Metal-free synthesis of imino-disaccharides and calix-iminosugars by photoinduced radical thiol-ene coupling (TEC)

Renaud Zelli, Pascal Dumy and Alberto Marra*

Institut des Biomolécules Max Mousseron (IBMM), UMR 5247, CNRS, Université de Montpellier, Ecole Nationale Supérieure de Chimie de Montpellier, 8 Rue de l'Ecole Normale, 34296 Montpellier cedex 5, France.

E-mail: Alberto.Marra@umontpellier.fr

Electronic Supplementary Information

Table of contents page

Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (40-63 μm). Optical rotations were measured at 20±2 °C in the stated solvent; $[\alpha]_D$ values are given in deg mL g^{-1} dm^{-1}. ^{1}H NMR (400 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in the stated solvent at room temperature unless otherwise specified. In the ^{1}H NMR spectra reported below, the n and m values quoted in geminal or vicinal proton-proton coupling constants $J_{n,m}$ refer to the number of the corresponding sugar protons. High resolution mass spectrometry (Waters Micromass Q-TOF) analyses were carried out at the *Laboratoire de Mesures Physiques*, University of Montpellier. The thiol-ene coupling (TEC) was carried out in a glass vial (diameter: 1 cm; wall thickness: 0.65 mm), closed with a natural rubber septum, located 2.5 cm away from the household UV-A (λ_{max} 365 nm) lamp apparatus equipped with four 15 W tubes (1.5 x 27 cm each). The commercially available photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DPAP) was used without further purification.

***N*-[4-(1'-thio-β-D-glucopyranosyl)-butyl]-1-deoxy-D-nojirimycin (14)**. A solution of *N*-butenyl-1-deoxy-D-nojirimycin **9** (26 mg, 0.12 mmol) and trifluoroacetic acid (26 μL, 0.35 mmol) in MeOH (240 μL) was stirred at room temperature for 5 min and then diluted with a solution of 1-thio-β-D-glucopyranose **10** (33 mg, 0.17 mmol) and DPAP (4.4 mg, 0.017 mmol) in MeOH (480 μL). The resulting solution was irradiated (365 nm) at room temperature for 30 min, then directly eluted from a short column (1 x 3.5 cm, d x h) of Dowex 1X8 ion exchange resin (OH^- form, activated immediately before use) with 3:1 MeOH-H_2O (15 mL) to give an eluate (≈16 mL) that was passed through a short column (0.5 x 4 cm, d x h) of Amberlyst 15 ion exchange resin (H^+ form). Then, the column was washed with 3:1 MeOH-H_2O (10 mL) to remove all the non-basic compounds. Finally, the imino-disaccharide **14** was released from the column upon elution with a 2M solution of ammonia in MeOH (15 mL) and removal of the solvent under vacuum (38.5 mg, 78%). $[\alpha]_D$ = -35.8 (*c* 0.4, H_2O). ^{1}H NMR (D_2O): δ 4.54 (d, 1H, $J_{1',2'}$ = 9.9 Hz, H-1'), 3.93 (dd, 1H, $J_{5,6a}$ = 2.0, $J_{6a,6b}$ = 12.3 Hz, H-6a), 3.91 (dd, 1H, $J_{5',6'a}$ = 2.0, $J_{6'a,6'b}$ = 12.2 Hz, H-6'a), 3.86 (dd, 1H, $J_{5',6'b}$ = 2.2 Hz, H-6'b), 3.72 (dd, 1H, $J_{5,6b}$ = 5.6 Hz, H-6b), 3.57 (ddd, 1H, $J_{1eq,2}$ = 4.6, $J_{2,3}$ = 9.3, $J_{1ax,2}$ = 11.1 Hz, H-2), 3.50 (dd, 1H, $J_{2',3'}$ = $J_{3',4'}$ = 8.7 Hz, H-3'), 3.46 (ddd, 1H, $J_{4',5'}$ = 8.7 Hz, H-5'), 3.43 (dd, 1H, H-4'), 3.41 (dd, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, H-4), 3.32 (dd, 1H, H-2'), 3.29 (dd, 1H, H-3), 3.07 (dd, 1H, $J_{1eq,1ax}$ = 11.5 Hz, H-1eq), 2.88-2.64 (m, 4H, CH_2N, CH_2S), 2.37 (dd, 1H, H-1ax), 2.32 (ddd, 1H, H-5), 1.71-1.57 (m, 4H, CH_2CH_2N, CH_2CH_2S). ^{13}C NMR (D_2O): δ 85.3 (CH), 79.8 (CH), 78.1 (CH), 77.2 (CH), 72.3 (CH), 69.9 (CH), 69.5 (CH), 68.7 (CH),

64.9 (CH), 60.8 (CH_2), 57.4 (CH_2), 55.1 (CH_2), 51.4 (CH_2), 29.7 (CH_2), 27.2 (CH_2), 21.9 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{16}H_{32}NO_9S$ $[M+H]^+$ 414.1798, found 414.1800.

***N*-[4-(2'-acetamido-2'-deoxy-1'-thio-β-D-glucopyranosyl)-butyl]-1-deoxy-D-nojirimycin (15)**. *N*-butenyl-1-deoxy-D-nojirimycin **9** (26 mg, 0.12 mmol) was allowed to react with the glycosyl thiol **11** (40 mg, 0.17 mmol) as described for the synthesis of **14** to give, after the same work-up and purification, **15** (40 mg, 74%) as an amorphous solid. $[\alpha]_D$ = -29.4 (*c* 0.4, H_2O). ^{1}H NMR (D_2O): δ 4.62 (d, 1H, $J_{1',2'}$ = 10.4 Hz, H-1'), 3.97-3.89 (m, 2H, $J_{5,6a}$ = 2.0 Hz, H-6a, H-6a') 3.85 (dd, 1H, $J_{5,6b}$ = 2.6, $J_{6a,6b}$ = 12.9 Hz, H-6b), 3.76 (dd, 1H, $J_{2',3'}$ = 9.9 Hz, H-2'), 3.73 (dd, 1H, $J_{5',6'b}$ = 1.6 Hz, H-6'b), 3.57 (ddd, 1H, $J_{1eq,2}$ = 4.9, $J_{2,3}$ = 9.2, $J_{1ax,2}$ = 11.0 Hz, H-2), 3.58-3.52 (m, 1H, H-5'), 3.51-3.45 (m, 2H, H-3', H-4'), 3.40 (dd, 1H, $J_{3,4}$ = 9.2, $J_{4,5}$ = 9.6 Hz, H-4), 3.28 (dd, 1H, H-3), 3.05 (dd, 1H, $J_{1eq,1ax}$ = 11.4 Hz, H-1eq), 2.88-2.64 (m, 4H, CH_2N, CH_2S), 2.37 (dd, 1H, H-1ax), 2.31 (ddd, 1H, H-5), 2.05 (s, 3H, CH_3), 1.71-1.58 (m, 4H, CH_2CH_2N, CH_2CH_2S). ^{13}C NMR (D_2O): δ 174.3 (C), 84.2 (CH), 79.9 (CH), 78.2 (CH), 75.1 (CH), 69.9 (CH), 69.7 (CH), 68.7 (CH), 64.9 (CH), 60.8 (CH_2), 57.3 (CH_2), 55.1 (CH_2), 54.8 (CH), 51.4 (CH_2), 29.8 (CH_2), 26.8 (CH_2), 22.5 (CH_3), 21.7 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{18}H_{35}N_2O_9S$ $[M+H]^+$ 455.2063, found 455.2064.

***N*-[4-(1'-thio-α-D-glucopyranosyl)-butyl]-1-deoxy-D-nojirimycin (16)**. *N*-butenyl-1-deoxy-D-nojirimycin **9** (26 mg, 0.12 mmol) was allowed to react with the glycosyl thiol **12** (33 mg, 0.17 mmol) as described for the synthesis of **14** to give, after the same work-up and purification, **16** (39.5 mg, 80%) as an amorphous solid. $[\alpha]_D$ = +12.0 (*c* 0.4, H_2O). ^{1}H NMR (D_2O): δ 5.44 (d, 1H, $J_{1',2'}$ = 5.5 Hz, H-1'), 4.07 (ddd, 1H, $J_{5',6'a}$ = 2.3, $J_{5',6'b}$ = 5.4, $J_{4',5'}$ = 10.0 Hz, H-5'), 3.94 (dd, 1H, $J_{5,6a}$ = 2.4, $J_{6a,6b}$ = 12.8 Hz, H-6a), 3.89 (dd, 1H, $J_{6'a,6'b}$ = 12.4 Hz, H-6'a), 3.86 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, H-6b), 3.84 (dd, 1H, $J_{2',3'}$ = 9.8 Hz, H-2'), 3.80 (dd, 1H, H-6'b), 3.50 (dd, 1H, $J_{3',4'}$ = 8.9 Hz, H-3'), 3.57 (ddd, 1H, $J_{1eq,2}$ = 4.9, $J_{2,3}$ = 9.2, $J_{1ax,2}$ = 10.7 Hz, H-2), 3.43 (dd, 1H, H-4'), 3.40 (dd, 1H, $J_{4,5}$ = 8.3, $J_{3,4}$ = 8.9 Hz, H-4), 3.29 (dd, 1H, H-3), 3.05 (dd, 1H, $J_{1eq,1ax}$ = 11.4 Hz, H-1eq), 2.84-2.62 (m, 4H, CH_2N, CH_2S), 2.35 (dd, 1H, H-1ax), 2.30 (ddd, 1H, H-5), 1.72-1.57 (m, 4H, CH_2CH_2N, CH_2CH_2S). ^{13}C NMR (D_2O): δ 85.6 (CH), 78.3 (CH), 73.7 (CH), 72.3 (CH), 70.9 (CH), 70.0 (CH), 69.7 (CH), 68.8 (CH), 64.9 (CH), 60.5 (CH_2), 57.5 (CH_2), 55.2 (CH_2), 51.4 (CH_2), 29.9 (CH_2), 26.8 (CH_2), 21.9 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{16}H_{32}NO_9S$ $[M+H]^+$ 414.1798, found 414.1798.

***N*-{4-[3-(α-D-glucopyranosyl)-propyl-1-thio]-butyl}-1-deoxy-D-nojirimycin (17)**. *N*-butenyl-1-

deoxy-D-nojirimycin **9** (26 mg, 0.12 mmol) was allowed to react with the freshly prepared glycosylpropyl thiol **13** (57 mg, 0.24 mmol, containing 5-10% of the corresponding disulfide derivative) as described for the synthesis of **14** to give, after the same work-up and purification, **17** (34 mg, 62%) as an amorphous solid. $[\alpha]_D$ = +32.8 (*c* 0.3, H_2O). ^{1}H NMR (D_2O): δ 3.98-3.85 (m, 1H, H-1'), 3.84-3.68 (m, 3H, H-6a, H-6b, H-6a'), 3.64-3.38 (m, 5H, H-2, H-2', H-4', H-5', H-6b'), 3.34-3.13 (m, 3H, H-3, H-3', H-4), 3.05 (dd, 1H, $J_{1eq,2}$ = 4.8, $J_{1eq,1ax}$ = 11.5 Hz, H-1eq), 2.90-2.44 (m, 6H, CH_2N, CH_2SCH_2) 2.37-2.18 (m, 2H, H-1ax, H-5), 1.86-1.41(m, 8H, 4 CH_2). ^{13}C NMR (D_2O): δ 75.4 (CH), 73.2 (CH), 72.4 (CH), 71.2 (CH), 70.3 (CH), 69.6 (CH), 68.4 (CH), 64.9 (CH), 61.0 (CH_2), 56.9 (CH_2), 54.9 (CH), 51.5 (CH_2), 30.8 (CH_2), 30.7 (CH_2), 26.5 (CH_2), 24.7 (CH_2), 22.7 (CH_2), 21.9 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{19}H_{38}NO_9S$ $[M+H]^+$ 456.2267, found 456.2271.

1-Allyl-2,3,4,6-tetra-*O*-benzyl-1-deoxy-β-L-*ido*-nojirimycin (20). To a cooled (0 °C), stirred solution of $(NH_4)_2Ce(NO_3)_6$ (6.10 g, 11.12 mmol) in THF (185 mL) and water (37 mL) was added dropwise a solution of *N*-(*p*-methoxybenzyl)-iminosugar **19** (1.90 g, 2.78 mmol) in THF (6.5 mL). The mixture was stirred at room temperature for 6 h, then diluted with saturated aqueous $NaHCO_3$ (100 mL) and extracted with AcOEt (3 x 100 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 4:1 toluene-Et_2O (containing 1% of Et_3N) to give **20** (1.22 g, 78%) as a colorless syrup. $[\alpha]_D$ = +10.4 (*c* 0.6, $CHCl_3$). ^{1}H NMR (C_6D_6): δ 7.32-7.04 (m, 20H, Ar), 5.95 (dddd, 1H, *J* = 6.1, 8.0, 10.1, 17.1 Hz, C*H*=CH_2), 5.10 (dddd, 1H, *J* = 1.6, 1.6, 2.5, 17.1 Hz, 1 H of CH=*CH*$_2$), 5.03 (dddd, 1H, *J* = 1.1, 1.1, 2.5, 10.1 Hz, 1 H of CH=*CH*$_2$), 4.53 and 4.47 (2 d, 2H, *J* = 11.6 Hz, Ph*CH*$_2$), 4.50 and 4.25 (2 d, 2H, *J* = 11.5 Hz, Ph*CH*$_2$), 4.37 and 4.30 (2 d, 2H, *J* = 12.0 Hz, Ph*CH*$_2$), 4.35 and 4.27 (2 d, 2H, *J* = 11.2 Hz, Ph*CH*$_2$), 3.90 (dd, 1H, $J_{2,3}$ = 2.7, $J_{3,4}$ = 2.7 Hz, H-3), 3.78 (ddd, 1H, $J_{2,4}$ = 0.7, $J_{4,5}$ = 1.6 Hz, H-4), 3.67-3.63 (m, 2H, H-6a, H-6b), 3.62-3.57 (m, 1H, H-5), 3.36 (ddd, 1H, $J_{1,2}$ = 2.1 Hz, H-2), 3.22 (ddd, 1H, $J_{1,CH2a}$ = $J_{1,CH2b}$ = 7.3 Hz, H-1), 2.49 (ddddd, 1H, *J* = 14.4 Hz, 1 H of *CH*$_2$-CH=CH_2), 2.35 (ddddd, 1H, 1 H of *CH*$_2$-CH=CH_2). ^{13}C NMR (C_6D_6): δ 139.4 (C), 139.3 (C), 139.2 (C), 138.8 (C), 137.1 (CH), 116.2 (CH_2), 75.4 (CH), 73.4 (CH_2), 73.0 (CH_2), 72.7 (CH), 72.3 (CH_2), 72.1 (CH_2), 71.6 (CH), 70.6 (CH_2), 56.3 (CH), 55.8 (CH), 37.3 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{37}H_{42}NO_4$ $[M+H]^+$ 564.3114, found 564.3116.

1-Allyl-1-deoxy-β-L-*ido*-nojirimycin (21). To cooled (-78 °C), stirred liquid ammonia (≈5 mL) sodium (125 mg, 5.43 mmol) was added in one portion. After complete dissolution of the sodium (blue solution), a solution of **20** (203 mg, 0.36 mmol) and allylamine (270 μL, 3.60 mmol) in anhydrous THF

(1.1 mL) was added dropwise. Then, the reaction mixture was diluted with water (0.6 mL) and allowed to warm to room temperature to remove the ammonia. The crude was diluted with more water (3 mL) and extracted with Et_2O (2 x 10 mL). The aqueous phase was treated with Amberlyst 15 ion exchange resin (H^+ form) under gentle stirring until neutral pH, then filtered and the resin washed with water. The iminosugar **21** was released from the resin upon elution with 1M aqueous NH_4OH (10 mL) and removal of the solvent under vacuum (73 mg, 100%, as a white foam). $[\alpha]_D$ = -4.8 (*c* 0.8, H_2O). ^1H NMR (D_2O): δ 5.83 (dddd, *J* = 7.2, 7.2, 10.2, 17.3 Hz, C*H*=CH_2), 5.15 (dddd, 1H, *J* = 1.3, 1.3, 1.9, 17.3 Hz, 1 H of CH=CH_2), 5.11 (dddd, 1H, *J* = 1.5, 1.5, 1.9, 10.2 Hz, 1 H of CH=CH_2), 3.98 (dd, 1H, $J_{2,3}$ = 3.2, $J_{3,4}$ = 3.9 Hz, H-3), 3.73 (ddd, 1H, $J_{2,4}$ = 1.5, $J_{4,5}$ = 1.7 Hz, H-4), 3.68 (dd, 1H, $J_{5,6a}$ = 6.5, $J_{6a,6b}$ = 11.1 Hz, H-6a), 3.64 (ddd, 1H, $J_{1,2}$ = 1.6 Hz, H-2), 3.60 (dd, 1H, $J_{5,6b}$ = 6.8 Hz, H-6b), 3.02 (ddd, 1H, H-5), 2.96 (ddd, 1H, $J_{1,CH2a} = J_{1,CH2a}$ = 7.3 Hz, H-1), 2.34-2.18 (m, 2H, CH_2-CH=CH_2). ^{13}C NMR (D_2O): δ 135.3 (CH), 117.4 (CH_2), 69.8 (CH), 69.4 (CH), 68.8 (CH), 62.2 (CH_2), 55.1 (CH), 53.2 (CH), 35.5 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_9H_{18}NO_4$ $[M+H]^+$ 204.1236, found 204.1240.

1-Deoxy-1-[3-(1'-thio-β-D-glucopyranosyl)-propyl]-β-L-*ido*-nojirimycin (22). 1-Allyl-1-deoxy-β-L-*ido*-nojirimycin **21** (20 mg, 0.10 mmol) was allowed to react with the glycosyl thiol **10** (27 mg, 0.14 mmol) as described for the synthesis of **14** to give, after the same work-up and purification, **22** (24 mg, 61%) as an amorphous solid. $[\alpha]_D$ = -18.3 (*c* 0.4, H_2O). ^1H NMR (D_2O): δ 4.55 (d, 1H, $J_{1',2'}$ = 9.9 Hz, H-1'), 4.04 (dd, 1H, $J_{3,4} = J_{2,3}$ = 3.2 Hz, H-3), 3.90 (dd, 1H, $J_{5',6'a}$ = 2.1, $J_{6'a,6'b}$ = 12.4 Hz, H-6'a), 3.80 (ddd, 1H, $J_{2,4}$ = 1.5, $J_{4,5}$ = 2.1 Hz, H-4), 3.72 (dd, 1H, $J_{5,6a}$ = 6.7, $J_{6a,6b}$ = 11.1 Hz, H-6a), 3.69 (ddd, 1H, $J_{1,2}$ = 1.6 Hz, H-2), 3.64 (dd, 1H, $J_{5,6b}$ = 6.6 Hz, H-6b), 3.60 (dd, 1H, $J_{5',6'b}$ = 6.5 Hz, H-6'b), 3.50 (dd, 1H, $J_{4',5'}$ = 8.7, $J_{3',4'}$ = 8.8 Hz, H-4'), 3.47 (ddd, 1H, H-5'), 3.41 (dd, 1H, $J_{2',3'}$ = 8.7 Hz, H-3'), 3.33 (dd, 1H, H-2'), 3.07 (ddd, 1H, H-5), 2.95 (ddd, 1H, H-1), 2.88-2.70 (m, 2H, CH_2S), 1.77-1.53 (m, 4H, $CH_2CH_2CH_2$S). ^{13}C NMR (D_2O): δ 85.3 (CH), 79.8 (CH), 77.1 (CH), 72.2 (CH), 69.4 (CH), 68.4 (CH), 68.4 (CH), 67.8 (CH), 61.0 (CH_2), 60.8 (CH_2), 55.3 (CH), 53.4 (CH), 29.8 (CH_2), 28.8 (CH_2), 25.4 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{15}H_{30}NO_9S$ $[M+H]^+$ 400.1641, found 400.1643.

1-Deoxy-1-[3-(2'-acetamido-2'-deoxy-1'-thio-β-D-glucopyranosyl)-propyl]-β-L-*ido*-nojirimycin (23). 1-Allyl-1-deoxy-β-L-*ido*-nojirimycin **21** (20 mg, 0.10 mmol) was allowed to react with the glycosyl thiol **11** (33 mg, 0.14 mmol) as described for the synthesis of **14** to give, after the same work-up and purification, **23** (28 mg, 65%) as an amorphous solid. $[\alpha]_D$ = +23.7 (*c* 0.3, H_2O). ^1H NMR (D_2O): δ 4.65 (d, 1H, $J_{1',2'}$ = 10.4 Hz, H-1'), 4.04 (dd, 1H, $J_{2,3} = J_{3,4}$ = 3.1 Hz, H-3), 3.93 (dd, 1H, $J_{5',6'a}$ =

1.41, $J_{6'a,6'b}$ = 12.4 Hz, H-6'a), 3.80-3.72 (m, 2H, H-5', H-6'b), 3.79 (ddd, 1H, $J_{2,4} = J_{4,5}$ = 1.5 Hz, H-4), 3.71 (dd, 1H, $J_{5,6a}$ = 6.7, $J_{6a,6b}$ = 11.1 Hz, H-6a), 3.68 (ddd, 1H, $J_{1,2}$ = 1.5 Hz, H-2), 3.65 (dd, 1H, $J_{5,6b}$ = 6.6 Hz, H-6b), 3.60-3.52 (m, 1H, H-2'), 3.50-3.46 (m, 2H, H-3', H-4'), 3.07 (ddd, 1H, H-5), 2.97-2.92 (m, 1H, H-1), 2.87-2.79 and 2.77-2.68 (2 m, 2H, CH_2S), 2.06 (s, 3H, CH_3), 1.75-1.50 (m, 4H, $CH_2CH_2CH_2S$). ^{13}C NMR (D_2O): δ 174.4 (C), 84.3 (CH), 79.8 (CH), 75.1 (CH), 69.7 (CH), 68.7 (CH), 68.6 (CH), 67.9 (CH), 61.3 (CH_2), 60.8 (CH_2), 55.3 (CH), 54.7 (CH), 53.3 (CH), 30.1 (CH_2), 29.0 (CH_2), 25.3 (CH_2), 22.1 (CH_3). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{17}H_{33}N_2O_9S$ $[M+H]^+$ 441.1907, found 441.1909.

1-Deoxy-1-[3-(1'-thio-α-D-glucopyranosyl)-propyl]-β-L-*ido*-nojirimycin (24). 1-Allyl-1-deoxy-β-L-*ido*-nojirimycin **21** (20 mg, 0.10 mmol) was allowed to react with the glycosyl thiol **12** (27 mg, 0.14 mmol) as described for the synthesis of **14** to give, after the same work-up and purification, **24** (22.5 mg, 57%) as an amorphous solid. $[\alpha]_D$ = +98.2 (*c* 0.3, H_2O). ^{1}H NMR (D_2O): δ 5.45 (d, 1H, $J_{1',2'}$ = 5.5 Hz, H-1') 4.07 (ddd, 1H, $J_{5',6'a}$ = 2.4, $J_{5',6'b}$ = 5.4, $J_{4',5'}$ = 10.0 Hz, H-5'), 4.04 (dd, 1H, $J_{2,3} = J_{3,4}$ = 3.2 Hz, H-3), 3.89 (dd, 1H, $J_{6'a,6'b}$ = 12.3 Hz, H-6'a), 3.85 (dd, 1H, $J_{2',3'}$ = 9.7 Hz, H-2'), 3.80 (dd, 1H, H-6'b), 3.79 (ddd, 1H, $J_{2,4}$ = 1.5, $J_{4,5}$ = 1.8 Hz, H-4), 3.72 (dd, 1H, $J_{5,6a}$ = 6.7, $J_{6a,6b}$ = 11.1 Hz, H-6a), 3.69 (ddd, 1H, $J_{1,2}$ = 1.5 Hz, H-2), 3.66 (dd, 1H, $J_{5,6b}$ = 6.6 Hz, H-6b), 3.61 (dd, 1H, $J_{3',4'}$ = 9.1 Hz, H-3'), 3.43 (dd, 1H, H-4'), 3.08 (ddd, 1H, H-5), 2.99-2.94 (m, 1H, H-1), 2.77-2.63 (m, 2H, CH_2S), 1.81-1.55 (m, 4H, $CH_2CH_2CH_2S$). ^{13}C NMR (D_2O): δ 85.4 (CH), 73.6 (CH), 72.2 (CH), 70.9 (CH), 69.6 (CH), 68.3 (CH), 68.2 (CH), 67.6 (CH), 60.7 (CH_2), 60.5 (CH_2), 55.6 (CH), 53.7 (CH), 29.7 (CH_2), 28.6 (CH_2), 24.8 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{15}H_{30}NO_9S$ $[M+H]^+$ 400.1641, found 400.1638.

1-Deoxy-1-{[3-(α-D-glucopyranosyl)-propyl-1-thio]-propyl}-β-L-*ido*-nojirimycin (25). 1-Allyl-1-deoxy-β-L-*ido*-nojirimycin **21** (20 mg, 0.10 mmol) was allowed to react with the freshly prepared glycosylpropyl thiol **13** (47 mg, 0.20 mmol, containing 5-10% of the corresponding disulfide derivative) as described for the synthesis of **14** to give, after the same work-up and purification, **25** (23.5 mg, 54%) as an amorphous solid. $[\alpha]_D$ = +17.8 (*c* 1.1, H_2O). ^{1}H NMR (D_2O): δ 3.96-3.84 (m, 2H, H-1', H-3), 3.77-3.64 (m, 2H, H-6a, H-4), 3.63-3.44 (m, 6H, H-2, H-2', H-5', H-6b, H-6a', H-6b'), 3.42-3.36 (m, 1H, H-4'), 3.25-3,16 (m, 1H, H-3'), 3.06-2.75 (m, 4H, H-1, H-5, CH_2S), 2.58-2.44 (m, 2H, CH_2S), 1.89-1.43 (m, 8H, 4 CH_2). ^{13}C NMR (D_2O): δ 75.4 (CH), 73.2 (CH), 72.4 (CH), 71.1 (CH), 70.2 (CH), 68.5 (CH), 67.8 (CH), 61.3 (CH_2), 61.1 (CH_2), 61.0 (CH), 55.3 (CH_2), 53.4 (CH_2), 30.8 (CH_2), 30.7 (CH_2), 29.0 (CH_2), 24.8 (CH_2), 24.6 (CH_2), 22.7 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for

$C_{18}H_{36}NO_9S$ $[M+H]^+$ 442.2111, found 442.2108.

2,3,4,6-Tetra-*O*-acetyl-*N*-(*S*-acetyl-4-thiobutyl)-1-deoxy-D-nojirimycin (27). A stirred solution of **26** (131 mg, 0.34 mmol), DPAP (26 mg, 0.10 mmol) and thioacetic acid (73 μL, 1.02 mmol) in CH_2Cl_2 (300 μL) was irradiated (365 nm) at room temperature for 30 min and then concentrated. The yellow residue was eluted from a column of silica gel with 1.5:1 cyclohexane-AcOEt to give **27** (141 mg, 90%) as a colorless syrup. $[\alpha]_D = +5.8$ (*c* 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 5.03-4.94 (m, 2H, H-3, H-4), 4.93-4.85 (m, 1H, H-2), 4.09 (d, 2H, $J_{5,6}$ = 2.6 Hz, H-6a, H-6b), 3.12 (dd, 1H, $J_{1eq,2}$ = 5.1, $J_{1eq,1ax}$ = 11.5 Hz, H-1eq), 2.81 (t, 2H, J = 6.7 Hz, CH_2S), 2.80-2.70 (m, 1H, 1 H of CH_2N), 2.57 (dt, 1H, $J_{4,5}$ = 8.9 Hz, H-5), 2.59-2.49 (m, 1H, 1 H of CH_2N), 2.26 (s, 3H, SAc), 2.23 (dd, 1H, $J_{1ax,2}$ = 10.5 Hz, H-1ax), 2.03-1.93 (4 s, 12H, 4 OAc), 1.56-1.32 (m, 4H, CH_2CH_2N, CH_2CH_2S). ^{13}C NMR ($CDCl_3$): δ 195.9 (C), 170.9 (C), 170.4 (C), 170.1(C), 169.8 (C), 74.7 (CH), 69.4 (CH), 69.3 (CH), 61.6 (CH), 59.5 (CH_2), 52.8 (CH_2), 51.0 (CH_2), 30.7 (CH_2), 28.8 (CH_2), 27.2 (CH_2), 24.1 (CH_3), 20.9 (CH_3), 20.8 (3 CH_3). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{20}H_{32}NO_9S$ $[M+H]^+$ 462.1798, found 462.1800.

***N*-(4-thiobutyl)-1-deoxy-D-nojirimycin (28)**. A solution of **27** (230 mg, 0.50 mmol) in a 2M solution of ammonia in MeOH (5 mL) was kept at room temperature under an argon atmosphere for 6 h, then concentrated to give **28** (125 mg, 100%) contaminated by ≈10% of its disulfide derivative. ^{1}H NMR (D_2O): δ 3.87 (dd, 1H, $J_{5,6a}$ = 2.3, $J_{6a,6b}$ = 12.7 Hz, H-6a), 3.78 (dd, 1H, $J_{5,6b}$ = 2.6 Hz, H-6b), 3.50 (ddd, 1H, $J_{1eq,2}$ = 4.9, $J_{2,3}$ = 9.4, $J_{1ax,2}$ = 10.6 Hz, H-2), 3.34 (dd, 1H, $J_{3,4}$ = 9.2, $J_{4,5}$ = 9.8 Hz, H-4), 3.21 (dd, 1H, H-3), 3.02-2.96 (m, 1H, H-1eq), 2.77-2.50 (m, 4H, CH_2N, CH_2S), 2.32-2.26 (m, 1H, H-1ax), 2.22 (ddd, 1H, H-5), 1.67-1.51 (m, 4H, CH_2CH_2N, CH_2CH_2S).

1-Allyl-*N*-acetyl-2,3,4,6-tetra-*O*-acetyl-1-deoxy-β-L-*ido*-nojirimycin (29). To cooled (-78 °C), stirred liquid ammonia (≈6 mL) sodium (140 mg, 6.00 mmol) was added in one portion. After complete dissolution of the sodium (blue solution), a solution of **20** (225 mg, 0.40 mmol) and allylamine (300 μL, 4.00 mmol) in anhydrous THF (1.2 mL) was added dropwise. Then, the reaction mixture was diluted with water (0.8 mL), allowed to warm to room temperature to remove the ammonia and then concentrated. A solution of the residue in pyridine (4 mL) and acetic anhydride (8 mL) was kept at room temperature for 14 h and then concentrated. The residue was diluted with AcOEt (100 mL), washed with water (2 x 10 mL), dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane-AcOEt to give **29** (165 mg, 95%, ≈1.2:1 mixture of rotamers

29-M and **29-m**) as a colorless syrup. $[\alpha]_D$ = +26.0 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$) for rotamer **29-M**: δ 5.73 (dddd, 1H, *J* = 6.9, 6.9, 10.1, 17.0, C*H*=CH_2), 5.52 (dd, 1H, $J_{2,3} = J_{3,4}$ = 10.4 Hz, H-3), 5.32 (ddd, 1H, $J_{1,2} = J_{1,CH2a}$ = 6.7, $J_{1,CH2b}$ = 8.1 Hz, H-1), 5.05 (dddd, 1H, *J* = 1.6, 1.6, 3.0, 17.0 Hz, 1 H of CH=CH_2), 5.00 (dddd, 1H, *J* = 1.6, 1.6, 2.2, 10.1 Hz, 1 H of CH=CH_2), 4.98 (dd, 1H, $J_{4,5}$ = 5.9 Hz, H-4), 4.89 (dd, 1H, H-2), 4.61 (ddd, 1H, $J_{5,6a} = J_{5,6b}$ = 5.9 Hz, H-5), 4.28 (d, 2H, H-6a, H-6b), 2.63-2.54 and 2.25-2.15 (2 m, 2H, CH_2CH=CH_2), 2.19 (s, 3H, Ac), 2.08, 2.06, 2.04, and 2.01 (4 s, 12H, 4 Ac). ^1H NMR ($CDCl_3$) for rotamer **29-m**: δ 5.73 (dddd, 1H, *J* = 6.9, 6.9, 10.1, 17.0, C*H*=CH_2), 5.61 (dd, 1H, $J_{2,3} = J_{3,4}$ = 10.6 Hz, H-3), 5.46 (ddd, 1H, $J_{4,5} = J_{5,6a}$ = 6.6, $J_{5,6b}$ = 7.5 Hz, H-5), 5.15 (dddd, 1H, *J* = 1.6, 1.6, 2.7, 17.0 Hz, 1 H of CH=CH_2), 5.13 (dddd, 1H, *J* = 1.6, 1.6, 2.2, 10.1 Hz, 1 H of CH=CH_2), 4.98 (dd, 1H, H-4), 4.89 (dd, 1H, $J_{1,2}$ = 6.3 Hz, H-2), 4.41 (ddd, 1H, $J_{1,CH2a}$ = 6.3, $J_{1,CH2b}$ = 9.0 Hz, H-1), 4.34 (dd, 1H, $J_{6a,6b}$ = 11.7 Hz, H-6a), 4.28 (dd, 1H, H-6b), 2.63-2.54 and 2.49-2.39 (2 m, 2H, CH_2CH=CH_2), 2.17 (s, 3H, Ac), 2.09, 2.07, 2.04, and 2.03 (4 s, 12H, 4 Ac). ^{13}C NMR ($CDCl_3$) for rotamer **29-M**: δ 171.2 (C), 171.1 (C), 170.3 (C), 170.2 (C), 169.5 (C), 135.1 (CH), 117.2 (CH_2), 70.6 (CH), 70.1 (CH), 67.0 (CH), 63.0 (CH_2), 53.5 (CH), 49.2 (CH), 35.1 (CH_2), 22.4 (CH_3), 21.1 (CH_3), 21.0 (CH_3), 20.9 (CH_3), 20.7 (CH_3). ^{13}C NMR ($CDCl_3$) for rotamer **29-m**: δ 171.2 (C), 171.1 (C), 170.3 (C), 170.2 (C), 169.5 (C), 133.9 (CH), 119.2 (CH_2), 71.5 (CH), 69.3 (CH), 67.1 (CH), 62.9 (CH_2), 54.9 (CH), 48.2 (CH), 34.5 (CH_2), 22.7 (CH_3), 21.1 (CH_3), 21.0 (CH_3), 20.9 (CH_3) 20.7 (CH_3). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{19}H_{28}NO_9$ $[M+H]^+$ 414.1764, found 414.1762.

***N*-Acetyl-2,3,4,6-tetra-*O*-acetyl-1-(*S*-acetyl-3-thiopropyl)-1-deoxy-β-L-*ido*-nojirimycin (30)**. A stirred solution of **29** (207 mg, 0.50 mmol), DPAP (38 mg, 0.15 mmol) and thioacetic acid (107 μL, 1.50 mmol) in CH_2Cl_2 (400 μL) was irradiated (365 nm) at room temperature for 30 min and then concentrated. The yellow residue was eluted from a column of silica gel with 1:1 cyclohexane-AcOEt to give **30** (225 mg, 92%, ≈3:1 mixture of rotamers **30-M** and **30-m**) as a colorless syrup. $[\alpha]_D$ = +11.6 (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$) for rotamer **30-M**: δ 5.47 (dd, 1H, $J_{2,3} = J_{3,4}$ = 10.1 Hz, H-3), 5.18 (ddd, 1H, $J_{1,CH2a}$ = 5.2, $J_{1,CH2b}$ = 6.0, $J_{1,2}$ = 7.5 Hz, H-1), 4.98 (dd, 1H, H-2), 4.94 (dd, 1H, $J_{4,5}$ = 6.6 Hz, H-4), 4.63 (ddd, 1H, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 8.4 Hz, H-5), 4.32 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, H-6a), 4.26 (dd, 1H, H-6b), 3.00-2.72 (m, 2H, CH_2S), 2.30 (s, 3H, Ac), 2.20 (s, 3H, Ac) 2.08 (s, 6H, 2 Ac), 2.03 (s, 6H, 2 Ac), 1.88-1.79 and 1.77-1.42 (2 m, 4H, $CH_2CH_2CH_2S$). ^1H NMR ($CDCl_3$) for rotamer **30-m**: δ 5.55 (dd, 1H, $J_{2,3} = J_{3,4}$ = 10.1 Hz, H-3), 5.51 (ddd, 1H, $J_{5,6a}$ = 5.7, $J_{4,5}$ = 6.7, $J_{5,6b}$ = 6.7 Hz, H-5), 4.94 (dd, 1H, H-4), 4.87 (dd, 1H, $J_{1,2}$ = 6.0 Hz, H-2), 4.35-4.31 (m, 1H, H-1), 4.31 (dd, 1H, $J_{6a,6b}$ = 11.8 Hz, H-6a), 4.19

(dd, 1H, H-6b), 3.00-2.72 (m, 2H, CH_2S), 2.35 (s, 3H, Ac), 2.19 (s, 3H, Ac), 2.08 (s, 6H, 2 Ac), 2.06 (s, 6H, 2 Ac), 1.77-1.42 (m, 4H, $CH_2CH_2CH_2S$). ^{13}C NMR ($CDCl_3$) for rotamer **30-M**: δ 195.6 (C), 171.3-169.4 (5 C), 70.6 (CH), 70.1 (CH), 67.1 (CH), 62.9 (CH_2), 53.6 (CH), 49.2 (CH), 30.8 (CH_3), 29.3 (CH_2), 28.7 (CH_2), 26.9 (CH_2), 22.4 (CH_3), 21.2-20.7 (4 CH_3). ^{13}C NMR ($CDCl_3$) for rotamer **30-m**: δ 195.7 (C), 171.3-169.4 (5 C), 71.4 (CH), 69.3 (CH), 67.2 (CH), 62.8 (CH_2), 54.9 (CH), 48.0 (CH), 30.6 (CH_3), 29.3 (CH_2), 28.7 (CH_2), 27.4 (CH_2), 22.6 (CH_3), 21.2-20.7 (4 CH_3). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{21}H_{32}NO_{10}S$ $[M+H]^+$ 490.1747, found 490.1749.

***N*-Acetyl-1-(3-thiopropyl)-1-deoxy-β-L-*ido*-nojirimycin (31)**. To a cooled (0 °C), stirred solution of **30** (98 mg, 0.20 mmol) in CH_3OH (600 μL) and CH_3CN (600 μL) was added a freshly prepared 0.5 M solution of CH_3ONa in CH_3OH (800 μL). The solution was stirred at 0 °C for 1 h under and an argon atmosphere, then neutralized at 0 °C with Amberlite IRA-120 ion exchange resin (H^+ form), filtered, and concentrated to afford the thiol **31** (56 mg, 100%, ≈1.5:1 mixture of rotamers **31-M** and **31-m**) contaminated by ≈10% of its disulfide derivative. The thiol **31** was used in the subsequent reactions without further purification. ^1H NMR (D_2O, 250 MHz): δ 5.08-5.00 (m, H-5*m*), 4.84-4.75 (m, H-1*M*), 4.41-4.32 (m, H-5*M*), 4.21-4.13 (m, H-1*m*), 4.10 (dd, 1H, $J_{5,6a}$ = 5.2, $J_{6a,6b}$ = 12.2 Hz, H-6a*m*), 4.05 (dd, 1H, $J_{5,6a}$ = 6.1, $J_{6a,6b}$ = 11.5 Hz, H-6a*M*), 3.76-3.51 (m, H-2, H-3, H-4, H-6b), 2.82-2.67 (m, CH_2Sm), 2.61-2.45 (m, CH_2SM), 2.24 (s, Ac*m*), 2.21 (s, Ac*M*), 1.80-1.40 (m, CH_2CH_2).

Calix[4]arene L-*ido*-nojirimycin cluster 34. A solution of tetra-*O*-allyl-calix[4]arene **32** (6.0 mg, 0.01 mmol), freshly prepared iminosugar thiol **31** (46 mg, 0.16 mmol, containing ca. 10% of the corresponding disulfide derivative) and DPAP (2.1 mg, 8.2 μmol) in DMF (150 μL), partially concentrated under vacuum (0.1 mbar) to remove the traces of Me_2NH, was irradiated (365 nm) at room temperature for 30 min and then concentrated. The residue was eluted from a Sephadex LH-20 column (1 x 80 cm) with MeOH to give the *N*-acetylated tetravalent cluster **33** that was diluted with hydrazine monohydrate (1 mL), stirred at 70 °C for 18 h and concentrated. The residue was eluted from a Sephadex LH-20 column (1 x 45 cm) with a 0.1 M solution of ammonia in CH_3OH to give **34** (11.8 mg, 75%) as a white foam. $[\alpha]_D$ = -3.5 (*c* 0.5, MeOH). ^1H NMR (CD_3OD): δ 6.71-6.51 (m, 12H, Ar), 4.44 and 3.18 (2 d, 8H, *J* = 13.3 Hz, 4 ArCH_2Ar), 4.02 (t, 8H, *J* = 7.2 Hz, 4 CH_2O), 3.95 (dd, 4H, $J_{2,3}$ = $J_{3,4}$ = 2.4 Hz, 4 H-3), 3.74-3.65 (m, 12H, 4 H-4, 4 H6a, 4 H-6b), 3.64-3.57 (m, 4H, 4 H-2), 3.18-3.08 (m, 4H, 4 H-5), 3.08-2.99 (m, 4H, 4 H-1), 2.78 (t, 8H, *J* = 7.1 Hz, 4 CH_2S), 2.64 (t, 8H, *J* = 6.4 Hz, 4 CH_2S), 2.29-2.11 (m, 8H, 4 CH_2CH_2O), 1.83-1.48 (m, 16H, 4 $CH_2CH_2CH_2S$). ^{13}C NMR (CD_3OD): δ

157.5 (C), 136.3 (C), 129.5 (CH), 123.4 (CH), 74.6 (CH_2), 70.8 (CH), 70.3 CH), 70.2 (CH), 63.3 (CH_2), 57.1 (CH), 55.1 (CH), 33.1 (CH_2), 29.8 (CH_2), 26.9 (CH_2), 23.4 (CH_2). HRMS (ESI/Q-TOF) *m/z* calcd. for $C_{76}H_{118}N_4O_{20}S_4/2$ $[(M+2H)/2]^+$ 767.3611, found 767.3617.

α-Glucosidase, β-glucosidase, α-mannosidase, and α-galactosidase inhibition assays. Inhibition constant (K_i) values were determined by spectrophotometry, measuring the residual hydrolytic activities of α-glucosidase (from yeast), β-glucosidase (from almond), α-mannosidase (from *Canavalia ensiformis*), and α-galactosidase (from green coffee bean) against the corresponding 4-nitrophenyl pyranoside. Each assay was carried out in phosphate–citrate buffer at pH 6.8 (α-glucosidase and α-galactosidase), pH 7.3 (β-glucosidase), pH 5.5 (α-mannosidase). The reactions were initiated by addition of the enzyme to a solution of the substrate in the absence or presence of various concentrations of iminosugar. The mixture was incubated for 10 min at 37 °C and the reaction was quenched by addition of 1M aqueous Na_2CO_3. The absorbance of the resulting mixture was determined at 405 nm. K_i determination and enzyme inhibition mode were determined from the slope of Lineweaver–Burk plots and double reciprocal analysis.

Trehalase inhibition assay. Inhibition constant (K_i) values were determined by spectrophotometry, measuring the residual hydrolytic activities of α-trehalase (from porcine kidney) against D-trehalose. To this aim, a glucose assay kit (GAGO-20), purchased from Sigma-Aldrich, allowed to measure the concentration of D-glucose. Each assay was carried out in phosphate–citrate buffer at pH 5.7. The reactions were initiated by addition of enzyme to a solution of the substrate in the absence or presence of various concentrations of iminosugar derivative. The mixture was incubated for 10 min at 37 °C and then submitted the glucose assay. The absorbance of the resulting mixture was determined at 540 nm. K_i determination and enzyme inhibition mode were determined from the slope of Lineweaver–Burk plots and double reciprocal analysis.

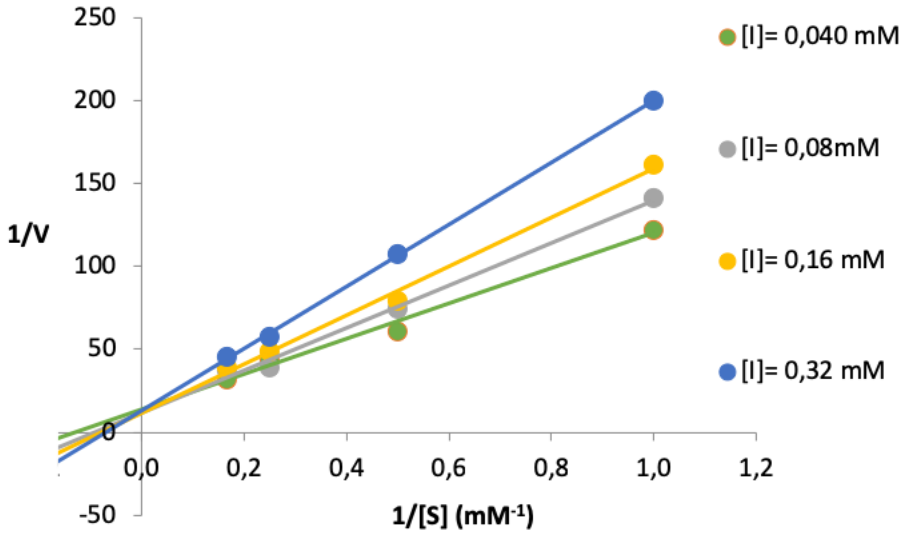


Figure S1. Lineweaver-Burk plot for K_i determination of **16** against β-glucosidase (from almond).

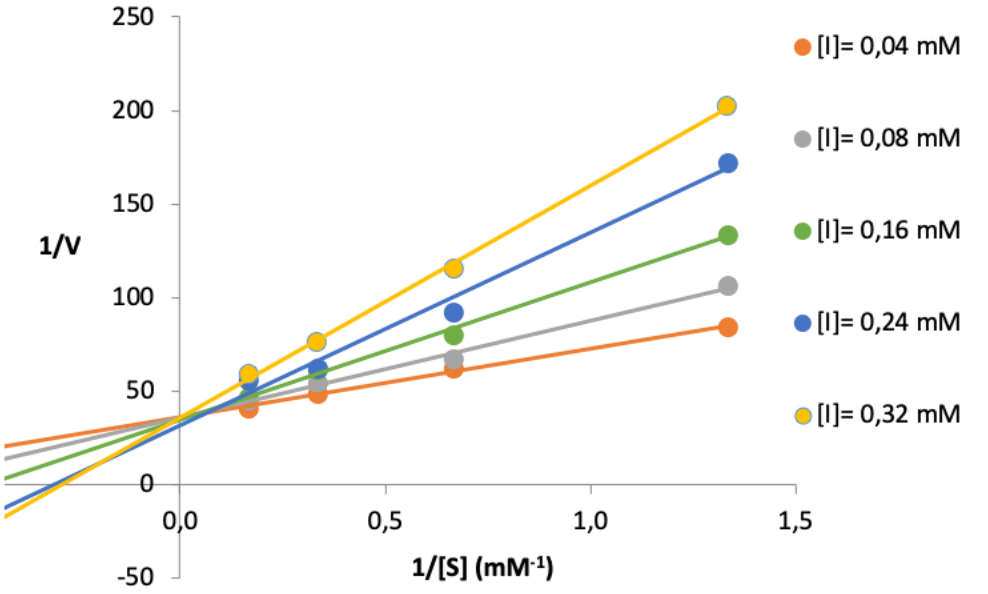


Figure S2. Lineweaver-Burk plot for K_i determination of **16** against α-galactosidase (green coffee).

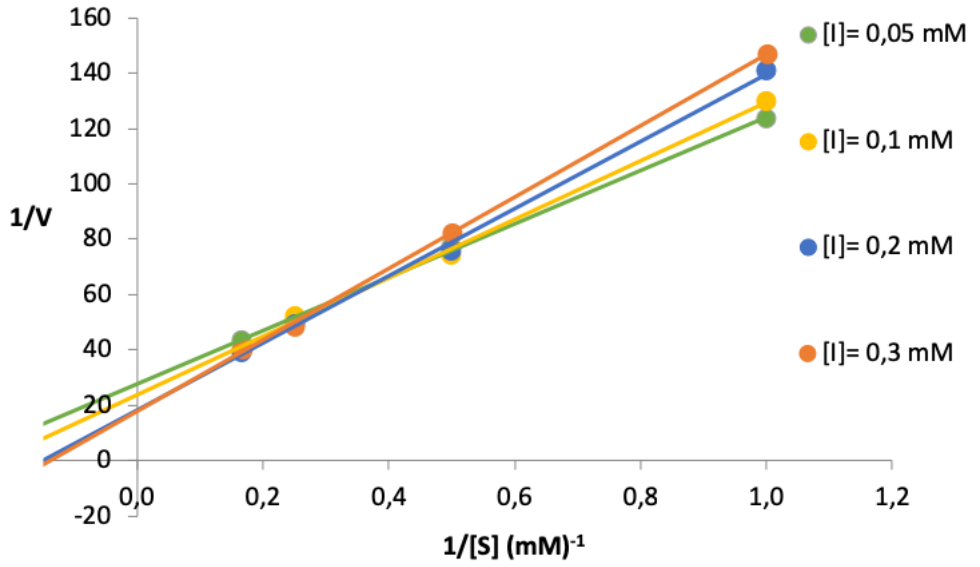


Figure S3. Lineweaver-Burk plot for K_i determination of **16** against Jack bean α-mannosidase.

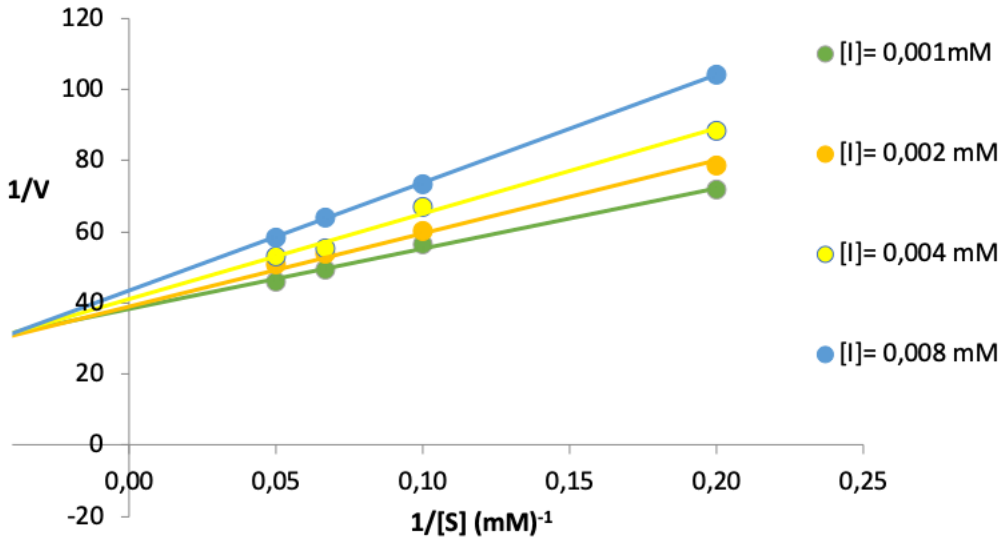


Figure S4. Lineweaver-Burk plot for K_i determination of **16** against trehalase (porcine kidney).

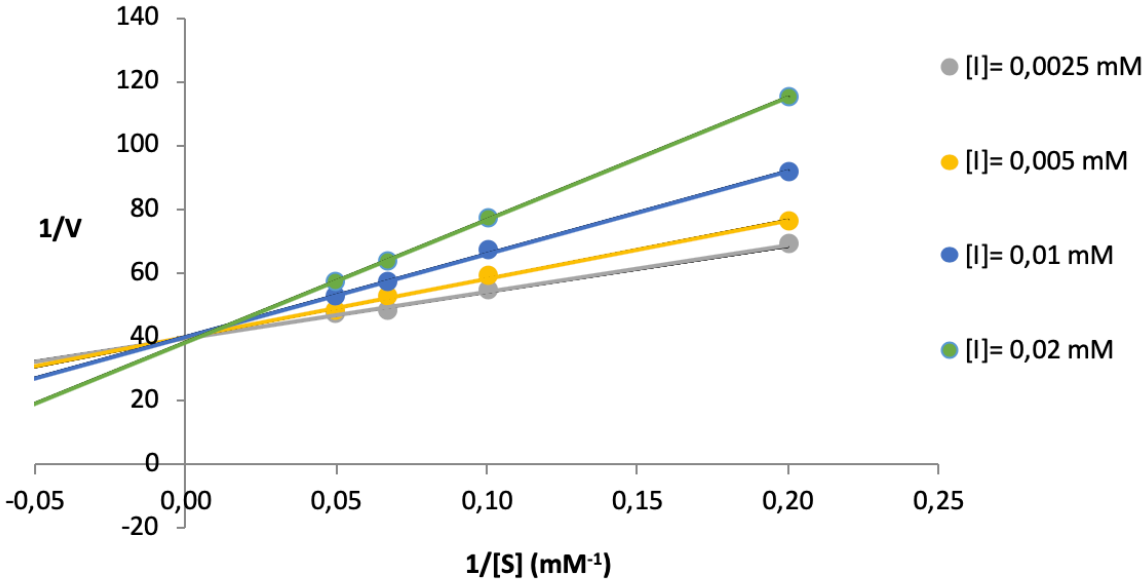


Figure S5. Lineweaver-Burk plot for K_i determination of 1-DNJ (**3**) against trehalase (porcine kidney).

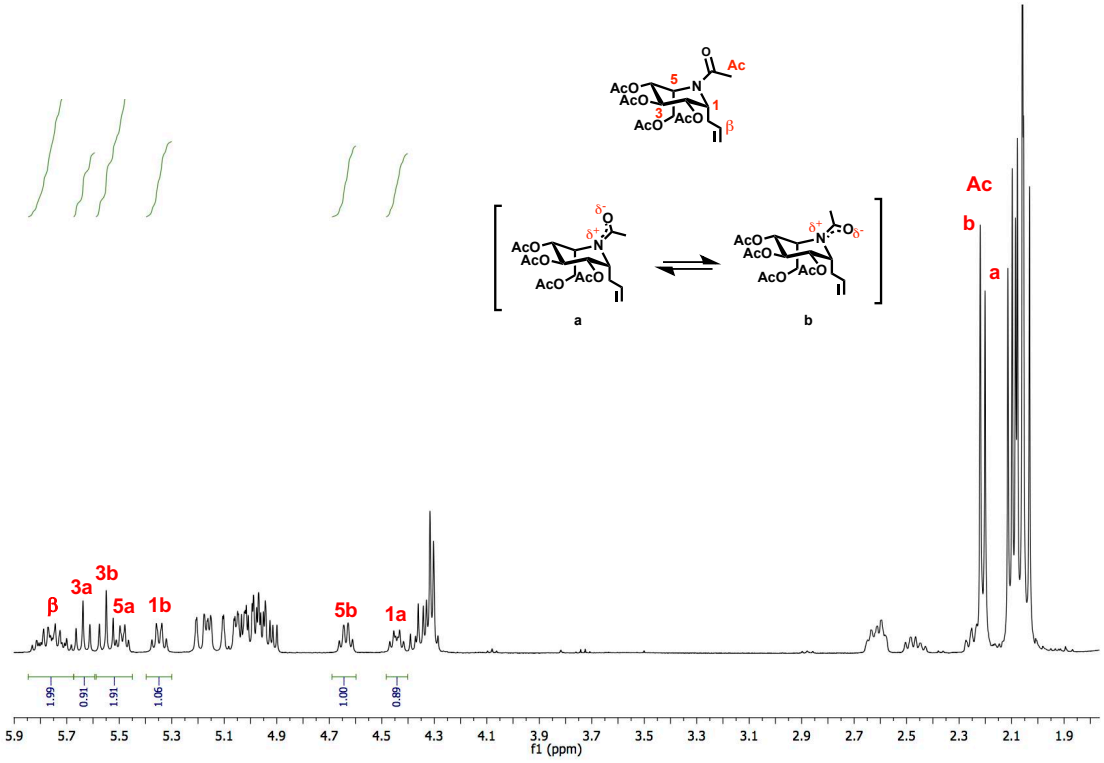
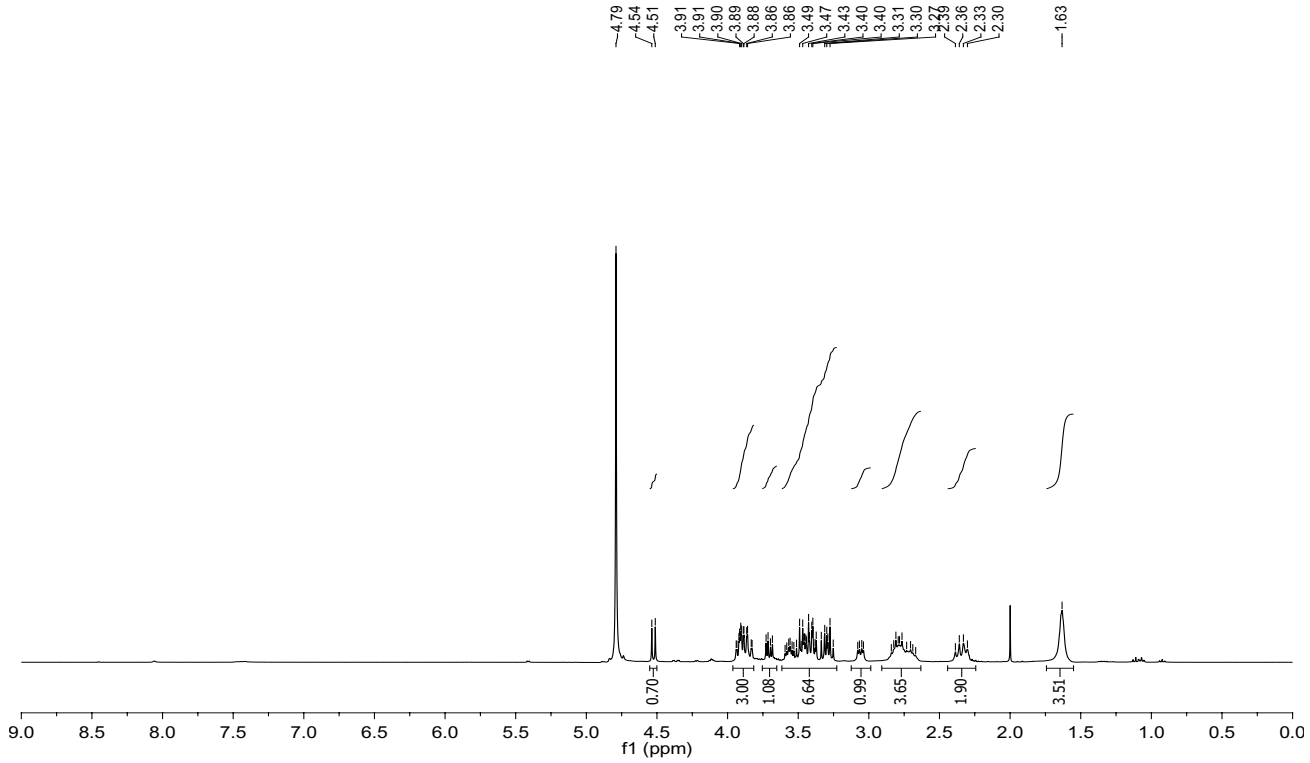
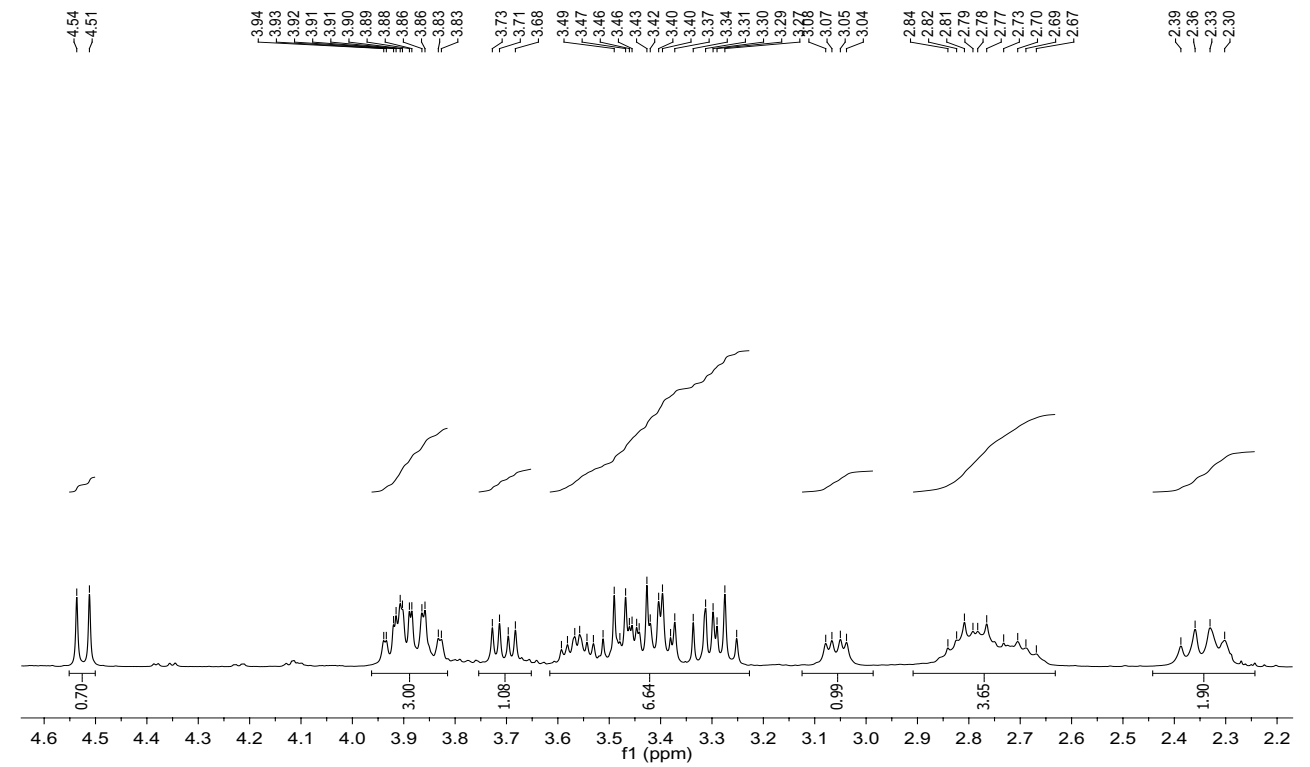


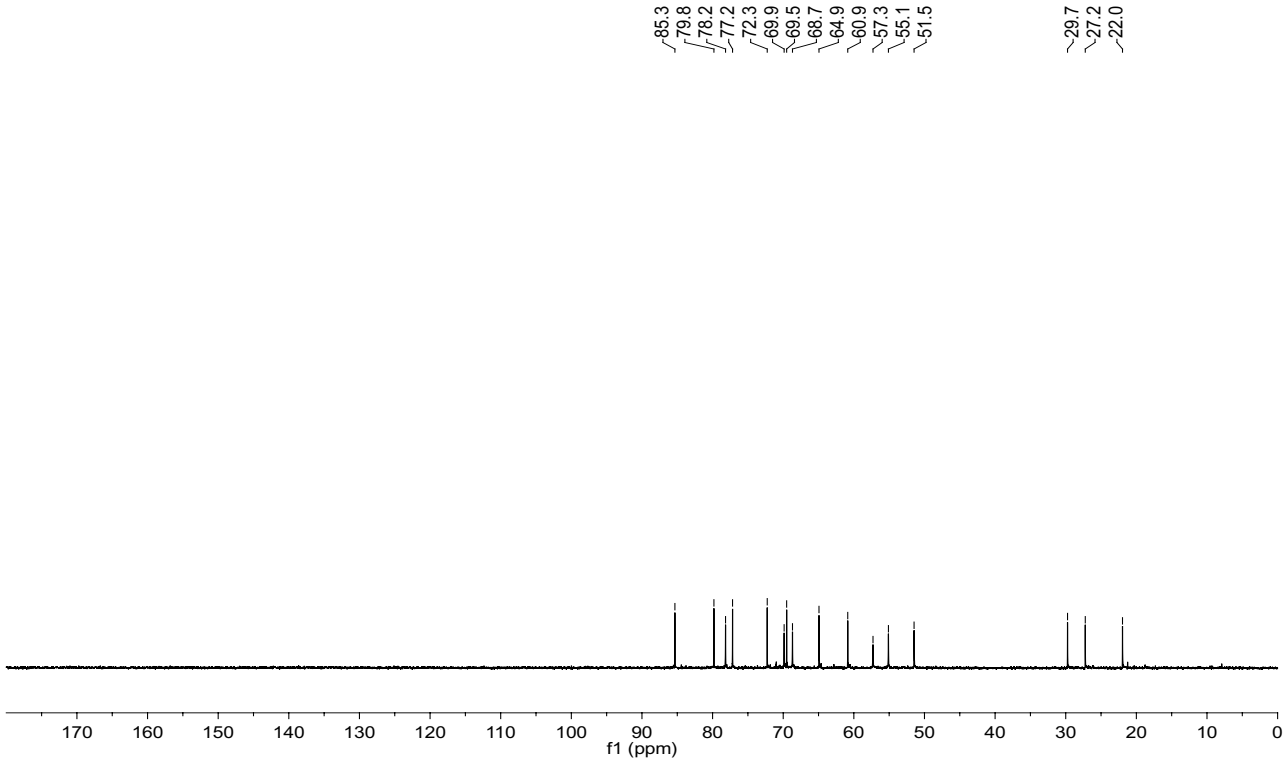
Figure S6. Assigned peaks for the two rotamers of the cyclic tertiary amide **29** (400 MHz, $CDCl_3$, r.t.).



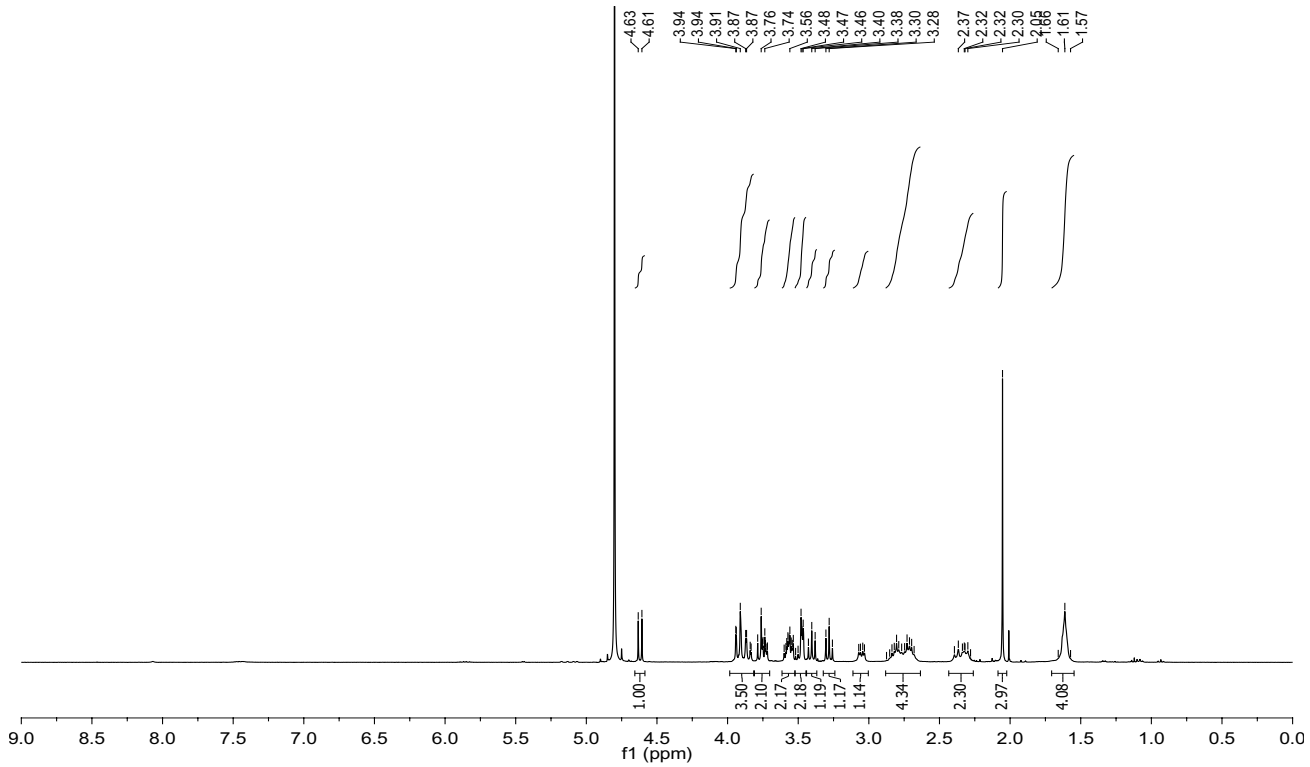
^{1}H-NMR spectrum of **14**



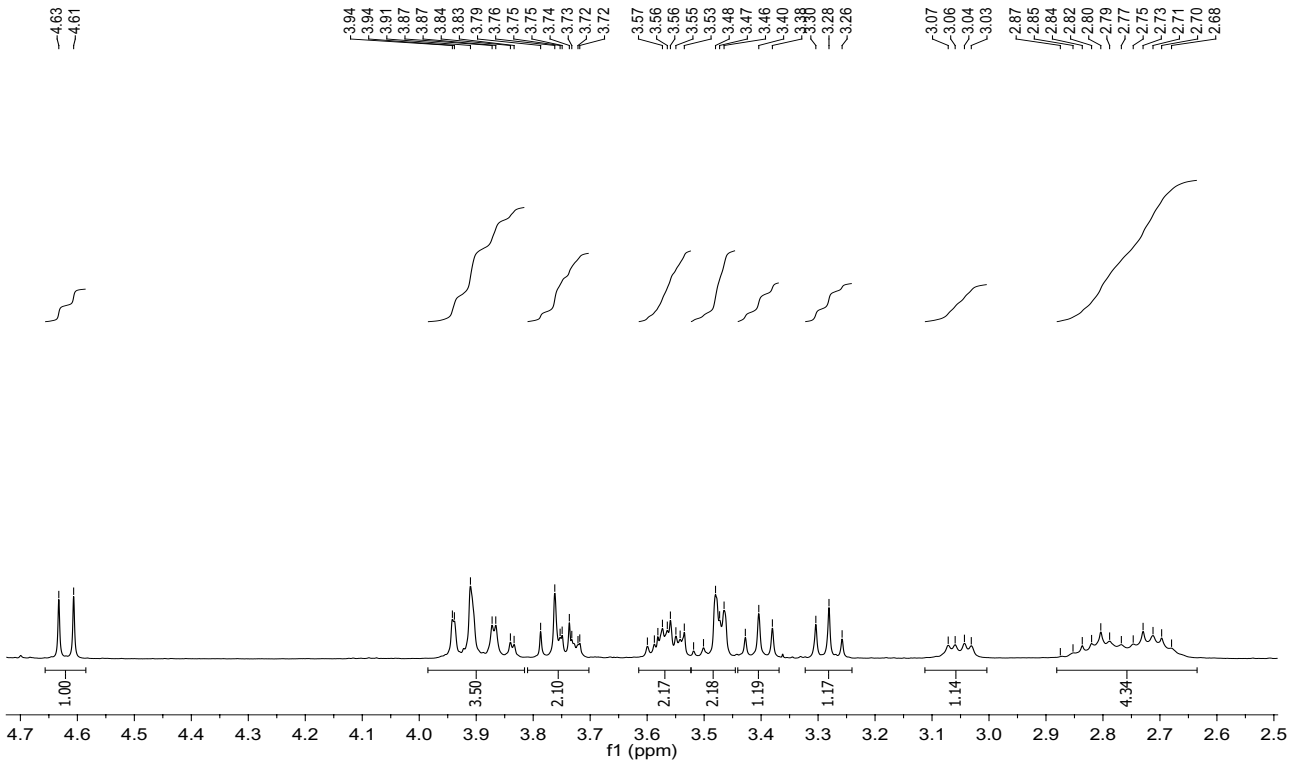
^{1}H-NMR spectrum (expansion) of **14**



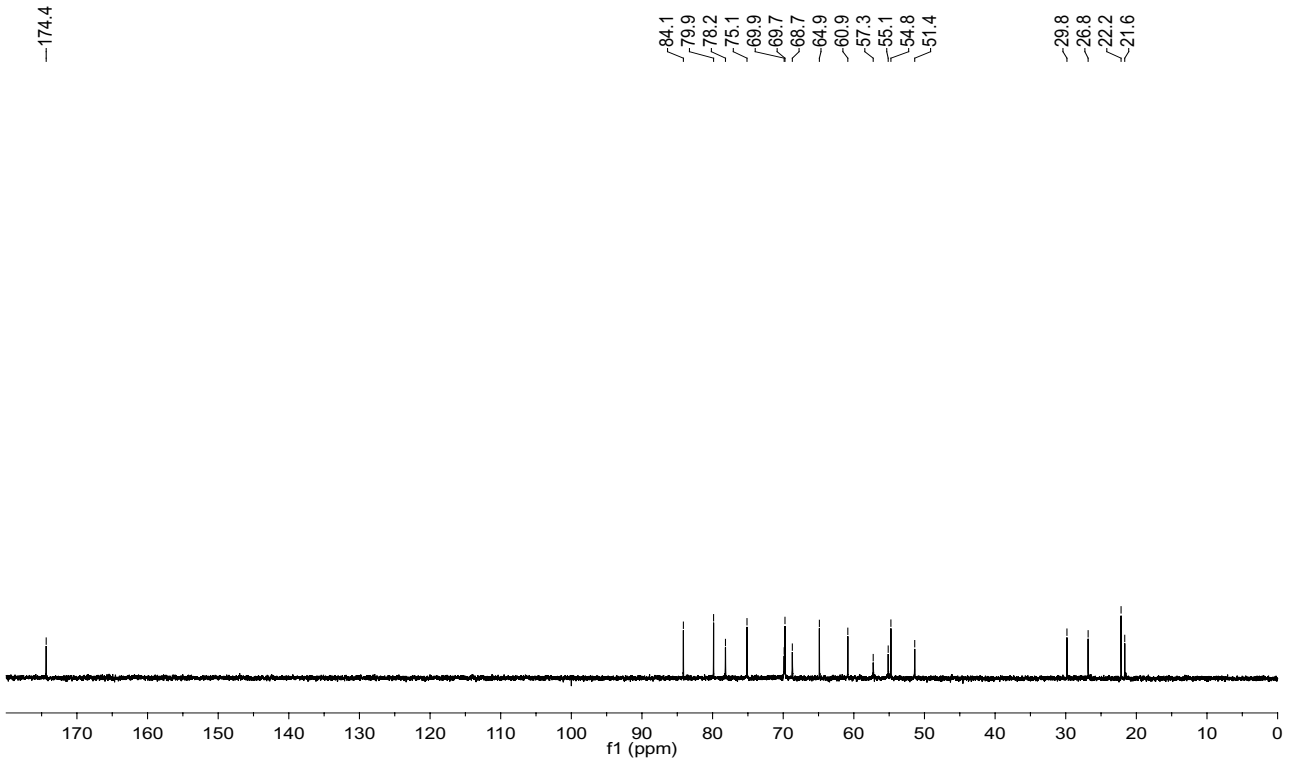
^{13}C-NMR spectrum of **14**



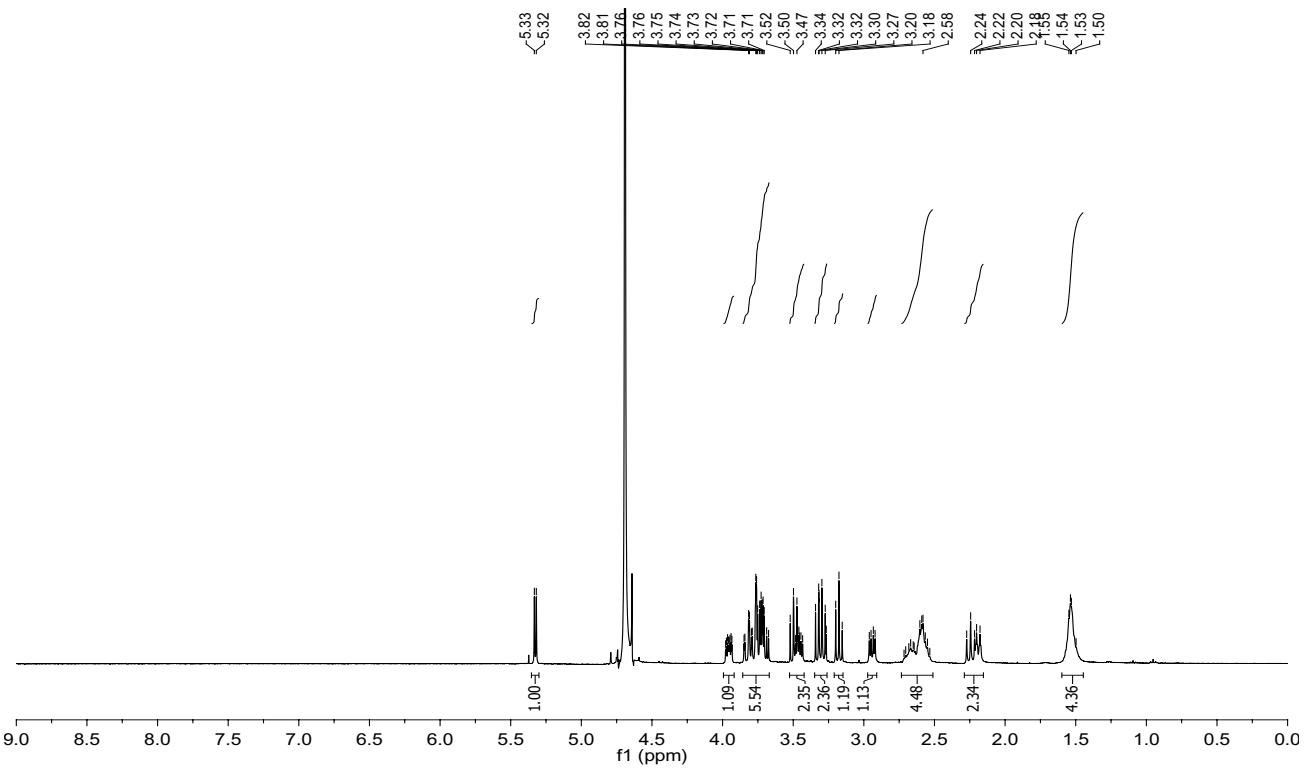
^{1}H-NMR spectrum of **15**



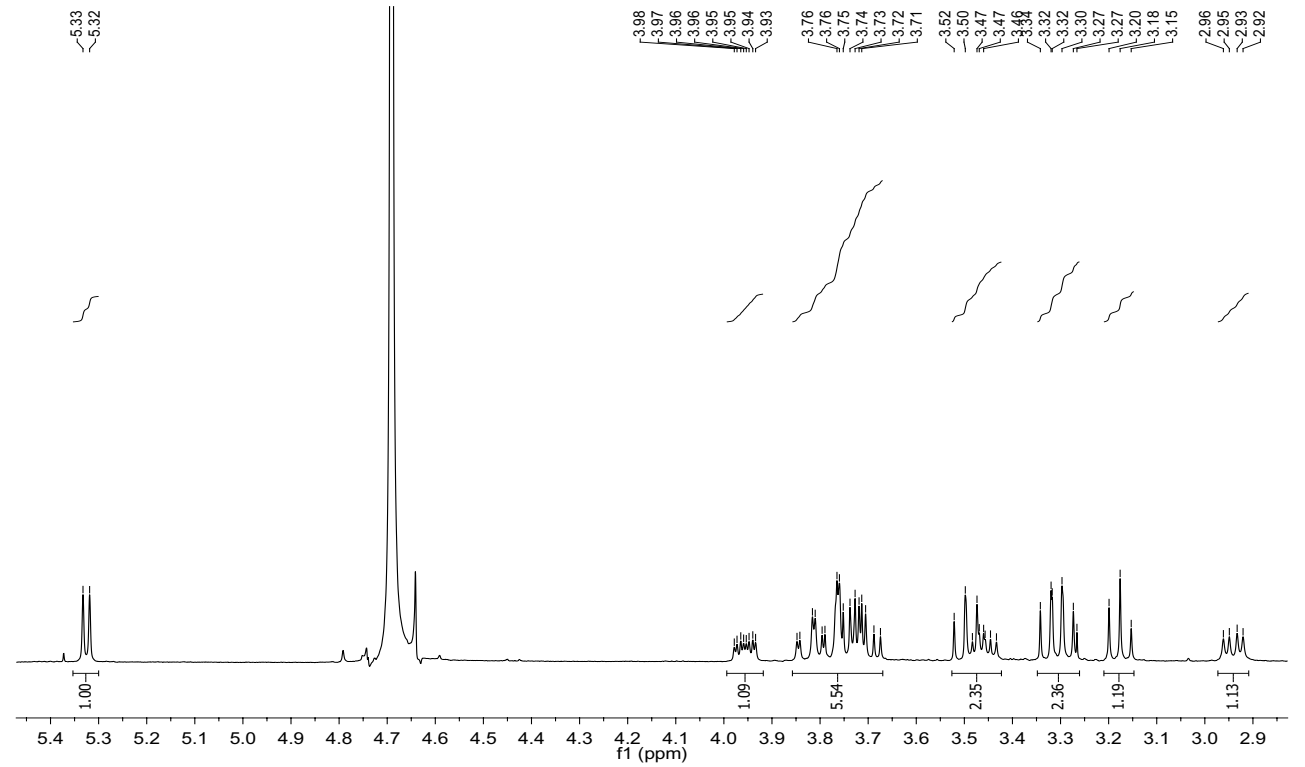
^{1}H-NMR spectrum (expansion) of **15**



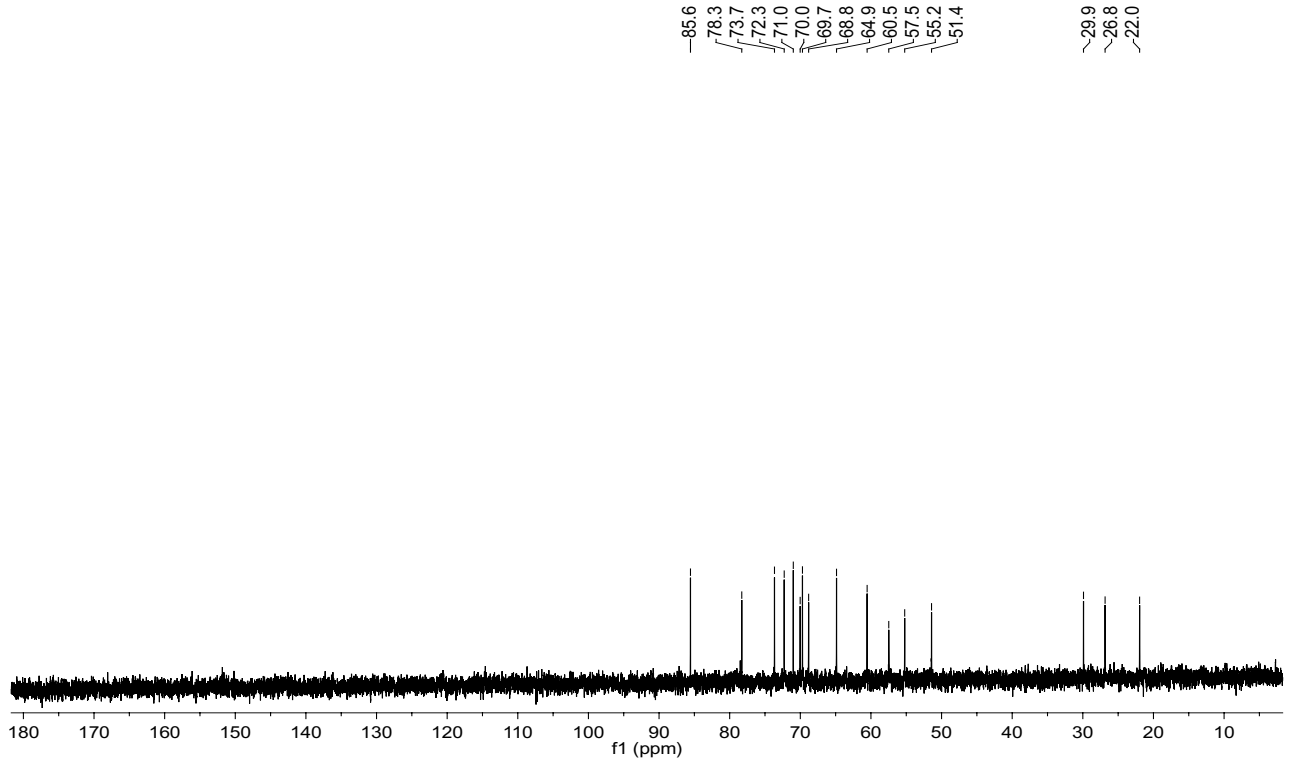
^{13}C-NMR spectrum of **15**



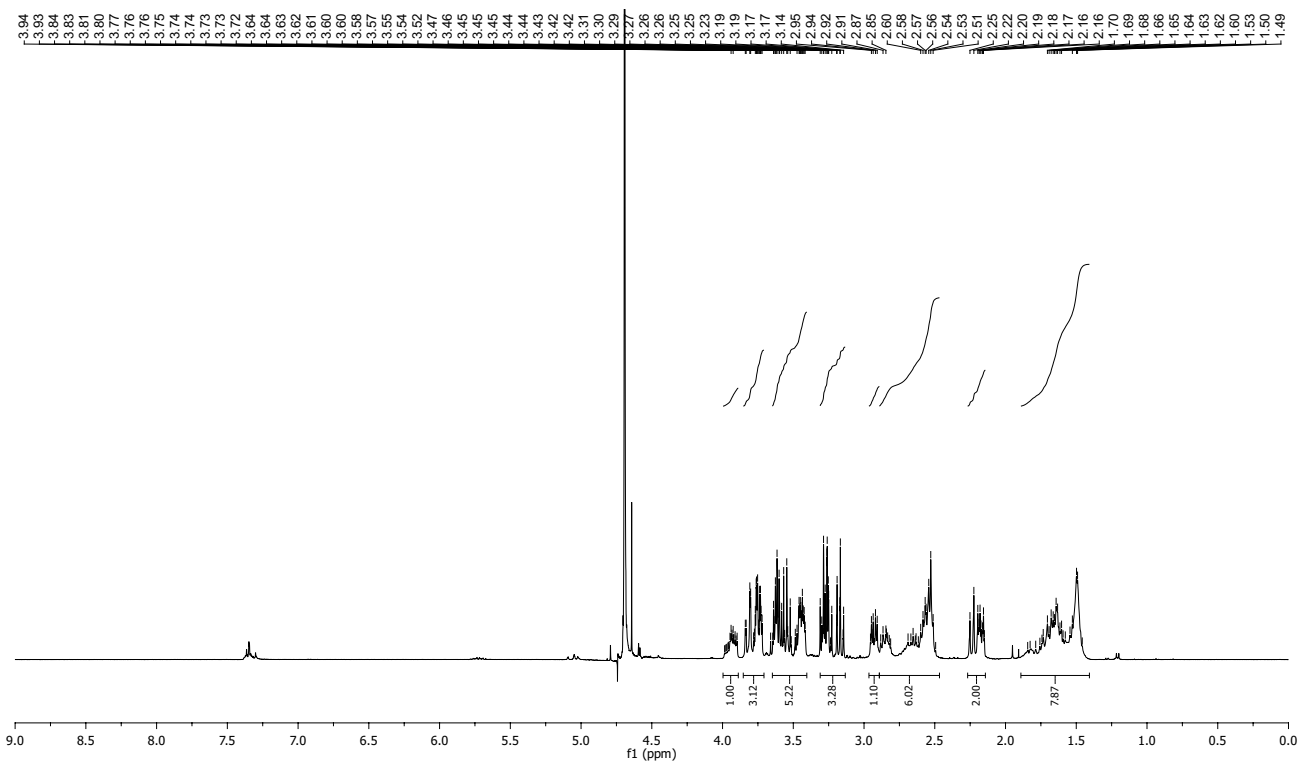
^{1}H-NMR spectrum of **16**



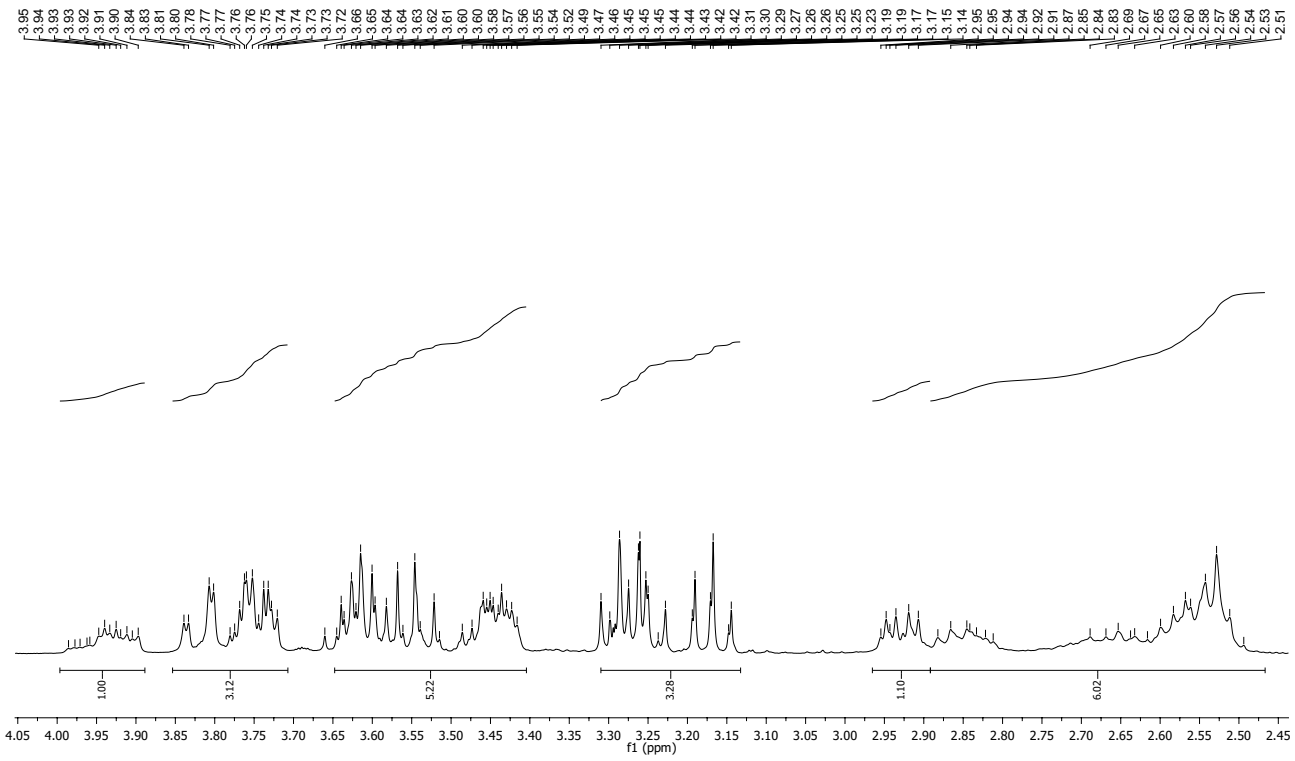
^{1}H-NMR spectrum (expansion) of **16**



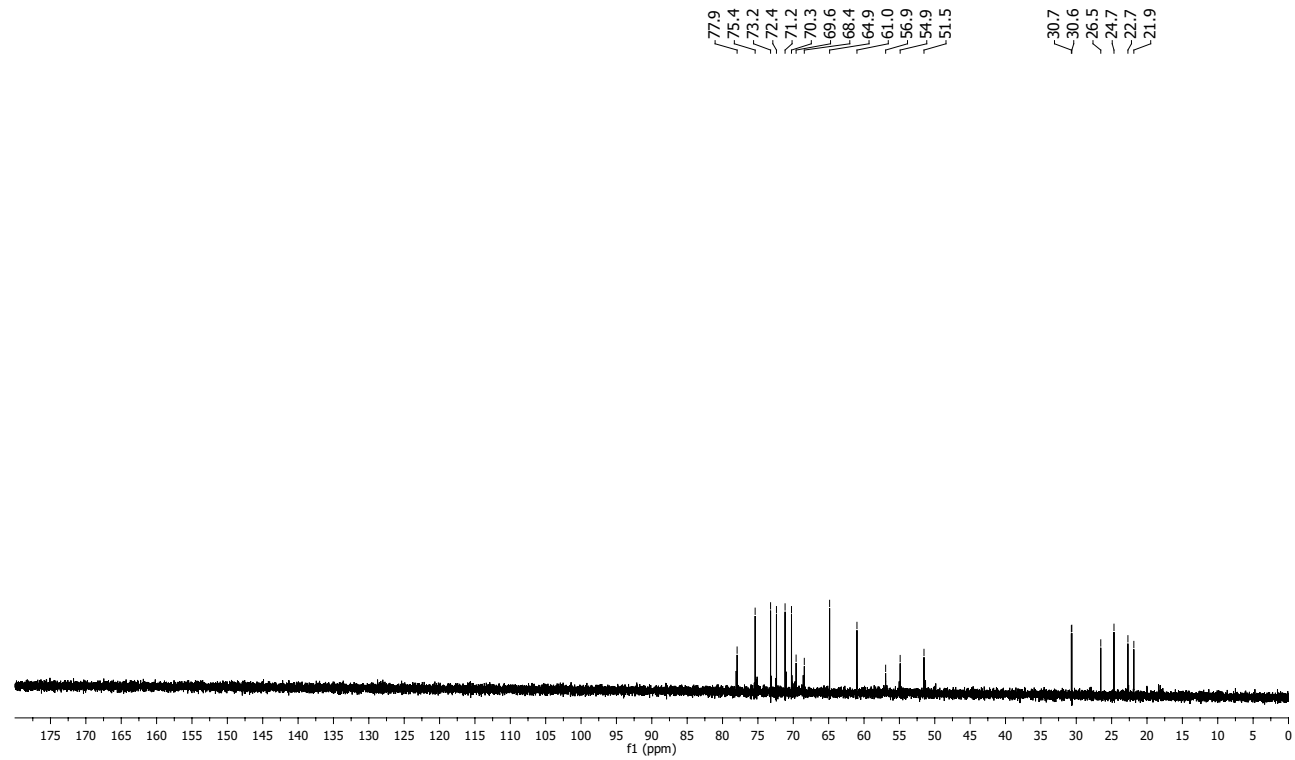
^{13}C-NMR spectrum of **16**



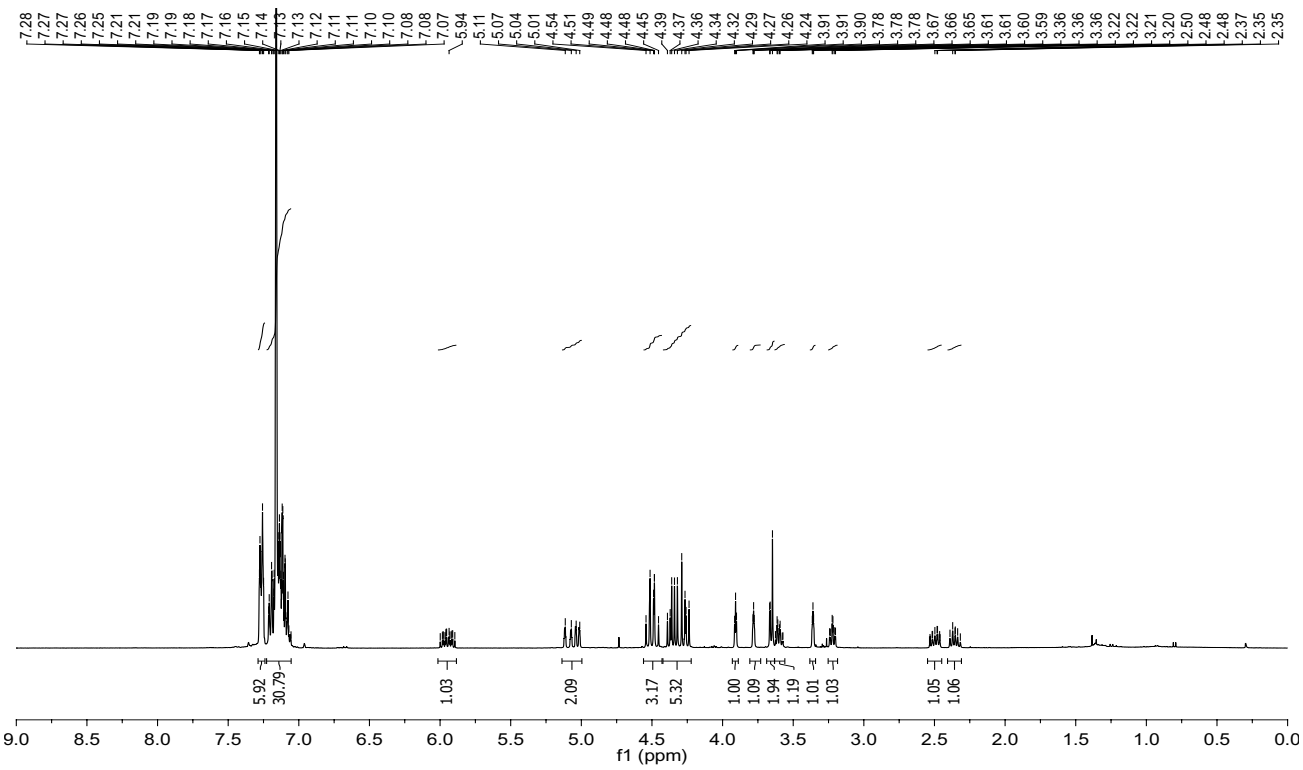
^{1}H-NMR spectrum of **17**



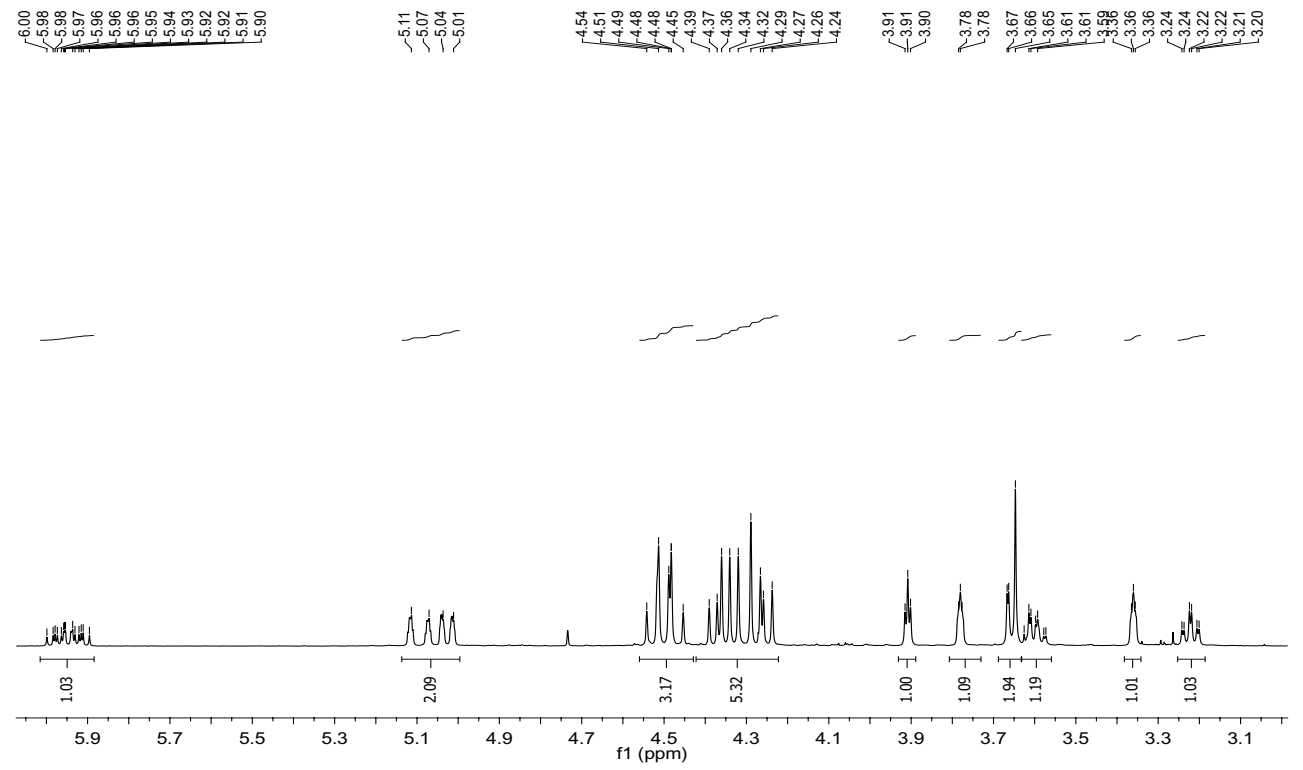
^{1}H-NMR spectrum (expansion) of **17**



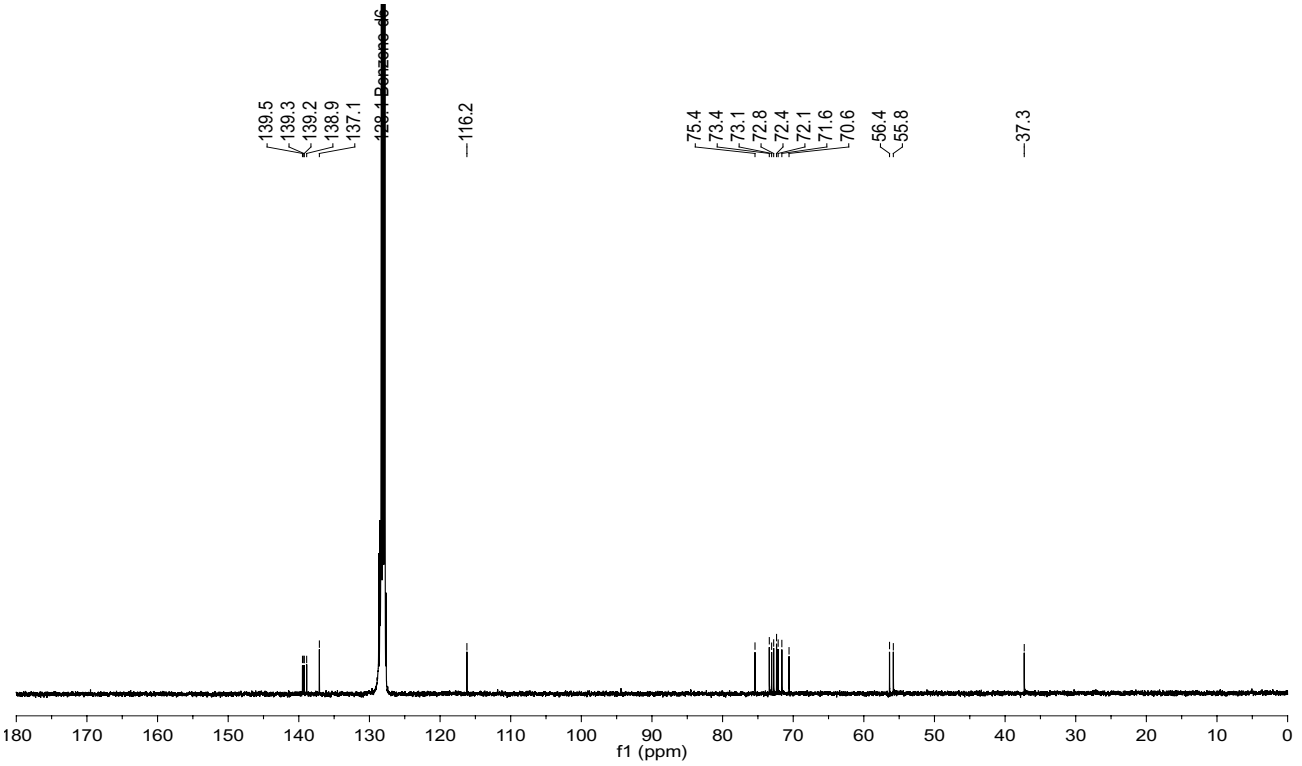
^{13}C-NMR spectrum of **17**



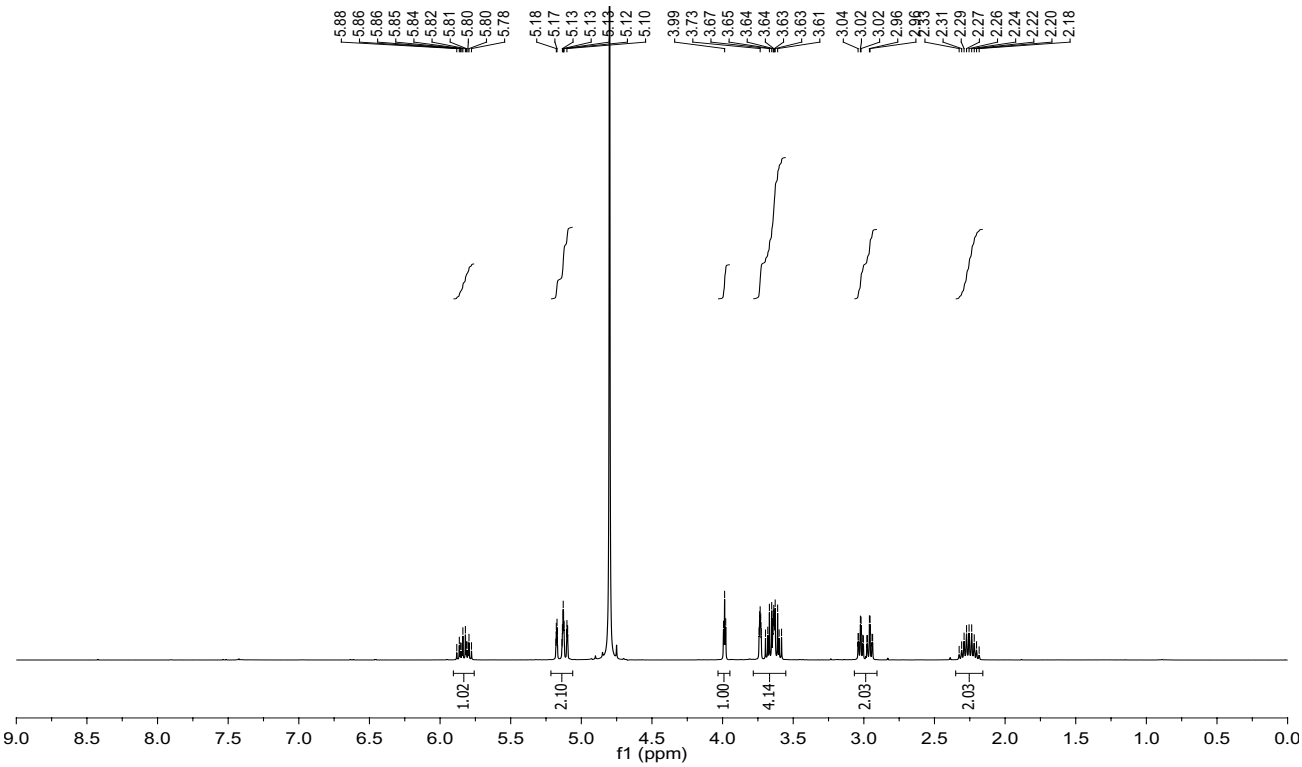
^{1}H-NMR spectrum of **20**



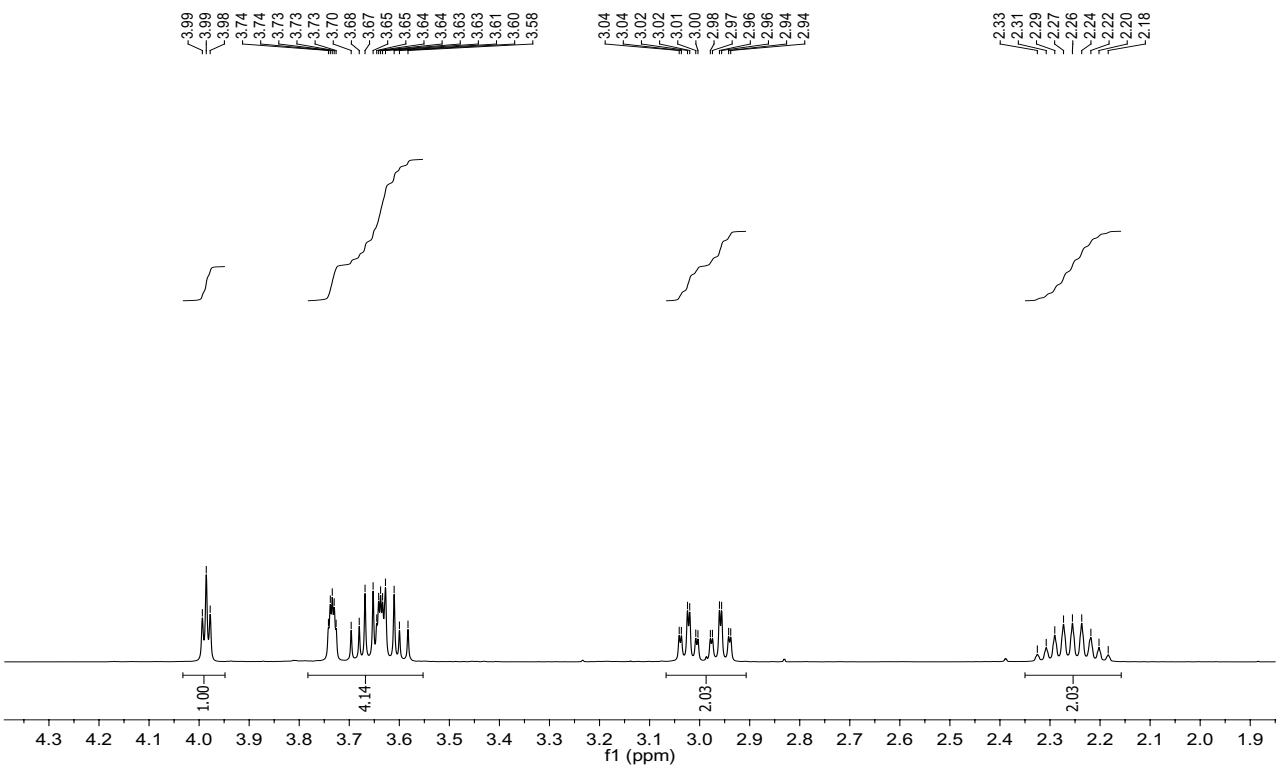
^{1}H-NMR spectrum (expansion) of **20**



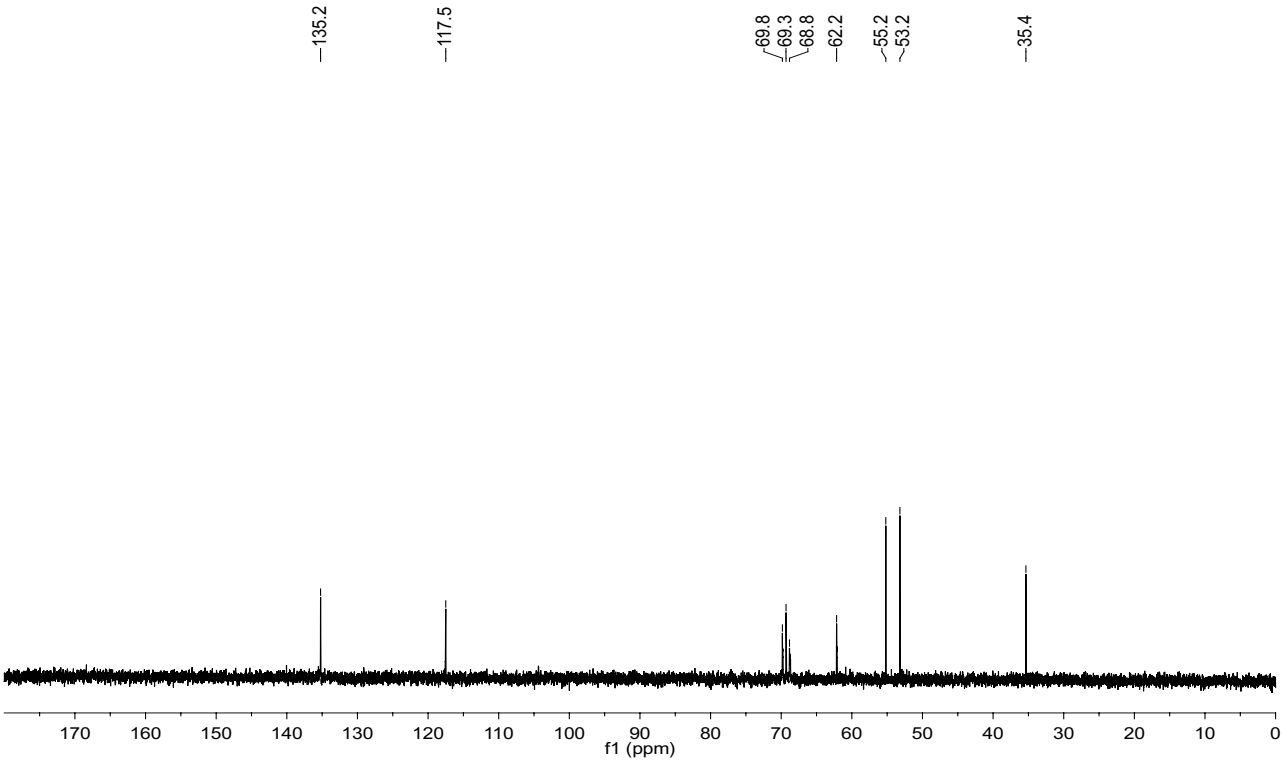
^{13}C-NMR spectrum of **20**



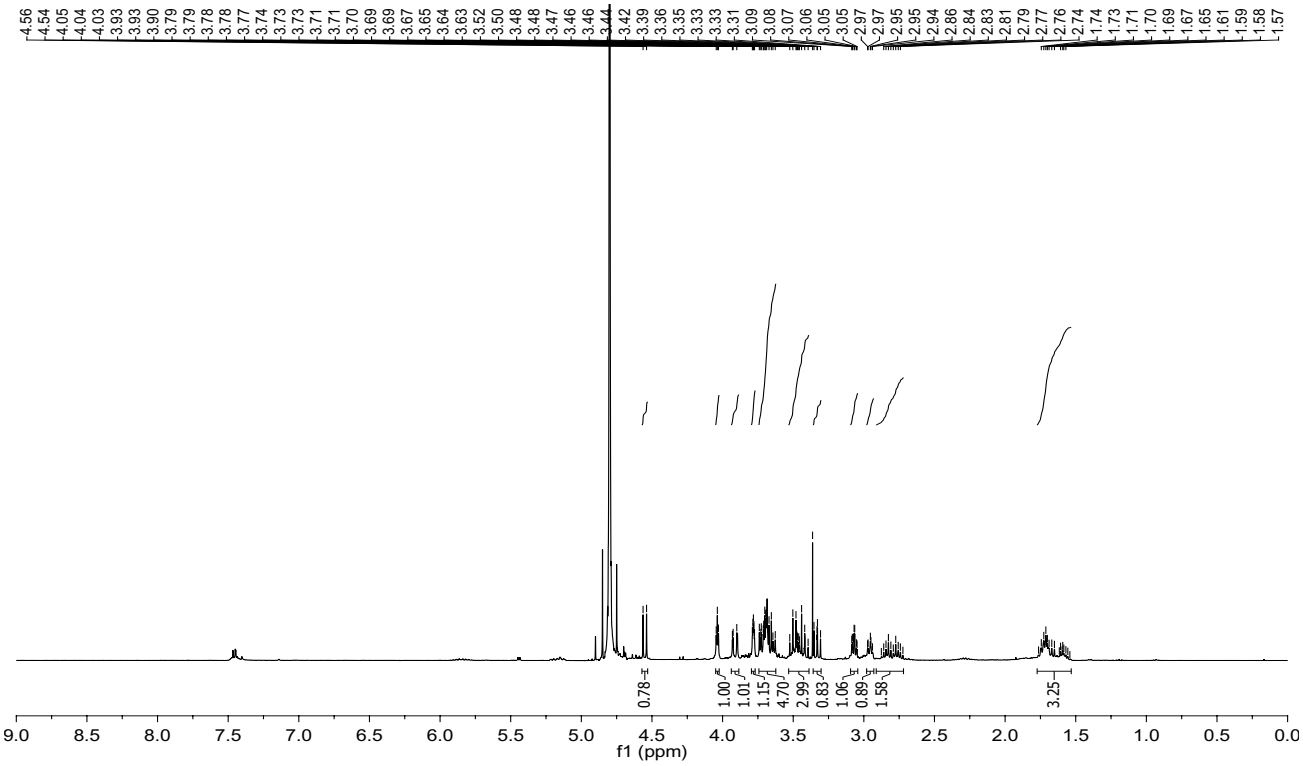
^{1}H-NMR spectrum of **21**



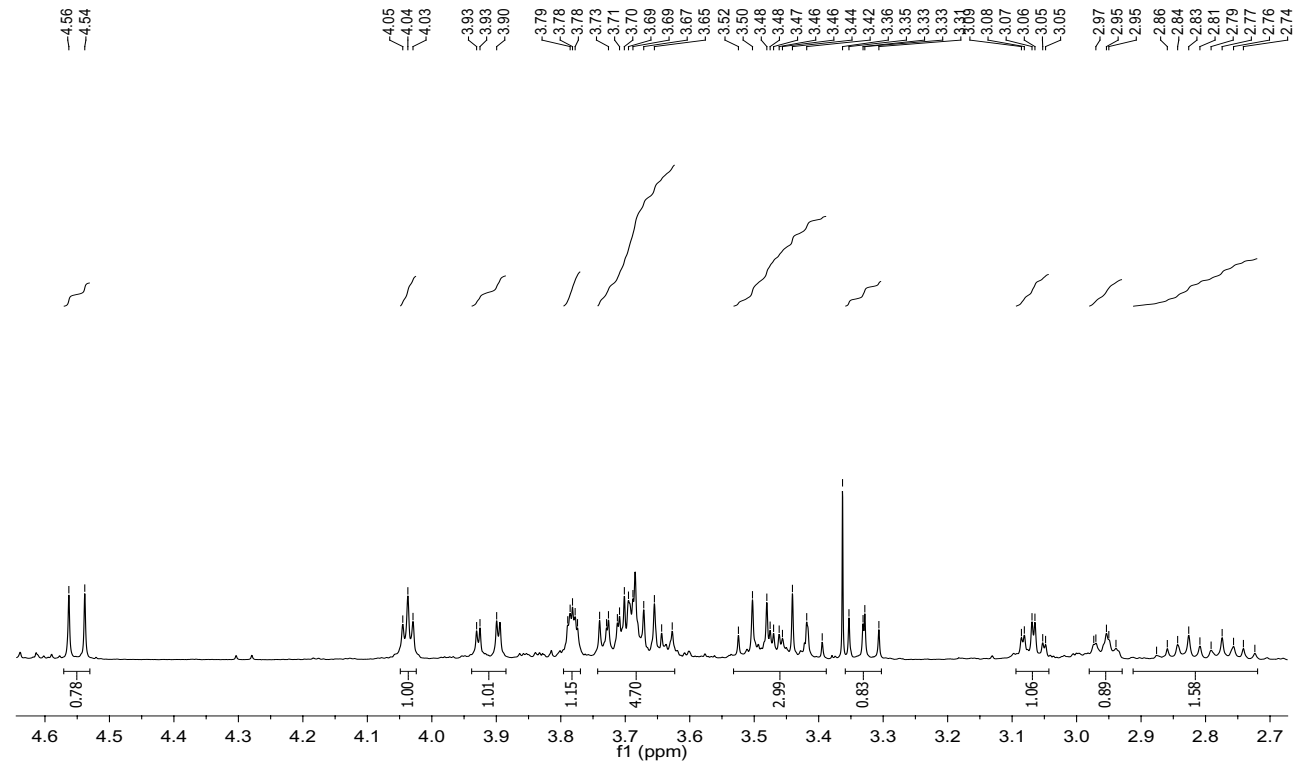
^{1}H-NMR spectrum (expansion) of **21**



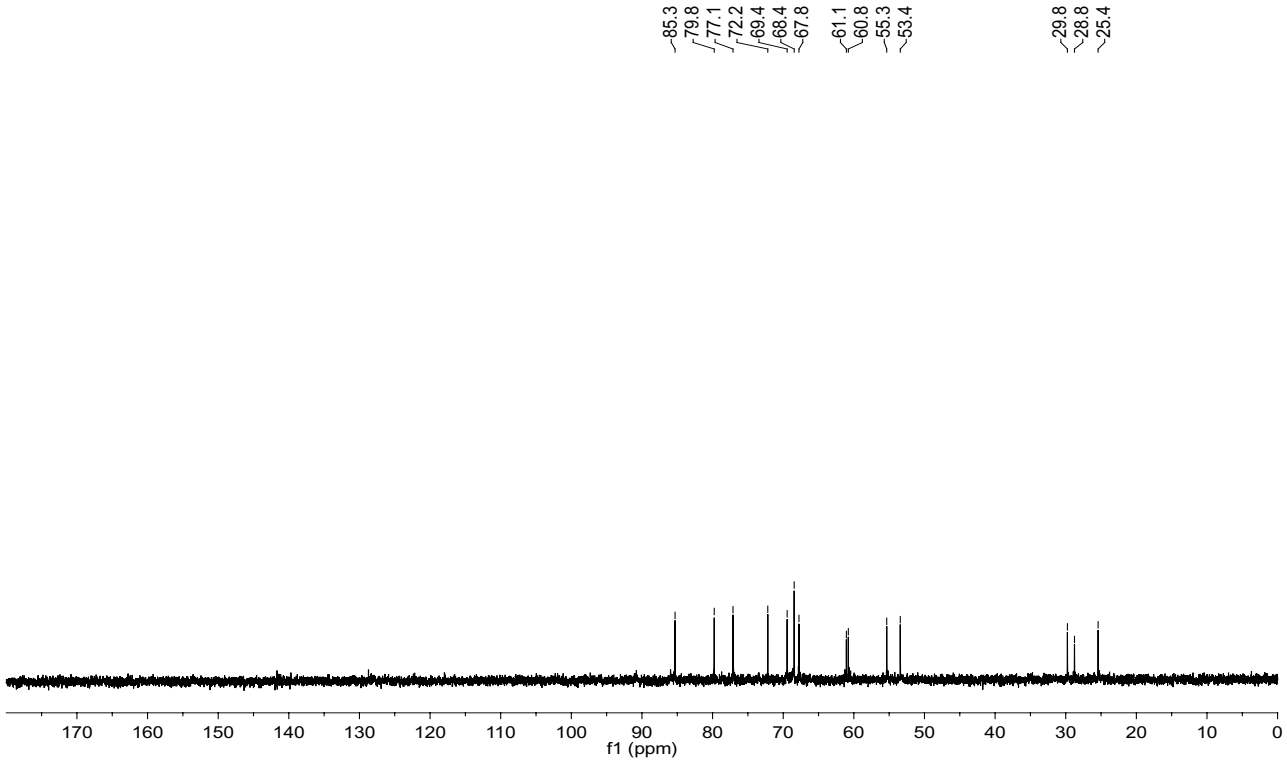
^{13}C-NMR spectrum of **21**



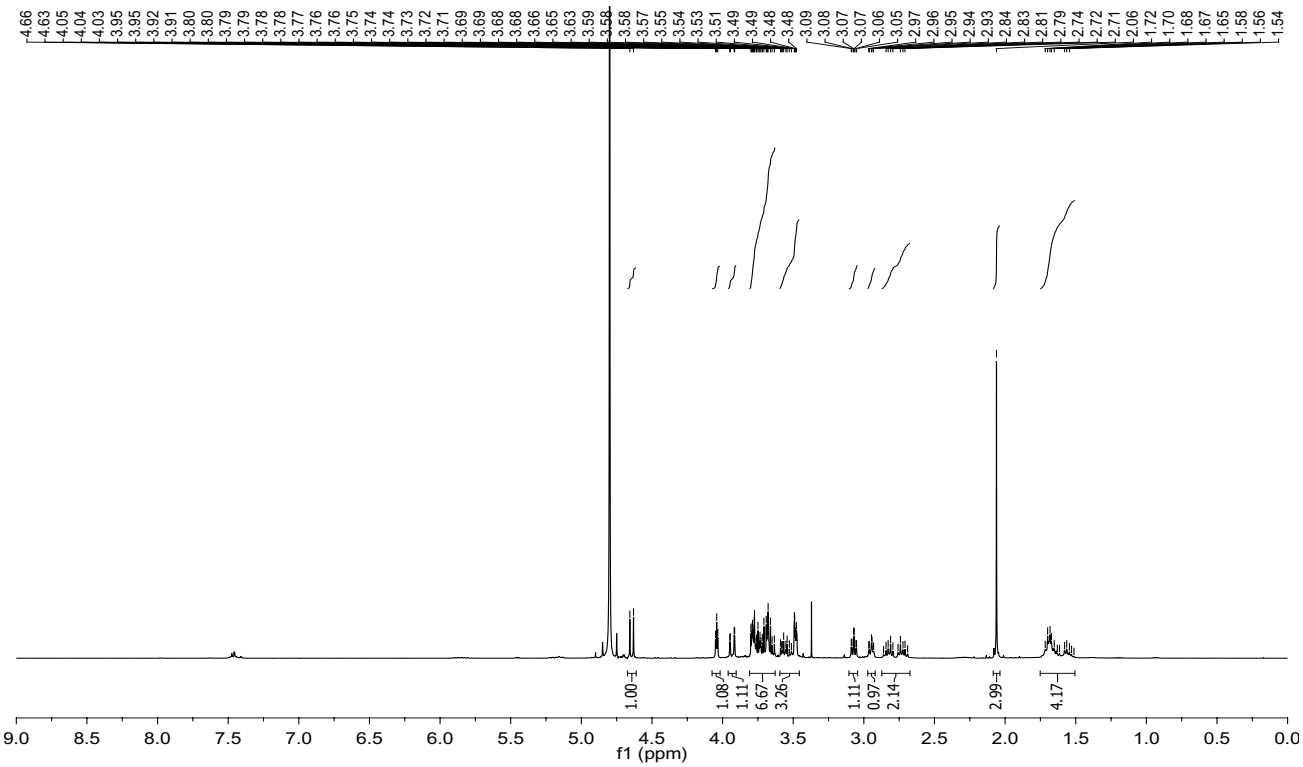
^{1}H-NMR spectrum of **22**



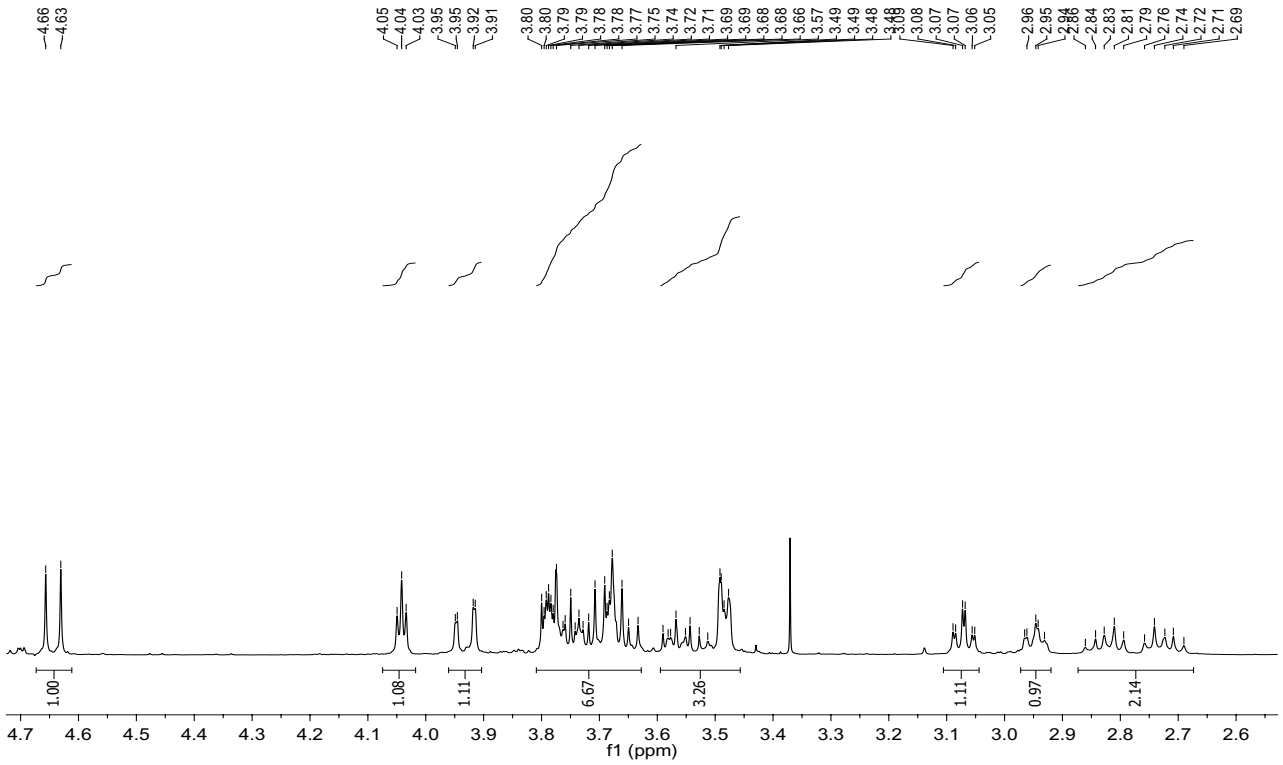
^{1}H-NMR spectrum (expansion) of **22**



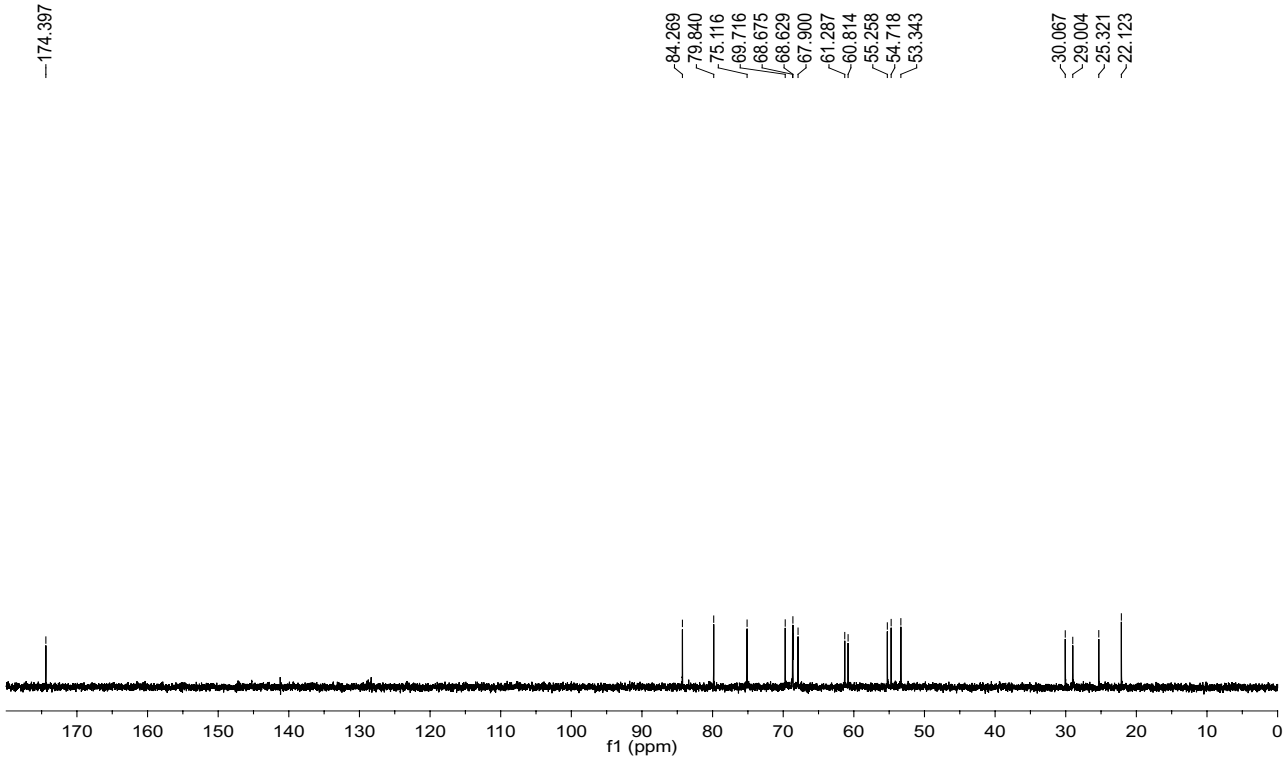
^{13}C-NMR spectrum of **22**



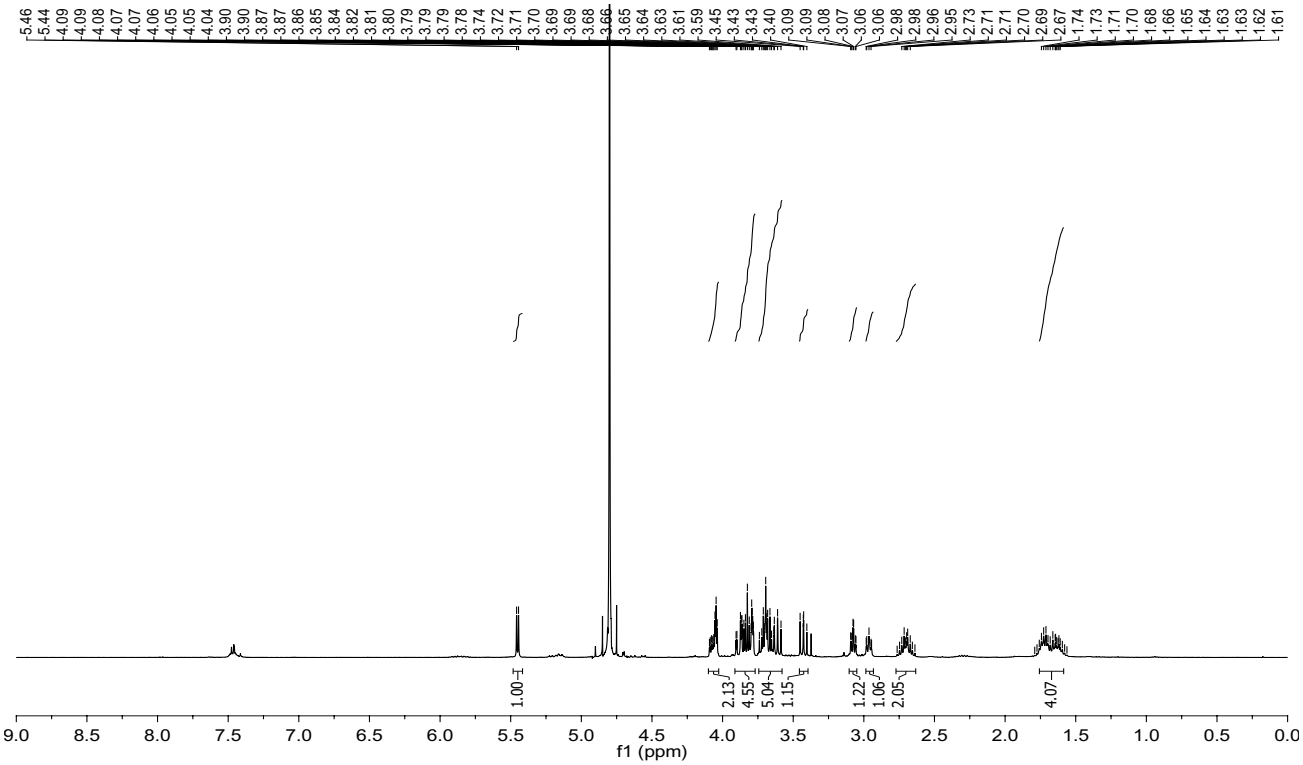
^{1}H-NMR spectrum of **23**



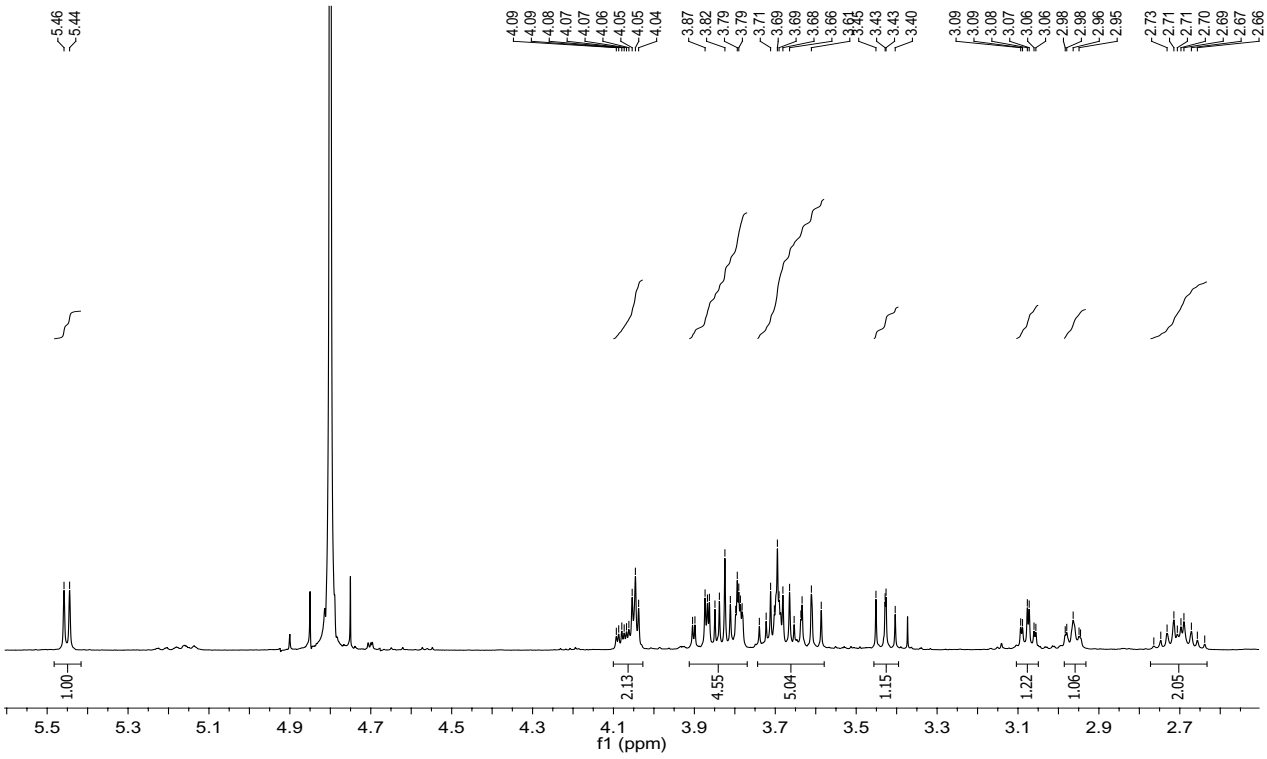
^{1}H-NMR spectrum (expansion) of **23**



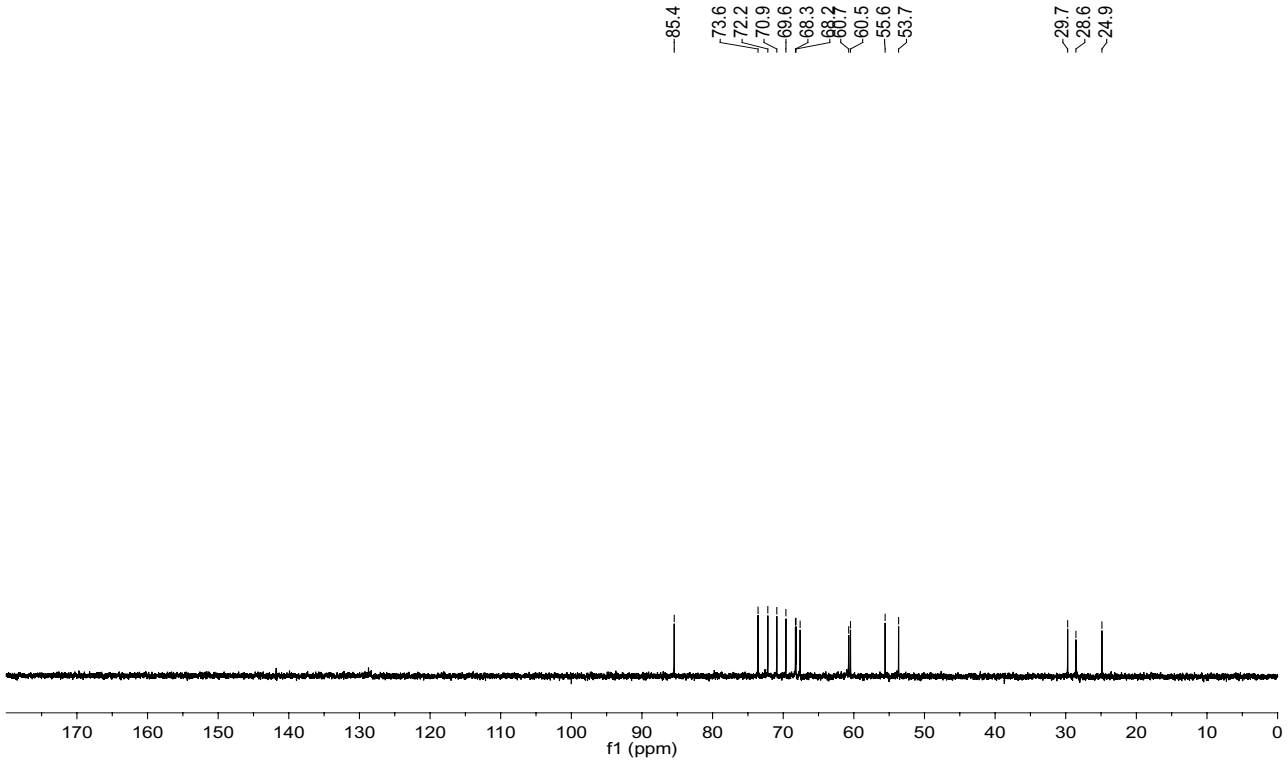
^{13}C-NMR spectrum of **23**



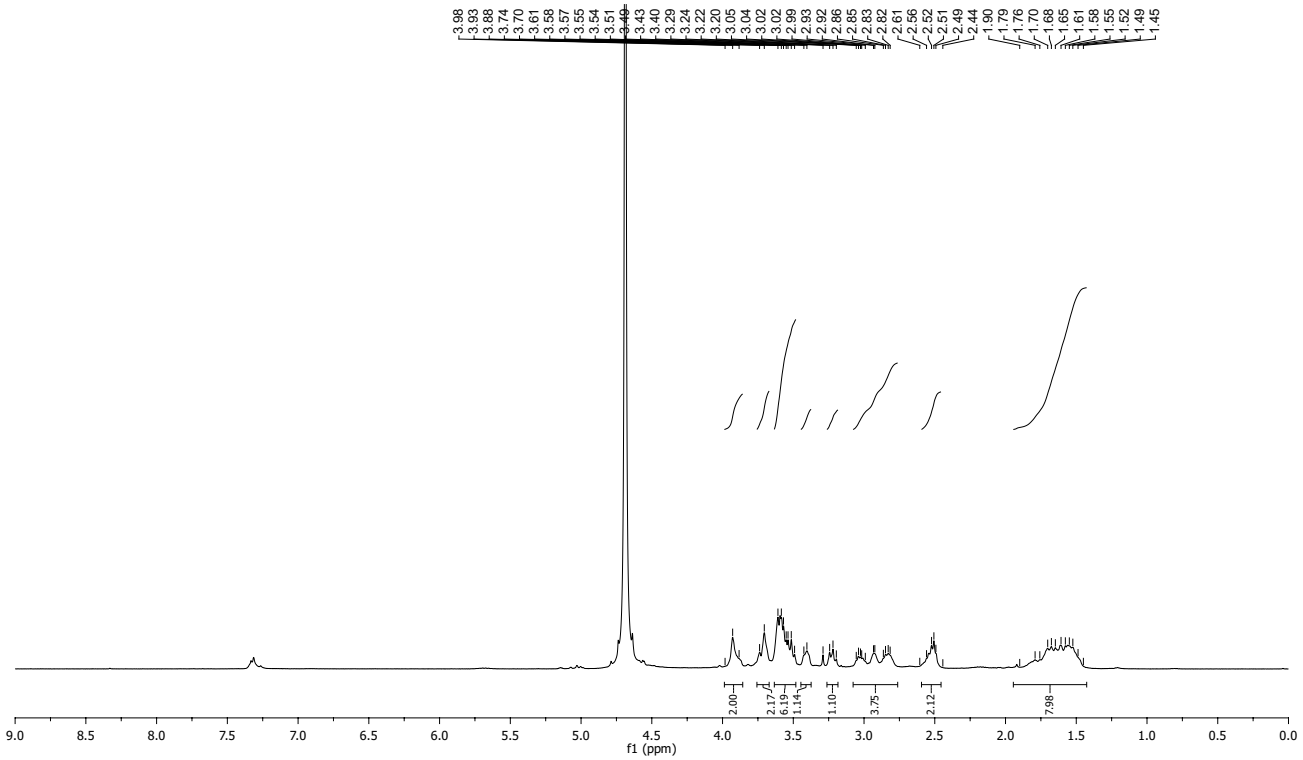
^{1}H-NMR spectrum of **24**



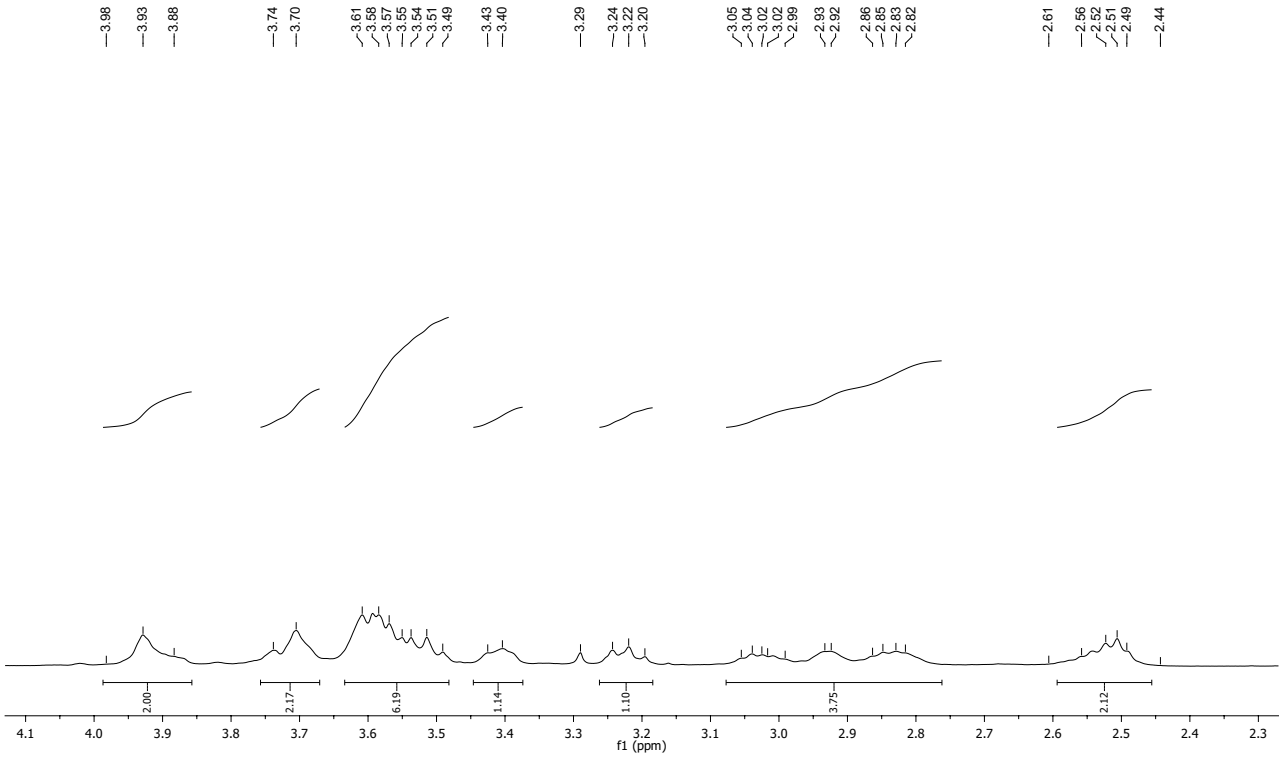
^{1}H-NMR spectrum (expansion) of **24**



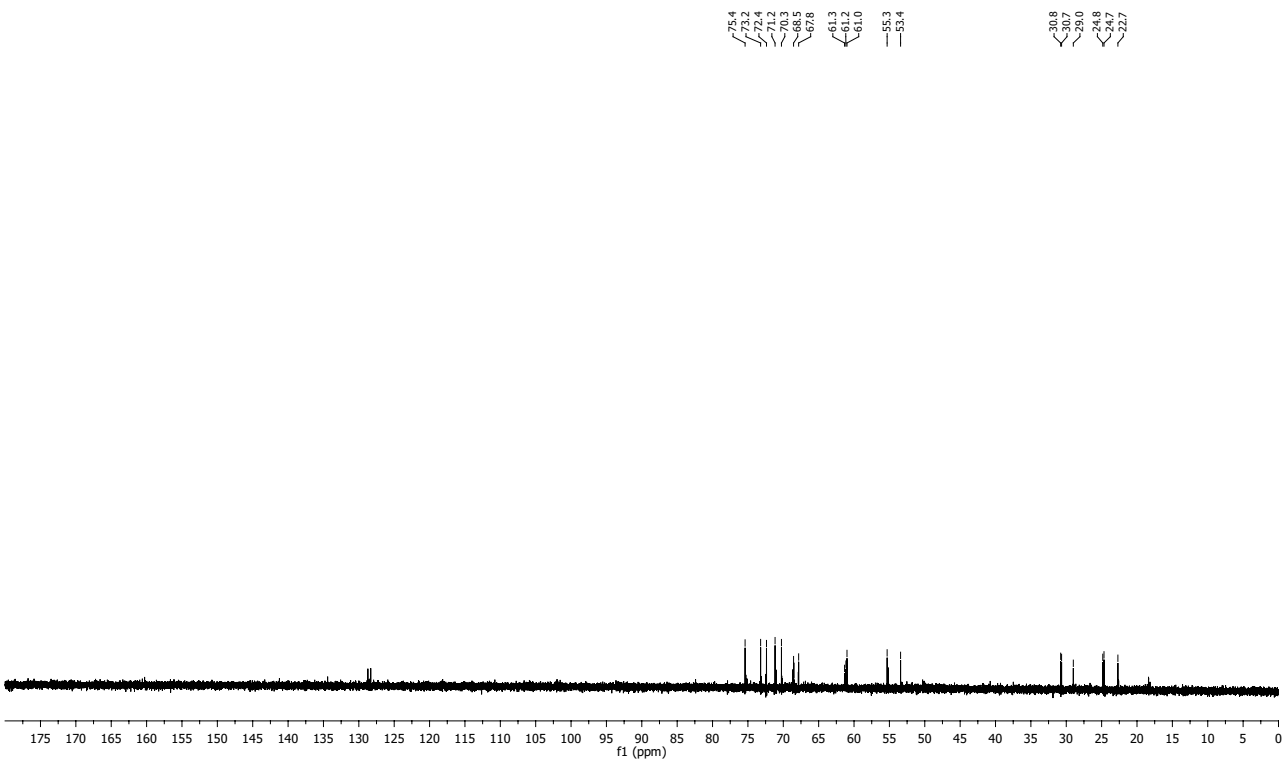
^{13}C-NMR spectrum of **24**



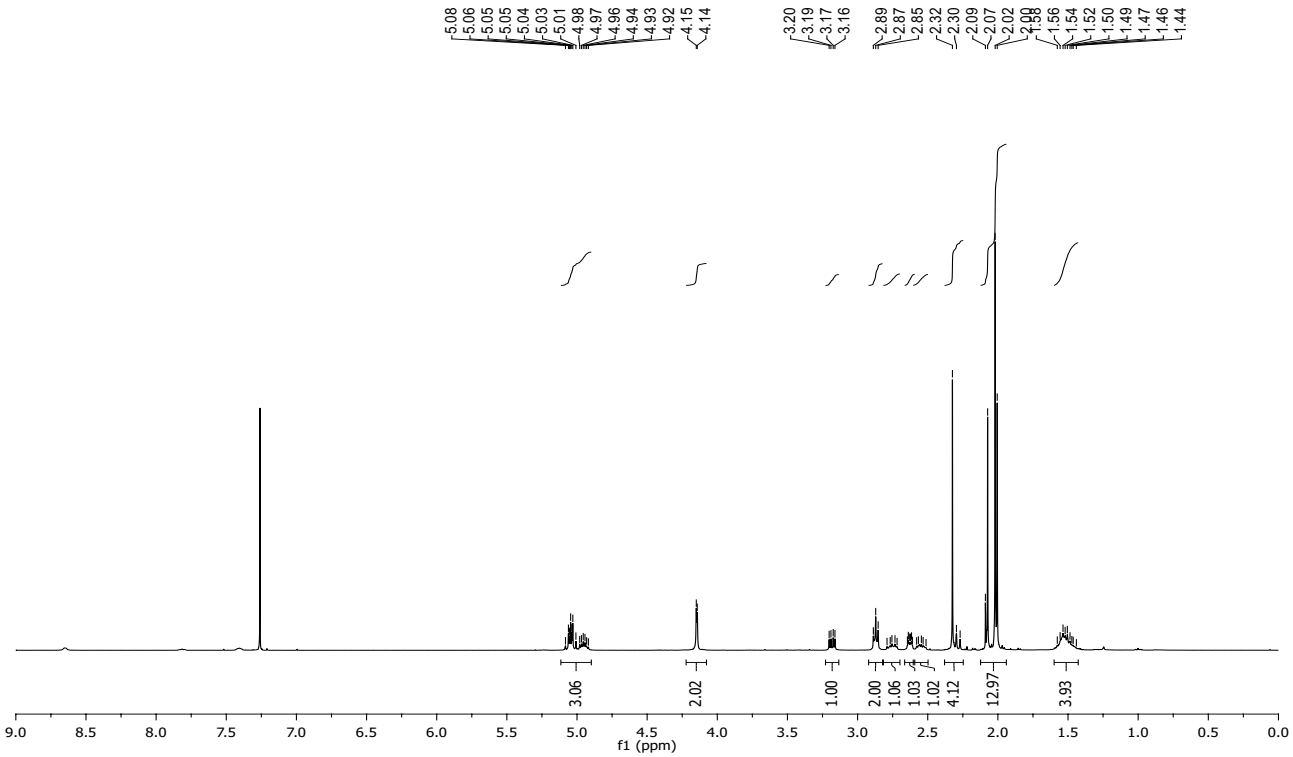
^{1}H-NMR spectrum of **25**



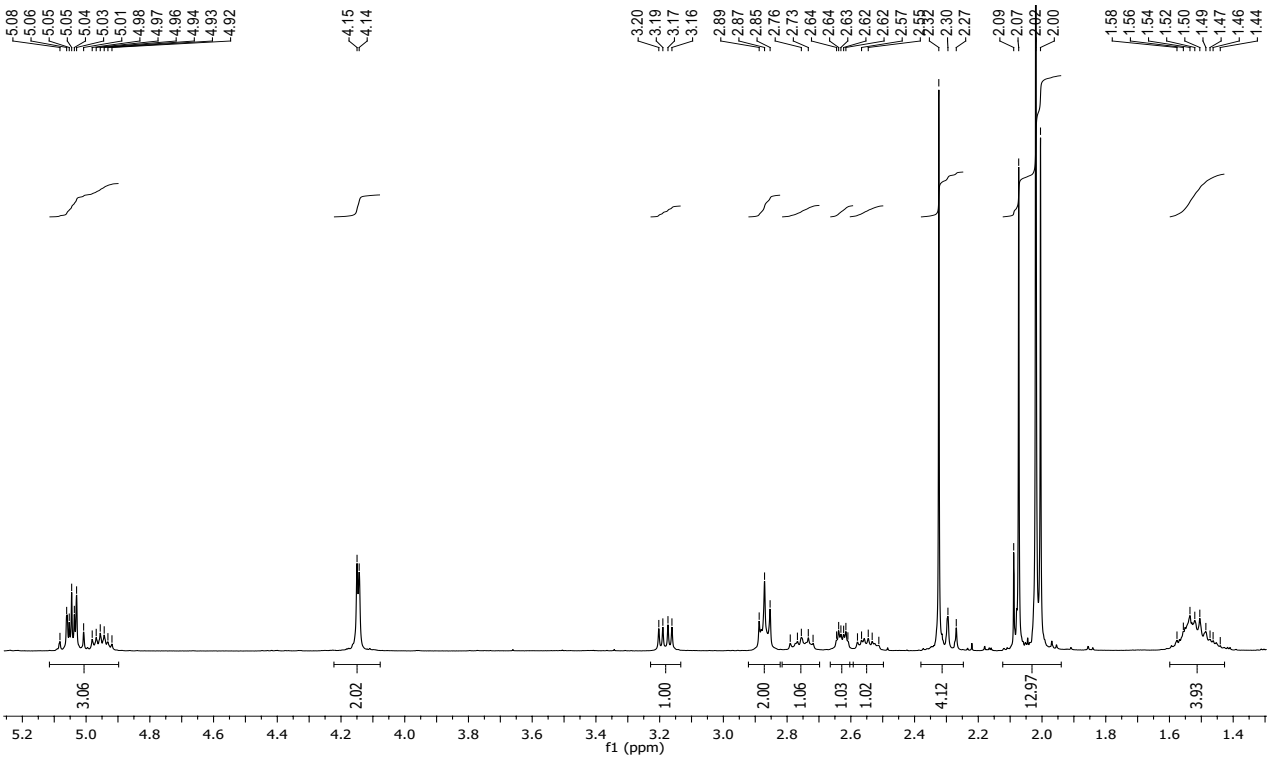
^{1}H-NMR spectrum (expansion) of **25**



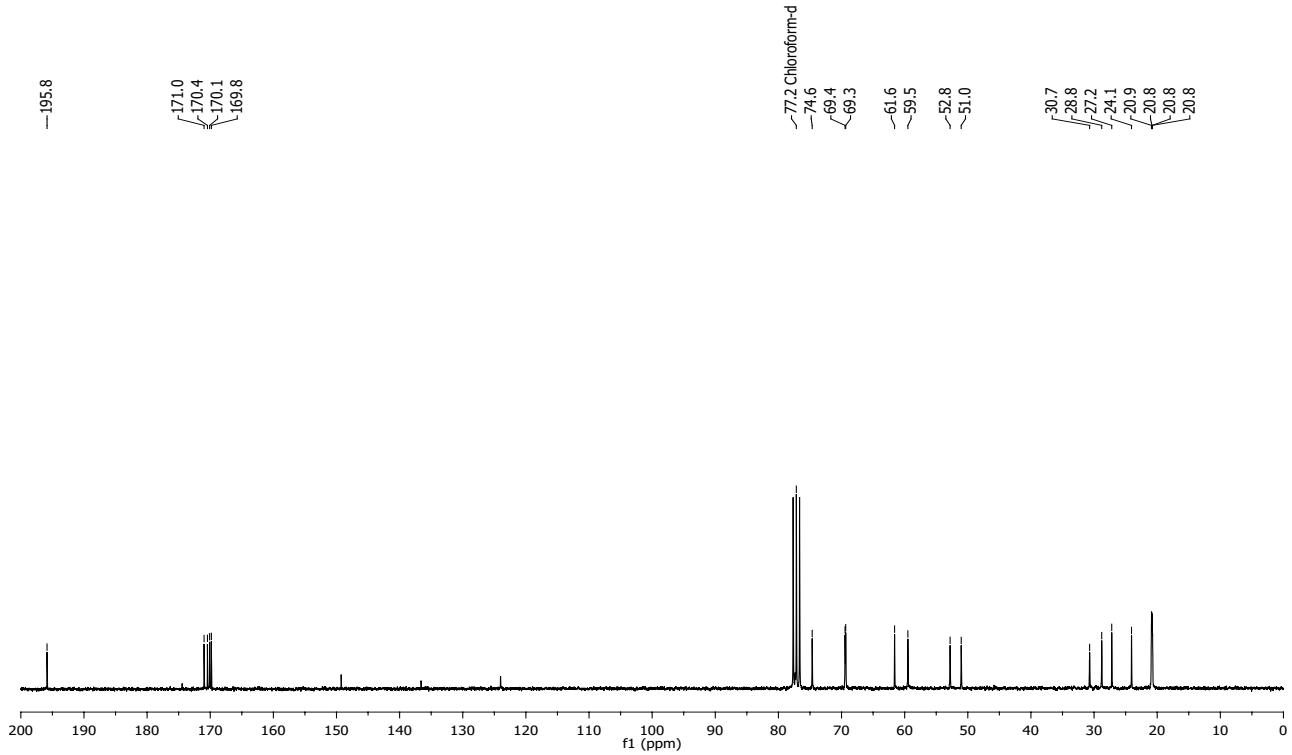
^{13}C-NMR spectrum of **25**



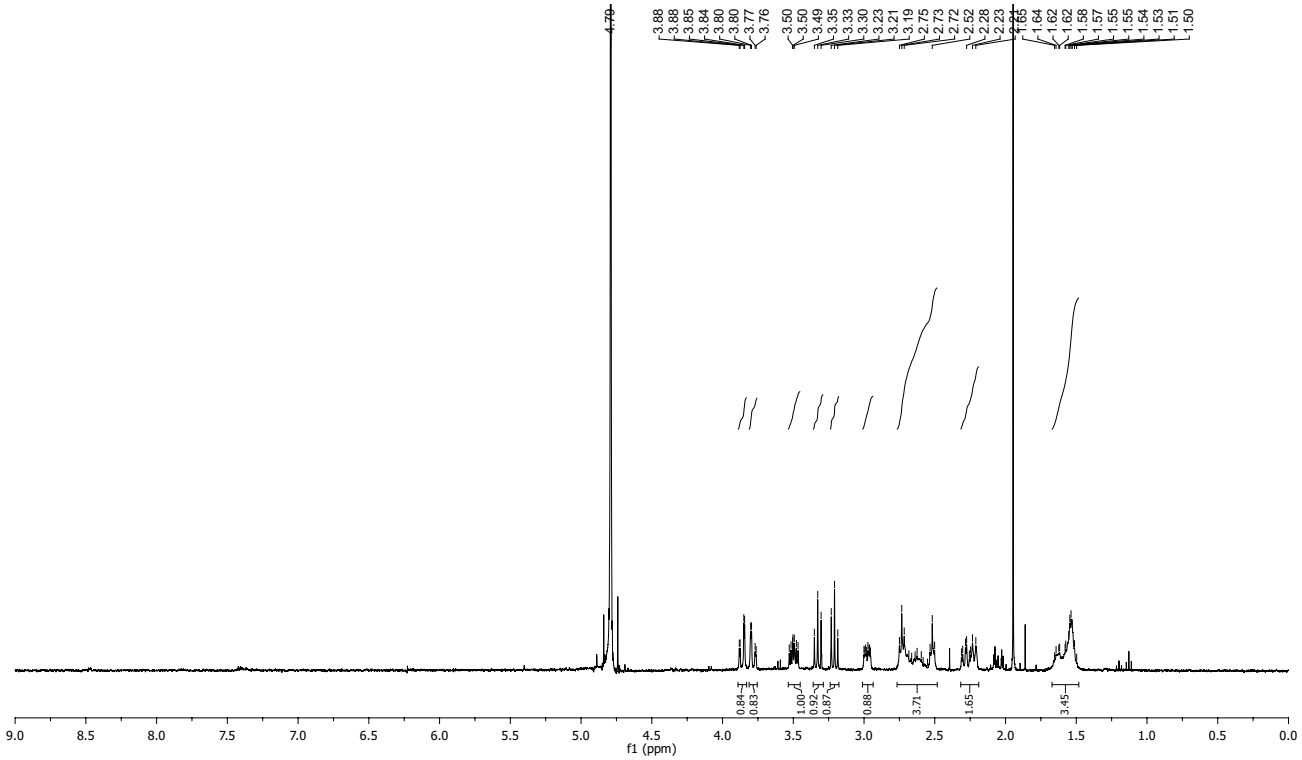
^{1}H-NMR spectrum of ***27***



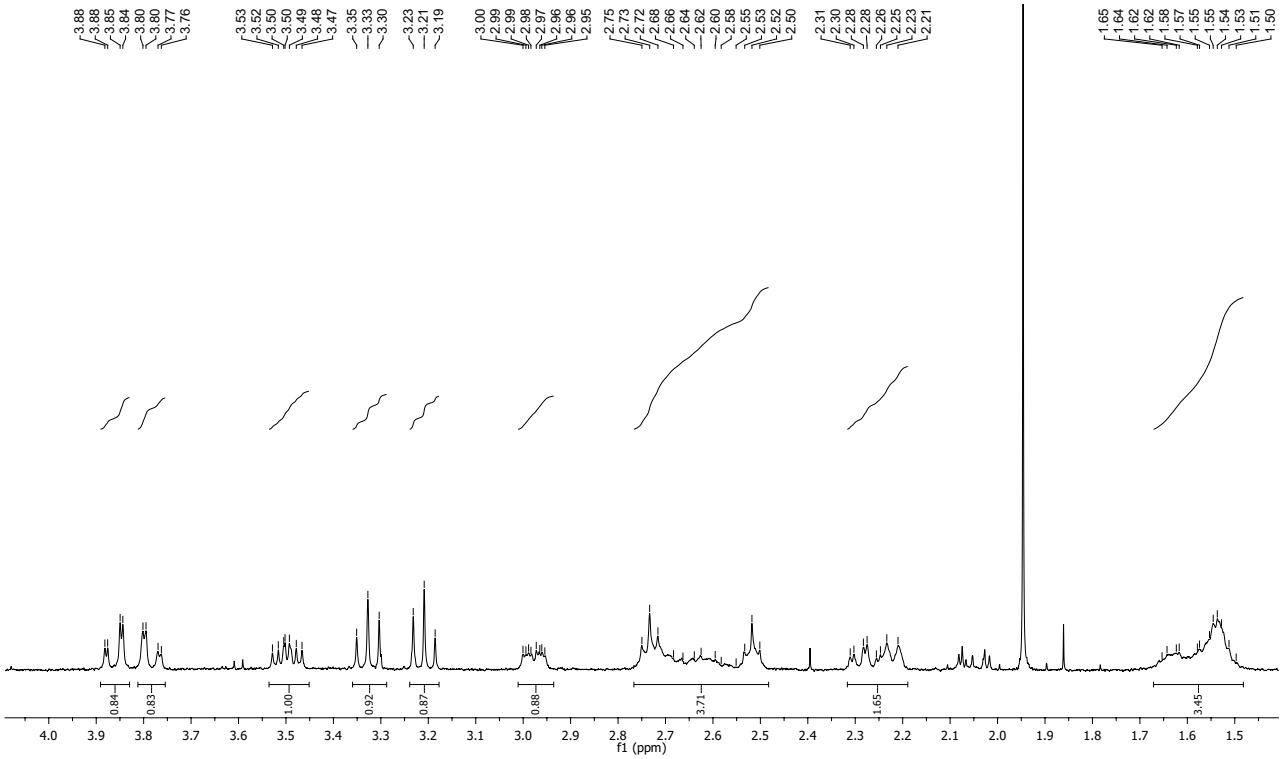
^{1}H-NMR spectrum (expansion) of ***27***



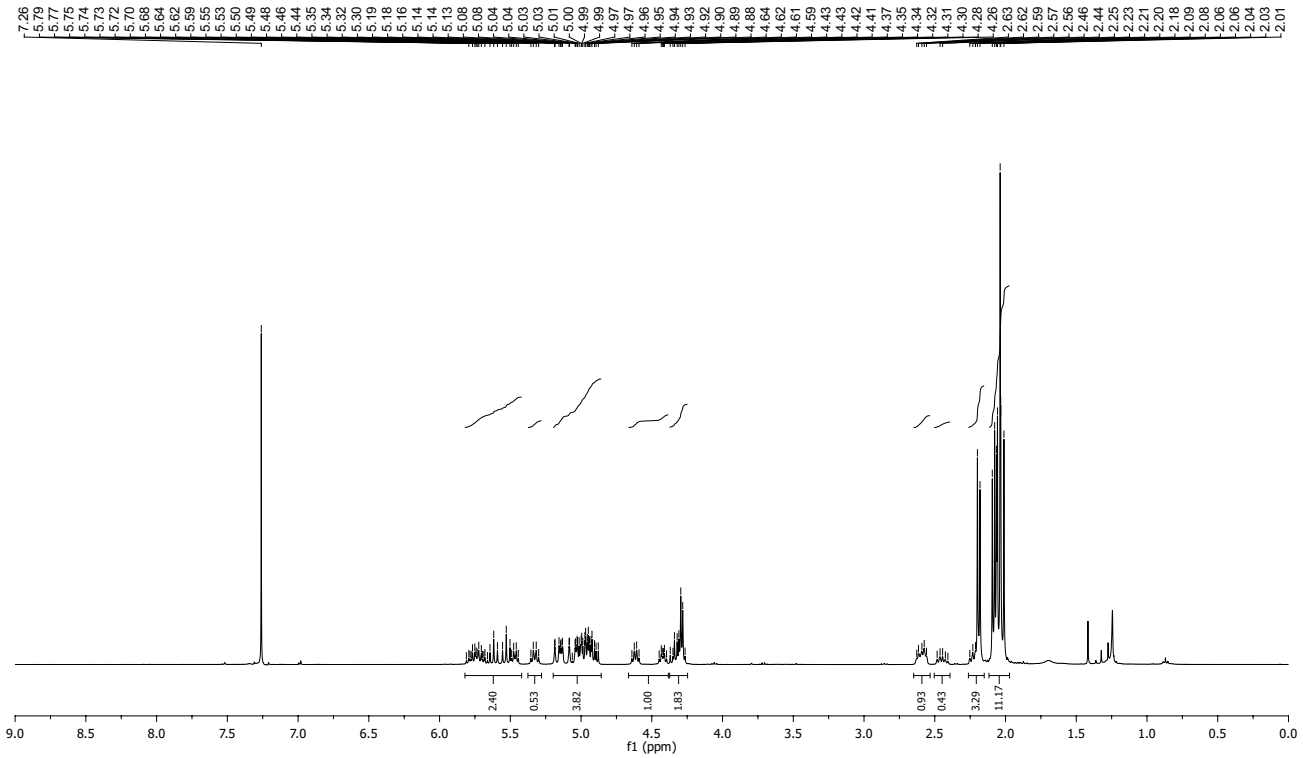
^{13}C-NMR spectrum of **27**



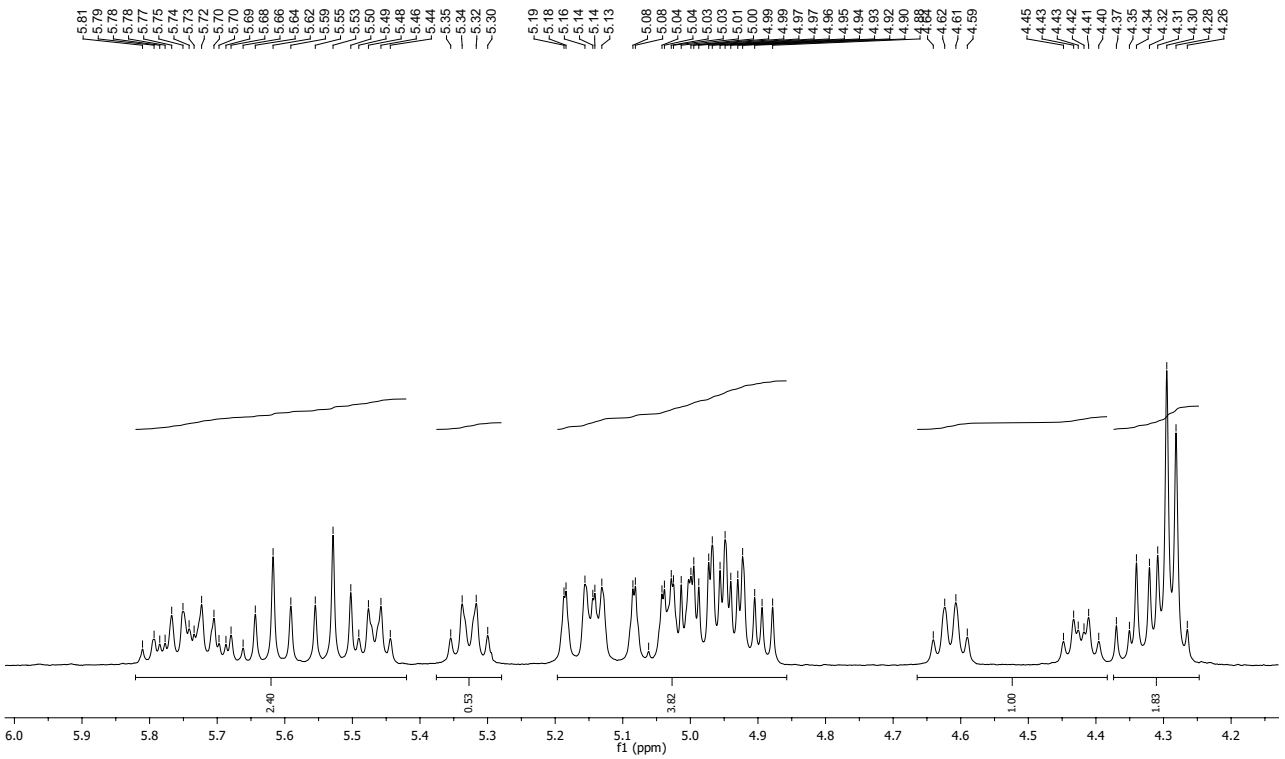
^{1}H-NMR spectrum of **28**



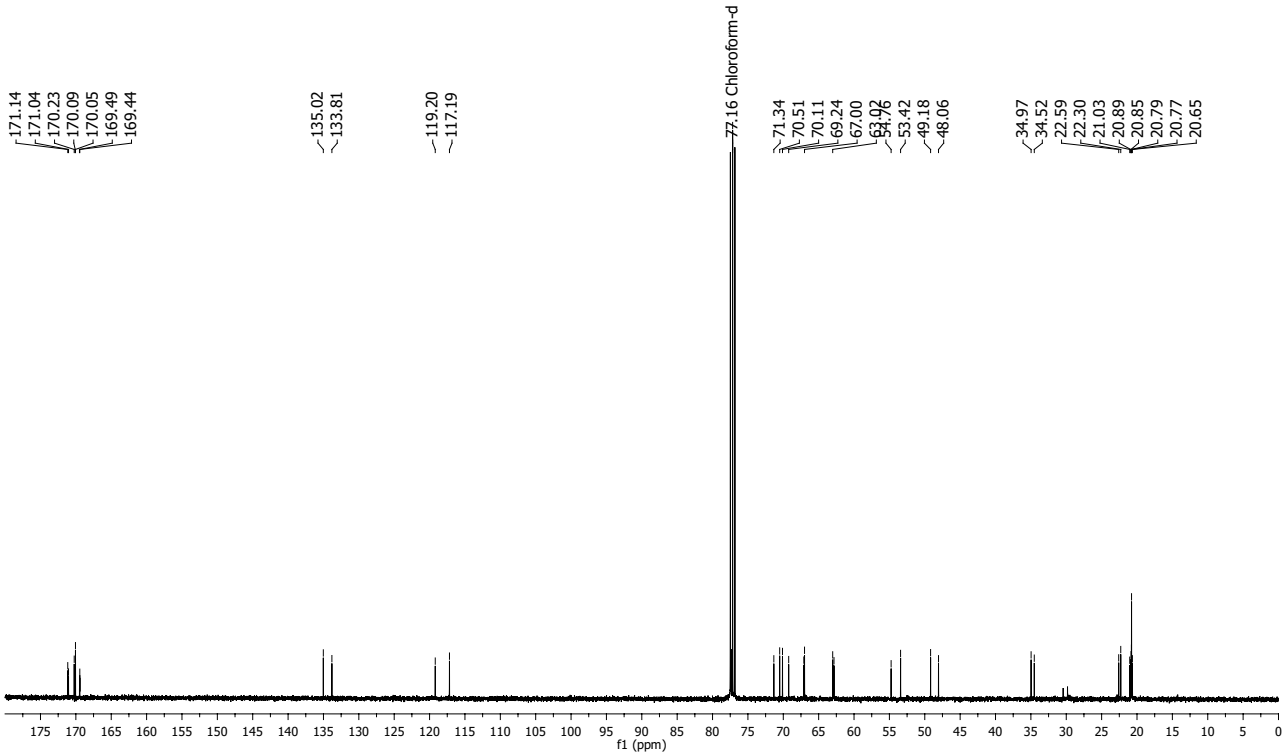
^{1}H-NMR spectrum (expansion) of **28**



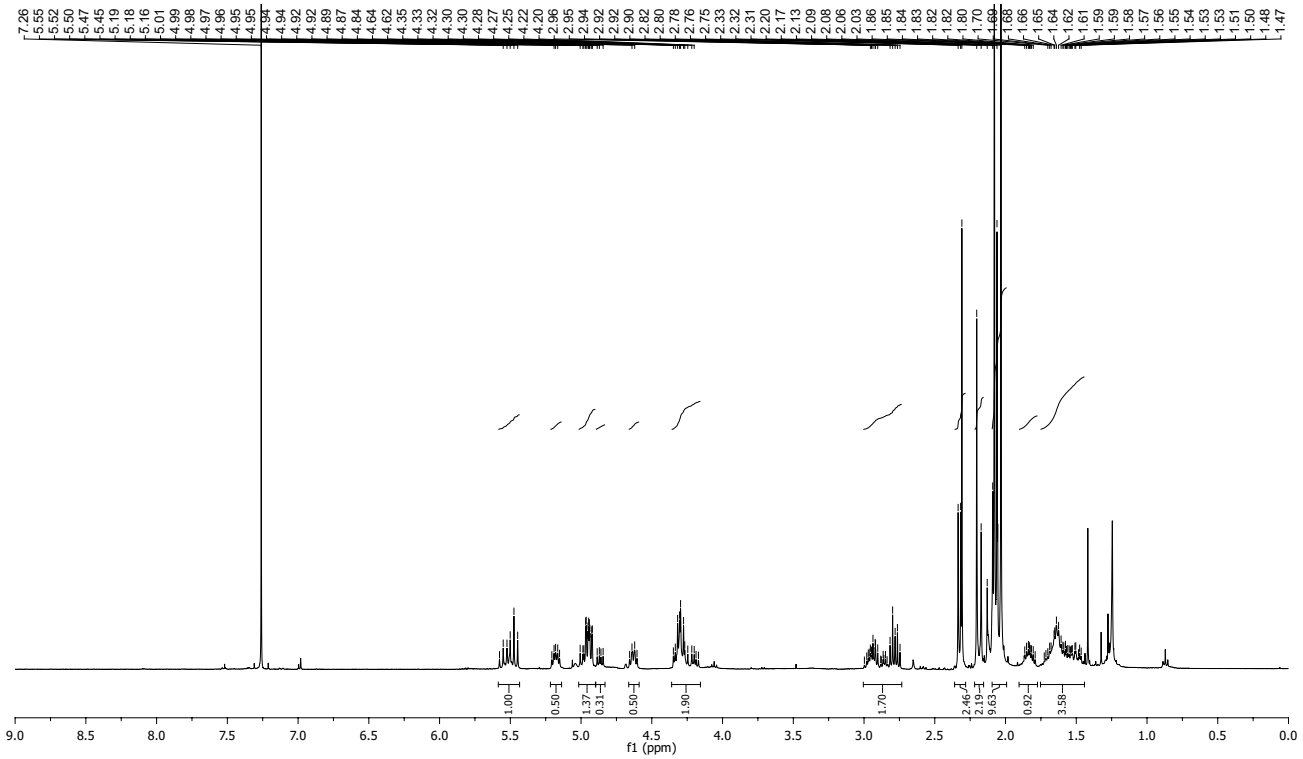
^{1}H-NMR spectrum of **29**



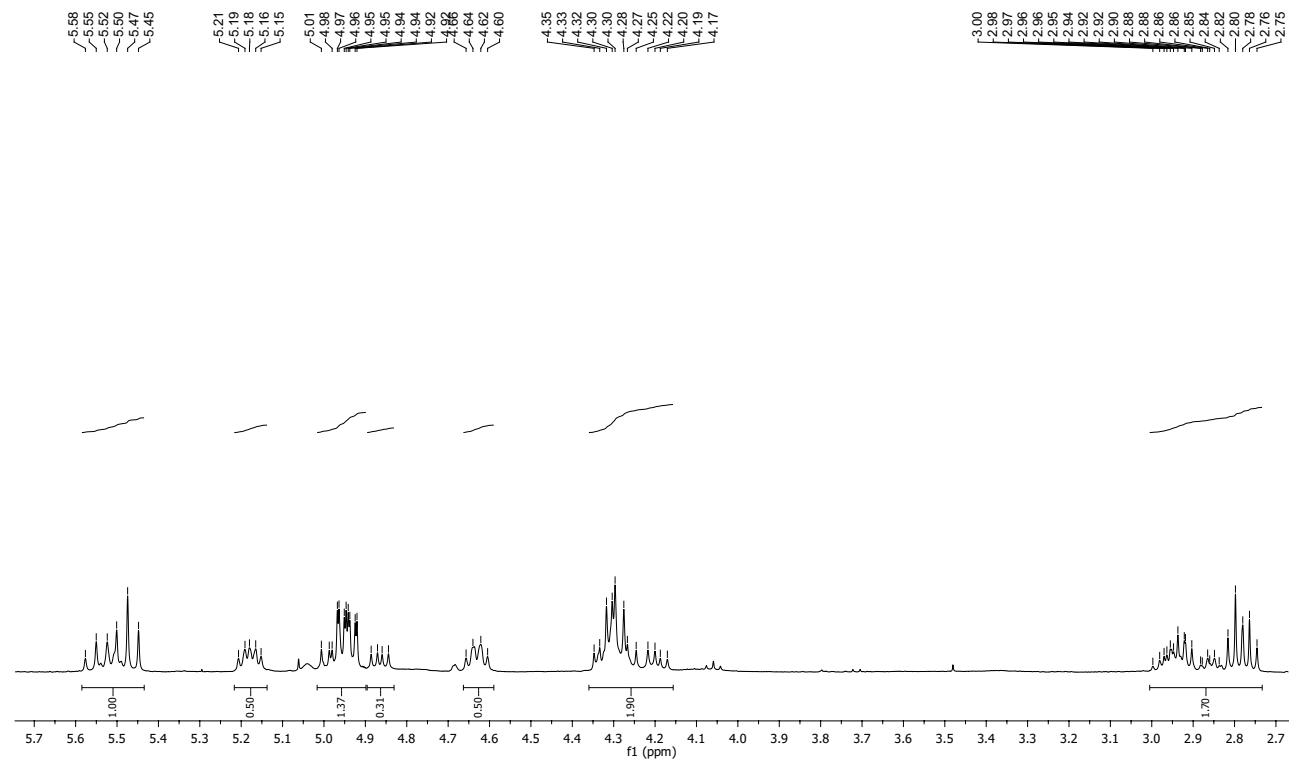
^{1}H-NMR spectrum (expansion) of **29**



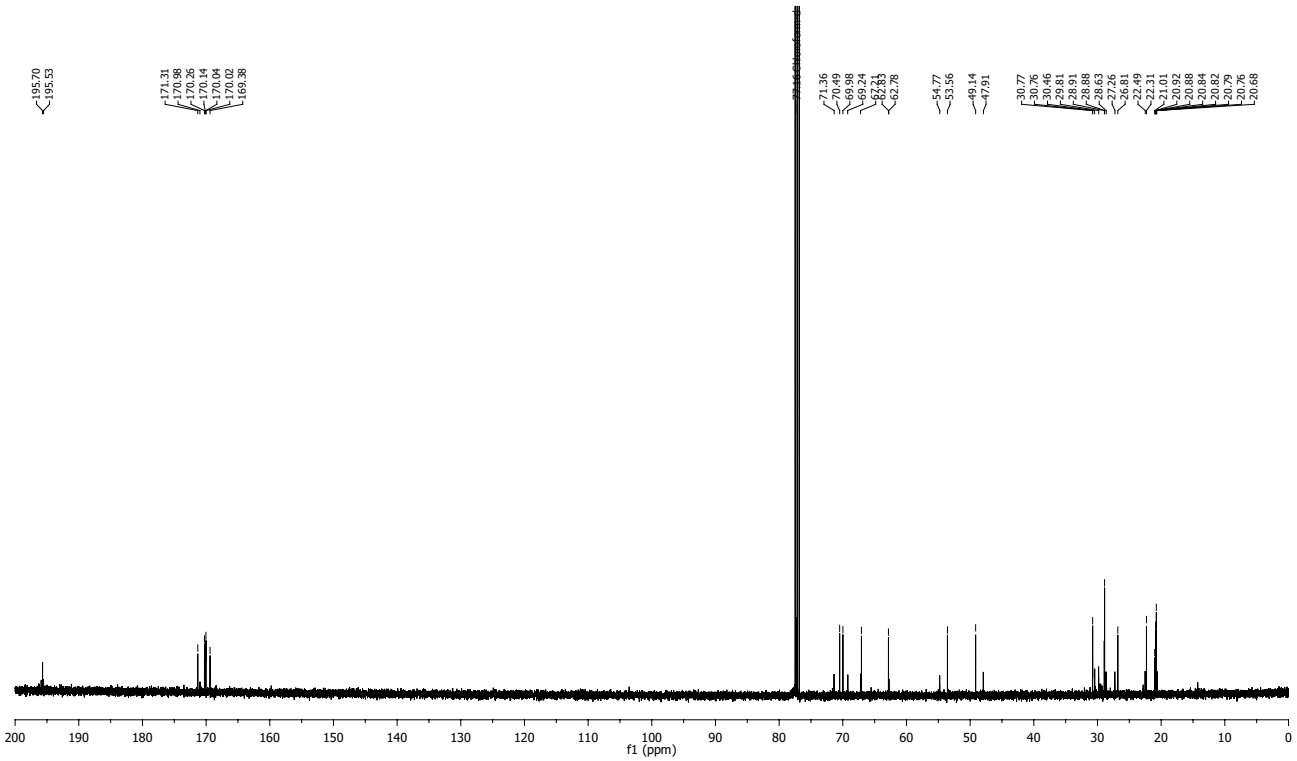
^{13}C-NMR spectrum of **29**



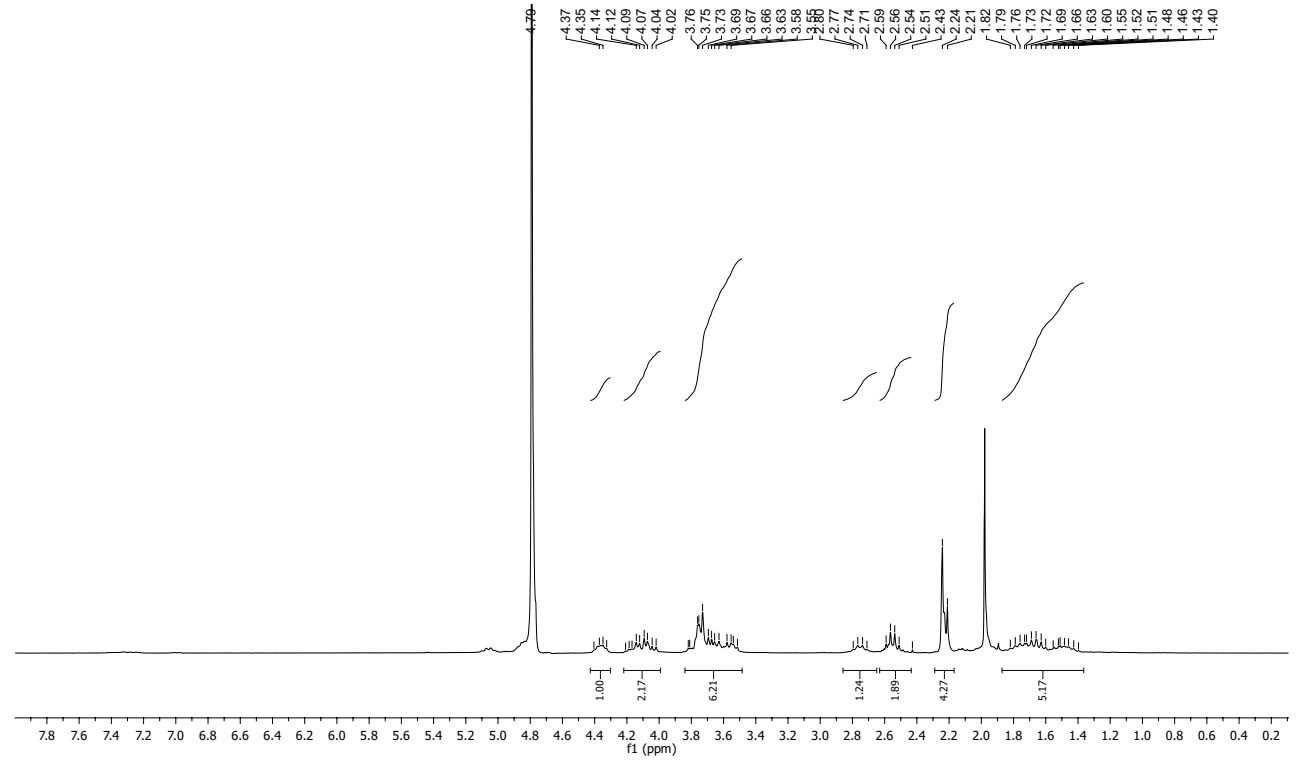
^{1}H-NMR spectrum of **30**



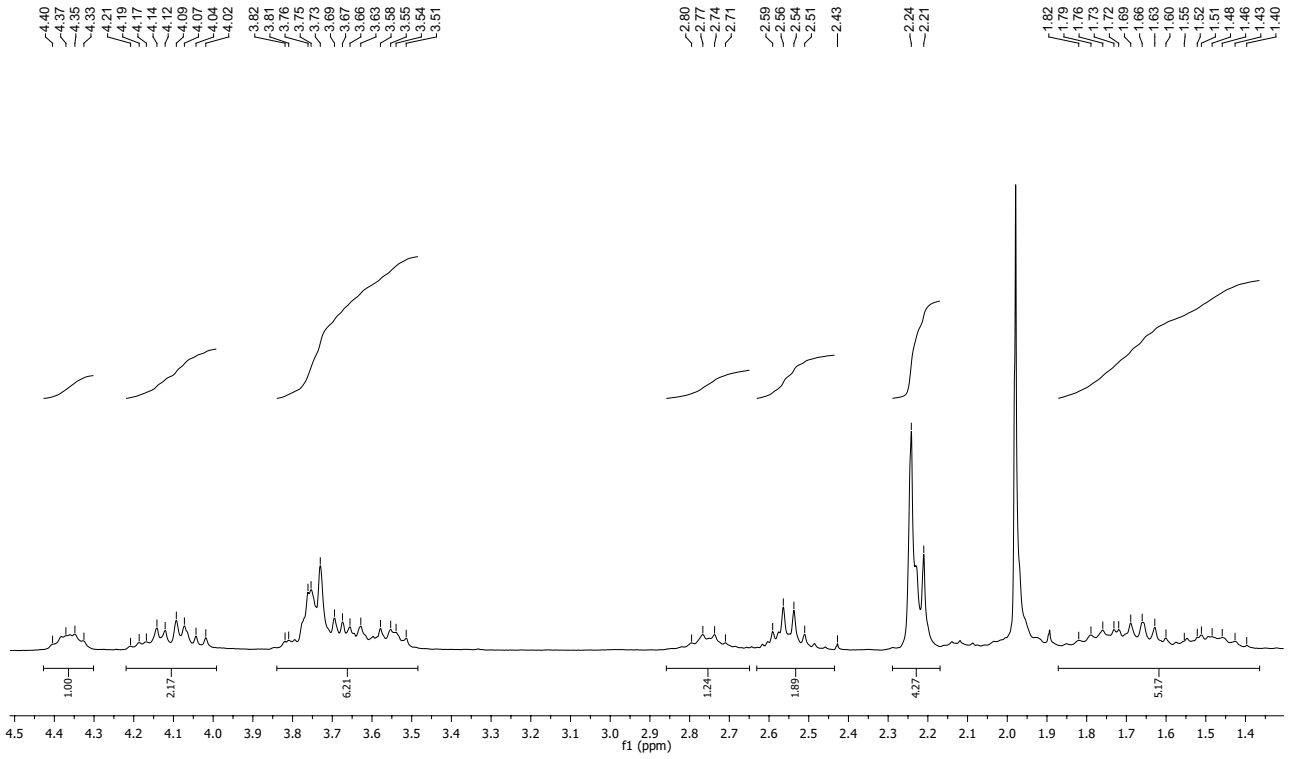
^{1}H-NMR spectrum (expansion) of **30**



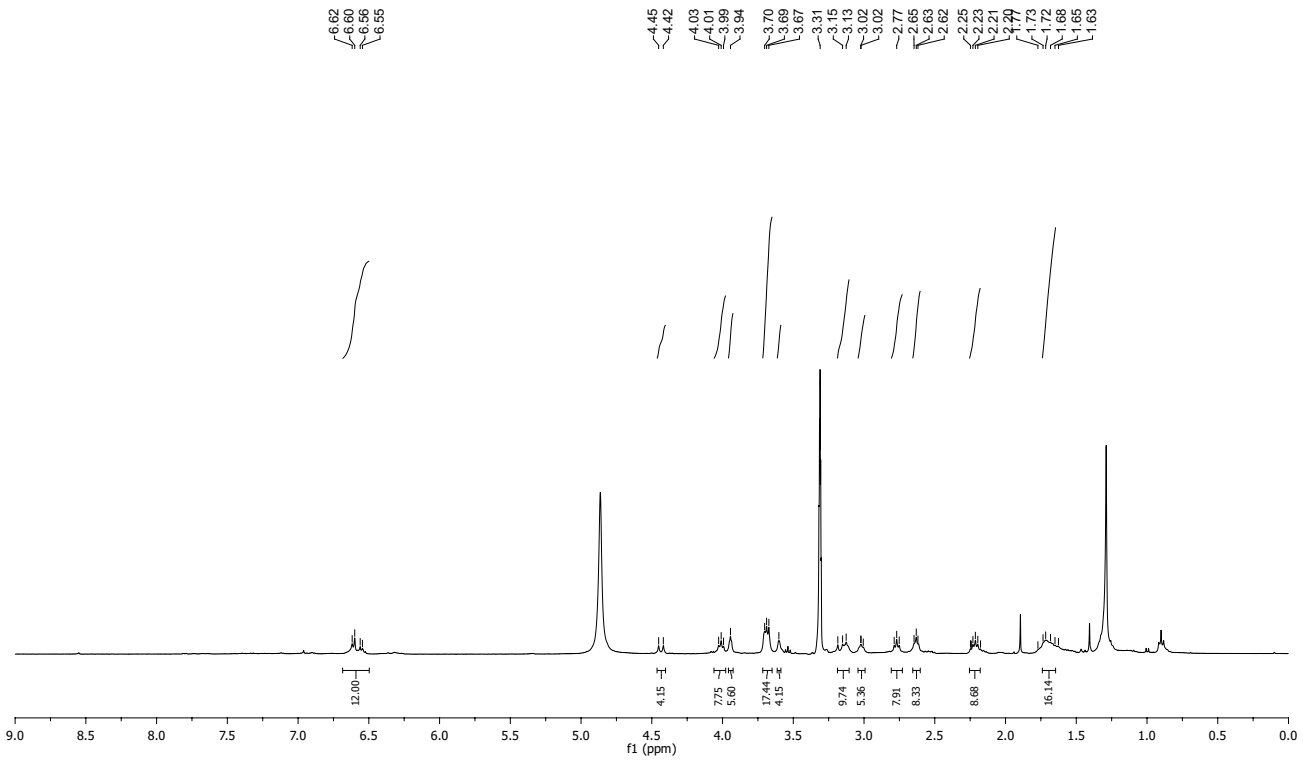
^{13}C-NMR spectrum of **30**



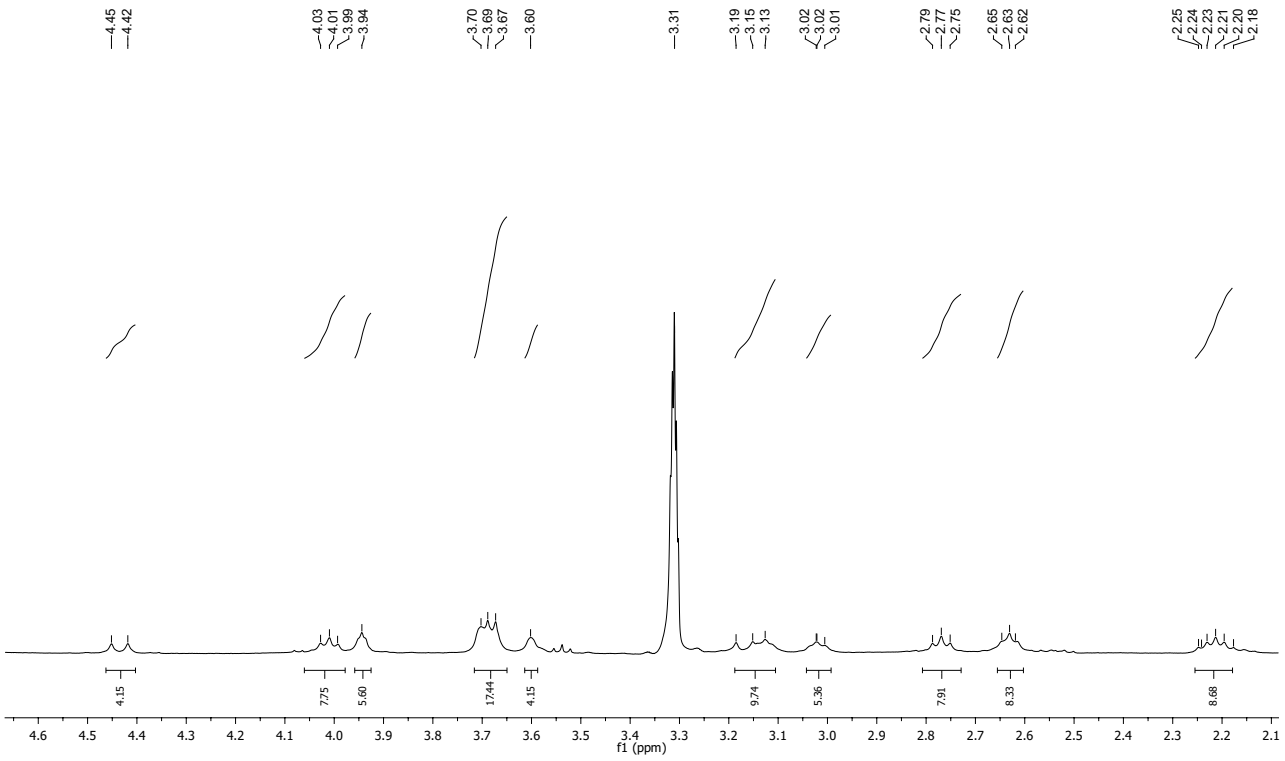
^{1}H-NMR spectrum of **31**



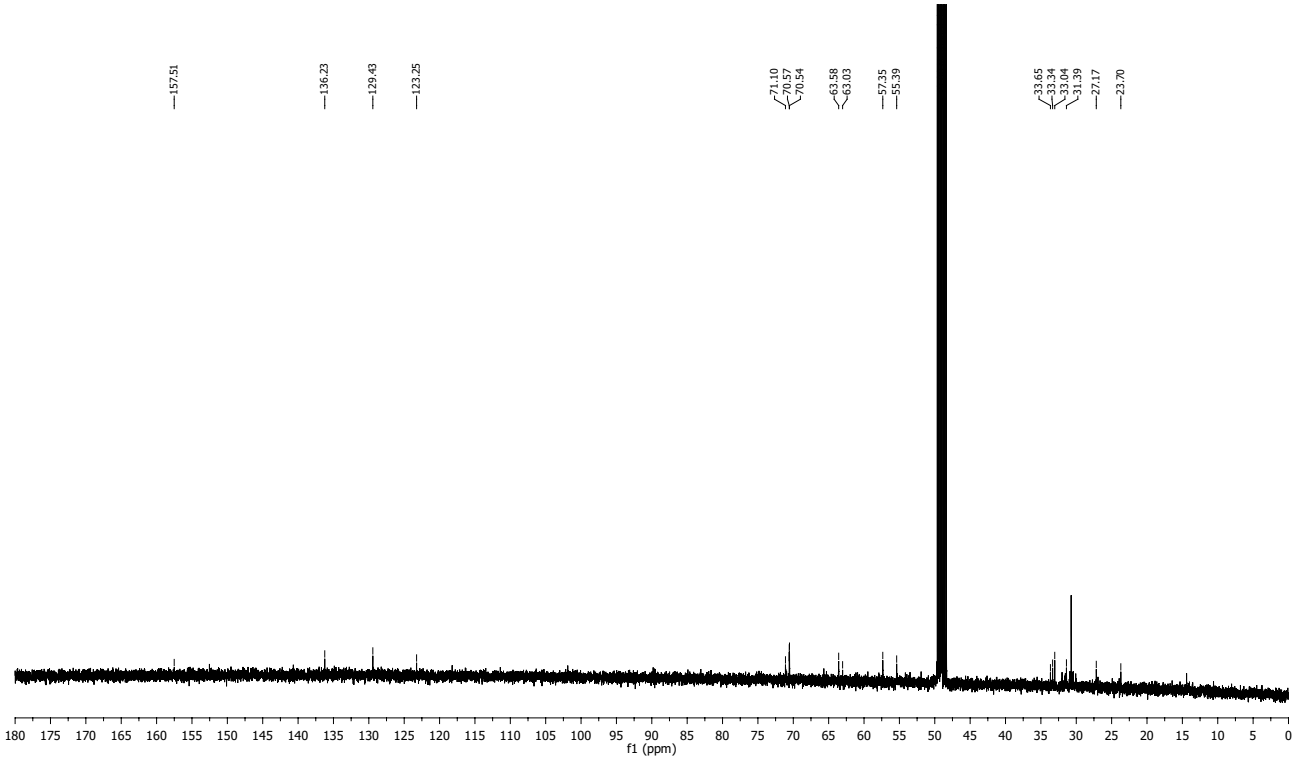
^{1}H-NMR spectrum (expansion) of **31**



^{1}H-NMR spectrum of **34**



^{1}H-NMR spectrum (expansion) of **34**



^{13}C-NMR spectrum of **34**