Supplementary Data

Modulating polybasic character of galactose-based glycosylated antitumor ether lipids for enhanced cytotoxic response

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Table of contents

List of Figures

1. EXPERIMENTAL SECTION

1.1 Chemistry. Reagents and solvents were purchased from Sigma Aldrich and AK Scientific, and lipids were purchased from Chem-Implex International and were used without further purification. The reaction progress was monitored by thin layer chromatography (TLC) using 0.25 mm silica gel 60 F254 plates from Merck and visualized under UV light, and by 20% H_2SO_4/MeOH stain, and by staining in ninhydrin solution. Products were purified using normal phase column chromatography using SiliaFlash P60 (40-63 μm) 60 Å silica gel. All the intermediates and final compounds were structurally characterized by ^1H, ^{13}C, and 2D (COSY, HSQC) NMR experiments recorded on a Bruker AMX-300 MHz, AMX-400 MHz, AMX-500 MHz NMR spectrometer. All masses were recorded on ESI-QTOF.

1.1.1 Scheme 1: General procedure A of benzoyl group and acetyl ester deprotection for the synthesis of compound Phenyl 2-azido-2-deoxy-1-thio-(α,β)-D-galactopyranoside (3): To a solution of compound **2** (obtained as reported before[1]) (1.2 g, 2.836 mmol) in methanol (5.0 mL), catalytic amount of sodium methoxide (0.110 g, 2.038 mmol) was added, and the reaction mixture was stirred for 3 hours at room temperature. After stopping the reaction with ion exchange resin (Dowex 50W hydrogen form), it was filtered under vacuum. The resultant filtrate was concentrated under a high vacuum. Then, the crude mixture was purified with column chromatography (100% ethyl acetate) to afford **3** as a white solid α/β (1:5) mixture (0.60 g, 71%) (8:2, α:β). ^1H NMR δ_H (400 MHz, MeOD) δ 7.46 (ddt, *J* = 12.3, 5.8, 1.6 Hz), 7.36 – 7.28 (m), 7.25 – 7.13 (m), 5.51 (0.80 H, d, *J* = 5.4 Hz, α H-1), 4.59 (0.23 H, d, *J* = 2.4 Hz, β H-1), 4.46 – 4.38 (m), 4.26 – 4.20 (m), 4.19 – 4.11 (m), 4.05 (dd, *J* = 5.5, 3.7 Hz), 4.00 (dd, *J* = 10.7, 5.4 Hz), 3.86 (dd, *J* = 3.3, 1.3 Hz), 3.78 – 3.73 (m), 3.73 – 3.66 (m), 3.66 – 3.62 (m), 3.60 (d, *J* = 7.8 Hz), 3.57 (s), 3.47 – 3.37 (m). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) δ 134.70, 133.97, 133.13, 132.35, 132.33, 131.69, 131.64, 128.66, 128.63, 128.60, 127.41, 127.26, 127.17, 88.11 (α C-1), 86.73 (β C-1), 83.56, 82.19, 79.32, 74.27, 73.86, 72.10, 72.00, 69.98, 69.12, 68.32, 63.17, 62.60, 61.24, 60.90, 60.89, 60.52. HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{12}H_{15}N_3O_4SNa^+$, 320.0675; found 320.0724.

1.1.2 Scheme 1: Synthesis of compound Phenyl 2-azido-2-deoxy-1-thio-6-*O*-tosyl-(α,β)-D-galactopyranoside (4): A dry flask with compound **3** (0.563 g, 1.895 mmol), toluene sulphonyl chloride (0.397 g, 2.084 mmol), and catalytic DMAP (0.046 g, 0.379 mmol) was cooled to 0°C and placed in vacuum. After 5-10 minutes, a nitrogen balloon was connected to the flask containing solids by replacing the vacuum setting. Then, dry pyridine (5.0 mL) was added to the flask and the reaction was stirred for 24 hours at room temperature. After 24 hours, the reaction was stopped by methanol, and the mixture was concentrated under high vacuum to evaporate pyridine and methanol. The crude mixture was subjected to extraction with ethyl acetate followed by 1M HCl wash (x3), sodium bicarbonate wash (x2), and water (x1). After drying and concentrating the organic layer, the brown residue was purified by column chromatography (35% ethyl acetate/hexane) to yield tosyl-protected compound **4** (0.45 g, 51%) (5.4:4.6, α:β). ^{1}H NMR δ_H (500 MHz, MeOD) δ 7.89 (d, *J* = 8.4 Hz), 7.78 – 7.72 (m), 7.68 – 7.62 (m), 7.56 – 7.47 (m), 7.48 – 7.39 (m), 7.38 – 7.31 (m), 7.31 – 7.24 (m), 5.65 (dd, *J* = 5.5, 4.1 Hz), 5.49 (0.54 H, d, *J* = 5.5 Hz, α H-1), 5.38 (dd, *J* = 3.5, 1.3 Hz), 4.52 (ddd, *J* = 8.2, 3.6, 1.4 Hz), 4.45 (0.46 H, d, *J* = 9.9 Hz, β H-1), 4.36 (dd, *J* = 10.8, 5.6 Hz), 4.31 – 4.26 (m), 4.22 (dd, *J* = 10.7, 3.7 Hz), 4.20 – 4.16 (m), 4.03 (dd, *J* = 10.7, 5.5 Hz), 3.86 (dd, *J* = 3.3, 1.3 Hz), 3.77 – 3.74 (m), 3.74 – 3.68 (m), 3.49 (dd, *J* = 9.6, 3.1 Hz), 3.44 (t, *J* = 9.7 Hz), 2.45 (d, *J* = 15.6 Hz), 2.40 (s), 2.38 (s). ^{13}C NMR δ_C (126 MHz, MeOD) δ 145.15, 145.12, 133.21, 132.89, 132.78, 132.68, 132.63, 132.61, 132.42, 132.15, 131.60, 129.69, 129.67, 129.60, 128.71, 128.68, 128.62, 128.58, 127.77, 127.70, 127.67, 127.57, 127.41, 127.28, 87.94, 87.70 (α C-1), 85.98 (β C-1), 76.08, 73.32, 70.89, 70.61, 69.67, 69.50, 69.44, 69.43, 68.88, 68.40, 68.03, 62.62, 61.07, 60.66, 60.50, 60.29, 60.14, 47.90, 20.19. HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{19}H_{21}N_3O_6S_2Na^+$, 474.0763; found 474.0825.

1.1.3 Scheme1: General procedure B of azide substitution at C-6 position of sugar for the synthesis of Phenyl 2,6-diazido-2,6-dideoxy-1-thio-(α,β)-D-galactopyranoside (5): To a solution of compound **4** (0.439 g, 0.973 mmol) in dry DMF (3.0 mL), NaN_3 (0.506 g, 7.785 mmol) was added and stirred for 24 hours at 70°C. Subsequently, DMF was removed under high vacuum and the residual liquid was extracted with ethyl acetate accompanied by cold

water wash (x3). The organic layer was dried, concentrated, and columned (30% ethyl acetate/hexane) to get pure compound **5** (0.22 g, 71%) (1.6:8.4, α:β). ^{1}H NMR δ_H (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.51 (m), 7.45 (tdd, *J* = 8.9, 4.2, 2.4 Hz), 7.37 (ddd, *J* = 12.2, 6.0, 2.8 Hz), 7.33 – 7.20 (m), 5.61 (0.16 H, d, *J* = 5.5 Hz, α H-1), 5.20 (d, *J* = 2.9 Hz), 4.57 (d, *J* = 3.8 Hz), 4.46 – 4.36 (0.84 H, broad m, β H-1), 4.38 – 4.17 (m), 4.15 – 3.96 (m), 3.98 – 3.79 (m), 3.61 (dd, *J* = 12.5, 7.0 Hz), 3.55 – 3.43 (m), 3.45 – 3.30 (m), 2.79 – 2.67 (m), 2.61 (d, *J* = 4.6 Hz), 2.58 – 2.49 (m), 2.31 (d, *J* = 3.9 Hz), 2.15 (t, *J* = 7.6 Hz), 2.05 – 1.75 (m). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) δ 133.44, 132.76, 132.30, 131.33, 131.27, 129.25, 129.19, 129.12, 128.55, 127.98, 86.97 (C-1), 77.23, 76.97, 73.77, 69.11, 68.33, 62.63, 60.96, 51.15, 29.72. HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{12}H_{14}N_6O_3SNa^+$, 345.0740; found 345.0790.

1.1.4 Scheme1: General procedure C of acetyl protection of hydroxyl group for the synthesis of compound Phenyl 3,4-di-*O*-acetyl-2,6-diazido-2,6-dideoxy-1-thio-(α,β)-D-galactopyranoside (6): In a dry flask, compound **5** (0.224 g, 0.695 mmol) and DMAP (0.017 g, 0.139 mmol) was added and placed in vacuum for 5-10 minutes. Then, nitrogen gas was purged in the flask after removing it from the vacuum line and pyridine (5.0 mL) was added to the mixture. The reaction mixture was placed in the ice bath and acetic anhydride (3.0 mL, 2.781 mmol) was slowly added to the flask. After stirring the reaction mixture for 24 hours, excess acetic anhydride was quenched with methanol. Methanol and pyridine were removed under high vacuum. The crude mixture was dissolved in ethyl acetate and washed with 2M HCl wash (x3), saturated sodium bicarbonate solution (x2), and distilled water (x2). Then, the organic layer was dried over anhydrous sodium sulfate and concentrated to purify with column chromatography (60 % v/v ethyl acetate/hexane) to give compound **6** (0.19 g, 70%) (7.6:2.7, α:β). ^{1}H NMR δ_H (400 MHz, $CDCl_3$) δ 7.59 – 7.53 (m), 7.50 – 7.45 (m), 7.32 – 7.22 (m), 5.64 (0.76 H d, *J* = 5.5 Hz, α H-1), 5.37 (dd, *J* = 3.3, 1.4 Hz), 5.25 (dd, *J* = 3.2, 1.1 Hz), 5.10 (dd, *J* = 11.1, 3.3 Hz), 4.81 – 4.75 (m), 4.59 (ddd, *J* = 8.3, 4.3, 1.4 Hz), 4.47 (0.27 H, d, *J* = 10.0 Hz, β H-1), 4.24 (dd, *J* = 11.1, 5.5 Hz), 4.05 (q, *J* = 7.1, 7.1, 7.1 Hz), 3.68 (ddd, *J* = 7.8, 4.9, 1.1 Hz), 3.59 (t, *J* = 10.2, 10.2 Hz), 3.44 (dd, *J* = 12.8, 7.8 Hz), 3.34 (dd, *J* = 12.9, 8.2 Hz), 3.11 (ddd, *J* = 17.0, 12.9, 4.6 Hz), 2.18 (s), 2.11 (s), 2.04 (s), 1.99 (d, *J* = 12.0 Hz). ^{13}C NMR δ_C (101 MHz,

$CDCl_3$) δ 169.95, 169.67, 169.55, 133.78, 132.56, 132.21, 129.30, 129.09, 128.76, 128.18, 87.24 (α C-1), 86.97 (β C-1), 75.85, 72.98, 70.09, 69.15, 68.18, 67.24, 59.40, 58.08, 50.84, 50.77, 20.63, 20.58. HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{16}H_{18}N_6O_5SNa^+$, 429.0951; found 429.0955.

1.1.5 Scheme1: General procedure D of glycosylation for the synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(3',4'-di-*O*-acetyl-2',6'-diazido-2′,6′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (7a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(3',4'-di-*O*-acetyl-2',6'-diazido-2′,6′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (7b): To a solution of compound **6** (0.153 g, 0.377 mmol) and glycosyl acceptor lipid (0.149 g, 0.452 mmol) in anhydrous DCM under nitrogen atmosphere, NIS (0.169 g, 0.754 mmol) and AgOTf (0.019 g, 0.075 mmol) were weighed in a glass vial and then, added to the reaction mixture under ice cold conditions. The reaction mixture was stirred for 3 hours and extracted with DCM. The organic layer was washed with saturated sodium thiosulphate solution (x3), brine (x1), and water (x1). The DCM layer was dried over anhydrous sodium sulfate and concentrated under vacuum followed by purification with slow column chromatography (10% v/v ethyl acetate/hexane) to afford α-anomer **7a** (0.04 g, 34%) and β-anomer **7b** (0.02g, 17%), obtained separately as colorless liquids. ^{1}H NMR **7a** δ_H (400 MHz, $CDCl_3$) 5.34 (1 H, dd, H-4), 5.29 (1 H, dd, H-3), 5.01 (1 H, d, *J* 3.5, H-1), 4.14 (1 H, m, CH), 3.84 (1 H, m, H-6a), 3.57 (1 H, m, H6b), 3.54 (1 H, m, H-2), 3.49 (1 H, dd, H-5), 3.47 (2 H, d, CH_2), 3.41 (3 H, s, OCH_3), 3.39 (2 H, m, CH_2), 3.35 (1 H, m, CH_2), 3.08 (1 H, dd, diastereotopic CH_2), 2.09 (3 H, s, acetyl CH_3), 1.99 (3 H, s, acetyl CH_3), 1.51 (2 H, d, CH_2), 1.19 (26 H, broad s, lipid CH_2), 0.81 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) 170.05 (CO), 169.78 (CO), 98.42 (C-1), 79.14 (C-5), 71.89 (CH_2), 69.56 (CH_2), 68.50 (C-4), 68.24 (CH), 68.01 (d, C-3, C-6), 58.04 (OCH_3), 57.41 (C-2), 50.75 (diastereotopic CH_2), 31.94 (CH_2), 29.69 (d, CH_2), 29.52 (CH_2), 29.38 (CH_2), 26.11 (CH_2), 22.71 (CH_2), 20.66 (d, acetyl CH_3 at C-3 and C-4), 14.14 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{30}H_{54}N_6O_8Na^+$, 649.3895; found 649.3302. ^{1}H NMR **7b** δ_H (400 MHz, $CDCl_3$) 5.21 (1 H, d, H-4), 4.69 (1 H, dd, H-3), 4.38 (1 H, d, *J* 8.1, H-1), 3.96 (1 H, dd, H-6a), 3.71 (1 H, m, H-5), 3.68 (1 H, m, H-6b), 3.63 (1 H, dd, H-2), 3.51 (1 H, broad d, CH), 3.48

(2 H, m, CH_2), 3.45 (1 H, d, diastereotopic CH_2), 3.40 (3 H, s, OCH_3), 3.38 (2 H, m, CH_2), 3.04 (1 H, dd, diastereotopic CH_2), 2.10 (3 H, d, acetyl CH_3), 1.99 (3 H, s, acetyl CH_3), 1.52 (2 H, broad s, CH_2), 1.19 (26 H, broad s, lipid CH_2), 0.81 (6 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) 170.07 (CO), 169.76 (CO), 102.49 (C-1), 79.82, 79.04, 72.94, 71.96, 71.85, 70.86 (C-3), 70.66, 69.81, 69.18, 67.30 (C-4), 62.74 (C-6), 60.89 (C-2), 58.03 (OCH_3), 50.61 (diastereotopic CH_2), 31.94, 29.69 (d, *J* 4.2), 29.62 (d, *J* 2.9), 29.52, 29.47, 29.38, 26.11 (d, *J* 3.9), 22.71, 20.64, 14.14, 1.03. HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{30}H_{54}N_6O_8Na^+$, 649.3895; found 649.3984.

1.1.6 Scheme1: Synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,6′-diazido-2′,6′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (8a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,6′-diazido-2′,6′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (8b): *General procedure A* was employed to deprotect the acetyl groups on compound **7a** (0.040 g, 0.063 mmol) and **7b** (0.020 g, 0.031 mmol) to obtain compound **8a** (0.020 g, 58%) and **8b** (0.014 g, 81%) as colorless liquids purified by column chromatography (20% **(8a)** and 25% **(8b)** for ethyl acetate/hexane). **8a** ^1H NMR δ_H (400 MHz, $CDCl_3$) 4.96 (1 H, d, *J* 3.6, H-1), 4.02 (1 H, d, H-3), 3.96 (1 H, t), 3.91 (1 H, broad s), 3.82 (1 H, dd), 3.56 (1 H, m, diastereotopic CH_2), 3.53 (1H, m), 3.46 (3 H, broad s), 3.40 (4 H, broad d, H-2, OCH_3), 3.36 (2 H, dd), 3.32 (1 H, d, diastereotopic CH_2), 2.43 – 2.39 (1 H, broad s, OH), 2.34 (1 H, d, OH), 1.49 (1H, broad s, CH_2) 1.19 (26 H, broad s, lipid CH_2), 0.81 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) 98.32 (C-1), 79.17, 71.87, 69.71, 69.42, 69.03, 67.90 (C-3), 67.48, 60.10 (C-2), 57.98 (OCH_3), 51.24 (diastereotopic CH_2), 31.94 (CH_2), 29.71 (CH_2), 29.66 (CH_2), 29.63 (CH_2), 29.52 (CH_2), 29.38 (CH_2), 26.11 (CH_2), 22.71 (CH_2), 14.14 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{26}H_{50}N_6O_6Na^+$, 565.3684; found 565.3696. **8b** ^1H NMR δ_H (400 MHz, $CDCl_3$) 4.30 (1 H, d, *J* 7.9, H-1), 3.97 – 3.92 (1 H, m, H-3), 3.79 (1 H, d), 3.69 – 3.65 (1 H, m, diastereotopic CH_2), 3.64 (1 H, broad d, H-4), 3.54 (1 H, dd), 3.51 – 3.50 (1 H, m), 3.49 (2 H, d), 3.46 (1 H, broad s, H-2), 3.39 (4 H, s), 3.38 – 3.33 (2 H, m), 3.27 (1 H, dd, diastereotopic CH_2), 2.46 (1 H, d, OH), 2.33 (1 H, d, OH), 1.52 (2 H, s, CH_2), 1.19 (26 H, s, lipid CH_2), 0.81 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, $CDCl_3$) 102.41 (C-1), 79.04, 74.07, 71.80 (CH_2), 71.74, 69.97, 68.73 (C-3,

C-4), 68.24, 63.97 (C-2), 58.00 (OCH_3), 50.94 (diastereotopic CH_2), 31.94 (CH_2), 29.72 (CH_2), 29.52 (CH_2), 29.38 (CH_2), 26.13 (CH_2), 22.71 (CH_2), 14.14 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{26}H_{50}N_6O_6Na^+$, 565.3684; found 565.3715.

1.1.7 Scheme1: General procedure D of azide group reduction for the synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2',6'-diamino-2',6'-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (9a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2',6'-diamino-2',6'-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (9b): Compound **8a** (0.020 g, 0.036 mmol) and **8b** (0.014 g, 0.025 mmol) were separately dissolved in THF/water (10:2) followed by addition of PMe_3 in 1M THF (2.0 mL). The reaction mixture was stirred for 3 hours at room temperature and concentrated under high vacuum. The residual suspension was subjected to column chromatography (10% v/v of 10% methanol-ammonia/DCM) to isolate the pure product **9a** (0.013 g, 72%) and **9b** (0.01 g, 79%). **9a** ^{1}H NMR δ_H (400 MHz, MeOD) 4.88 (1 H, d, *J* 3.6, H-1), 3.92 (1 H, ddd, CH), 3.80 (1 H, dd, H-4), 3.77 – 3.72 (1 H, m, H-6a), 3.63 (1 H, dd, H-3), 3.49 (2 H, m, H-6b, H-5), 3.45 (2 H, dd, CH_2), 3.41 – 3.33 (5 H, m, CH_2, OCH_3), 3.15 (1 H, dd, diastereotopic CH_2), 3.05 (1 H, dd, diastereotopic CH_2), 3.02 (1 H, dd, H-2), 1.51 – 1.43 (2 H, m, CH_2), 1.19 (26 H, broad s, lipid CH_2), 0.80 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, MeOD) 98.66 (C-1), 79.10 (C-5), 71.38 (CH_2), 70.10 (C-4), 69.46 (CH_2), 69.03 (C-3), 67.51 (C-6), 67.32 (CH), 56.67 (OCH_3), 50.70 (C-2), 41.05 (diastereotopic CH_2), 31.67 (CH_2), 29.38 (CH_2), 29.36 (CH_2), 29.21 (CH_2), 29.07 (CH_2), 25.85 (CH_2), 22.34 (CH_2), 13.04 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{26}H_{54}N_2O_6$, 491.4054; found 491.4079. **9b** ^{1}H NMR δ_H (400 MHz, MeOD) 4.11 (1 H, d, *J* 8.1, H-1), 3.89 – 3.84 (1 H, m, H-6a), 3.64 (1 H, dd, H-4), 3.58 (1 H, dd, H-6b), 3.53 – 3.48 (2 H, m, CH, H-5), 3.45 (2H, m, CH_2), 3.40 – 3.34 (5 H, m, CH_2, OCH_3), 3.31 (1 H, dd, H-3), 3.07 (1 H, dd, diastereotopic CH_2), 2.93 (1 H, dd, diastereotopic CH_2), 2.83 (1 H, dd, H-2), 1.47 (2 H, t, CH_2), 1.19 (26 H, broad s, lipid CH_2), 0.83 – 0.77 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (101 MHz, MeOD) 103.77 (C-1), 79.17 (C-5), 72.79 (C-3), 72.77 (CH), 71.30 (CH_2), 69.88 (CH_2), 69.06 (C-4), 68.57 (C-6), 56.82 (OCH_3), 52.84 (C-2), 41.12 (diastereotopic CH_2), 31.68 (CH_2), 29.38 (CH_2), 29.35 (CH_2), 29.21 (CH_2),

29.07 (CH_2), 25.83 (CH_2), 22.34 (CH_2), 13.04 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{26}H_{54}N_2O_6$, 491.4054; found 491.4071.

1.1.8 Scheme 2: synthesis of compound Phenyl 6-*O*-acetyl-2,4-diazido-2,4-dideoxy-3-*O*-benzoyl-1-thio-β-D-galactopyranoside (11): Compound **10** was prepared by following a previously reported scheme by Ayan et al[2] and the NMR data was in agreement with the previously reported information[2]. The key intermediate compound **11** was prepared from compound **10** (0.140 g, 0.328 mmol) using the general procedure C of acetyl protection of the C-6 hydroxyl group. The reaction mixture was subjected to purification by column chromatography (20% ethyl acetate/hexane) to yield intermediate **11** (0.1 g, 70%). Compound **11** ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 8.11 – 8.07 (2 H, m), 7.62 (3 H, tt), 7.48 (2 H, t), 7.40 – 7.35 (3 H, m), 5.22 (1 H, dd, H-3), 4.53 (1 H, d, *J* 10.0, H-1), 4.36 (1 H, dd, H-6a), 4.21 (1 H, dd, H-6b), 4.19 – 4.17 (1 H, m, H-4), 3.91 – 3.85 (2 H, m, H-5, H-2), 2.09 (3 H, s, acetyl CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 170.38 (CO), 165.46 (CO), 134.01, 133.53, 130.88, 130.05, 129.11, 128.68 (d, *J* 4.2), 128.27, 86.74 (C-1), 75.26 (C-3), 74.53 (C-5), 62.69 (C-6), 59.89 (C-2), 59.70 (C-4), 20.73 (acetyl CH_3). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{21}H_{20}N_6O_5SNa^+$ 491.1108; found: 491.1139.

1.1.9 Scheme 2: Synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(6′-*O*-acetyl-2′,4′-diazido-2′,4′-dideoxy-3′-*O*-benzoyl-α-D-galactopyranosyl)-*sn*-glycerol (12a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(6′-*O*-acetyl-2′,4′-diazido-2′,4′-dideoxy-3′-*O*-benzoyl-β-D-galactopyranosyl)-*sn*-glycerol (12b): For glycosylation of compound **11** (0.20 g, 0.4272 mmol), general procedure D was followed, and the anomeric mixture was subjected to column chromatography (8% ethyl acetate/hexane) to obtain α-glycosylated compound **12a** (0.044 g, 15%) and β-anomer **12b** (0.165 g, 56%), separately. **12a** ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 8.16 – 8.10 (2 H, m, aromatic meta-CH), 7.65 – 7.59 (1 H, m, aromatic para-CH), 7.49 (2 H, t, aromatic ortho-CH), 5.70 (1 H, dd, H-3), 5.07 (1 H, d, *J* 3.5, H-1), 4.29 (1 H, m, H-5), 4.27 (1 H, d, H-6), 4.25 (1 H, m, H-4), 4.19 (1H, m, H-6), 3.88 – 3.84 (1 H, m, diastereotopic CH_2), 3.81 (1 H, dd, H-2), 3.62 (1 H, m, diastereotopic CH_2), 3.55 (1 H, m, CH), 3.54 (2 H, broad s, CH_2), 3.47 (3 H, s, OCH_3), 3.45 (2 H, dd, CH_2), 2.09 (3 H, s, acetyl CH_3), 1.57 (2 H, p, CH_2), 1.25 (26 H, s, lipid CH_2), 0.88 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 170.29

(CO), 165.55 (CO), 133.86 (aromatic CH), 130.09 (aromatic CH), 128.63 (aromatic CH), 128.51 (aromatic CH), 98.44 (C-1), 79.06 (CH), 71.85 (CH_2), 70.52 (C-3), 69.61 (CH_2), 67.82 (CH_2), 66.50 (C-5), 62.73 (C-6), 60.94 (C-4), 57.93 (C-2, OCH_3), 31.91 (CH_2), 29.68 (CH_2), 29.67 (CH_2), 29.64 (CH_2), 29.62 (CH_2), 29.60 (CH_2), 29.48 (CH_2), 29.34 (CH_2), 26.08 (CH_2), 22.67 (CH_2), 20.72 (acetyl CH_3), 14.10 (terminal CH_3). ES-MS: m/z $[M+Na]^+$ calculated for $C_{35}H_{56}N_6O_8Na^+$ 711.4051, found 711.4056. **12b** ^1H NMR δ_H (300 MHz, $CDCl_3$) 8.17 – 8.11 (2 H, m, aromatic meta-CH), 7.69 – 7.62 (1 H, m, aromatic para-CH), 7.52 (2 H, dd, ortho-aromatic CH), 5.14 (1 H, dd, H-3), 4.45 (1 H, d, *J* 7.9, H-1), 4.37 (1 H, dd, H-6), 4.22 (1 H, dd, H-6), 4.13 (1 H, dd, H-4), 4.02 – 3.95 (1 H, m, diastereotopic CH_2), 3.92 (1 H, dd, H-2), 3.87 – 3.80 (1 H, m, H-5), 3.79 – 3.73 (1 H, m, diastereotopic CH_2), 3.60 (1 H, d, CH), 3.58 (2 H, s, CH_2), 3.49 (3 H, s, OCH_3), 3.46 (2 H, dd, CH_2), 2.12 (3 H, s, acetyl CH_3), 1.60 (2 H, s, CH_2), 1.27 (26 H, s, lipid CH_2), 0.94 – 0.86 (3 H, m, terminal CH_3). ^{13}C NMR δ_C (75 MHz, $CDCl_3$) 170.35 (CO), 165.54 (CO), 133.96 (aromatic CH), 130.11 (aromatic CH), 128.69 (aromatic CH), 128.45 (aromatic CH), 102.57 (C-1), 79.05 (CH), 73.28 (C-3), 71.84 (CH_2), 70.69 (C-5), 69.81 (CH_2), 69.11 (CH_2), 62.37 (C-6), 61.33 (C-2), 59.72 (C-4), 58.02 (OCH_3), 31.94 (CH_2), 29.71 (CH_2), 29.67 (CH_2), 29.63 (CH_2), 29.51 (CH_2), 29.37 (CH_2), 26.13 (CH_2), 22.70 (CH_2), 20.74 (acetyl CH_3), 14.12 (terminal CH_3). ES-MS: m/z $[M+Na]^+$ calculated for $C_{35}H_{56}N_6O_8Na^+$ 711.4051, found 711.4018.

1.1.10 Scheme 2: synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′-diazido-2′,4′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (13a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′-diazido-2′,4′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (13b): Simultaneous deprotection of acetyl and benzoyl group was done by general procedure A and the products were separately purified by column chromatography (35% ethyl acetate/hexane) to give **13a** (0.058 g, 92%) and **13b** (0.140 g, 94%). **13a** ^1H NMR δ_H (500 MHz, MeOD) 4.88 (1 H, d, *J* 3.6, H-1), 4.25 (1 H, dd, H-3), 3.97 (1 H, dd, H-4), 3.93 (1 H, td), 3.84 – 3.80 (1 H, m, diastereotopic CH_2), 3.63 (2 H, d), 3.58 – 3.54 (1 H, m), 3.53 (2 H, d, *J* 8.3), 3.50 (1 H, dd, diastereotopic CH_2), 3.46 (2 H, dd, CH_2), 3.44 (3 H, s, OCH_3), 3.37 (1 H, dd, H-2), 1.59 – 1.53 (2 H, m, CH_2), 1.29 (26 H, broad s, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 98.50 (C-1), 79.09, 71.21 (CH_2), 69.62, 69.38, 67.89 (C-3), 66.71 (diastereotopic CH_2), 63.66 (C-4),

60.86, 60.17 (C-2), 56.76 (OCH_3), 31.65 (CH_2), 29.37 (CH_2), 29.35 (CH_2), 29.33 (CH_2), 29.31 (CH_2), 29.30 (CH_2), 29.26 (CH_2), 29.13 (CH_2), 29.04 (CH_2), 25.80 (CH_2), 22.30 (CH_2), 13.01 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{26}H_{50}N_6O_6Na^+$, 565.3684 ; found 565.3674. **13b** ^1H NMR δ_H (500 MHz, MeOD) 4.28 (1 H, d, *J* 8.1, H-1), 3.89 (1 H, dd diastereotopic CH_2), 3.85 (1 H, dd, H-4), 3.71 – 3.68 (1 H, m, H-3), 3.68 – 3.67 (1 H, m), 3.66 (1 H, d), 3.64 (1 H, d), 3.58 (1 H, dd), 3.56 – 3.54 (1 H, m), 3.54 – 3.49 (2 H, m), 3.46 (2 H, dq), 3.43 (3 H, s, OCH_3), 3.38 (1 H, dd, H-2), 1.59 – 1.53 (2 H, m, CH_2), 1.29 (26 H, broad s, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 102.30 (C-1), 79.08, 73.45, 72.15 (C-3), 71.19, 69.65, 68.19 (diastereotopic CH_2), 64.56 (C-2), 62.26 (C-4), 60.63, 56.70 (OCH_3), 48.19, 31.64 (CH_2), 29.36 (CH_2), 29.34 (CH_2), 29.32 (CH_2), 29.29 (CH_2), 29.23 (CH_2), 29.12 (CH_2), 29.04 (CH_2), 25.79 (CH_2), 22.30 (CH_2), 13.00 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{26}H_{50}N_6O_6Na^+$, 565.3684; found: 565.3724.

1.1.11 Scheme 2: synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′-diamino-2,4′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (14a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′-diamino-2′,4′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (14b): The final compounds were obtained by reduction of azide group using general procedure D and pure products were separately isolated by column chromatography (10% v/v of 10% methanol-ammonia/DCM) to afford α-anomeric compound **14a** (0.025 g, 91%) and β-anomer **14b** (0.042 g, 93%). **14a** ^1H NMR δ_H (500 MHz, MeOD) 3.92 (1 H, d, H-5), 3.88 – 3.82 (1 H, m, diastereotopic CH_2), 3.72 (1 H, dd, H-6a), 3.69 (1 H, broad s, H-3), 3.67 – 3.62 (1 H, m, H-6b), 3.57 (1 H, broad s, CH), 3.54 (2 H, dd, CH_2), 3.49 (1 H, broad d, diastereotopic CH_2), 3.45 (5 H, broad d, OCH_3, CH_2), 3.14 (1 H, broad s, H-4), 2.90 (1 H, broad dt, H-2), 1.55 (2 H, q, CH_2), 1.28 (26 H, broad d, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 98.89 (C-1), 79.09 (CH), 71.27 (CH_2), 70.03 (C-5), 69.80 (C-3), 69.75 (CH_2), 66.81 (diastereotopic CH_2), 61.45 (C-6), 56.62 (OCH_3), 52.08 (C-4), 51.02 (C-2), 31.64 (CH_2), 29.35 (CH_2), 29.32 (CH_2), 29.17 (CH_2), 29.04 (CH_2), 25.82 (CH_2), 22.30 (CH_2), 13.00 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{26}H_{54}N_2O_6$ 491.4054, found: 491.4066. **14b** ^1H NMR δ_H (500 MHz, MeOD) 4.75 (1 H, d, *J* 8.7, H-1), 4.22 (1 H, dd, H-3), 4.00 (1 H, dd), 3.88 (1 H, d), 3.85 (1 H, d), 3.83 – 3.81 (1 H, m), 3.81 – 3.78 (1 H, m), 3.71 (1 H, broad d, H-4), 3.64 (1 H, p,

CH), 3.57 (2 H, qd, CH_2), 3.48 (3 H, s, OCH_3), 3.46 (2 H, dd, CH_2), 3.12 (1 H, dd, H-2), 1.56 (2 H, p, CH_2), 1.28 (26 H, broad s, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 99.53 (C-1), 78.83 (CH), 71.34, 71.31 (CH_2), 69.57 (CH_2) 68.76, 66.27 (C-3), 60.44, 56.88 (OCH_3), 53.13 (C-2), 52.75 (C-4), 31.64 (CH_2), 29.35 (CH_2), 29.32 (CH_2), 29.18 (CH_2), 29.04 (CH_2), 25.81 (CH_2), 22.30 (CH_2), 13.02 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{26}H_{54}N_2O_6$ 491.4054, found: 491.4095.

1.1.12 Scheme 2: Synthesis of compound 3-Azido-1-*O*-hexadecyl-2-*O*-(6′-*O*-acetyl-2′,4′-diazido-2′,4′-dideoxy-3′-*O*-benzoyl-α-D-galactopyranosyl)-*sn*-glycerol (15a), 3-Azido-1-*O*-hexadecyloxyl-2-*O*-(6′-*O*-acetyl-2′,4′-diazido-2′,4′-dideoxy-3′-*O*-benzoyl-β-D-galactopyranosyl)-*sn*-glycerol (15b): Intermediate **11** (0.234 g, 0.499 mmol) was glycosylated with the modified lipid (L-2) using NIS (0.224 g, 0.999 mmol) and AgOTf (0.025 g, 0.099 mmol) as described in general procedure D. The resulting anomeric mixture (3:1, α:β) was subjected to column chromatography to yield α-isomer **15a** (0.148 g, 42%) and β-isomer **15b** (0.054 g, 15%), separately. **15a** ^{1}H NMR δ_H (300 MHz, $CDCl_3$) 8.15 (2 H, m, aromatic ortho-CH), 7.64 (1 H, m, aromatic para-CH), 7.51 (2 H, dd, aromatic para-CH), 5.70 (1 H, dd, H-3), 5.22 (1 H, d, *J* 3.6, H-1), 4.45 (1 H, td, H-5), 4.28 (1 H, m, H-4), 4.22 (2 H, m, H-6), 3.93 (1 H, m, CH), 3.90 (1 H, m, H-2), 3.61 (1 H, m, diastereotopic CH_2), 3.56 (2 H, m, CH_2), 3.49 (1 H, q, diastereotopic CH_2), 3.45 (2 H, m, CH_2), 2.11 (3 H, s, acetyl CH_3), 1.56 (2 H, CH_2), 1.28 (26 H, s, lipid CH_2), 0.94 – 0.86 (3 H, m, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 170.19 (CO), 165.55 (CO), 133.89 (aromatic CH), 130.09 (aromatic CH), 128.64 (aromatic CH), 128.46 (aromatic CH), 98.05 (C-1), 76.95 (CH), 71.83 (CH_2), 70.70 (C-3), 70.27 (CH_2), 66.71 (C-5), 62.60 (C-6), 60.81 (C-4), 57.99 (C-2), 52.01 (CH_2), 31.91 (CH_2), 29.69 (CH_2), 29.64 (CH_2), 29.61 (CH_2), 29.56 (CH_2), 29.48 (CH_2), 29.34 (CH_2), 26.08 (CH_2), 22.67 (CH_2), 20.71 (acetyl CH_3), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{34}H_{53}N_9O_7Na^+$ 722.3960, found: 722. 3937. **15b** ^{1}H NMR δ_H (400 MHz, $CDCl_3$) 8.14 (2 H, m, aromatic *o*-CH), 7.66 (1 H, t, aromatic *p*-CH), 7.52 (2 H, t, *m*-CH), 5.13 (1 H, dd, H-3), 4.67 (1 H, d, *J* 7.9, H-1), 4.38 (1 H, dd, H-6), 4.22 (1 H, dd, H-6), 4.13 (1 H, d, H-4), 4.08 (1 H, CH), 3.93 (1 H, dd, H-2), 3.84 (1 H, t, H-5), 3.62 (2 H, m, CH_2), 3.53 (1 H, m, diastereotopic CH_2), 3.48 (2 H, t, CH_2), 3.40 (1 H, dd, diastereotopic CH_2), 2.12 (3 H, s, acetyl CH_3), 1.56 (2 H, d, CH_2),

1.27 (26 H, d, lipid CH_2), 0.90 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 170.38 (CO), 165.51 (CO), 133.94 (aromatic CH), 130.09 (aromatic CH), 128.66 (aromatic CH), 128.38 (aromatic CH), 102.09 (C-1), 77.65 (CH), 73.13 (C-3), 71.93 (CH_2), 70.67 (C-5), 70.49 (CH_2), 62.41 (C-6), 61.07 (C-2), 59.57 (C-4), 52.12 (CH_2), 31.91 (CH_2), 29.82 – 29.52 (m, CH_2), 29.46 (CH_2), 29.34 (CH_2), 26.07 (CH_2), 22.67 (CH_2), 20.72 (acetyl CH_3), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{34}H_{53}N_9O_7Na^+$ 722.3960, found: 722. 3936.

1.1.13 Scheme 2: Synthesis of compound 3-Azido-1-*O*-hexadecyloxyl-2-*O*-(2′,4′-diazido-2′,4′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (16a), 3-Azido-1-*O*-hexadecyloxyl-2-*O*-(2′,4′-diazido-2′,4′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (16b): The respective α-glycoside **15a** (0.119 g, 0.170 mmol) and β-glycoside **15b** (0.054 g, 0.077 mmol) were subjected to deprotection of acetyl and benzoyl protecting groups using general procedure A. The products were purified by column chromatography (8% ethyl acetate/hexane) yielding α-isomer **16a** (0.090 g, 96%) and (12% ethyl acetate/hexane) β-isomer **16b** (0.039 g, 92%). **16a** ^1H NMR δ_H (500 MHz, $CDCl_3$) 5.14 (1 H, d, *J* 3.7, H-1), 4.26 (1 H, dd, H-3), 4.19 (1 H, broad d, H-5), 3.99 (1 H, broad s, H-4), 3.90 (1 H, q, CH), 3.84 (1 H, broad t, H-6), 3.77 – 3.70 (1 H, m, H-6b), 3.59 – 3.56 (1 H, m, diastereotopic CH_2), 3.52 (2 H, dd, CH_2), 3.44 (2 H, d, CH_2), 3.40 (1 H, d, diastereotopic CH_2), 2.54 (1 H, broad s, C3-O*H*), 1.98 (1 H, s, C6-O*H*), 1.27 (26 H, d, lipid CH_2), 0.88 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 97.82 (C-1), 76.85 (CH), 71.85 (CH_2), 70.48 (CH_2), 69.58 (C-5), 68.74 (C-3), 62.77 (C-4), 62.35 (C-6), 60.80 (C-2), 52.02 (diastereotopic CH_2), 31.91 (CH_2), 29.68 (CH_2), 29.66 (CH_2), 29.64 (CH_2), 29.61 (CH_2), 29.50 (CH_2), 29.44 (CH_2), 29.34 (CH_2), 26.06 (CH_2), 22.67 (CH_2), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{25}H_{47}N_9O_5Na^+$ 576.3592, found: 576.3661. **16b** ^1H NMR δ_H (500 MHz, MeOD) 4.54 – 4.49 (1 H, broad d, H-1), 4.04 (1 H, dd, CH), 3.86 (1 H, d, H-4), 3.69 (1 H, d, H-3), 3.67 (2 H, broad t, H-6a, H-6b), 3.58 (1 H, broad s, H-5), 3.56 (2 H, d, CH_2), 3.50 (1 H, d, diastereotopic CH_2), 3.47 (2 H, d, CH_2), 3.44 – 3.38 (1 H, m, H-2), 3.35 (1 H, broad s, diastereotopic CH_2), 1.58 (2 H, dt, CH_2), 1.28 (26 H, d, lipid CH_2), 0.90 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 101.88 (H-1), 77.08 (CH), 73.35 (C-5), 72.04 (C-6), 71.23 (CH_2), 70.00 (CH_2), 64.44 (C-2), 62.13 (C-4), 60.62 (C-3), 51.82 (diastereotopic CH_2), 31.71 (CH_2), 29.43 (CH_2), 29.40 (CH_2), 29.37 (CH_2), 29.21 (CH_2), 29.13 (CH_2), 25.85 (CH_2),

22.38 (CH_2), 13.09 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ calculated for $C_{25}H_{47}N_9O_5Na^+$ 576.3592; found: 576.3569.

1.1.14 Scheme 2: synthesis of compound 3-Amino-1-*O*-hexadecyloxyl-2-*O*-(2′,4′-diamino-2′,4′-dideoxy-α-D-galactopyranosyl)-*sn*-glycerol (17a), 3-Amino-1-*O*-hexadecyloxyl-2-*O*-(2′,4′-diamino-2′,4′-dideoxy-β-D-galactopyranosyl)-*sn*-glycerol (17b): The final compounds were obtained by azide reduction by following general procedure D and purified using column chromatography (10% v/v of 10% methanol-ammonia/DCM). The purification resulted in **17a** (0.040 g, 80%) and **17b** (0.028 g, 83%). **17a** ^{1}H NMR δ_H (500 MHz, MeOD) 5.55 (1 H, d, *J* 3.7, H-1), 4.47 (1 H, dd, H-3), 4.30 (1 H, broad s), 4.23 (1 H, broad s), 3.80 (2 H, q), 3.77 – 3.75 (1 H, m), 3.73 (1 H, broad d, H-4), 3.72 – 3.63 (1 H, m), 3.48 (2 H, q, CH_2), 3.46 – 3.42 (1 H, m, H-2), 3.41 – 3.31 (2 H, m, CH_2), 1.59 (2 H, broad t, CH_2), 1.27 (26 H, broad s, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 96.34 (C-1), 75.73, 71.62 (CH_2), 70.41, 67.02, 63.33 (C-3), 60.79, 53.21 (C-4), 50.50 (C-2), 41.06 (CH_2), 31.64 (CH_2), 29.36 (CH_2), 29.32 (CH_2), 29.26 (CH_2), 29.03 (CH_2), 25.85 (CH_2), 22.30 (CH_2), 13.00 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{25}H_{53}N_3O_5$ 476.4057; found: 476.4032. **17b** ^{1}H NMR δ_H (500 MHz, MeOD) 4.96 (1 H, d, *J* 8.2, H-1), 4.29 (1 H, broad s, CH), 4.23 (1 H, d, H-3), 3.97 (1 H, broad s, H-5), 3.85 (2 H, broad s, H-6a, 6b), 3.70 (1 H, broad d, H-4), 3.64 (2 H, broad s, CH_2), 3.51 (2 H, broad d, CH_2), 3.39 (1 H, broad d, H-2), 3.22 (1 H, d, diastereotopic CH_2), 3.09 (1 H, t, diastereotopic CH_2), 1.59 (2 H, broad d, CH_2), 1.27 (26 H, d, lipid CH_2), 0.88 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 98.24 (C-1), 74.14 (CH), 71.86(C-5), 71.61 (CH_2), 69.76 (CH_2), 66.04 (C-3), 60.49 (C-6), 52.98 (C-2), 52.82 (C-4), 40.82 (diastereotopic CH_2), 31.63 (CH_2), 29.35 (CH_2), 29.32 (CH_2), 29.23 (CH_2), 29.18 (CH_2), 29.03 (CH_2), 25.74 (CH_2), 22.29 (CH_2), 13.00 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{25}H_{53}N_3O_5$ 476.4057; found: 476.4070.

1.1.15 Scheme 3: synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triazido-2′,4′,6′-trideoxy-3′-*O*-benzoyl-α-D-galactopyranosyl)-*sn*-glycerol (19a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triazido-2′,4′,6′-trideoxy-3′-*O*-benzoyl-β-D-galactopyranosyl)-*sn*-glycerol (19b): Compound **18** was obtained in two steps from compound **10** by following a previously method. Subsequently, the triazide compound **18**

(0.230 g, 0.509 mmol) was subjected to glycosylation with commercially available lipid using general procedure D. The resulting anomeric mixture (1:3, α:β) was purified by column chromatography (10% ethyl acetate/hexane) to obtain separate α-anomeric compound **19a** (0.059 g,17%) and β-glycoside **19b** (0.155 g, 45%). **19a** ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 8.16 – 8.10 (2 H, m, aromatic *o*-CH), 7.66 – 7.59 (1 H, m, aromatic *p*-CH), 7.50 (2 H, t, aromatic *m*-CH), 5.70 (1 H, dd, H-3), 5.08 (1 H, d, *J* 3.5, H-1), 4.24 – 4.17 (2 H, m, H-6a), 4.22 (1 H, dd, H-4), 4.21 – 4.18 (1 H, m, CH), 3.90 (1 H, dd, H-6a), 3.80 (1 H, dd, H-2), 3.67 – 3.62 (1 H, m, H-6b), 3.61 – 3.57 (1 H, m, diastereotopic CH_2), 3.55 (3 H, broad s, H-5, CH_2), 3.48 (3 H, s, OCH_3), 3.45 (2 H, dd, CH_2), 3.33 (1 H, dd, diastereotopic CH_2), 1.59 (4 H, broad d, CH_2), 1.26 (26 H, broad s, lipid CH_2), 0.88 (3 H, t, terminal CH_3).^{13}C NMR δ_C (126 MHz, $CDCl_3$) 165.50 (benzoyl CO), 133.88 (aromatic CH), 130.10 (aromatic CH), 128.63 (aromatic CH), 128.45 (aromatic CH), 98.42 (C-1), 79.10 (C-5), 71.87 (CH_2), 70.58 (C-3), 69.50 (CH_2), 67.89 (C-6), 67.74 (C-5), 61.10 (C-4), 57.99 (OCH_3), 57.88 (C-2), 51.26 (diastereotopic CH_2), 31.91 (CH_2), 29.66 (d, CH_2), 29.61 (CH_2), 29.49 (CH_2), 29.35 (CH_2), 26.09 (CH_2), 22.68 (CH_2), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ $C_{33}H_{53}N_9O_6Na^+$ 694.4011; found: 694.4034. **19b** ^{1}H NMR δ_H (300 MHz, $CDCl_3$) 8.14 (2 H, m, aromatic *o*-CH), 7.65 (1 H, m, aromatic *p*-CH), 7.52 (2 H, dd, aromatic *m*-CH), 5.15 (1 H, dd, H-3), 4.48 (1 H, d, *J* 7.9, H-1), 4.11 (1 H, d, H-4), 4.03 (1 H, H-6), 3.92 (1 H, dd, H-2), 3.78 (1 H, dd, H-6), 3.75 (2 H, d, CH_2), 3.70 (1 H, d, diastereotopic CH_2), 3.59 (1 H, m, CH), 3.57 (1 H, broad d, H-5), 3.48 (3 H, s, OCH_3), 3.46 (2 H, dd, CH_2), 3.33 (1 H, dd, diastereotopic CH_2), 1.56 (2 H, m, CH_2), 1.28 (26 H, s, lipid CH_2), 0.90 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (75 MHz, $CDCl_3$) 165.47 (benzoyl CO), 133.98 (aromatic CH), 130.13 (aromatic CH), 128.69 (aromatic CH), 128.38 (aromatic CH), 102.51 (C-1), 79.02 (CH), 73.30 (C-3), 72.41 (CH_2), 71.83 (CH_2), 69.86 (C-5), 69.02 (C-6), 61.25 (C-2), 59.91 (C-4), 58.01 (OCH_3), 51.15 (CH_2), 31.94 (CH_2), 29.71 (CH_2), 29.67 (CH_2), 29.64 (CH_2), 29.51 (CH_2), 29.37 (CH_2), 26.14 (CH_2), 22.70 (CH_2), 14.12 (CH_3). HRMS (ESI) m/z; $[M+Na]^+$ $C_{33}H_{53}N_9O_6Na^+$ 694.4011; found: 694.4041.

1.1.16 Scheme 3: synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triazido-2′,4′,6′-trideoxy-α-D-galactopyranosyl)-*sn*-glycerol (20a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triazido-2′,4′,6′-trideoxy-β-D-galactopyranosyl)-*sn*-glycerol (20b):

The glycosylated products **19a** (0.059 g, 0.087 mmol) and **19b** (0.155 g, 0.231 mmol) were separately subjected to deprotection of protecting groups using general procedure A. The products were purified with column chromatography (20% ethyl acetate/ hexane) to yield **20a** (0.045 g, 90%) and **20b** (0.120 g, 92%). **20a** ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 5.00 (1 H, d, *J* 3.5, H-1), 4.28 (1 H, dd, H-3), 4.06 (1 H, t, CH), 3.93 (1 H, d, H-4), 3.86 (1 H, dd, H-6a), 3.62 – 3.56 (2 H, m, H-6b, diastereotopic CH_2), 3.53 (1H, broad s, H-5),3.52 (2 H, broad s, CH_2), 3.49 (1 H, dd, H-2), 3.46 (3 H, s, OCH_3), 3.43 (2 H, dd, CH_2), 3.32 (1 H, dd, diastereotopic CH_2), 2.43 (1 H, broad s, OH), 1.56 (2 H, d, CH_2), 1.26 (26 H, broad s, lipid CH_2), 0.88 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 98.12 (C-1), 79.10 (C-5), 71.85 (CH_2), 69.53 (CH_2), 68.59 (C-3), 68.12 (CH), 67.57 (C-6), 62.84 (C-4), 60.45 (C-2), 57.94 (OCH_3), 51.38 (diastereotopic CH_2), 31.91 (CH_2), 29.68 (CH_2), 29.66 (CH_2), 29.64 (CH_2), 29.62 (CH_2), 29.60 (CH_2), 29.48 (CH_2), 29.34 (CH_2), 26.08 (CH_2), 22.67 (CH_2), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ $C_{26}H_{49}N_9O_5Na^+$ 590.3748; found: 590.3782. **20b** ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 4.33 (1 H, d, *J* 7.5, H-1), 4.00 – 3.95 (1 H, m, CH), 3.84 (1 H, d, H-4), 3.72 – 3.66 (2 H, m, H-6a, diastereotopic CH_2), 3.64 (1 H, t, H-3), 3.63 – 3.58 (2 H, m, H-6b, H-2), 3.57 (1 H, broad s, H-5), 3.53 (2 H, s, CH_2), 3.45 (3 H, s, OCH_3), 3.45 – 3.40 (2 H, m, CH_2), 3.29 (1 H, dd, diastereotopic CH_2), 2.62 (1 H, d, C3-O*H*), 1.56 (2 H, broad d, CH_2), 1.26 (26 H, broad s, lipid CH_2), 0.88 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, $CDCl_3$) 102.48 (C-1), 78.96 (C-5), 72.73 (C-6), 72.45 (C-3), 71.77 (CH_2), 69.87 (CH_2), 68.74 (CH), 64.01 (C-2), 61.02 (C-4), 57.97 (OCH_3), 51.24 (diastereotopic CH_2), 31.91 (CH_2), 29.68 (CH_2), 29.67 (CH_2), 29.64 (CH_2), 29.62 (CH_2), 29.58 (CH_2), 29.48 (CH_2), 29.34 (CH_2), 26.09 (CH_2), 22.67 (CH_2), 14.10 (terminal CH_3). HRMS (ESI) m/z; $[M+Na]^+$ $C_{26}H_{49}N_9O_5Na^+$ 590.3748; found: 590.3786.

1.1.19 Scheme 3: synthesis of compound 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triamino-2′,4′,6′-trideoxy-α-D-galactopyranosyl)-*sn*-glycerol (21a), 1-*O*-Hexadecyl-2-*O*-methyl-3-*O*-(2′,4′,6′-triamino-2′,4′,6′-trideoxy-β-D-galactopyranosyl)-*sn*-glycerol (21b): The final tribasic scaffold was obtained by reduction of azide groups on **20a** (0.045 g, 0.079 mmol) and **20b** (0.040 g, 0.070 mmol) by following general procedure D. The reaction mixture was purified in each case by column chromatography (10% v/v of 10% methanol-ammonia/DCM). The purification resulted in **21a** (0.036 g, 93%) and **21b** (0.032 g, 93%). **21a**

^{1}H NMR δ_H (500 MHz, MeOD) 5.17 (1 H, d, *J* 3.8, H-1), 4.27 – 4.23 (1 H, m, CH), 4.12 (1 H, dd, H-3), 3.91 (1 H, m), 3.69 – 3.64 (2 H, m), 3.63 – 3.60 (1 H, m), 3.57 – 3.51 (1 H, m), 3.47 (3 H, s), 3.47 – 3.44 (2 H, m), 3.44 – 3.39 (2 H, m), 3.26 – 3.18 (2 H, m), 1.57 (2 H, p, CH_2), 1.36 – 1.26 (26 H, m, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 96.41 (C-1), 78.88, 71.44, 69.04, 68.36, 65.83 (CH), 65.09 (C-3), 56.42, 52.63, 50.22, 40.49, 31.64 (CH_2), 29.35 (CH_2), 29.32 (CH_2), 29.20 (CH_2), 29.03 (CH_2), 25.80 (CH_2), 22.30 (CH_2), 13.00 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ $C_{26}H_{55}N_3O_5$ 490.4214; found 490.4216. **21b** ^{1}H NMR δ_H (500 MHz, MeOD) 4.16 (1 H, d, *J* 8.0, H-1), 3.94 (1 H, dd, H-6a), 3.67 (1 H, dd, H-6b), 3.56 (2 H, dq), 3.50 (2 H, dt), 3.47 (1 H, d), 3.45 – 3.41 (5 H, m), 2.96 (1 H, dd, diastereotopic CH_2), 2.90 (1 H, dd, H-4), 2.79 (1 H, dd, diastereotopic CH_2), 2.75 (1 H, dd, H-2), 1.56 (2 H, p, CH_2), 1.29 (26 H, broad d, lipid CH_2), 0.89 (3 H, t, terminal CH_3). ^{13}C NMR δ_C (126 MHz, MeOD) 104.34 (C-1), 79.13, 75.14, 72.95, 71.23, 69.93, 68.31 (C-6), 56.70 (OCH_3), 52.99 (C-2), 51.97 (C-4), 41.83 (diastereotopic CH_2), 31.64 (CH_2), 29.35 (CH_2), 29.32 (CH_2), 29.16 (CH_2), 29.04 (CH_2), 25.81 (CH_2), 22.30 (CH_2), 13.01 (terminal CH_3). HRMS (ESI) m/z; $[M+H]^+$ calculated for $C_{26}H_{55}N_3O_5$ 490.4214, found: 490.4242.

2. Biological section

2.1 Cytotoxicity cell viability assay. Frozen stocks of cell lines originally obtained from ATCC were cultured by incubation with 5% CO_2 in a humidified atmosphere at 37°C. DU-145, JIMT-1, MDA-MB-231, HEYC2, COV362, HepG2, and BxPC3 cells were grown in DMEM supplemented with 10% FBS, MIAPaCa-2 in DMEM supplemented with 10% FBS and 2.5% horse serum, BT-474 in DMEM/F12 supplemented with 10% FBS, OVCAR-3 in RPMI supplemented with 10% FBS and 0.01 mg/mL insulin. Penicillin/streptomycin (0.5 to 1.0 mL of 10,000 U/mL solution per 100 mL) was also added to all media. The cytotoxic effect of GAELs on the cell viability of various epithelial cancer cell lines was evaluated using PrestoBlue cell viability assay. Equal number of cells (5000-DU-145, 8000-JIMT-1, 8000-MDA-MB-231, 8000-HEYC2, 7500-COV362, 8000-HepG2, 7500-BxPC3, 7500-MIAPaCa-2, 10,500-BT-474, 7500-OVCAR-3) were plated in 96-well plates. The wells with media and no cells served as blanks. After 24-hour incubation, the cells were incubated with increasing concentrations of drug prepared from stock solution (30 mM) for 48 hours. Subsequently,

PrestoBlue cell viability reagent (10% v/v Invitrogen) was added to assess the cell viability, and the plates were incubated in the CO_2 incubator for an additional 40-45 minutes. The fluorescence was measured with excitation and emission wavelengths of 560 nm and 590 nm, respectively, using a SpectraMax M2 plate reader from Molecular Devices. The cell viability was interpreted as previously reported[3–5]. The readings from blank wells were subtracted from the corresponding experimental wells with cells and the cell viability was obtained relative to that of vehicle treated cells. The data was plotted as line graphs using excel. The results in the excel plots indicate the mean ± standard deviation of two independent experiments, with five experimental wells per concentration. CC_{50} values ± standard error was obtained from non-linear regression (curve fit) analysis of all the data sets from two experiments on GraphPad Prism. Standard error was then converted to standard deviation ($SE = SD\sqrt{(sample\ size)}$ for consistent data presentation.

2.2 Caspase inhibition assay. DU-145 cells were grown in DMEM supplemented with 10% FBS and penicillin/streptomycin. An equal number of cells (5000) were dispersed into 96-well plates. After 24 hours, cells were incubated with caspase inhibitor, MX1013 (70 µM) for 2 hours and the rest of the wells received vehicle. Subsequently, varying concentrations of the drug (0-8 µM) were added to all the wells and incubated for 48 hours. Cell viability was determined as previously described in 2.1. The data was plotted and analyzed on GraphPad

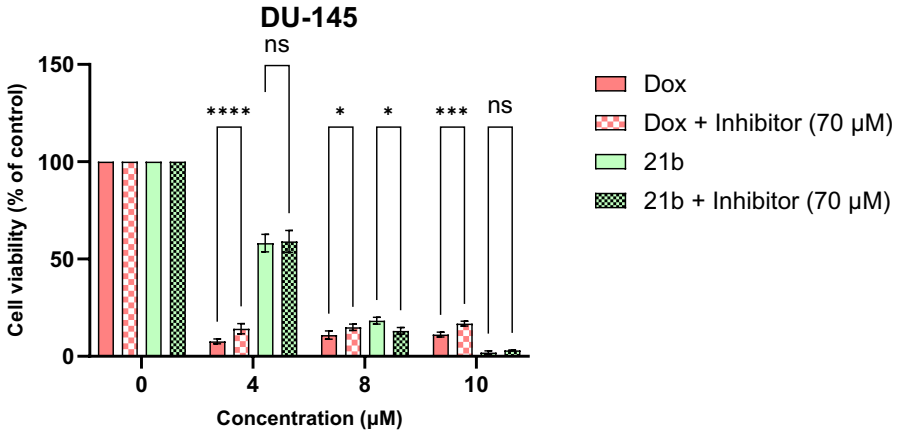

Figure 1: *Pan-caspase inhibition of DU-145 cells on treatment with varying concentrations of doxorubicin and* ***21b****, with and without MX1013 caspase inhibitor (70 µM). Asterisks (*) represent a significant difference in drug response with and without inhibitor analyzed by two-way ANOVA analysis on GraphPad Prism version 10.2.1.*

Prism version 10.2.1. The results represent the mean ± standard deviation of 6 independent determinations obtained from two independent experiments.

2.3 Statistical analysis. Statistical significance was determined using GraphPad Prism version 10.2.1. For dose-response cell viability experiments, the mean values were subjected to a one-way analysis of variance (ANOVA). The comparisons were carried out between the cell viability of vehicle or drug-treated cells to determine statistically significant differences. For comparison between the two groups, a student t-test analysis was performed to indicate a significant difference in cytotoxic concentration to kill 50% of the cells (CC_{50}) in a specific cell line. A two-way ANOVA was performed for the caspase inhibition assay to evaluate the cell viability of DU-145 cells with the drug in the absence and presence of the caspase inhibitor. The comparisons were analyzed between vehicle and drug-treated cells in the absence and presence of the caspase inhibitor. A P-value < 0.05 indicates statistically significant differences.

3. References

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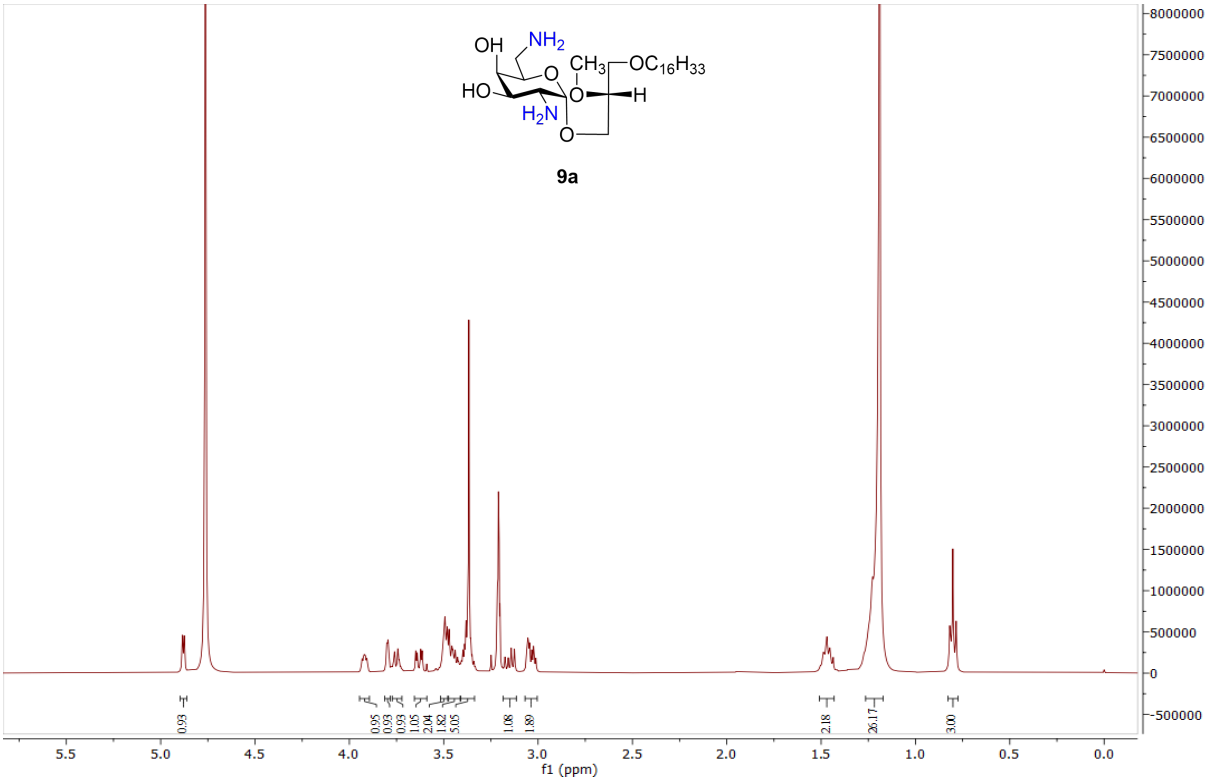
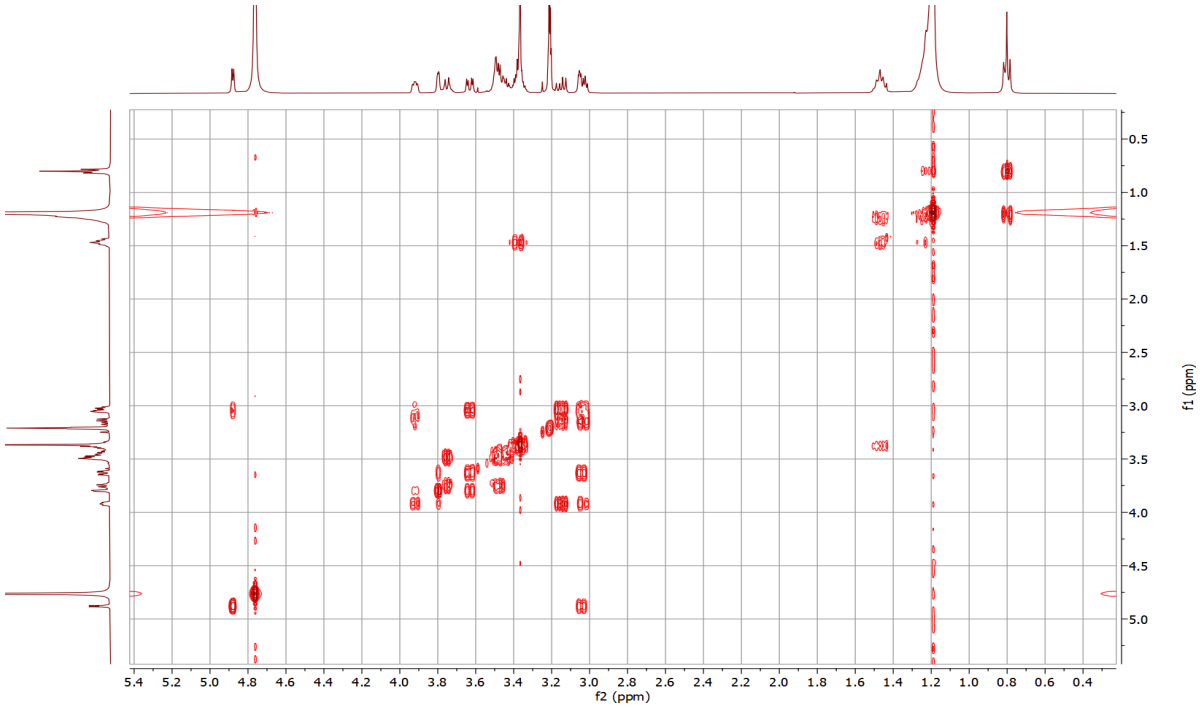
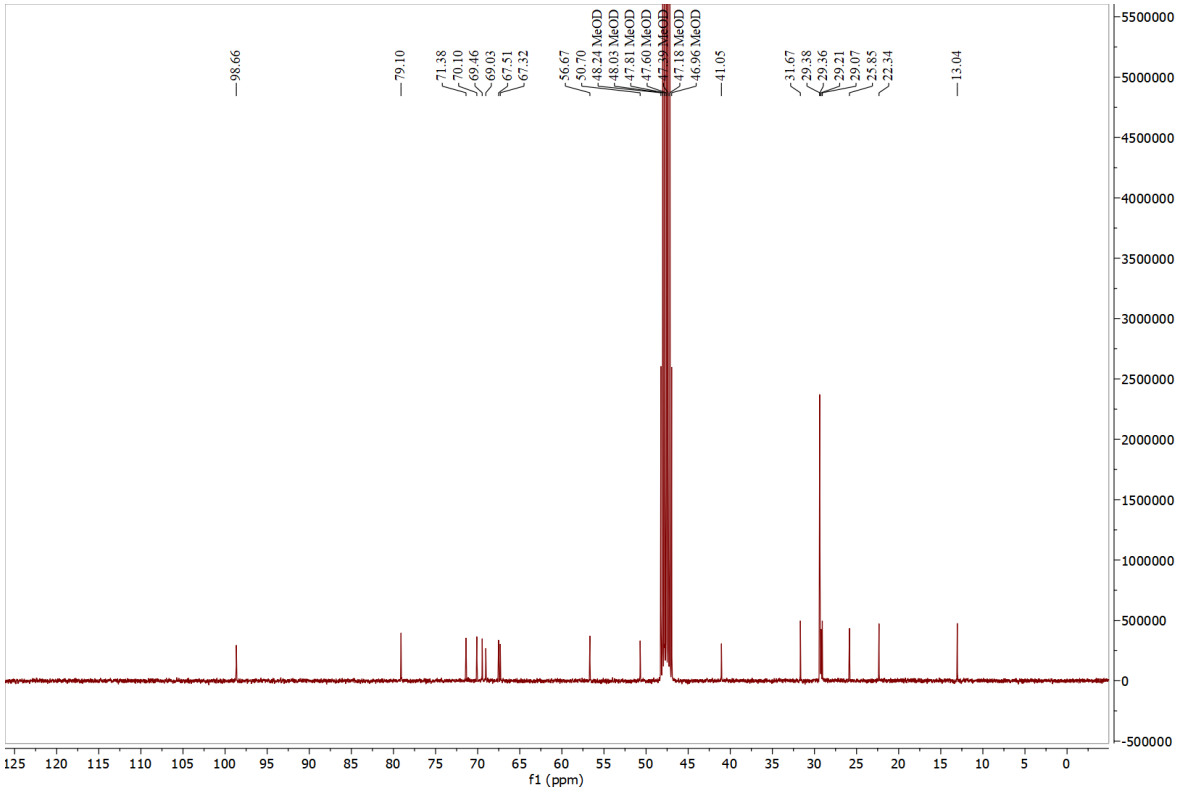
4. NMR data

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 9a



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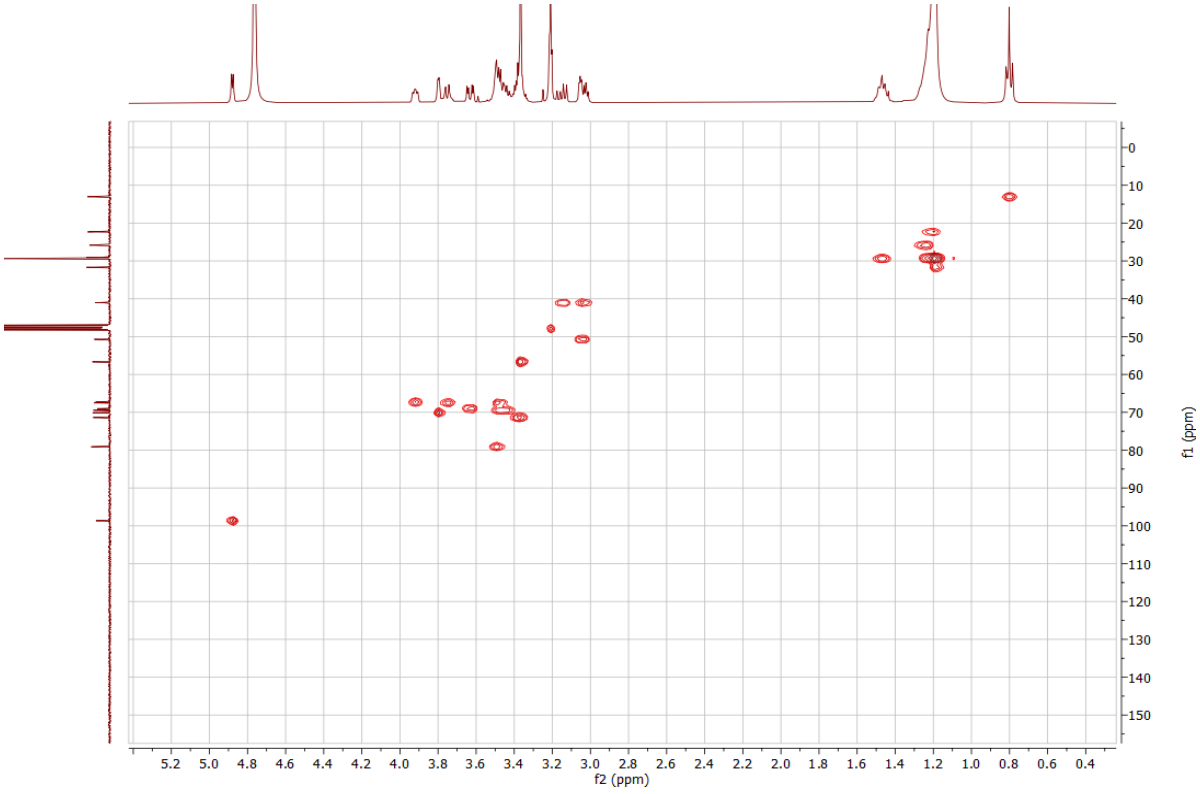
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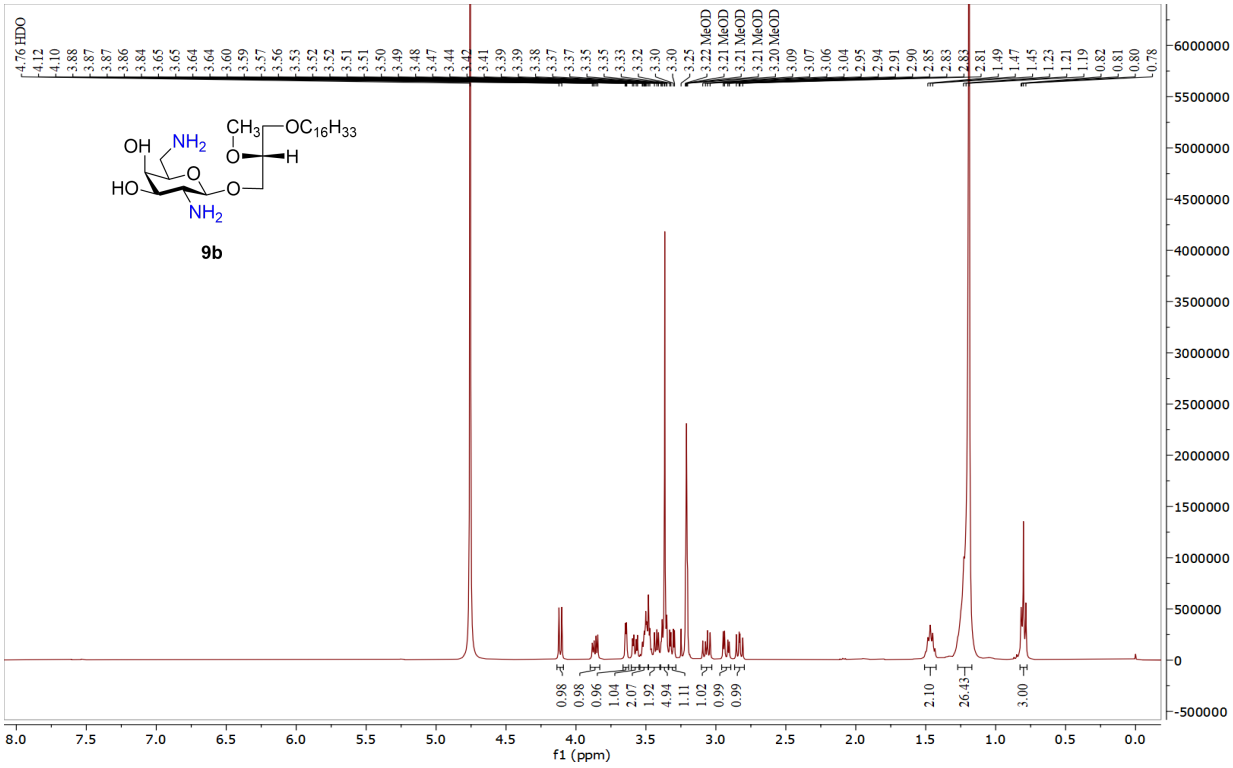
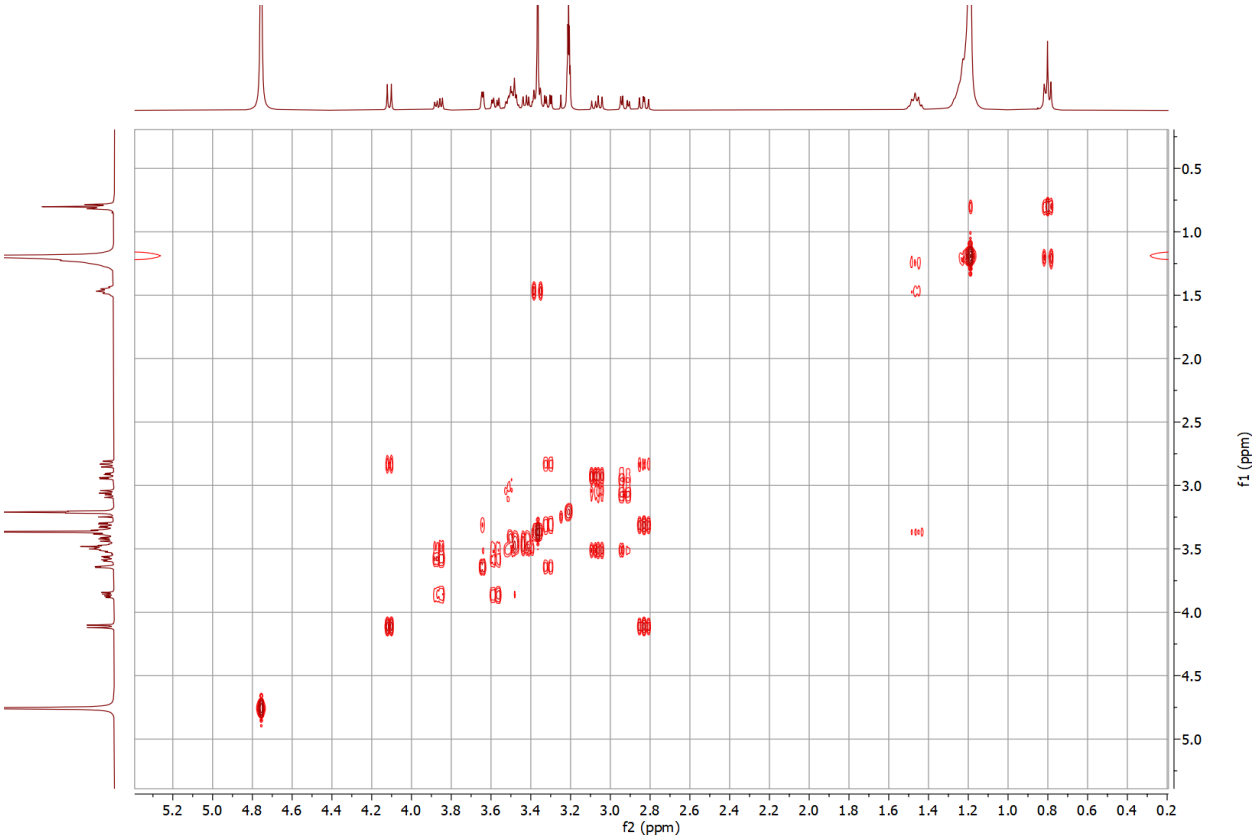
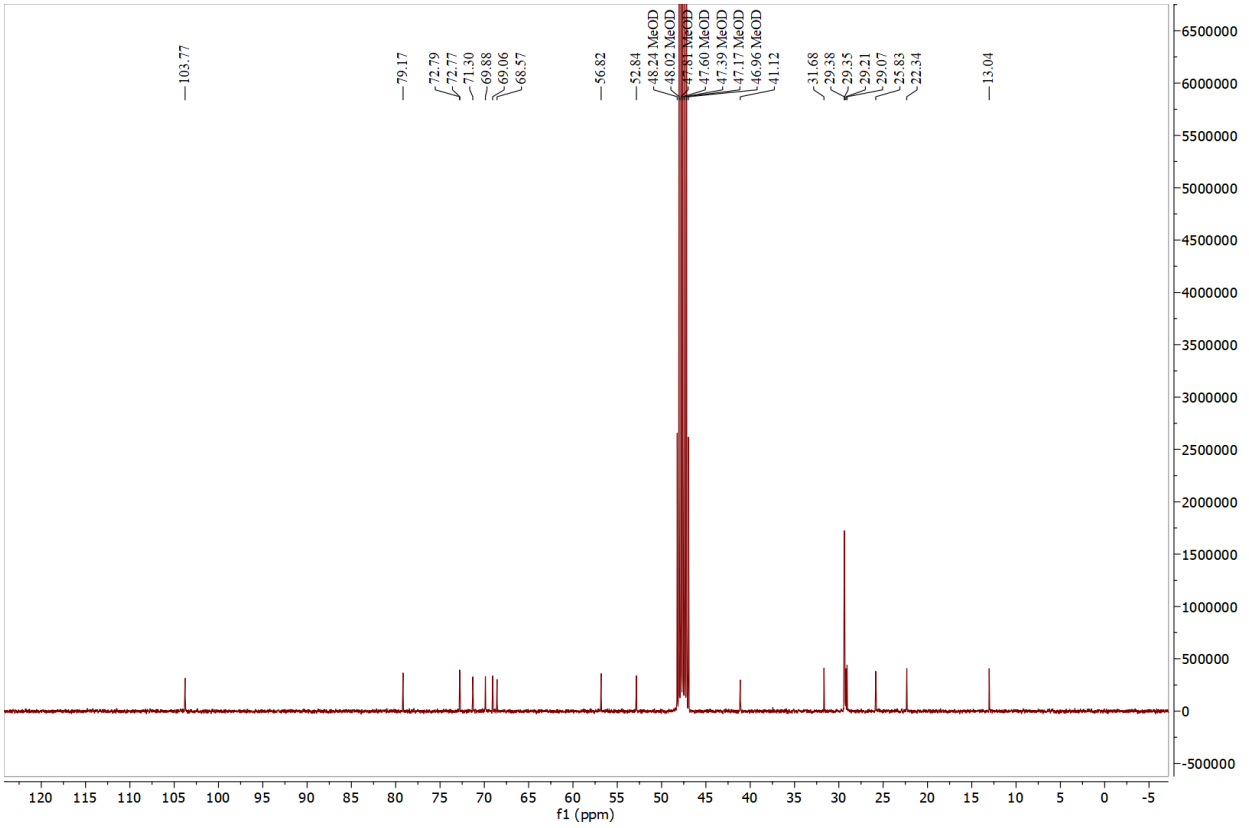
^{1}H, COSY, ^{13}C, and HSQC of compound 9b



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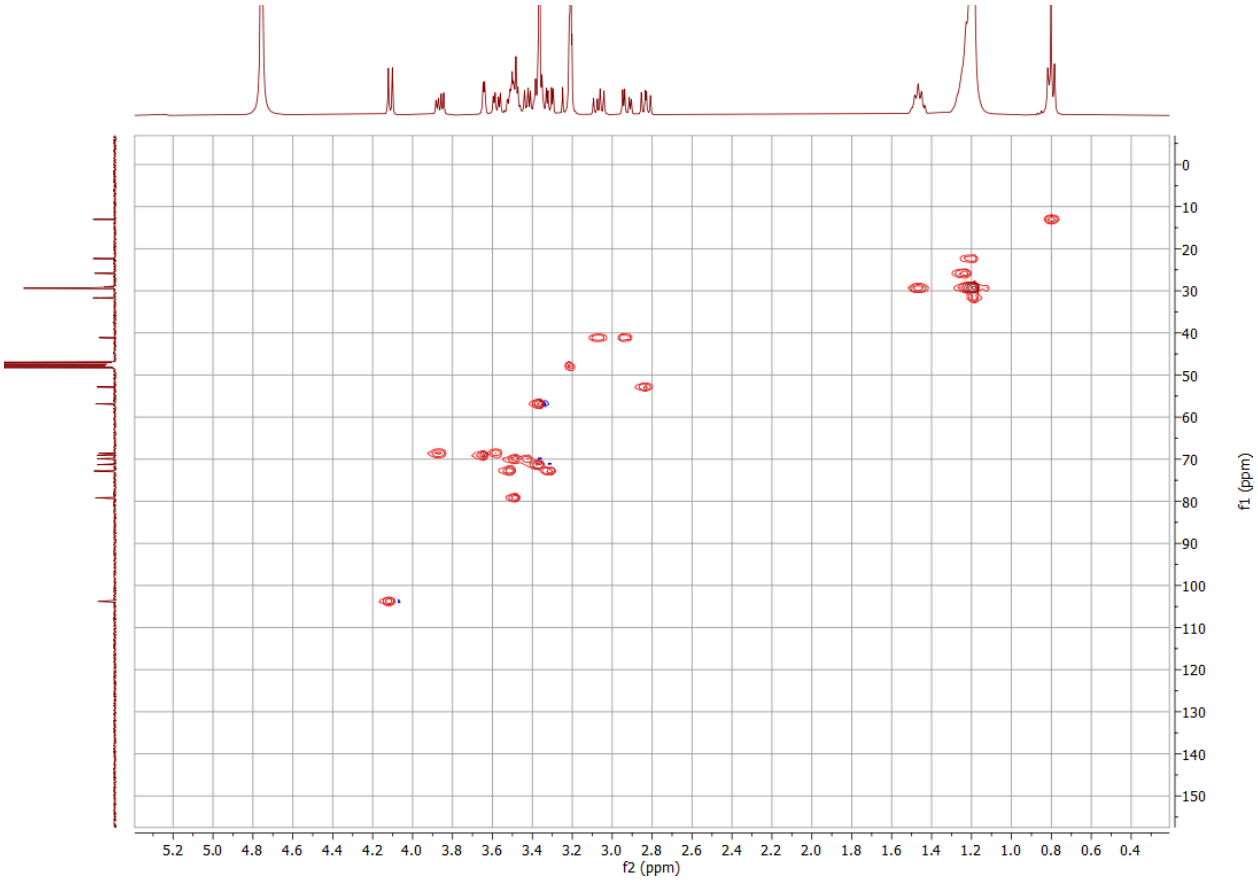
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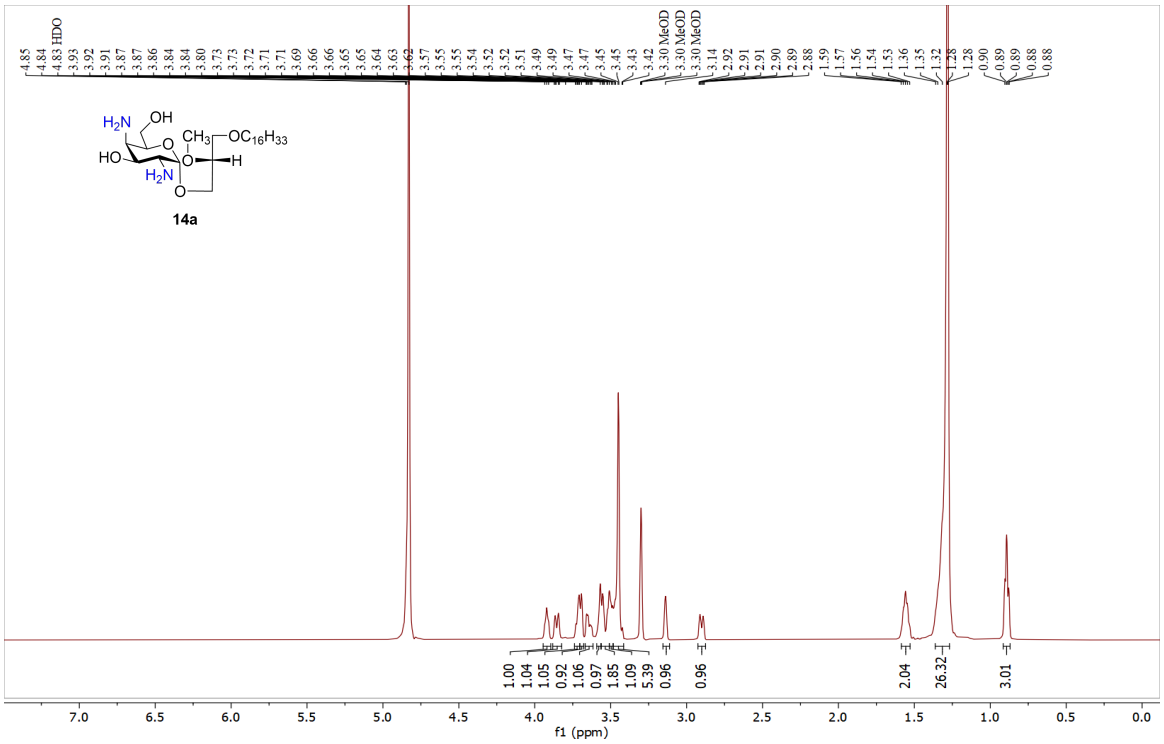
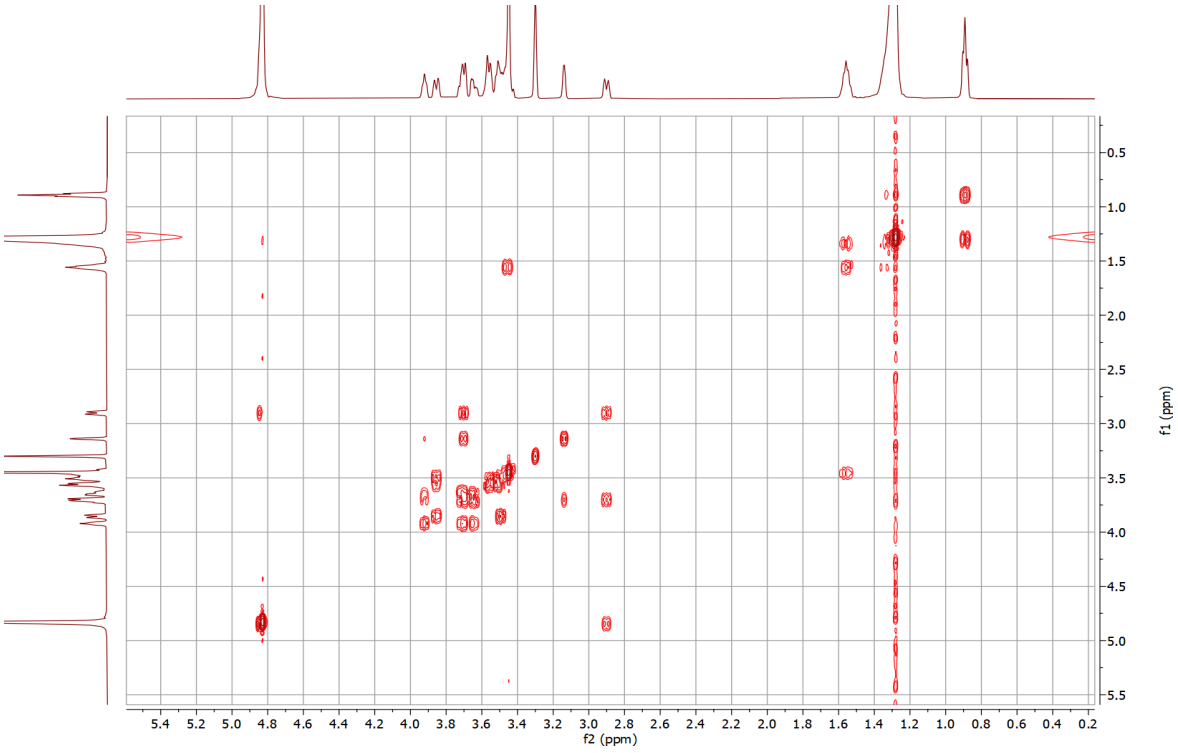
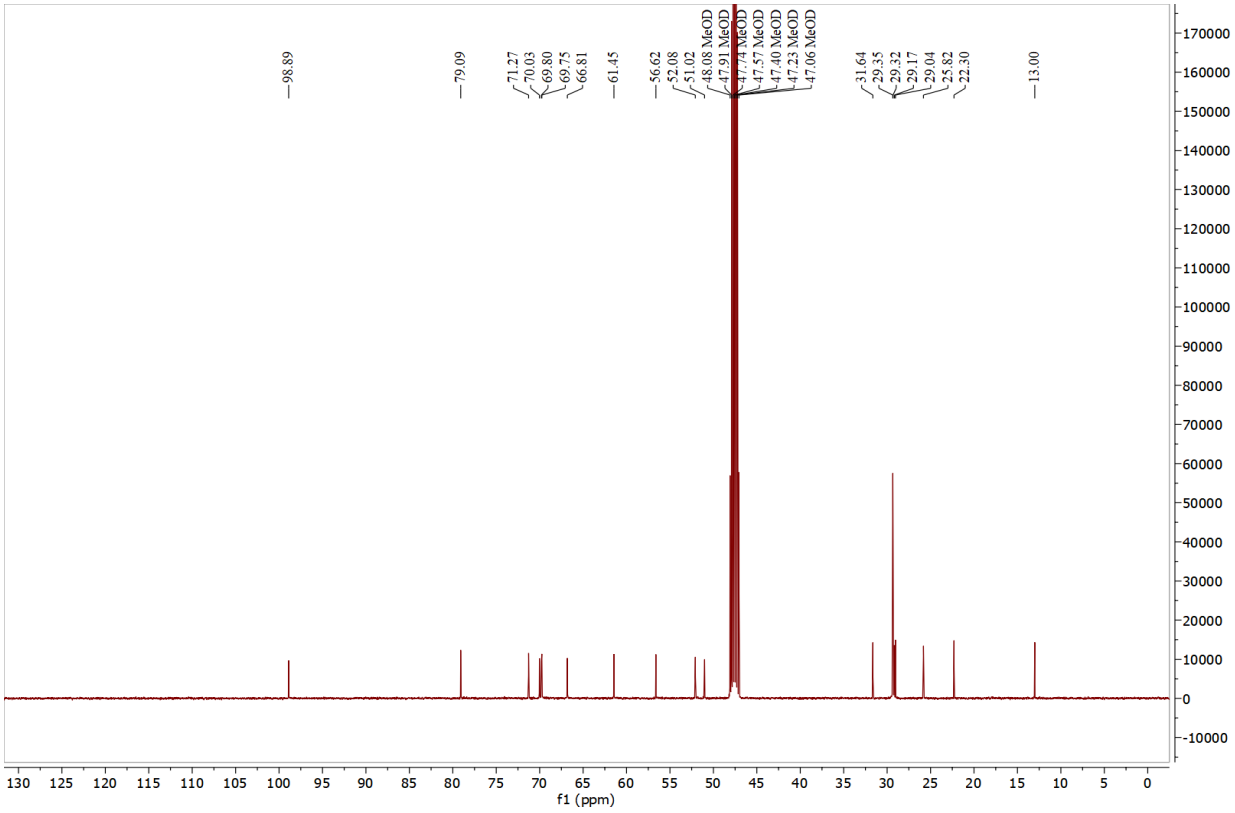
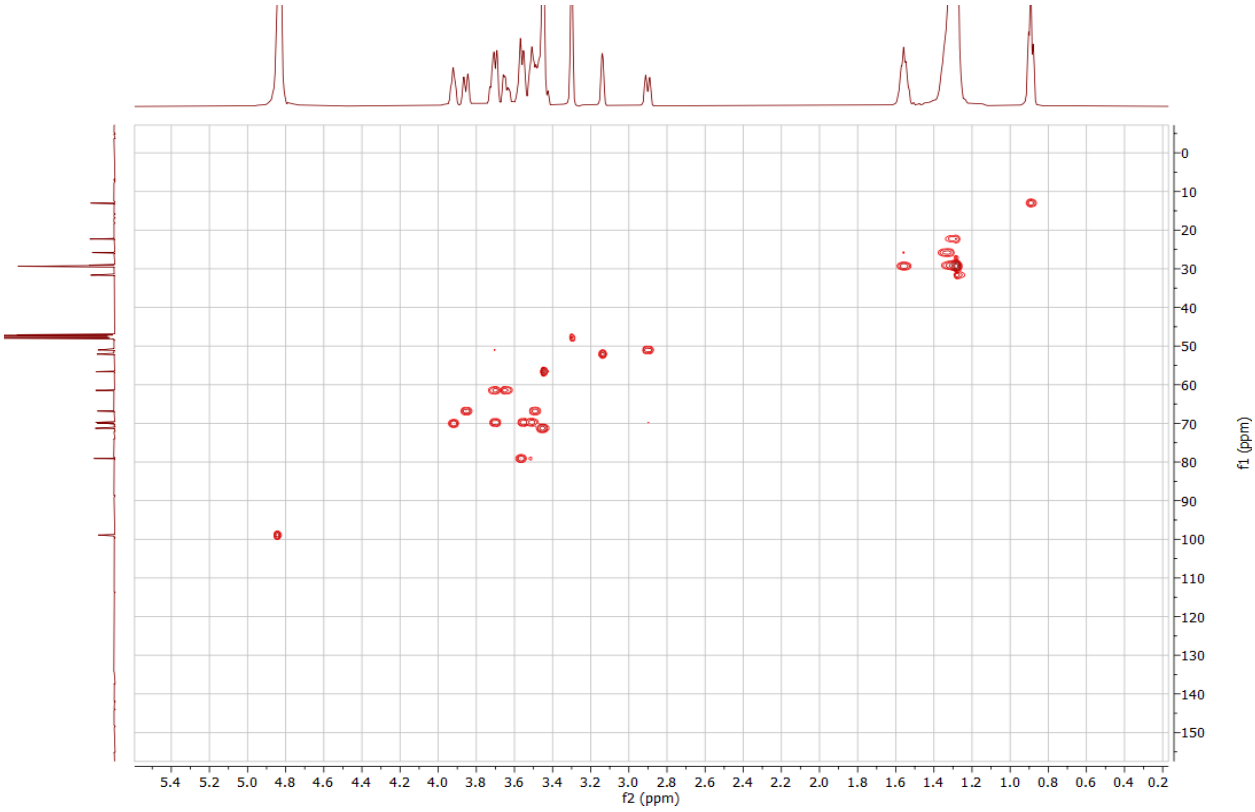
^{1}H, COSY, ^{13}C, and HSQC of compound 14a

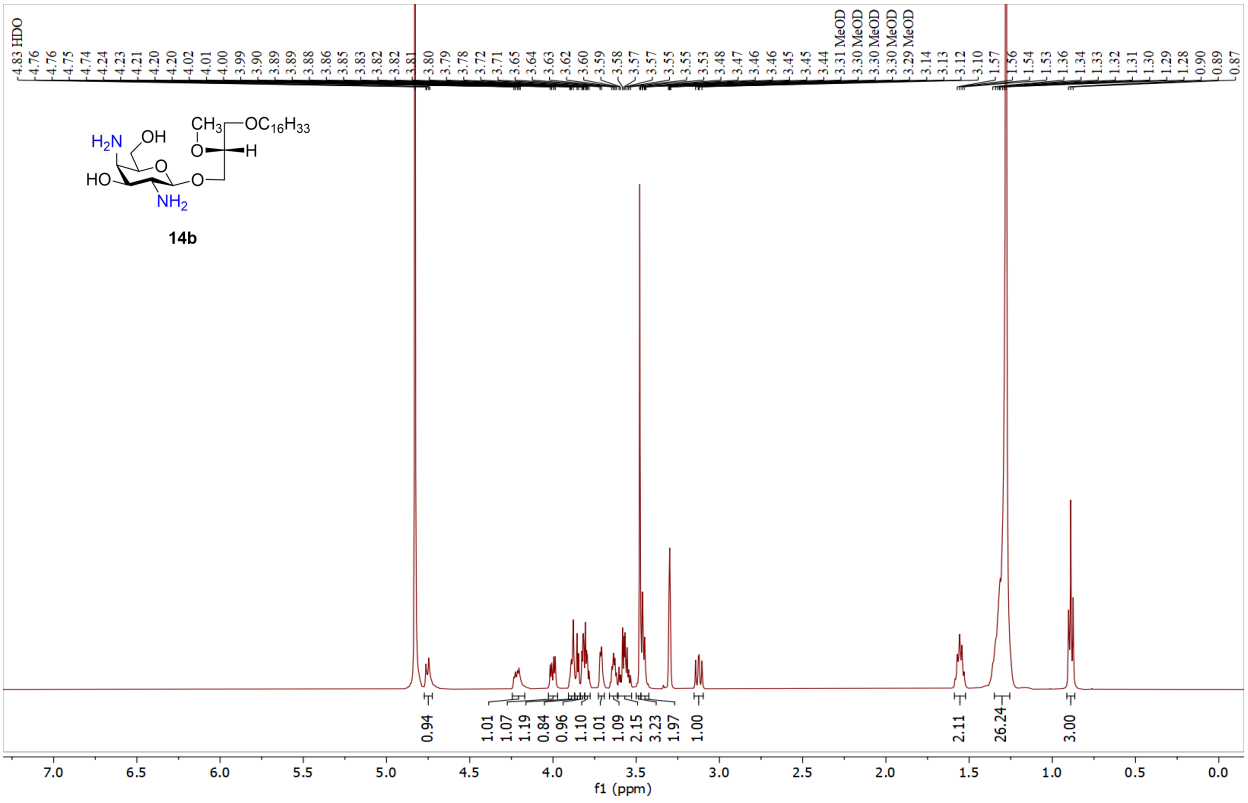


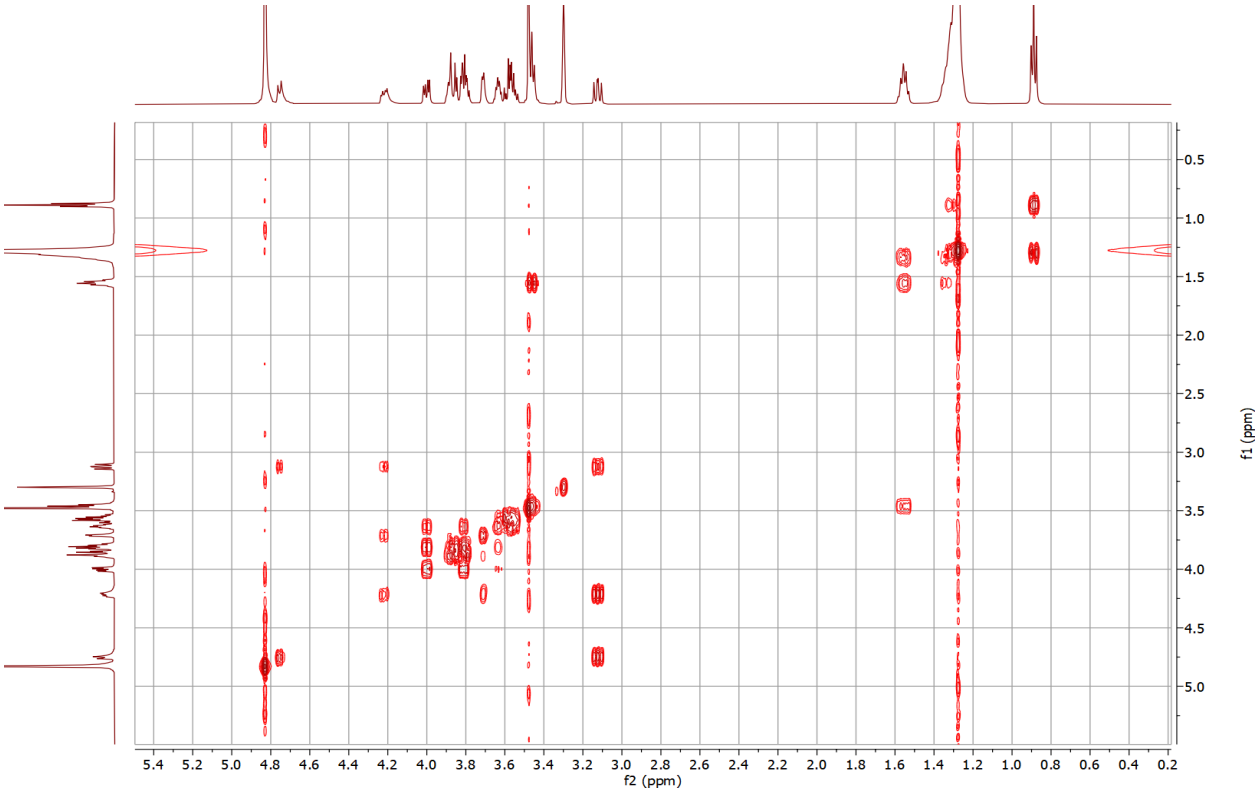


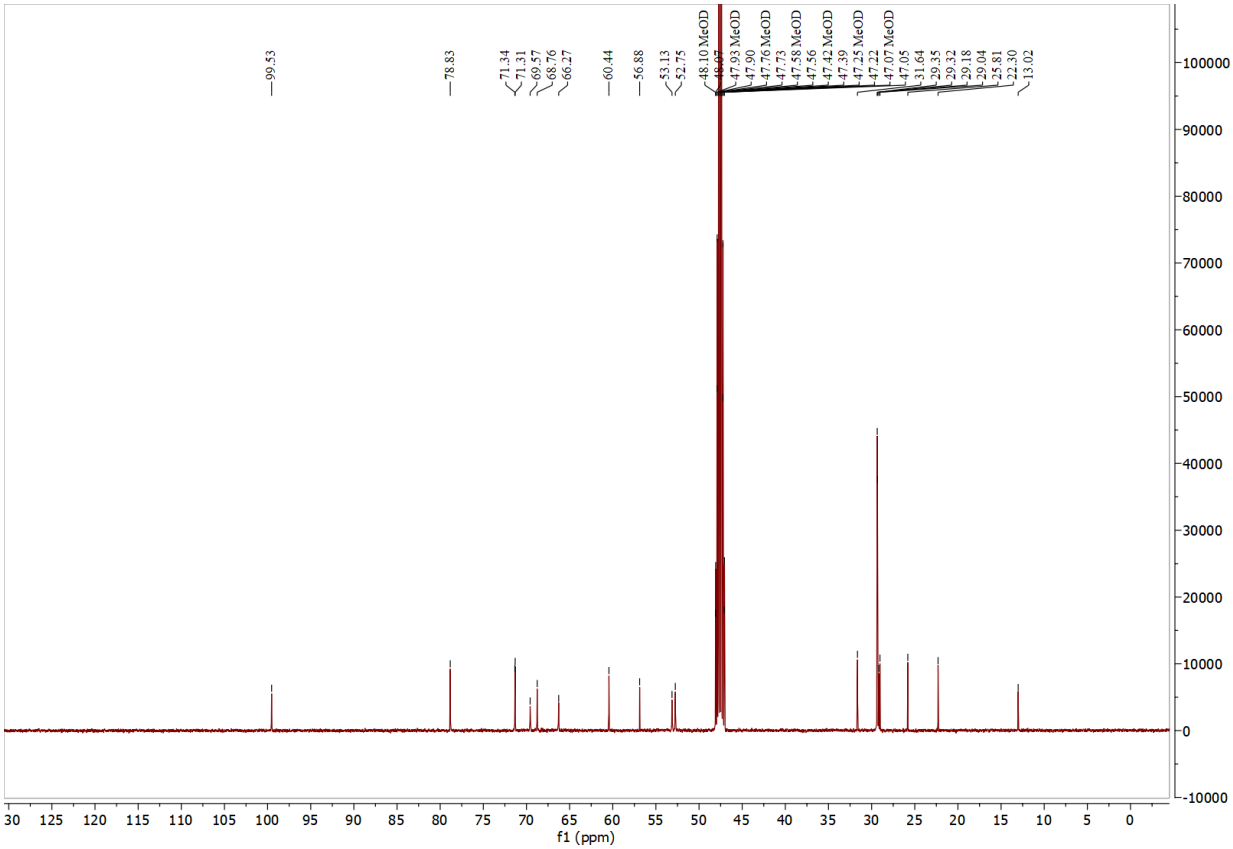

98.89
79.09
71.27
70.03
69.80
69.75
66.81
61.45
56.62
52.08
51.02
48.08 MeOD
47.91 MeOD
47.74 MeOD
47.57 MeOD
47.40 MeOD
47.23 MeOD
47.06 MeOD
31.64
29.35
29.32
29.17
29.04
25.82
22.30
13.00
f1 (ppm)

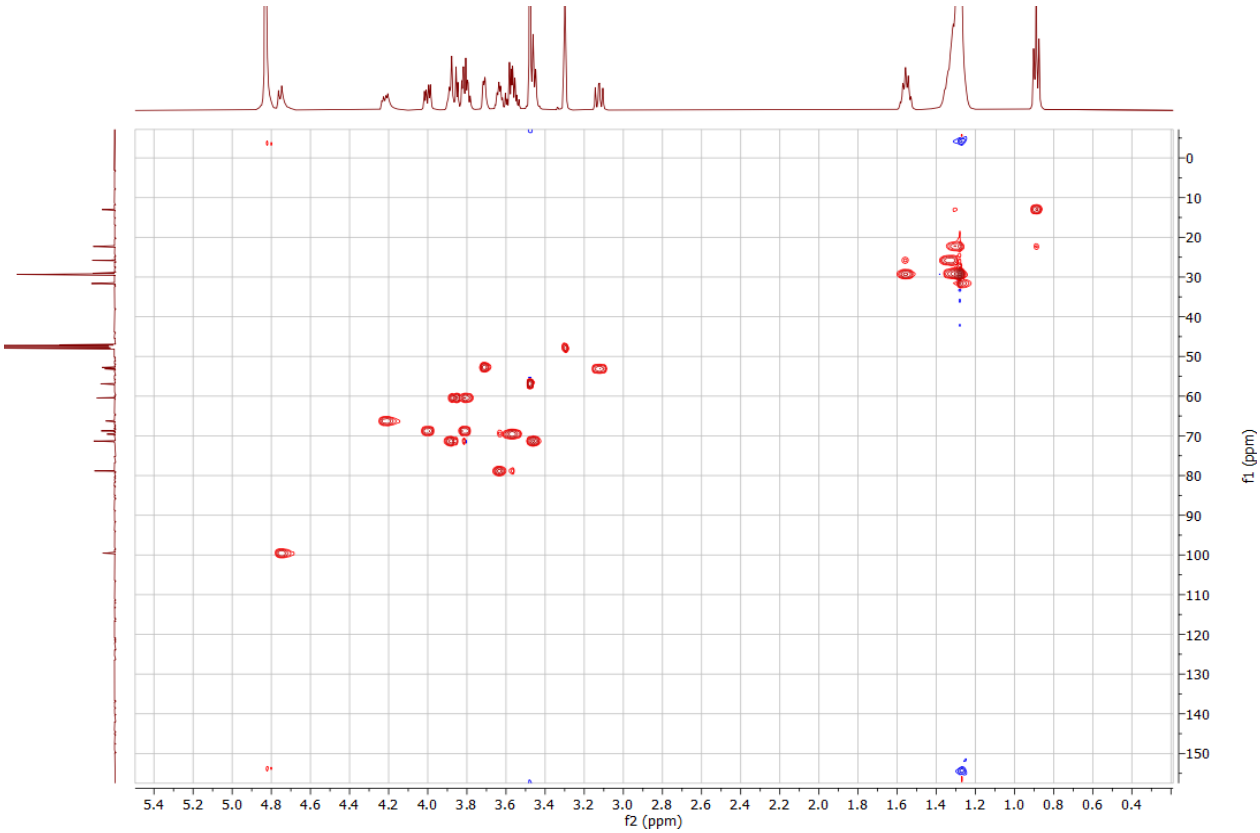

f2 (ppm)
f1 (ppm)

^{1}H, COSY, and ^{13}C NMR of compound 14b

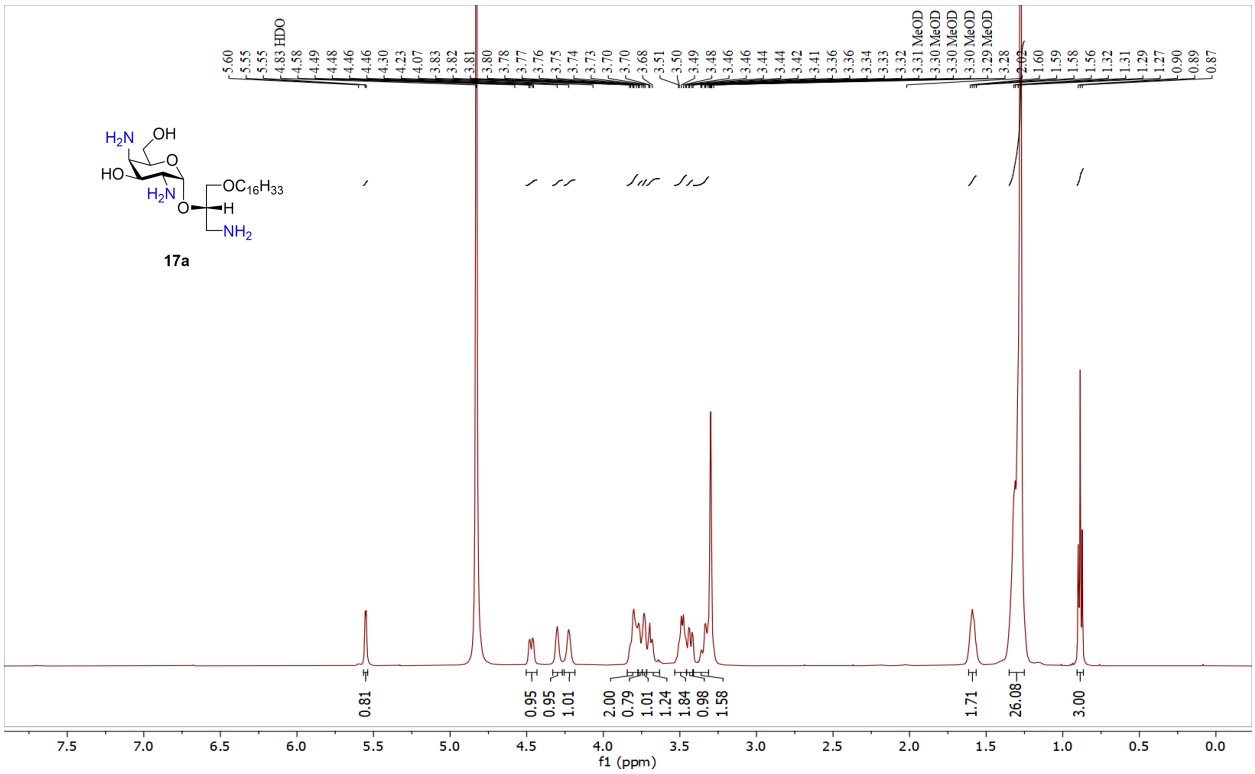


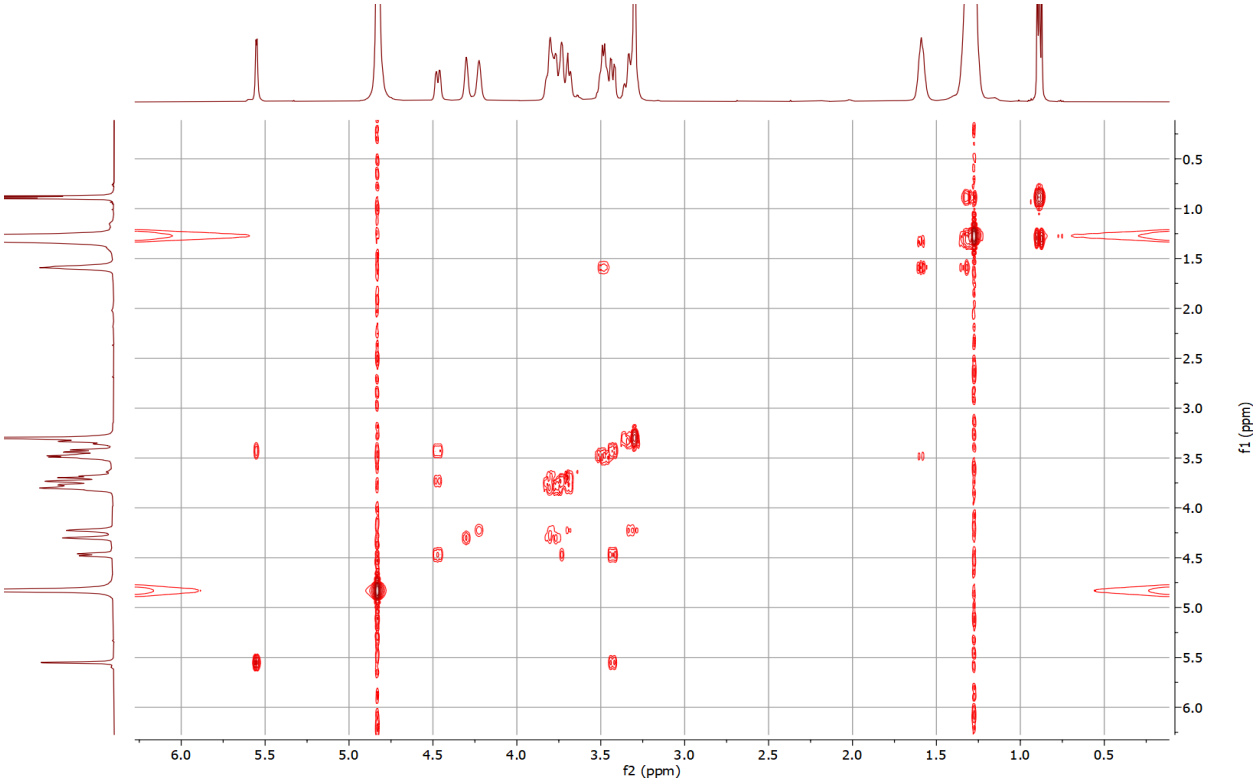


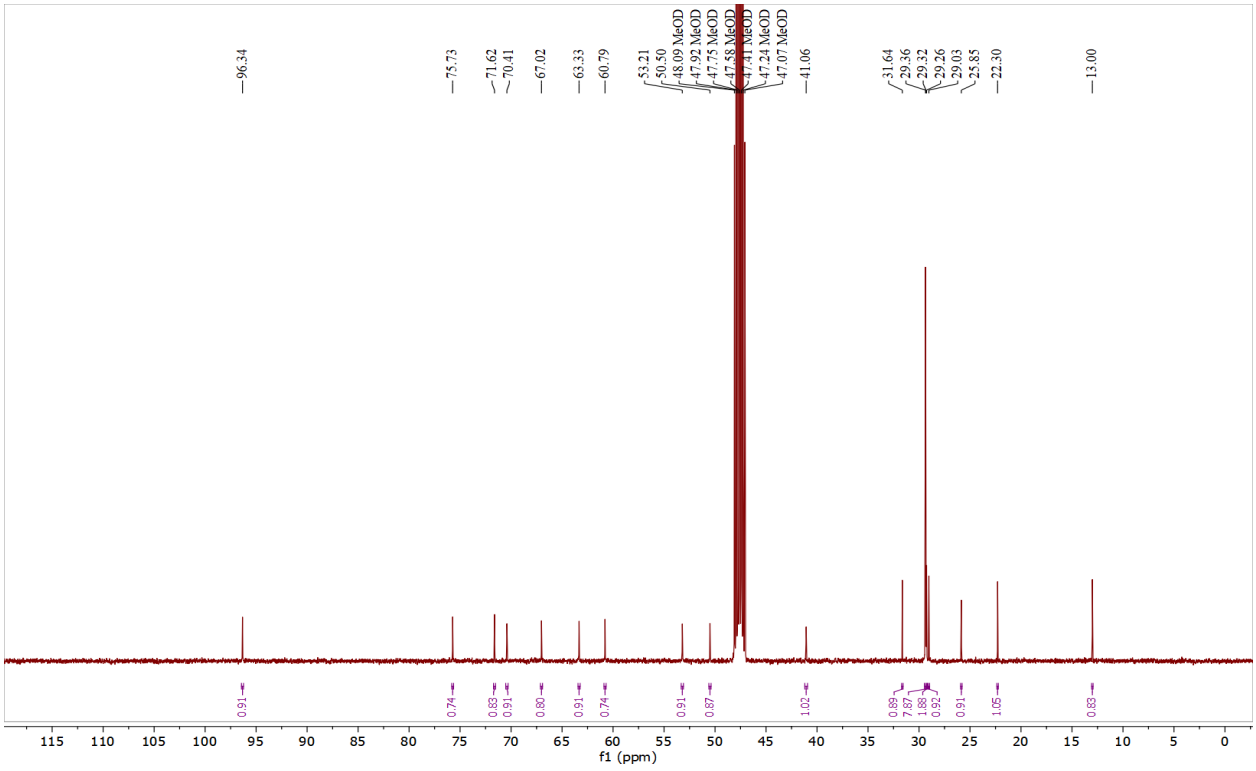

99.53
78.83
71.34
71.31
69.57
68.76
66.27
60.44
56.88
53.13
52.75
48.10 MeOD
47.93 MeOD
47.90
47.76 MeOD
47.73
47.58 MeOD
47.56
47.42 MeOD
47.39
47.25 MeOD
47.22
47.07 MeOD
47.05
31.64
29.35
29.32
29.18
29.04
25.81
22.30
13.02
f1 (ppm)

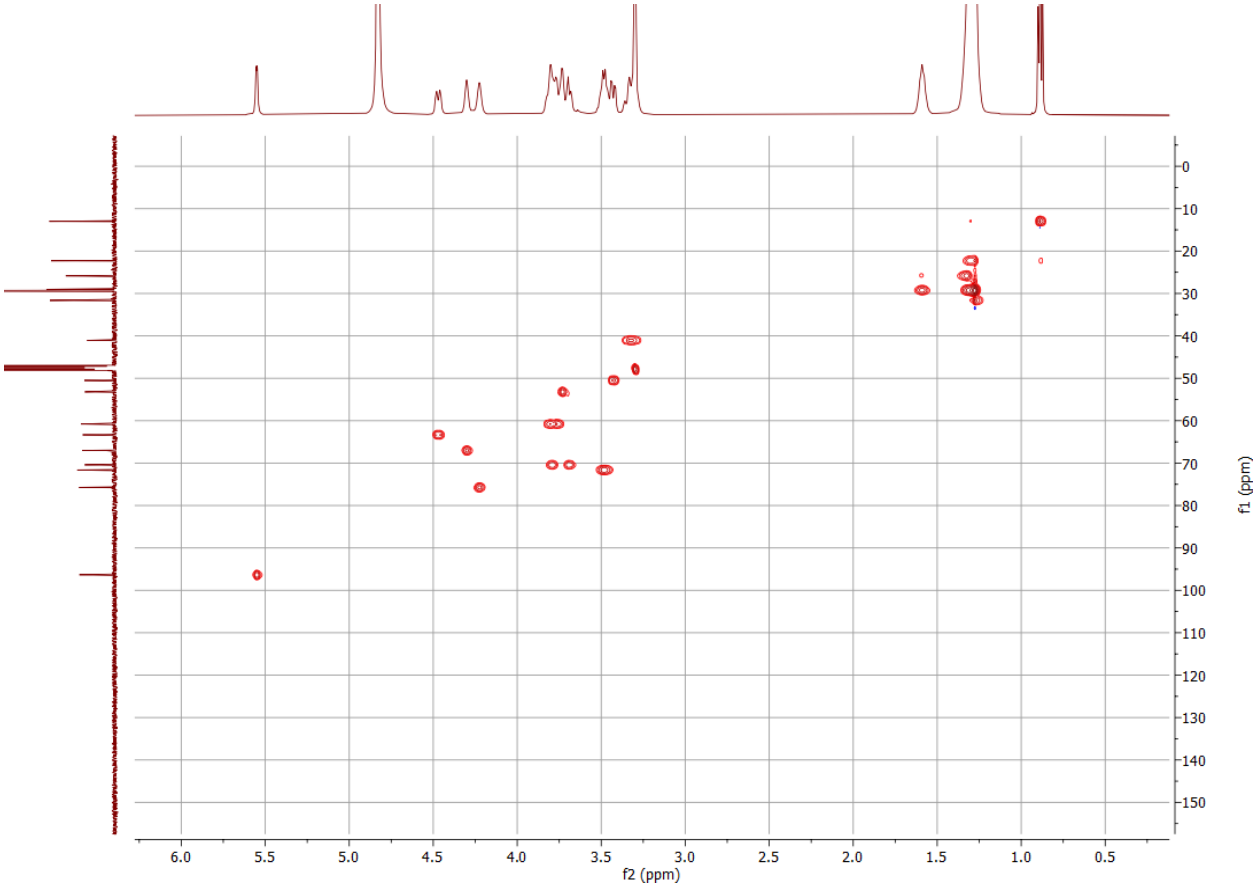

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQCNMR of compound 17a

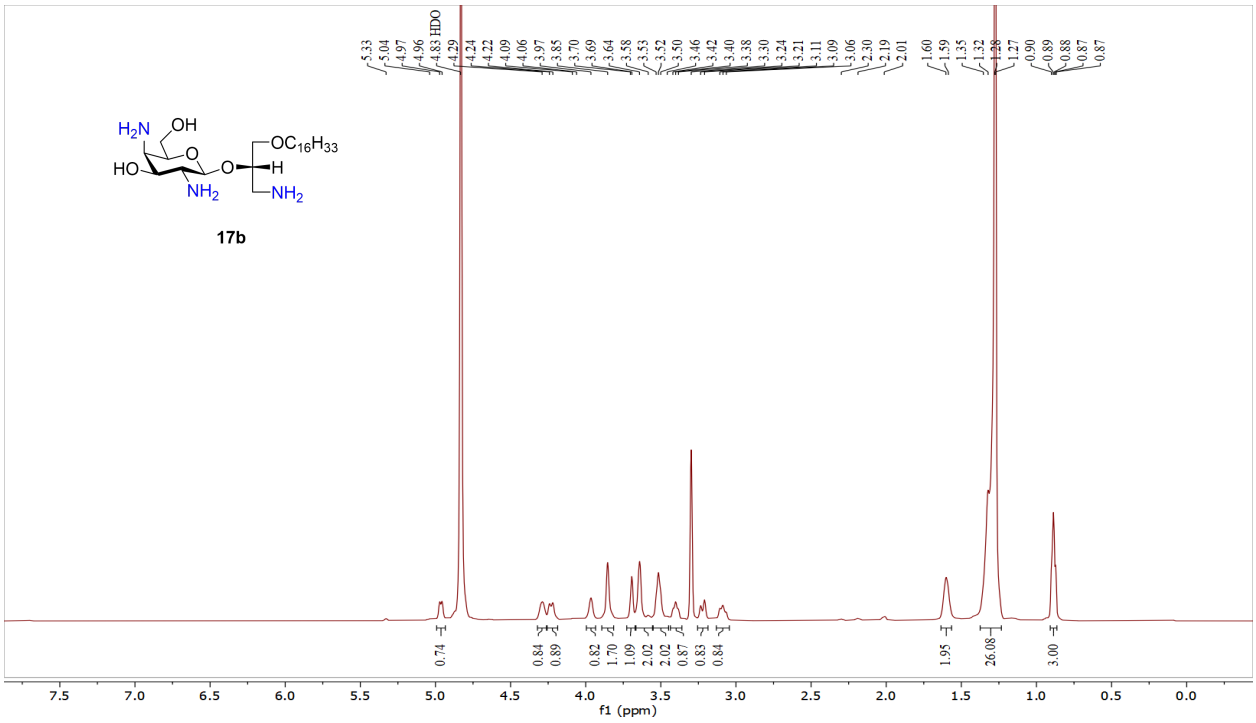


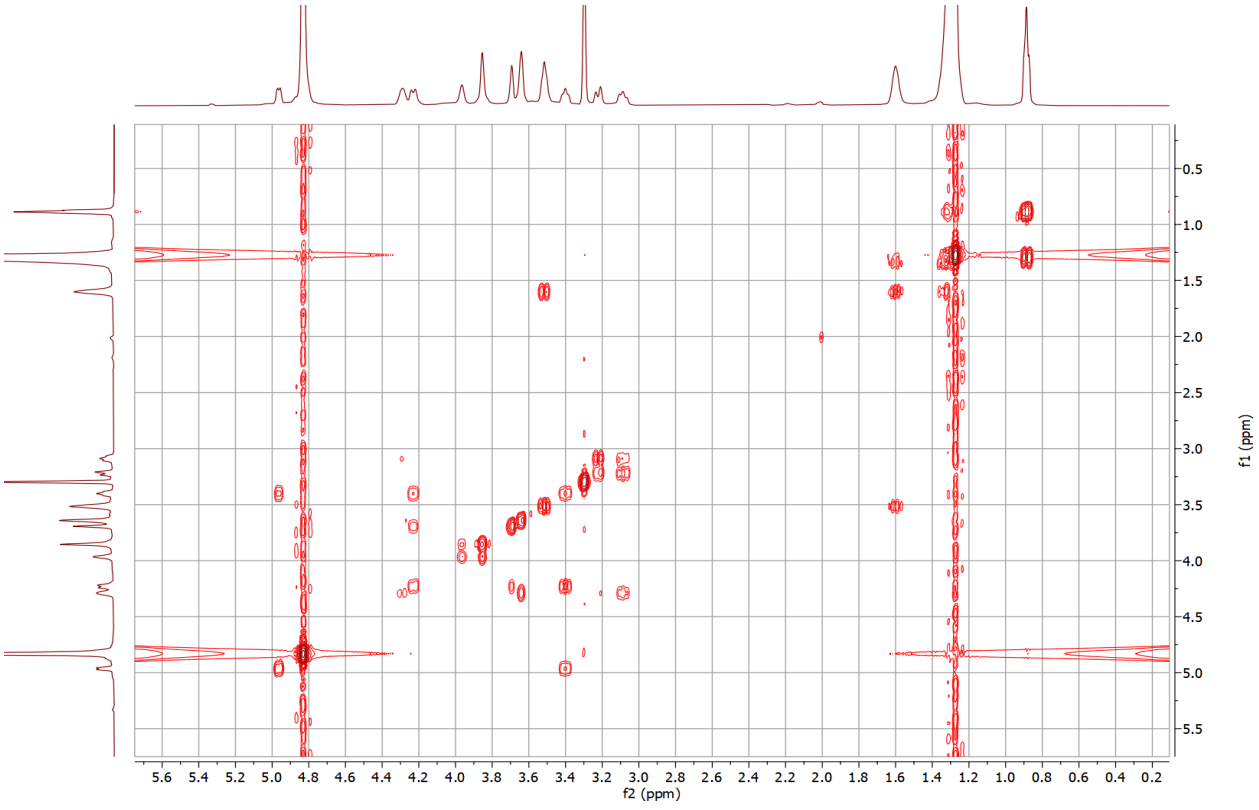


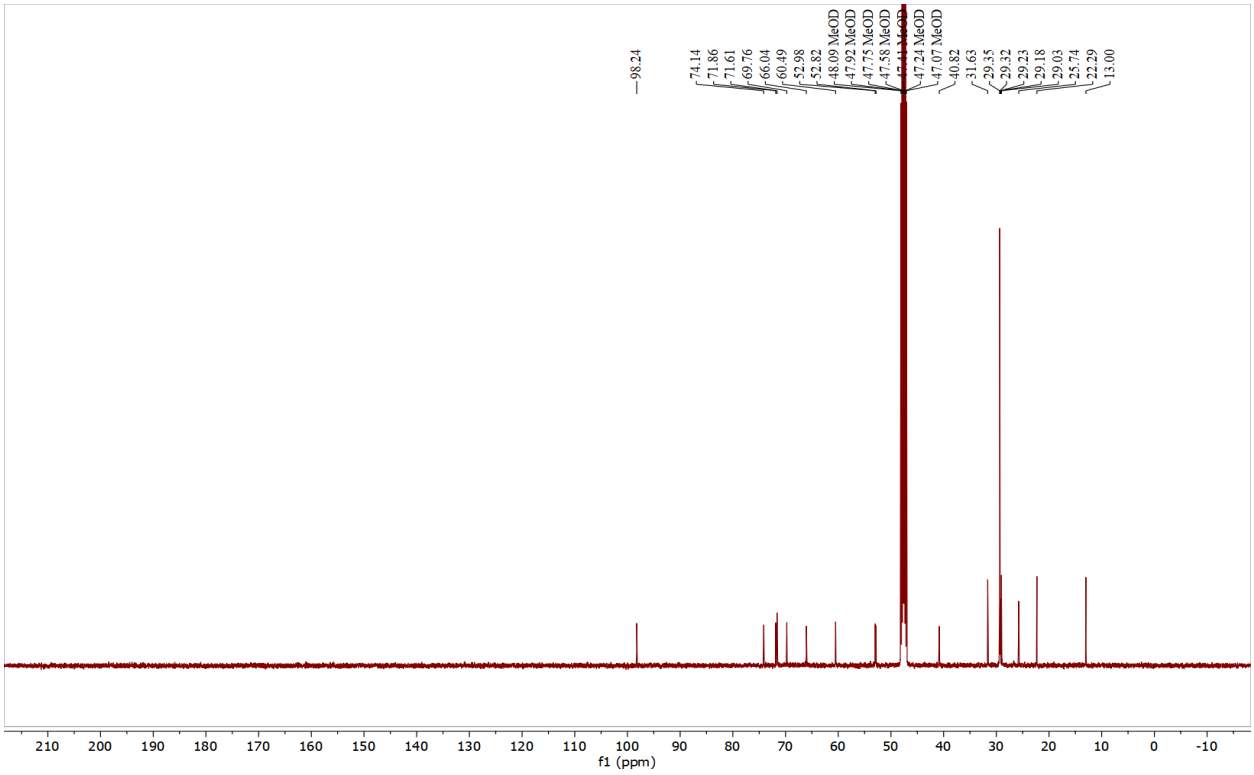

96.34
75.73
71.62
70.41
67.02
63.33
60.79
53.21
50.50
48.09 MeOD
47.92 MeOD
47.75 MeOD
47.58 MeOD
47.41 MeOD
47.24 MeOD
47.07 MeOD
41.06
31.64
29.36
29.32
29.26
29.03
25.85
22.30
13.00
0.91
0.74
0.83
0.91
0.80
0.91
0.74
0.91
0.87
1.02
0.89
7.87
1.88
0.92
0.91
1.05
0.83
f1 (ppm)

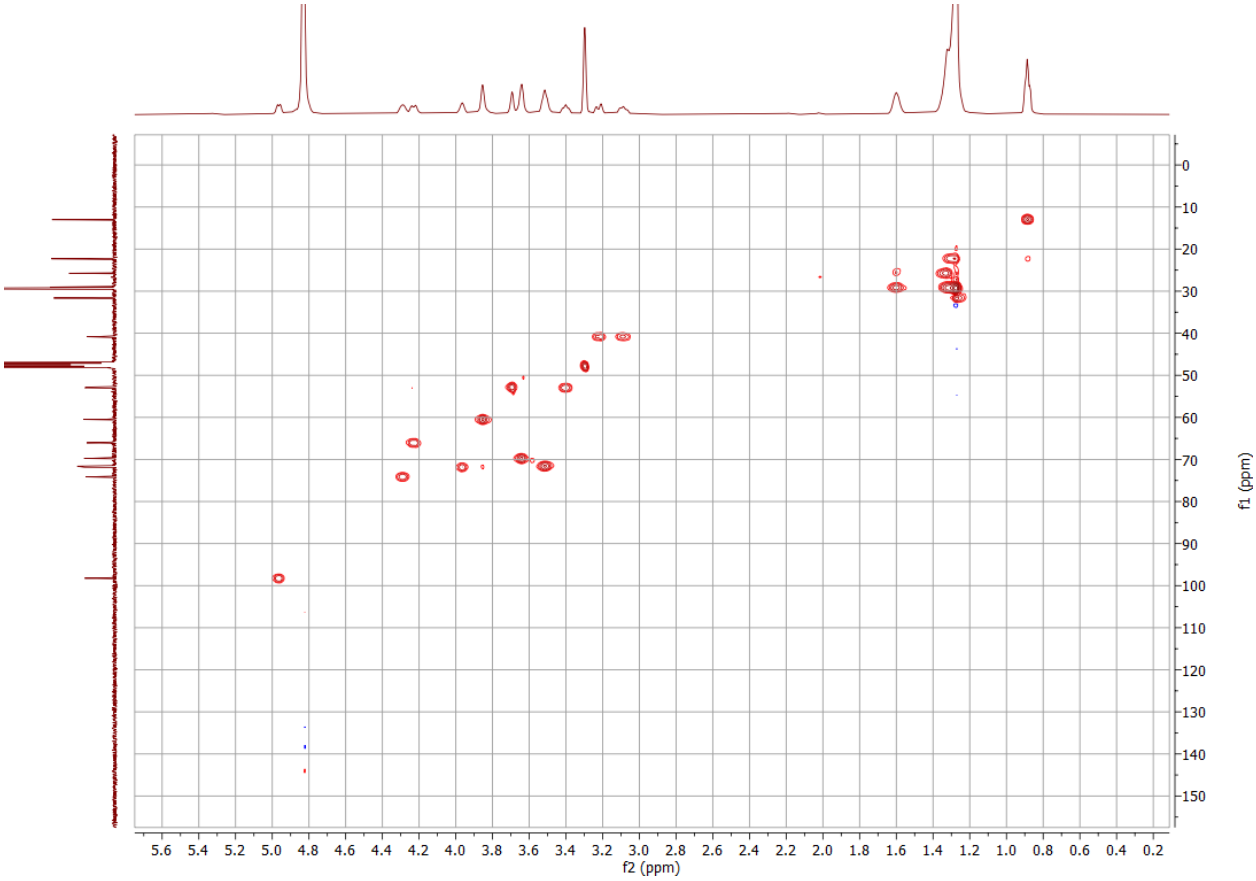

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 17b

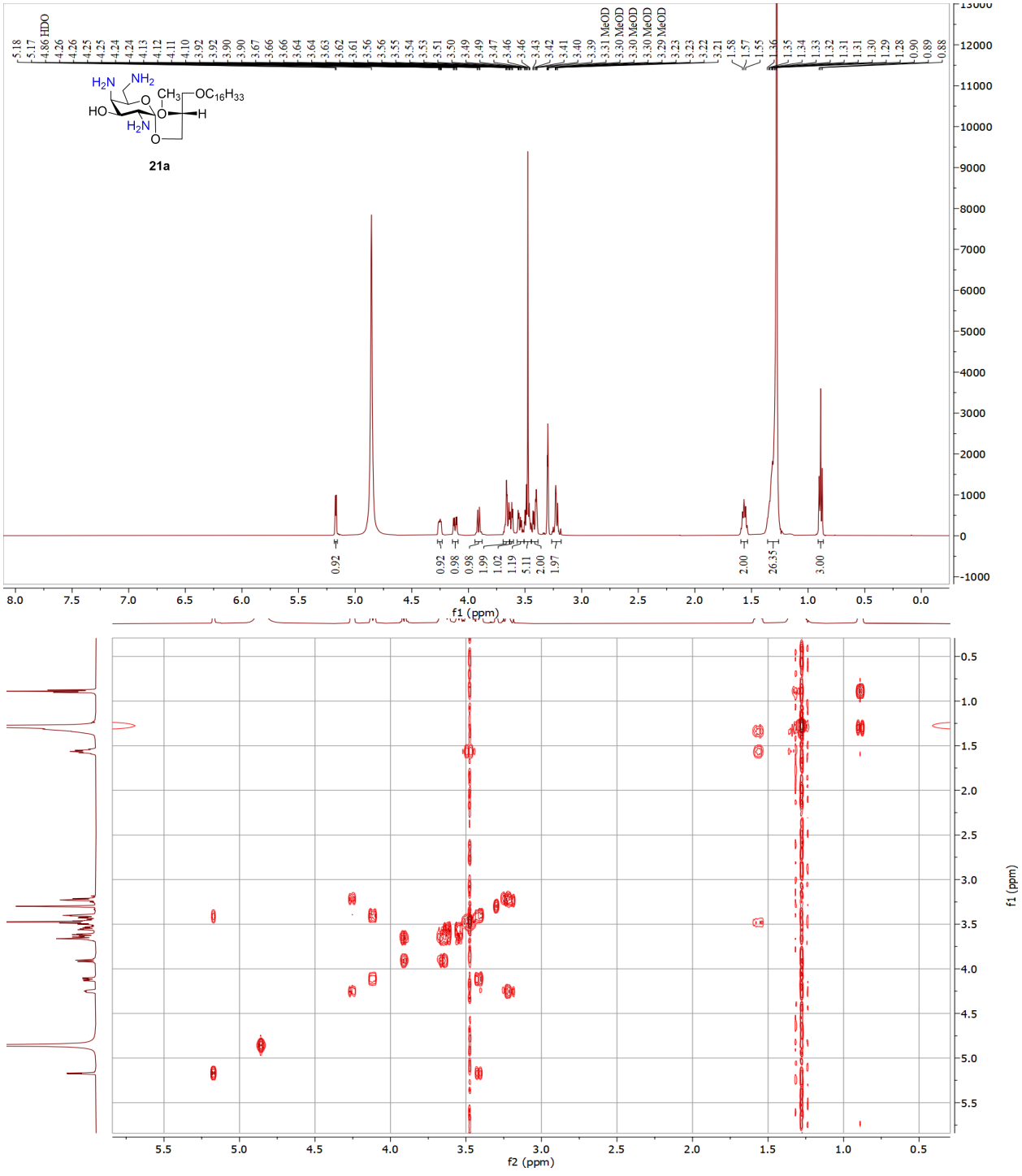


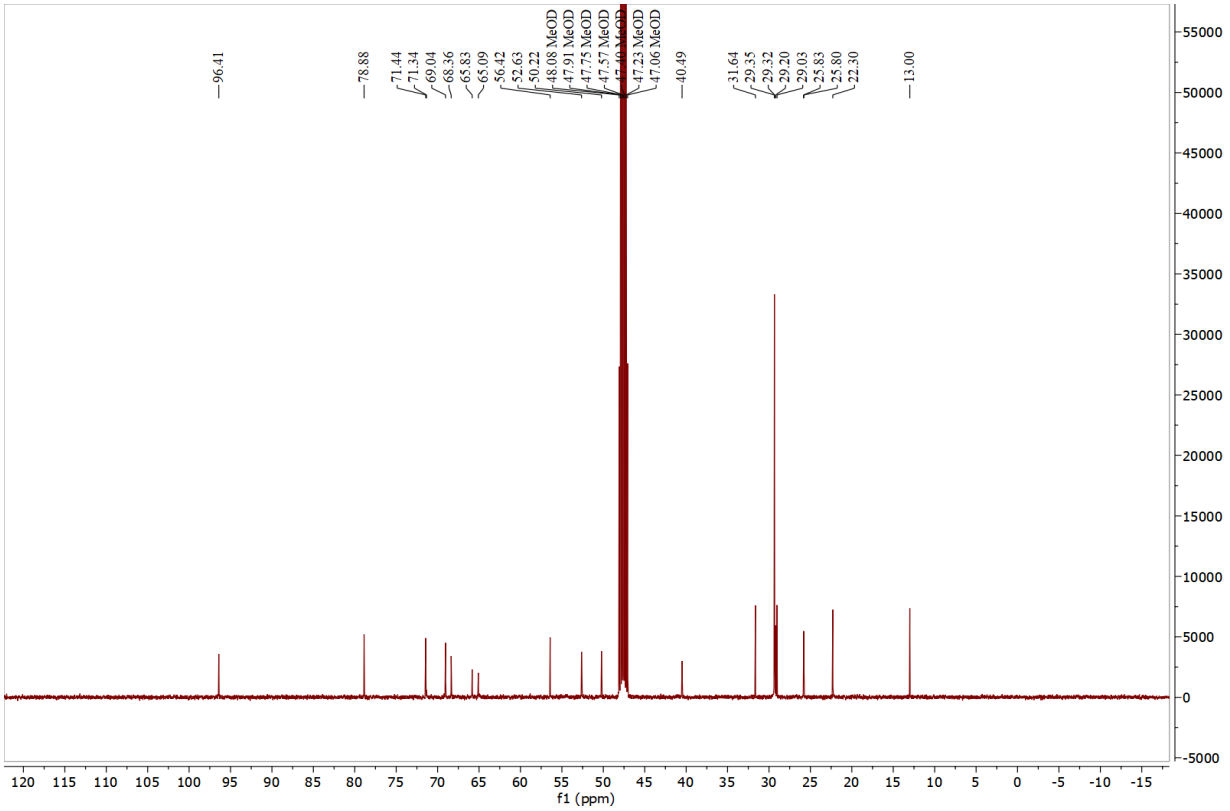


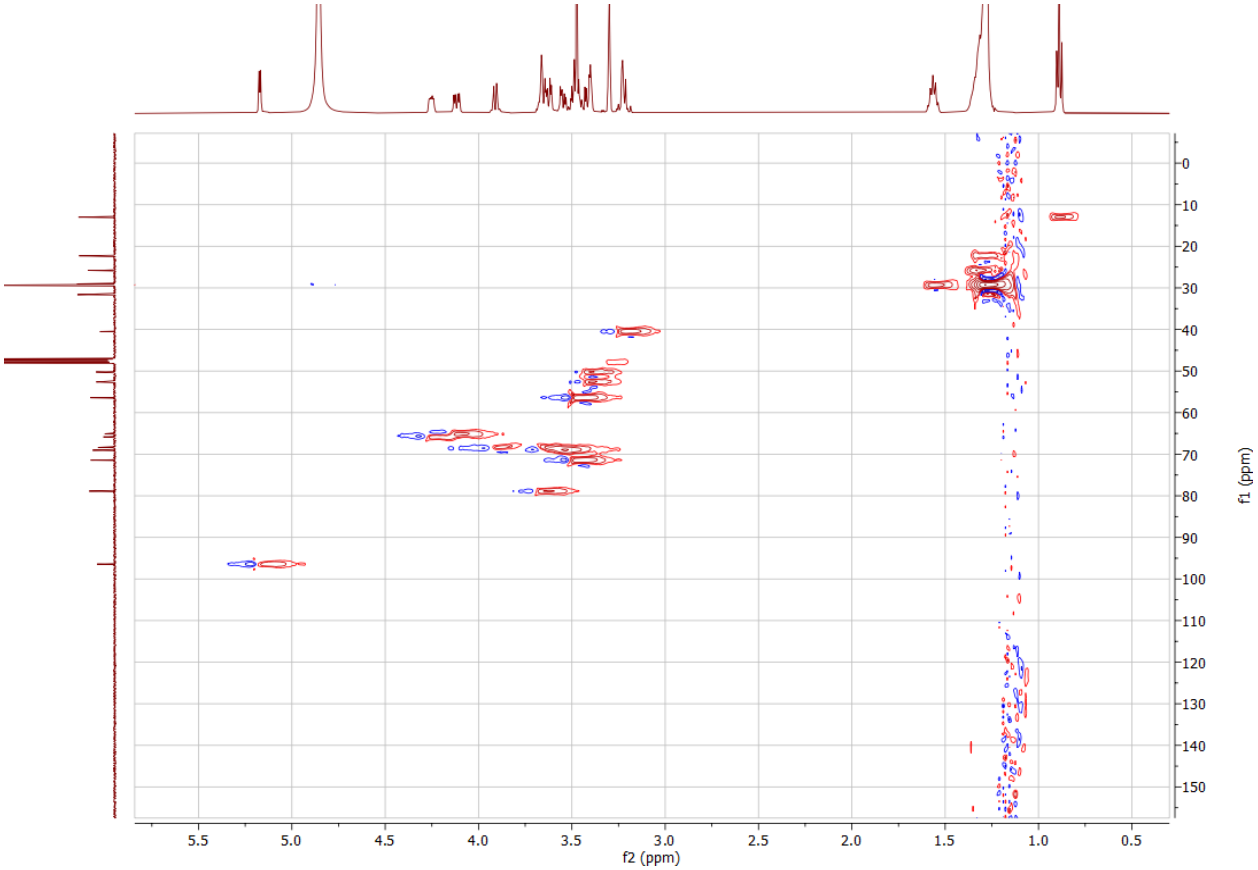

98.24
74.14
71.86
71.61
69.76
66.04
60.49
52.98
52.82
48.09 MeOD
47.92 MeOD
47.75 MeOD
47.58 MeOD
47.41 MeOD
47.24 MeOD
47.07 MeOD
40.82
31.63
29.35
29.32
29.23
29.18
29.03
25.74
22.29
13.00
f1 (ppm)


f2 (ppm)
f1 (ppm)

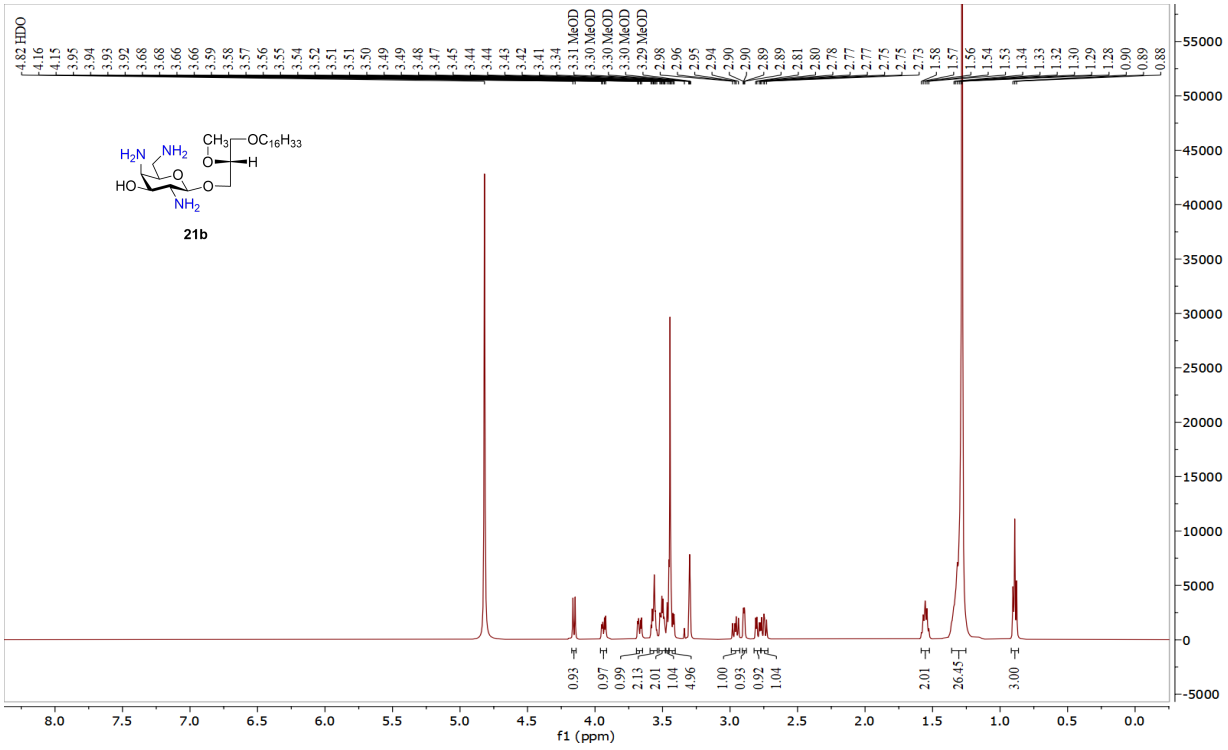
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 21a

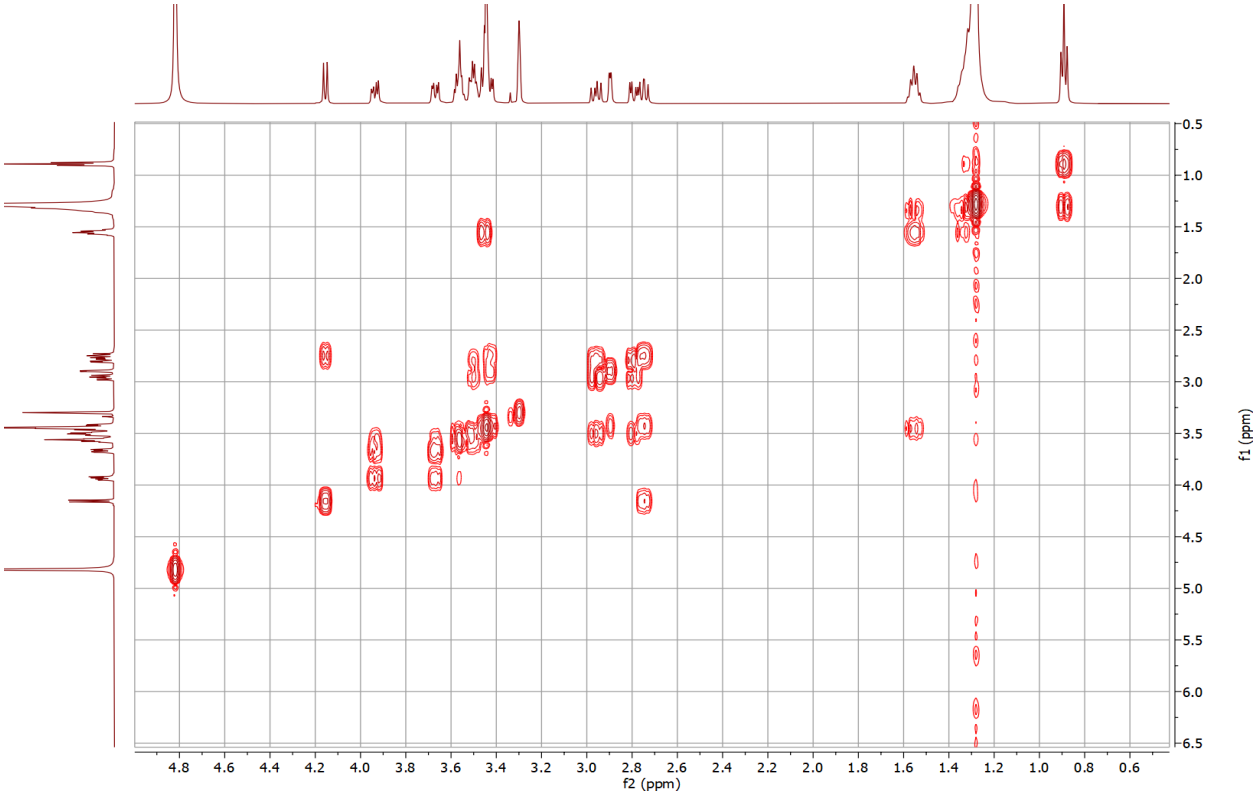


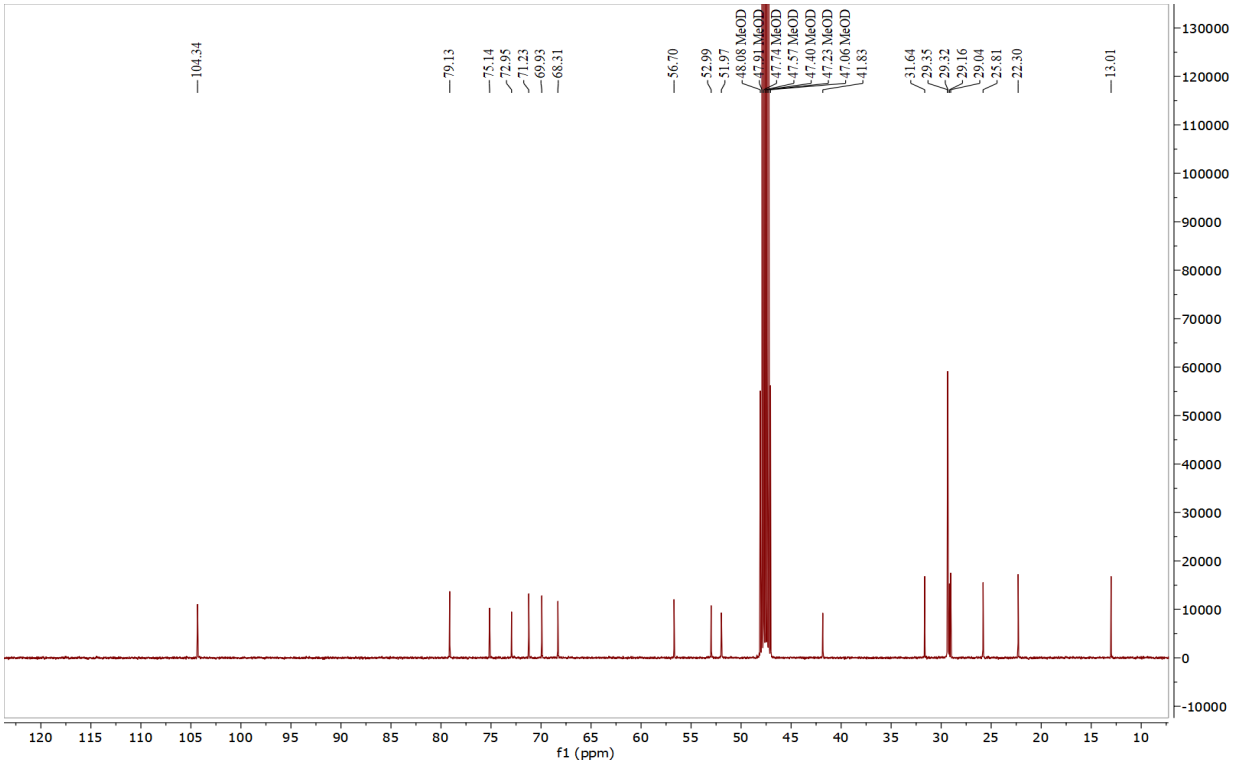

96.41
78.88
71.44
71.34
69.04
68.36
65.83
65.09
56.42
52.63
50.22
48.08 MeOD
47.91 MeOD
47.75 MeOD
47.57 MeOD
47.40 MeOD
47.23 MeOD
47.06 MeOD
40.49
31.64
29.35
29.32
29.20
29.03
25.83
25.80
22.30
13.00
f1 (ppm)

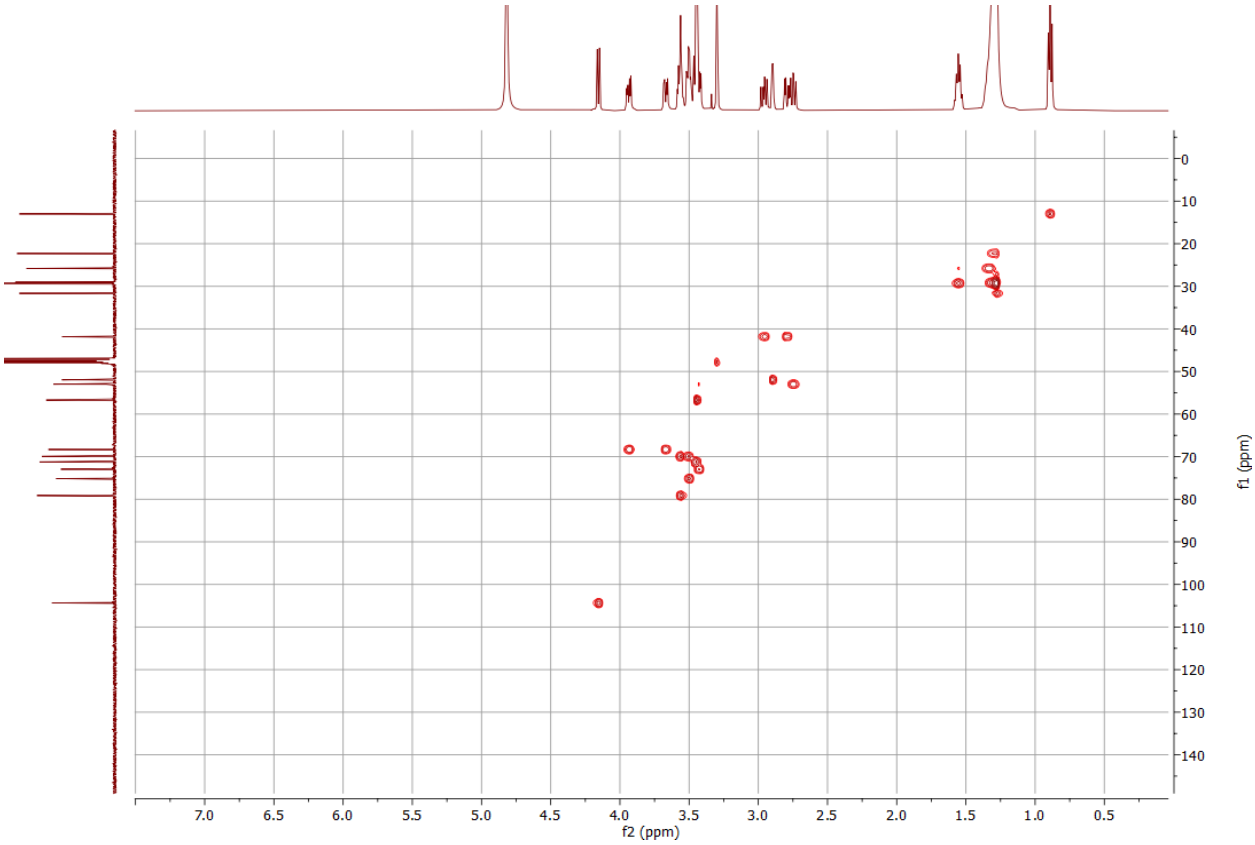

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 21b

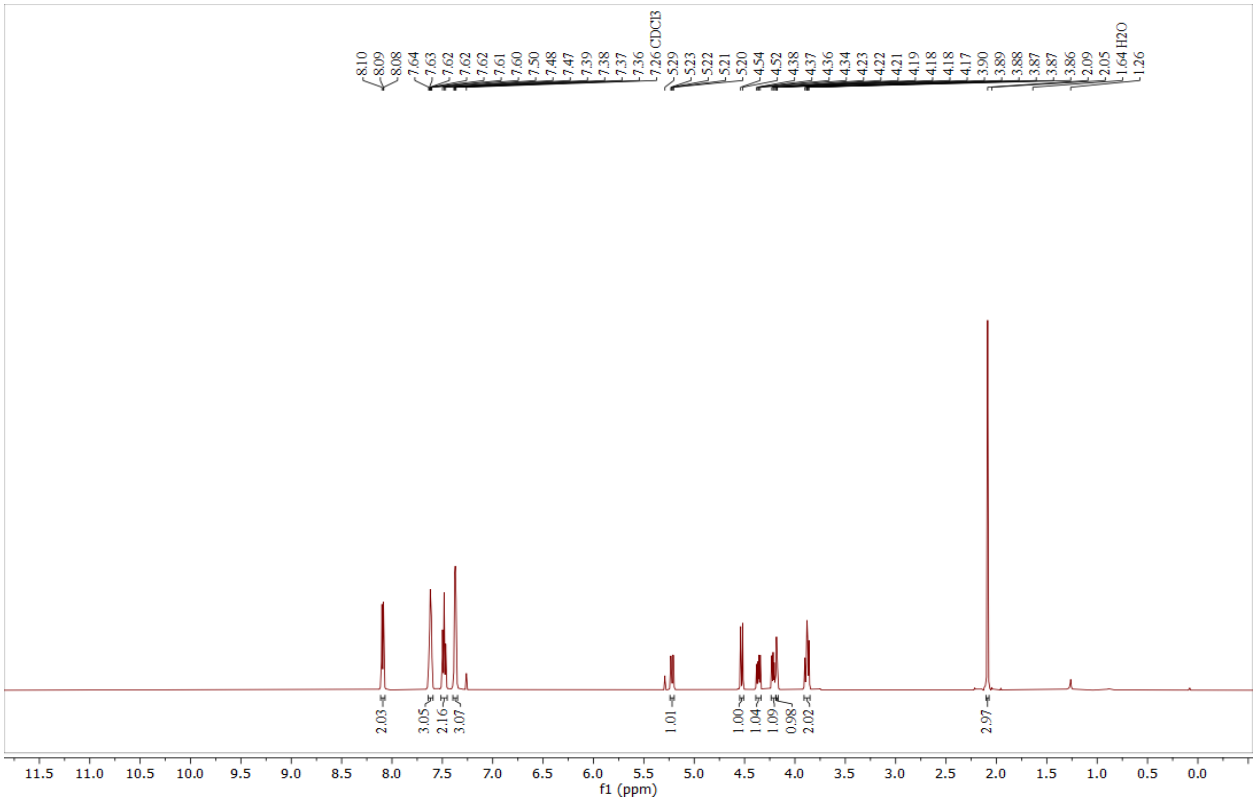


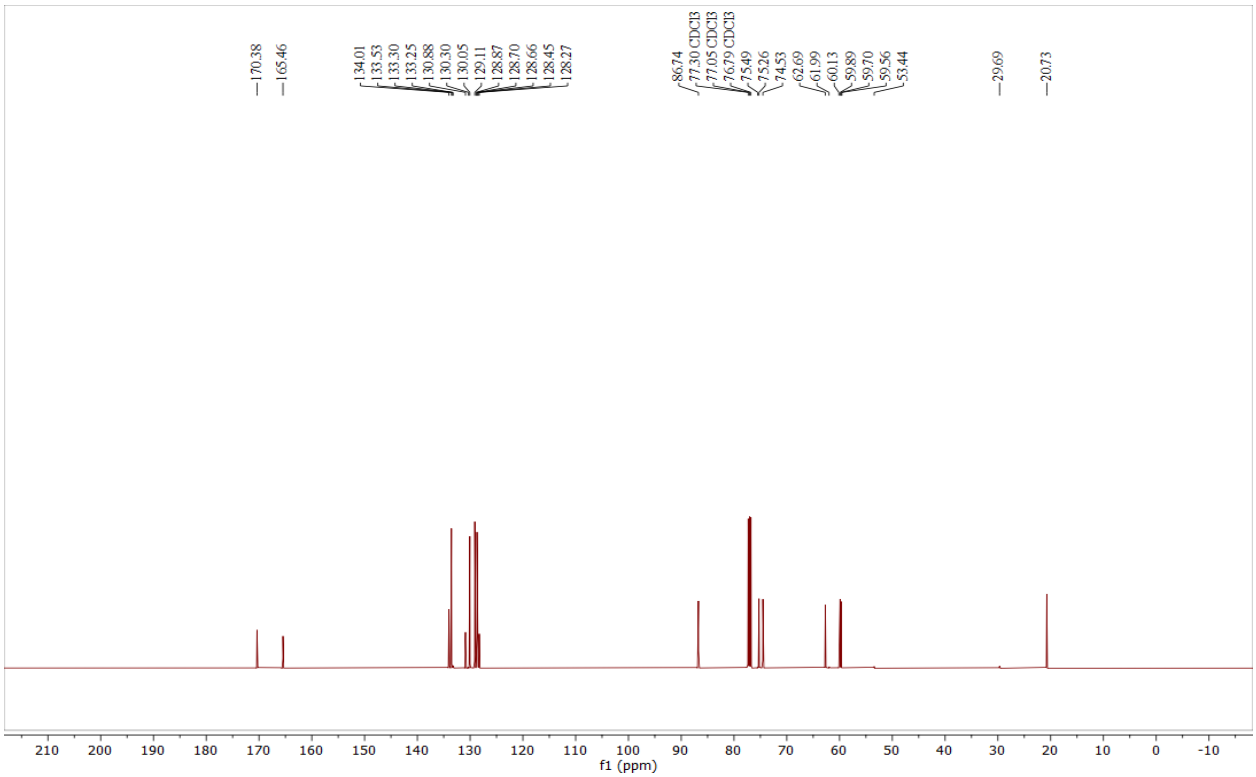


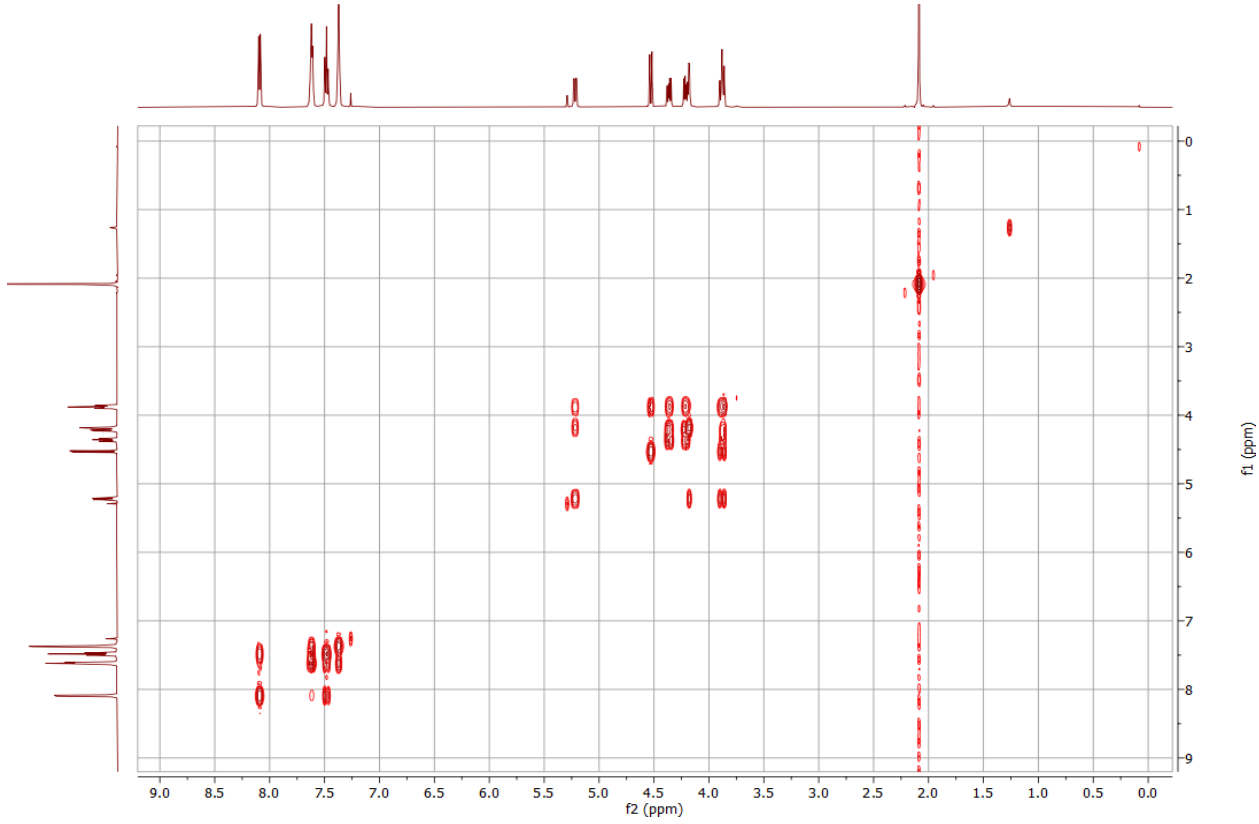

104.34
79.13
75.14
72.95
71.23
69.93
68.31
56.70
52.99
51.97
48.08 MeOD
47.91 MeOD
47.74 MeOD
47.57 MeOD
47.40 MeOD
47.23 MeOD
47.06 MeOD
41.83
31.64
29.35
29.32
29.16
29.04
25.81
22.30
13.01
f1 (ppm)

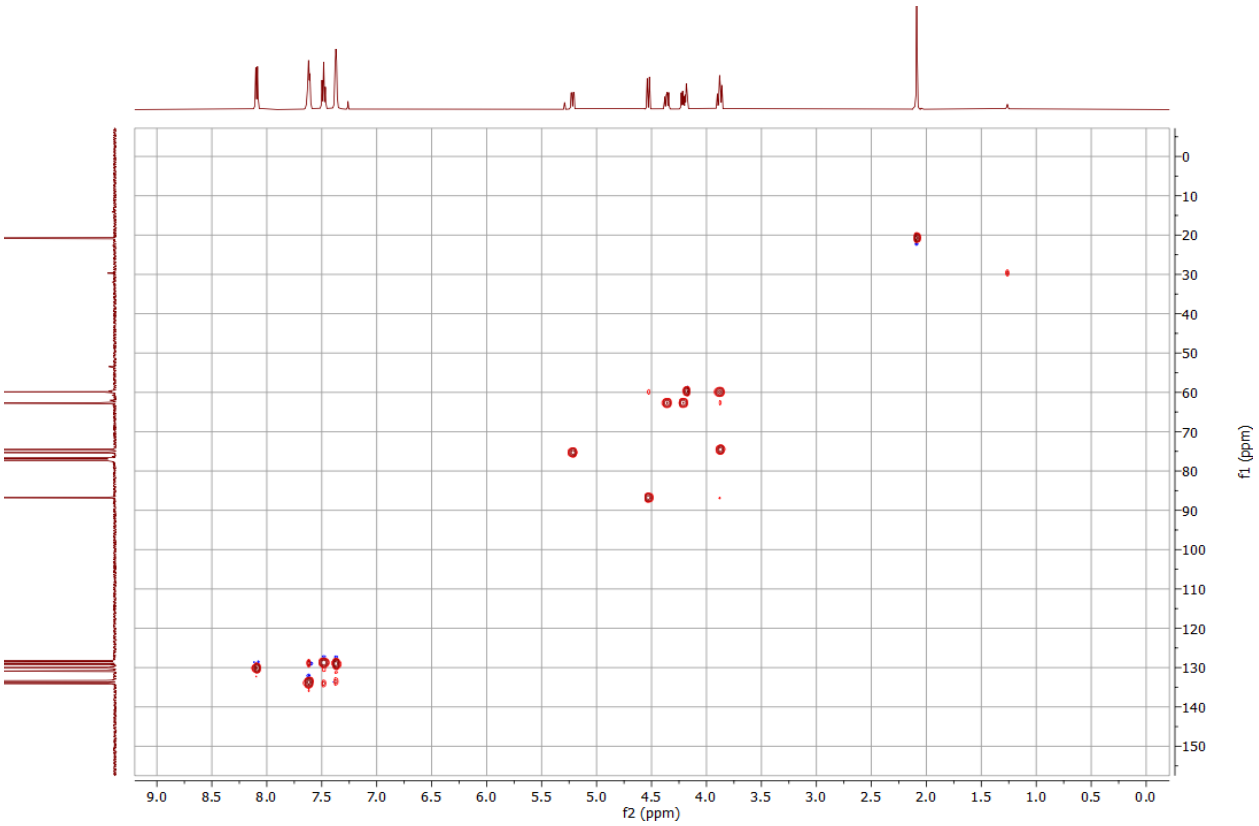

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 11

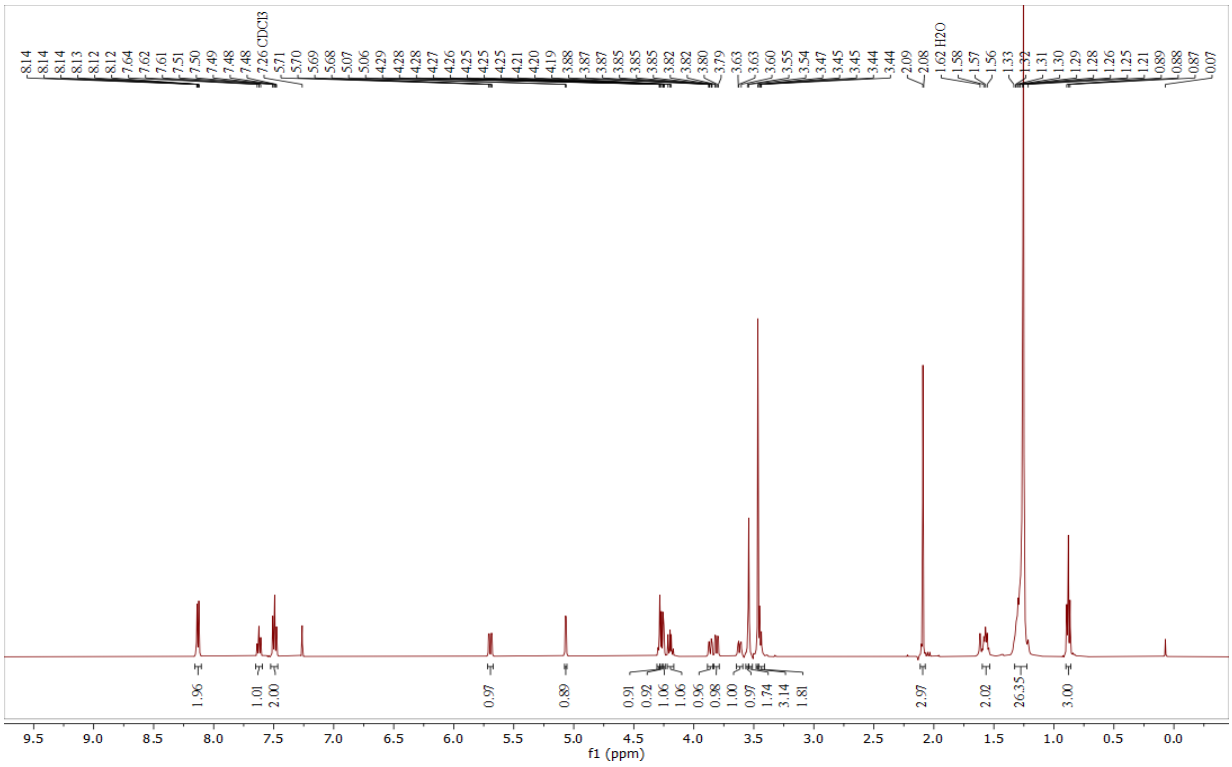


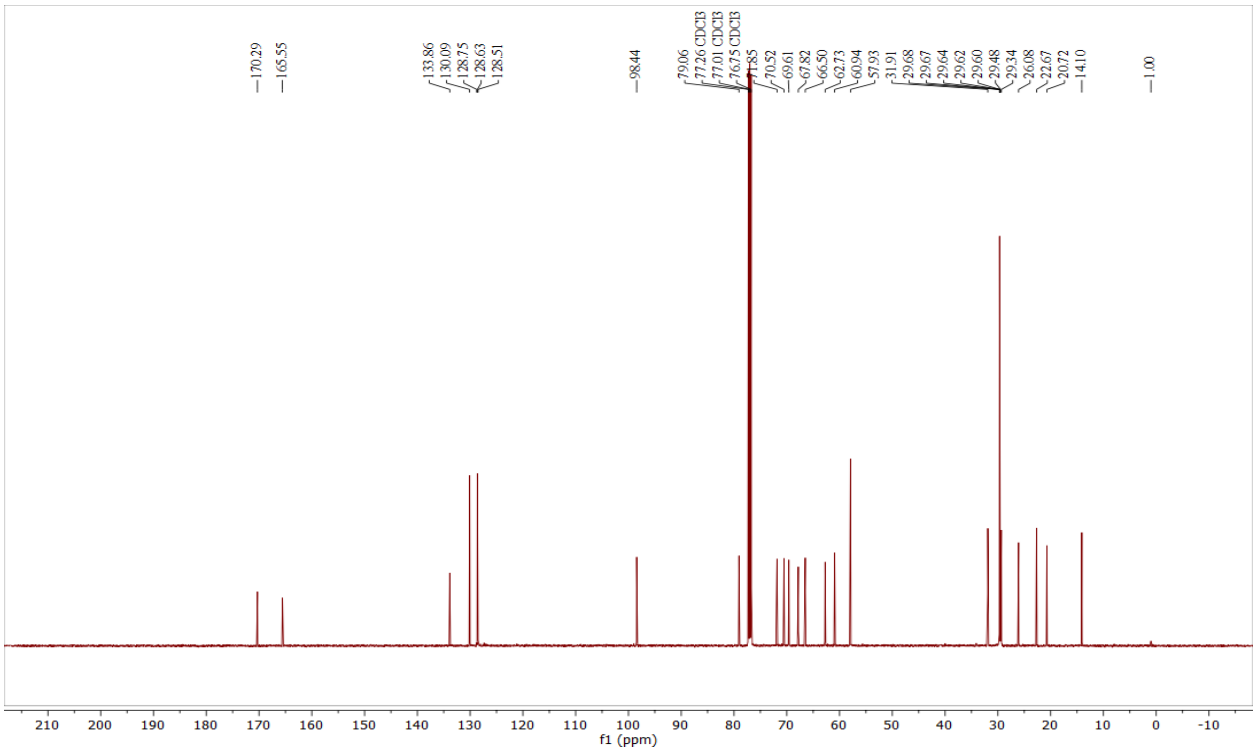


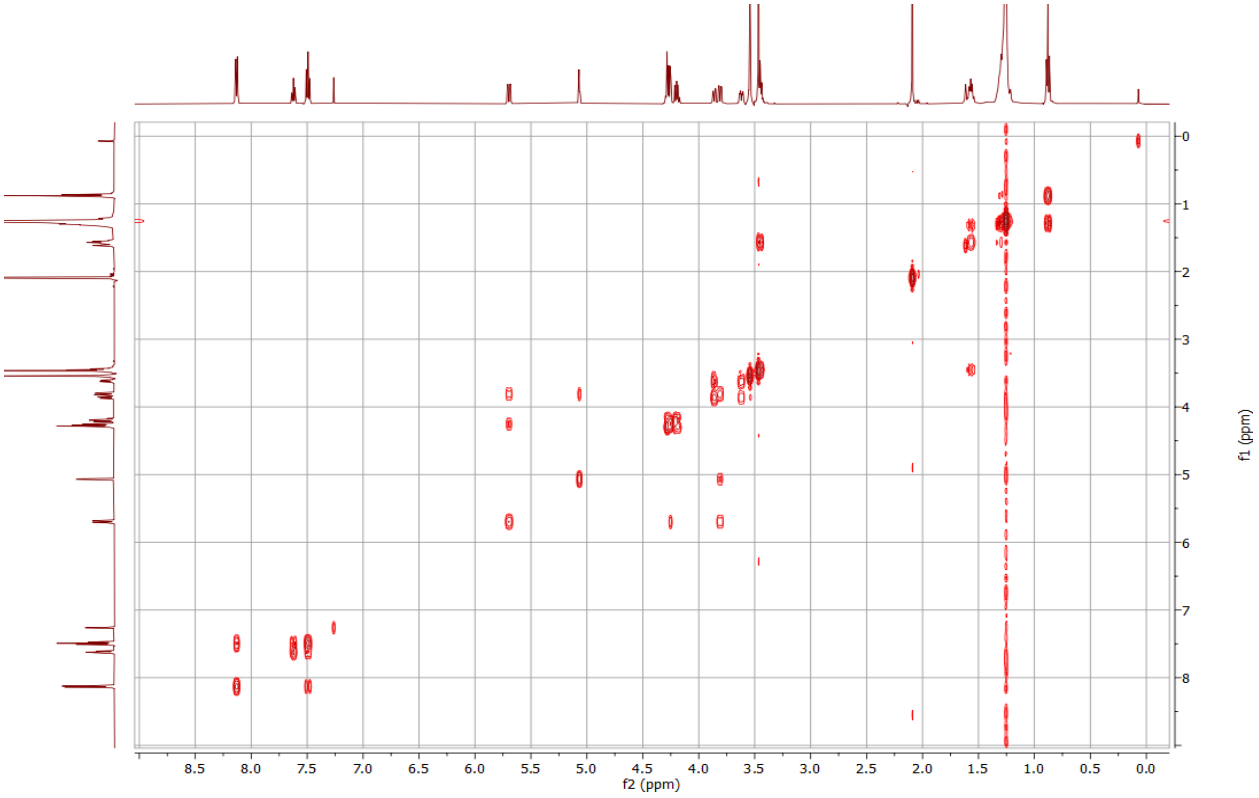

f2 (ppm)
f1 (ppm)

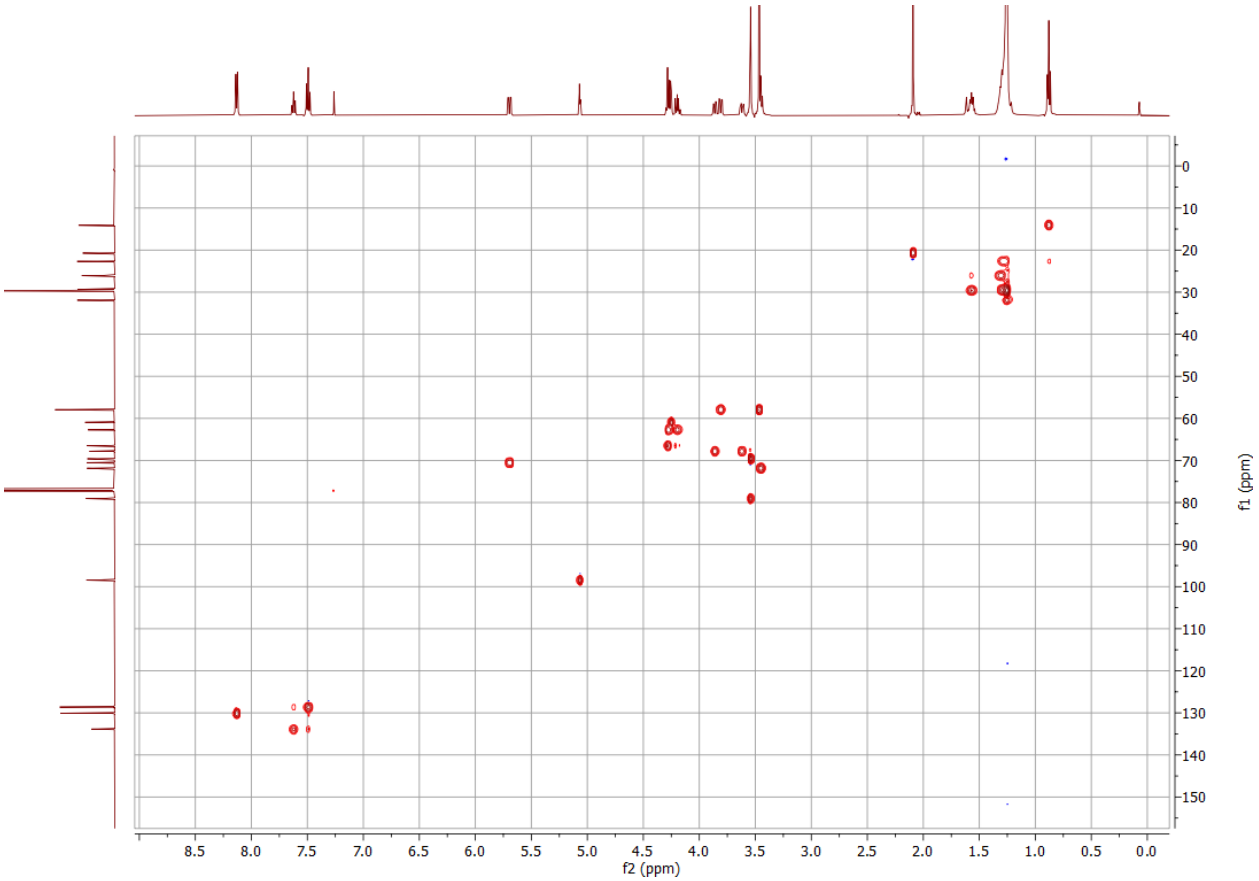

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 12a

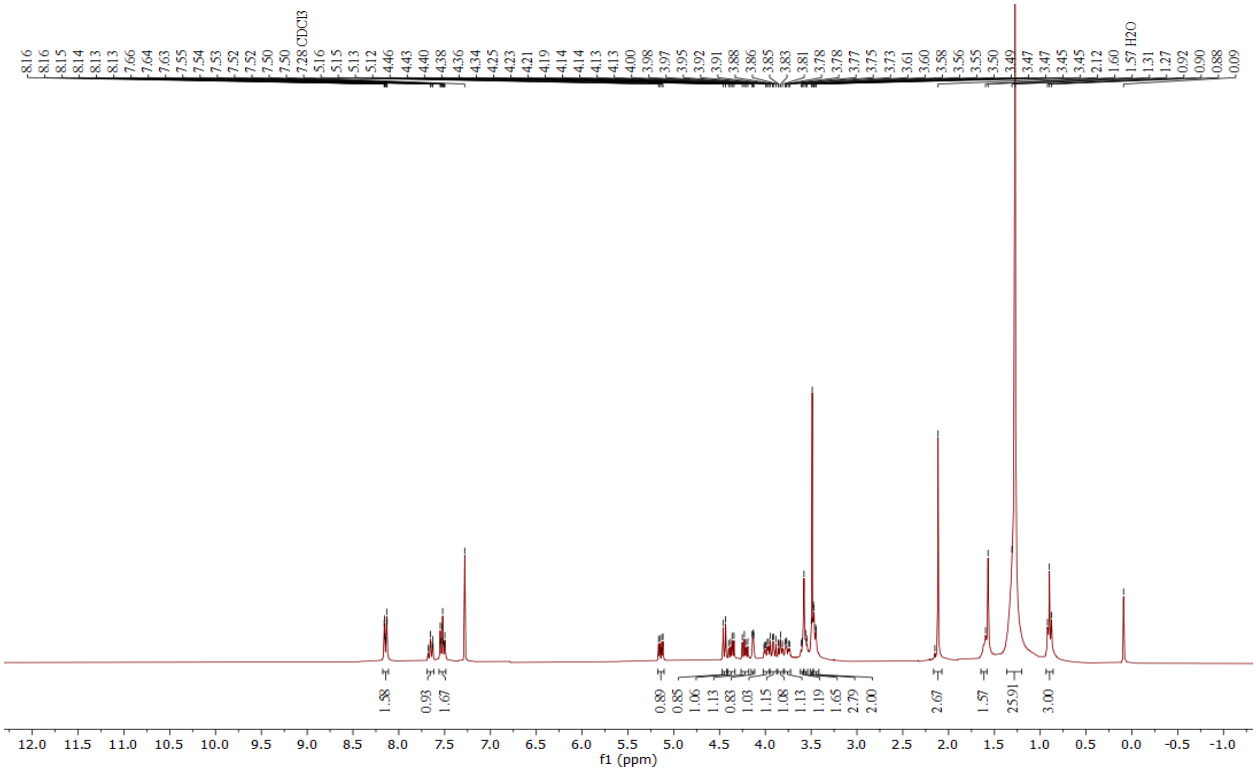


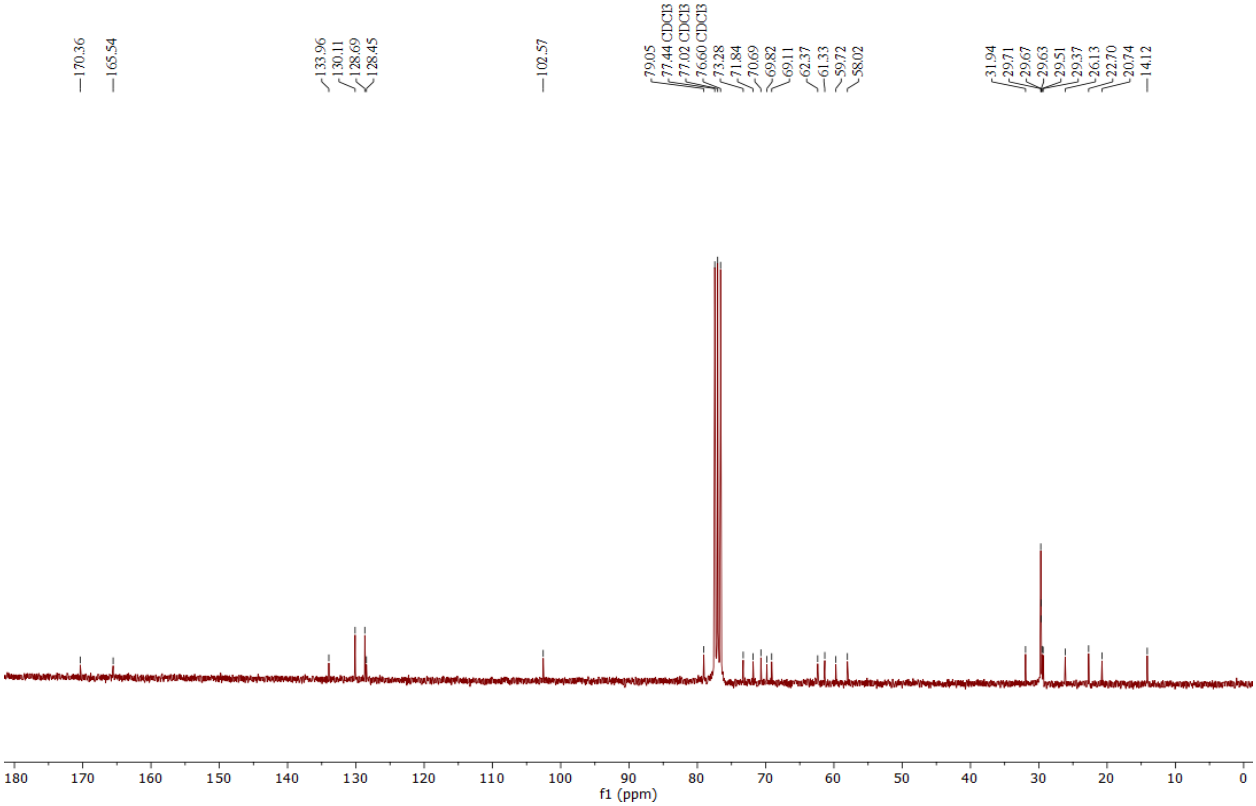


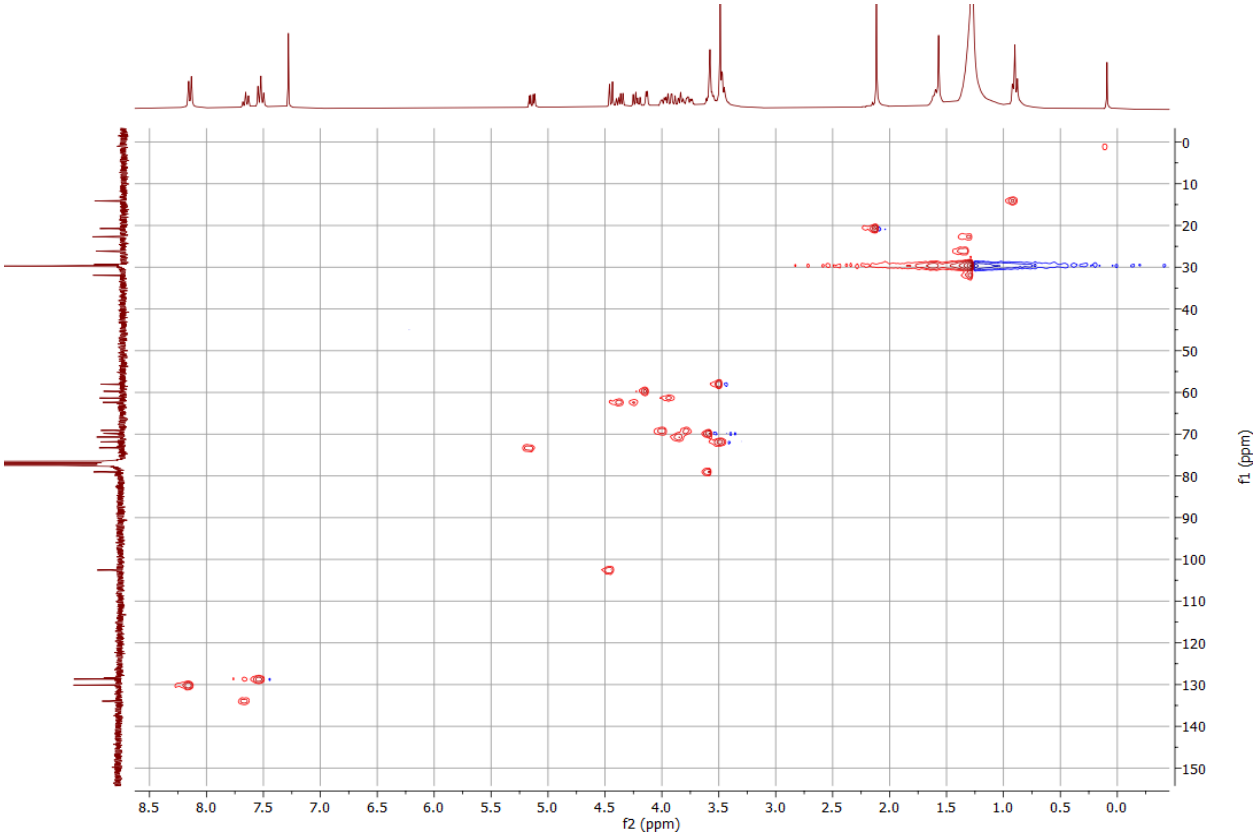

f2 (ppm)
f1 (ppm)

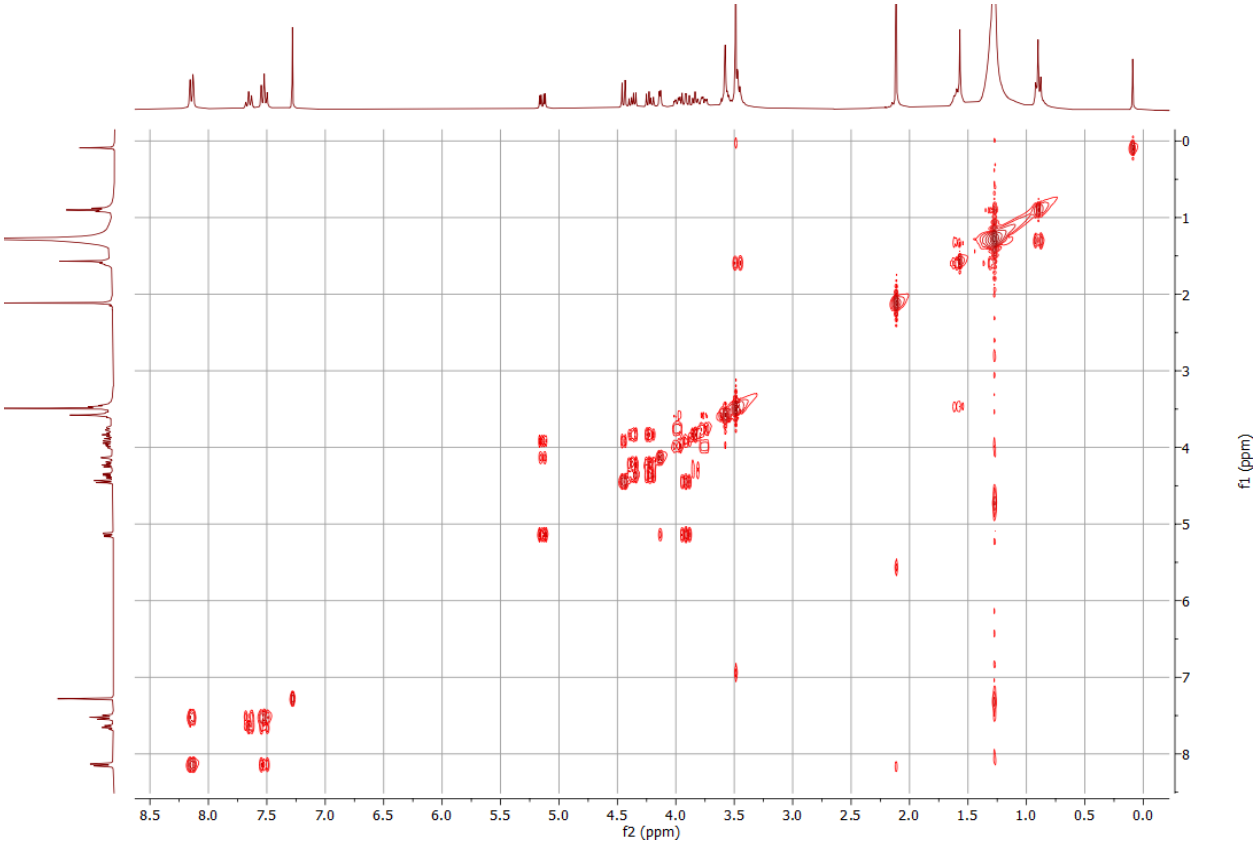

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 12b

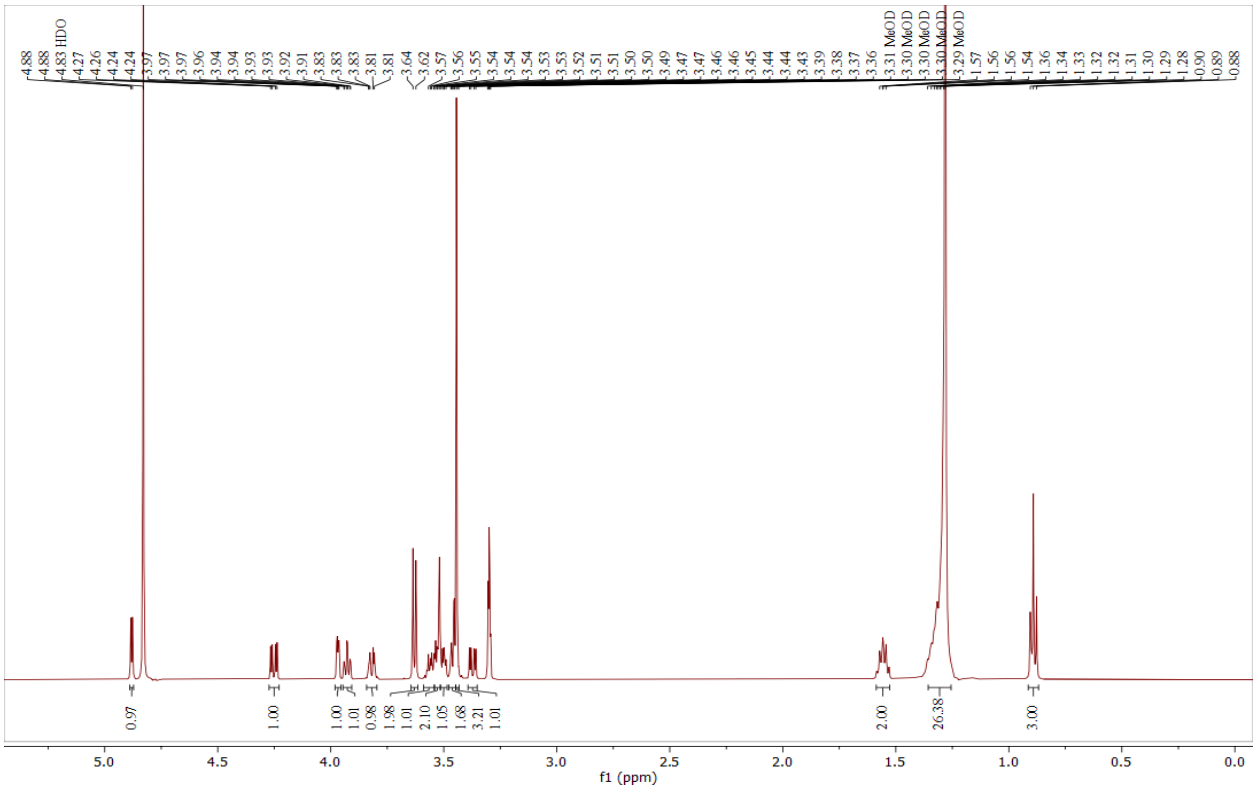


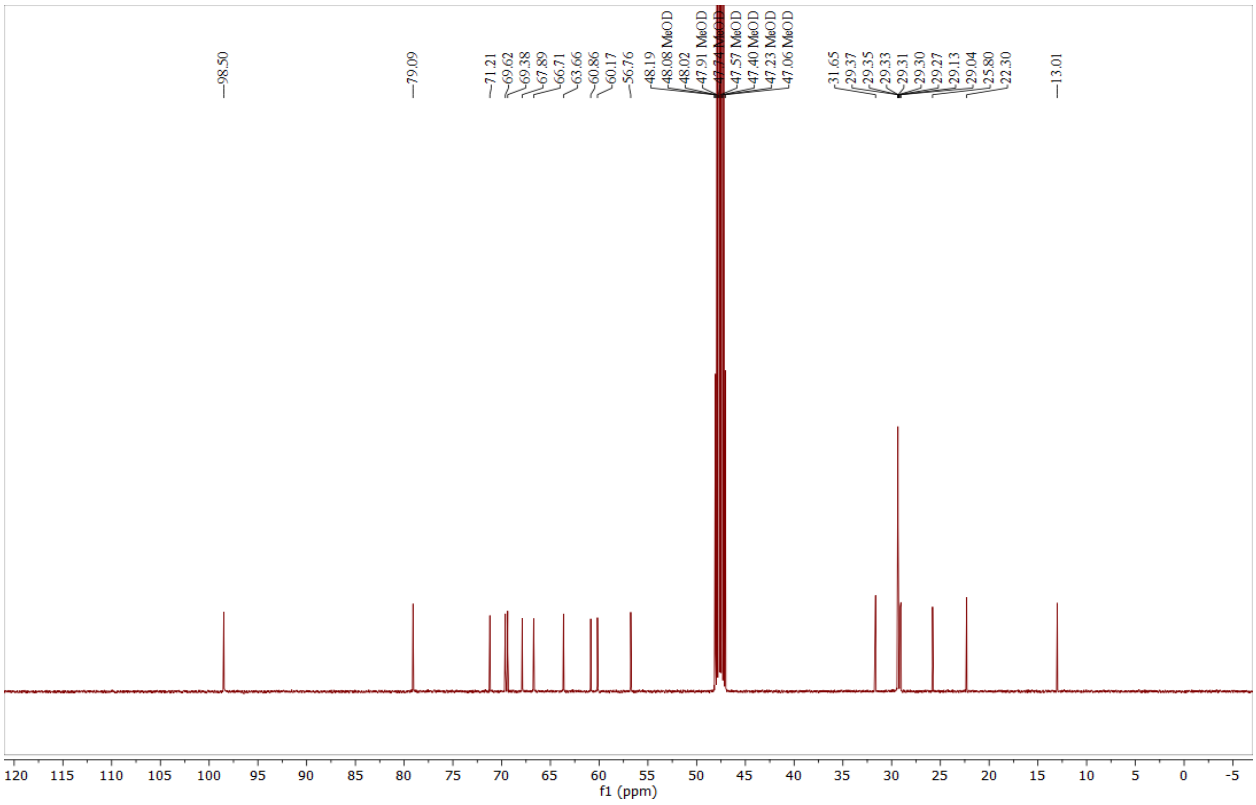


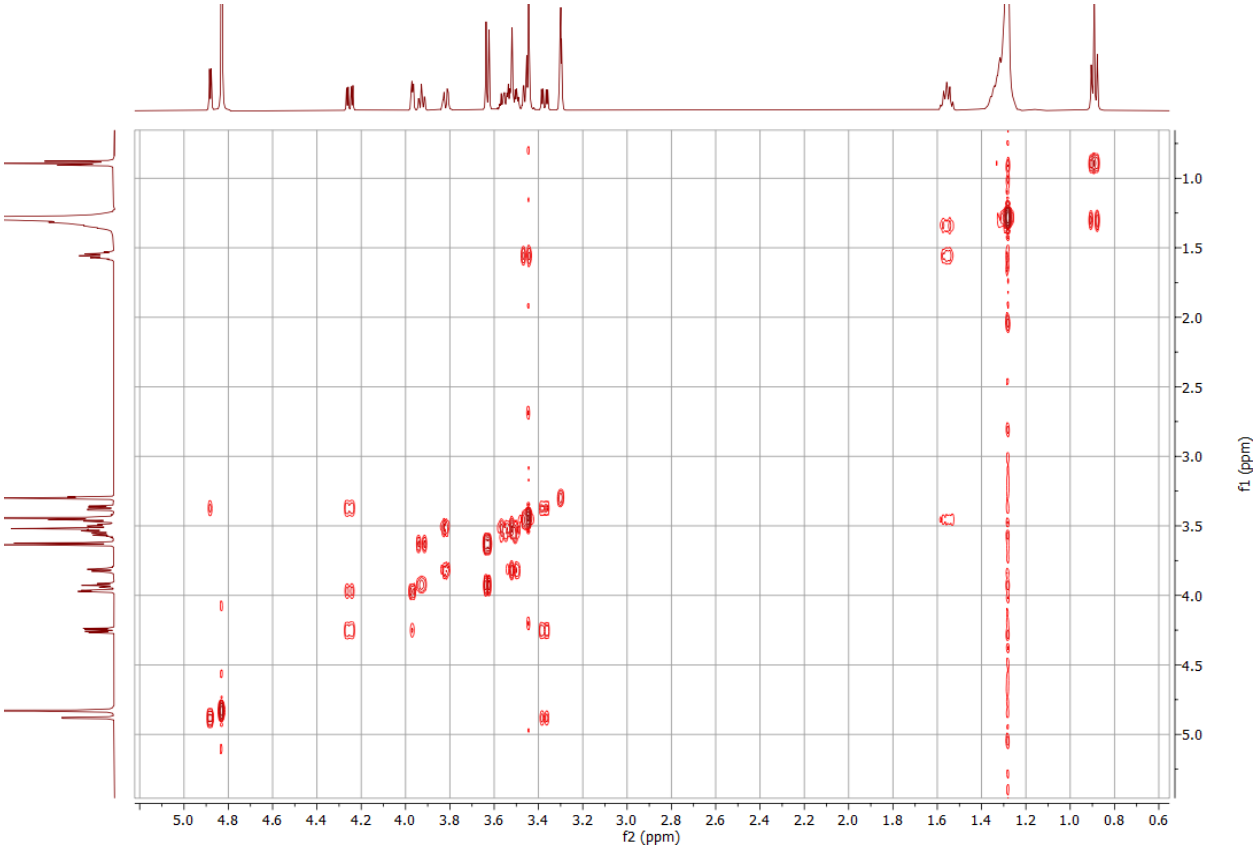

f2 (ppm)
f1 (ppm)

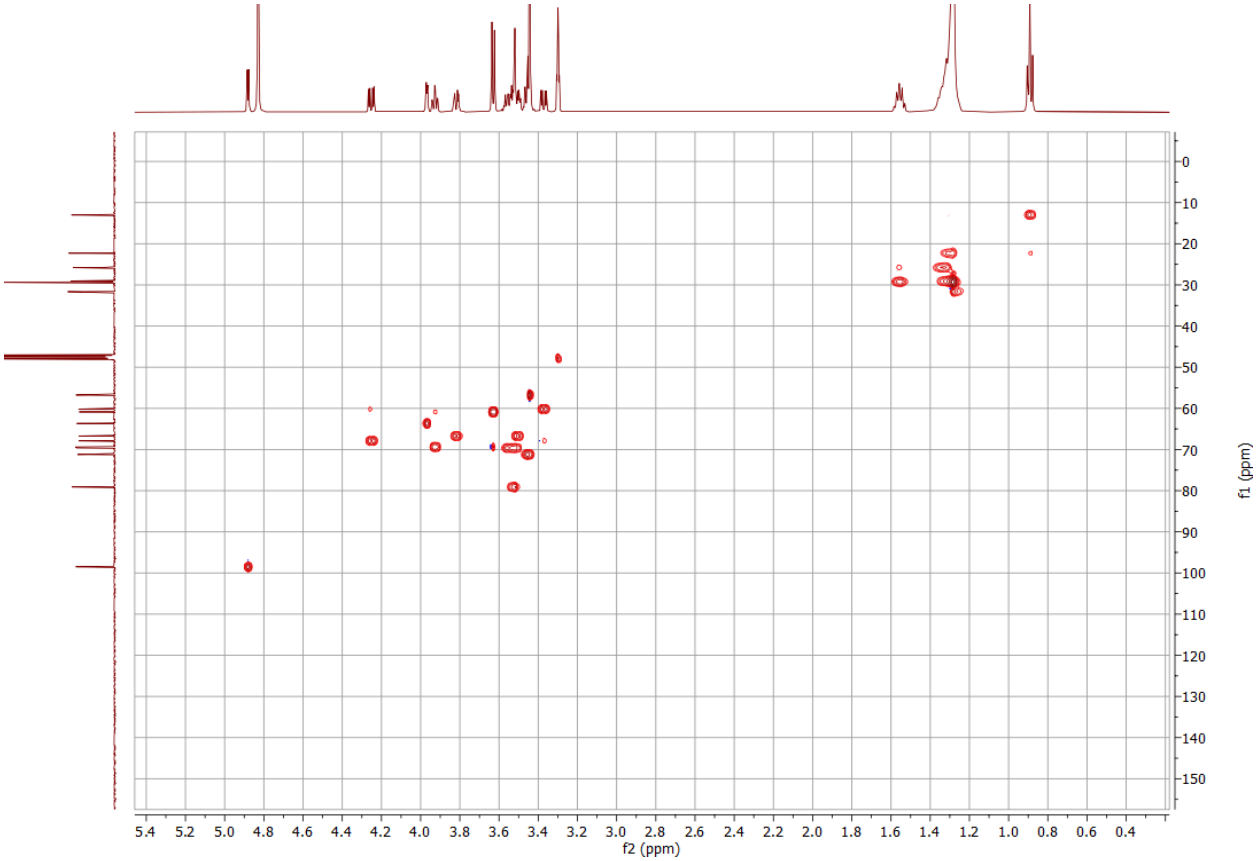

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 13a

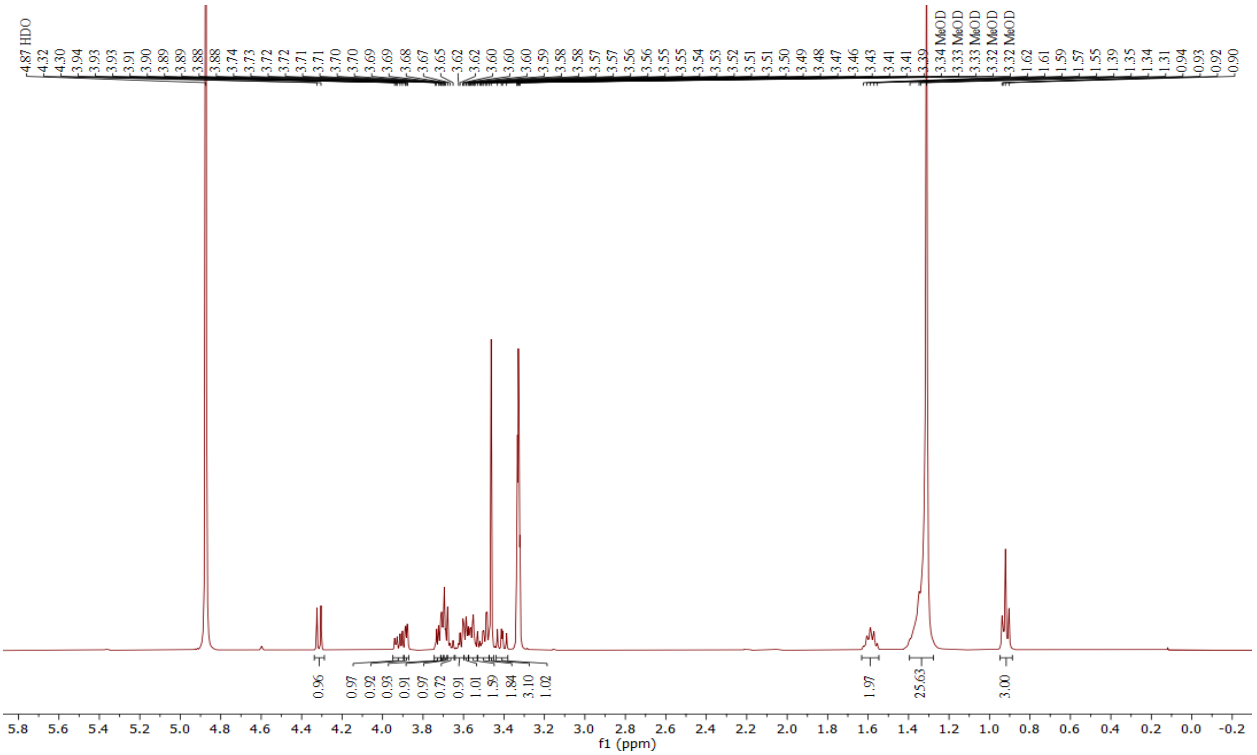


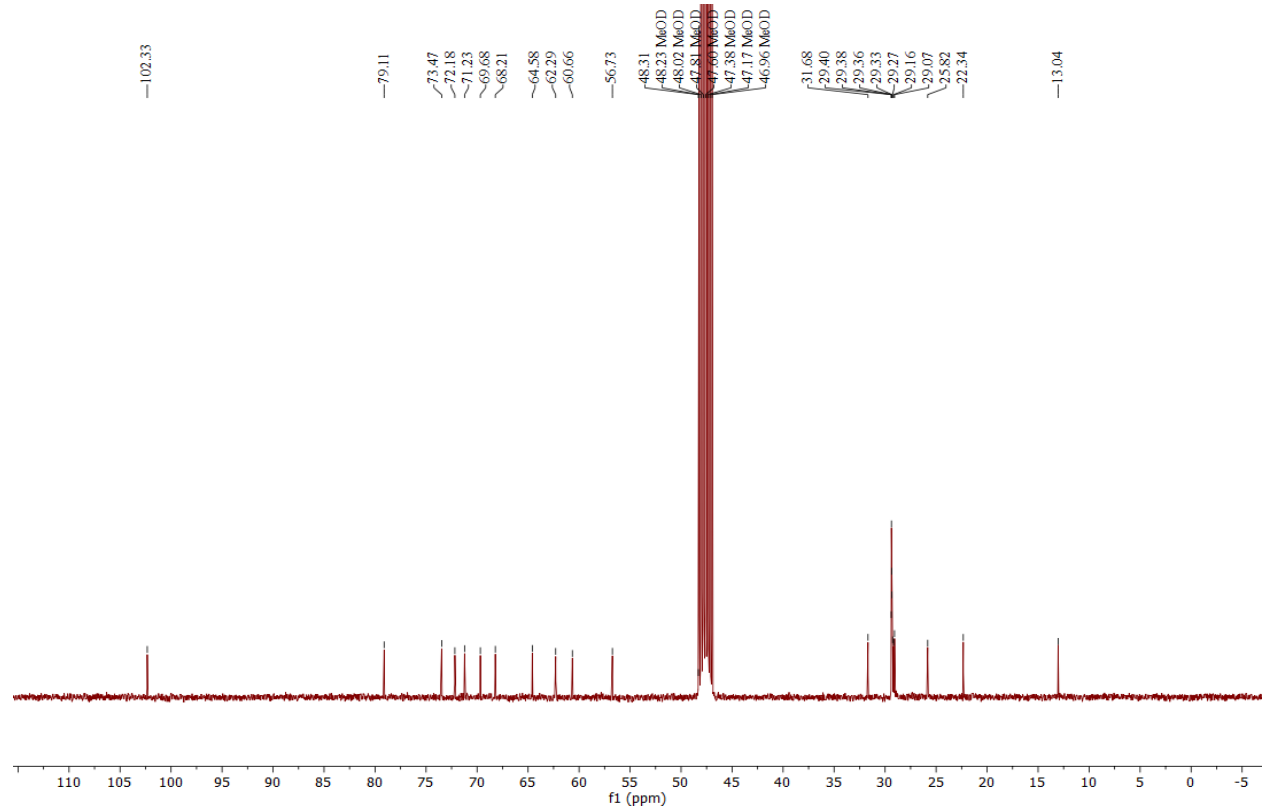


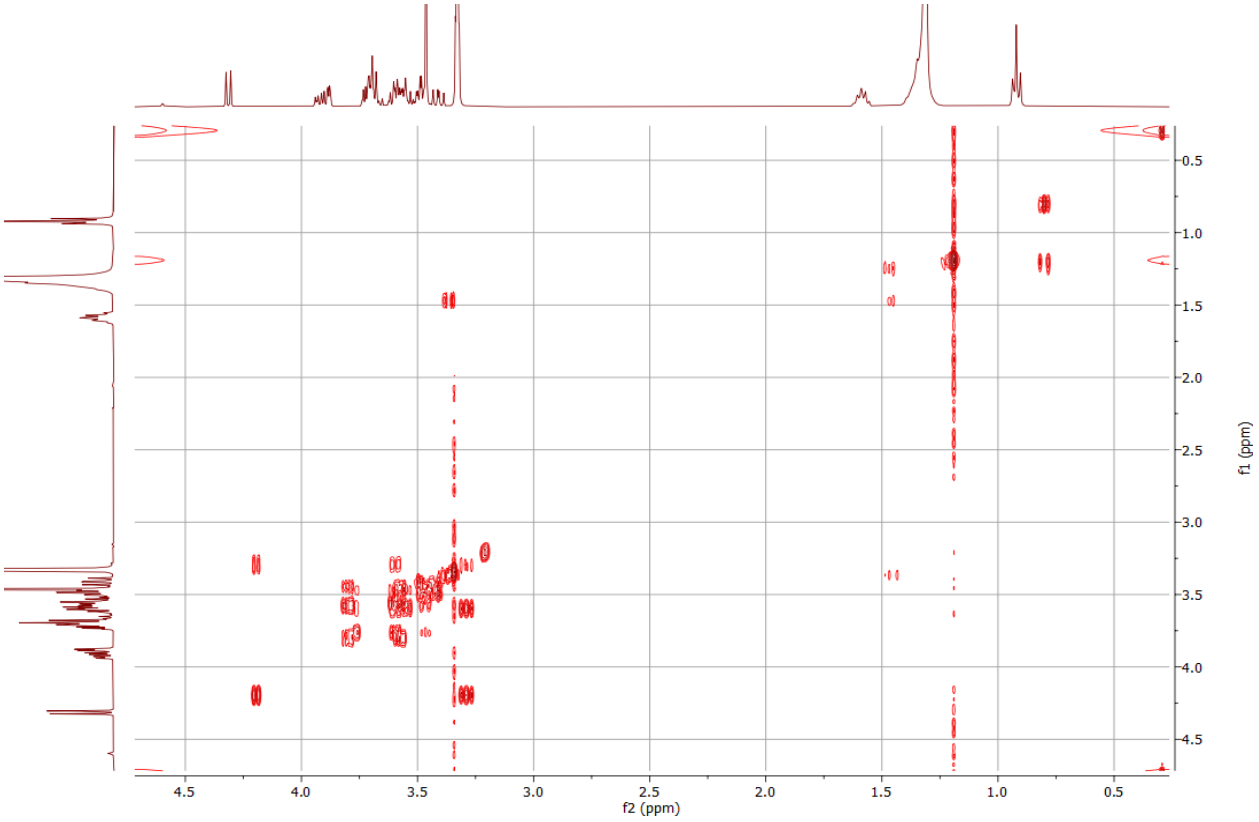

f2 (ppm)
f1 (ppm)

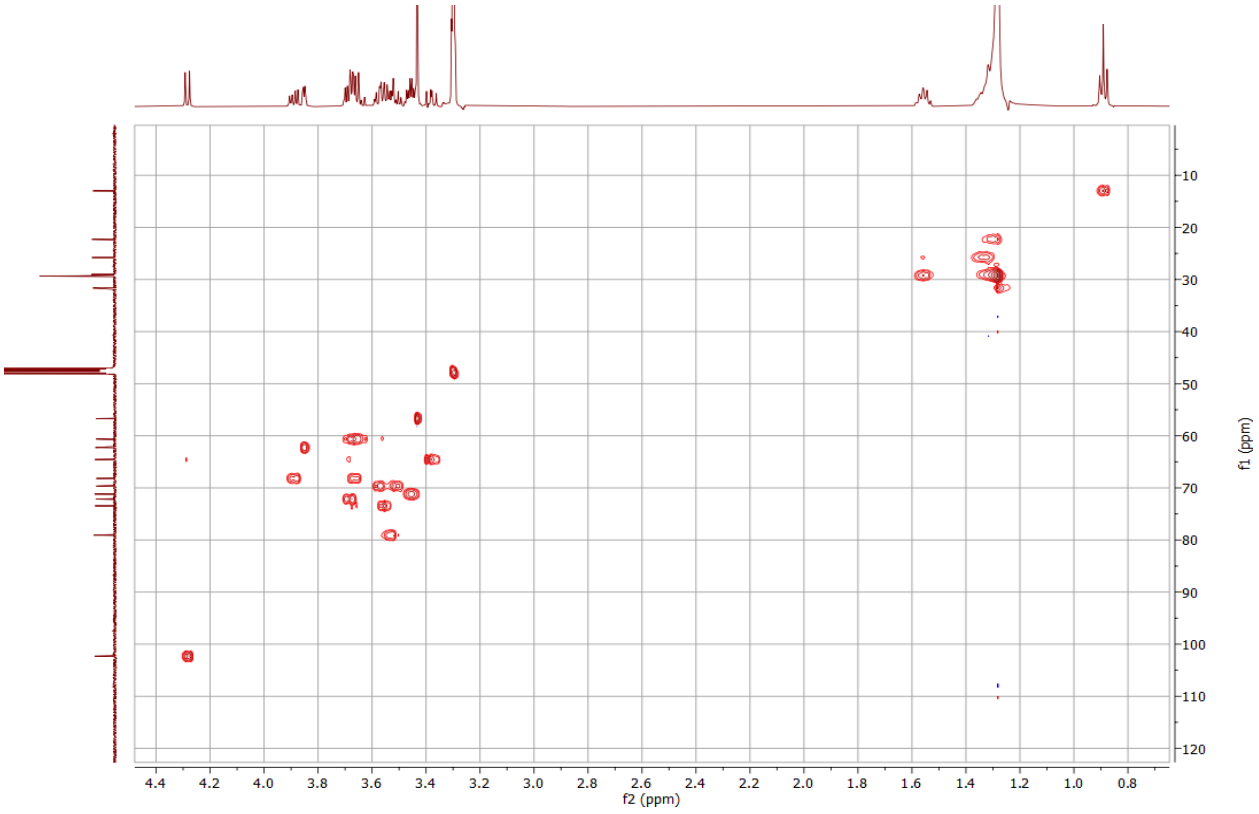

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 13b

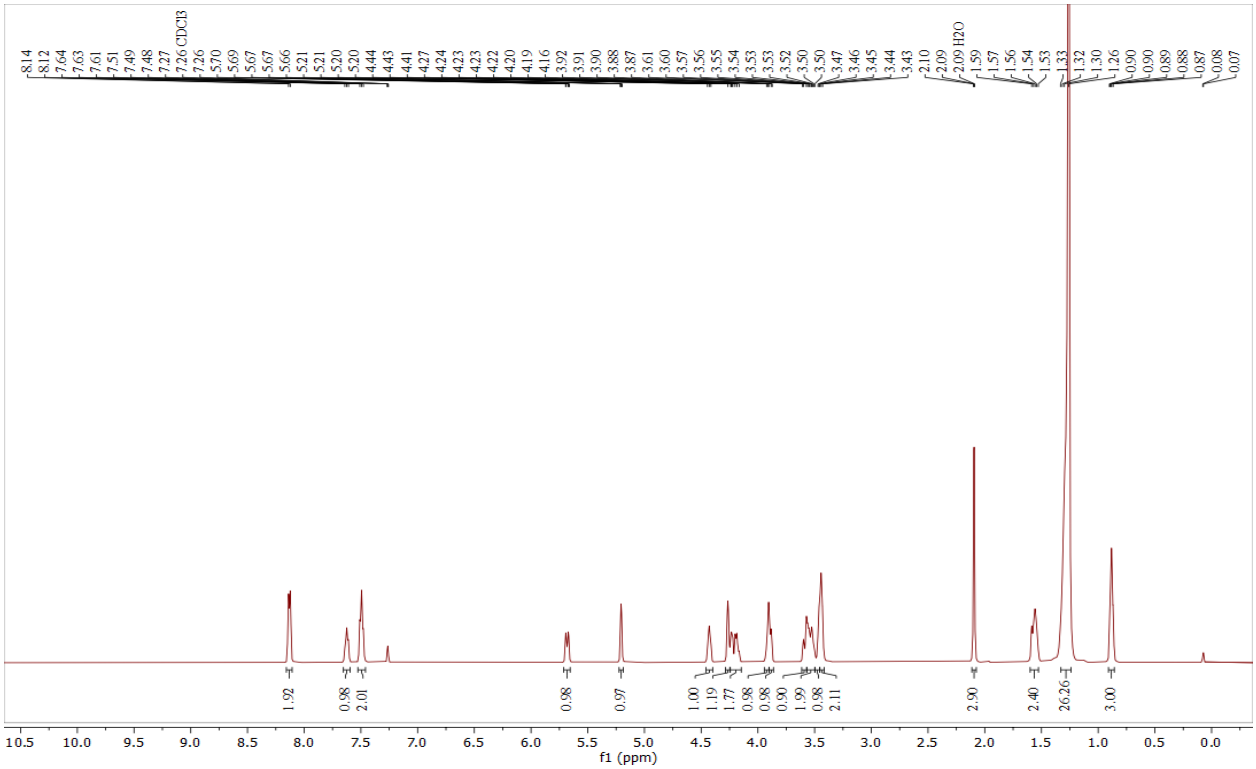


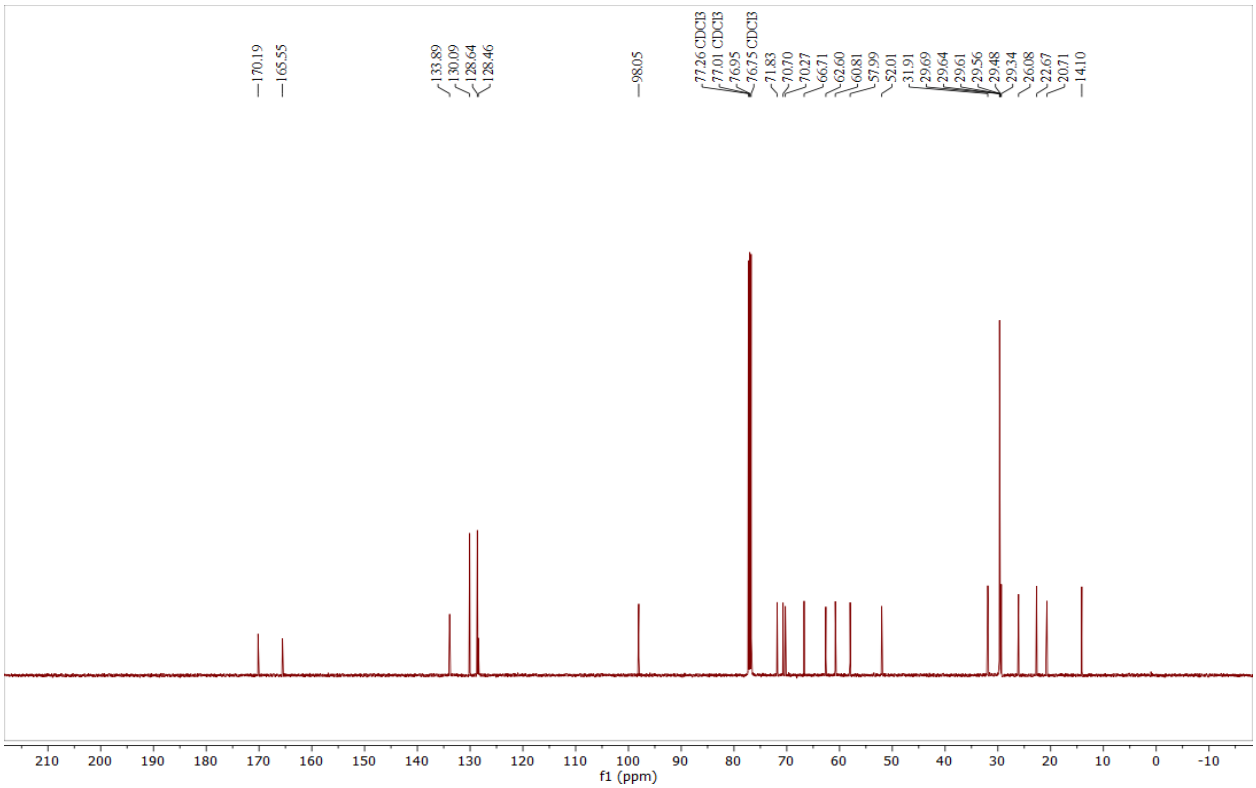


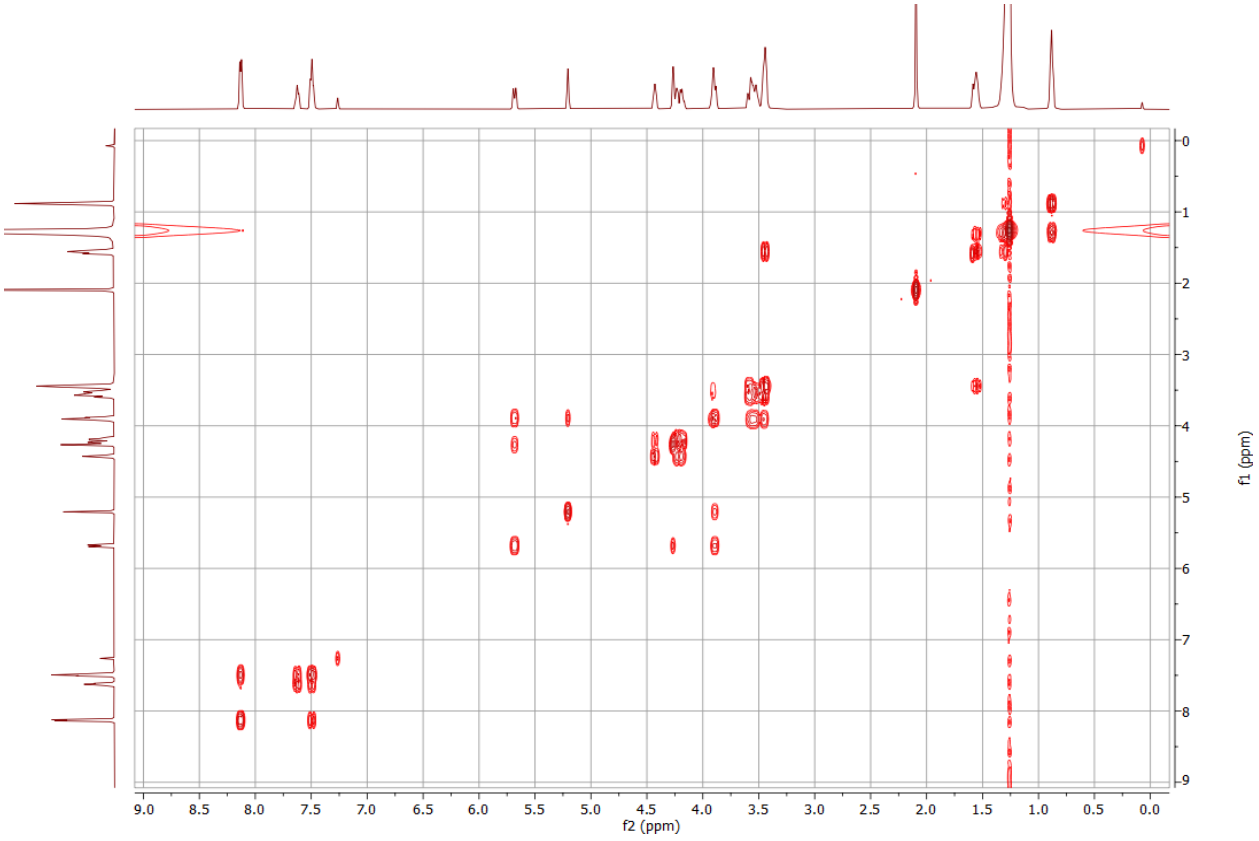

0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)

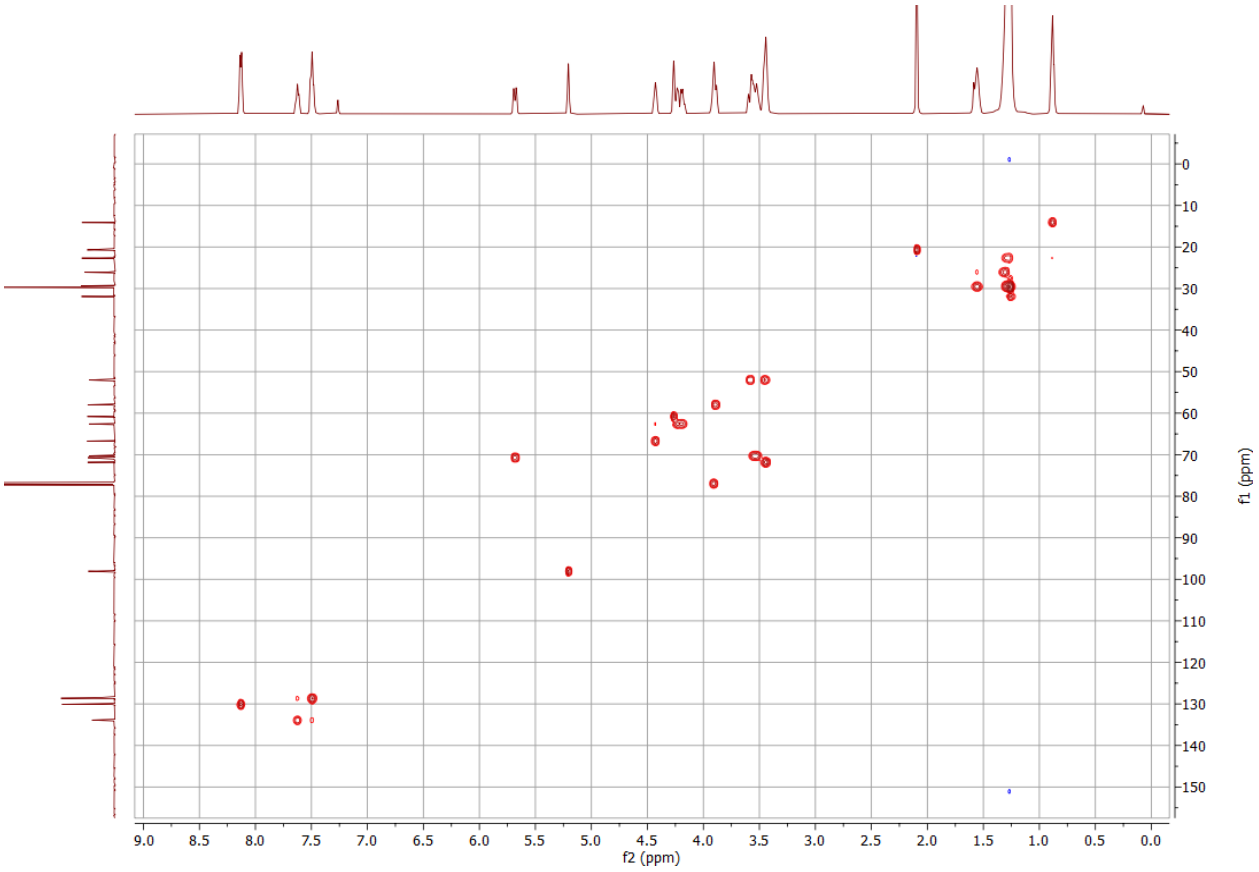

10
20
30
40
50
60
70
80
90
100
110
120
f1 (ppm)
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
f2 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 15a

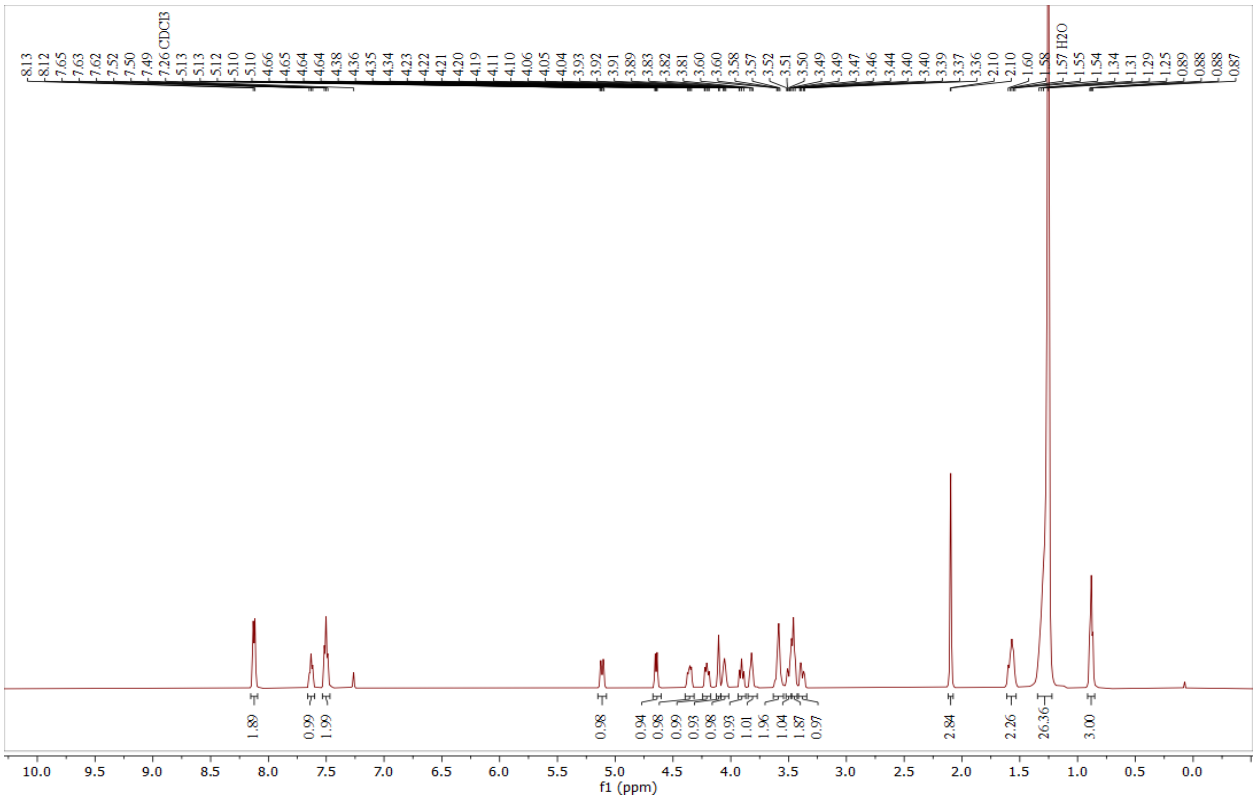


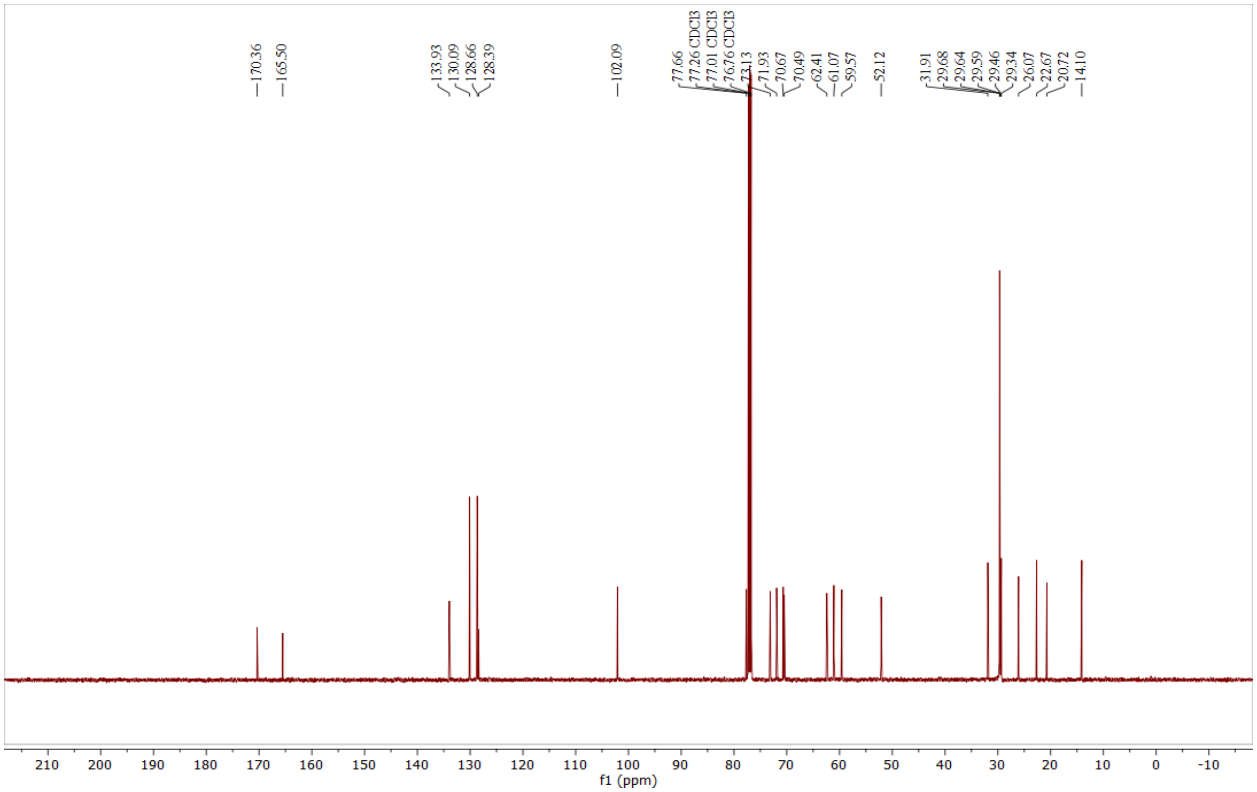


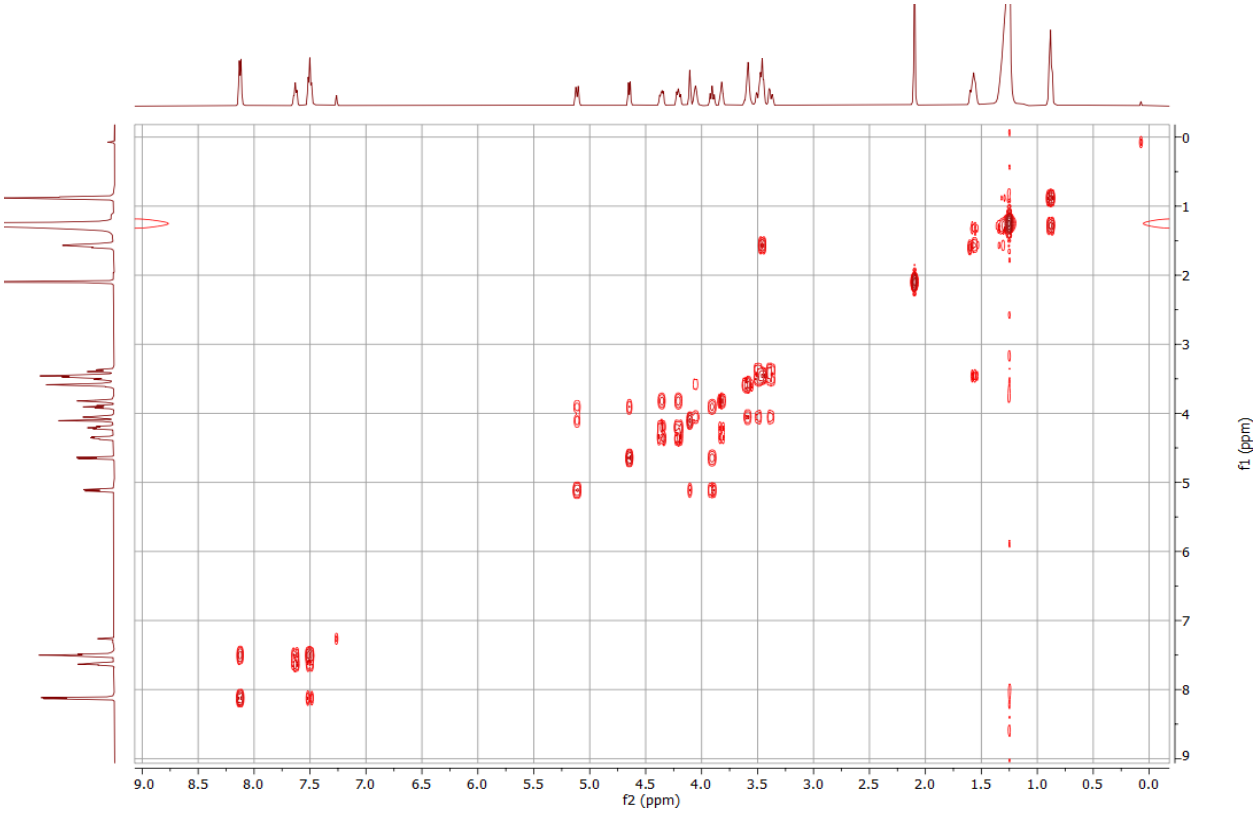

f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 15b



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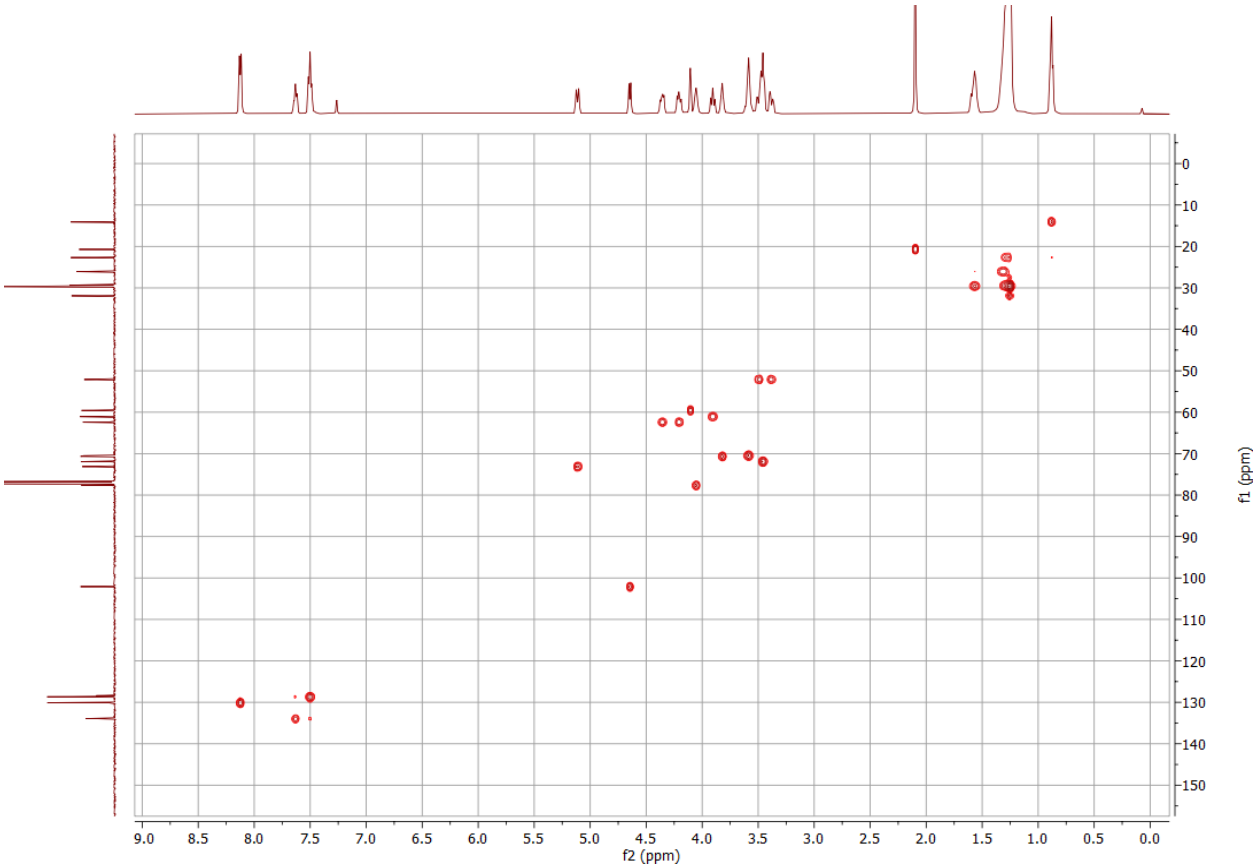
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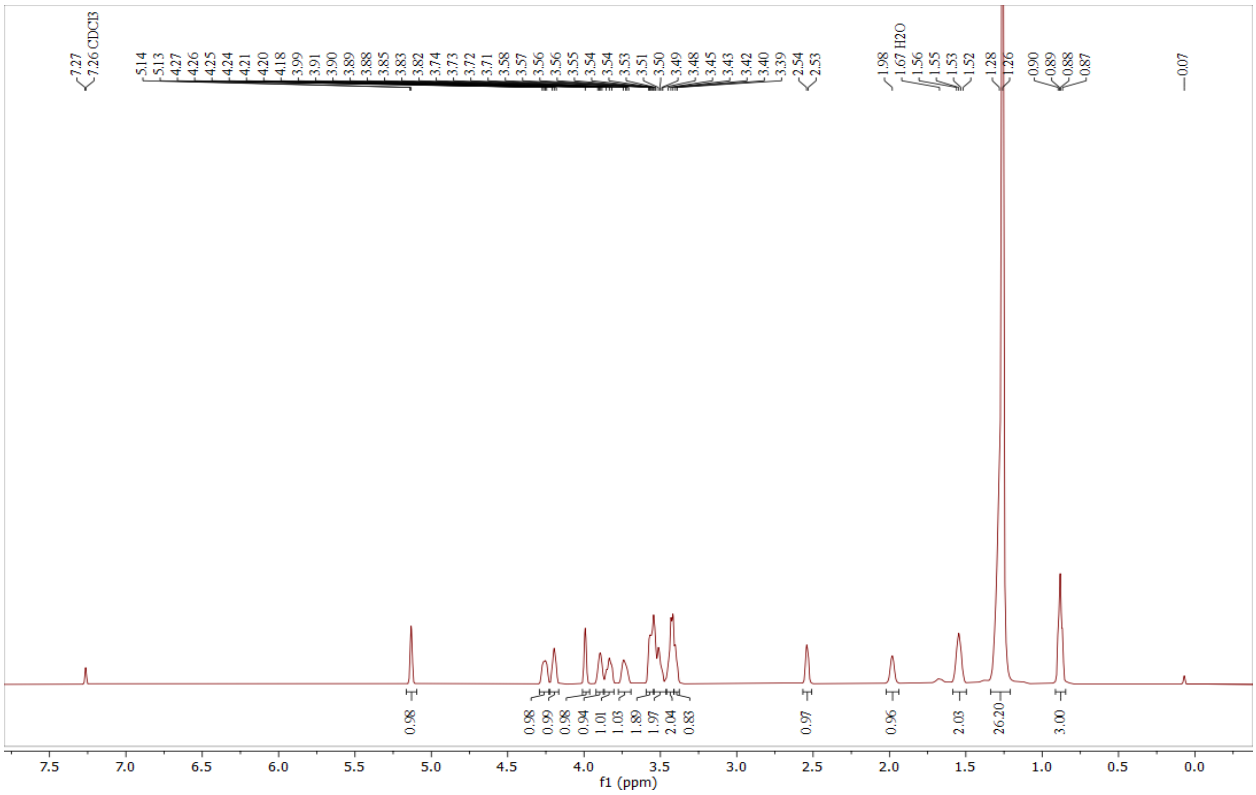
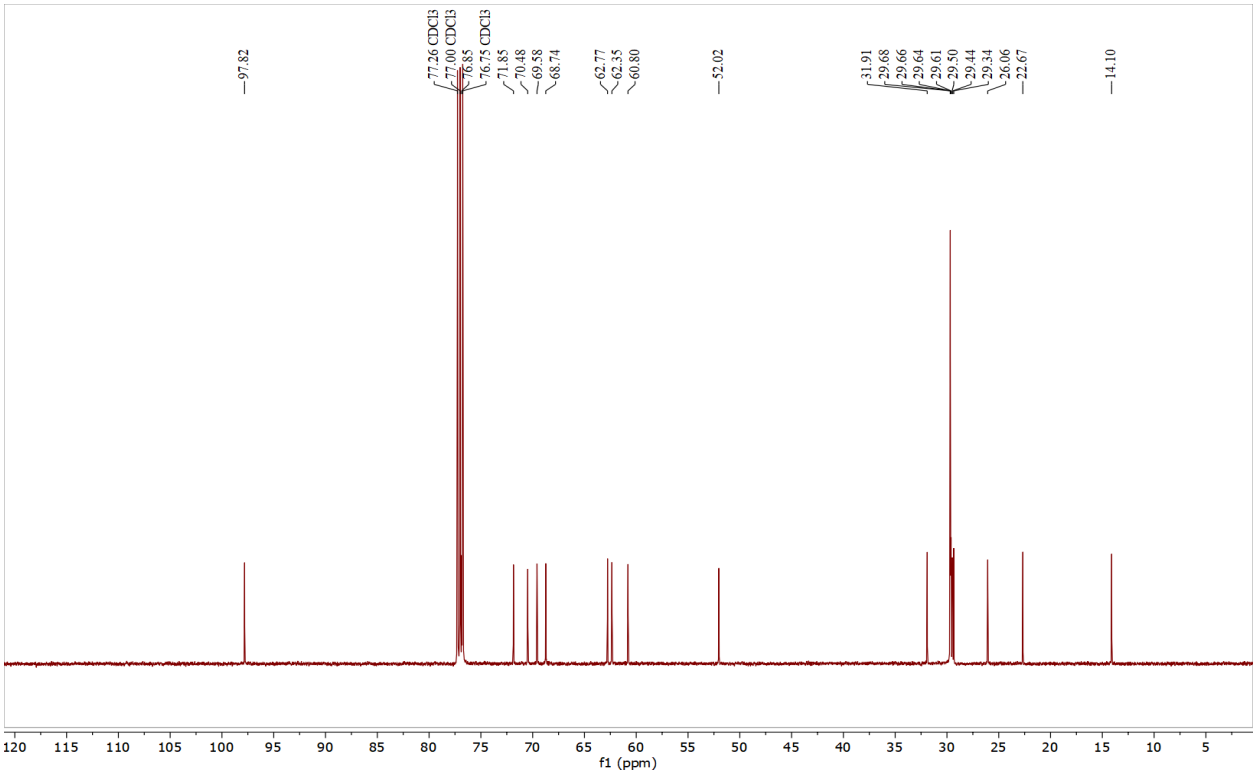
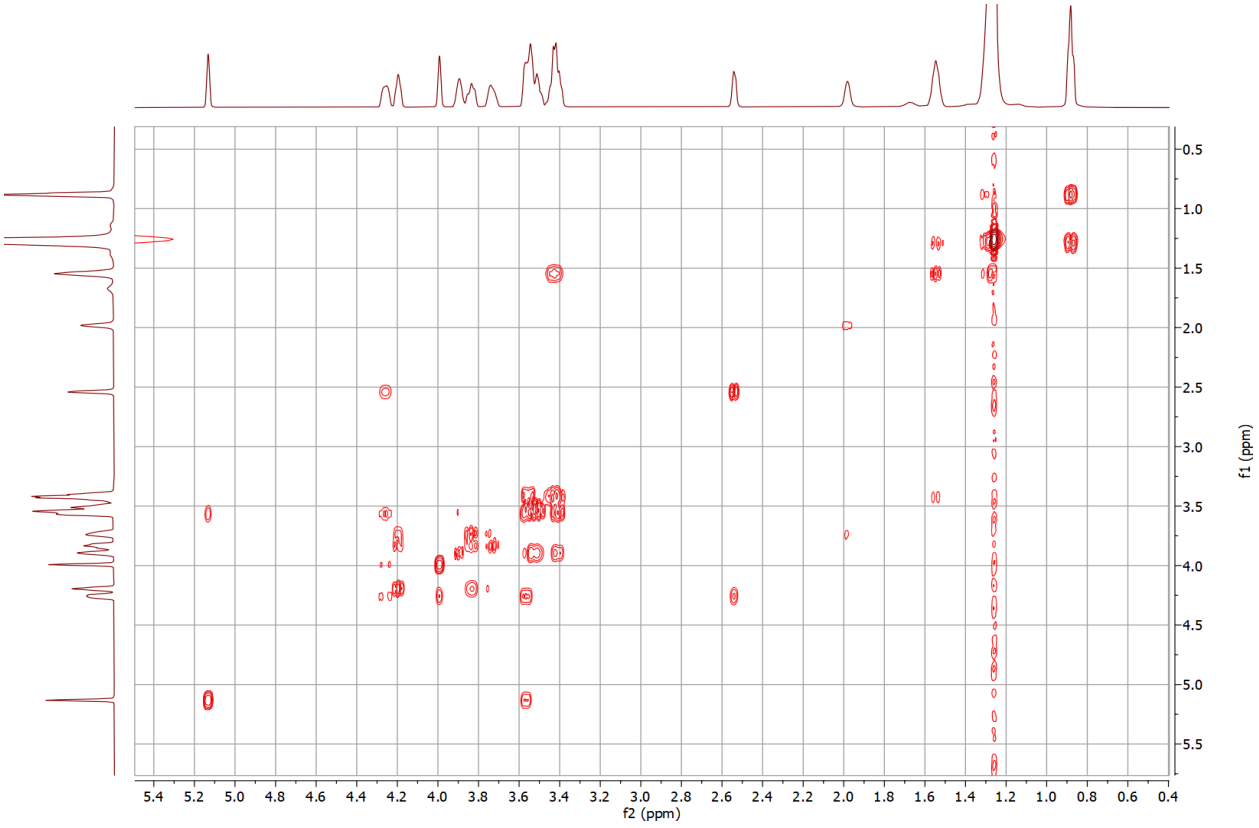
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 16a



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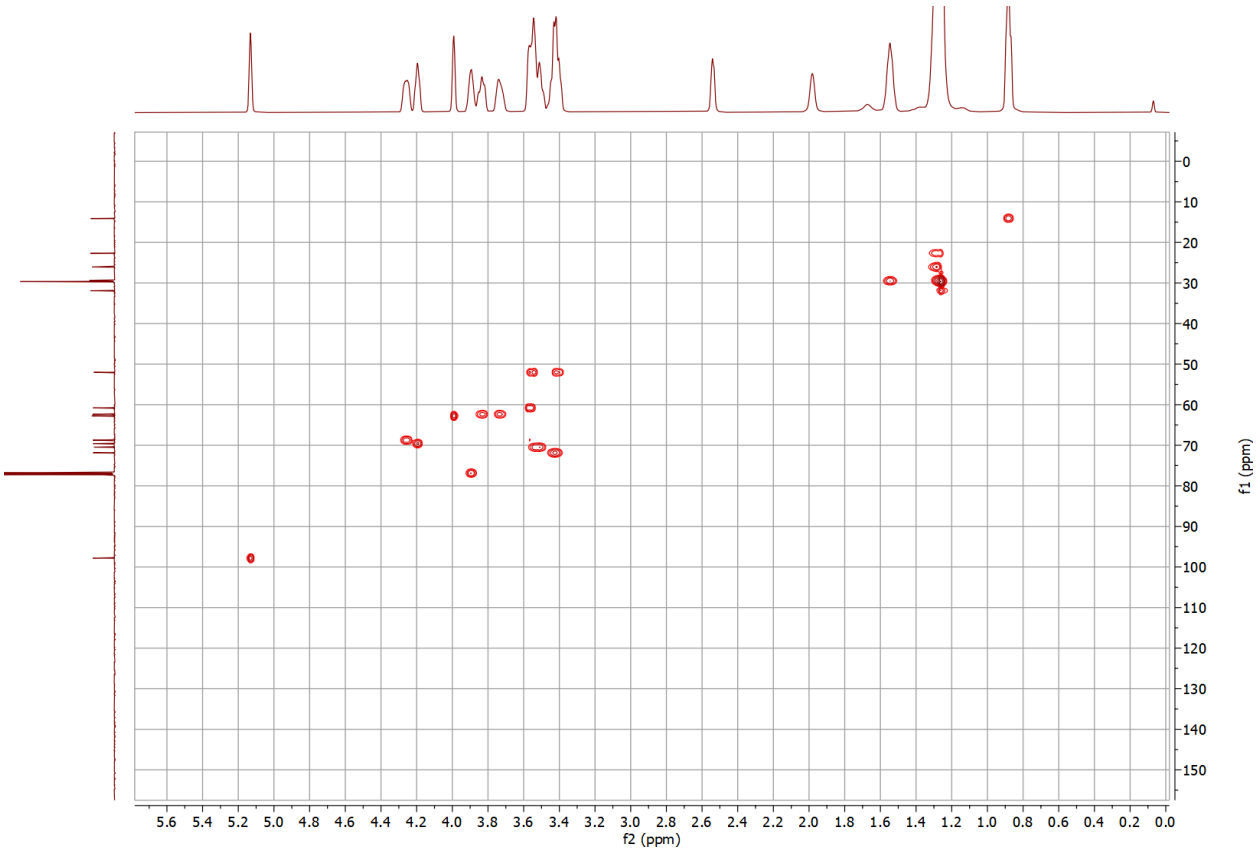
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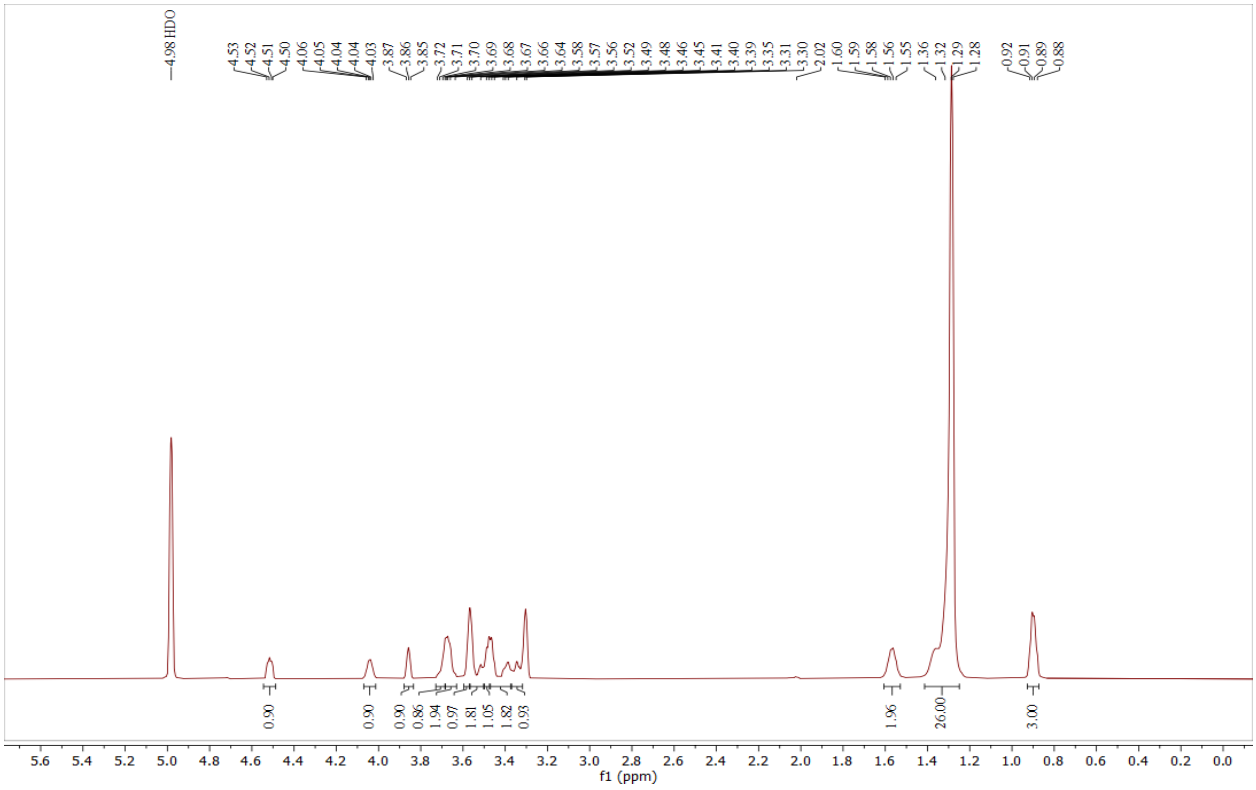
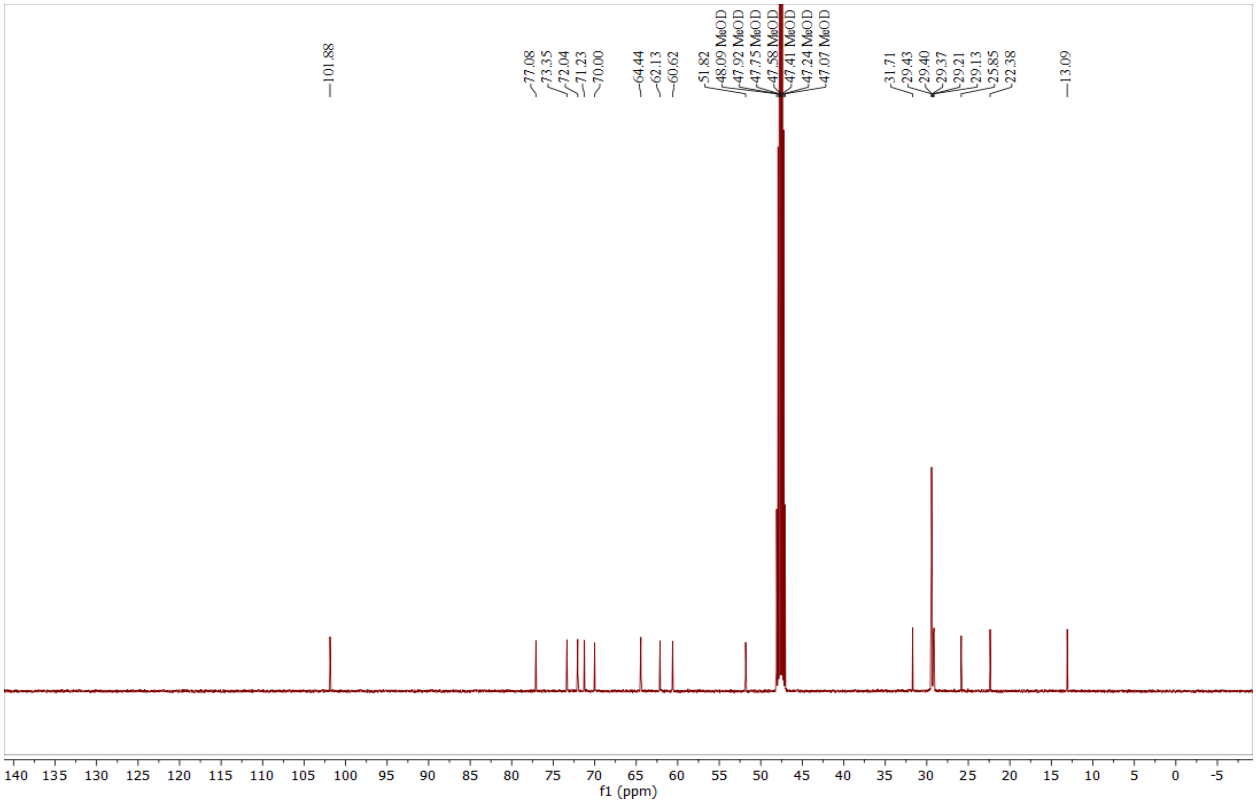
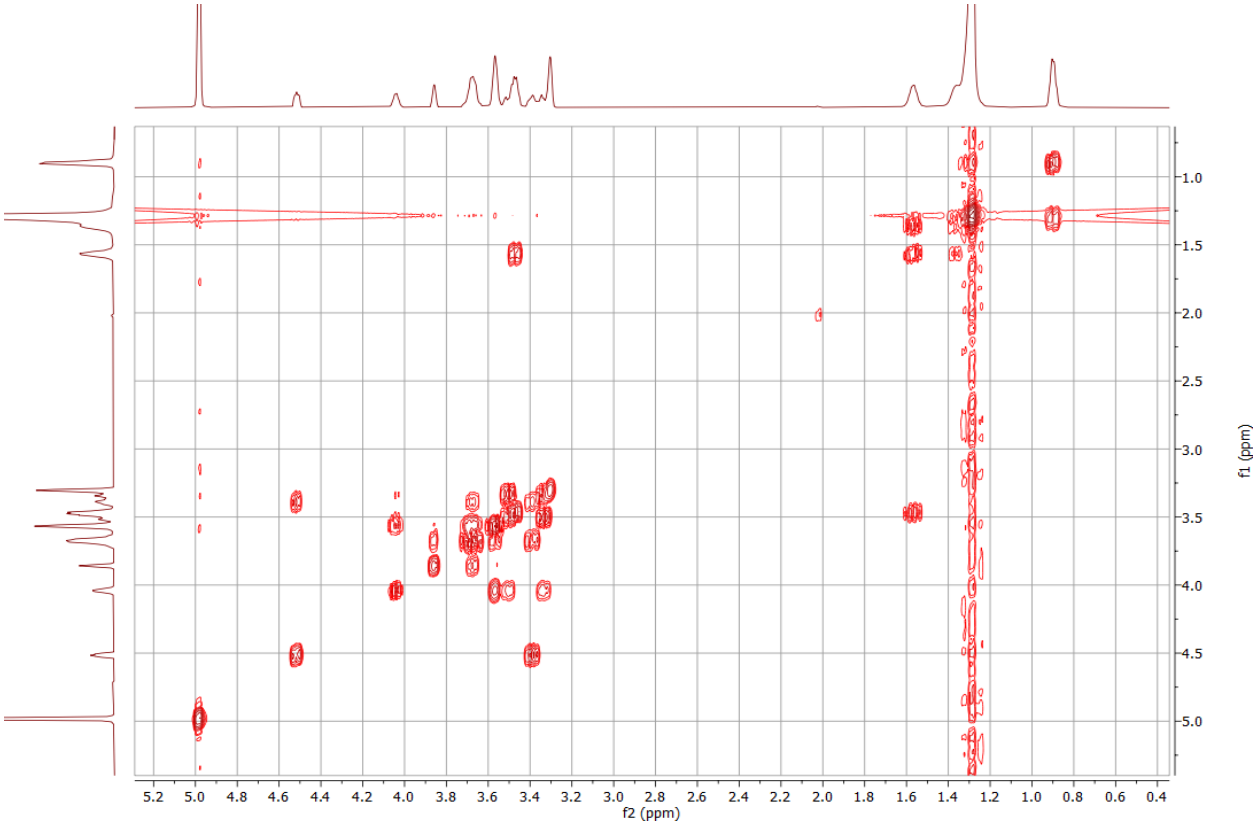
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 16b



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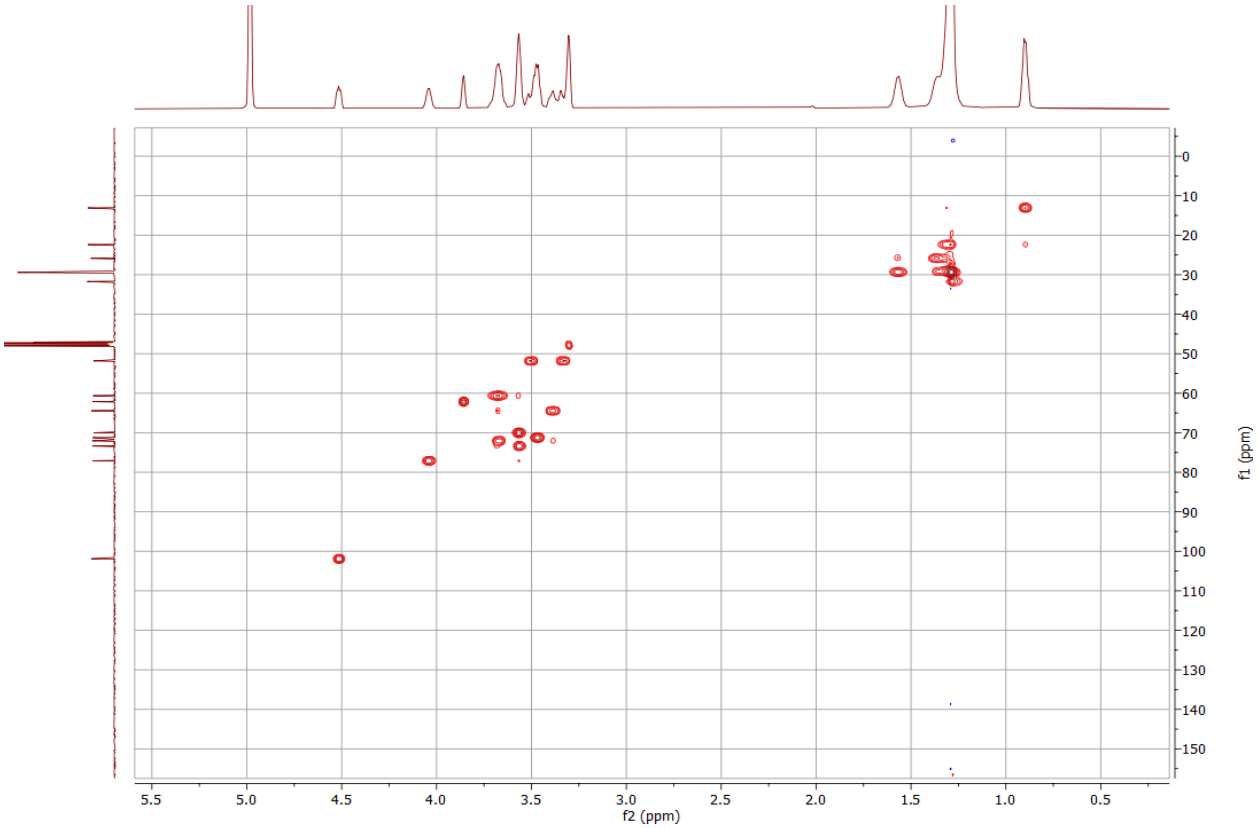
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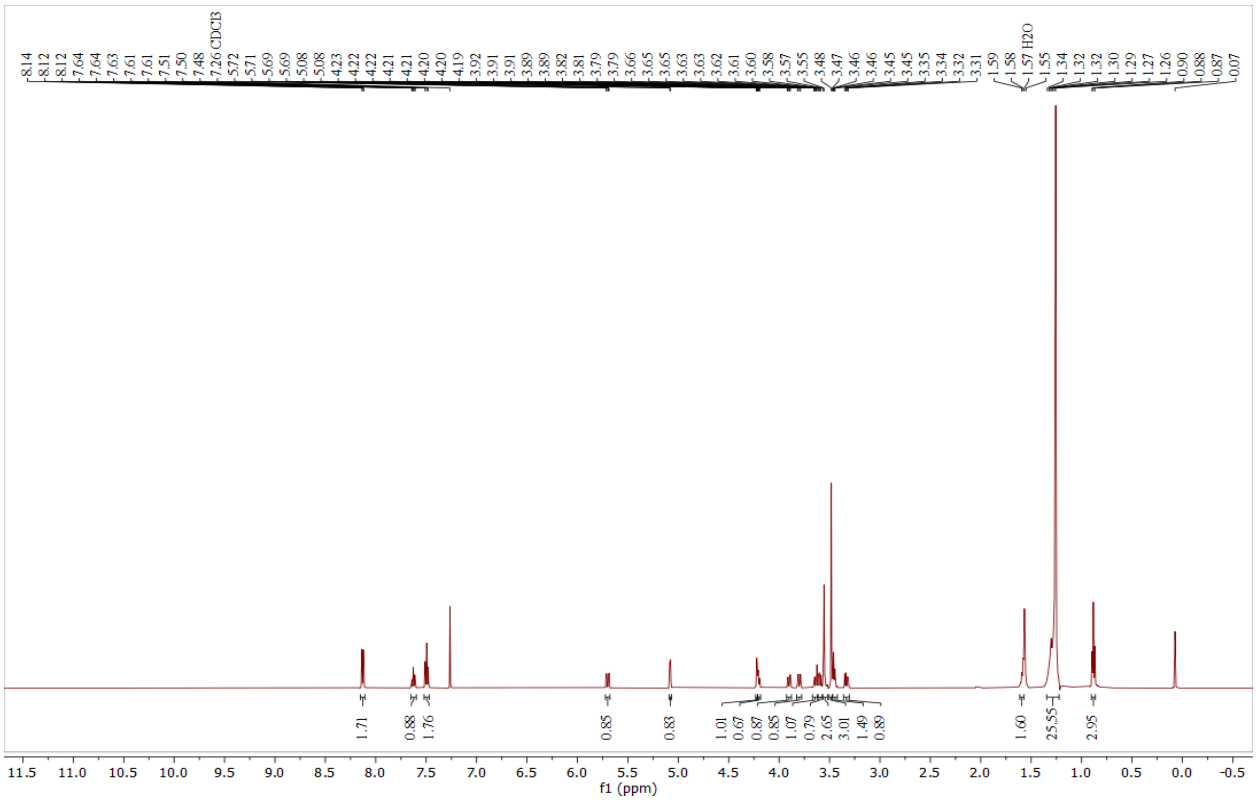
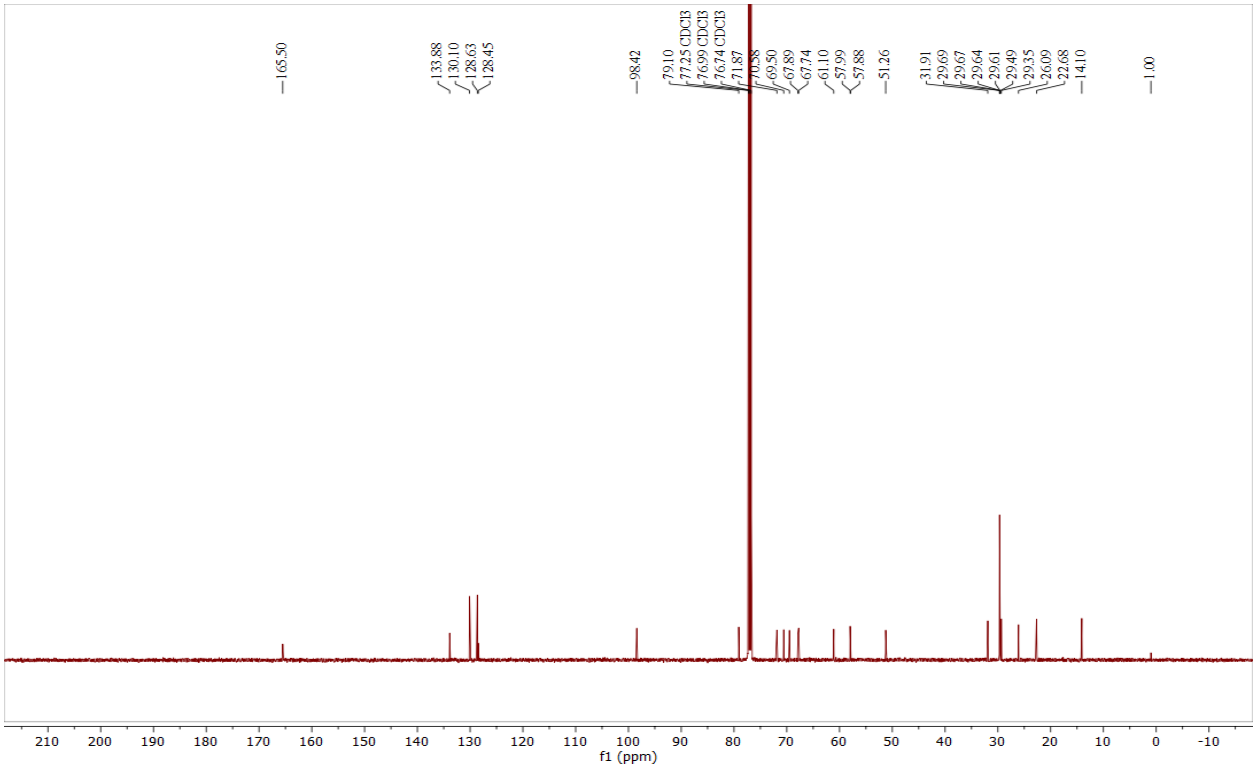
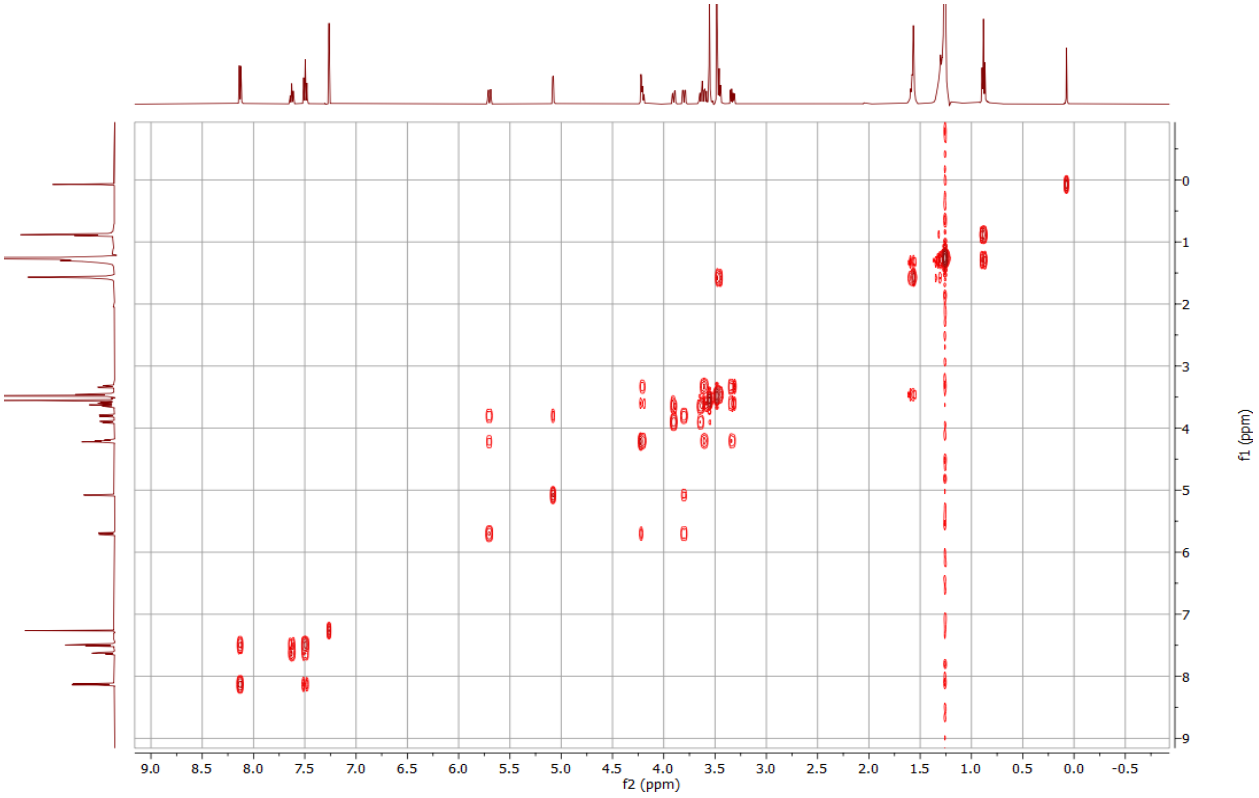
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 19a



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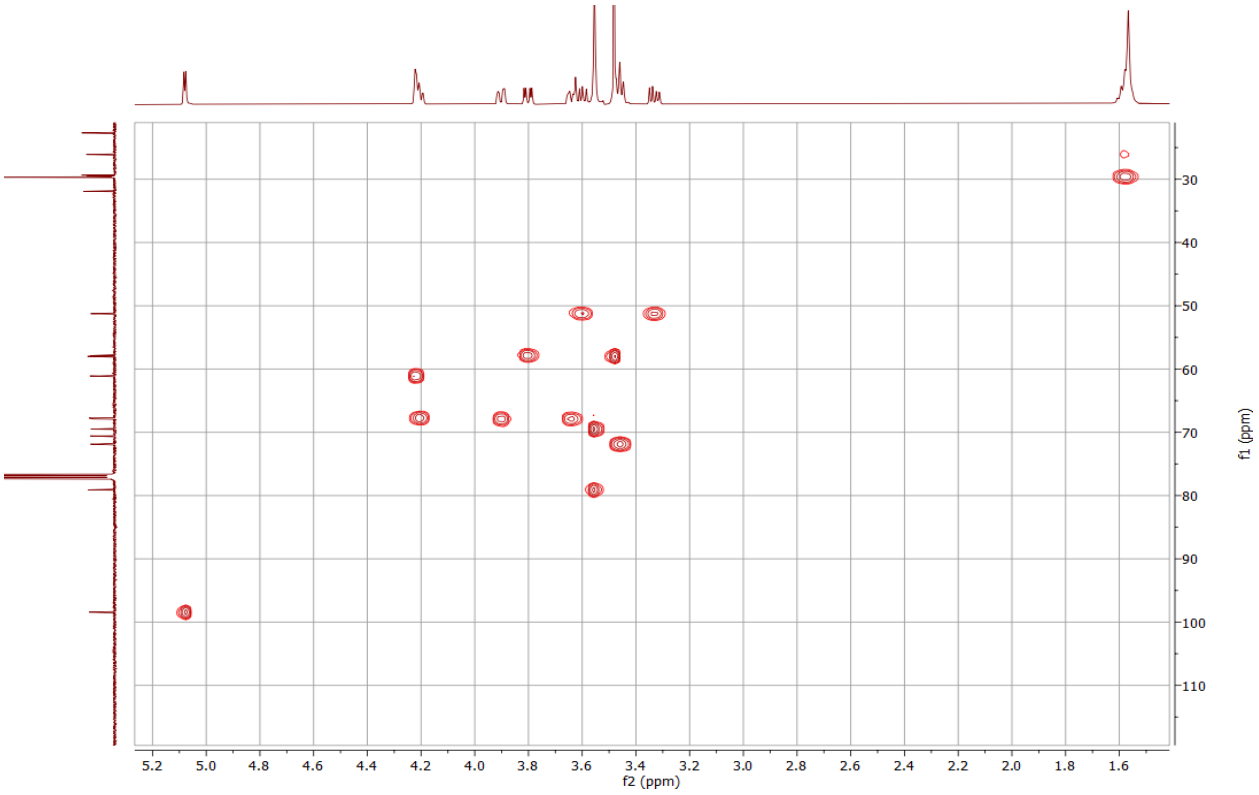
f1 (ppm)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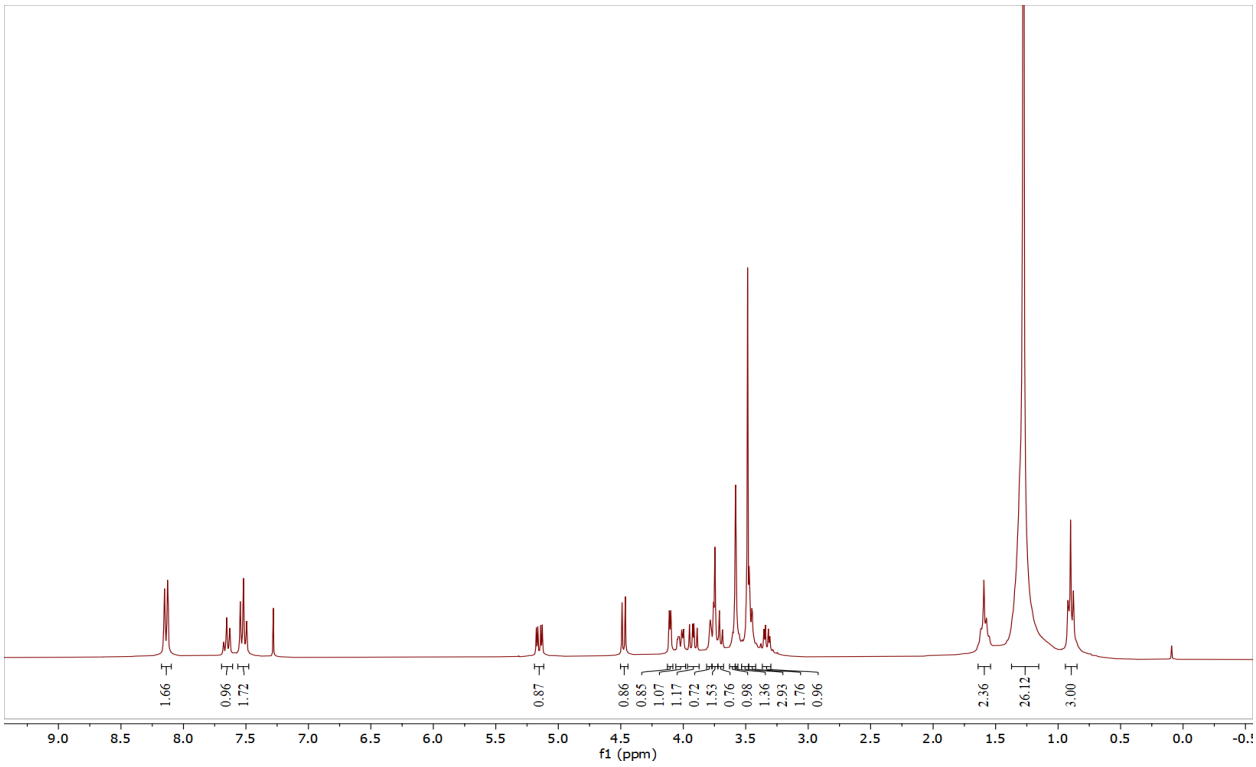
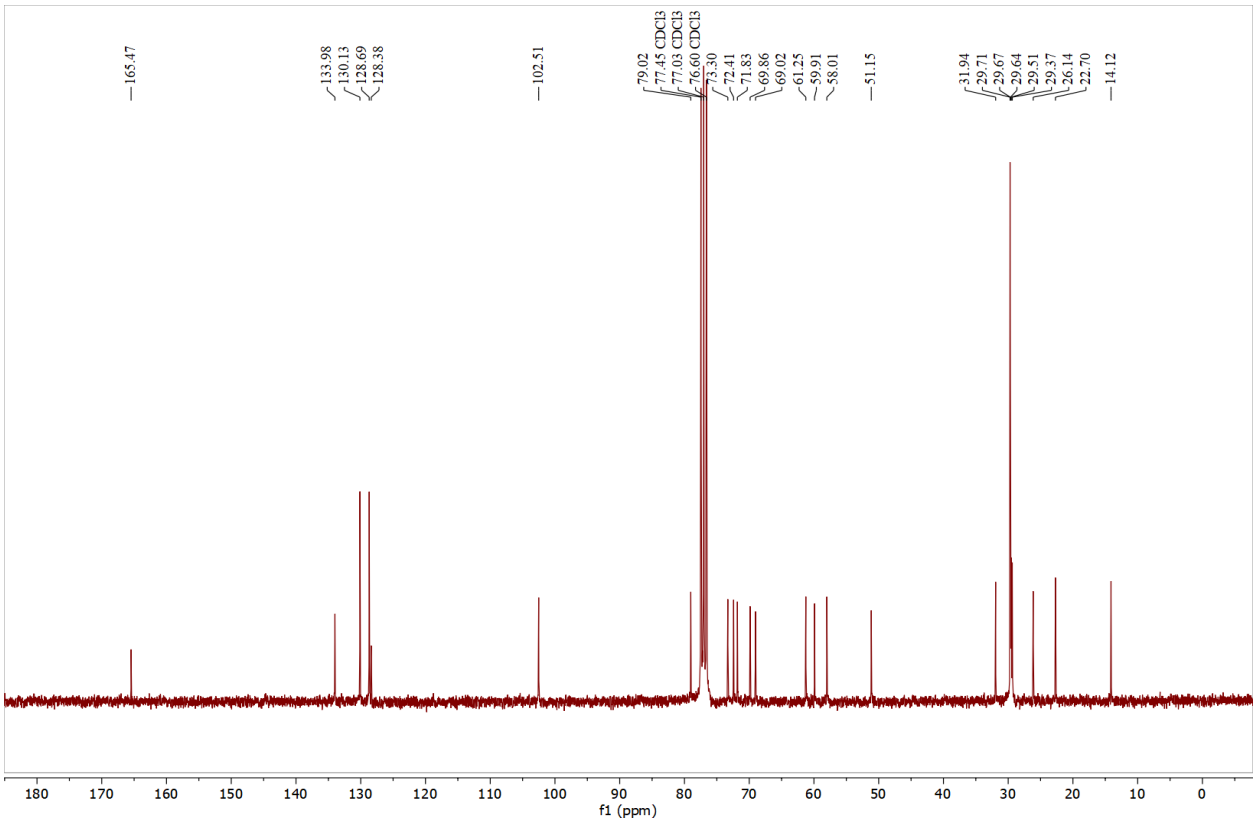
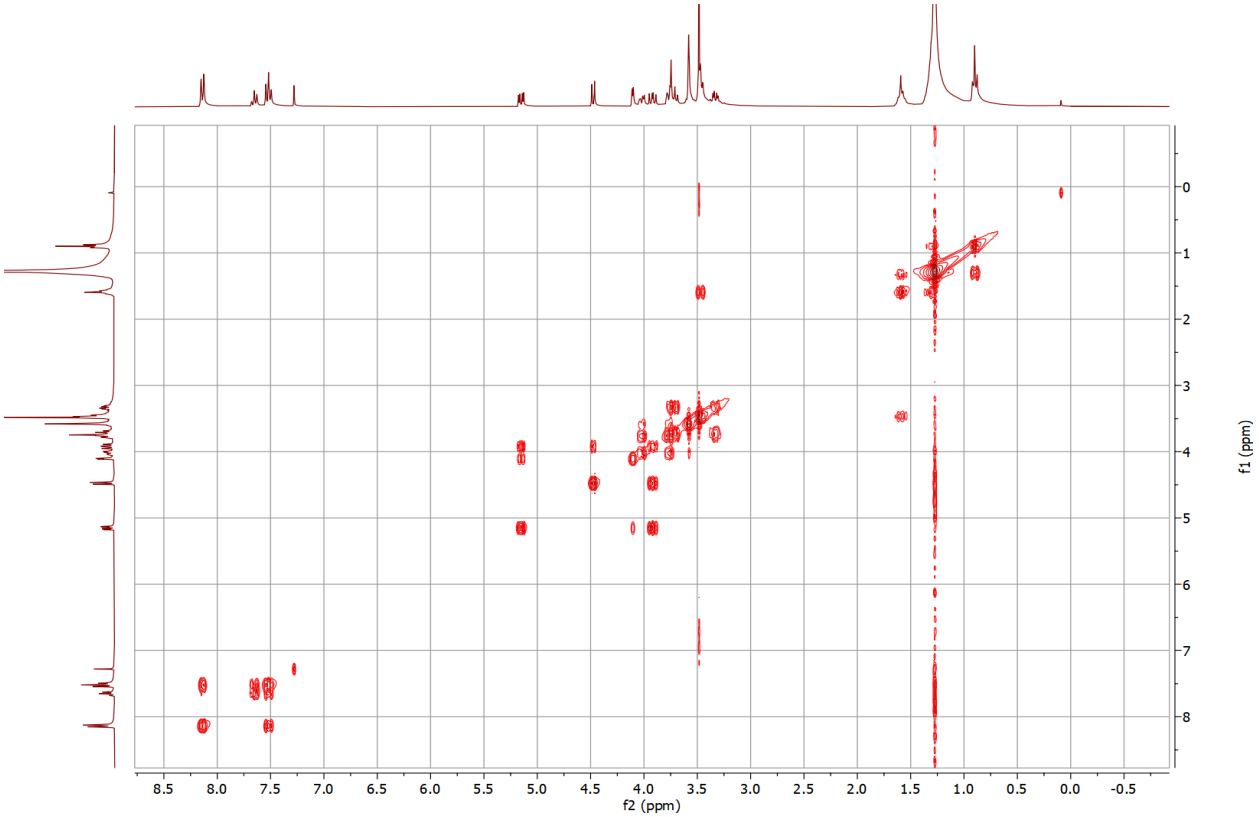
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 19b



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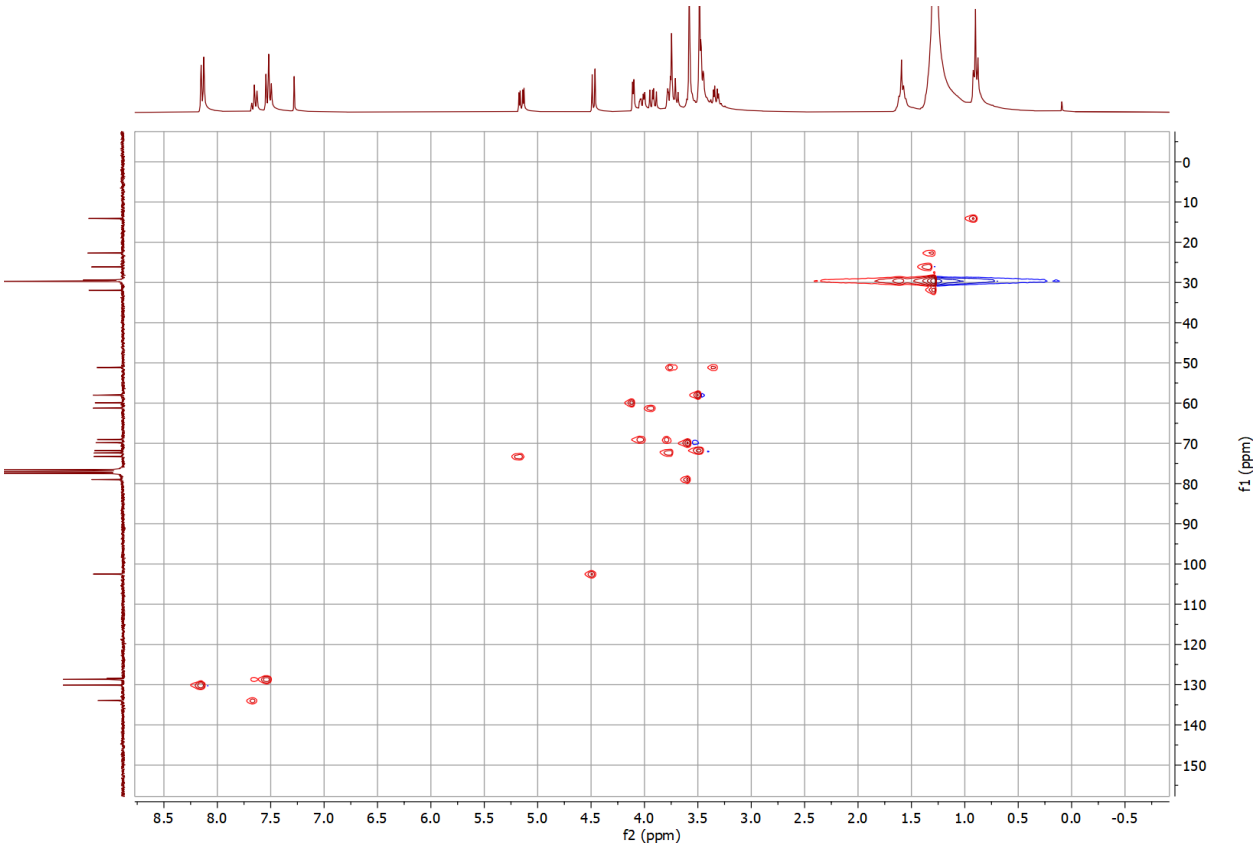
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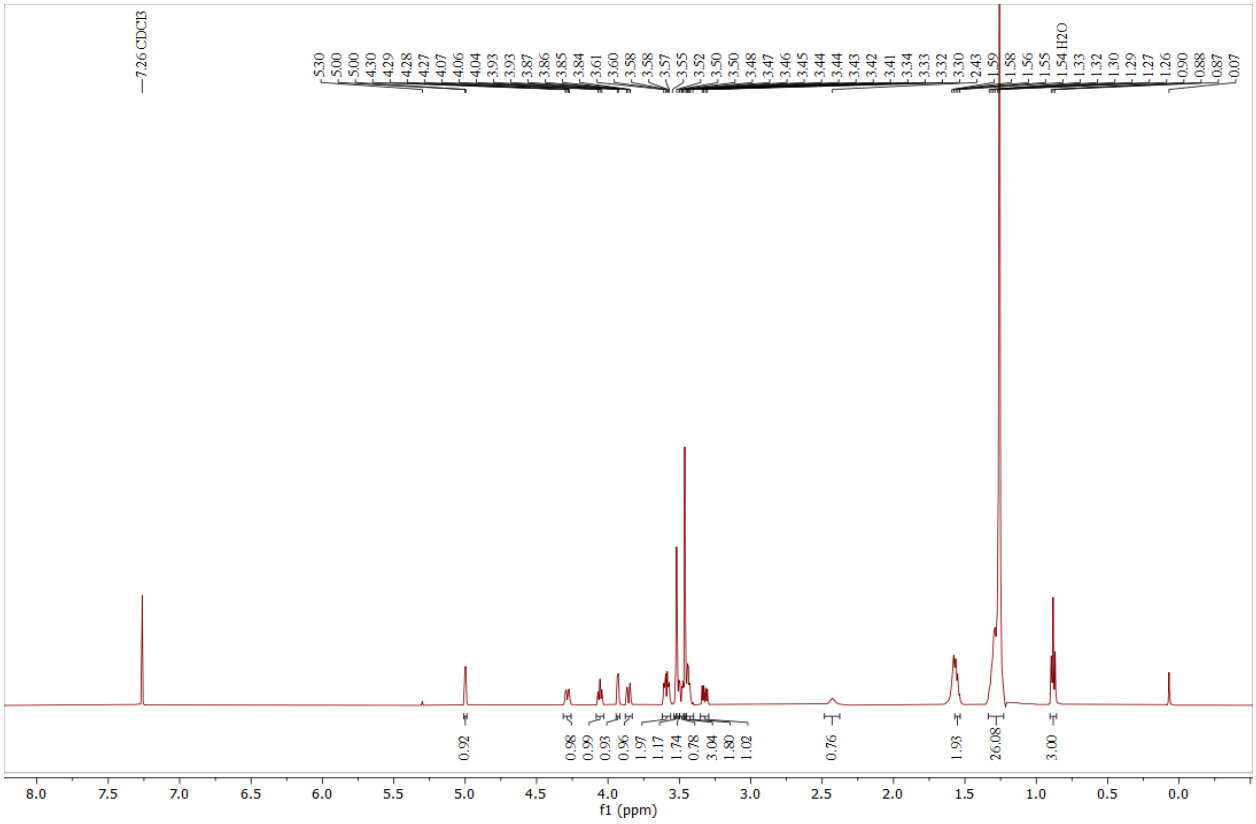
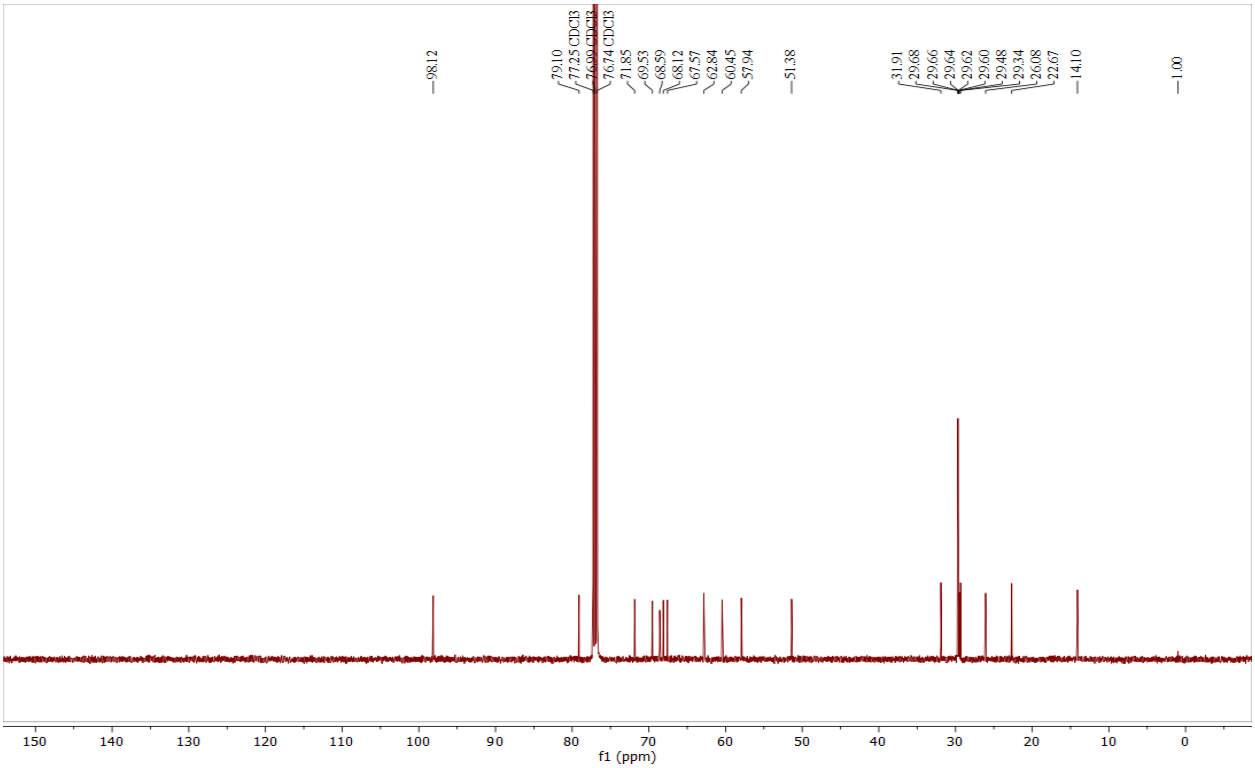
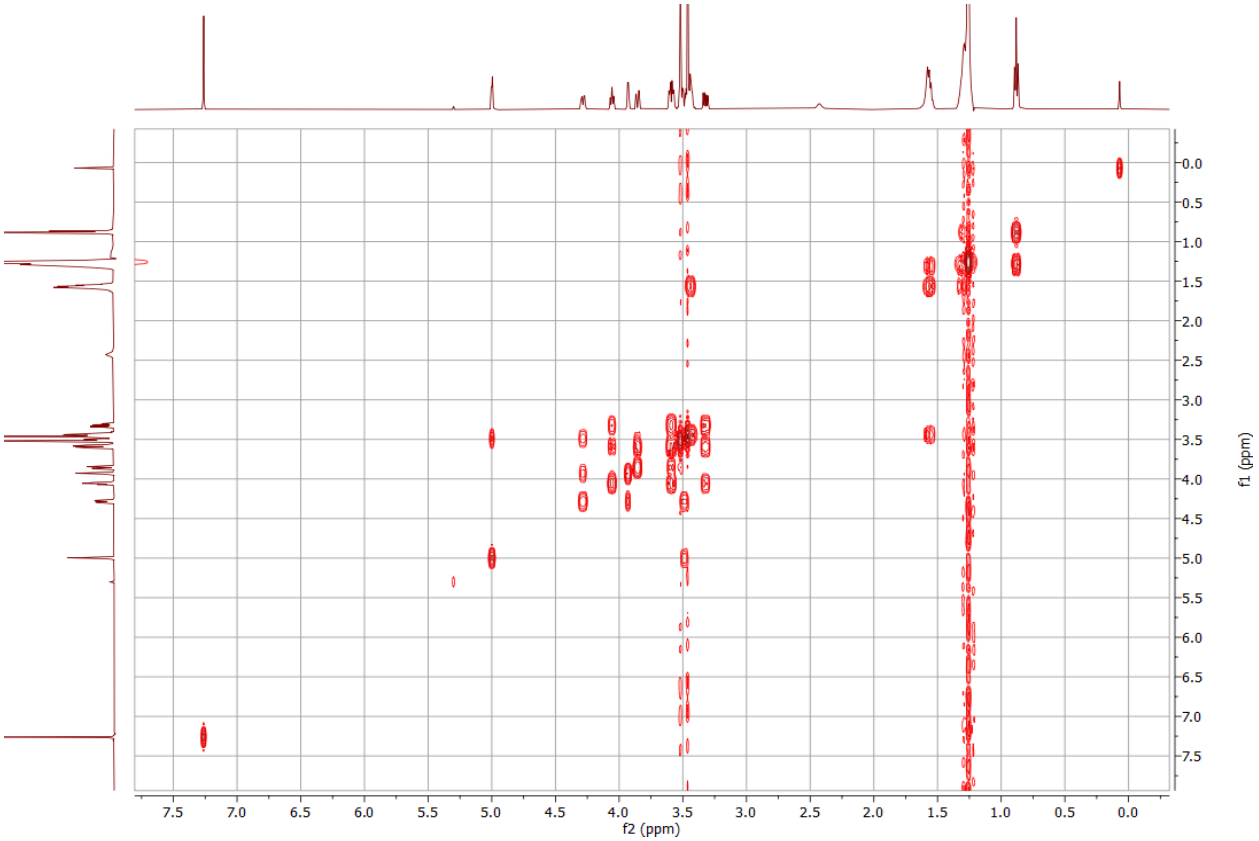
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 20a



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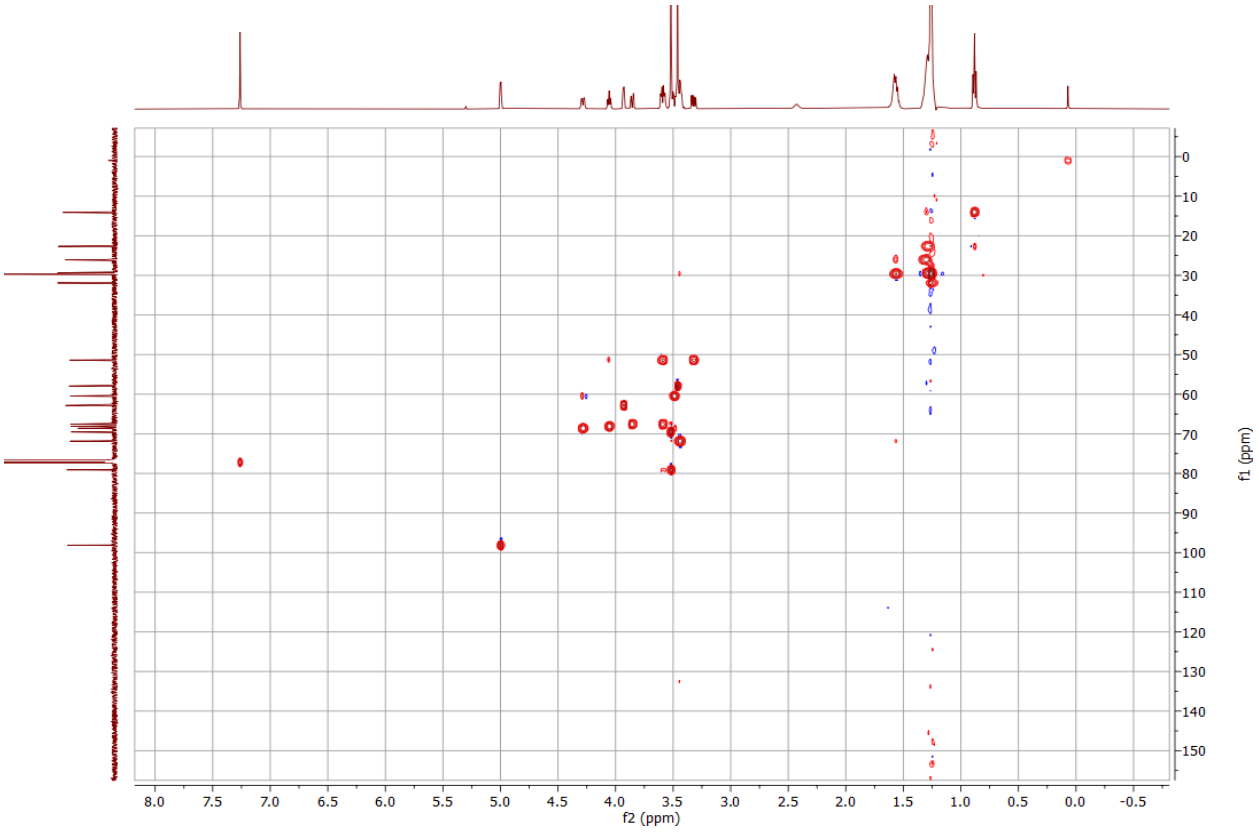
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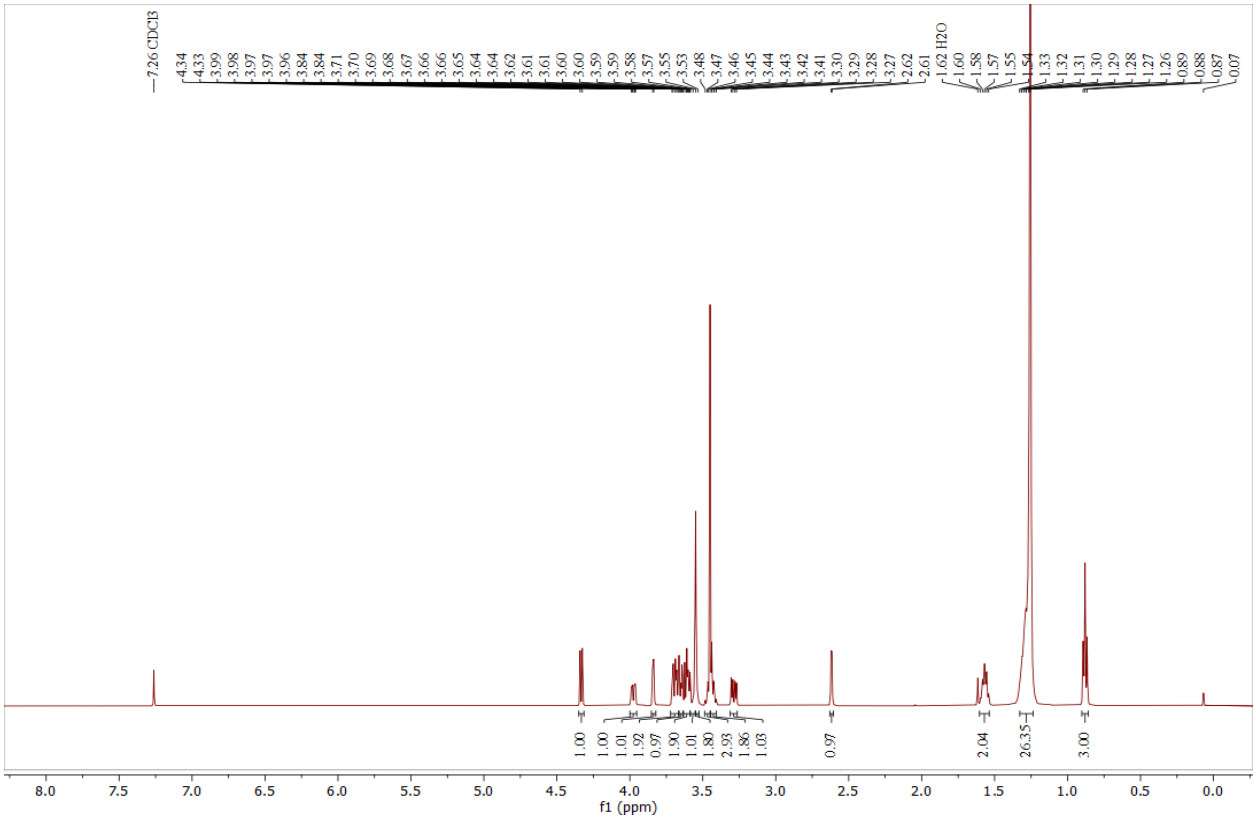
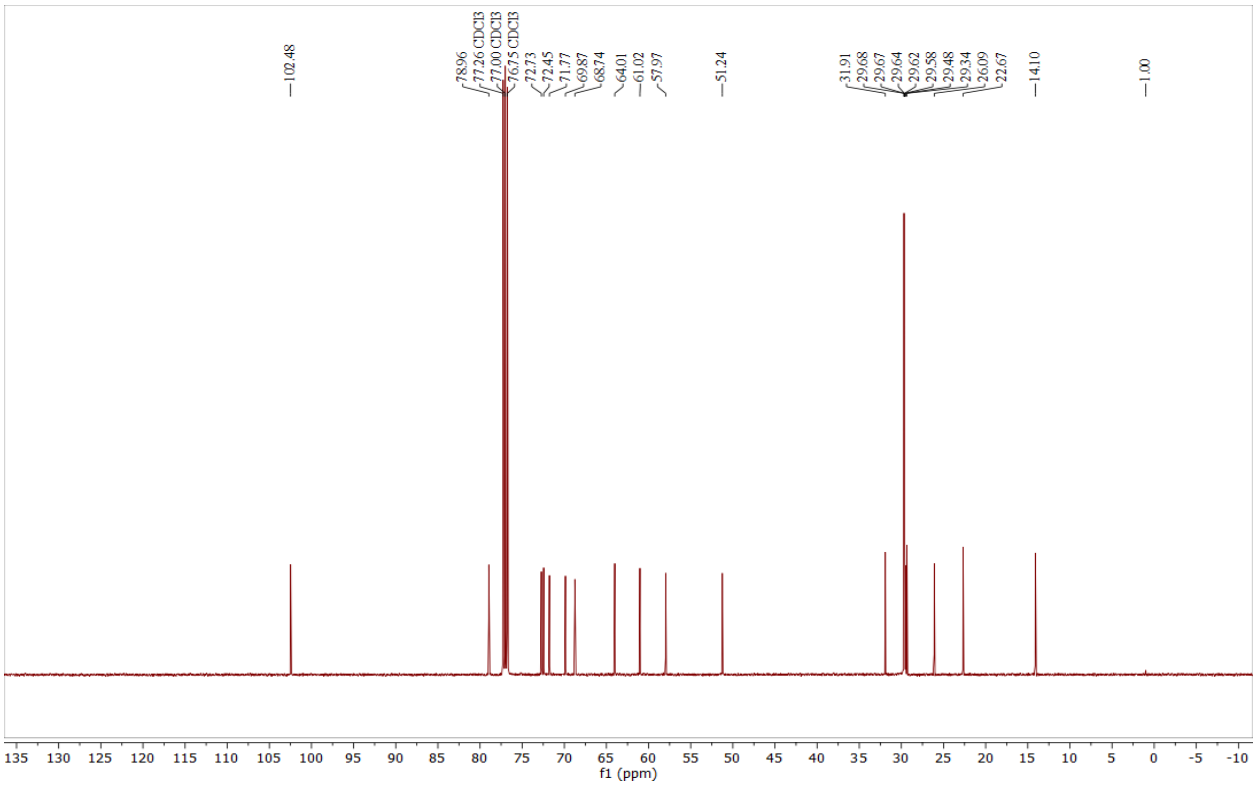
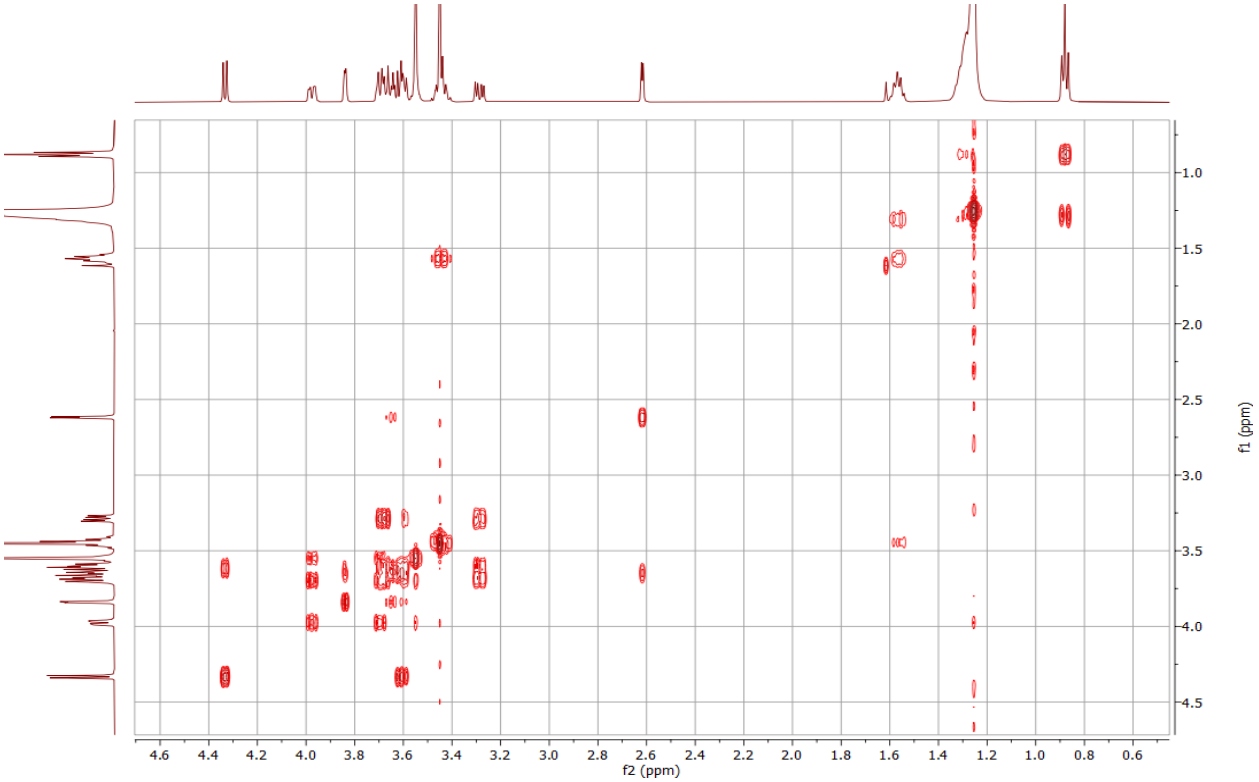
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 20b



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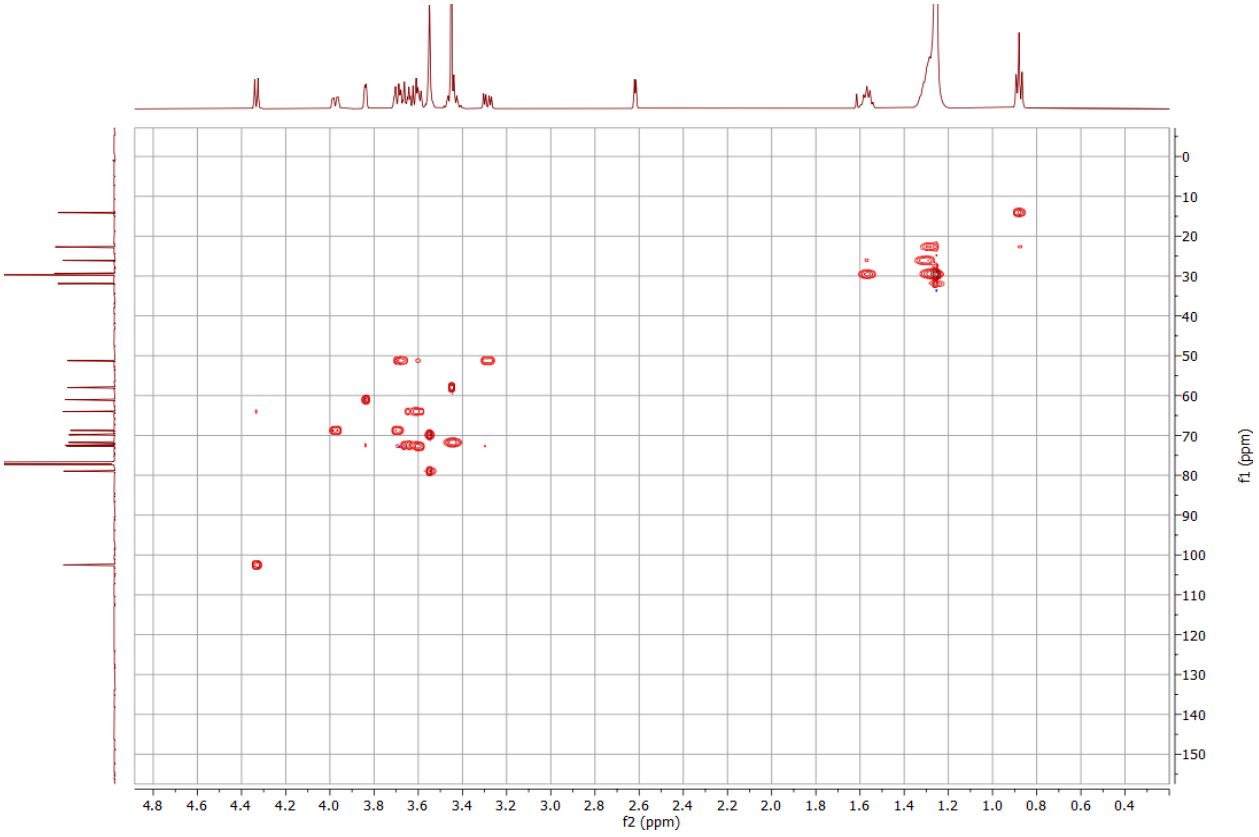
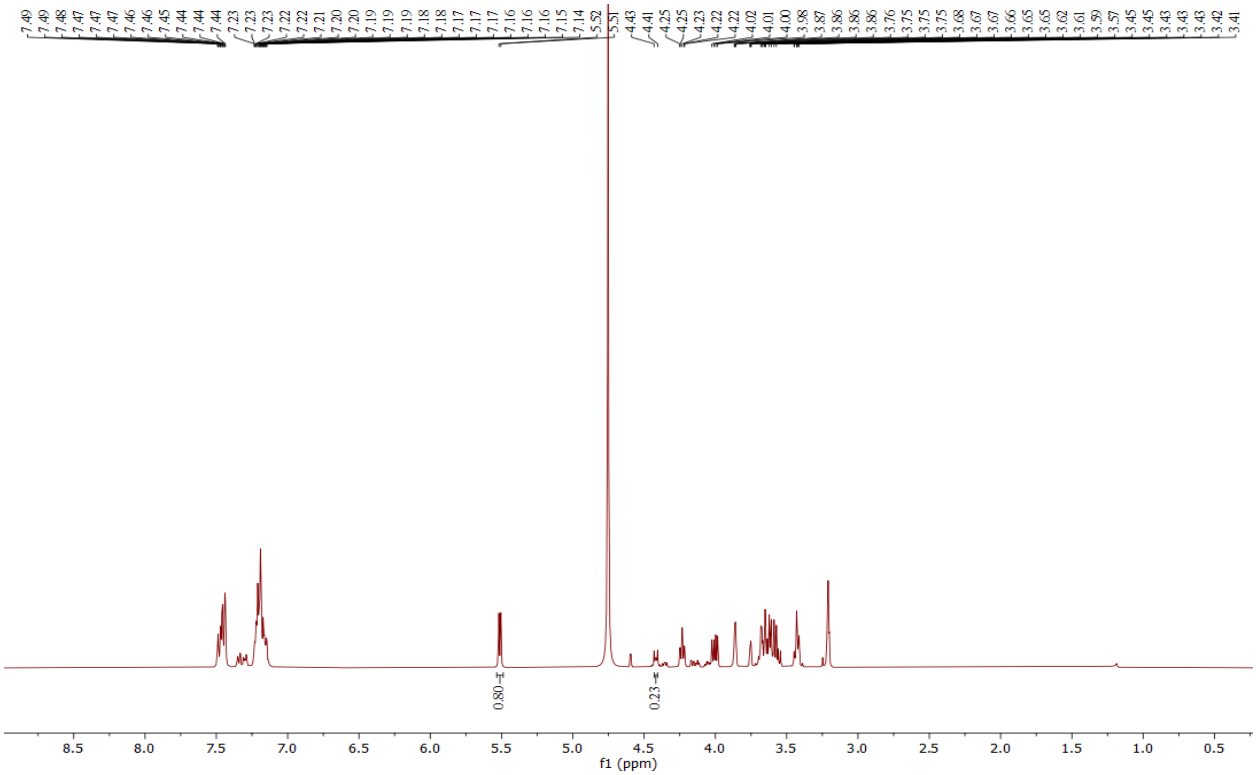
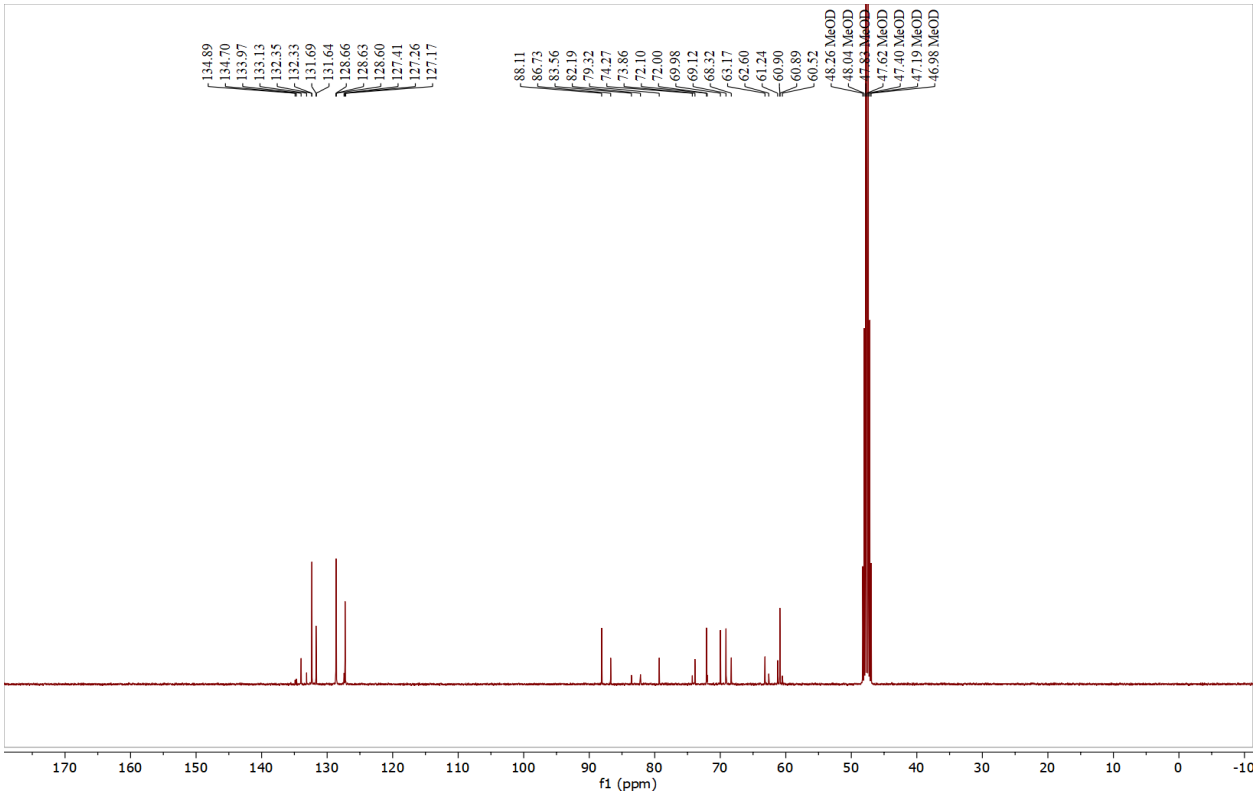
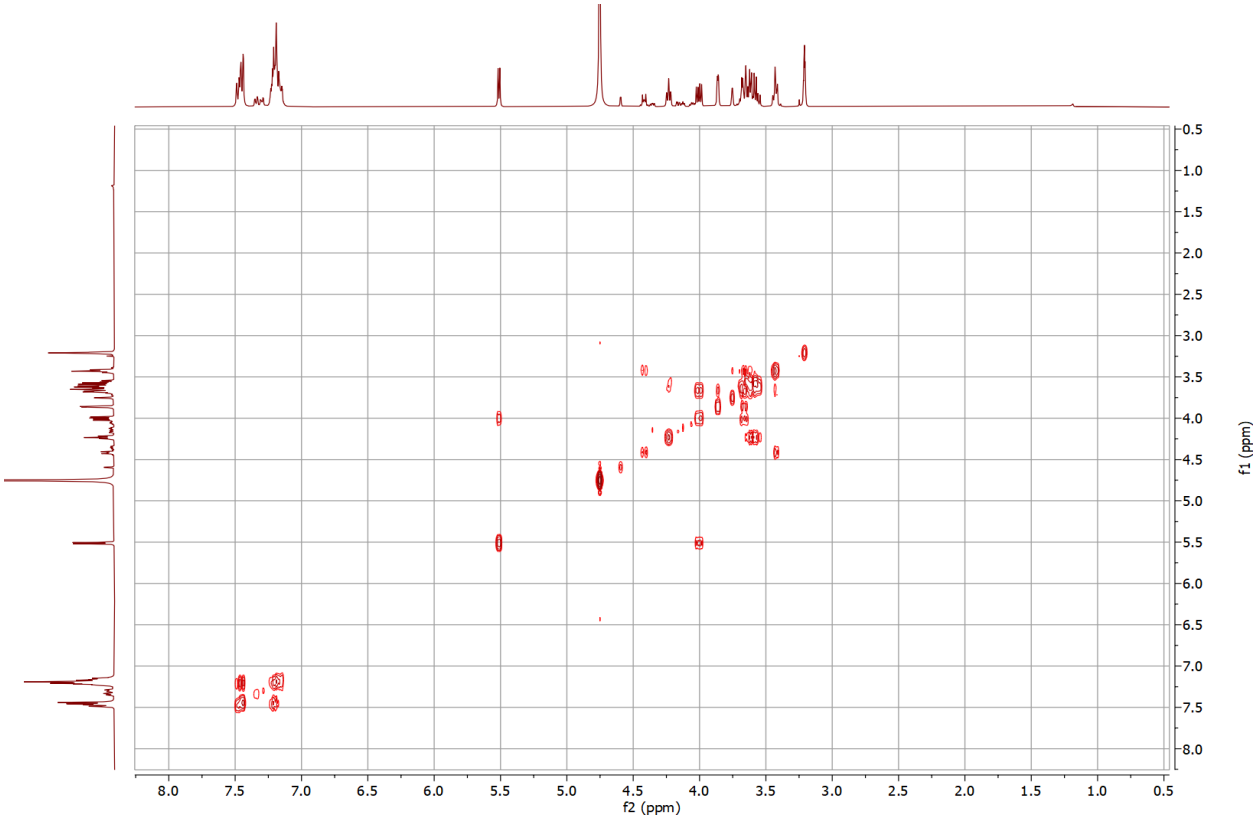

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 3



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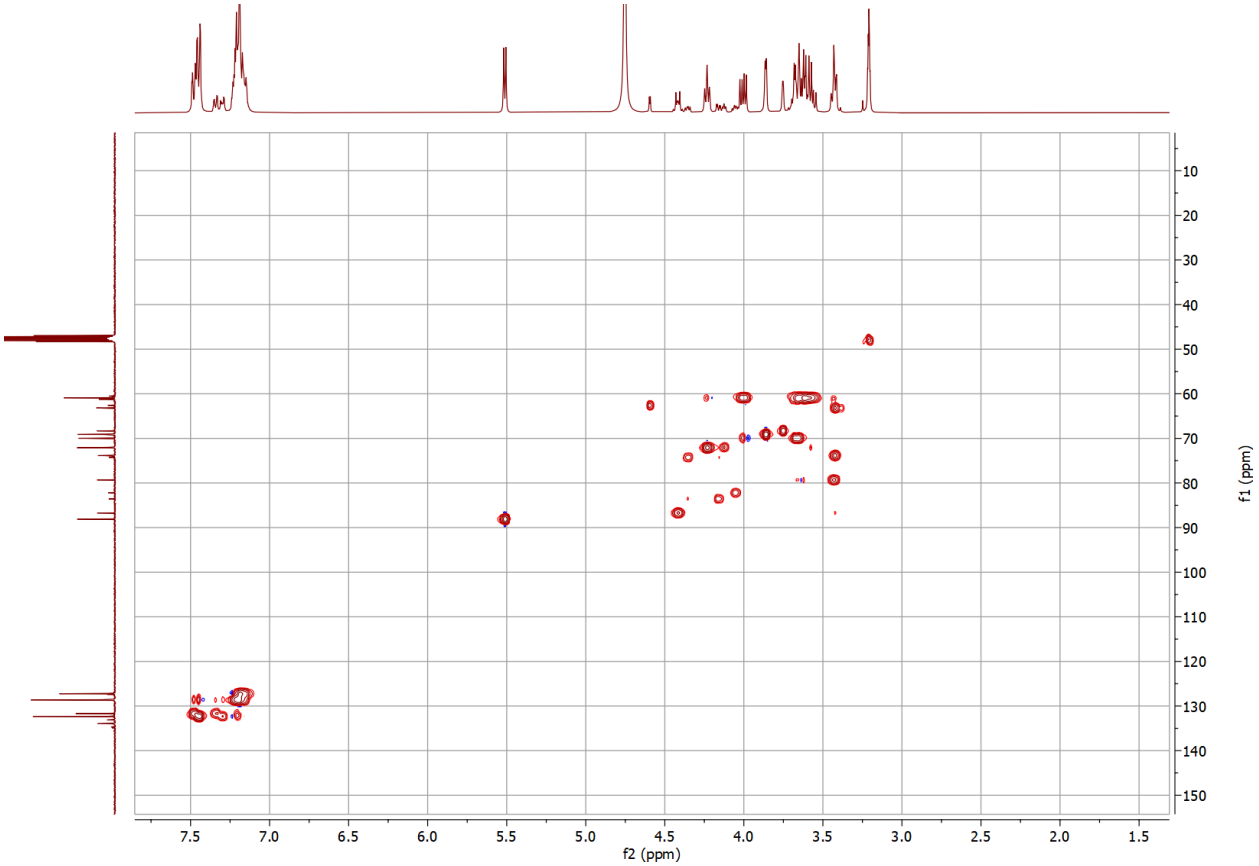
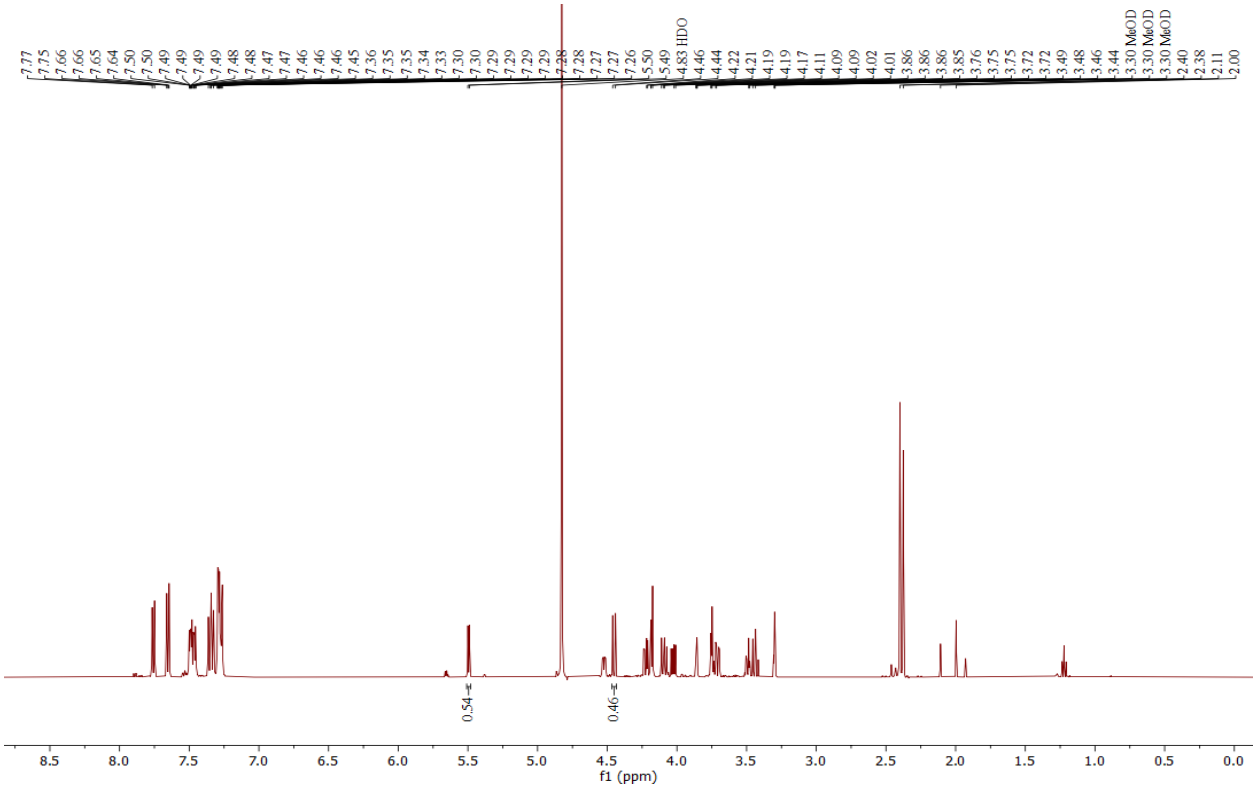
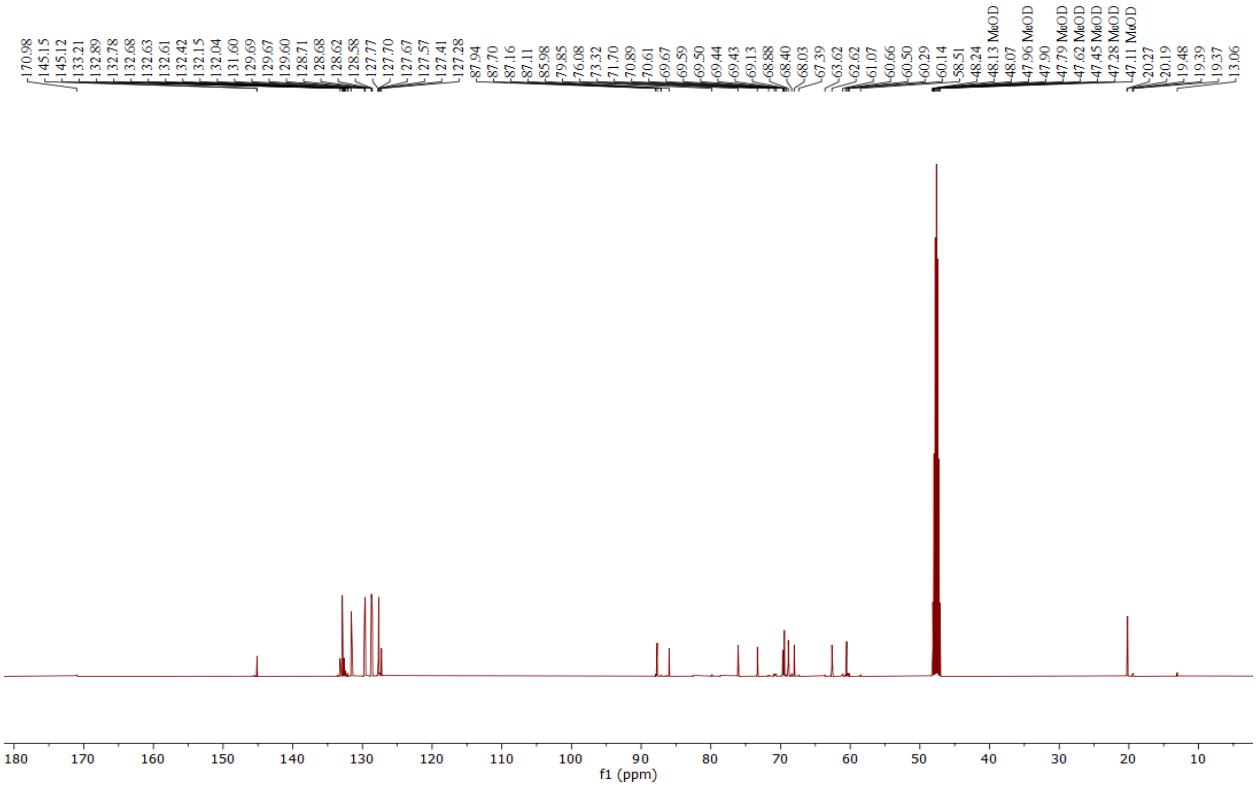
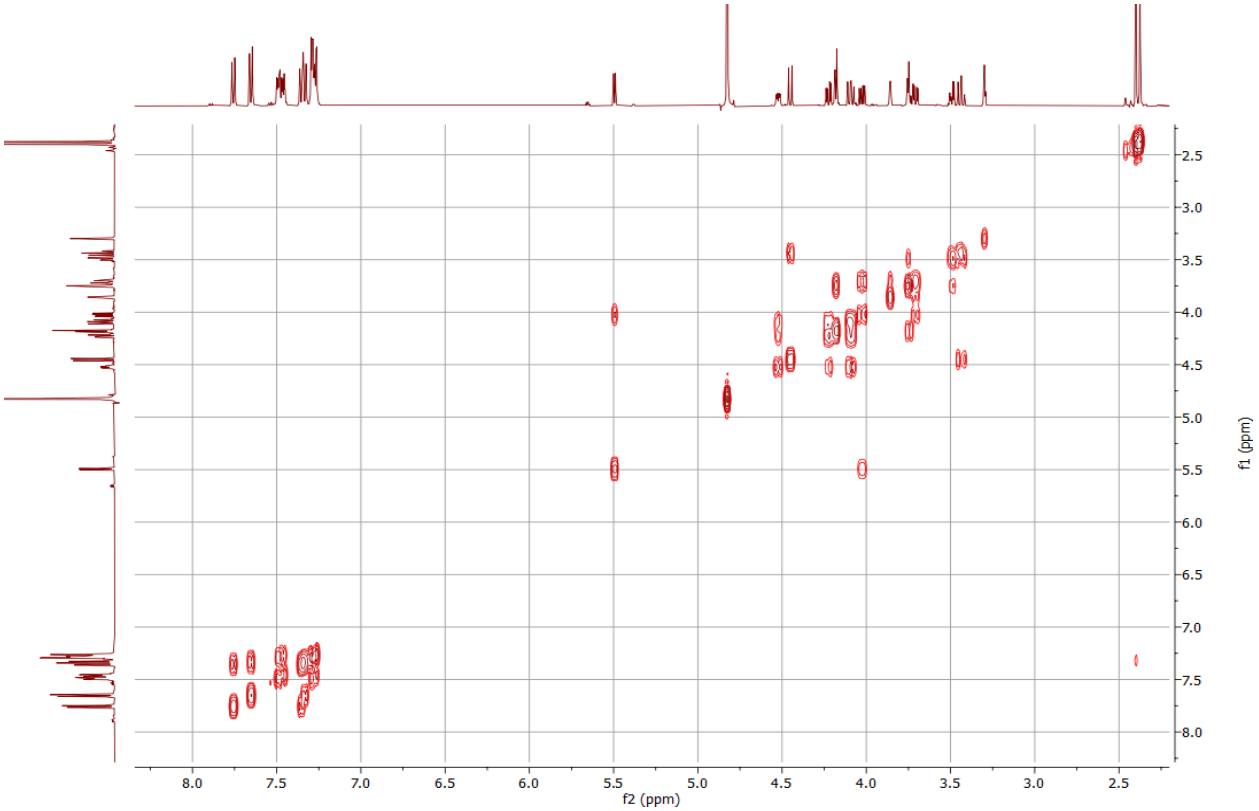

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 4



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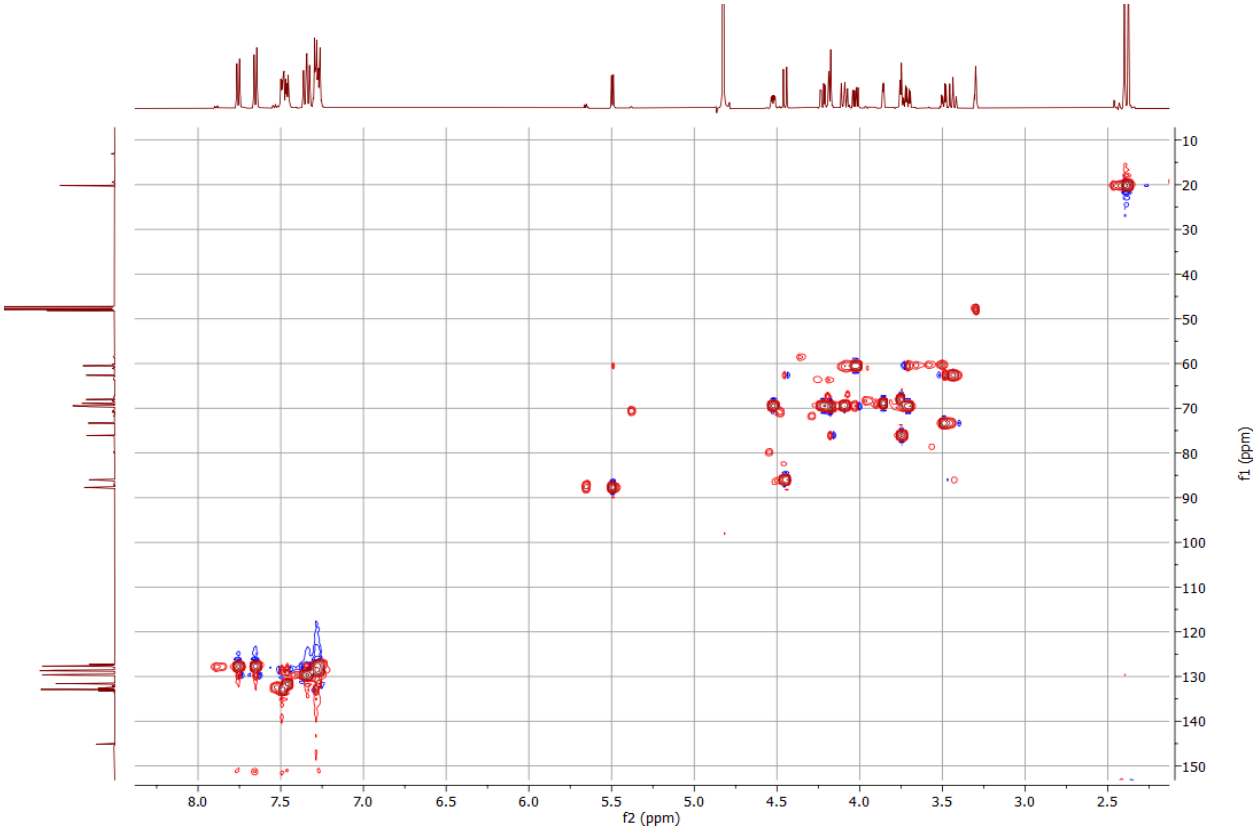
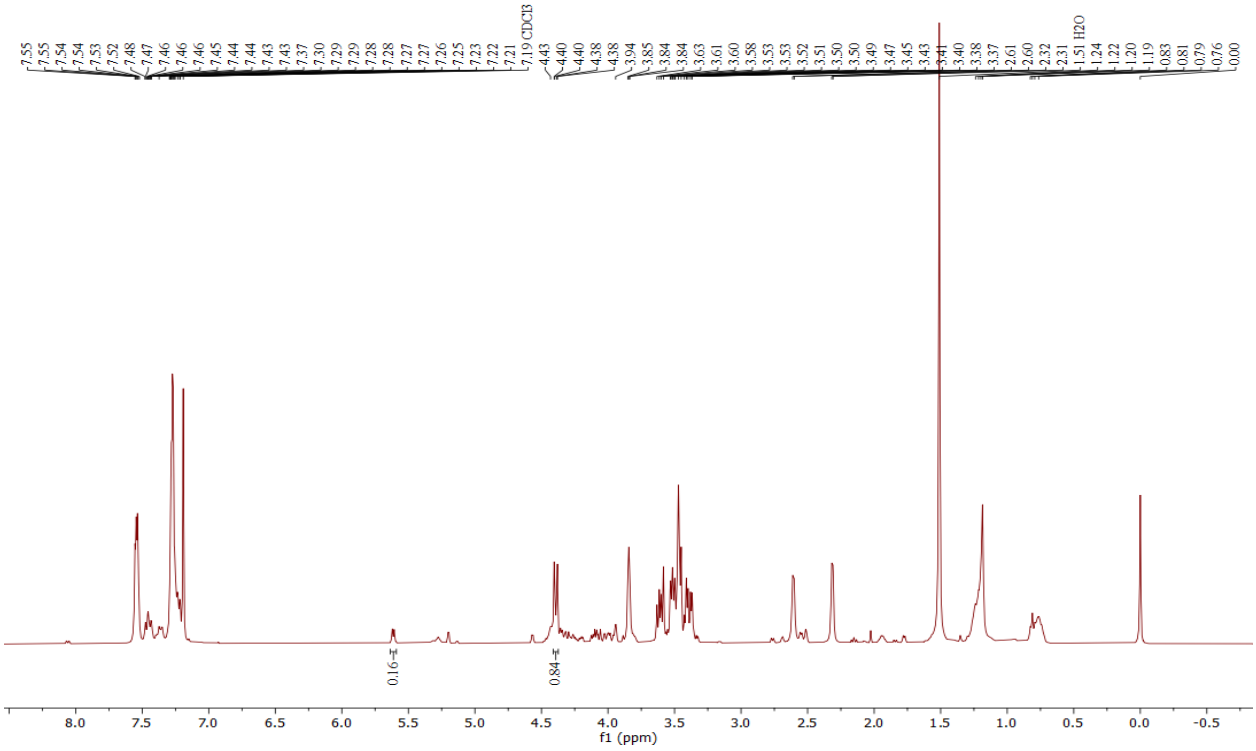
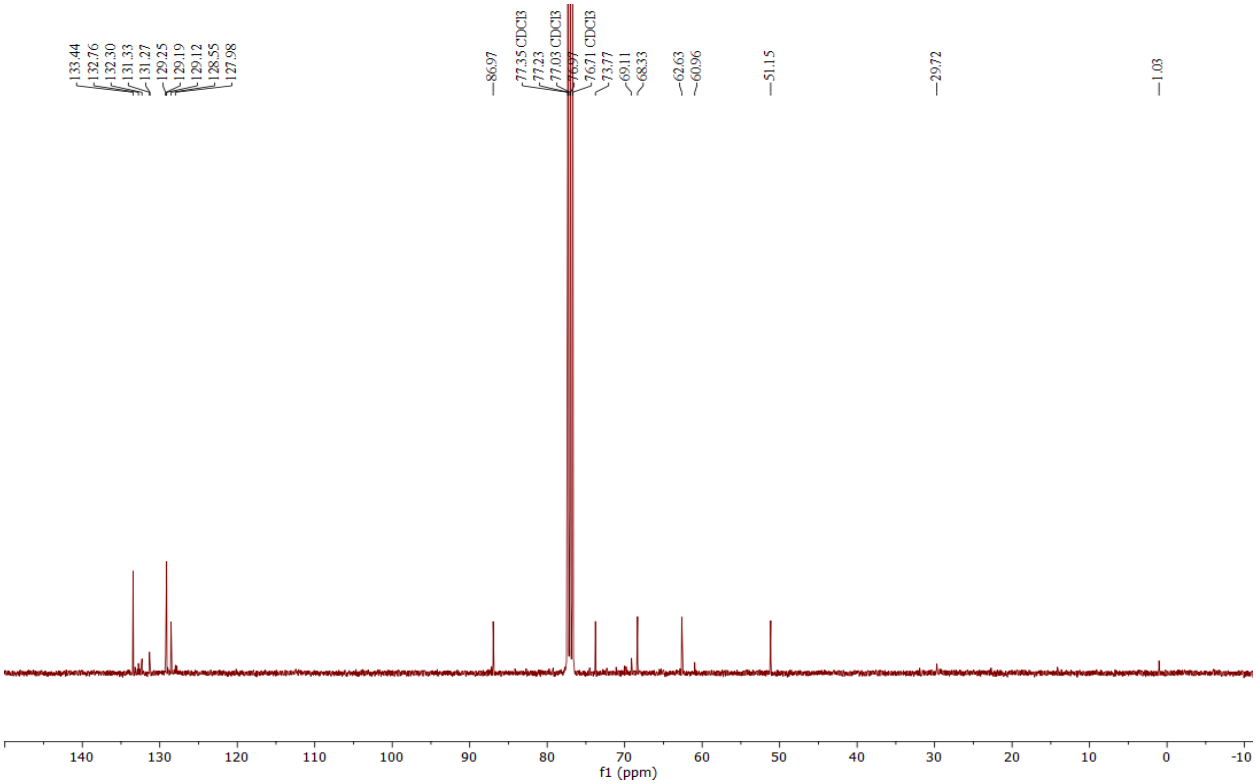

f2 (ppm)
f1 (ppm)

^{1}H, COSY, ^{13}C, and HSQC NMR of compound 5






f2 (ppm)
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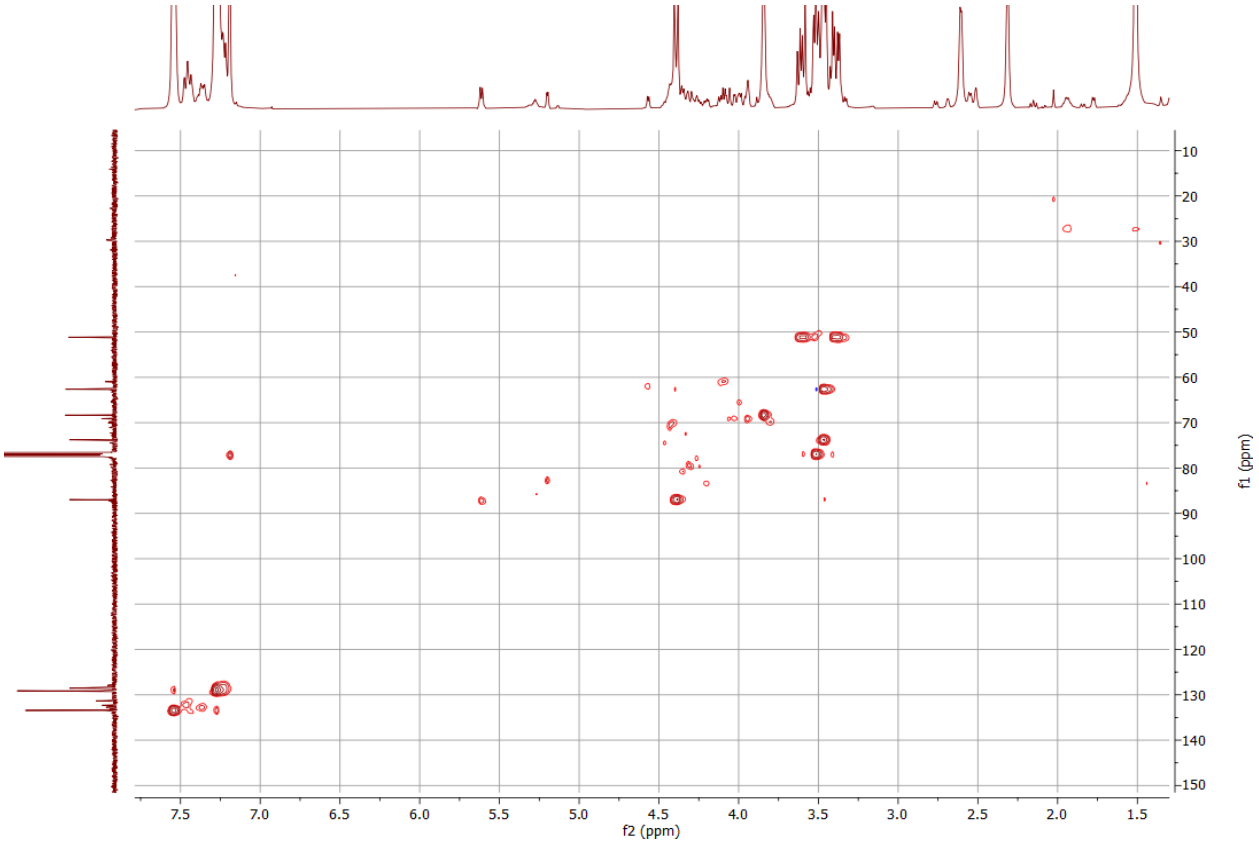
f2 (ppm)
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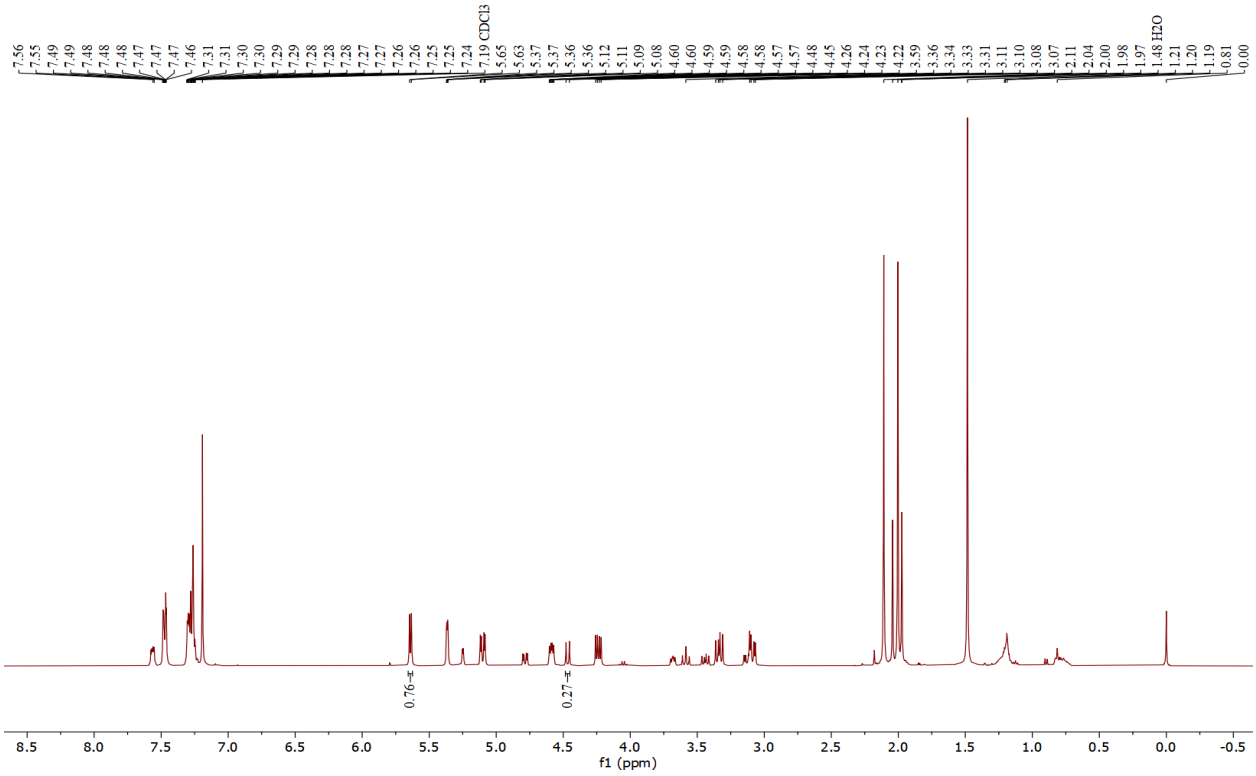
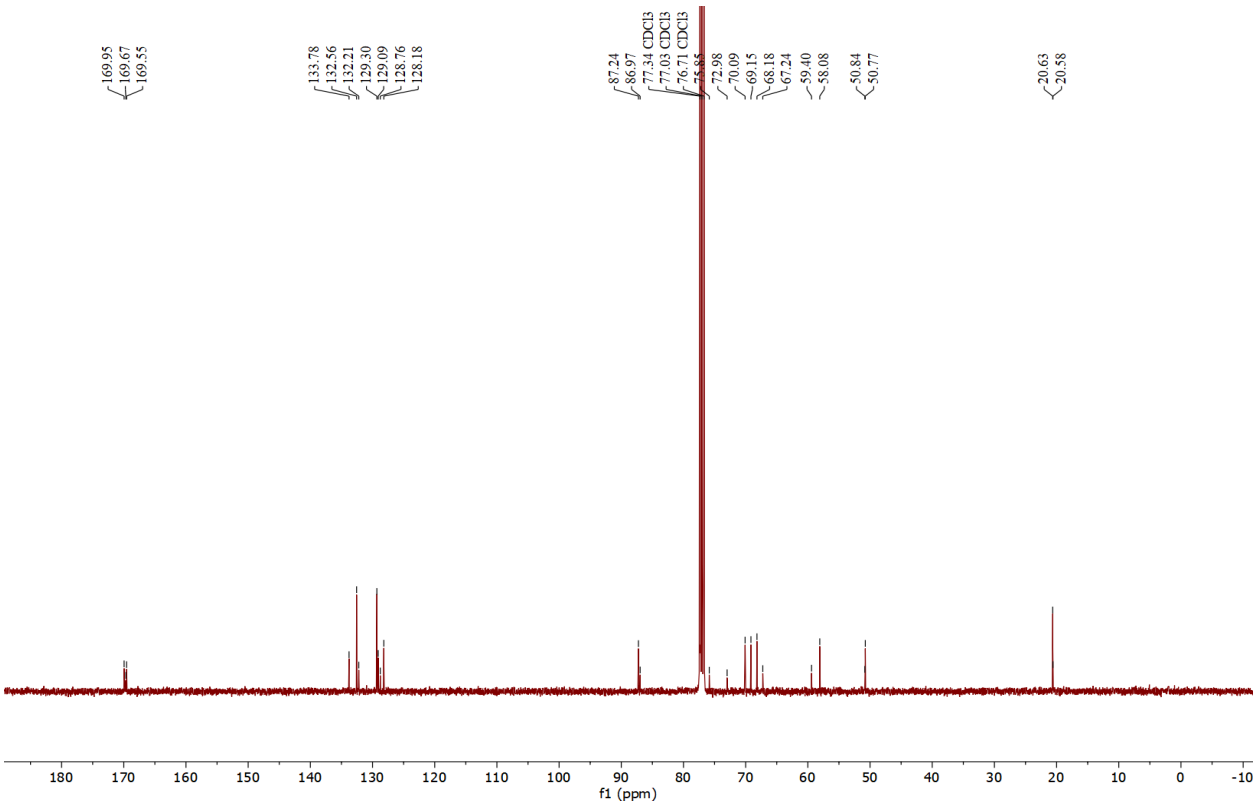
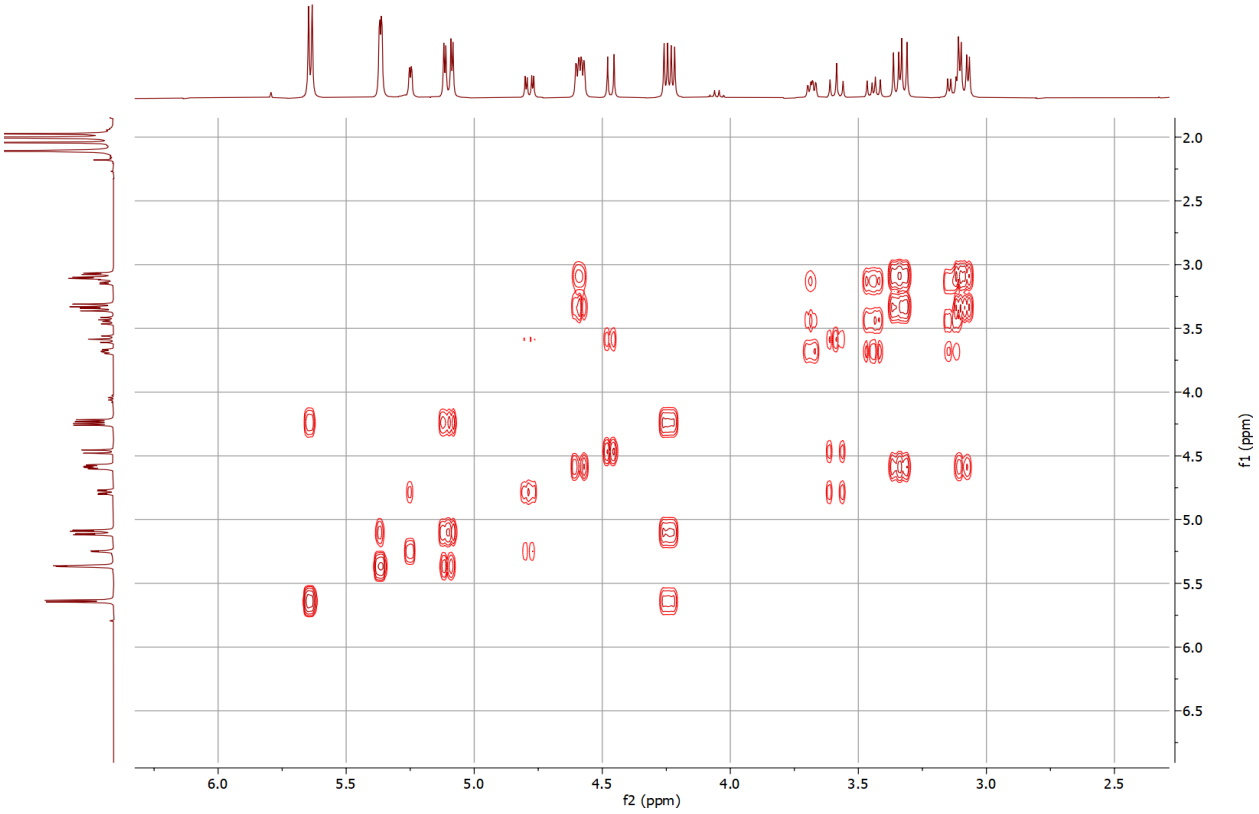
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 6



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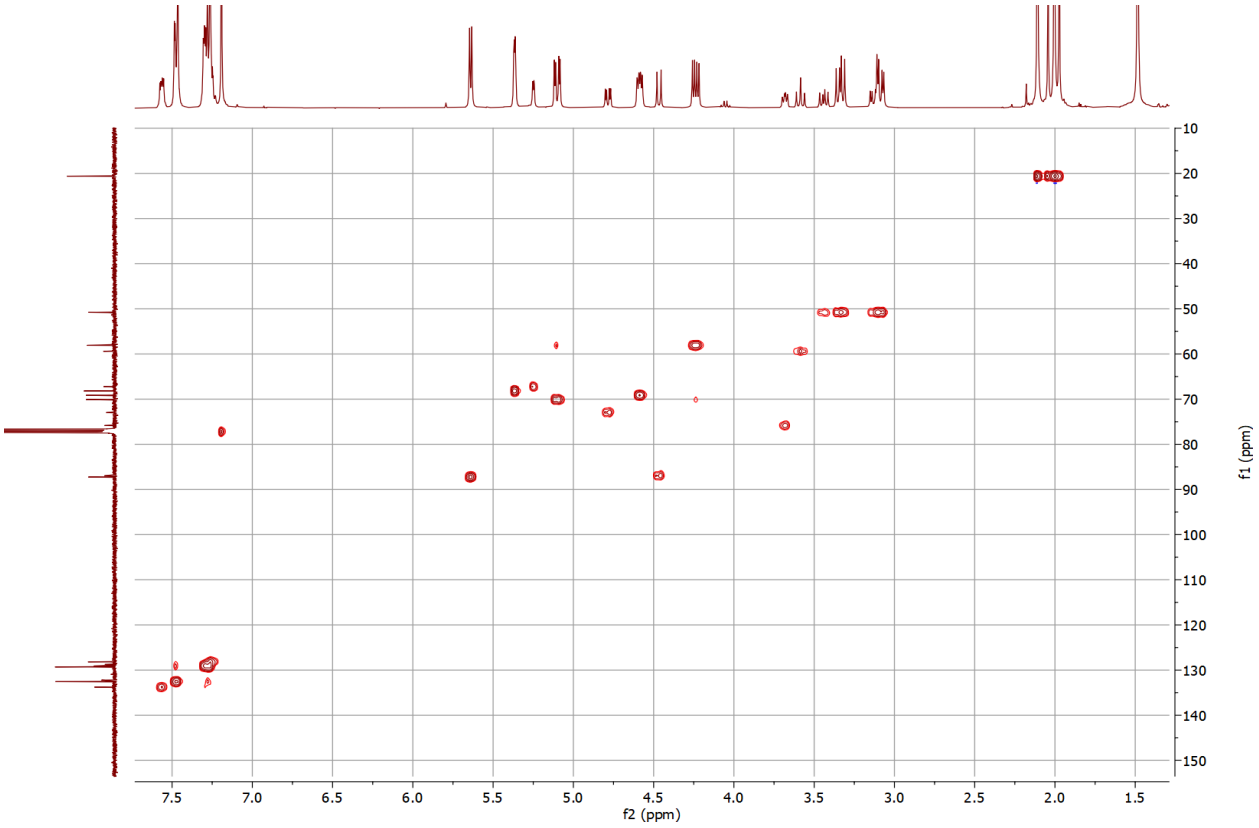
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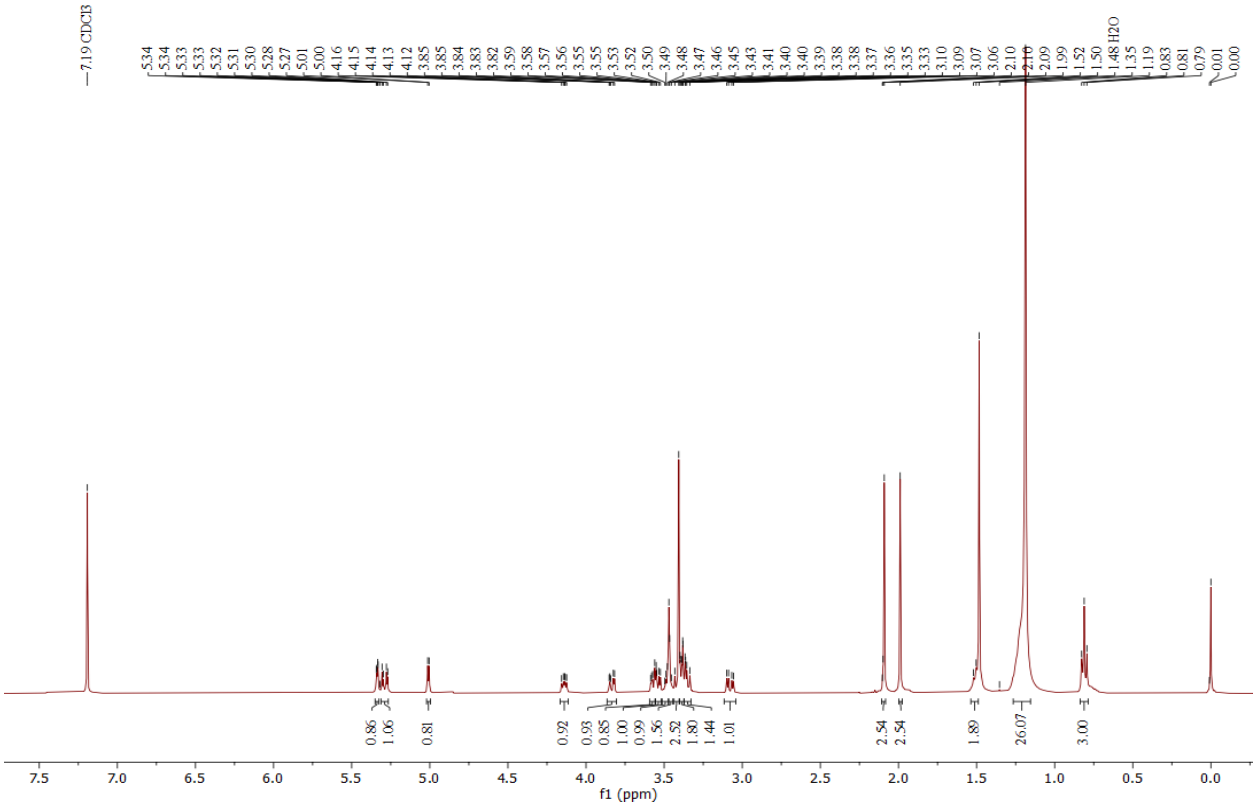
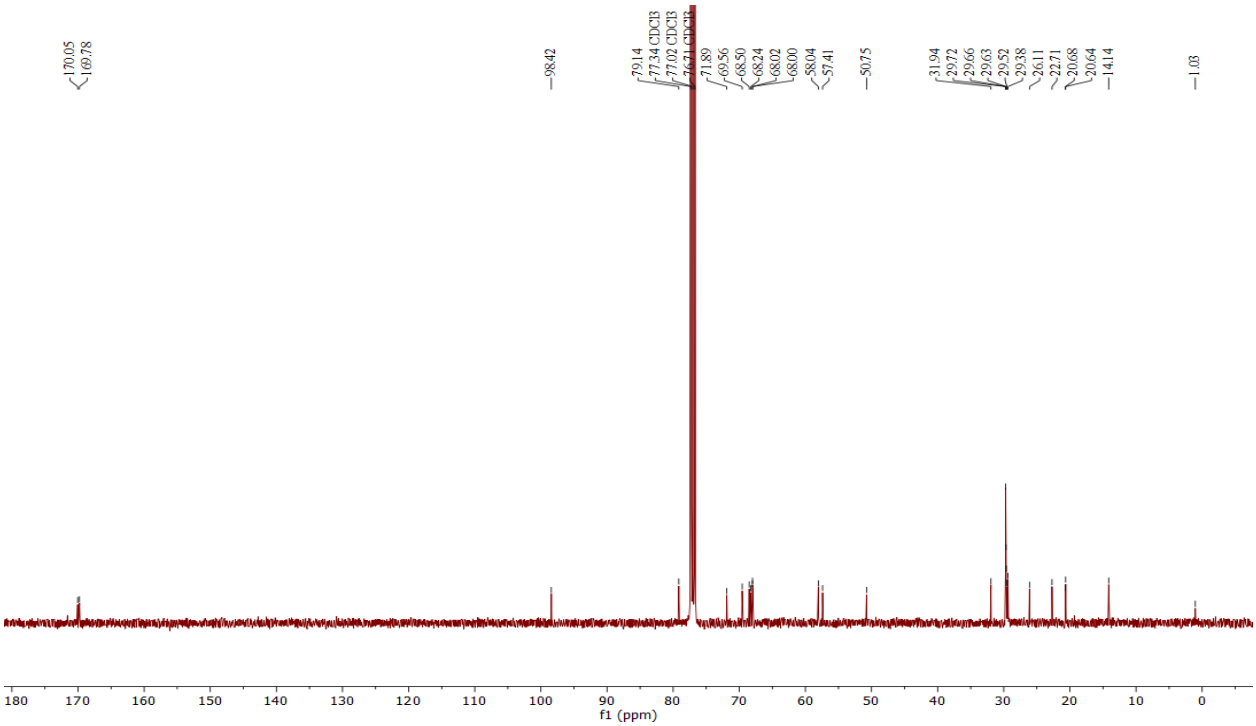
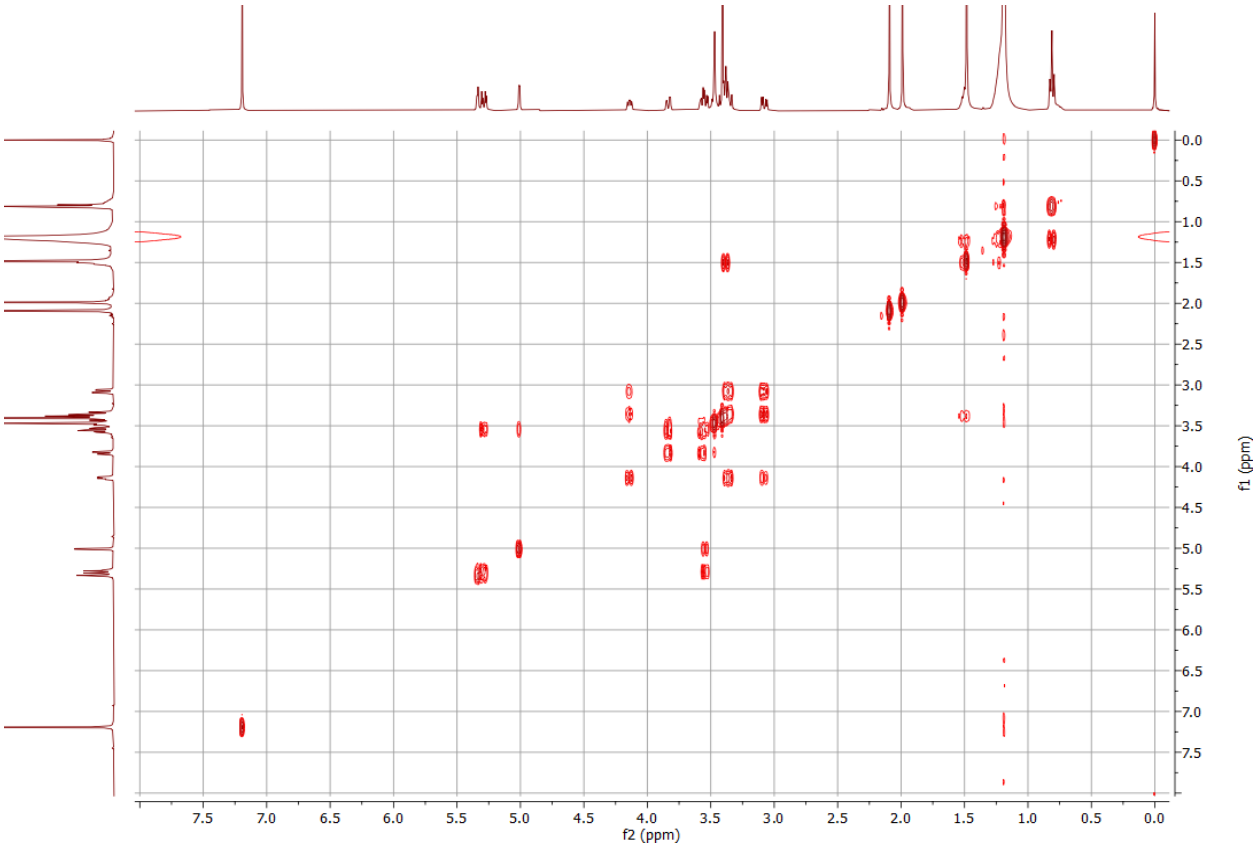
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 7a



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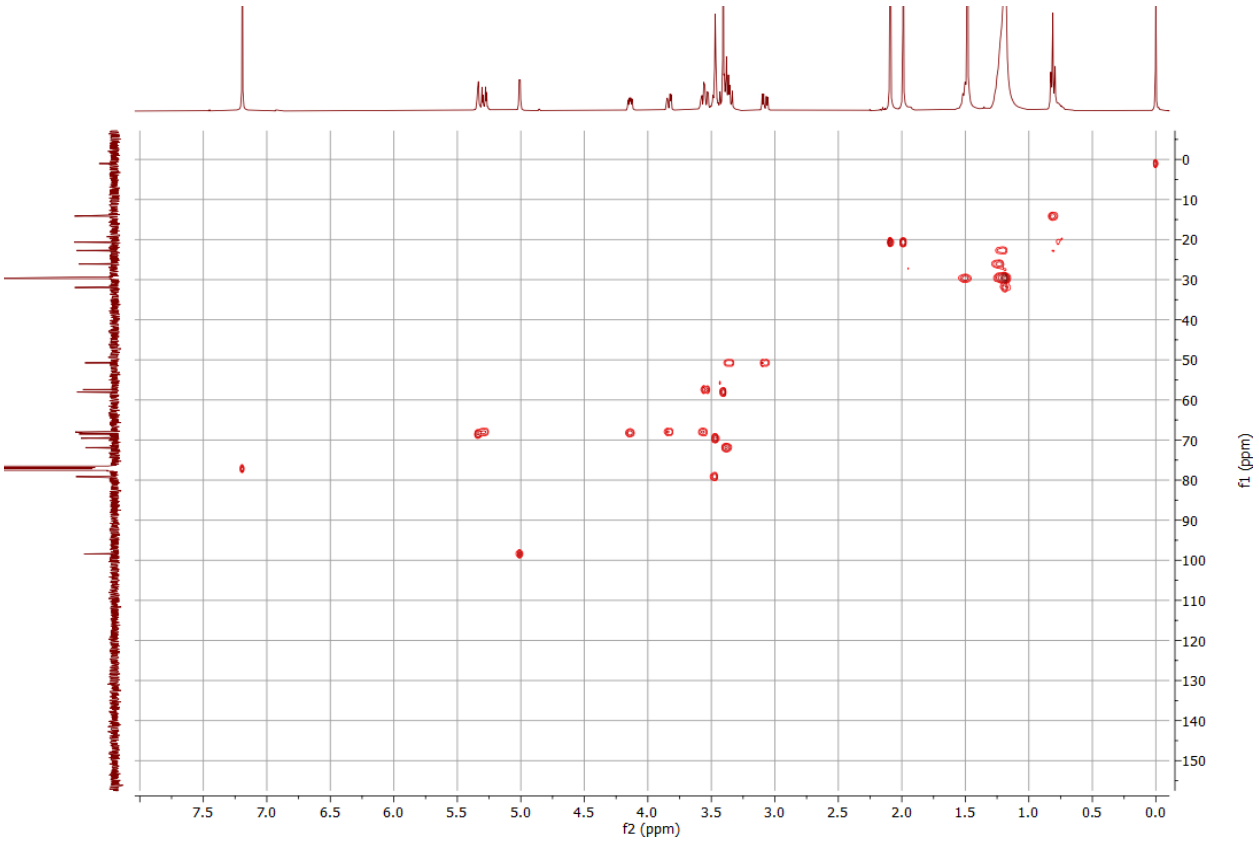
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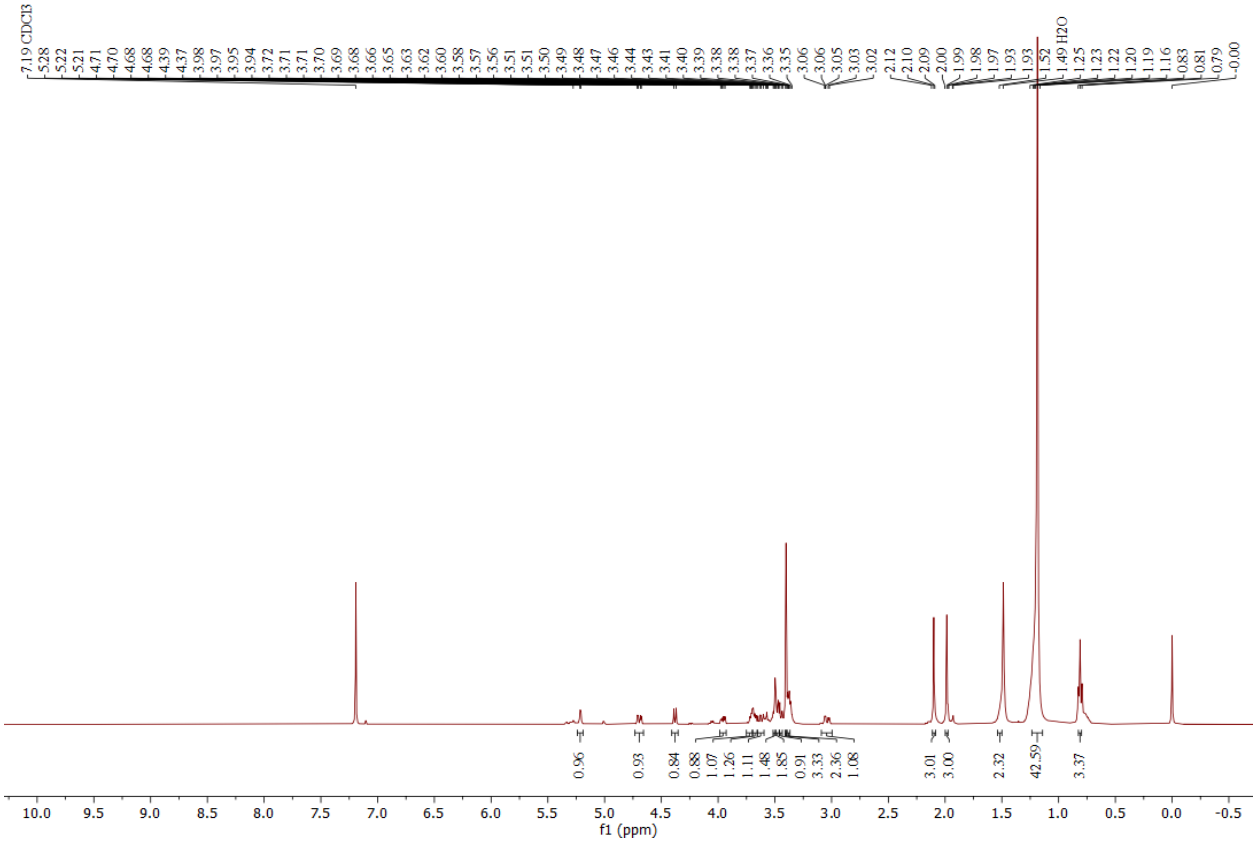
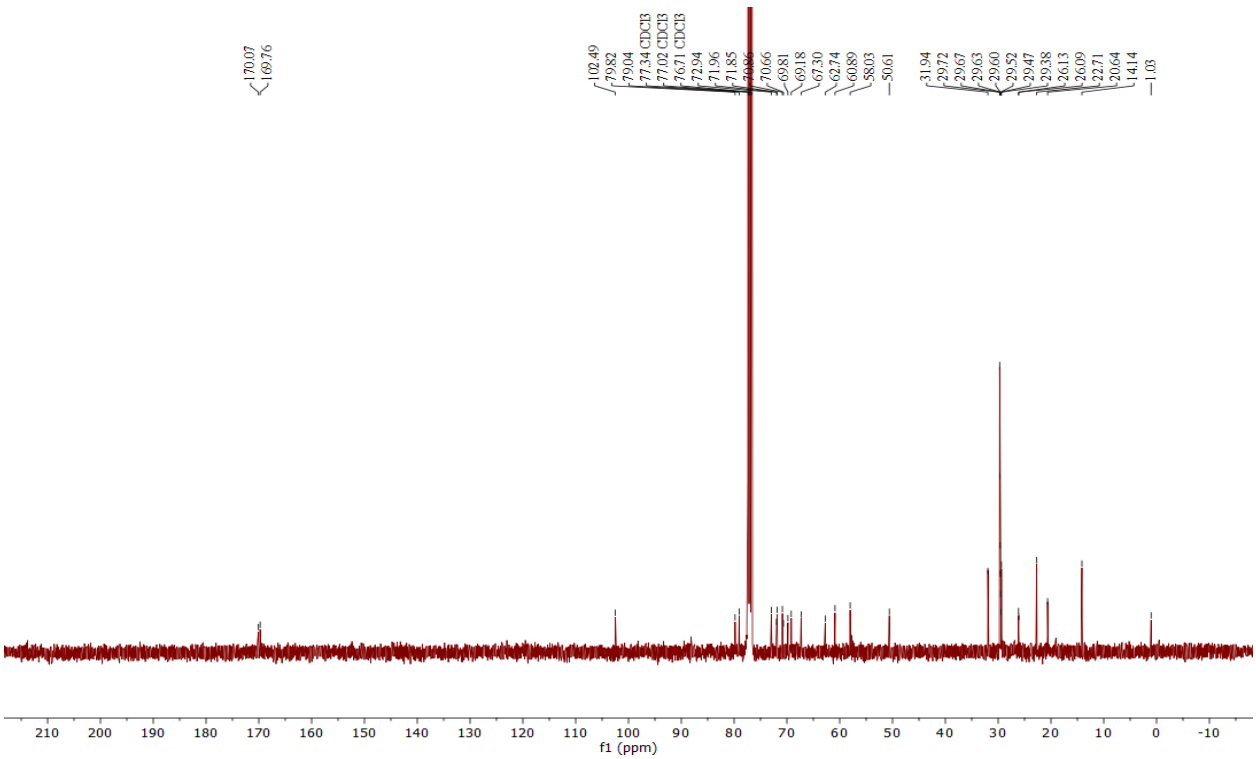
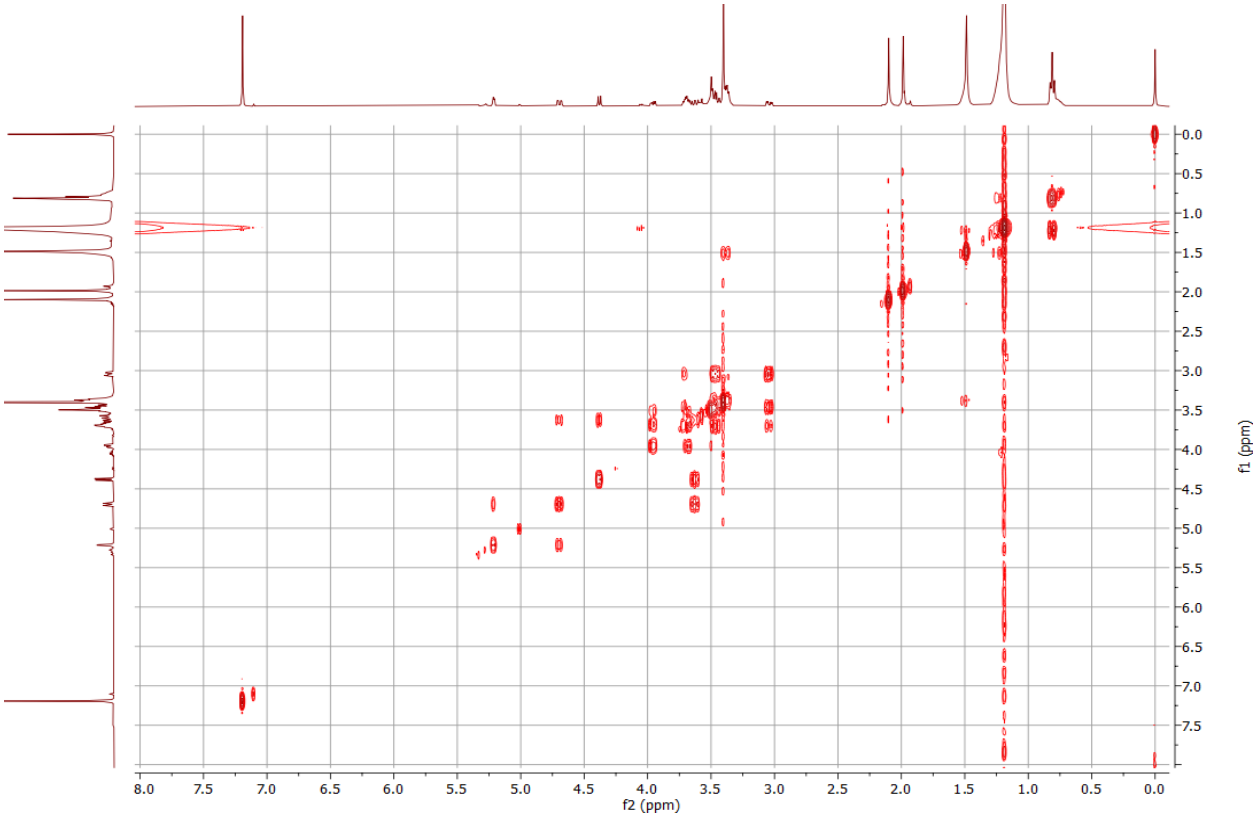
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 7b



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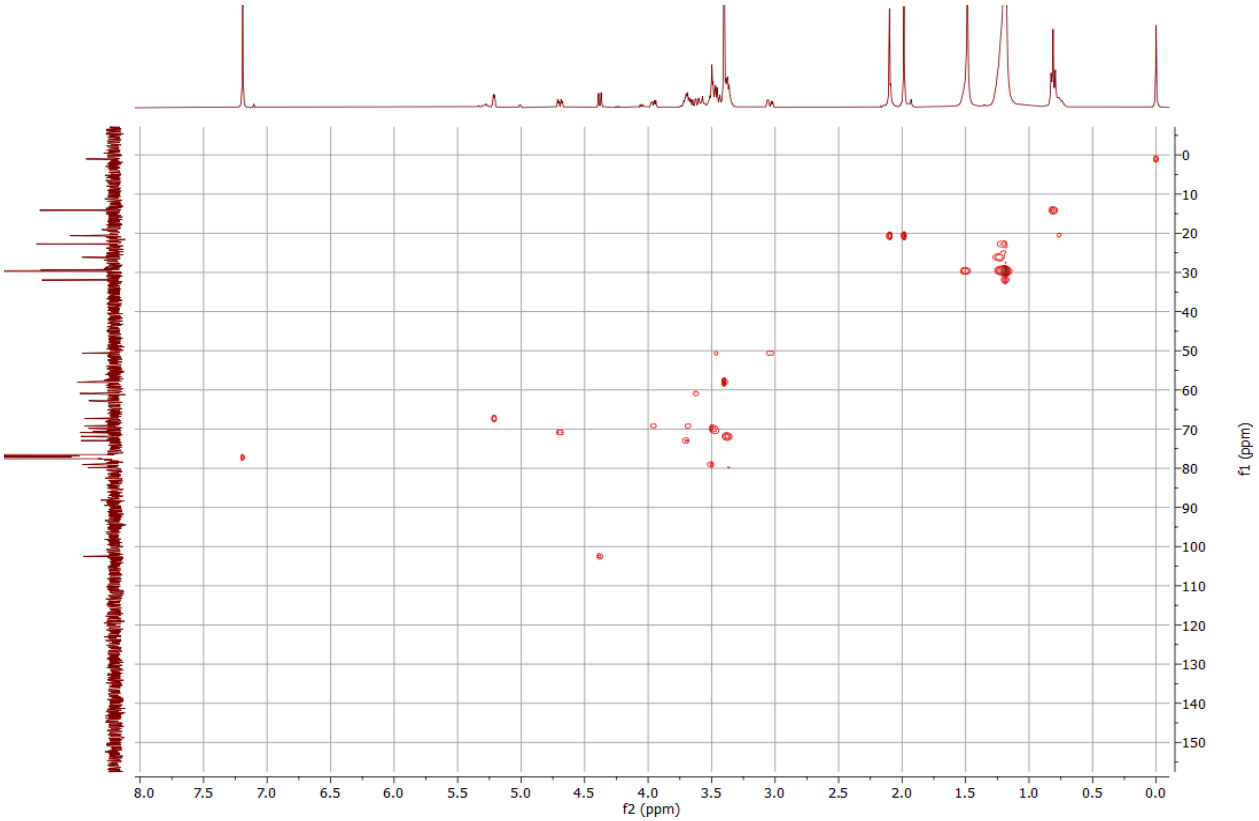
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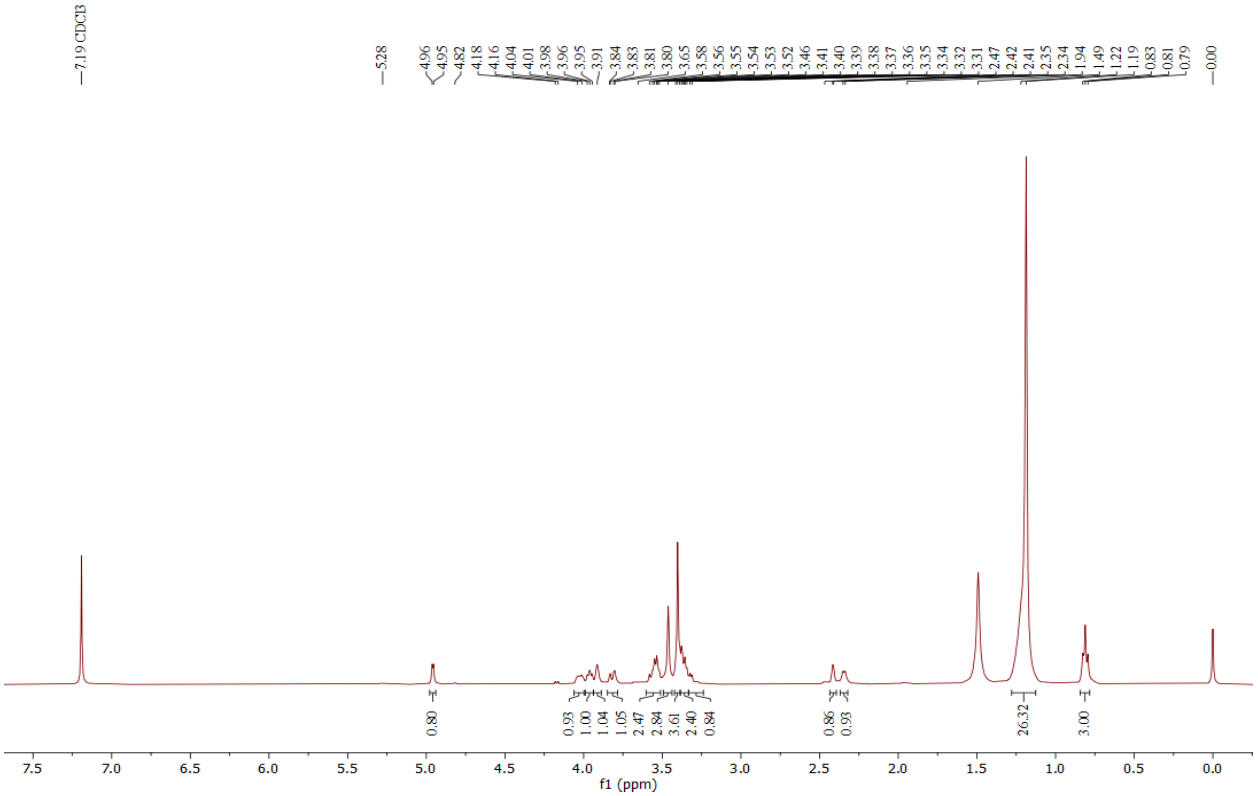
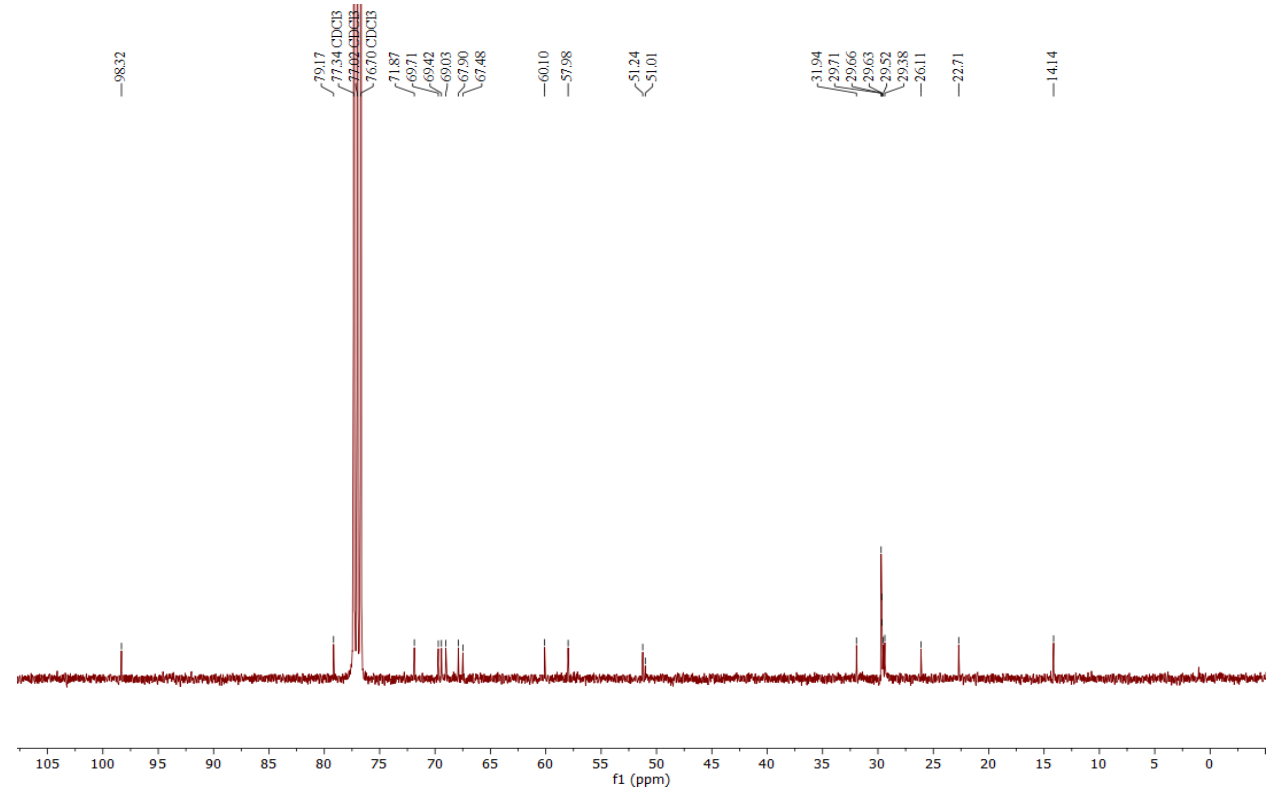
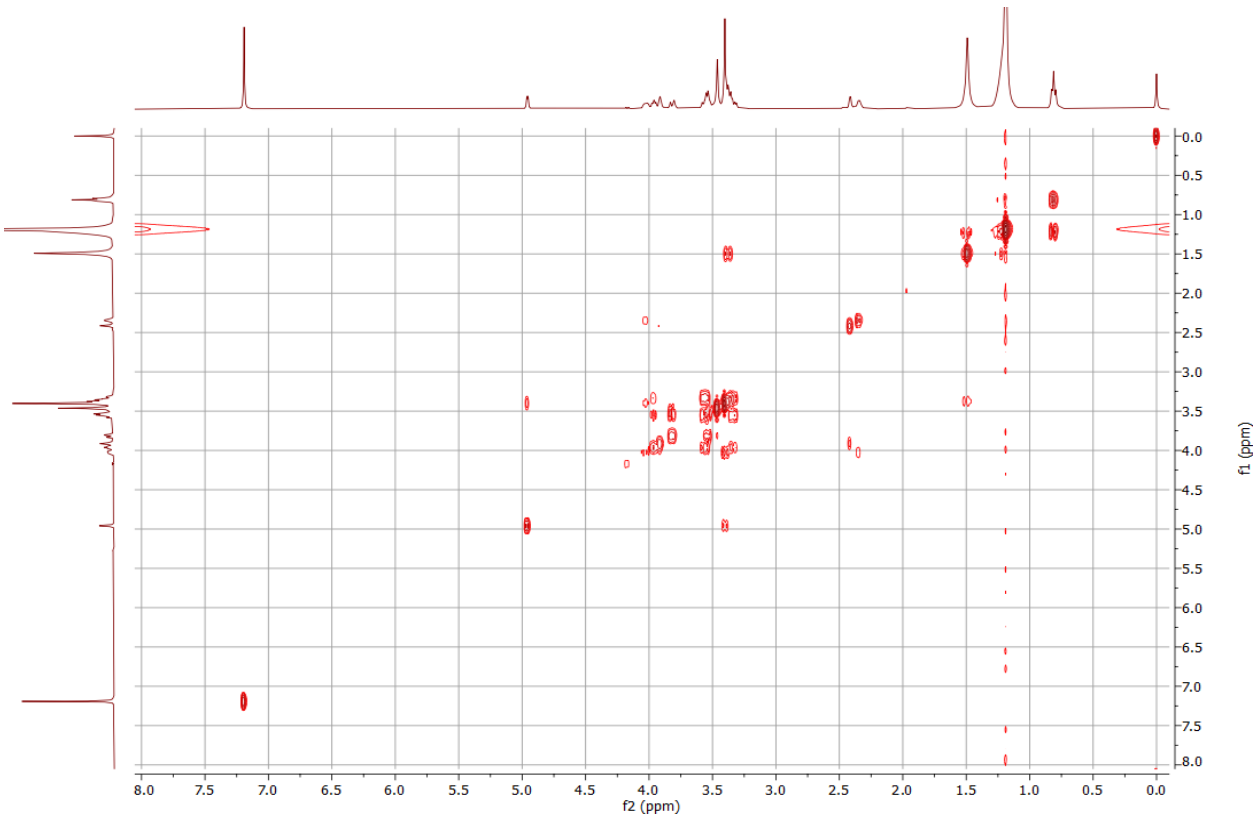
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 8a






f2 (ppm)
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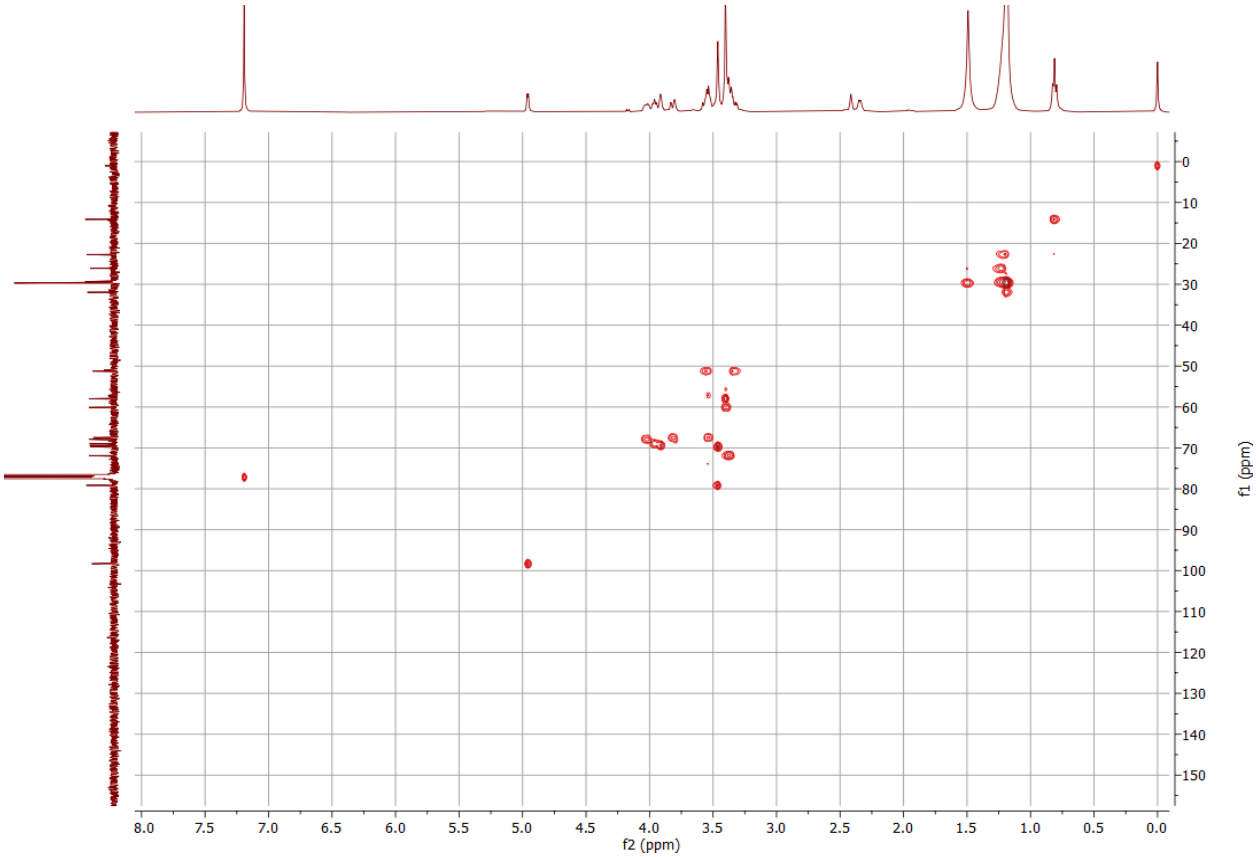
f2 (ppm)
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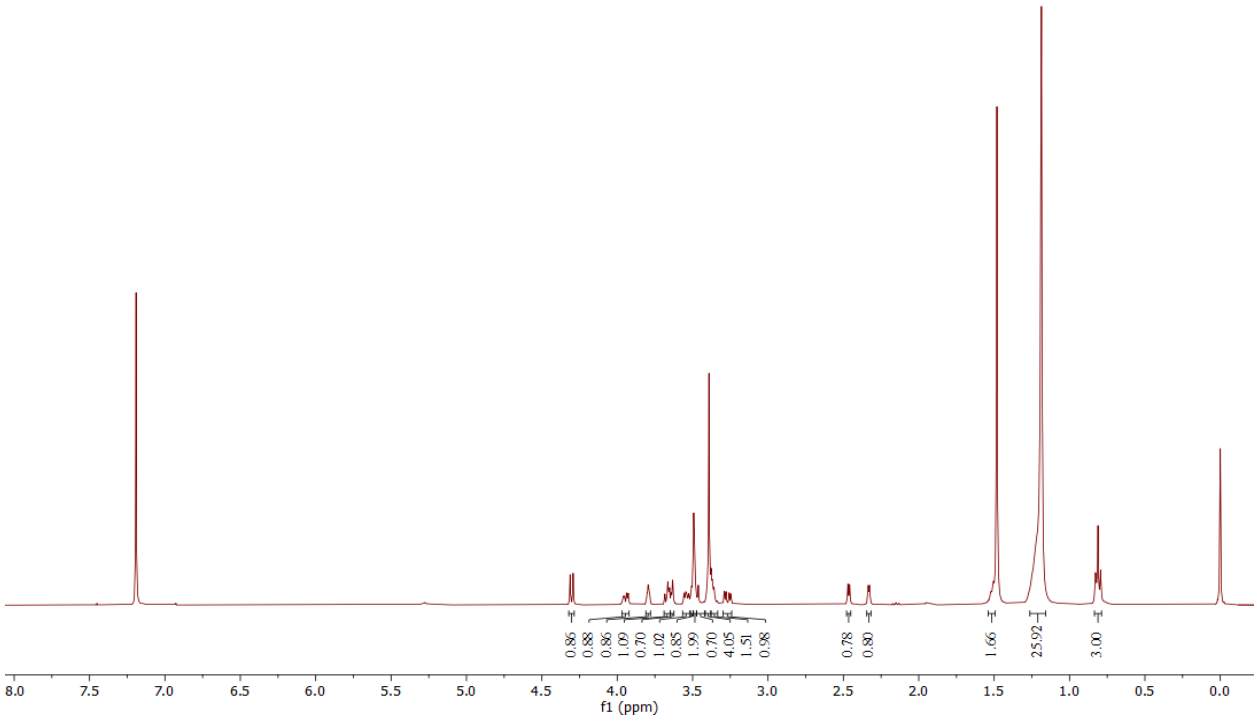
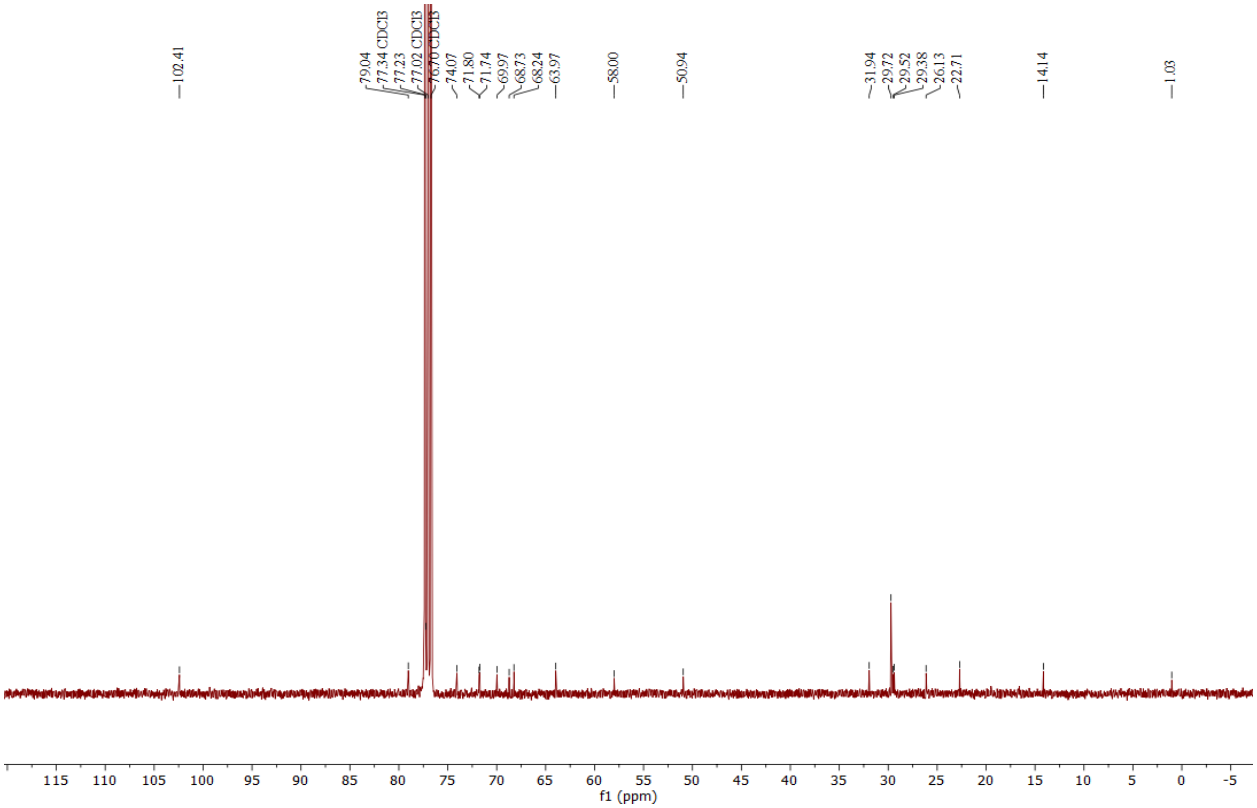
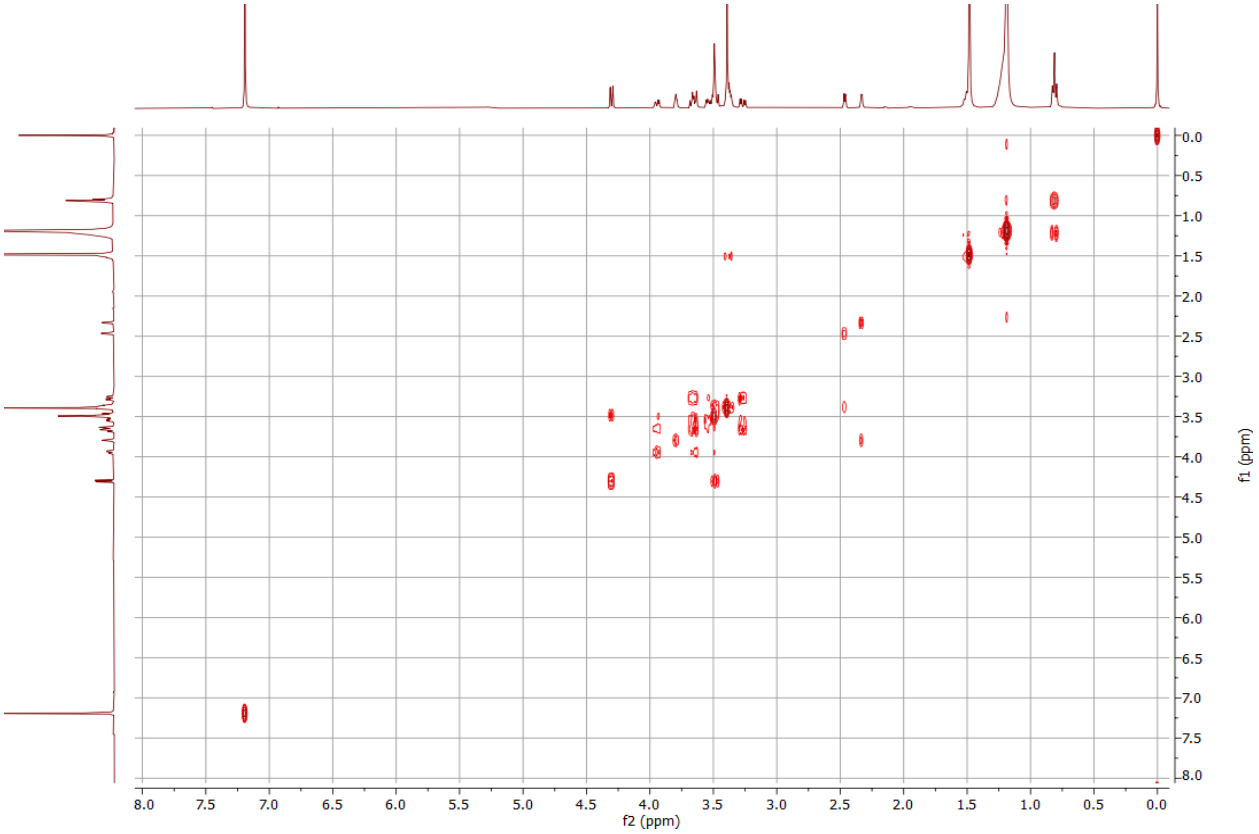
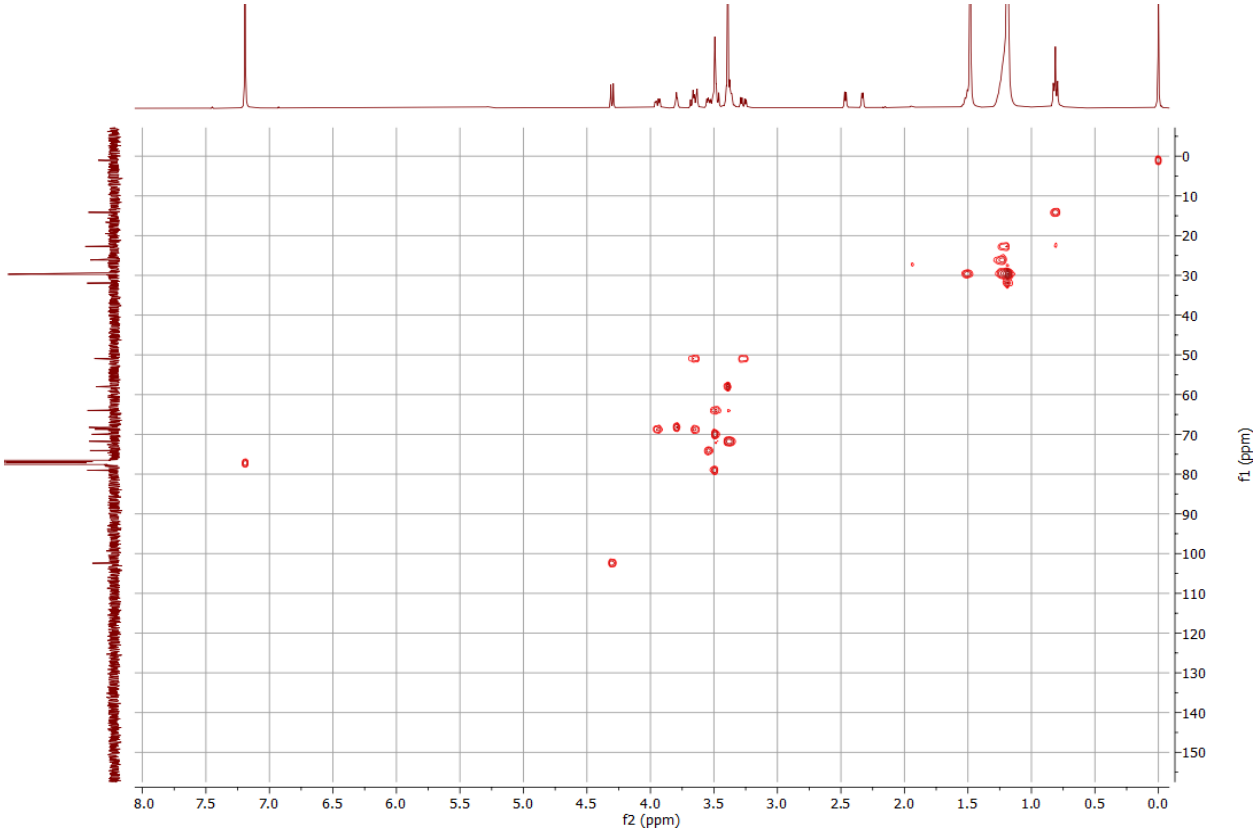
^{1}H, COSY, ^{13}C, and HSQC NMR of compound 8b






f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)