Stereoselective Alkylation of (*S*)-*N*-Acyl-4-isopropyl-1,3-thiazolidine-2-thiones Catalyzed by $(Me_3P)_2NiCl_2$

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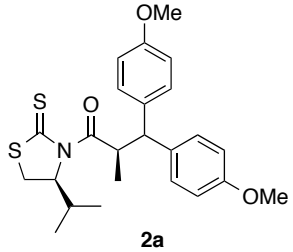
1. General Experimental Methods

Unless otherwise noted, reactions were conducted in oven-dried glassware under inert atmosphere of N_2 with anhydrous solvents. The solvents and reagents were dried and purified when necessary according to standard procedures. Commercially available reagents were used as received. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60 F_{254} plates and analyzed by UV (254 nm) and stained with phosphomolybdic acid and *p*-anisaldehyde; R_f values are approximate. Specific rotations ($[\alpha]_D$) were determined at 20 °C on a Perkin-Elmer 241 MC polarimeter. IR spectra (Attenuated Total Reflectance, ATR) were recorded on a Nicolet 6700 FT-IR Thermo Scientific spectrometer and only the more representative frequencies (ν) are reported in cm^{-1}. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a Varian Mercury 400. Chemical shifts (δ) are quoted in ppm and referenced to internal TMS (δ 0.00 for ^1H NMR) or $CDCl_3$ (δ 77.0 for ^{13}C NMR); coupling constants (*J*) are quoted in Hz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet (and their corresponding combinations); where necessary, 2D techniques (NOESY, COSY, HSQC) were also used to assist on structure elucidation. High resolution mass spectra (HRMS) were obtained with an Agilent 1100 spectrometer by the Unitat d'Espectrometria de Masses (CCiTUB), Universitat de Barcelona. Column chromatographies were carried under low pressure (flash) conditions and performed on SDS silica gel 60 (35–70 μm).

2. Alkylation of 1 with 4,4'-Dimethoxybenzhydryl Methyl Ether



2a

A 0.05 M solution of $(Me_3P)_2NiCl_2$ (100 μL, 5 μmol, 1 mol %)[1] was added to a solution of **1**[2] (109 mg, 0.5 mmol) and 4,4'-dimethoxybenzhydryl methyl ether[3] (194 mg, 0.75 mmol) in CH_2Cl_2 (0.9 mL) at room temperature under N_2. This mixture was cooled at –20 °C. Then, TESOTf (130 μL, 0.575 mmol) was added. Finally, 2,6-lutidine (87 μL, 0.75 mmol) was added four minutes later. The resultant mixture was stirred at –20 °C for 5 h.

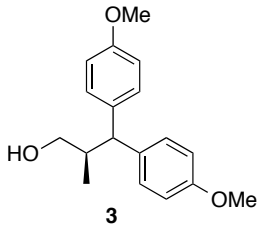
The reaction was quenched by addition of sat NH_4Cl (1.2 mL) and the mixture was stirred vigorously for five minutes at room temperature. It was partitioned with CH_2Cl_2 (2 × 20 mL) and water (20 mL).

[1] The stock solution was prepared by dissolving 14.1 mg (0.05 mmol) of $(Me_3P)_2NiCl_2$ in 1 mL of CH_2Cl_2.
[2] (*S*) 4-Isopropyl-*N*-propanoyl-1,3-thiazolidine-2-thione (**1**) was prepared as reported. See Gálvez, E.; Romea, P.; Urpí, F. *Org. Synth.* **2009**, *86*, 70–80.
[3] 4,4'-Dimethoxybenzhydryl methyl ether was prepared by stirring overnight at room temperature a mixture of commercially available 4,4'-dimethoxybenzhydrol (428 mg, 1.75 mmol), $HC(OMe)_3$ (710 μL, 6.5 mmol), MeOH (440 μL, 10.85 mmol), and Amberlyst-15®. It was filtered and concentrated to afford the desired pure ether.

The aqueous layer was further extracted with CH_2Cl_2 (20 mL) and the combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc 85:15) to afford 205 mg (0.46 mmol, 92% yield) of **2a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.30. **mp** 175–176 °C. $[\alpha]^{20}_D$ +316.7 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2959, 2925, 2829, 1683, 1601, 1501, 1464, 1360, 1238, 1145, 1030 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.32–7.18 (4H, m, Ar<u>H</u>), 6.83–6.73 (4H, m, Ar<u>H</u>), 6.07 (1H, dq, *J* = 11.5, 6.8 Hz, COC<u>H</u>), 5.18 (1H, ddd, *J* = 8.5, 5.2, 1.1 Hz, NC<u>H</u>), 4.19 (1H, d, *J* = 11.5 Hz, COCHC<u>H</u>), 3.74 (3H, s, OC<u>H</u>$_3$), 3.71 (3H, s, OC<u>H</u>$_3$), 3.36 (1H, dd, *J* = 11.5, 8.5 Hz, SC<u>H</u>$_a$H$_b$), 2.84 (1H, dd, *J* = 11.5, 1.1 Hz, SCH$_a$<u>H</u>$_b$), 1.69–1.61 (1H, m, C<u>H</u>$(CH_3)_2$), 1.07 (3H, d, *J* = 6.8 Hz, COCHC<u>H</u>$_3$), 0.78 (3H, d, *J* = 6.8 Hz, C<u>H</u>$_3$), 0.64 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.2 (C), 176.9 (C), 158.1 (C), 157.9 (C), 136.5 (C), 135.1 (C), 129.0 (CH), 128.8 (CH), 114.0 (CH), 113.9 (CH), 71.5 (CH), 55.2 (CH_3), 55.2 (CH_3), 54.2 (CH), 42.0 (CH), 30.7 (CH), 28.3 (CH_2), 18.7 (CH_3), 17.2 (CH_3), 17.1 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{24}H_{30}NO_3S_2$ $[M+H]^+$: 444.1662; found: 444.1672.

3. Removal of the Chiral Auxiliary from 2a

Synthesis of (*R*) 3,3-di(4-methoxyphenyl)-2-methyl-1-propanol (3)

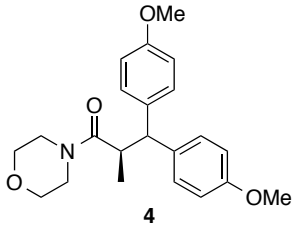


3

A 2 M solution of $LiBH_4$ in THF (336 μL, 0.67 mmol) was added to a solution of **2a** (150 mg, 0.34 mmol) in THF (2 mL) at –78 °C under N_2. The resultant mixture was stirred at –78 °C for 30 min, at room temperature for 15 h, and quenched by adding sat NH_4Cl (1.5 mL) at 0 °C.

It was diluted with Et_2O (60 mL) and washed with 2 M NaOH (3 × 20 mL). The aqueous layers were extracted with Et_2O (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated to afford 92 mg (0.32 mmol, 95% yield) of **3** as a colorless oil. A small portion of this material was further purified by column chromatrography (hexanes/EtOAc 50:10). R_f (hexanes/EtOAc 50:10) 0.30. $[\alpha]^{20}_D$ –24.2 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 3377, 2959, 2825, 1601, 1504, 1459, 1237, 1170, 1027 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.22–7.16 (4H, m, Ar<u>H</u>), 6.84–6.76 (4H, m, Ar<u>H</u>), 3.75 (3H, s, OC<u>H</u>$_3$), 3.74 (3H, s, OC<u>H</u>$_3$), 3.61 (1H, d, *J* = 10.9 Hz, C<u>H</u>Ar_2), 3.56 (1H, dd, *J* =10.8, 3.8 Hz, HOC<u>H</u>$_a$H$_b$), 3.38 (1H, dd, *J* =10.8, 5.9 Hz, HOCH$_a$<u>H</u>$_b$), 2.49–2.39 (1H, m, C<u>H</u>CH_3), 0.94 (3H, d, *J* = 6.7 Hz, CHC<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 157.7 (2 × C), 136.4 (2 × C), 128.8 (2 × CH), 128.6 (2 × CH), 114.0 (2 × CH), 113.8 (2 × CH), 66.5 (CH_2), 55.1 (2 × CH_3), 53.5 (CH), 39.4 (CH), 16.1 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{18}H_{26}NO_3$ $[M+NH_4]^+$: 304.1907; found: 304.1904.

Synthesis of *N*-[(*R*)-3,3-di(4-methoxyphenyl)-2-methylpropanoyl]morpholine (4)



4

A solution of **2a** (147 mg, 0.33 mmol), morpholine (64 μL, 0.73 mmol), Et_3N (46 μL, 0.33 mmol), and DMAP (40 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) was stirred 15 h at room temperature.

It was diluted with Et_2O (60 mL) and washed with 2 M NaOH (3 × 20 mL). The aqueous layers were extracted with Et_2O (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (hexanes/EtOAc 70:30) to afford 98 mg (0.27 mmol, 80% yield) of **4** as a white solid. R_f (hexanes/EtOAc 70:30) 0.05. **mp** 122–126 °C. $[\alpha]^{20}_D$ –47.4 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2959, 2836, 1619, 1499, 1459, 1241, 1183, 1023 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.22–7.12 (4H, m, Ar<u>H</u>), 6.86–6.74 (4H, m, Ar<u>H</u>), 4.17 (1H, d, J = 11.2 Hz, C<u>H</u>Ar_2), 3.77 (3H, s, OC<u>H</u>$_3$), 3.73 (3H, s, OC<u>H</u>$_3$), 3.60–3.12 (9H, m, heterocyclic ring & COC<u>H</u>), 1.06 (3H, d, *J* = 6.6 Hz, CHC<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 174.1, 158.1, 158.0, 136.0, 134.6, 129.3, 128.6, 113.9, 113.7, 66.8, 66.5, 55.2, 53.5, 46.0, 42.0, 39.8, 17.3. **HRMS** (+ESI): *m/z* calc. for $C_{22}H_{28}NO_4$ $[M+H]^+$: 370.2013; found: 370.2017.

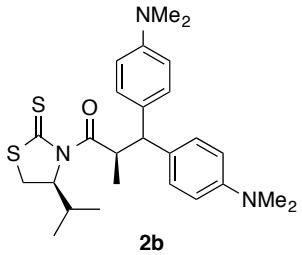
4. General Procedure for the Alkylation of 1

Complex $(Me_3P)_2NiCl_2$ (7.0 mg, 25 μmol, 5 mol %) was added to a solution of **1** (109 mg, 0.5 mmol) and the corresponding methyl ether (0.75 mmol) in CH_2Cl_2 (1 mL) at room temperature under N_2. This mixture was cooled at –20 °C. Then, TESOTf (136 μL, 0.6 mmol) was added. Finally, 2,6-lutidine (87 μL, 0.75 mmol) was added four minutes later. The resultant mixture was stirred at –20 °C for 15 h.

The reaction was quenched by addition of sat NH_4Cl (1.2 mL) and the mixture was stirred vigorously for five minutes at room temperature. It was partitioned with CH_2Cl_2 (2 × 20 mL) and water (20 mL). The aqueous layer was further extracted with CH_2Cl_2 (20 mL) and the combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography to afford the desired pure adducts **2**.

5. Physical and Spectroscopic Data for 2b–2d

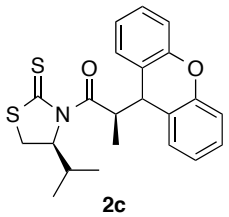
(*S*) *N*-[(*R*)-3,3-Di(4-dimethylaminophenyl)-2-methylpropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (2b)



2b

The reaction was performed from **1** (109 mg, 0.5 mmol) and 4,4'-bis(dimethylamino)benzhydryl methyl ether (213 mg, 0.75 mmol)[4] according to the general procedure to afford 226 mg (0.48 mmol, 96% yield) of **2b** as a blue solid. R_f (hexanes/EtOAc 70:30) 0.60. **mp** 159–160 °C. $[\alpha]^{20}_D$ +167.3 (*c* 0.01, $CHCl_3$). **IR** (ATR) ν 2955, 2925, 2788, 1698, 1675, 1605, 1516, 1342, 1238, 1145, 1123 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.25–7.23 (2H, m, ArH), 7.16–7.14 (2H, m, ArH), 6.67–6.65 (2H, m, ArH), 6.63–6.60 (2H, m, ArH), 6.01 (1H, dq, *J* = 11.4, 6.8 Hz, COCH), 5.20 (1H, ddd, *J* = 8.7, 5.0, 1.0 Hz, NCH), 4.09 (1H, d, *J* = 11.4 Hz, COCHCH), 3.36 (1H, dd, *J* = 11.4, 8.7 Hz, SCH_aH_b), 2.88 (6H, s, $N(CH_3)_2$), 2.83 (1H, dd, *J* = 11.4, 1.0 Hz, SCH_aH_b), 2.83 (6H, s, $N(CH_3)_2$), 1.68–1.56 (1H, m, $CH(CH_3)_2$), 1.08 (3H, d, *J* = 6.8 Hz, $COCHCH_3$), 0.77 (3H, d, *J* = 6.8 Hz, CH_3), 0.65 (3H, d, *J* = 7.0 Hz, CH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.9 (C), 177.4 (C), 149.1 (2 × C), 133.2 (C), 131.6 (C), 128.7 (CH), 128.3 (CH), 113.3 (CH), 113.0 (CH), 71.5 (CH), 54.2 (CH), 42.1 (CH), 40.9 (2 × CH_3), 40.7 (2 × CH_3), 30.7 (CH), 28.0 (CH_2), 18.8 (CH_3), 17.2 (CH_3), 17.0 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{18}H_{25}N_2OS_2$ $[M-C_8H_{11}N]^+$: 349.1403; found: 349.1412; calc. for $C_{26}H_{32}N_3OS_2$ $[M+H]^+$: 470.2294; found: 470.2299.

(*S*) 4-Isopropyl-*N*-[(*R*)-2-methyl-3-(9*H*-xanthen-9-yl)propanoyl]-1,3-thiazolidine-2-thione (2c)



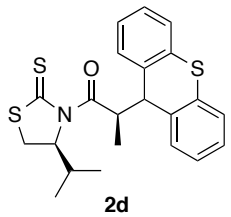
2c

The reaction was performed from **1** (109 mg, 0.5 mmol) and methyl 9*H*-xanthen-9-yl ether (159 mg, 0.75 mmol)[5] according to the general procedure to afford 190 mg (0.48 mmol, 95% yield) of **2c** as a yellow solid. R_f (hexanes/EtOAc 80:20) 0.60. **mp** 92–93 °C. $[\alpha]^{20}_D$ +163.4 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2962, 2922, 2866, 1676, 1472, 1449, 1249, 1238, 1153 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.34–6.98 (8H, m, ArH), 5.08 (1H, dd, *J* = 8.2, 5.5, 0.9 Hz, NCH), 4.94 (1H, dq, *J* = 7.7, 6.9 Hz, COCH), 4.50 (1H, d, *J* = 7.7 Hz, COCHCH), 3.34 (1H, dd, *J* = 11.5, 8.2 Hz, SCH_aH_b), 2.89 (1H, dd, *J* = 11.5, 0.9 Hz, SCH_aH_b), 2.29–2.17 (1H, m, $CH(CH_3)_2$), 1.00 (3H, d, *J* = 6.9 Hz, $COCHCH_3$), 0.91 (3H, d, *J* = 7.0 Hz, CH_3), 0.90 (3H, d, *J* =

[4] 4,4'-Bis(dimethylamino)benzhydryl methyl ether was prepared as described in Ref. 3.
[5] Methyl 9*H*-xanthen-9-yl ether was prepared as described in Ref. 3.

6.8 Hz, C$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.5 (C), 175.9 (C), 153.6 (2 × C), 130.1 (CH), 128.9 (CH), 128.0 (CH), 127.9 (CH), 124.6 (C), 123.1 (CH), 122.9 (C), 122.6 (CH), 116.6 (CH), 116.4 (CH), 71.9 (CH), 45.0 (CH), 42.2 (CH), 30.8 (CH), 29.1 (CH_2), 19.1 (CH_3), 17.0 (CH_3), 15.6 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{22}H_{24}NO_2S_2$ $[M+H]^+$: 398.1243; found: 398.1260; calc. for $C_{22}H_{23}NNaO_2S_2$ $[M+Na]^+$: 420.1062; found: 420.1077.

(*S*) 4-Isopropyl-*N*-[(*R*)-2-methyl-3-(9*H*-thioxanthen-9-yl)propanoyl]-1,3-thiazolidine-2-thione (2d)



2d

The reaction was performed from **1** (109 mg, 0.5 mmol) and methyl 9*H*-thioxanthen-9-yl ether (171 mg, 0.75 mmol)[6] according to the general procedure to afford 125 mg (0.30 mmol, 60% yield) of **2d** as a yellow solid. ***R*$_f$** (hexanes/EtOAc 90:10) 0.35. **mp** 160–162 °C. **[α]$^{20}_D$** +112.5 (*c* 1.30, $CHCl_3$). **IR** (ATR) ν 2959, 2925, 2866, 1683, 1457, 1349, 1242, 1153 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.45–7.11 (8H, m, Ar$\underline{H}$), 5.36 (1H, dq, *J* = 10.6, 6.9 Hz, COC$\underline{H}$), 5.08 (1H, ddd, *J* = 8.4, 5.8, 0.9 Hz, NC$\underline{H}$), 4.51 (1H, d, *J* = 10.6 Hz, COCHC$\underline{H}$), 3.26 (1H, ddd, *J* = 11.5, 8.4, 1.0 Hz, SC$\underline{H}_a$H$_b$), 2.79 (1H, dt, *J* = 11.5, 1.1 Hz, SCH$_a$H$_b$), 1.84–1.75 (1H, m, C$\underline{H}$(CH$_3$)$_2$), 0.94 (3H, d, *J* = 6.9 Hz, COCHC$\underline{H}_3$), 0.70 (3H, d, *J* = 7.0 Hz, C$\underline{H}_3$), 0.67 (3H, d, *J* = 6.8 Hz, C$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 201.8 (C), 176.4 (C), 136.2 (C), 135.5 (C), 133.6 (C), 133.3 (C), 130.6 (CH), 130.5 (CH), 127.3 (CH), 127.1 (CH), 126.8 (CH), 126.6 (CH), 126.0 (CH), 126.0 (CH), 71.3 (CH), 51.9 (CH), 37.6 (CH), 30.6 (CH), 28.7 (CH_2), 18.9 (CH_3), 17.4 (CH_3), 16.8 (CH_3). HRMS (+ESI): *m/z* calcd. for $C_{22}H_{23}NNaOS_3$ $[M+Na]^+$: 436.0834; found 436.0834.

6. Synthesis of Chiral *N*-Acyl Thiazolidinethiones 5–13

General Procedure

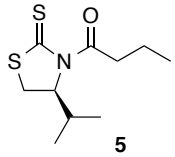
A 1.6 M solution of *n*-BuLi in hexanes (1.1 equiv) was added dropwise to a solution of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione[7] (1 mmol) in THF (2 mL) at –78 °C under N_2. The reaction mixture was stirred for 15 min and the corresponding acyl chloride (1.3 equiv) was carefully added. The resulting clear solution was stirred for 5 min and the solution was allowed to warm to room temperature and stirred for 1.5 h.

The reaction mixture was cooled with an ice bath and quenched with a saturated solution of NH_4Cl (2.5 mL) and water (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The resultant oil was purified

[6] Methyl 9*H*-thioxanthen-9-yl ether was prepared as described in Ref. 3.
[7] For the synthesis of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione see Ref. 2.

through flash column chromatography to afford the corresponding (*S*)-*N*-acyl-4-isopropyl-1,3-thiazolidine-2-thione.

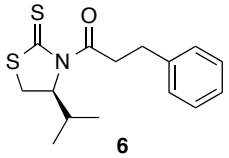
(*S*) *N*-Butanoyl-4-isopropyl-1,3-thiazolidine-2-thione (5)



5

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (484 mg, 3.0 mmol) with butanoyl chloride (405 μL mg, 3.9 mmol) was carried out according to the general procedure to afford 512 mg (2.2 mmol, 74% yield) of **5** as a yellow oil. R_f (hexanes/EtOAc 90:10) 0.30. $[\alpha]^{20}_D$ +407.0 (*c* 1.10, $CHCl_3$). **IR** (ATR) ν 2957, 2927, 2867, 1690, 1460, 1360, 1300, 1252 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.17 (1H, ddd, *J* = 8.0, 6.1, 1.3 Hz, NC<u>H</u>), 3.50 (1H, dd, *J* = 11.5, 8.0 Hz, SC<u>H</u>$_a$H$_b$), 3.33 (1H, ddd, *J* = 17.0, 8.4, 6.1 Hz, COC<u>H</u>$_a$H$_b$), 3.11 (1H, ddd, *J* = 17.0, 8.4, 6.5 Hz, COCH$_a$<u>H</u>$_b$), 3.01 (1H, dd, *J* = 11.5, 1.3 Hz, SCH$_a$<u>H</u>$_b$), 2.44–2.28 (1H, m, C<u>H</u>(CH$_3$)$_2$), 1.83–1.58 (2H, m, C<u>H</u>$_2$CH$_3$), 1.06 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$), 0.97 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$), 0.97 (3H, t, *J* = 7.4 Hz, CH$_2$C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.6 (C), 173.9 (C), 71.6 (CH), 40.0 (CH_2), 30.8 (CH), 30.4 (CH_2), 19.0 (CH_3), 18.3 (CH_2), 17.7 (CH_3), 13.6 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{10}H_{17}NNaOS_2$ $[M+Na]^+$: 254.0644; found: 254.0643.

(*S*) 4-Isopropyl-*N*-(3-phenylpropanoyl)-1,3-thiazolidine-2-thione (6)

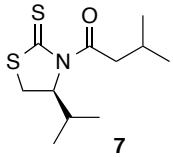


6

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (484 mg, 3.0 mmol) with 3-phenylpropanoyl chloride (579 μL mg, 3.9 mmol) was carried out according to the general procedure to afford 687 mg (2.4 mmol, 79% yield) of **6** as a yellow solid. R_f (hexanes/CH_2Cl_2 20:80) 0.65. **mp** 84–85 °C [lit.[8] **mp** 84 °C]. $[\alpha]^{20}_D$ +321.6 (*c* 0.95, $CHCl_3$). **IR** (ATR) ν 3052, 3022, 2957, 2920, 2867, 1698, 1360, 1255, 1234 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.31–7.18 (5H, m, Ar<u>H</u>), 5.11 (1H, ddd, *J* = 8.0, 6.2, 1.2 Hz, NC<u>H</u>), 3.67 (1H, ddd, *J* = 17.1, 9.0, 5.9 Hz, COC<u>H</u>$_a$H$_b$), 3.52 (1H, ddd, *J* = 17.1, 8.9, 6.6 Hz, COCH$_a$<u>H</u>$_b$), 3.45 (1H, dd, *J* = 11.5, 8.0 Hz, SC<u>H</u>$_a$H$_b$), 3.10–2.93 (2H, m, C<u>H</u>$_2$Ph), 2.99 (1H, dd, *J* = 11.5, 1.2 Hz, SCH$_a$<u>H</u>$_b$), 2.40–2.28 (1H, m, C<u>H</u>(CH$_3$)$_2$), 1.04 (3H, d, *J* = 6.8 Hz, C<u>H</u>$_3$), 0.96 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7 (C), 173.1 (C), 140.5 (C), 128.5 (CH), 128.4 (CH), 126.2 (CH), 71.6 (CH), 39.6 (CH_2), 30.9 (CH_2), 30.7 (CH), 30.4 (CH_2), 19.0 (CH_3), 17.7 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{15}H_{20}NOS_2$ $[M+H]^+$: 294.0981; found: 294.0974.

[8] Ferstl, E. M.; Venkatesan, H.; Ambhaikar, N. B.; Snyder, J. P.; Liotta, D. C. *Synthesis* **2002**, 2075.

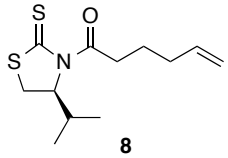
(*S*) 4-Isopropyl-*N*-(3-methylbutanoyl)-1,3-thiazolidine-2-thione (7)



7

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (484 mg, 3.0 mmol) with 3-methylbutanoyl chloride (475 μL, 3.9 mmol) was carried out according to the general procedure to afford 697 mg (2.8 mmol, 95% yield) of **7** as a yellow oil.[9] R_f (hexanes/CH_2Cl_2 50:50) 0.40. $[\alpha]^{20}_D$ +382.9 (*c* 1.05, $CHCl_3$). **IR** (ATR) ν 2955, 2930, 2870, 1688, 1464, 1359, 1293, 1255, 1154, 1086, 1033 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.17 (1H, ddd, *J* = 8.0, 6.2, 1.2 Hz, NC$\underline{H}$), 3.49 (1H, dd, *J* = 11.5, 8.0 Hz, SC$\underline{H}_a$H$_b$), 3.23 (1H, dd, *J* = 16.5, 6.1 Hz, COC$\underline{H}_a$H$_b$), 3.06 (1H, dd, *J* = 16.5, 7.4 Hz, COCH$_a\underline{H}_b$), 3.01 (1H, dd, *J* = 11.5, 1.2 Hz, SCH$_a\underline{H}_b$), 2.43–2.31 (1H, m, NCHC$\underline{H}$), 2.27–2.16 (1H, m, $CH_2C\underline{H}$), 1.06 (3H, d, *J* = 6.8 Hz, CHCHC$\underline{H}_3$), 0.99 (3H, d, *J* = 6.5 Hz, $CH_2CHC\underline{H}_3$), 0.97 (3H, d, *J* = 6.6 Hz, CHCHC$\underline{H}_3$), 0.96 (3H, d, *J* = 6.6 Hz, $CH_2CHC\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7 (C), 173.2 (C), 71.6 (CH), 46.5 (CH_2), 30.8 (CH), 30.4 (CH_2), 25.4 (CH), 22.5 (CH_3), 22.2 (CH_3), 19.1 (CH_3), 17.7 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{11}H_{20}NOS_2$ $[M+H]^+$: 246.0981; found: 246.0982.

(*S*) *N*-(5-Hexenoyl)-4-isopropyl-1,3-thiazolidine-2-thione (8)

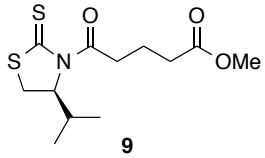


8

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (419 mg, 2.6 mmol) with 5-hexenoyl chloride (398 mg, 3.0 mmol) was carried out according to the general procedure to afford 429 mg (1.7 mmol, 64% yield) of **8** as a yellow oil. R_f (hexanes/CH_2Cl_2 50:50) 0.50. $[\alpha]^{20}_D$ +379.2 (*c* 0.92, $CHCl_3$). **IR** (ATR) ν 3074, 2960, 2872, 1691, 1638, 1466, 1363, 1256, 1150 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.80 (1H, ddt, *J* = 17.0, 10.2, 6.7 Hz, $CH_2C\underline{H}$=CH_2), 5.16 (1H, ddd, *J* = 8.0, 6.2, 1.2 Hz, NC$\underline{H}$), 5.03 (1H, dtd, *J* = 17.0, 3.5, 1.6 Hz, CH=C$\underline{H}_a$H$_b$), 4.98 (1H, dtd, *J* = 10.2, 2.2, 1.6 Hz, CH=CH$_a\underline{H}_b$), 3.50 (1H, dd, *J* = 11.5, 8.0 Hz, SC$\underline{H}_a$H$_b$), 3.36 (1H, ddd, *J* = 17.2, 8.8, 5.9 Hz, COC$\underline{H}_a$H$_b$), 3.15 (1H, ddd, *J* = 17.2, 8.8, 6.2 Hz, COCH$_a\underline{H}_b$), 3.01 (1H, dd, *J* = 11.5, 1.2 Hz, SCH$_a\underline{H}_b$), 2.40–2.30 (1H, m, C$\underline{H}$(CH_3)$_2$), 2.16–2.08 (2H, m, $C\underline{H}_2CH$=CH_2), 1.87–1.70 (2H, m, $COCH_2C\underline{H}_2$), 1.06 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.97 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.6 (C), 173.9 (C), 137.8 (CH), 115.2 (CH_2), 71.6 (CH), 37.5 (CH_2), 32.9 (CH_2), 30.8 (CH), 30.4 (CH_2), 24.1 (CH_2), 19.0 (CH_3), 17.7 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $[M+H]^+$ $C_{12}H_{20}NOS_2$ $[M+H]^+$: 258.0981; found: 258.0991.

[9] Physical and NMR data have been reported previously. See Ref. 8.

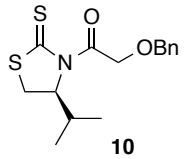
(*S*) 4-Isopropyl-*N*-[5-methoxy-5-oxopentanoyl]-1,3-thiazolidine-2-thione (9)



9

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (806 mg, 5.0 mmol) with methyl 5-chloro-5-oxopentanoate (760 μL, 5.5 mmol) was carried out according to the general procedure to afford 1.35 g (4.7 mmol, 93% yield) of **9** as a yellow oil. R_f (hexanes/EtOAc 70:30) 0.45. **$[\alpha]^{20}_D$** +305.4 (*c* 1.05, $CHCl_3$). **IR** (ATR) ν 2957, 2872, 1732, 1690, 1434, 1363, 1307, 1252, 1139, 1088, 1030 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.16 (1H, ddd, *J* = 8.0, 6.2, 1.1 Hz, NC$\underline{H}$), 3.68 (3H, s, OC$\underline{H}_3$), 3.51 (1H, dd, *J* = 11.5, 8.0 Hz, SC$\underline{H}_a$H$_b$), 3.42 (1H, ddd, *J* = 17.6, 7.9, 6.5 Hz, NCOC$\underline{H}_a$H$_b$), 3.20 (1H, ddd, *J* = 17.6, 7.8, 6.7 Hz, NCOCH$_a\underline{H}_b$), 3.02 (1H, dt, *J* = 11.5, 1.1 Hz, SCH$_a\underline{H}_b$), 2.44–2.30 (1H, m, C$\underline{H}$(CH$_3$)$_2$), 2.41 (2H, t, *J* = 7.3 Hz, C$\underline{H}_2$CO$_2$), 2.12–1.90 (2H, m, COCH$_2$C$\underline{H}_2$), 1.06 (3H, d, *J* = 6.8 Hz, C$\underline{H}_3$), 0.97 (3H, d, *J* = 6.9 Hz, C$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7 (C), 173.4 (C), 173.1 (C), 71.5 (CH), 51.5 (CH_3), 37.4 (CH_2), 32.9 (CH_2), 30.8 (CH), 30.4 (CH_2), 20.1 (CH_2), 19.0 (CH_3), 17.7 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{12}H_{20}NO_3S_2$ $[M+H]^+$: 290.0879; founf: 290.0880.

(*S*) *N*-(2-Benzyloxyacetyl)-4-isopropyl-1,3-thiazolidine-2-thione (10)

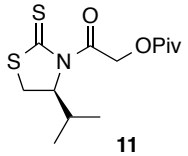


10

The acylation of (*S*) 4-isopropyl-1,3-thiazolidine-2-thione (484 mg, 3.0 mmol) with 2-benzyloxyacetyl chloride (615 μL, 3.9 mmol) was carried out according to the general procedure to afford 881 mg (2.9 mmol, 95% yield) of **10** as a yellow oil.[10] R_f (hexanes/EtOAc 70:30) 0.60. **$[\alpha]^{20}_D$** +233.6 (*c* 1.10, $CHCl_3$). **IR** (ATR) ν 3059, 3025, 2959, 2872, 1701, 1463, 1363, 1307, 1260 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.42–7.28 (5H, m, Ar$\underline{H}$), 5.18 (1H, ddd, *J* = 8.1, 6.4, 1.0 Hz, NC$\underline{H}$), 5.05 (1H, d, *J* = 17.7 Hz, COC$\underline{H}_a$H$_b$), 4.97 (1H, d, *J* = 17.7 Hz, COCH$_a\underline{H}_b$), 4.67 (1H, d, *J* = 11.6 Hz, OC$\underline{H}_a$H$_b$Ph), 4.63 (1H, d, *J* = 11.6 Hz, OCH$_a\underline{H}_b$Ph), 3.59 (1H, dd, *J* = 11.5, 8.1 Hz, SC$\underline{H}_a$H$_b$), 3.08 (1H, dd, *J* = 11.5, 1.0 Hz, SCH$_a\underline{H}_b$), 2.45–2.32 (1H, m, C$\underline{H}$(CH$_3$)$_2$), 1.07 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.99 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.1 (C), 171.0 (C), 137.2 (C), 128.4 (CH), 128.0 (CH), 127.9 (CH), 73.4 (CH_2), 72.0 (CH_2), 71.3 (CH), 31.4 (CH_2), 30.7 (CH), 19.0 (CH_3), 17.6 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{15}H_{20}NO_2S_2$ $[M+H]^+$: 310.0930; found: 310.0930.

[10] Physical and spectroscopic data have been reported previously, Nagao, Y.; Dai, W.-M.; Ochiai, M.; Tsukagoshi, S.; Fujita, E. *J. Org. Chem.* **1990**, *55*, 1148.

(*S*) 4-Isopropyl-*N*-(2-pivaloyloxyacetyl)-1,3-thiazolidine-2-thione (11)



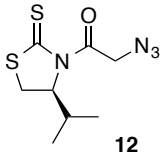
11

A mixture of pivaloyl chloride (4.4 mL, 36 mmol) and glycolic acid (1.52 g, 20 mmol) was stirred for 60 h at room temperature under N_2. Then, the volatiles were eliminated under vacuum and the product, 2-pivaloyloxy acetic acid, was used in the next step without further purification.

A solution of this product, (*S*) 4-isopropyl-1.3-thiazolidine-2-thione (2.74 g, 17 mmol), EDC·HCl (4.89 g, 25.5 mmol), and DMAP (104 mg, 0.85 mmol) in CH_2Cl_2 (27 mL) was stirred at 0 °C for 15 min and at room temperature for 16 h under N_2.

The resulting yellow mixture was diluted in Et_2O (50 mL) and washed with 0.5 M HCl (3 × 40 mL), 0.5 M NaOH (3 × 40 mL), and brine (50 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed and the crude product was purified by flash column chromatography on silica gel (hexanes/EtOAc 90:10) to give 4.11 g (13.5 mmol, 80%) of **11** as a thick yellow oil.[11] R_f (hexanes/CH_2Cl_2 70:30) 0.50. $[\alpha]^{20}_D$ +232.8 (*c* 1.0, $CHCl_3$). **IR** (ATR) ν 2965, 2874, 1740, 1714, 1141 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.44 (2H, s, $COCH_2$), 5.11 (1H, ddd, *J* = 8.1, 5.9, 1.1 Hz, NC<u>H</u>), 3.63 (1H, dd, *J* = 11.5, 8.1 Hz, SC<u>H</u>$_a$H$_b$), 3.09 (1H, dd, *J* = 11.5, 1.1 Hz, SCH$_a$<u>H</u>$_b$), 2.43–2.32 (1H, m, C<u>H</u>$(CH_3)_2$), 1.27 (9H, s, CH$(C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 6.8 Hz, C<u>H</u>$_3$), 0.98 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.5 (C), 177.9 (C), 168.1 (C), 71.4 (CH), 65.0 (CH_2), 38.7 (C), 31.4 (CH), 30.7 (CH_2), 27.1 (CH_3), 19.0 (C<u>H</u>$_3$), 17.5 (C<u>H</u>$_3$). **HRMS** (+ESI): *m/z* calcd. for $C_{13}H_{22}NO_3S_2$ [M+H]+: 304.1036; found: 304.1037; calcd. for $C_{13}H_{21}NNaO_3S_2$ [M+Na]+: 326.0855; found: 326.0859.

(*S*) *N*-(2-Azidoacetyl)-4-isopropyl-1,3-thiazolidine-2-thione (12)



12

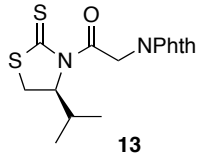
A 1.6 M solution of *n*-BuLi in hexanes (3.5 mL, 5.6 mmol) was added dropwise to a solution of (*S*)-4-isopropyl-1,3-thiazolidine-2-thione (806 mg, 5.0 mmol) in THF (0.5 mL) at –78 °C under N_2. The reaction mixture was stirred for 15 min at –78 °C and 2-azidoacetyl chloride (831 mg, 7.0 mmol) was carefully added *via cannula* (1.5 mL THF). After stirring for 5 min, the resulting clear solution was allowed to warm to room temperature and stirred for 2.5 h.

The reaction mixture was cooled with an ice bath and quenched with a saturated solution of NH_4Cl (2.2 mL) and water (6 mL). This mixture was extracted with Et_2O (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The resultant oil was purified through flash column chromatography (CH_2Cl_2/hexanes 70:30) to afford 950 mg (3.9 mmol, 78% yield) of **12** as a yellow oil.

[11] Physical and spectroscopic data have been reported previously by our group, see Baiget, J.; Caba, M.; Gálvez, E.; Romea, P.; Urpí, F.; Font-Bardia, M. *J. Org. Chem.* **2012**, *77*, 8809.

***R*$_f$** (CH_2Cl_2/hexanes 70:30) 0.45. **[α]$^{20}_D$** +239.9 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2961, 2097, 1692, 1467, 1304, 1168, 1037 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.22–5.17 (1H, m, NC<u>H</u>), 4.92 (1H, d, *J* = 18.3 Hz, COC<u>H</u>$_a$H$_b$), 4.73 (1H, d, *J* = 18.3 Hz, COCH$_a$<u>H</u>$_b$), 3.62 (1H, dd, *J* = 11.6, 8.1 Hz, SC<u>H</u>$_a$H$_b$), 3.10 (1H, dd, *J* = 11.6, 1.0 Hz, SCH$_a$<u>H</u>$_b$), 2.40–2.30 (1H, m, C<u>H</u>(CH$_3$)$_2$), 1.08 (3H, d, *J* = 6.9 Hz, C<u>H</u>$_3$), 0.96 (3H, d, *J* = 6.9 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.5, 168.7, 71.6, 55.0, 31.1, 30.7, 19.0, 17.5. **HRMS** (+ESI): *m/z* calcd, for $C_8H_{13}N_4OS_2$ $[M+H]^+$: 245.0525; found: 245.0530.

(*S*) 4-Isopropyl-*N*-(*N,N*-phtaloyl-2-aminoacetyl)-1,3-thiazolidine-2-thione (13)



13

Neat EDC·HCl (1.150 g, 6.0 mmol) was added to a solution of (*S*)-4-isopropyl-1,3-thiazolidine-2-thione (647 mg, 4.0 mmol), *N*,*N*-phtaloylglicine (983 mg, 4.8 mmol) and DMAP (22 mg, 0.2 mmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2. The resultant mixture was stirred for 96 h at room temperature.

The yellow solution was diluted with ether (10 mL) and extracted with 0.5 M HCl (3 × 20 mL), 0.5 M NaOH (3 × 30 mL), and brine (1 × 40 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resultant oil was purified through flash column chromatography (CH_2Cl_2/hexanes 90:10) to afford 976 mg (2.8 mmol, 70%) of **13** as a yellow oil. ***R*$_f$** (CH_2Cl_2/hexanes 90:10) 0.35. **[α]$^{20}_D$** +264.4 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2953, 1771, 1715, 1704, 1699, 1468, 1409, 1235, 1177, 1117 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.90–7.88 (2H, br s, Ar<u>H</u>), 7.76–7.74 (2H, br s, Ar<u>H</u>), 5.51 (1H, d, *J* = 17.9 Hz, COC<u>H</u>$_a$H$_b$), 5.17 (1H, d, *J* = 17.9 Hz, COCH$_a$<u>H</u>$_b$), 5.12 (1H, ddd, *J* = 8.0, 5.8, 0.9 Hz, NC<u>H</u>), 3.65 (1H, dd, *J* = 11.1, 8.3 Hz, SC<u>H</u>$_a$H$_b$), 3.10 (1H, dd, *J* = 11.1, 8.0 Hz, SCH$_a$<u>H</u>$_b$), 2.42–2.30 (1H, m, C<u>H</u>(CH$_3$)$_2$), 1.07 (3H, d, *J* = 6.9 Hz, C<u>H</u>$_3$), 0.96 (3H, d, *J* = 6.9 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7, 167.6, 167.1 (× 2), 134.1 (× 2), 132.1 (× 2), 123.5 (× 2), 71.7, 44.0, 31.1, 30.8, 19.0, 17.6. **HRMS** (+ESI): *m/z* calcd. for $C_{16}H_{16}N_2NaO_3S_2$ $[M+Na]^+$: 371.0495; found: 371.0503

7. General Procedure for the Alkylation of 5–13

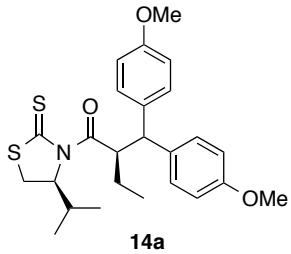
Complex $(Me_3P)_2NiCl_2$ (7.0 mg, 25 μmol, 5 mol %) was added to a solution of *N*-acyl thiomide (0.5 mmol) and 4,4'-dimethoxybenzhydryl methyl ether (194 mg, 0.75 mmol) in CH_2Cl_2 (1 mL) at room temperature under N_2. This mixture was cooled at –20 °C. Then, TESOTf (170 μL, 0.75 mmol) was added. Finally, 2,6-lutidine (87 μL, 0.75 mmol) was added four minutes later. The resultant mixture was stirred at –20 °C for 15 h.

The reaction was quenched by addition of sat NH_4Cl (1.2 mL) and the mixture was stirred vigorously for five minutes at room temperature. It was partitioned with CH_2Cl_2 (2 × 20 mL) and water (20 mL). The aqueous layer was further extracted with CH_2Cl_2 (20 mL) and the combined organic extracts were

washed with brine (30 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography to afford the desired pure adducts **14a–22a**.

8. Physical and Spectroscopic Data for 14a–22a

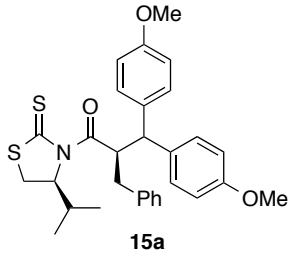
(*S*)-*N*-[(*R*)-3,3-Di(4-methoxyphenyl)-2-ethylpropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (14a)



14a

The reaction was performed from **5** (116 mg, 0.5 mmol) according to the general procedure to afford 213 mg (0.465 mmol, 93% yield) of **14a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.30. **mp** 183–185 °C. $[\alpha]^{20}_D$ +292.1 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2957, 2832, 1691, 1505, 1241, 1146 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.40–7.35 (2H, m, ArH), 7.25–7.21 (2H, m, ArH), 6.84–6.80 (2H, m, ArH), 6.76–6.71 (2H, m, ArH), 6.25 (1H, ddd, *J* = 11.5, 8.5, 4.1 Hz, COCH), 5.21 (1H, ddd, *J* = 8.2, 5.7, 0.8 Hz, NCH), 4.18 (1H, d, *J* = 11.5 Hz, CHAr$_2$), 3.75 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.35 (1H, dd, *J* = 11.5, 8.2 Hz, SCH$_a$H$_b$), 2.86 (1H, dd, *J* = 11.5, 0.8 Hz, SCH$_a$H$_b$), 1.79–1.67 (1H, m, CH(CH_3)$_2$), 1.65–1.46 (2H, m, COCHCH_2), 0.85 (3H, t, *J* = 7.5 Hz, CH$_2$CH_3), 0.77 (3H, d, *J* = 6.8 Hz, CHCH_3), 0.61 (3H, d, *J* = 6.9 Hz, CHCH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.6 (C), 175.9 (C), 158.1 (C), 157.9 (C), 136.3 (C), 135.3 (C), 129.2 (CH), 128.9 (CH), 114.1 (CH), 113.8 (CH), 71.6 (CH), 55.2 (CH_3), 55.1 (CH_3), 53.4 (CH), 46.8 (CH), 30.7 (CH), 28.9 (CH_2), 25.5 (CH_2), 18.6 (CH_3), 17.4 (CH_3), 10.3 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{25}H_{32}NO_3S_2$ $[M+H]^+$: 458.1818; found: 458.1831.

(*S*)-*N*-[(*R*)-2-Benzyl-3,3-di(4-methoxyphenyl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (15a)

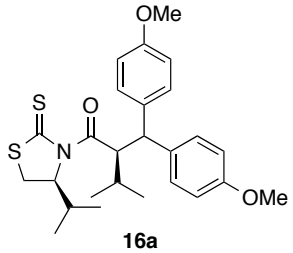


15a

The reaction was performed from **6** (147 mg, 0.5 mmol) according to the general procedure to afford 249 mg (0.48 mmol, 95% yield) of **15a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.30. **mp** 142–144 °C. $[\alpha]^{20}_D$ +291.2 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2957, 2872, 1687, 1605, 1508, 1370, 1243, 1145 cm^{-1}. **^{1}H**

NMR ($CDCl_3$, 400 MHz) δ 7.49–7.43 (2H, m, ArH), 7.41–7.36 (2H, m, ArH), 7.25–7.09 (5H, m, ArH), 6.92–6.87 (2H, m, ArH), 6.74–6.69 (2H, m, ArH), 6.45 (1H, td, *J* = 11.1, 5.0, Hz, COCH), 4.70 (1H, ddd, *J* = 7.2, 5.4, 2.9 Hz, NCH), 4.25 (1H, d, *J* = 11.1 Hz, $CHAr_2$), 3.79 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 2.90 (1H, dd, *J* = 12.8, 5.0 Hz, CH_aH_bPh), 2.62 (1H, dd, *J* = 12.8, 11.1 Hz, CH_aH_bPh), 2.58–2.50 (2H, m, SCH_2), 1.84–1.73 (1H, m, $CH(CH_3)_2$), 0.74 (3H, d, *J* = 6.7 Hz, $CHCH_3$), 0.42 (3H, d, *J* = 6.9 Hz, $CHCH_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.8 (C), 175.3 (C), 158.2 (C), 157.9 (C), 137.8 (C), 135.6 (C), 135.2 (C), 129.7 (CH), 129.0 (CH), 128.9 (CH), 128.2 (CH), 126.6 (CH), 114.3 (CH), 113.6 (CH), 71.3 (CH), 55.2 (2 × CH_3), 54.9 (CH), 47.2 (CH), 41.0 (CH_2), 30.2 (CH_2 & CH), 18.3 (CH_3), 18.2 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{30}H_{33}NNaO_3S_2$ $[M+Na]^+$: 542.1794; found: 542.1794.

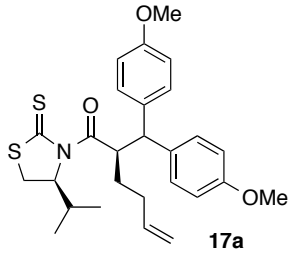
(*S*)-*N*-[(*R*)-3,3-Di(4-methoxyphenyl)-2-isopropylpropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (16a)



16a

The reaction was performed from **7** (123 mg, 0.5 mmol) according to the general procedure to afford 228 mg (0.47 mmol, 94% yield) of **16a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.38. **mp** 147–149 °C. **$[\alpha]^{20}_D$** +283.0 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2954, 2830, 1685, 1604, 1505, 1240, 1141 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.46–7.41 (2H, m, ArH), 7.31–7.26 (2H, m, ArH), 6.85–6.80 (2H, m, ArH), 6.74–6.70 (2H, m, ArH), 6.37 (1H, dd, *J* = 11.6, 4.1 Hz, COCH), 5.16 (1H, ddd, *J* = 8.2, 5.9, 1.0 Hz, NCH), 4.27 (1H, d, *J* = 11.6 Hz, $CHAr_2$), 3.75 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.34 (1H, dd, *J* = 11.5, 8.2 Hz, SCH_aH_b), 2.86 (1H, dd, *J* = 11.5, 1.0 Hz, SCH_aH_b), 1.91–1.73 (2H, m, 2 × $CH(CH_3)_2$), 0.96 (3H, t, *J* = 7.0 Hz, CH_2CHCH_3), 0.90 (3H, d, *J* = 6.8 Hz, $CHCH_3$), 0.77 (3H, d, *J* = 6.9 Hz, $CHCH_3$), 0.55 (3H, t, *J* = 7.0 Hz, CH_2CHCH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 204.1 (C), 173.8 (C), 158.1 (C), 157.8 (C), 136.4 (C), 135.4 (C), 129.5 (CH), 128.8 (CH), 114.1 (CH), 113.7 (CH), 71.7 (CH), 55.2 (2 × CH_3), 52.0 (CH), 49.5 (CH), 30.6 (CH), 29.7 (CH), 29.4 (CH_2), 20.5 (CH_3), 18.5 (CH_3), 17.7 (CH_3), 17.5 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{26}H_{34}NO_3S_2$ $[M+H]^+$: 472.1975; found: 472.1971.

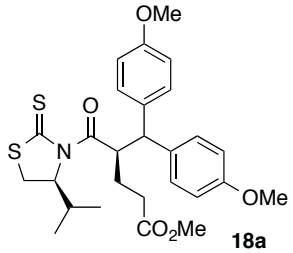
(*S*)-*N*-[(*R*)-2-(3-Butenyl)-3,3-di(4-methoxyphenyl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (17a)



17a

The reaction was performed from **8** (129 mg, 0.5 mmol) according to the general procedure to afford 228 mg (0.47 mmol, 94% yield) of **17a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.35. **mp** 189–191 °C. **[α]$^{20}_D$** +251.1 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2929, 2839, 1686, 1604, 1505, 1242, 1144 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.39–7.34 (2H, m, ArH), 7.27–7.22 (2H, m, ArH), 6.85–6.80 (2H, m, ArH), 6.75–6.71 (2H, m, ArH), 6.30 (1H, ddd, *J* = 11.3, 7.8, 5.3 Hz, COCH), 5.64 (1H, ddt, *J* = 17.0, 10.2, 6.5 Hz, CH=CH_2), 5.22–5.18 (1H, m, NCH), 4.93 (1H, dq, *J* = 17.0, 1.7 Hz, CH=CH_aH_b), 4.87 (1H, dq, *J* = 10.2, 1.7 Hz, CH=CH_aH_b), 4.15 (1H, d, *J* = 11.3 Hz, CHAr_2), 3.75 (3H, s, ArOCH_3), 3.70 (3H, s, ArOCH_3), 3.32 (1H, dd, *J* = 11.5, 8.4 Hz, SCH_aH_b), 2.83 (1H, dd, *J* = 11.5, 0.7 Hz, SCH_aH_b), 2.12–1.96 (2H, m, CH_2CH=CH_2), 1.72–1.58 (3H, m, C$H(CH_3)_2$, COCHCH_2), 0.72 (3H, d, *J* = 6.8 Hz, CHCH_3), 0.62 (3H, d, *J* = 7.0 Hz, CHCH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.6 (C), 176.0 (C), 158.1 (C), 157.9 (C), 138.0 (CH), 135.8 (C), 135.2 (C), 129.3 (CH), 128.9 (CH), 114.8 (CH_2), 114.1 (CH), 113.8 (CH), 71.6 (CH), 55.2 (2 × CH_3), 54.4 (CH), 45.7 (CH), 32.2 (CH_2), 30.8 (CH), 30.5 (CH_2), 28.4 (CH_2), 18.6 (CH_3), 17.1 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{27}H_{33}NNaO_3S_2$ $[M+Na]^+$: 506.1794; found: 506.1798.

(*S*)-*N*-[(*R*)-3,3-Di(4-methoxyphenyl)-2-(3-methoxy-3-oxopropyl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (18a)

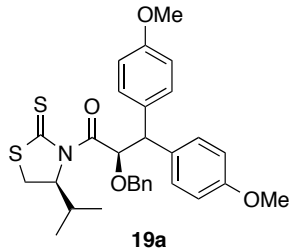


18a

The reaction was performed from **9** (145 mg, 0.5 mmol) according to the general procedure to afford 232 mg (0.45 mmol, 90% yield) of **18a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.15. **mp** 151–153 °C. **[α]$^{20}_D$** +263.9 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2949, 2833, 1738, 1686, 1604, 1506, 1241, 1144 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.37–7.33 (2H, m, ArH), 7.27–7.23 (2H, m, ArH), 6.85–6.81 (2H, m, ArH), 6.76–6.71 (2H, m, ArH), 6.36 (1H, ddd, *J* = 11.6, 8.2, 3.8 Hz, COCH), 5.18–5.13 (1H, m, NCH), 4.18 (1H, d, *J* = 11.6 Hz, CHAr_2), 3.75 (3H, s, ArOCH_3), 3.70 (3H, s, ArOCH_3), 3.61 (3H, s, COOCH_3), 3.43 (1H, dd, *J* = 11.4, 8.4 Hz, SCH_aH_b), 2.84 (1H, dd, *J* = 11.5, 0.8 Hz, SCH_aH_b), 2.41–2.22 (2H, m, CH_2CO_2Me), 2.02–1.91 (1H, m, COCHCH_aH_b), 1.86–1.75 (1H, m, COCHCH_aH_b), 1.72–1.62 (1H, m, C$H(CH_3)_2$), 0.73 (3H, d, *J* = 6.8 Hz, CHCH_3), 0.60 (3H, d, *J* = 7.0 Hz, CHCH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.8 (C), 175.3 (C), 173.3

(C), 158.2 (C), 158.0 (C), 135.7 (C), 134.7 (C), 129.2 (CH), 128.9 (CH), 114.2 (CH), 113.8 (CH), 71.7 (CH), 55.2 (2 × CH_3), 53.4 (CH), 51.6 (CH_3), 44.9 (CH) 30.7 (CH), 30.3 (CH_2), 28.6 (CH_2), 26.7 (CH_2), 18.6 (CH_3), 17.2 (CH_3). **HRMS** (+ESI): *m/z* calc. for $C_{27}H_{33}NNaO_5S_2$ $[M+Na]^+$: 538.1692; found: 538.1694.

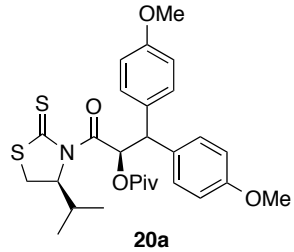
(*S*)-*N*-[(*R*)-2-Benzyloxy-3,3-di(4-methoxyphenyl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (19a)



19a

The reaction was performed from **10** (162 mg, 0.5 mmol) according to the general procedure to afford 251 mg (0.47 mmol, 94% yield) of **19a** as a yellow solid. R_f (hexanes/EtOAc 80:20) 0.30. **mp** 136–138 °C. $[\alpha]^{20}_D$ +160.3 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2955, 2834, 1697, 1604, 1505, 1363, 1243, 1157 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.40–7.35 (2H, m, ArH), 7.31–7.27 (2H, m, ArH), 7.27–7.23 (3H, m, ArH), 7.19–7.14 (2H, m, ArH), 7.02 (1H, d, *J* = 7.4 Hz, COCH), 6.86–6.81 (2H, m, ArH), 6.76–6.71 (2H, m, ArH), 4.97 (1H, ddd, *J* = 8.7, 4.6, 1.1 Hz, NCH), 4.65 (1H, d, *J* = 7.4 Hz, $CHAr_2$), 4.50 (1H, d, *J* = 12.1 Hz, OCH_aH_bPh), 4.46 (1H, d, *J* = 12.1 Hz, OCH_aH_bPh), 3.78 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 3.15 (1H, dd, *J* = 11.4, 8.1 Hz, SCH_aH_b), 2.79 (1H, dd, *J* = 11.4, 1.2 Hz, SCH_aH_b), 1.63–1.53 (1H, m, $CH(CH_3)_2$), 0.67 (3H, d, *J* = 7.1 Hz, $CHCH_3$), 0.65 (3H, d, *J* = 7.2 Hz, $CHCH_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7 (C), 172.3 (C), 158.3 (C), 158.2 (C), 137.7 (C), 132.9 (C), 132.8 (C), 130.2 (CH), 130.1 (CH), 128.0 (3 × CH), 127.6 (C), 113.7 (CH), 113.6 (CH), 79.0 (CH), 73.4 (CH_2), 71.6 (CH), 55.2 (2 × CH_3), 53.0 (CH), 30.5 (CH), 28.8 (CH_2), 18.7 (CH_3), 16.6 (CH_3); **HRMS** (+ESI): *m/z* calc. for $C_{30}H_{33}NNaO_4S_2$ $[M+Na]^+$: 558.1743; found: 558.1745.

(*S*)-*N*-[(*R*)-3,3-Di(4-methoxyphenyl)-2-pivaloyloxypropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (20a)

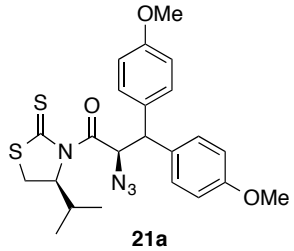


20a

The reaction was performed from **11** (152 mg, 0.5 mmol) according to the general procedure to afford 250 mg (0.47 mmol, 95% yield) of **20a** as a yellow solid. R_f (hexanes/EtOAc 85:15) 0.25. **mp** 75–77 °C. $[\alpha]^{20}_D$ +150.4 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2959, 2835, 1728, 1704, 1508, 1244, 1140 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.35–7.30 (3H, m, COCH, ArH), 7.25–7.20 (2H, m, ArH), 6.86–6.81 (2H, m, ArH), 6.79–6.75 (2H, m, ArH), 5.20 (1H, ddd, *J* = 9.0, 4.6, 1.4 Hz, NCH), 5.07 (1H, d, *J* = 5.5 Hz, $CHAr_2$), 3.78

(3H, s, OC$\underline{H}_3$), 3.75 (3H, s, OC$\underline{H}_3$), 3.53 (1H, dd, *J* = 11.5, 9.0 Hz, SC$\underline{H}_a$H$_b$), 2.93 (1H, dd, *J* = 11.5, 1.4 Hz, SCH$_a\underline{H}_b$), 1.70–1.59 (1H, m, C$\underline{H}$(CH$_3$)$_2$), 1.15 (9H, s, C(C$\underline{H}_3$)$_3$), 0.84 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.76 (3H, d, *J* = 7.0 Hz, CHC$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.4 (C), 178.0 (C), 169.1 (C), 158.6 (C), 158.2 (C), 132.5 (C), 131.0 (CH), 130.7 (C), 129.5 (CH), 113.5 (CH), 113.4 (CH), 74.9 (CH), 71.6 (CH), 55.2 (2 × CH_3), 49.7 (CH), 38.5 (C), 30.6 (CH), 29.2 (CH_2), 26.9 (CH_3), 18.9 (CH_3), 16.7 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{28}H_{36}NO_5S_2$ $[M+H]^+$: 530.2029; found: 530.2045.

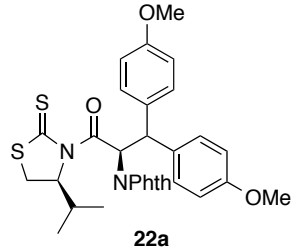
(*S*)-*N*-[(*R*)-2-Azido-3,3-di(4-methoxyphenyl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (21a)



21a

The reaction was performed from **12** (122 mg, 0.5 mmol) according to the general procedure to afford 216 mg (0.46 mmol, 92% yield) of **21a** as a yellow solid. ***R**f* (hexanes/EtOAc 85:15) 0.25. **mp** 133–135 °C. **[α]$^{20}_D$** +129.7 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2958, 2833, 2101, 1697, 1506, 1462, 1361, 1244, 1160 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.33–7.27 (5H, m, Ar$\underline{H}$, COC$\underline{H}$), 6.90–6.85 (2H, m, Ar$\underline{H}$), 6.80–6.75 (2H, m, Ar$\underline{H}$), 5.22 (1H, ddd, *J* = 8.6, 5.4, 1.1 Hz, NC$\underline{H}$), 4.57 (1H, d, *J* = 10.8 Hz, C$\underline{H}$Ar), 3.78 (3H, s, OC$\underline{H}_3$), 3.73 (3H, s, OC$\underline{H}_3$), 3.46 (1H, dd, *J* = 11.6, 8.6 Hz, SC$\underline{H}_a$H$_b$), 2.91 (1H, dd, *J* = 11.6, 1.1 Hz, SCH$_a\underline{H}_b$), 1.77–1.68 (1H, m, C$\underline{H}$(CH$_3$)$_2$), 0.72 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.66 (3H, d, *J* = 7.0 Hz, CHC$\underline{H}_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.4 (C), 169.4 (C), 158.7 (C), 158.6 (C), 132.3 (C), 132.2 (C), 129.6 (CH), 129.2 (CH), 114.2 (CH), 114.0 (CH), 71.5 (CH), 60.8 (CH), 55.2 (2 × CH_3), 51.9 (CH), 30.6 (CH), 28.9 (CH_2), 18.6 (CH_3), 17.0 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{23}H_{26}KN_4O_3S_2$ $[M+K]^+$: 509.1078; found: 509.1082.

(*S*)-*N*-[(*R*)-3,3-Di(4-methoxyphenyl)-*N*-phatloyl-2-aminopropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (22a)

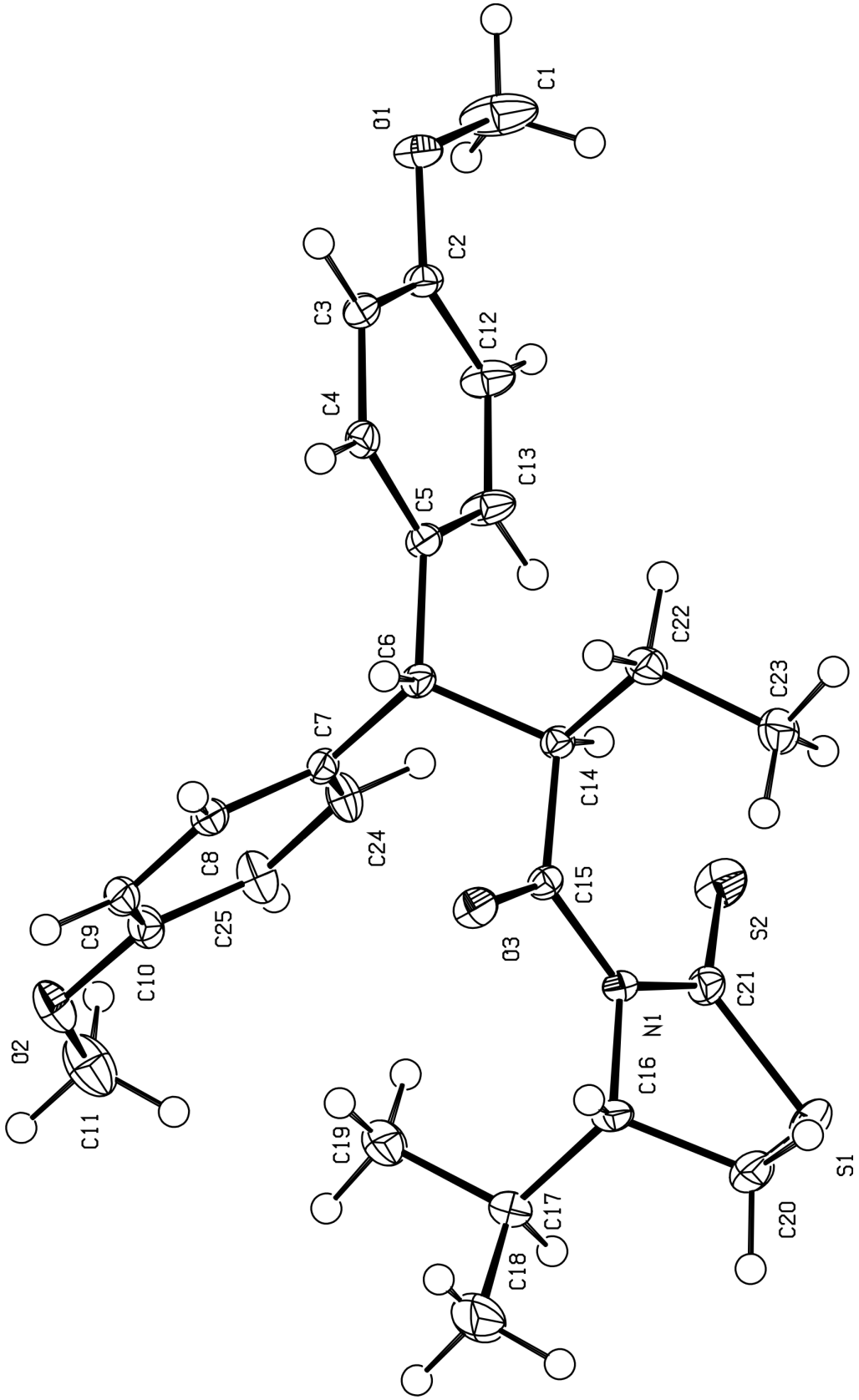


22a

The reaction was performed from **13** (174 mg, 0.5 mmol) according to the general procedure to afford 262 mg (0.46 mmol, 91% yield) of **22a** as a yellow solid. ***R**f* (hexanes/EtOAc 80:20) 0.10. **mp** 203–205 °C. **[α]$^{20}_D$** +525.7 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2964, 2836, 1774, 1715, 1687, 1510, 1383, 1247, 1177 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.71– 7.62 (4H, m, Ar$\underline{H}$), 7.44–7.39 (2H, m, Ar$\underline{H}$), 7.24 (1H, d, *J* = 11.0 Hz, COC$\underline{H}$), 7.04–6.98 (2H, m, Ar$\underline{H}$), 6.92–6.86 (2H, m, Ar$\underline{H}$), 6.56–6.51 (2H, m, Ar$\underline{H}$), 5.11 (1H, d, *J* =

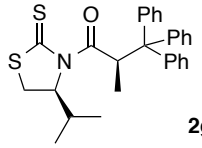
11.0 Hz, C<u>H</u>Ar_2), 4.79 (1H, ddd, *J* = 7.6, 5.9, 0.8 Hz, NC<u>H</u>), 3.79 (3H, s, OC<u>H_3</u>), 3.59 (3H, s, OC<u>H_3</u>), 3.30 (1H, dd, *J* = 11.3, 7.6 Hz, SC<u>H_a</u>H_b), 2.93 (1H, dd, *J* = 11.3, 0.8 Hz, SCH_a<u>H_b</u>), 2.41–2.30 (1H, m, C<u>H</u>$(CH_3)_2$), 0.94 (3H, d, *J* = 6.8 Hz, CHC<u>H_3</u>), 0.89 (3H, d, *J* = 7.0 Hz, CHC<u>H_3</u>). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 201.6 (C), 169.5 (C), 158.2 (2 × C), 134.1 (CH), 133.3 (C), 132.3 (C), 130.9 (C), 130.1 (CH), 129.1 (CH), 123.2 (CH), 114.1 (CH), 113.4 (CH), 73.8 (CH), 55.5 (CH), 55.2 (CH_3), 55.1 (CH_3), 49.6 (CH), 31.5 (CH_2), 31.2 (CH), 19.0 (CH_3), 17.6 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{31}H_{30}N_2NaO_5S_2$ $[M+Na]^+$: 597.1488; found: 597.1487.

9. X-Ray Structure of 14a



10. Alkylation of 1 with Methyl Trityl Ether and Tropylium Cations

Alkylation with methyl trityl ether

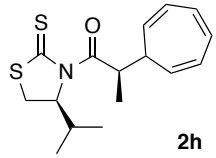


2g

Solid $(Me_3P)_2NiCl_2$ (7.0 mg, 25 μmol, 5 mol %) was added to a solution of **1** (109 mg, 0.5 mmol) and methyl trityl ether (173 mg, 0.75 mmol) in CH_2Cl_2 (1.0 mL) at room temperature under N_2. The resulting solution was cooled at –20 °C. Then, TESOTf (170 μL, 0.75 mmol) was added. Finally, four minutes later 2,6-lutidine (87 μL, 0.75 mmol) was added dropwise and the resultant mixture was stirred at –20 °C for 15 h.

The reaction was quenched with sat NH_4Cl (1.2 mL) and the mixture was stirred vigorously for five minutes at room temperature. It was then partitioned with H_2O (20 mL) and CH_2Cl_2 (20 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo and the crude was purified by flash column chromatography (hexanes/EtOAc 80:20) to afford 50 mg (0.11 mmol, 22% yield) of (*S*) 4-isopropyl-*N*-[(*R*)-2-methyl-3,3,3-triphenylpropanoyl]-1,3-thiazolidine-2-thione (**2g**) as a yellow solid. R_f (hexanes/EtOAc 80:20) 0.50. **mp** 190–192 °C. $[\alpha]^{20}_D$ +185.0 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 2962, 2836, 1697, 1707, 1488, 1362, 1241, 1134 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.54–7.03 (16H, m, ArH, COCH), 5.07 (1H, ddd, *J* = 8.2, 5.3, 0.9 Hz, NCH), 3.32 (1H, dd, *J* = 11.5, 8.2 Hz, SCH_aH_b), 2.90 (1H, dd, *J* = 11.5, 0.9 Hz, SCH_aH_b), 2.10–2.00 (1H, m, $CH(CH_3)_2$), 1.10 (3H, d, *J* = 7.2 Hz, CH_3), 1.04 (3H, d, *J* = 6.9 Hz, CH_3), 0.83 (3H, d, *J* = 6.9 Hz, CH_3). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 203.7 (C), 175.2 (C), 144.0 (C), 128.7 (CH), 127.7 (CH), 126.9 (CH) 72.2 (CH), 60.5 (C), 42.7 (CH), 30.7 (CH), 28.4 (CH_2), 19.0 (CH_3), 17.4 (CH_3), 16.6 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{28}H_{30}NOS_2$ $[M+H]^+$: 460.1763; found: 460.1767.

Alkylation with tropylium tetrafluoroborate



2h

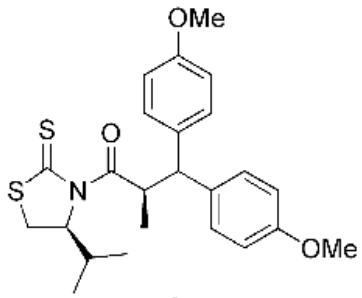
Solid $(Me_3P)_2NiCl_2$ (28.0 mg, 0.10 mmol, 20 mol %) was added to a solution of **1** (109 mg, 0.5 mmol) and tropylium tetrafluoroborate (133 mg, 0.75 mmol) in CH_2Cl_2 (1.0 mL) at room temperature under N_2. This mixture was cooled at –20 °C. Then, TESOTf (57 μL, 0.25 mmol) was added. Finally, 2,6-lutidine (88 μL, 0.75 mmol) was added four minutes later. The resultant mixture was stirred at –20 °C for 2 h.

The reaction was quenched by addition of sat NH_4Cl (1.2 mL) and the mixture was stirred vigorously for five minutes at room temperature. It was partitioned with CH_2Cl_2 (20 mL) and water (20 mL). The aqueous layer was further extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic extracts were

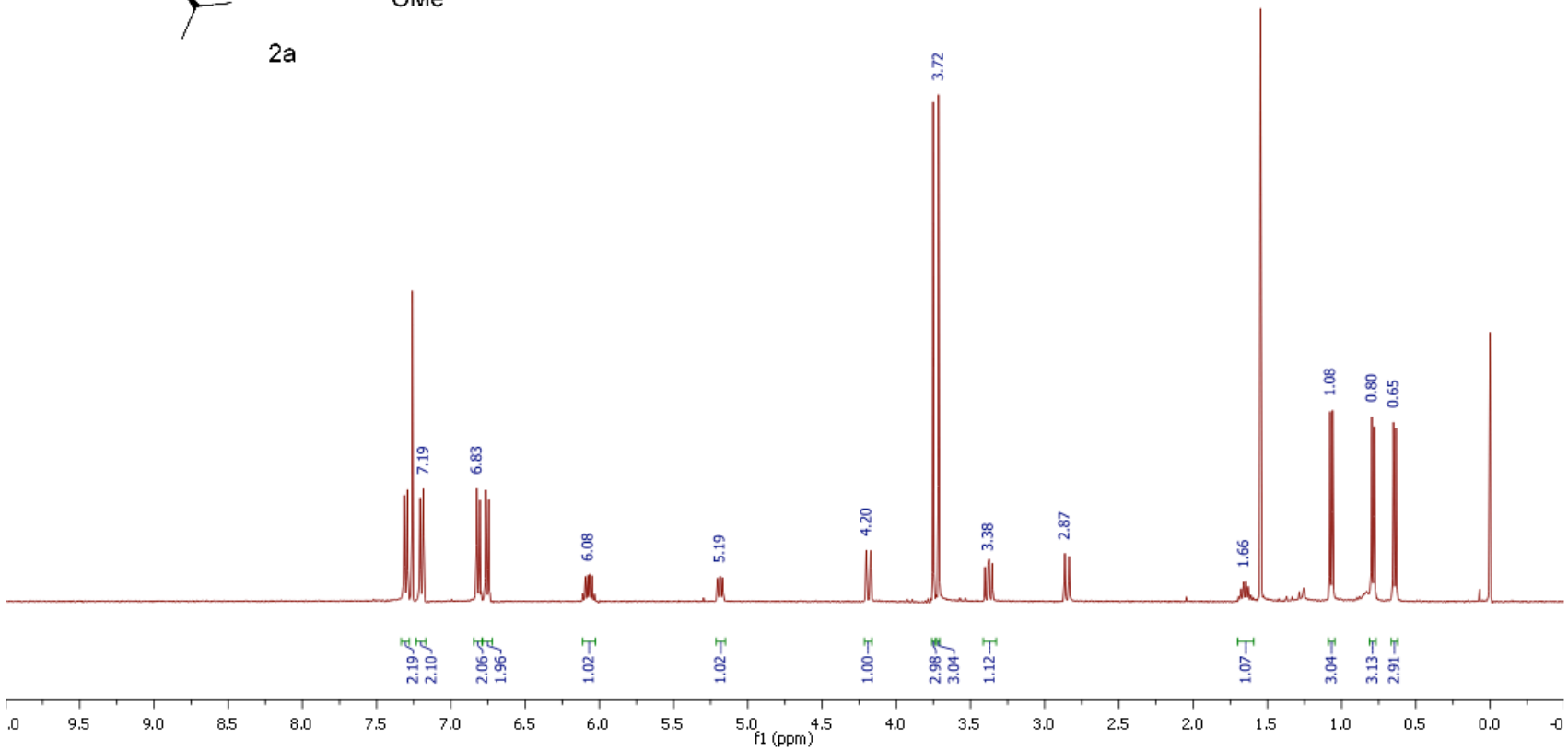
washed with brine (30 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (from hexanes/CH_2Cl_2 30:70 to 20:80) to afford 114 mg (0.37 mmol, 74% yield) of (*S*)-*N*-[(*R*)-2-(cyclohepta-2,4,6-trien-1-yl)propanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (**2h**) as a yellow oil. $\boldsymbol{R_f}$ (hexanes/ CH_2Cl_2 30:70) 0.70. $\boldsymbol{[\alpha]^{20}_D}$ +225.0 (*c* 1.00, $CHCl_3$). **IR** (ATR) ν 3011, 2959, 2925, 2870, 1683, 1457, 1360, 1253, 1231, 1145 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.68–6.62 (2H, m, COCHCHCH=CHC<u>H</u>=C<u>H</u>), 6.27–6.15 (2H, m, C<u>H</u>=CHCHCH=C<u>H</u>), 5.32 (2H, dt, *J* = 9.5, 5.8 Hz, CH=C<u>H</u>CHC<u>H</u>=CH), 5.21 (1H, ddd, *J* = 8.1, 6.0, 1.2 Hz, NC<u>H</u>), 5.09 (1H, dq, *J* = 8.4, 6.9 Hz, COC<u>H</u>), 3.47 (1H, dd, *J* = 11.5, 8.1 Hz, SC<u>H</u>$_a$H$_b$), 2.98 (1H, dd, *J* = 11.5, 1.2 Hz, SCH$_a$<u>H</u>$_b$), 2.38–2.32 (1H, m, C<u>H</u>$(CH_3)_2$), 2.23 (1H, dtt, *J* = 8.4, 5.8, 1.2 Hz, COCHC<u>H</u>), 1.27 (3H, d, *J* = 6.9 Hz, COCHC<u>H</u>$_3$), 1.04 (3H, d, *J* = 6.8 Hz, C<u>H</u>$_3$), 0.97 (3H, d, *J* = 7.0 Hz, C<u>H</u>$_3$). **^{13}C NMR** ($CDCl_3$, 100.6 MHz) δ 202.7 (C), 176.9 (C), 131.0 (CH), 130.6 (CH), 125.4 (CH), 125.0 (CH), 124.6 (CH), 122.6 (CH), 71.9 (CH), 42.0 (CH), 39.6 (CH), 30.8 (CH), 29.7 (CH_2), 19.2 (CH_3), 17.6 (CH_3), 15.1 (CH_3). **HRMS** (+ESI): *m/z* calcd. for $C_{16}H_{22}NOS_2$ $[M+H]^+$: 308.1137; found: 308.1139.

11. ^{1}H and ^{13}C Spectra

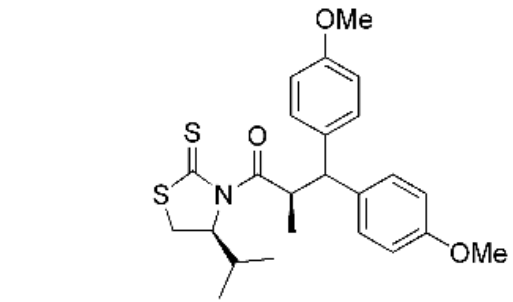
^{1}H NMR (400 MHz, $CDCl_3$)



2a

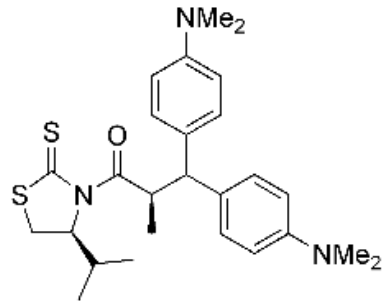


^{13}C NMR (100.6 MHz, $CDCl_3$)



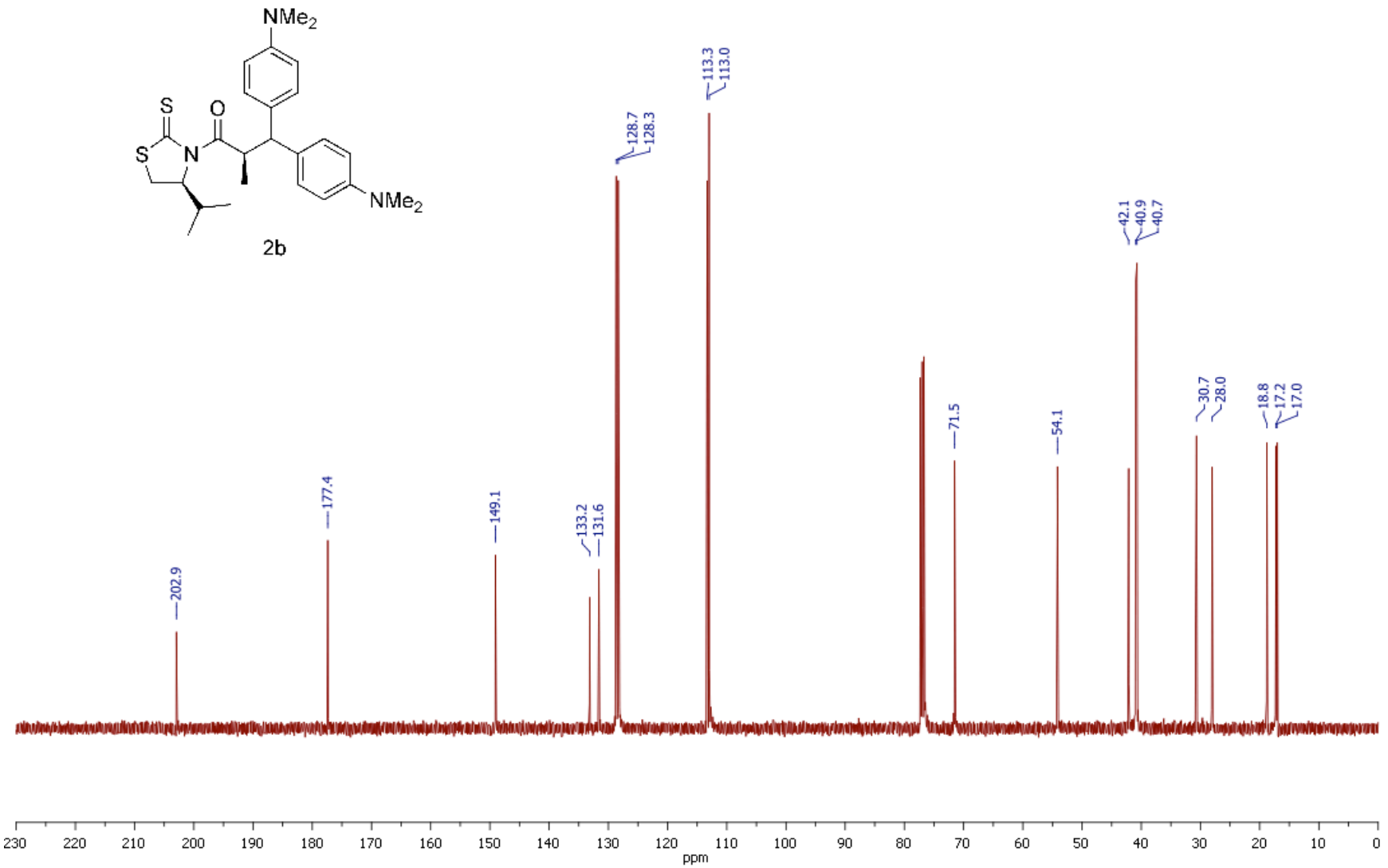
2a

^{1}H NMR (400 MHz, $CDCl_3$)

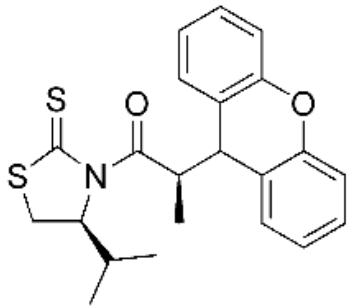


2b

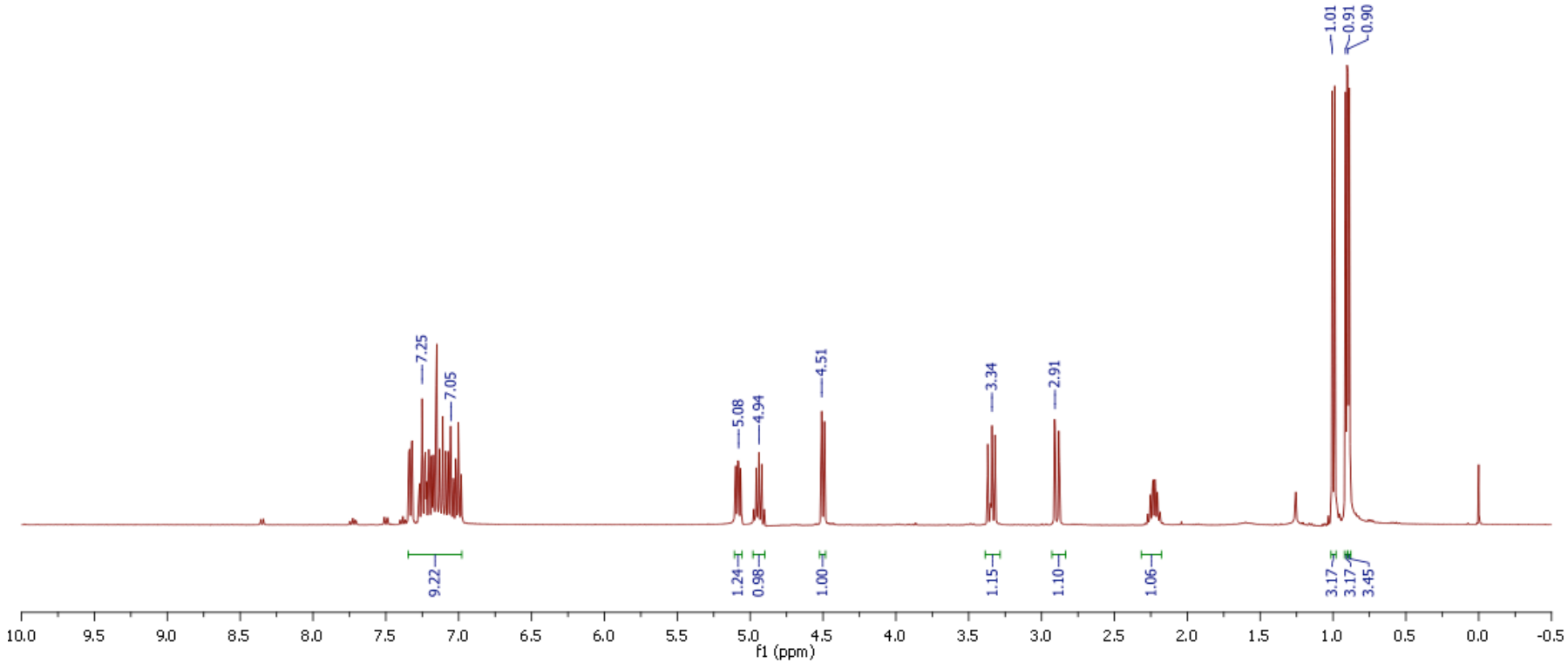
^{13}C NMR (100.6 MHz, $CDCl_3$)



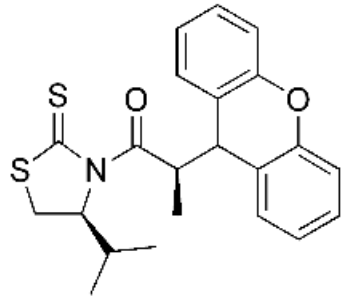
^{1}H NMR (400 MHz, $CDCl_3$)



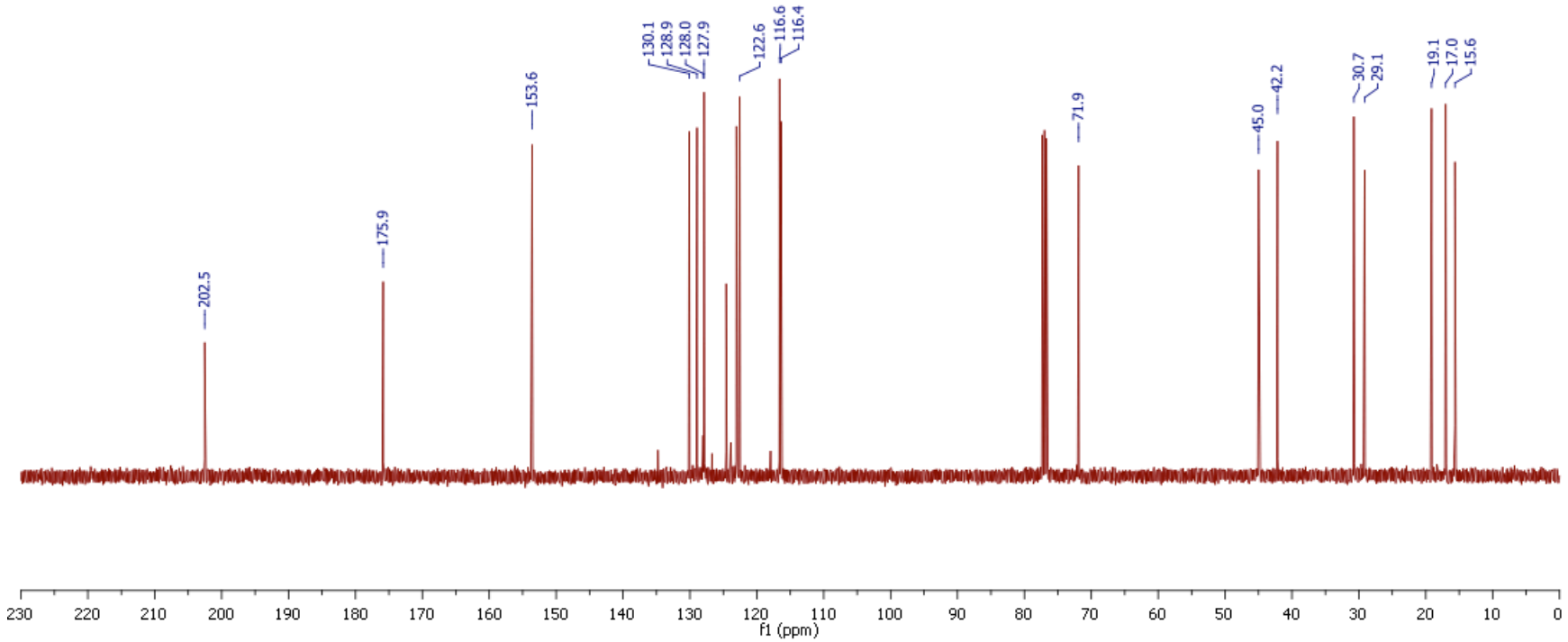
2c



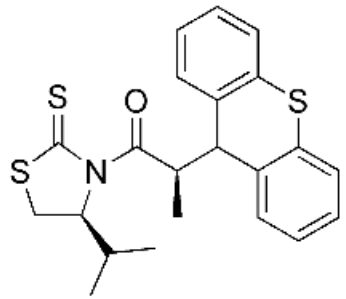
^{13}C NMR (100.6 MHz, $CDCl_3$)



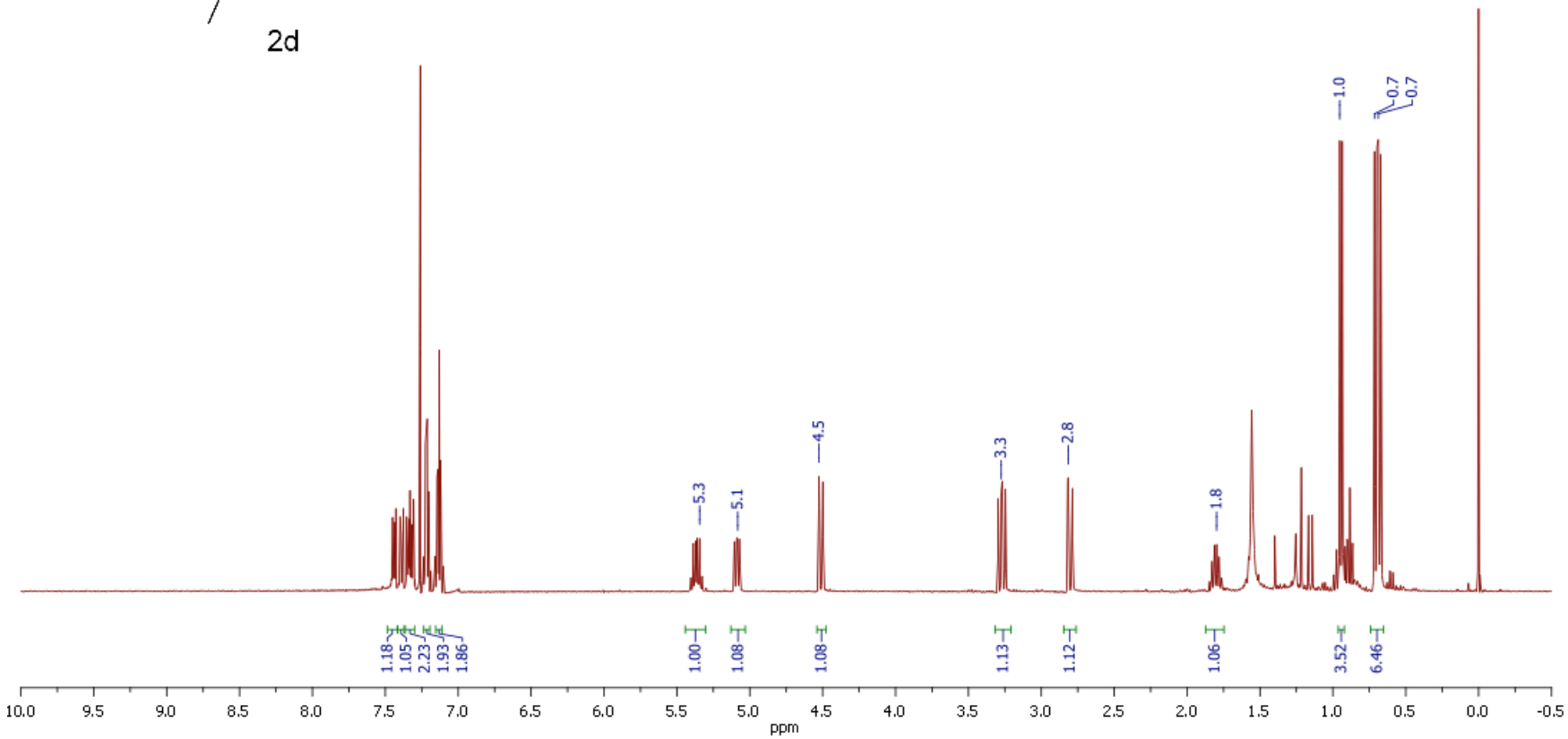
2c



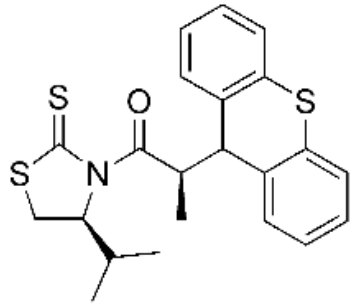
^{1}H NMR (400 MHz, $CDCl_3$)



2d

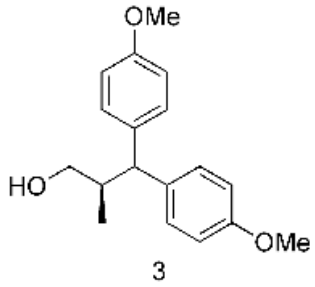


^{13}C NMR (100.6 MHz, $CDCl_3$)



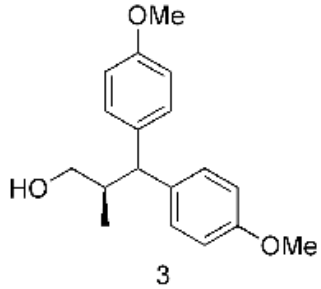
2d

^{1}H NMR (400 MHz, $CDCl_3$)



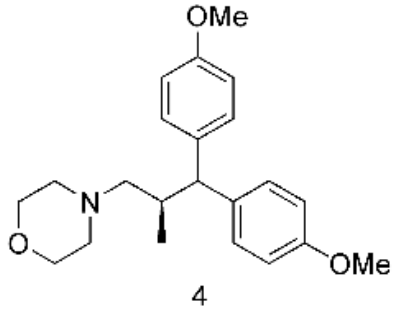
3

^{13}C NMR (100.6 MHz, $CDCl_3$)



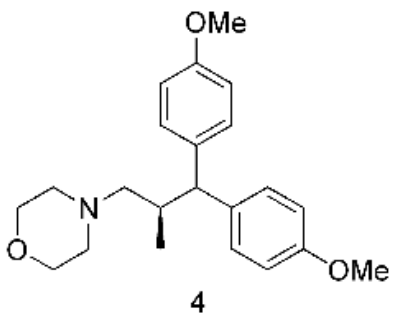
3

^{1}H NMR (400 MHz, $CDCl_3$)



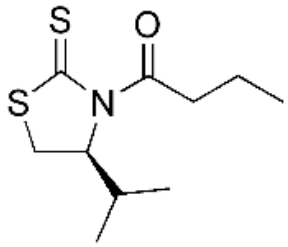
4

^{13}C NMR (100.6 MHz, $CDCl_3$)

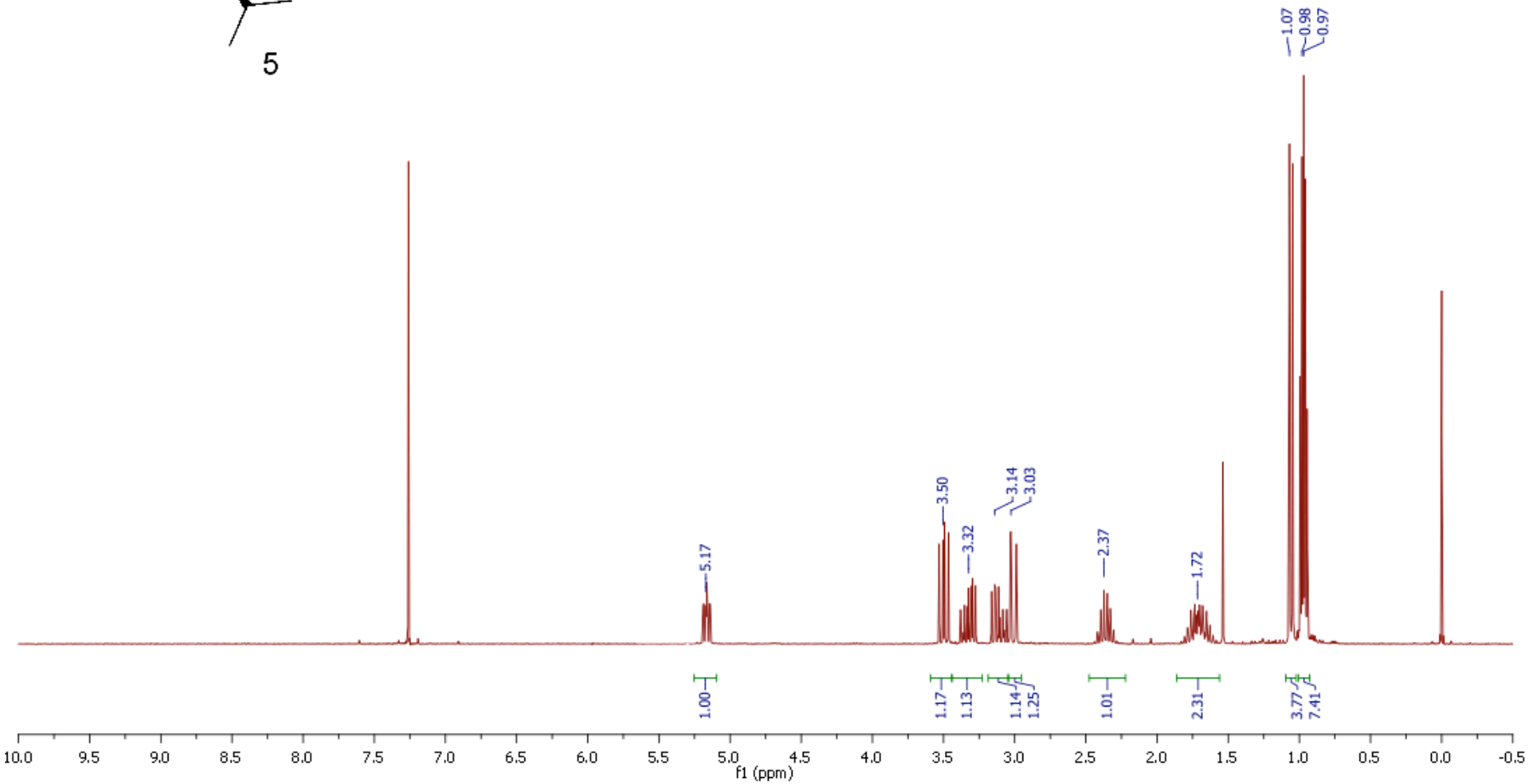


4

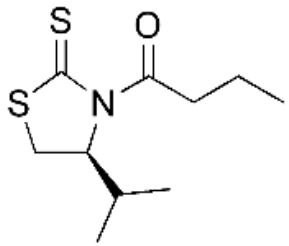
^{1}H NMR (400 MHz, $CDCl_3$)



5



^{13}C NMR (100.6 MHz, $CDCl_3$)



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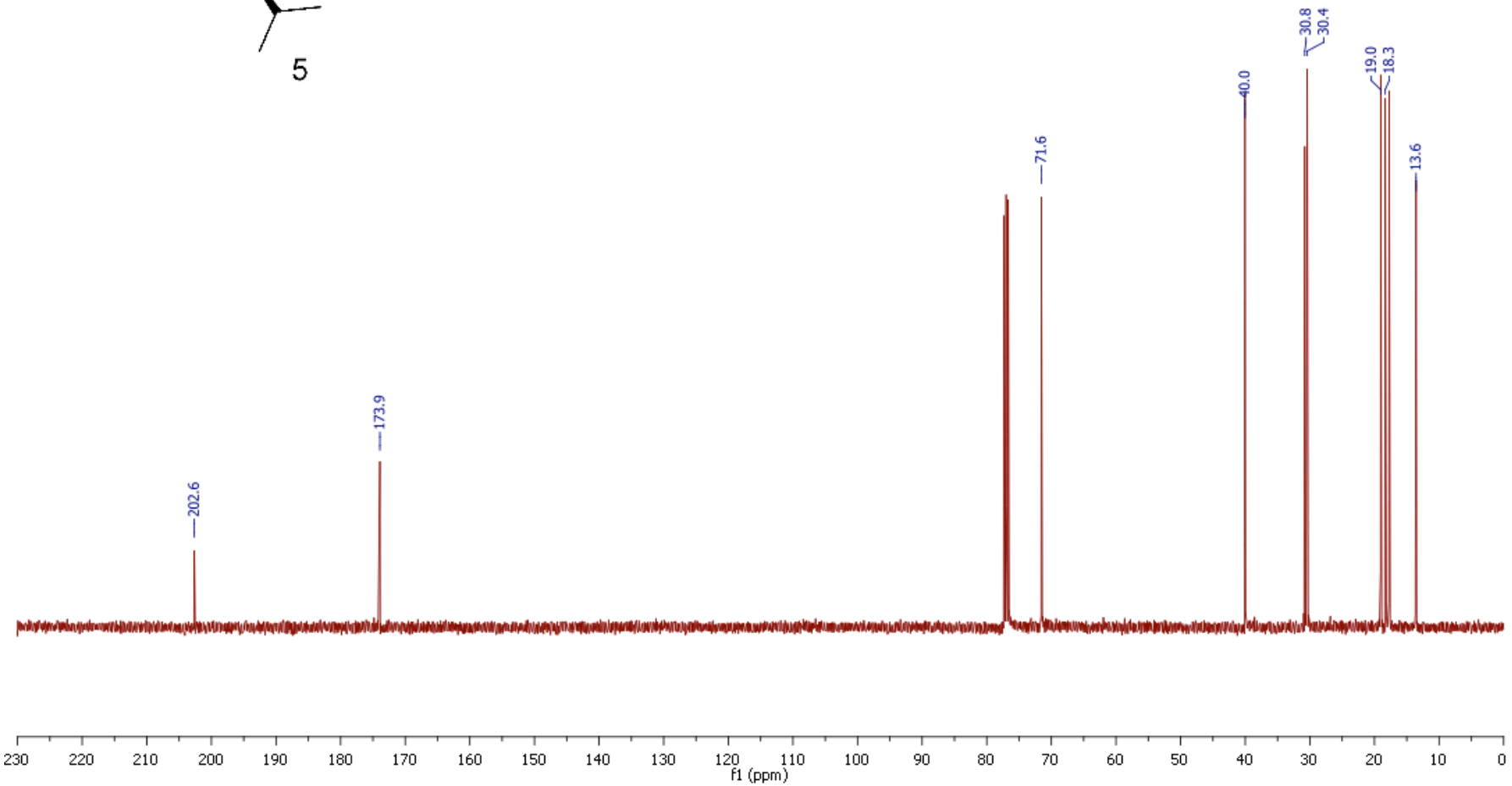
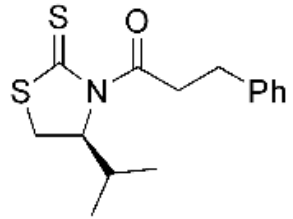
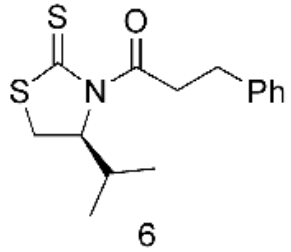


^{1}H NMR (400 MHz, $CDCl_3$)



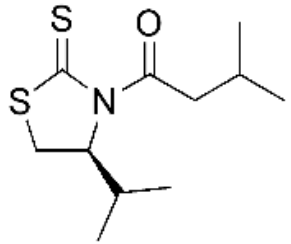
6

^{13}C NMR (100.6 MHz, $CDCl_3$)



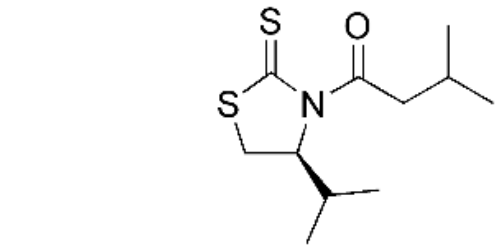
6

^{1}H NMR (400 MHz, $CDCl_3$)



7

^{13}C NMR (100.6 MHz, $CDCl_3$)



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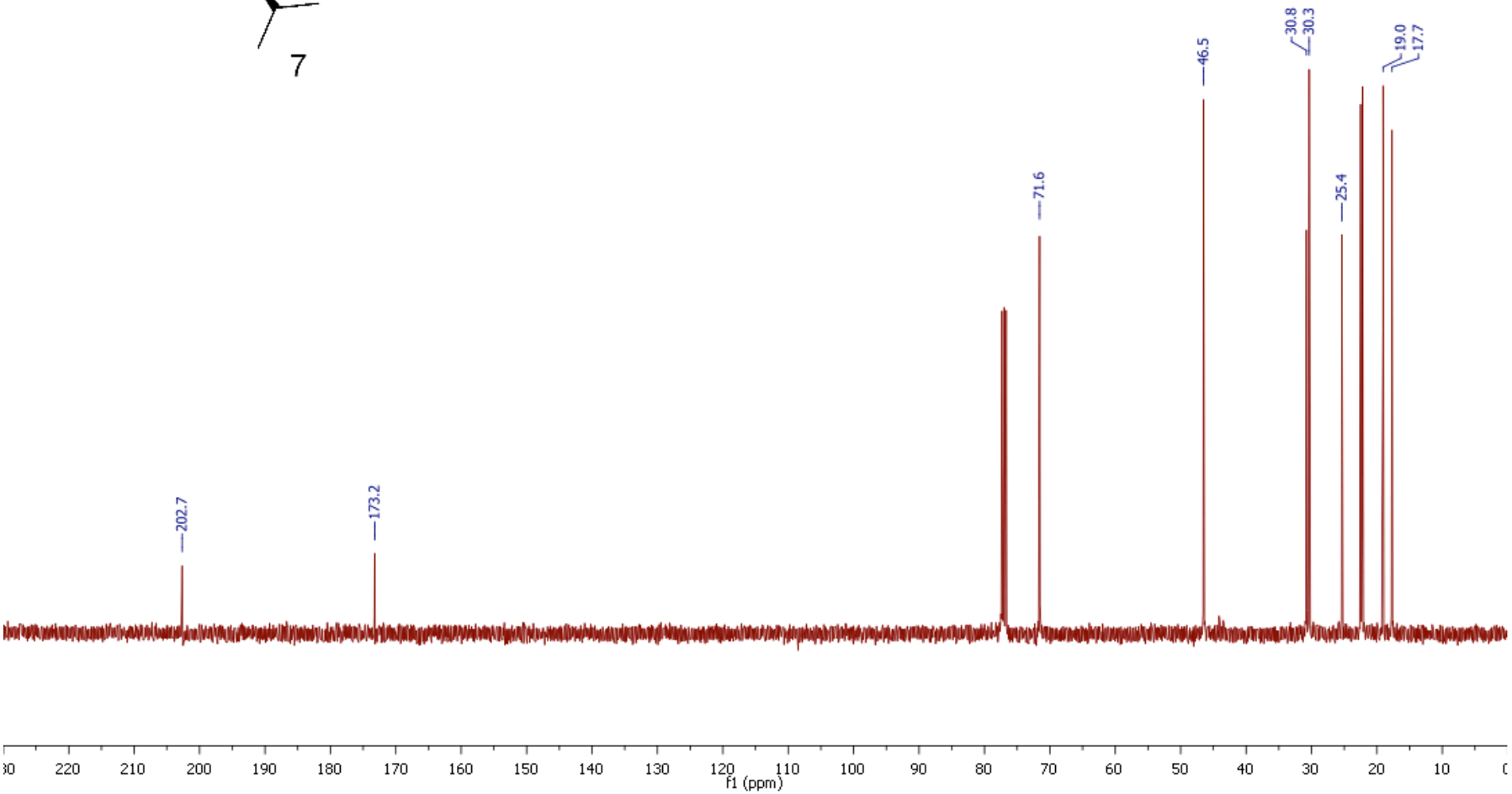
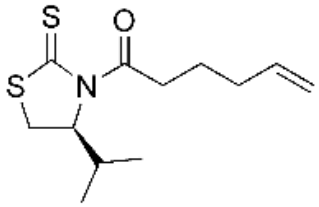


^{1}H NMR (400 MHz, $CDCl_3$)



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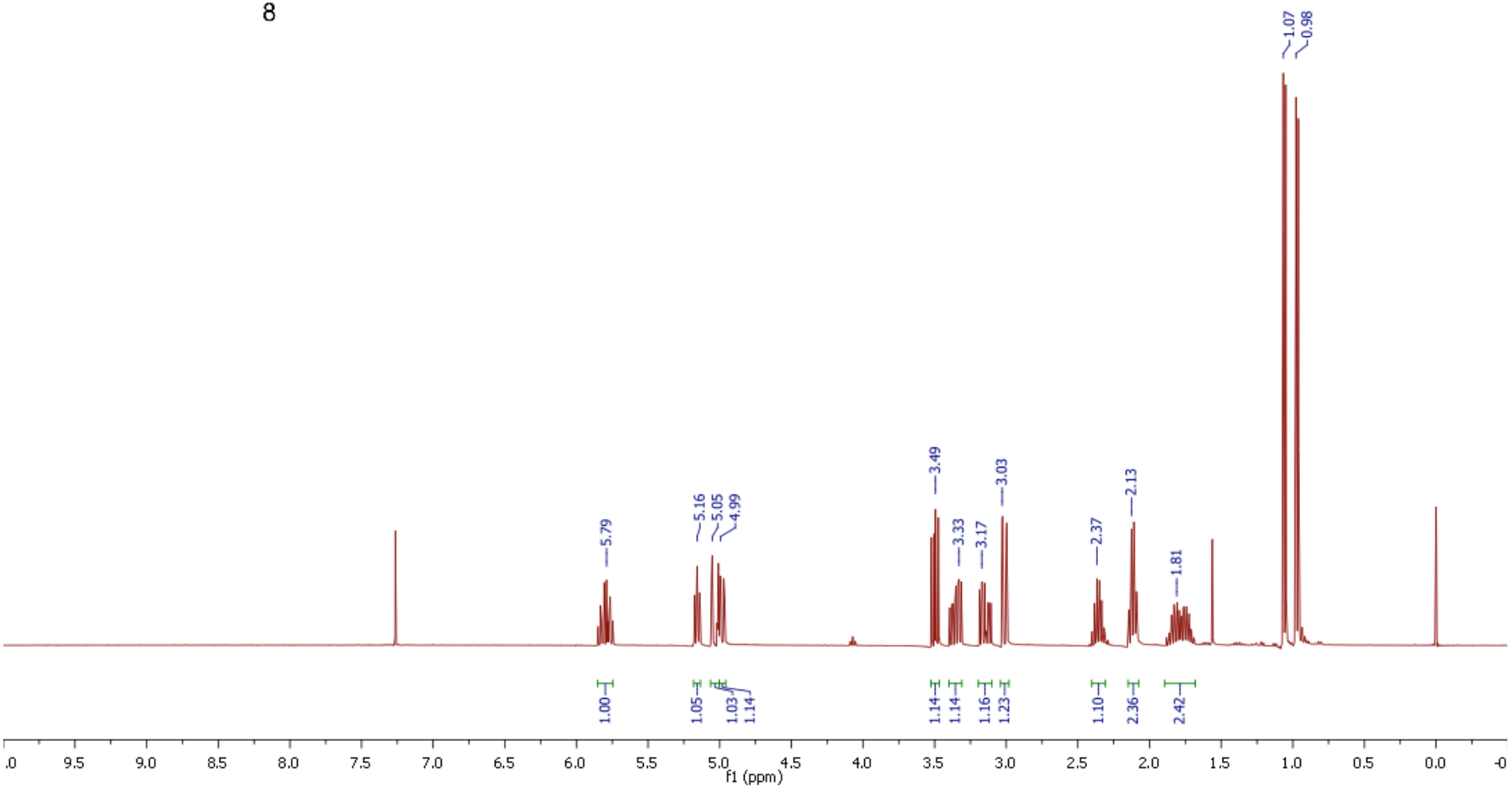
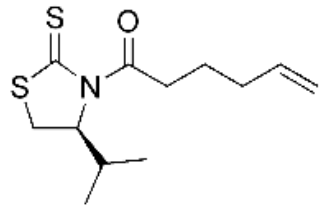
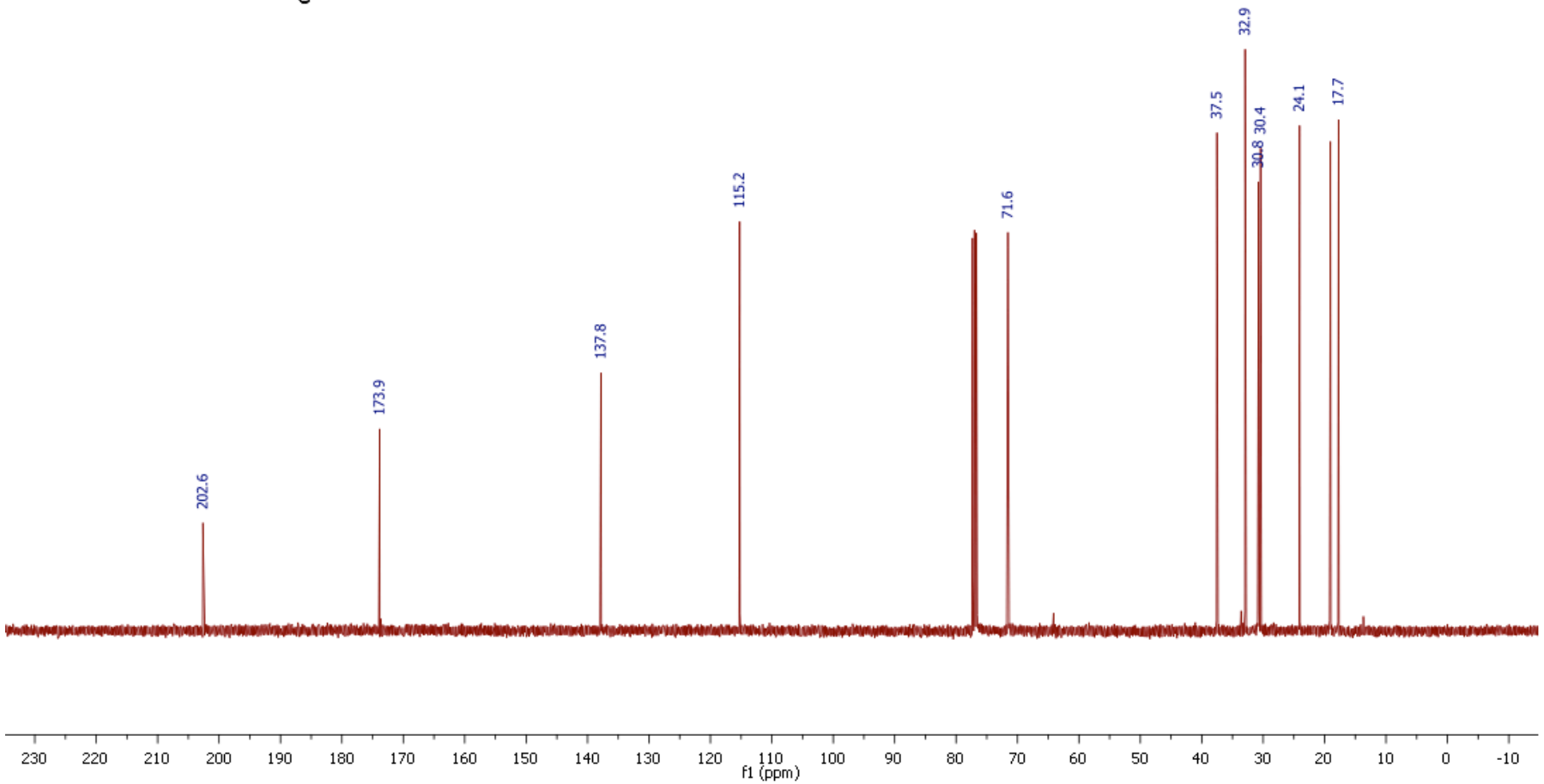


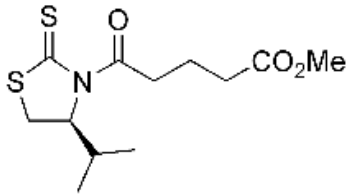
^{13}C NMR (100.6 MHz, $CDCl_3$)



8

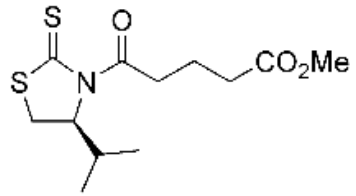


^{1}H NMR (400 MHz, $CDCl_3$)

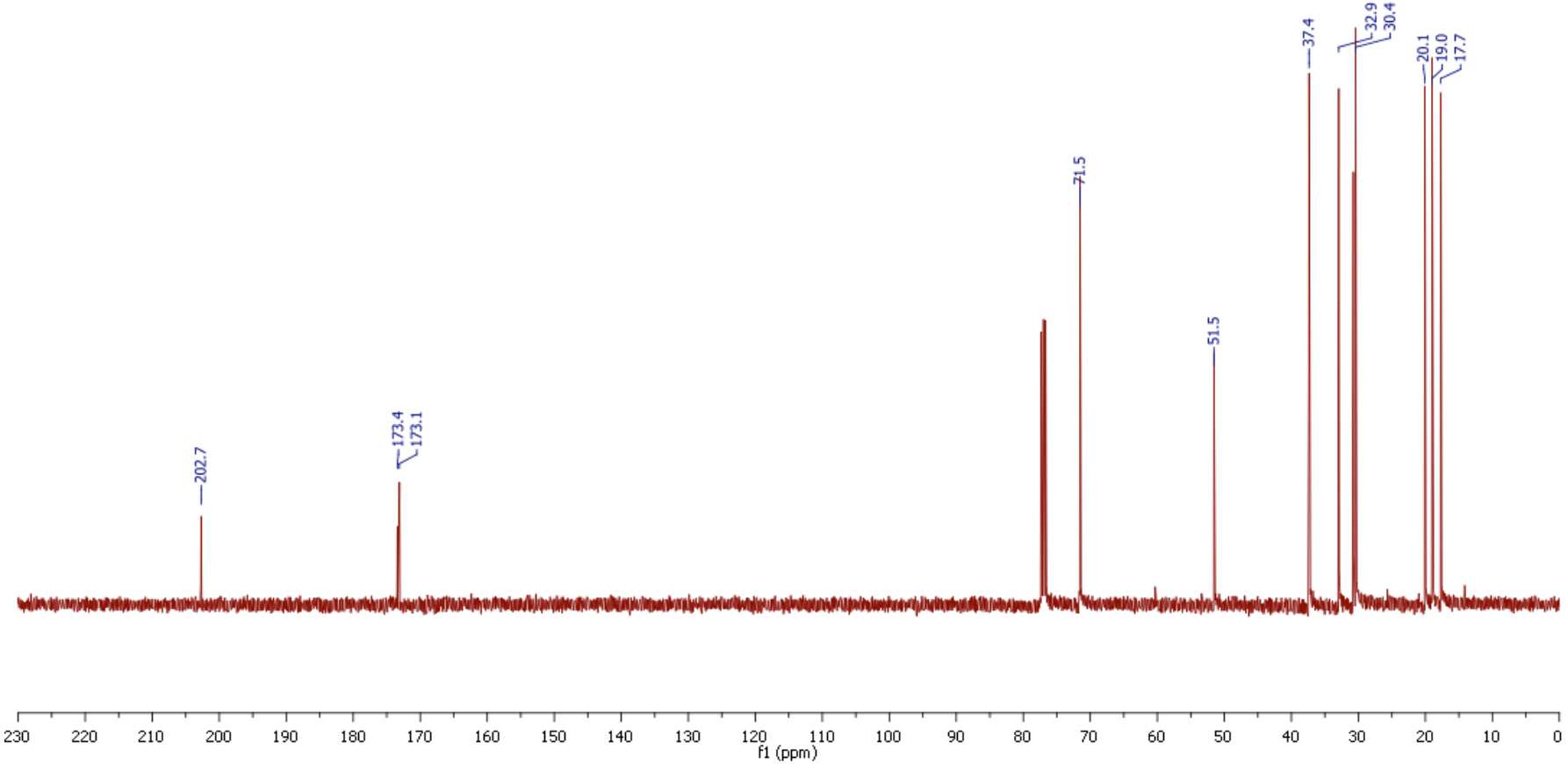


9

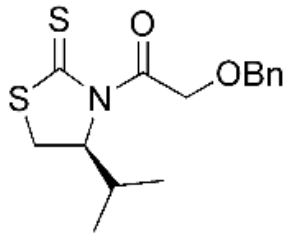
^{13}C NMR (100.6 MHz, $CDCl_3$)



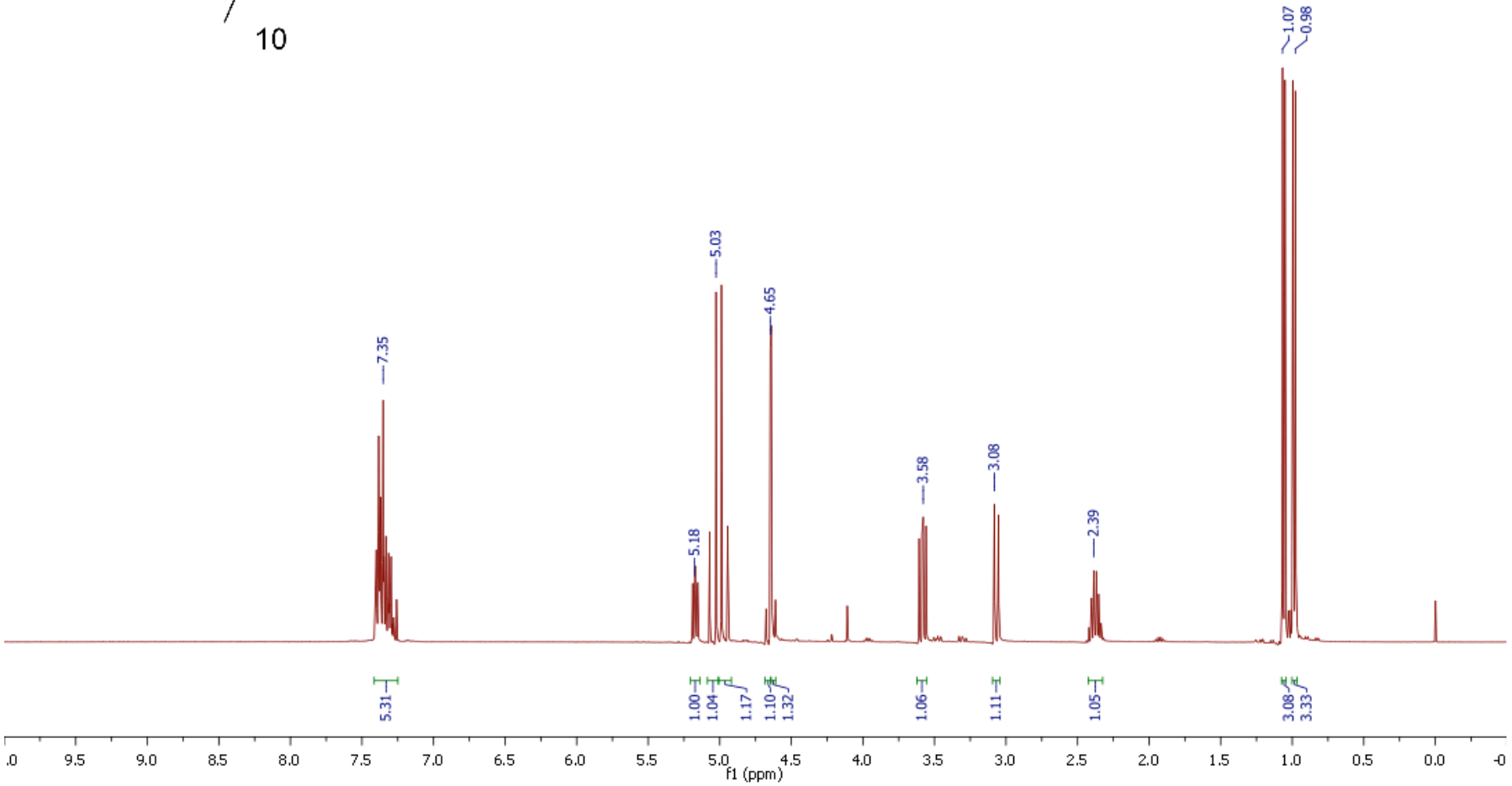
9



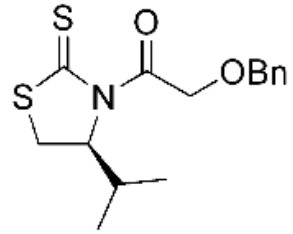
^{1}H NMR (400 MHz, $CDCl_3$)



10

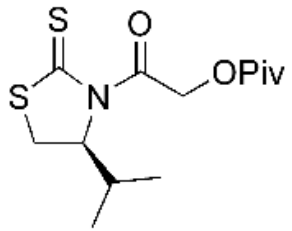


^{13}C NMR (100.6 MHz, $CDCl_3$)



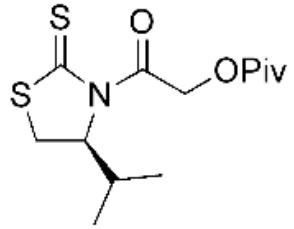
10

^{1}H NMR (400 MHz, $CDCl_3$)



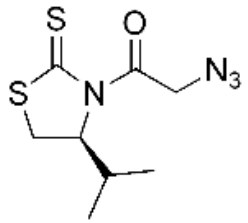
11

^{13}C NMR (100.6 MHz, $CDCl_3$)



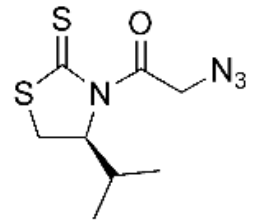
11

^{1}H NMR (400 MHz, $CDCl_3$)

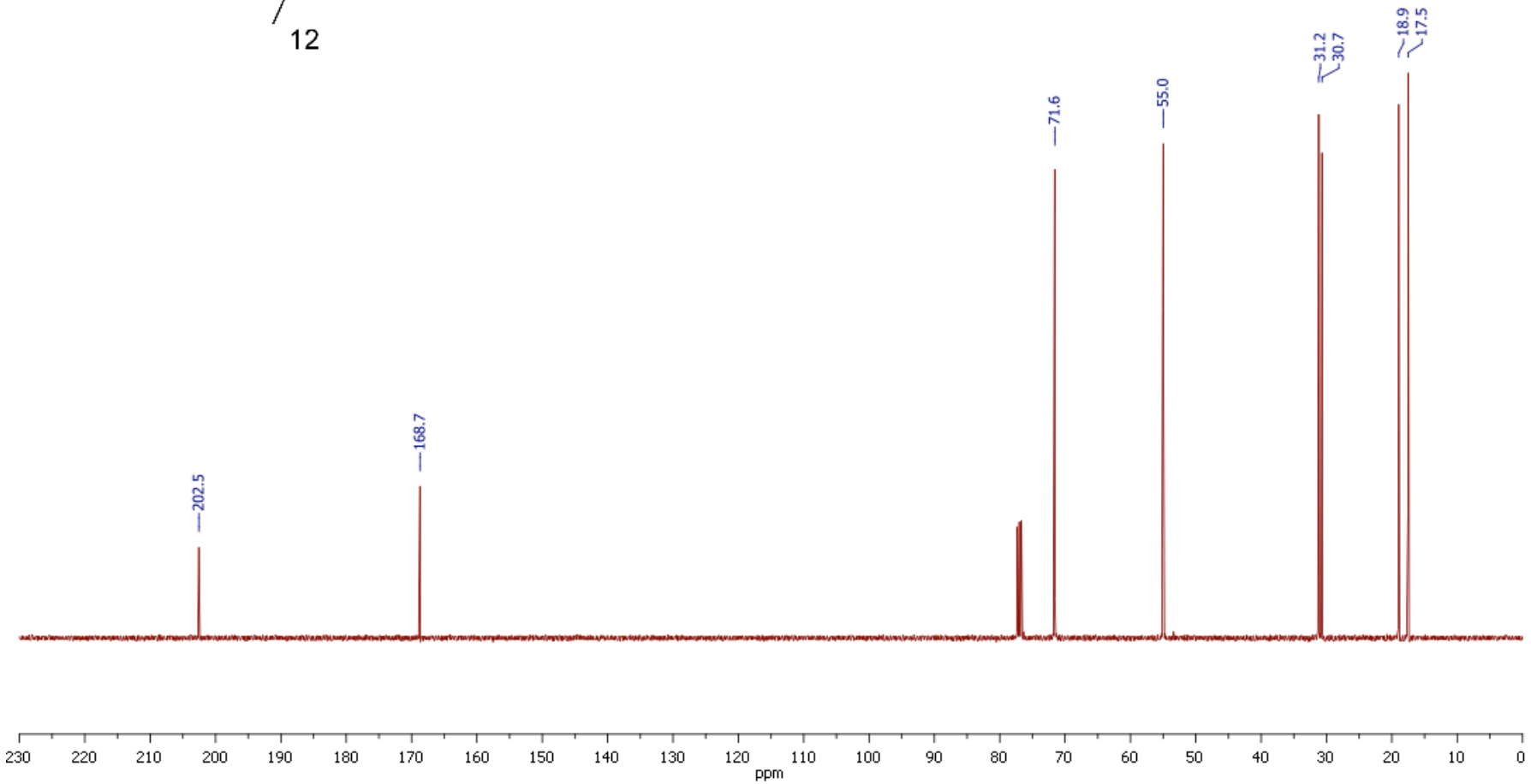


12

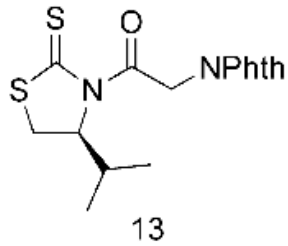
^{13}C NMR (100.6 MHz, $CDCl_3$)



12

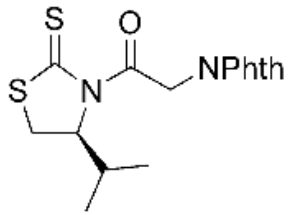


^{1}H NMR (400 MHz, $CDCl_3$)

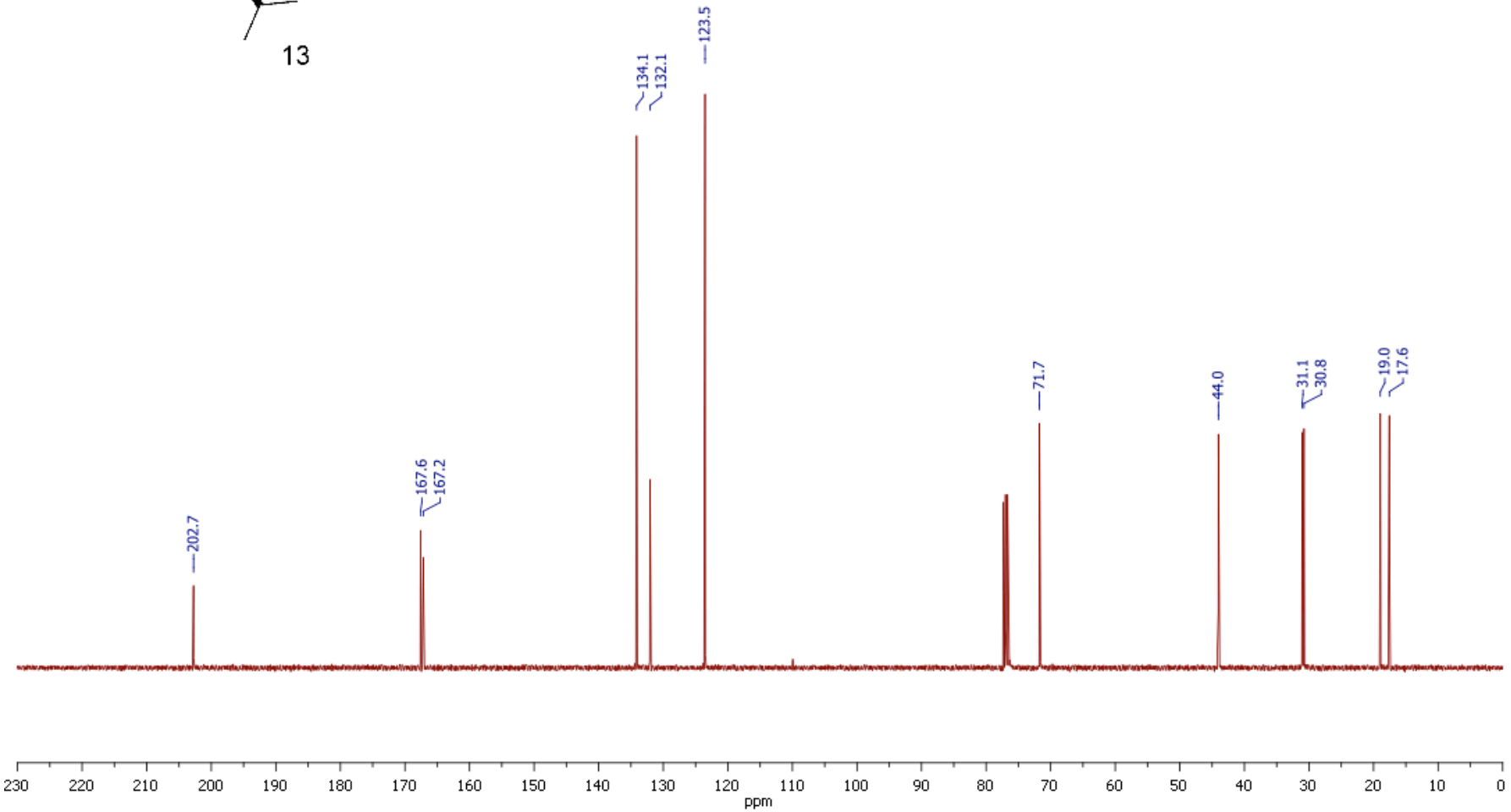


13

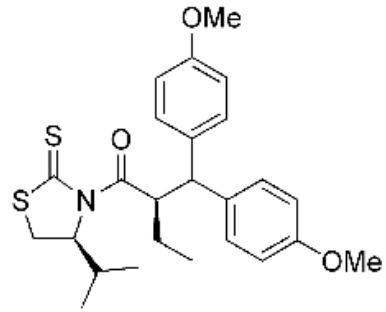
^{13}C NMR (100.6 MHz, $CDCl_3$)



13

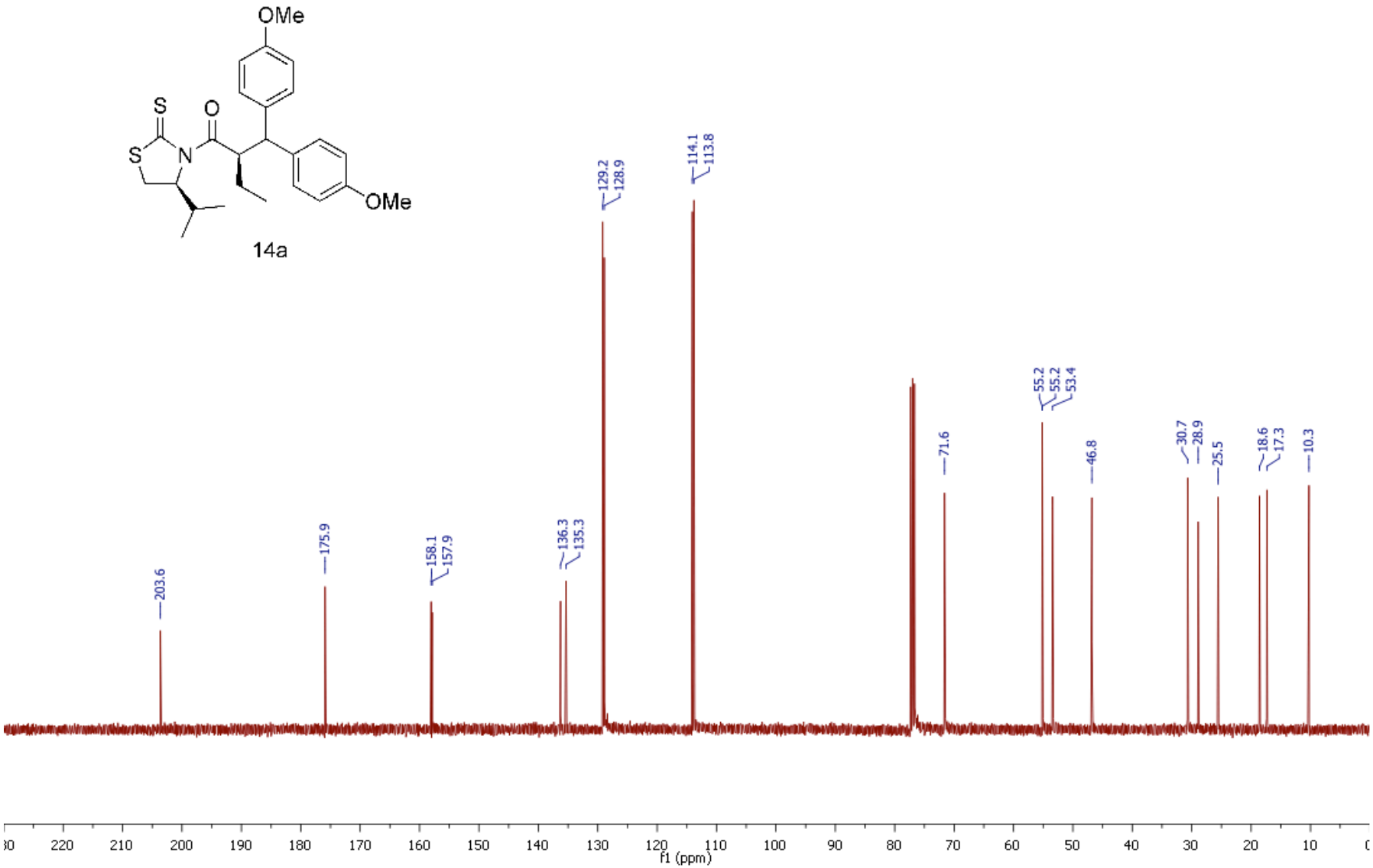


^{1}H NMR (400 MHz, $CDCl_3$)

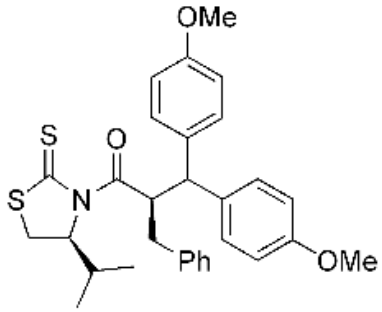


14a

^{13}C NMR (100.6 MHz, $CDCl_3$)

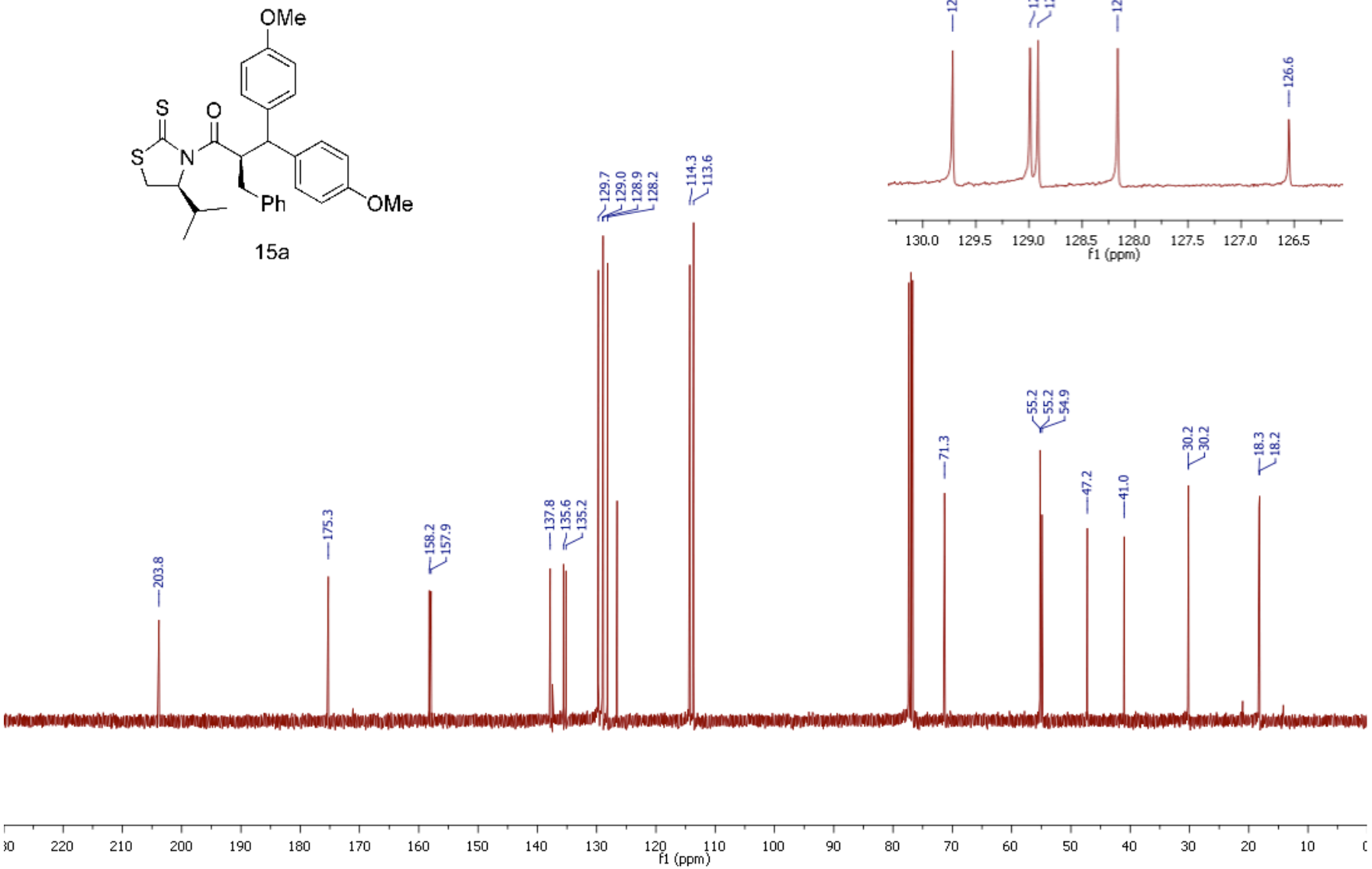


^{1}H NMR (400 MHz, $CDCl_3$)

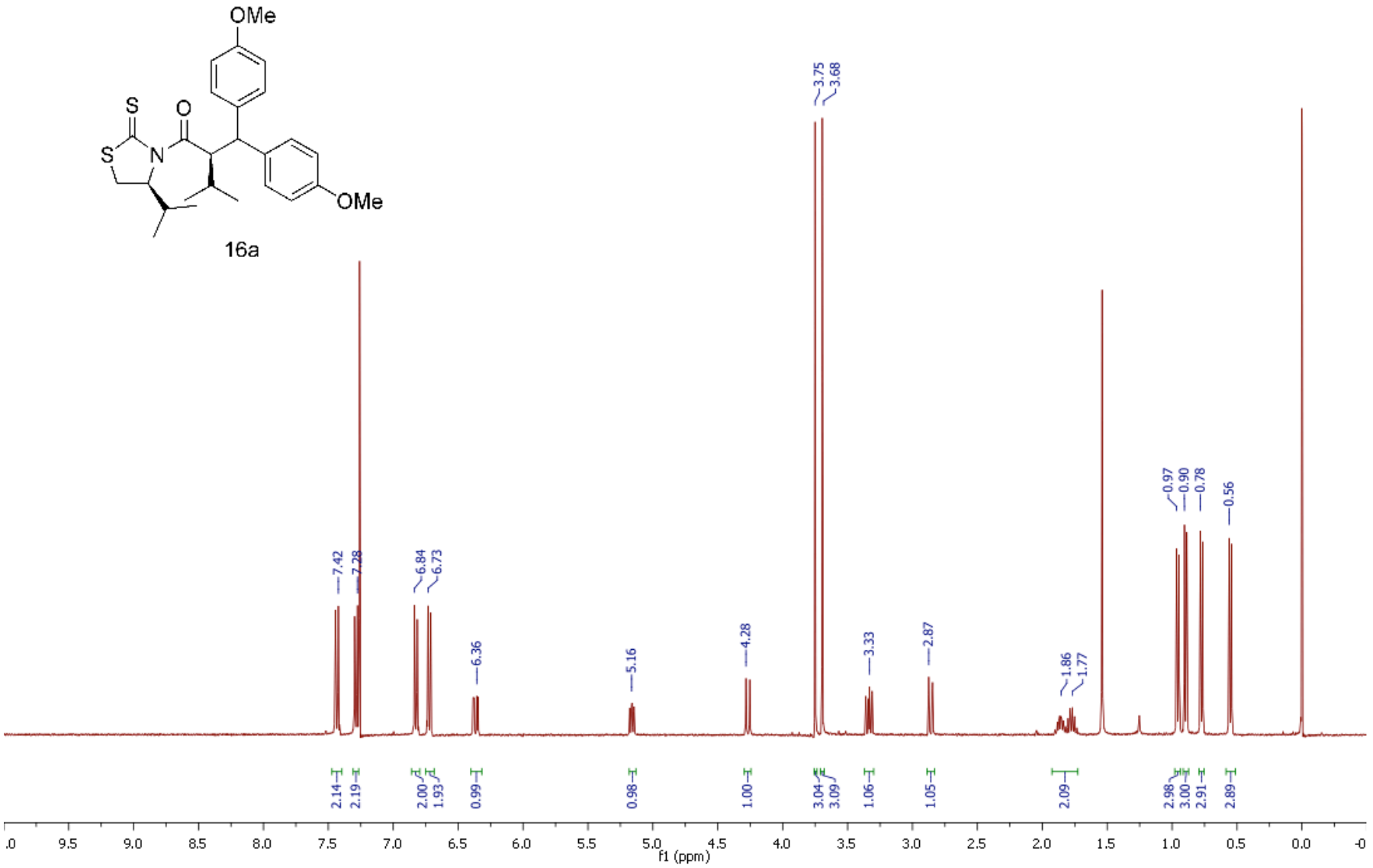


15a

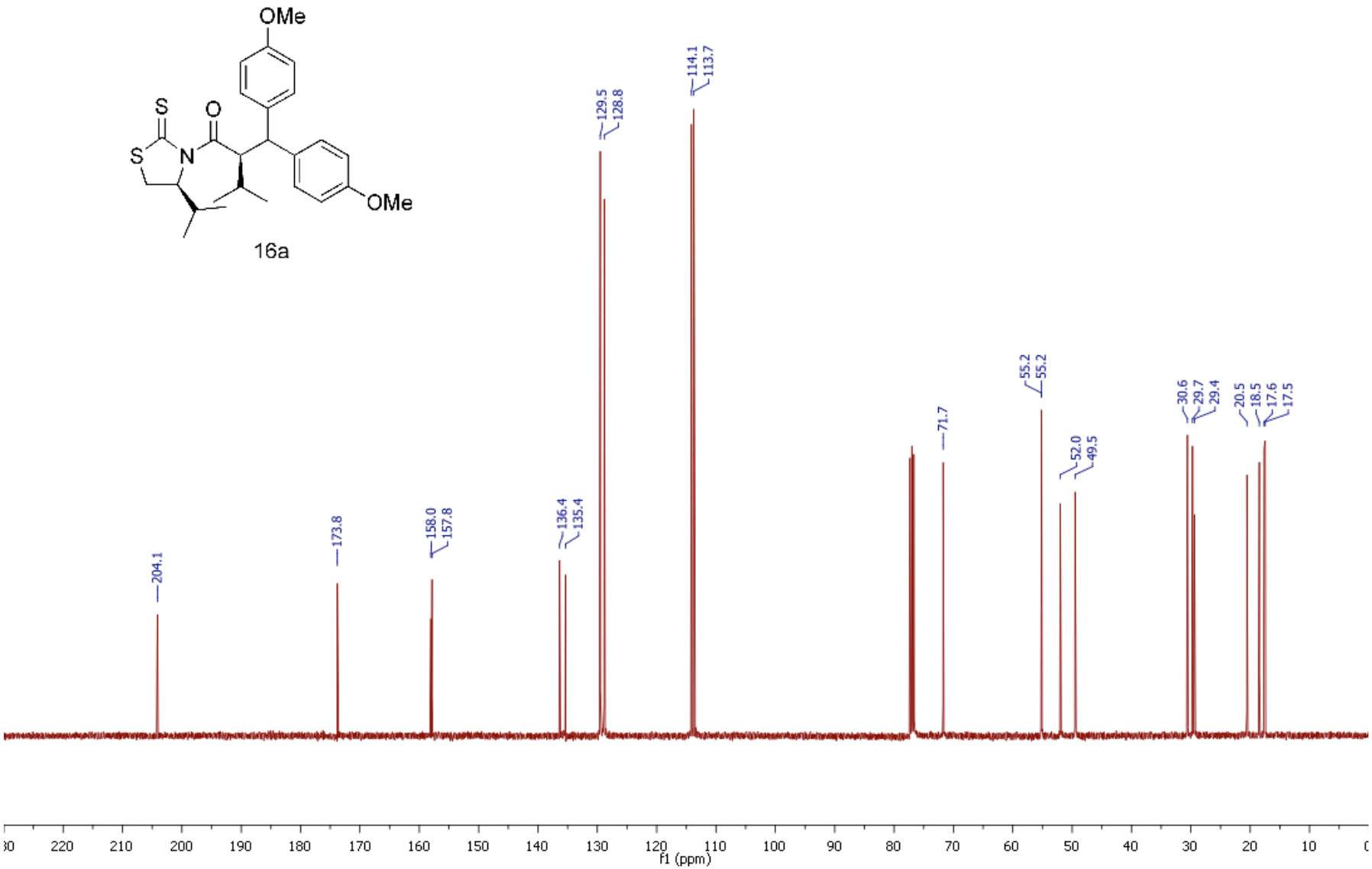
^{13}C NMR (100.6 MHz, $CDCl_3$)



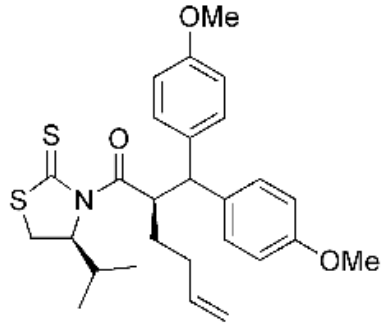
^{1}H NMR (400 MHz, $CDCl_3$)



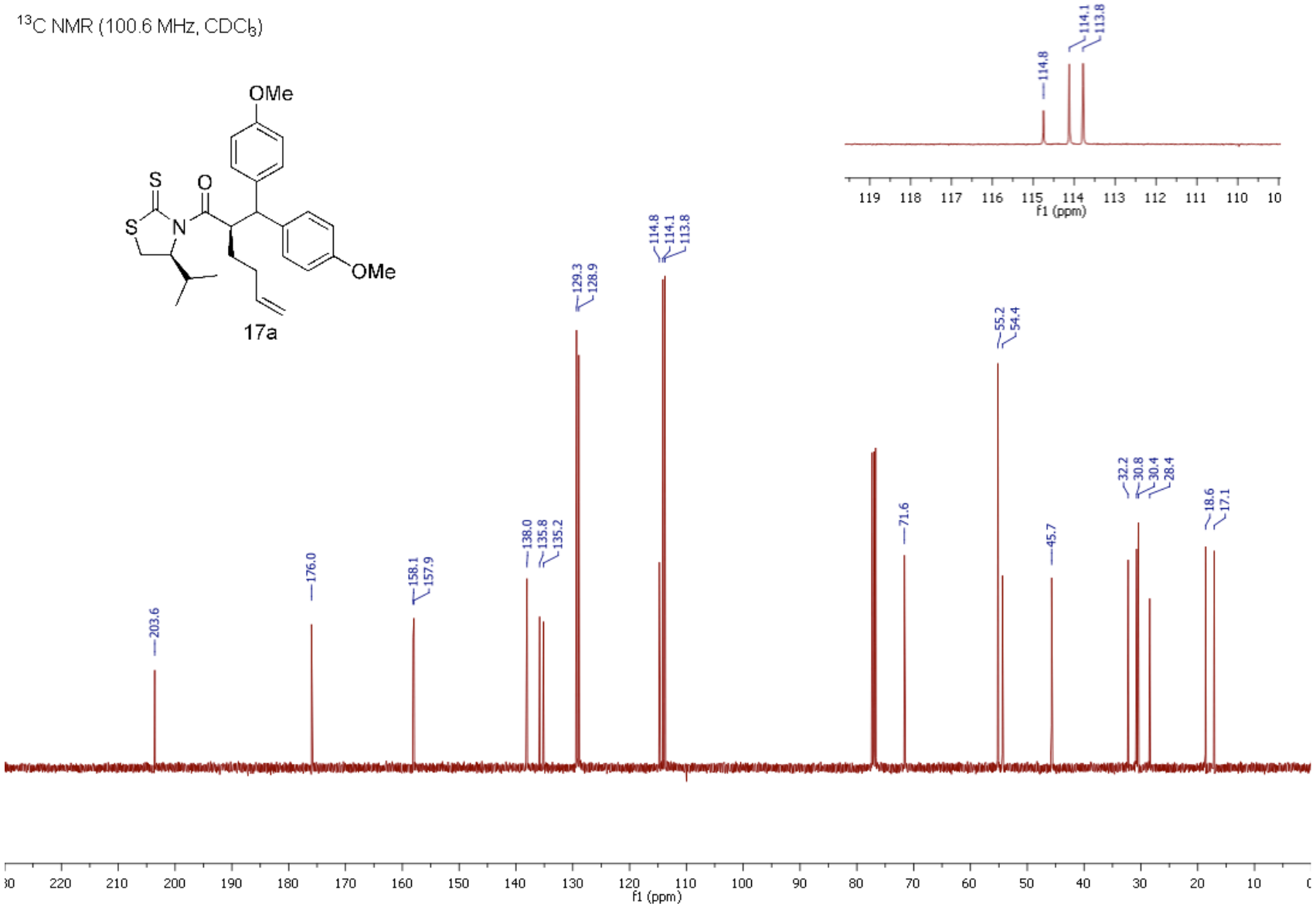
^{13}C NMR (100.6 MHz, $CDCl_3$)



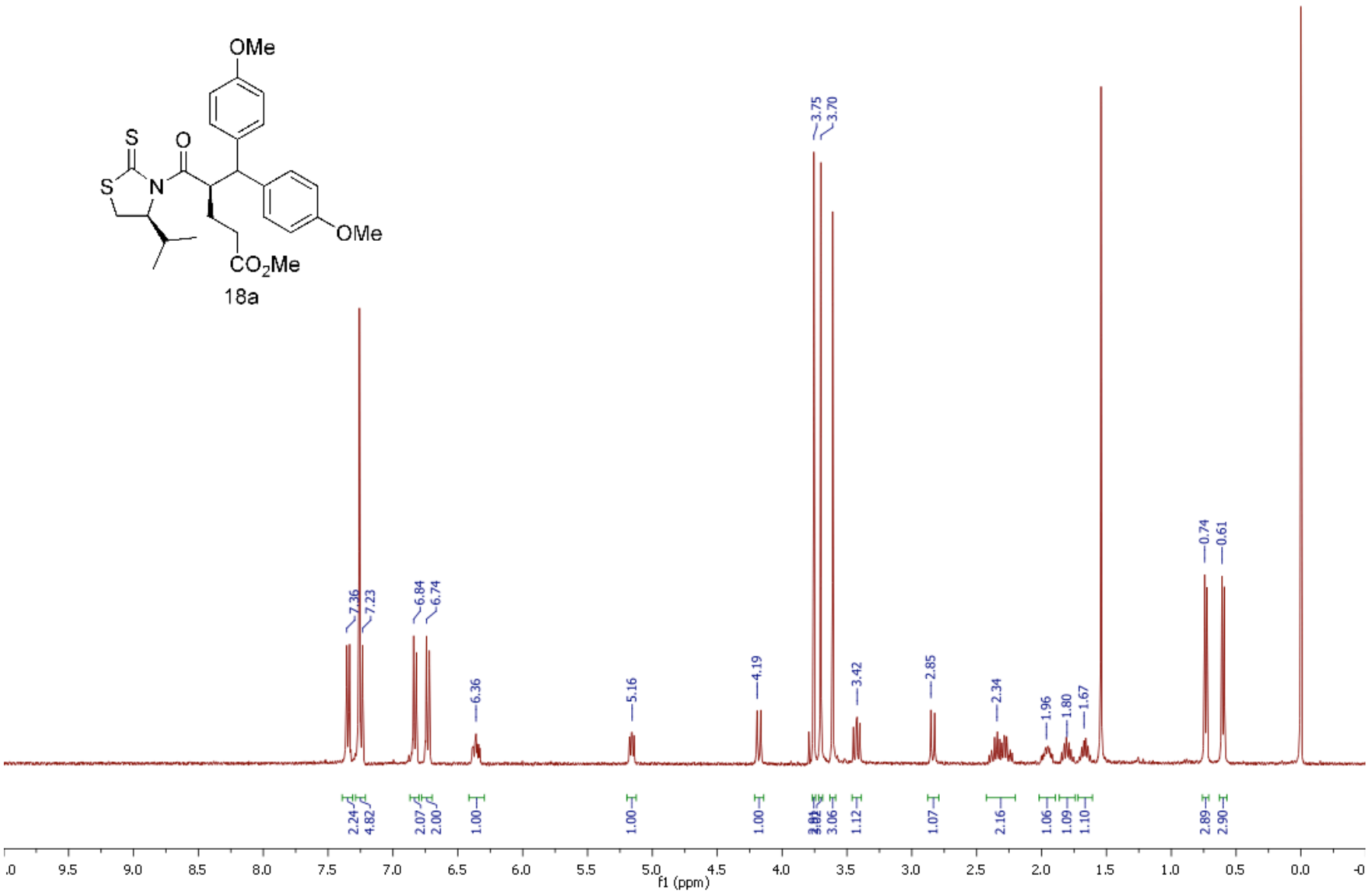
^{1}H NMR (400 MHz, $CDCl_3$)



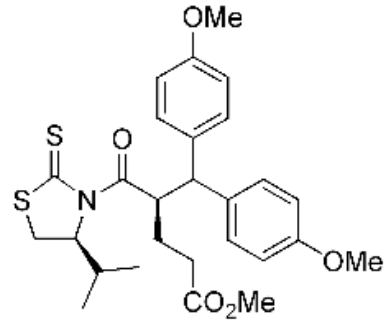
17a


^{13}C NMR (100.6 MHz, $CDCl_3$)
OMe
S
O
S
N
OMe
17a
114.8
114.1
113.8
119 118 117 116 115 114 113 112 111 110 10
f1 (ppm)
203.6
176.0
158.1
157.9
138.0
135.8
135.2
129.3
128.9
114.8
114.1
113.8
71.6
55.2
54.4
45.7
32.2
30.8
30.4
28.4
18.6
17.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

^{1}H NMR (400 MHz, $CDCl_3$)

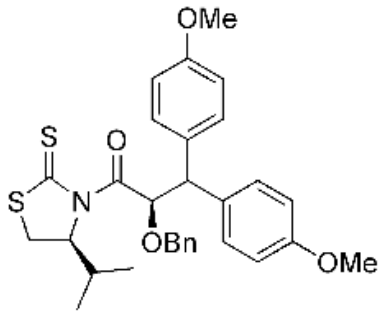


^{13}C NMR (100.6 MHz, $CDCl_3$)



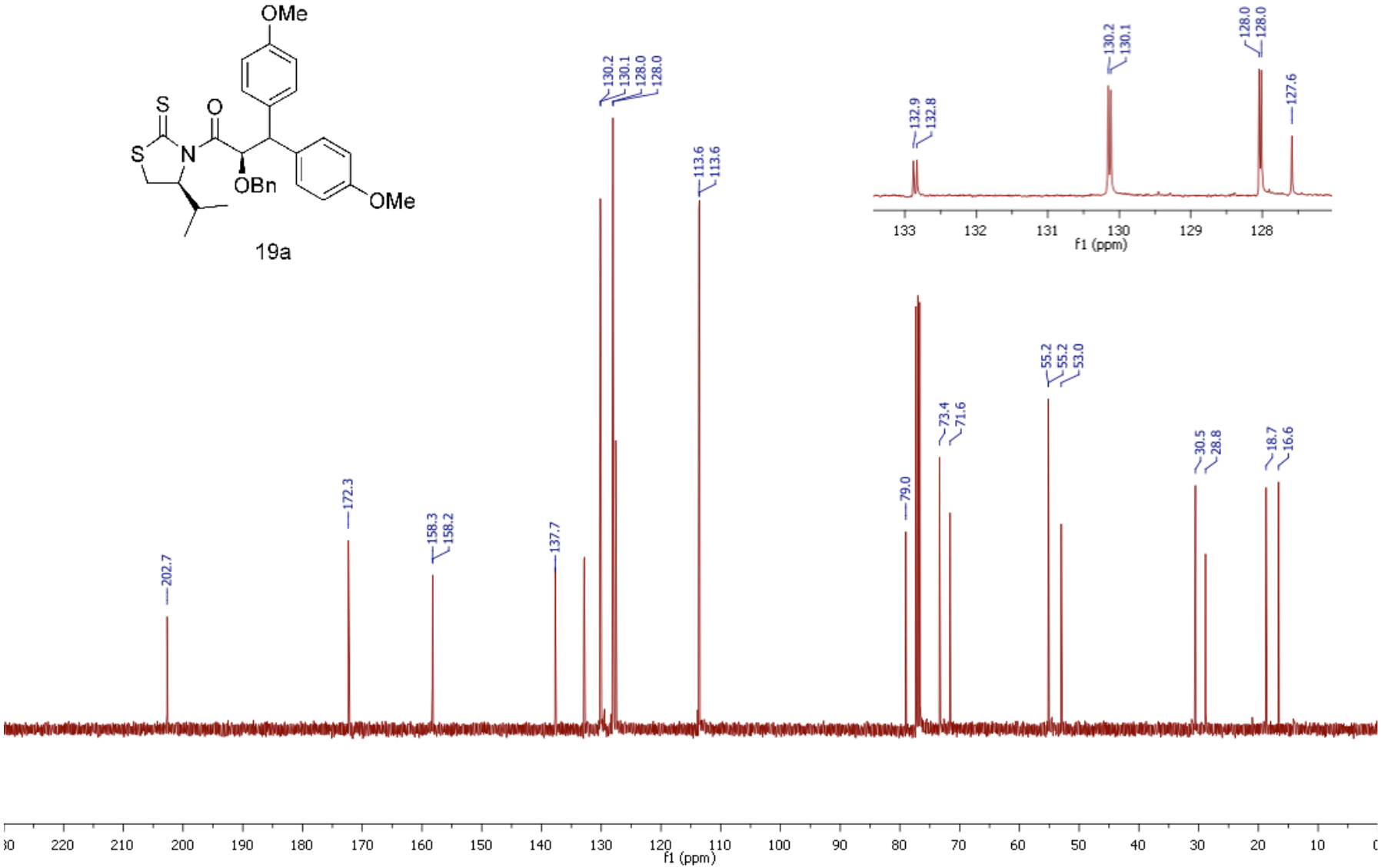
18a

^{1}H NMR (400 MHz, $CDCl_3$)

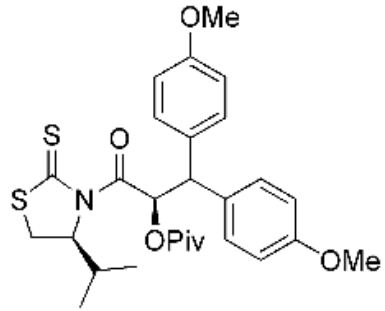


19a

^{13}C NMR (100.6 MHz, $CDCl_3$)

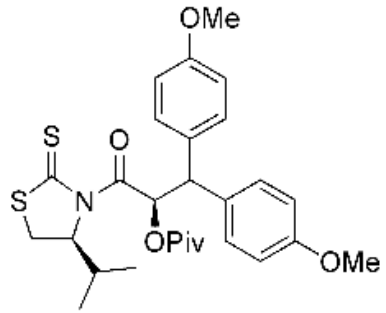


^{1}H NMR (400 MHz, $CDCl_3$)



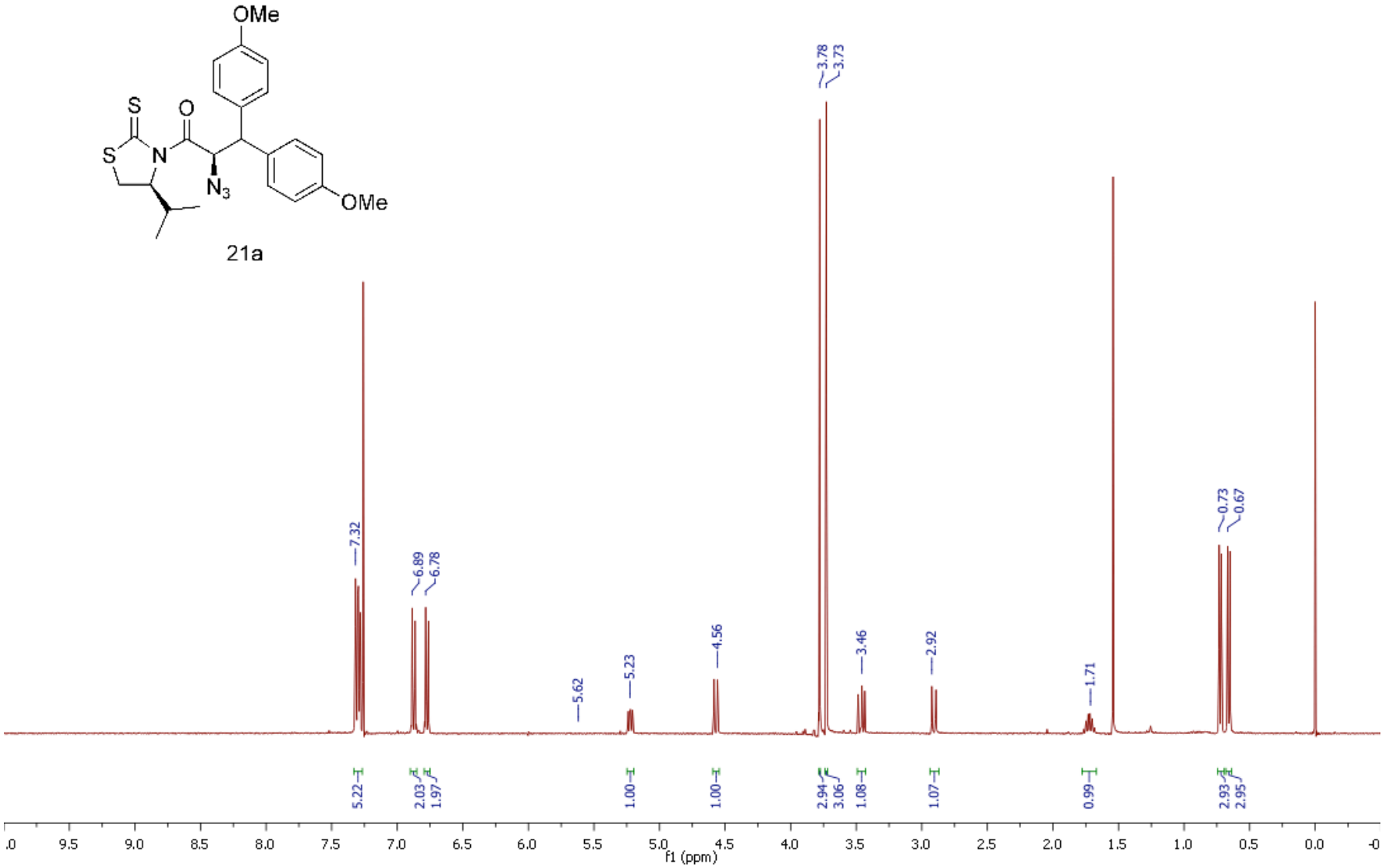
20a

^{13}C NMR (100.6 MHz, $CDCl_3$)

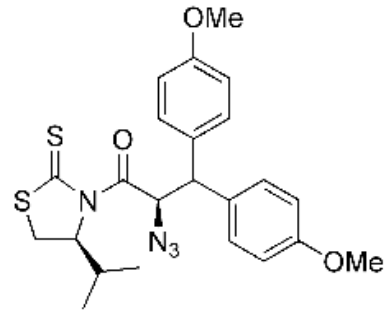


20a

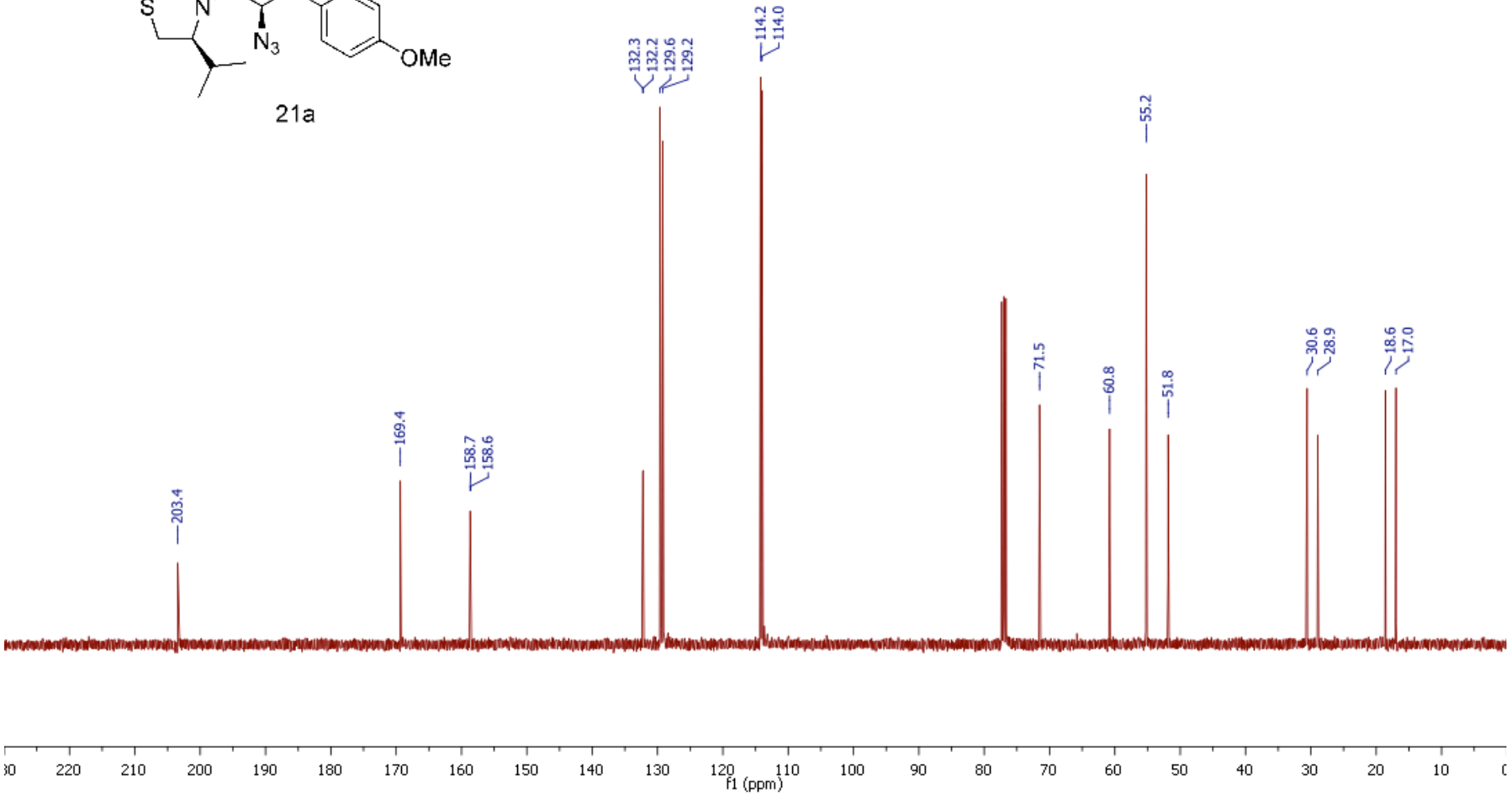
^{1}H NMR (400 MHz, $CDCl_3$)



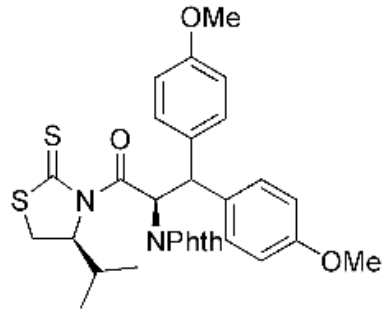
^{13}C NMR (100.6 MHz, $CDCl_3$)



21a

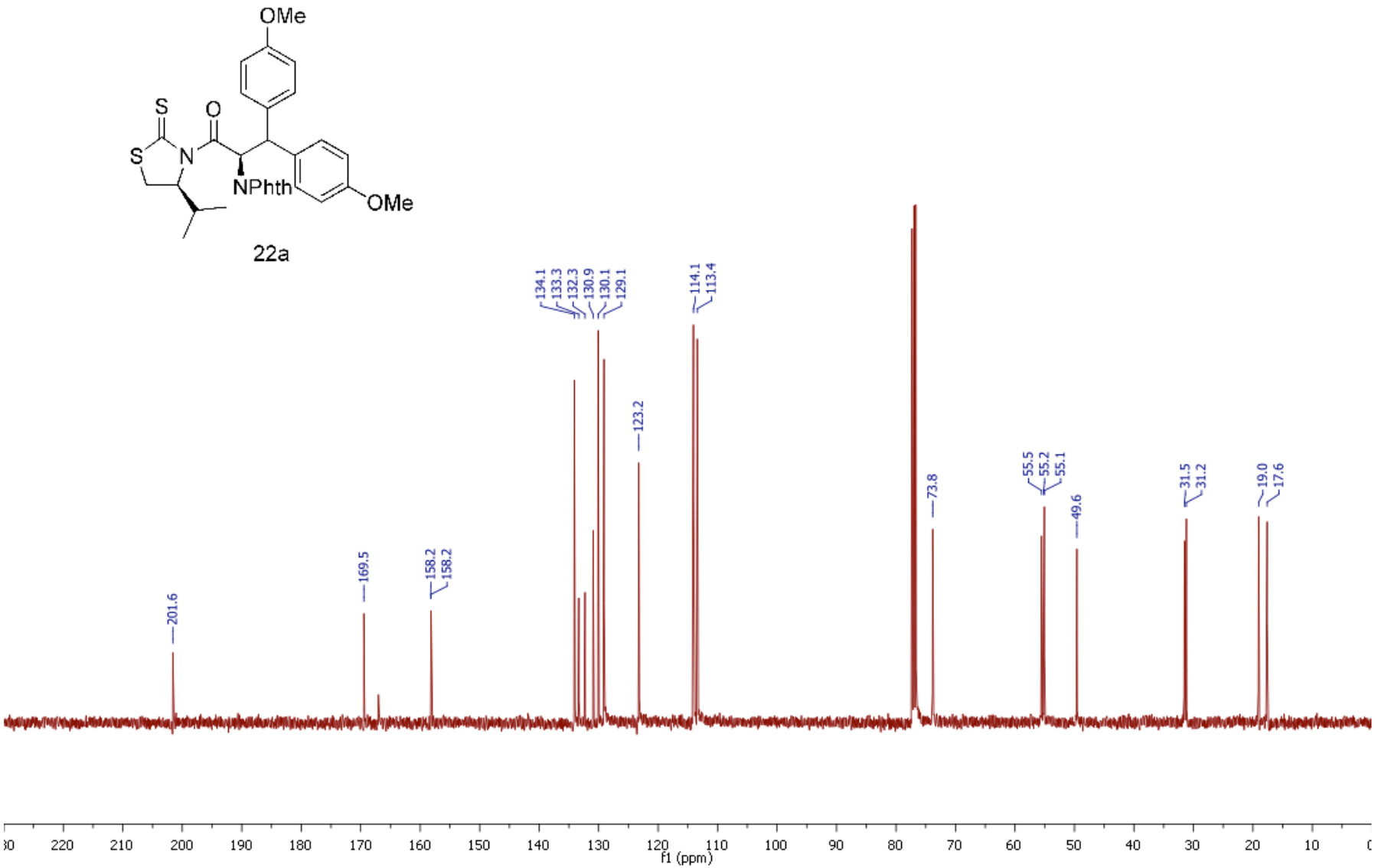


^{1}H NMR (400 MHz, $CDCl_3$)

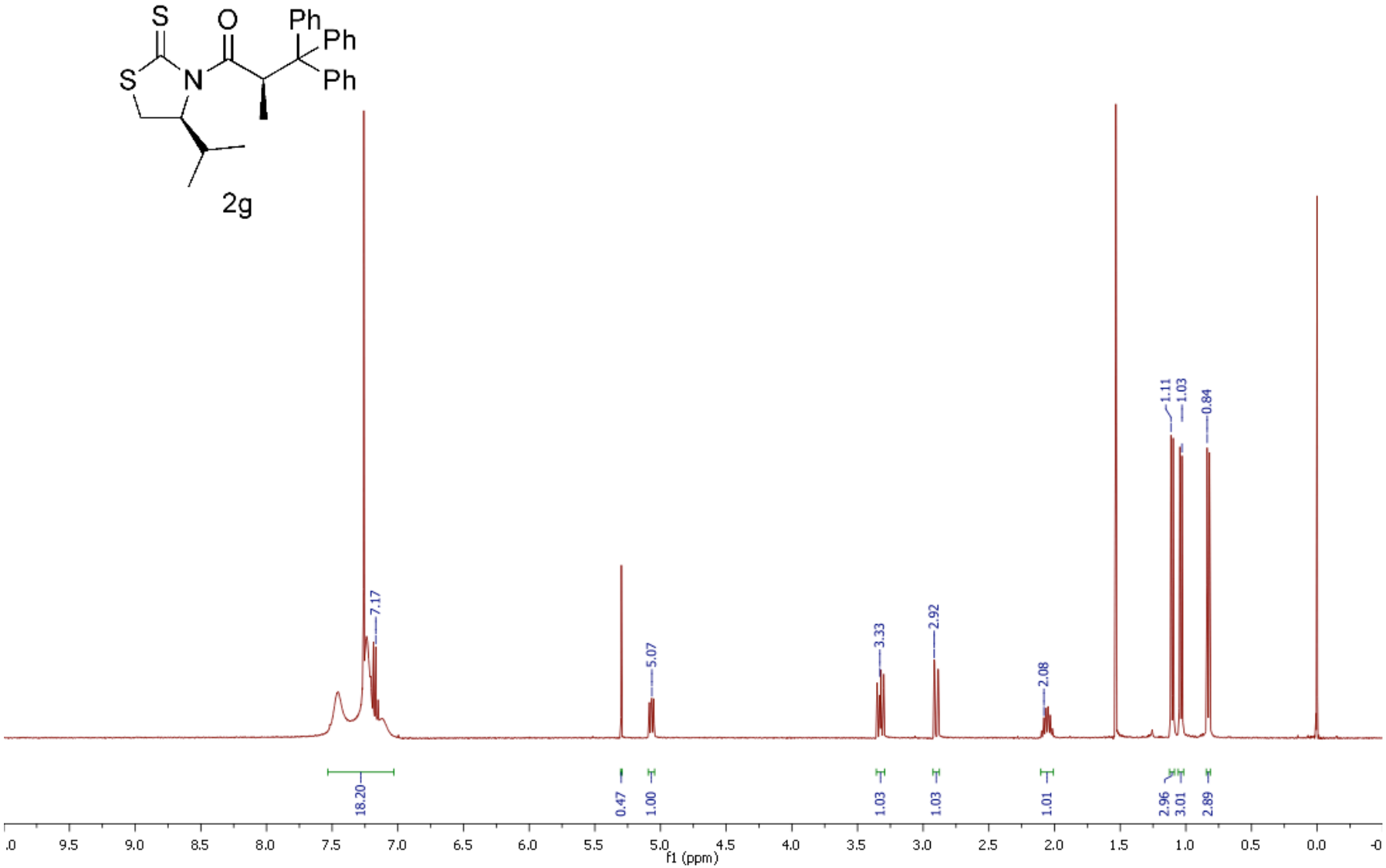


22a

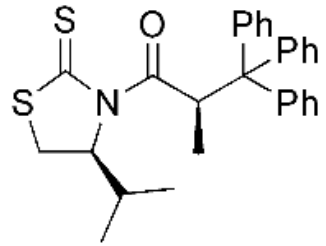
^{13}C NMR (100.6 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)

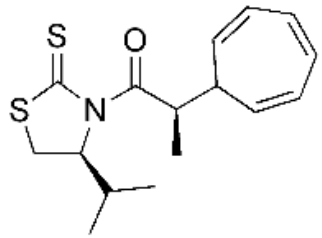


^{13}C NMR (100.6 MHz, $CDCl_3$)



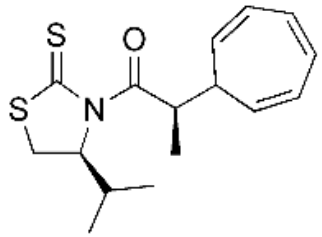
2g

^{1}H NMR (400 MHz, $CDCl_3$)



2h

^{13}C NMR (100.6 MHz, $CDCl_3$)



2h