

Supporting information

for

Comparison of the Reactivity of β -Thiolactones and β -Lactones Toward Ring-opening by Thiols and Amines.

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| Compound | Expt | Spectra |
|--|------|---------|
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| Figure 3 | S3 | / |
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Reactions were performed using oven dried glasswares under an atmosphere of argon. All separations were carried out under flash-chromatographic conditions on silica gel (Redi Sep prepacked column, 230–400 mesh) at medium pressure (20 psi) with use of a CombiFlash Companion. Reactions were monitored by thin-layer chromatography on Merck silica gel plates (60 F₂₅₄ aluminum sheets) which were rendered visible by ultraviolet light and/or spraying with KMnO₄ (1 g), Na₂CO₃ (2 g) in H₂O (100 mL) followed by heating. THF, CH₂Cl₂, MeOH and CH₃CN were purchased from Acros Organics at the highest commercial quality and used without further purification. Reagent-grade chemicals were obtained from diverse commercial suppliers (Sigma-Aldrich, Acros Organics, TCI and Alfa-Aesar) and were used as received.

¹H NMR (500 or 300 MHz) and **¹³C NMR** (125 or 75 MHz) **spectra** were recorded on Bruker Avance spectrometers at 298 K unless otherwise stated. Chemical shifts are given in ppm (δ) and are referenced to the internal solvent signal or to TMS used as an internal standard. Multiplicities are declared as follow: *s* (singlet), *brs* (broad singlet), *d* (doublet), *t* (triplet), *q* (quadruplet), *dd* (doublet of doublet), *ddd* (doublet of doublet of doublet), *dt* (doublet of triplet), *m* (multiplet). Coupling constants *J* are given in Hz. Carbon multiplicities were determined by DEPT135 experiment. Diagnostic correlations were obtained by two-dimensional COSY, HSQC and HMBC experiments.

Infrared spectra (IR) were recorded on a Perkin-Elmer FT-IR system using diamond window Dura SamplIR II and the data are reported in reciprocal centimeters (cm⁻¹). **Melting points** were recorded in open capillary tubes on a Büchi B-540 apparatus and are uncorrected.

High resolution mass spectra (HRMS) were recorded using a Micromass LCT Premier XE instrument (Waters) and were determined by electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI).

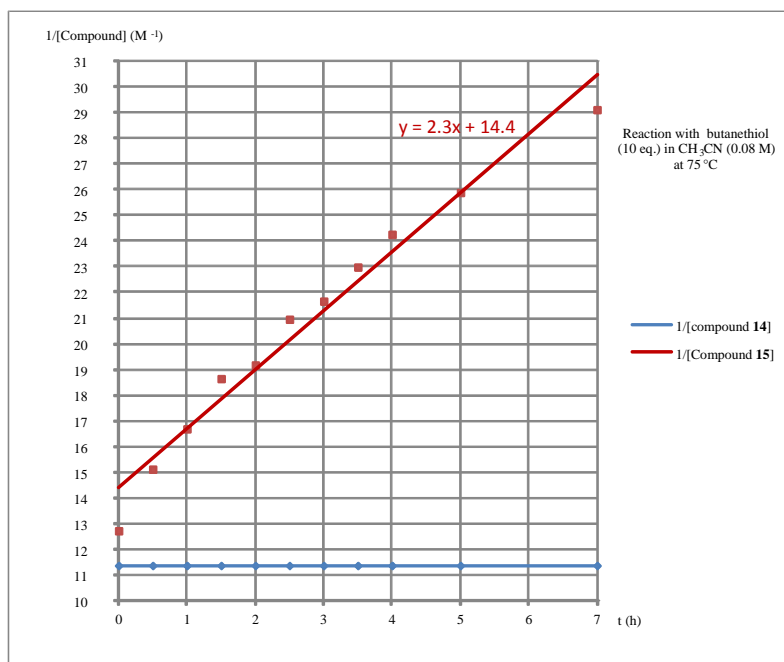


Figure 2: Plot with $1/[\text{compound}] = f(t)$ for reactions of compounds **14** and **15** with butanethiol in acetonitrile at 75 °C.

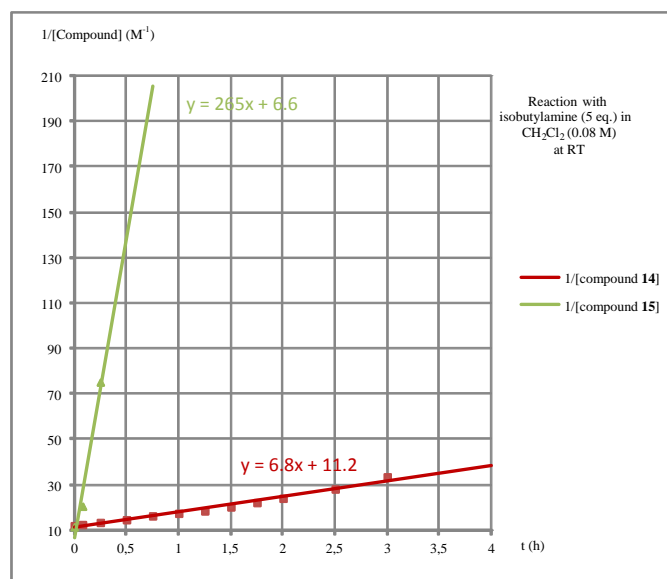


Figure 3: Plot with $1/[\text{compound}] = f(t)$ for reactions of compounds **14** and **15** with isobutylamine in dichloromethane at RT

3-Ethyl-3-(hydroxymethyl)oxetan-2-one (2). Triethylamine (0.38 mL, 2.7 mmol) was added to a solution of 2,2-bis(hydroxymethyl)butanoic acid (200 mg, 1.35 mmol) in CH₂Cl₂ (6.75 mL). After stirring for 5 min, the mixture was cooled down to -10 °C and benzenesulfonyl chloride (0.19 mL, 1.5 mmol) was added dropwise. The mixture was allowed stirred for 2 h at -10 °C. The product was extracted with water. The organic layer was dried over Na₂SO₄ and the solvent was removed under vacuum. After purification on a silica cartridge (ether/MeOH, 99.8:0.2), the desired product was

obtained as a colorless oil (60.6 mg, 34%). IR ν_{\max} (cm⁻¹): 3395 (OH), 1818 (C(O)O); ¹H NMR (500 MHz, CDCl₃): δ 4.43 (d, J = 4.9 Hz, 1 H), 4.15 (d, J = 4.9 Hz, 1 H), 3.93 (d, J = 11.5 Hz, 1 H), 3.72 (d, J = 11.5 Hz, 1 H), 1.95 (br s, 1H), 1.84-1.68 (m, 2 H), 1.05 (t, J = 7.5 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 173.5 (C), 66.2 (CH₂), 64.6 (C), 61.9 (CH₂), 22.5 (CH₂), 8.6 (CH₃); MS (ESI⁺) m/z (%) 153.1 ([M+Na]⁺, 100); ESIHRMS calcd for C₆H₁₀NaO₃ (M+Na) 153.0528, found 153.0527.

S-((3-Ethyl-2-oxooxetan-3-yl)methyl) ethanethioate (3). DEAD (40% in toluene) (1.7 mL, 3.73 mmol) was added dropwise to a solution of diphenyl-[4-(1H,1H,2H,2H-perfluorodecyl)phenyl] phosphine (2.6 g, 3.68 mmol) in CH₂Cl₂ (8.8 mL) at 0 °C and the mixture was stirred at this temperature for 1 h. Compound **2** (320 mg, 2.45 mmol) was solubilized in CH₂Cl₂ (4.0 mL) and the solution was added to the previous mixture, followed by AcSH (0.18 mL, 2.45 mmol). The mixture was stirred at room temperature for 3 h. The mixture was acidified and the organic layer was extracted with CH₂Cl₂. After purification on a silica cartridge (Heptane/AcOEt 70:30), the product was obtained as a colorless oil (274.3 mg, 59%). IR ν_{\max} (cm⁻¹): 1818 (C(O)O), 1694 (S(O)); ¹H NMR (500 MHz, CDCl₃): δ 4.01 (d, J = 5.5 Hz, 1 H), 4.03 (d, J = 5.5 Hz, 1 H), 3.23 (d, J = 14.5 Hz, 1 H), 3.20 (d, J = 14.5 Hz, 1 H), 2.34 (s, 3 H), 1.75-1.82 (m, 2 H), 1.01 (t, J = 7.5 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 194.2 (C), 171.8 (C), 67.8 (CH₂), 62.0 (C), 30.4 (CH₂), 30.0 (CH₃), 25.4 (CH₂), 8.6 (CH₃); MS (ESI⁺) m/z (%) 211.1 ([M+Na]⁺, 100); ESIHRMS calcd for C₈H₁₂NaO₃S (M+Na) 211.0405, found 211.0399.

3-Ethyl-3-(mercaptomethyl)oxetan-2-one (4). A solution of compound **3** (35 mg, 0.19 mmol) in acetonitrile (1.1 mL) was added to hydrazine acetate (19.9 mg, 0.22 mmol). The reaction mixture was stirred at room temperature for 2 h. The mixture was acidified with 1 M HCl and the organic layer was extracted with AcOEt. The solvent was removed under vacuum to give the desired product as a colorless oil without further purification (to avoid oxidation) (23.6 mg, 87%). IR ν_{\max} (cm⁻¹): 2569 (SH), 1817 (C(O)O); ¹H NMR (500 MHz, CDCl₃): δ 4.34 (d, J = 5.1 Hz, 1 H), 4.15 (d, J = 5.1 Hz, 1 H), 2.92 (dd, J = 14.3, 8.5 Hz, 1 H), 2.73 (dd, J = 14.3, 8.5 Hz, 1 H), 1.84-1.91 (m, 2 H), 1.55 (t, J = 8.5 Hz, 1 H), 1.07 (t, J = 7.4 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 172.3 (C), 67.5 (CH₂), 63.8 (C), 26.2 (CH₂), 25.0 (CH₂), 8.7 (CH₃); MS (NCI NH₃) m/z (%) 145.0 ([M-H]⁻, 100).

2-(Hydroxymethyl)-2-(mercaptomethyl)butanoic acid (5). Compound **3** (206 mg, 1.09 mmol) in HBF₄ (48% in water) (5.4 mL) was heated at 60 °C for 4 h. Saturated aqueous Na₂CO₃ was added and the organic compound was extracted with AcOEt. The aqueous layer was acidified with oxalic acid and extracted with AcOEt, the organic layer was dried over Na₂SO₄ and the solvent was removed under vacuum. The desired product was obtained as a colorless oil after purification on a silica cartridge (Heptane/ AcOEt 90:10) (127.8 mg, 71%). IR ν_{\max} (cm⁻¹): 3100 (OH), 2572 (SH), 1699 (C(O)OH); ¹H NMR (500 MHz, CD₃OD): δ 7.61 (br s, 1 H), 3.97 (d, J = 11.3 Hz, 1 H), 3.84 (d, J = 11.3 Hz, 1 H), 2.93 (d, J = 14.1 Hz, 1 H), 2.81 (d, J = 14.1 Hz, 1 H), 1.73 (q, J = 7.5 Hz, 2 H), 1.32 (s, 2 H), 0.91 (t, J = 7.5 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 179.9 (C), 63.3 (CH₂), 52.7 (C), 26.3 (CH₂), 25.3 (CH₂), 8.3 (CH₃); MS (ESI⁻) m/z (%) 163.0 ([M-H]⁻, 100), 327.1 ([2M-H]⁻, 25); ESIHRMS calcd for C₆H₁₁O₃S (M-H) 163.0429, found 163.0435.

3-Ethyl-3-(hydroxymethyl)thietan-2-one (7). To a solution of compound **5** (100 mg, 0.61 mmol) in CH₂Cl₂ (1.1 mL) was added triethylamine (0.17 mL, 1.22 mmol) and TFAA (81.2 μ L, 0.57 mmol). The reaction mixture was stirred at room temperature for 2 h. The mixture was quenched with saturated Na₂CO₃ and the organic layer was extracted with CH₂Cl₂. The solvent was removed under vacuum to give the desired product as a colorless oil after filtration on a silice pad with CH₂Cl₂ (9 mg, 10%). IR

ν_{\max} (cm^{-1}): 3376 (OH), 1735 (C(O)S); ^1H NMR (300 MHz, CDCl_3): δ 3.88 (d, $J = 11.4$ Hz, 1 H), 3.71 (d, $J = 11.4$ Hz, 1 H), 3.07 (d, $J = 8.7$ Hz, 1 H), 2.84 (d, $J = 8.7$ Hz, 1 H), 1.66-1.90 (m, 3 H), 1.07 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 192.7 (C), 81.5 (C), 64.5 (CH_2), 25.1 (CH_2), 23.6 (CH_2), 8.1 (CH_3); MS (ESI^+) m/z (%) no answer.

2-(Mercaptomethyl)-2-((2,2,2-trifluoroacetoxy)methyl)butanoic acid (9). To a solution of compound **5** (200 mg, 1.22 mmol) in CH_2Cl_2 (2.2 mL) was added triethylamine (0.34 mL, 2.45 mmol) and TFAA (0.16 mL, 1.13 mmol). The reaction was stirred at room temperature for 3.5 h. The solvent was removed under vacuum. The crude product was purified on a silica cartridge (Heptane/AcOEt 70:30) to give the compound **9** as a colorless oil, in a mixture with compound **7** (8:2) (196.8 mg, 67%). IR ν_{\max} (cm^{-1}): 3466 (COOH), 2965 (SH), 1725 (C(O)S); ^1H NMR (300 MHz, CDCl_3): δ 10.58 (br s, 1 H), 4.68 (d, $J = 11.3$ Hz, 1 H), 4.58 (d, $J = 11.3$ Hz, 1 H), 2.93 (dd, $J = 14.2, 9.2$ Hz, 1 H), 2.77 (dd, $J = 14.1, 9.2$ Hz, 1 H), 1.74 (q, $J = 7.5$ Hz, 2 H), 1.40 (t, $J = 9.2$ Hz, 1 H), 0.92 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 178.7 (C), 156.9 (q, $J_{\text{CF}} = 42.8$ Hz, C), 114.35 (q, $J_{\text{CF}} = 285.5$ Hz, C), 66.1 (CH_2), 51.7 (C), 26.6 (CH_2), 26.1 (CH_2), 8.3 (CH_3); MS (ESI^-) m/z (%) 519.1 (100, $[\text{2M-H}]^-$); ESIHRMS calcd for $\text{C}_{16}\text{H}_{21}\text{F}_6\text{O}_8\text{S}_2$ (2M-H) 519.0577, found 519.0588.

Methyl 2-(mercaptomethyl)-2-(hydroxymethyl)butanoate (10). To a solution of compound **9** containing 20% of **7** (50.9 mg, 0.20 mmol) in MeOH (1 mL) was added 2 M trimethylsilyl diazomethane in hexane (0.20 mL, 0.40 mmol). The reaction was stirred at room temperature for 10 min. The solvent was removed under vacuum. The crude was purified on a silica cartridge (Heptane/AcOEt 80:20) to give methylester **10** as a colorless oil, containing 10% of compound **7** (32.1 mg, 90%). IR ν_{\max} (cm^{-1}): 3366 (OH), 2965 (SH); ^1H NMR (300 MHz, CDCl_3): δ 3.86 (d, $J = 11.3$ Hz, 1 H), 3.80 (d, $J = 11.3$ Hz, 1 H), 3.74 (s, 3 H), 2.96 (dd, $J = 14.0, 9.0$ Hz, 1 H), 2.74 (dd, $J = 14.0, 9.0$ Hz, 1 H), 1.91 (br s, 1 H), 1.69 (q, $J = 7.5$ Hz, 2 H), 1.41 (t, $J = 9.0$ Hz, 1 H), 0.85 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 175.3 (C), 63.7 (CH_2), 52.9 (C), 52.0 (CH_3), 27.2 (CH_2), 25.9 (CH_2), 8.6 (CH_3); MS (ESI^+) m/z (%) 377.1 (90, $[\text{2M-2H+Na}]^+$), 400.2 (100, $[\text{2M-2H+HCOOH}]^+$); ESIHRMS calcd for $\text{C}_{14}\text{H}_{26}\text{NaO}_6\text{S}_2$ (2M-2H+Na) 377.1063, found 377.1070.

(3-ethyl-2-oxothietan-3-yl)methyl 4-nitrobenzoate (11). Triethylamine (34 μL , 0.24 mmol) and trifluoroacetic anhydride (16.2 μL , 0.12 mmol) were added to a solution of compound **7** (20 mg, 0.12 mmol) in CH_2Cl_2 (0.6 mL). The reaction mixture was stirred at room temperature for 3 h 30. Saturated Na_2CO_3 was added and the organic layer was extracted with CH_2Cl_2 , the aqueous phase was acidified with oxalic acid and the organic layer was extracted with CH_2Cl_2 and was dried over Na_2SO_4 and the solvent was removed under vacuum. Pyridine (12.2 μL , 1.15 mmol), 4-nitrobenzoyl chloride (16.8 mg, 0.09 mmol) were added to a solution of crude product in CH_2Cl_2 (0.75 mL). The reaction mixture was stirred at room temperature for 50 min, was quenched with 1 M HCl and the organic layer was extracted with CH_2Cl_2 . After purification on a silica plate (Heptane/AcOEt 70:30), the desired product was obtained as a colorless oil (3.8 mg, 11%). IR ν_{\max} (cm^{-1}): 1731 (CO), 1528 (NO_2); ^1H NMR (500 MHz, CDCl_3): δ 8.32 (d, $J = 9.0$ Hz, 2 H), 8.25 (d, $J = 9.0$ Hz, 2 H), 4.50 (d, $J = 11.6$ Hz, 1 H), 4.44 (d, $J = 11.6$ Hz, 1 H), 3.11 (d, $J = 8.8$ Hz, 1 H), 2.96 (d, $J = 8.8$ Hz, 1 H), 1.93 (sext., $J = 7.3$ Hz, 1 H), 1.80 (sext., $J = 7.3$ Hz, 1 H), 1.13 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 195.2 (C), 164.2 (C), 150.8 (C), 134.8 (C), 130.9 (2 CH), 123.7 (2 CH), 78.7 (C), 66.0 (CH_2), 25.9 (CH_2), 24.5 (CH_2), 8.1 (CH_3); MS (ESI^+) m/z (%) 318.0 ($[\text{M+Na}]^+$, 100), 608.1 ($[\text{2M+NH}_4]^+$, 15); ESIHRMS calcd for $\text{C}_{13}\text{H}_{13}\text{NaO}_5\text{S}$ (M+Na) 318.0412, found 318.0415.

3-Ethylthietane-3-carboxylic acid (13). To a solution of compound **4** (78 mg, 0.53 mmol) in THF (1.3 mL) was added 1 M NaOH (1.3 mL). The reaction mixture was stirred at room temperature for 2 h. The mixture was acidified with 1 M HCl and the organic layer was extracted with CHCl₃. The mixture was solubilized in warm ether and slowly cooled to room temperature to give the desired product as a white solid (3.6 mg, 5%). Mp = 269-272 °C; IR ν_{\max} (cm⁻¹): 3034-2850 (OH), 1708 (C(O)O); ¹H NMR (300 MHz, CD₃OD): δ 3.38 (d, *J* = 14.7 Hz, 2 H), 2.95 (d, *J* = 14.7 Hz, 2 H), 1.66 (q, *J* = 7.6 Hz, 2 H), 0.86 (t, *J* = 7.6 Hz, 3 H); ¹³C NMR (75 MHz, CD₃OD): δ 178.6 (C), 54.4 (C), 43.9 (2 CH₂), 33.0 (CH₂), 9.4 (CH₃); MS (ESI⁻) *m/z* (%) 145.0 ([M-H]⁻, 10), 247.1 ([2M-CO₂-H]⁻, 100); ESIHRMS calcd for C₆H₉O₂S (M-H) 145.0323, found 145.0316.

2-Benzyl-3-(butylthio)propanoic acid (16). To a solution of compound **14** (18 mg, 0.11 mmol) in CH₃CN (0.55 mL) at 75 °C was added butanethiol (60 μ L, 0.55 mmol) and the reaction mixture was stirred at this temperature overnight. After purification on a silica cartridge (Heptane/AcOEt 80:20) the desired product was obtained as a colorless oil (2.2 mg, 8%); starting material was recovered (91%). IR ν_{\max} (cm⁻¹): 1709 (COOH); ¹H NMR (300 MHz, CDCl₃): δ 7.56 (br s, 1 H), 7.18-7.32 (m, 5 H), 3.00-3.08 (m, 1 H), 2.88-2.98 (m, 2 H), 2.78 (dd, *J* = 13.3, 7.5 Hz, 1 H), 2.65 (dd, *J* = 13.3, 5.2 Hz, 1 H), 2.38-2.48 (m, 2 H), 1.51 (quint., *J* = 7.4 Hz, 2 H), 1.38 (sext., *J* = 7.4 Hz, 2 H), 0.88 (t, *J* = 7.4 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 177.6 (C), 138.3 (C), 129.0 (2 CH), 128.6 (2 CH), 126.7 (CH), 47.5 (CH), 37.4 (CH₂), 32.9 (CH₂), 32.3 (CH₂), 31.6 (CH₂), 21.9 (CH₂), 13.6 (CH₃); MS (ESI⁻) *m/z* (%) 251.1 ([M-H]⁻, 65), 503.2 ([2M-H]⁻, 100); ESIHRMS calcd for C₁₄H₁₉O₂S (M-H) 251.1106, found 251.1118.

2-Benzyl-3-(butylthio)propanethioic S-acid (17). To a solution of compound **15** (20 mg, 0.11 mmol) in CH₃CN (0.55 mL) at 75 °C was added butanethiol (60 μ L, 0.55 mmol) and the reaction mixture was stirred at this temperature overnight. After purification on a silica cartridge (Heptane/AcOEt 80:20) the desired product was obtained as a colorless oil (15.9 mg, 54%). IR ν_{\max} (cm⁻¹): 2570 (SH), 1678 (CO); ¹H NMR (300 MHz, CDCl₃): δ 7.12-7.33 (m, 5 H), 2.95-3.10 (m, 2 H), 2.75-2.94 (m, 4 H), 2.61 (ddd, *J* = 13.4, 8.8, 4.6 Hz, 1 H), 1.51 (quint., *J* = 7.3 Hz, 2 H), 1.49 (s, 1 H), 1.32 (sext., *J* = 7.3 Hz, 2 H), 0.90 (t, *J* = 7.3 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 201.1 (C), 138.0 (C), 129.1 (2 CH), 128.5 (2 CH), 126.7 (CH), 58.9 (CH), 37.9 (CH₂), 31.5 (CH₂), 28.7 (CH₂), 25.7 (CH₂), 21.8 (CH₂), 13.6 (CH₃); MS (ESI⁺) *m/z* (%) 179.1 ([M-BuS]⁺, 100), 503.2 ([2M-SH]⁺, 50); ESIHRMS calcd for C₁₆H₂₄NOS₂ (M+CH₃CN+H) 310.1299, found 310.1306.

2-Benzyl-3-(isobutylamino)propanoic acid (18). To a solution of compound **14** (44 mg, 0.27 mmol) in CH₂Cl₂ (1.6 mL) was added isobutylamine (0.15 mL, 1.50 mmol) and the reaction mixture was stirred at room temperature for 6 h. The solvent was removed under vacuum and product **18** was obtained (together with compound **19**) and isolated after precipitation in AcOEt as a white solid (17 mg, 27%). Mp = 159.8-161.3 °C; IR ν_{\max} (cm⁻¹): 3450 (OH), 1586 (C(O)OH); ¹H NMR (300 MHz, CDCl₃): δ 9.88 (br s, 2 H), 7.11-7.37 (m, 5 H), 3.31 (br d, *J* = 12.4 Hz, 1 H), 2.70-2.94 (m, 5 H), 2.56 (dd, *J* = 11.4, 7.2 Hz, 1 H), 2.00-2.16 (m, 1 H), 1.00 (d, *J* = 6.5 Hz, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ 178.3 (C), 139.3 (C), 128.9 (2 CH), 128.5 (2 CH), 126.3 (CH), 54.4 (CH₂), 48.7 (CH₂), 42.8 (CH), 36.5 (CH₂), 25.7 (CH), 20.2 (CH₃), 20.1 (CH₃); MS (ESI⁺) *m/z* (%) 236.2 ([M+H]⁺, 100); ESIHRMS calcd for C₁₄H₂₂NO₂ (M+H) 236.1651, found 236.1641.

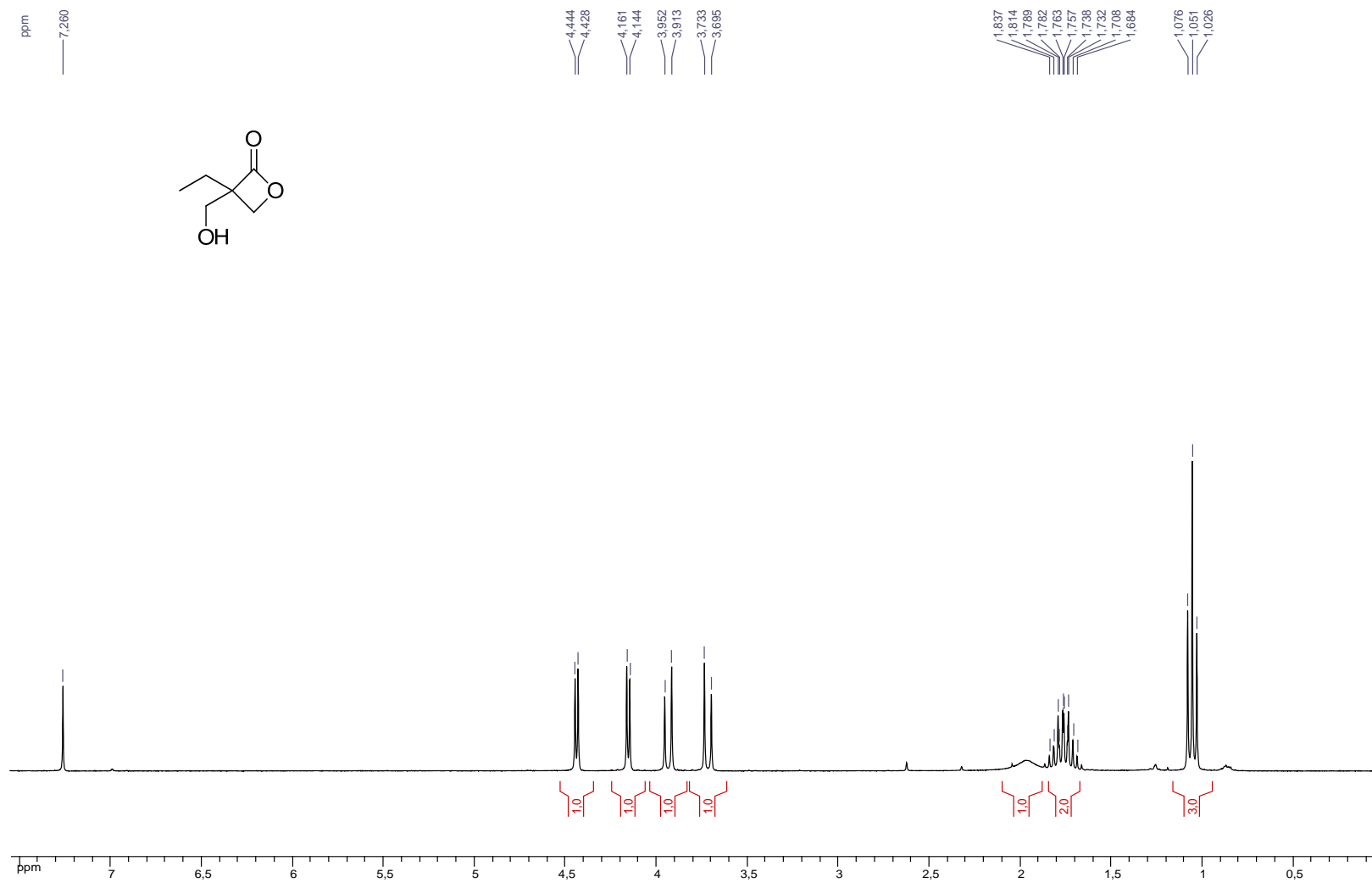
2-Benzyl-3-hydroxy-N-isobutylpropanamide (19). This product was obtained after purification of the solution on a silica plate (Heptane/AcOEt 50:50) as a white solid (45.6 mg, 72%, mp = 79.8-81.0 °C). Mp = 79.8-81.0 °C; IR ν_{\max} (cm⁻¹): 3306 (OH), 1641 (C(O)N); ¹H NMR (300 MHz, CDCl₃): δ 7.10-7.36 (m,

5 H), 5.50 (br s, 1 H), 3.81 (dd, $J = 10.9, 3.6$ Hz, 1 H), 3.76 (dd, $J = 10.9, 5.9$ Hz, 1 H), 3.10-2.75 (m, 5 H), 2.45-2.57 (m, 1 H), 1.62 (sept., $J = 6.7$ Hz, 1 H), 2.25 (br s, 1 H), 0.79 (d, $J = 6.7$ Hz, 3 H), 0.78 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 174.4 (C), 139.2 (C), 128.9 (2 CH), 128.6 (2 CH), 126.6 (CH), 63.4 (CH_2), 50.6 (CH), 46.7 (CH_2), 35.4 (CH_2), 28.3 (CH), 19.98 (CH_3), 19.96 (CH_3); MS (APCI) m/z (%) 236.2 ($[\text{M}+\text{H}]^+$, 100); APCIHRMS calcd for $\text{C}_{14}\text{H}_{22}\text{NO}_2$ (M+H) 236.1651, found 236.1641.

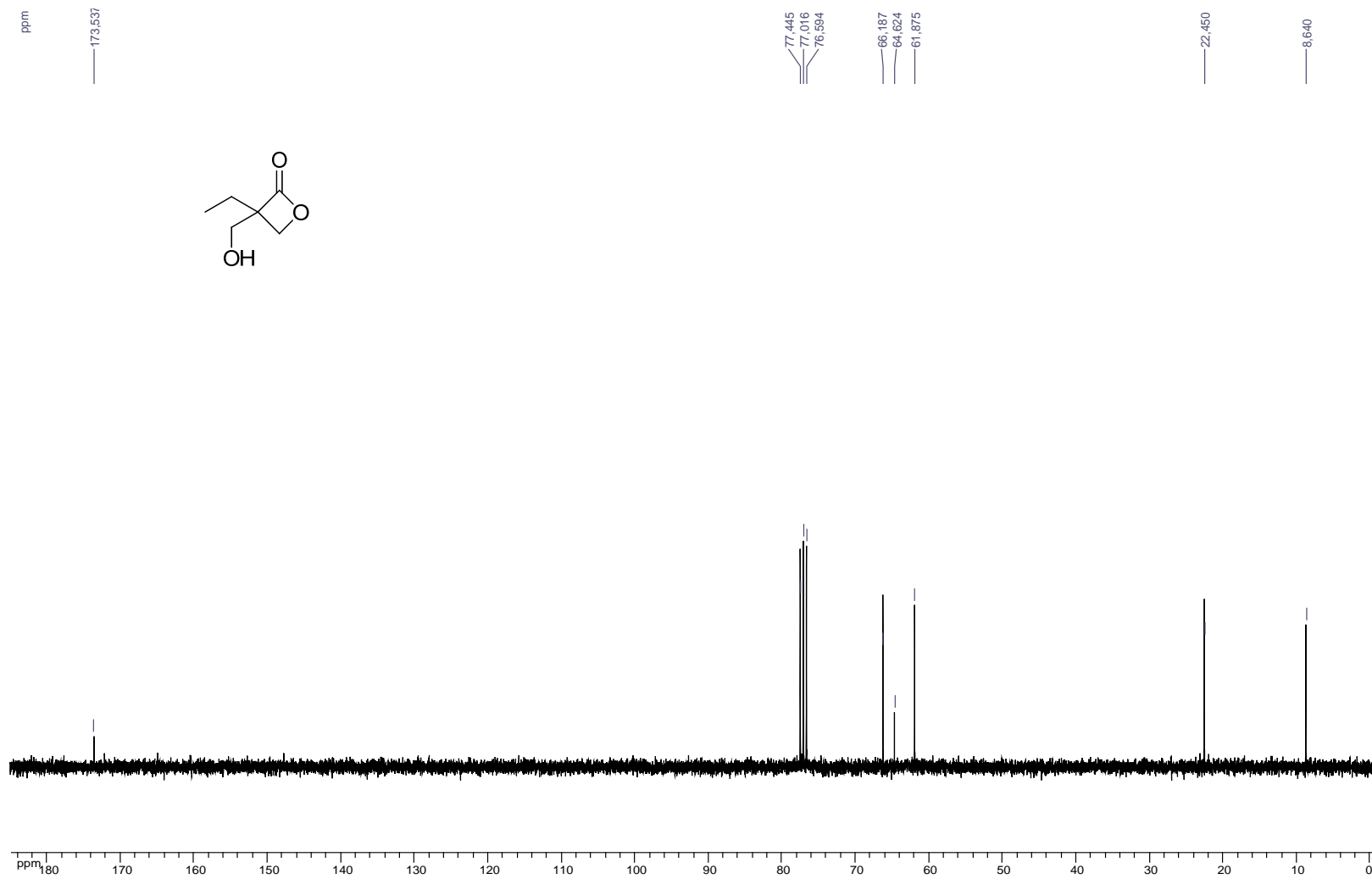
2-Benzyl-N-isobutyl-3-mercaptopropanamide (20). To a solution of compound **15** (20 mg, 0.11 mmol) in CH_2Cl_2 (0.55 mL) was added isobutylamine (66 μL , 0.66 mmol) and the reaction mixture was stirred at room temperature for 72 h. The solvent was removed under vacuum and the desired product was obtained after purification on a silica plate (Heptane/AcOEt 70:30) as a colorless oil (9.6 mg, 35%). Disulfide **21** was also obtained (11.6 mg, 42%). IR ν_{max} (cm^{-1}): 3294 (NH), 2560 (SH), 1643 (C(O)N); ^1H NMR (300 MHz, CDCl_3): δ 7.15-7.32 (m, 5 H), 5.60 (br t, $J = 5.8$ Hz, 1 H), 2.84-3.08 (m, 5 H), 2.72-2.84 (m, 2 H), 1.65 (t, $J = 7.1$ Hz, 1 H), 1.59 (sept., $J = 6.7$ Hz, 1 H), 0.738 (d, $J = 6.7$ Hz, 3 H), 0.735 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 172.8 (C), 138.9 (C), 128.9 (2 CH), 128.6 (2 CH), 126.6 (CH), 49.2 (CH), 46.9 (CH_2), 40.4 (CH_2), 38.4 (CH_2), 28.3 (CH), 20.0 (2 CH_3); MS (APCI) m/z (%) 501.3 ($[\text{2M-H}]^+$, 100), 1023.5 ($[\text{4M-4H+Na}]^+$, 90); APCIHRMS calcd for $\text{C}_{28}\text{H}_{41}\text{N}_2\text{O}_2\text{S}_2$ (2M-H) 501.2609, found 501.2617.

3,3'-Disulfanediylbis(2-benzyl-N-isobutylpropanamide) (21). This product was obtained as a colorless oil (31.4 mg, 57%). IR ν_{max} (cm^{-1}): 3297 (NH), 1644 (C(O)N); ^1H NMR (300 MHz, CDCl_3): δ 7.11-7.33 (m, 10 H), 5.89 (br t, $J = 5.9$ Hz, 2 H), 2.96-3.08 (m, 4 H), 2.73-2.96 (m, 8 H), 2.62-2.73 (m, 2 H), 1.59 (sept., $J = 6.7$ Hz, 2 H), 0.751 (d, $J = 6.7$ Hz, 6 H), 0.745 (d, $J = 6.7$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ 173.0 (2 C), 139.0 (2 C), 128.9 (4 CH), 128.5 (4 CH), 126.5 (2 CH), 48.4 (2 CH), 47.0 (2 CH_2), 39.7 (2 CH_2), 38.3 (2 CH_2), 28.3 (2 CH), 20.1 (4 CH_3); MS (APCI) m/z (%) 501.3 ($[\text{2M-H}]^+$, 100), 1023.5 ($[\text{4M-4H+Na}]^+$, 90); APCIHRMS calcd for $\text{C}_{28}\text{H}_{41}\text{N}_2\text{O}_2\text{S}_2$ (2M-H) 501.2609, found 501.2619.

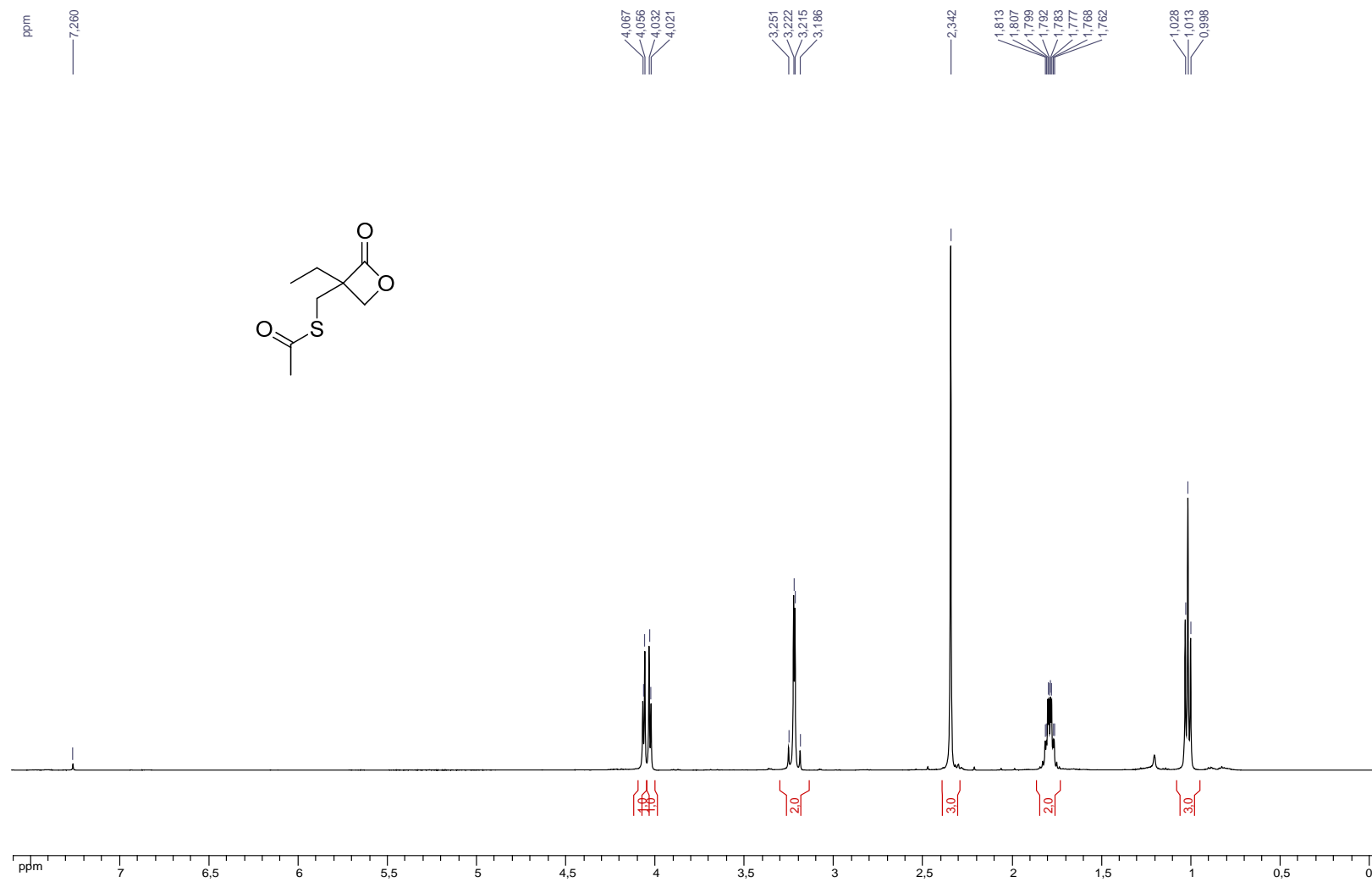
^1H NMR (500 MHz, CDCl_3) of compound **2**.



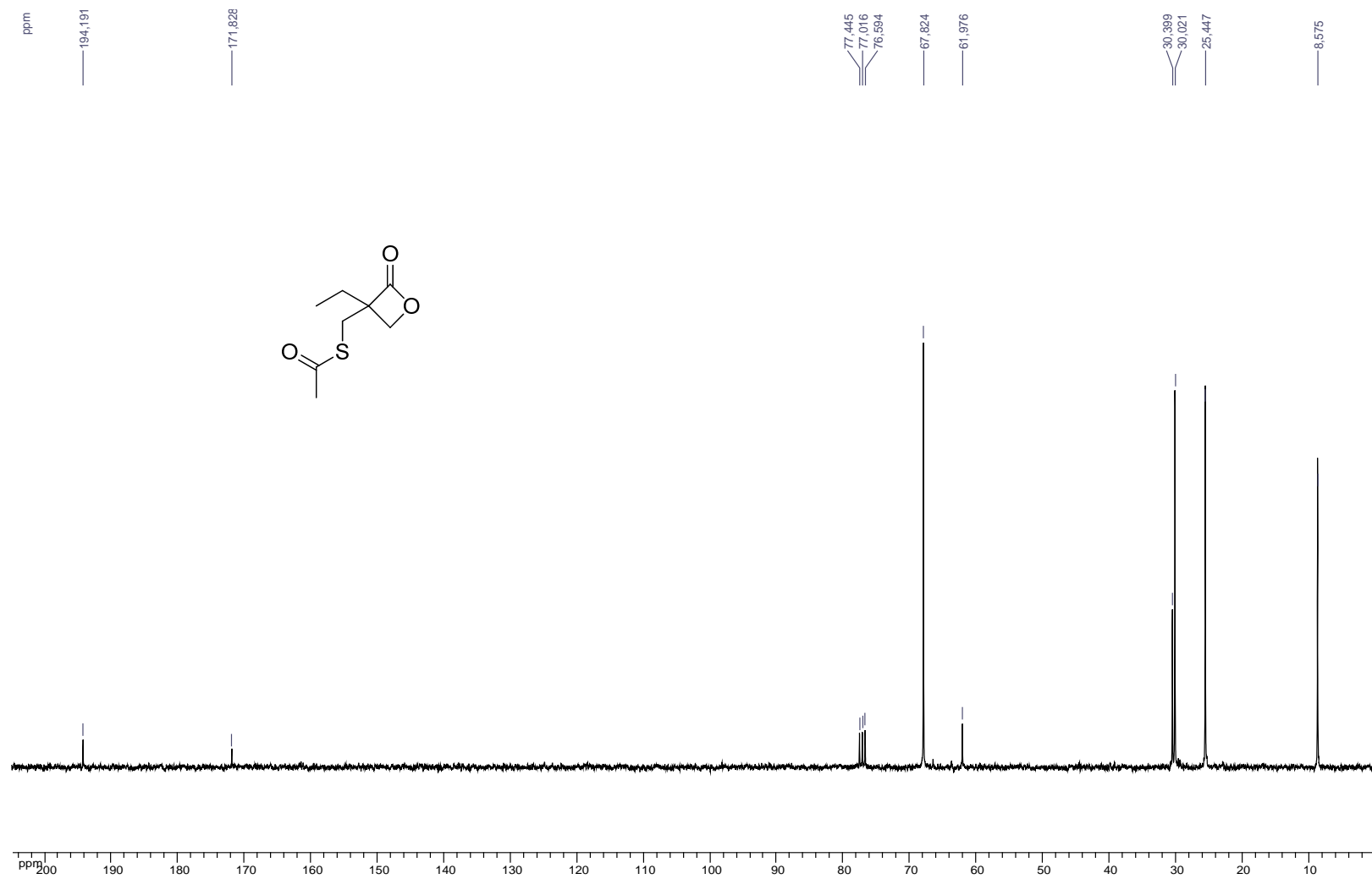
^{13}C NMR (75 MHz, CDCl_3) of compound **2**.



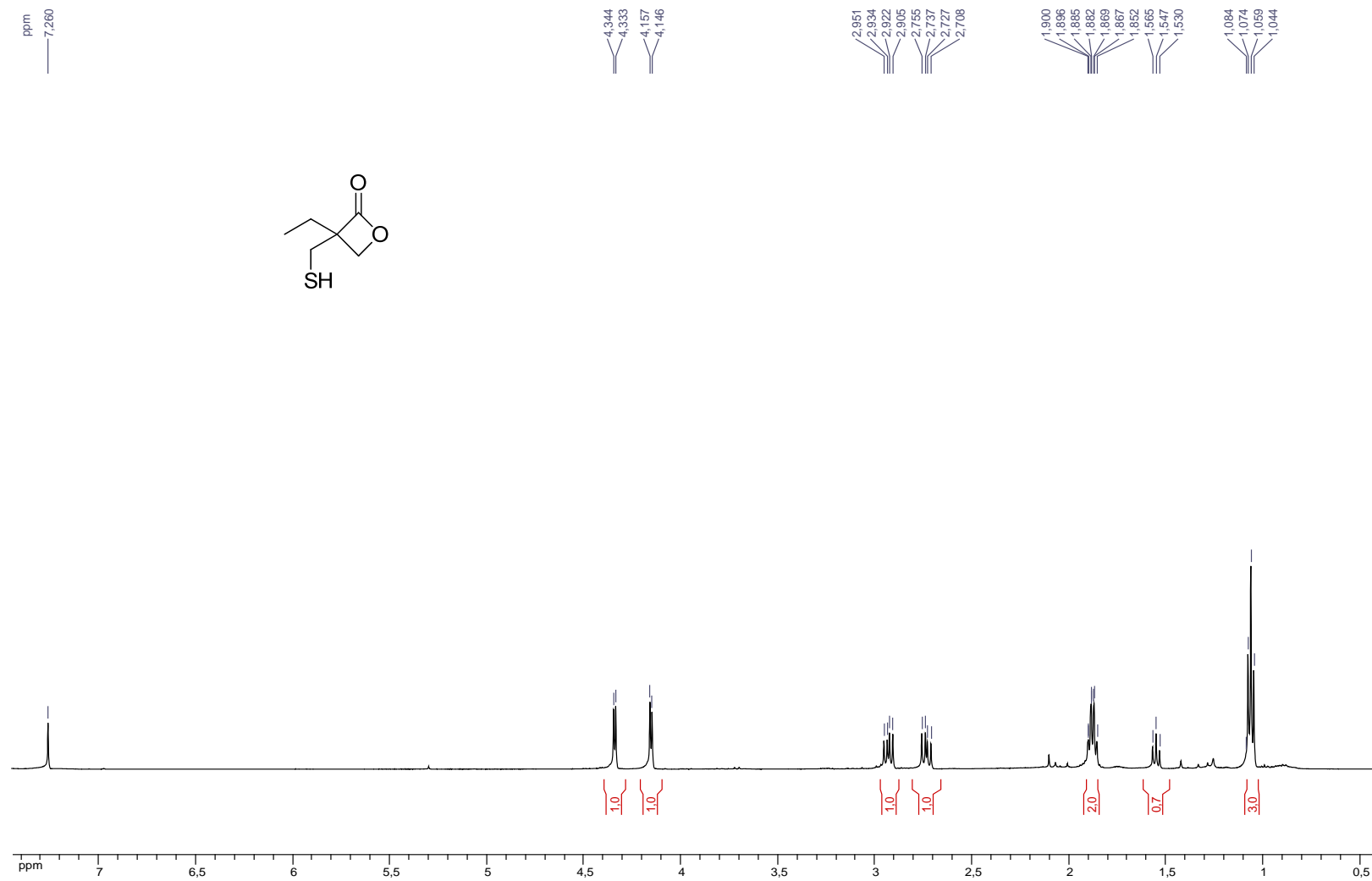
^1H NMR (500 MHz, CDCl_3) of compound **3**.



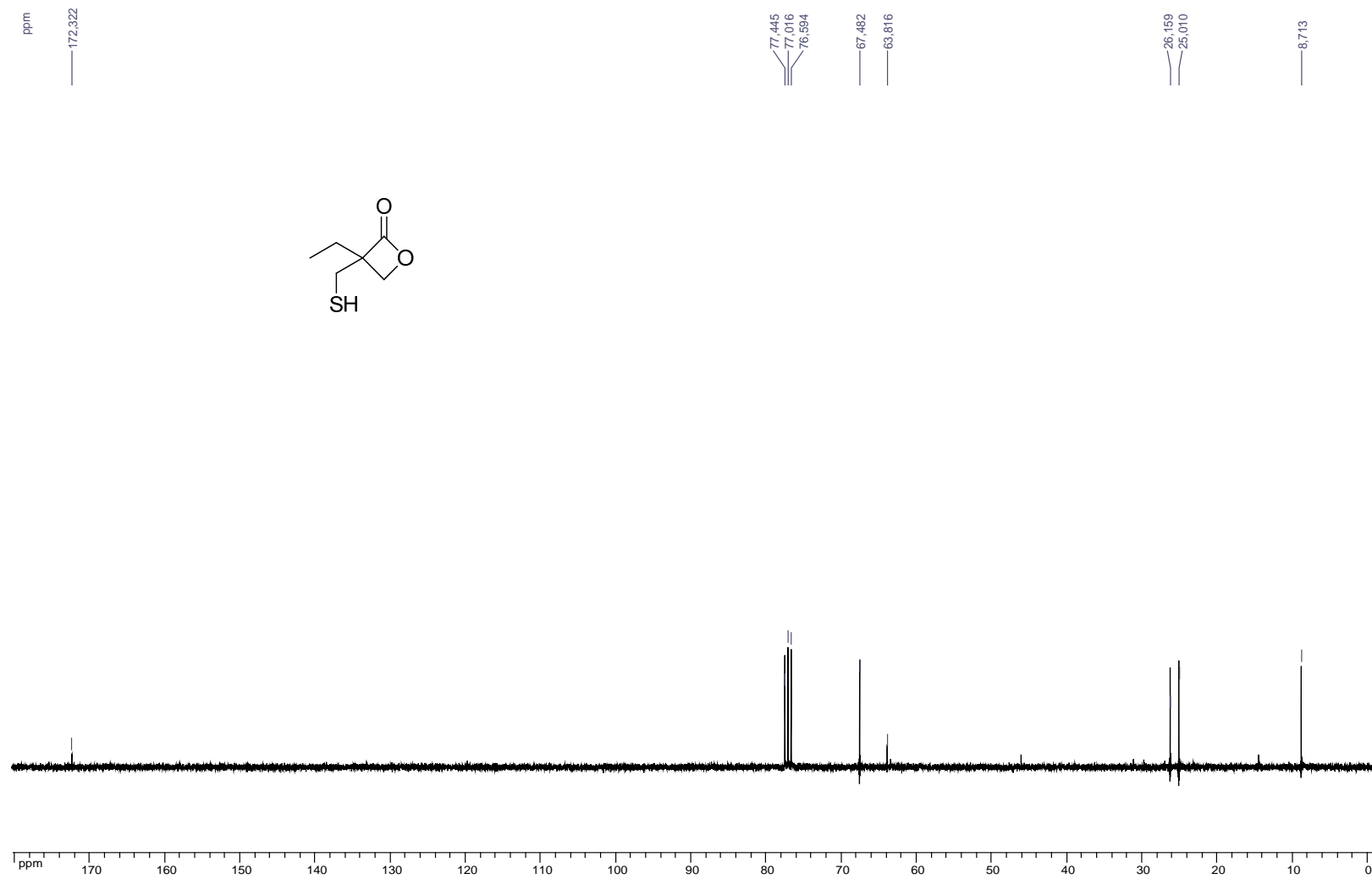
^{13}C NMR (75 MHz, CDCl_3) of compound **3**.



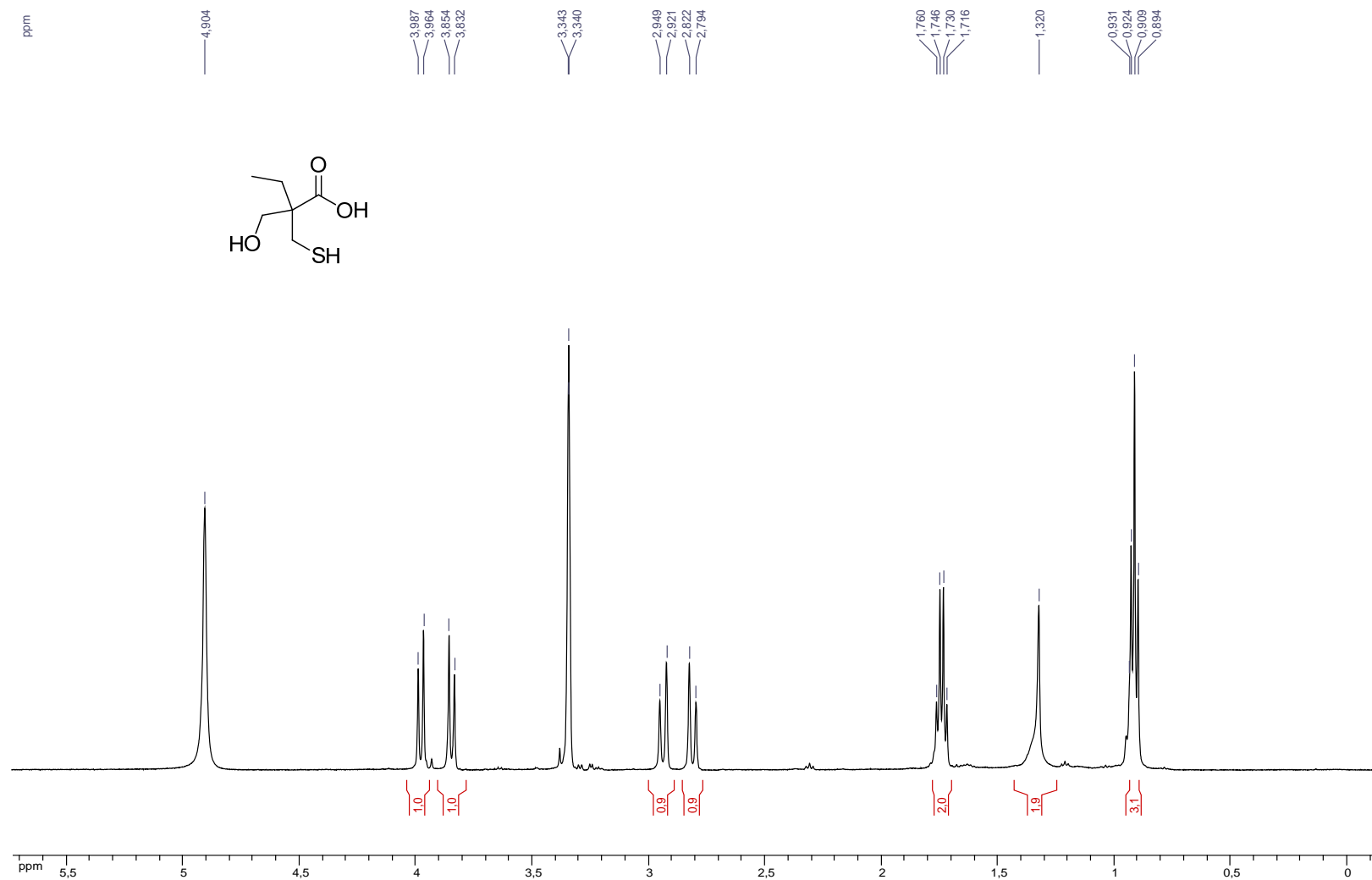
^1H NMR (500 MHz, CDCl_3) of compound **4**.



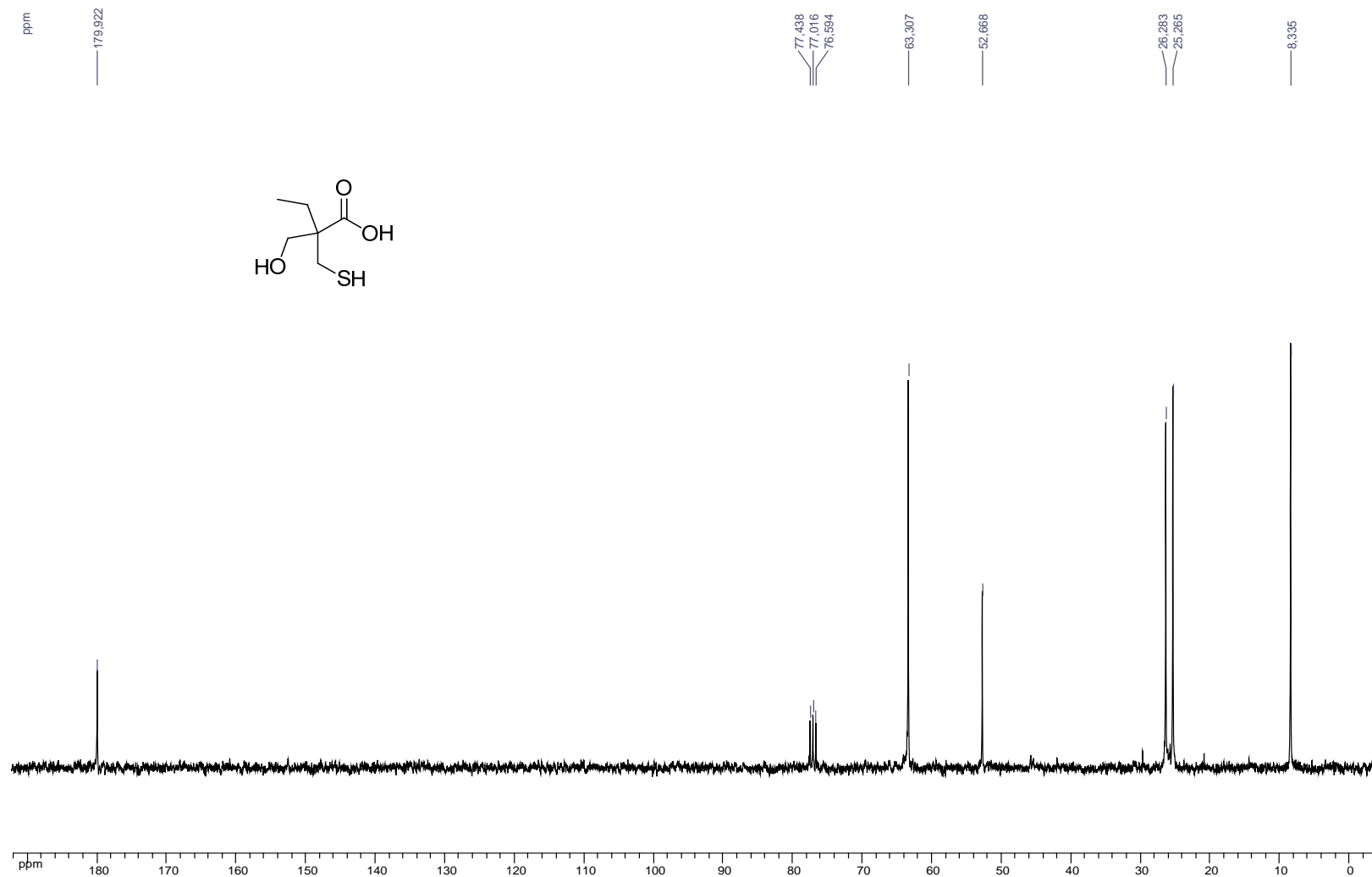
^{13}C NMR (75 MHz, CDCl_3) of compound **4**.



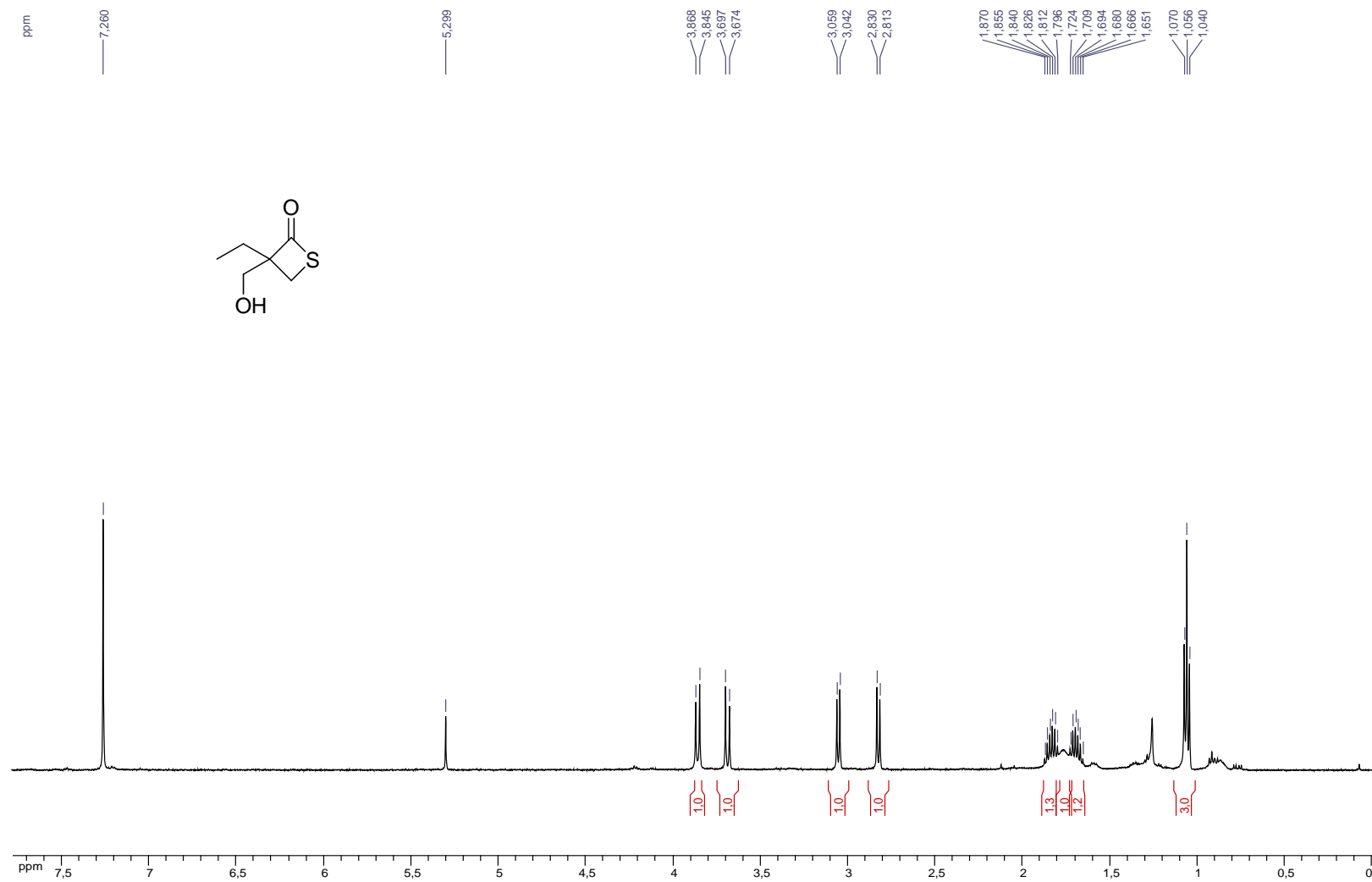
^1H NMR (500 MHz, CD_3OD) of compound **5**.



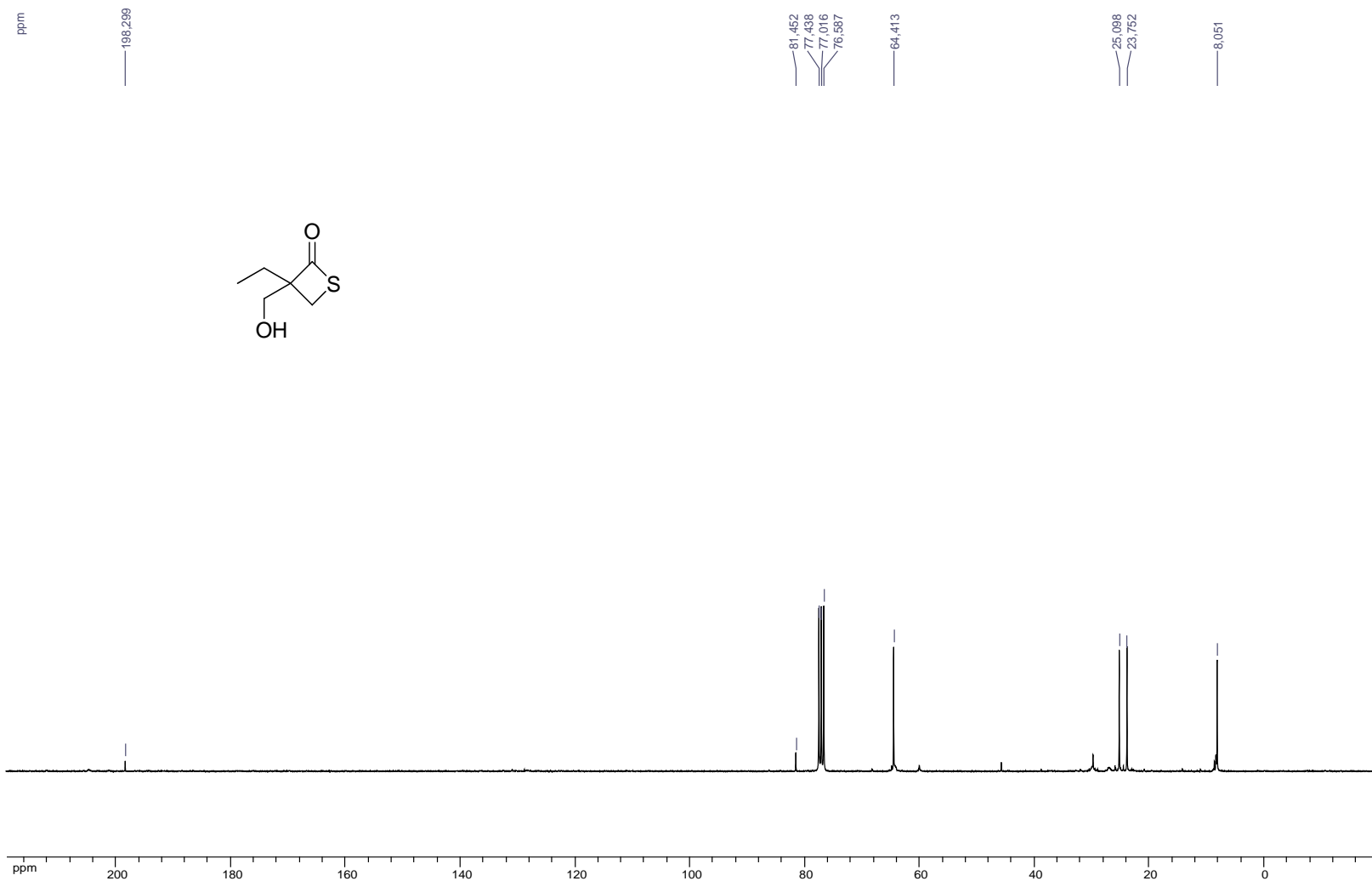
^{13}C NMR (75 MHz, CD_3OD) of compound 5.



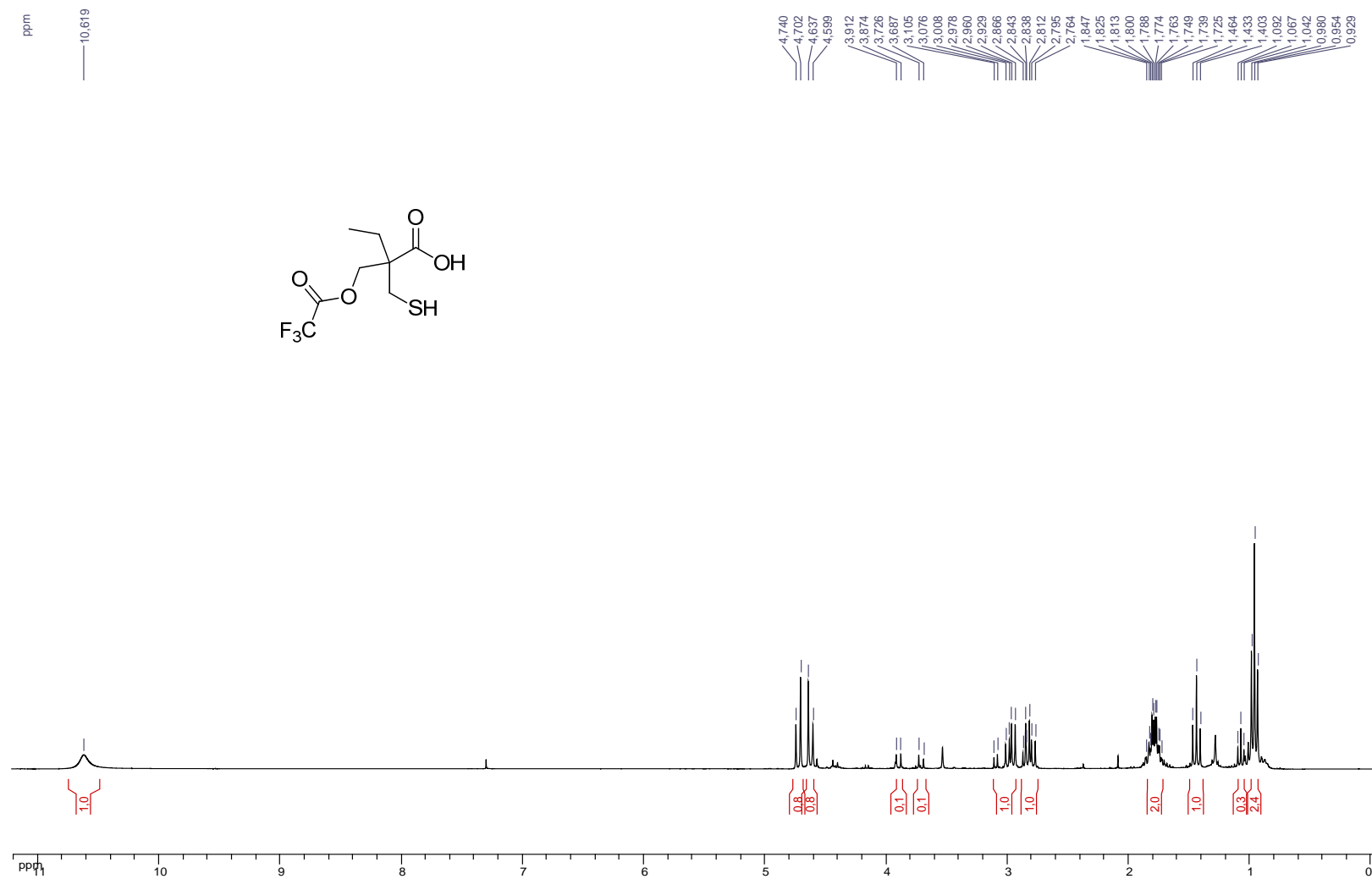
^1H NMR (300 MHz, CDCl_3) of compound **7**.



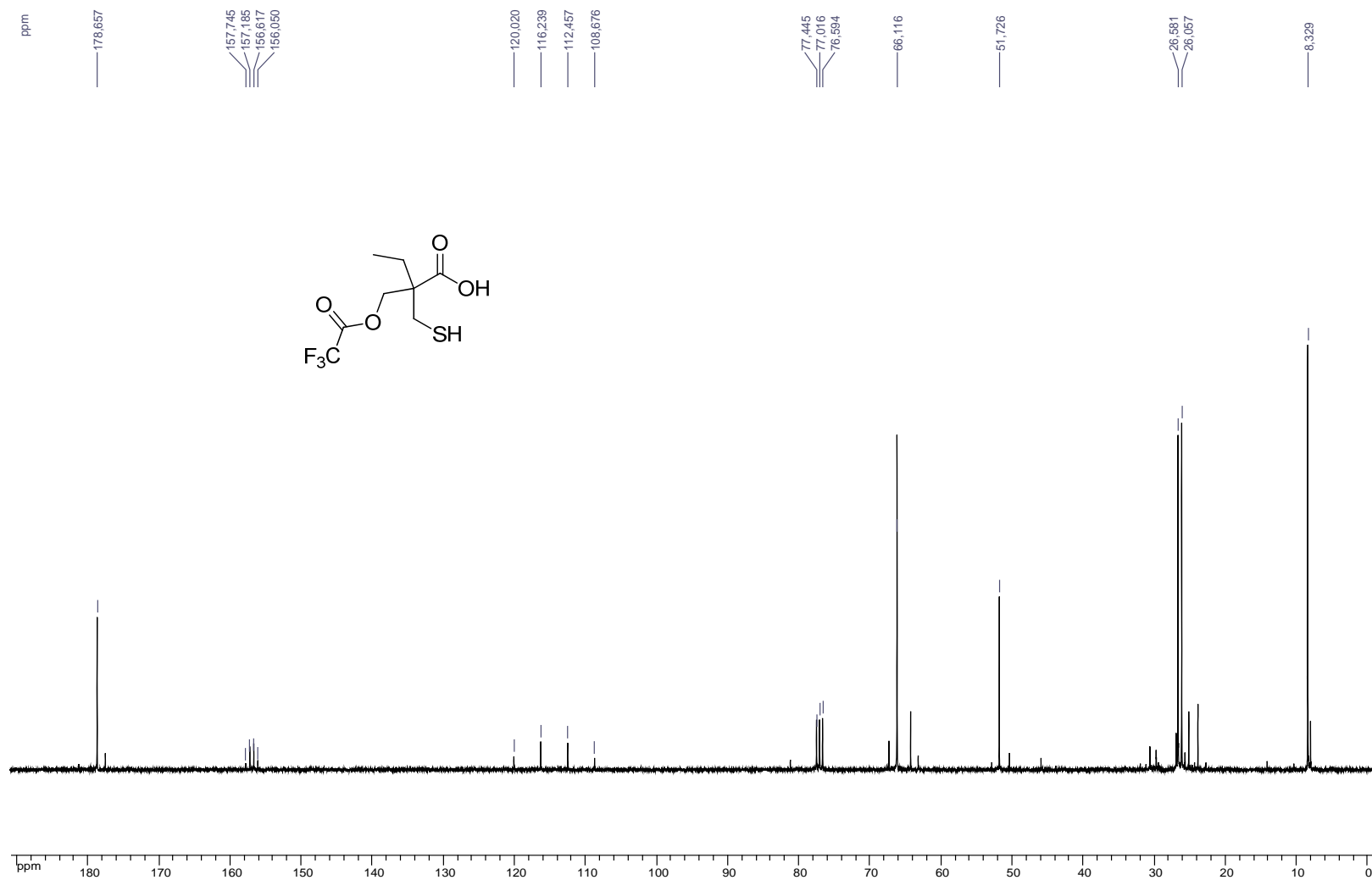
^{13}C NMR (75 MHz, CDCl_3) of compound 7.



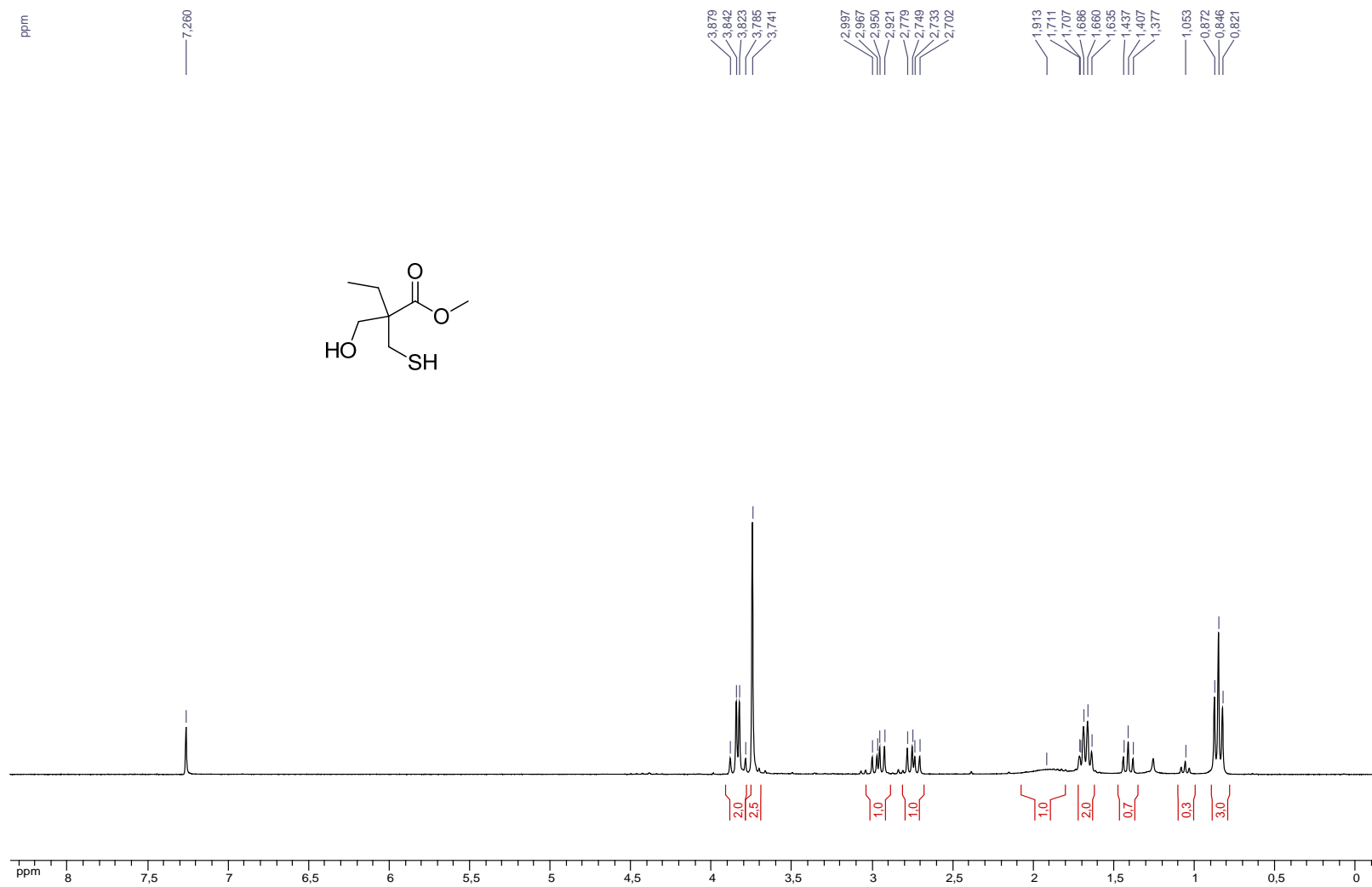
^1H NMR (300 MHz, CDCl_3) of compound **9**.



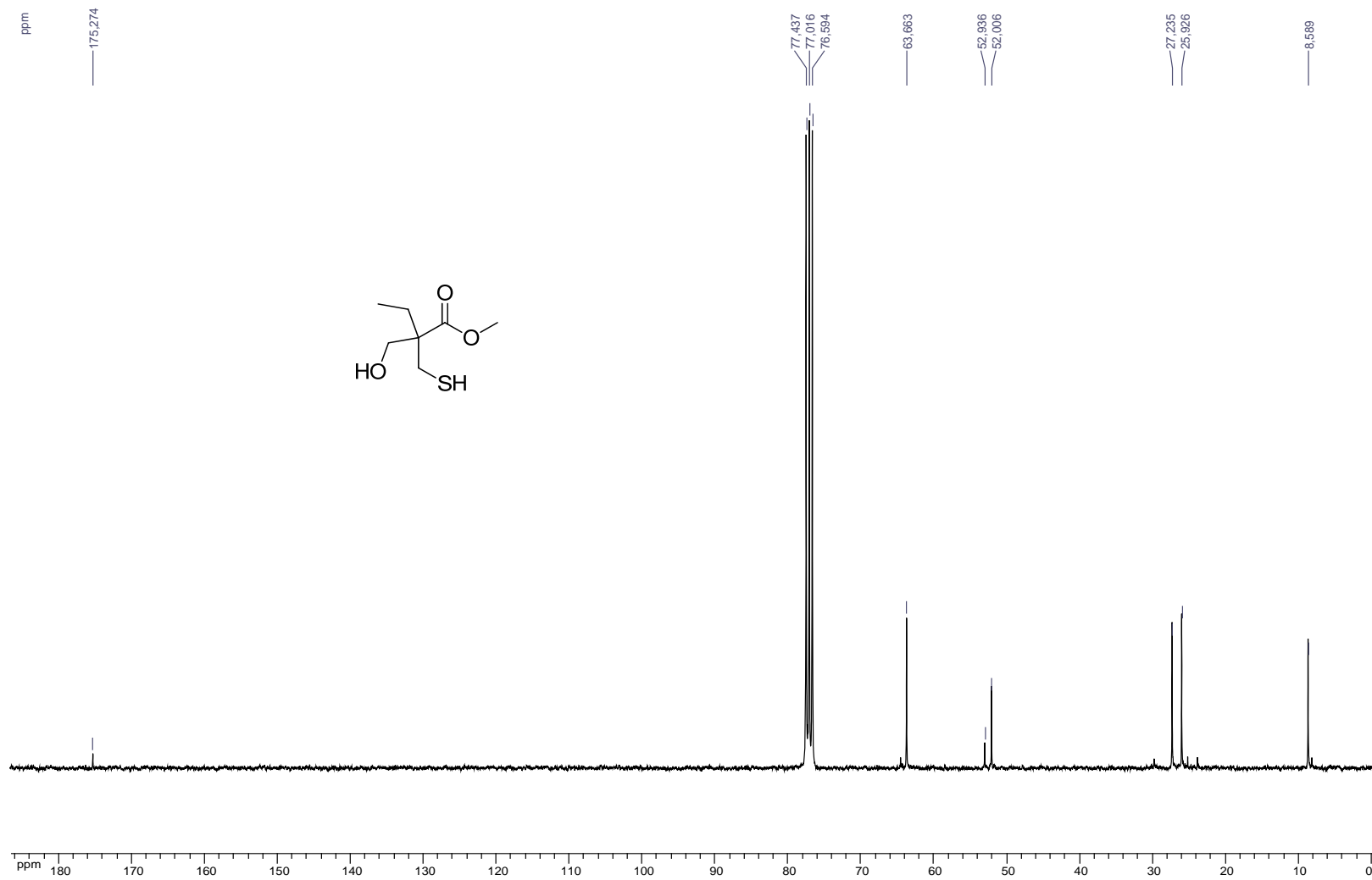
^{13}C NMR (75 MHz, CDCl_3) of compound 9.



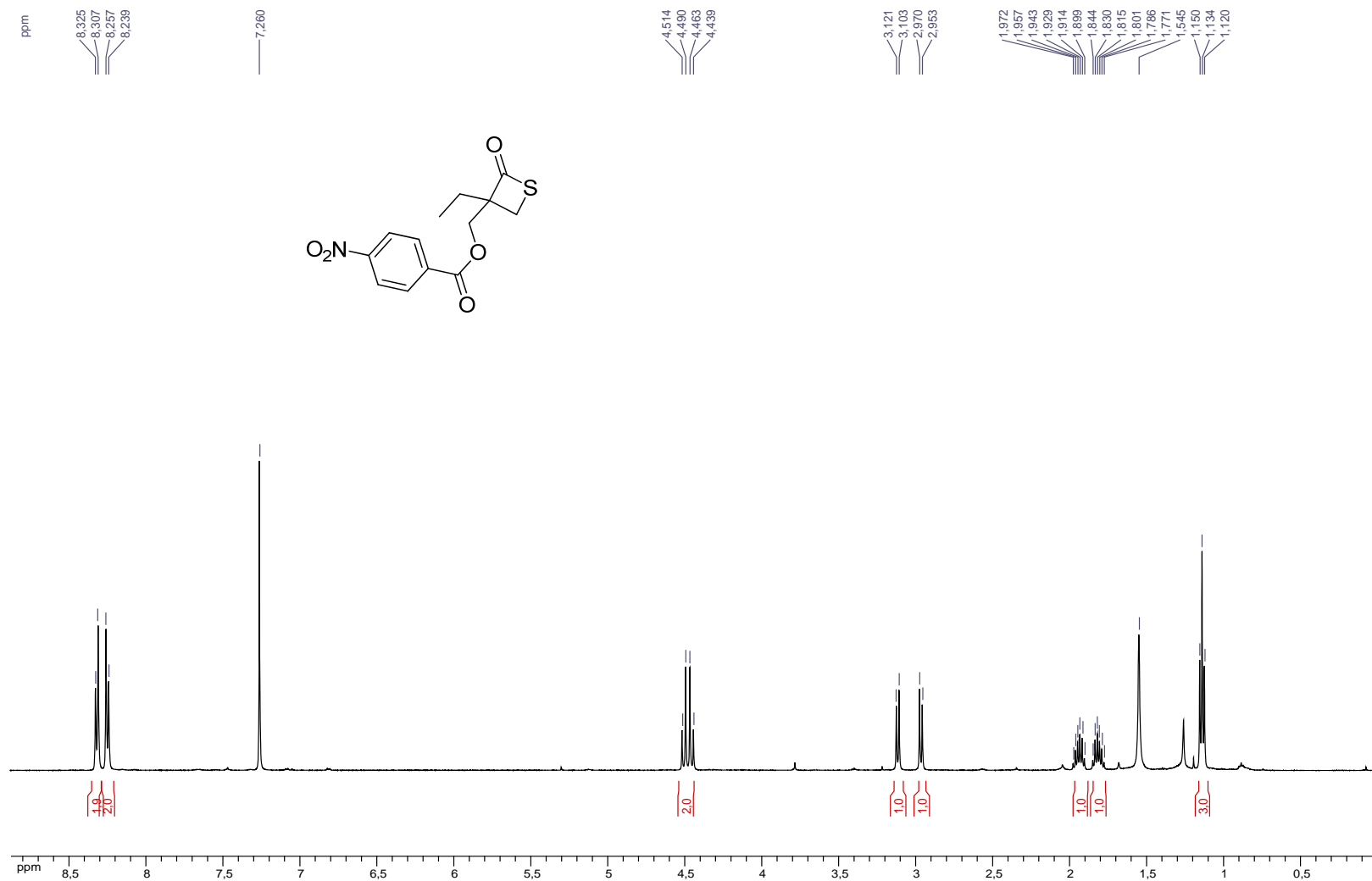
^1H NMR (300 MHz, CDCl_3) of compound **10**.



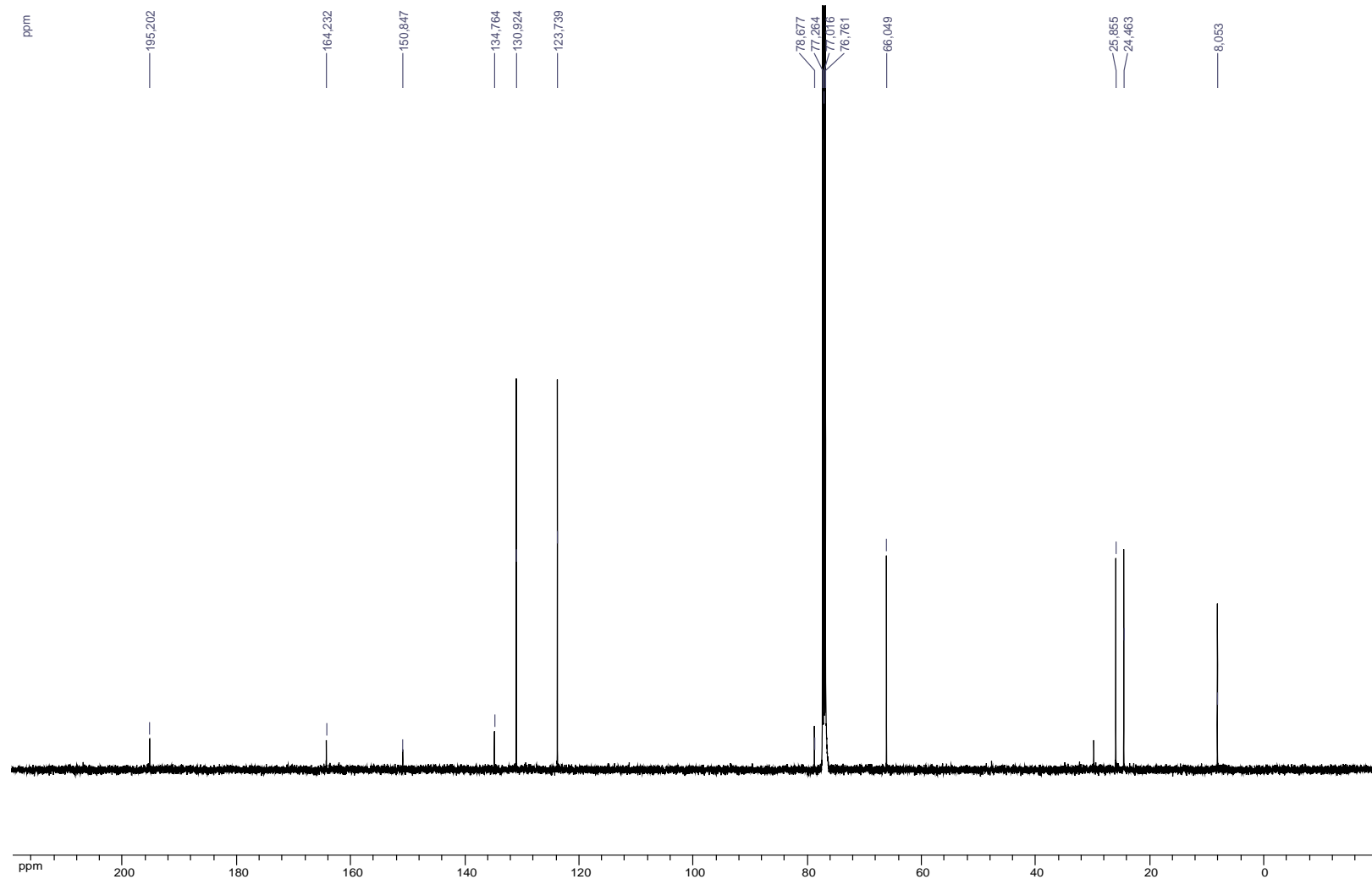
^{13}C NMR (75 MHz, CDCl_3) of compound **10**.



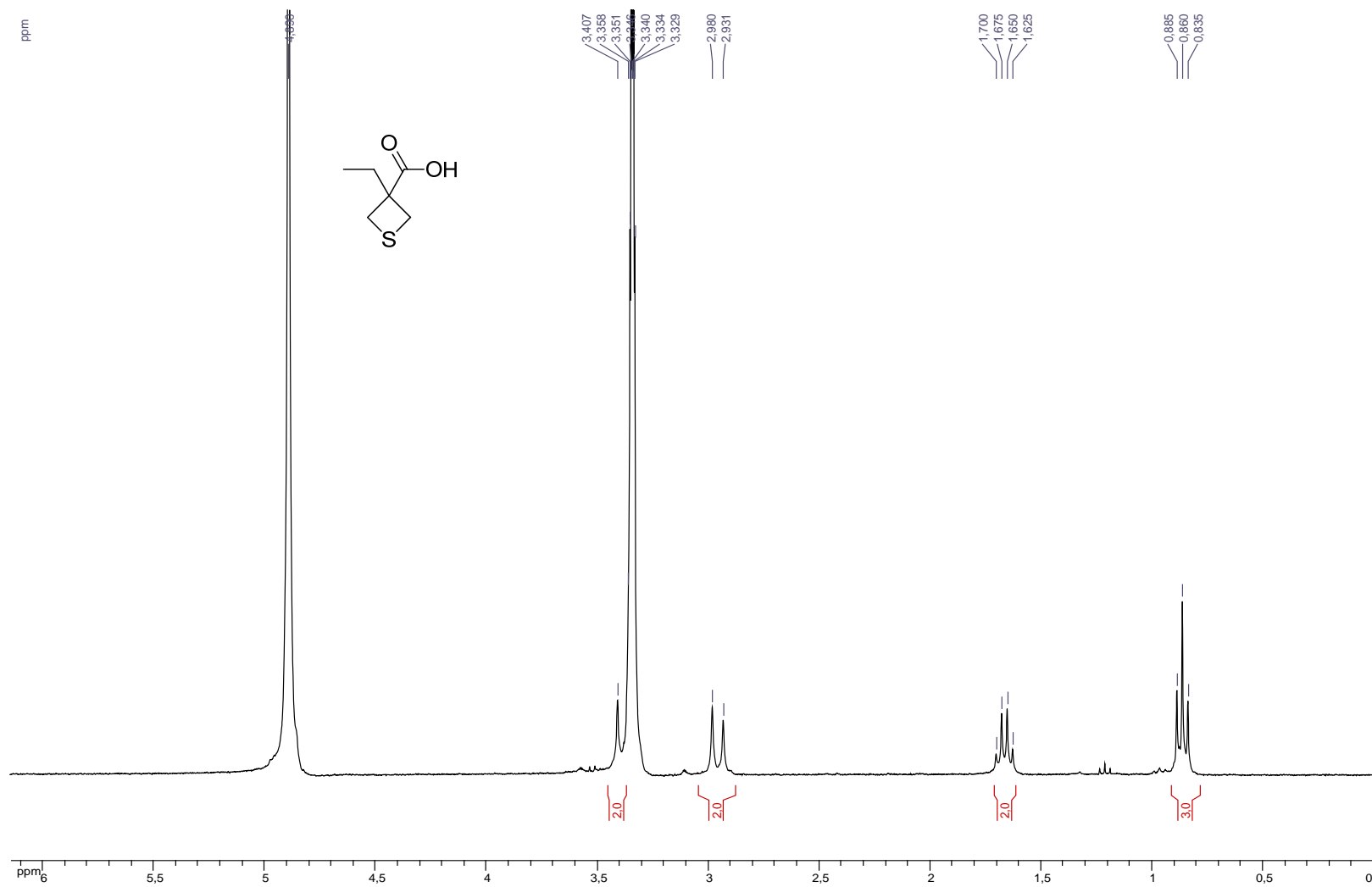
^1H NMR (500 MHz, CDCl_3) of compound **11**.



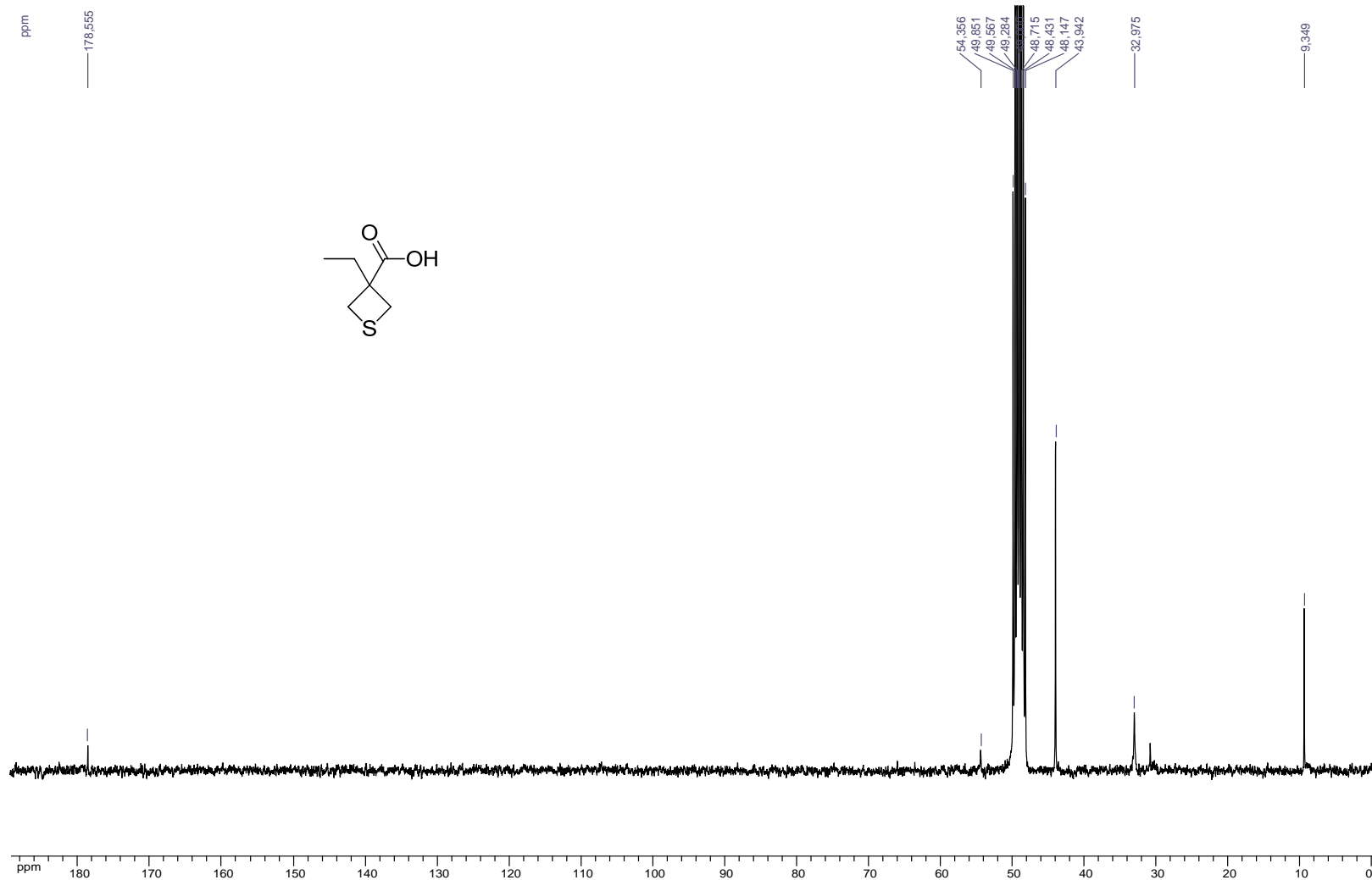
^{13}C NMR (75 MHz, CDCl_3) of compound **11**.



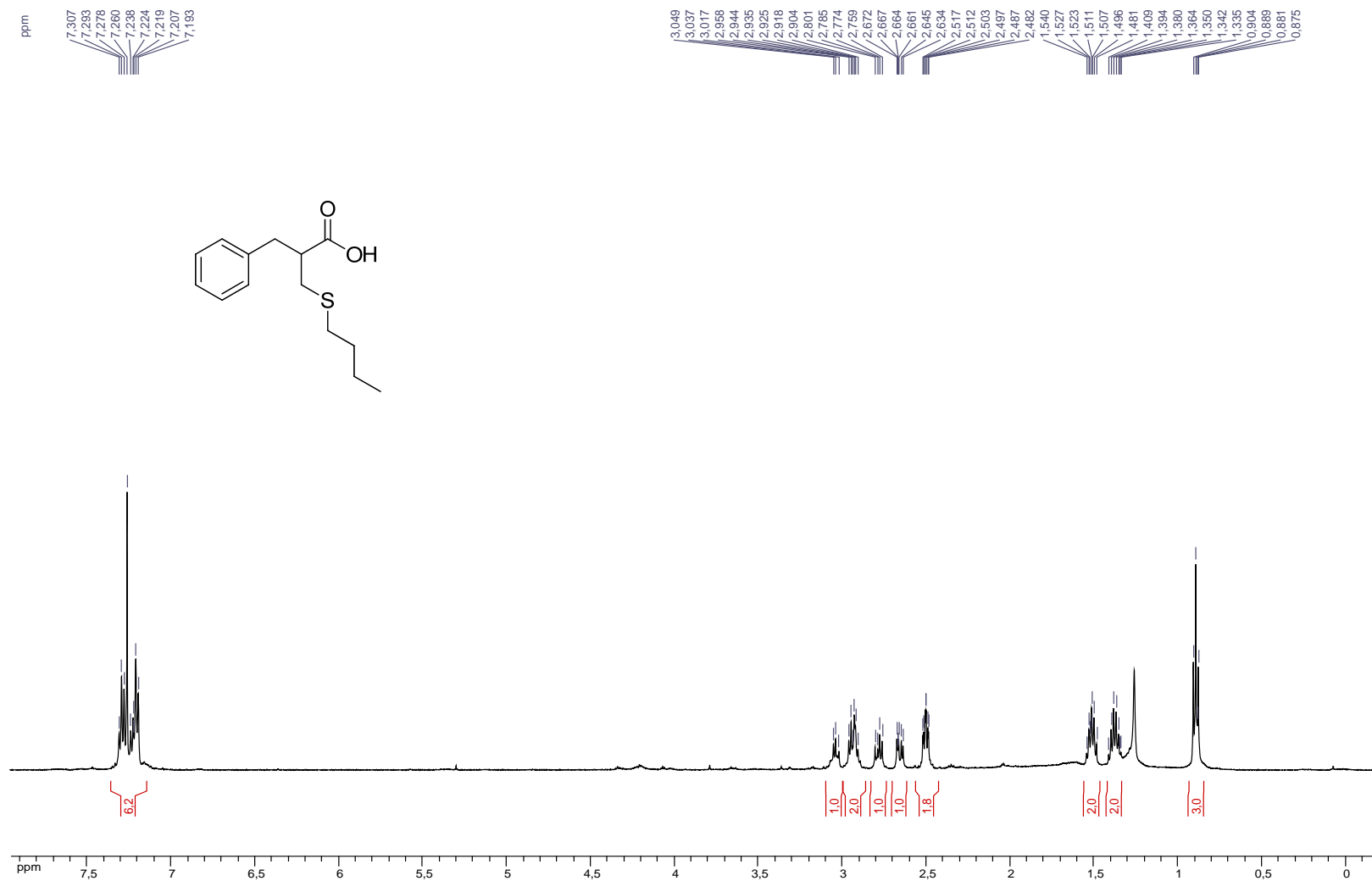
^1H NMR (300 MHz, CD_3OD) of compound **13**.



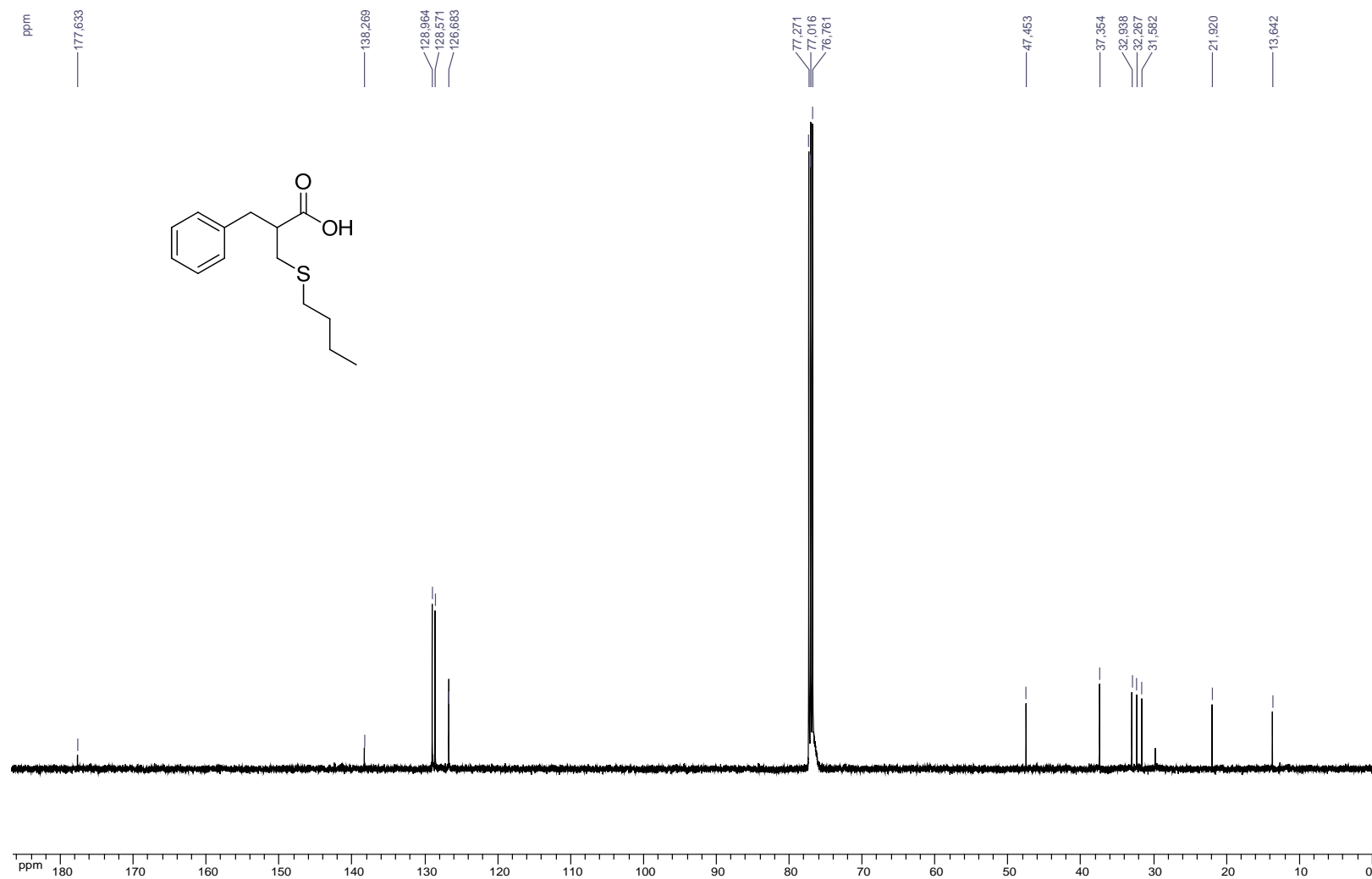
^{13}C NMR (75 MHz, CD_3OD) of compound **13**.



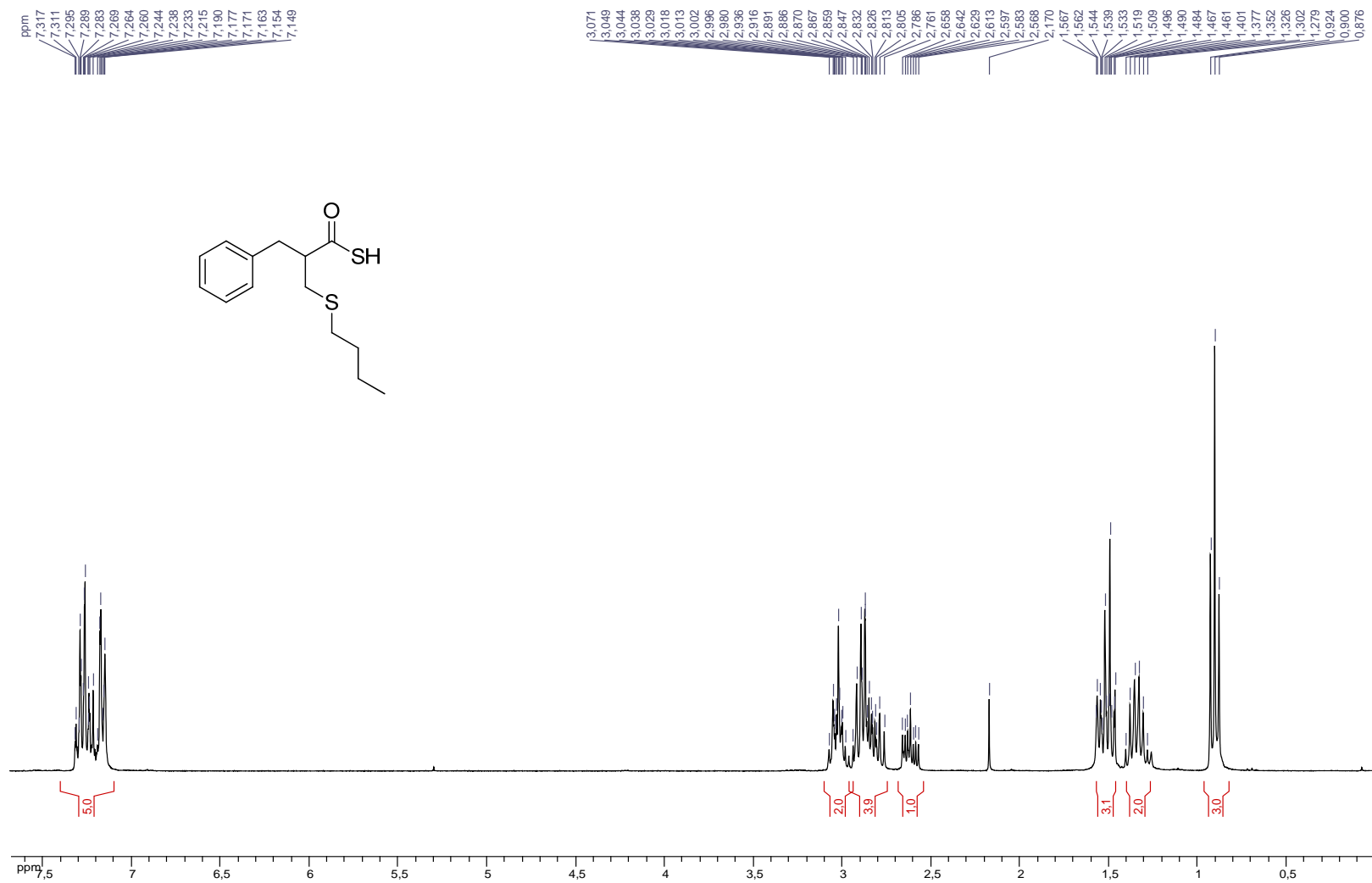
^1H NMR (300 MHz, CDCl_3) of compound **16**.



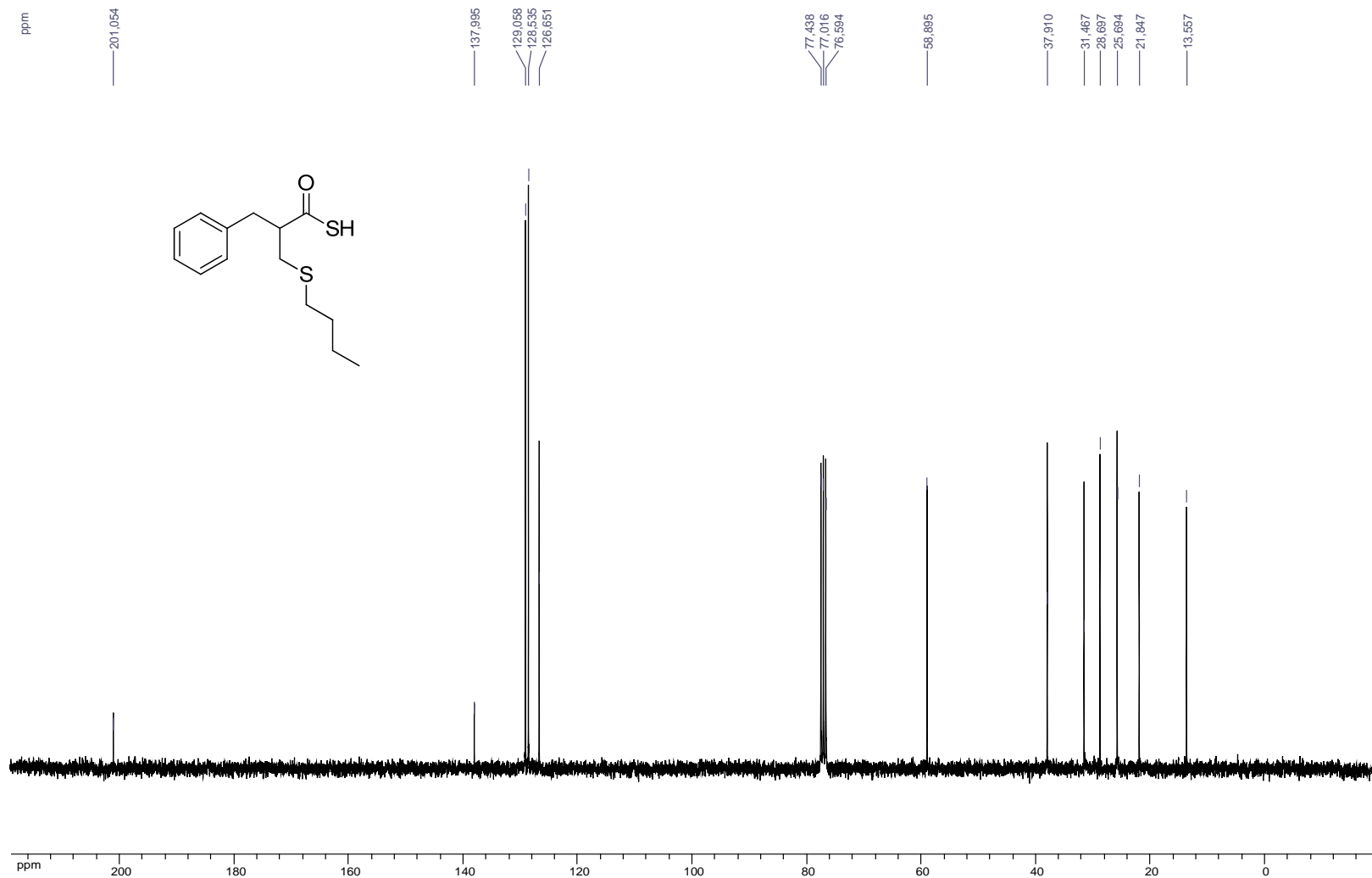
^{13}C NMR (75 MHz, CDCl_3) of compound **16**.



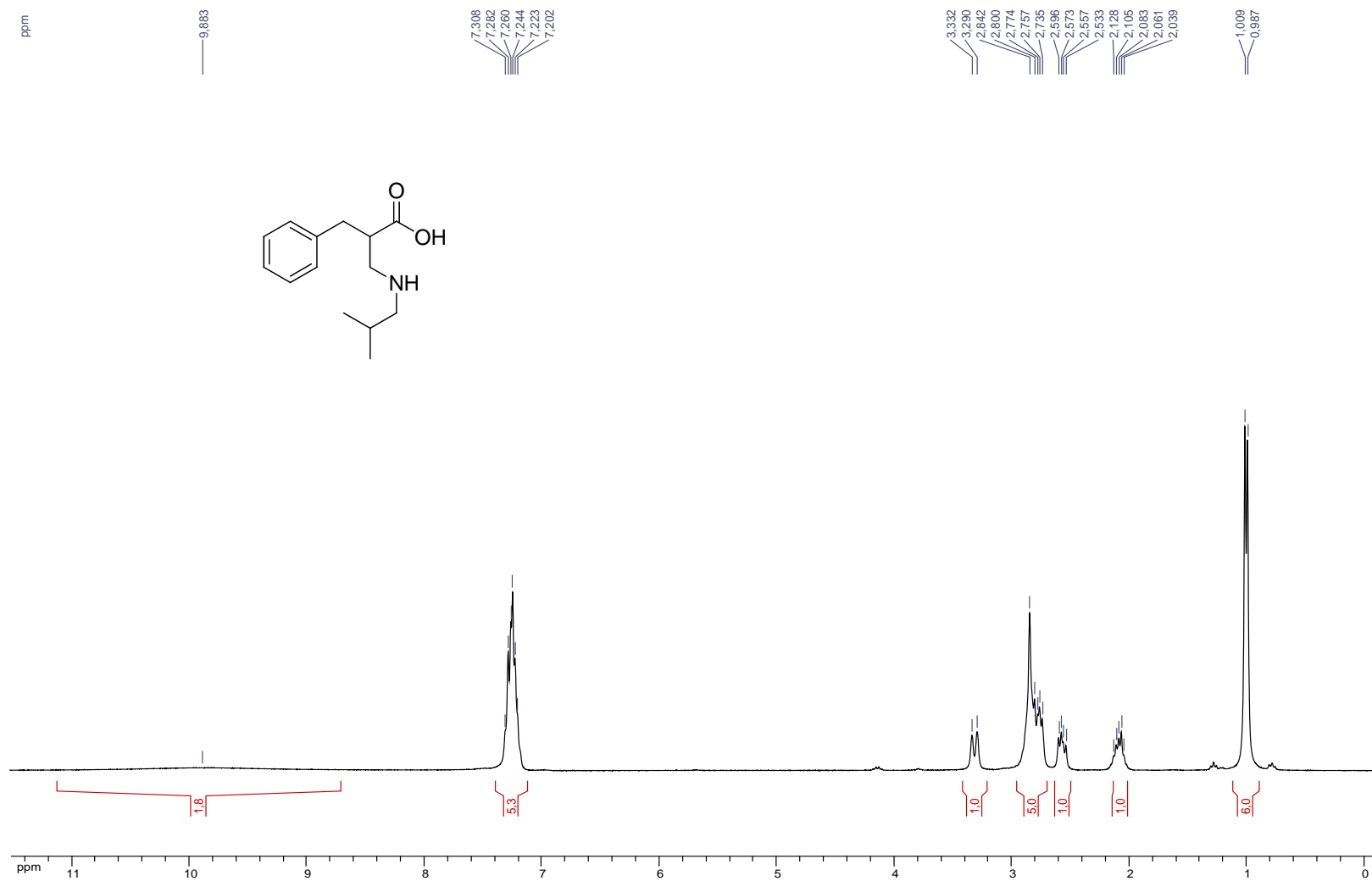
^1H NMR (300 MHz, CDCl_3) of compound **17**.



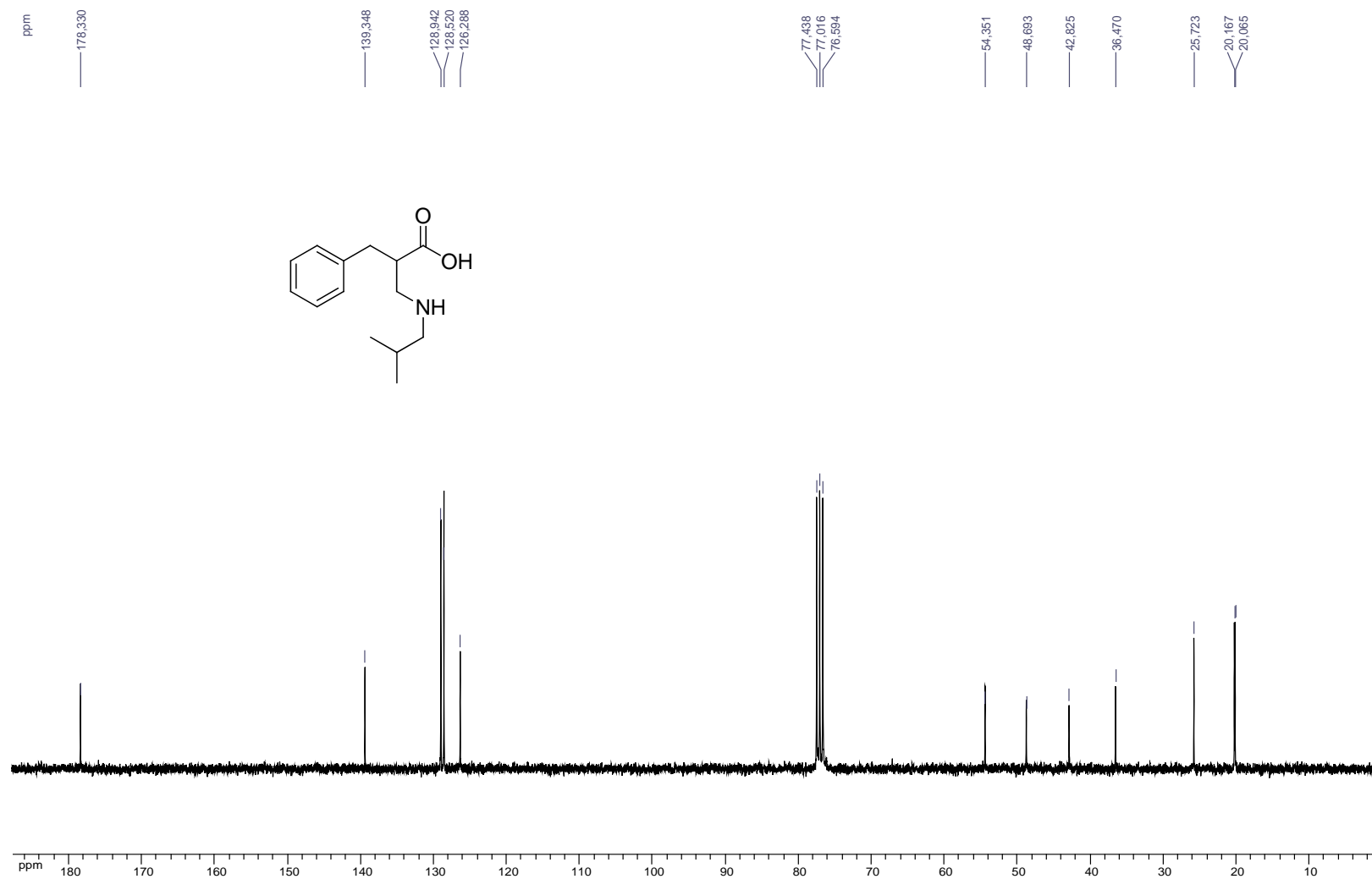
^{13}C NMR (75 MHz, CDCl_3) of compound **17**.



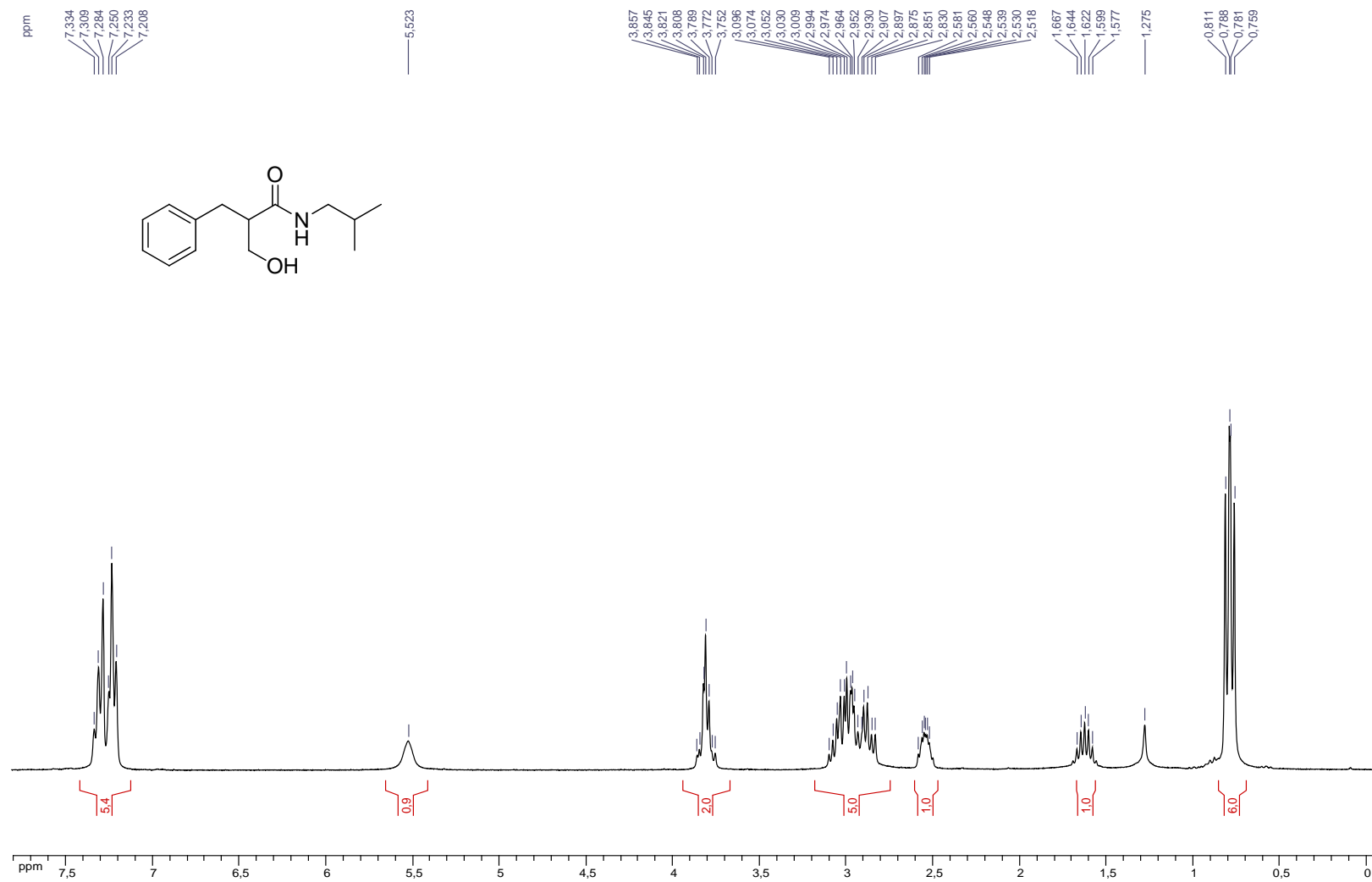
^1H NMR (300 MHz, CDCl_3) of compound **18**.



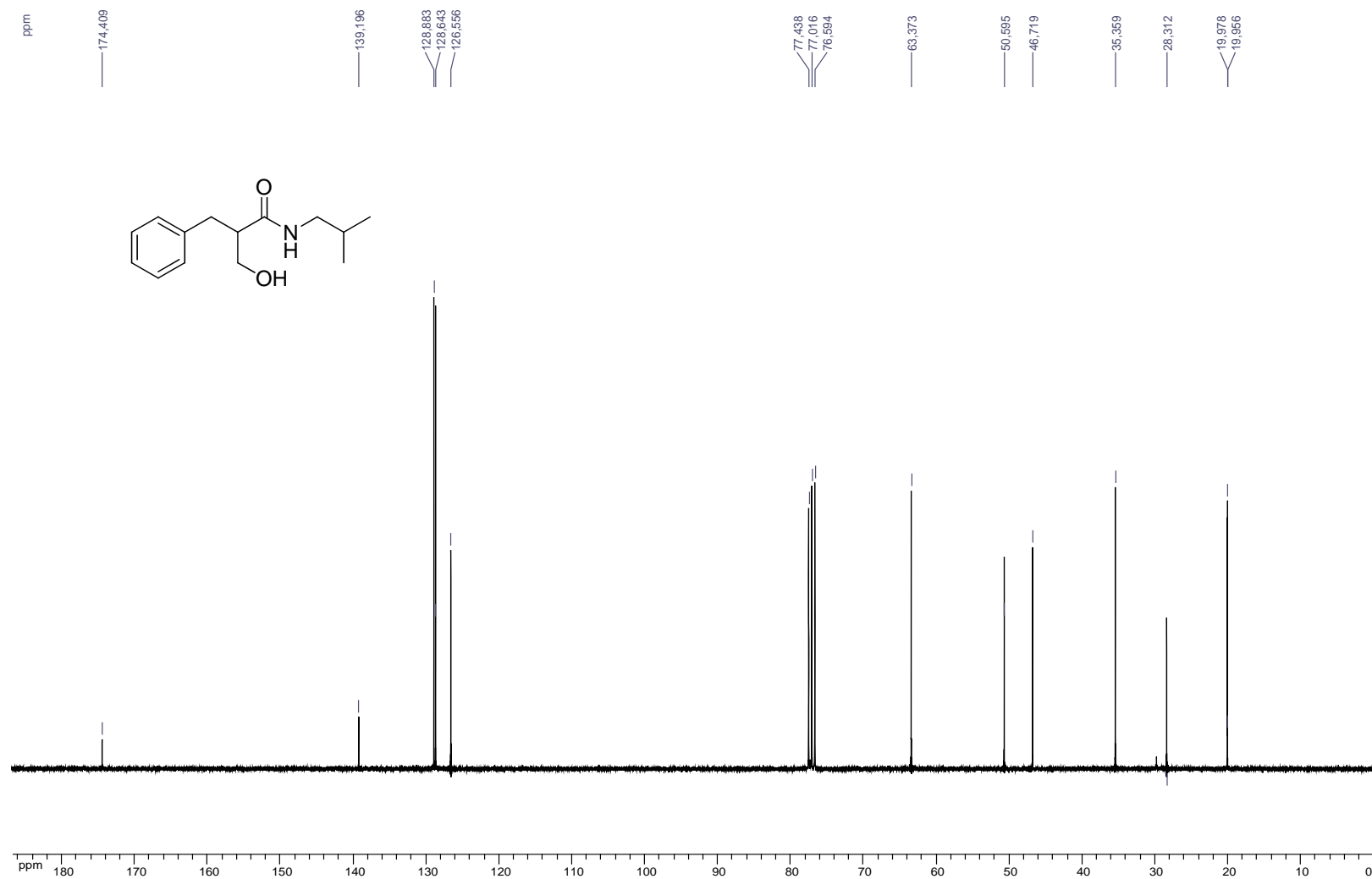
^{13}C NMR (75 MHz, CDCl_3) of compound **18**.



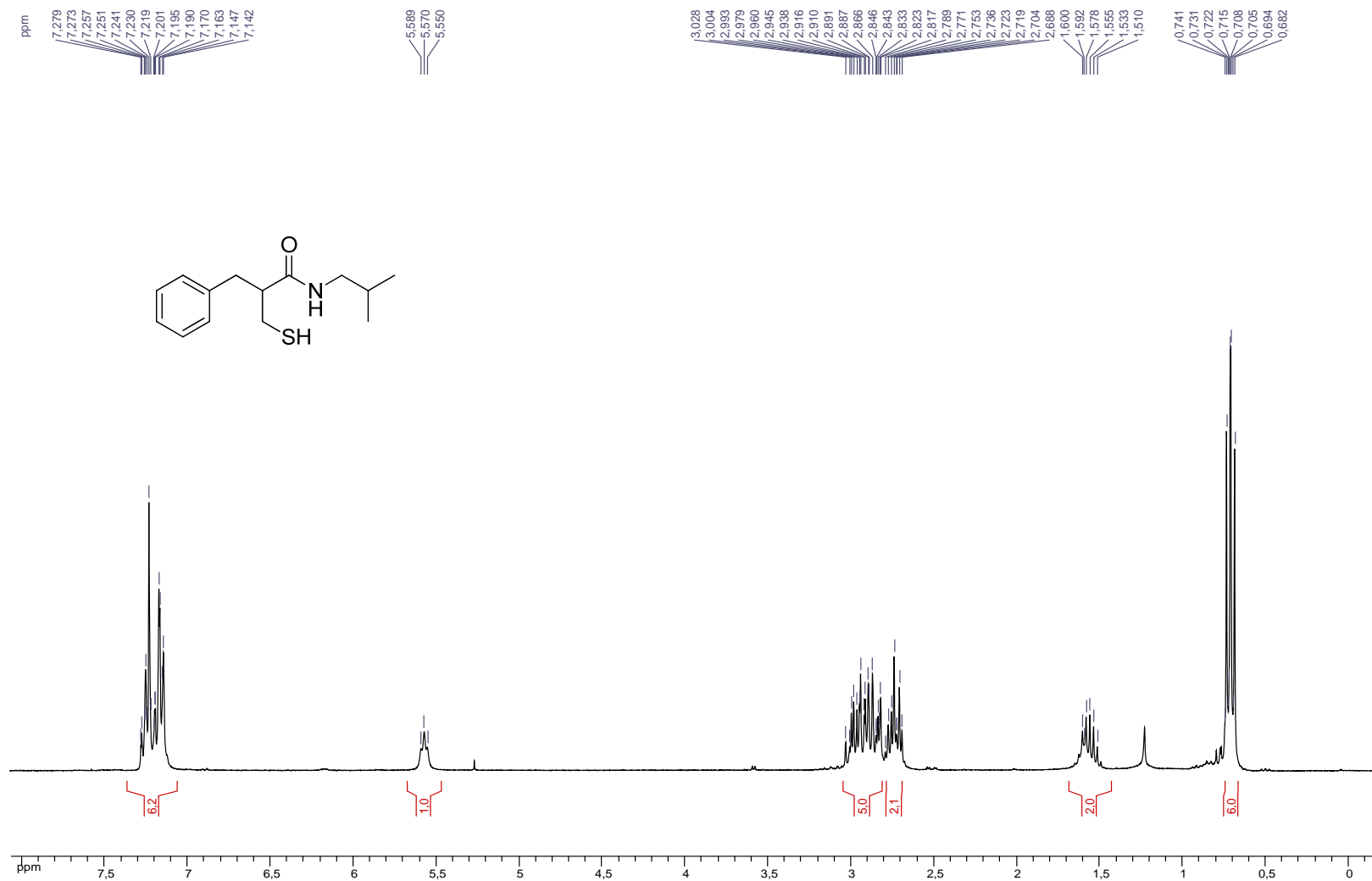
¹H NMR (300 MHz, CDCl₃) of compound **19**.



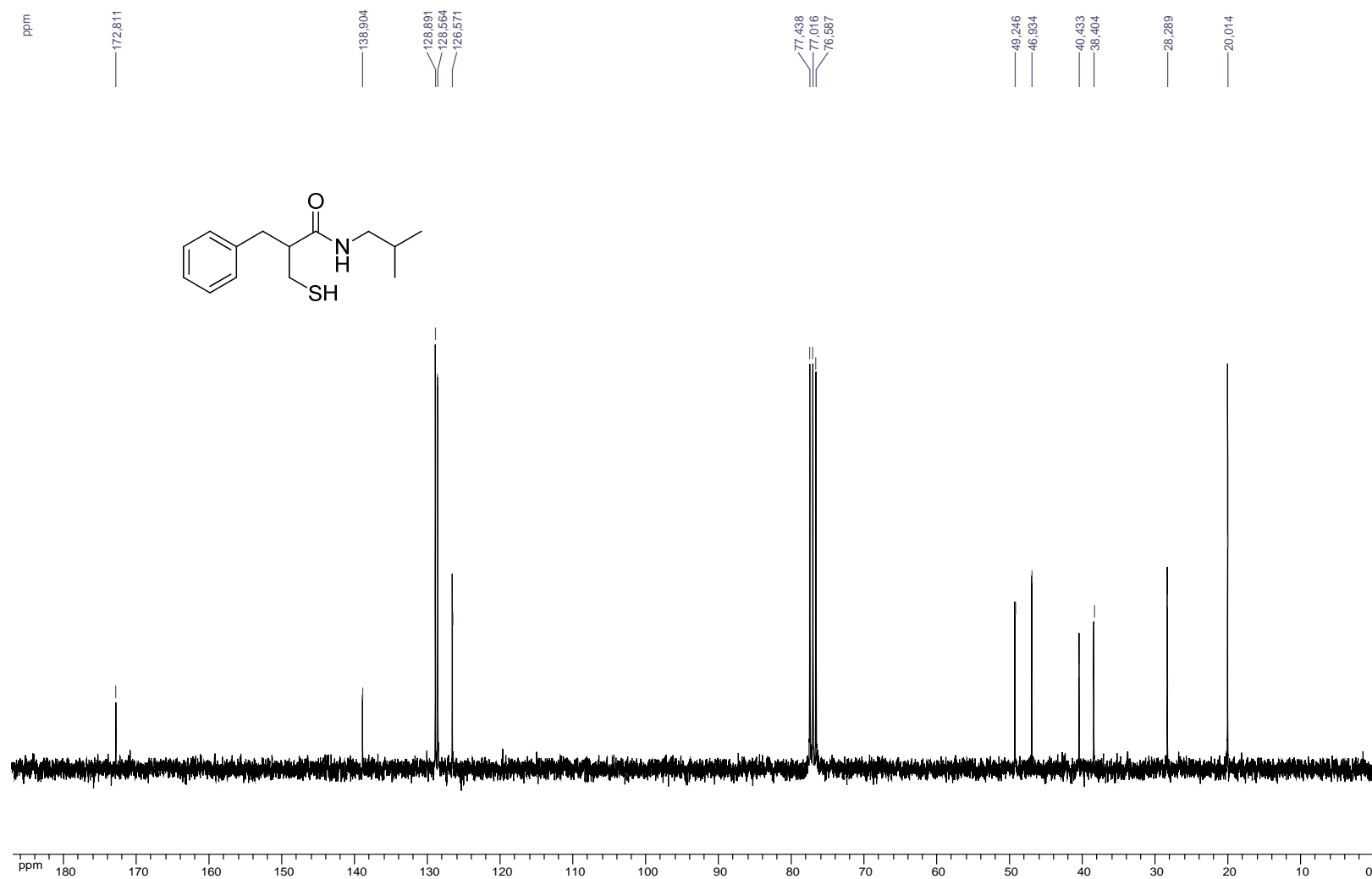
^{13}C NMR (75 MHz, CDCl_3) of compound **19**.



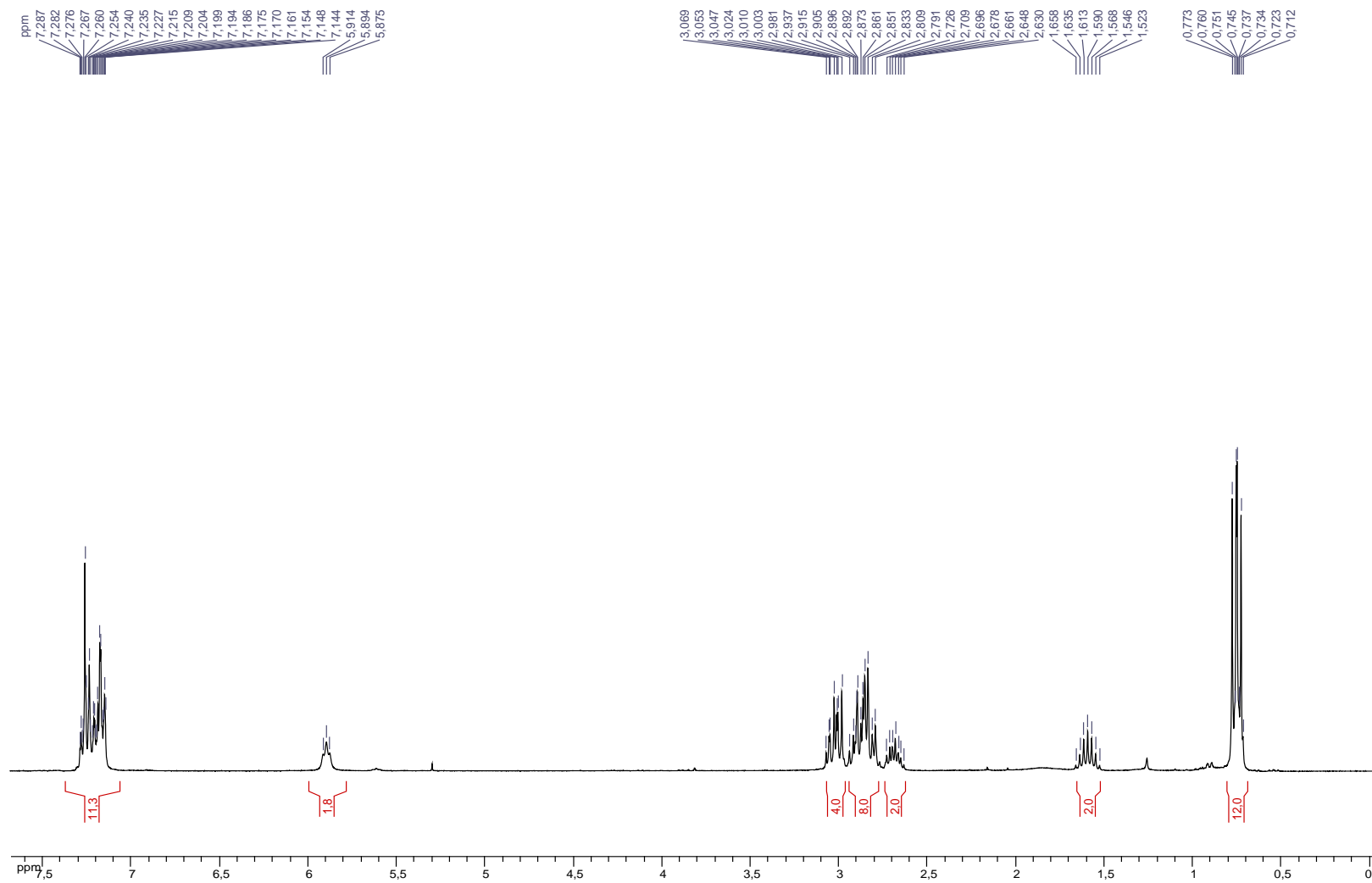
^1H NMR (300 MHz, CDCl_3) of compound **20**.



^{13}C NMR (75 MHz, CDCl_3) of compound **20**.



^1H NMR (300 MHz, CDCl_3) of compound **21**.



^{13}C NMR (75 MHz, CDCl_3) of compound **21**.

