4.1079044	1.8549131	-1.0511346
H	-3.6494302	-0.9364590	3.0449767	Si	-1.1381285	-1.9000329	-2.6896966
H	-4.2904817	0.9916374	4.4634361	C	-2.1527259	-1.5371793	-4.2167448
H	-3.0435759	3.1341257	4.3110834	H	-3.1734220	-1.2389649	-3.9553040
H	-1.1730943	3.3681546	2.6851813	H	-2.2135301	-2.4276039	-4.8543539
H	-2.0727596	-1.8994409	1.2036466	H	-1.7006501	-0.7335877	-4.8086418
H	0.2452203	2.3179812	0.8748734	C	-1.9660086	-3.1558534	-1.5812611
H	0.3328288	-1.8028106	0.5488197	H	-2.1176378	-4.0860635	-2.1432947
H	6.5944901	0.1213692	1.1162801	H	-2.9452219	-2.8099204	-1.2357527

H	-1.3532564	-3.3955732	-0.7068963	H	0.7065577	-3.2627364	-3.6232110
C	0.6348344	-2.3205057	-3.0673726	H	1.2210530	-2.4246484	-2.1474852
H	1.1016251	-1.5339047	-3.6702730				

(11R*,10aS*)-endo-3a

E(TPSS-D3/def2-TZVP) = -2011.222372045 (conv) Lowest Freq. = 15.86 cm⁻¹

57, (11R*,10aS*)-endo-3a (009c1/opt)

C	-1.9579634	-0.2445479	2.0827880	C	3.2416464	4.1279029	2.2577275
C	-2.2889871	0.7289963	3.0275684	O	3.1088955	2.9405016	-0.1272989
C	-1.8676252	2.0503906	2.8591190	H	2.8202364	4.8527819	1.5573439
C	-1.0977851	2.4086431	1.7498917	H	4.3156854	4.0277037	2.0864023
C	-0.7792930	1.4400386	0.8023579	H	3.0351350	4.4070490	3.2899533
C	-1.2174720	0.1159702	0.9602839	C	-1.2121390	-0.2324971	-1.5327980
C	-0.7614606	-0.7942351	-0.1421865	C	-0.6324267	1.1989998	-1.6817444
C	0.1111644	1.6080348	-0.4035533	H	0.0545234	1.1968166	-2.5302209
N	1.2499979	0.6474947	-0.2191624	H	-1.4315436	1.9162287	-1.8863490
C	0.7923564	-0.7657627	-0.1929087	O	-2.6274227	-0.3031060	-1.7374732
C	2.1656454	0.9355187	0.7832206	O	-0.6785109	-1.0469122	-2.5435247
C	2.5209736	-0.0935324	1.5963924	C	-3.5186138	0.4998095	-0.9575321
C	2.6993006	2.3295136	0.8407914	H	-3.7007906	0.0608075	0.0275052
C	3.5921515	-0.0825186	2.5922856	H	-4.4508814	0.5331750	-1.5263028
S	1.6159285	-1.5784469	1.2541300	H	-3.1395127	1.5195020	-0.8238539
O	3.4958496	-1.1795792	3.3989787	Si	-1.4617970	-2.3092343	-3.3378244
C	4.5266109	-1.2717317	4.4073921	C	-2.7271129	-1.6808109	-4.5711807
O	4.4708096	0.7553237	2.7054599	H	-3.5932309	-1.2434526	-4.0663071
H	-2.2763071	-1.2749954	2.2184497	H	-3.0775651	-2.4982902	-5.2140856
H	-2.8702810	0.4556078	3.9034594	H	-2.2887623	-0.9127943	-5.2192719
H	-2.1253916	2.7987558	3.6030402	C	-2.2443566	-3.5189482	-2.1302396
H	-0.7411701	3.4288979	1.6325990	H	-2.6788587	-4.3675270	-2.6740034
H	-1.1184175	-1.8205270	-0.0340572	H	-3.0440773	-3.0462304	-1.5512614
H	0.5333620	2.6099222	-0.4958294	H	-1.5038121	-3.9251645	-1.4307010
H	1.1217903	-1.2749113	-1.0991902	C	-0.0413919	-3.1333844	-4.2433729
H	4.4668586	-0.4166337	5.0853812	H	0.4541476	-2.4297342	-4.9221460
H	4.3249996	-2.2036477	4.9347778	H	-0.3955305	-3.9817518	-4.8416351
H	5.5122745	-1.2911352	3.9359717	H	0.7127938	-3.5093304	-3.5424343
O	2.6073532	2.8369875	2.0851783				

(11S*,10aS*)-endo-3a

E(TPSS-D3/def2-TZVP) = -2011.226858990 (conv) Lowest Freq. = 15.34 cm⁻¹

57, (11S*,10aS*)-endo-3a (024c1/opt)

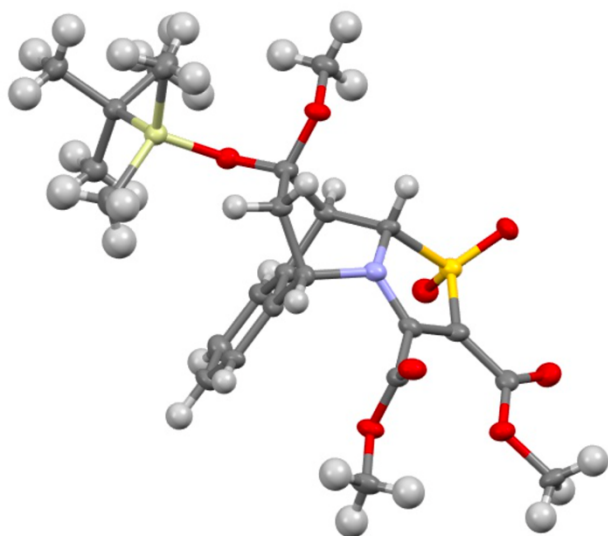
C	-1.8496273	-0.4134942	1.7301183	C	2.5353378	0.3261293	0.8897786
C	-2.2924345	0.7616555	2.3431683	C	2.7507548	-0.5360210	1.9180941
C	-1.7649375	1.9989185	1.9671817	C	3.0981546	1.7038386	0.7621461
C	-0.7867860	2.0743723	0.9723214	C	3.6867482	-0.3537869	3.0264417
C	-0.3575889	0.9045488	0.3544604	S	1.8543011	-2.0542167	1.7327038
C	-0.8831068	-0.3398979	0.7328640	O	3.4574298	-1.2908706	3.9930032
C	-0.3116678	-1.4876345	-0.0500808	C	4.3494723	-1.2110296	5.1265146
C	0.7053429	0.7743777	-0.7068176	O	4.5685209	0.4847323	3.1048587
N	1.7569412	-0.1413190	-0.1579243	H	-2.2570495	-1.3765724	2.0258601
C	1.2303937	-1.5107857	0.0765369	H	-3.0492633	0.7120263	3.1208405

H	-2.1122458	2.9055233	2.4544334	O	-2.0198072	-1.1671965	-1.6657700
H	-0.3648862	3.0342438	0.6847665	C	-0.6238362	-3.5271523	-2.2314473
H	-0.7397732	-2.4467370	0.2481532	H	-0.2296842	-3.9962284	-1.3198990
H	1.1866364	1.7192199	-0.9632868	H	-0.2988703	-4.1048459	-3.0982240
H	1.6365628	-2.1893619	-0.6776413	H	-1.7171762	-3.5004103	-2.1879800
H	4.2318271	-0.2484433	5.6305211	Si	-3.0628292	-0.2853505	-2.6319128
H	4.0539027	-2.0322595	5.7788403	C	-2.4944145	-0.2747275	-4.4224940
H	5.3856118	-1.3226875	4.7975719	H	-1.5475514	0.2589239	-4.5587448
O	2.8716663	2.4288445	1.8735783	H	-3.2434114	0.2129682	-5.0591725
C	3.5152888	3.7264303	1.8890527	H	-2.3531617	-1.2969491	-4.7914646
O	3.6395509	2.1255756	-0.2419308	C	-3.2517965	1.4625809	-1.9686608
H	3.1996517	4.3150266	1.0244976	H	-4.1002101	1.9606203	-2.4551292
H	4.5990673	3.5918595	1.8707703	H	-2.3672320	2.0868125	-2.1351039
H	3.1946226	4.1882434	2.8217288	H	-3.4429941	1.4439877	-0.8897168
C	-0.6161649	-1.2079945	-1.5560964	C	-4.6845858	-1.2058837	-2.4559618
C	0.1209798	0.0962042	-1.9548587	H	-4.5994472	-2.2341117	-2.8256297
H	0.9230270	-0.1552451	-2.6524009	H	-5.4838989	-0.7110767	-3.0206028
H	-0.5654486	0.7866090	-2.4482776	H	-4.9931648	-1.2502660	-1.4052700
O	-0.0867403	-2.2117166	-2.4183071				

8. X-Ray Crystal Structure Analysis of 6

X-Ray diffraction: Data sets for compound **6** were collected with a Bruker D8 Venture PHOTON III diffractometer. Programs used:¹⁰ data collection: APEX3 V2019.1-0; cell refinement: SAINT V8.40A; data reduction: SAINT V8.40A; absorption correction, SADABS V2016/2. Structure solution *SHELXT-2015*,¹¹ and structure refinement *SHELXL-2015*.¹² *R*-values are given for observed reflections, and *wR*² values are given for all reflections.

Structure analysis of 6 (gar10289): CCDC Nr.: 2164595



Ellipsoids are given at a 50% probability level

A pale yellow, plate-like specimen of $C_{24}H_{33}NO_8SSi$, approximate dimensions 0.043 mm x 0.079 mm x 0.113 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a single crystal diffractometer Bruker D8 Venture Photon III system equipped with a micro focus tube Cu I μ S (CuK α , λ = 1.54178 Å) and a MX mirror monochromator. A total of 1774 frames were collected. The total exposure time was 24.32 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 23665 reflections to a maximum θ angle

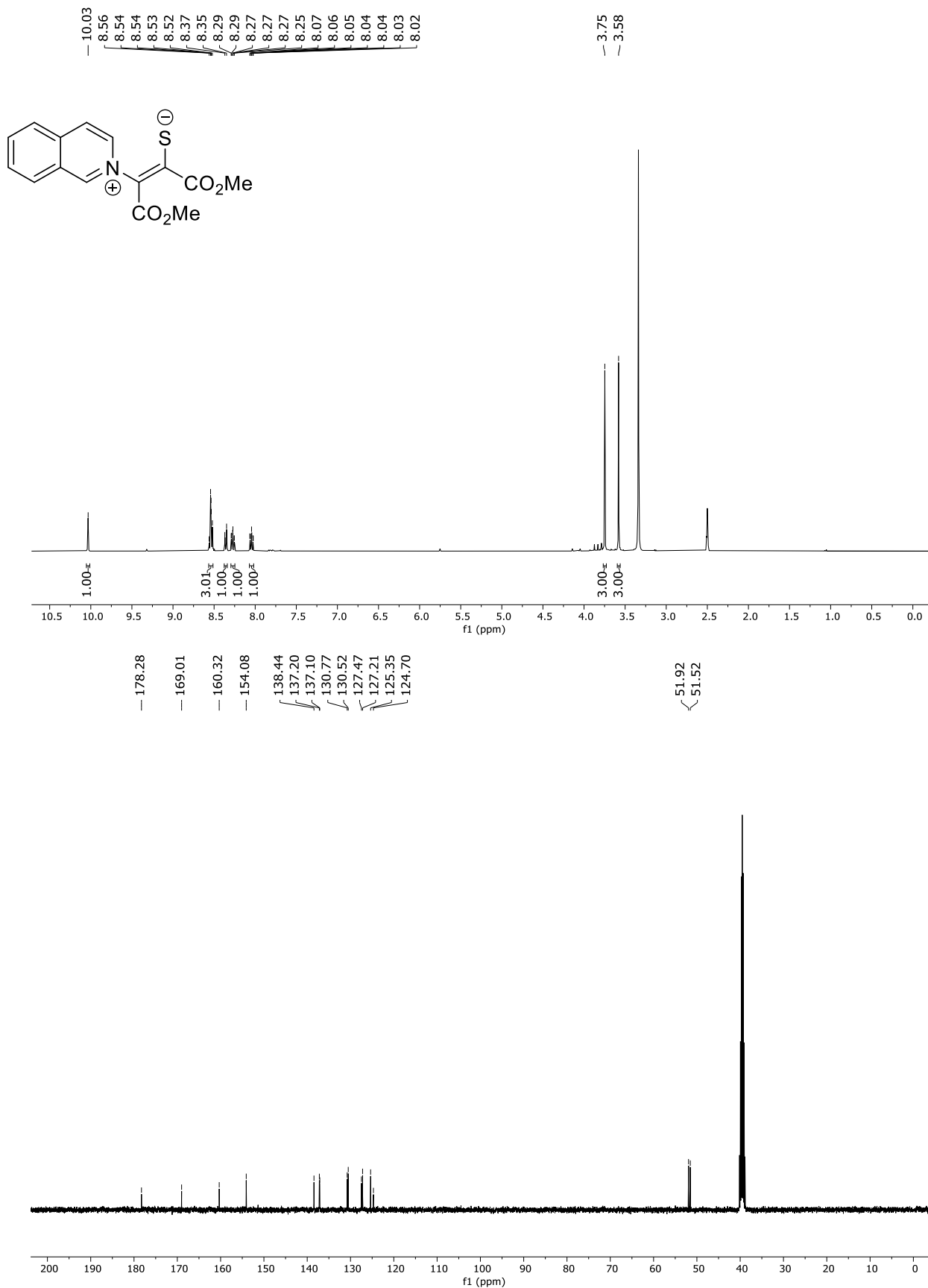
= 1269.23(11) Å³, are based upon the refinement of the XYZ-centroids of 5299 reflections above 2θ σ (I) with 6.344° < 2θ < 133.1°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.774. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.8050 and 0.9190. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group *P*-1, with Z = 2 for the formula unit, C₂₄H₃₃NO₈SSi. The final anisotropic full-matrix least-squares refinement on F² with 325 variables converged at R1 = 6.27%, for the observed data and wR2 = 17.10% for all data. The goodness-of-fit was 1.031. The largest peak in the final difference electron density synthesis was 0.364 e⁻/Å³ and the largest hole was -0.603 e⁻/Å³ with an RMS deviation of 0.085 e⁻/Å³. On the basis of the final model, the calculated density was 1.370 g/cm³ and F(000), 556 e⁻.

9. References

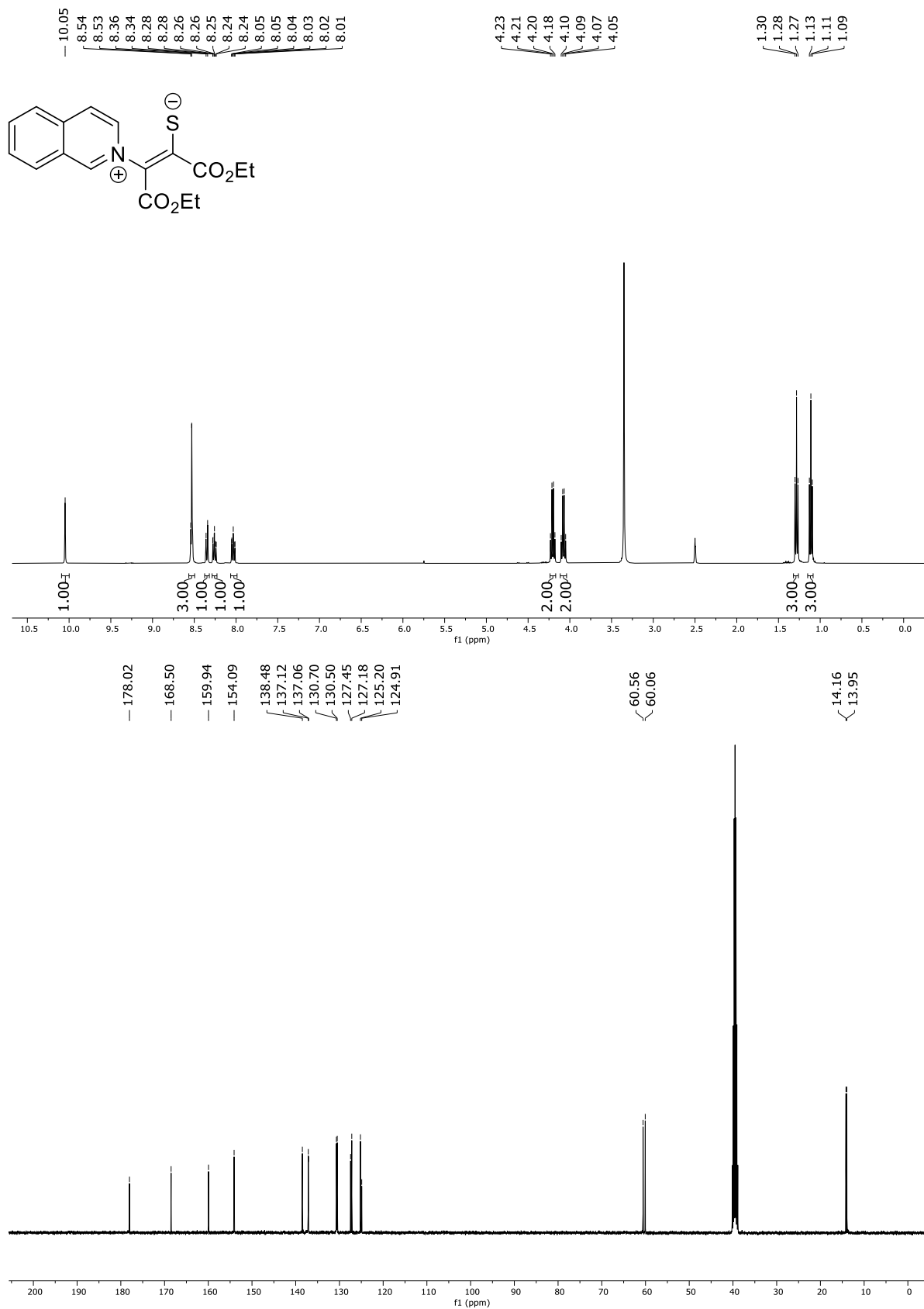
1. A. G. Wenzel and E. N. Jacobsen, *J. Am. Chem. Soc.* 2002, **124**, 12964-12965.
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11. Sheldrick, G. M., *SHELXT – Integrated space-group and crystal-structure determination*, *Acta Cryst.* 2015, **A71**, 3-8.
12. Sheldrick, G.M., *Crystal structure refinement with SHELXL*, *Acta Cryst.* 2015, **C71**, 3-8.

10. NMR Collection

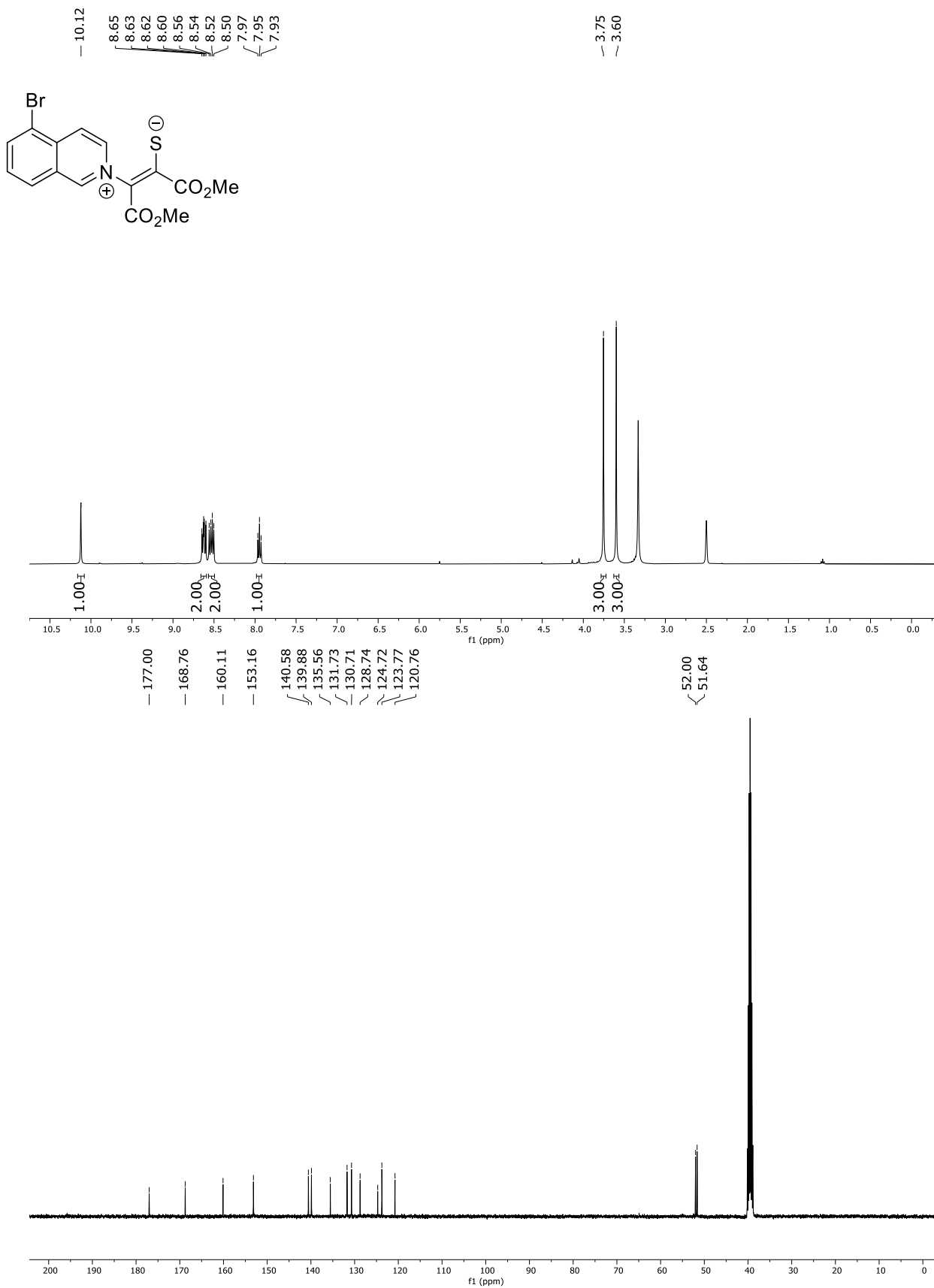
$^1\text{H-NMR}$ (400 MHz, DMSO-d_6) and $^{13}\text{C-NMR}$ (100 MHz, DMSO-d_6) for 1a



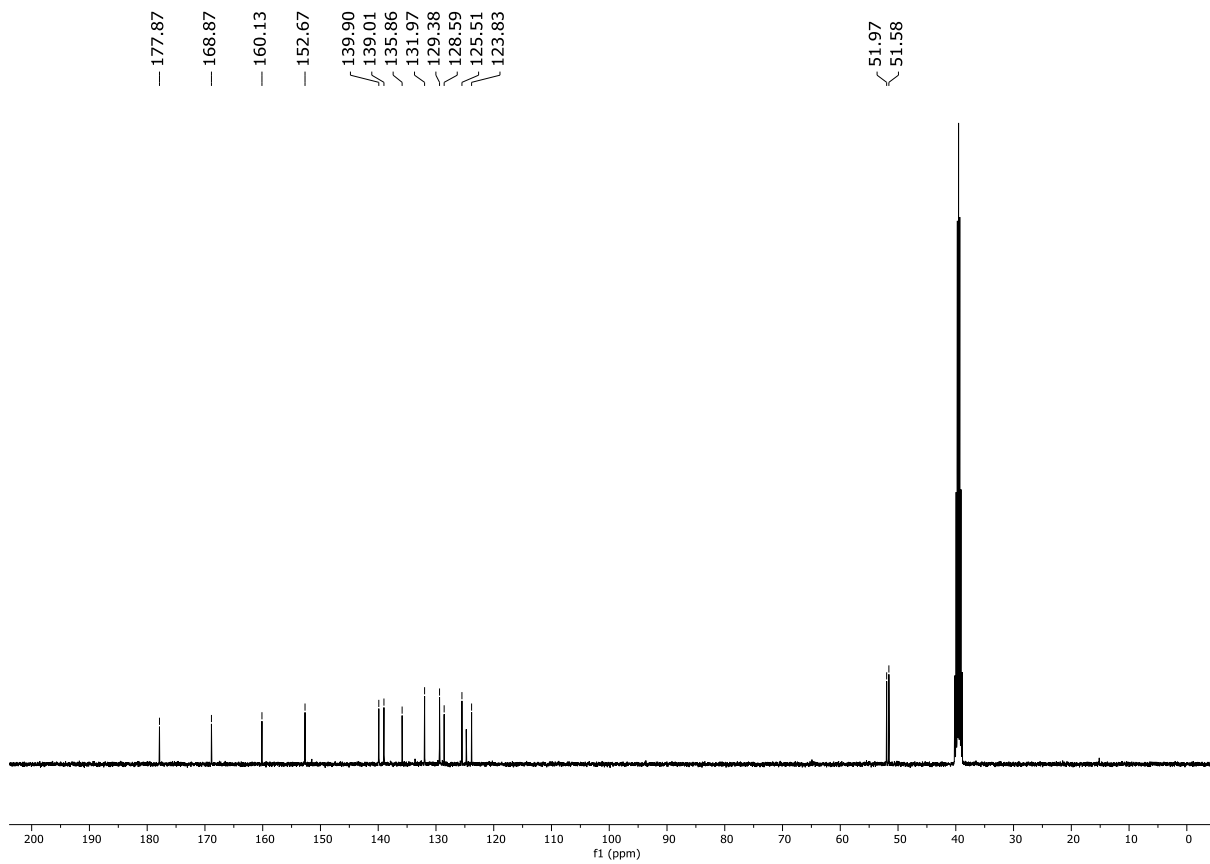
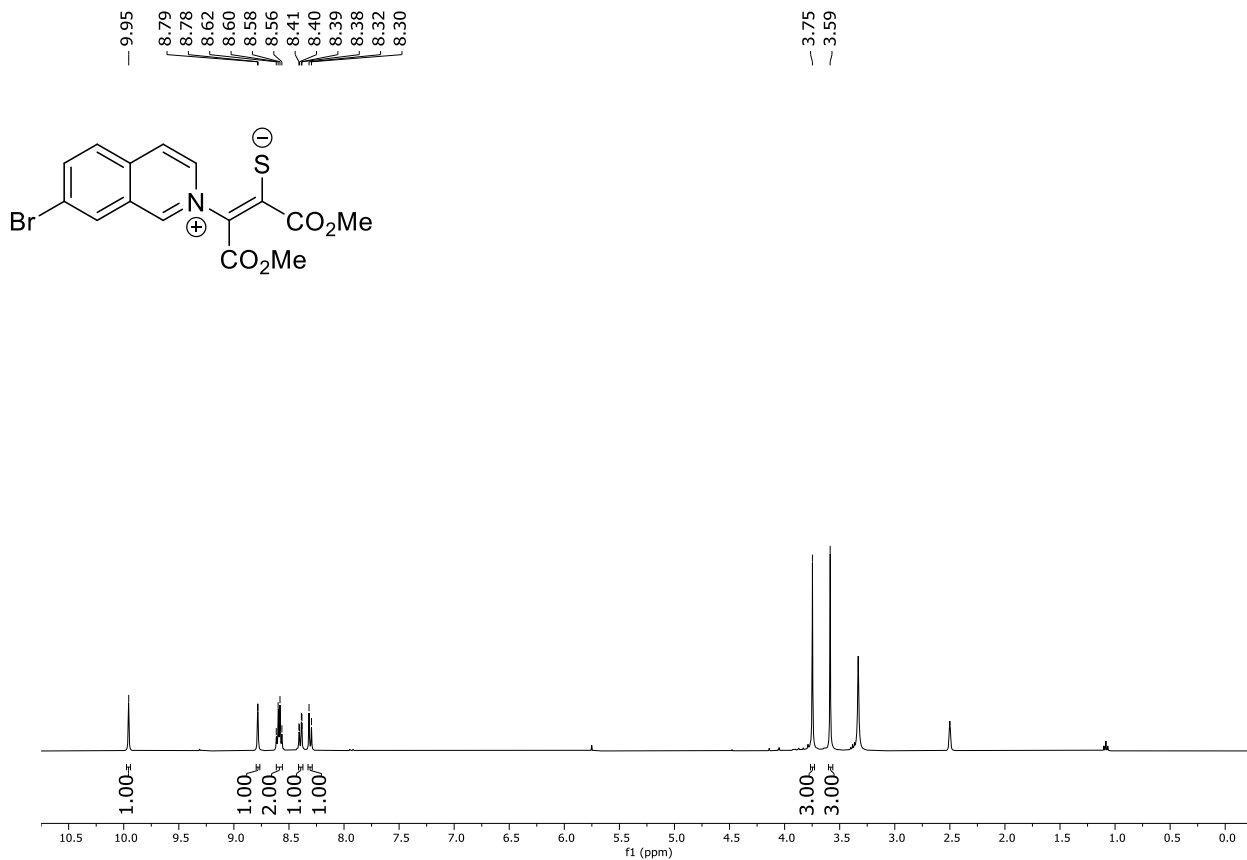
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1b



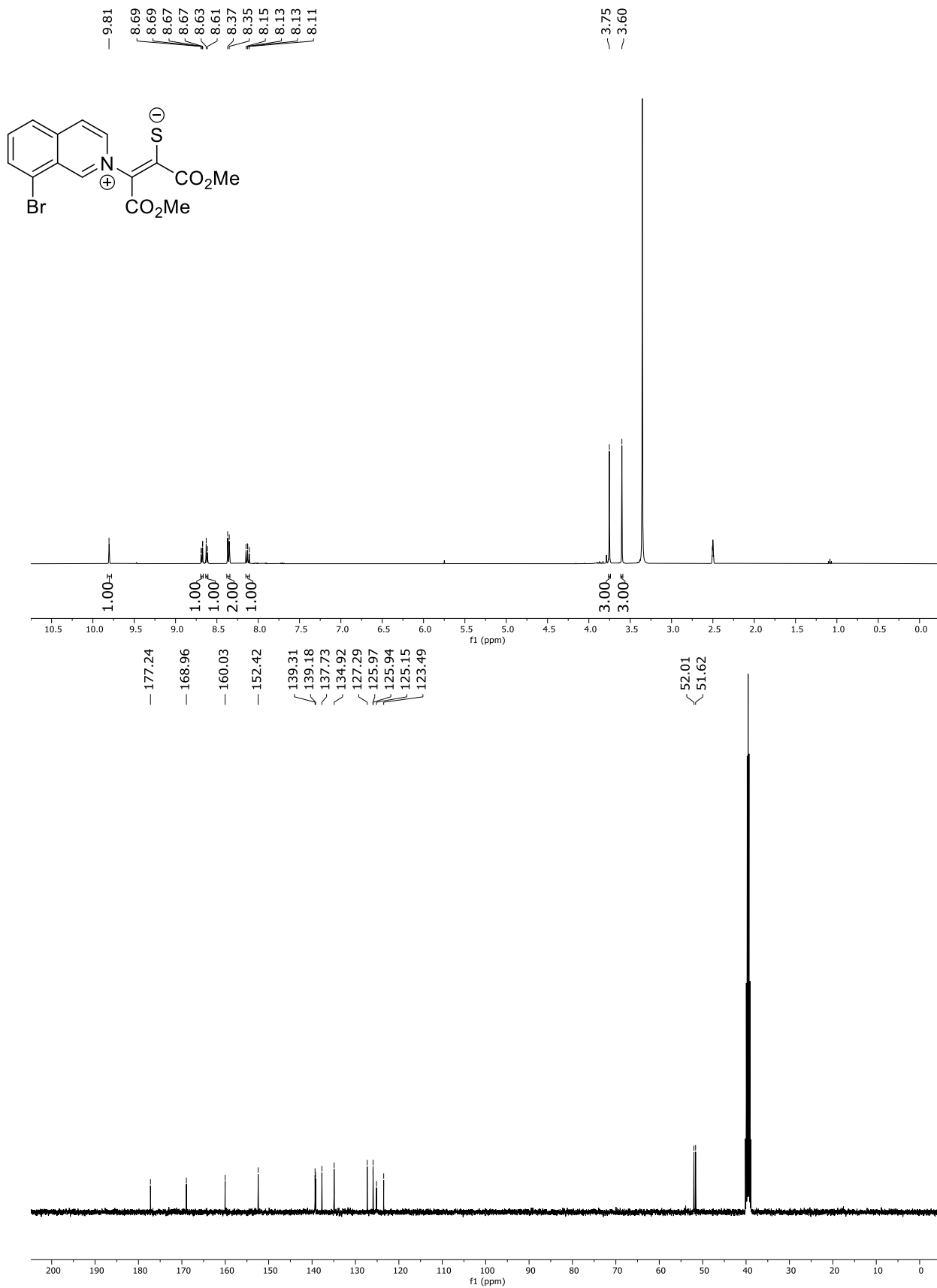
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1c



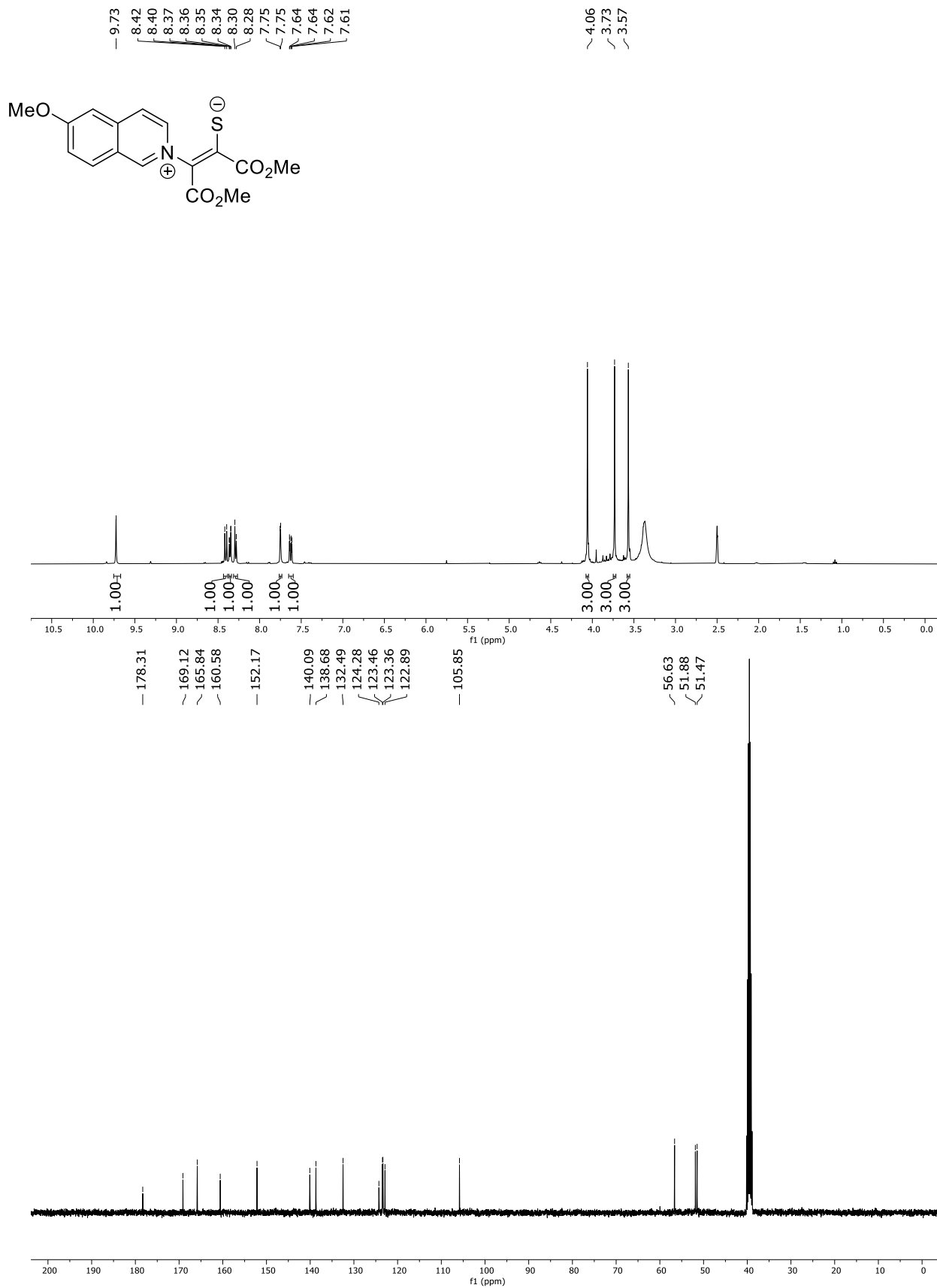
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1d



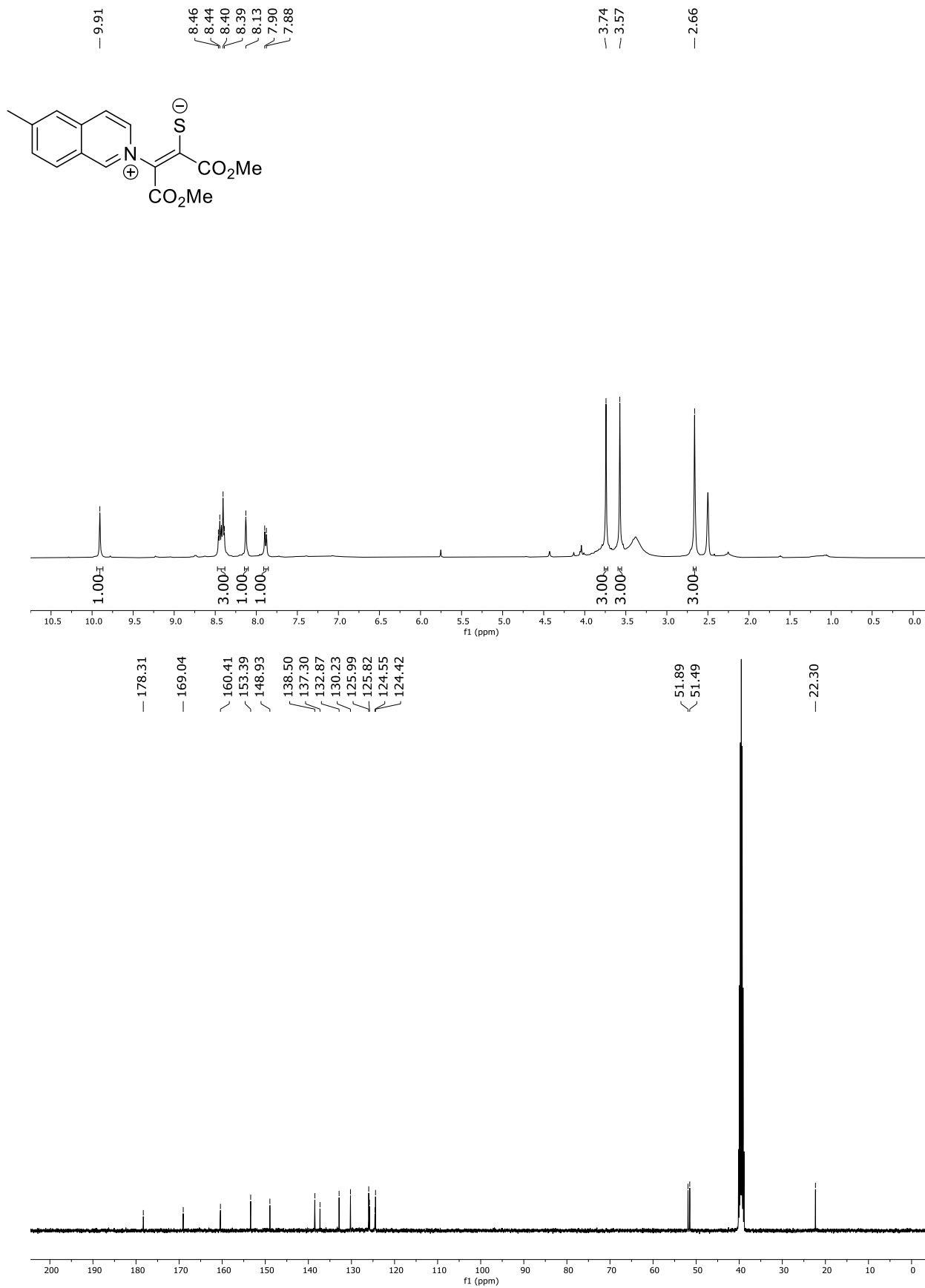
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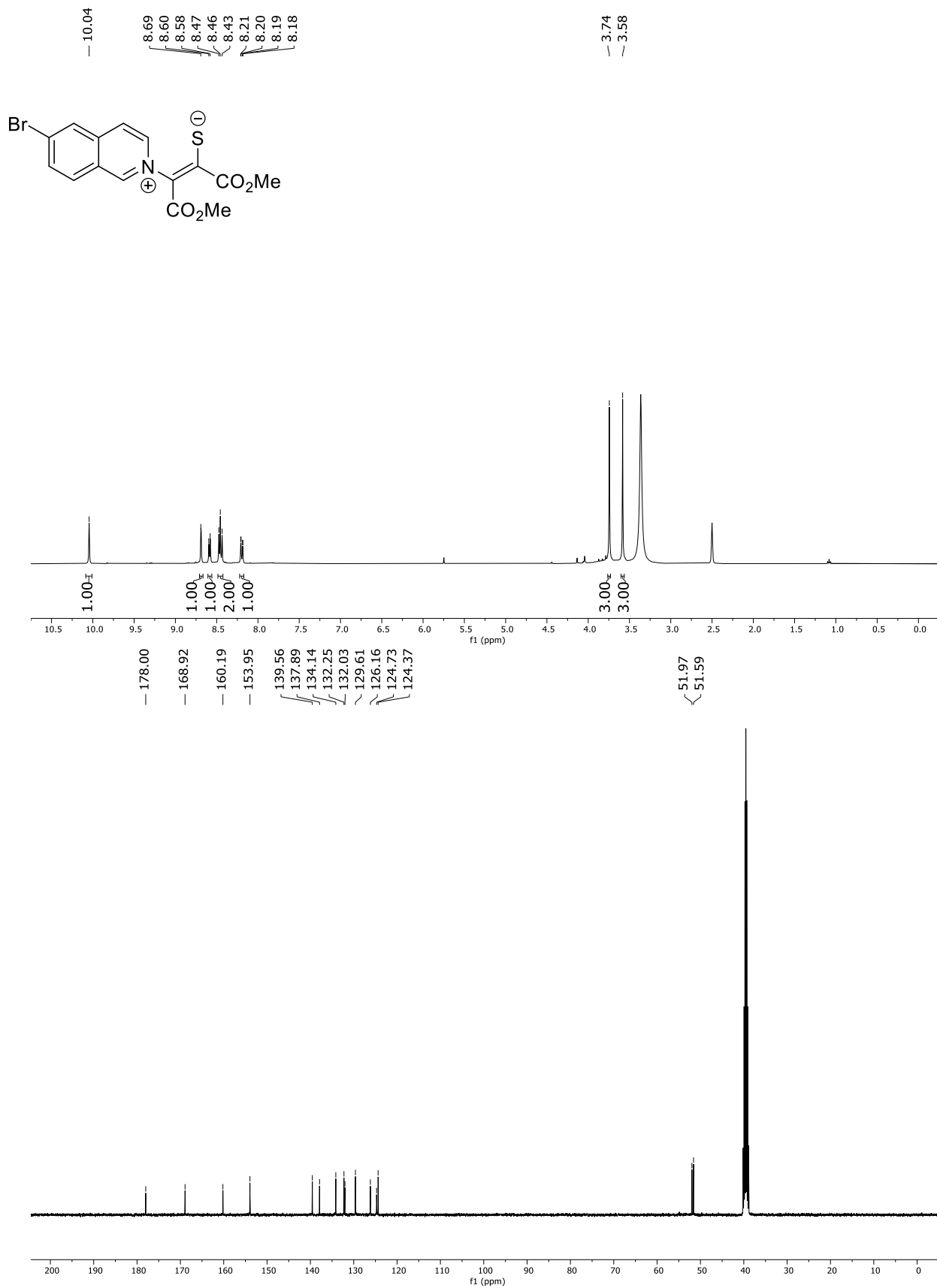
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1f



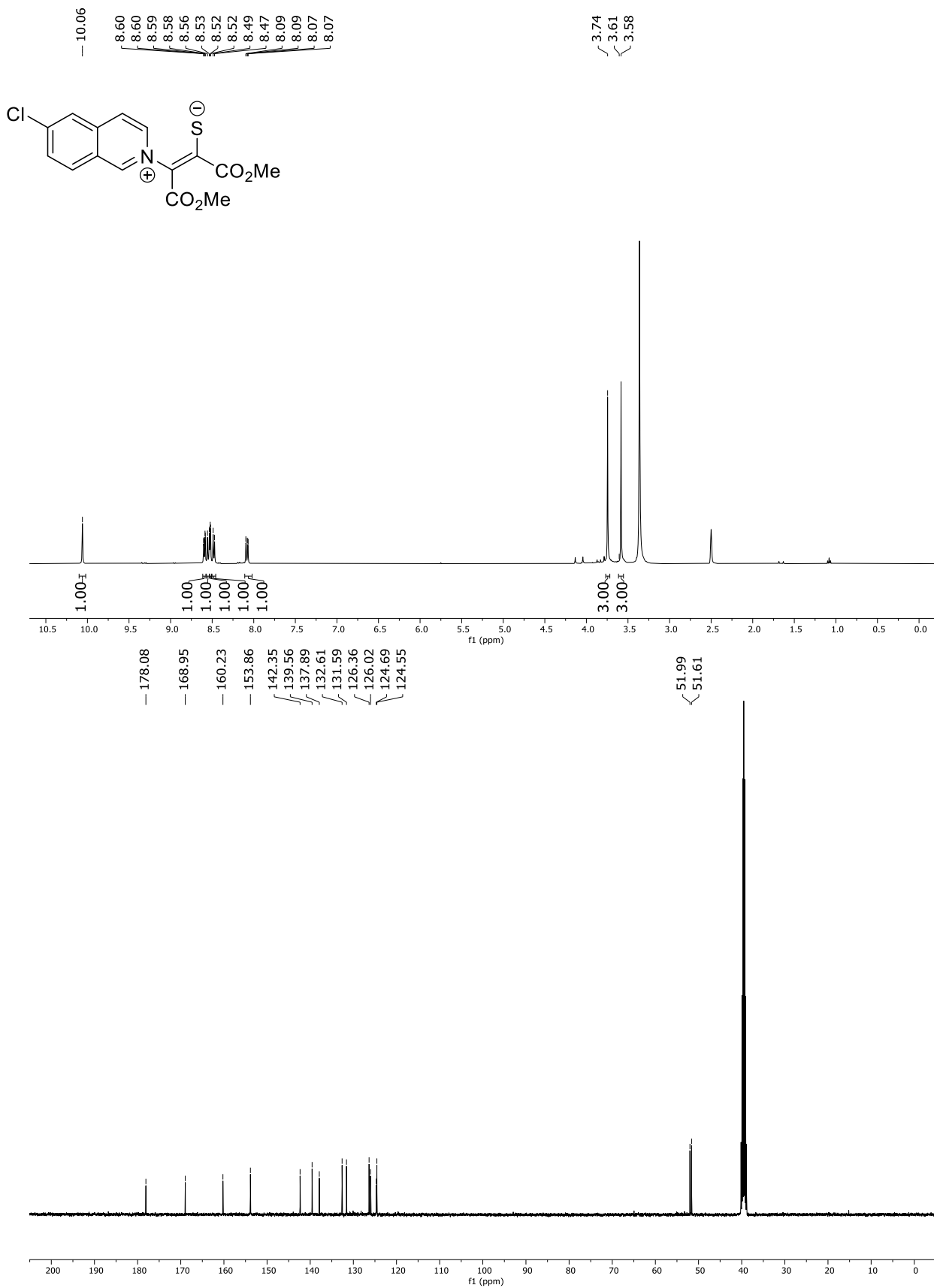
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1g



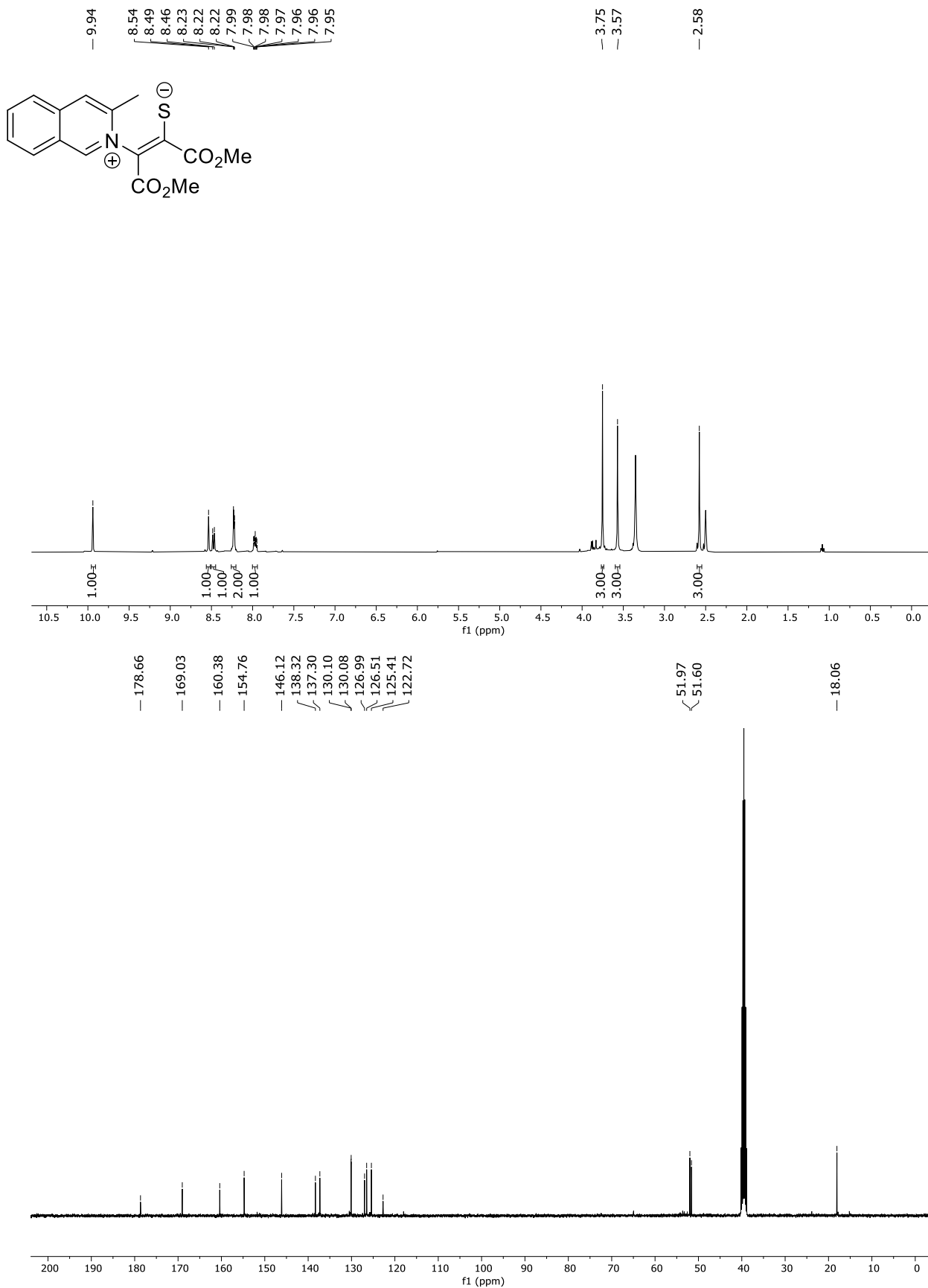
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1h



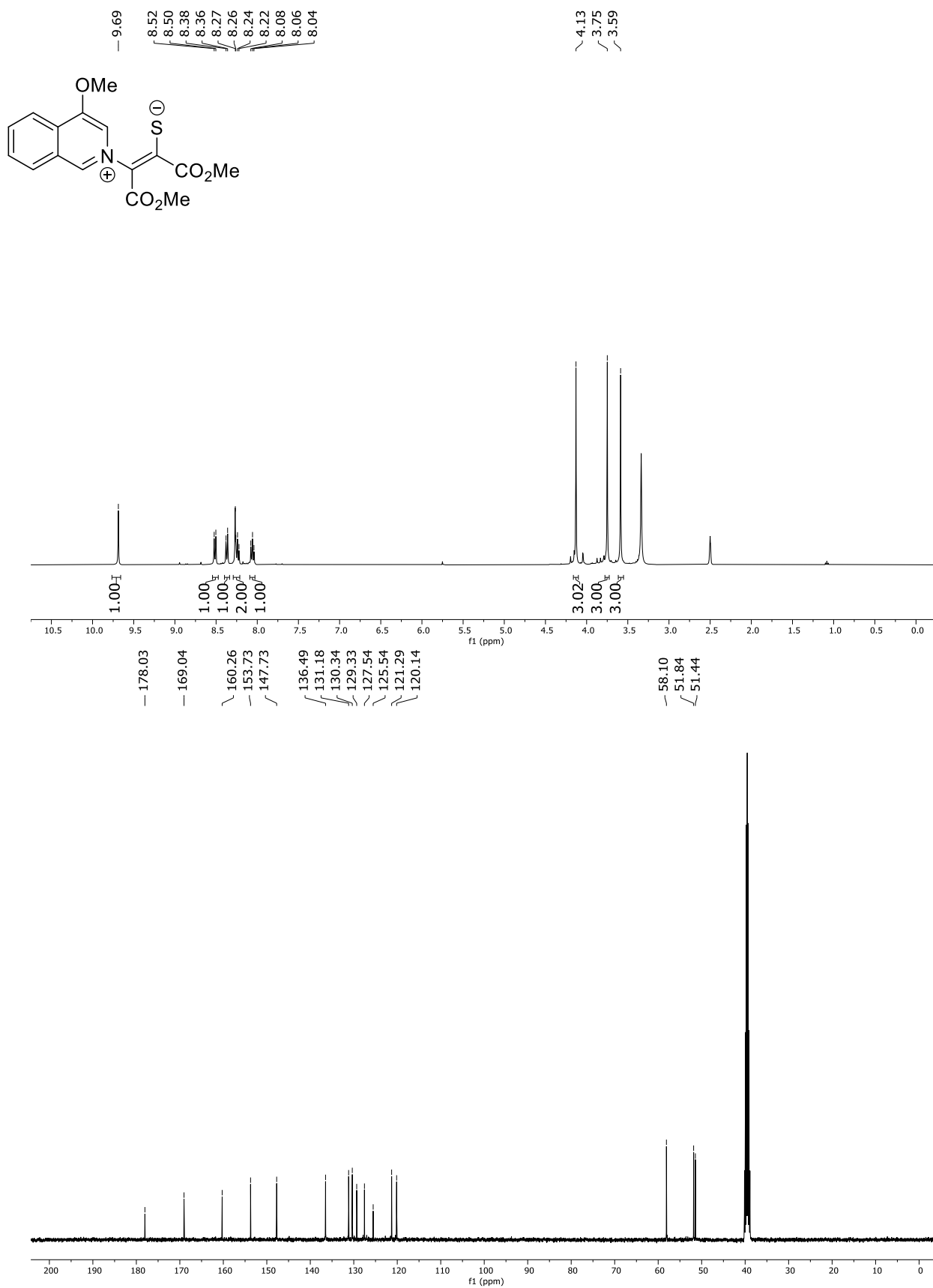
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1i



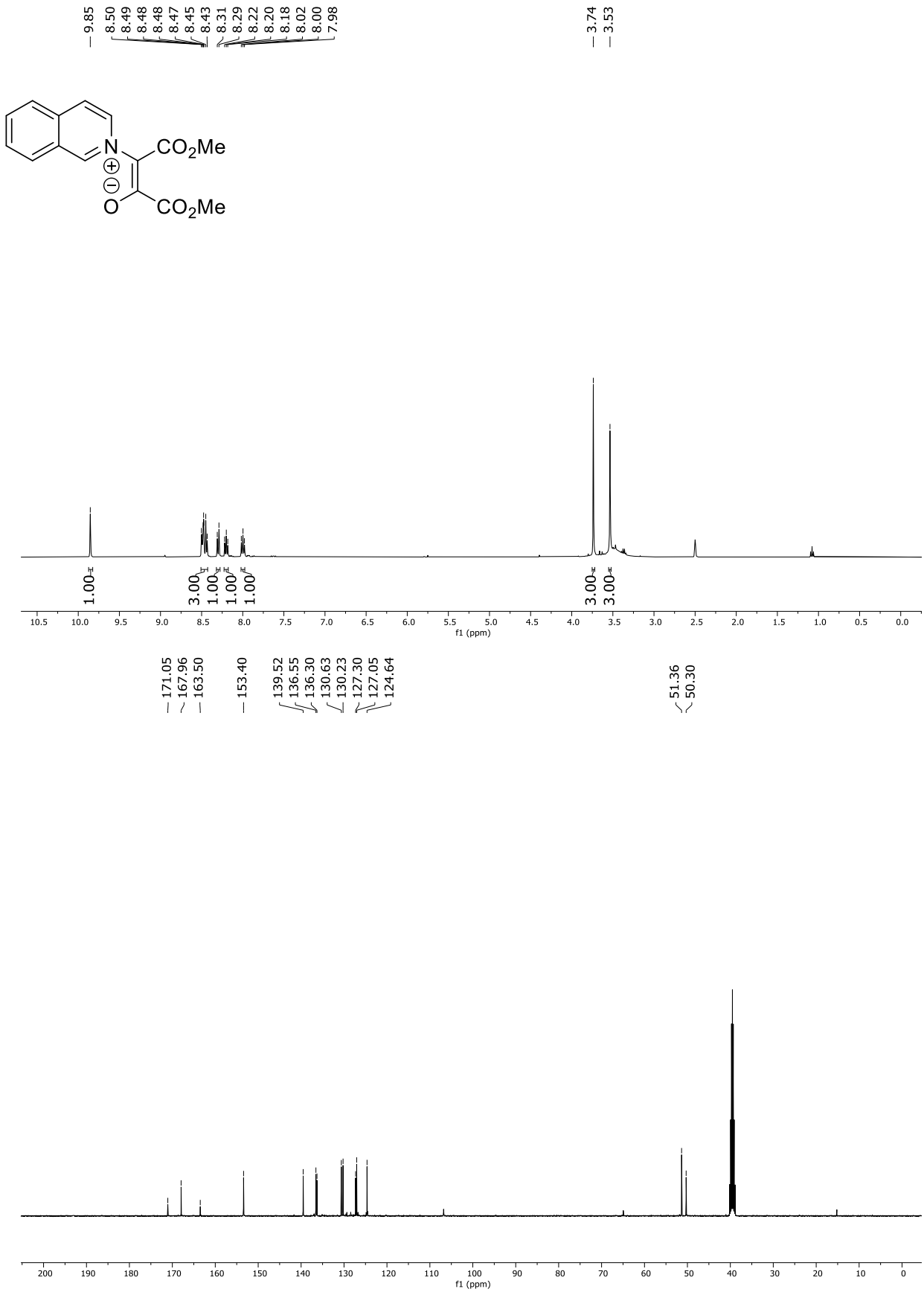
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1j



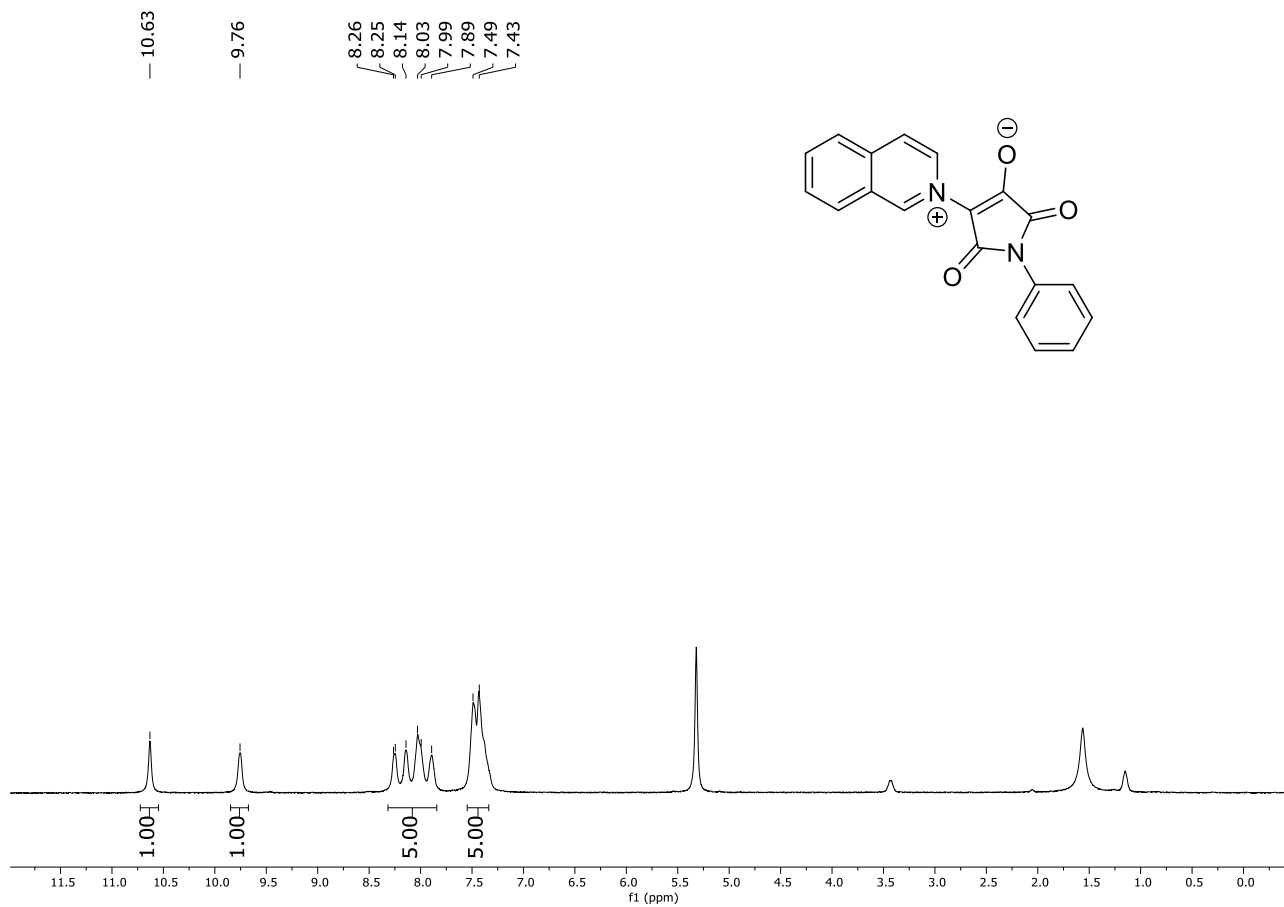
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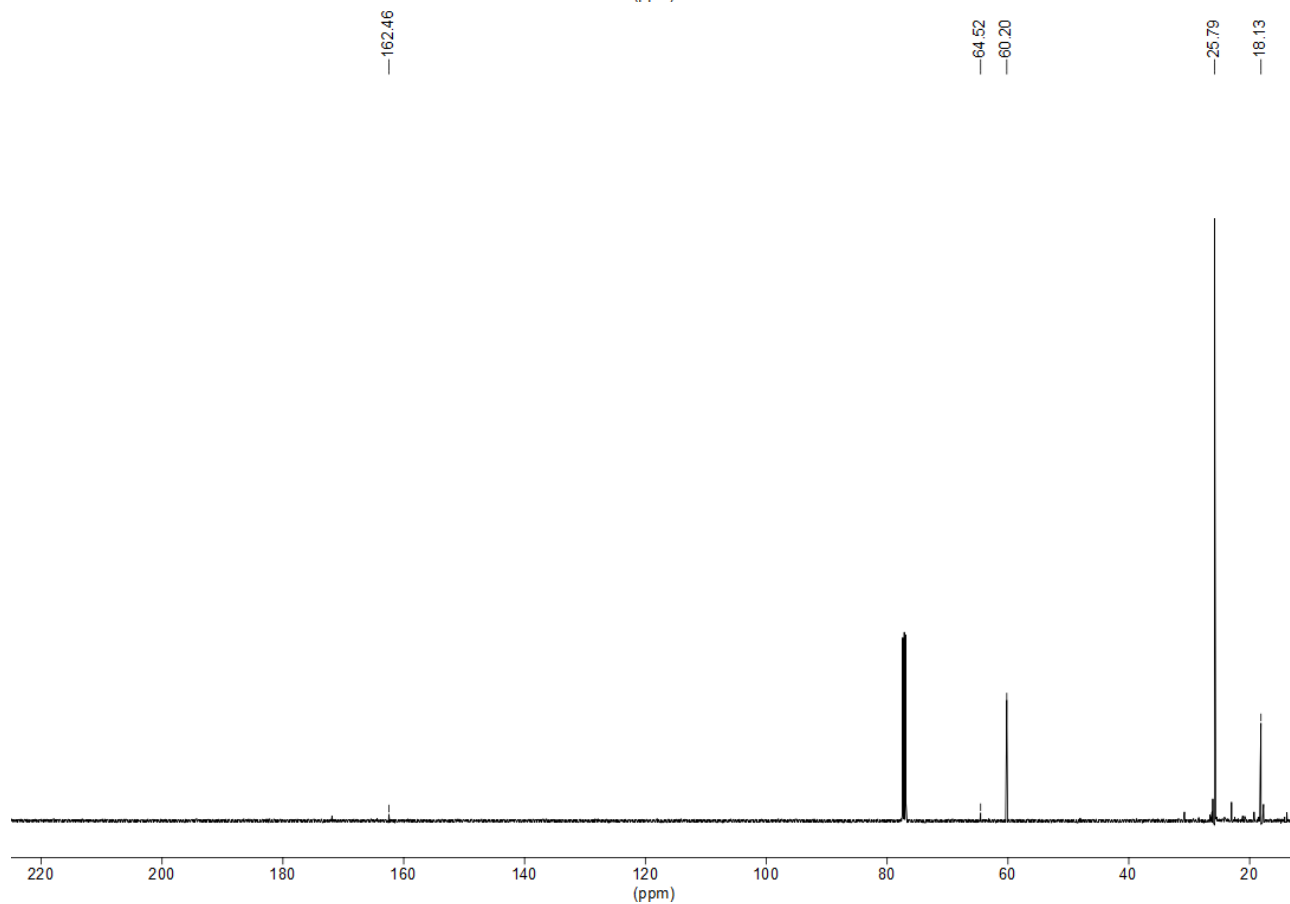
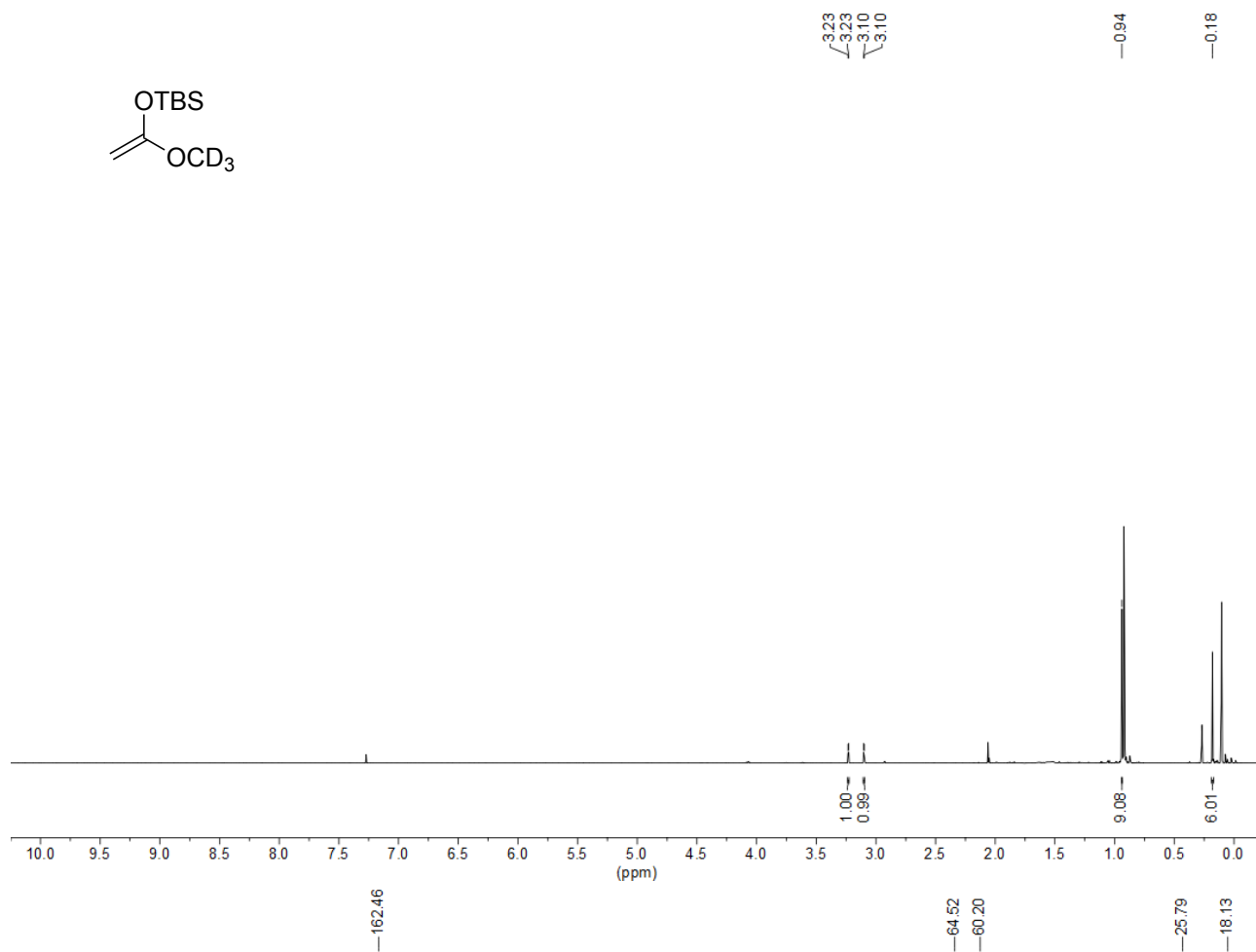
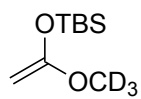
¹H-NMR (400 MHz, DMSO-d₆) and ¹³C-NMR (100 MHz, DMSO-d₆) for 1I



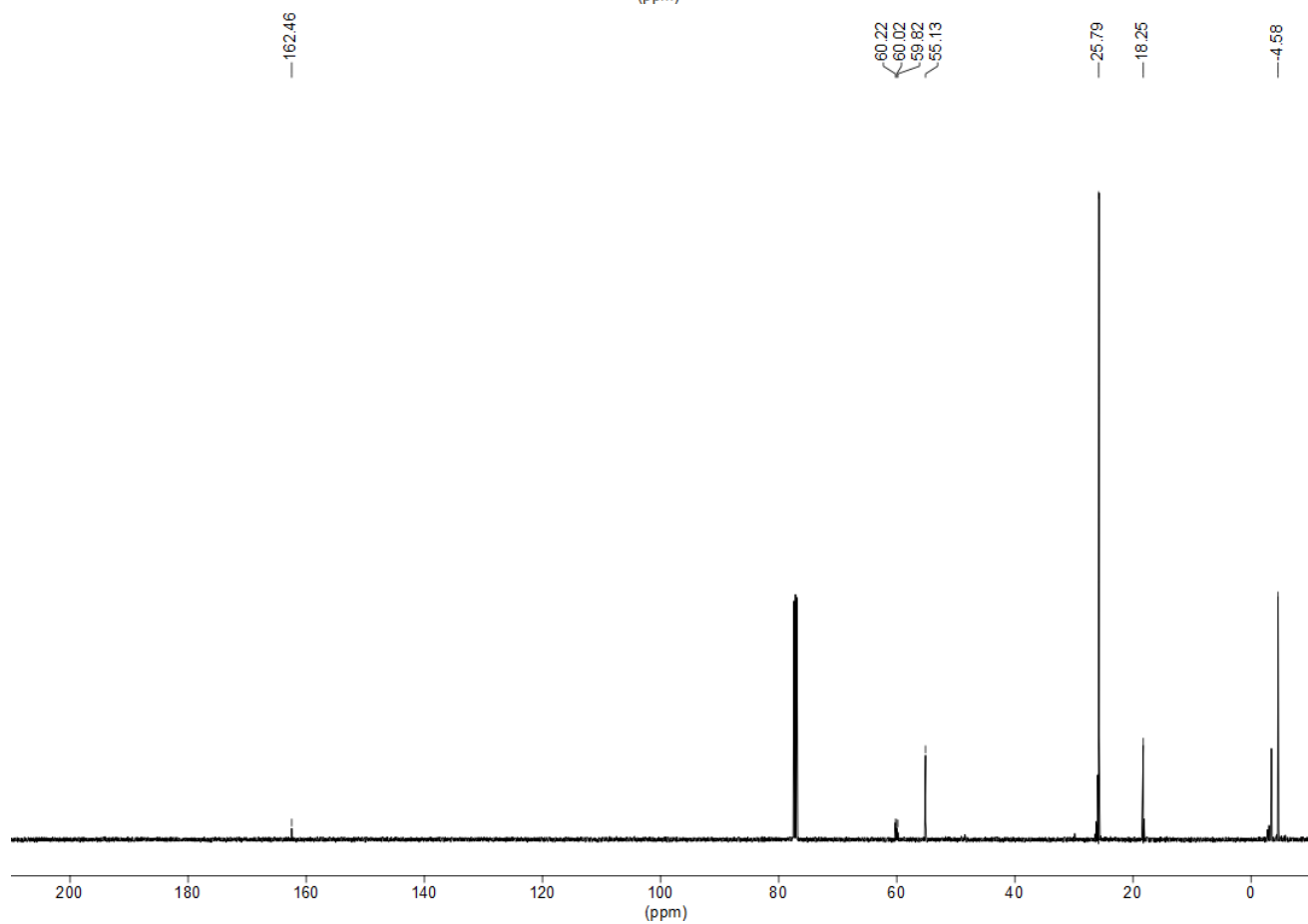
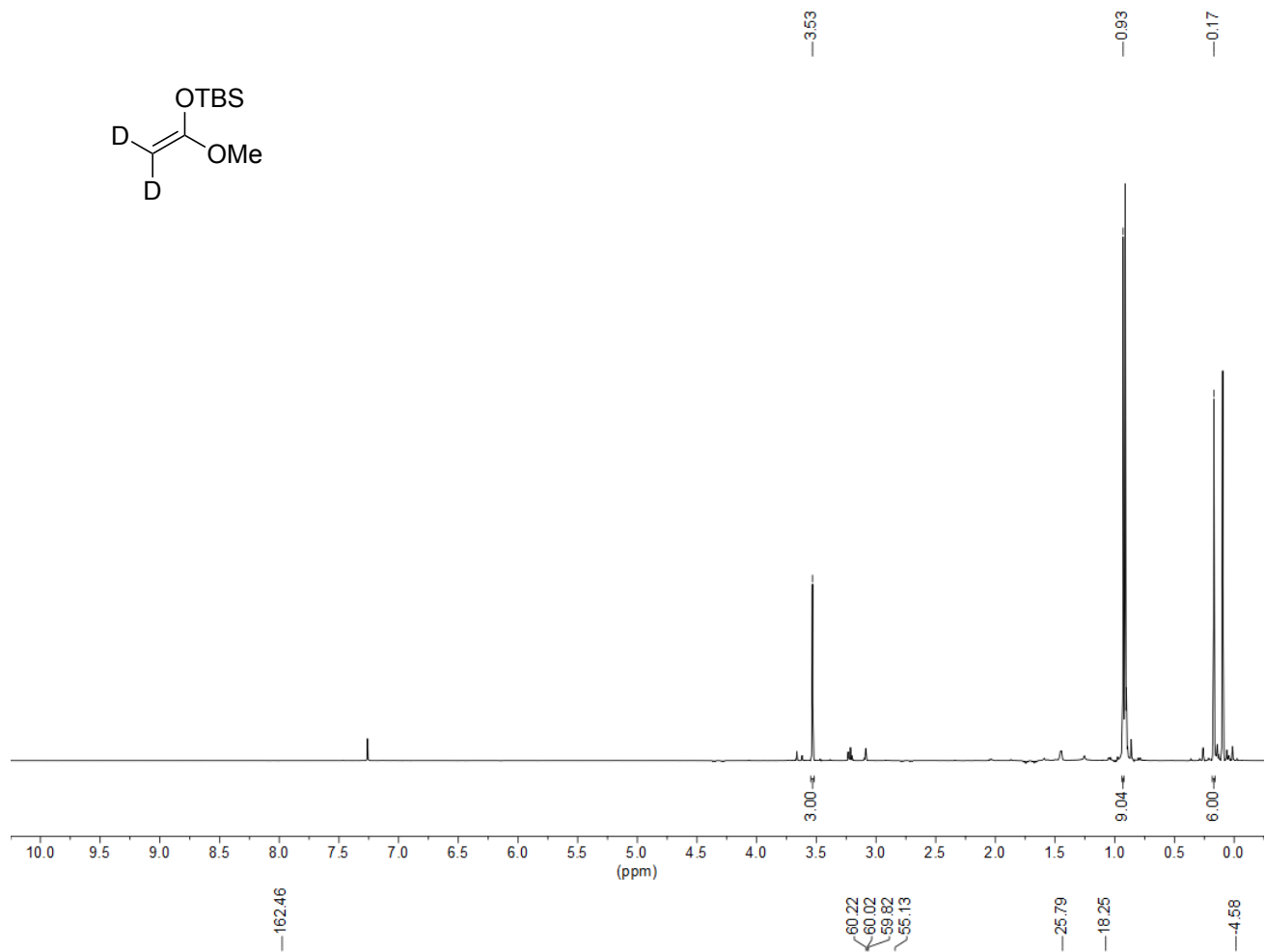
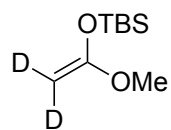
¹H-NMR (400 MHz, CD₂Cl₂) for 1m



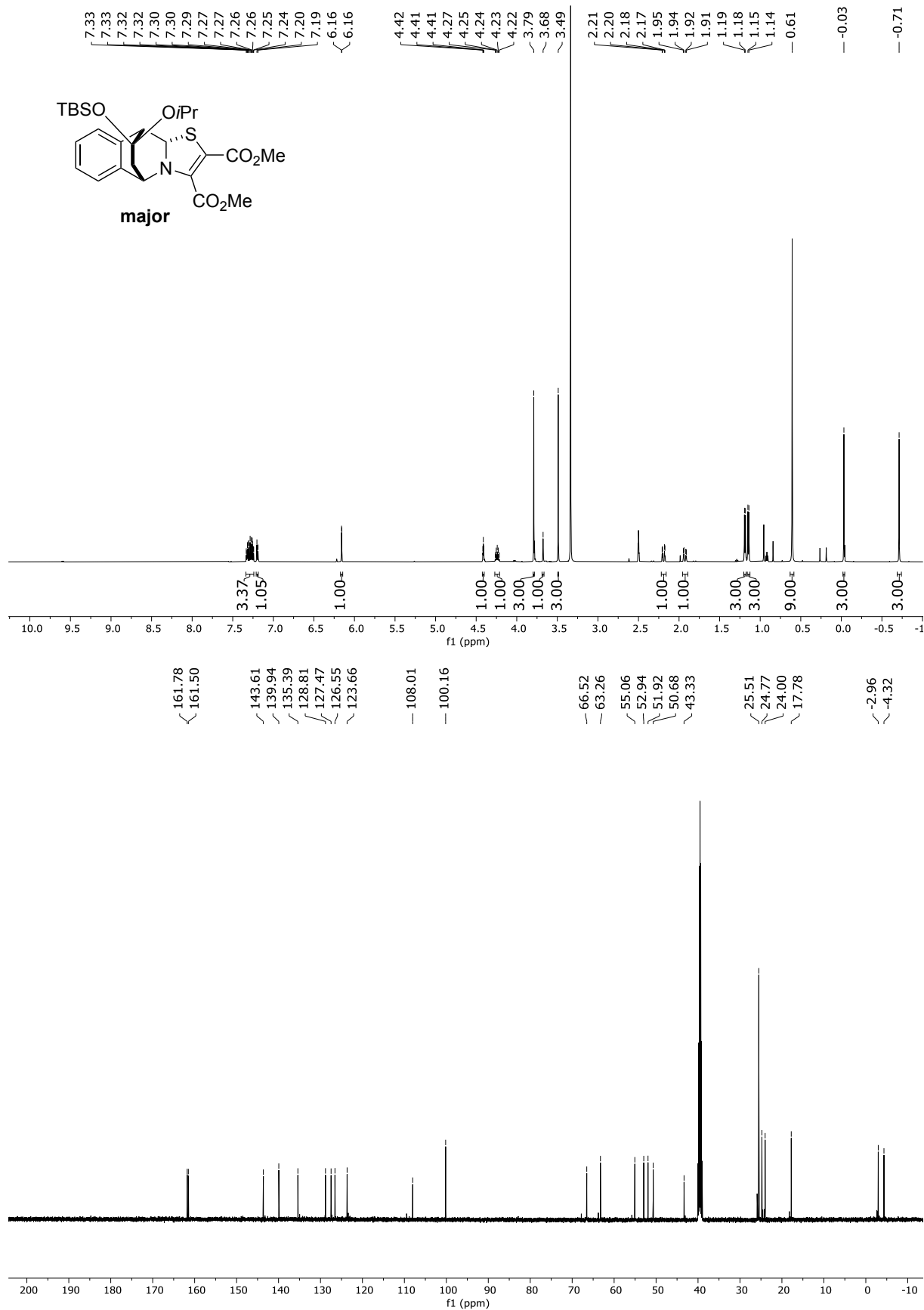
¹H-NMR (600 MHz, CDCl₃) and ¹³C-NMR (150 MHz, CDCl₃) for 2b-D



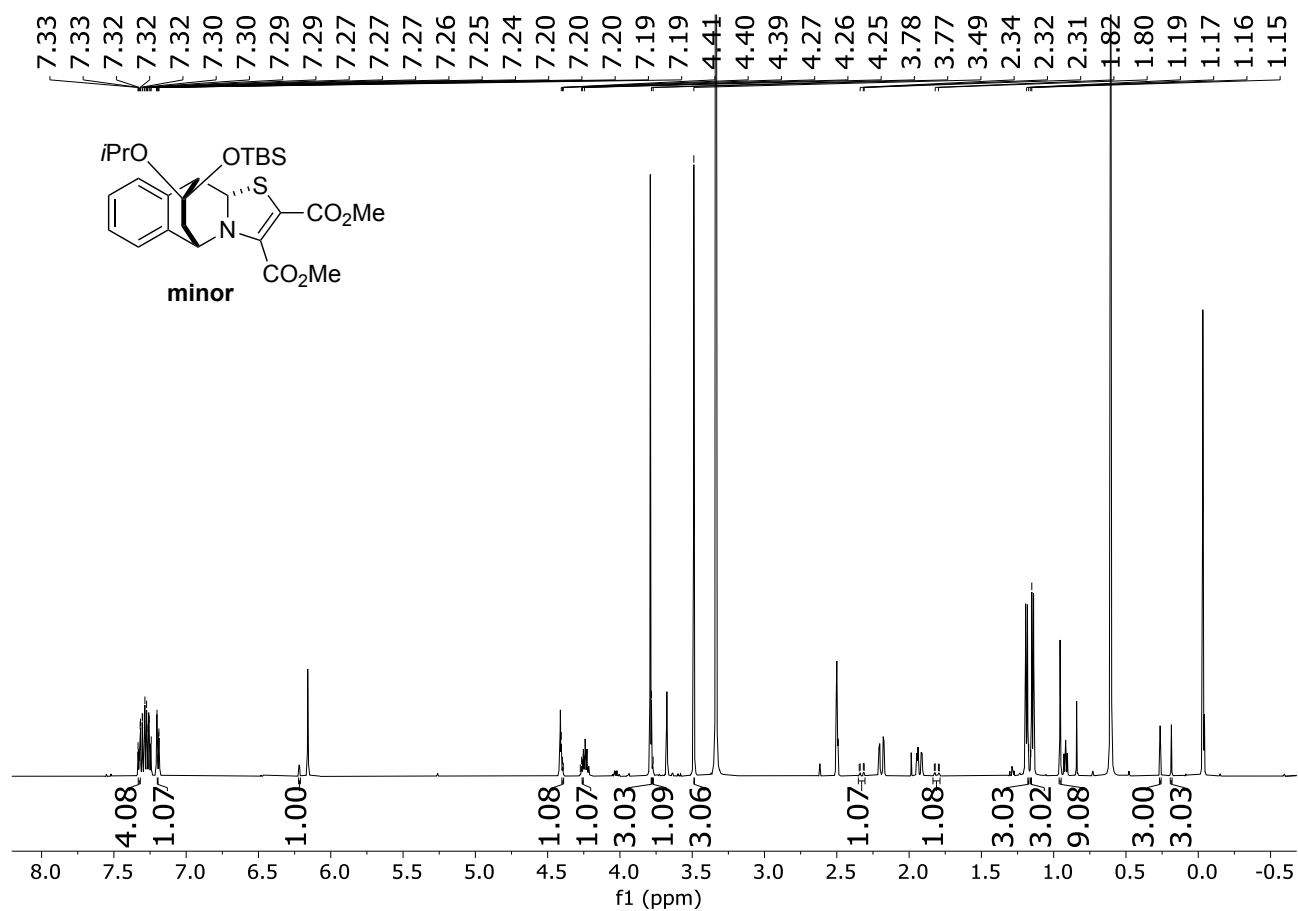
¹H-NMR (600 MHz, CDCl₃) and ¹³C-NMR (150 MHz, CDCl₃) for 2b-D'



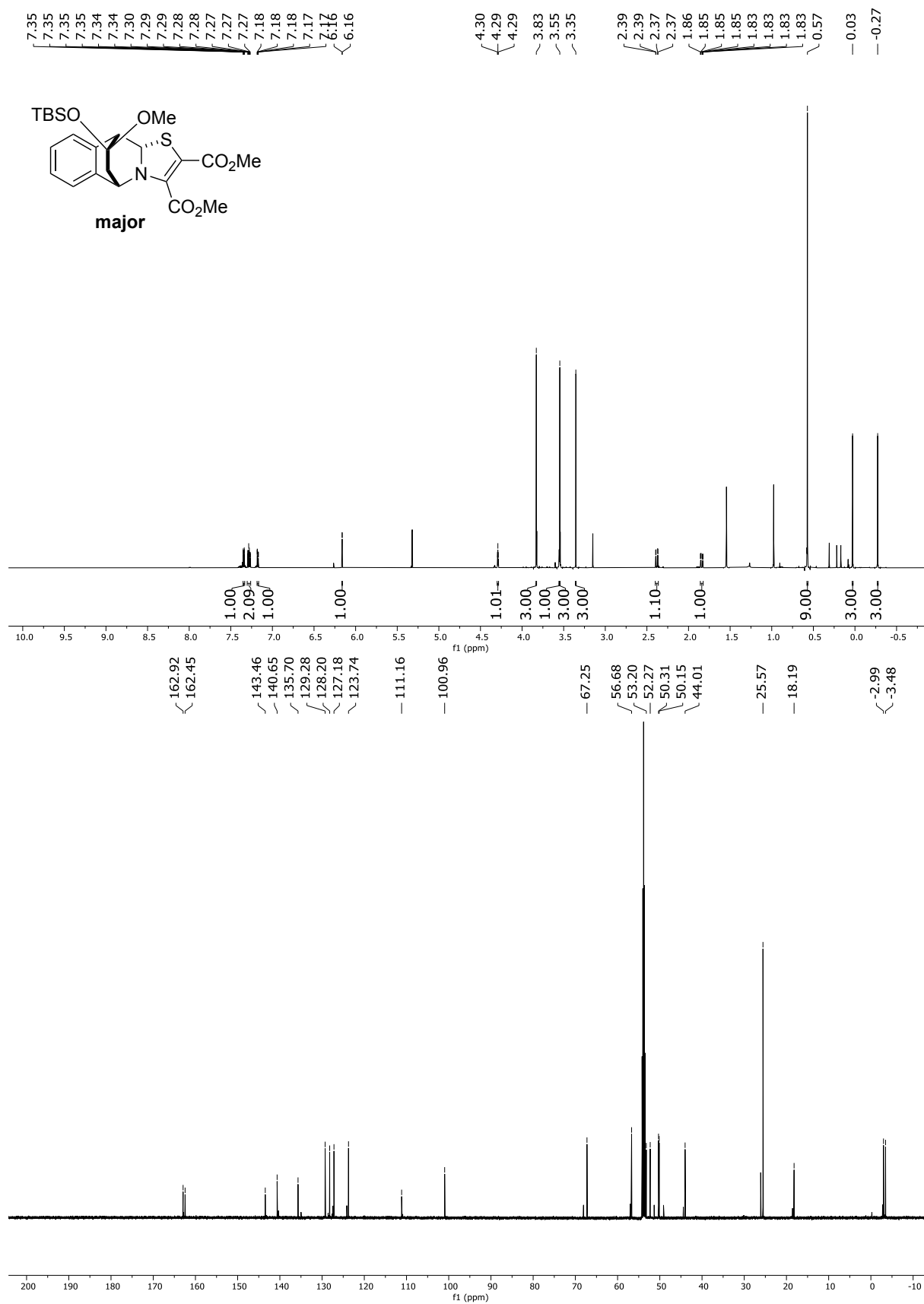
¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 3a-major



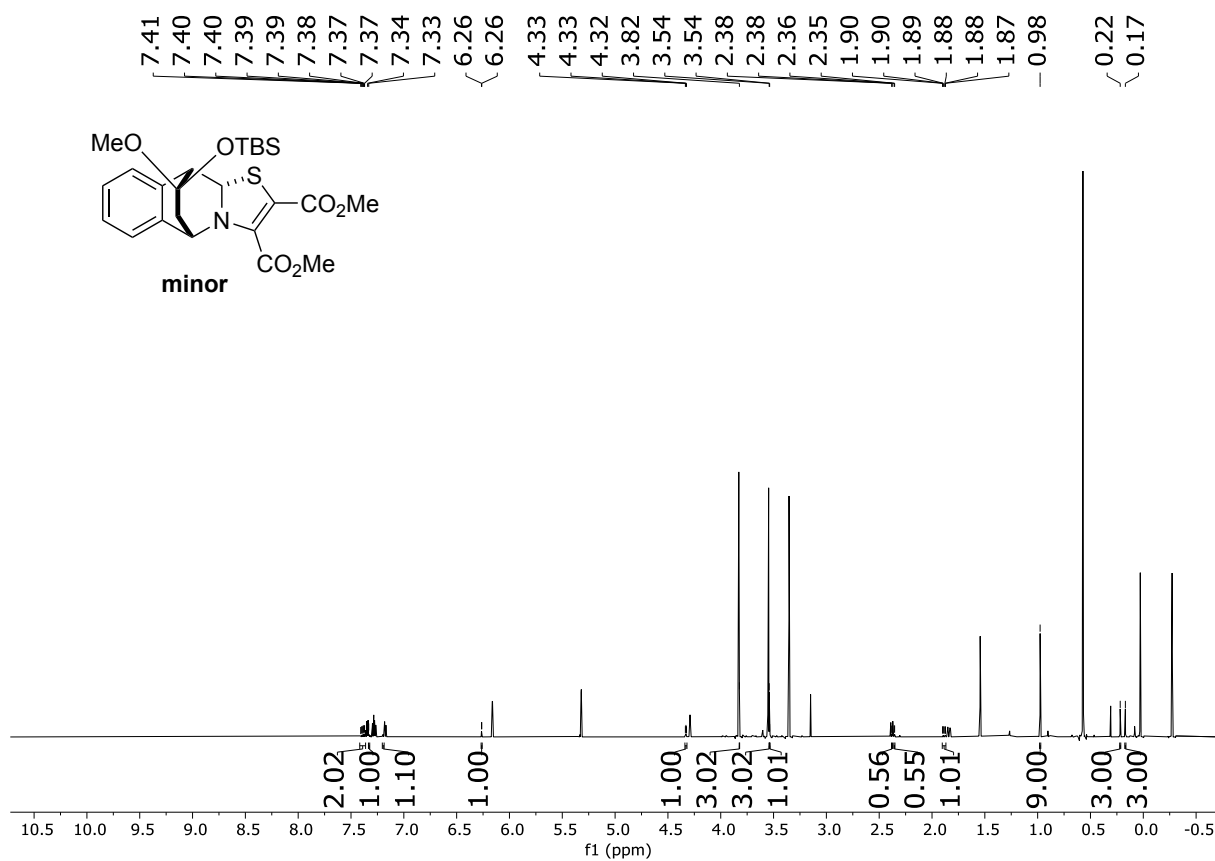
¹H-NMR (500 MHz, CD₂Cl₂) for 3a-minor (representative signals)



¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3b-major



¹H-NMR (600 MHz, CD₂Cl₂) for 3b-minor (representative signals)

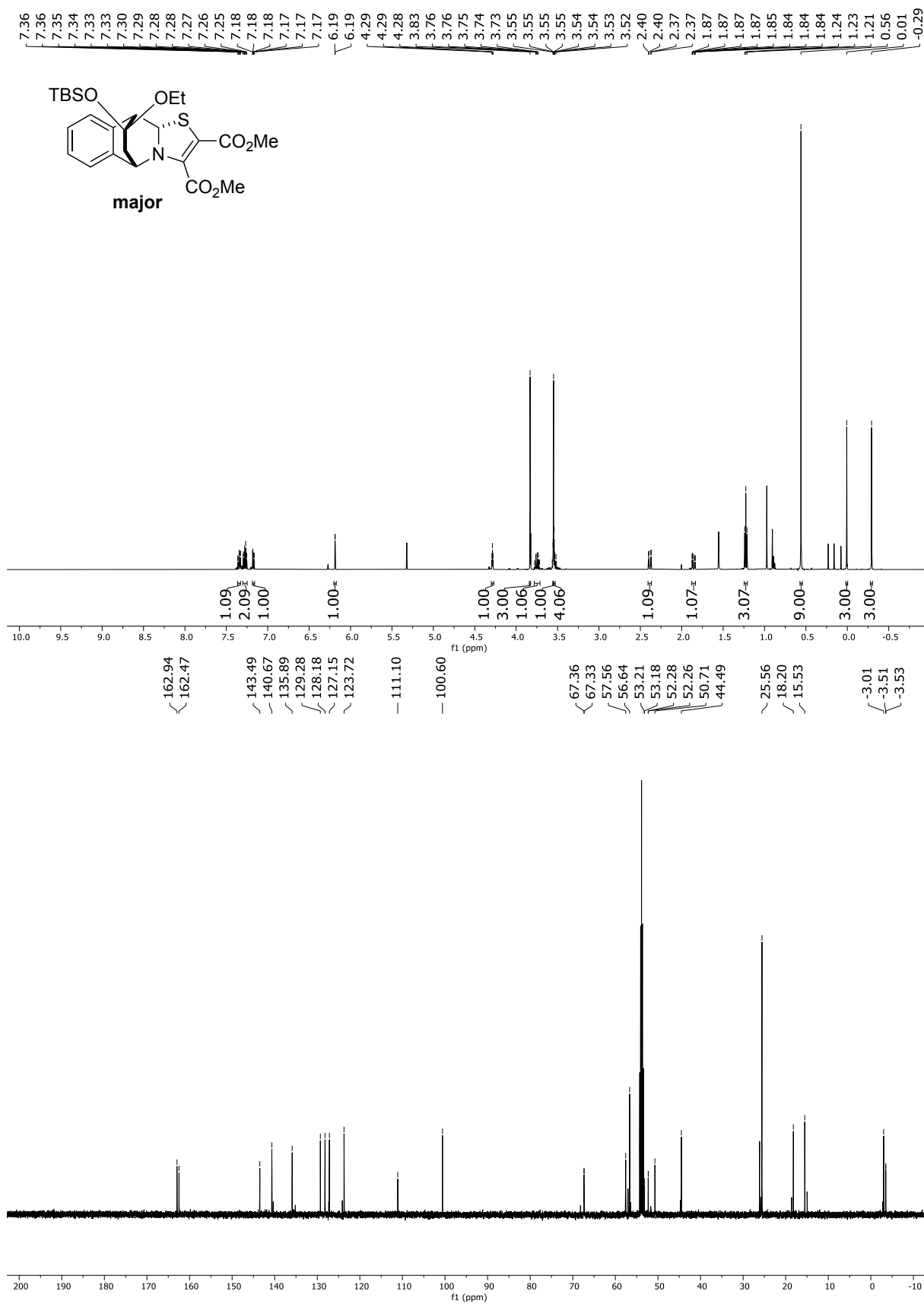


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7.40
7.39
7.39
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7.37
7.37
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7.33
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6.26
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4.33
4.32
3.82
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3.54
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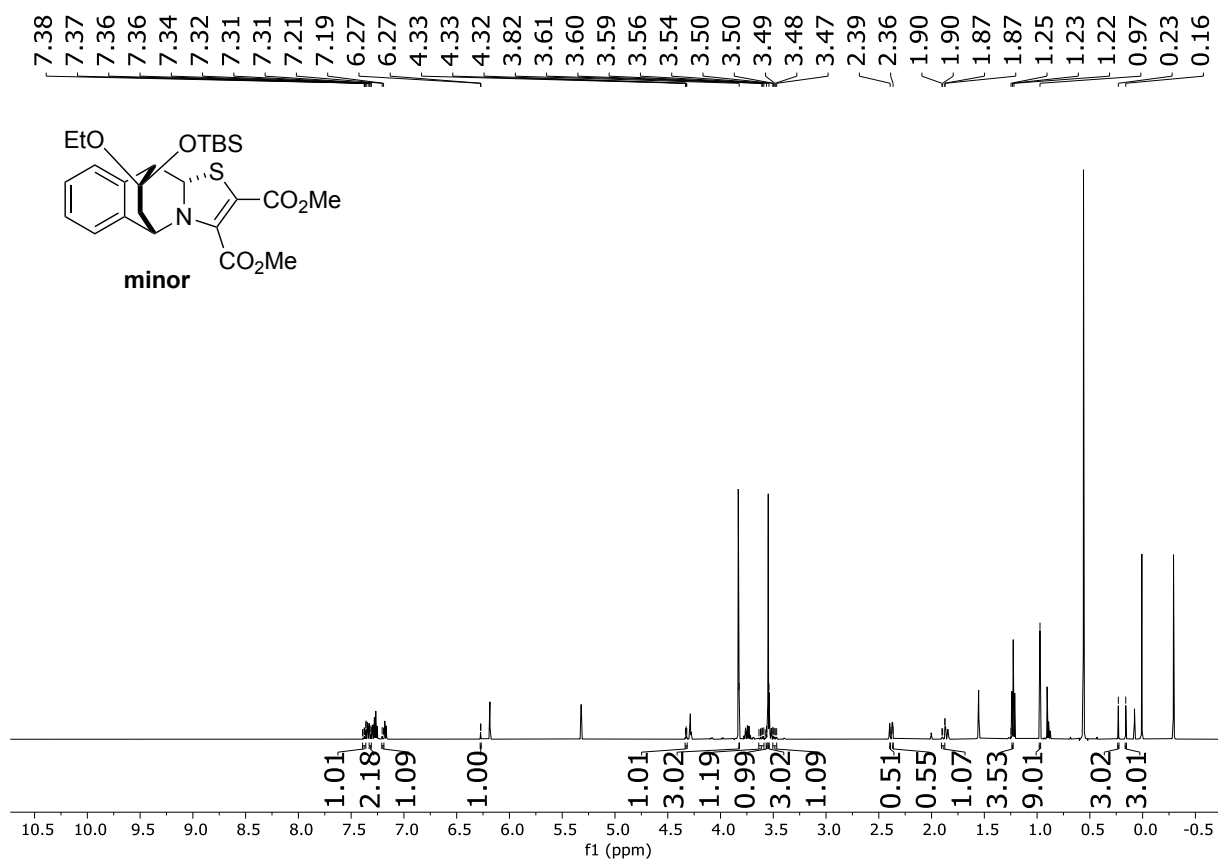
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f1 (ppm)

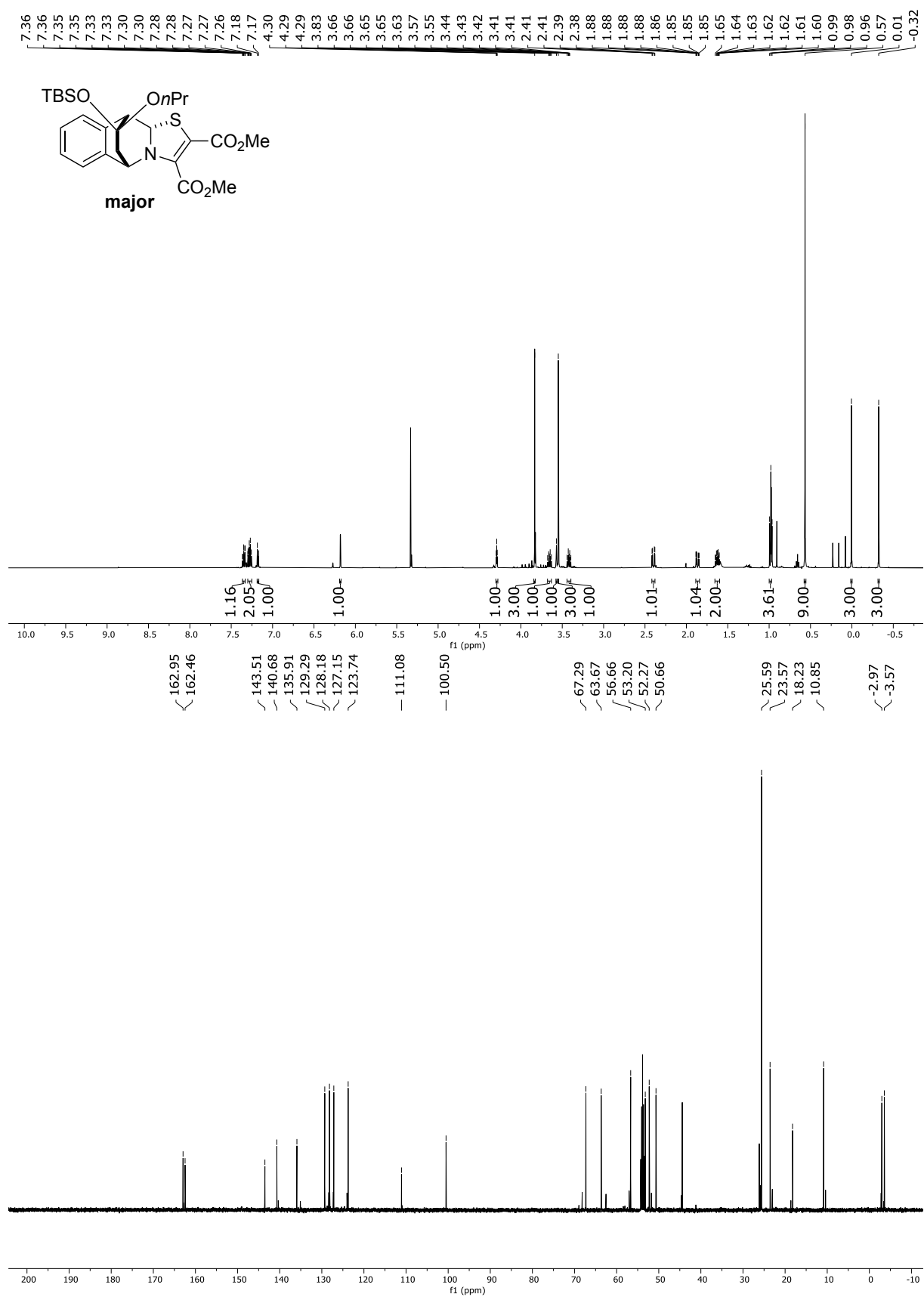
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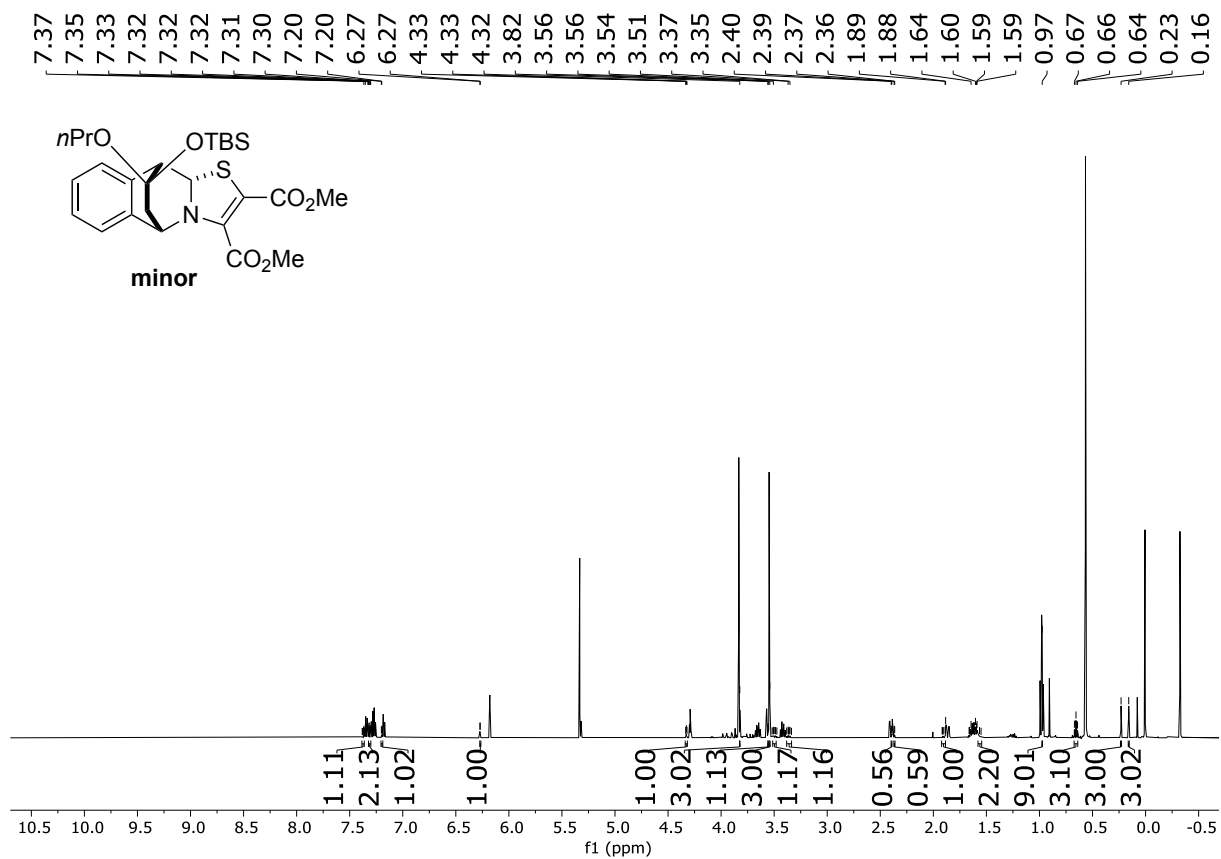
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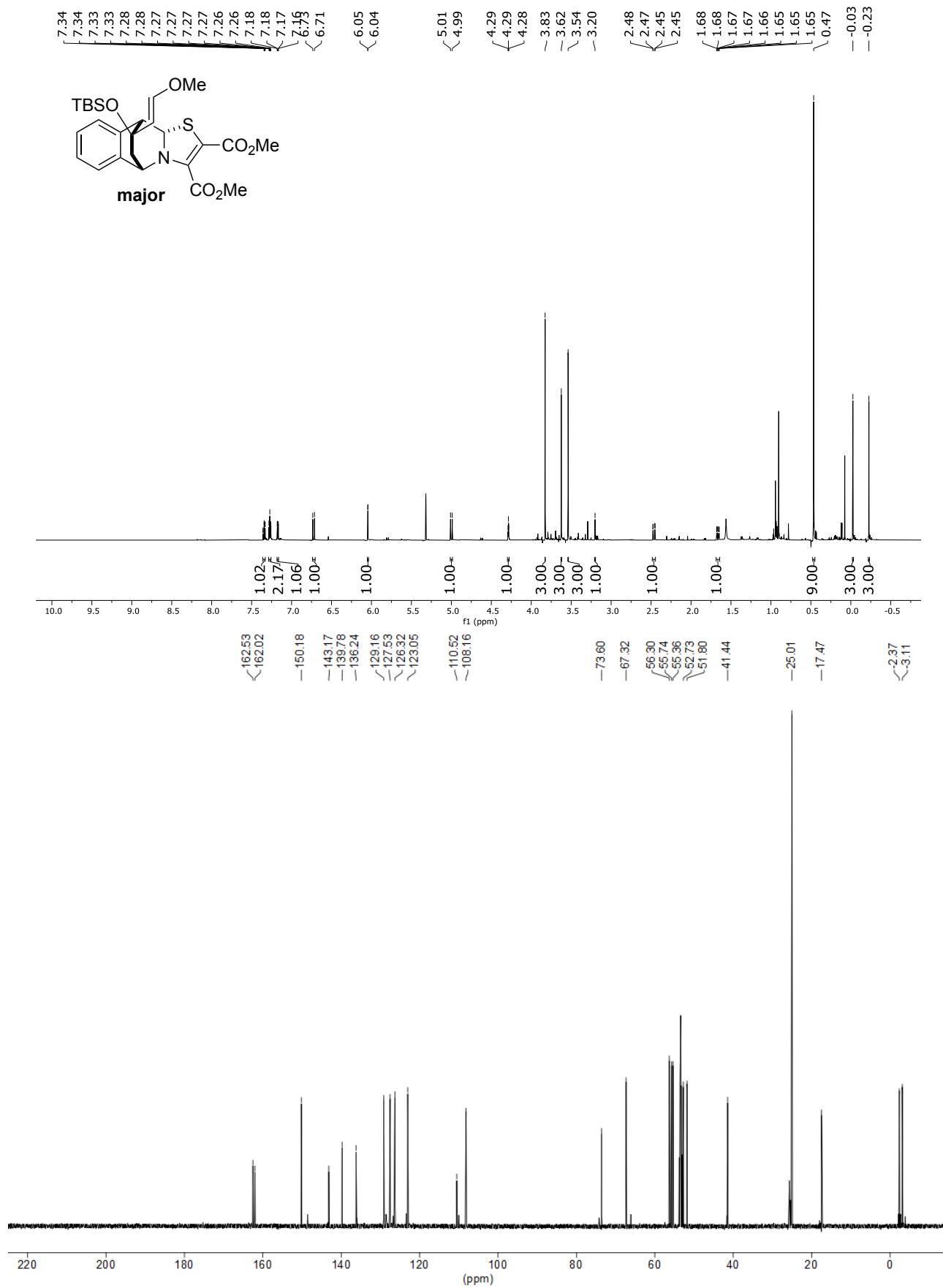
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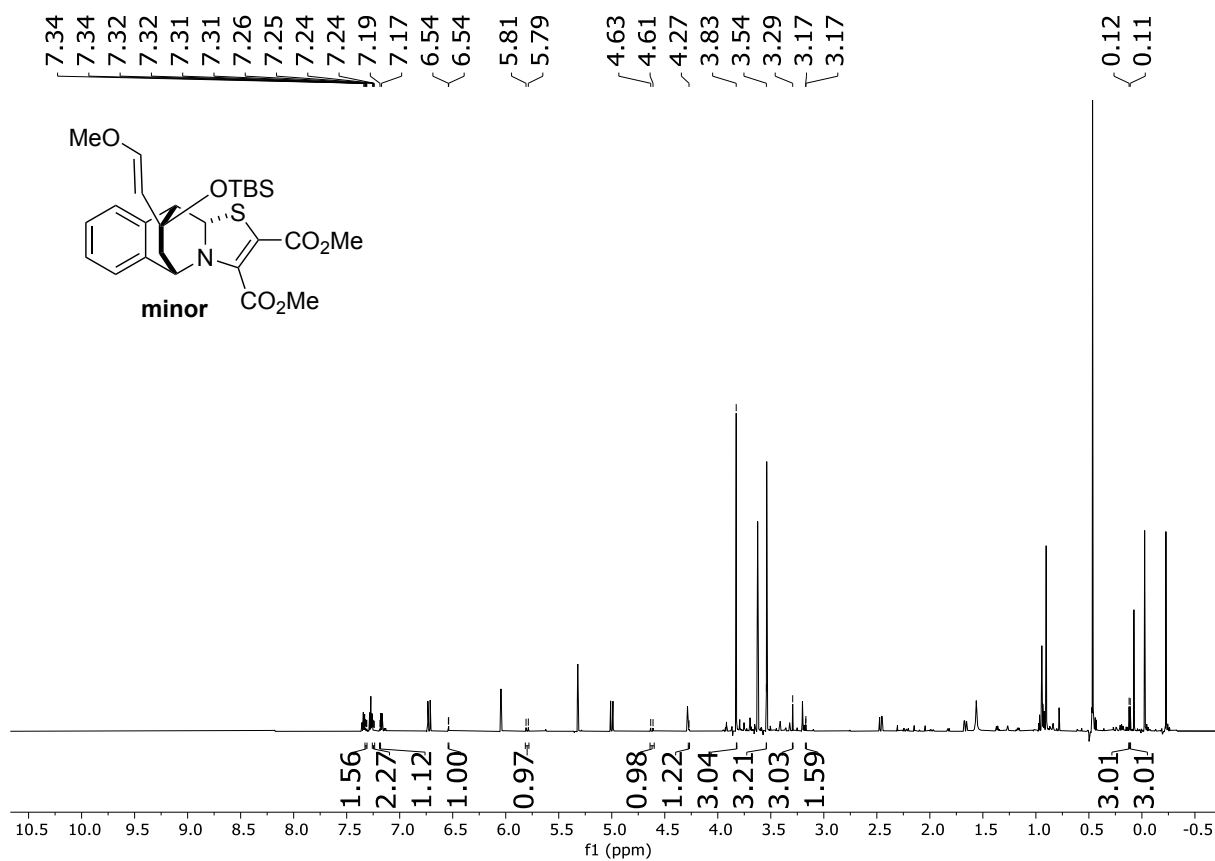
¹H-NMR (500 MHz, CD₂Cl₂) for 3d-minor (representative signals)



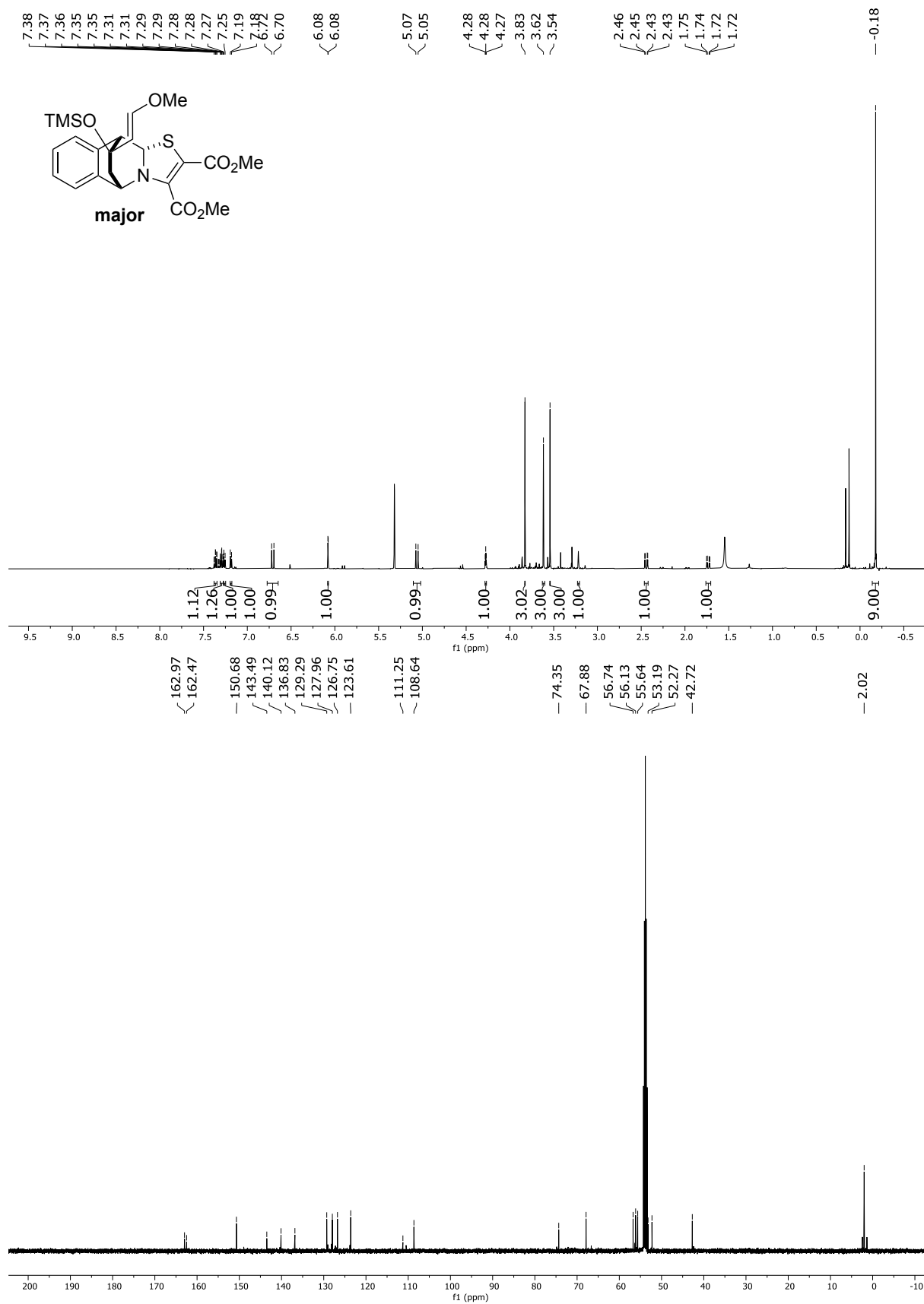
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3e-major



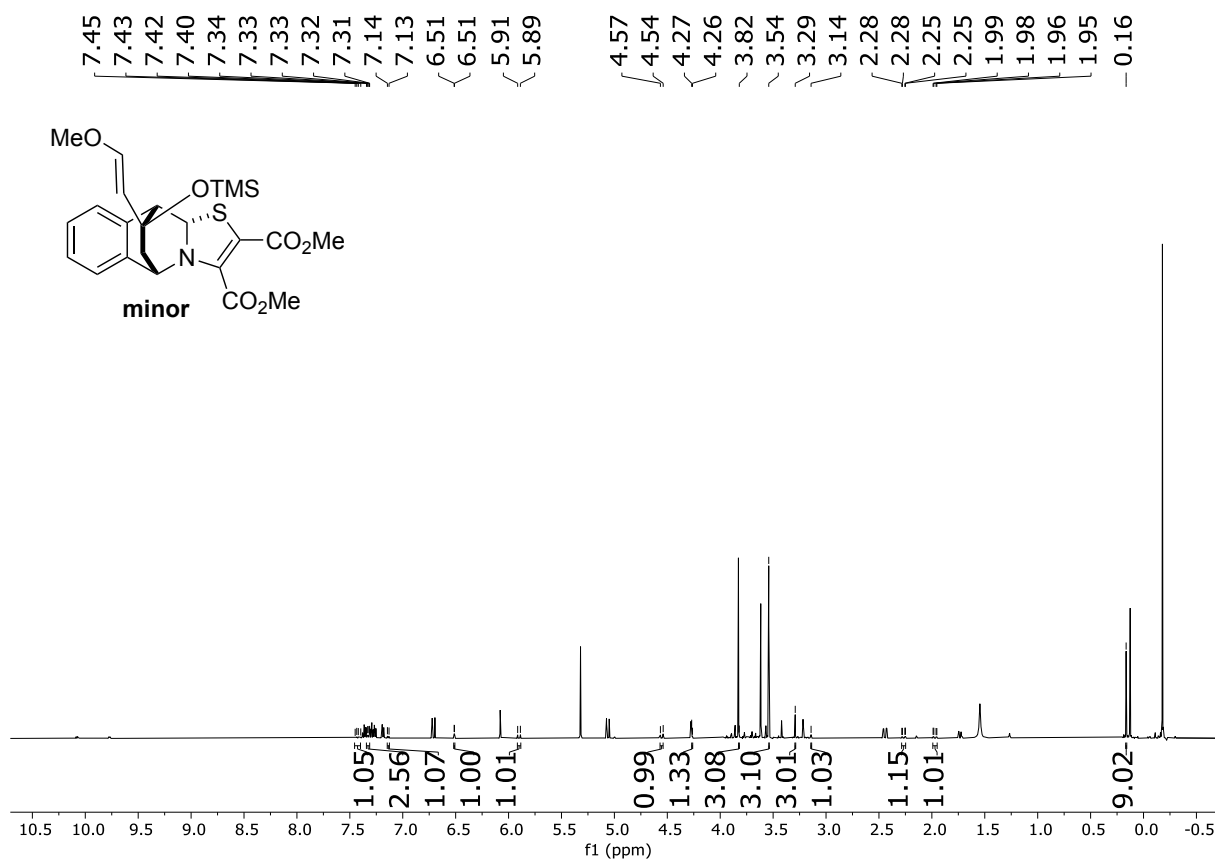
¹H-NMR (600 MHz, CD₂Cl₂) for 3e-minor (representative signals)



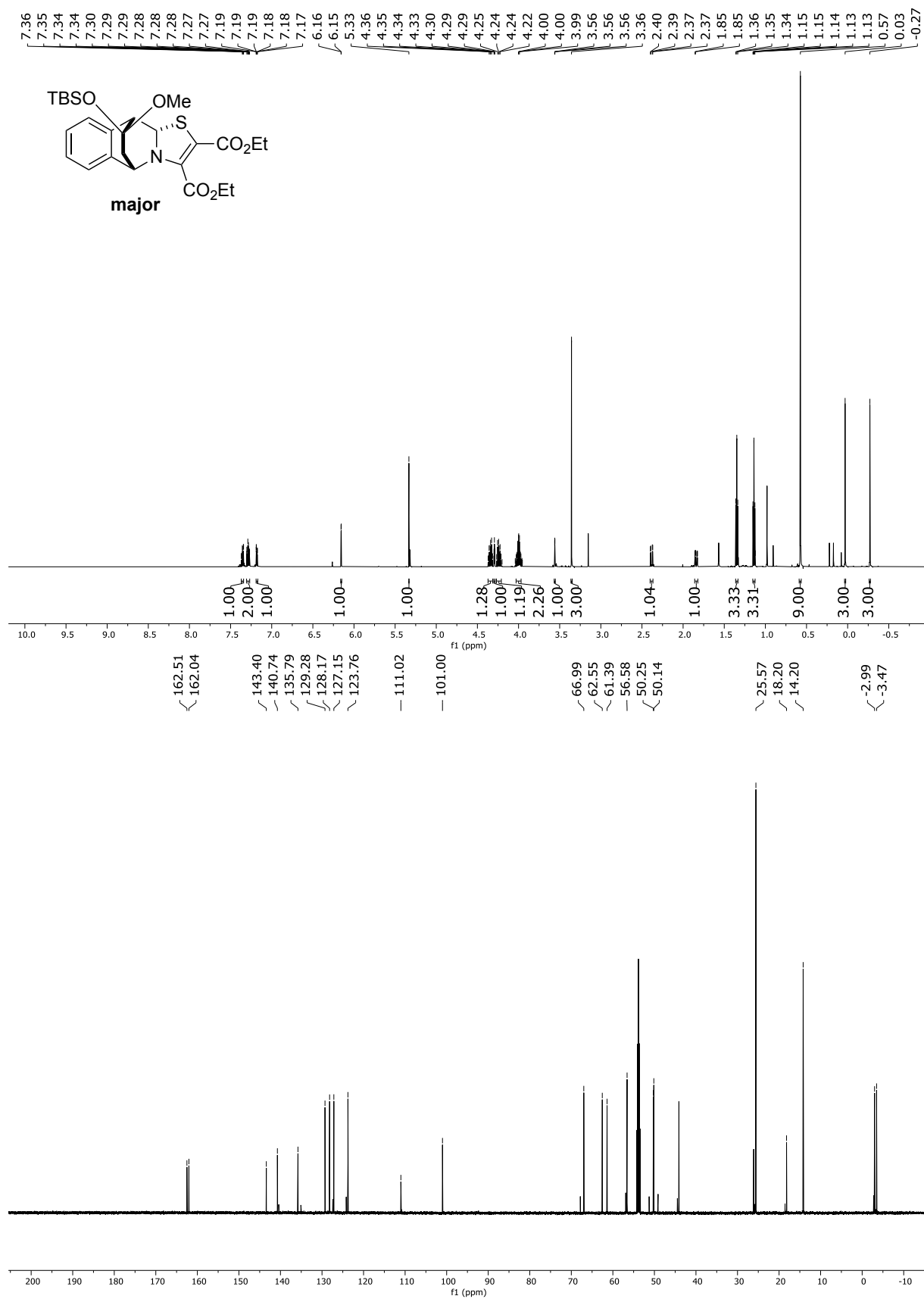
¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 3f-major



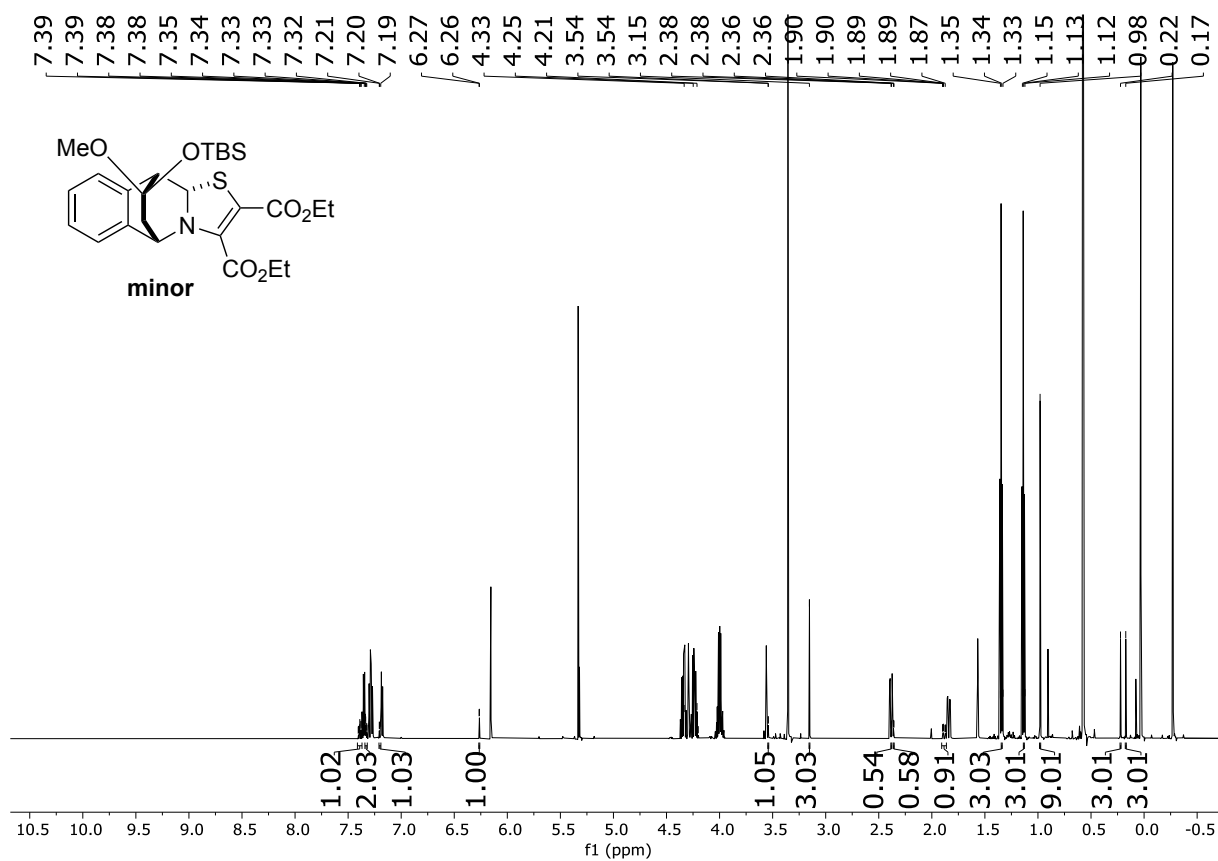
¹H-NMR (500 MHz, CD₂Cl₂) for 3f-minor (representative signals)



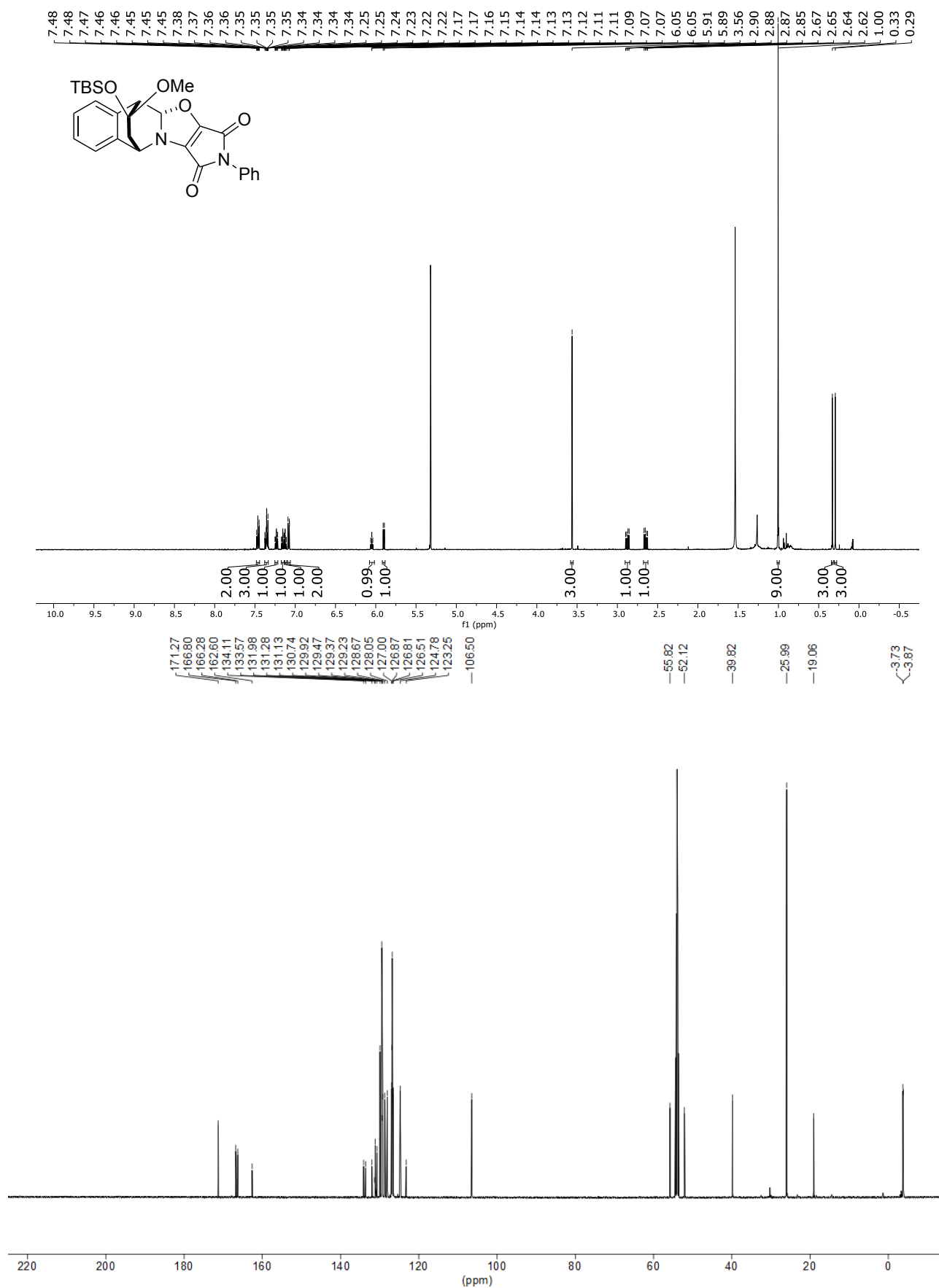
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3g-major



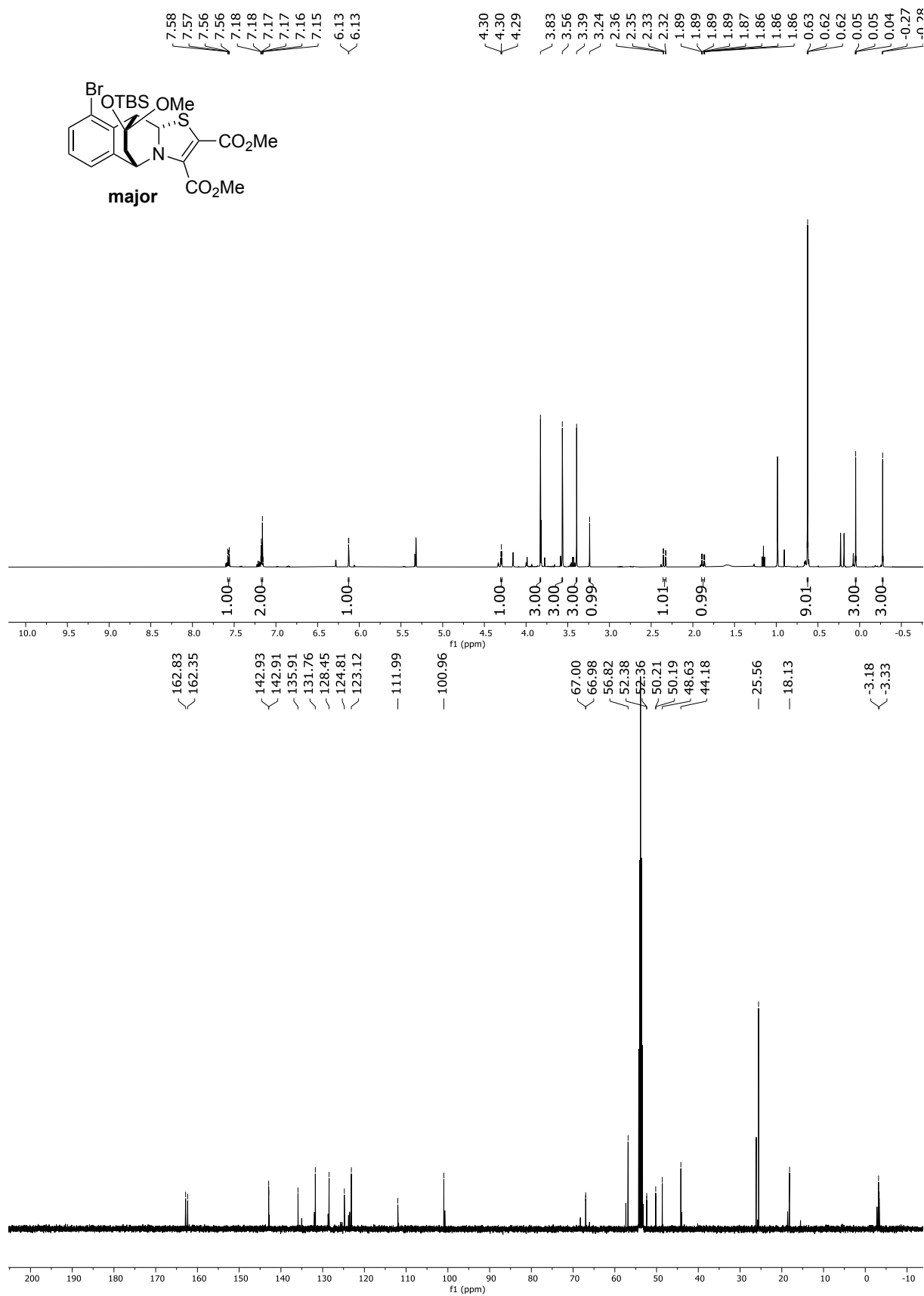
¹H-NMR (600 MHz, CD₂Cl₂) for 3g-minor (representative signals)



¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 3h

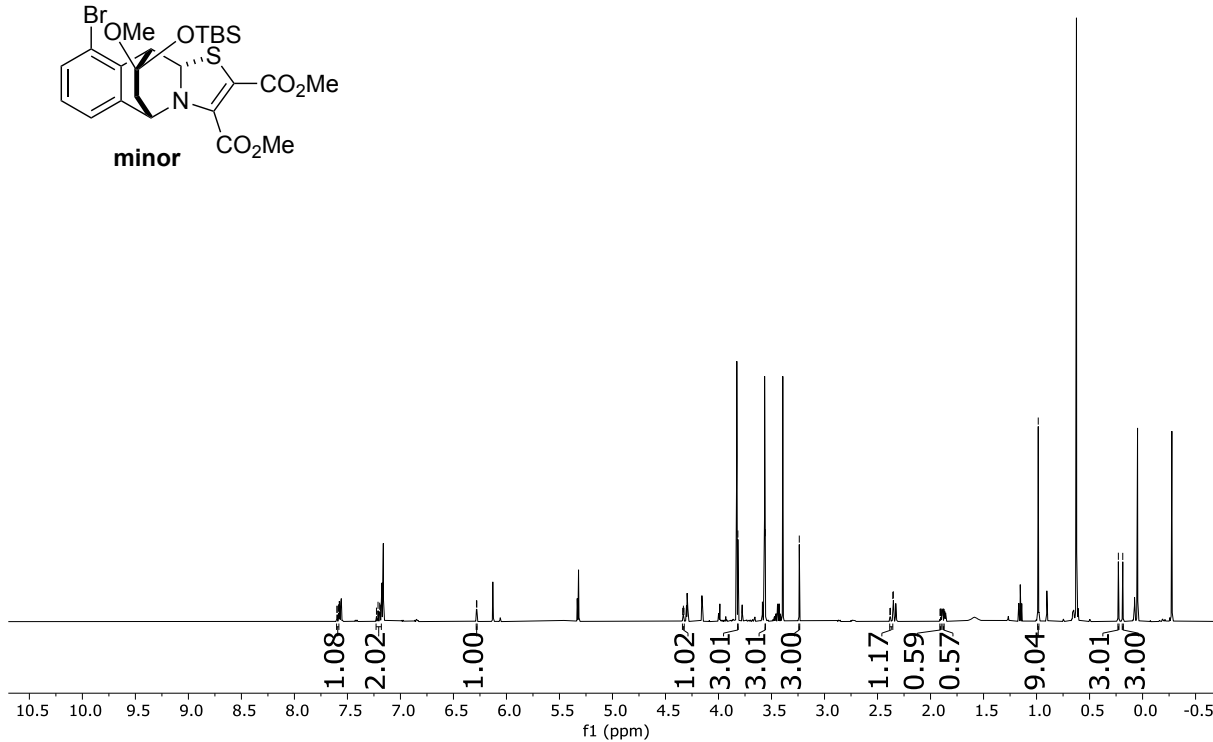
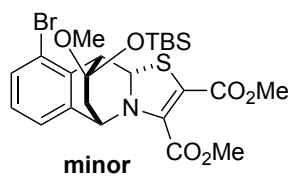


¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 3i-major

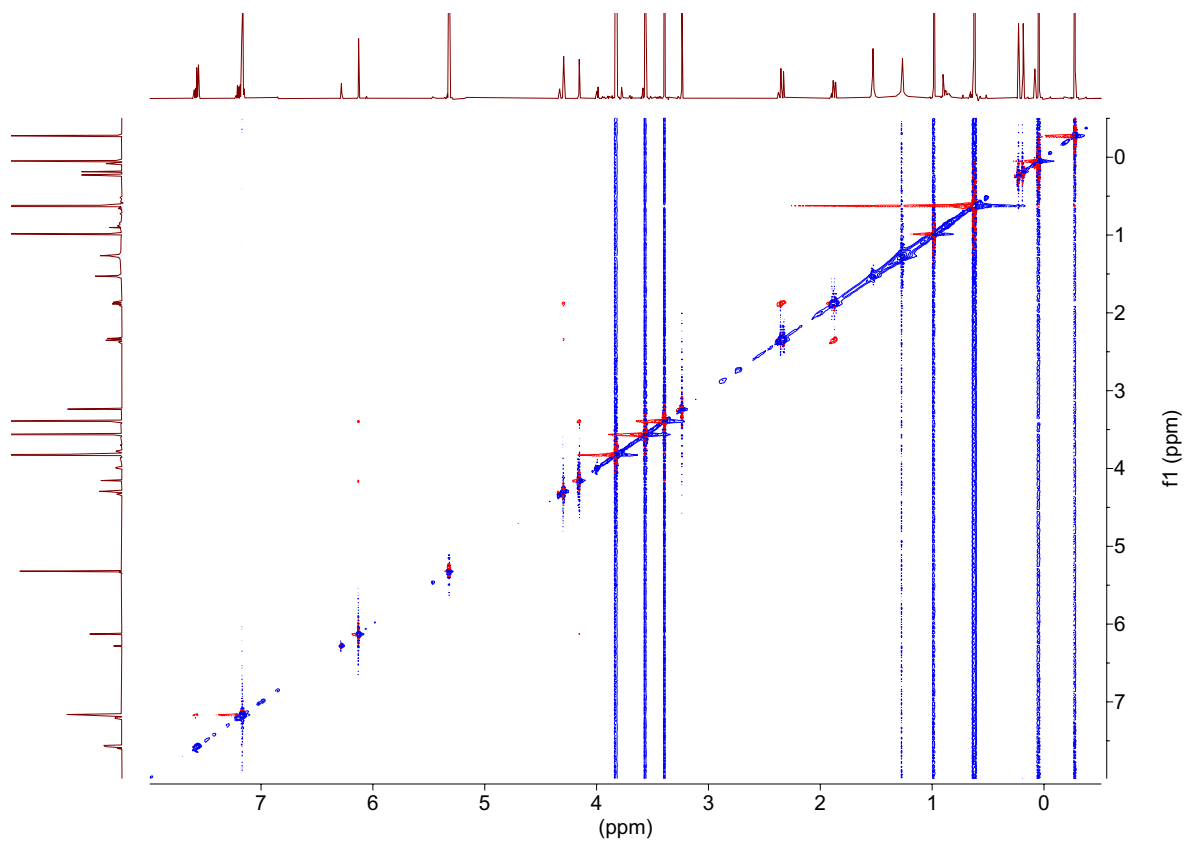


¹H-NMR (500 MHz, CD₂Cl₂) for 3i-minor (representative signals)

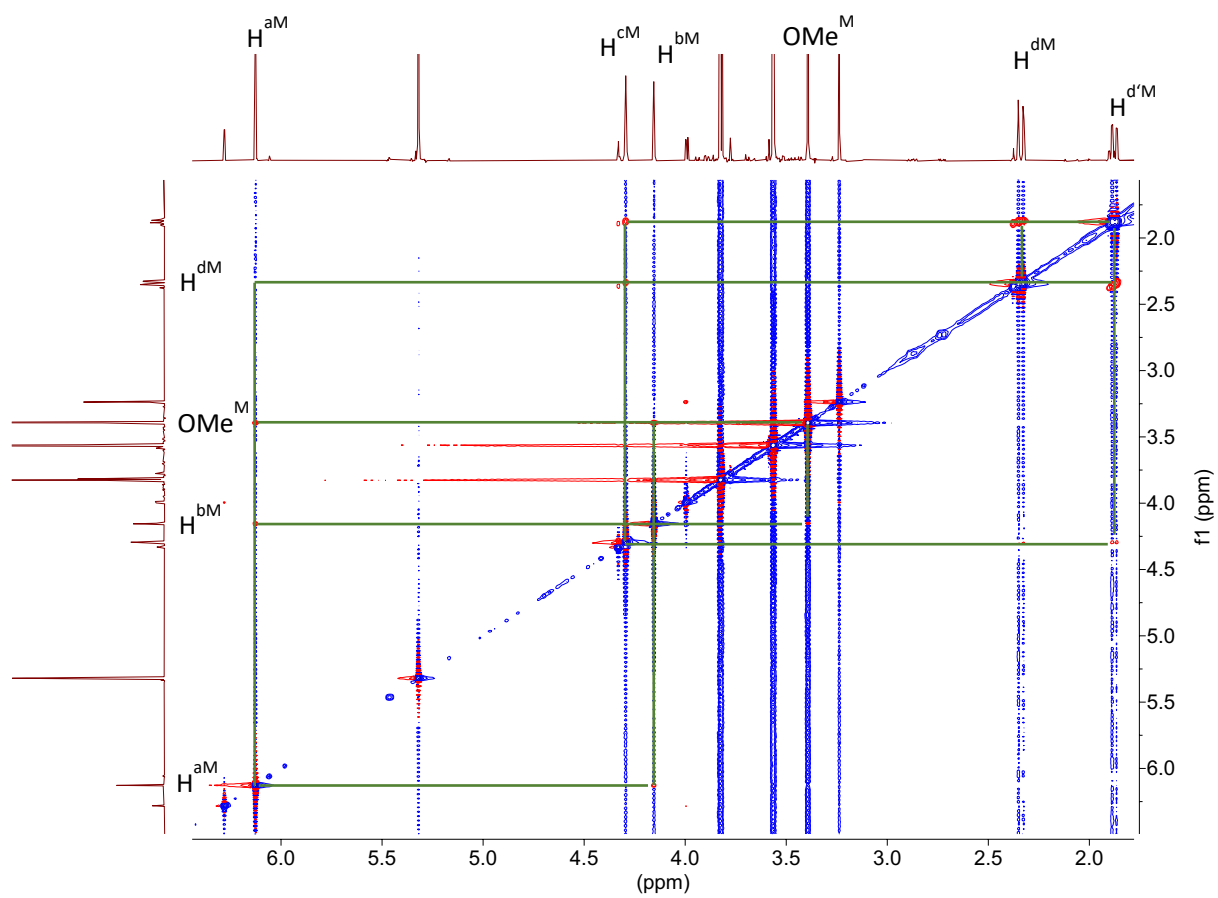
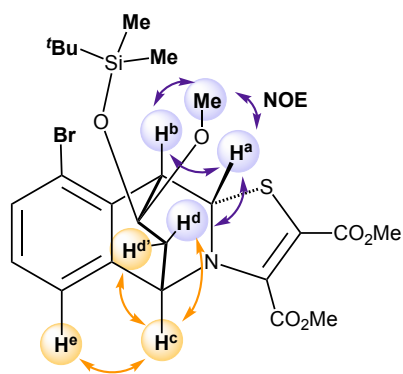
7.60 7.60 7.58 7.58 7.23 7.21 7.20 7.19 6.28 6.28 4.34 4.33 4.33 3.82 3.56 3.24 2.38 2.38 2.36 2.35 1.91 1.91 1.90 1.90 1.88 1.88 1.87 1.87 0.98 0.23 0.19



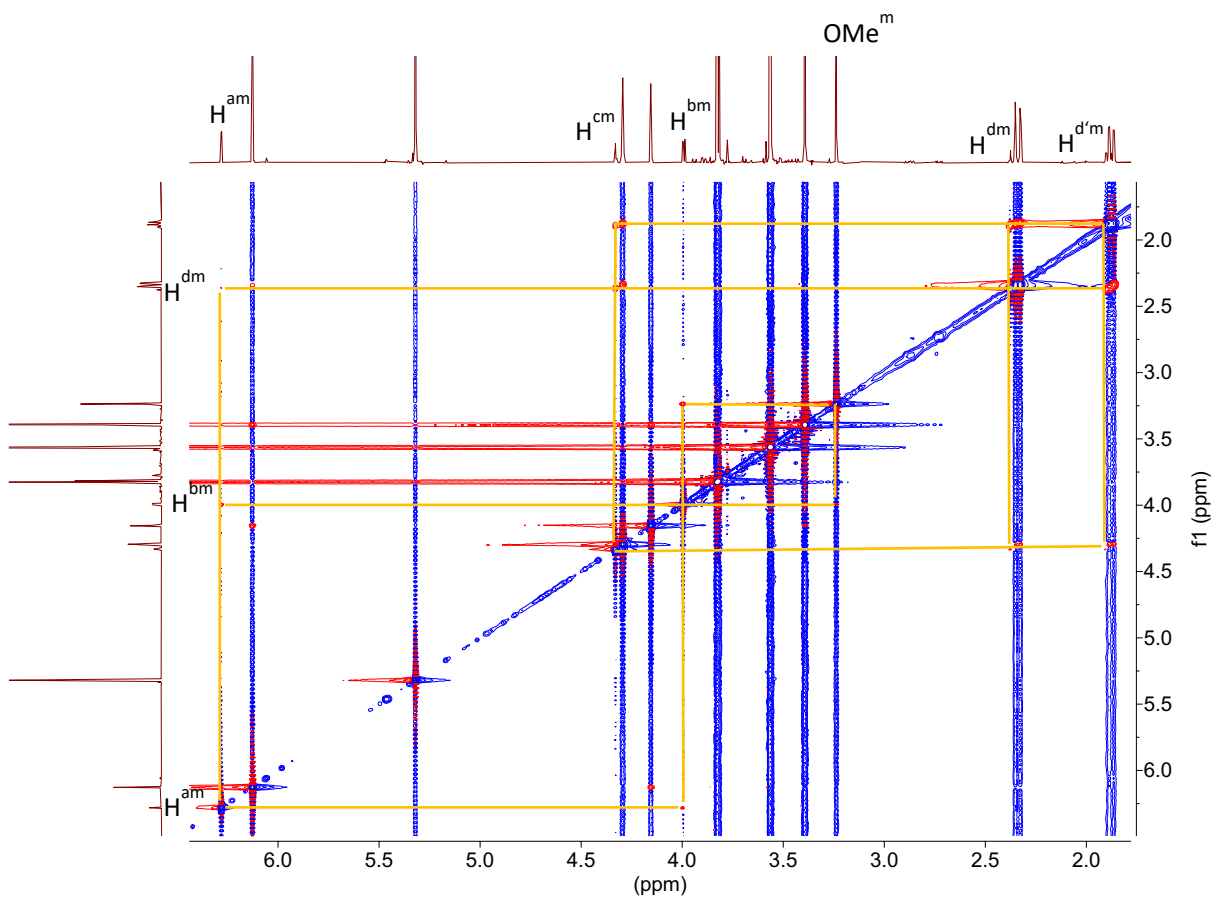
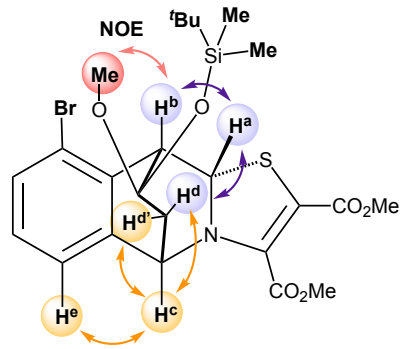
2D-NOESY (600 MHz, CD₂Cl₂) of for 3i (full spectrum)



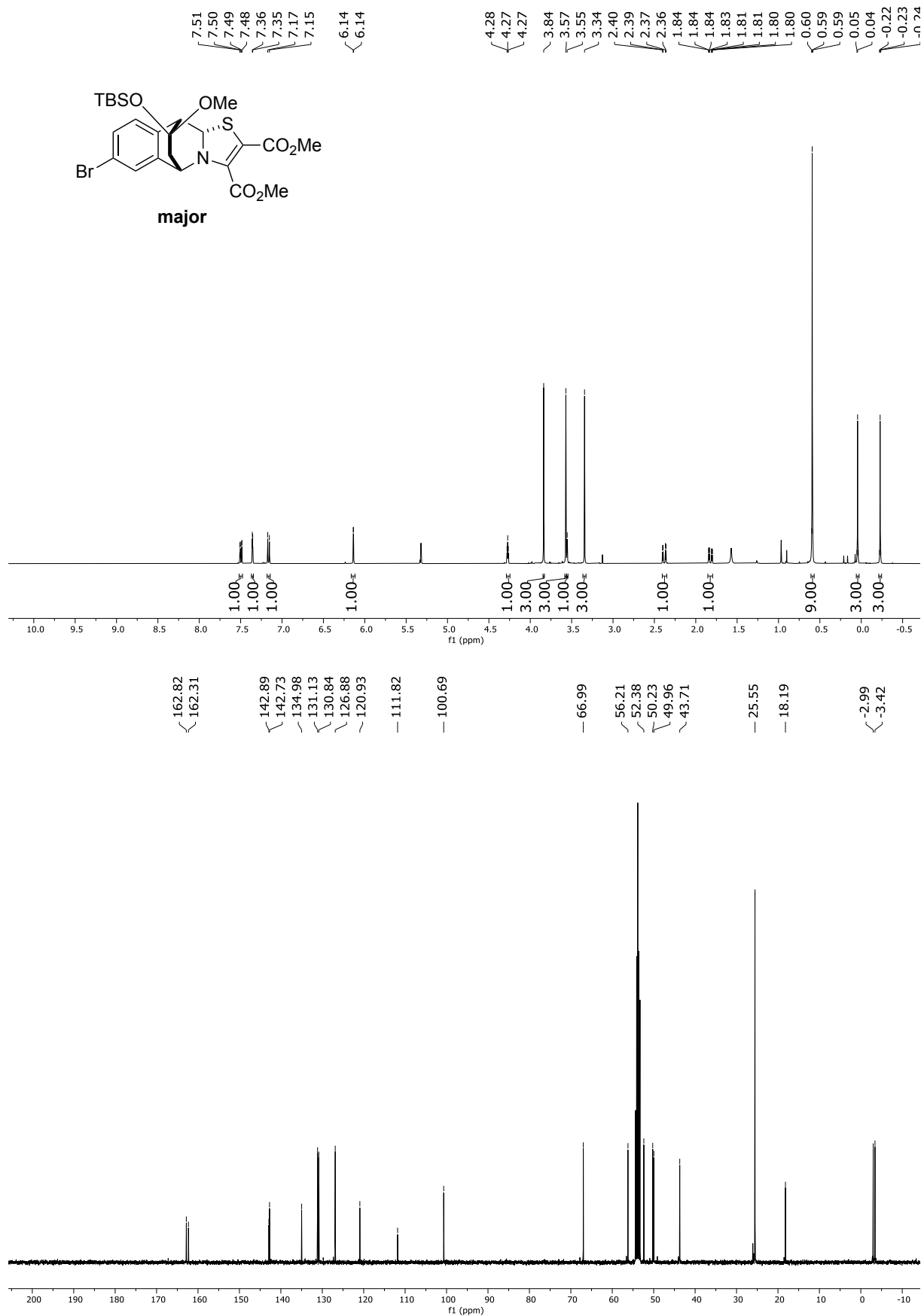
3i - Major Isomer



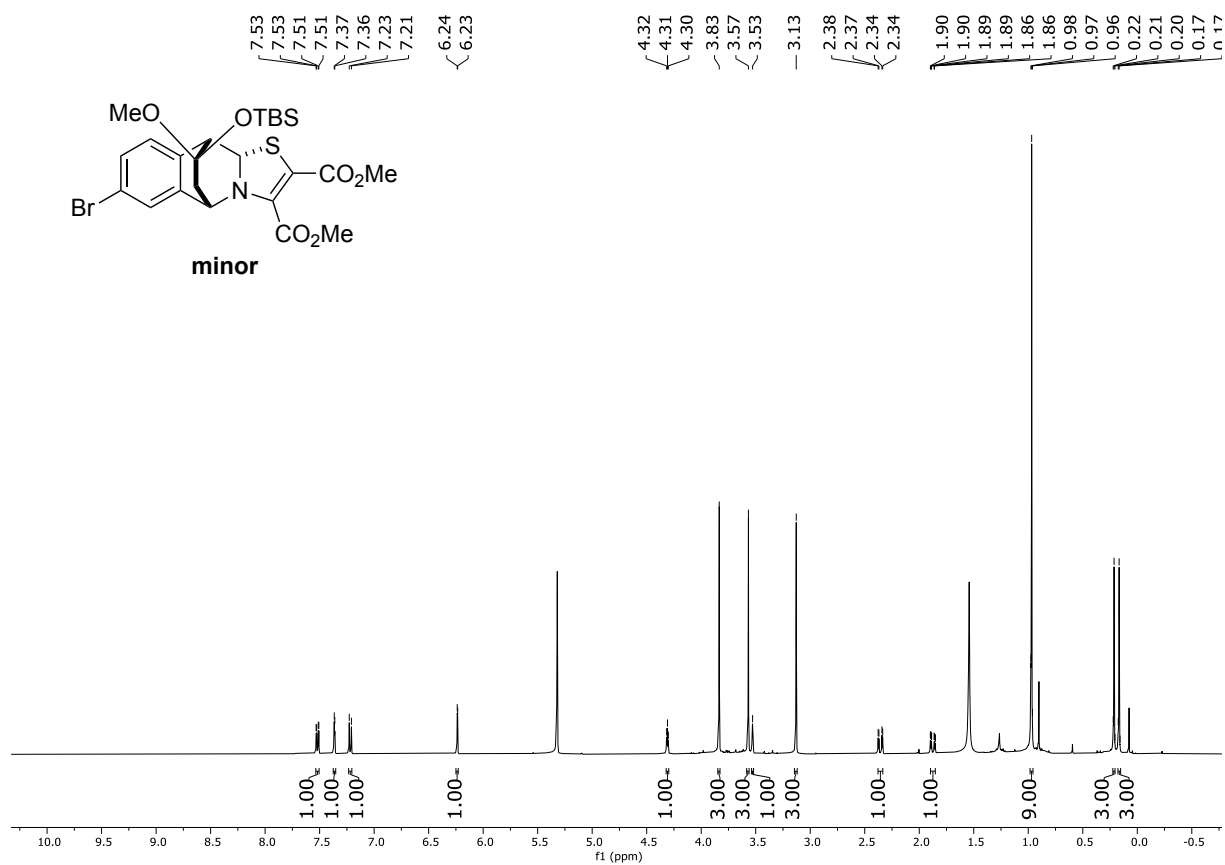
3i - Minor Isomer



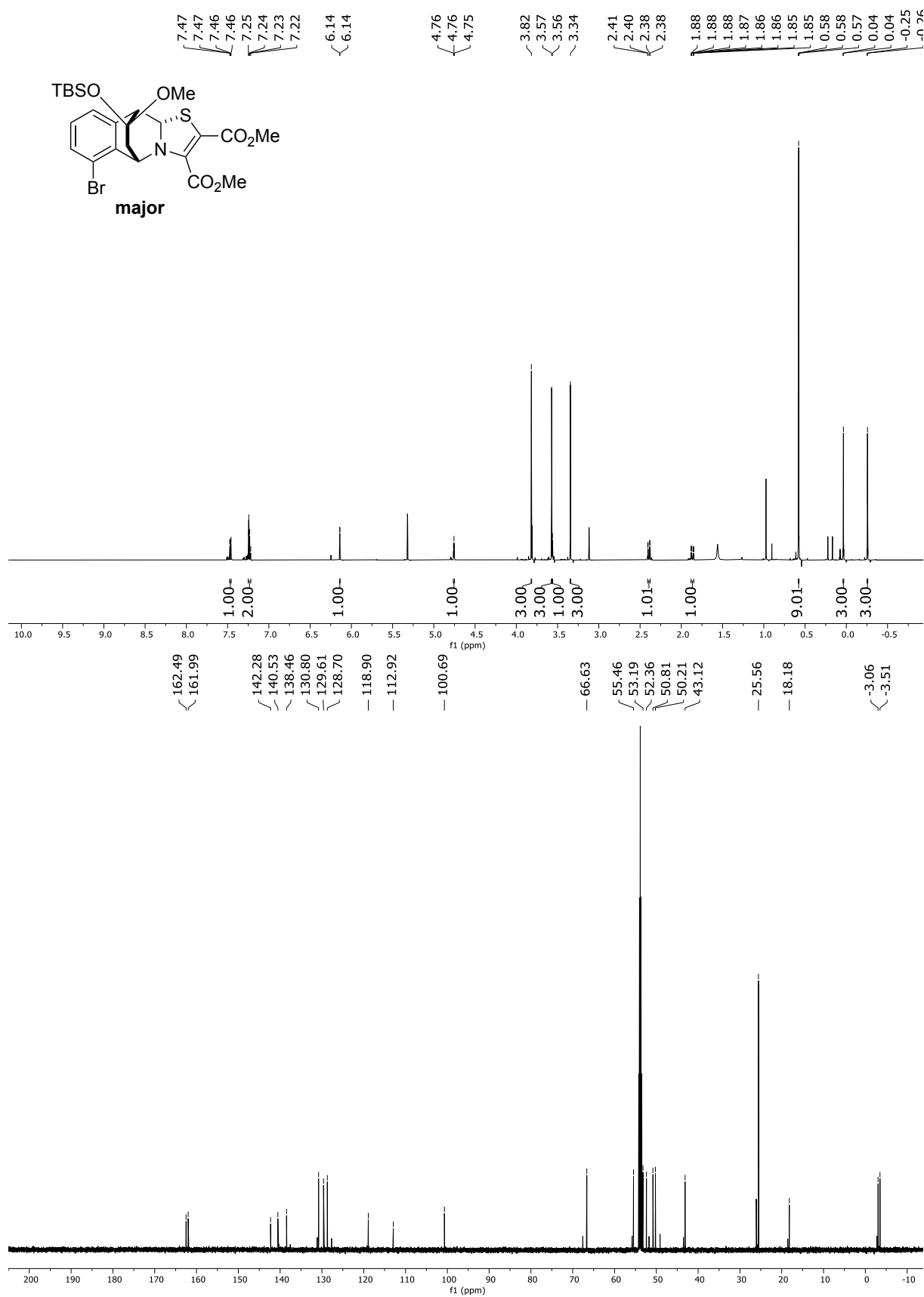
$^1\text{H-NMR}$ (400 MHz, CD_2Cl_2) and $^{13}\text{C-NMR}$ (100 MHz, CD_2Cl_2) for 3j-major



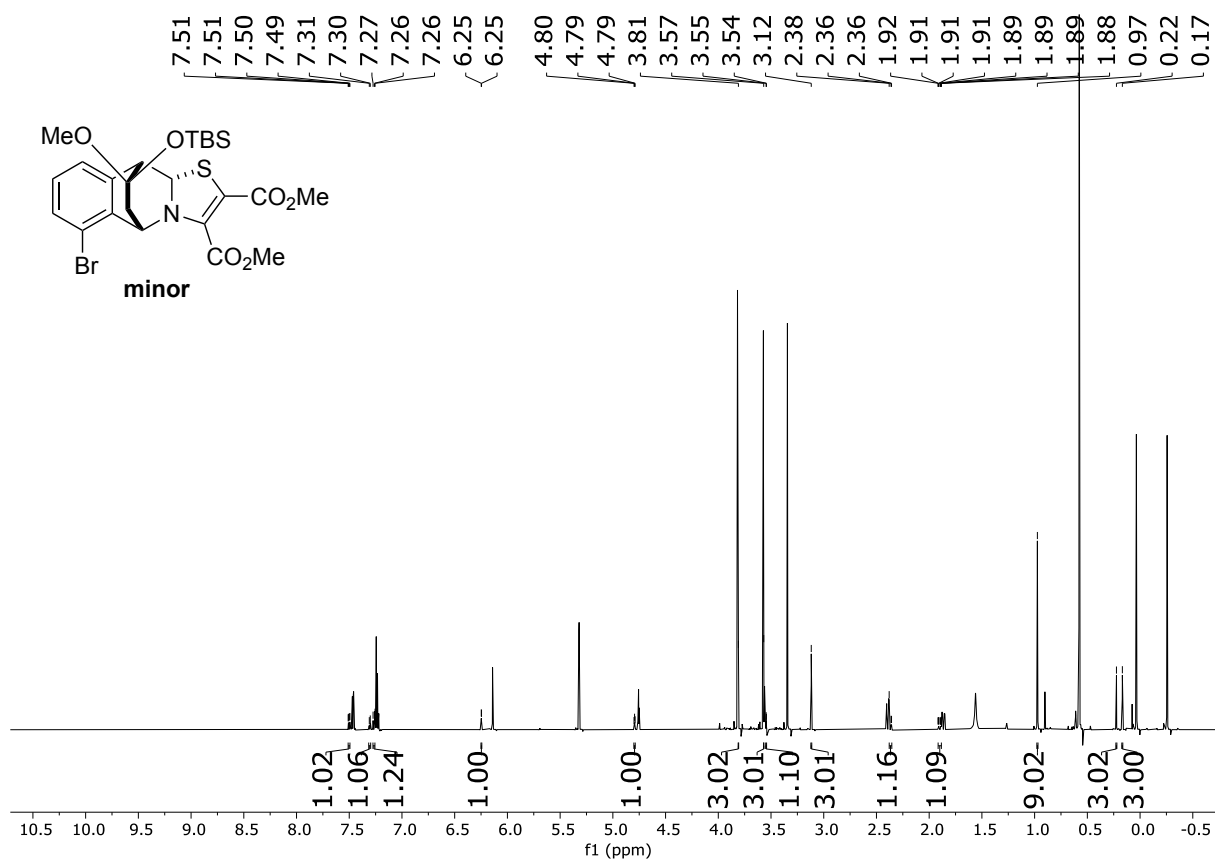
¹H-NMR (400 MHz, CD₂Cl₂) for 3j-minor (representative signals)



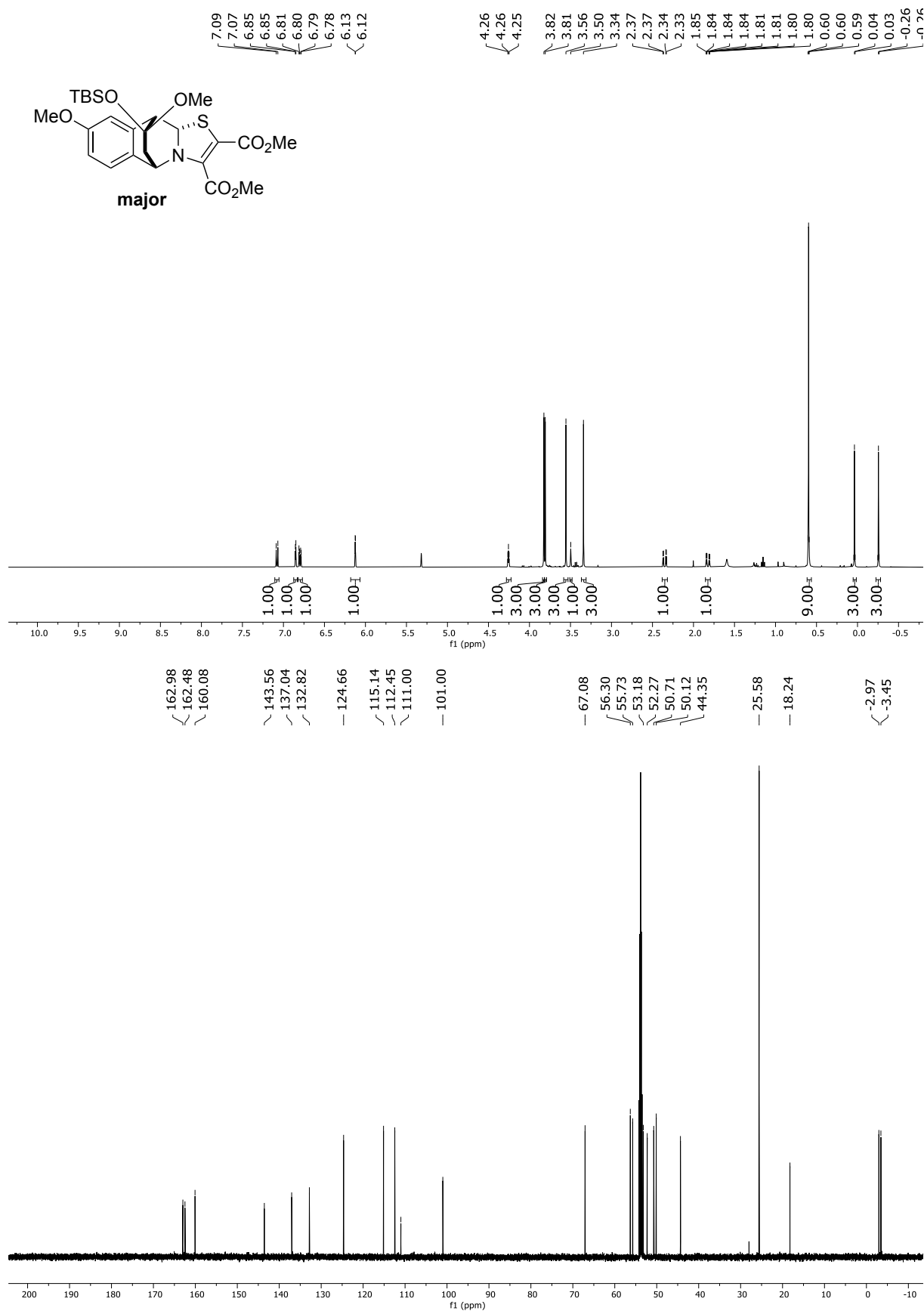
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3k-major



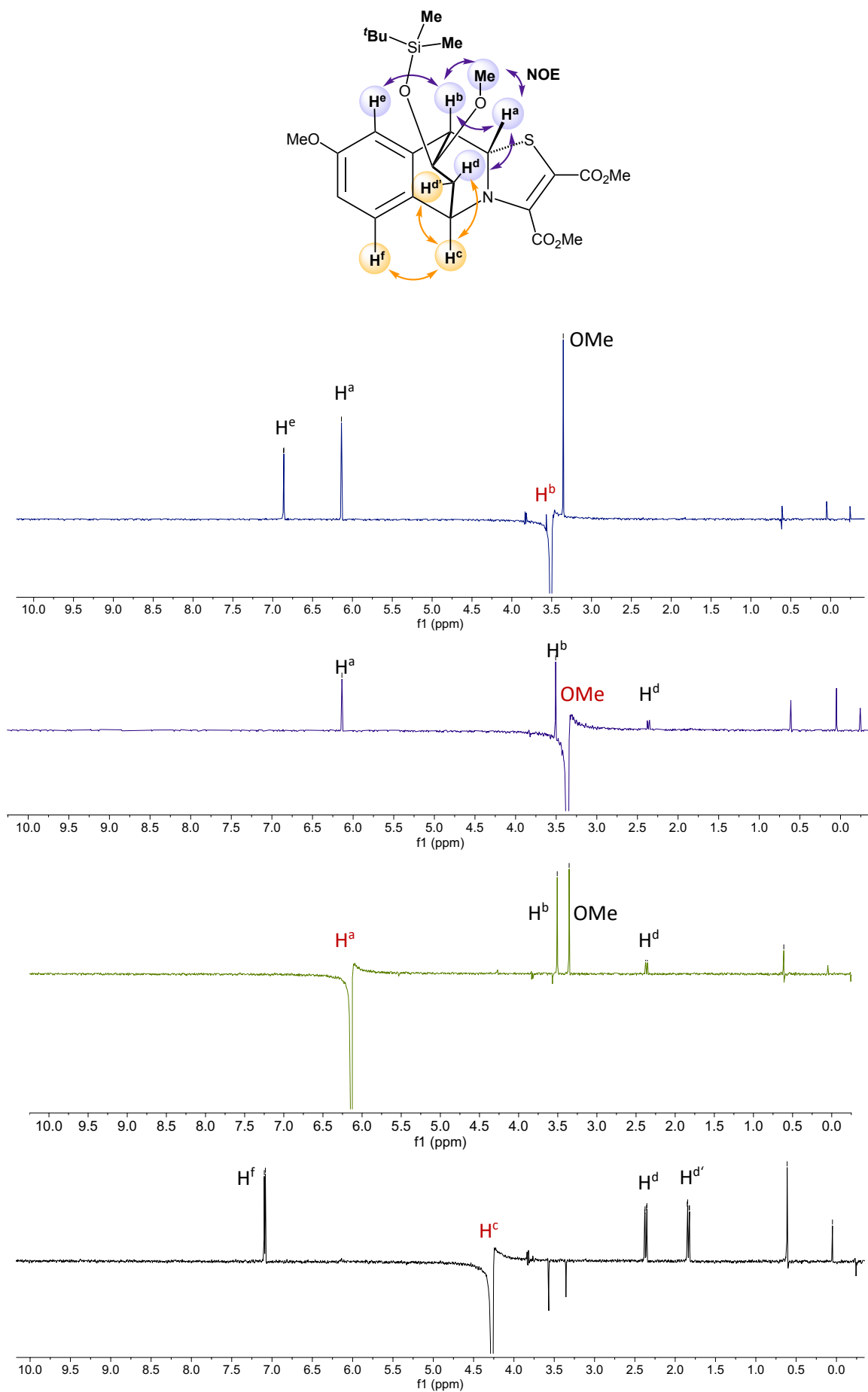
¹H-NMR (600 MHz, CD₂Cl₂) for 3k-minor (representative signals)



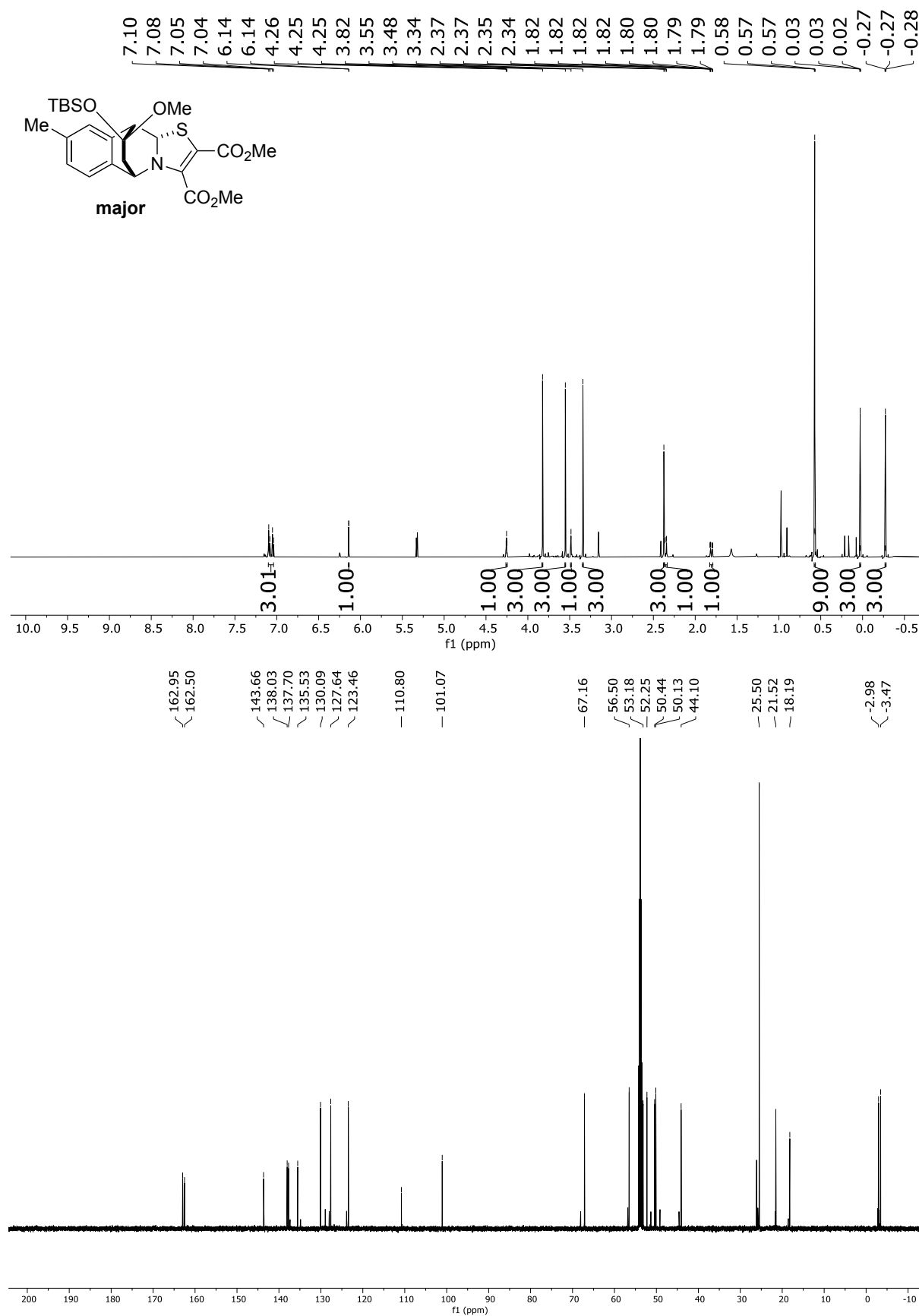
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3I



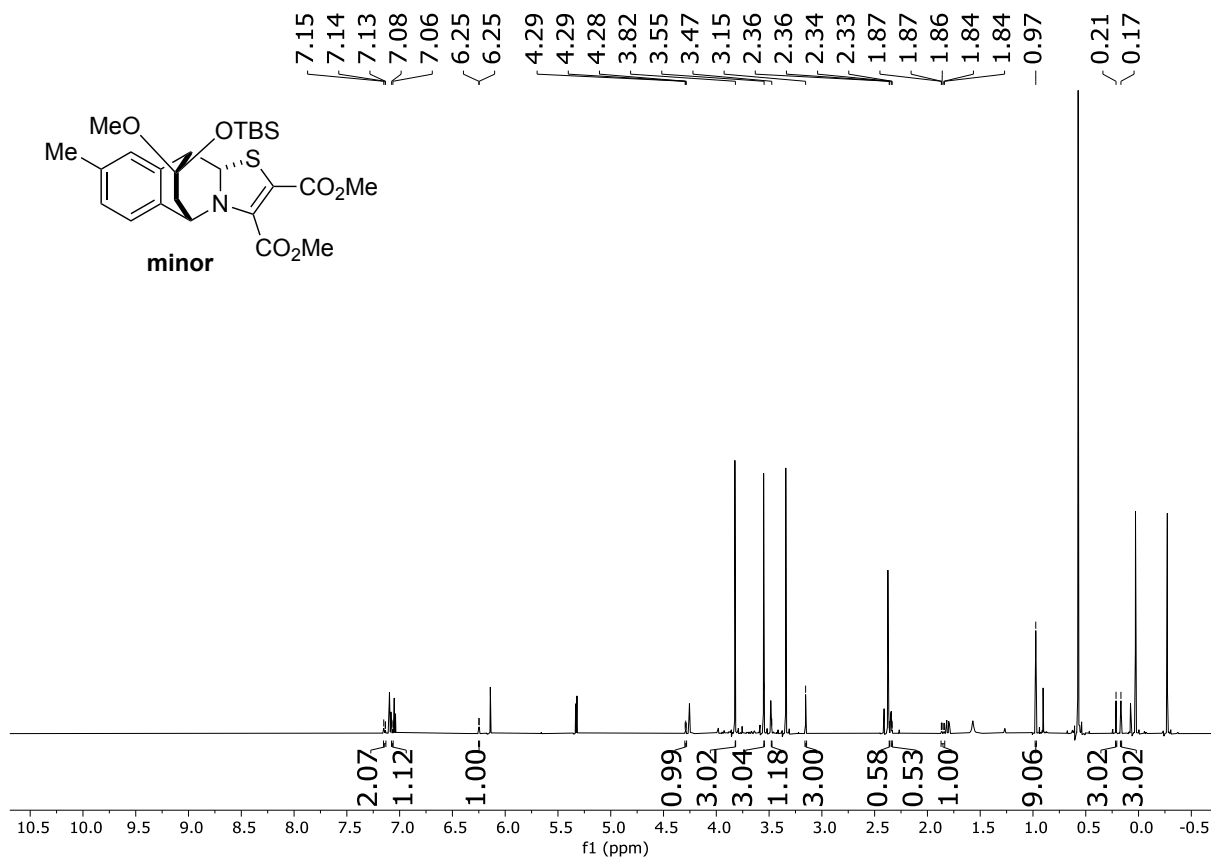
¹D-NOESY (600 MHz, CD₂Cl₂) analysis of representative signals for 31



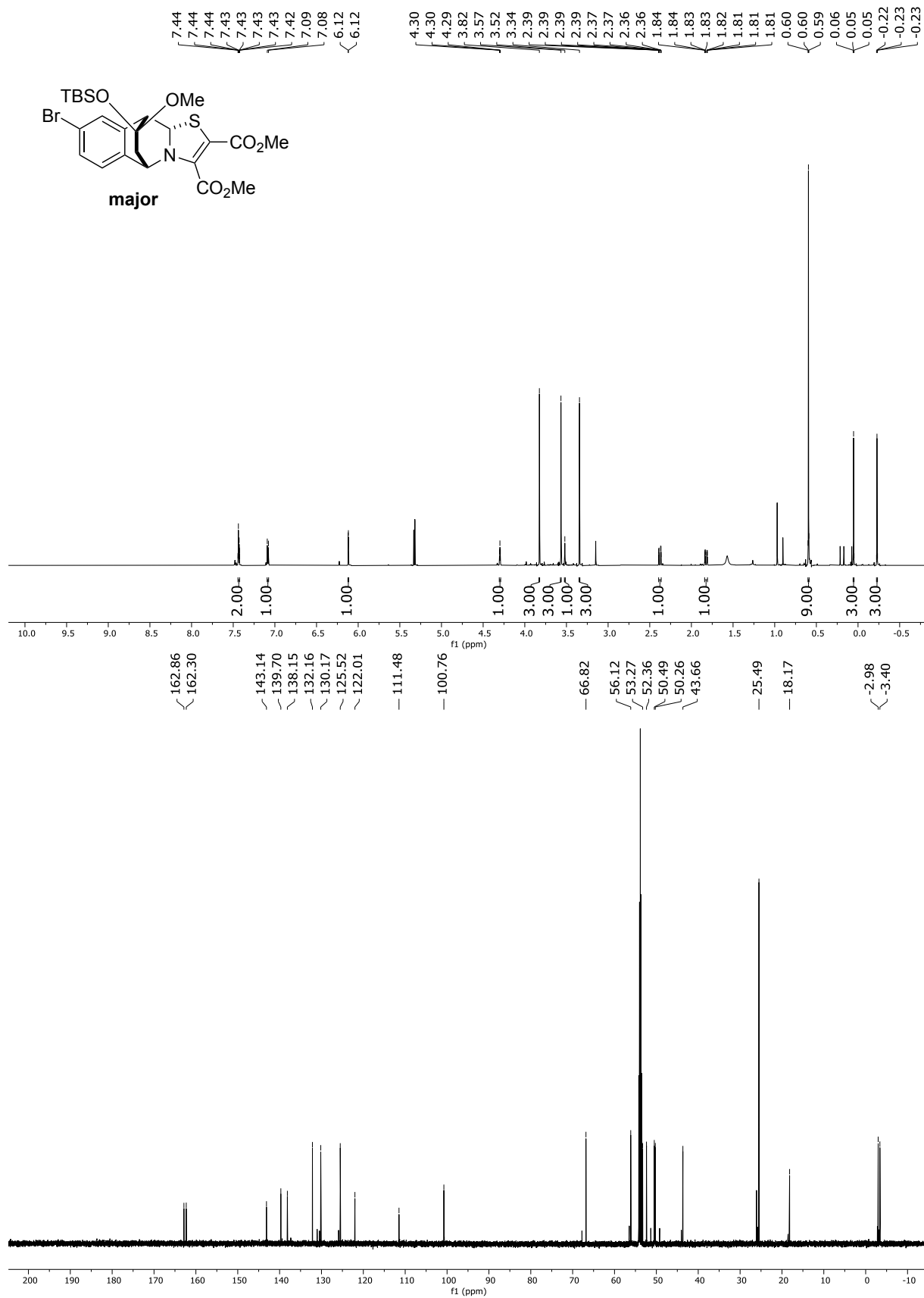
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3m-major



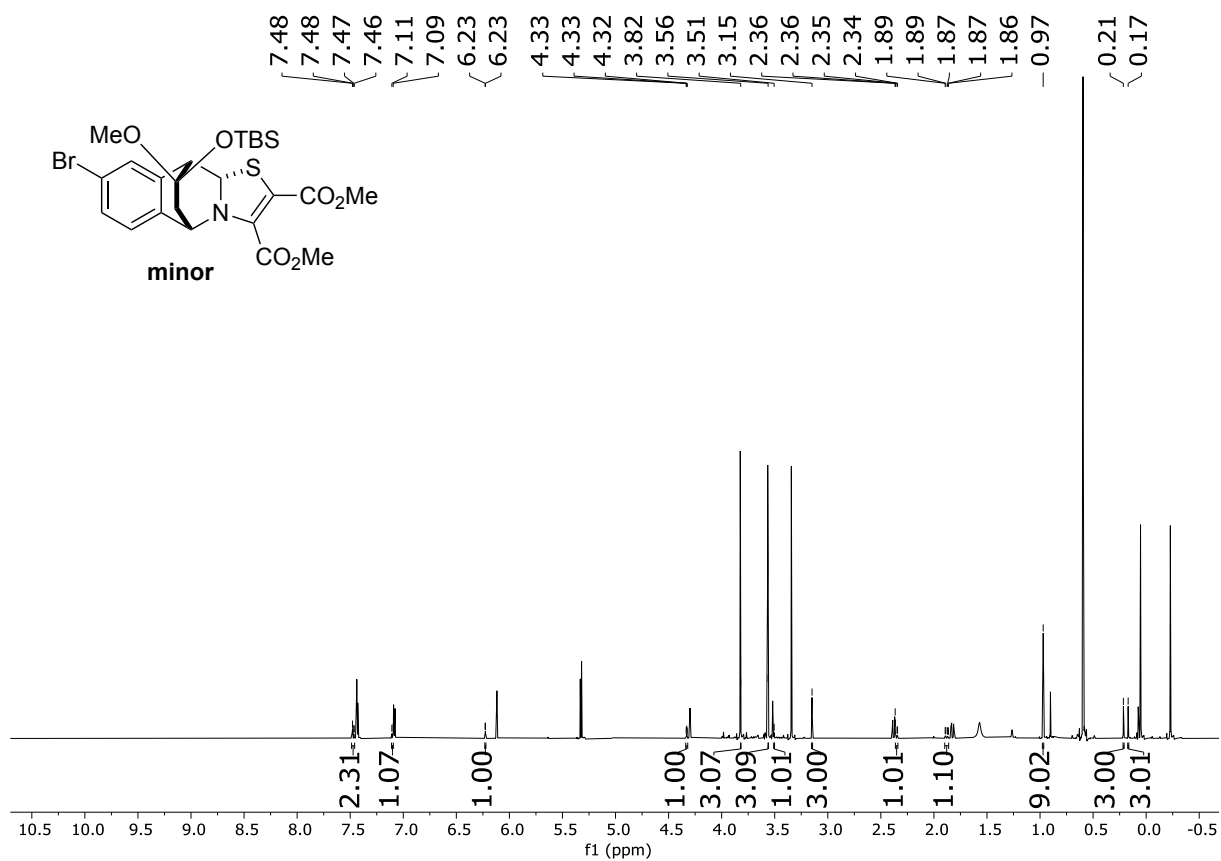
¹H-NMR (600 MHz, CD₂Cl₂) for 3m-minor (representative signals)



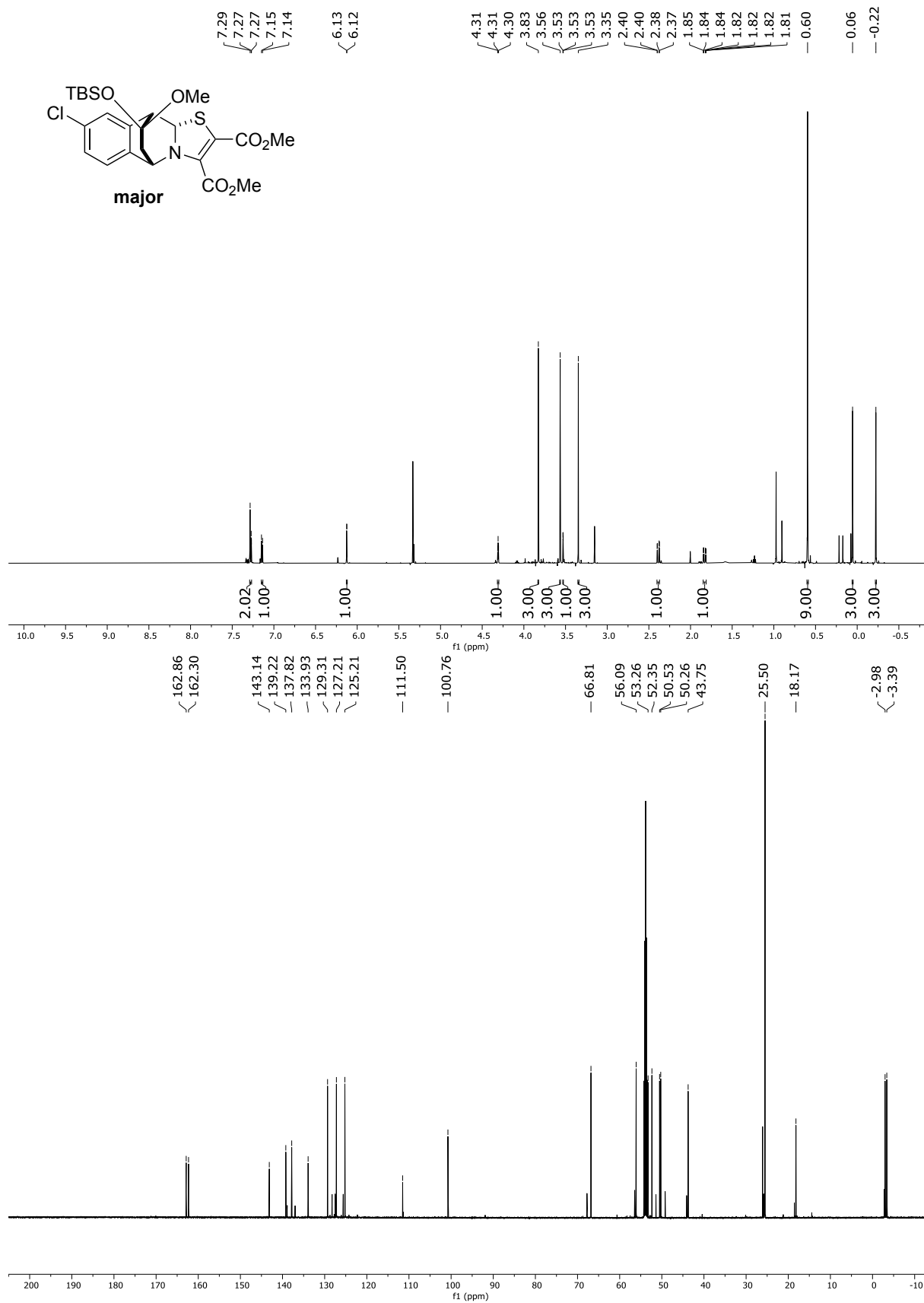
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3n-major



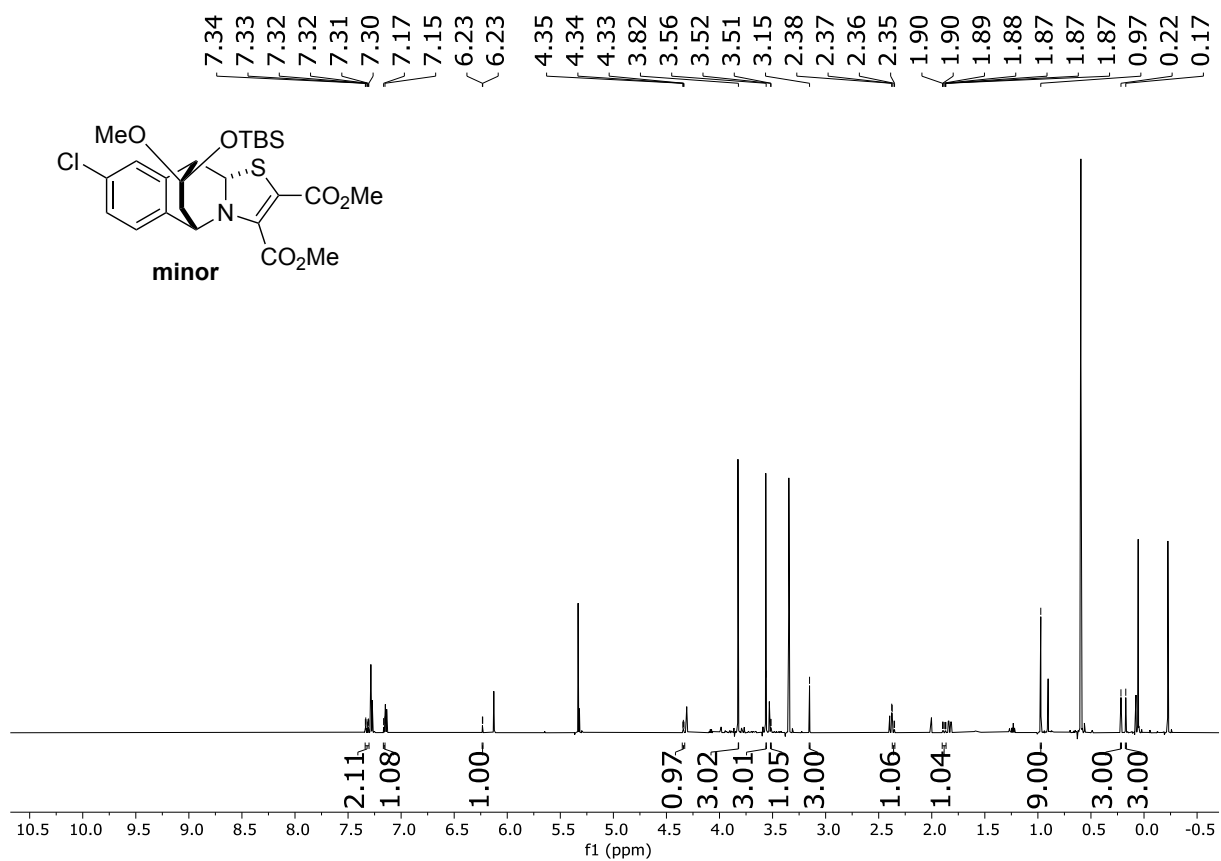
¹H-NMR (600 MHz, CD₂Cl₂) for 3n-minor (representative signals)



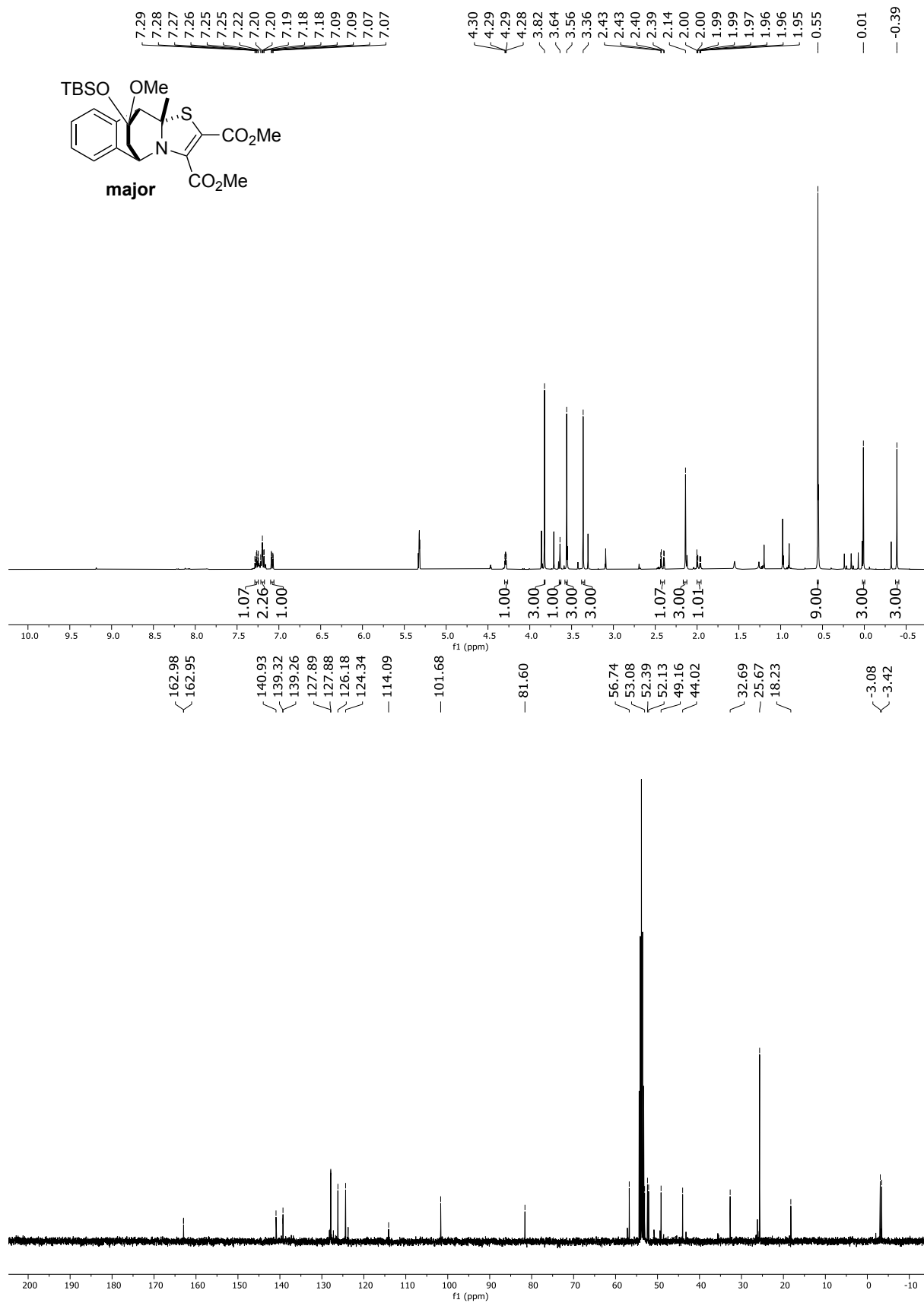
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3o-major



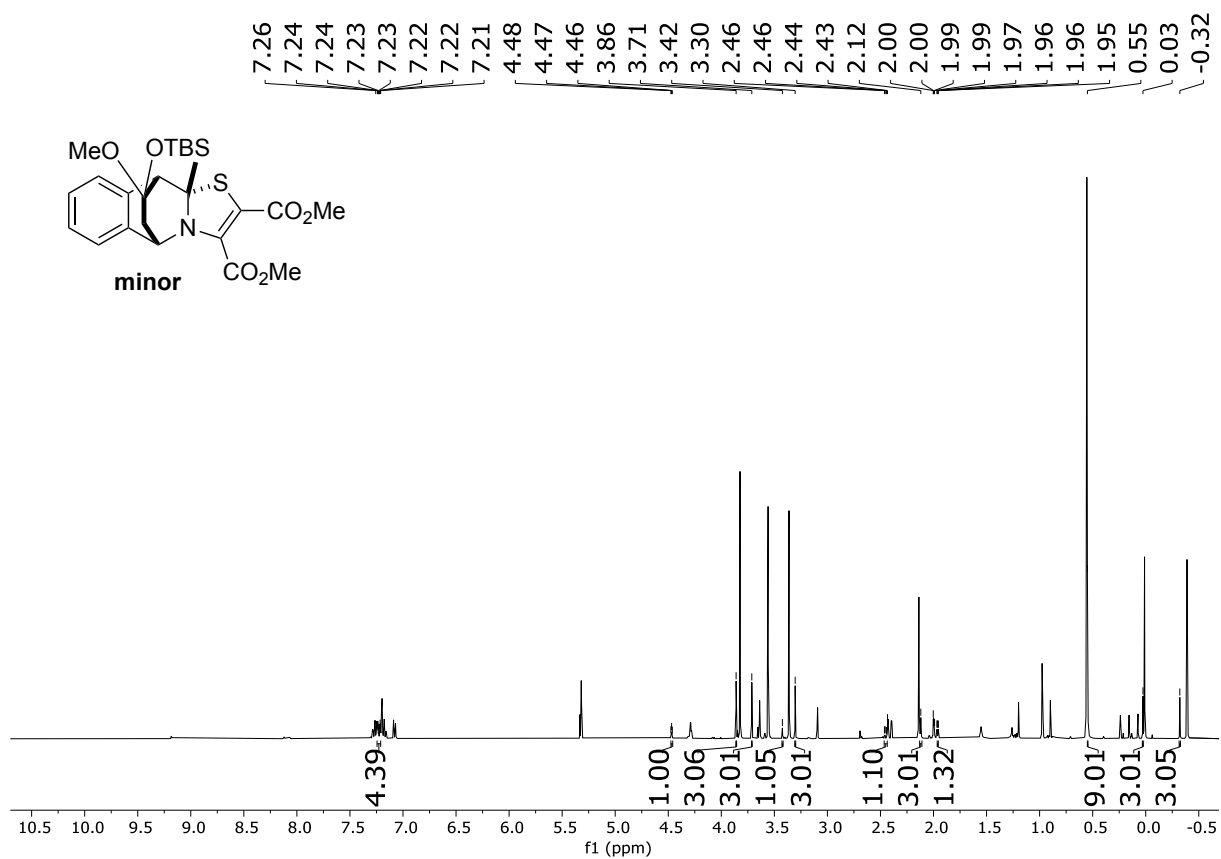
¹H-NMR (600 MHz, CD₂Cl₂) for 3o-minor (representative signals)



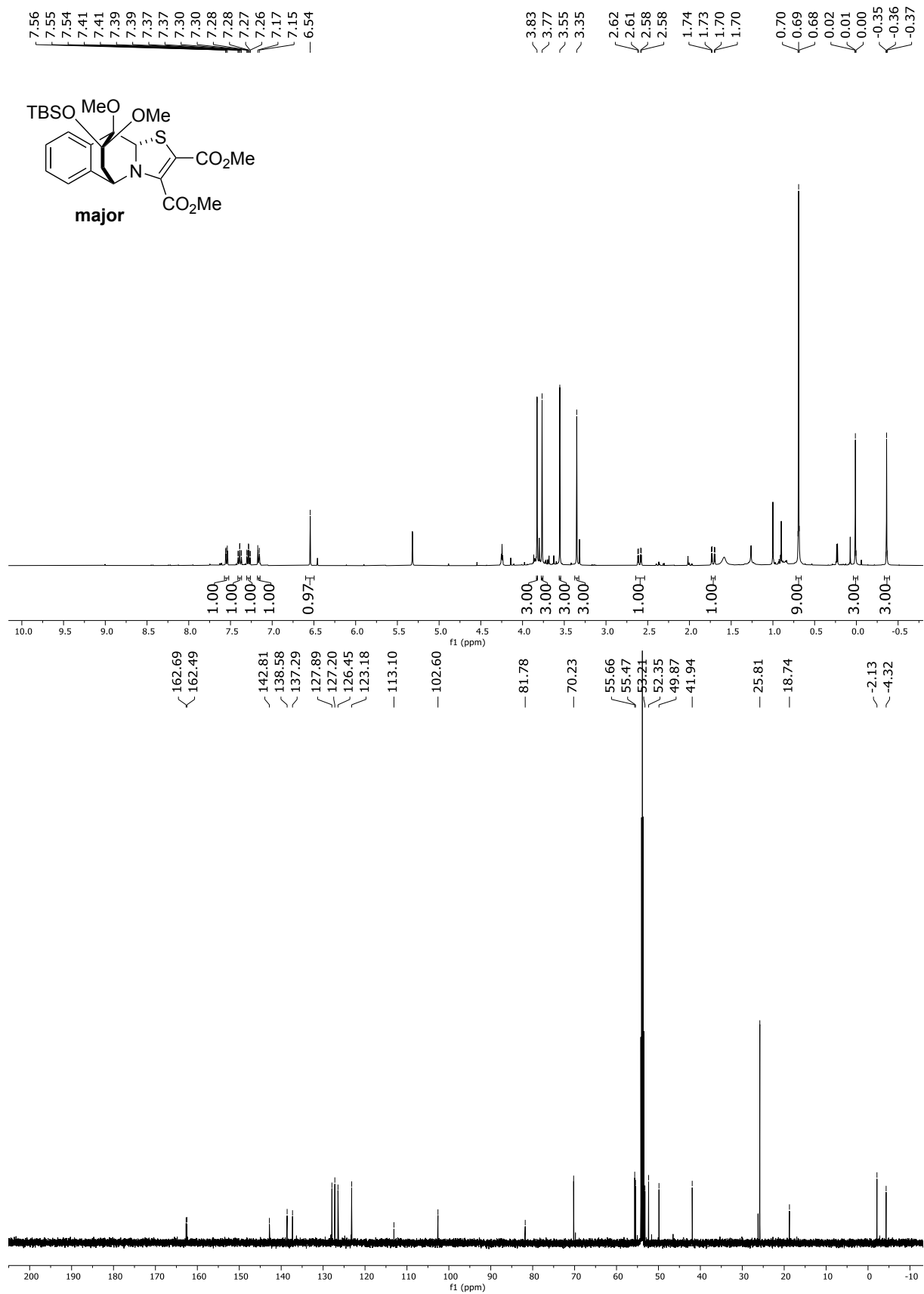
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 3p-major



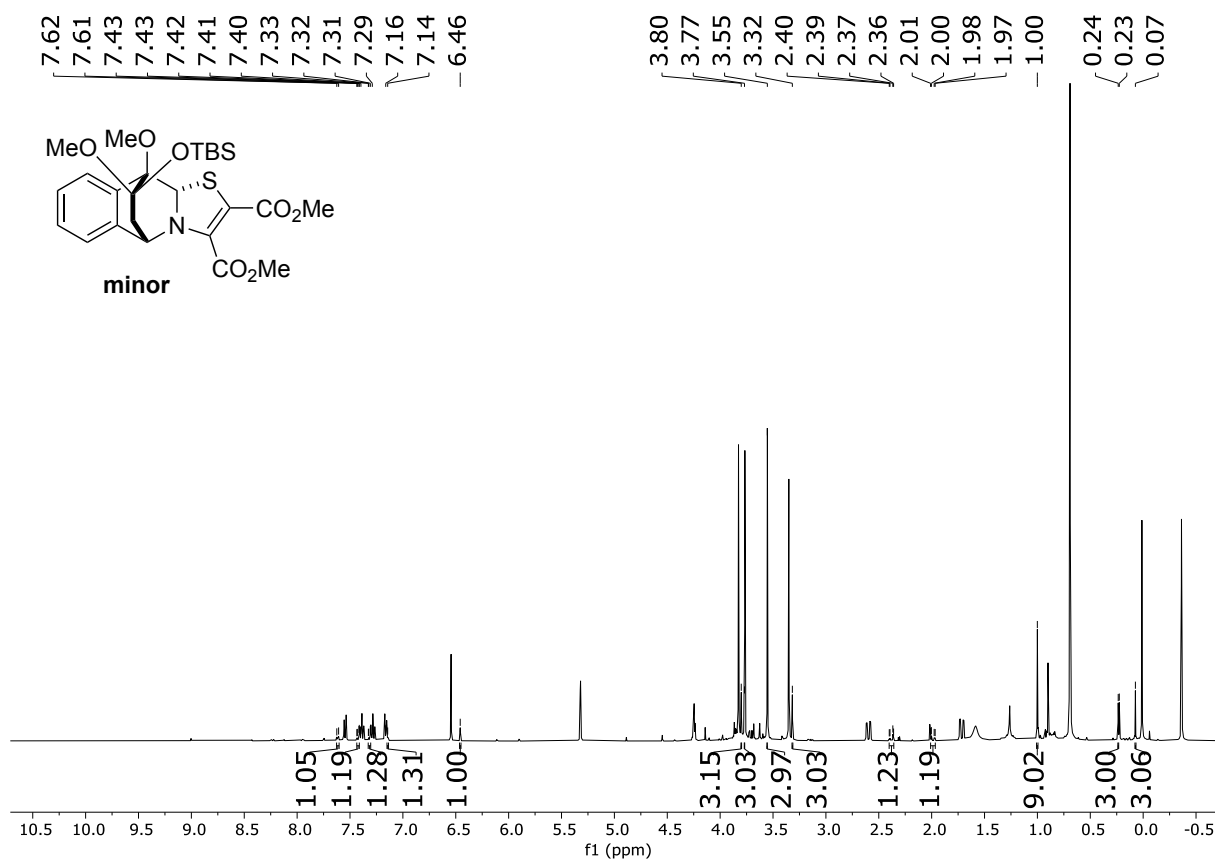
¹H-NMR (400 MHz, CD₂Cl₂) for 3p-minor (representative signals)



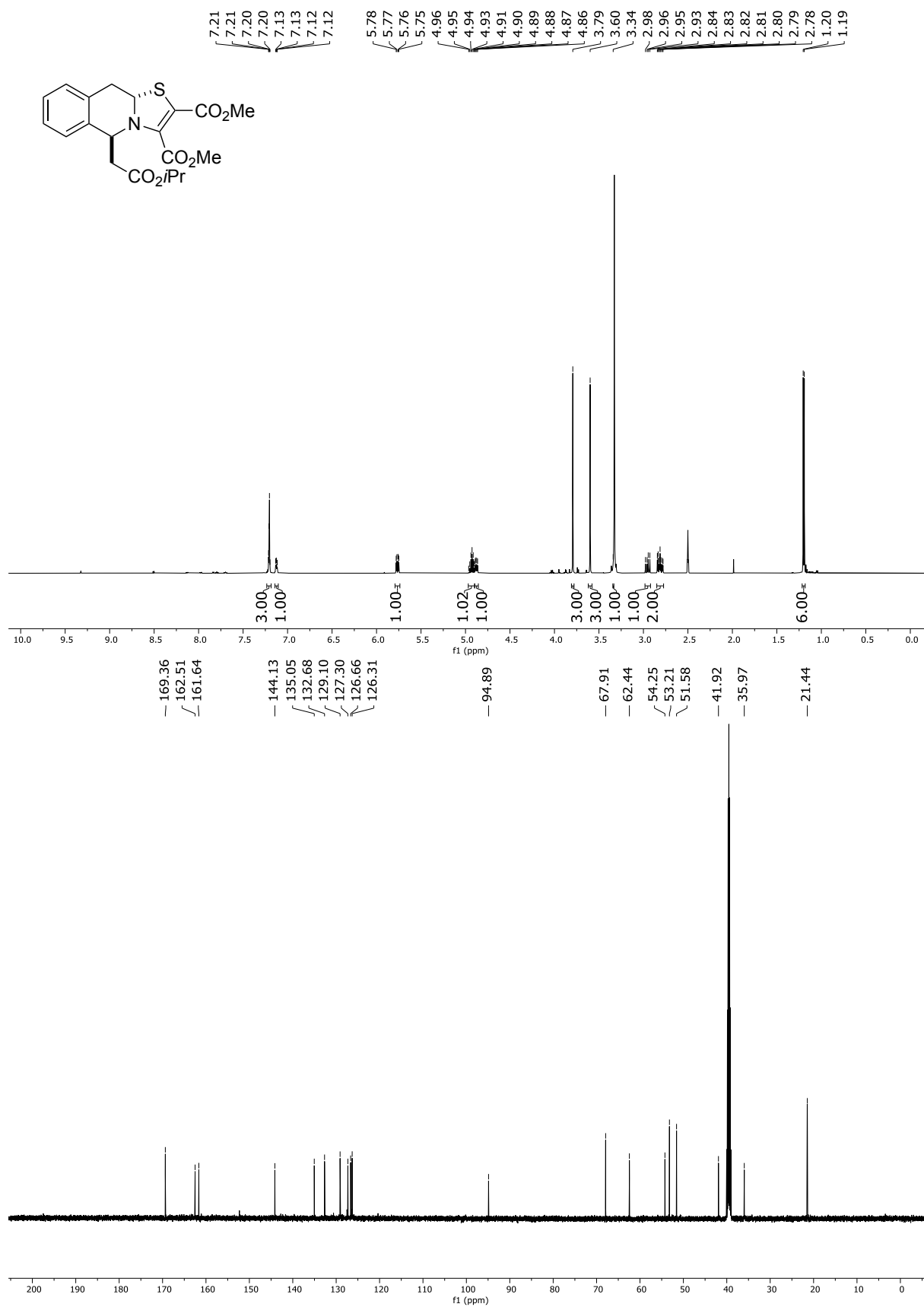
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 3q-major



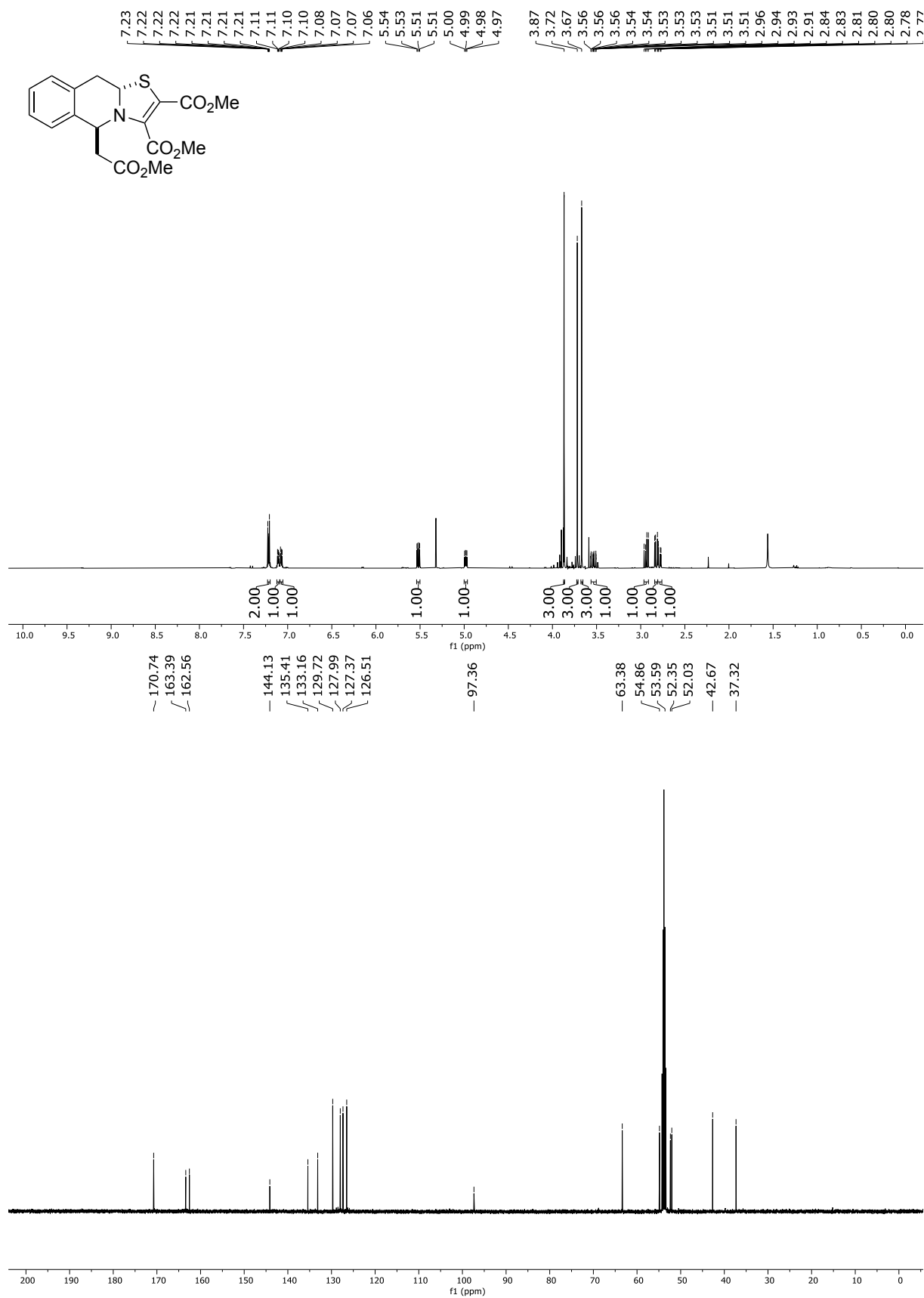
¹H-NMR (600 MHz, CD₂Cl₂) for 3q-minor (representative signals)



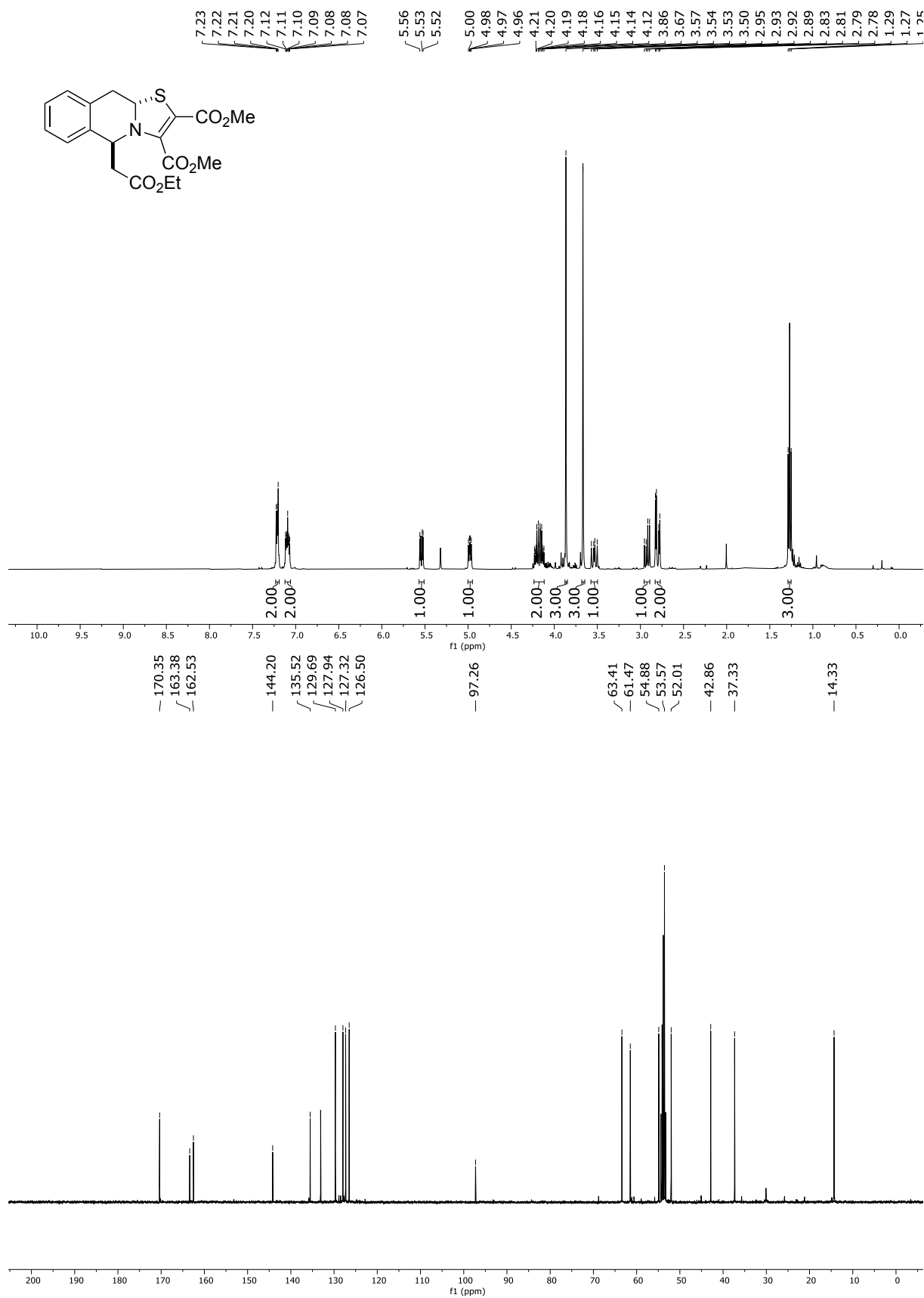
¹H-NMR (500 MHz, DMSO-d₆) and ¹³C-NMR (125 MHz, DMSO-d₆) for 4a



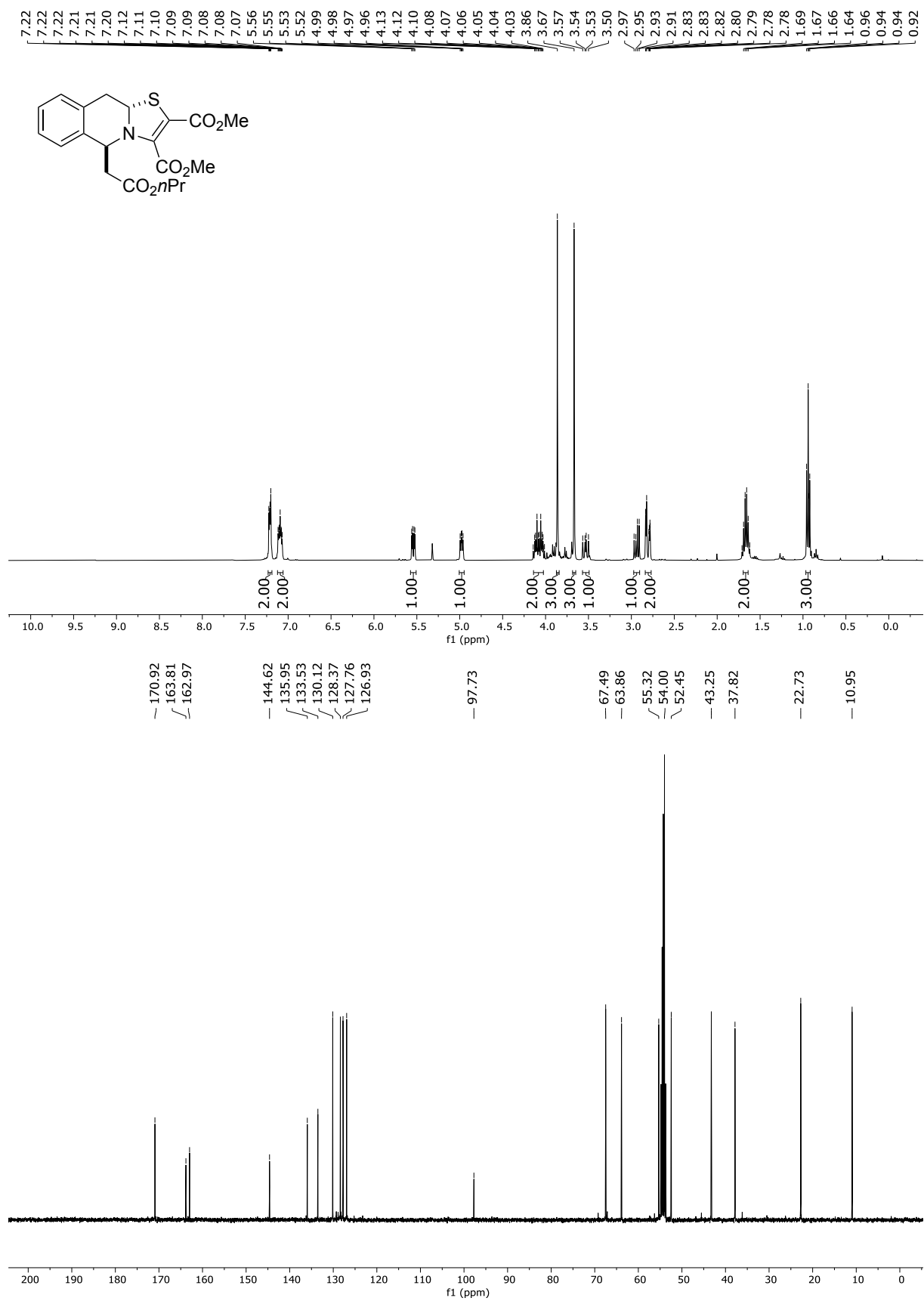
¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 4b



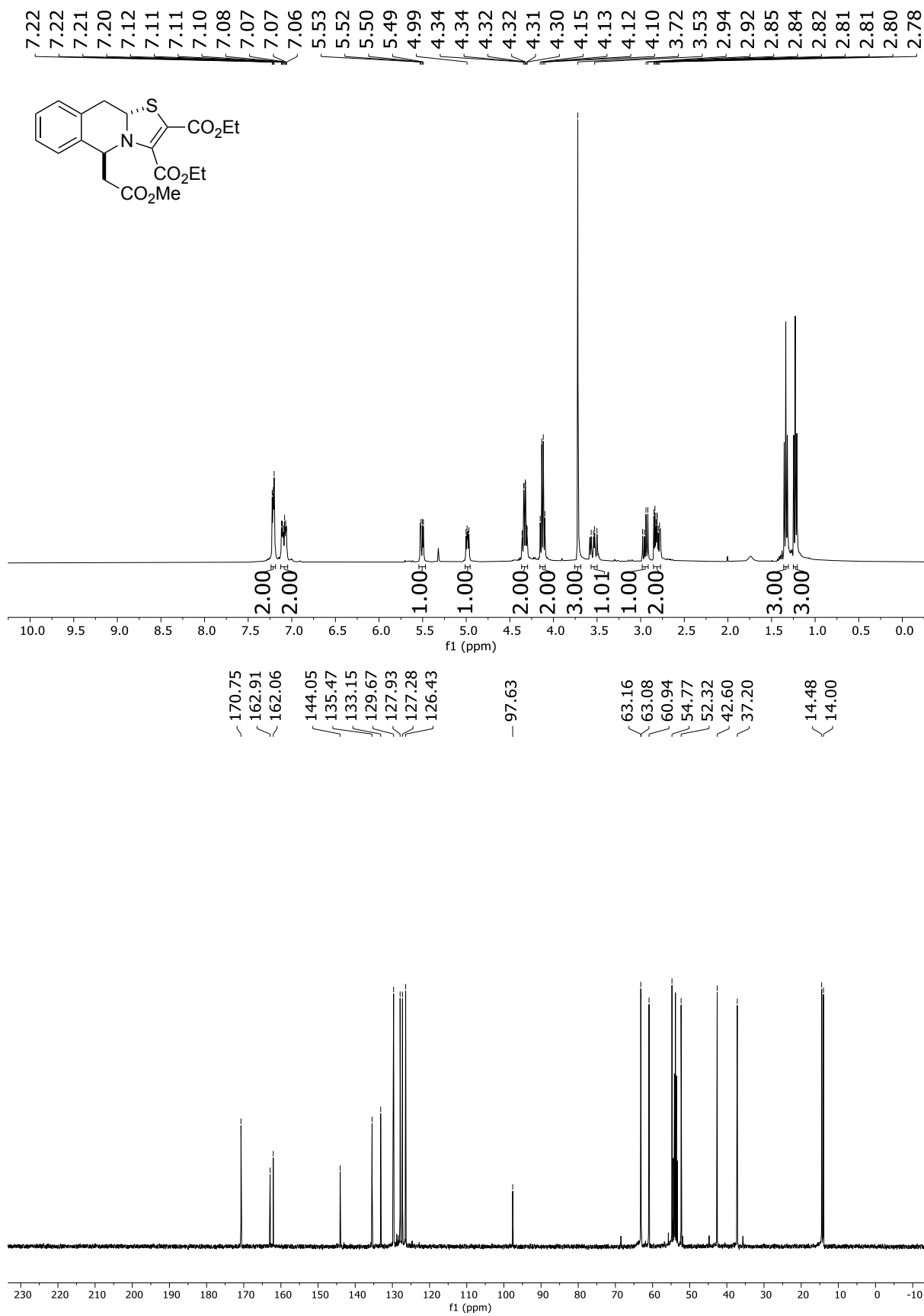
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4c



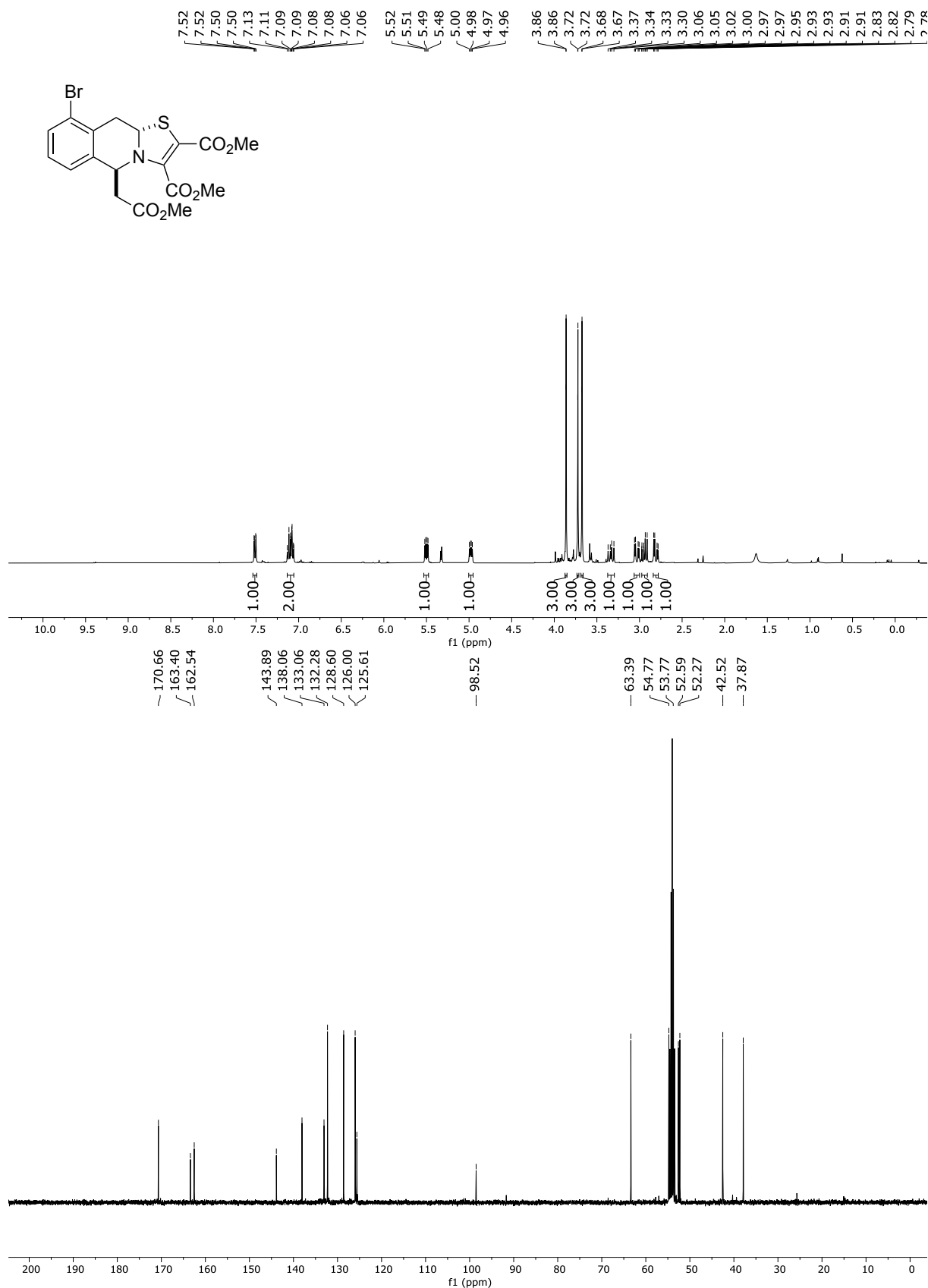
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4d



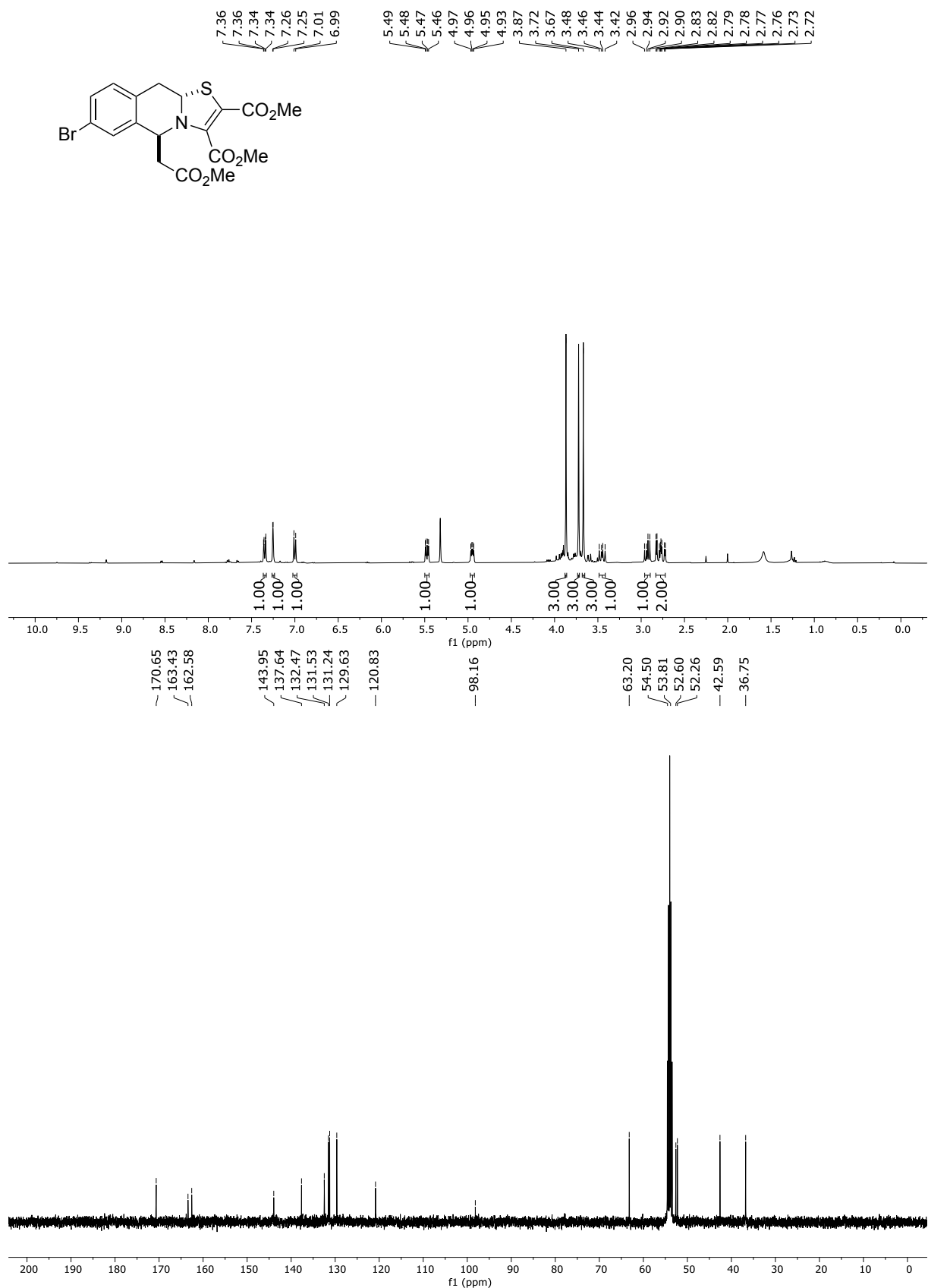
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4e



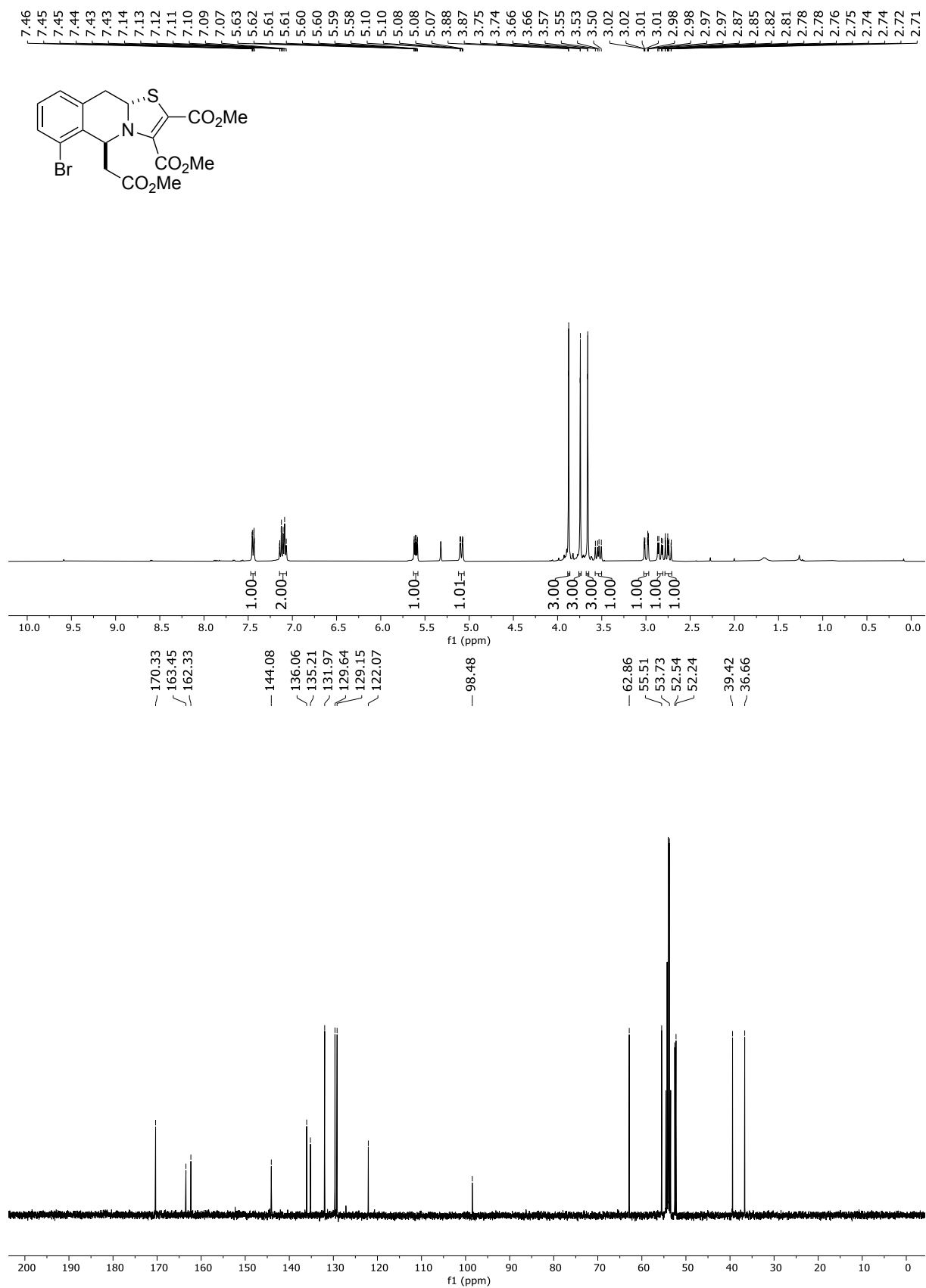
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4f



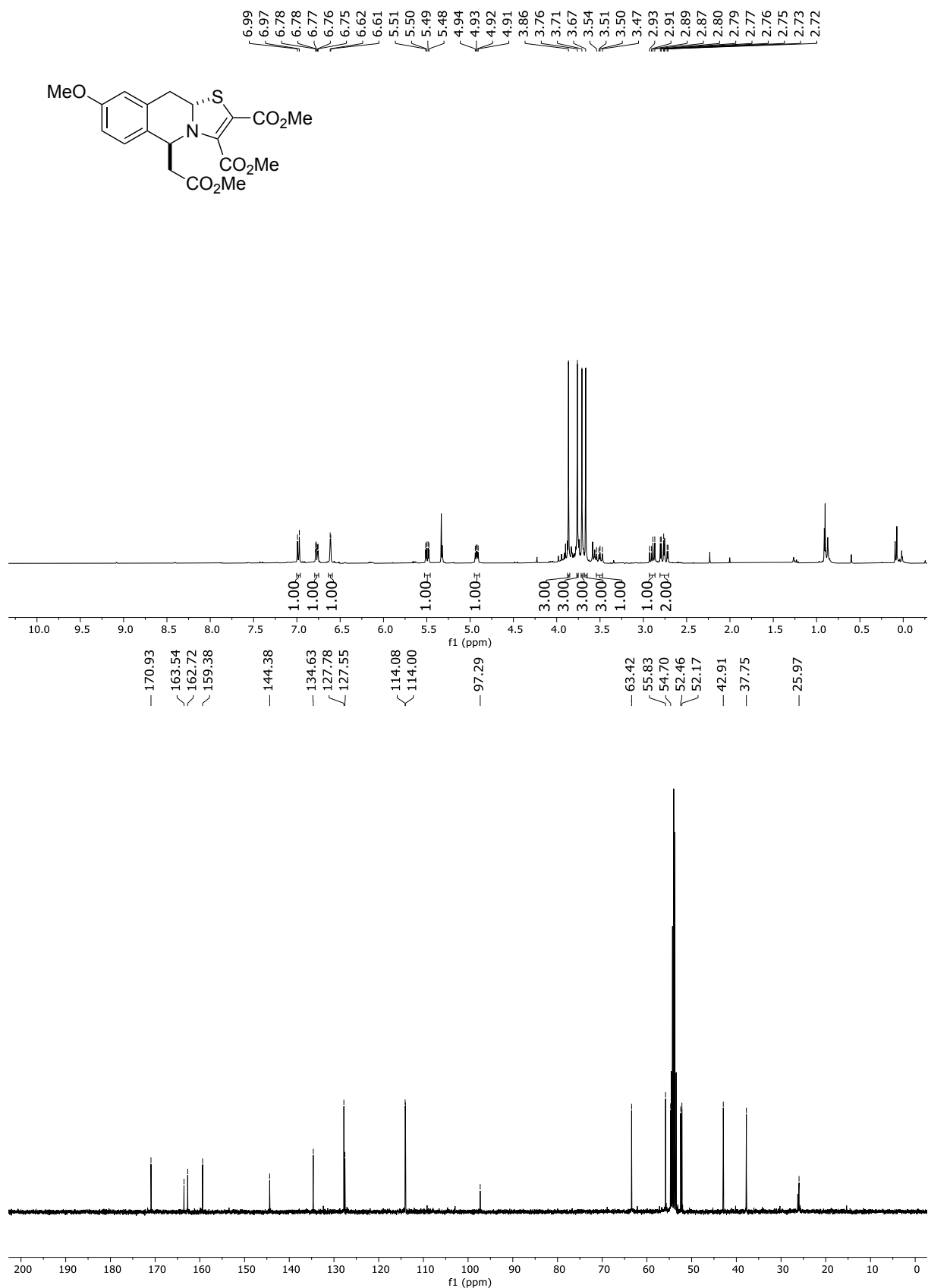
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4g



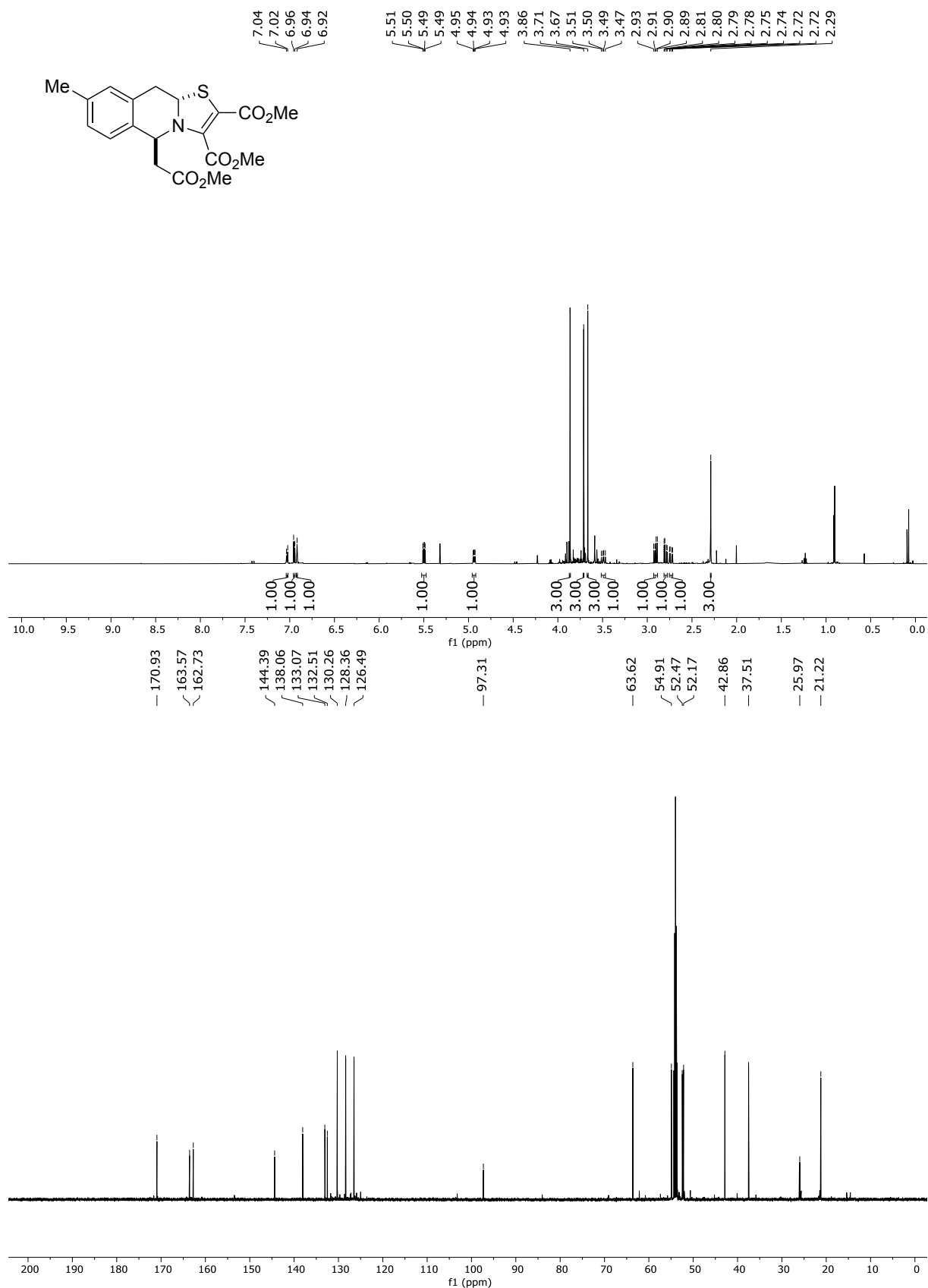
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4h



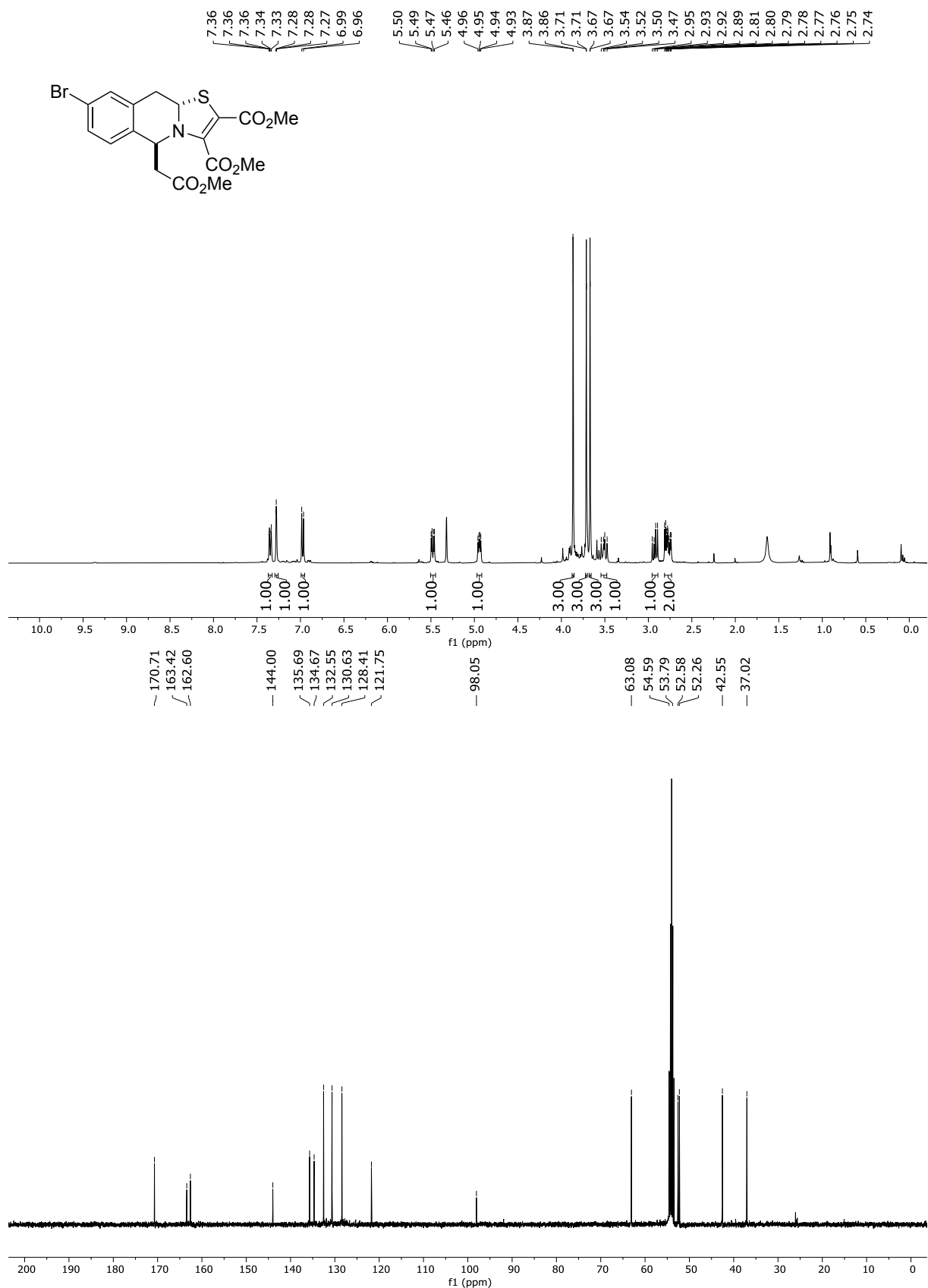
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4i



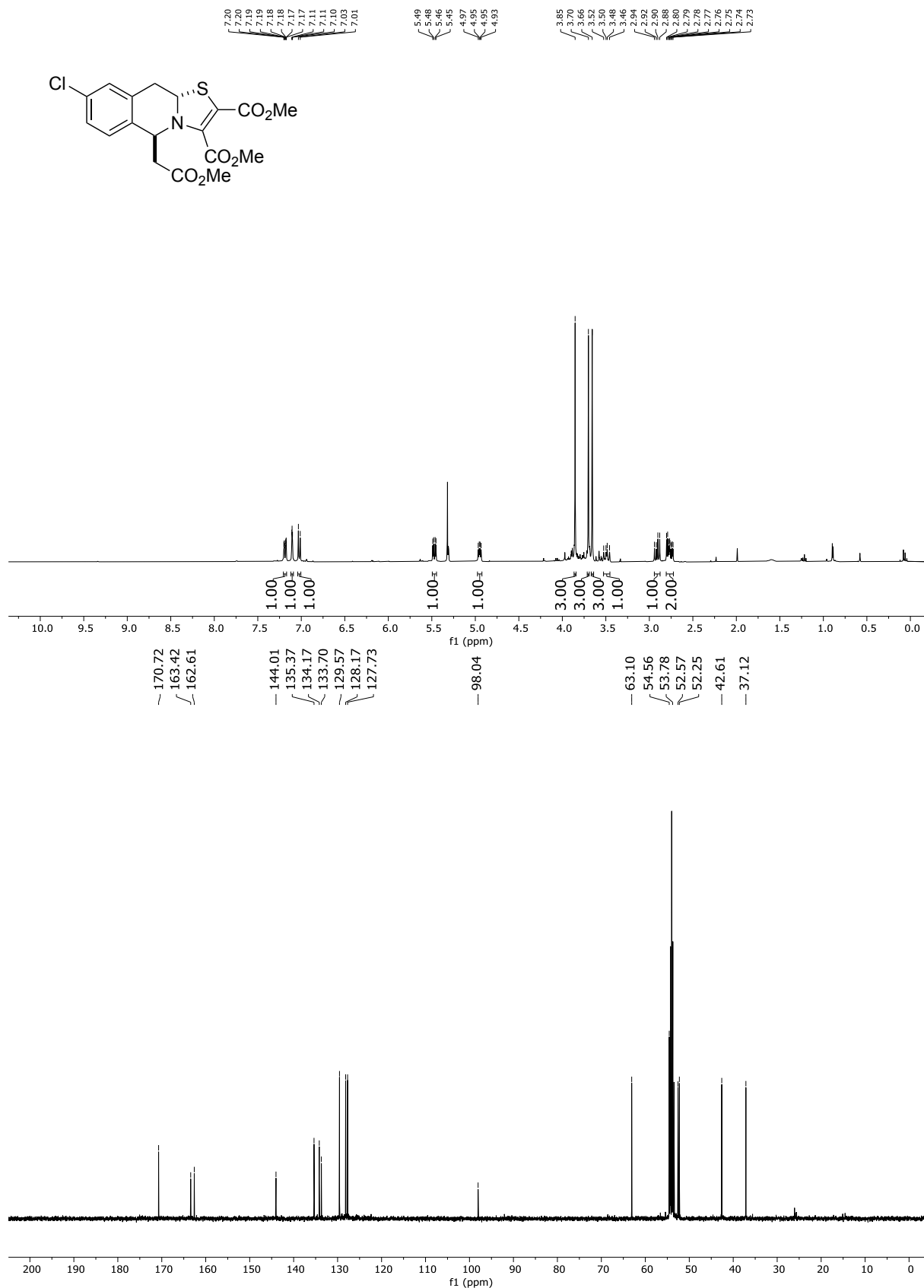
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 4j



¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4k



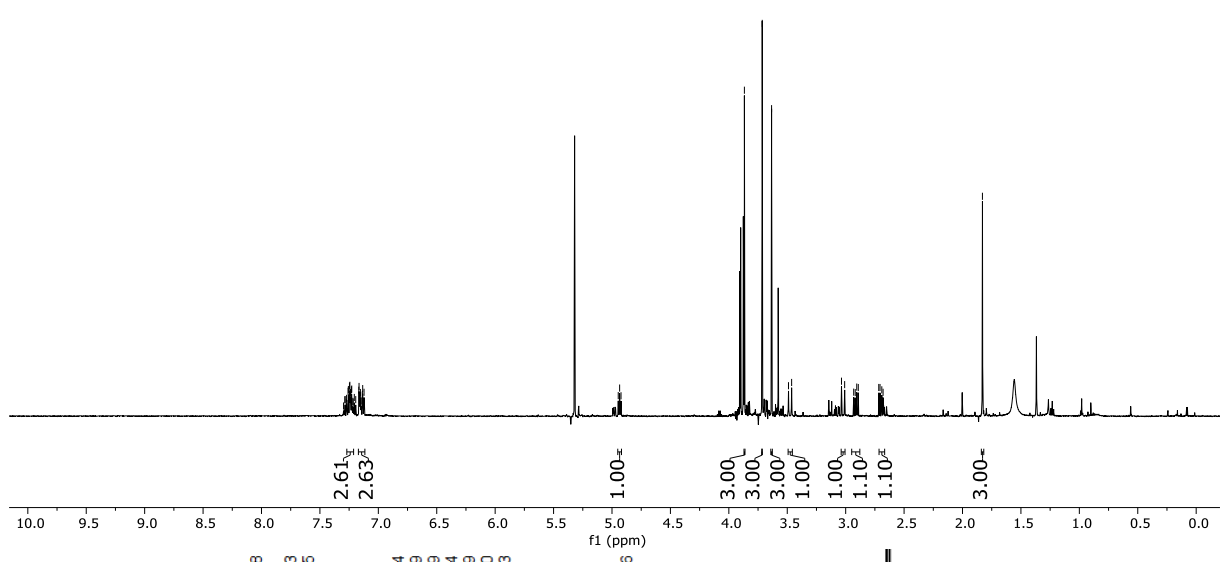
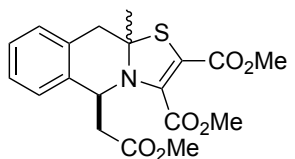
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 4I



¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 4m-major

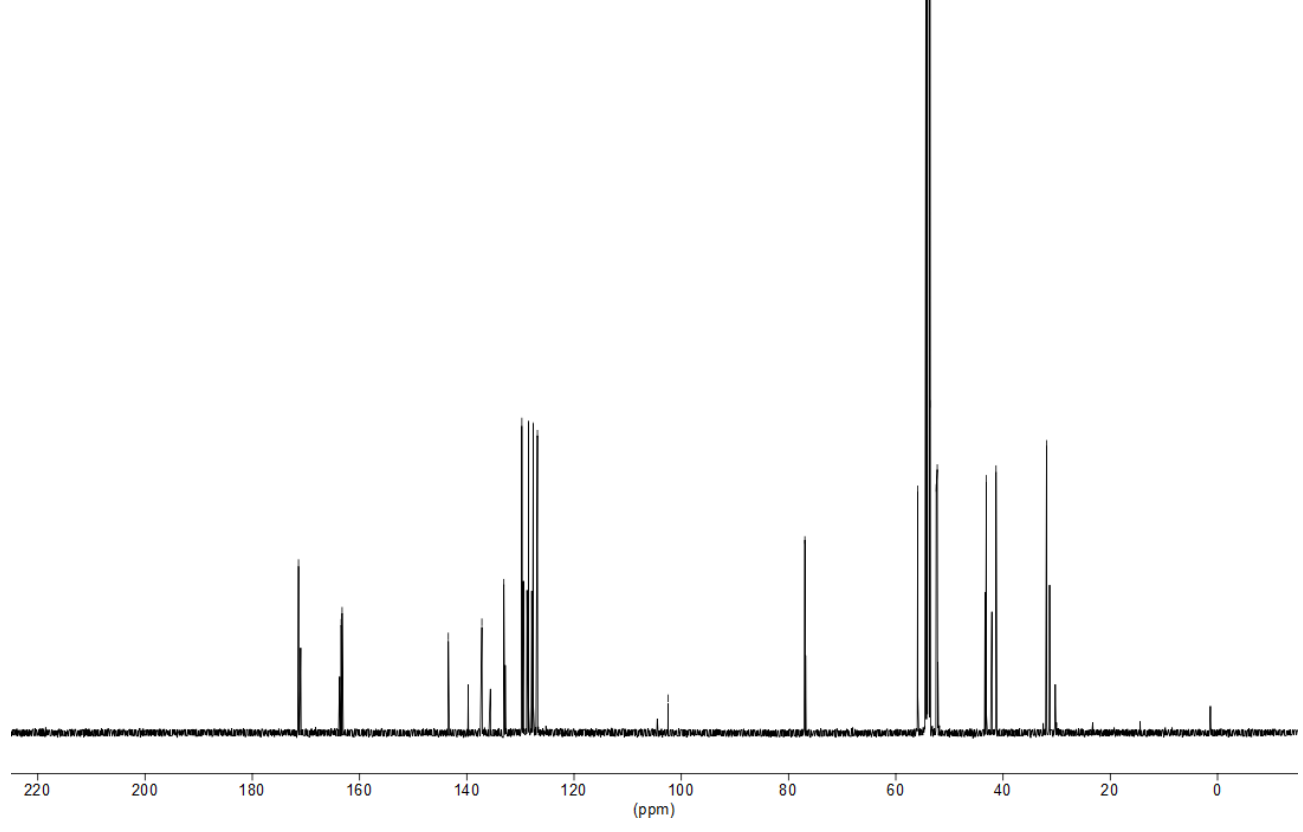
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4.92

3.87
3.71
3.63
3.49
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2.93
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2.71
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2.68
1.83

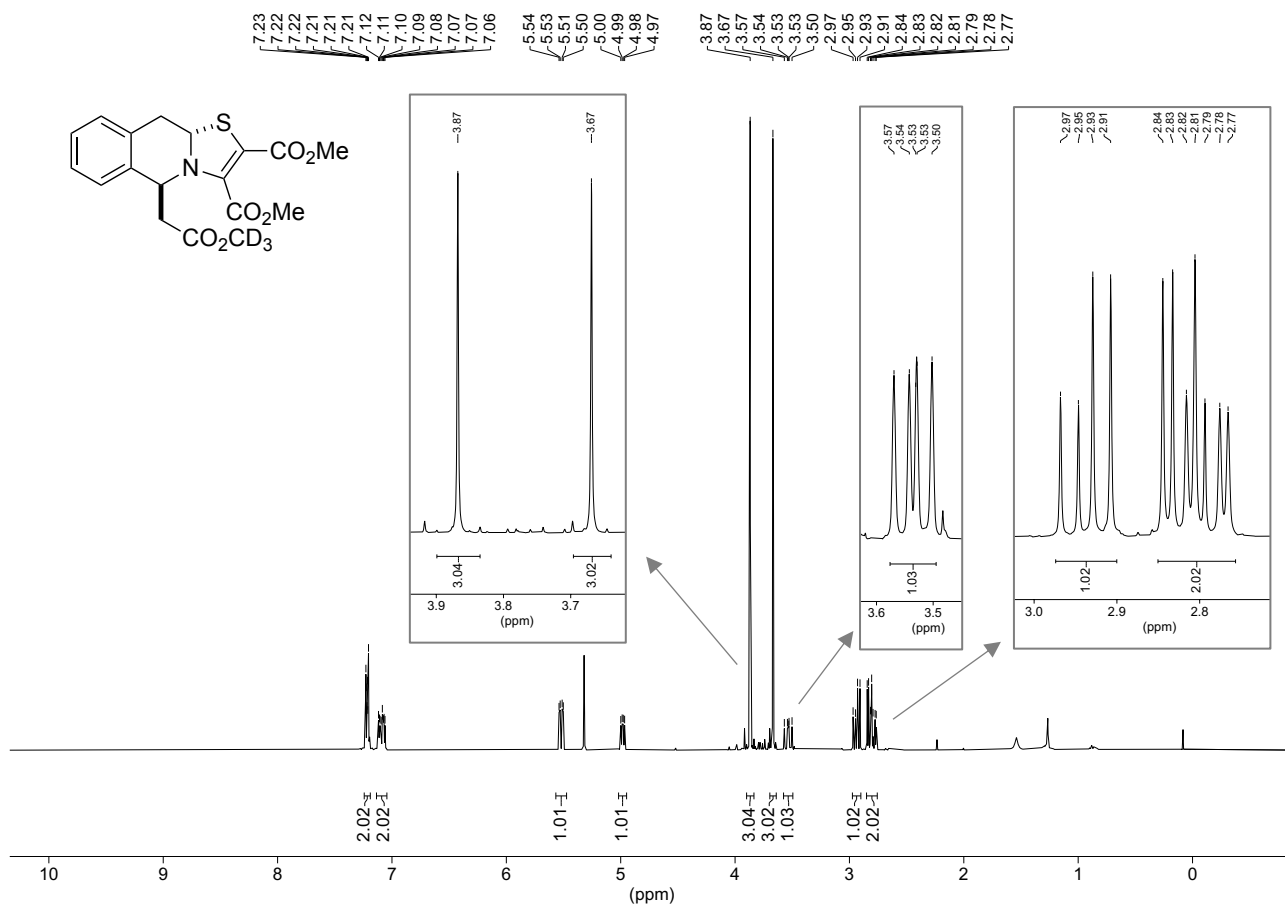


10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

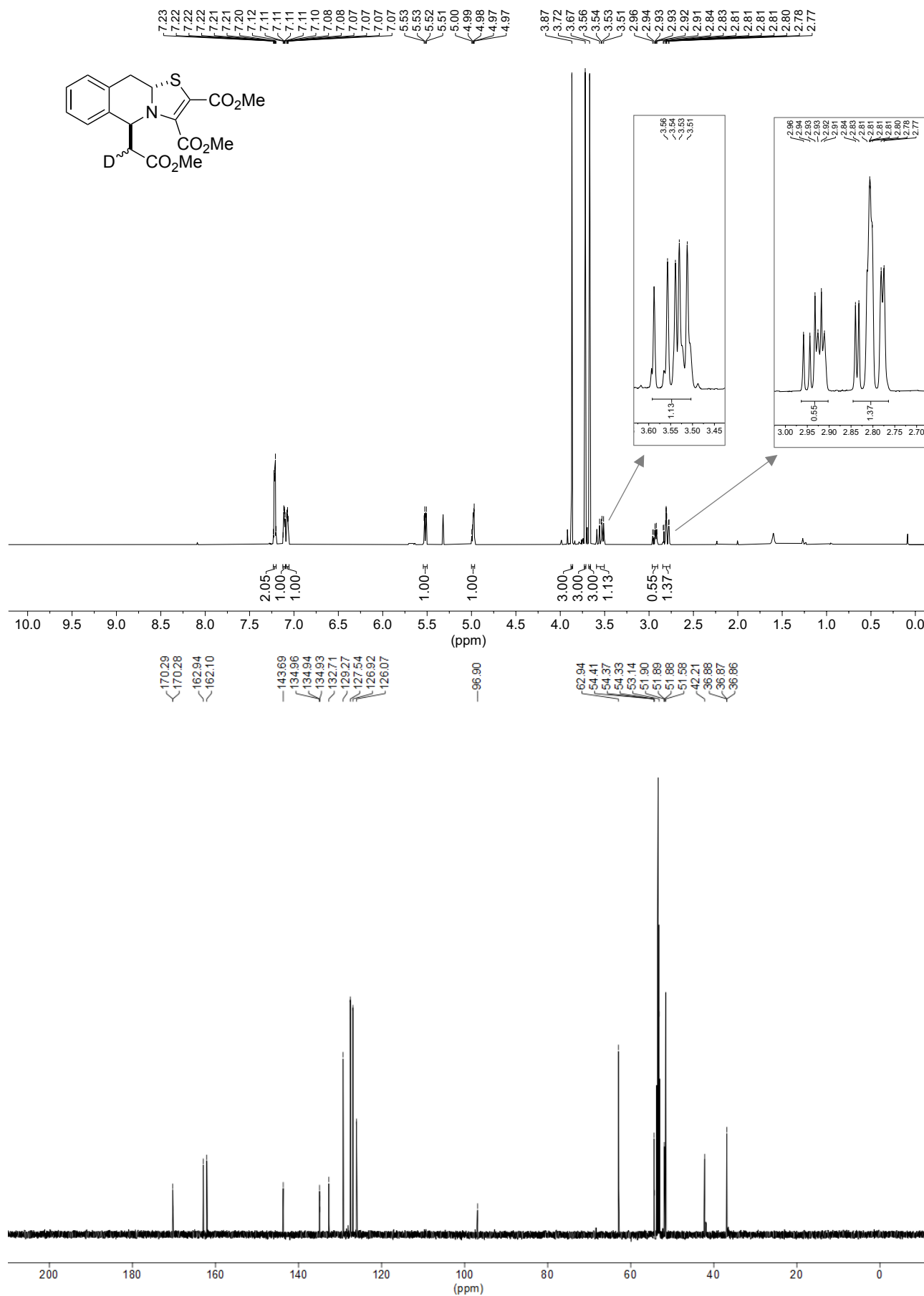
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55.91
53.62
52.75
52.27
43.12
41.31
31.88



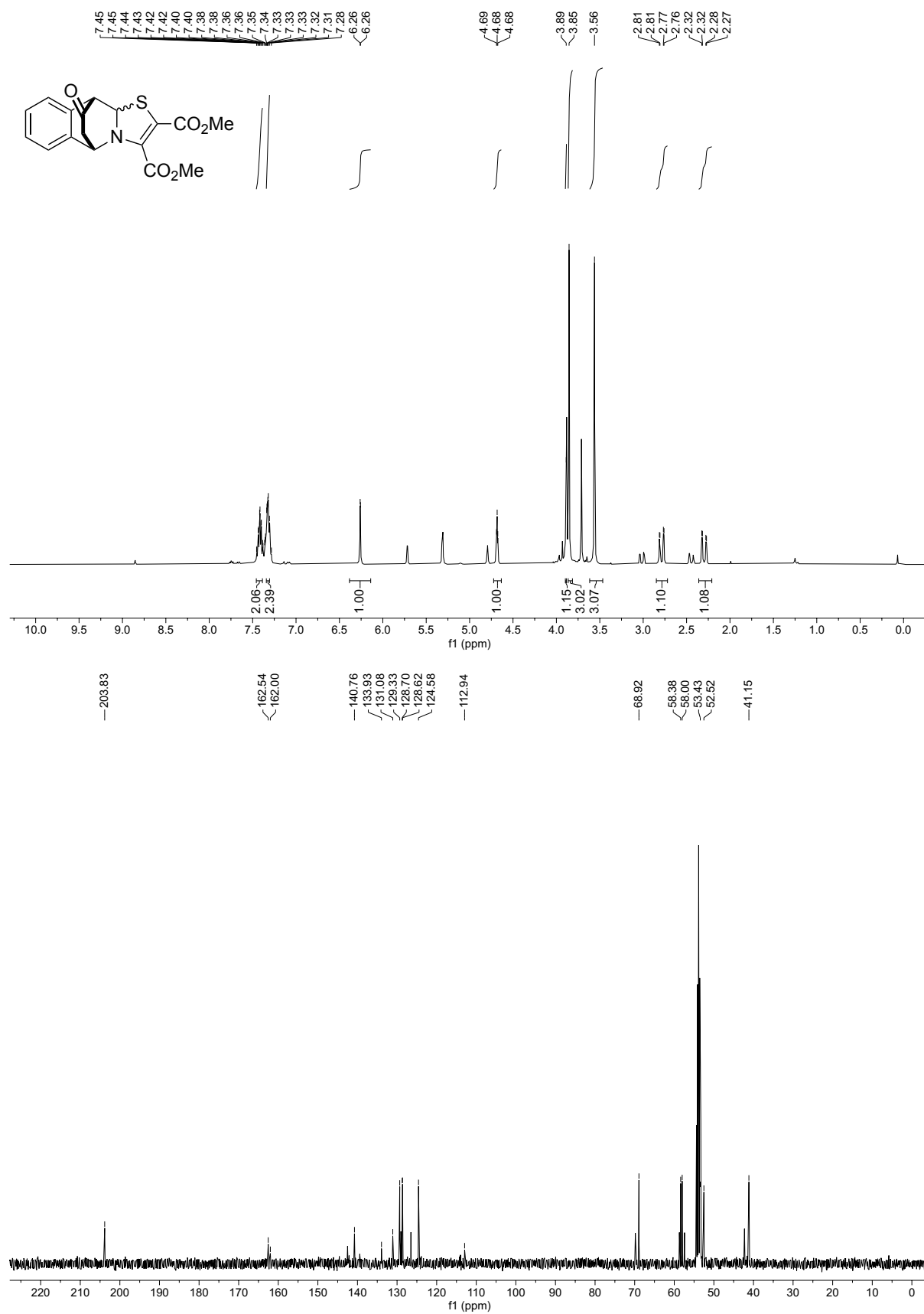
¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 4b-D



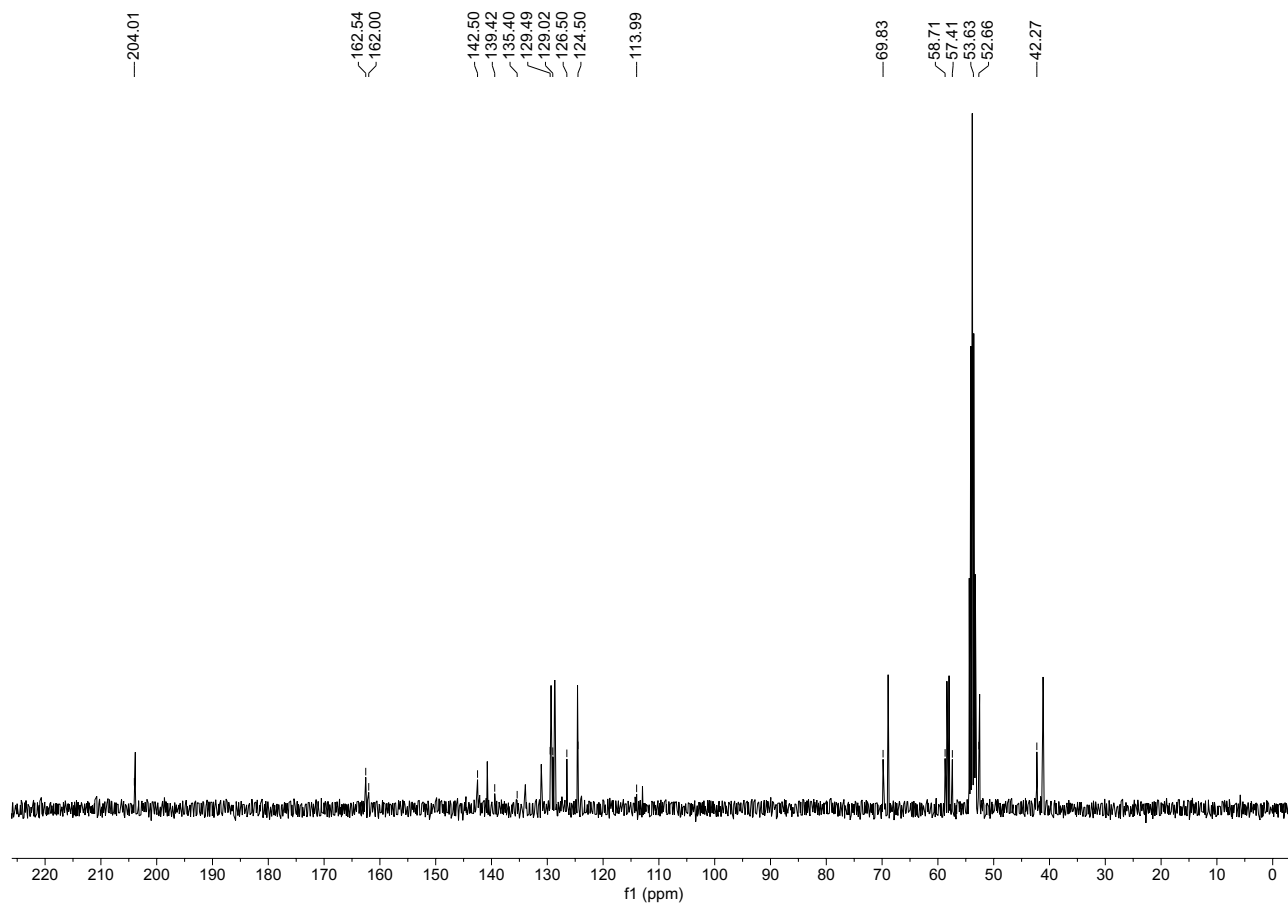
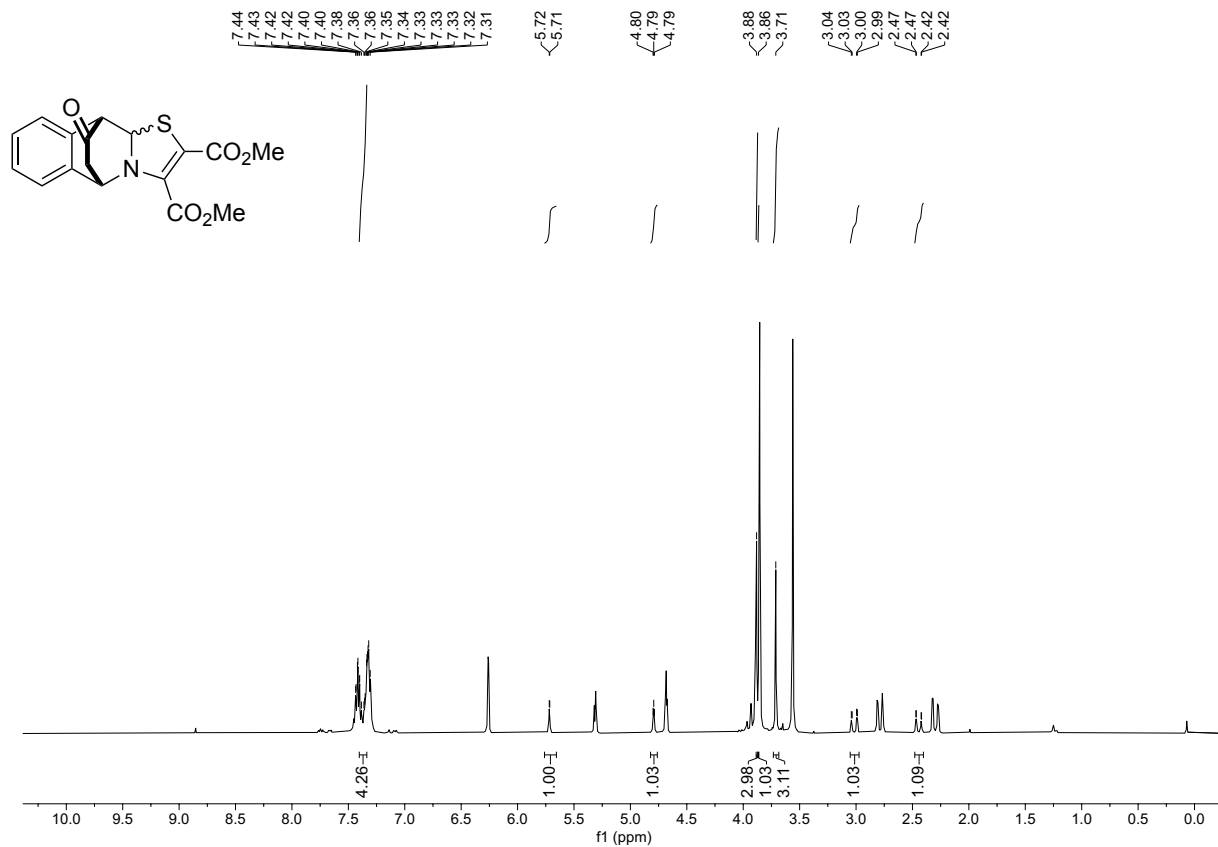
¹H-NMR (600 MHz, CD₂Cl₂) and ¹³C-NMR (150 MHz, CD₂Cl₂) for 4b-D'



¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 5-major



¹H-NMR (400 MHz, CD₂Cl₂) and ¹³C-NMR (100 MHz, CD₂Cl₂) for 5-minor (representative signals)



¹H-NMR (500 MHz, CD₂Cl₂) and ¹³C-NMR (125 MHz, CD₂Cl₂) for 6

