

Supporting Information

Modular Approach to Substituted Pyridoazepinones

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General experimental methods

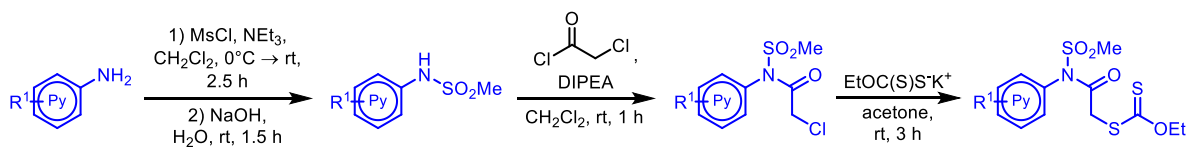
Reactions sensitive to air and/or moisture were performed under nitrogen atmosphere. For the reactions that require heating, an oil bath or a DrySyn heating block was used as the heat source.

Flash column chromatography was carried out on silica gel 60 (40-63 μm). Thin layer chromatography (TLC) was performed on alumina plates precoated with silica gel (Merck silica gel, 60 F₂₅₄). Products spots were visualized by exposure to the UV light ($\lambda_{\text{max}} = 254 \text{ nm}$) and/or by staining with vanillin in acidic ethanol solution and/or basic aqueous KMnO_4 , followed by heating. Preparative TLC was performed on glass plates coated with silica gel (Merck PLC silica gel, 60 F₂₅₄). Petroleum ether refers to the fraction of petroleum boiling between 40°C and 60°C.

Nuclear magnetic resonance spectra were recorded at ambient temperature on a Bruker Avance DPX 400 instrument. Proton magnetic resonance spectra (^1H NMR) were recorded at 400 MHz and coupling constants (J) are reported to $\pm 0.5 \text{ Hz}$. The following abbreviations were utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Carbon magnetic resonance spectra (^{13}C NMR) were recorded at 101 MHz. Chemical shifts (H, C) are quoted in parts per million (ppm) and are referenced to the residual solvent peak (CDCl_3 : $\delta\text{H} = 7.26$ and $\delta\text{C} = 77.2$; DMSO: $\delta\text{H} = 2.50$ and $\delta\text{C} = 39.5$; Acetone: $\delta\text{H} = 2.05$ and $\delta\text{C} = 29.8$).

High resolution mass spectrometry experiments were performed on a tims-TOF mass spectrometer (Bruker, France). Electrospray source has been used in positive mode. The quoted masses are accurate to $\pm 5 \text{ ppm}$. Infrared spectra were recorded on a Perkin-Elmer Spectrum Two apparatus. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}). Melting points were recorded in degrees Celsius ($^{\circ}\text{C}$), using a Stuart SMP40 Automatic Melting Point apparatus.

Synthesis of starting xanthates



2-*R*¹-5-amino:

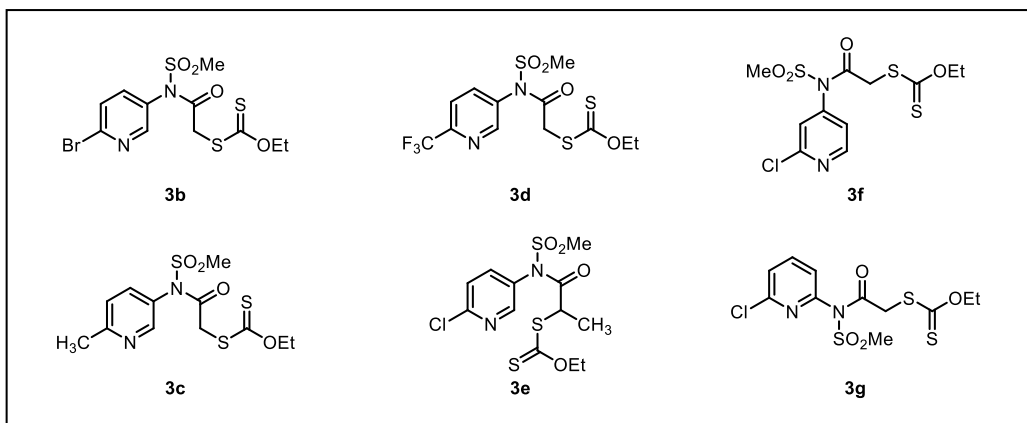
R ¹ = Br, R ² = H	1b (99%)	2b (76%)	3b (82%)
R ¹ = CH ₃ , R ² = H	1c (65%)	2c (59%)	3c (80%)
R ¹ = CF ₃ , R ² = H	1d (98%)	2d (73%)	3d (80%)
R ¹ = Cl, R ² = CH ₃		2e (57%)	3e (72%)

2-*R*¹-4-amino:

R ¹ = Cl, R ² = H	1f (65%)	2f (55%)	3f (71%)
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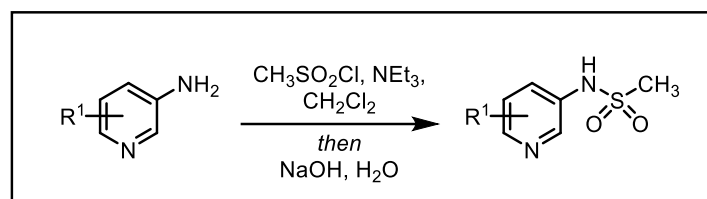
2-*R*¹-6-amino:

R ¹ = Cl, R ² = H	1g (87%)	2g (77%)	3g (63%)
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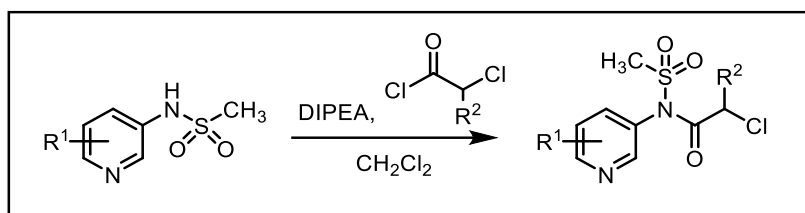
General experimental procedures

General procedure A (Sulfonylation of aminopyridines)



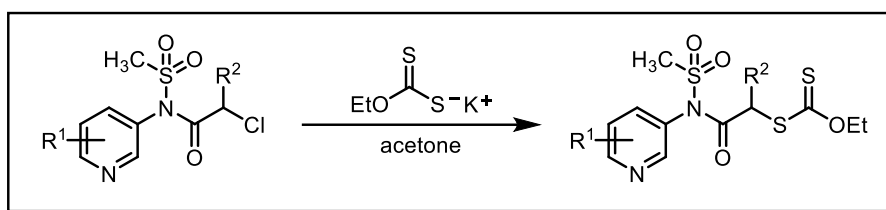
According to a modified literature procedure¹, aminopyridine (1 eq.) was dissolved in DCM (1 M solution), then Et₃N (2.25 eq.) was added. The reaction mixture was cooled to 0°C, and a solution of methanesulfonyl chloride (2.25 eq.) in DCM was added dropwise under N₂ atmosphere. Reaction mixture was stirred at r.t. for 2.5-4 h, then concentrated under reduced pressure. A 2.5 M aqueous solution of NaOH (10 eq.) was added, and the reaction mixture was stirred for 1.5-4 h (until all solid material dissolved). The mixture was then diluted with 2.0 M HCl aqueous solution (ca. 10 eq.) to ensure the acidic pH, and extracted with EtOAc. The extract was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure to afford target product, which could be further recrystallized or used directly for the next step.

General procedure B (Acylation of sulfonamide)



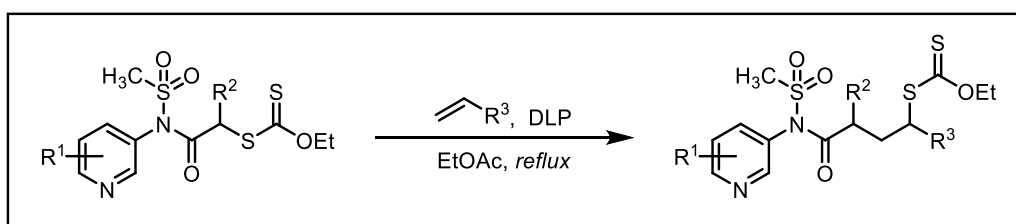
Sulfonamide (1 eq.) was mixed with DCM (0.5 M), and the mixture was cooled to 0°C. DIPEA (1.5 eq.) and chloroacetyl or chloropropionyl chloride (2.0 eq.) were added under N₂ atmosphere, and the mixture was stirred at r.t. for 1-2 h. It was then diluted with DCM, and poured into sat. NH₄Cl solution. The organic layer was washed with sat. NH₄Cl solution and brine, dried over Na₂SO₄ and concentrated under reduced pressure. The crude material was recrystallized from EtOAc or purified by column chromatography to afford the target product.

General procedure C (Substitution of chlorine to xanthate)



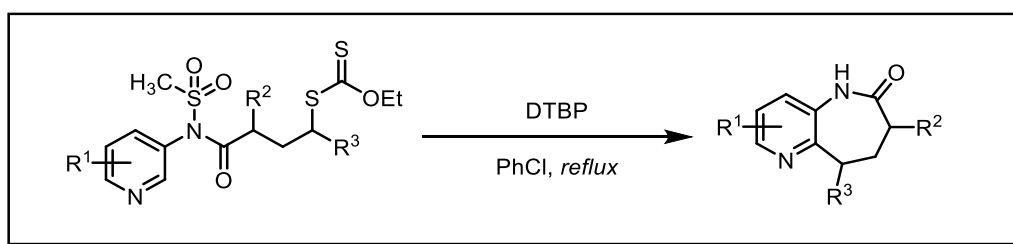
Chloride (1 eq.) was dissolved in acetone (0.3 M solution with respect to chloride) at r.t., and potassium ethyl xanthogenate (1.05 eq.) was added. The reaction mixture was stirred at r.t. for 3-4 h, then concentrated under reduced pressure. The residue was dissolved in EtOAc and washed with brine, the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography to afford the target product.

General procedure D (Xanthate addition-transfer process)



A stirred solution of the xanthate (1 eq.) and the olefin (1.1-2 eq.) in EtOAc (1.0 M of xanthate) was refluxed for 15-20 min under N_2 . Lauroyl peroxide (DLP) (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to yield the desired compounds.

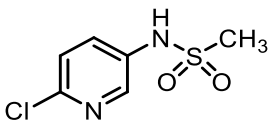
General procedure E (Radical cyclization)



A stirred solution of xanthate (1 eq.) in chlorobenzene (0.01-0.02 M of xanthate) was refluxed for 15-20 min under N_2 . Di-*tert*-butylperoxide (DTBP) (5 eq.) was then added by portions to

the refluxing solution. The reaction was monitored by TLC every hour until the starting xanthate was completely consumed. The reaction mixture was then cooled down to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel or recrystallized to yield the desired compounds.

Experimental procedures and spectroscopic data

N-(6-chloropyridin-3-yl)methanesulfonamide (1a)	
	Chemical Formula: C ₆ H ₇ ClN ₂ O ₂ S Molecular Weight: 206.64

Following the general procedure A, the reaction was carried out with the solution of 5-amino-2-chloropyridine (10.0 g, 77.8 mmol, 1 eq.) in DCM (78 mL), Et₃N (24.0 mL, 175 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (13.6 mL, 175 mmol, 2.25 eq.) in DCM (39 mL) during 2.5 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (310 mL) for 1.5 h. It was followed by the addition of 2.0 M HCl solution (390 mL), and extraction with EtOAc (3 × 200 mL). Concentration of the solution under reduced pressure afforded crude target material (15.8 g). Recrystallization from PE/EtOAc in freezer afforded pure target product **1a** (13.5 g, 84%) as light brown crystals.

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.18 (s, 1H, NH), 8.24 (dd, *J* = 2.9, 0.7 Hz, 1H, CH_{Ar}), 7.67 (dd, *J* = 8.6, 2.9 Hz, 1H, CH_{Ar}), 7.50 (dd, *J* = 8.6, 0.7 Hz, 1H, CH_{Ar}), 3.09 (s, 3H, SO₂CH₃).

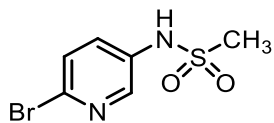
¹³C NMR (101 MHz, DMSO-*d*₆) δ 144.7 (C_{Ar}), 141.0 (CH_{Ar}), 134.8 (C_{Ar}), 130.6 (CH_{Ar}), 124.7 (CH_{Ar}), 39.8 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 3095, 3026, 2778, 1578, 1463, 1371, 1321, 1260, 1144, 1105, 965, 836.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₆H₈ClN₂O₂S 206.9990; Found 206.9992.

R_f = 0.4 (PE/EtOAc = 50%).

m.p. = 132-134°C (crystallized from PE/EtOAc).

N-(6-bromopyridin-3-yl)methanesulfonamide (1b)

Chemical Formula: C₆H₇BrN₂O₂S
Molecular Weight: 251.10

Following the general procedure A, the reaction was carried out with the solution of 2-amino-5-bromopyridine (2.00 g, 11.6 mmol, 1 eq.) in DCM (12 mL), Et₃N (3.70 mL, 26.0 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (2.00 mL, 26.0 mmol, 2.25 eq.) in DCM (6 mL) during 3 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (46 mL) for 4 h. It was followed by addition of 2.0 M HCl solution (58 mL), and extraction with EtOAc (3 × 50 mL). Concentration of the solution under reduced pressure afforded target material (2.86 g, 99%) as light brown crystals, sufficiently pure for the next step.

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.18 (s, 1H, NH), 8.23 (dd, *J* = 2.8, 0.8 Hz, 1H, CH_{Ar}), 7.62 (dd, *J* = 8.6, 0.8 Hz, 1H, CH_{Ar}), 7.57 (dd, *J* = 8.6, 2.8 Hz, 1H, CH_{Ar}), 3.09 (s, 3H, SO₂CH₃).

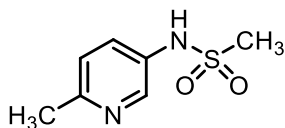
¹³C NMR (101 MHz, DMSO-*d*₆) δ 141.5 (CH_{Ar}), 135.2 (C_{Ar}), 135.0 (C_{Ar}), 130.3 (CH_{Ar}), 128.4 (CH_{Ar}), 39.9 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 2897, 1573, 1486, 1458, 1367, 1318, 1257, 1144, 1093, 964, 920, 836.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₆H₈BrN₂O₂S 250.9484; Found 250.9495.

R_f = 0.37 (PE/EtOAc = 50%).

m.p. = 150-151°C.

N-(6-methylpyridin-3-yl)methanesulfonamide (1c)

Chemical Formula: C₇H₁₀N₂O₂S
Molecular Weight: 186.23

Following the general procedure A, the reaction was carried out with the solution of 5-amino-2-methylpyridine (2.00 g, 18.5 mmol, 1 eq.) in DCM (18 mL), Et₃N (5.80 mL, 41.6 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (3.20 mL, 41.6 mmol, 2.25 eq.) in DCM (9 mL) during 3 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (74 mL) for 4 h. It was followed by addition of 2.0 M HCl solution (92 mL). Then the mixture was neutralized with saturated NaHCO₃ solution (150 mL) to pH \approx 7-8, and extracted with EtOAc (4 \times 50 mL). Concentration of the solution under reduced pressure afforded target material (2.24 g, 65%) as yellowish crystals, sufficiently pure for the next step.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.79 (s, 1H, NH), 8.30 (dd, *J* = 2.6, 0.8 Hz, 1H, CH_{Ar}), 7.51 (ddd, *J* = 8.4, 2.6 Hz, 1H, CH_{Ar}), 7.23 (dt, *J* = 8.4, 0.8 Hz, 1H, CH_{Ar}), 3.00 (s, 3H, SO₂CH₃), 2.42 (s, 3H, CH₃).

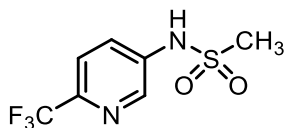
¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.7 (C_{Ar}), 141.5 (CH_{Ar}), 132.4 (C_{Ar}), 128.5 (CH_{Ar}), 123.3 (CH_{Ar}), 39.4 (SO₂CH₃), 23.3 (CH₃).

IR (neat), ν (cm⁻¹): 3010, 1580, 1492, 1377, 1315, 1290, 1262, 1136, 981, 935, 843, 730.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₇H₁₁N₂O₂S 187.0536; Found 187.0544.

R_f = 0.28 (EtOAc).

m.p. = 169-172°C.

N-(6-(trifluoromethyl)pyridin-3-yl)methanesulfonamide (1d)

Chemical Formula: C₇H₇F₃N₂O₂S
Molecular Weight: 240.20

Following the general procedure A, the reaction was carried out with the solution of 5-amino-2-(trifluoromethyl)pyridine (2.00 g, 12.3 mmol, 1 eq.) in DCM (12 mL), Et₃N (3.90 mL, 27.8 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (2.20 mL, 27.8 mmol, 2.25 eq.) in DCM (6 mL) during 3.5 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (50 mL) for 3 h. It was followed by addition of 2.0 M HCl solution (64 mL), and extraction with EtOAc (3 × 50 mL). Concentration of the solution under reduced pressure afforded target material (2.91 g, 98%) as white crystals, sufficiently pure for the next step.

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.62 (s, 1H, NH), 8.55 (dd, *J* = 2.6, 1.0 Hz, 1H, CH_{Ar}), 7.88 (dd, *J* = 8.6, 1.0 Hz, 1H, CH_{Ar}), 7.82 (dd, *J* = 8.6, 2.6 Hz, 1H, CH_{Ar}), 3.19 (s, 3H, SO₂CH₃).

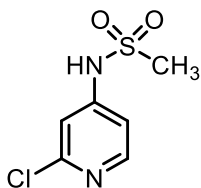
¹³C NMR (101 MHz, DMSO-*d*₆) δ 140.6 (C-F, ²*J*_{C-F} = 34.4 Hz, C_{Ar}), 140.3 (CH_{Ar}), 138.3 (C_{Ar}), 126.0 (CH_{Ar}), 121.8 (C-F, ¹*J*_{C-F} = 273.2 Hz, CF₃), 121.6 (C-F, ³*J*_{C-F} = 2.9 Hz, CH_{Ar}), 40.3 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 3221, 1586, 1473, 1332, 1317, 1245, 1130, 1022, 980, 906, 838, 766.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₇H₈F₃N₂O₂S 241.0253; Found 241.0263.

R_f = 0.47 (PE/EtOAc = 50%).

m.p. = 122-124°C.

N-(2-chloropyridin-4-yl)methanesulfonamide (1f)

Chemical Formula: C₆H₇ClN₂O₂S
Molecular Weight: 206.64

Following the general procedure A, the reaction was carried out with the solution of 2-chloropyridin-4-amine (2.50 g, 19.5 mmol, 1 eq.) in DCM (20 mL), Et₃N (6.10 mL, 43.8 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (3.40 mL, 43.8 mmol, 2.25 eq.) in DCM (10 mL) during 2 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (78 mL) for 2 h. It was followed by addition of 2.0 M HCl solution (100 mL), and extraction with EtOAc (100 mL + 2 x 50 mL). Concentration of the solution under reduced pressure and recrystallization from EtOAc afforded target material (2.63 g, 65%) as white crystals.

¹H NMR (400 MHz, Acetone-*d*₆) δ 9.50 (s, 1H, NH), 8.25 (dd, *J* = 5.6, 0.6 Hz, 1H, CH_{Ar}), 7.28 (dd, *J* = 2.0, 0.5 Hz, 1H, CH_{Ar}), 7.23 (dd, *J* = 5.6, 2.0 Hz, 1H, CH_{Ar}), 3.24 (s, 3H, SO₂CH₃).

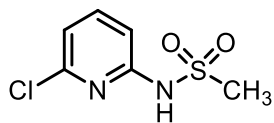
¹³C NMR (101 MHz, Acetone-*d*₆) δ 152.9 (C_{Ar}), 151.4 (CH_{Ar}), 149.2 (C_{Ar}), 112.2 (CH_{Ar}), 112.2 (CH_{Ar}), 40.7 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 2761, 1593, 1491, 1328, 1233, 1144, 1087, 1002, 985, 853, 749.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₆H₈ClN₂O₂S 206.9990; Found 206.9991.

R_f = 0.16 (PE/EtOAc = 40%).

m.p. = 144-146°C (crystallized from EtOAc).

N-(6-chloropyridin-2-yl)methanesulfonamide (1g)

Chemical Formula: C₆H₇ClN₂O₂S
Molecular Weight: 206.64

Following the general procedure A, the reaction was carried out with the solution of 6-chloropyridin-2-amine (2.50 g, 19.5 mmol, 1 eq.) in DCM (20 mL), Et₃N (6.10 mL, 43.8 mmol, 2.25 eq.), and a solution of methanesulfonyl chloride (3.40 mL, 43.8 mmol, 2.25 eq.) in DCM (10 mL) during 2 h. After concentration of the reaction mixture, the second step was carried out with 2.5 M solution of NaOH (78 mL) for 2 h. It was followed by addition of 2.0 M HCl solution (100 mL), and extraction with EtOAc (3 × 100 mL). Concentration of the solution under reduced pressure and purification by column chromatography (eluent: PE/EtOAc = 40%) afforded target material **1g** (3.50 g, 87%) as white crystals. The product was recrystallized from Et₂O for analytical purposes.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.11 (s, 1H), 7.62 (dd, *J* = 8.1, 7.8 Hz, 1H, CH_{Ar}), 7.09 (dd, *J* = 8.1, 0.7 Hz, 1H, CH_{Ar}), 7.04 (dd, *J* = 7.8, 0.7 Hz, 1H, CH_{Ar}), 3.29 (s, 3H, SO₂CH₃).

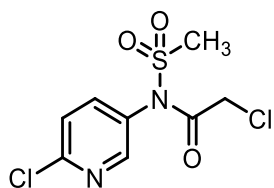
¹³C NMR (101 MHz, Chloroform-*d*) δ 150.9 (C_{Ar}), 149.9 (C_{Ar}), 141.2 (CH_{Ar}), 119.5 (CH_{Ar}), 110.3 (CH_{Ar}), 41.7 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 3240, 1586, 1570, 1434, 1376, 1318, 1142, 969, 938, 881, 787.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₆H₈ClN₂O₂S 206.9990; Found 206.9993.

R_f = 0.48 (PE/EtOAc = 40%).

m.p. = 98-100°C (crystallized from Et₂O).

2-chloro-N-(6-chloropyridin-3-yl)-N-(methylsulfonyl)acetamide (2a)

Chemical Formula: C₈H₈Cl₂N₂O₃S
Molecular Weight: 283.12

Following the general procedure B, the reaction was carried out with sulfonamide **1a** (13.2 g, 63.9 mmol, 1 eq.) in DCM (128 mL), DIPEA (16.8 mL, 95.8 mmol, 1.5 eq.) and chloroacetyl chloride (10.2 mL, 127.8 mmol, 2 eq.) during 1 h. For work-up, DCM (200 mL) and sat. NH₄Cl solution (200 mL + 100 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **2a** as light brown crystals (12.2 g, 67%).

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.60 (d, *J* = 2.8 Hz, 1H, CH_{Ar}), 8.10 (dd, *J* = 8.5, 2.8 Hz, 1H, CH_{Ar}), 7.72 (d, *J* = 8.5 Hz, 1H, CH_{Ar}), 4.31 (s, 2H, CH₂), 3.64 (s, 3H, SO₂CH₃).

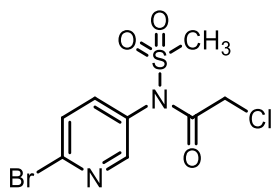
¹³C NMR (101 MHz, DMSO-*d*₆) δ 166.3 (C=O), 151.5 (C_{Ar}), 151.3 (CH_{Ar}), 141.6 (CH_{Ar}), 130.9 (C_{Ar}), 125.3 (CH_{Ar}), 44.8 (CH₂), 41.8 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 3043, 1705, 1566, 1459, 1360, 1296, 1235, 1168, 1109, 1029, 971, 884, 773, 742.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₈H₉Cl₂N₂O₃S 282.9705; Found 282.9707.

R_f = 0.70 (PE/EtOAc = 50%).

m.p. = 152-156°C (crystallized from EtOAc).

N-(6-bromopyridin-3-yl)-2-chloro-N-(methylsulfonyl)acetamide (2b)

Chemical Formula: C₈H₈BrClN₂O₃S
Molecular Weight: 327.58

Following the general procedure B, the reaction was carried out with sulfonamide **1b** (2.68 g, 10.7 mmol, 1 eq.) in DCM (21 mL), DIPEA (2.80 mL, 16.0 mmol, 1.5 eq.) and chloroacetyl chloride (1.70 mL, 21.4 mmol, 2 eq.) during 2 h. For work-up, DCM (30 mL) and sat. NH₄Cl solution (50 mL + 30 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **2b** as white crystals (2.65 g, 76%).

¹H NMR (400 MHz, DMSO-d₆) δ 8.57 (dd, J = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.98 (dd, J = 8.5, 2.8 Hz, 1H, CH_{Ar}), 7.85 (dd, J = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.31 (s, 2H, CH₂), 3.63 (s, 3H, SO₂CH₃).

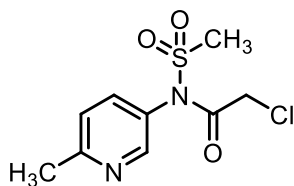
¹³C NMR (101 MHz, DMSO-d₆) δ 166.2 (C=O), 151.7 (CH_{Ar}), 142.6 (C_{Ar}), 141.4 (CH_{Ar}), 131.3 (C_{Ar}), 129.0 (CH_{Ar}), 44.8 (CH₂), 41.8 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 3037, 1704, 1561, 1454, 1358, 1296, 1234, 1167, 1113, 1090, 969, 882, 70, 736, 665.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₈H₉BrClN₂O₃S 326.9200; Found 326.9215.

R_f = 0.60 (PE/EtOAc = 50%).

m.p. = 173-175°C (crystallized from EtOAc).

2-chloro-N-(6-methylpyridin-3-yl)-N-(methylsulfonyl)acetamide (2c)

Chemical Formula: C₉H₁₁ClN₂O₃S
Molecular Weight: 262.71

Following the general procedure B, the reaction was carried out with sulfonamide **1c** (2.07 g, 11.1 mmol, 1 eq.) in DCM (22 mL), DIPEA (2.90 mL, 16.7 mmol, 1.5 eq.) and chloroacetyl chloride (1.80 mL, 22.2 mmol, 2 eq.) during 2 h. For work-up, DCM (30 mL) and sat. NH₄Cl solution (50 mL + 2 x 30 mL) were used. The crude material was purified by column chromatography (eluent: PE/EtOAc = 60%) to afford the target product **2c** as brown non-crystalline solid (1.72 g, 59%).

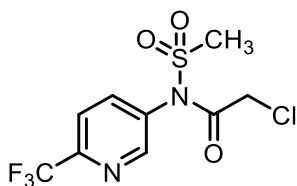
¹H NMR (400 MHz, Chloroform-*d*) δ 8.46 (ddd, *J* = 2.7 Hz, 1H, CH_{Ar}), 7.60 (dd, *J* = 8.3, 2.7 Hz, 1H, CH_{Ar}), 7.33 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 3.91 (s, 2H, CH₂), 3.50 (s, 3H, SO₂CH₂), 2.65 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 166.9 (C=O), 161.7 (C_{Ar}), 149.4 (CH_{Ar}), 137.8 (CH_{Ar}), 128.9 (C_{Ar}), 124.6 (CH_{Ar}), 43.2 (CH₂), 42.3 (SO₂CH₃), 24.5 (CH₃).

IR (neat), ν (cm⁻¹): 3013, 1718, 1621, 1561, 1487, 1317, 1147, 966, 894, 766.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₉H₁₂ClN₂O₃S 263.0252; Found 263.0265.

R_f = 0.33 (PE/EtOAc = 60%).

2-chloro-N-(methylsulfonyl)-N-(6-(trifluoromethyl)pyridin-3-yl)acetamide (2d)

Chemical Formula: C₉H₈ClF₃N₂O₃S
Molecular Weight: 316.68

Following the general procedure B, the reaction was carried out with sulfonamide **1d** (2.72 g, 11.3 mmol, 1 eq.) in DCM (23 mL), DIPEA (3.00 mL, 17.0 mmol, 1.5 eq.) and chloroacetyl chloride (1.80 mL, 22.6 mmol, 2 eq.) during 2 h. Then it was diluted with DCM (30 mL), and poured into sat. NH₄Cl solution (50 mL). The aqueous layer was extracted with DCM (30 mL) and EtOAc (30 mL), and combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The crude material was recrystallized from EtOAc in freezer to afford the target product **2d** as white crystals (2.63 g, 73%).

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.94 (d, *J* = 2.4 Hz, 1H, CH_{Ar}), 8.36 (dd, *J* = 8.4, 2.4 Hz, 1H, CH_{Ar}), 8.13 (dd, *J* = 8.4 Hz, 1H, CH_{Ar}), 4.34 (s, 2H, CH₂), 3.68 (s, 3H, SO₂CH₃).

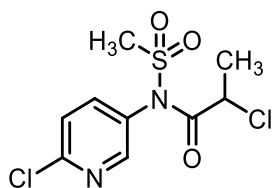
¹³C NMR (101 MHz, DMSO-*d*₆) δ 166.2 (C=O), 151.6 (CH_{Ar}), 147.1 (C-F, ²*J*_{C-F} = 34.4 Hz, C_{Ar}), 140.6 (CH_{Ar}), 134.3 (C_{Ar}), 121.9 (C-F, ³*J*_{C-F} = 2.8 Hz, CH_{Ar}), 121.3 (C-F, ¹*J*_{C-F} = 274.4 Hz, CF₃), 44.8 (CH₂), 41.9 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 2939, 1729, 1333, 1238, 1139, 1082, 1030, 968, 895, 778, 760, 705.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₉H₉ClF₃N₂O₃S 316.9969; Found 316.9982.

R_f = 0.65 (PE/EtOAc = 50%).

m.p. = 187-189°C (crystallized from EtOAc).

2-chloro-N-(6-chloropyridin-3-yl)-N-((methylthio)peroxy)propanamide (2e)

Chemical Formula: C₉H₁₀Cl₂N₂O₃S
Molecular Weight: 297.15

Following the general procedure B, the reaction was carried out with sulfonamide **1e** (2.50 g, 12.1 mmol, 1 eq.) in DCM (24 mL), DIPEA (3.20 mL, 18.2 mmol, 1.5 eq.) and chloropropionyl chloride (2.40 mL, 24.2 mmol, 2 eq.) during 2 h. For work-up, DCM (2 x 30 mL) and sat. NH₄Cl solution (50 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **2e** as white crystals (2.06 g, 57%).

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.65 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 8.14 (dd, *J* = 8.5, 2.8 Hz, 1H, CH_{Ar}), 7.74 (dd, *J* = 8.5, 0.7 Hz, 1H, CH_{Ar}), 4.36 (q, *J* = 6.4 Hz, 1H, CH), 3.65 (s, 3H, SO₂CH₃), 1.52 (d, *J* = 6.4 Hz, 3H, CH₃).

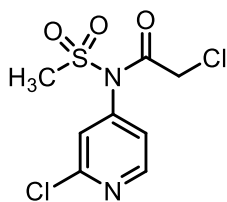
¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.7 (C=O), 151.4 (C_{Ar}), 151.4 (CH_{Ar}), 141.8 (CH_{Ar}), 131.0 (C_{Ar}), 125.1 (CH_{Ar}), 51.8 (CH), 41.6 (SO₂CH₃), 20.1 (CH₃).

IR (neat), ν (cm⁻¹): 3069, 1712, 1562, 1456, 1343, 1273, 1154, 1115, 963, 861, 775, 748.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₉H₁₁Cl₂N₂O₃S 296.9862; Found 296.9876.

R_f = 0.60 (PE/EtOAc = 50%).

m.p. = 134-137°C (crystallized from EtOAc).

2-chloro-N-(2-chloropyridin-4-yl)-N-(methylsulfonyl)acetamide (2f)

Chemical Formula: C₈H₈Cl₂N₂O₃S
Molecular Weight: 283.12

Following the general procedure B, the reaction was carried out with sulfonamide **1f** (2.50 g, 12.1 mmol, 1 eq.) in DCM (24 mL), DIPEA (3.20 mL, 18.2 mmol, 1.5 eq.) and chloroacetyl chloride (1.90 mL, 24.2 mmol, 2 eq.) during 2 h. For work-up, DCM (50 mL + 25 mL) and sat. NH₄Cl solution (2 x 50 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **2f** as white crystals (1.89 g, 55%).

¹H NMR (400 MHz, Acetone-*d*₆) δ 8.61 (dd, *J* = 5.2, 0.6 Hz, 1H, CH_{Ar}), 7.78 (dd, *J* = 1.8, 0.6 Hz, 1H, CH_{Ar}), 7.66 (dd, *J* = 5.2, 1.8 Hz, 1H, CH_{Ar}), 4.34 (s, 2H, CH₂), 3.62 (s, 3H, SO₂CH₃).

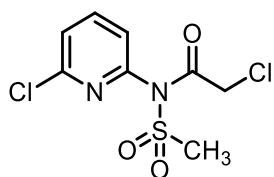
¹³C NMR (101 MHz, Acetone-*d*₆) δ 166.4 (C=O), 153.0 (C_{Ar}), 152.2 (CH_{Ar}), 145.9 (C_{Ar}), 126.9 (CH_{Ar}), 125.6 (CH_{Ar}), 44.9 (CH₂), 42.5 (SO₂CH₃).

IR (neat), ν (cm⁻¹): 1725, 1697, 1578, 1461, 1356, 1251, 1154, 1120, 1084, 965, 911, 777, 747.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₈H₉Cl₂N₂O₃S 282.9705; Found 282.9707.

R_f = 0.48 (PE/EtOAc = 40%).

m.p. = 122-125°C (crystallized from EtOAc).

2-chloro-N-(6-chloropyridin-2-yl)-N-(methylsulfonyl)acetamide (2g)

Chemical Formula: C₈H₈Cl₂N₂O₃S
Molecular Weight: 283.12

Following the general procedure B, the reaction was carried out with sulfonamide **1g** (3.20 g, 15.5 mmol, 1 eq.) in DCM (31 mL), DIPEA (4.10 mL, 23.2 mmol, 1.5 eq.) and chloroacetyl chloride (2.50 mL, 31.5 mmol, 2 eq.) during 2 h. For work-up, DCM (50 mL + 25 mL) and sat. NH₄Cl solution (2 x 50 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **2g** as white crystals (3.89 g, 77%).

¹H NMR (400 MHz, Acetone-*d*₆) δ 8.13 (dd, *J* = 7.7 Hz, 1H, CH_{Ar}), 7.71 (dd, *J* = 6.0, 0.7 Hz, 1H, CH_{Ar}), 7.69 (dd, *J* = 6.3, 0.7 Hz, 1H, CH_{Ar}), 4.31 (s, 2H, CH₂), 3.57 (s, 3H, SO₂CH₃).

¹³C NMR (101 MHz, Acetone-*d*₆) δ 167.2 (C=O), 151.2 (C_{Ar}), 149.2 (C_{Ar}), 143.1 (CH_{Ar}), 127.1 (CH_{Ar}), 126.0 (CH_{Ar}), 44.7 (CH₂), 42.3 (SO₂CH₃).

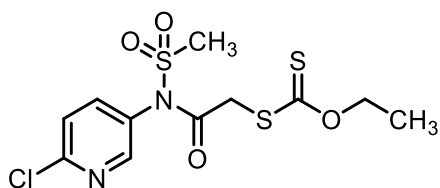
IR (neat), ν (cm⁻¹): 2939, 1728, 1579, 1569, 1429, 1359, 1319, 1158, 1026, 967, 779, 747.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₈H₉Cl₂N₂O₃S 282.9705; Found 282.9708.

R_f = 0.58 (PE/EtOAc = 40%).

m.p. = 151-153°C (crystallized from EtOAc).

S-(2-(N-(6-chloropyridin-3-yl)methylsulfonamido)-2-oxoethyl) O-ethyl carbonodithioate (3a)



Chemical Formula: C₁₁H₁₃ClN₂O₄S₃
Molecular Weight: 368.87

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2a** (12.0 g, 42.4 mmol, 1 eq.) in acetone (140 mL) and potassium ethyl xanthogenate (7.14 g, 44.5 mmol, 1.05 eq.) during 3 h. For work-up, EtOAc 200 mL) and brine (2 × 150 mL) were used. The crude material was purified by flash column chromatography (eluent: PE/EtOAc = 40%) to afford the target product **3a** as a brown oil, that solidified upon time (14.2 g, 91%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.46 (dd, J = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.78 (dd, J = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.51 (dd, J = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.61 (q, J = 7.1 Hz, 2H, CH₂), 3.80 (s, 2H, CH₂), 3.49 (s, 3H, SO₂CH₃), 1.41 (t, J = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 213.4 (C=S), 167.2 (C=O), 153.4 (C_{Ar}), 150.4 (CH_{Ar}), 140.4 (CH_{Ar}), 131.1 (C_{Ar}), 125.7 (CH_{Ar}), 71.7 (CH₂), 42.5 (SO₂CH₃), 41.4 (CH₂), 13.8 (CH₃).

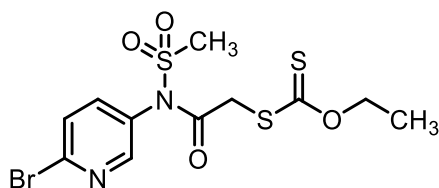
IR (neat): 2985, 2931, 1713, 1562, 1454, 1355, 1288, 1149, 1108, 1045, 961, 871, 771, 746.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₁H₁₄ClN₂O₄S₃ 368.9799; Found 368.9801.

R_f = 0.74 (PE/EtOAc = 40%).

m.p. = 103-105°C.

S-(2-(N-(6-bromopyridin-3-yl)methylsulfonamido)-2-oxoethyl) O-ethyl carbonodithioate (3b)



Chemical Formula: C₁₁H₁₃BrN₂O₄S₃
Molecular Weight: 413.32

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2b** (2.54 g, 25.9 mmol, 1 eq.) in acetone (26 mL) and potassium ethyl xanthogenate (1.31 g, 8.14 mmol, 1.05 eq.) during 4 h. For work-up, EtOAc (50 mL + 25 mL) and water (50 mL) were used. The crude material was purified by flash column chromatography (eluent: PE/EtOAc = 40%) to afford the target product as a white solid (2.61 g, 82%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.44 (dd, *J* = 2.0, 1.5 Hz, 1H, CH_{Ar}), 7.67 (m, 1H, CH_{Ar}), 7.66 (m, 1H, CH_{Ar}), 4.61 (q, *J* = 7.1 Hz, 2H, CH₂), 3.79 (s, 2H, CH₂), 3.49 (s, 3H, SO₂CH₃), 1.41 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 213.3 (C=S), 167.1 (C=O), 150.8 (CH_{Ar}), 144.1 (C_{Ar}), 140.1 (CH_{Ar}), 131.5 (C_{Ar}), 129.6 (CH_{Ar}), 71.7 (CH₂), 42.5 (SO₂CH₃), 41.4 (CH₂), 13.8 (CH₃).

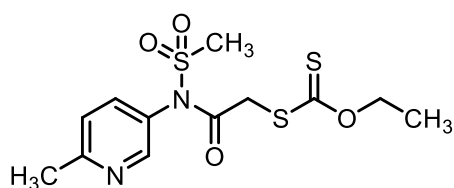
IR (neat), ν (cm⁻¹): 3048, 1698, 1555, 1449, 1345, 1307, 1217, 1150, 1090, 1045, 962, 891, 768.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₄BrN₂O₄S₃ 412.9294; Found 412.9310.

R_f = 0.63 (PE/EtOAc = 40%).

m.p. = 118-122°C.

O-ethyl S-(2-(N-(6-methylpyridin-3-yl)methylsulfonamido)-2-oxoethyl) carbonodithioate (3c)



Chemical Formula: C₁₂H₁₆N₂O₄S₃
Molecular Weight: 348.45

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2c** (1.65 g, 6.28 mmol, 1 eq.) in acetone (21 mL) and potassium ethyl xanthogenate (1.06 g, 6.59 mmol, 1.05 eq.) during 4 h. For work-up, EtOAc (50 mL + 25 mL) and water (50 mL) were used. The crude material was purified by flash column chromatography (eluent: PE/EtOAc = 50/50 → 40/60) to afford the target product **3c** as a white solid (1.76 g, 80%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.53 (dd, *J* = 2.7, 0.8 Hz, 1H, CH_{Ar}), 7.67 (dd, *J* = 8.3, 2.7 Hz, 1H, CH_{Ar}), 7.32 (dd, *J* = 8.3, 0.8 Hz, 1H, CH_{Ar}), 4.59 (q, *J* = 7.1 Hz, 2H, CH₂), 3.75 (s, 2H, CH₂), 3.47 (s, 3H, SO₂CH₃), 2.62 (s, 3H, CH₃), 1.39 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 213.2 (C=S), 167.5 (C=O), 161.2 (C_{Ar}), 149.6 (CH_{Ar}), 137.8 (CH_{Ar}), 129.4 (C_{Ar}), 124.5 (CH_{Ar}), 71.4 (CH₂), 42.3 (SO₂CH₃), 41.4 (CH₂), 24.5 (CH₃), 13.8 (CH₃).

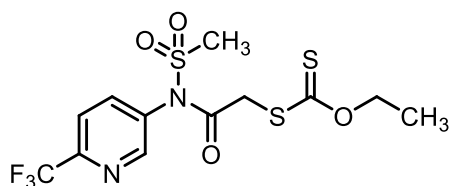
IR (neat), ν (cm⁻¹): 2988, 1701, 1484, 1343, 1306, 1215, 1150, 1109, 1045, 964, 893, 764.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₇N₂O₄S₃ 349.0345; Found 349.0358.

R_f = 0.19 (PE/EtOAc = 40%).

m.p. = 117-118°C.

O-ethyl S-(2-oxo-2-(N-(6-(trifluoromethyl)pyridin-3-yl)methylsulfonamido)ethyl) carbonodithioate (3d)



Chemical Formula: C₁₂H₁₃F₃N₂O₄S₃
Molecular Weight: 402.42

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2d** (2.49 g, 7.85 mmol, 1 eq.) in acetone (26 mL) and potassium ethyl xanthogenate (1.32 g, 8.24 mmol, 1.05 eq.) during 2.5 h. For work-up, EtOAc (50 + 30 mL) and brine (50 mL) were used. The crude material was purified by flash column chromatography (eluent: PE/EtOAc = 80/20 → 60/40) to afford the target product **3d** as a yellow oil (2.54 g, 80%), that solidified into a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.79 (dd, *J* = 2.5, 0.8 Hz, 1H, CH_{Ar}), 8.02 (dd, *J* = 8.4, 2.5 Hz, 1H, CH_{Ar}), 7.87 (dd, *J* = 8.4, 0.8 Hz, 1H, CH_{Ar}), 4.62 (q, *J* = 7.1 Hz, 2H, CH₂), 3.82 (s, 2H, CH₂), 3.53 (s, 3H, SO₂CH₃), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 213.4 (C=S), 167.0 (C=O), 150.9 (CH_{Ar}), 149.6 (C-F, ²*J*_{C-F} = 35.7 Hz, C_{Ar}), 139.6 (CH_{Ar}), 134.5 (C_{Ar}), 121.8 (C-F, ³*J*_{C-F} = 2.8 Hz, CH_{Ar}), 121.0 (C-F, ¹*J*_{C-F} = 274.6 Hz, CF₃), 71.8 (CH₂), 42.5 (SO₂CH₃), 41.6 (CH₂), 13.8 (CH₃).

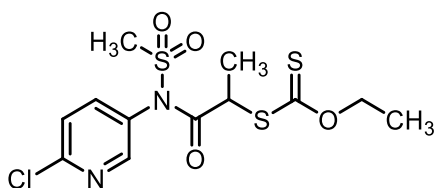
IR (neat), ν (cm⁻¹): 2898, 1714, 1360, 1338, 1242, 1158, 1130, 1086, 1040, 964, 904, 774, 755.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₄F₃N₂O₄S₃ 403.0062; Found 403.0080.

R_f = 0.71 (PE/EtOAc = 40%).

m.p. = 107-109°C.

S-(1-((6-chloropyridin-3-yl)((methylthio)peroxy)amino)-1-oxopropan-2-yl) O-ethyl carbonodithioate (3e)



Chemical Formula: C₁₂H₁₅ClN₂O₄S₃
Molecular Weight: 382.89

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2e** (1.92 g, 6.45 mmol, 1 eq.) in acetone (22 mL) and potassium ethyl xanthogenate (1.09 g, 6.77 mmol, 1.05 eq.) during 2.5 h. For work-up, EtOAc (100 mL + 50 mL) and brine (100 mL) were used. The crude material was recrystallized from PE/EtOAc in freezer to afford the target product **3e** as white crystals (1.77 g, 72%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.45 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.77 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.63 – 4.47 (m, 2H, CH₂), 4.21 (q, *J* = 7.1 Hz, 1H, CH), 3.49 (s, 3H, SO₂CH₃), 1.49 (d, *J* = 7.1 Hz, 3H, CH₃), 1.38 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 211.9 (C=S), 171.3 (C=O), 153.2 (C_{Ar}), 150.7 (CH_{Ar}), 140.7 (CH_{Ar}), 130.7 (C_{Ar}), 125.4 (CH_{Ar}), 71.5 (CH₂), 48.4 (CH), 42.4 (SO₂CH₃), 16.7 (CH₃), 13.8 (CH₃).

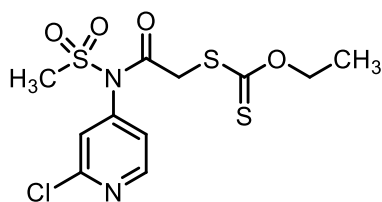
IR (neat), ν (cm⁻¹): 2987, 1701, 1565, 1451, 1339, 1233, 1211, 1143, 1026, 954, 864, 768, 750.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₆ClN₂O₄S₃ 382.9955; Found 382.9973.

R_f = 0.70 (PE/EtOAc = 40%).

m.p. = 128-130°C (crystallized from PE/EtOAc).

S-(2-(N-(2-chloropyridin-4-yl)methylsulfonamido)-2-oxoethyl) O-ethyl carbonodithioate (3f)



Chemical Formula: C₁₁H₁₃ClN₂O₄S₃
Molecular Weight: 368.87

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2f** (1.75 g, 6.18 mmol, 1 eq.) in acetone (20 mL) and potassium ethyl xanthogenate (1.04 g, 6.49 mmol, 1.05 eq.) during 2 h. For work-up, EtOAc (30 mL) and brine (30 mL) were used. The crude material was purified by column chromatography (eluent: PE/EtOAc = 80/20 → 70/30) to afford the target product **3f** as yellow oil (1.63 g, 71%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.57 (d, *J* = 5.2 Hz, 1H, CH_{Ar}), 7.45 (d, *J* = 1.8 Hz, 1H, CH_{Ar}), 7.36 (dd, *J* = 5.2, 1.8 Hz, 1H, CH_{Ar}), 4.61 (q, *J* = 7.1 Hz, 2H, CH₂), 3.81 (s, 2H, CH₂), 3.48 (s, 3H, SO₂CH₃), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

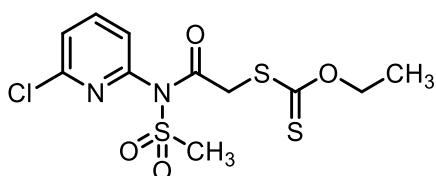
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.3 (C=S), 166.6 (C=O), 153.2 (C_{Ar}), 151.6 (CH_{Ar}), 144.8 (C_{Ar}), 125.7 (CH_{Ar}), 123.8 (CH_{Ar}), 71.7 (CH₂), 42.7 (SO₂CH₃), 41.3 (CH₂), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 1716, 1578, 1461, 1359, 1231, 1151, 1113, 1046, 965, 773.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₄ClN₂O₄S₃ 368.9799; Found 368.9800.

R_f = 0.59 (PE/EtOAc = 40%).

S-(2-(N-(6-chloropyridin-2-yl)methylsulfonamido)-2-oxoethyl) O-ethyl carbonodithioate (3g)



Chemical Formula: C₁₁H₁₃ClN₂O₄S₃
Molecular Weight: 368.87

Following the general procedure for the formation of xanthate (procedure C), the reaction was carried out with chloride **2g** (3.20 g, 11.3 mmol, 1 eq.) in acetone (38 mL) and potassium ethyl xanthogenate (1.90 g, 11.9 mmol, 1.05 eq.) during 2 h. For work-up, EtOAc (3 x 30 mL) and H₂O (2 x 30 mL) were used. The crude material was recrystallized from EtOAc in freezer to afford the target product **3g** as white crystals (2.63 g, 63%).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.89 (dd, *J* = 7.9, 7.7 Hz, 1H, CH_{Ar}), 7.52 (dd, *J* = 7.7, 0.8 Hz, 1H, CH_{Ar}), 7.49 (dd, *J* = 7.9, 0.8 Hz, 1H, CH_{Ar}), 4.62 (q, *J* = 7.1 Hz, 2H, CH₂), 3.86 (s, 2H, CH₂), 3.50 (s, 3H, SO₂CH₃), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 212.2 (C=S), 167.3 (C=O), 151.1 (C_{Ar}), 148.4 (C_{Ar}), 141.2 (CH_{Ar}), 126.1 (CH_{Ar}), 124.7 (CH_{Ar}), 71.2 (CH₂), 42.0 (SO₂CH₃), 41.3 (CH₂), 13.7 (CH₃).

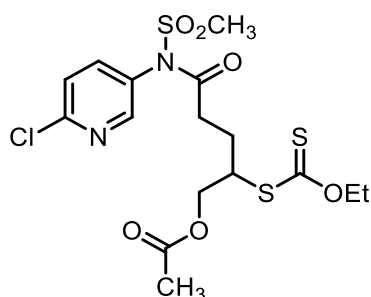
IR (neat), ν (cm⁻¹): 1717, 1578, 1561, 1427, 1357, 1228, 1146, 1044, 963, 875, 772, 731.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₄ClN₂O₄S₃ 368.9799; Found 368.9803.

R_f = 0.67 (PE/EtOAc = 40%).

m.p. = 99-100°C (crystallized from EtOAc).

5-(N-(6-chloropyridin-3-yl)methylsulfonamido)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl acetate (4aa)



Chemical Formula: C₁₆H₂₁ClN₂O₆S₃
Molecular Weight: 468.98

Following the general procedure D, the reaction was carried out with the solution of **3a** (304 mg, 0.82 mmol, 1 eq.) and allyl acetate (0.18 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.1 eq. of DLP (32 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4aa** (330 mg, 85%) as a yellowish oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.61 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.47 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.64 (q, *J* = 7.1 Hz, 2H, CH₂), 4.28 (dd, *J* = 11.4, 4.9 Hz, 1H, CH_{A1}H), 4.19 (dd, *J* = 11.5, 6.1 Hz, 1H, CH_HA₂), 4.06 – 3.91 (m, 1H, S-CH), 3.50 (s, 3H, SO₂CH₃), 2.35 – 2.17 (m, 3H, CH₂ and CH_{B1}H), 2.06 (s, 3H, CH₃), 1.92 – 1.80 (m, 1H, CH_HB₂), 1.43 (t, *J* = 7.1 Hz, 3H, CH₃).

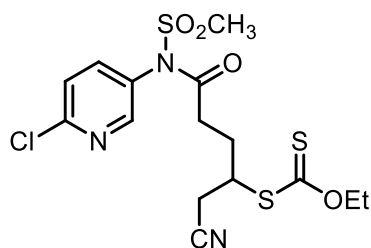
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.3 (C=S), 172.3 (C=O), 170.7 (C=O), 153.2 (C_{Ar}), 150.2 (CH_{Ar}), 140.1 (CH_{Ar}), 131.3 (C_{Ar}), 125.7 (CH_{Ar}), 71.0 (CH₂), 65.8 (CH₂), 49.0 (S-CH), 42.6 (SO₂CH₃), 34.2 (CH₂), 25.8 (CH₂), 20.9 (CH₃), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 2984, 2934, 1735, 1712, 1562, 1455, 1355, 1222, 1151, 1109, 1039, 963, 909, 776, 731.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₂ClN₂O₆S₃ 469.0323; Found 469.0328.

R_f = 0.50 (PE/EtOAc = 40%).

5-(*N*-(6-chloropyridin-3-yl)methylsulfonamido)-1-cyano-5-oxopentan-2-yl *O*-ethyl carbonodithioate (4ab**)**



Chemical Formula: C₁₅H₁₈ClN₃O₄S₃
Molecular Weight: 435.96

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and allyl cyanide (0.13 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 50%) afforded target product **4ab** (280 mg, 79%) as a yellowish oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.63 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.48 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.65 (qd, *J* = 7.1, 0.7 Hz, 2H, CH₂), 3.98 – 3.89 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 2.89 – 2.84 (m, 2H, CH₂), 2.39 – 2.22 (m, 3H, CH₂ and CH_{Ar}H), 2.06 – 1.94 (m, 1H, CHH_{A2}), 1.44 (t, *J* = 7.1 Hz, 3H, CH₃).

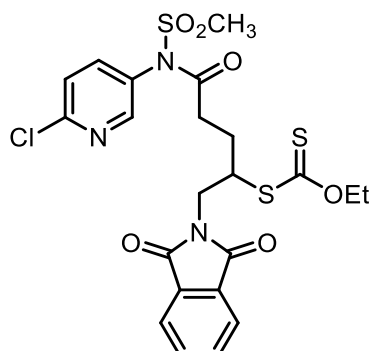
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.0 (C=S), 171.9 (C=O), 153.2 (C_{Ar}), 150.2 (CH_{Ar}), 140.1 (CH_{Ar}), 131.2 (C_{Ar}), 125.8 (CH_{Ar}), 117.0 (CN), 71.2 (CH₂), 45.8 (S-CH), 42.6 (SO₂CH₃), 34.1 (CH₂), 27.4 (CH₂), 24.4 (CH₂), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 2931, 1709, 1562, 1454, 1354, 1224, 1151, 1109, 1043, 962, 910, 776.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₁₉ClN₃O₄S₃ 436.0221; Found 436.0229.

R_f = 0.26 (PE/EtOAc = 40%).

5-(*N*-(6-chloropyridin-3-yl)methylsulfonamido)-1-(1,3-dioxoisindolin-2-yl)-5-oxopentan-2-yl *O*-ethyl carbonodithioate (4ac**)**



Chemical Formula: C₂₂H₂₂ClN₃O₆S₃
Molecular Weight: 556.06

Following the general procedure D, the reaction was carried out with the solution of **3a** (302 mg, 0.82 mmol, 1 eq.) and *N*-allyl phthalimide (302 mg, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.1 eq. of DLP (35 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 10% → 40% → 50%) afforded target product **4ac** (367 mg, 81%) as a white foam.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.86 – 7.82 (m, 2H, CH_{Phth}), 7.75 – 7.71 (m, 2H, CH_{Phth}), 7.62 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.46 (dd, *J* = 8.4, 0.8 Hz, 1H, CH_{Ar}), 4.59 (q, *J* = 7.1 Hz, 2H, CH₂), 4.16 – 4.07 (m, 1H, S-CH), 3.94 (dd, *J* = 14.1, 7.2 Hz, 1H, CH_{A1}H), 3.86 (dd, *J* = 14.1, 7.5 Hz, 1H, CH_{H_{A2}}), 3.49 (s, 3H, SO₂CH₃), 2.38 – 2.30 (m, 2H, CH₂), 2.25 – 2.12 (m, 1H, CH_{B1}H), 1.93 – 1.81 (m, 1H, CH_{H_{B2}}), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

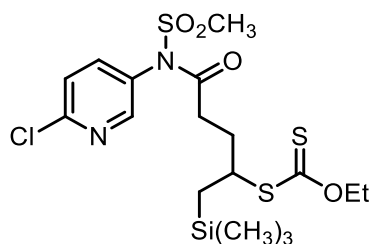
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.5 (C=S), 172.2 (C=O), 168.2 (C=O), 153.1 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 134.4 (2C, CH_{Phth}), 131.8 (2C, C_{Phth}), 131.3 (C_{Ar}), 125.7 (CH_{Ar}), 123.7 (2C, CH_{Phth}), 70.9 (CH₂), 48.7 (S-CH), 42.6 (SO₂CH₃), 40.8 (CH₂), 34.0 (CH₂), 26.2 (CH₂), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 2934, 1711, 1456, 1394, 1356, 1223, 1155, 1110, 1046, 963, 777, 716.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₂H₂₃ClN₃O₆S₃ 556.0432; Found 556.0436.

R_f = 0.27 (PE/EtOAc = 40%).

5-(*N*-(6-chloropyridin-3-yl)methylsulfonamido)-5-oxo-1-(trimethylsilyl)pentan-2-yl *O*-ethyl carbonodithioate (4ad)



Chemical Formula: C₁₇H₂₇ClN₂O₄S₃Si
Molecular Weight: 483.13

Following the general procedure D, the reaction was carried out with the solution of **3a** (304 mg, 0.82 mmol, 1 eq.) and allyltrimethylsilane (0.26 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 10% → 30%) afforded target product **4ad** (325 mg, 82%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.29 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.59 (dd, *J* = 8.4, 2.7 Hz, 1H, CH_{Ar}), 7.44 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.62 (qd, *J* = 7.1, 2.8 Hz, 2H, CH₂), 3.92 – 3.82 (m, 1H, C-S), 3.50 (s, 3H, SO₂CH₃), 2.31 – 2.16 (m, 3H, CH₂ and CH_{Al}H), 1.82 – 1.70 (m, 1H, CHH_{A2}), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃), 1.08 (dd, *J* = 14.9, 7.1 Hz, 1H, CH_{B1}H), 0.94 (dd, *J* = 14.9, 8.1 Hz, 1H, CHH_{B2}), 0.06 (s, 9H, Si(CH₃)₃).

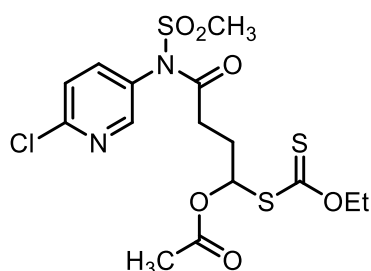
¹³C NMR (101 MHz, Chloroform-*d*) δ 215.0 (C=S), 172.6 (C=O), 153.0 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.4 (C_{Ar}), 125.6 (CH_{Ar}), 70.3 (CH₂), 48.4 (S-CH), 42.6 (SO₂CH₃), 34.5 (CH₂), 32.1 (CH₂), 24.2 (CH₂), 14.0 (CH₃), -0.7 (3C, Si(CH₃)₃).

IR (neat), ν (cm⁻¹): 2947, 1711, 1562, 1455, 1356, 1248, 1212, 1153, 1109, 1046, 963, 845, 776, 732.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₈ClN₂O₄S₃Si 483.0664; Found 483.0682.

R_f = 0.68 (PE/EtOAc = 40%).

4-(N-(6-chloropyridin-3-yl)methylsulfonamido)-1-((ethoxycarbonothioyl)thio)-4-oxobutyl acetate (4ae)



Chemical Formula: C₁₅H₁₉ClN₂O₆S₃
Molecular Weight: 454.96

Following the general procedure D, the reaction was carried out with the solution of **3a** (304 mg, 0.82 mmol, 1 eq.) and vinyl acetate (0.15 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 10% → 40%) afforded target product **4ae** (278 mg, 74%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.33 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.64 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.48 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 6.59 (dd, *J* = 7.1, 5.2 Hz, 1H, S-CH), 4.69 – 4.55 (m, 2H, OCH₂), 3.51 (s, 3H, SO₂CH₃), 2.41 – 2.11 (m, 4H, 2 × CH₂), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

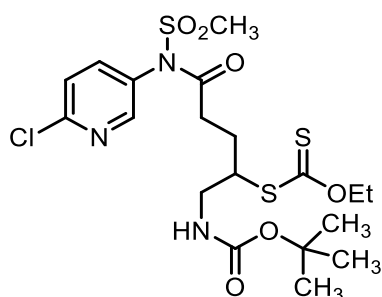
¹³C NMR (101 MHz, Chloroform-*d*) δ 209.8 (C=S), 171.5 (C=O), 170.1 (C=O), 153.2 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.3 (C_{Ar}), 125.7 (CH_{Ar}), 79.8 (S-CH), 70.7 (CH₂), 42.5 (SO₂CH₃), 32.8 (CH₂), 28.5 (CH₂), 21.0 (CH₃), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 2986, 2935, 1742, 1712, 1562, 1455, 1358, 1223, 1155, 1110, 1049, 1027, 962, 909, 777, 733.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₂₀ClN₂O₆S₃ 455.0167; Found 455.0178.

R_f = 0.47 (PE/EtOAc = 40%).

***tert*-butyl (5-(*N*-(6-chloropyridin-3-yl)methylsulfonamido)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl)carbamate (**4af**)**



Chemical Formula: C₁₉H₂₈ClN₃O₆S₃
Molecular Weight: 526.08

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and *tert*-butyl allylcarbamate (145 mg, 0.92 mmol, 1.1 eq.) in EtOAc (0.82 mL) with 0.3 eq. of DLP (105 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 50%) afforded target product **4af** (268 mg, 63%) as a colorless oil. Product contained traces of the reduced starting material (*N*-(6-chloropyridin-3-yl)-*N*-(methylsulfonyl)acetamide) inseparable by column chromatography.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.62 (dd, *J* = 8.4, 2.7 Hz, 1H, CH_{Ar}), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.84 (t, br, *J* = 5.4 Hz, 1H, NH), 4.62 (qd, *J* = 7.1, 0.8 Hz, 2H, CH₂), 3.85 – 3.76 (m, 1H, S-CH), 3.48 (s, 3H, SO₂CH₃), 3.45 – 3.36 (m, 1H, CH_{A1}H), 3.35 – 3.23 (m, 1H, CH_HA₂), 2.37 – 2.26 (m, 2H, CH₂), 2.22 – 2.09 (m, 1H, CH_{B1}H), 1.88 – 1.76 (m, 1H, CH_HB₂), 1.45 – 1.38 (m, 12H, 4 x CH₃).

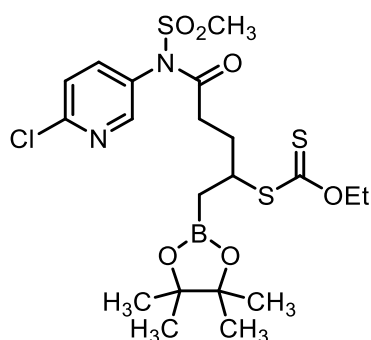
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.5 (C=S), 172.4 (C=O), 156.0 (C=O), 153.0 (C_{Ar}), 150.2 (CH_{Ar}), 140.2 (C_{Ar}), 131.4 (CH_{Ar}), 125.6 (C_{Ar}), 79.9 (C), 70.8 (CH₂), 51.1 (S-CH), 43.6 (CH₂), 42.5 (SO₂CH₃), 34.2 (CH₂), 28.4 (3C, CH₃), 26.0 (CH₂), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 3389, 2978, 2931, 1705, 1512, 1455, 1359, 1221, 1157, 1111, 1047, 965, 777, 733, 549.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₂₉ClN₃O₆S₃ 526.0902; Found 526.0915.

R_f = 0.62 (PE/EtOAc = 40%).

5-(*N*-(6-chloropyridin-3-yl)methylsulfonamido)-5-oxo-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl *O*-ethyl carbonodithioate (4ag**)**



Chemical Formula: C₂₀H₃₀BClN₂O₆S₃
Molecular Weight: 536.91

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.31 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4ag** (316 mg, 72%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.59 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.61 (qd, *J* = 7.1, 1.3 Hz, 2H, CH₂), 3.94 – 3.85 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 2.32 – 2.07 (m, 3H, CH₂ and CH_{Ar}H), 1.99 – 1.86 (m, 1H, CHH_{A2}), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃), 1.24 – 1.20 (m, 2H, CH₂-B), 1.23 (s, 6H, 2 x CH₃), 1.21 (s, 6H, 2 x CH₃).

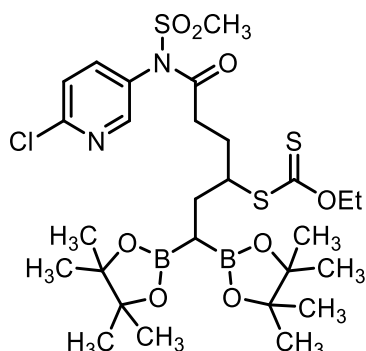
¹³C NMR (101 MHz, Chloroform-*d*) δ 214.7 (C=S), 172.7 (C=O), 153.0 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.5 (C_{Ar}), 125.6 (CH_{Ar}), 83.8 (2C, C-O), 70.2 (CH₂), 47.3 (S-CH), 42.6 (SO₂CH₃), 34.7 (CH₂), 31.0 (CH₂), 24.9 (2C, CH₃), 24.9 (2C, CH₃), 13.9 (CH₃). B-CH₂ signal is not observed.

IR (neat), ν (cm⁻¹): 2924, 2853, 1712, 1562, 1455, 1359, 1214, 1142, 1109, 1048, 965, 845, 776, 735.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₃₁BClN₂O₆S₃ 537.1120; Found 537.1138.

R_f = 0.57 (PE/EtOAc = 40%).

S-(6-(N-(6-chloropyridin-3-yl)methylsulfonamido)-6-oxo-1,1-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-3-yl) O-ethyl carbonodithioate (4ah)



Chemical Formula: C₂₇H₄₃B₂ClN₂O₈S₃
Molecular Weight: 676.90

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and 4,4,5,5-tetramethyl-2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-1,3,2-dioxaborolane² (278 mg, 0.90 mmol, 1.1 eq.) in EtOAc (0.82 mL) with 0.4 eq. of DLP (140 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 30%) afforded target product **4ah** (347 mg, 63%) as a white foam.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.29 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.59 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.44 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.58 (q, *J* = 7.2 Hz, 1H, CH₂), 3.71 – 3.61 (m, 1H, S-CH), 3.48 (s, 3H, SO₂CH₃), 2.37 – 2.11 (m, 3H, CH₂ and CH_{Ar}H), 1.99 – 1.87 (m, 1H, CH_{B1}H), 1.86 – 1.69 (m, 2H, CHH_{A2} and CHH_{B2}), 1.39 (t, *J* = 7.1 Hz, 3H, CH₃), 1.21 (s, 12H, 4 x CH₃), 1.20 – 1.19 (m, 12H, 4 x CH₃), 0.75 (dd, *J* = 9.1, 6.6 Hz, 1H, B-CH).

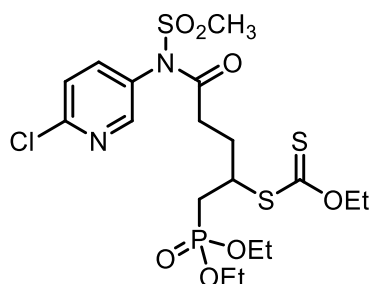
¹³C NMR (101 MHz, Chloroform-*d*) δ 215.1 (C=S), 172.6 (C=O), 152.9 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.5 (C_{Ar}), 125.5 (CH_{Ar}), 83.4 (4C, C-O), 70.3 (CH₂), 53.7 (S-CH), 42.6 (SO₂CH₃), 34.4 (CH₂), 30.2 (CH₂), 29.9 (CH₂), 25.0 (2C, CH₃), 25.0 (2C, CH₃), 24.7 (2C, CH₃), 24.7 (2C, CH₃), 13.9 (CH₃). B-CH signal is not observed.

IR (neat), *ν* (cm⁻¹): 2978, 2931, 1713, 1455, 1359, 1314, 1266, 1215, 1133, 1110, 1049, 966, 848, 776, 734.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₇H₄₄B₂ClN₂O₈S₃ 677.2129; Found 677.2145.

R_f = 0.55 (PE/EtOAc = 40%).

S-(5-(N-(6-chloropyridin-3-yl)methylsulfonamido)-1-(diethoxyphosphoryl)-5-oxopentan-2-yl) O-ethyl carbonodithioate (4ai)



Chemical Formula: C₁₈H₂₈ClN₂O₇PS₃
Molecular Weight: 547.03

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and diethyl allylphosphonate (160 mg, 0.90 mmol, 1.1 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Then N₂ was flushed at heating to 130°C during 30 min. Flash column chromatography on silica gel (eluent: PE/EtOAc = 80% → 100%) afforded target product **4ai** (308 mg, 69%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.61 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.44 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.60 (qd, *J* = 7.1, 2.0 Hz, 2H, CH₂), 4.15 – 4.01 (m, 4H, 2 x CH₂), 4.01 – 3.89 (m, 1H, S-CH), 3.46 (s, 3H, SO₂CH₃), 2.49 – 2.21 (m, 4H, CH_{A1}H, CH_{B1}H, CH₂), 2.12 – 1.86 (m, 2H, CH_{H A2} and CH_{H B2}), 1.39 (t, *J* = 7.1 Hz, 3H, CH₃), 1.34 – 1.27 (m, 6H, 2 x CH₃).

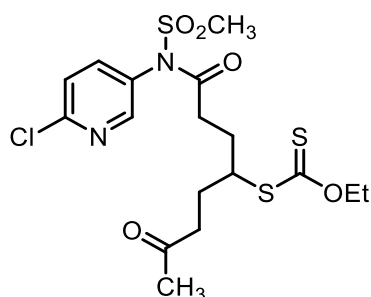
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.9 (C=S), 172.2 (C=O), 152.9 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.4 (C_{Ar}), 125.6 (CH_{Ar}), 70.5 (CH₂), 62.5 – 61.2 (m, 2C, CH₂), 44.9 (d, *J* = 1.9 Hz, S-CH), 42.5 (SO₂CH₃), 34.4 (CH₂), 31.9 (d, *J* = 137.5 Hz, CH₂), 28.7 (d, *J* = 4.3 Hz, CH₂), 16.7 – 16.1 (m, 2C, CH₃), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 2983, 1710, 1563, 1455, 1354, 1223, 1154, 1109, 1040, 959, 775, 734.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₉ClN₂O₇PS₃ 547.0558; Found 547.0574.

R_f = 0.61 (EtOAc).

S-(1-(N-(6-chloropyridin-3-yl)methylsulfonamido)-1,7-dioxooctan-4-yl) O-ethyl carbonodithioate (4aj)



Chemical Formula: C₁₇H₂₃ClN₂O₅S₃
Molecular Weight: 467.01

Following the general procedure D, the reaction was carried out with the solution of **3a** (304 mg, 0.82 mmol, 1 eq.) and 5-hexen-2-one (0.19 mL 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4aj** (306 mg, 80%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.30 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.61 (dd, *J* = 8.4, 2.7 Hz, 1H, CH_{Ar}), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.62 (q, *J* = 7.1 Hz, 2H, CH₂), 3.75 – 3.66 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 2.58 (t, *J* = 7.2 Hz, 2H, CH₂), 2.31 – 2.24 (m, 2H, CH₂), 2.21 – 2.06 (m, 1H, CH_{A1}H), 2.12 (s, 3H, CH₃), 2.06 – 1.92 (m, 1H, CH_{B1}H), 1.89 – 1.71 (m, 2H, CH_HA₂ and CH_HB₂), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃).

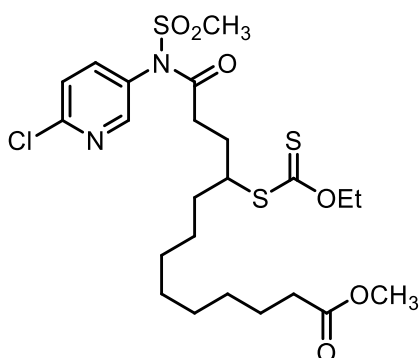
¹³C NMR (101 MHz, Chloroform-*d*) δ 214.6 (C=S), 207.6 (C=O), 172.5 (C=O), 153.0 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.4 (C_{Ar}), 125.6 (CH_{Ar}), 70.7 (CH₂), 50.6 (S-CH), 42.6 (SO₂CH₃), 40.7 (CH₂), 34.3 (CH₂), 30.2 (CH₃), 29.6 (CH₂), 28.3 (CH₂), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 2929, 1709, 1562, 1454, 1353, 1215, 1150, 1108, 1043, 963, 884, 776.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₄ClN₂O₅S₃ 467.0530; Found 467.0535.

R_f = 0.33 (PE/EtOAc = 40%).

**methyl 13-(N-(6-chloropyridin-3-yl)methylsulfonamido)-10-
((ethoxycarbonothioyl)thio)-13-oxotridecanoate (4ak)**



Chemical Formula: C₂₃H₃₅ClN₂O₆S₃
Molecular Weight: 567.17

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and methyl 10-undecenoate (0.37 mL 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 30%) afforded target product **4ak** (396 mg, 86%) as a yellow oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.29 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.59 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.44 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.68 – 4.56 (m, 2H, CH₂), 3.76 – 3.68 (m, 1H, S-CH), 3.65 (s, 3H, CH₃), 3.49 (s, 3H, SO₂CH₃), 2.32 – 2.12 (m, 5H, 2 x CH₂ and CH_{Ar}H), 1.81 – 1.69 (m, 1H, CHH_{A2}), 1.69 – 1.53 (m, 4H, 2 x CH₂), 1.41 (t, *J* = 7.1 Hz, 3H, CH₃), 1.38 – 1.19 (m, 10H, 5 x CH₂).

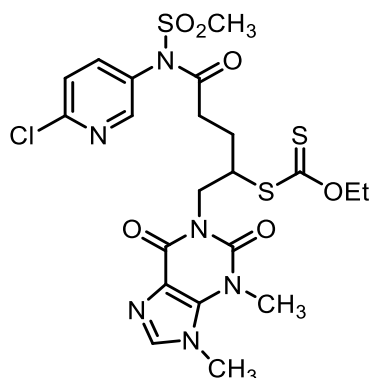
¹³C NMR (101 MHz, Chloroform-*d*) δ 215.2 (S=O), 174.4 (C=O), 172.7 (C=O), 153.0 (C_{Ar}), 150.3 (CH_{Ar}), 140.2 (CH_{Ar}), 131.4 (C_{Ar}), 125.6 (CH_{Ar}), 70.5 (CH₂), 51.6 (CH₃), 51.1 (S-CH), 42.6 (SO₂CH₃), 35.0 (CH₂), 34.4 (CH₂), 34.2 (CH₂), 29.3 (CH₂), 29.3 (CH₂), 29.3 (CH₂), 29.2 (CH₂), 29.2 (CH₂), 26.9 (CH₂), 25.0 (CH₂), 13.9 (CH₃).

IR (neat), *v* (cm⁻¹): 2927, 2854, 1720, 1562, 1455, 1357, 1212, 1156, 1109, 1048, 965, 777.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₃H₃₆ClN₂O₆S₃ 567.1419; Found 567.1420.

R_f = 0.41 (PE/EtOAc = 30%).

S-(5-(N-(6-chloropyridin-3-yl)methylsulfonamido)-1-(3,9-dimethyl-2,6-dioxo-2,3,6,9-tetrahydro-1H-purin-1-yl)-5-oxopentan-2-yl) O-ethyl carbonodithioate (4aI)



Chemical Formula: C₂₁H₂₅ClN₆O₆S₃
Molecular Weight: 589.10

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1.5 eq.) and 1-allyl-3,9-dimethyl-3,9-dihydro-1H-purine-2,6-dione (120 mg, 0.54 mmol, 1 eq.) in EtOAc (0.82 mL) with 0.6 eq. of DLP (132 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 80% → 100%) afforded target product **4aI** (195 mg, 61%) as a yellow oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.32 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.64 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.50 (q, *J* = 0.6 Hz, 1H, CH), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.56 (q, *J* = 7.1 Hz, 2H, CH₂), 4.27 (dd, *J* = 12.7, 8.1 Hz, 1H, CH_{A1}H), 4.22 – 4.13 (m, 1H, S-CH), 4.09 (dd, *J* = 12.7, 6.5 Hz, 1H, CH_{H_{A2}}), 3.95 (d, *J* = 0.6 Hz, 3H, CH₃), 3.54 (s, 3H, CH₃), 3.48 (s, 3H, SO₂CH₃), 2.46 – 2.25 (m, 2H, CH₂), 2.22 – 2.09 (m, 1H, CH_{B1}H), 2.01 – 1.87 (m, 1H, CH_{H_{B2}}), 1.37 (t, *J* = 7.1 Hz, 3H, CH₃).

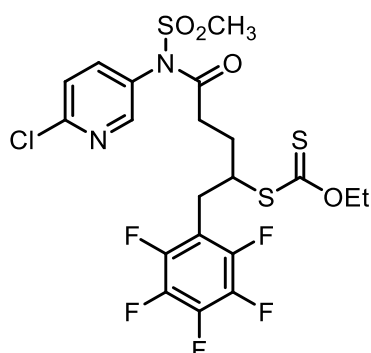
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.3 (C=S), 172.4 (C=O), 155.1 (C=O), 153.0 (C_{Ar}), 151.5 (C=O), 150.3 (CH_{Ar}), 149.1 (C), 141.9 (CH), 140.2 (CH_{Ar}), 131.4 (C_{Ar}), 125.6 (CH_{Ar}), 107.5 (C), 70.6 (CH₂), 48.4 (S-CH), 43.1 (CH₂), 42.5 (SO₂CH₃), 34.2 (CH₂), 33.7 (CH₃), 29.9 (CH₃), 26.6 (CH₂), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 2930, 1705, 1658, 1548, 1455, 1355, 1225, 1155, 1111, 1047, 965, 736.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₂₁H₂₅ClN₆NaO₆S₃ 611.0578; Found 611.0584.

R_f = 0.31 (EtOAc).

S-(5-(N-(6-chloropyridin-3-yl)methylsulfonamido)-5-oxo-1-(perfluorophenyl)pentan-2-yl) O-ethyl carbonodithioate (4am)



Chemical Formula: C₂₀H₁₈ClF₅N₂O₄S₃
Molecular Weight: 577.00

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and allylpentafluorobenzene (0.25 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.2 eq. of DLP (64 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 30%) afforded target product **4am** (331 mg, 71%) as a yellow oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.27 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.58 (dd, *J* = 8.4, 2.7 Hz, 1H, CH_{Ar}), 7.45 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.60 (q, *J* = 7.1 Hz, 2H, CH₂), 4.07 – 3.95 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 3.14 – 2.97 (m, 2H, CH₂), 2.35 – 2.25 (m, 2H, CH₂), 2.25 – 2.13 (m, 1H, CH_{Ar}H), 1.88 – 1.77 (m, 1H, CHH_{A2}), 1.41 (t, *J* = 7.1 Hz, 3H, CH₃).

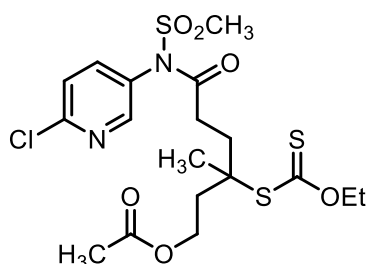
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.2 (C=S), 172.2 (C=O), 153.2 (C_{Ar}), 150.2 (CH_{Ar}), 140.1 (CH_{Ar}), 131.3 (C_{Ar}), 125.7 (CH_{Ar}), 111.3 (C_{Ar}), 71.0 (CH₂), 49.7 (S-CH), 42.6 (SO₂CH₃), 34.3 (CH₂), 28.3 (CH₂), 28.2 (CH₂), 13.8 (CH₃). C-F signals are not observed.

IR (neat), ν (cm⁻¹): 2933, 1712, 1520, 1502, 1455, 1357, 1222, 1151, 1110, 1045, 963, 777, 735.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₁₉ClF₅N₂O₄S₃ 577.0110; Found 577.0112.

R_f = 0.60 (PE/EtOAc = 40%).

6-(N-(6-chloropyridin-3-yl)methylsulfonamido)-3-((ethoxycarbonothioyl)thio)-3-methyl-6-oxohexyl acetate (4an)



Chemical Formula: C₁₈H₂₅ClN₂O₆S₃
Molecular Weight: 497.04

Following the general procedure D, the reaction was carried out with the solution of **3a** (300 mg, 0.81 mmol, 1 eq.) and 3-methylbut-3-en-1-yl acetate (210 mg, 1.64 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.3 eq. of DLP (96 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 20% → 60%) afforded target product **4an** (294 mg, 73%) as a yellow oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 2.8 Hz, 1H, CH_{Ar}), 7.65 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.49 (d, *J* = 8.4 Hz, 1H, CH_{Ar}), 4.70 – 4.60 (m, 2H, CH₂), 4.15 (t, *J* = 7.0 Hz, 2H, CH₂), 3.47 (s, 3H, SO₂CH₃), 2.45 – 2.18 (m, 4H, CH₂, CH_{A1}H, CH_{B1}H), 2.08 – 2.00 (m, 1H, CHH_{A2}), 2.02 (s, 3H, CH₃), 2.00 – 1.87 (m, 1H, CHH_{B2}), 1.47 (t, *J* = 7.1 Hz, 3H, CH₃), 1.23 (s, 3H, CH₃).

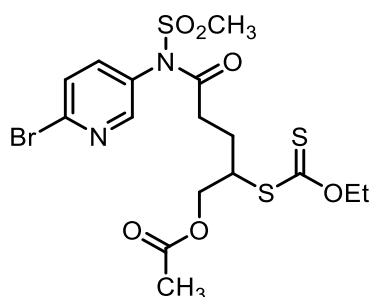
¹³C NMR (101 MHz, Chloroform-*d*) δ 211.7 (C=S), 172.5 (C=O), 171.0 (C=O), 153.2 (C_{Ar}), 150.1 (CH_{Ar}), 140.1 (CH_{Ar}), 131.4 (C_{Ar}), 125.8 (CH_{Ar}), 70.2 (CH₂), 60.9 (CH₂), 55.9 (C), 42.7 (SO₂CH₃), 38.1 (CH₂), 34.1 (CH₂), 32.3 (CH₂), 24.8 (CH₃), 21.1 (CH₃), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 2932, 1721, 1456, 1358, 1233, 1156, 1110, 1037, 965, 777, 735.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₂₆ClN₂O₆S₃ 497.0636; Found 497.0630.

R_f = 0.26 (PE/EtOAc = 40%).

5-(N-(6-bromopyridin-3-yl)methylsulfonamido)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl acetate (4ba)



Chemical Formula: C₁₆H₂₁BrN₂O₆S₃
Molecular Weight: 513.44

Following the general procedure D, the reaction was carried out with the solution of **3b** (300 mg, 0.73 mmol, 1 eq.) and allyl acetate (0.16 mL, 1.45 mmol, 2 eq.) in EtOAc (0.73 mL) with 0.2 eq. of DLP (60 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4ba** (292 mg, 78%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.28 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.62 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 7.49 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 4.64 (q, *J* = 7.1 Hz, 2H, CH₂), 4.27 (dd, *J* = 11.5, 4.9 Hz, 1H, CH_{A1}H), 4.18 (dd, *J* = 11.5, 6.1 Hz, 1H, CH_HA₂), 4.02 – 3.93 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 2.33 – 2.25 (m, 2H, CH₂), 2.26 – 2.15 (m, 1H, CH_{B1}H), 2.05 (s, 3H, CH₃), 1.92 – 1.79 (m, 1H, CH_HB₂), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃).

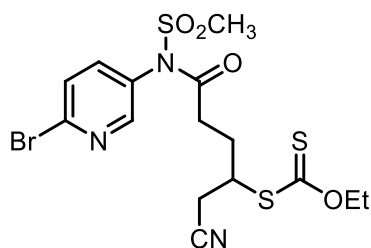
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.2 (C=S), 172.2 (C=O), 170.7 (C=O), 150.6 (CH_{Ar}), 143.8 (C_{Ar}), 139.9 (CH_{Ar}), 131.8 (C_{Ar}), 129.5 (CH_{Ar}), 71.0 (CH₂), 65.8 (CH₂), 48.9 (S-CH), 42.6 (SO₂CH₃), 34.2 (CH₂), 25.8 (CH₂), 20.9 (CH₃), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 1733, 1712, 1451, 1355, 1222, 1151, 1089, 1039, 964, 884, 771, 745, 547.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₂BrN₂O₆S₃ 512.9818; Found 512.9819.

R_f = 0.37 (PE/EtOAc = 40%).

S-(5-(N-(6-bromopyridin-3-yl)methylsulfonamido)-1-cyano-5-oxopentan-2-yl) O-ethyl carbonodithioate (4bb)



Chemical Formula: C₁₅H₁₈BrN₃O₄S₃
Molecular Weight: 480.41

Following the general procedure D, the reaction was carried out with the solution of **3b** (300 mg, 0.73 mmol, 1 eq.) and allyl cyanide (0.12 mL, 1.45 mmol, 2 eq.) in EtOAc (0.73 mL) with 0.3 eq. of DLP (90 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 50%) afforded target product **4bb** (260 mg, 75%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.28 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.62 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 7.52 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 4.63 (d, *J* = 7.1 Hz, 2H, CH₂), 3.95 – 3.86 (m, 1H, S-CH), 3.47 (s, 3H, SO₂CH₃), 2.91 – 2.81 (m, 2H, CH₂), 2.37 – 2.29 (m, 2H, CH₂), 2.28 – 2.19 (m, 1H, CH_{Ar}H), 2.05 – 1.91 (m, 1H, CH_HA₂), 1.42 (t, *J* = 7.1 Hz, 3H, CH₃).

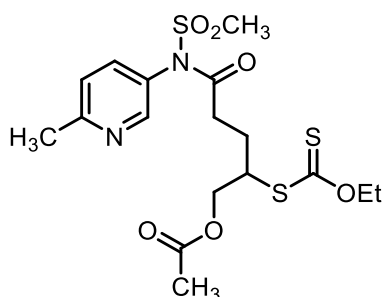
¹³C NMR (101 MHz, Chloroform-*d*) δ 211.9 (C=S), 171.8 (C=O), 150.6 (CH_{Ar}), 143.7 (C_{Ar}), 139.9 (CH_{Ar}), 131.6 (C_{Ar}), 129.5 (CH_{Ar}), 117.0 (CN), 71.2 (CH₂), 45.7 (CH), 42.5 (SO₂CH₃), 34.1 (CH₂), 27.3 (CH₂), 24.3 (CH₂), 13.8 (CH₃).

IR (neat), *v* (cm⁻¹): 1708, 1450, 1353, 1224, 1149, 1089, 1043, 962, 772, 734, 546.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₁₉BrN₃O₄S₃ 479.9716; Found 479.9717.

R_f = 0.31 (PE/EtOAc = 40%).

2-((ethoxycarbonothioyl)thio)-5-(N-(6-methylpyridin-3-yl)methylsulfonamido)-5-oxopentyl acetate (4ca)



Chemical Formula: C₁₇H₂₄N₂O₆S₃
Molecular Weight: 448.57

Following the general procedure D, the reaction was carried out with the solution of **3c** (300 mg, 0.86 mmol, 1 eq.) and allyl acetate (0.19 mL, 1.72 mmol, 2 eq.) in EtOAc (0.86 mL) with 0.2 eq. of DLP (70 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 20% → 60%) afforded target product **4ca** (341 mg, 88%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.37 (dd, *J* = 2.7, 0.7 Hz, 1H, CH_{Ar}), 7.50 (dd, *J* = 8.1, 2.7 Hz, 1H, CH_{Ar}), 7.28 (dd, *J* = 8.1, 0.7 Hz, 1H, CH_{Ar}), 4.62 (q, *J* = 7.1 Hz, 2H, CH₂), 4.24 (dd, *J* = 11.4, 4.8 Hz, 1H, CH_{A1}H), 4.16 (dd, *J* = 11.4, 6.1 Hz, 1H, CH_HA₂), 3.99 – 3.90 (m, 1H, S-CH), 3.47 (s, 3H, SO₂CH₃), 2.62 (s, 3H, CH₃), 2.31 – 2.24 (m, 2H, CH₂), 2.24 – 2.13 (m, 1H, CH_{B1}H), 2.03 (s, 3H, CH₃), 1.90 – 1.79 (m, 1H, CH_HB₂), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

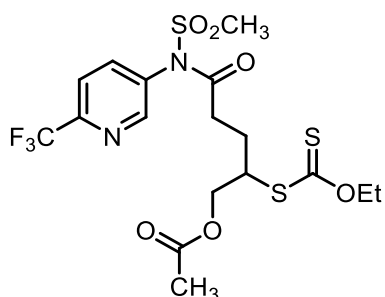
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.0 (C=S), 172.7 (C=O), 170.7 (C=O), 160.9 (C_{Ar}), 149.5 (CH_{Ar}), 137.6 (CH_{Ar}), 129.7 (C_{Ar}), 124.4 (CH_{Ar}), 70.8 (CH₂), 65.7 (CH₂), 48.8 (S-CH), 42.4 (CH₃), 34.1 (CH₂), 25.7 (CH₂), 24.5 (CH₃), 20.8 (CH₃), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 1737, 1707, 1486, 1352, 1222, 1151, 1039, 964, 762, 734, 546.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₅N₂O₆S₃ 449.0869; Found 449.0870.

R_f = 0.32 (PE/EtOAc = 50%).

2-((ethoxycarbonothioyl)thio)-5-oxo-5-(N-(6-(trifluoromethyl)pyridin-3-yl)methylsulfonamido)pentyl acetate (4da)



Chemical Formula: C₁₇H₂₁F₃N₂O₆S₃
Molecular Weight: 502.54

Following the general procedure D, the reaction was carried out with the solution of **3d** (286 mg, 0.71 mmol, 1 eq.) and allyl acetate (0.16 mL, 1.42 mmol, 2 eq.) in EtOAc (0.71 mL) with 0.2 eq. of DLP (60 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4da** (211 mg, 59%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.62 (dd, *J* = 2.3, 0.9 Hz, 1H, CH_{Ar}), 7.86 (ddd, *J* = 8.3, 2.3 Hz, 1H, CH_{Ar}), 7.82 (dd, *J* = 8.3, 0.9 Hz, 1H, CH_{Ar}), 4.61 (q, *J* = 7.1 Hz, 2H, CH₂), 4.25 (dd, *J* = 11.5, 4.9 Hz, 1H, CH_{A1}H), 4.17 (dd, *J* = 11.5, 6.0 Hz, 1H, CH_HA₂), 4.00 – 3.92 (m, 1H, S-CH), 3.50 (s, 3H, SO₂CH₃), 2.33 – 2.26 (m, 2H, CH₂), 2.26 – 2.16 (m, 1H, CH_{B1}H), 2.03 (s, 3H, CH₃), 1.92 – 1.78 (m, 1H, CH_HB₂), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

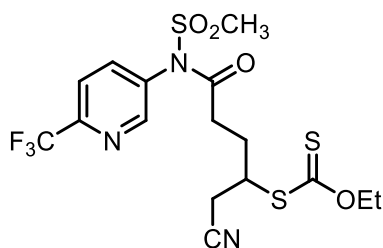
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.2 (C=S), 172.0 (C=O), 170.7 (C=O), 150.6 (CH_{Ar}), 149.2 (C-F, ²*J*_{C-F} = 35.6 Hz, C_{Ar}), 139.3 (CH_{Ar}), 134.7 (C_{Ar}), 121.7 (C-F, ³*J*_{C-F} = 2.7 Hz, CH_{Ar}), 121.0 (C-F, ¹*J*_{C-F} = 274.7 Hz, CF₃), 71.0 (CH₂), 65.7 (CH₂), 48.9 (S-CH), 42.6 (SO₂CH₃), 34.3 (CH₂), 25.8 (CH₂), 20.8 (CH₃), 13.8 (CH₃).

IR (neat), *ν* (cm⁻¹): 1731, 1714, 1335, 1226, 1143, 1041, 966, 777, 761, 602, 540.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₂₂F₃N₂O₆S₃ 503.0587; Found 503.0588.

R_f = 0.44 (PE/EtOAc = 40%).

S-(1-cyano-5-oxo-5-(N-(6-(trifluoromethyl)pyridin-3-yl)methylsulfonamido)pentan-2-yl) O-ethyl carbonodithioate (4db)



Chemical Formula: C₁₆H₁₈F₃N₃O₄S₃
Molecular Weight: 469.51

Following the general procedure D, the reaction was carried out with the solution of **3d** (306 mg, 0.76 mmol, 1 eq.) and allyl cyanide (0.12 mL, 1.49 mmol, 2 eq.) in EtOAc (0.75 mL) with 0.2 eq. of DLP (60 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4db** (267 mg, 75%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.64 (dd, *J* = 2.3, 1.0 Hz, 1H, CH_{Ar}), 7.88 (dd, *J* = 8.3, 2.3 Hz, 1H, CH_{Ar}), 7.84 (dd, *J* = 8.3, 1.0 Hz, 1H, CH_{Ar}), 4.66 (q, *J* = 7.1 Hz, 2H, CH₂), 4.01 – 3.92 (m, 1H, S-CH), 3.52 (s, 3H, SO₂CH₃), 2.92 – 2.82 (m, 2H, CH₂), 2.40 – 2.33 (m, 2H, CH₂), 2.33 – 2.23 (m, 1H, CH_{Ar}H), 2.08 – 1.98 (m, 1H, CHH_{A2}), 1.44 (t, *J* = 7.1 Hz, 3H, CH₃).

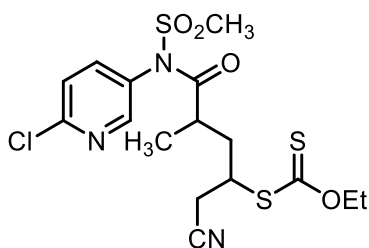
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.0 (C=S), 171.7 (C=O), 150.6 (CH_{Ar}), 149.5 (C-F, ²*J*_{C-F} = 35.9 Hz, C_{Ar}), 139.3 (CH_{Ar}), 134.6 (C_{Ar}), 121.9 (C-F, ³*J*_{C-F} = 2.5 Hz, CH_{Ar}), 121.0 (C-F, ¹*J*_{C-F} = 274.9 Hz, CF₃), 117.0 (CN), 71.3 (CH₂), 45.9 (S-CH), 42.8 (SO₂CH₃), 34.3 (CH₂), 27.5 (CH₂), 24.5 (CH₂), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 2346, 1714, 1358, 1336, 1235, 1151, 1088, 1047, 966, 759.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₁₉F₃N₃O₄S₃ 470.0484; Found 470.0486.

R_f = 0.48 (PE/EtOAc = 40%).

S-(5-(N-(6-chloropyridin-3-yl)methylsulfonamido)-1-cyano-4-methyl-5-oxopentan-2-yl) O-ethyl carbonodithioate (4eb)



Chemical Formula: C₁₆H₂₀ClN₃O₄S₃
Molecular Weight: 449.98

Following the general procedure D, the reaction was carried out with the solution of **3e** (300 mg, 0.78 mmol, 1 eq.) and allyl cyanide (0.13 mL, 1.57 mmol, 2 eq.) in EtOAc (0.78 mL) with 0.7 eq. of DLP (210 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 40%) afforded target product **4eb** (178 mg, 50%) as a white foam. Mixture of two diastereomers (d.r. = 1.2:1). Product contained traces of the reduced starting material (*N*-(6-chloropyridin-3-yl)-*N*-(methylsulfonyl)propionamide), inseparable by column chromatography.

Isomer 1:

¹H NMR (400 MHz, Chloroform-*d*) δ 8.26 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.59 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.44 (dd, *J* = 8.5, 0.7 Hz, 1H, CH_{Ar}), 4.83 – 4.70 (m, 2H, CH₂), 3.98 – 3.87 (m, 1H, S-CH), 3.46 (s, 3H, SO₂CH₃), 2.91 (dd, *J* = 17.1, 5.6 Hz, 1H, CH_{A1}H), 2.86 – 2.76 (m, 1H, CHH_{A2}), 2.63 – 2.52 (m, 1H, CH), 2.39 – 2.19 (m, 1H, CH_{B1}H), 1.81 – 1.69 (m, 1H, CHH_{B2}), 1.50 (t, *J* = 7.1 Hz, 3H, CH₃), 1.14 (d, *J* = 6.9 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 211.1 (C=S), 175.8 (C=O), 153.1 (C_{Ar}), 149.9 (CH_{Ar}), 140.1 (CH_{Ar}), 130.9 (C_{Ar}), 125.4 (CH_{Ar}), 116.7 (CN), 71.5 (CH₂), 45.2 (S-CH), 42.4 (SO₂CH₃), 37.6 (CH), 36.0 (CH₂), 25.1 (CH₂), 18.4 (CH₃), 13.9 (CH₃).

Isomer 2:

¹H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 2.8, 0.7 Hz, 1H, CH_{Ar}), 7.64 (dd, *J* = 8.4, 2.8 Hz, 1H, CH_{Ar}), 7.48 (dd, *J* = 8.4, 0.7 Hz, 1H, CH_{Ar}), 4.70 – 4.62 (m, 2H, CH₂), 3.82 – 3.72 (m, 1H, S-CH), 3.49 (s, 3H, SO₂CH₃), 2.86 – 2.76 (m, 2H, CH₂), 2.50 – 2.40 (m, 1H, CH), 2.39 – 2.19 (m, 1H, CH_{B1}H), 1.97 – 1.86 (m, 1H, CHH_{B2}), 1.45 (t, *J* = 7.1 Hz, 3H, CH₃), 1.16 (d, *J* = 6.9 Hz, 3H, CH₃).

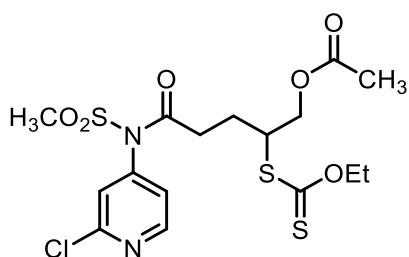
^{13}C NMR (101 MHz, Chloroform-*d*) δ 212.0 (C=S), 175.9 (C=O), 153.1 (C_{Ar}), 150.0 (CH_{Ar}), 140.1 (CH_{Ar}), 131.2 (C_{Ar}), 125.6 (CH_{Ar}), 116.9 (CN), 71.3 (CH_2), 45.3 (S-CH), 42.4 (SO_2CH_3), 37.7 (CH), 35.6 (CH_2), 24.8 (CH_2), 17.6 (CH_3), 13.8 (CH_3).

IR (neat), ν (cm^{-1}): 1706, 1454, 1356, 1224, 1150, 1107, 1041, 959, 775, 732, 547.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{21}\text{ClN}_3\text{O}_4\text{S}_3$ 450.0377; Found 450.0378.

$R_f = 0.42$ (PE/EtOAc = 40%).

5-(N-(2-chloropyridin-4-yl)methylsulfonamido)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl acetate (4fa)



Chemical Formula: C₁₆H₂₁ClN₂O₆S₃
Molecular Weight: 468.98

Following the general procedure D, the reaction was carried out with the solution of **3f** (300 mg, 0.81 mmol, 1 eq.) and allyl acetate (0.18 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.15 eq. of DLP (48 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 10% → 40%) afforded target product **4fa** (275 mg, 72%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.54 (dd, *J* = 5.3, 0.6 Hz, 1H, CH_{Ar}), 7.29 (dd, *J* = 1.8, 0.6 Hz, 1H, CH_{Ar}), 7.19 (dd, *J* = 5.3, 1.8 Hz, 1H, CH_{Ar}), 4.65 (q, *J* = 7.1 Hz, 2H, CH₂), 4.28 (dd, *J* = 11.5, 4.9 Hz, 1H, CH_{A1}H), 4.19 (dd, *J* = 11.4, 6.1 Hz, 1H, CH_HA₂), 4.04 – 3.95 (m, 1H, S-CH), 3.50 (s, 3H, SO₂CH₃), 2.36 – 2.29 (m, 2H, CH₂), 2.29 – 2.18 (m, 1H, CH_{B1}H), 2.05 (s, 3H, CH₃), 1.91 – 1.80 (m, 1H, CH_HB₂), 1.43 (t, *J* = 7.1 Hz, 3H, CH₃).

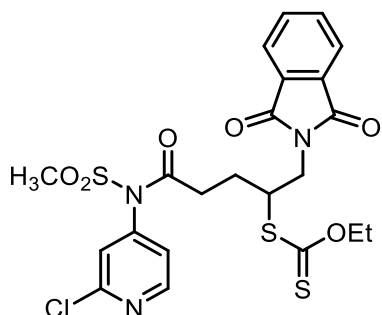
¹³C NMR (101 MHz, Chloroform-*d*) δ 213.4 (C=S), 171.6 (C=O), 170.7 (C=O), 153.3 (C_{Ar}), 151.5 (CH_{Ar}), 145.2 (C_{Ar}), 125.6 (CH_{Ar}), 123.7 (CH_{Ar}), 71.1 (CH₂), 65.8 (CH₂), 49.1 (CH), 42.8 (SO₂CH₃), 34.0 (CH₂), 25.8 (CH₂), 20.9 (CH₃), 13.9 (CH₃).

IR (neat), *v* (cm⁻¹): 1732, 1713, 1579, 1555, 1461, 1356, 1221, 1148, 1038, 964, 787, 734.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₂ClN₂O₆S₃ 469.0323; Found 469.0327.

R_f = 0.36 (PE/EtOAc = 40%).

S-(5-(N-(2-chloropyridin-4-yl)methylsulfonamido)-1-(1,3-dioxisoindolin-2-yl)-5-oxopentan-2-yl) O-ethyl carbonodithioate (4fc)



Chemical Formula: C₂₂H₂₂ClN₃O₆S₃
Molecular Weight: 556.06

Following the general procedure D, the reaction was carried out with the solution of **3f** (307 mg, 0.83 mmol, 1 eq.) and allyl phthalimide (312 mg, 1.66 mmol, 2 eq.) in EtOAc (0.83 mL) with 0.1 eq. of DLP (35 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 25% → 45%) afforded target product **4fc** (417 mg, 90%) as a white foam.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.53 (d, *J* = 5.2 Hz, 1H, CH_{Ar}), 7.88 – 7.82 (m, 2H, CH_{Phth}), 7.76 – 7.71 (m, 2H, CH_{Phth}), 7.31 (d, *J* = 1.8 Hz, 1H, CH_{Ar}), 7.21 (dd, *J* = 5.2, 1.8 Hz, 1H, CH_{Ar}), 4.60 (q, *J* = 7.1 Hz, 2H, CH₂), 4.18 – 4.08 (m, 1H, S-CH), 3.95 (dd, *J* = 14.0, 7.2 Hz, 1H, CH_{A1}H), 3.87 (dd, *J* = 14.0, 7.5 Hz, 1H, CH_{H_{A2}}), 3.49 (s, 3H, SO₂CH₃), 2.36 (t, *J* = 6.8 Hz, 2H, CH₂), 2.28 – 2.11 (m, 1H, CH_{B1}H), 1.95 – 1.79 (m, 1H, CH_{H_{B2}}), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

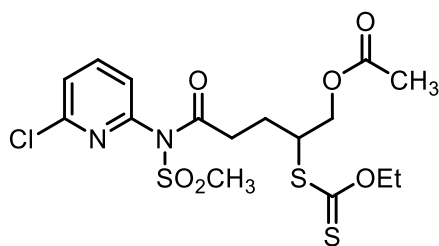
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.6 (C=S), 171.6 (C=O), 168.2 (C=O), 153.2 (C_{Ar}), 151.5 (CH_{Ar}), 145.2 (C_{Ar}), 134.4 (2C, CH_{Phth}), 131.9 (2C, C_{Phth}), 125.7 (CH_{Ar}), 123.8 (CH_{Ar}), 123.7 (2C, CH_{Phth}), 71.0 (CH₂), 48.9 (S-CH), 42.8 (SO₂CH₃), 40.8 (CH₂), 33.9 (CH₂), 26.3 (CH₂), 13.8 (CH₃).

IR (neat), *v* (cm⁻¹): 1772, 1713, 1579, 1395, 1358, 1223, 1154, 1047, 967, 751, 720.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₂H₂₃ClN₃O₆S₃ 556.0432; Found 556.0433.

R_f = 0.26 (PE/EtOAc = 40%).

5-(N-(6-chloropyridin-2-yl)methylsulfonamido)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl acetate (4ga)



Chemical Formula: C₁₆H₂₁ClN₂O₆S₃
Molecular Weight: 468.98

Following the general procedure D, the reaction was carried out with the solution of 3g (300 mg, 0.81 mmol, 1 eq.) and allyl acetate (0.18 mL, 1.63 mmol, 2 eq.) in EtOAc (0.82 mL) with 0.15 eq. of DLP (48 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 10% → 30%) afforded target product **4ga** (231 mg, 61%) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 8.0, 7.6 Hz, 1H, CH_{Ar}), 7.47 (dd, *J* = 8.0, 0.8 Hz, 1H, CH_{Ar}), 7.39 (dd, *J* = 7.6, 0.8 Hz, 1H, CH_{Ar}), 4.62 (d, *J* = 7.1 Hz, 2H, CH₂), 4.26 (dd, *J* = 11.4, 4.8 Hz, 1H, CH_{A1}H), 4.17 (dd, *J* = 11.4, 6.2 Hz, 1H, CH_HA₂), 3.97 – 3.88 (m, 1H, S-CH), 3.47 (s, 3H, SO₂CH₃), 2.43 – 2.29 (m, 2H, CH₂), 2.28 – 2.17 (m, 1H, CH_{B1}H), 2.06 (s, 3H, CH₃), 1.97 – 1.84 (m, 1H, CH_HB₂), 1.41 (t, *J* = 7.1 Hz, 3H, CH₃).

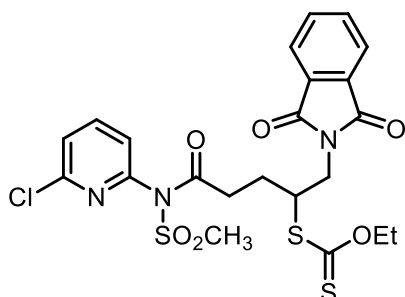
¹³C NMR (101 MHz, Chloroform-*d*) δ 212.7 (C=S), 172.4 (C=O), 170.7 (C=O), 151.2 (C_{Ar}), 148.8 (C_{Ar}), 141.4 (CH_{Ar}), 126.1 (CH_{Ar}), 124.7 (CH_{Ar}), 70.7 (CH₂), 65.7 (CH₂), 48.6 (S-CH), 41.9 (SO₂CH₃), 34.2 (CH₂), 25.8 (CH₂), 20.9 (CH₃), 13.9 (CH₃).

IR (neat), ν (cm⁻¹): 1739, 1715, 1579, 1562, 1429, 1358, 1225, 1162, 1043, 967, 753.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₂ClN₂O₆S₃ 469.0323; Found 469.0324.

R_f = 0.51 (PE/EtOAc = 40%).

S-(5-(N-(6-chloropyridin-2-yl)methylsulfonamido)-1-(1,3-dioxoisindolin-2-yl)-5-oxopentan-2-yl) O-ethyl carbonodithioate (4gc)



Chemical Formula: C₂₂H₂₂ClN₃O₆S₃
Molecular Weight: 556.06

Following the general procedure D, the reaction was carried out with the solution of **3g** (200 mg, 0.54 mmol, 1 eq.) and allyl phthalimide (203 mg, 1.08 mmol, 2 eq.) in EtOAc (0.54 mL) with 0.1 eq. of DLP (22 mg). Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 25% → 45%) afforded target product **4gc** (265 mg, 88%) as a white foam.

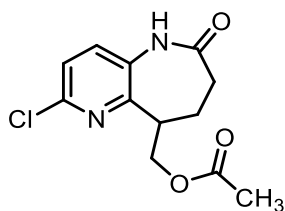
¹H NMR (400 MHz, Chloroform-*d*) δ 7.87 – 7.79 (m, 3H, CH_{Ar} and CH_{Phth}), 7.76 – 7.68 (m, 2H, CH_{Phth}), 7.45 (dd, *J* = 8.0, 0.6 Hz, 1H, CH_{Ar}), 7.40 (dd, *J* = 7.7, 0.6 Hz, 1H, CH_{Ar}), 4.57 (q, *J* = 7.2 Hz, 2H, CH₂), 4.12 – 4.03 (m, 1H, S-CH), 3.94 (dd, *J* = 14.0, 7.4 Hz, 1H, CH_{A1}H), 3.85 (dd, *J* = 14.0, 7.3 Hz, 1H, CH_{H_{A2}}), 3.45 (s, 3H, SO₂CH₃), 2.49 – 2.27 (m, 2H, CH₂), 2.23 – 2.12 (m, 1H, CH_{B1}H), 1.96 – 1.82 (m, 1H, CH_{H_{B2}}), 1.40 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 212.1 (C=S), 172.3 (C=O), 168.1 (C=O), 151.2 (C_{Ar}), 148.8 (C_{Ar}), 141.4 (CH_{Ar}), 134.3 (2C, CH_{Phth}), 131.9 (2C, C_{Phth}), 126.0 (CH_{Ar}), 124.7 (CH_{Ar}), 123.6 (2C, CH_{Phth}), 70.6 (CH₂), 48.6 (S-CH), 41.9 (SO₂CH₃), 40.9 (CH₂), 34.1 (CH₂), 26.4 (CH₂), 13.8 (CH₃).

IR (neat), ν (cm⁻¹): 1710, 1498, 1393, 1355, 1220, 1150, 1043, 965, 726, 714, 607.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₂H₂₃ClN₃O₆S₃ 556.0432; Found 556.0432.

R_f = 0.26 (PE/EtOAc = 40%).

(2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate (5aa)

Chemical Formula: C₁₂H₁₃ClN₂O₃
Molecular Weight: 268.70

Following the general procedure E, the reaction was carried out with the solution of **4aa** (590 mg, 1.26 mmol, 1 eq.) in chlorobenzene (63 mL) with 5 eq. of DTBP (1.20 mL) for 1.5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 40% → 70%) afforded target product **5aa** (217 mg, 64%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.29 (s, 1H, NH), 7.32 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.21 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 4.70 (dd, *J* = 11.2, 6.3 Hz, 1H, OCH_{A1}H), 4.37 (dd, *J* = 11.2, 7.5 Hz, 1H, OCH_{H_{A2}}), 3.52 – 3.41 (m, 1H, CH), 2.64 – 2.50 (m, 1H, CH_{B1}H), 2.43 – 2.34 (m, 2H, CH₂), 2.02 (s, 3H, CH₃), 2.07 – 1.93 (m, 1H, CH_{H_{B2}}).

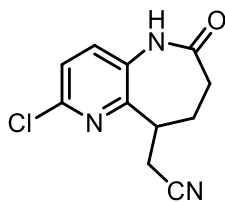
¹³C NMR (101 MHz, Chloroform-*d*) δ 175.4 (C=O), 171.1 (C=O), 154.0 (C_{Ar}), 147.1 (C_{Ar}), 133.2 (C_{Ar}), 131.9 (CH_{Ar}), 123.1 (CH_{Ar}), 64.8 (CH₂), 40.2 (CH), 32.4 (CH₂), 31.3 (CH₂), 21.0 (CH₃).

IR (neat), ν (cm⁻¹): 3036, 2930, 1733, 1681, 1435, 1364, 1252, 1196, 1159, 1121, 1027, 936, 919, 828, 798, 767.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₄ClN₂O₃ 269.0687; Found 269.0693.

R_f = 0.26 (PE/EtOAc = 70%).

m.p. = 176-180°C.

2-(2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)acetonitrile (5ab)

Chemical Formula: C₁₁H₁₀ClN₃O
Molecular Weight: 235.67

Following the general procedure E, the reaction was carried out with the solution of **4ab** (280 mg, 0.64 mmol, 1 eq.) in chlorobenzene (65 mL) with 5 eq. of DTBP (0.60 mL) for 3 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50% → 70%) afforded target product **5ab** (90 mg, 60%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.80 (s, 1H, NH), 7.47 – 7.41 (m, 2H, CH_{Ar}), 3.49 – 3.36 (m, 1H, CH), 2.96 (dd, *J* = 16.7, 7.5 Hz, 1H, CH_{A1}H), 2.86 (dd, *J* = 16.7, 6.0 Hz, 1H, CH_HA₂), 2.49 – 2.41 (m, 1H, CH_{B1}H), 2.37 – 2.25 (m, 1H, CH_{C1}H), 2.23 – 2.13 (m, 1H, CH_HC₂), 1.99 – 1.86 (m, 1H, CH_HB₂).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 173.5 (C=O), 153.9 (C_{Ar}), 145.5 (C_{Ar}), 135.4 (C_{Ar}), 133.5 (C_{Ar}), 124.2 (CH_{Ar}), 120.7 (CN), 38.3 (CH), 33.9 (CH₂), 33.4 (CH₂), 20.1 (CH₂).

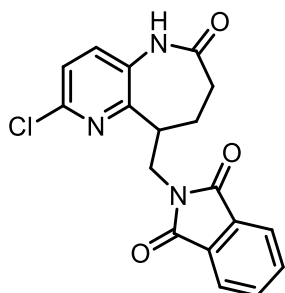
IR (neat), ν (cm⁻¹): 3206, 2934, 1676, 1441, 1368, 1192, 1161, 1136, 927, 835, 766, 734.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₁ClN₃O 236.0585; Found 236.0591.

R_f = 0.30 (PE/EtOAc = 70%).

m.p. = 217-218°C.

2-((2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl)isoindoline-1,3-dione (5ac)



Chemical Formula: C₁₈H₁₄ClN₃O₃
Molecular Weight: 355.78

Following the general procedure E, the reaction was carried out with the solution of **4ac** (250 mg, 0.45 mmol, 1 eq.) in chlorobenzene (45 mL) with 5 eq. of DTBP (0.42 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50% → 70%) afforded target product **5ac** (91 mg, 57%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.76 (s, br, 1H, NH), 7.93 – 7.78 (m, 4H, CH_{Phth}), 7.42 (s, 2H, CH_{Ar}), 4.10 – 3.92 (m, 2H, CH₂), 3.59 – 3.46 (m, 1H, CH), 2.43 – 2.24 (m, 2H, CH₂), 2.18 – 2.09 (m, 1H, CH_{Ar}H), 1.91 – 1.78 (m, 1H, CH_HA₂).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 172.7 (C=O), 168.1 (C=O), 153.7 (C_{Ar}), 144.4 (C_{Ar}), 134.5 (C_{Ar}), 134.3 (2C, CH_{Phth}), 132.4 (CH_{Ar}), 131.7 (2C, C_{Phth}), 123.0 (2C, CH_{Phth}), 122.9 (CH_{Ar}), 40.2 (CH₂), 38.9 (CH), 32.3 (CH₂), 31.2 (CH₂).

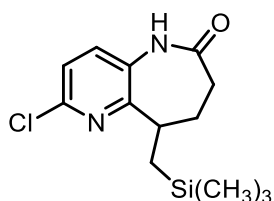
IR (neat), ν (cm⁻¹): 3218, 2937, 1771, 1707, 1676, 1438, 1399, 1369, 1228, 1165, 930, 907, 721.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₁₅ClN₃O₃ 356.0796; Found 356.0804.

R_f = 0.39 (PE/EtOAc = 70%).

Melting is not observed in the 20-225°C range.

**2-chloro-9-((trimethylsilyl)methyl)-5,7,8,9-tetrahydro-6H-pyrido[3,2-b]azepin-6-one
(5ad)**



Chemical Formula: C₁₃H₁₉ClN₂OSi
Molecular Weight: 282.84

Following the general procedure E, the reaction was carried out with the solution of **4ad** (303 mg, 0.63 mmol, 1 eq.) in chlorobenzene (63 mL) with 5 eq. of DTBP (0.58 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 30% → 50%) afforded target product **5ad** (90 mg, 51%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.42 (s, 1H, NH), 7.26 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.19 (dd, *J* = 8.2, 0.5 Hz, 1H, CH_{Ar}), 3.37 – 3.23 (m, 1H, CH), 2.58 – 2.44 (m, 1H, CH_{Ar}H), 2.39 – 2.26 (m, 2H, CH₂), 2.03 – 1.87 (m, 1H, CHH_{A2}), 1.46 (dd, *J* = 14.7, 8.2 Hz, 1H, CH_{B1}H), 0.87 (dd, *J* = 14.7, 6.3 Hz, 1H, CHH_{B2}), -0.07 (s, 9H, Si(CH₃)₃).

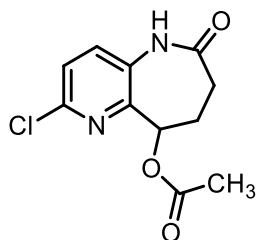
¹³C NMR (101 MHz, Chloroform-*d*) δ 175.4 (C=O), 158.2 (C_{Ar}), 147.1 (C_{Ar}), 132.9 (C_{Ar}), 131.6 (CH_{Ar}), 122.4 (CH_{Ar}), 38.2 (CH), 37.6 (CH₂), 33.2 (CH₂), 19.1 (CH₂), -0.6 (3C, Si(CH₃)₃).

IR (neat), ν (cm⁻¹): 3202, 2942, 1671, 1436, 1363, 1246, 1164, 1133, 839, 766.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₃H₂₀ClN₂OSi 283.1028; Found 283.1038.

R_f = 0.41 (PE/EtOAc = 50%).

m.p. = 148-150°C (crystallized from PE/EtOAc).

2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl acetate (5ae)Chemical Formula: C₁₁H₁₁ClN₂O₃

Molecular Weight: 254.67

Following the general procedure E, the reaction was carried out with the solution of **4ae** (457 mg, 1.00 mmol, 1 eq.) in chlorobenzene (100 mL) with 5 eq. of DTBP (0.93 mL) for 2.5 h. The mixture was washed with Et₂O to afford target product **5ae** (184 mg, 72%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.86 (s, 1H, NH), 7.45 (d, *J* = 0.8 Hz, 2H, CH_{Ar}), 5.74 (dd, *J* = 8.3, 6.8 Hz, 1H, CH), 2.61 – 2.53 (m, 1H, CH_{A1}H), 2.39 – 2.29 (m, 2H, CH₂), 2.29 – 2.18 (m, 1H, CH_{H_{A2}}), 2.08 (s, 3H, CH₃).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 172.4 (C=O), 169.5 (C=O), 149.7 (C_{Ar}), 144.2 (C_{Ar}), 133.2 (C_{Ar}), 133.0 (CH_{Ar}), 124.0 (CH_{Ar}), 71.9 (CH), 31.4 (CH₂), 30.7 (CH₂), 20.8 (CH₃).

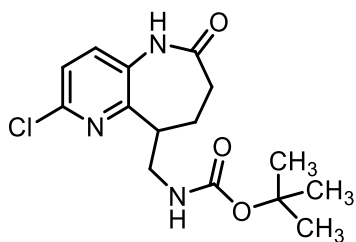
IR (neat), ν (cm⁻¹): 2935, 1728, 1664, 1442, 1369, 1236, 1161, 1138, 1048, 764.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₂ClN₂O₃ 255.0531; Found 255.0537.

R_f = 0.17 (PE/EtOAc = 50%).

m.p = 220-223°C (crystallized from Et₂O).

***tert*-butyl ((2-chloro-6-oxo-6,7,8,9-tetrahydro-5*H*-pyrido[3,2-*b*]azepin-9-yl)methyl)carbamate (**5af**)**



Chemical Formula: C₁₅H₂₀ClN₃O₃
Molecular Weight: 325.79

Following the general procedure E, the reaction was carried out with the solution of **4af** (268 mg, 0.59 mmol, 1 eq.) in chlorobenzene (59 mL) with 5 eq. of DTBP (0.55 mL) for 3 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50% → 70%) afforded target product **5af** (94 mg, 63%) as a yellow oil. For analytical purposes it was crystallized from PE/EtOAc to yield white crystals.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.16 (s, 1H, NH), 7.32 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.22 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 5.31 (t, *J* = 6.5 Hz, 1H, NH), 3.70 – 3.49 (m, 2H, CH₂), 3.42 – 3.24 (m, 1H, CH), 2.53 – 2.38 (m, 1H, CH_{Ar}H), 2.38 – 2.26 (m, 2H, CH₂), 2.07 – 1.90 (m, 1H, CHH_{A2}), 1.40 (s, 9H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 175.4 (C=O), 156.2 (C_{Ar}), 155.6 (C=O), 147.0 (C_{Ar}), 133.8 (C_{Ar}), 132.1 (CH_{Ar}), 122.9 (CH_{Ar}), 79.4 (C), 41.6 (CH), 41.1 (CH₂), 32.6 (CH₂), 31.4 (CH₂), 28.5 (3C, CH₃).

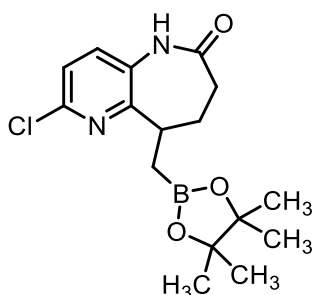
IR (neat), ν (cm⁻¹): 3226, 2976, 2933, 1680, 1501, 1439, 1365, 1277, 1252, 1164, 1137, 914, 731.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₂₁ClN₃O₃ 326.1266; Found 326.1273.

R_f = 0.31 (PE/EtOAc = 70%).

m.p. = 177-179°C (crystallized from PE/EtOAc).

2-chloro-9-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-5,7,8,9-tetrahydro-6H-pyrido[3,2-b]azepin-6-one (5ag)



Chemical Formula: C₁₆H₂₂BClN₂O₃
Molecular Weight: 336.62

Following the general procedure E, the reaction was carried out with the solution of **4ag** (316 mg, 0.59 mmol, 1 eq.) in chlorobenzene (59 mL) with 5 eq. of DTBP (0.55 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50% → 70%) afforded target product **5ag** (102 mg, 52%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.23 (s, 1H, NH), 7.26 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.13 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 3.48 – 3.36 (m, 1H, CH), 2.56 – 2.44 (m, 1H, CH_{A1}H), 2.43 – 2.25 (m, 2H, CH₂), 2.08 – 1.96 (m, 1H, CH_{H_{A2}}), 1.43 – 1.32 (m, 1H, CH_{C1}H), 1.18 (s, 6H, 2 x CH₃), 1.10 – 1.04 (m, 1H, CH_{H_{C2}}), 1.09 (s, 6H, 2 x CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 175.9 (C=O), 157.9 (C_{Ar}), 146.7 (C_{Ar}), 133.0 (C_{Ar}), 131.5 (CH_{Ar}), 122.2 (CH_{Ar}), 83.0 (2C, C-O), 37.6 (CH), 36.7 (CH₂), 33.2 (CH₂), 25.0 (2C, CH₃), 24.7 (2C, CH₃). B-CH₂ signal is not observed.

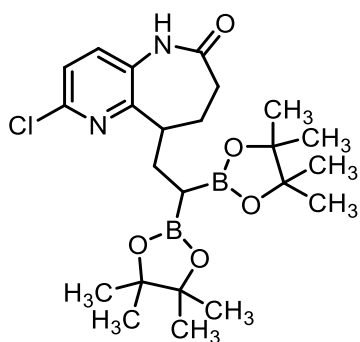
IR (neat), ν (cm⁻¹): 3211, 2977, 1673, 1438, 1371, 1318, 1165, 1143, 967, 921, 846, 735.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₂₃BClN₂O₃ 337.1315; Found 337.1495.

R_f = 0.59 (PE/EtOAc = 70%).

m.p. = 198-200°C (crystallized from PE/EtOAc).

9-(2,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2-chloro-5,7,8,9-tetrahydro-6H-pyrido[3,2-b]azepin-6-one (5ah)



Chemical Formula: $C_{23}H_{35}B_2ClN_2O_5$
Molecular Weight: 476.61

Following the general procedure E, the reaction was carried out with the solution of **4ah** (320 mg, 0.47 mmol, 1 eq.) in chlorobenzene (48 mL) with 5 eq. of DTBP (0.44 mL) for 3.5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 40% → 70%) afforded target product **5ah** (88 mg, 39%) as a yellow oil.

1H NMR (400 MHz, Chloroform-*d*) δ 8.54 (s, 1H, NH), 7.21 (d, $J = 8.3$ Hz, 1H, CH_{Ar}), 7.12 (d, $J = 8.3$ Hz, 1H, CH_{Ar}), 3.22 – 3.07 (m, 1H, CH), 2.56 – 2.42 (m, 1H, CH_{AlH}), 2.38 – 2.18 (m, 3H, CH_2 and CH_{BlH}), 1.97 – 1.79 (m, 2H, CH_{HA2} and CH_{HB2}), 1.18 (s, 24H, CH_3), 0.75 (dd, $J = 9.1, 6.6$ Hz, 1H, B-CH).

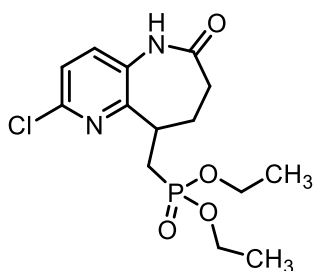
^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.5 (C=O), 157.3 (C_{Ar}), 147.0 (C_{Ar}), 133.1 (C_{Ar}), 131.5 (CH_{Ar}), 122.2 (CH_{Ar}), 83.2 (C), 83.1 (4C, C-O), 43.3 (CH), 33.8 (CH_2), 32.9 (CH_2), 27.1 (CH_2), 24.6 (4C, CH_3), 24.8 (4C, CH_3). B-CH is not observed.

IR (neat), ν (cm^{-1}): 2977, 1674, 1437, 1359, 1310, 1250, 1135, 967, 848, 734.

HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{23}H_{36}B_2ClN_2O_5$ 477.2493; Found 477.2503.

$R_f = 0.24$ (PE/EtOAc = 50%).

diethyl ((2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl)phosphonate (5ai)



Chemical Formula: C₁₄H₂₀ClN₂O₄P
Molecular Weight: 346.75

Following the general procedure E, the reaction was carried out with the solution of **4ai** (244 mg, 0.45 mmol, 1 eq.) in chlorobenzene (45 mL) with 5 eq. of DTBP (0.41 mL) for 4.5 h. Flash column chromatography on silica gel (eluent: EtOAc/MeOH = 10%) afforded target product **5ai** (38 mg, 24%) as a yellow oil.

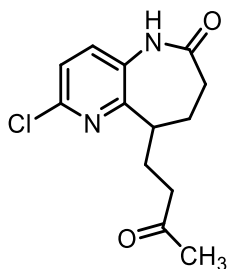
¹H NMR (400 MHz, Acetone-*d*₆) δ 8.92 (s, 1H, NH), 7.49 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.35 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 4.14 – 3.96 (m, 4H, 2 x CH₂), 3.61 – 3.48 (m, 1H, CH), 2.75 – 2.60 (m, 2H, CH_{A1}H and CH_{B1}H), 2.42 – 2.29 (m, 1H, CH_{C1}H), 2.27 – 2.17 (m, 1H, CH_{H2}), 2.09 – 1.88 (m, 2H, CH_{H2} and CH_{H2}), 1.22 (t, *J* = 7.1 Hz, 3H, CH₃), 1.22 (t, *J* = 7.1 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Acetone-*d*₆) δ 173.3 (C=O), 156.2 (d, *J* = 10.8 Hz, C_{Ar}), 146.3 (C_{Ar}), 135.4 (C_{Ar}), 133.1 (CH_{Ar}), 123.5 (CH_{Ar}), 62.0 – 61.6 (m, 2C, CH₂), 37.0 (d, *J* = 2.3 Hz, CH), 35.9 (d, *J* = 8.8 Hz, CH₂), 33.5 (CH₂), 28.0 (d, *J* = 141.5 Hz, CH₂), 17.0 – 16.5 (m, 2C, CH₃).

IR (neat), ν (cm⁻¹): 3197, 2982, 2926, 1677, 1439, 1363, 1220, 1166, 1051, 1022, 963, 831, 796.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₄H₂₁ClN₂O₄P 347.0922; Found 347.0936.

R_f = 0.32 (EtOAc/MeOH = 10%).

2-chloro-9-(3-oxobutyl)-5,7,8,9-tetrahydro-6H-pyrido[3,2-b]azepin-6-one (5aj)

Chemical Formula: C₁₃H₁₅ClN₂O₂
Molecular Weight: 266.73

Following the general procedure E, the reaction was carried out with the solution of **4aj** (286 mg, 0.61 mmol, 1 eq.) in chlorobenzene (61 mL) with 5 eq. of DTBP (0.57 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 70%) afforded target product **5aj** (77 mg, 47%) as a non-crystalline white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.34 (s, 1H, NH), 7.30 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.17 (dd, *J* = 8.3 Hz, 1H, CH_{Ar}), 3.19 – 3.03 (m, 1H, CH), 2.61 – 2.23 (m, 6H, 2 x CH₂, CH_{A1}H, CH_{B1}H), 2.09 (s, 3H, CH₃), 1.97 – 1.78 (m, 2H, CHH_{A2} and CHH_{B2}).

¹³C NMR (101 MHz, Chloroform-*d*) δ 208.8 (C=O), 175.7 (C=O), 156.0 (C_{Ar}), 146.9 (C_{Ar}), 133.6 (C_{Ar}), 131.9 (CH_{Ar}), 122.6 (CH_{Ar}), 41.7 (CH₂), 40.4 (CH), 34.5 (CH₂), 32.8 (CH₂), 30.0 (CH₃), 25.2 (CH₂).

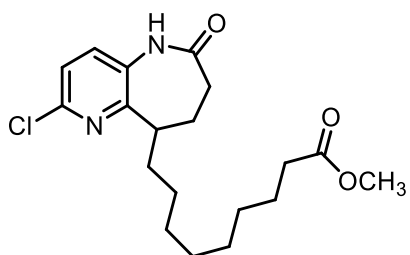
IR (neat), ν (cm⁻¹): 2929, 1668, 1583, 1435, 1359, 1257, 1158, 1134, 917, 831, 730.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₃H₁₆ClN₂O₂ 267.0895; Found 267.0898.

R_f = 0.30 (PE/EtOAc = 70%).

m.p. = 125-134°C.

**methyl 9-(2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)nonanoate
(5ak)**



Chemical Formula: C₁₉H₂₇ClN₂O₃
Molecular Weight: 366.89

Following the general procedure E, the reaction was carried out with the solution of **4ak** (346 mg, 0.64 mmol, 1 eq.) in chlorobenzene (61 mL) with 5 eq. of DTBP (0.56 mL) for 5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50%) afforded target product **5ak** (100 mg, 44%) as a yellow non-crystalline solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.05 (s, 1H, NH), 7.27 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.16 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 3.63 (s, 3H, CH₃), 3.16 – 2.97 (m, 1H, CH), 2.56 – 2.41 (m, 1H, CH_{A1}H), 2.38 – 2.30 (m, 2H, CH₂), 2.27 (t, *J* = 7.5 Hz, 2H, CH₂), 2.09 – 1.95 (m, 1H, CH_{B1}H), 1.93 – 1.82 (m, 1H, CH_HA₂), 1.65 – 1.52 (m, 3H, CH₂ and CH_HB₂), 1.34 – 1.19 (m, 10H, 5 x CH₂).

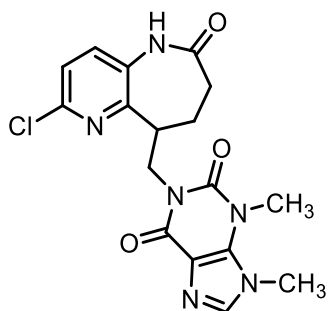
¹³C NMR (101 MHz, Chloroform-*d*) δ 175.9 (C=O), 174.4 (C=O), 157.3 (C_{Ar}), 147.0 (C_{Ar}), 133.3 (C_{Ar}), 131.7 (CH_{Ar}), 122.3 (CH_{Ar}), 51.5 (CH₃), 41.5 (CH), 34.2 (CH₂), 34.2 (CH₂), 32.9 (CH₂), 31.4 (CH₂), 29.6 (CH₂), 29.3 (CH₂), 29.2 (CH₂), 29.2 (CH₂), 27.6 (CH₂), 25.0 (CH₂).

IR (neat), ν (cm⁻¹): 2926, 2854, 1733, 1671, 1435, 1361, 1254, 1160, 1134, 915, 829, 729.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₂₈ClN₂O₃ 367.1783; Found 367.1785.

R_f = 0.30 (PE/EtOAc = 50%).

1-((2-chloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl)-3,9-dimethyl-3,9-dihydro-1H-purine-2,6-dione (5al)



Chemical Formula: C₁₇H₁₇ClN₆O₃
Molecular Weight: 388.81

Following the general procedure E, the reaction was carried out with the solution of **4al** (180 mg, 0.31 mmol, 1 eq.) in chlorobenzene (30 mL) with 5 eq. of DTBP (0.28 mL) for 5.5 h. Recrystallization from EtOAc in freezer afforded target product **5al** (48 mg, 40%) as a yellow solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.42 (s, 1H, NH), 7.53 (d, *J* = 0.7 Hz, 1H, CH), 7.24 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.17 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 4.75 (dd, *J* = 13.6, 9.8 Hz, 1H, CH_{A1}H), 4.37 (dd, *J* = 13.6, 4.2 Hz, 1H, CH_HA₂), 3.97 (d, *J* = 0.6 Hz, 3H, CH₃), 3.67 – 3.57 (m, 1H, CH), 3.56 (s, 3H, CH₃), 2.41 – 2.28 (m, 3H, CH₂, CH_{B1}H), 2.24 – 2.08 (m, 1H, CH_HB₂).

¹³C NMR (101 MHz, Chloroform-*d*) δ 174.5 (C=O), 155.5 (C=O), 155.3 (C_{Ar}), 151.8 (C=O), 149.0 (C), 146.8 (C_{Ar}), 141.8 (CH), 133.1 (C_{Ar}), 131.7 (CH_{Ar}), 122.8 (CH_{Ar}), 107.7 (C), 43.4 (CH₂), 39.5 (CH), 33.8 (CH₃), 32.5 (CH₂), 31.9 (CH₂), 29.9 (CH₃).

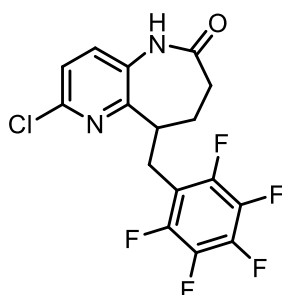
IR (neat), ν (cm⁻¹): 3249, 2939, 1702, 1657, 1444, 1362, 1231, 1138, 763, 739.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₁₈ClN₆O₃ 389.1123; Found 389.1129.

R_f = 0.08 (EtOAc/MeOH = 2%).

m.p. = 155-165°C (with decomposition).

2-chloro-9-((perfluorophenyl)methyl)-5,7,8,9-tetrahydro-6H-pyrido[3,2-b]azepin-6-one (5am)



Chemical Formula: C₁₆H₁₀ClF₅N₂O
Molecular Weight: 376.71

Following the general procedure E, the reaction was carried out with the solution of **4am** (274 mg, 0.47 mmol, 1 eq.) in chlorobenzene (48 mL) with 5 eq. of DTBP (0.44 mL) for 3 h. Flash column chromatography on silica gel with (eluent: PE/EtOAc = 30% → 45%) afforded target product **5am** (139 mg, 77%) as a yellow solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.61 (s, 1H, NH), 7.30 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.23 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 3.52 – 3.41 (m, 1H, CH), 3.37 (dd, *J* = 14.1, 5.6 Hz, 1H, CH_{A1}H), 3.21 (dd, *J* = 14.1, 9.2 Hz, 1H, CH_{H_{A2}}), 2.47 – 2.26 (m, 3H, CH₂ and CH_{B1}H), 2.10 – 1.96 (m, 1H, CH_{H_{B2}}).

¹³C NMR (101 MHz, Chloroform-*d*) δ 174.8 (C=O), 155.2 (C_{Ar}), 147.4 (C_{Ar}), 133.0 (C_{Ar}), 131.9 (CH_{Ar}), 123.2 (CH_{Ar}), 113.3 (C_{Ar}), 40.2 (CH), 33.6 (CH₂), 32.6 (CH₂), 24.9 (CH₂). C-F signals are not observed.

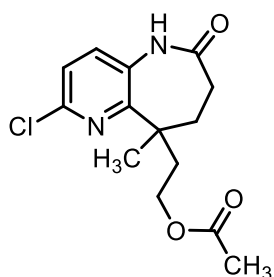
IR (neat), ν (cm⁻¹): 2938, 1675, 1520, 1500, 1439, 1368, 1190, 1124, 1049, 962, 739.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₆H₁₁ClF₅N₂O 377.0475; Found 377.0480.

R_f = 0.43 (PE/EtOAc = 50%).

m.p. = 146-150°C.

2-(2-chloro-9-methyl-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)ethyl acetate (5an)



Chemical Formula: C₁₄H₁₇ClN₂O₃
Molecular Weight: 296.75

Following the general procedure E, the reaction was carried out with the solution of **4an** (275 mg, 0.55 mmol, 1 eq.) in chlorobenzene (55 mL) with 5 eq. of DTBP (0.51 mL) for 3 h. Flash column chromatography on silica gel with (eluent: PE/EtOAc = 0% → 50% → 70%) afforded target product **5an** (75 mg, 46%) as a yellow non-crystalline solid.

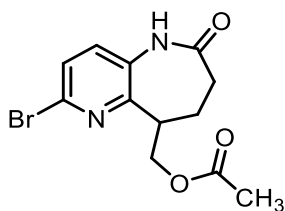
¹H NMR (400 MHz, Chloroform-*d*) δ 9.28 (s, 1H, NH), 7.29 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.13 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 4.07 – 3.88 (m, 2H, CH₂), 2.61 – 2.45 (m, 2H, CH₂), 2.36 – 2.10 (m, 3H, CH₂, CH_{Ar}/H), 2.09 – 1.99 (m, 1H, CHH_{A2}), 1.91 (s, 3H, CH₃), 1.45 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 176.4 (C=O), 171.0 (C=O), 155.4 (C_{Ar}), 145.2 (C_{Ar}), 132.9 (CH_{Ar}), 132.4 (C_{Ar}), 122.9 (CH_{Ar}), 61.4 (CH₂), 43.4 (C), 40.0 (CH₂), 36.5 (CH₂), 32.1 (CH₂), 28.3 (CH₃), 21.0 (CH₃).

IR (neat), ν (cm⁻¹): 2965, 2932, 1733, 1673, 1440, 1369, 1237, 1149, 1034, 913, 833.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₄H₁₈ClN₂O₃ 297.1000; Found 297.0997.

R_f = 0.29 (PE/EtOAc = 50%).

(2-bromo-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate (5ba)

Chemical Formula: C₁₂H₁₃BrN₂O₃
Molecular Weight: 313.15

Following the general procedure E, the reaction was carried out with the solution of **4ba** (270 mg, 0.53 mmol, 1 eq.) in chlorobenzene (52 mL) with 5 eq. of DTBP (0.49 mL) for 5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 40% → 70%) afforded target product **5ba** (91 mg, 55%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H, NH), 7.38 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.20 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 4.72 (dd, *J* = 11.2, 6.2 Hz, 1H, CH_{A1}H), 4.39 (dd, *J* = 11.2, 7.5 Hz, 1H, CH_{H_{A2}}), 3.54 – 3.43 (m, 1H, CH), 2.64 – 2.51 (m, 1H, CH_{B1}H), 2.44 – 2.34 (m, 2H, CH₂), 2.04 (s, 3H, CH₃), 2.02 – 1.94 (m, 1H, CH_{H_{B2}}).

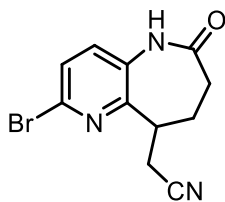
¹³C NMR (101 MHz, Chloroform-*d*) δ 174.9 (C=O), 171.1 (C=O), 154.7 (C_{Ar}), 137.4 (C_{Ar}), 133.6 (C_{Ar}), 131.6 (CH_{Ar}), 126.9 (CH_{Ar}), 64.9 (CH₂), 40.3 (CH), 32.5 (CH₂), 31.3 (CH₂), 21.0 (CH₃).

IR (neat), ν (cm⁻¹): 3220, 2940, 1737, 1675, 1438, 1369, 1240, 1040, 832, 760.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₄BrN₂O₃ 313.0182; Found 313.0186.

R_f = 0.18 (PE/EtOAc = 50%).

m.p. = 186-187°C (crystallized from PE/EtOAc).

2-(2-bromo-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)acetonitrile (5bb)

Chemical Formula: C₁₁H₁₀BrN₃O
Molecular Weight: 280.13

Following the general procedure E, the reaction was carried out with the solution of **4bb** (231 mg, 0.48 mmol, 1 eq.) in chlorobenzene (48 mL) with 5 eq. of DTBP (0.45 mL) for 4.5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 70%) afforded target product **5bb** (65 mg, 48%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.79 (s, 1H, NH), 7.58 (dd, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.33 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 3.47 – 3.36 (m, 1H, CH), 2.95 (dd, *J* = 16.6, 7.5 Hz, 1H, CH_{A1}H), 2.86 (dd, *J* = 16.6, 6.0 Hz, 1H, CH_{H_{A2}}), 2.48 – 2.40 (m, 1H, CH_{B1}H), 2.38 – 2.26 (m, 1H, CH_{C1}H), 2.23 – 2.13 (m, 1H, CH_{H_{C2}}), 1.99 – 1.85 (m, 1H, CH_{H_{B2}}).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 172.4 (C=O), 153.5 (C_{Ar}), 135.0 (C_{Ar}), 134.8 (C_{Ar}), 132.2 (C_{Ar}), 127.0 (CH_{Ar}), 119.6 (CN), 37.3 (CH), 32.8 (CH₂), 32.4 (CH₂), 19.1 (CH₂).

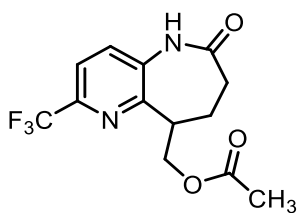
IR (neat), ν (cm⁻¹): 1666, 1436, 1374, 1330, 1181, 1156, 1130, 1079, 920, 831, 752, 631, 536.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₁BrN₃O 280.0080; Found 280.0083.

R_f = 0.32 (PE/EtOAc = 70%).

m.p. = 206-209°C (with decomposition).

(6-oxo-2-(trifluoromethyl)-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate (5da)



Chemical Formula: C₁₃H₁₃F₃N₂O₃
Molecular Weight: 302.25

Following the general procedure E, the reaction was carried out with the solution of **4da** (182 mg, 0.36 mmol, 1 eq.) in chlorobenzene (36 mL) with 5 eq. of DTBP (0.34 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50% → 60%) afforded target product **5da** (61 mg, 56%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H, NH), 7.60 (d, *J* = 8.2 Hz, 1H, CH_{A1}), 7.47 (d, *J* = 8.2 Hz, 1H, CH_{A1}), 4.80 (dd, *J* = 11.2, 6.5 Hz, 1H, CH_{A1}H), 4.42 (dd, *J* = 11.2, 7.1 Hz, 1H, CH_{A2}), 3.65 – 3.51 (m, 1H, CH), 2.68 – 2.53 (m, 1H, CH_{B1}H), 2.53 – 2.36 (m, 2H, CH₂), 2.10 – 2.03 (m, 1H, CH_{B2}), 2.02 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 174.8 (C=O), 171.1 (C=O), 154.2 (C_{A1}), 144.4 (C-F, ²*J*_{C-F} = 35.3 Hz, C_{A1}), 136.6 (C_{A1}), 129.5 (CH_{A1}), 121.4 (C-F, ¹*J*_{C-F} = 273.7 Hz, CF₃), 119.6 (C-F, ³*J*_{C-F} = 2.4 Hz, CH_{A1}), 64.7 (CH₂), 40.5 (CH), 32.6 (CH₂), 30.9 (CH₂), 20.9 (CH₃).

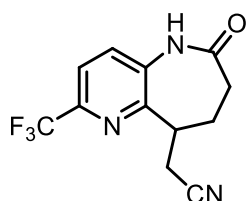
IR (neat), *ν* (cm⁻¹): 1737, 1678, 1586, 1471, 1368, 1337, 1237, 1133, 1115, 1042, 848, 737.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₃H₁₄F₃N₂O₃ 303.0951; Found 303.0954.

*R*_f = 0.27 (PE/EtOAc = 50%).

m.p. = 164-167°C (crystallized from PE/EtOAc).

2-(6-oxo-2-(trifluoromethyl)-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)acetonitrile (5db)



Chemical Formula: C₁₂H₁₀F₃N₃O
Molecular Weight: 269.23

Following the general procedure E, the reaction was carried out with the solution of **4db** (262 mg, 0.56 mmol, 1 eq.) in chlorobenzene (56 mL) with 5 eq. of DTBP (0.52 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 70%) afforded target product **5db** (69 mg, 46%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 9.15 (s, 1H, NH), 7.66 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.53 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 3.70 – 3.57 (m, 1H, CH), 3.07 (dd, *J* = 16.9, 6.5 Hz, 1H, CH_{A1}H), 2.90 (dd, *J* = 16.9, 7.5 Hz, 1H, CHH_{A2}), 2.83 – 2.69 (m, 1H, CH_{B1}H), 2.55 – 2.38 (m, 2H, CH₂), 2.15 – 2.03 (m, 1H, CHH_{B2}).

¹³C NMR (101 MHz, Chloroform-*d*) δ 174.5 (C=O), 152.8 (C_{Ar}), 144.4 (C-F, ²*J*_{C-F} = 35.6 Hz, C_{Ar}), 136.6 (C_{Ar}), 129.9 (CH_{Ar}), 121.3 (C-F, ¹*J*_{C-F} = 273.8 Hz, CF₃), 120.3 (C-F, ³*J*_{C-F} = 2.8 Hz, CH_{Ar}), 118.6 (CN), 38.2 (CH), 33.4 (CH₂), 32.6 (CH₂), 20.0 (CH₂).

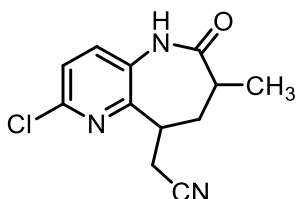
IR (neat), ν (cm⁻¹): 1678, 1588, 1472, 1371, 1336, 1263, 1178, 1132, 1110, 932, 735.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₁F₃N₃O 270.0849; Found 270.0850.

R_f = 0.30 (PE/EtOAc = 70%).

m.p. = 176-178°C (crystallized from PE/EtOAc).

2-(2-chloro-7-methyl-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)acetonitrile (5eb)



Chemical Formula: C₁₂H₁₂ClN₃O
Molecular Weight: 249.70

Following the general procedure E, the reaction was carried out with the solution of **4eb** (145 mg, 0.32 mmol, 1 eq.) in chlorobenzene (32 mL) with 5 eq. of DTBP (0.30 mL) for 4.5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50%) afforded target product **5eb** (37 mg, 46%) as a white non-crystalline solid. Mixture of two diastereomers (d.r. = 2.8:1).

Isomer 1:

¹H NMR (400 MHz, Chloroform-*d*) δ 9.11 (s, 1H, NH), 7.36 (d, *J* = 8.5 Hz, 1H, CH_{Ar}), 7.26 (d, *J* = 8.5 Hz, 1H, CH_{Ar}), 3.66 – 3.55 (m, 1H, CH), 2.89 – 2.84 (m, 2H, CH₂), 2.77 – 2.64 (m, 1H, CH), 2.59 – 2.50 (m, 1H, CH_{A1}H), 2.05 – 1.92 (m, 1H, CH_{H_{A2}}), 1.13 (d, *J* = 6.9 Hz, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 177.4 (C=O), 151.5 (C_{Ar}), 146.3 (C_{Ar}), 132.9 (CH_{Ar}), 132.6 (C_{Ar}), 124.1 (CH_{Ar}), 118.1 (CN), 41.3 (CH), 39.0 (CH₂), 37.0 (CH), 22.5 (CH₂), 17.0 (CH₃).

Isomer 2:

¹H NMR (400 MHz, Chloroform-*d*) δ 8.97 (s, 1H, NH), 7.35 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 7.27 (d, *J* = 8.3 Hz, 1H, CH_{Ar}), 3.58 – 3.48 (m, 1H, CH), 3.02 – 2.90 (m, 1H, CH_{A1}H), 2.84 – 2.78 (m, 1H, CH_{H_{A2}}), 2.51 – 2.43 (m, 1H, CH), 2.39 – 2.27 (m, 1H, CH_{B1}H), 2.16 – 2.07 (m, 1H, CH_{H_{B2}}), 1.12 (d, *J* = 6.4 Hz, 3H, CH₃).

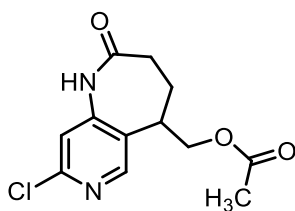
¹³C NMR (101 MHz, Chloroform-*d*) δ 176.6 (C=O), 153.4 (C_{Ar}), 147.3 (C_{Ar}), 132.6 (C_{Ar}), 132.3 (CH_{Ar}), 123.6 (CH_{Ar}), 118.8 (CN), 43.3 (CH₂), 37.3 (CH), 35.4 (CH), 19.8 (CH₂), 15.4 (CH₃).

IR (neat), ν (cm⁻¹): 2933, 1671, 1580, 1443, 1394, 1273, 1137, 915, 834, 734.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₃ClN₃O 250.0742; Found 250.0743.

$R_f = 0.53$ (PE/EtOAc = 70%).

m.p. = 130-132°C.

(8-chloro-2-oxo-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]azepin-5-yl)methyl acetate (5fa)

Chemical Formula: C₁₂H₁₃ClN₂O₃
Molecular Weight: 268.70

Following the general procedure E, the reaction was carried out with the solution of **4fa** (236 mg, 0.50 mmol, 1 eq.) in chlorobenzene (50 mL) with 5 eq. of DTBP (0.46 mL) for 3 h. Flash column chromatography on silica gel (eluent: DCM/MeOH = 4%), followed by the recrystallization from EtOAc, afforded target product **5fa** (75 mg, 55%) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 8.74 (s, 1H, NH), 8.20 (d, *J* = 5.3 Hz, 1H, CH_{Ar}), 6.86 (d, *J* = 5.3 Hz, 1H, CH_{Ar}), 4.39 – 4.25 (m, 2H, CH₂), 4.14 – 4.03 (m, 1H, CH), 2.67 – 2.49 (m, 2H, CH₂), 2.46 – 2.36 (m, 1H, CH_{Ar}H), 2.29 – 2.16 (m, 1H, CHH_{A2}), 1.96 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 175.0 (C=O), 170.8 (C=O), 154.0 (C_{Ar}), 148.6 (CH_{Ar}), 147.2 (C_{Ar}), 125.4 (C_{Ar}), 116.2 (CH_{Ar}), 64.4 (CH₂), 37.5 (CH), 32.5 (CH₂), 27.2 (CH₂), 20.9 (CH₃).

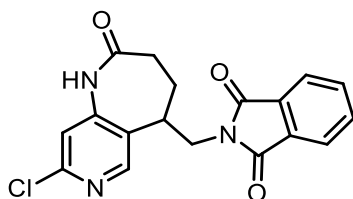
IR (neat), ν (cm⁻¹): 1738, 1678, 1575, 1464, 1368, 1228, 1034, 842, 733, 659, 603.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₄ClN₂O₃ 269.0687; Found 269.0689.

R_f = 0.31 (PE/EtOAc = 70%).

m.p. = 168-172°C (crystallized from EtOAc).

2-((8-chloro-2-oxo-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]azepin-5-yl)methyl)isoindoline-1,3-dione (5fc)



Chemical Formula: C₁₈H₁₄ClN₃O₃
Molecular Weight: 355.78

Following the general procedure E, the reaction was carried out with the solution of **4fc** (417 mg, 0.75 mmol, 1 eq.) in chlorobenzene (75 mL) with 5 eq. of DTBP (0.69 mL) for 4 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 45% → 75%) afforded target product **5fc** (151 mg, 57%) as a white solid.

¹H NMR (400 MHz, DMSO-*d*₆) δ 10.35 (s, 1H, NH), 8.07 (d, *J* = 5.3 Hz, 1H, CH_{Ar}), 7.85 – 7.73 (m, 4H, CH_{Phth}), 6.99 (d, *J* = 5.3 Hz, 1H, CH_{Ar}), 4.08 – 3.94 (m, 2H, CH and CH_{A1}H), 3.82 – 3.69 (m, 1H, CHH_{A2}), 2.56 – 2.45 (m, 1H, CH_{B1}H), 2.44 – 2.35 (m, 1H, CH_{C1}H), 2.34 – 2.25 (m, 1H, CHH_{B2}), 2.23 – 2.10 (m, 1H, CHH_{C2}).

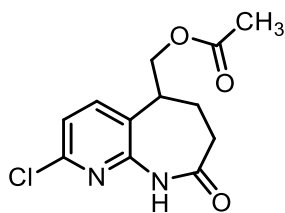
¹³C NMR (101 MHz, DMSO-*d*₆) δ 173.5 (C=O), 167.4 (C=O), 152.3 (C_{Ar}), 149.0 (C_{Ar}), 148.2 (CH_{Ar}), 134.5 (2C, CH_{Phth}), 131.2 (2C, C_{Phth}), 125.1 (C_{Ar}), 123.1 (2C, CH_{Phth}), 116.6 (CH_{Ar}), 39.7 (CH₂), 36.7 (CH), 32.5 (CH₂), 28.5 (CH₂).

IR (neat), ν (cm⁻¹): 1706, 1680, 1580, 1466, 1348, 1168, 1001, 941, 722, 714.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₈H₁₅ClN₃O₃ 356.0796; Found 356.0800.

R_f = 0.27 (PE/EtOAc = 70%).

m.p. = 216-219°C (crystallized from PE/EtOAc).

(2-chloro-8-oxo-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-5-yl)methyl acetate (5ga)

Chemical Formula: C₁₂H₁₃ClN₂O₃
Molecular Weight: 268.70

Following the general procedure E, the reaction was carried out with the solution of **4ga** (199 mg, 0.42 mmol, 1 eq.) in chlorobenzene (42 mL) with 5 eq. of DTBP (0.39 mL) for 6 h. Flash column chromatography on silica gel (eluent: DCM/MeOH = 2%) afforded target product **5ga** (11.3 mg, 10%) as a yellow oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.80 (s, 1H, NH), 7.55 (d, *J* = 8.0 Hz, 1H, CH_{Ar}), 7.14 (d, *J* = 8.0 Hz, 1H, CH_{Ar}), 4.44 (dd, *J* = 11.4, 7.4 Hz, 1H, CH_{A1}H), 4.32 (dd, *J* = 11.4, 6.0 Hz, 1H, CH_HA₂), 3.37 – 3.25 (m, 1H, CH), 2.58 – 2.38 (m, 3H, CH₂ and CH_{B1}H), 2.04 (s, 3H, CH₃), 2.02 – 1.88 (m, 1H, CH_HB₂).

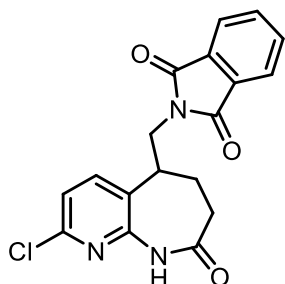
¹³C NMR (101 MHz, Chloroform-*d*) δ 173.3 (C=O), 170.8 (C=O), 151.1 (C_{Ar}), 148.5 (C_{Ar}), 139.3 (CH_{Ar}), 125.8 (C_{Ar}), 120.7 (CH_{Ar}), 64.5 (CH₂), 38.0 (CH), 32.9 (CH₂), 30.0 (CH₂), 20.9 (CH₃).

IR (neat), ν (cm⁻¹): 2945, 1738, 1683, 1568, 1441, 1367, 1236, 1118, 1043, 768.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₂H₁₄ClN₂O₃ 269.0687; Found 269.0689.

R_f = 0.41 (PE/EtOAc = 60%).

2-((2-chloro-8-oxo-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-5-yl)methyl)isoindoline-1,3-dione (5gc)



Chemical Formula: C₁₈H₁₄ClN₃O₃
Molecular Weight: 355.78

Following the general procedure E, the reaction was carried out with the solution of **4gc** (265 mg, 0.48 mmol, 1 eq.) in chlorobenzene (48 mL) with 5 eq. of DTBP (0.44 mL) for 3 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 35% → 55%), followed by the crystallization from Et₂O, afforded target product **5gc** (37 mg, 22%) as a white solid.

¹H NMR (400 MHz, Chloroform-d) δ 7.90 (s, 1H, NH), 7.82 – 7.78 (m, 2H, CH_{Phth}), 7.73 – 7.69 (m, 2H, CH_{Phth}), 7.65 (d, J = 8.0 Hz, 1H, CH_{Ar}), 7.05 (d, J = 8.0 Hz, 1H, CH_{Ar}), 4.12 (dd, J = 13.7, 8.0 Hz, 1H, CH_{A1}H), 3.91 (dd, J = 13.7, 7.4 Hz, 1H, CH_{H_{A2}}), 3.60 – 3.49 (m, 1H, CH), 2.52 – 2.37 (m, 3H, CH₂ and CH_{B1}H), 2.05 – 1.93 (m, 1H, CH_{H_{B2}}).

¹³C NMR (101 MHz, Chloroform-d) δ 173.2 (C=O), 168.2 (C=O), 151.1 (C_{Ar}), 148.5 (C_{Ar}), 139.5 (CH_{Ar}), 134.4 (2C, CH_{Phth}), 131.6 (2C, C_{Phth}), 125.7 (C_{Ar}), 123.6 (2C, CH_{Phth}), 120.5 (CH_{Ar}), 40.3 (CH₂), 37.9 (CH), 32.8 (CH₂), 31.0 (CH₂).

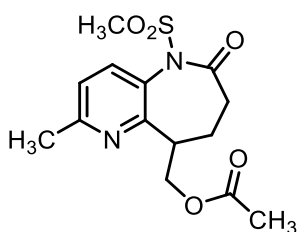
IR (neat), ν (cm⁻¹): 1772, 1709, 1580, 1563, 1430, 1357, 1155, 968, 727.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₁₅ClN₃O₃ 356.0796; Found 356.0798.

R_f = 0.31 (PE/EtOAc = 50%).

m.p. = 143-144°C (crystallized from Et₂O).

(2-methyl-5-(methylsulfonyl)-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate (6ca)



Chemical Formula: C₁₄H₁₈N₂O₅S
Molecular Weight: 326.37

Following the general procedure E, the reaction was carried out with the solution of **4ca** (300 mg, 0.67 mmol, 1 eq.) in chlorobenzene (67 mL) with 5 eq. of DTBP (0.62 mL) for 5 h. Flash column chromatography on silica gel (eluent: PE/EtOAc = 50%) afforded sulfonylated product **6ca** (121 mg, 55%) as a yellow oil, that solidified thereafter.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 7.14 (d, *J* = 8.2 Hz, 1H, CH_{Ar}), 4.78 (dd, *J* = 11.2, 5.9 Hz, 1H, CH_{A1}H), 4.45 (dd, *J* = 11.2, 7.8 Hz, 1H, CH_HA₂), 3.53 (s, 3H, SO₂CH₃), 3.50 – 3.39 (m, 1H, CH), 2.61 – 2.52 (m, 1H, CH_{B1}H), 2.54 (s, 3H, CH₃), 2.51 – 2.42 (m, 1H, CH_{C1}H), 2.31 – 2.19 (m, 1H, CH_HC₂), 2.05 (s, 3H, CH₃), 1.80 – 1.69 (m, 1H, CH_HB₂).

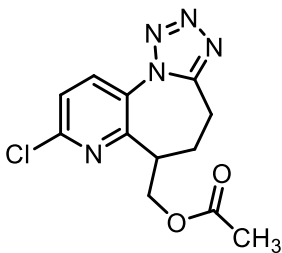
¹³C NMR (101 MHz, Chloroform-*d*) δ 173.2 (C=O), 171.3 (C=O), 159.2 (C_{Ar}), 154.1 (C_{Ar}), 135.7 (CH_{Ar}), 129.1 (C_{Ar}), 122.0 (CH_{Ar}), 65.1 (CH₂), 43.2 (SO₂CH₃), 38.7 (CH), 34.3 (CH₂), 30.4 (CH₂), 24.4 (CH₃), 21.1 (CH₃).

IR (neat), ν (cm⁻¹): 1731, 1706, 1460, 1350, 1236, 1163, 1128, 1033, 965, 912, 763, 732.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₄H₁₉N₂O₅S 327.1009; Found 327.1009.

R_f = 0.60 (PE/EtOAc = 70%).

Derivatization of the pyridoazepinone 5aa

(8-chloro-5,6-dihydro-4H-pyrido[2,3-f]tetrazolo[1,5-a]azepin-6-yl)methyl acetate (7)	
	Chemical Formula: C ₁₂ H ₁₂ ClN ₅ O ₂ Molecular Weight: 293.71

According to a modified literature procedure³, to a solution of xanthate **5aa** (100 mg, 0.37 mmol, 1 eq.) in pyridine (0.56 mL) was added diphenylphosphoryl azide (0.16 mL, 0.74 mmol, 2 eq.), and the reaction mixture was refluxed under nitrogen for 15 h. Then it was diluted with EtOAc (30 mL) and washed with sat. aq. NH₄Cl solution (3 x 30 mL). The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. The residue was subjected to a column chromatography on silica gel (eluent: PE/EtOAc = 25% → 45%) to yield target product **7** (76 mg, 69%) as a white solid.

¹H NMR (400 MHz, Chloroform-d) δ 8.12 (d, J = 8.4 Hz, 1H, CH_{Ar}), 7.49 (d, J = 8.4 Hz, 1H, CH_{Ar}), 4.67 (dd, J = 11.4, 5.9 Hz, 1H, CH_{Ar}H), 4.37 (dd, J = 11.4, 7.2 Hz, 1H, CH_HA₂), 3.55 – 3.45 (m, 1H, CH_BH), 3.19 – 3.07 (m, 1H, CH), 2.97 – 2.84 (m, 1H, CH_HB₂), 2.69 – 2.57 (m, 1H, CH_CH), 2.29 – 2.17 (m, 1H, CH_HC₂), 1.99 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-d) δ 170.8 (C=O), 154.4 (C_{Ar}), 153.0 (C_{Ar}), 151.6 (C=N), 133.6 (CH_{Ar}), 129.2 (C_{Ar}), 124.2 (CH_{Ar}), 64.4 (CH₂), 41.3 (CH), 30.6 (CH₂), 20.9 (CH₃), 20.4 (CH₂).

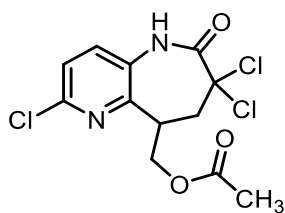
IR (neat), ν (cm⁻¹): 2951, 1735, 1468, 1368, 1235, 1144, 1079, 1040, 921, 732.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₂H₁₃ClN₅O₂ 294.0752; Found 294.0752.

R_f = 0.44 (PE/EtOAc = 50%).

m.p. = 117-119°C (crystallized from PE/EtOAc).

(2,7,7-trichloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate
(8)



Chemical Formula: C₁₂H₁₁Cl₃N₂O₃
Molecular Weight: 337.58

According to a modified literature procedure⁴, to a solution of xanthate **5aa** (100 mg, 0.37 mmol, 1 eq.) in toluene (3.7 mL) was added PCl₅ (317 mg, 1.52 mmol, 4 eq.), and the reaction mixture was stirred at 80°C under nitrogen for 1.5 h. Then it was cooled to rt and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) and washed with sat. aq. NaHCO₃ solution (20 mL). Aqueous layer was extracted with EtOAc (2 x 20 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. The residue was subjected to a column chromatography on silica gel with (eluent: PE/EtOAc = 15% → 35%) to yield target product **8** (80 mg, 64%) as a yellow foam. For analytical purposes it was recrystallized from Et₂O to give white crystals.

¹H NMR (400 MHz, Chloroform-d) δ 8.11 (s, 1H, NH), 7.30 (d, J = 8.4 Hz, 1H, CH_{Ar}), 7.26 (d, J = 8.4 Hz, 1H, CH_{Ar}), 4.75 (dd, J = 11.4, 5.1 Hz, 1H, CH_{A1}H), 4.42 (dd, J = 11.5, 8.2 Hz, 1H, CH_{H_{A2}}), 3.74 – 3.64 (m, 1H, CH), 3.44 (dd, J = 15.3, 6.6 Hz, 1H, CH_{B1}H), 3.08 (dd, J = 15.3, 11.9 Hz, 1H, CH_{H_{B2}}), 2.08 (s, 3H, CH₃).

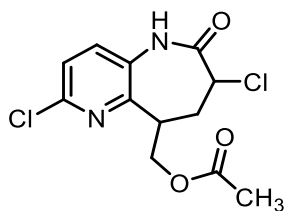
¹³C NMR (101 MHz, Chloroform-d) δ 171.0 (C=O), 165.2 (C=O), 151.3 (C_{Ar}), 147.7 (C_{Ar}), 132.2 (C_{Ar}), 130.9 (CH_{Ar}), 123.8 (CH_{Ar}), 84.6 (CCl₂), 64.6 (CH₂), 53.2 (CH₂), 39.5 (CH), 21.1 (CH₃).

IR (neat), ν (cm⁻¹): 3228, 1700, 1450, 1365, 1236, 1140, 1037, 901, 835, 771.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₂H₁₂Cl₃N₂O₃ 336.9908; Found 336.9905.

R_f = 0.72 (PE/EtOAc = 50%).

m.p. = 180-181°C (crystallized from Et₂O).

(2,7-dichloro-6-oxo-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]azepin-9-yl)methyl acetate (9)

Chemical Formula: C₁₂H₁₂Cl₂N₂O₃
Molecular Weight: 303.14

Solution of xanthate **5aa** (100 mg, 0.37 mmol, 1 eq.) in dry DCM (3.8 mL) was added dropwise to a suspension of PCl₅ (315 mg, 1.51 mmol, 4 eq.) at 0°C under argon. The reaction mixture was stirred 2 h, slowly warming to rt. Then it was diluted with DCM (20 mL) and washed with sat. aq. NaHCO₃ solution (20 mL). Aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. The residue was subjected to a column chromatography on silica gel with eluent gradient PE/EtOAc = 10% → 40% to yield target product **9** (72 mg, 64%) as a white solid. For analytical purposes it was crystallized from DCM to give white crystals. Mixture of two diastereomers (d.r. = 1.25:1; determined by the NMR analysis of the crude mixture).

Isomer 1:

¹H NMR (400 MHz, Chloroform-*d*) δ 8.85 (s, 1H, NH), 7.35 (d, J = 7.5 Hz, 1H, CH_{Ar}), 7.30 – 7.23 (m, 1H, CH_{Ar}), 4.66 (dd, J = 11.2, 6.1 Hz, 1H, CH_{A1}H), 4.37 (dd, J = 11.2, 7.8 Hz, 1H, CH_HA₂), 3.70 – 3.50 (m, 1H, CH), 3.19 – 3.07 (m, 1H, CH_{B1}H), 2.44 – 2.31 (m, 1H, CH_HB₂), 2.03 (s, 3H, CH₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 171.0 (C=O), 170.3 (C=O), 153.0 (C_{Ar}), 147.6 (C_{Ar}), 132.3 (C_{Ar}), 131.9 (CH_{Ar}), 123.7 (CH_{Ar}), 64.7 (CH₂), 56.1 (CH), 41.3 (CH₂), 39.9 (CH), 21.0 (CH₃).

Isomer 2:

¹H NMR (400 MHz, Chloroform-*d*) δ 9.06 (s, 1H, NH), 7.40 (d, J = 7.6 Hz, 1H, CH_{Ar}), 7.30 – 7.27 (m, 1H, CH_{Ar}), 4.73 (dd, J = 11.3, 5.4 Hz, 1H, CH_{A1}H), 4.48 – 4.41 (m, 2H, CH_HA₂ and CH), 3.67 – 3.50 (m, 1H, CH), 2.84 – 2.70 (m, 1H, CH_{B1}H), 2.65 – 2.53 (m, 1H, CH_HB₂), 2.06 (s, 3H, CH₃).

^{13}C NMR (101 MHz, Chloroform- d) δ 171.1 (C=O), 169.7 (C=O), 153.2 (C_{Ar}), 148.4 (C_{Ar}), 132.6 (CH_{Ar}), 131.6 (C_{Ar}), 123.7 (CH_{Ar}), 64.4 (CH_2), 55.6 (CH), 42.9 (CH_2), 39.1 (CH), 21.0 (CH_3).

IR (neat), ν (cm^{-1}): 3218, 1699, 1446, 1368, 1240, 1194, 1139, 1039, 890, 835, 757.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_3$ 303.0298; Found 303.0298.

R_f = 0.44 (PE/EtOAc = 50%).

m.p. = 206-209°C (crystallized from DCM).

Gram-scale preparation of the pyridoazepinone **5aa**

Step 1.

A stirred solution of the xanthate **3a** (3.00 g, 8.13 mmol, 1 eq.) and allyl acetate (1.80 mL, 16.7 mmol, 2 eq.) in EtOAc (8 mL, 1.0 M of the xanthate) was refluxed for 15 min under nitrogen. A portion of DLP (325 mg, 0.81 mmol, 0.1 eq.) was then added to the refluxing solution, followed by one additional portion (325 mg, 0.81 mmol, 0.1 eq.) after 1 h. The reaction mixture was then refluxed for 1 h until the starting xanthate was completely consumed. The reaction mixture was cooled to room temperature, concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (eluent: PE/EtOAc = 40%) to yield the target product **4aa** (3.38 g, 89%).

Step 2.

A stirred solution of xanthate **4aa** (3.38 g, 7.21 mmol, 1 eq.) in chlorobenzene (360 mL, 0.02 M of the xanthate) was refluxed for 15 min under nitrogen. DTBP (6.6 mL, 36.0 mmol, 5 eq.) was then added to the refluxing solution, and the reaction mixture was refluxed under nitrogen for 3 h. The reaction mixture was then cooled to the room temperature, concentrated under reduced pressure. The crude mixture was crystallized from the small volume of chlorobenzene, to yield the product **5aa** (1.11 g, 57%) as light brown solid. The mother liquor was concentrated under reduced pressure and purified by column chromatography (eluent: PE/EtOAc = 40% → 70%) to yield additional portion of **5aa** (0.15 g, 8%). Total yield of **5aa**: 1.26 g (65%). For analytical purposes the product was recrystallized from EtOAc.



One-pot synthesis of the pyridoazepinone **5aa**

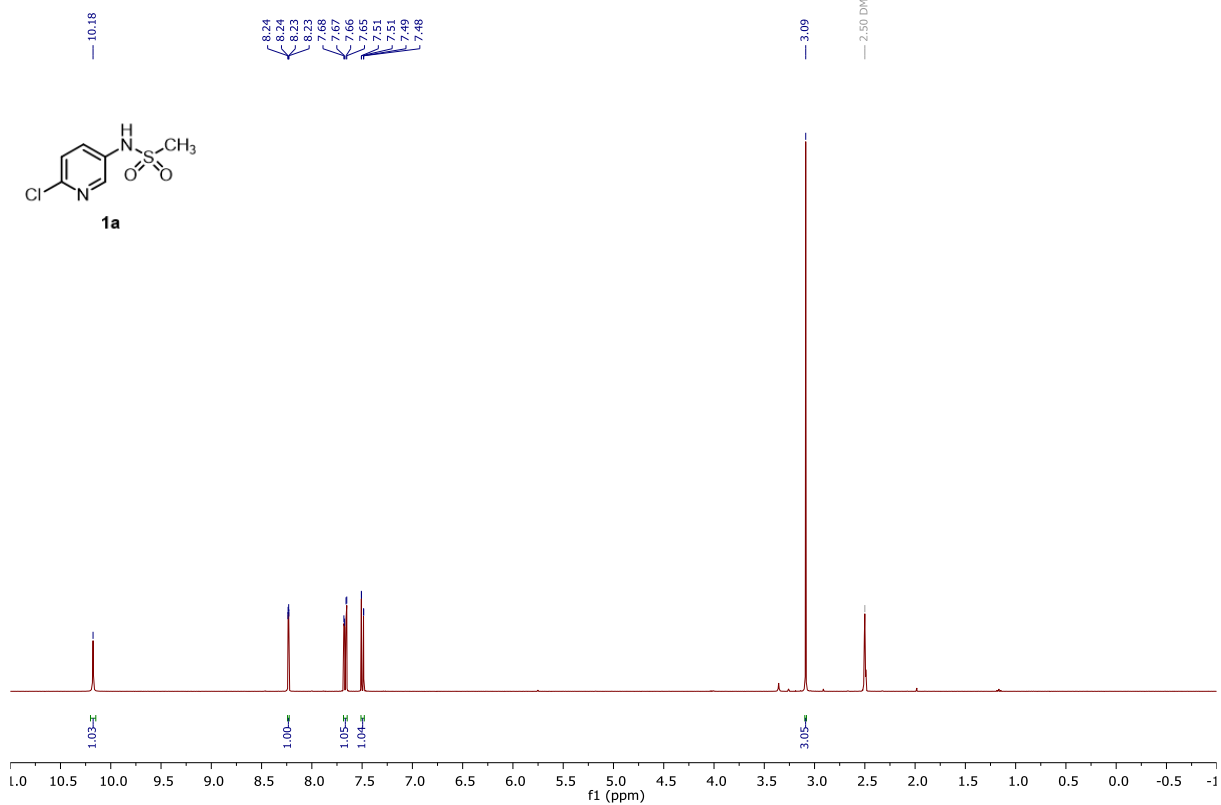
A stirred solution of the xanthate **3a** (250 mg, 0.68 mmol, 1 eq.) and allyl acetate (0.15 mL, 1.36 mmol, 2 eq.) in chlorobenzene (0.7 mL, 1.0 M of the xanthate, degassed with N₂) was heated to 90°C under nitrogen. A portion of DLP (27 mg, 0.07 mmol, 0.1 eq.) was then added to the refluxing solution, followed by one additional portion (27 mg, 0.07 mmol, 0.1 eq.) after 1 h. The reaction mixture was then refluxed for 1 h until the starting xanthate was completely consumed. The reaction mixture was concentrated by blowing N₂ at 90°C. The residue was diluted with chlorobenzene (34 mL, 0.01 M, degassed with N₂) and DTBP (0.63 mL, 3.43 mmol, 5 eq.) was added. The reaction mixture was refluxed under nitrogen for 2 h, then cooled down to the room temperature and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (eluent: PE/EtOAc = 0% → 50% → 75%), then the resulting white solid was washed with pentane (ca. 5 mL) to yield the target product **5aa** (114 mg, 63%).

References

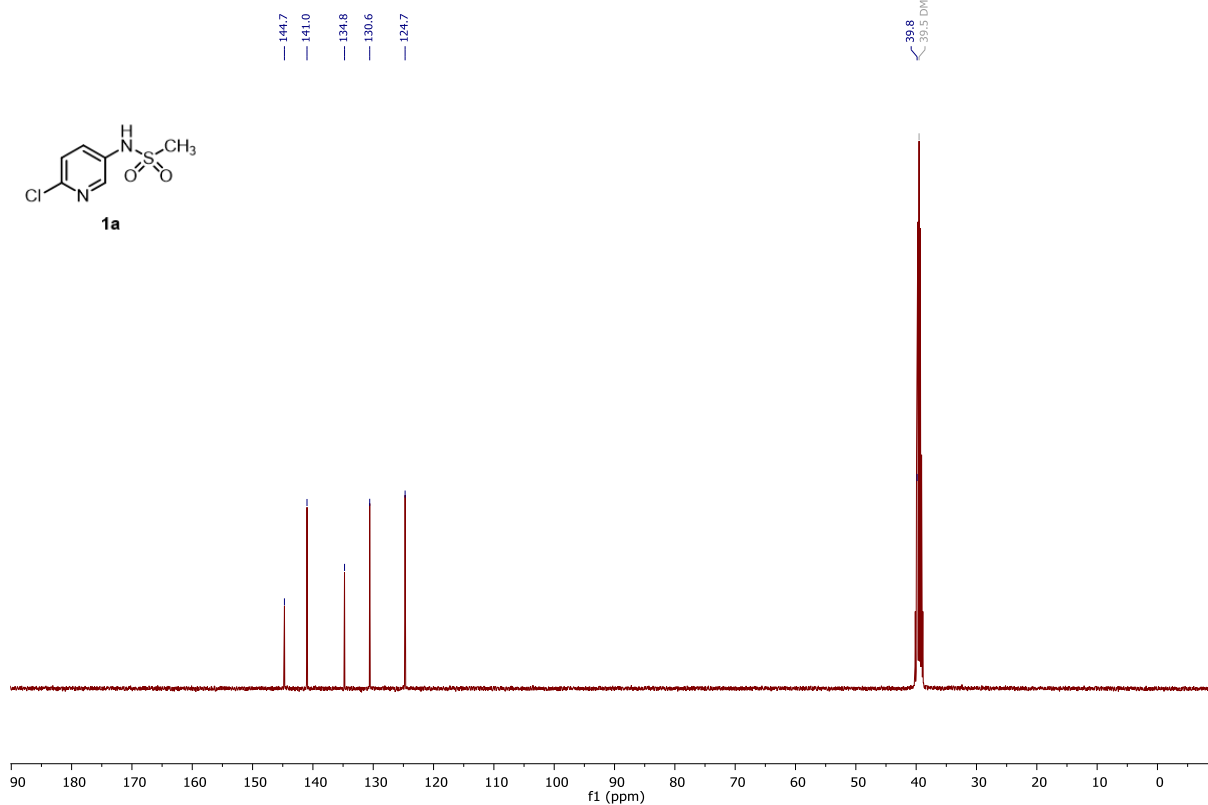
- (1) Kosinski, S.; Wojciechowski, K. Reactions of Pyridine Analogues of Aza-Ortho-Xylylenes Generated from 1,3-Dialkylpyridosultams. *Eur. J. Org. Chem.* **2000**, 1263–1270.
- (2) Huang, Q.; Zard, S. Z. Radical Fragment Coupling Route to Geminal Bis(Boronates). *Org. Lett.* **2018**, 20 (17), 5304–5308.
- (3) Ishihara, K.; Shioiri, T.; Matsugi, M. An Expeditious Approach to Tetrazoles from Amides Utilizing Phosphorazidates. *Org. Lett.* **2020**, 22 (16), 6244–6247.
- (4) Watthey, J. W. H.; Stanton, J. L.; Desai, M.; Babiarz, J. E.; Finn, B. M. Synthesis and Biological Properties of (Carboxyalkyl)Amino-Substituted Bicyclic Lactam Inhibitors of Angiotensin Converting Enzyme. *J. Med. Chem.* **1985**, 28 (10), 1511–1516.

Copies of NMR spectra

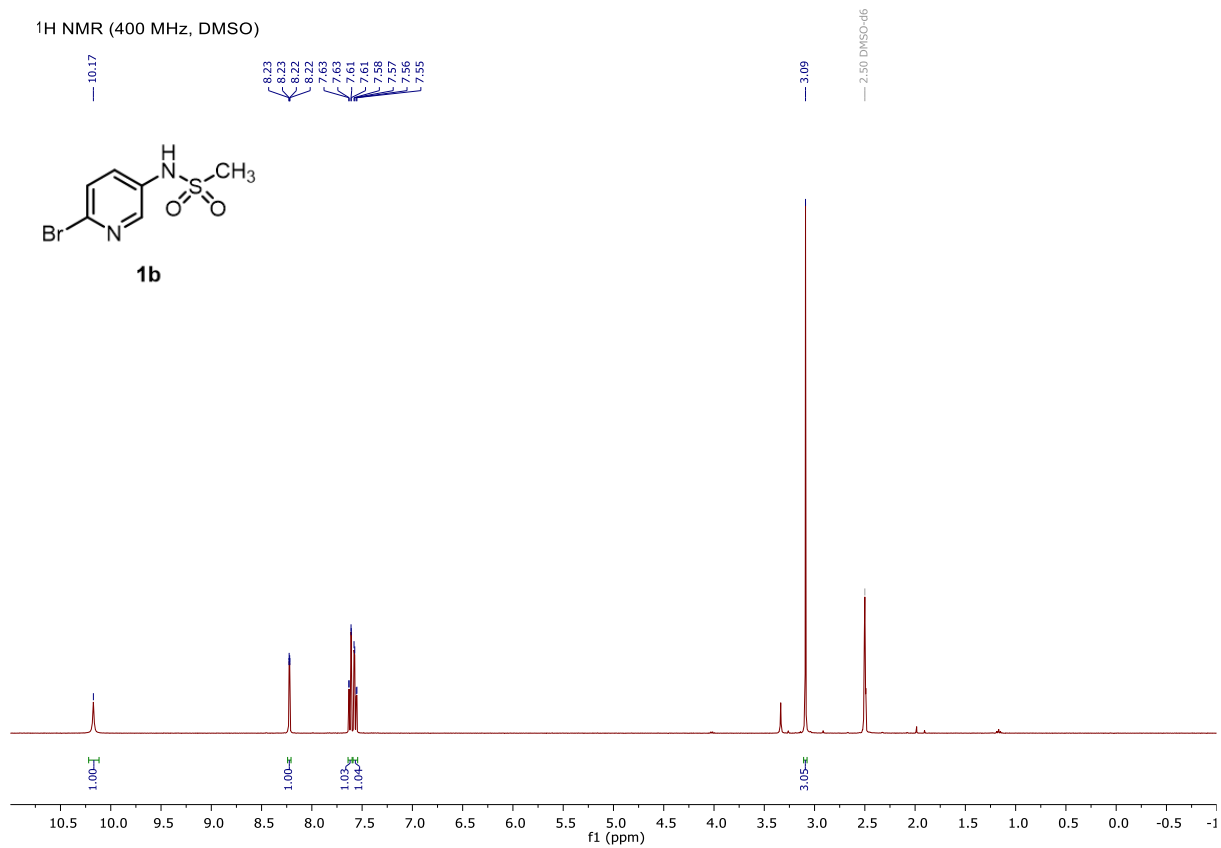
¹H NMR (400 MHz, DMSO)



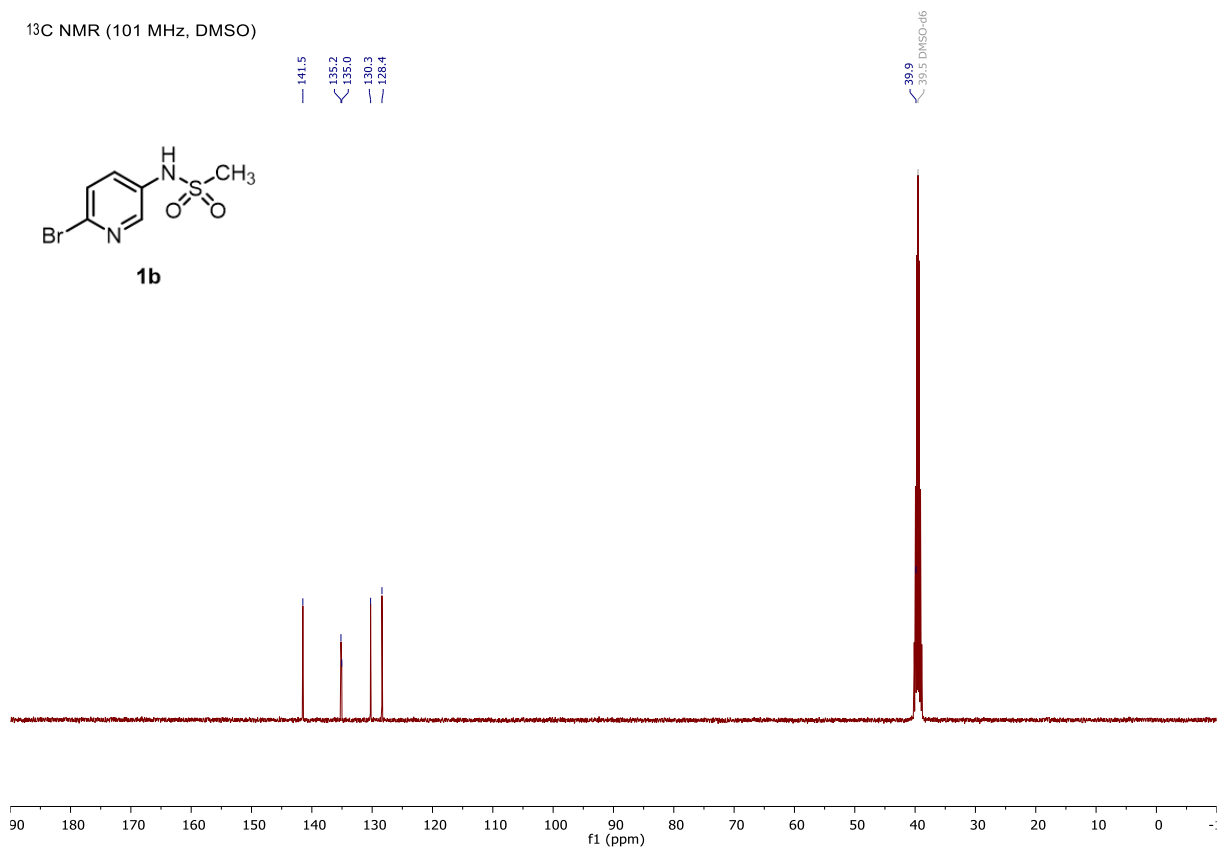
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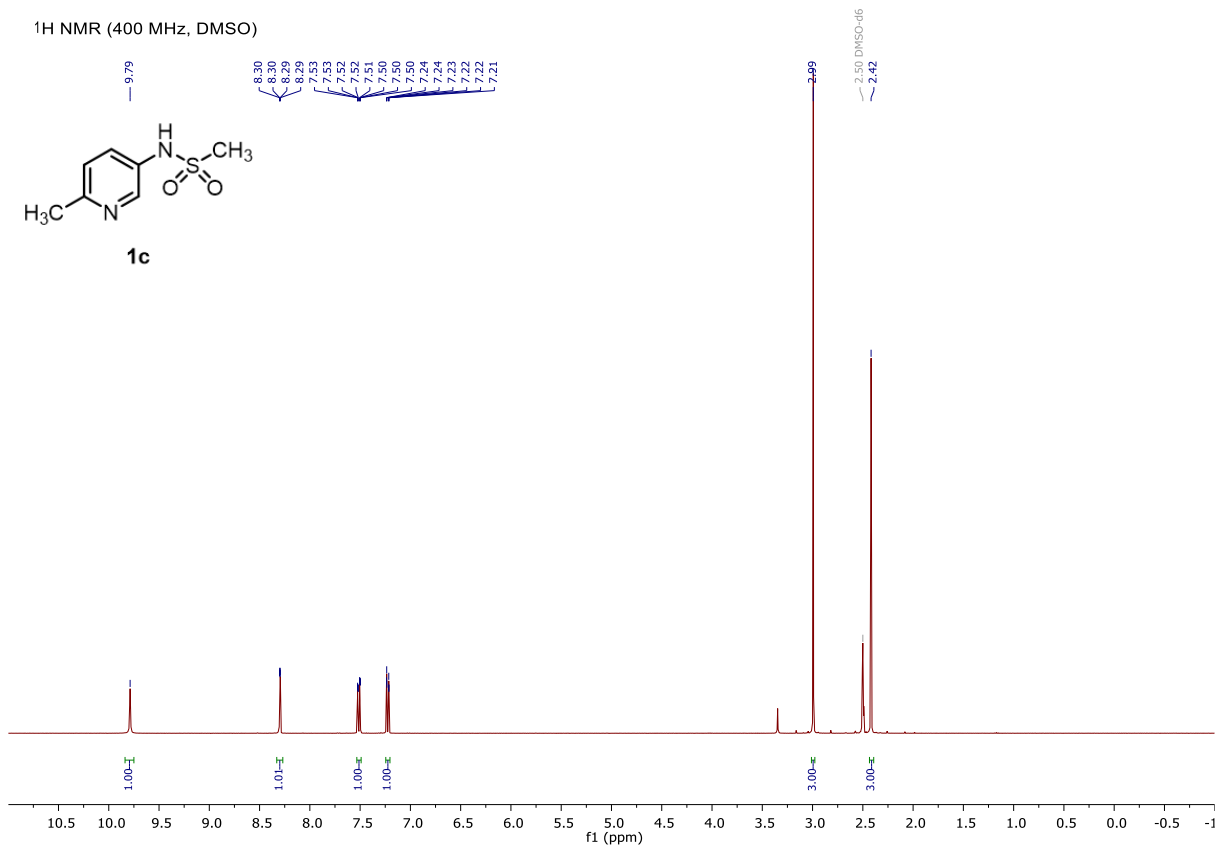
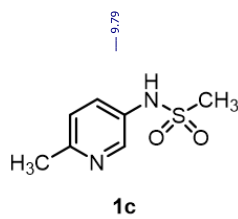
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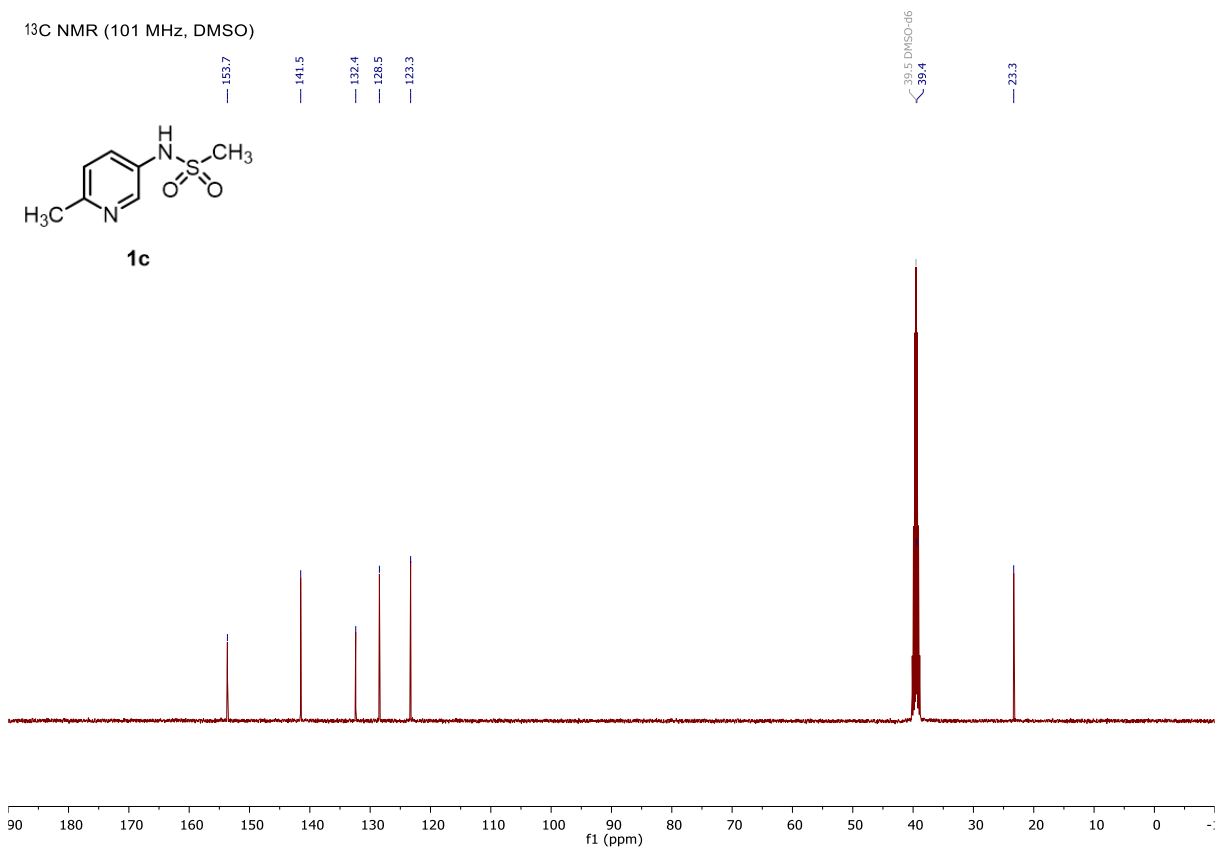
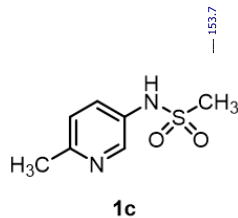
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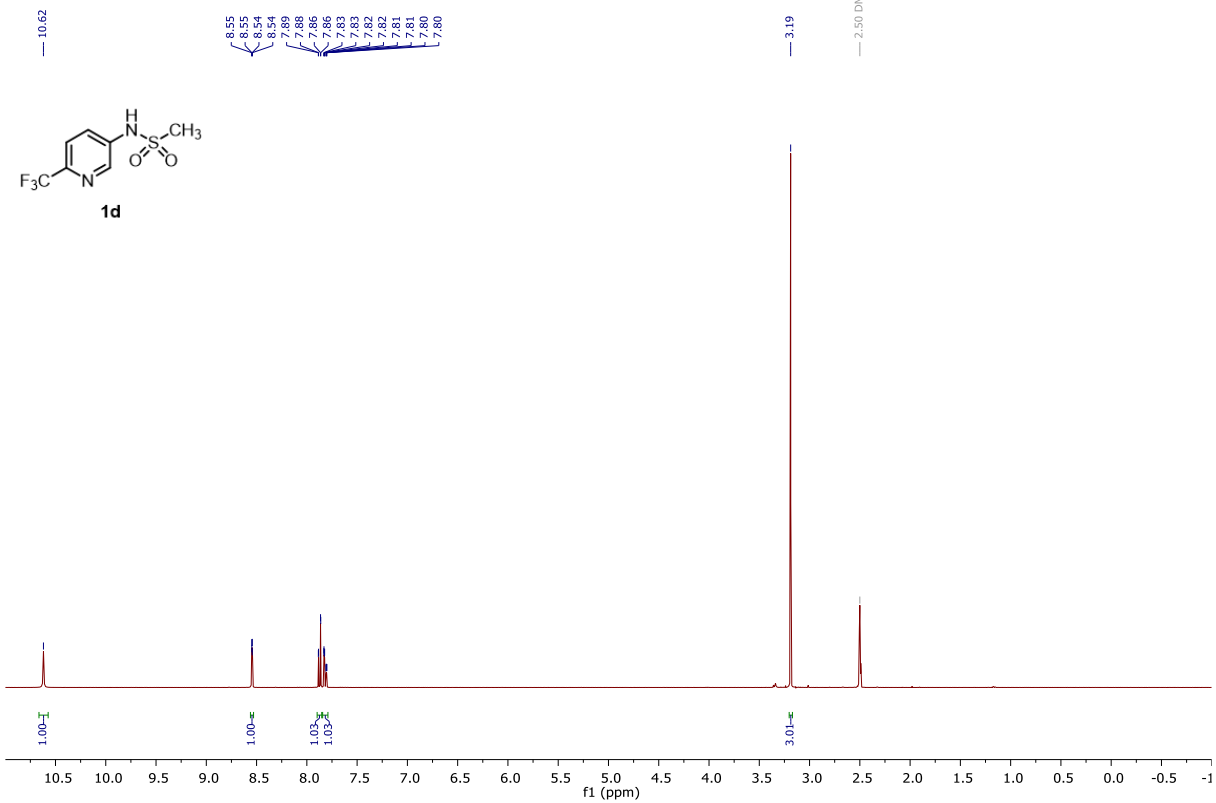
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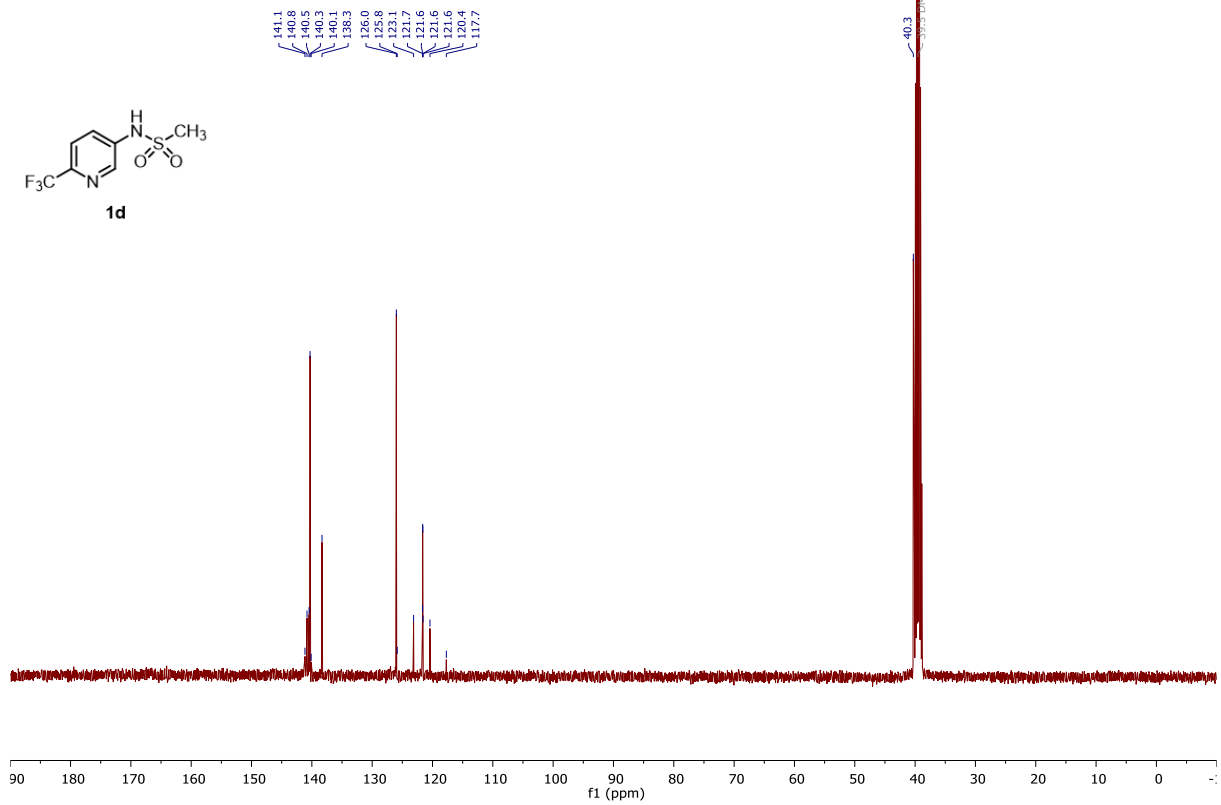
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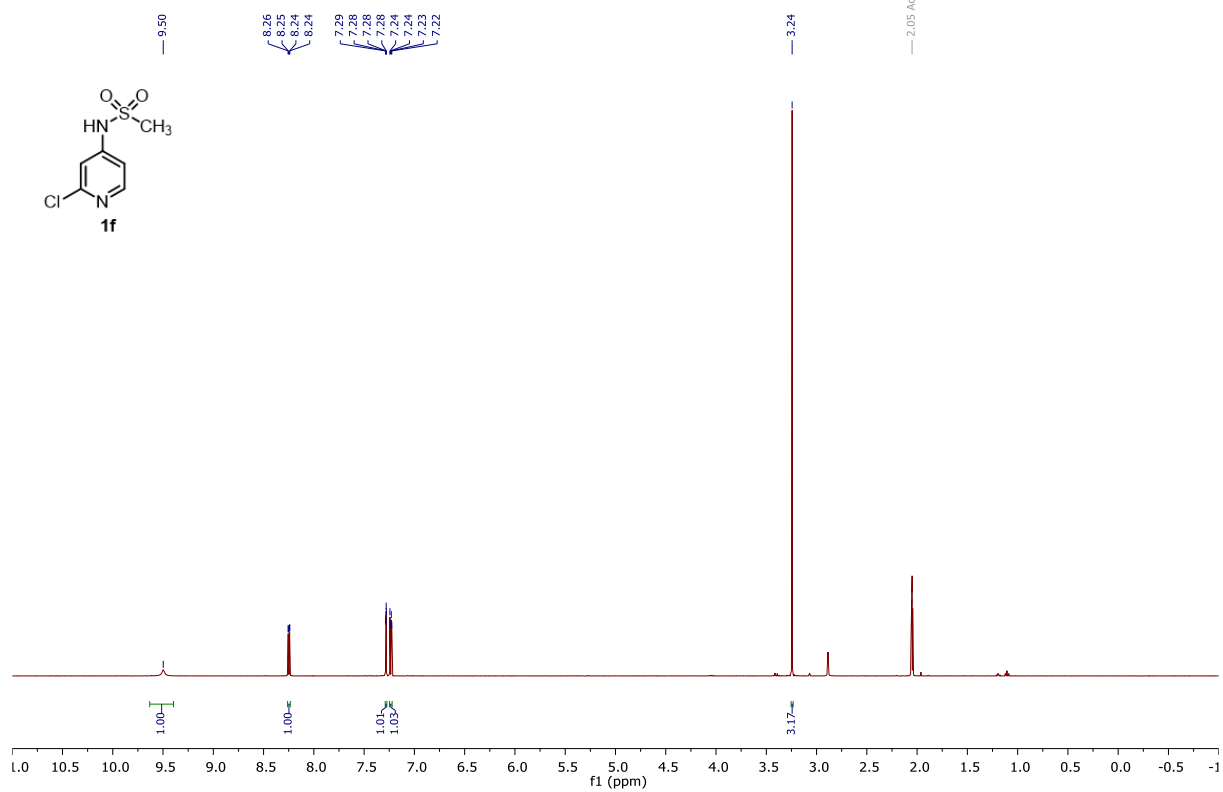
¹H NMR (400 MHz, DMSO)



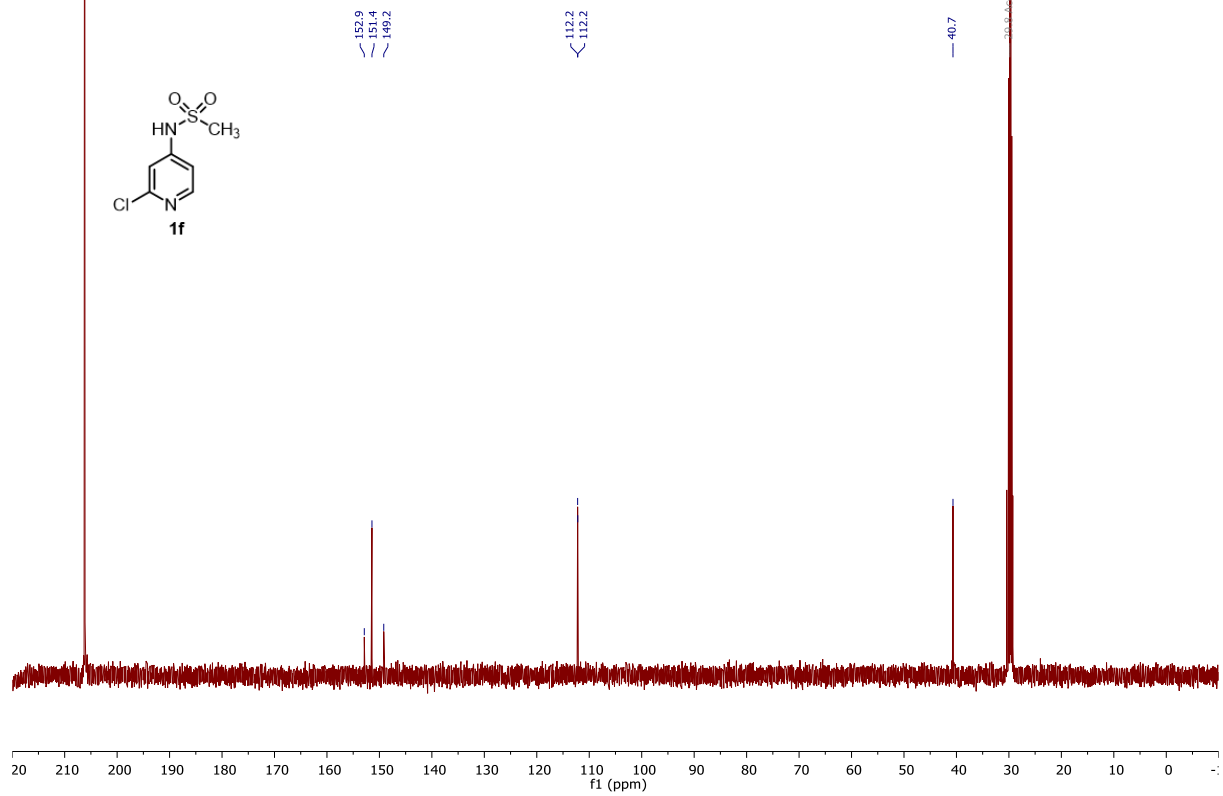
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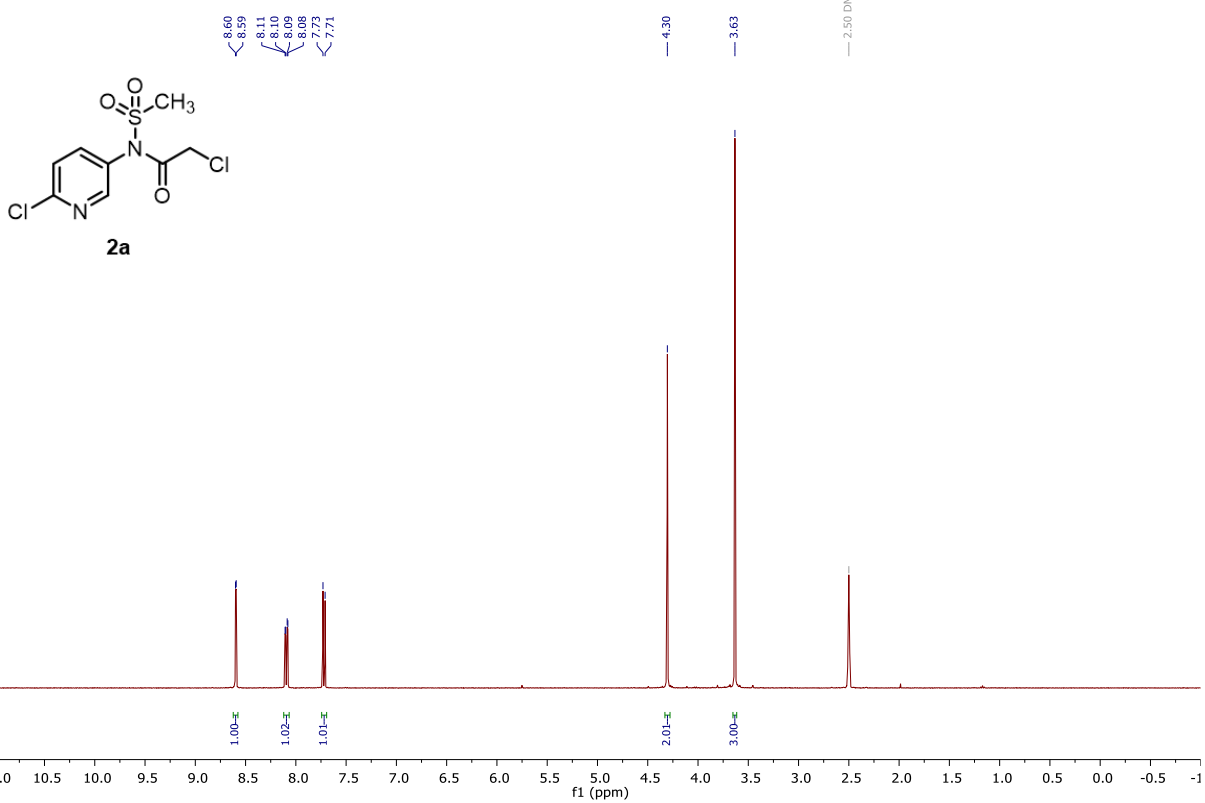
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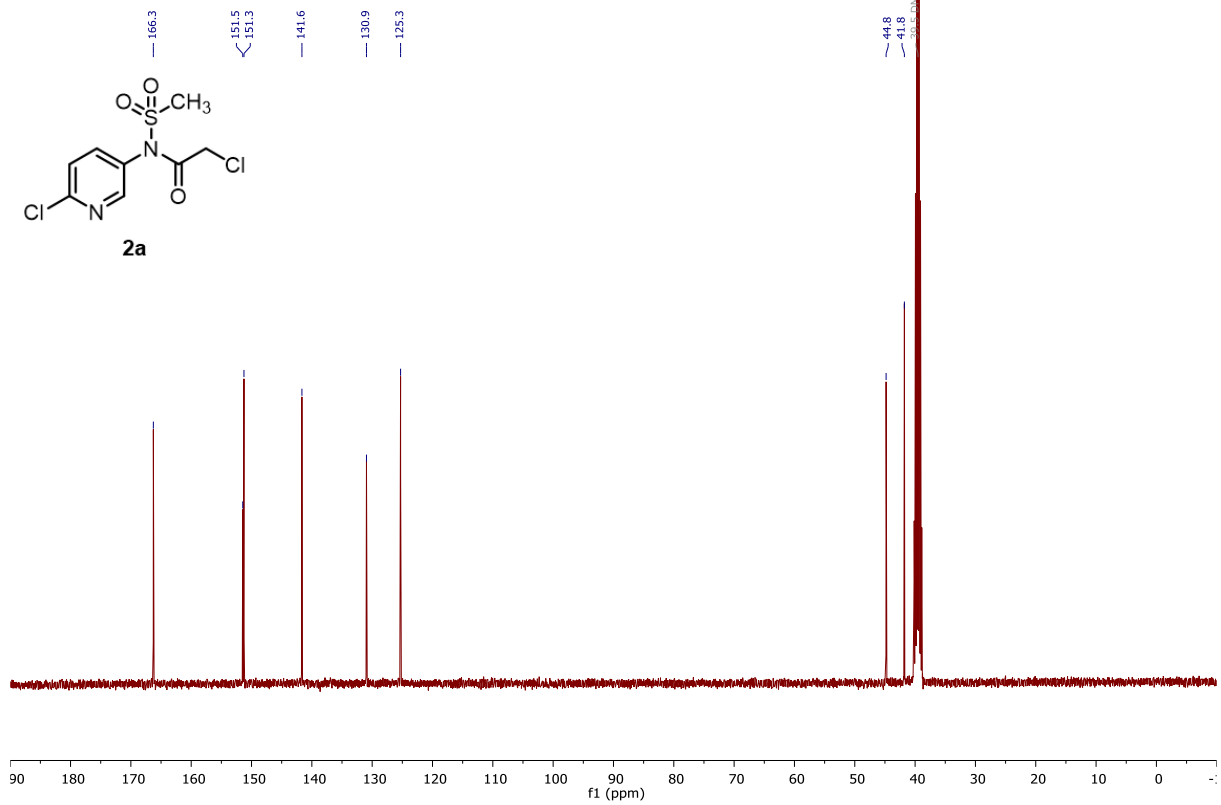
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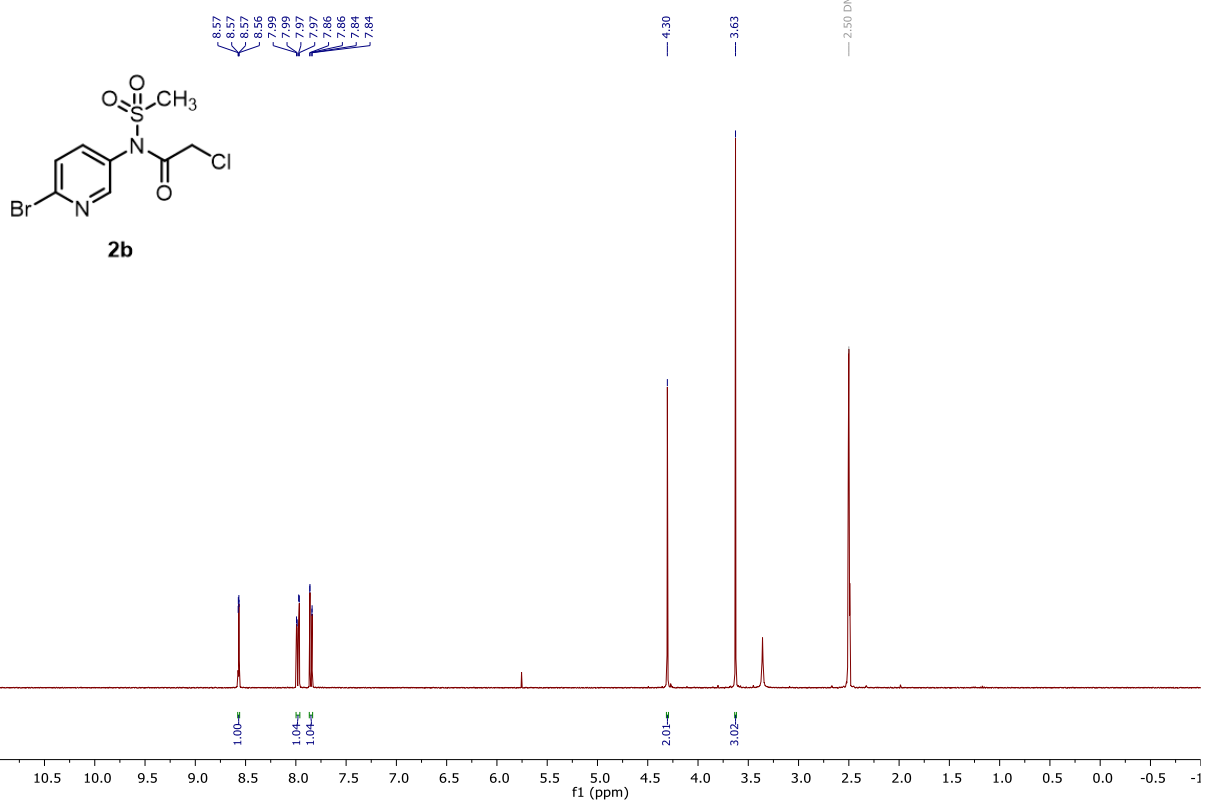
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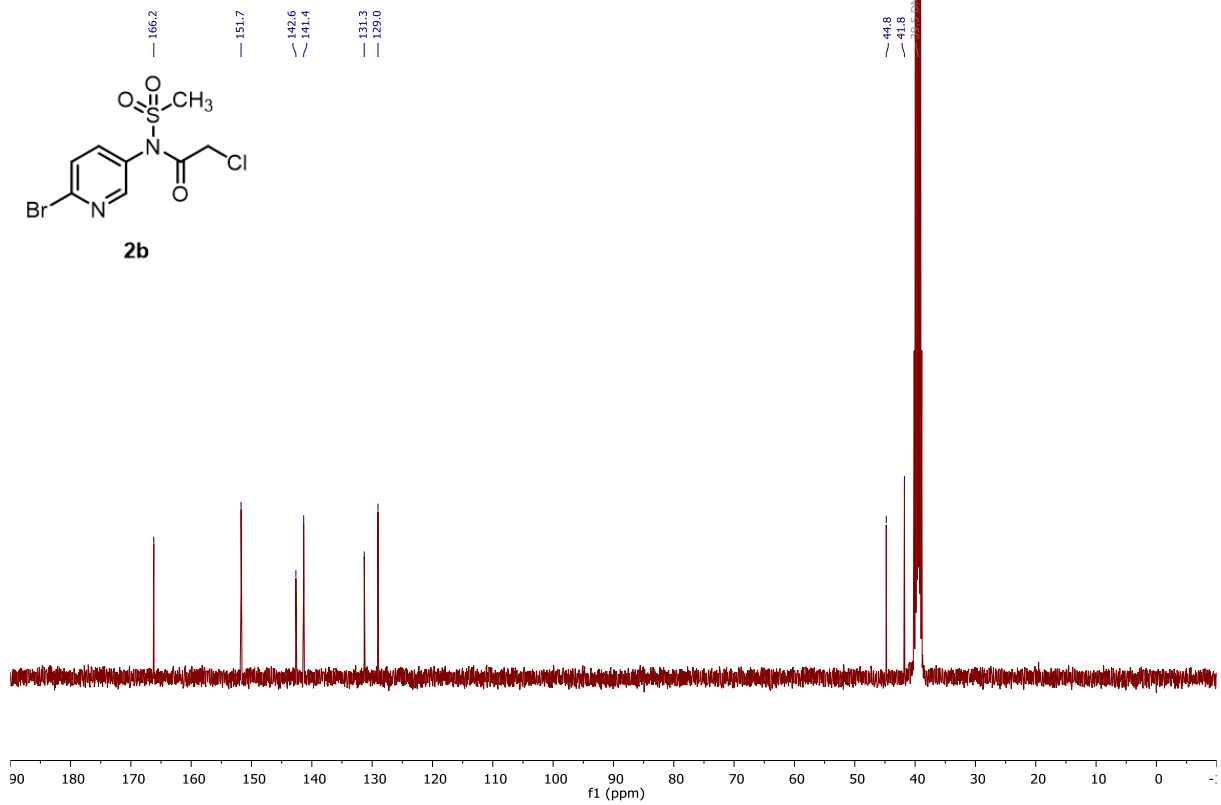
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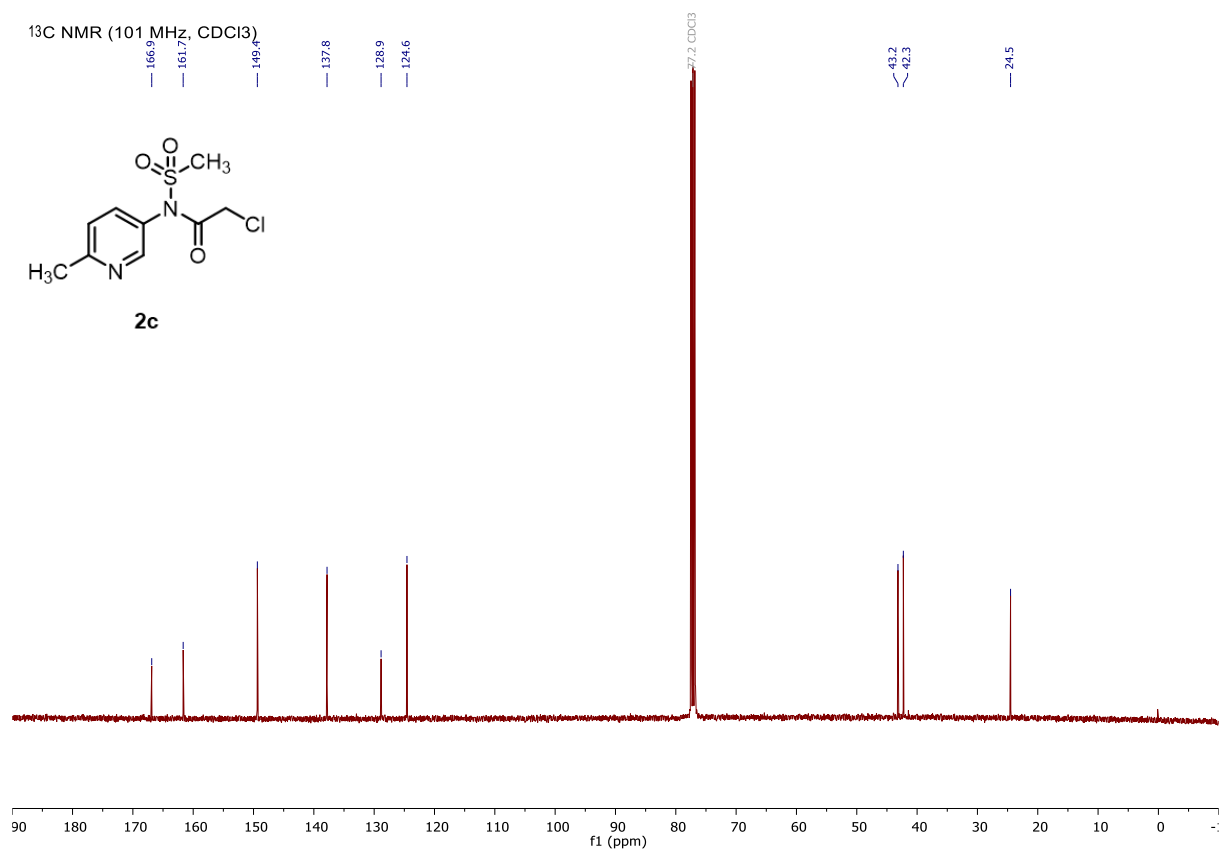
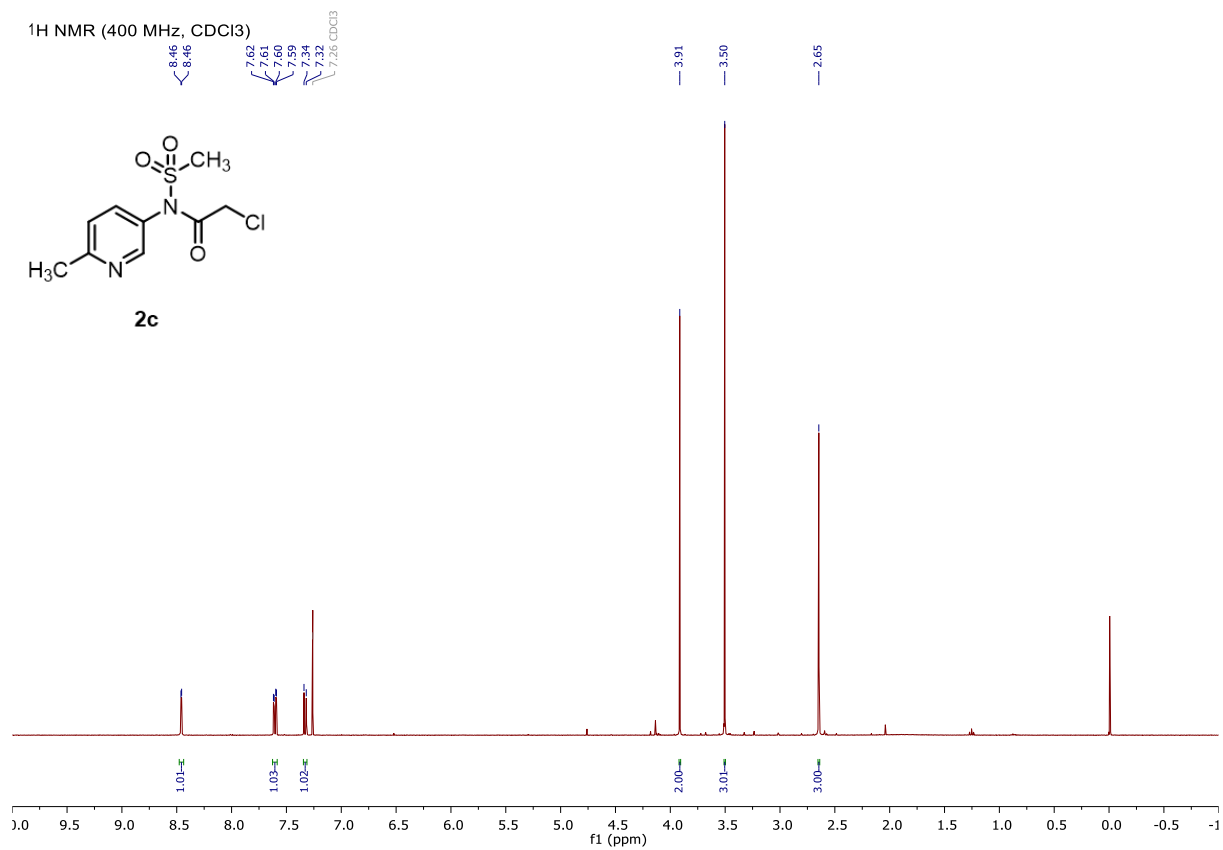


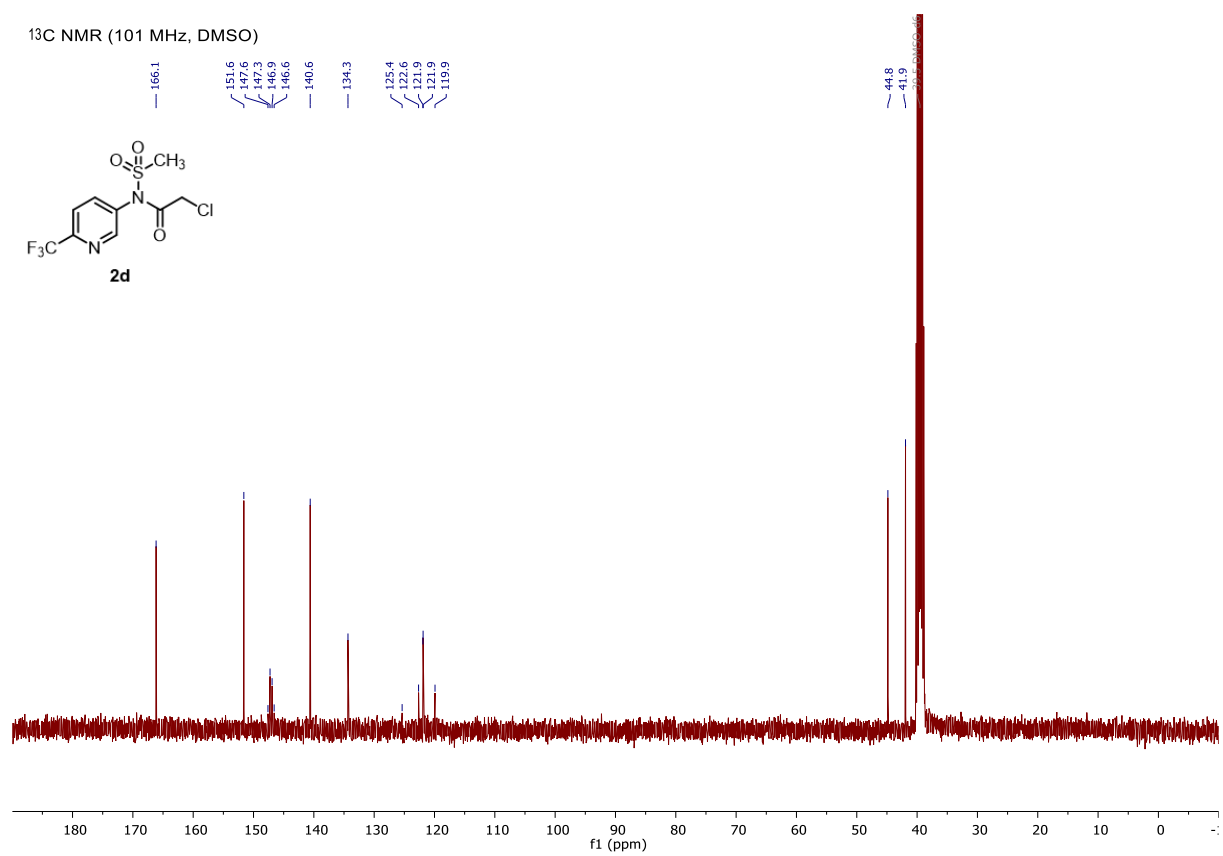
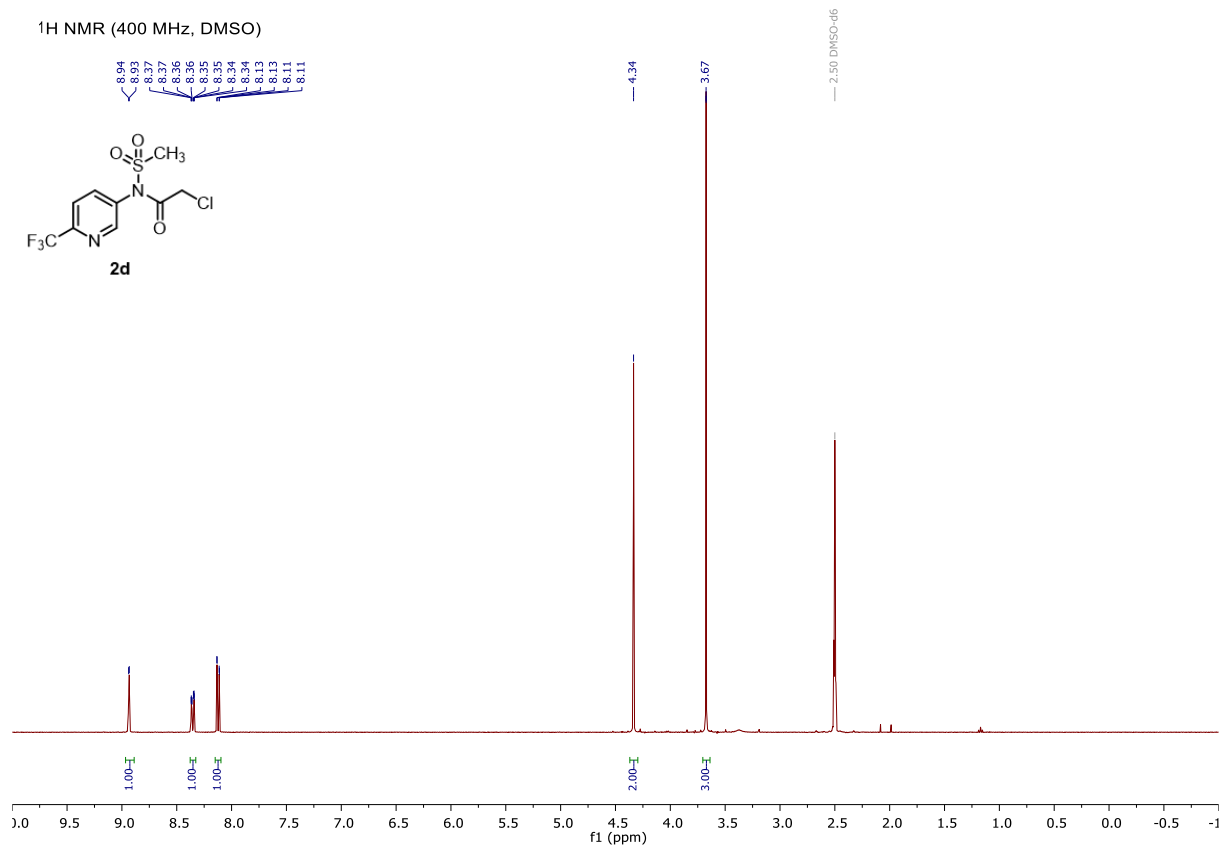
¹H NMR (400 MHz, DMSO)



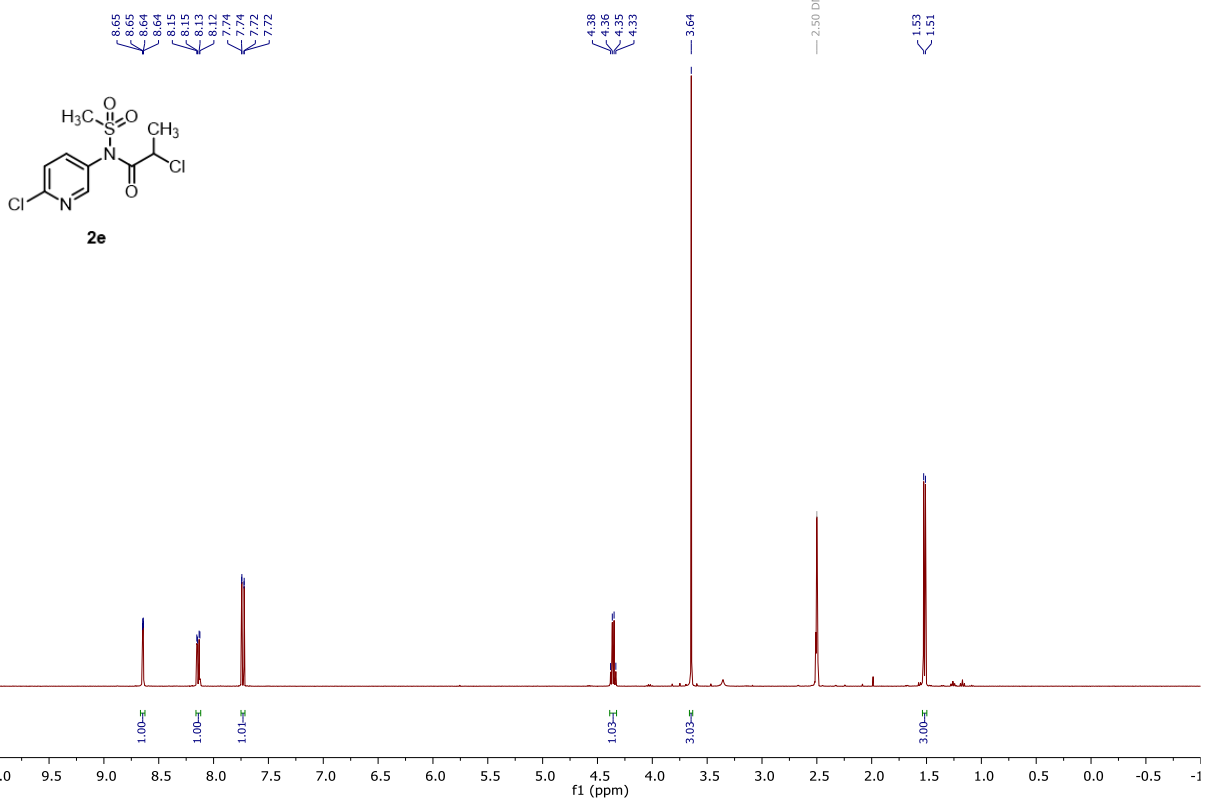
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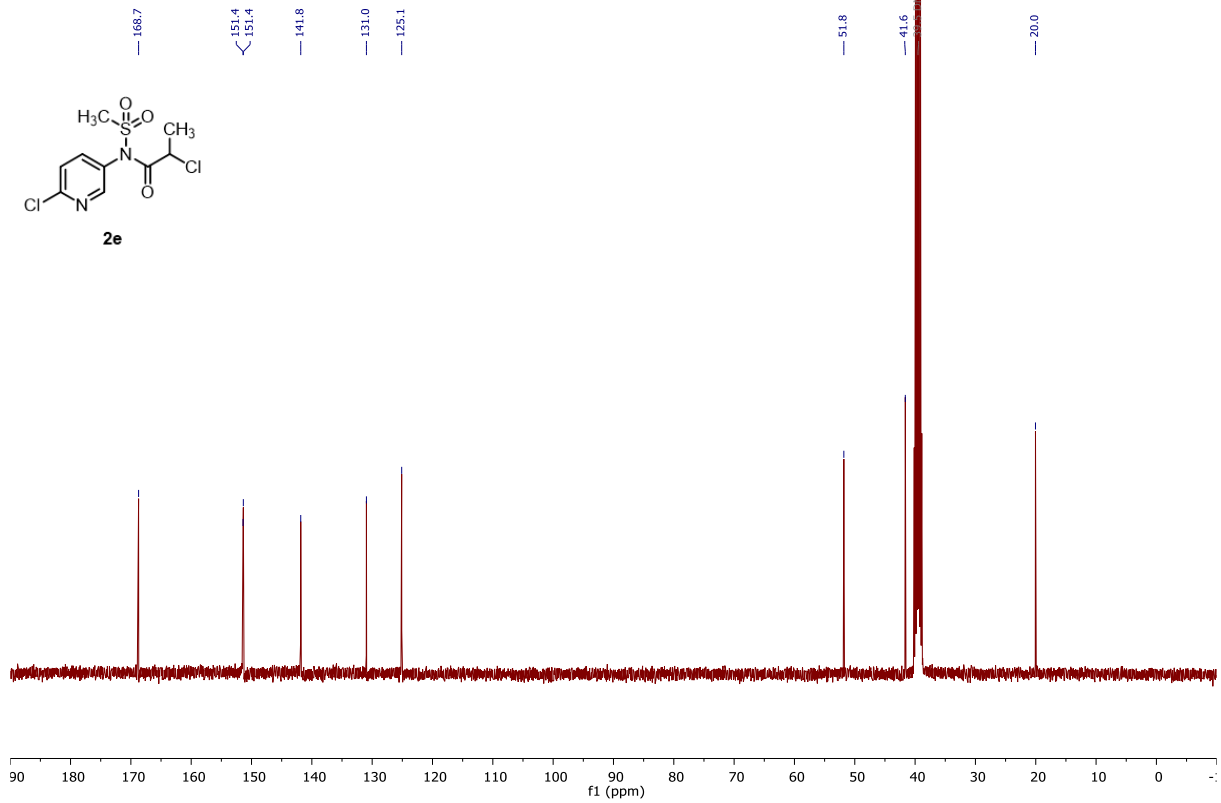




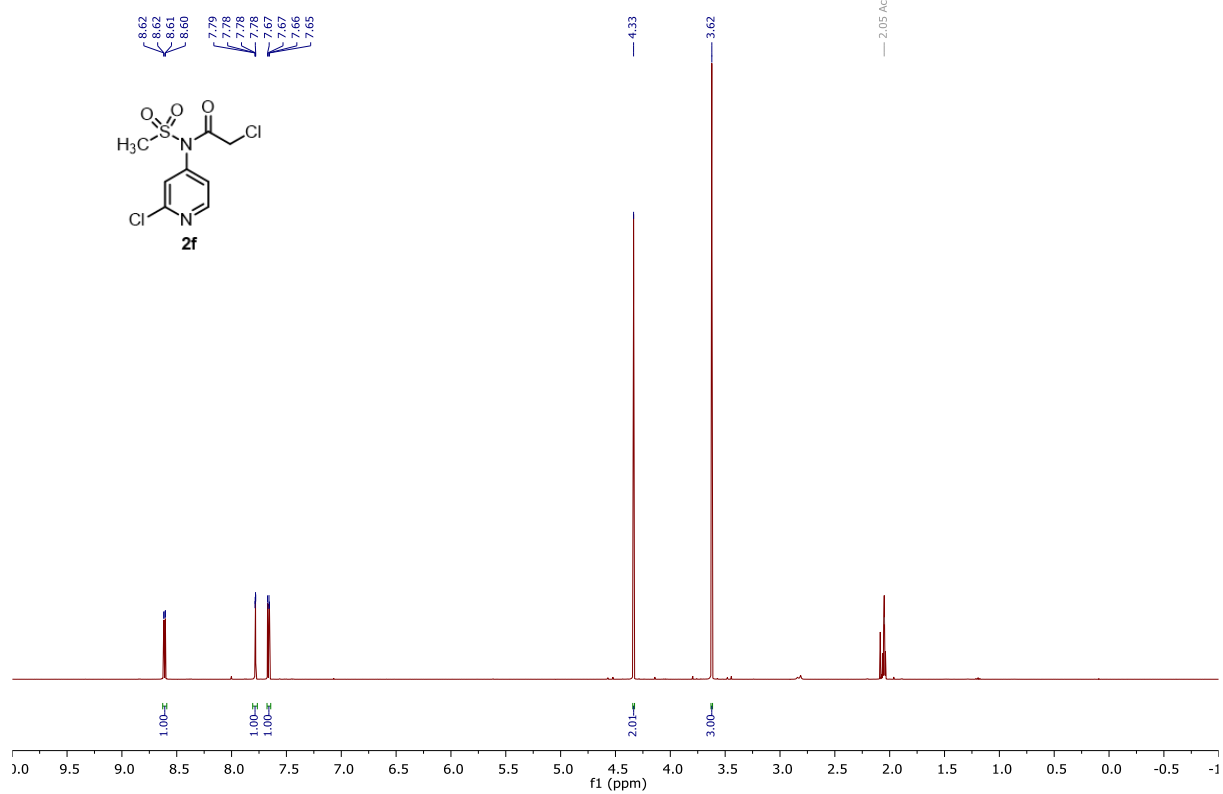
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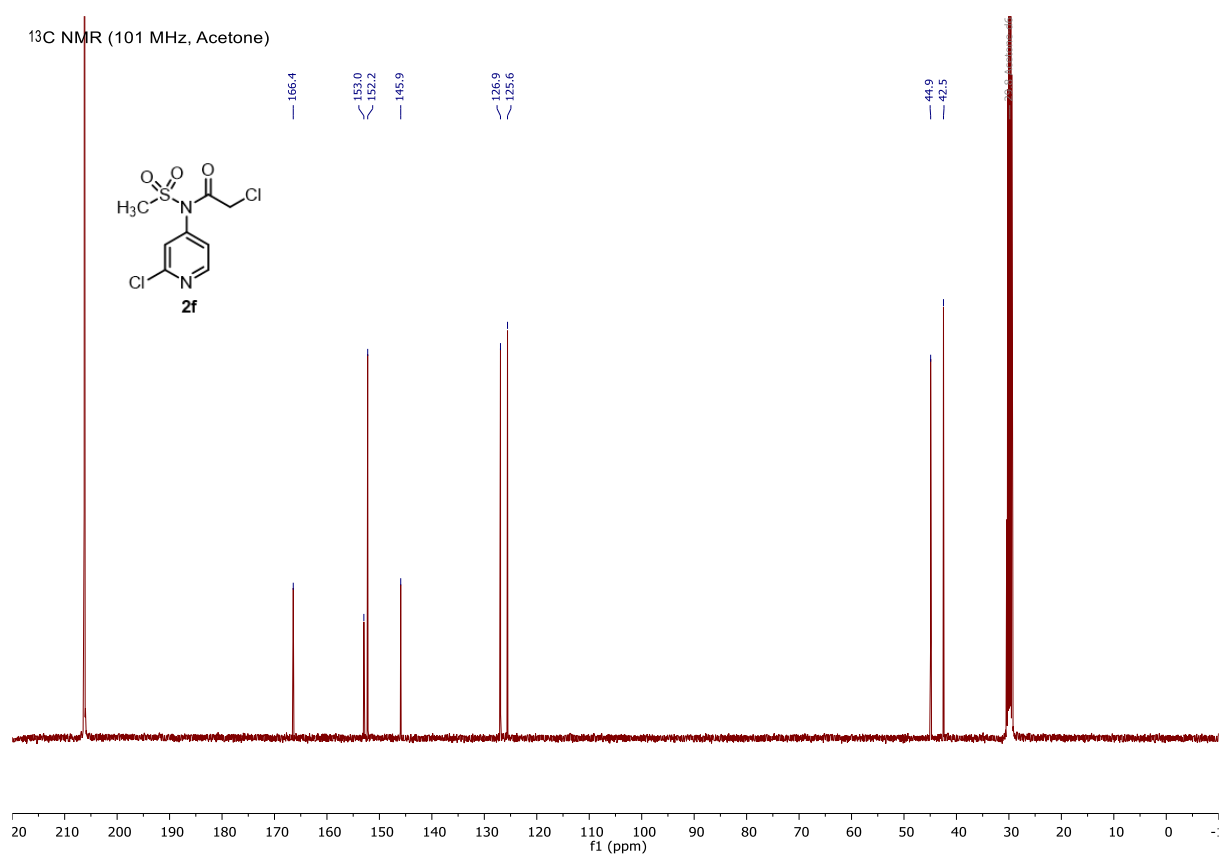
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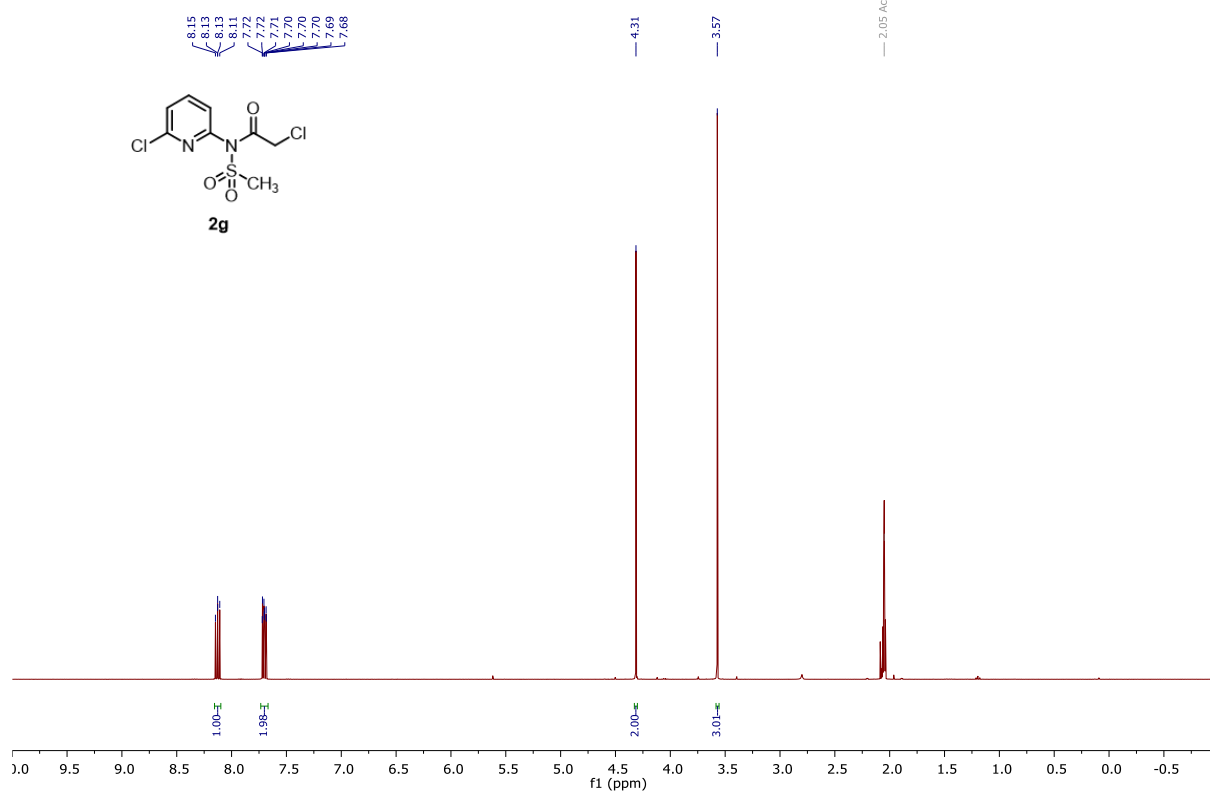
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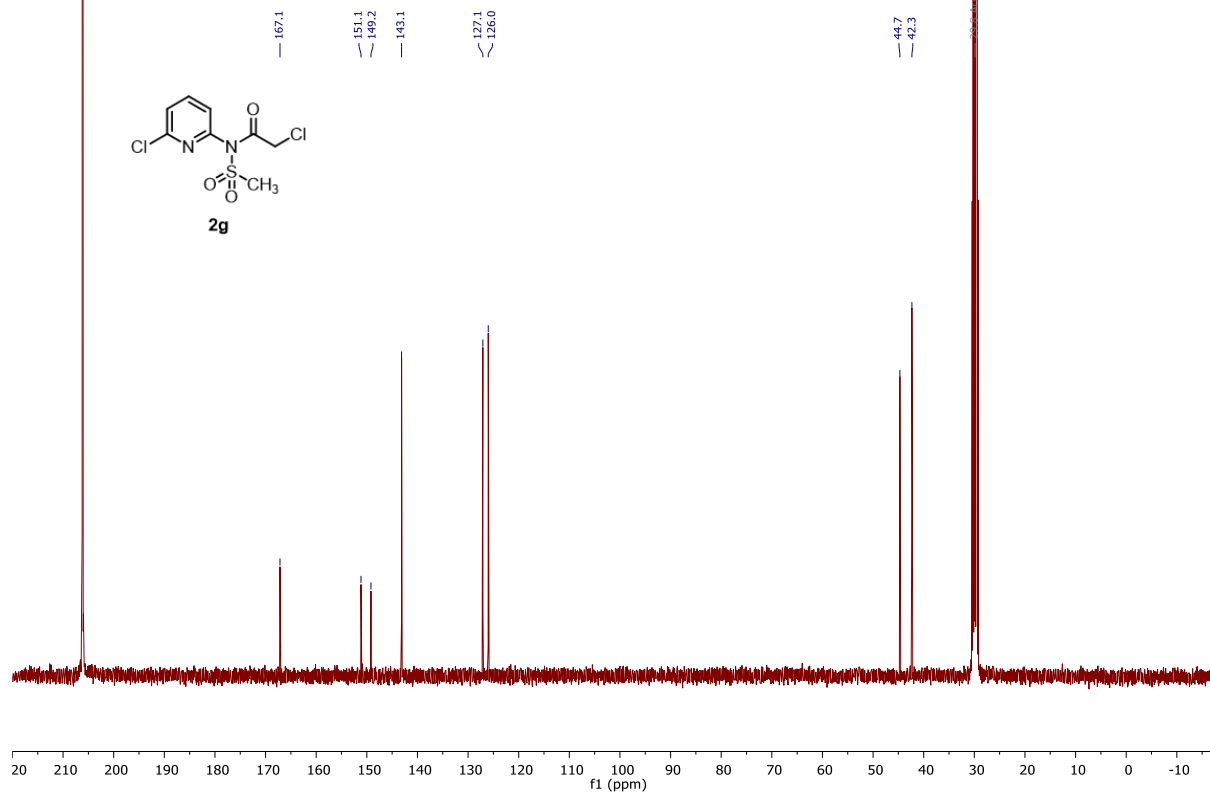
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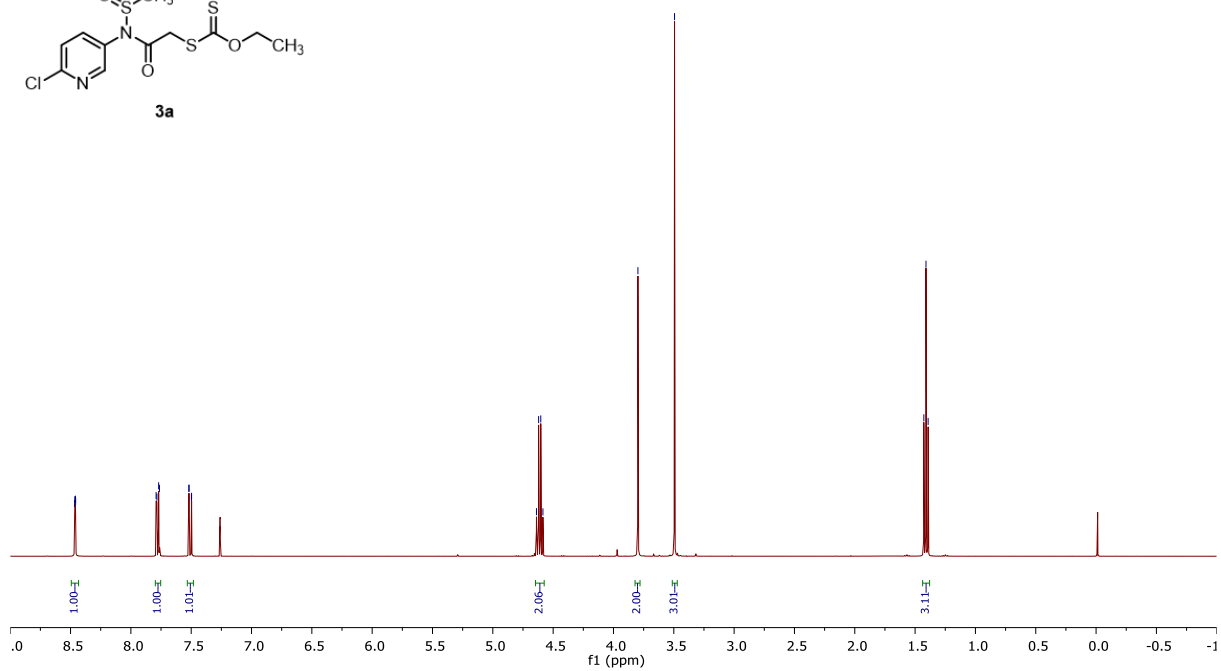
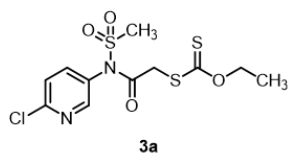


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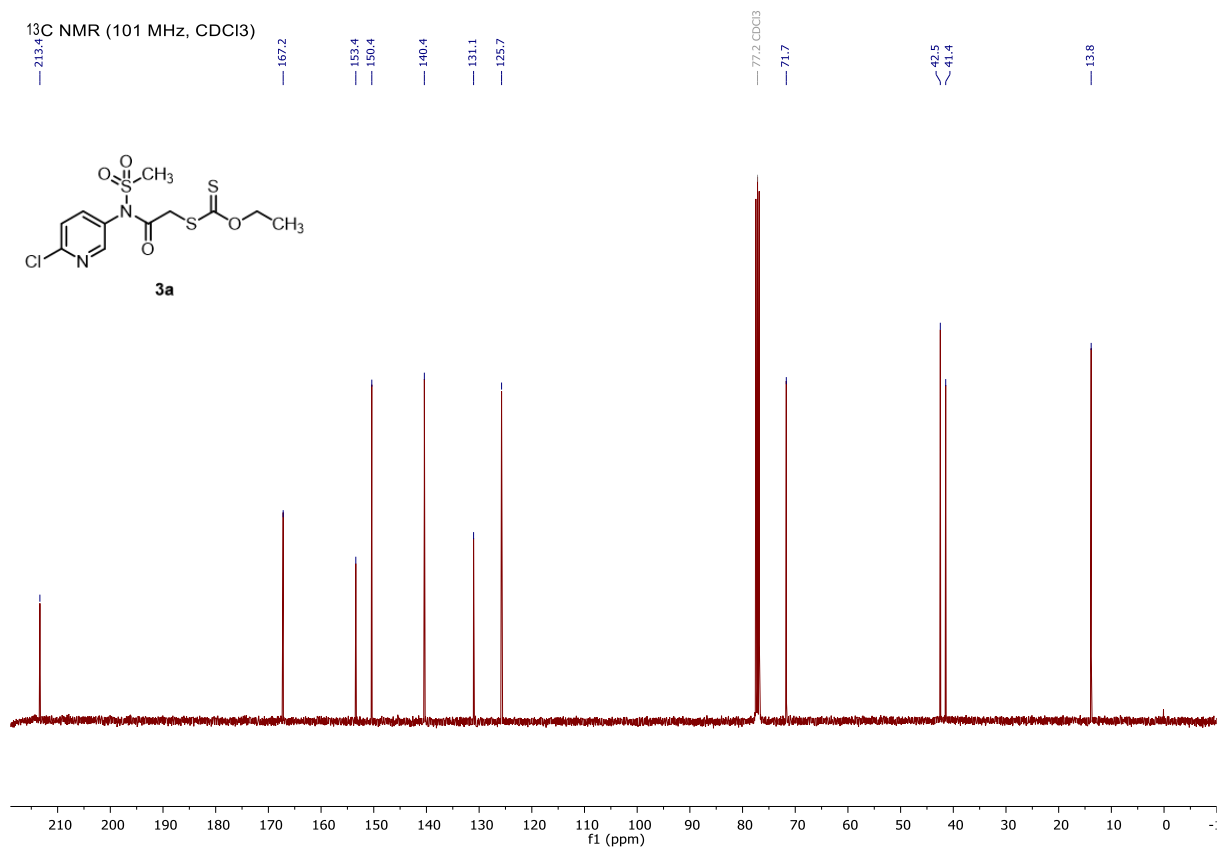
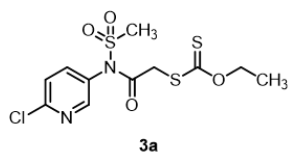
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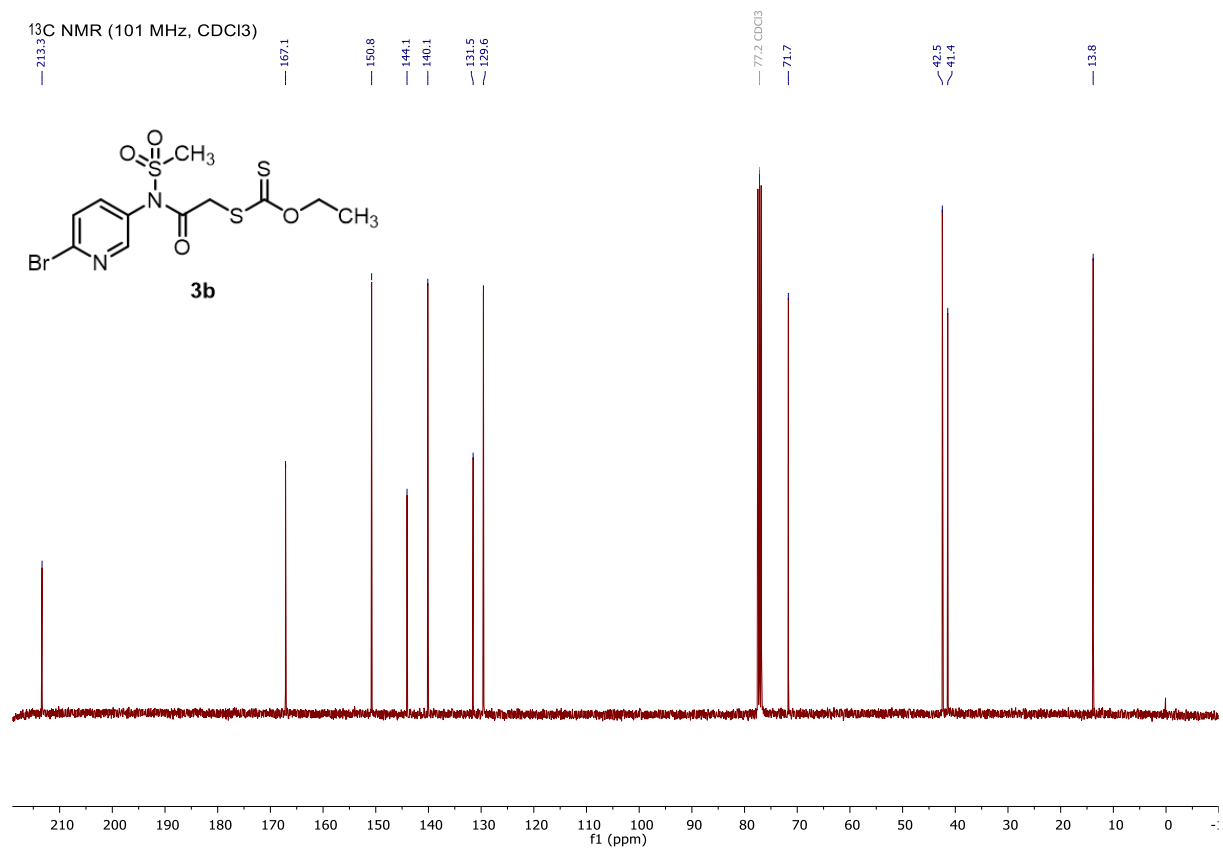
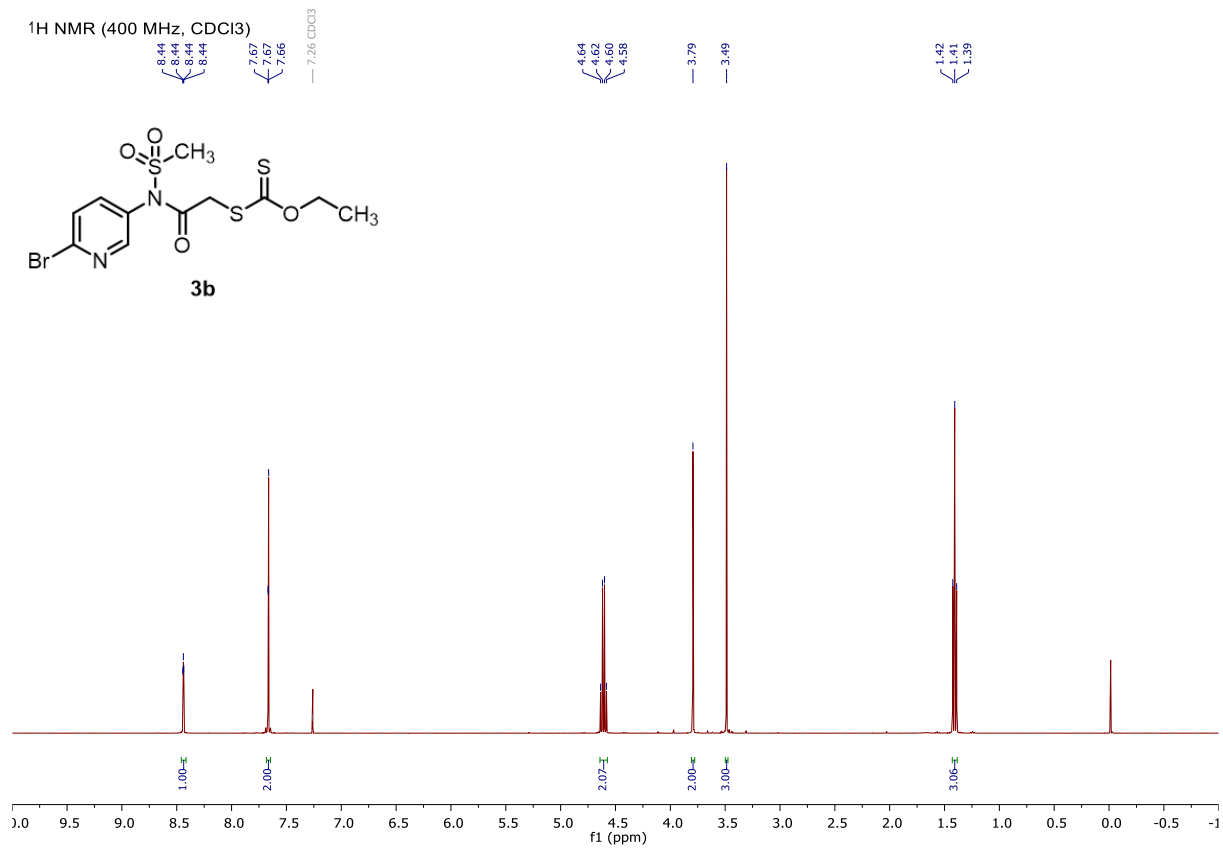
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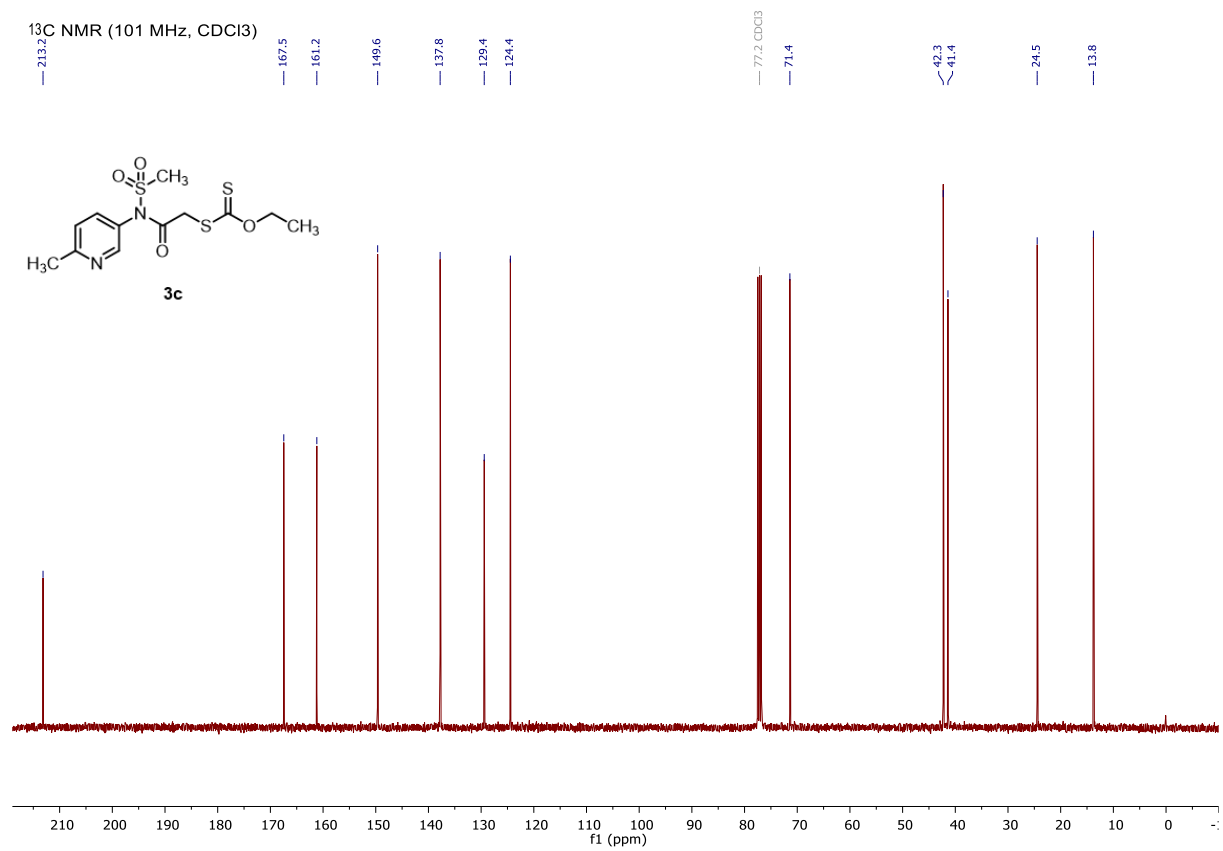
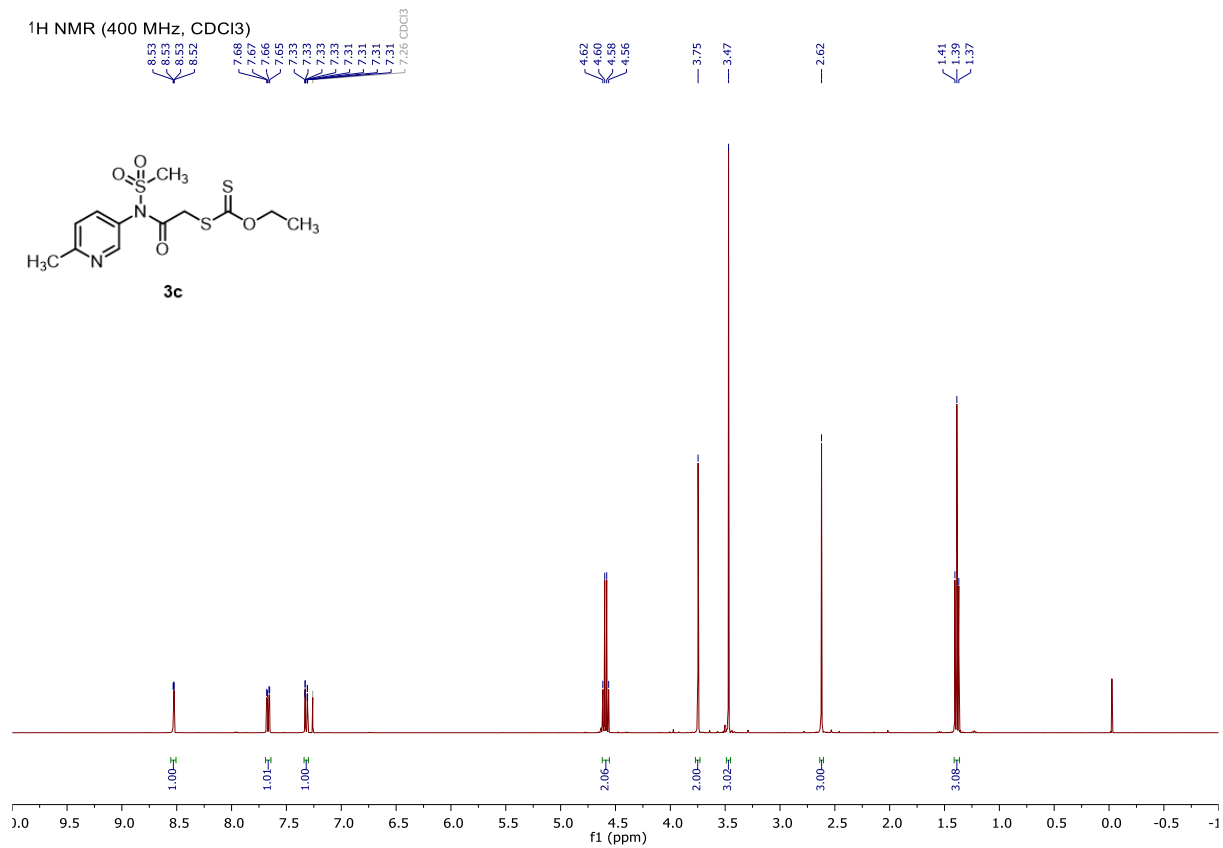


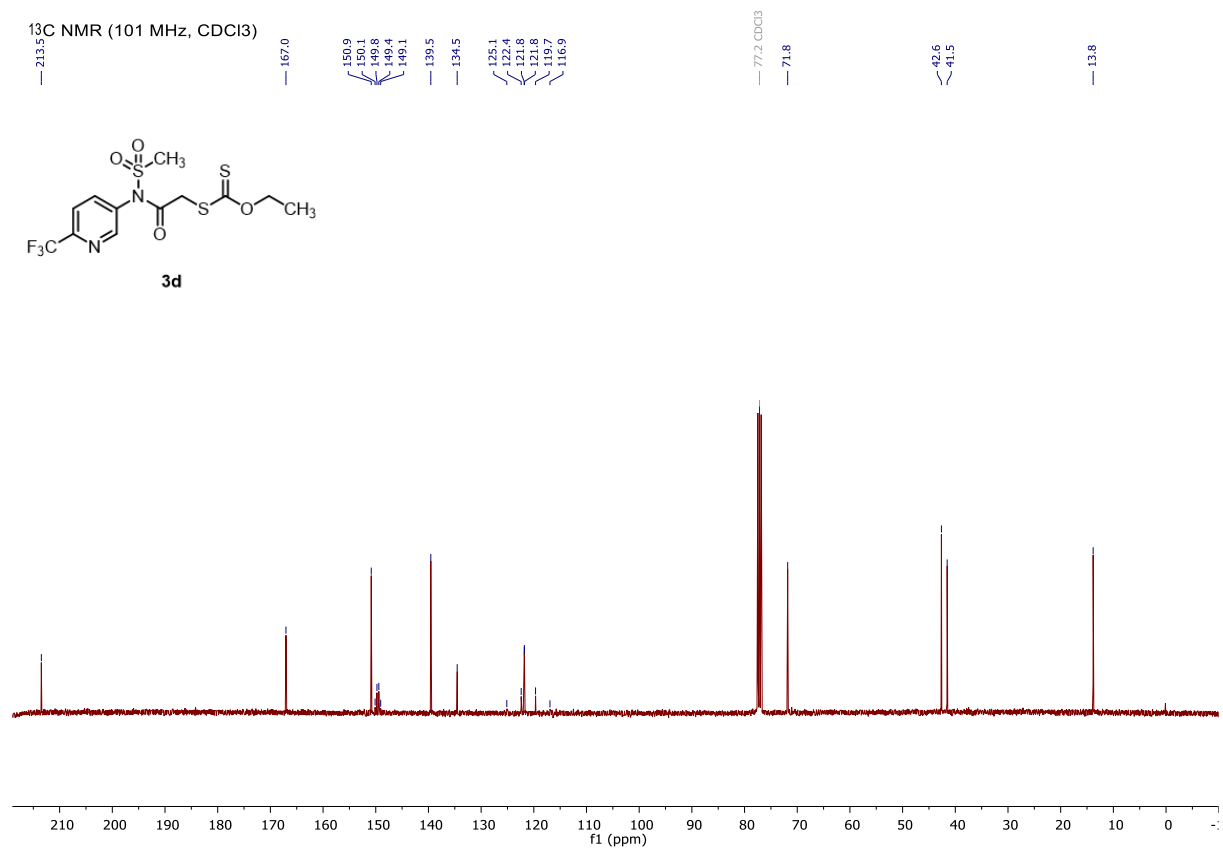
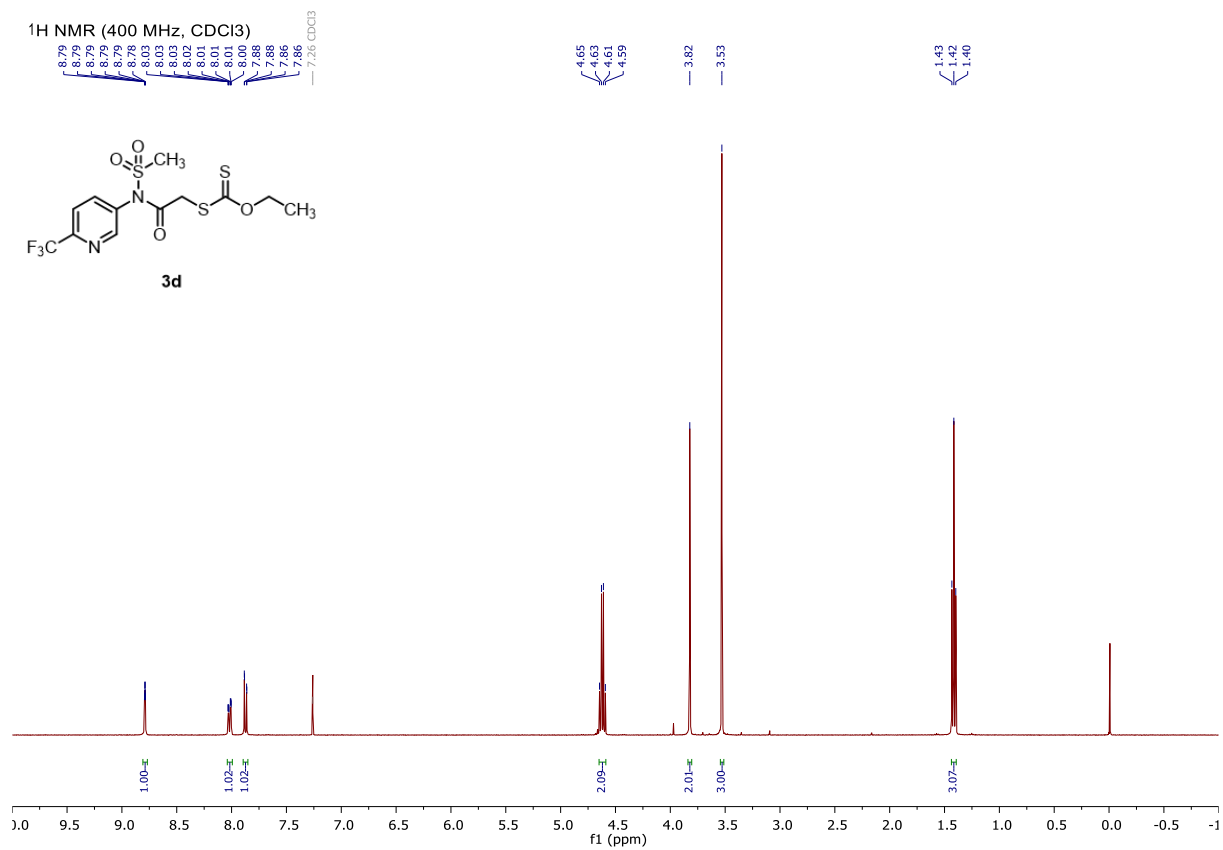
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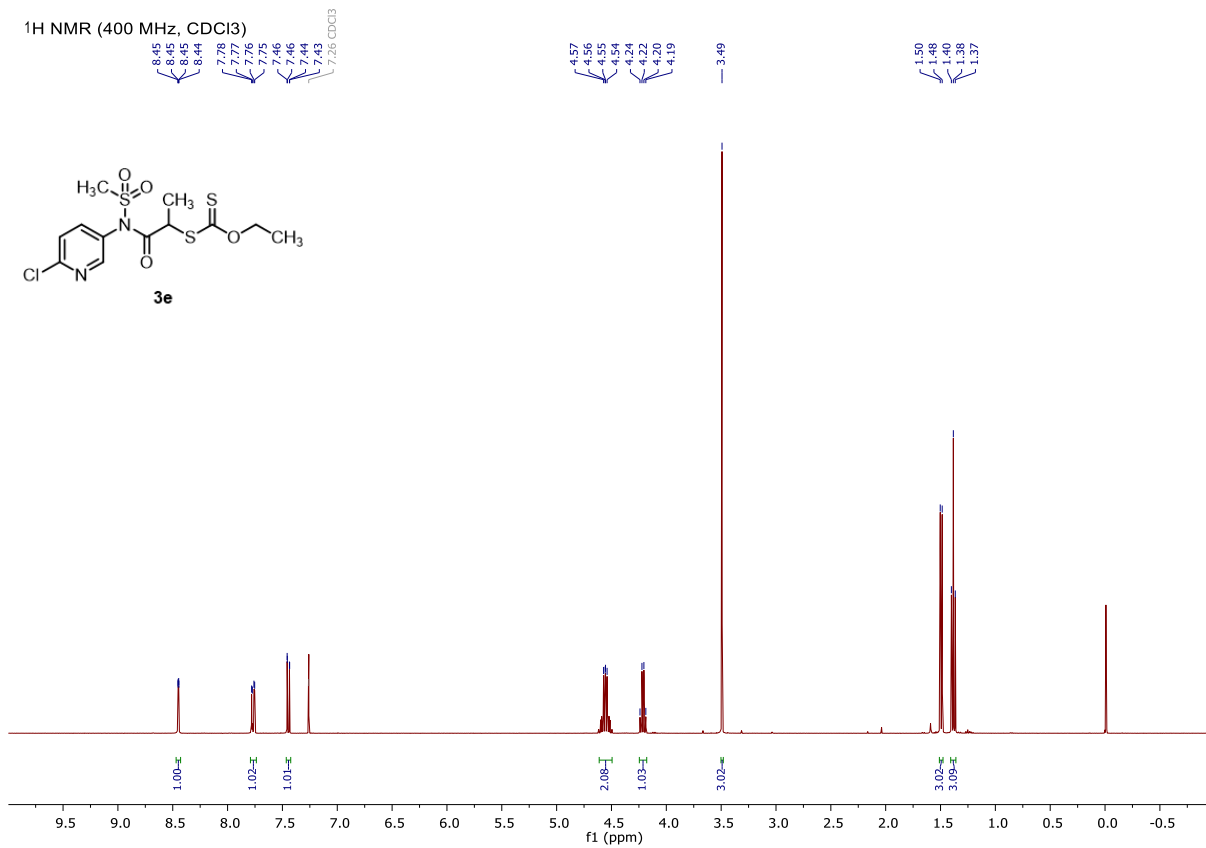
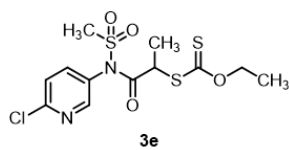




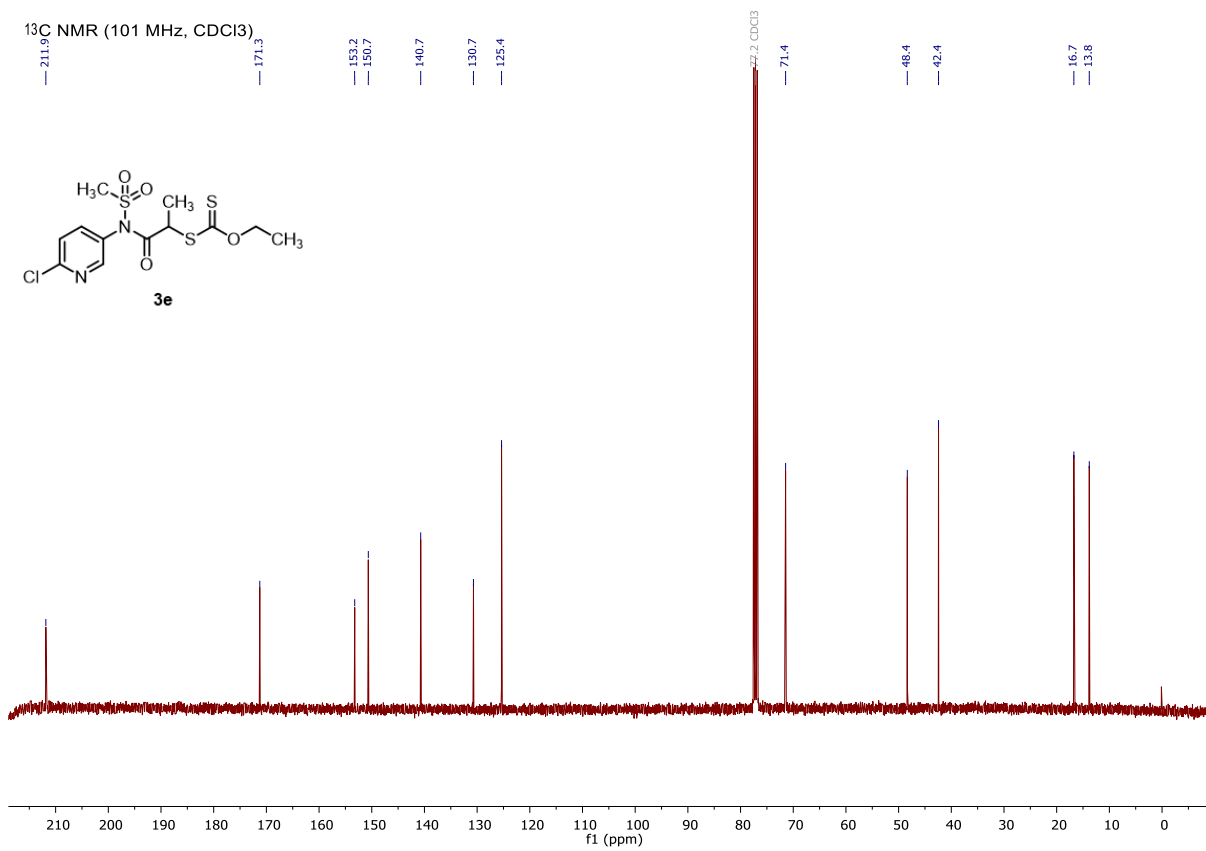
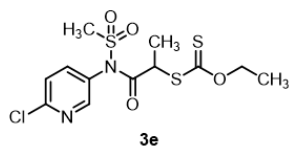




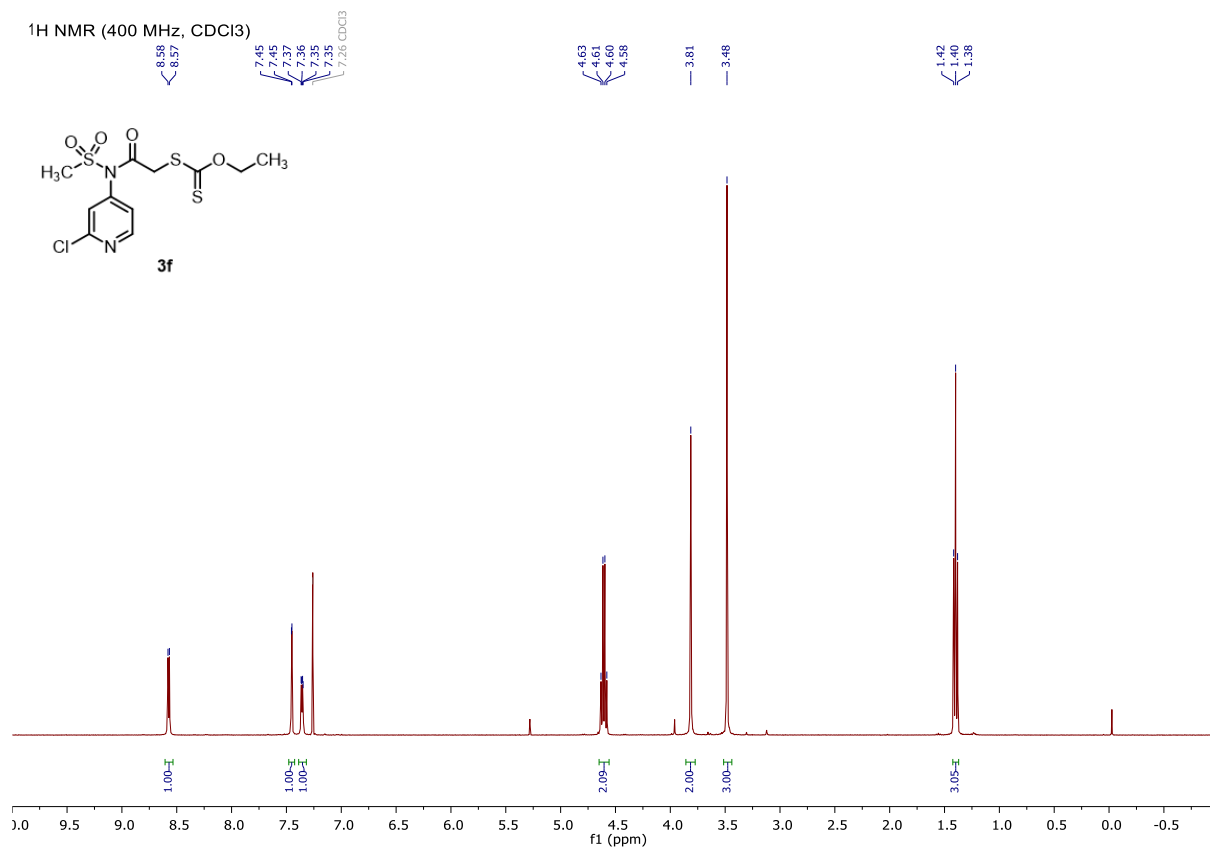
¹H NMR (400 MHz, CDCl₃)



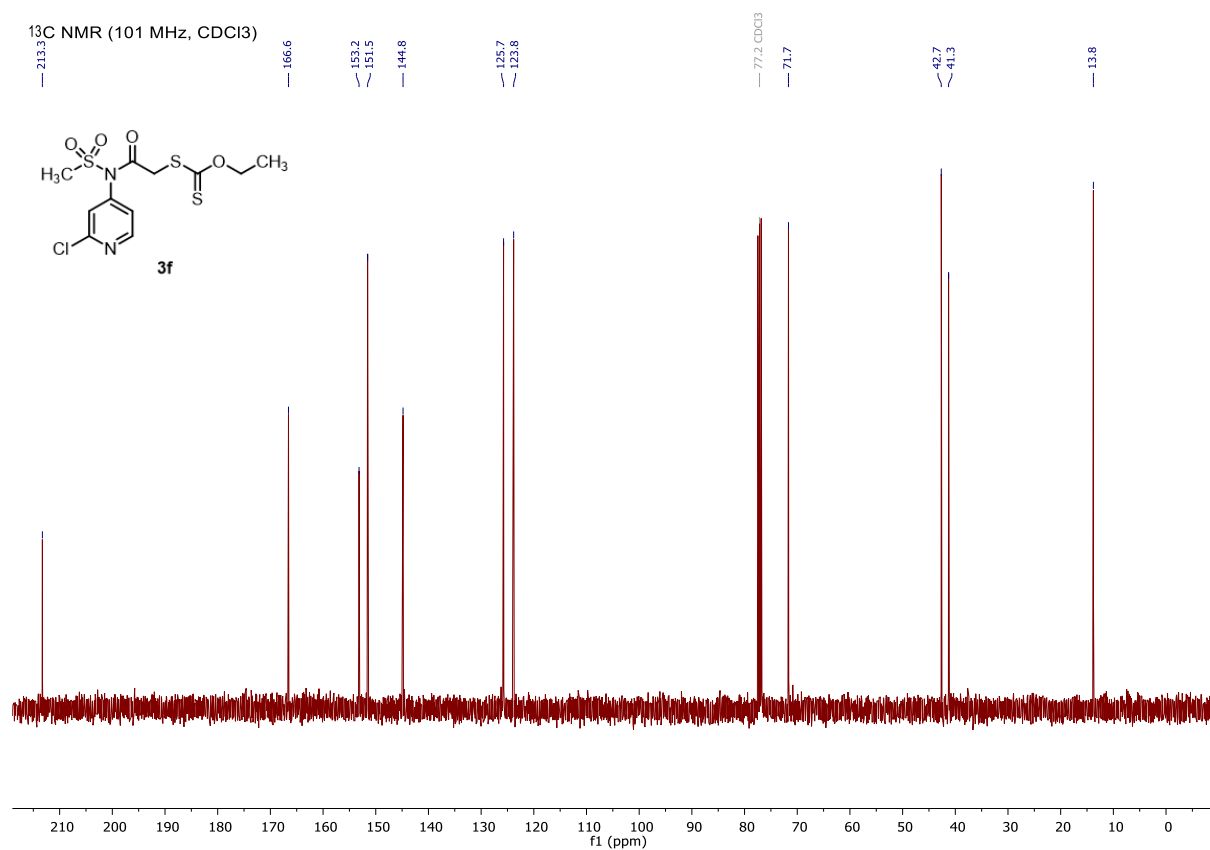
¹³C NMR (101 MHz, CDCl₃)



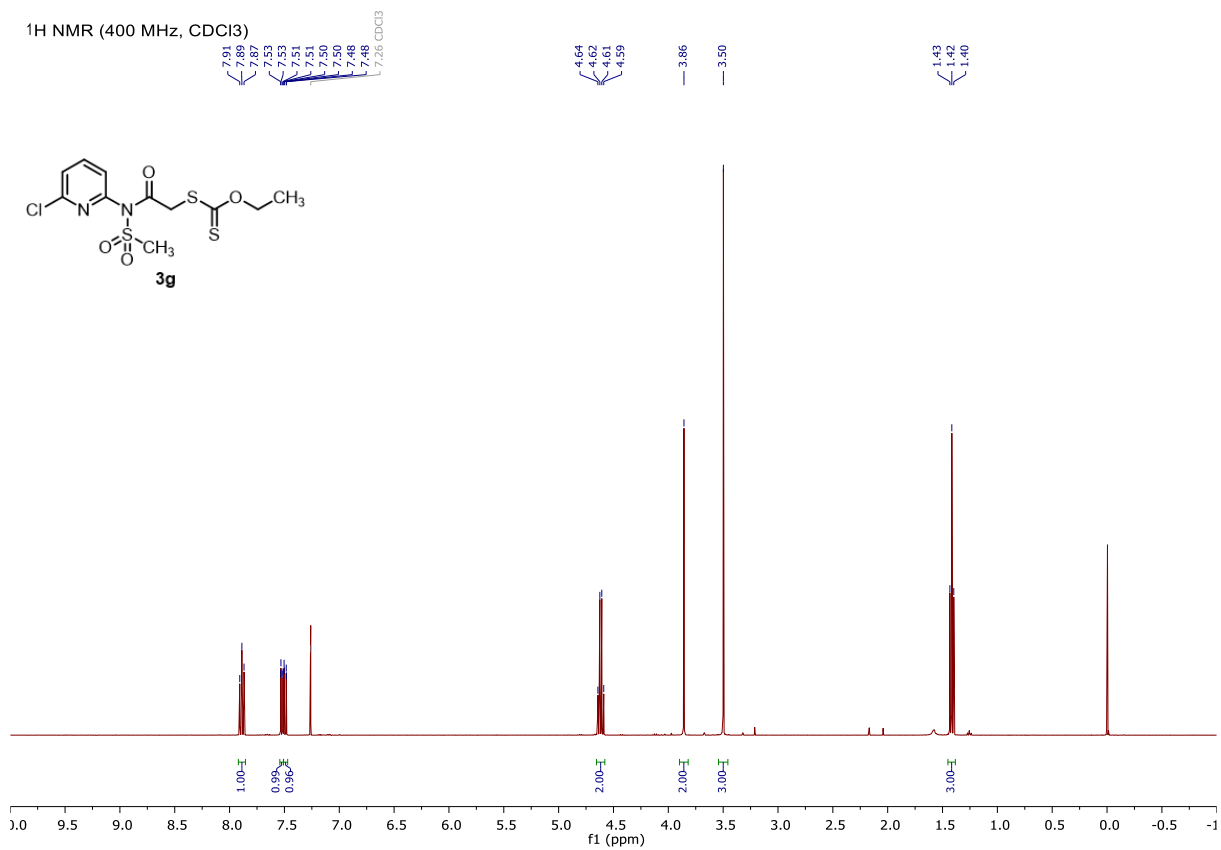
¹H NMR (400 MHz, CDCl₃)



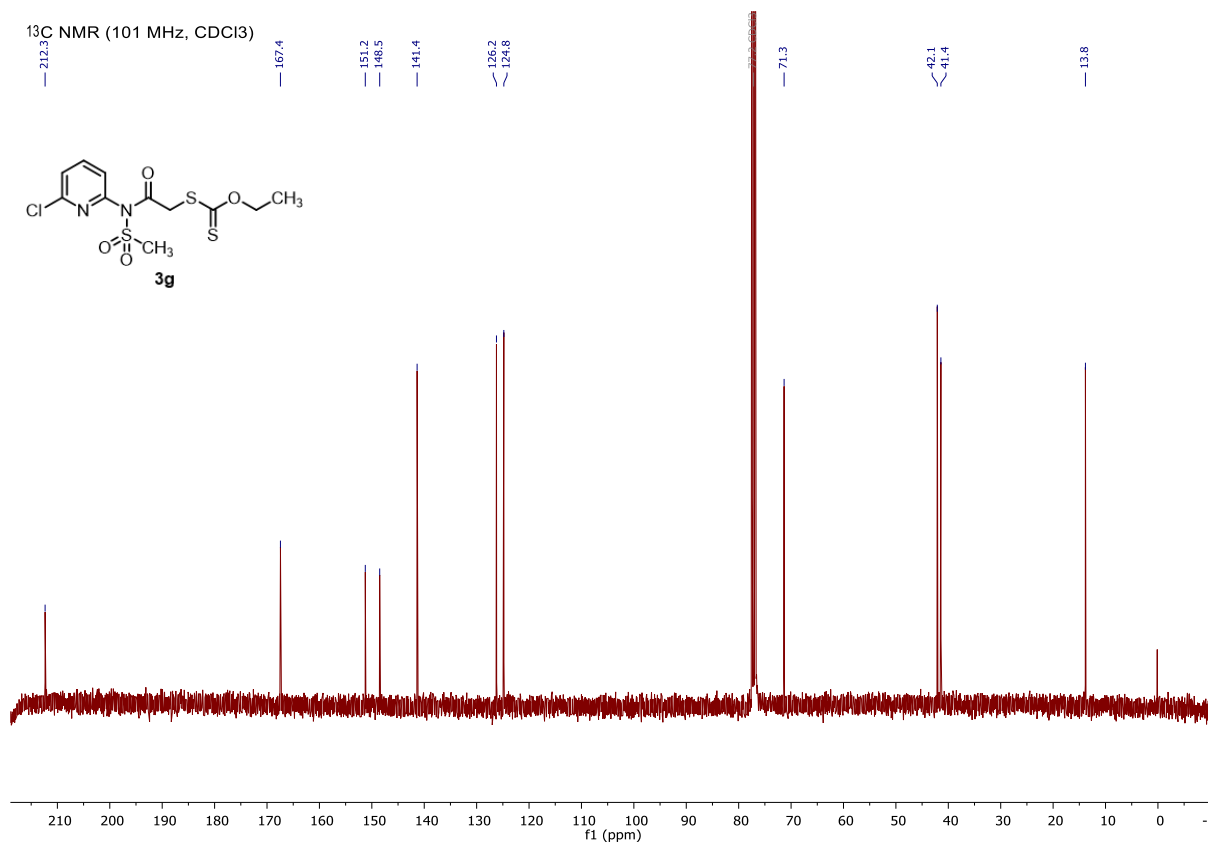
¹³C NMR (101 MHz, CDCl₃)

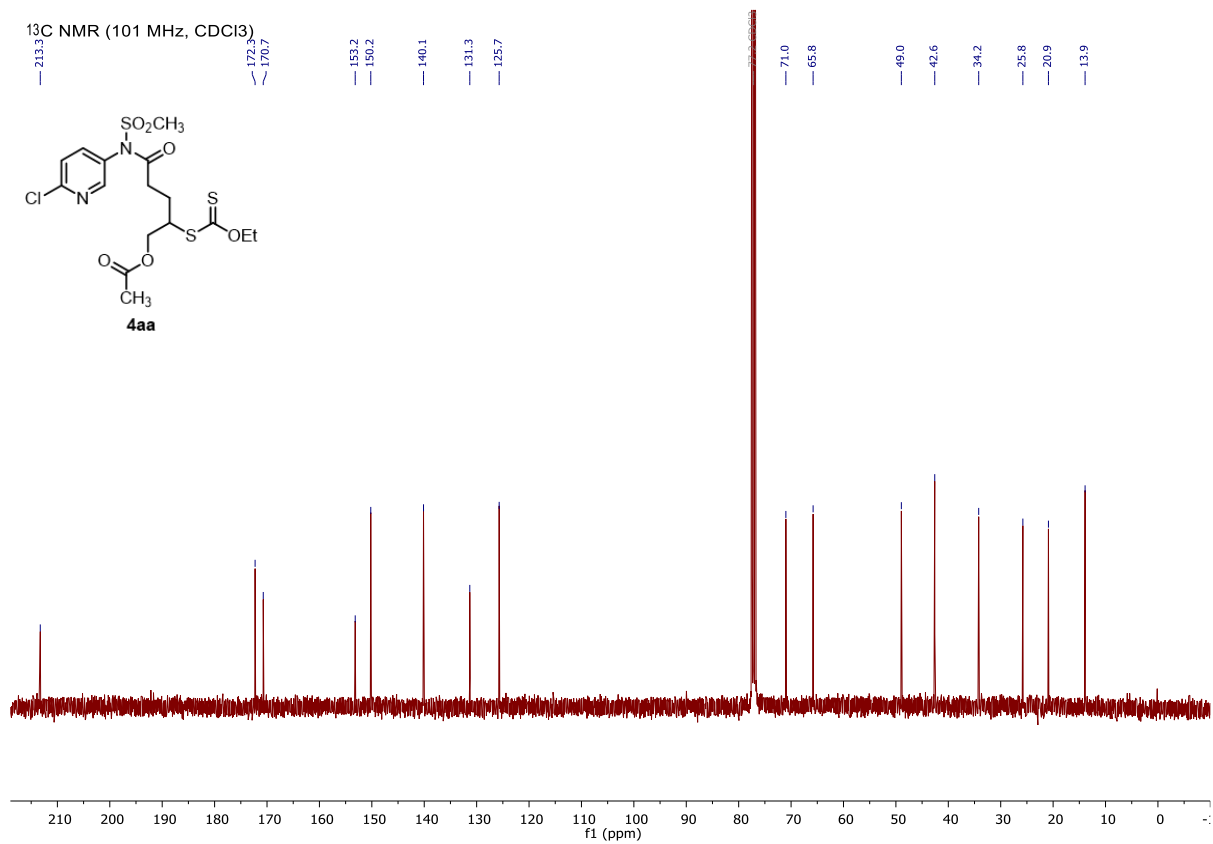
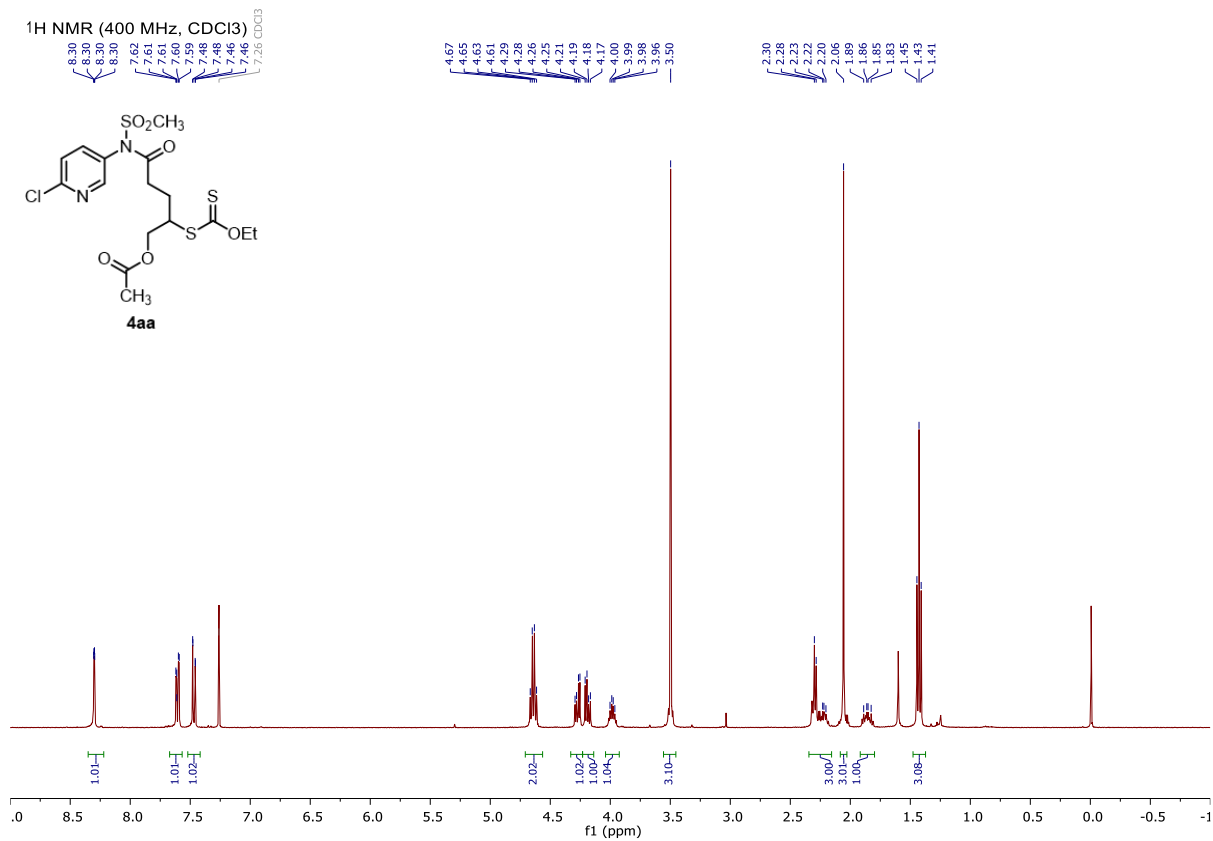


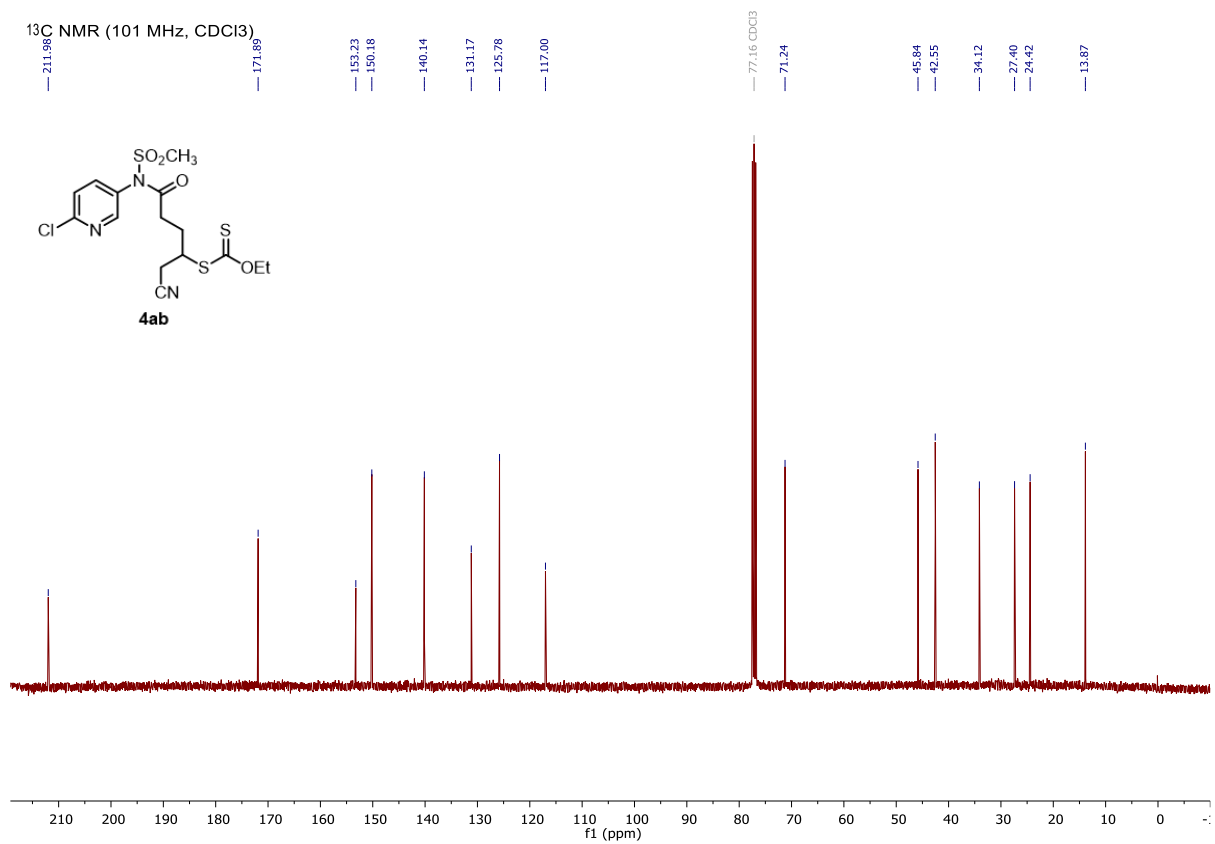
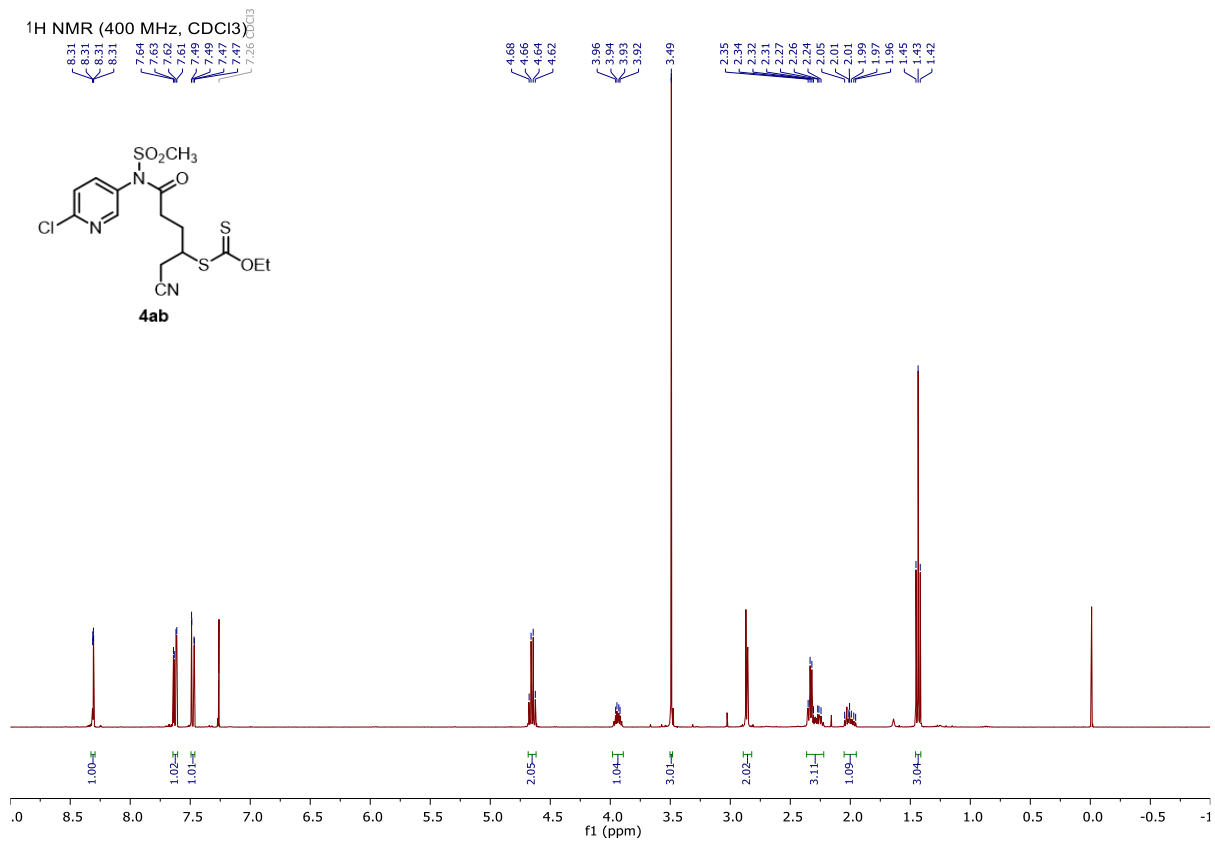
¹H NMR (400 MHz, CDCl₃)

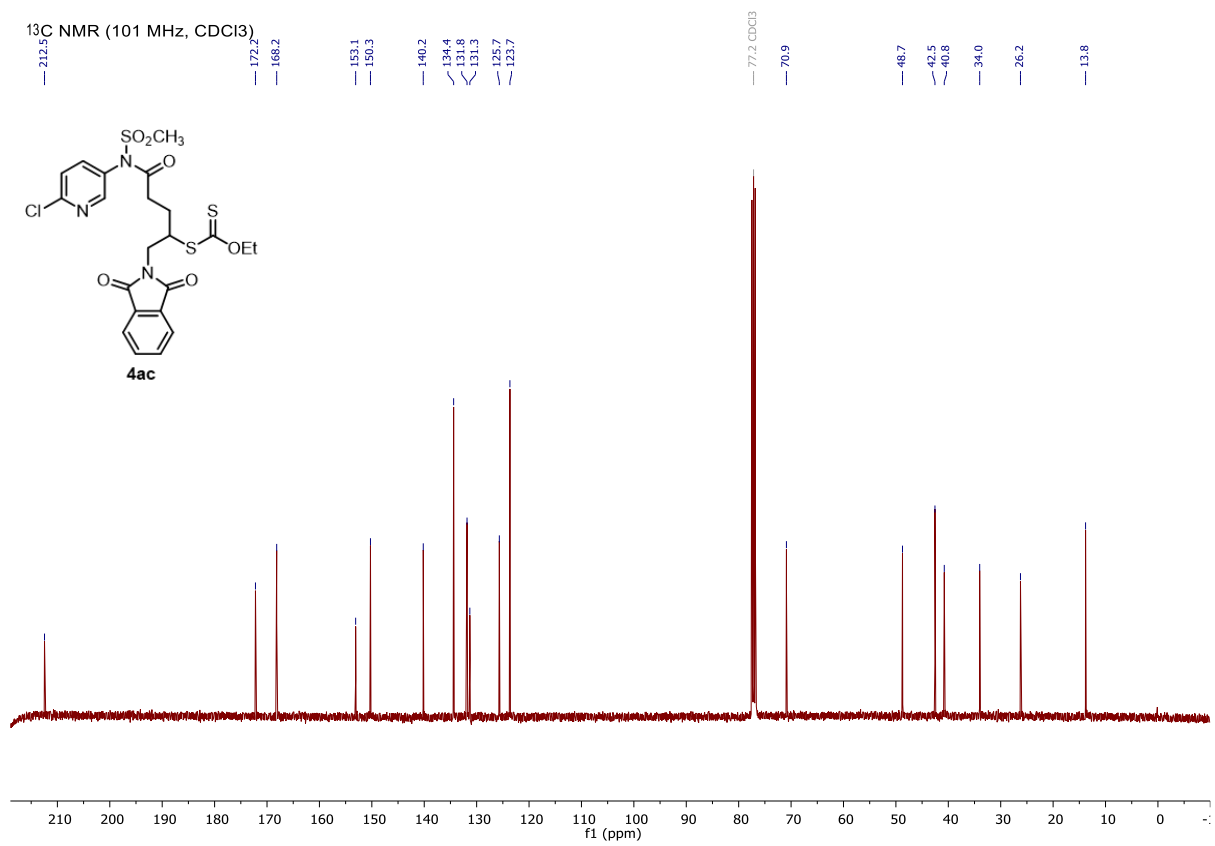
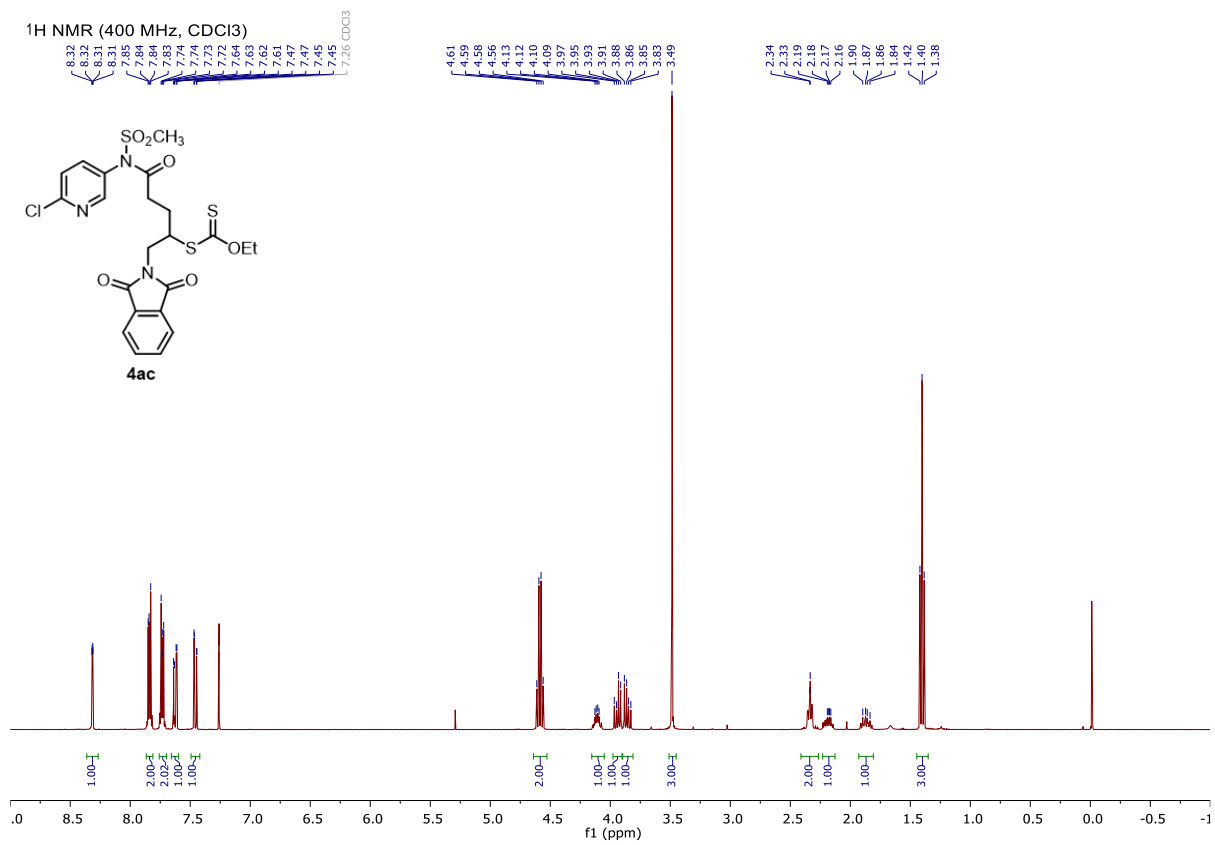


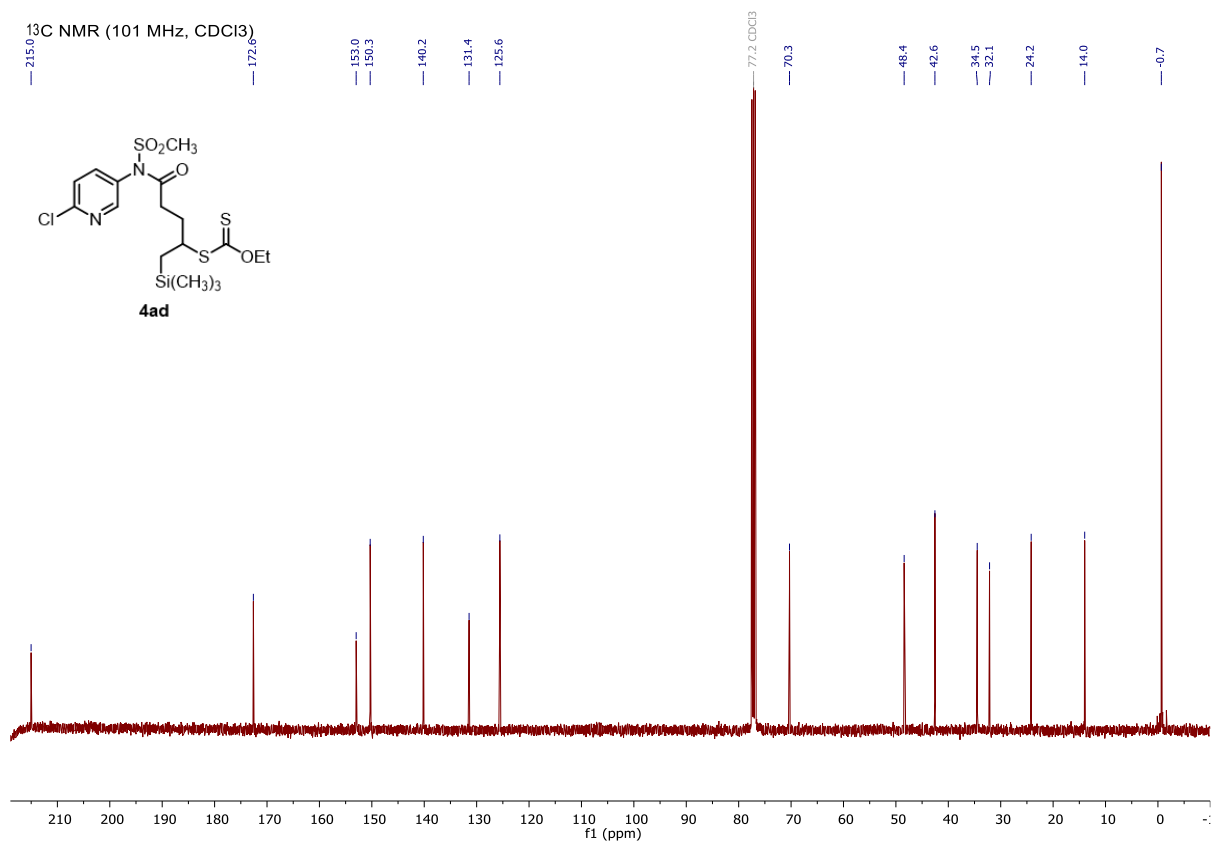
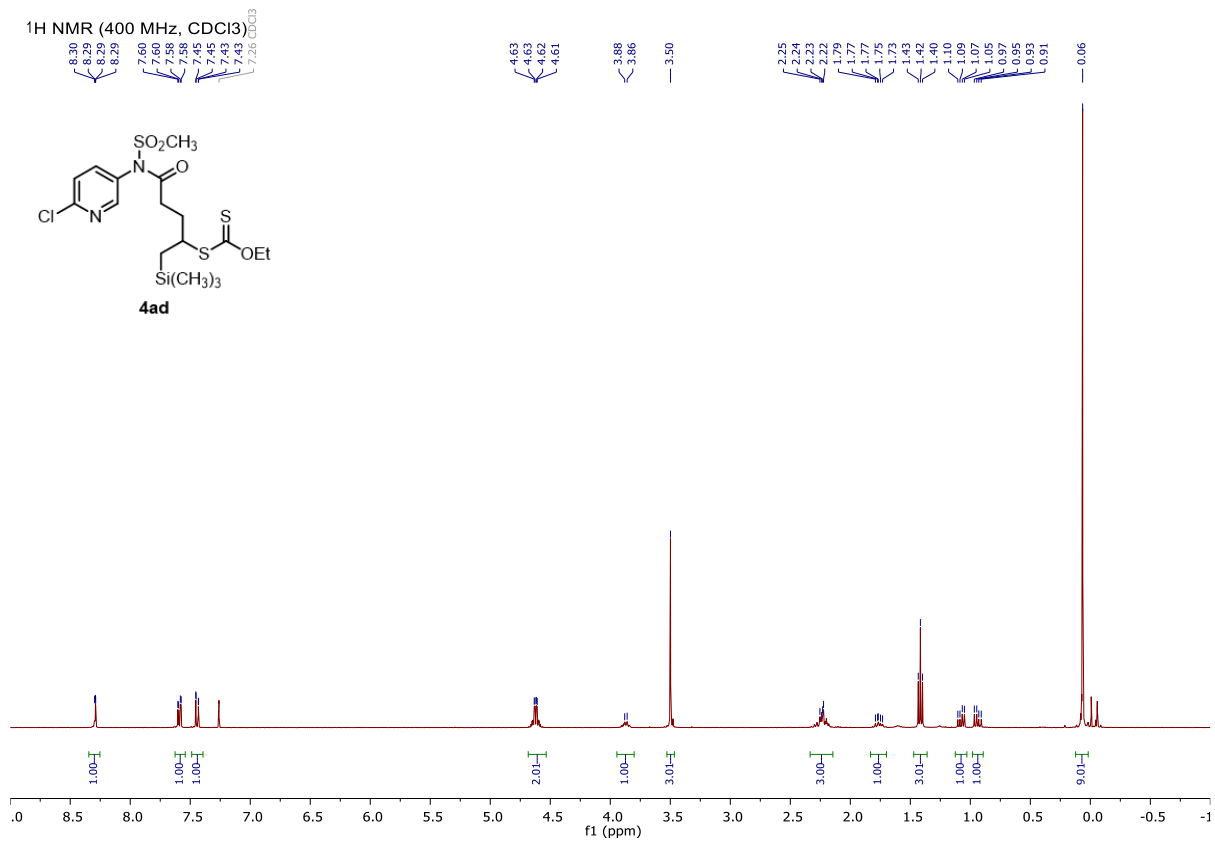
¹³C NMR (101 MHz, CDCl₃)

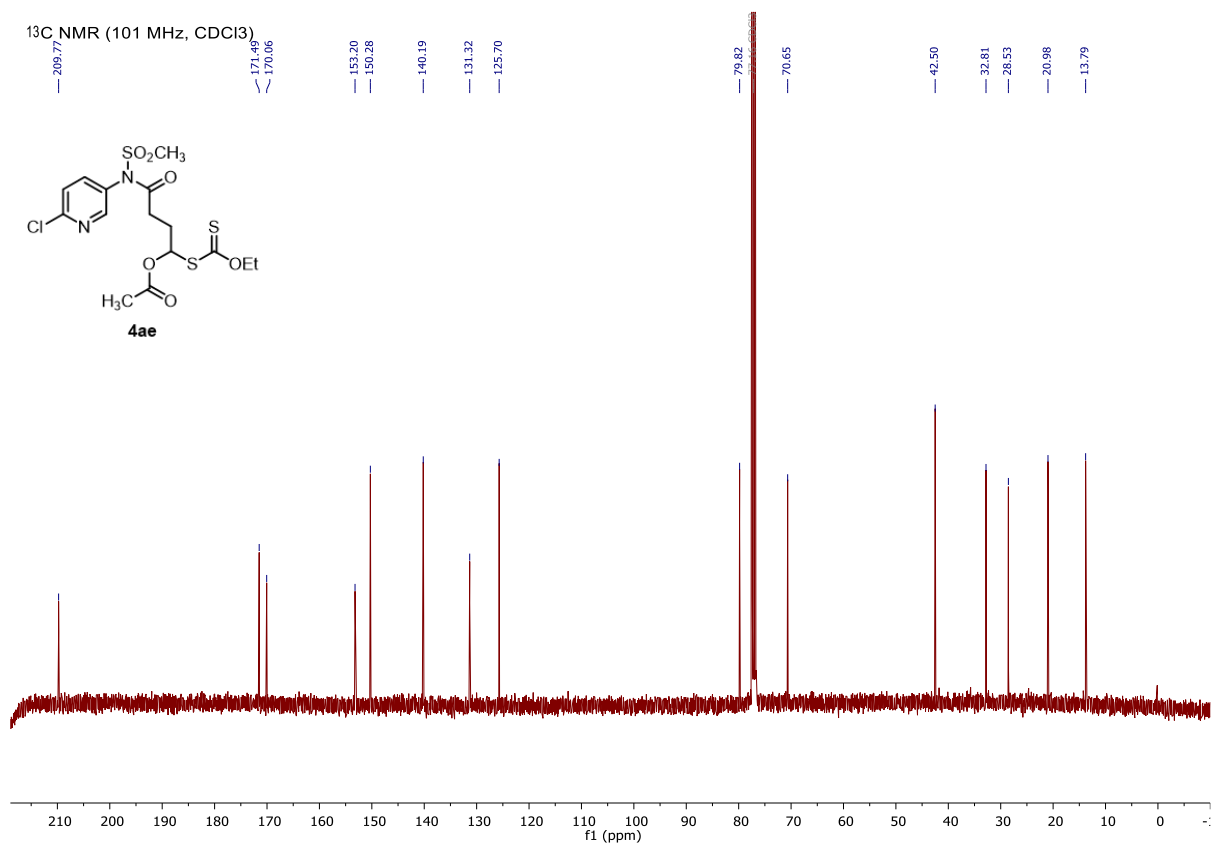
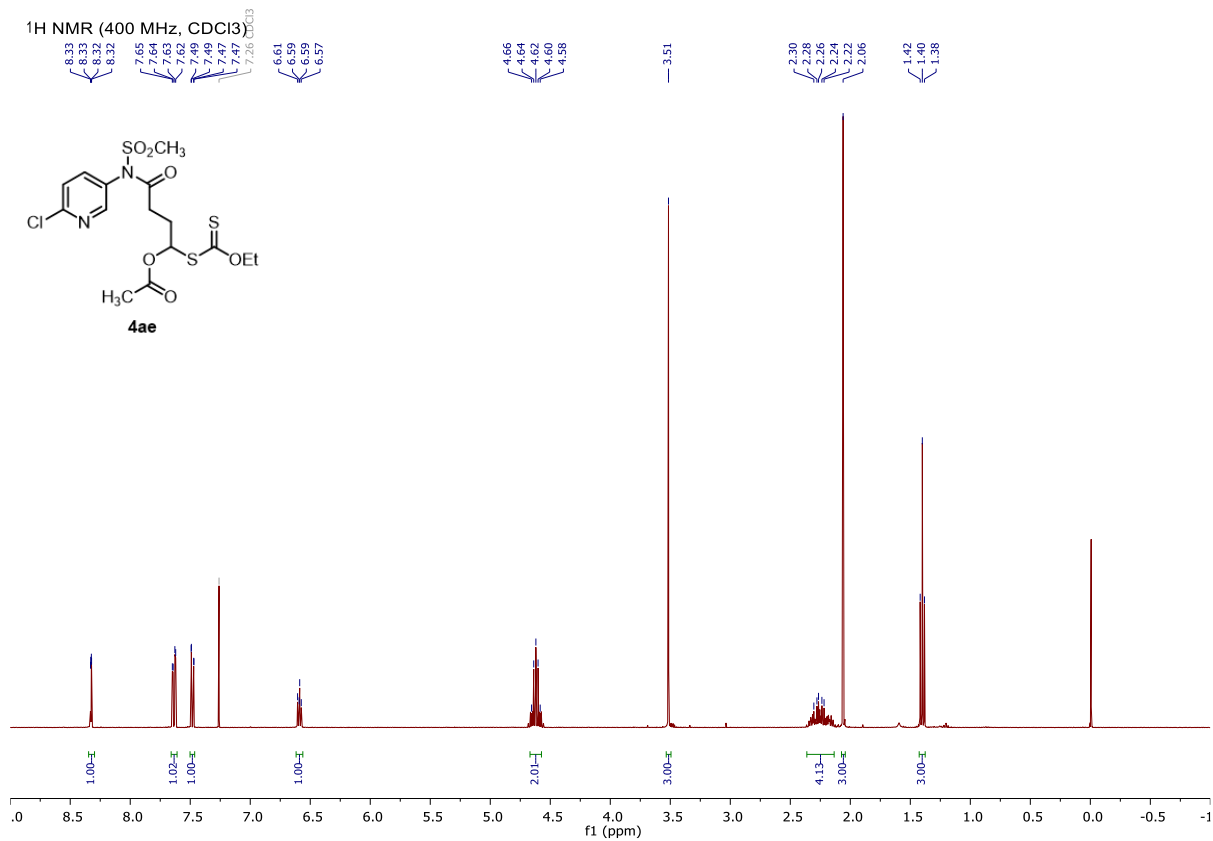




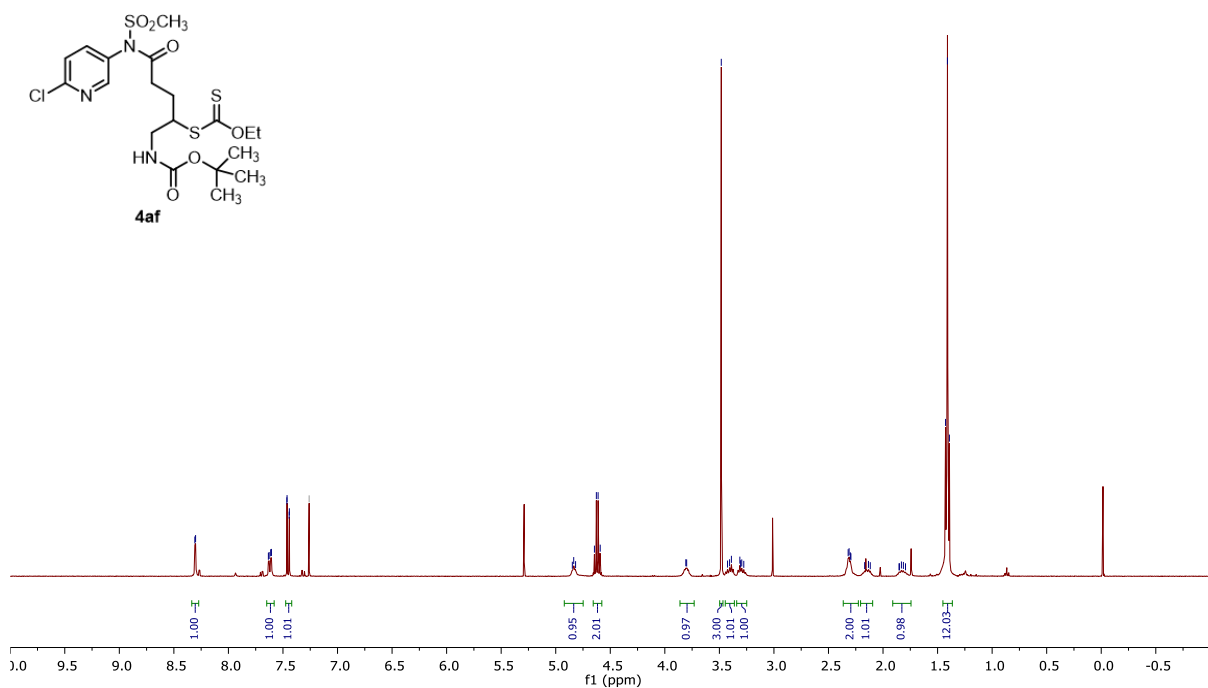




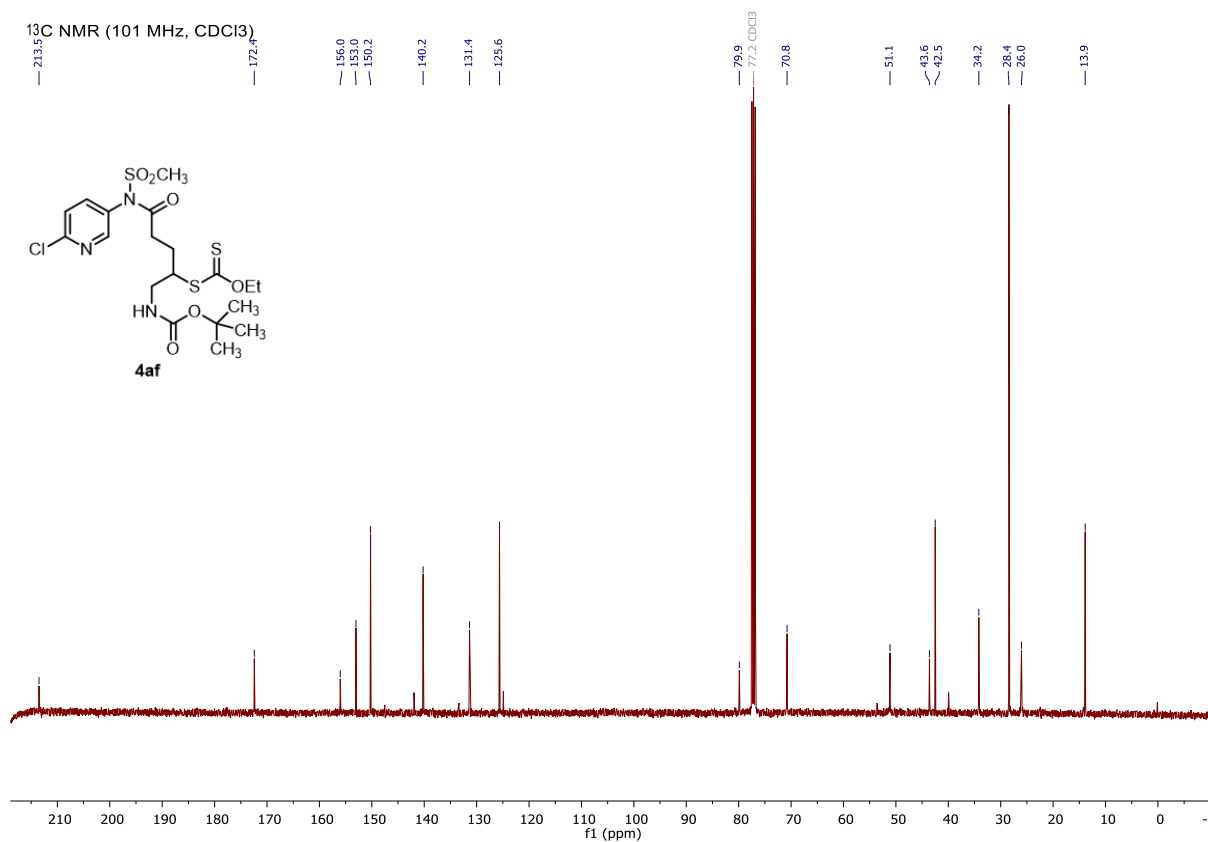




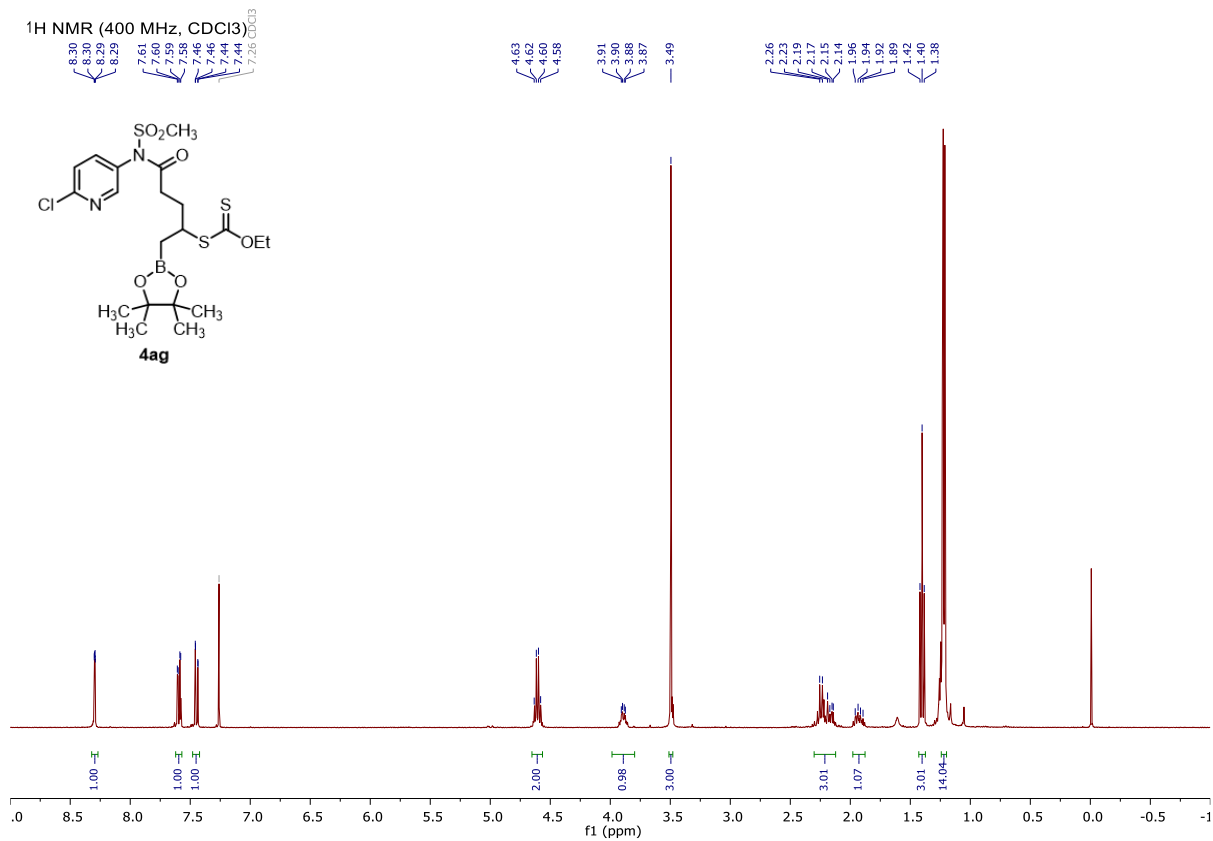
¹H NMR (400 MHz, CDCl₃)



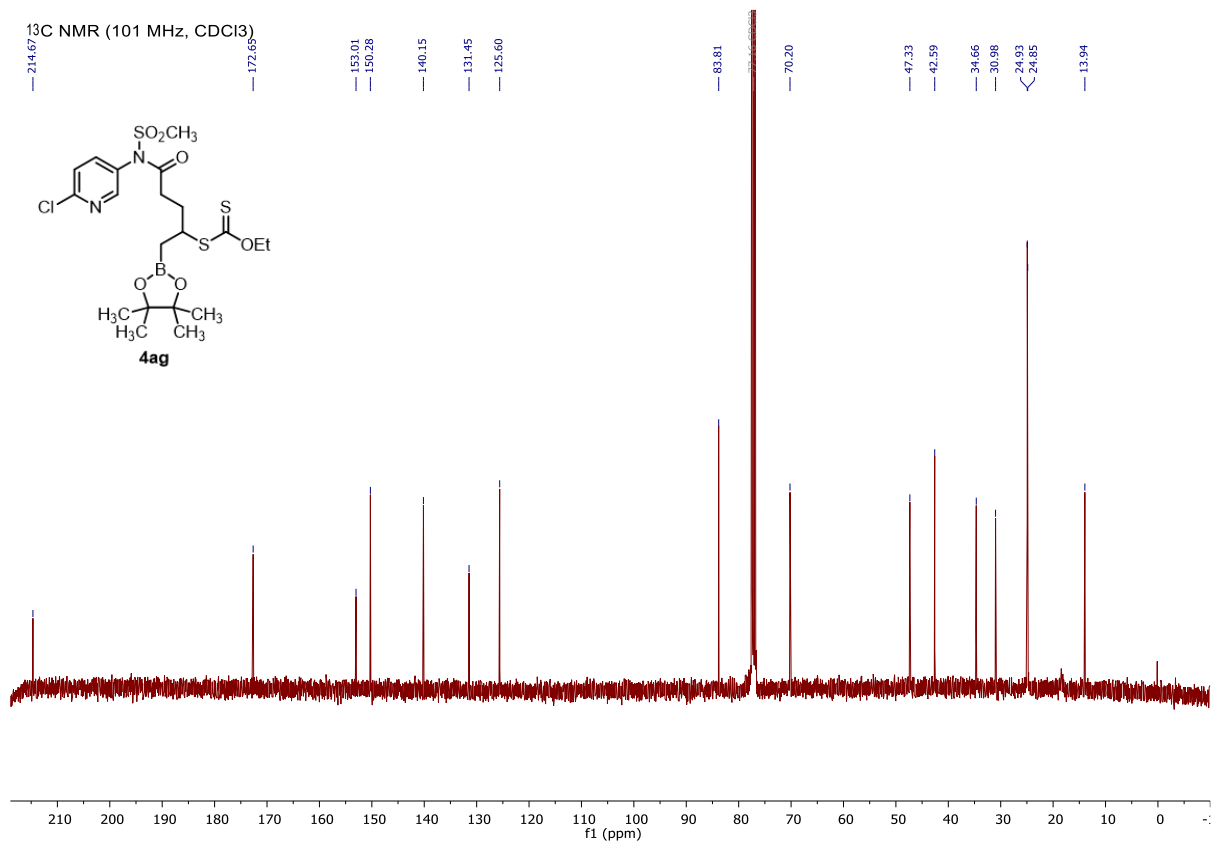
¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)



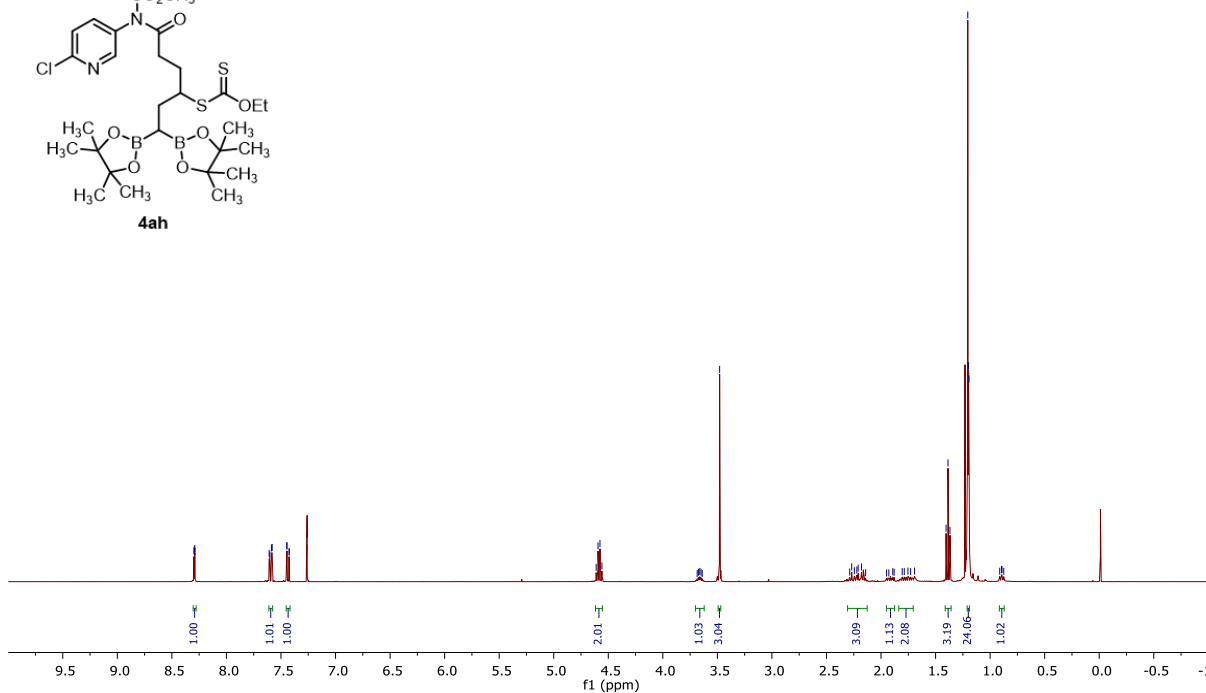
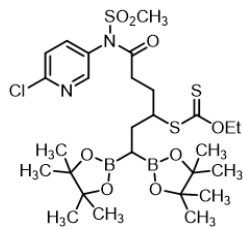
¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)

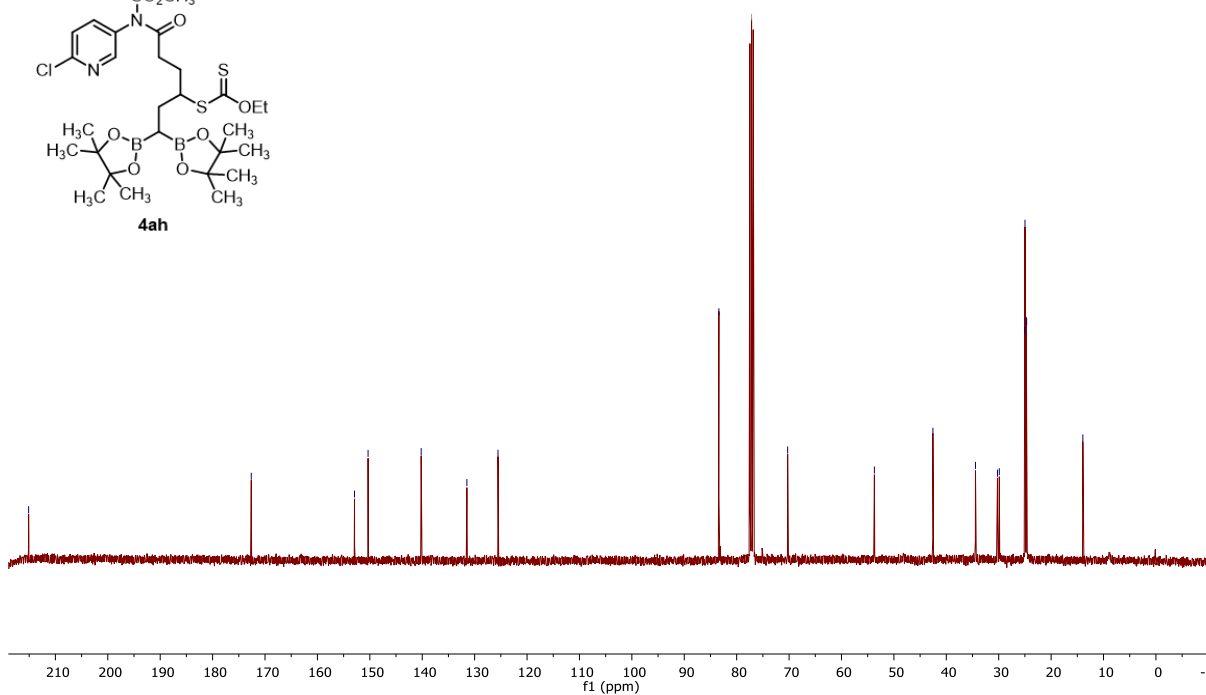
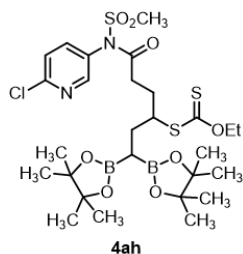
8.30
8.29
8.29
7.61
7.59
7.58
7.45
7.44
7.43
7.42
7.26 CDCl₃

4.61
4.59
4.58
4.56
3.69
3.66
3.65
3.64
3.48
2.29
2.27
2.24
2.22
2.21
2.18
2.14
1.95
1.93
1.89
1.88
1.81
1.79
1.75
1.73
1.69
1.40
1.39
1.37
1.24
1.21
1.19
1.19
0.91
0.90
0.89



¹³C NMR (101 MHz, CDCl₃)

215.1
172.6
152.9
150.3
140.2
131.5
125.5
83.4
77.2 CDCl₃
70.3
53.7
42.6
34.4
30.2
29.9
25.0
25.0
24.7
24.7
13.9

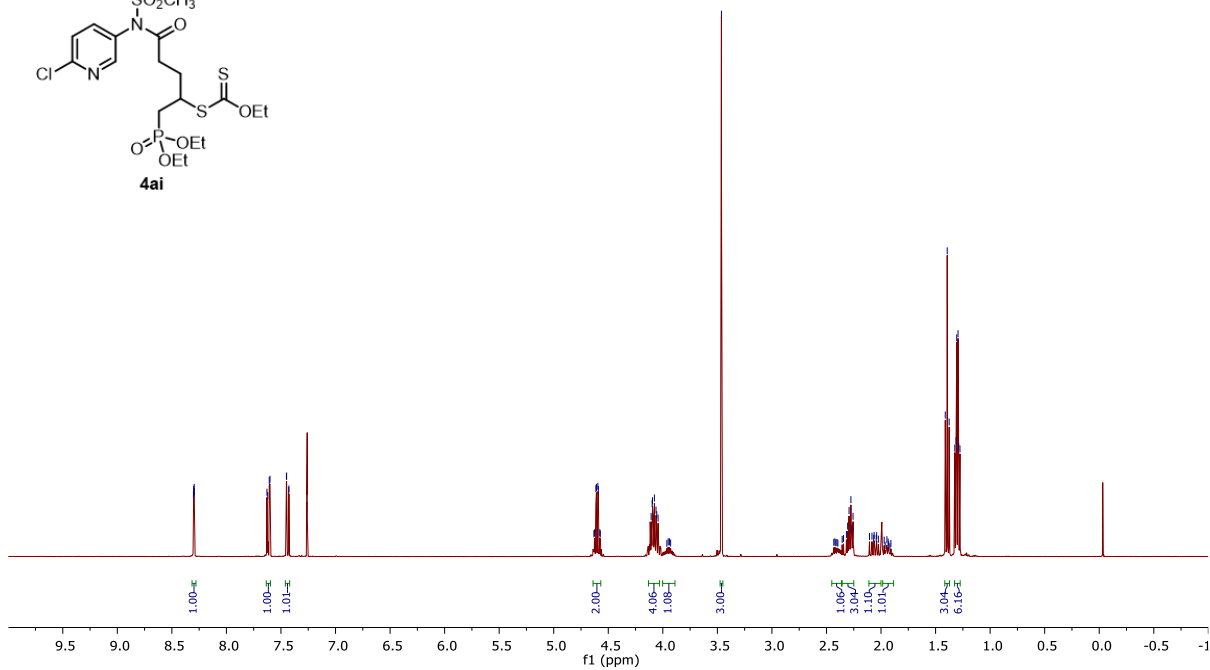
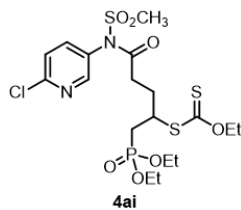


¹H NMR (400 MHz, CDCl₃)

8.30
8.30
8.29
7.63
7.61
7.60
7.45
7.43
7.43
7.26 CDCl₃

4.63
4.61
4.61
4.60
4.59
4.58
4.57
4.11
4.10
4.09
4.08
4.06
4.06
4.04
3.96
3.95
3.94
3.93
3.92
3.46

2.43
2.42
2.41
2.40
2.40
2.36
2.34
2.32
2.31
2.29
2.28
2.27
2.26
2.11
2.08
2.06
2.04
2.04
2.02
1.97
1.95
1.93
1.91
1.89
1.41
1.39
1.38
1.32
1.31
1.29
1.29
1.28



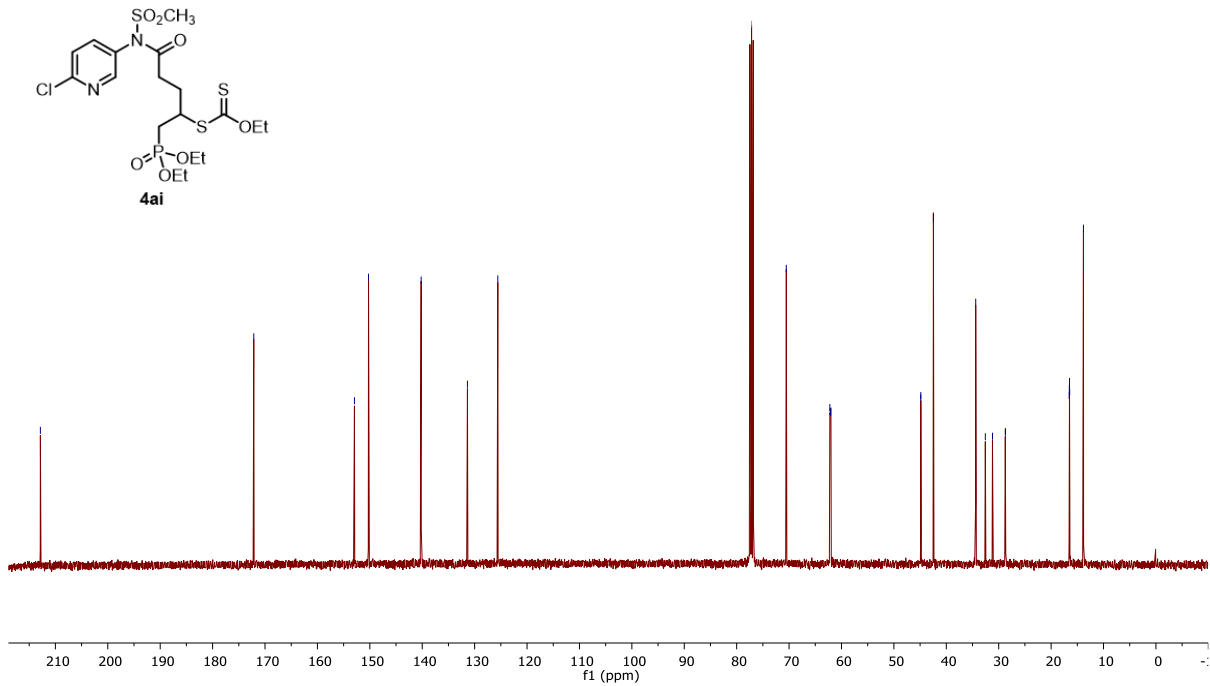
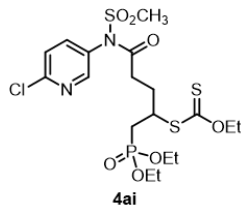
¹³C NMR (101 MHz, CDCl₃)

212.9
172.1

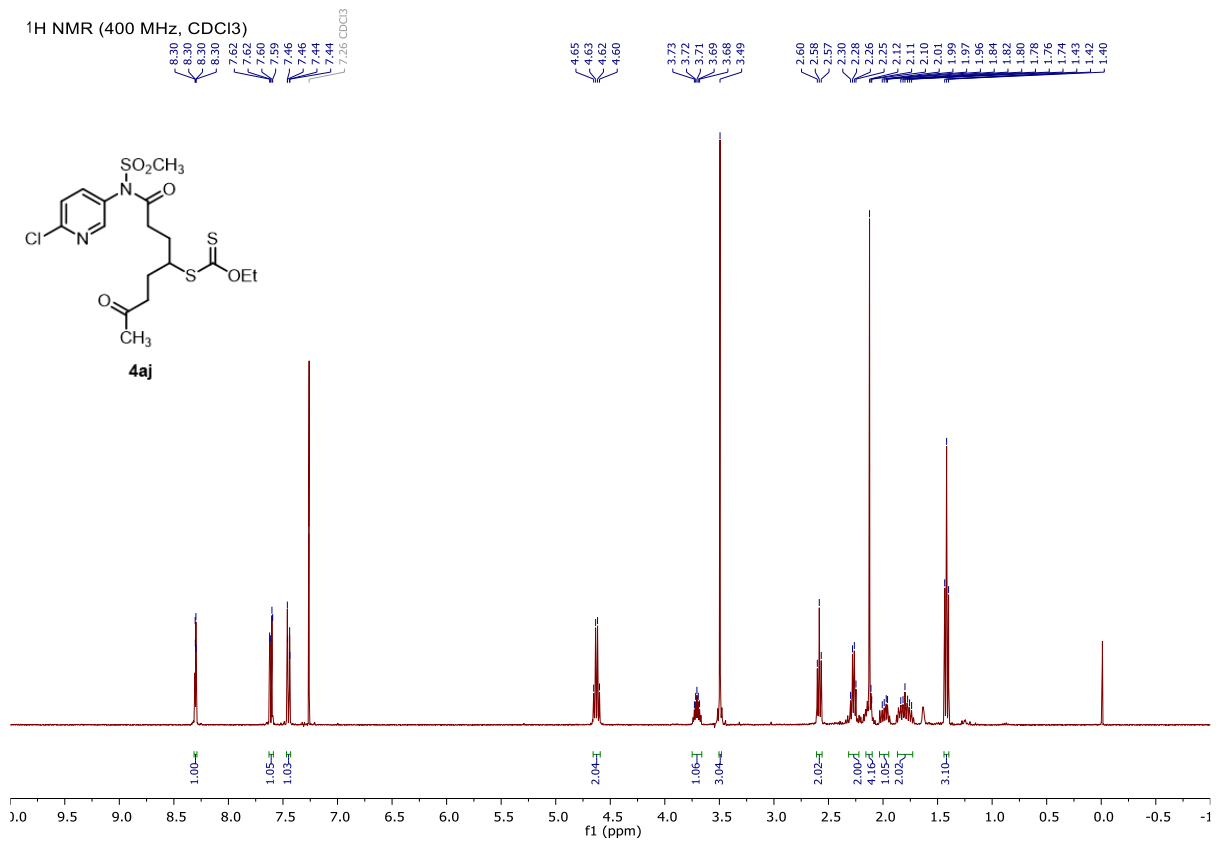
152.9
150.2
140.2
131.4
125.6

77.2 CDCl₃

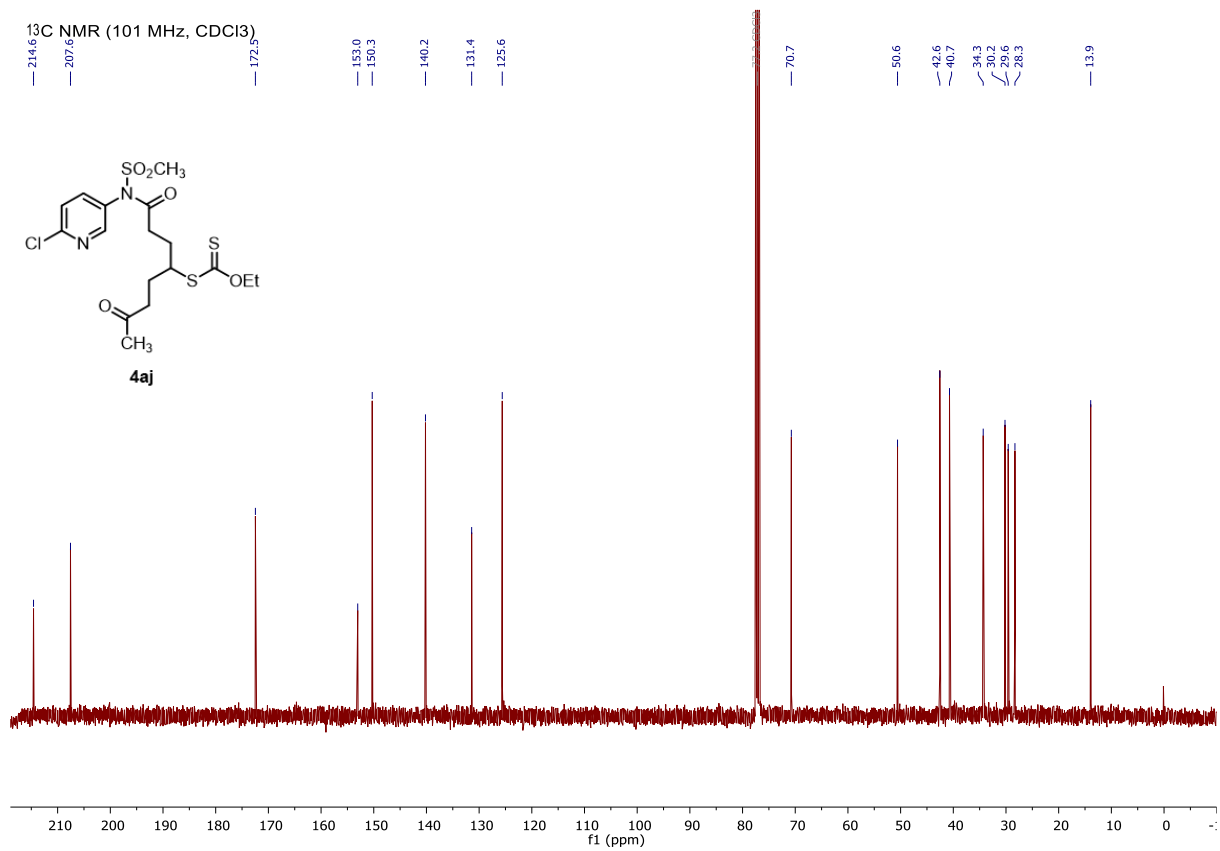
70.5
62.2
62.2
62.1
62.0
44.9
42.5
34.4
34.4
31.2
28.7
28.7
16.6
16.5
16.5
16.5
13.8



¹H NMR (400 MHz, CDCl₃)



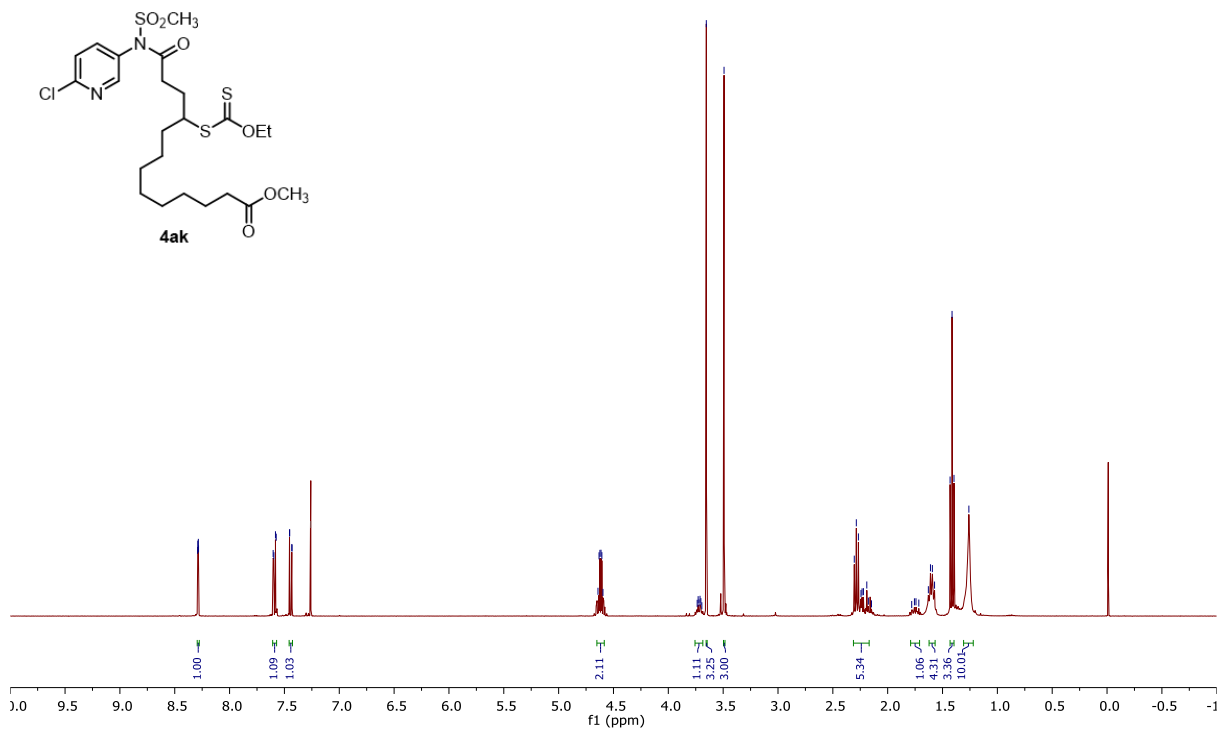
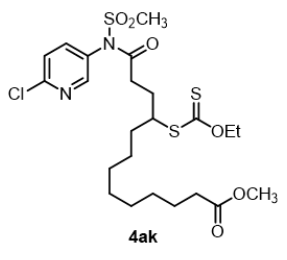
¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)

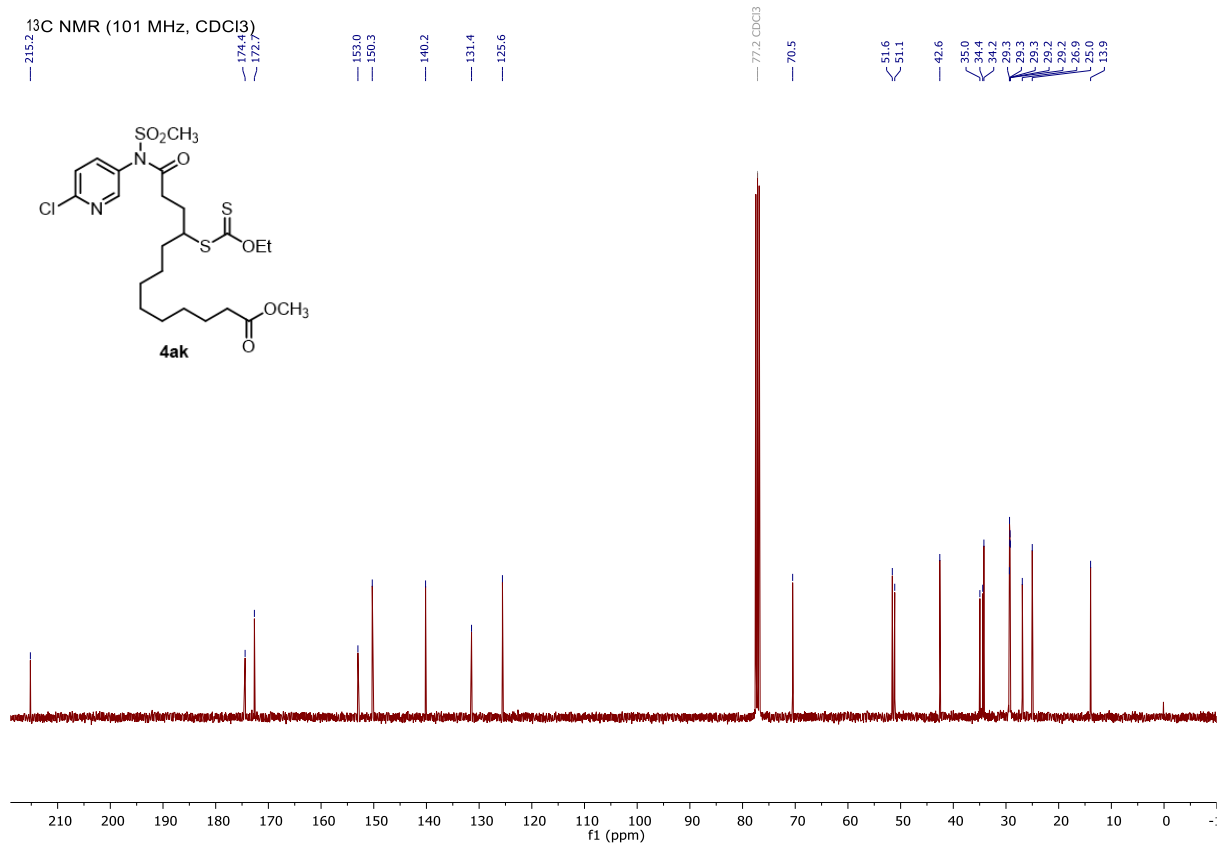
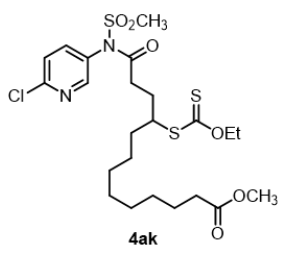
8.29
8.29
8.28
7.60
7.60
7.57
7.45
7.45
7.43
7.43
7.26 CDCl₃

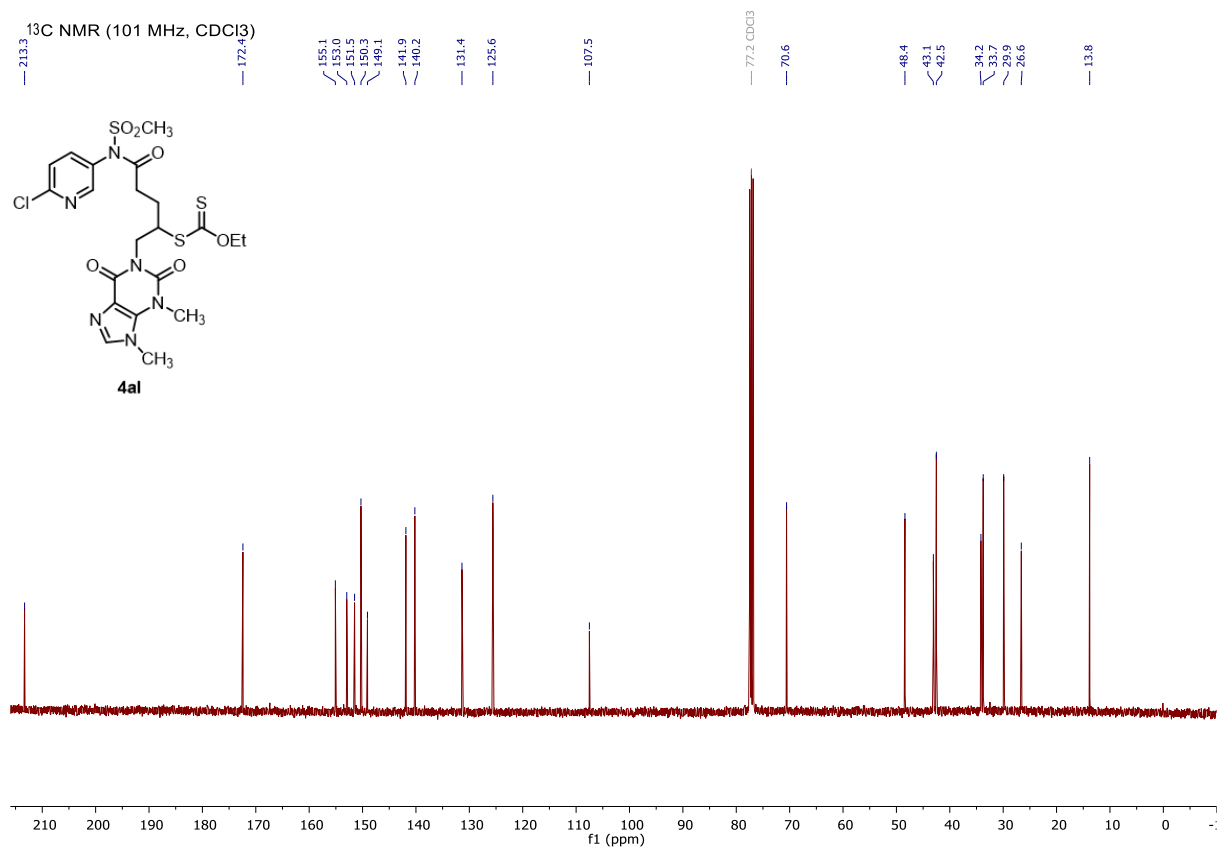
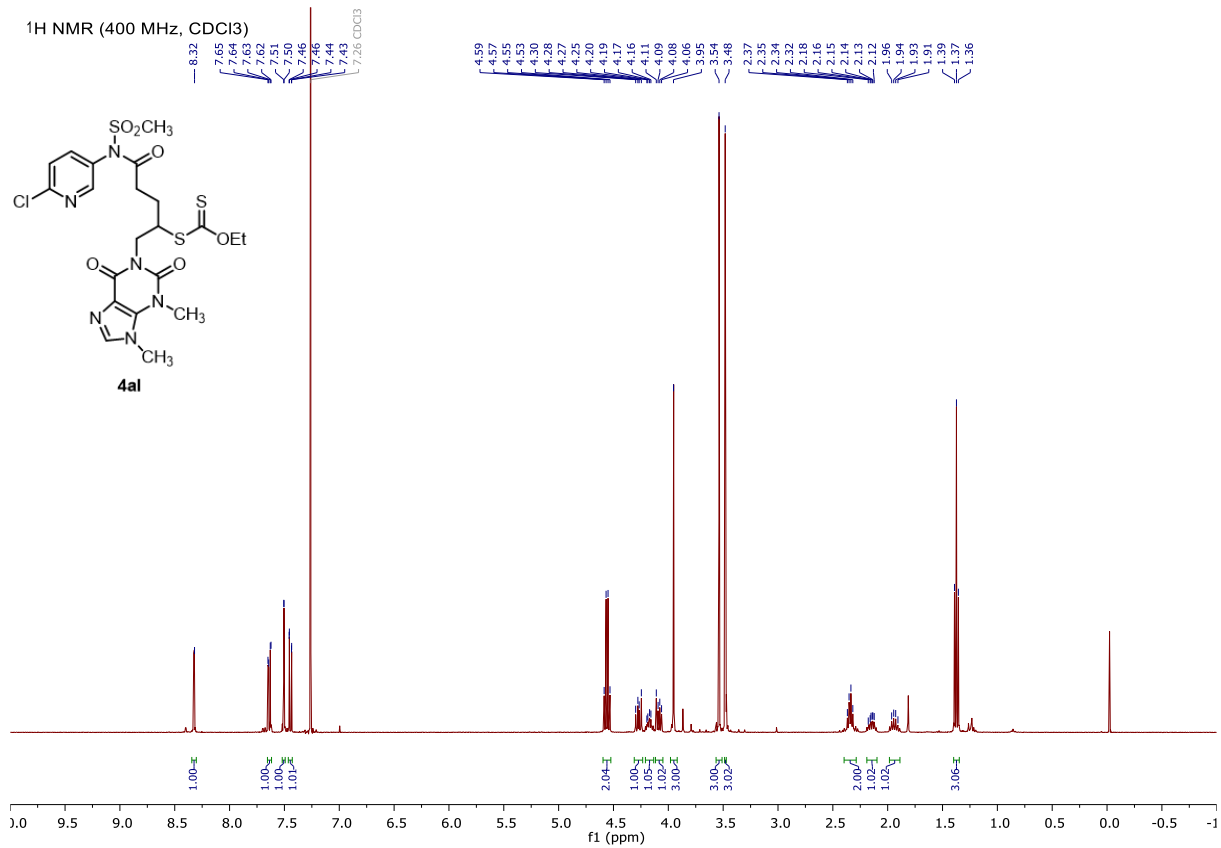
4.64
4.63
4.62
4.61
4.61
4.60
3.74
3.73
3.72
3.71
3.70
3.69
3.65
3.49
2.30
2.29
2.27
2.24
2.23
2.22
2.19
2.18
2.18
1.78
1.76
1.74
1.72
1.63
1.61
1.59
1.57
1.53
1.43
1.41
1.40
1.26



¹³C NMR (101 MHz, CDCl₃)

215.2
174.4
172.7
153.0
150.3
140.2
131.4
125.6
77.2 CDCl₃
70.5
51.6
51.1
42.6
35.0
34.4
34.4
29.3
29.3
29.3
29.2
29.2
26.9
23.0
13.9

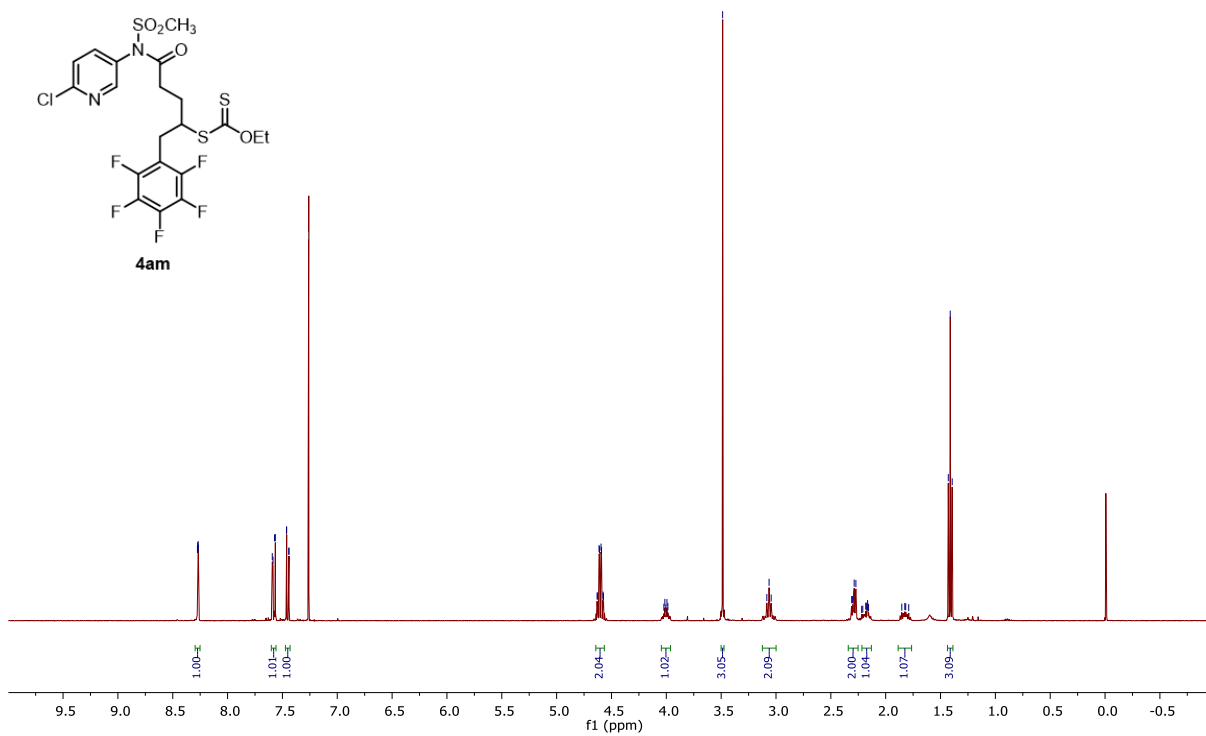
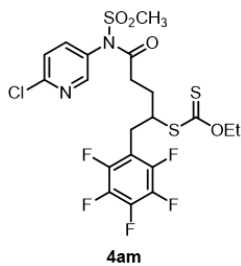




¹H NMR (400 MHz, CDCl₃)

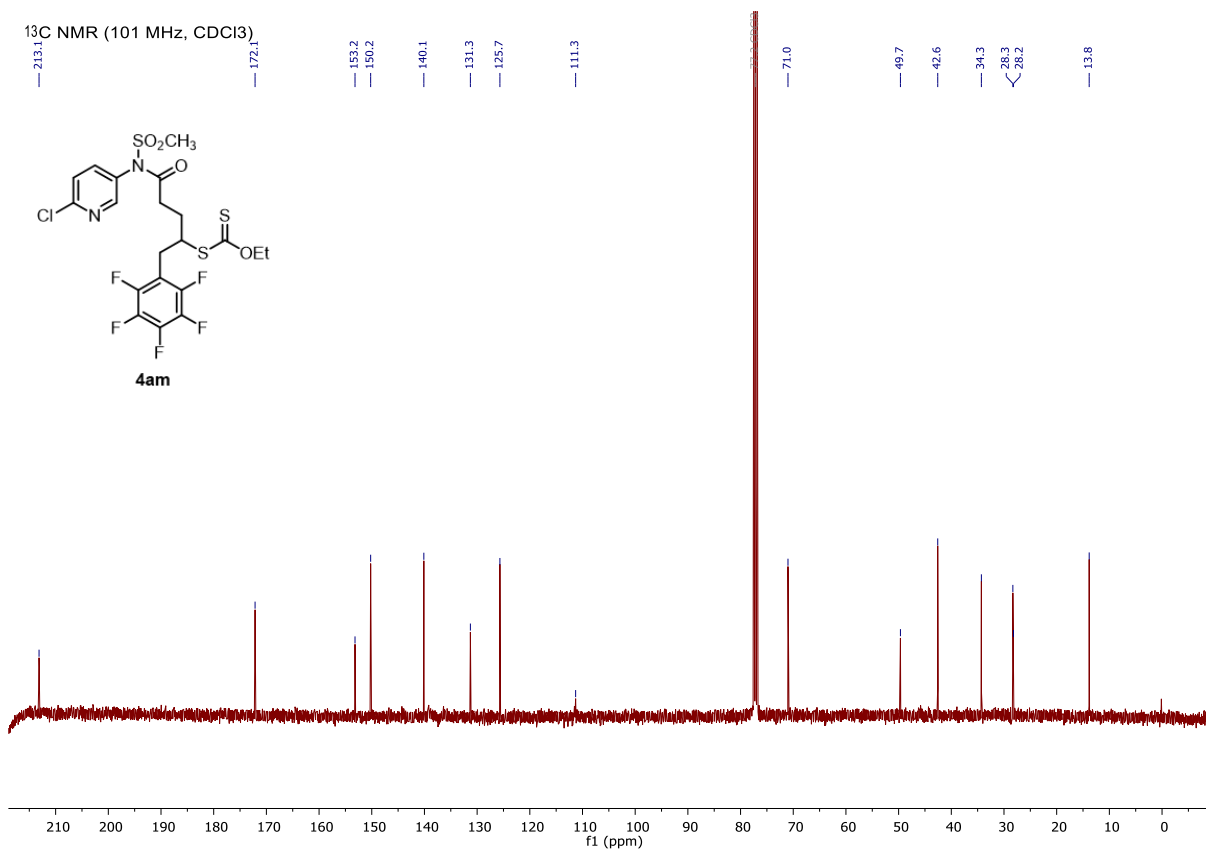
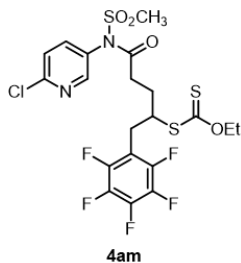
8.27, 8.27, 8.27, 7.99, 7.99, 7.56, 7.46, 7.46, 7.44, 7.44, 7.26 CDCl₃

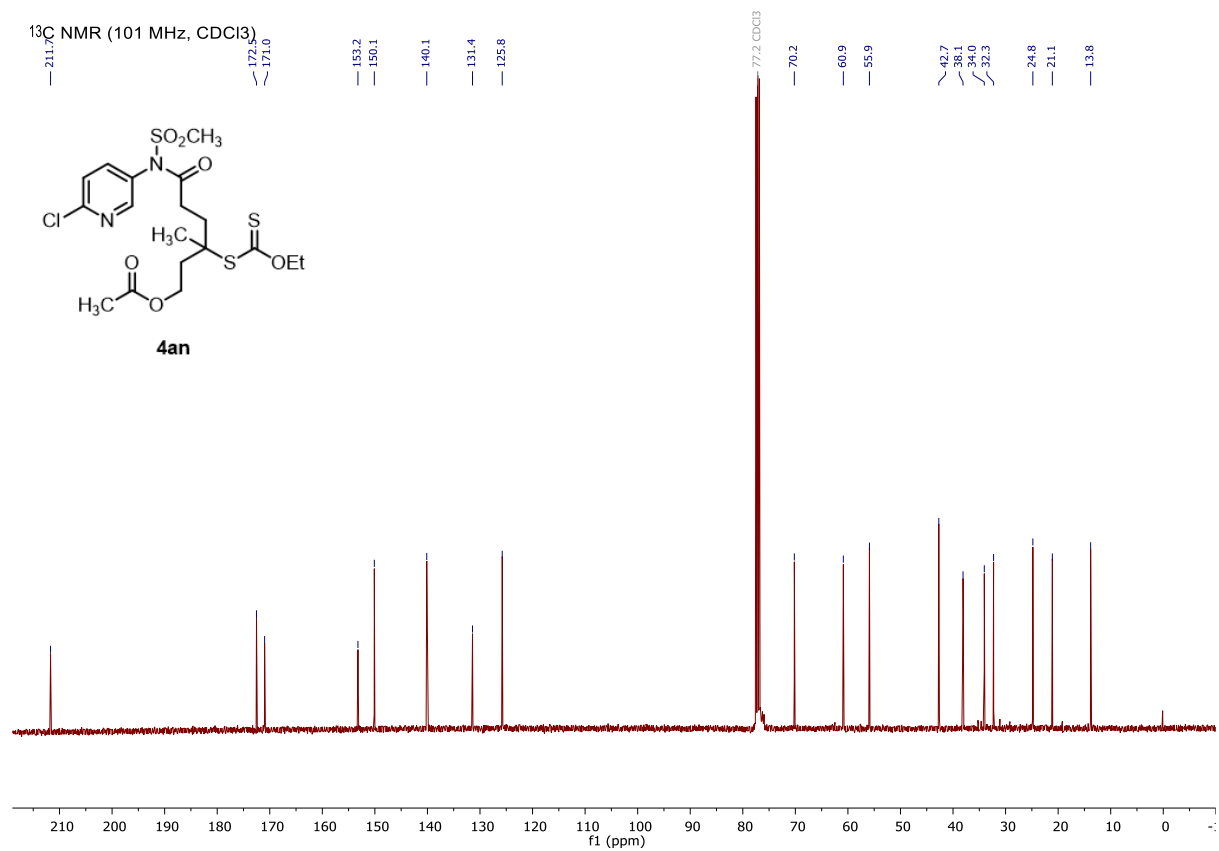
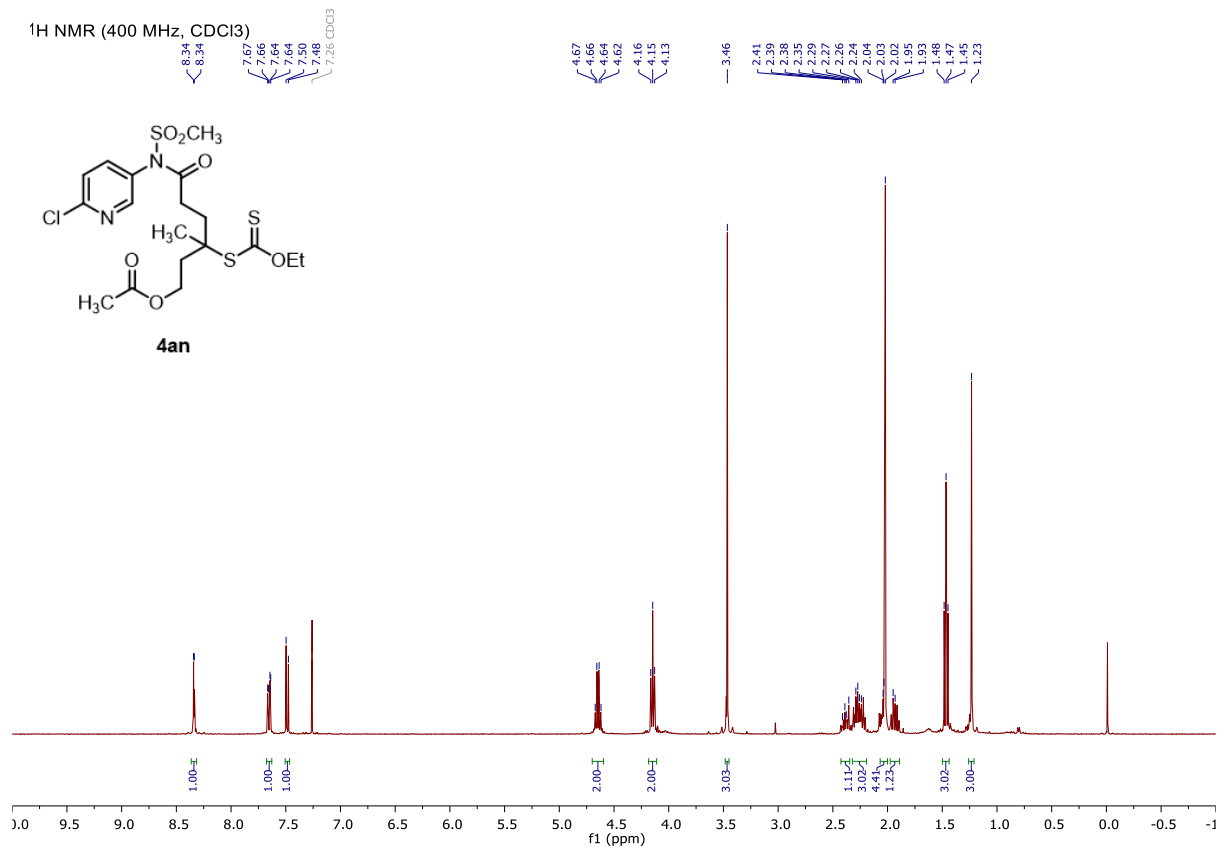
4.63, 4.63, 4.61, 4.61, 4.60, 4.59, 4.59, 4.58, 4.10, 4.01, 4.00, 3.99, 3.99, 3.49, 3.08, 3.06, 3.04, 2.31, 2.30, 2.29, 2.27, 2.22, 2.21, 2.19, 2.17, 2.16, 1.85, 1.83, 1.82, 1.79, 1.43, 1.42, 1.41, 1.39



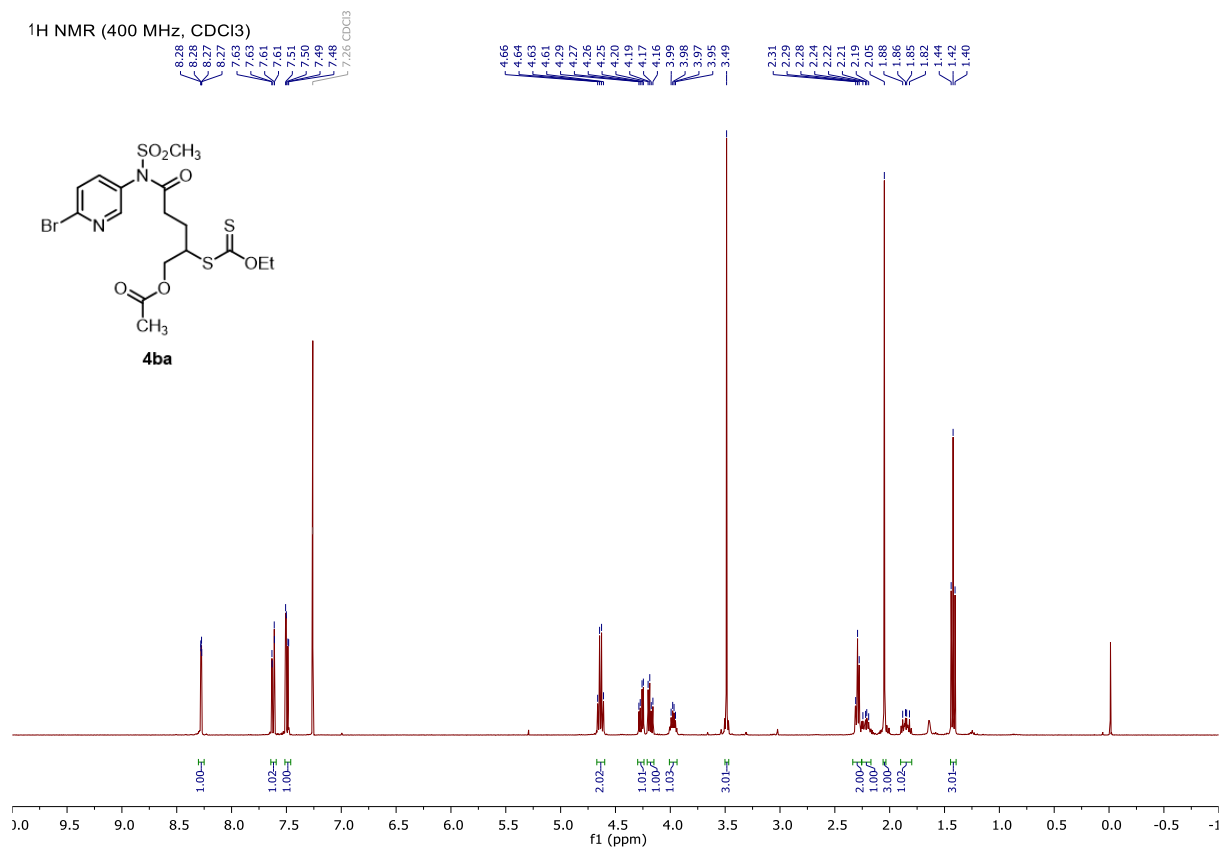
¹³C NMR (101 MHz, CDCl₃)

213.1, 172.1, 153.2, 150.2, 140.1, 131.3, 125.7, 111.3, 71.0, 49.7, 42.6, 34.3, 28.3, 28.2, 13.6

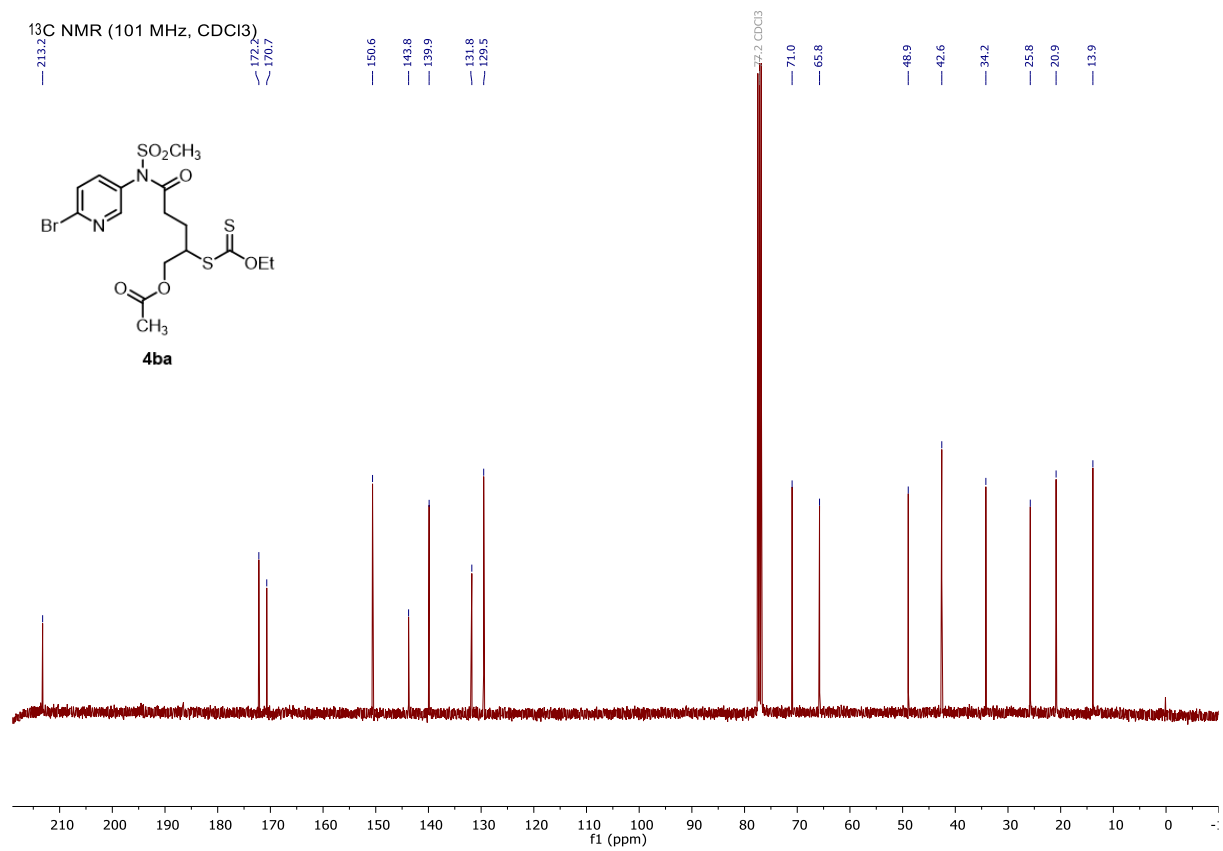


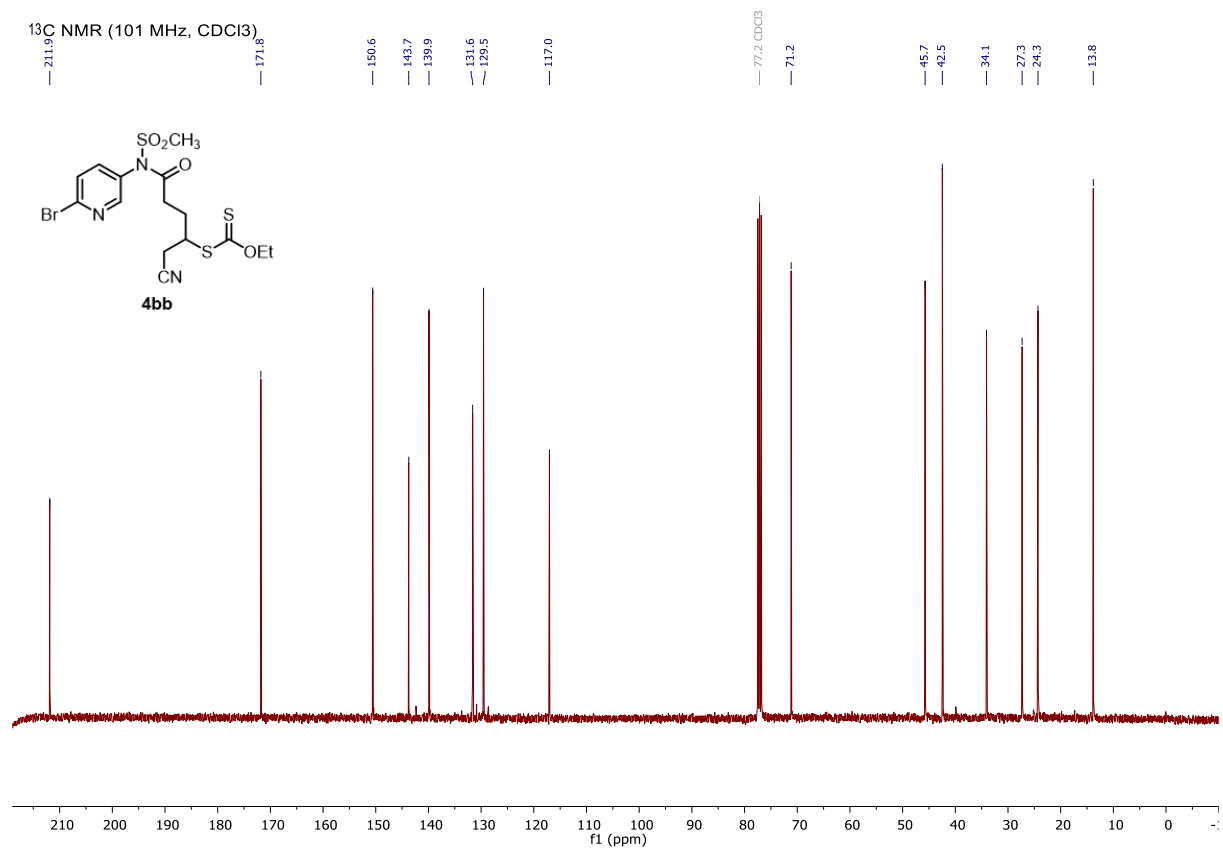
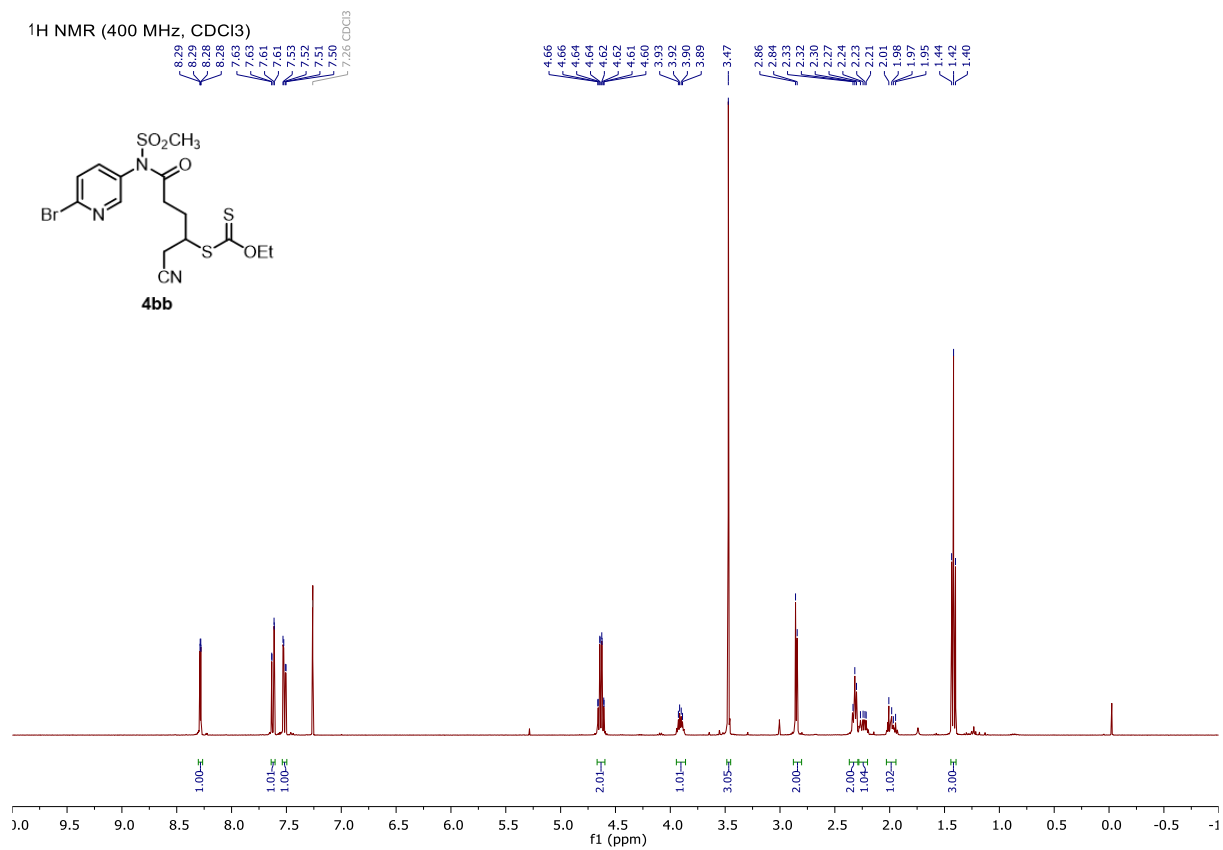


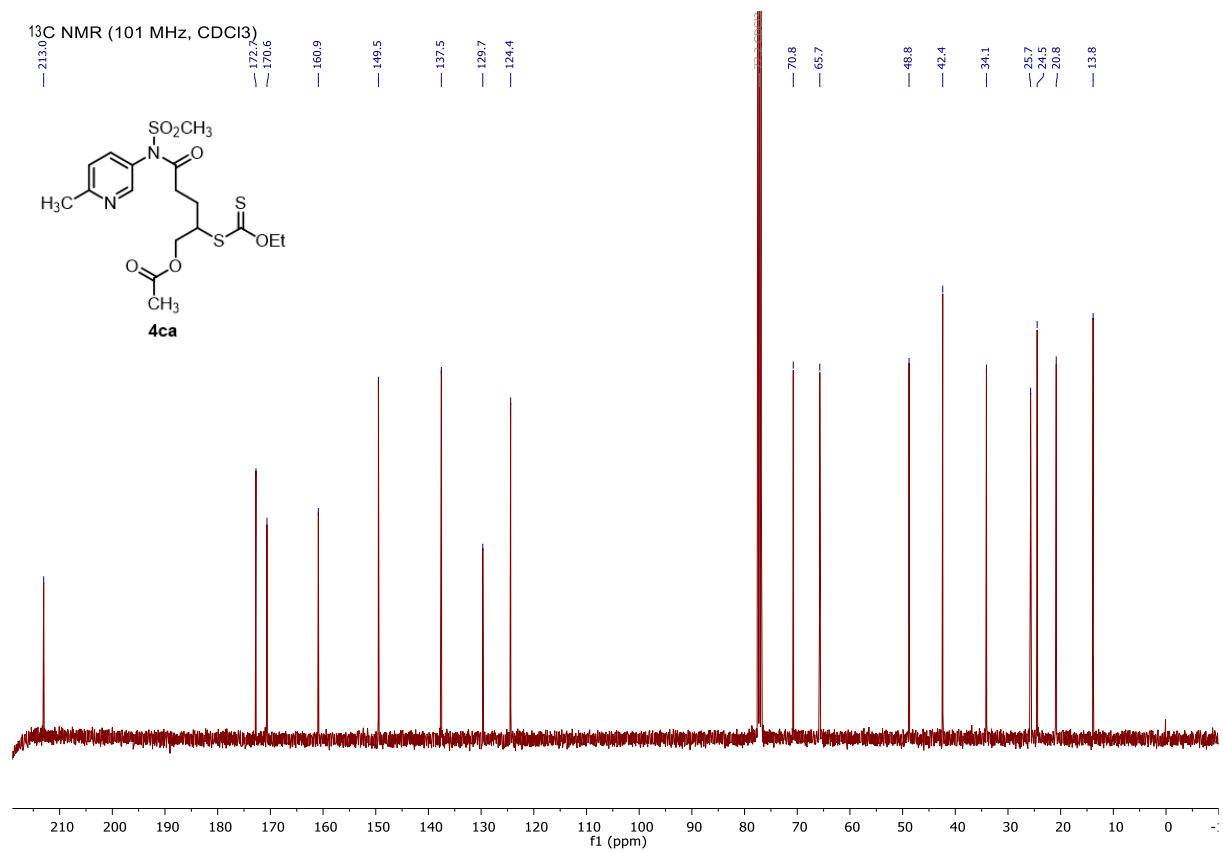
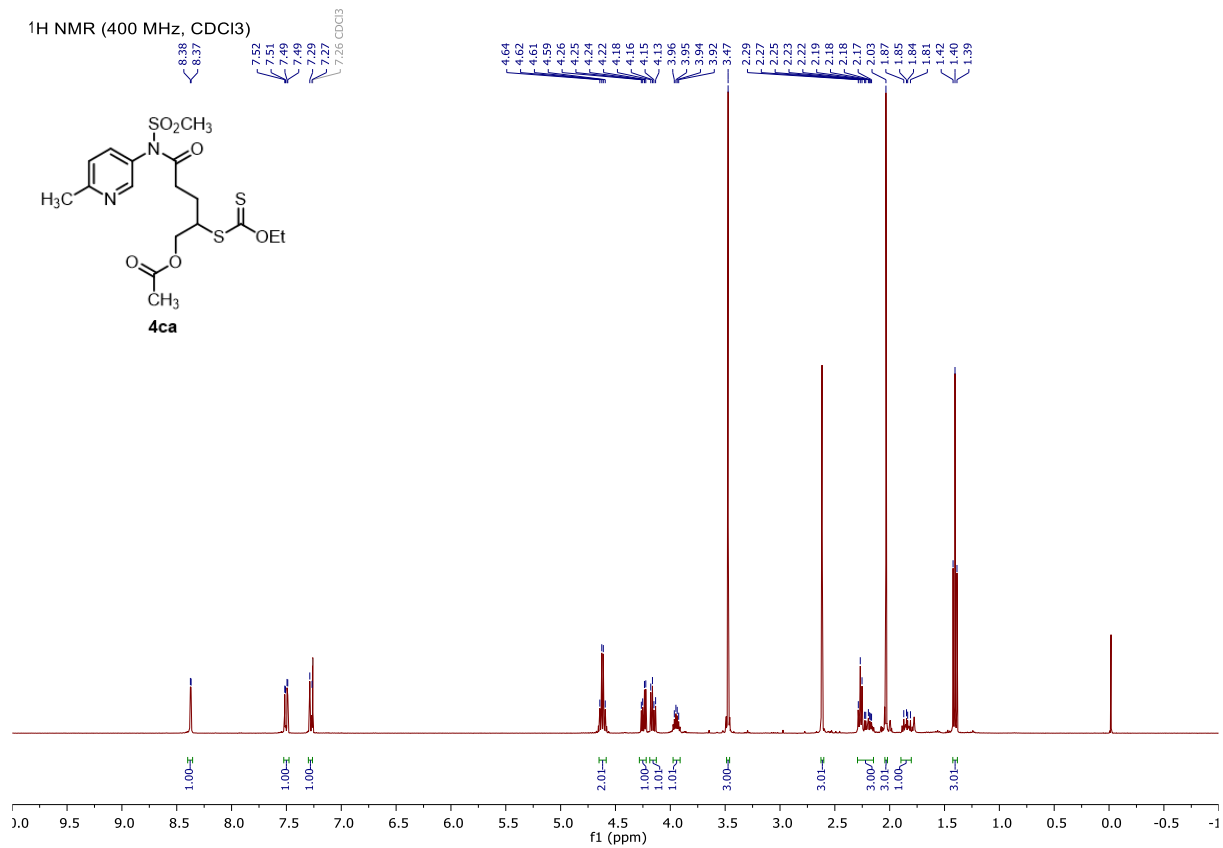
¹H NMR (400 MHz, CDCl₃)



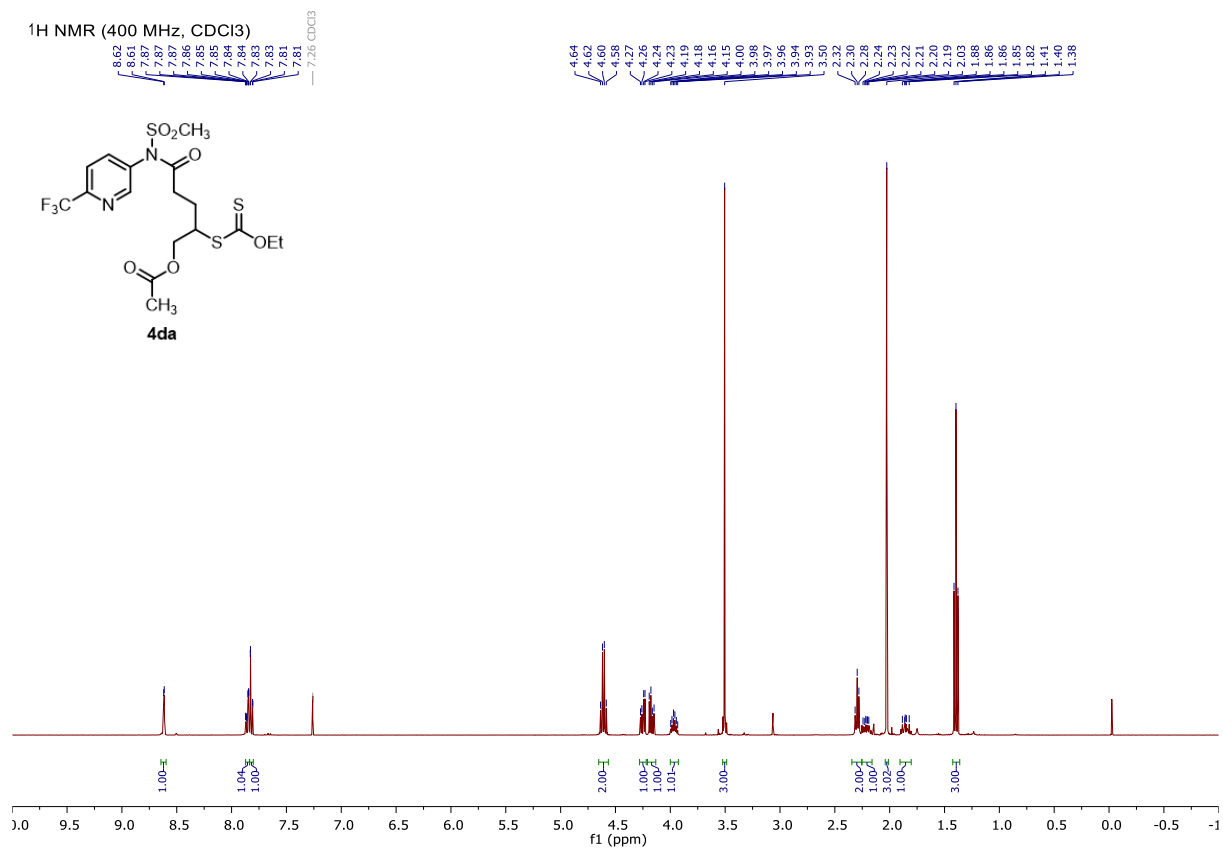
¹³C NMR (101 MHz, CDCl₃)



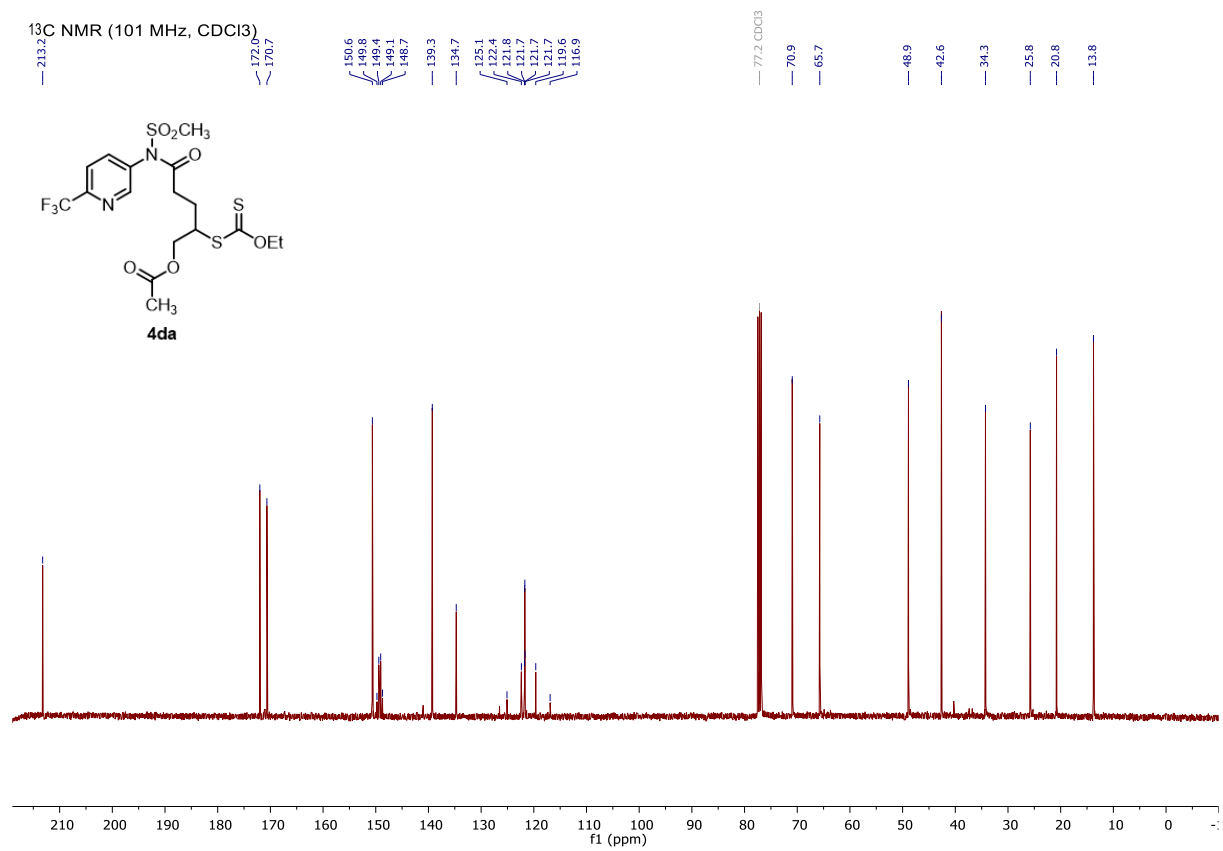


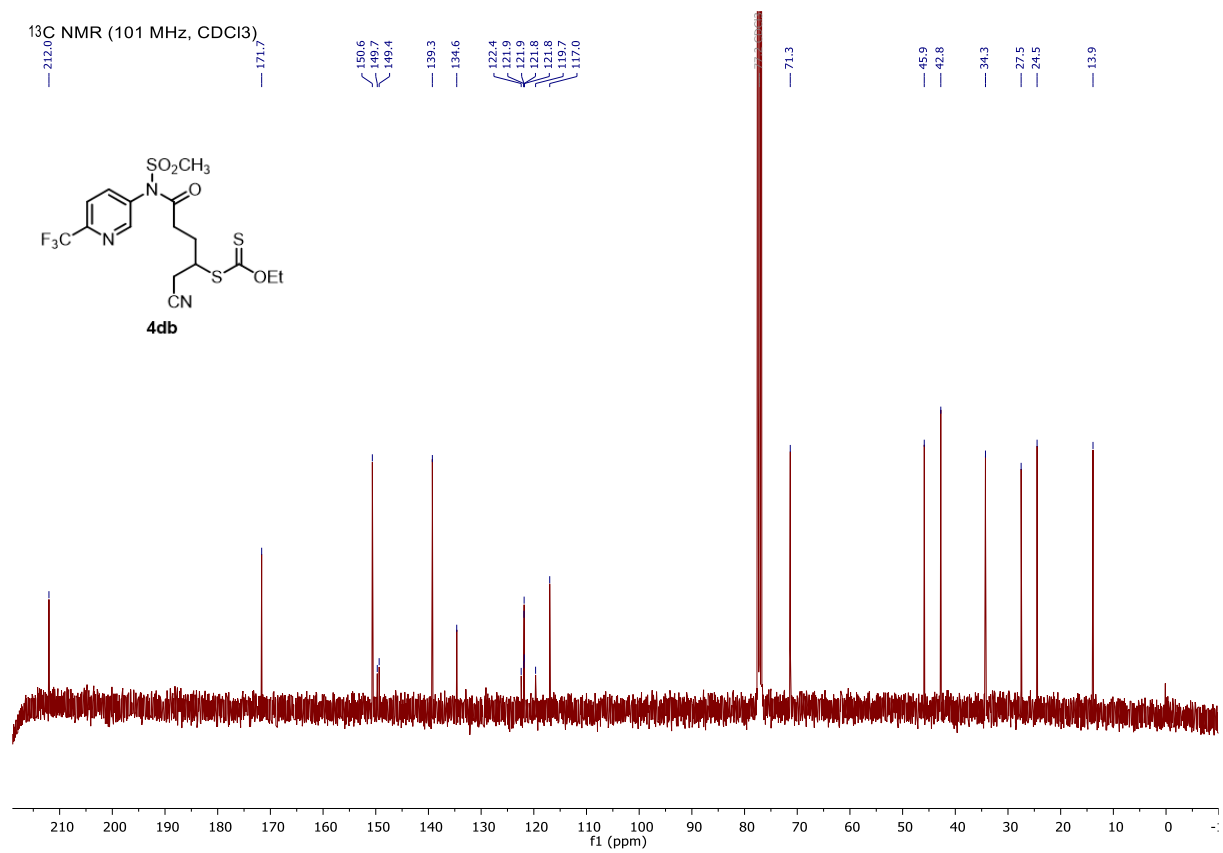
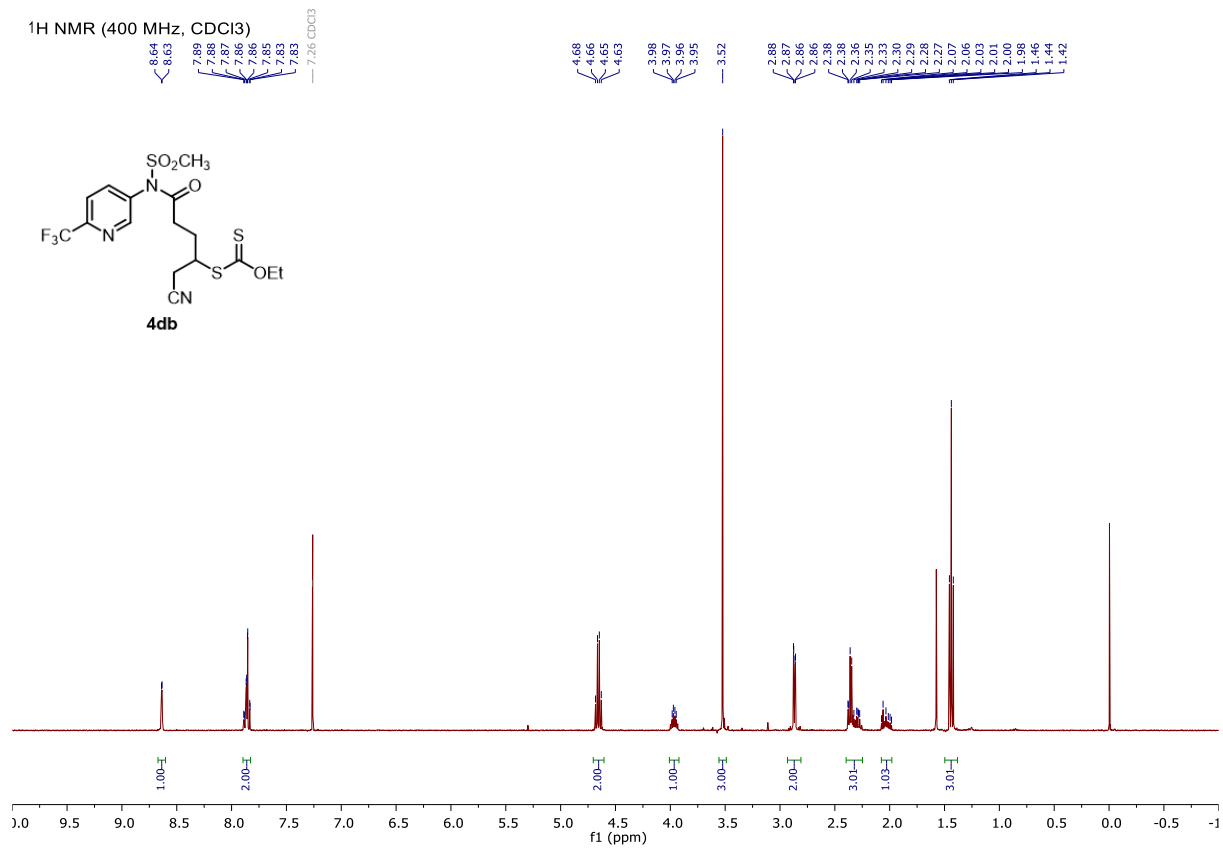


¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

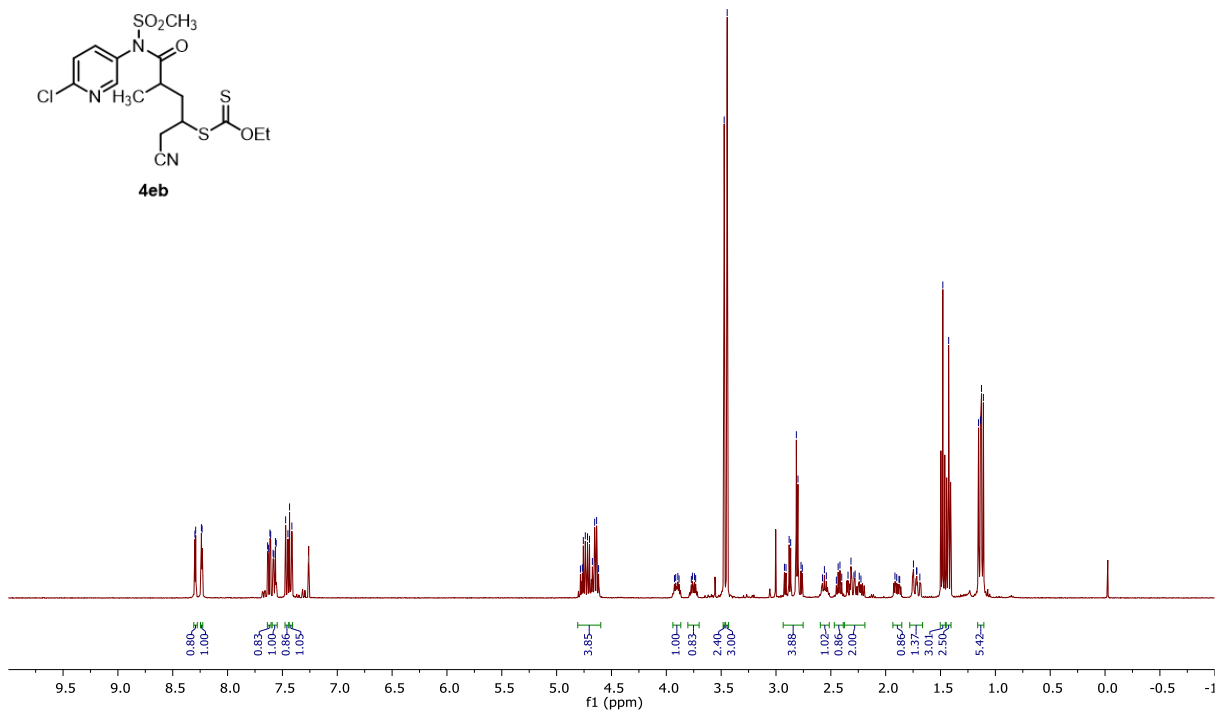
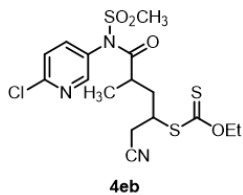




¹H NMR (400 MHz, CDCl₃)

8.30
8.29
8.24
8.23
7.63
7.61
7.58
7.56
7.47
7.46
7.43
7.41
7.26 CDCl₃

4.79
4.77
4.76
4.74
4.72
4.70
4.67
4.65
4.64
4.62
3.93
3.91
3.89
3.88
3.77
3.76
3.74
3.73
3.47
3.44
2.92
2.91
2.89
2.87
2.81
2.80
2.77
2.76
2.59
2.56
2.54
2.43
2.42
2.40
2.34
2.32
2.29
2.28
2.24
2.23
1.92
1.90
1.87
1.87
1.75
1.72
1.72
1.69
1.48
1.43
1.15
1.14
1.13
1.11



¹³C NMR (101 MHz, CDCl₃)

212.0
211.1

175.9
175.8

153.1
152.1
150.0

149.9

140.1

131.3
131.2
130.9

125.6
125.4

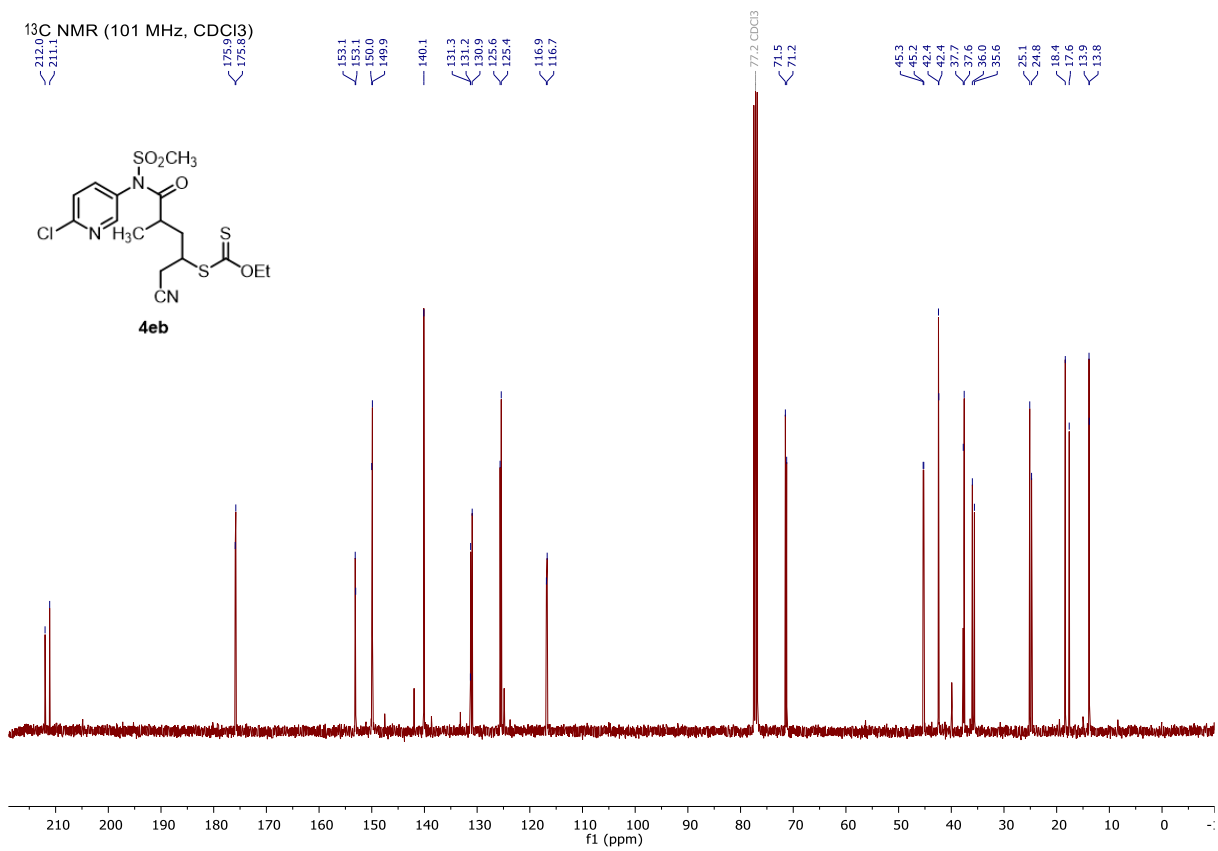
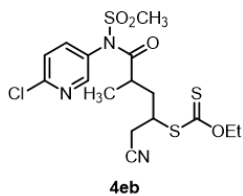
116.9
116.7

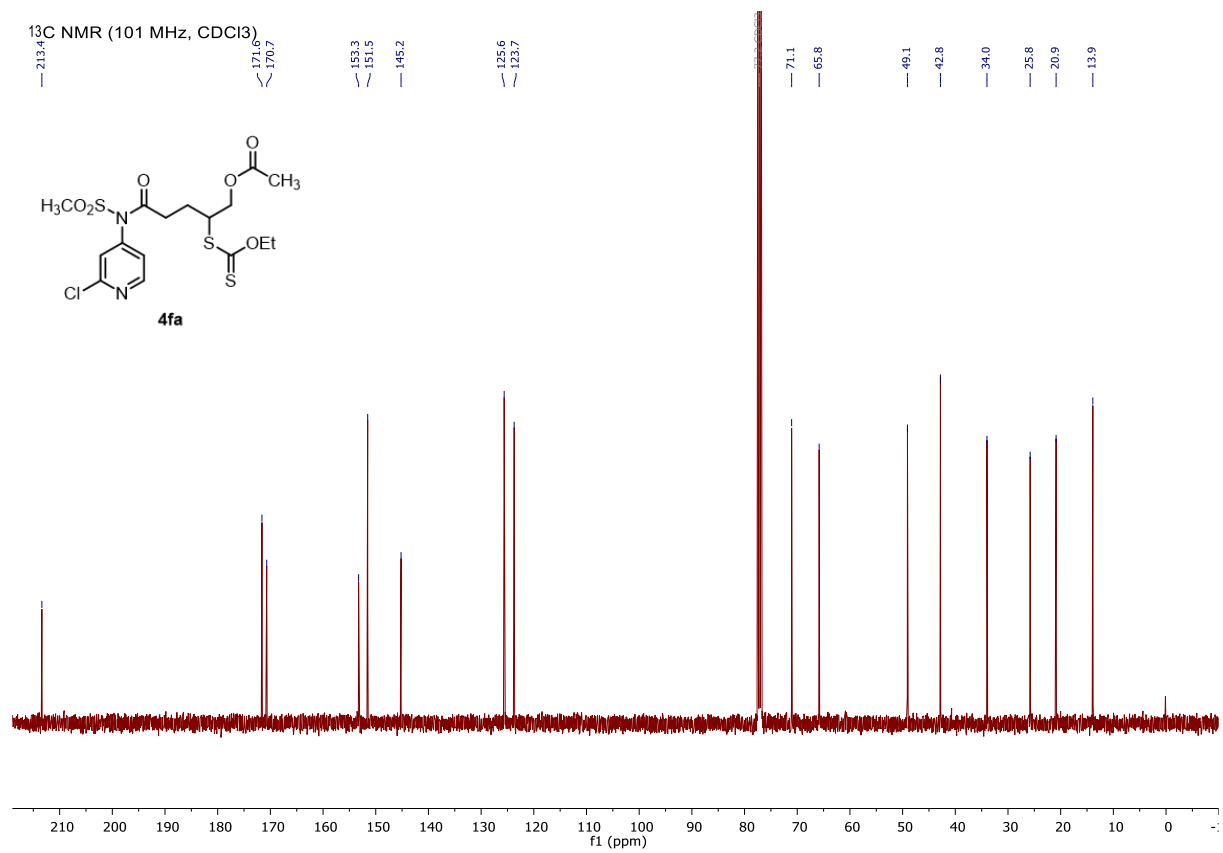
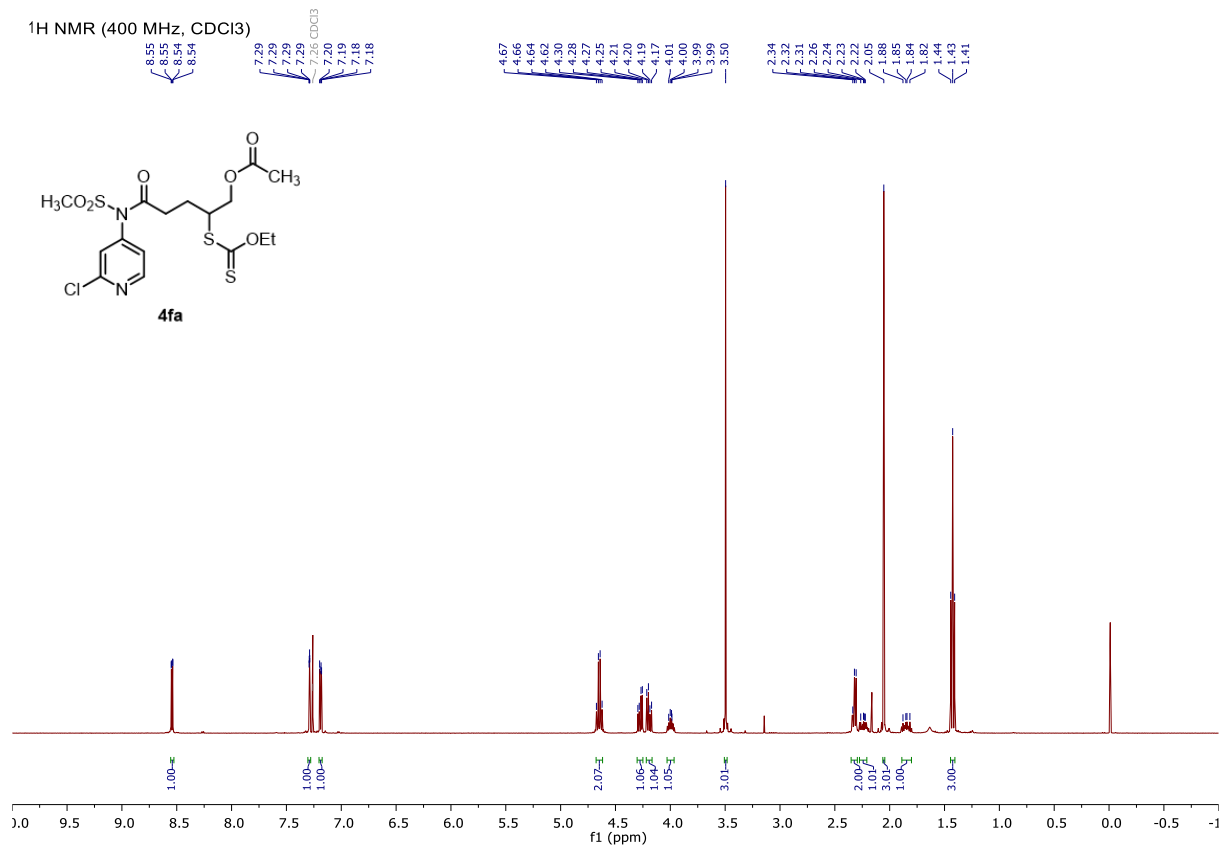
77.2 CDCl₃

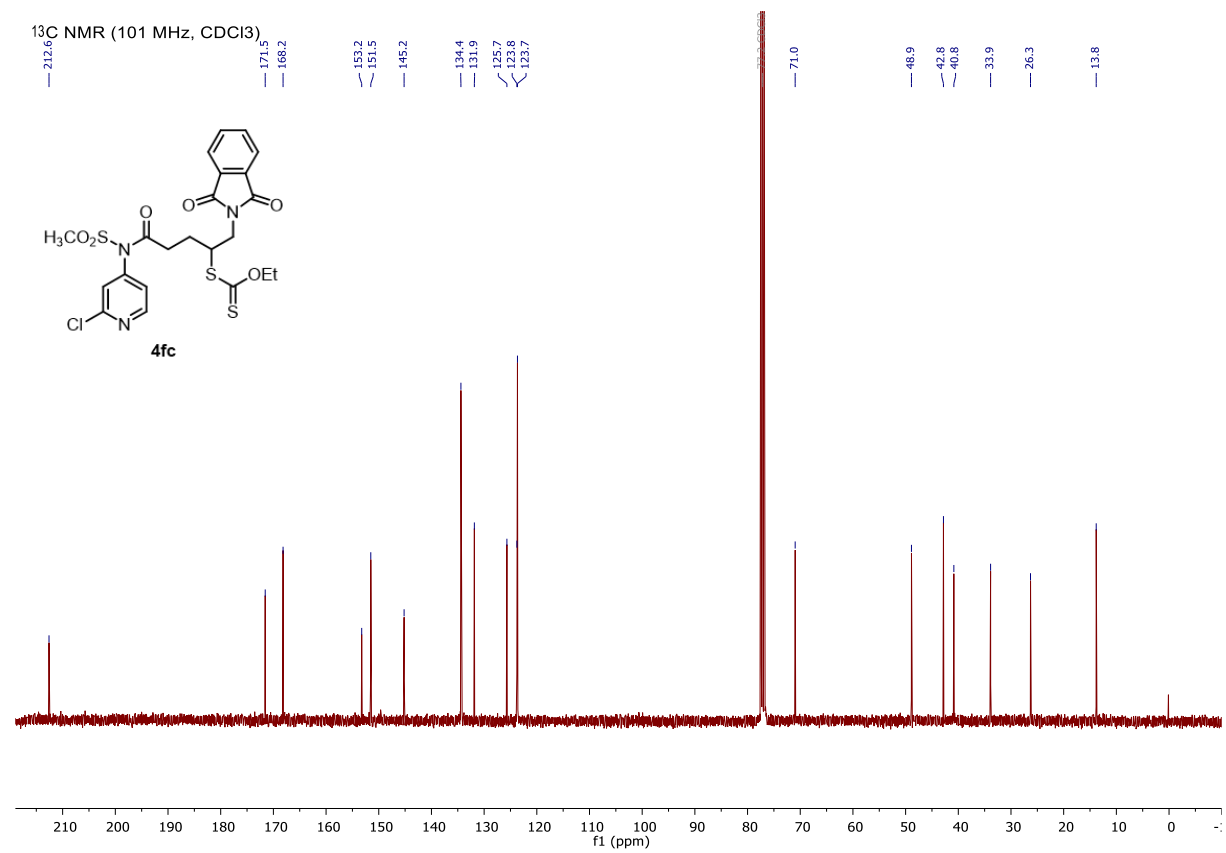
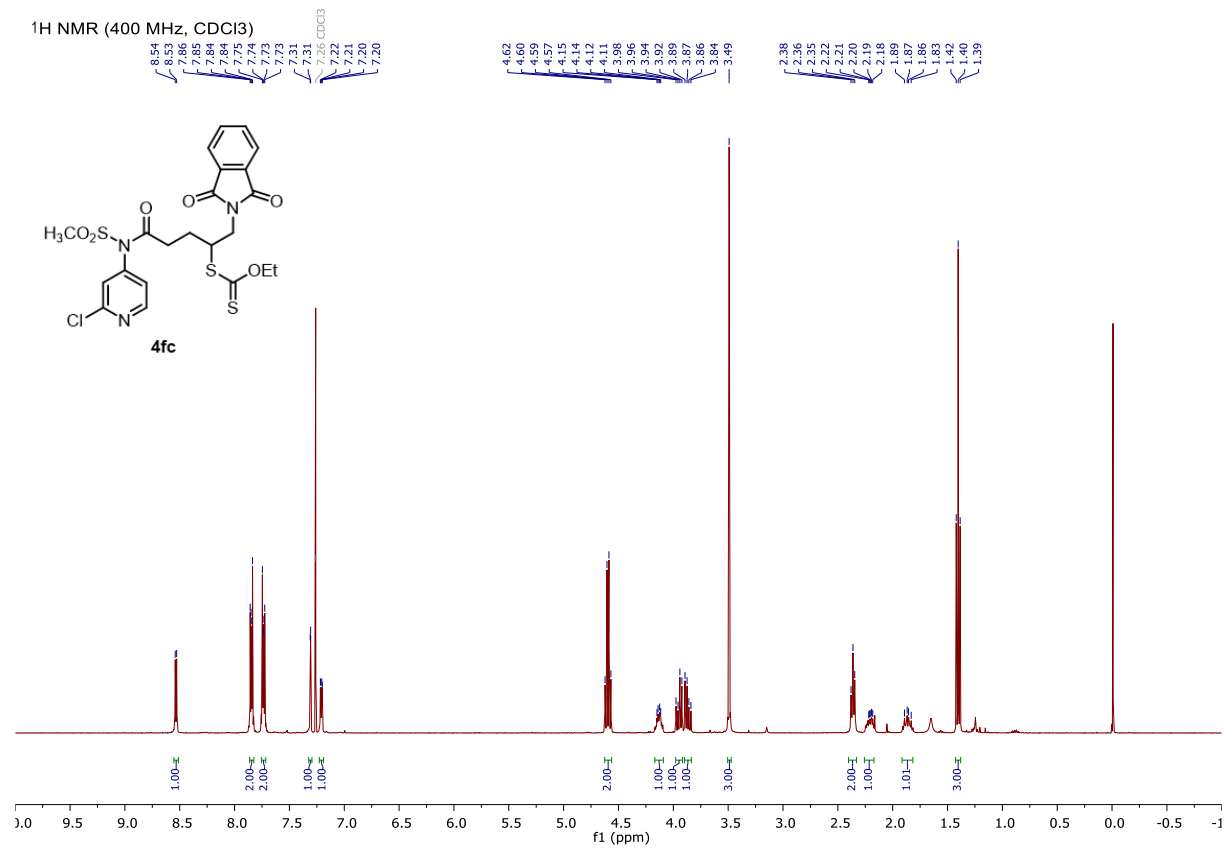
71.5
71.2

45.3
45.2
45.1
42.4
42.4
37.7
36.0
35.6

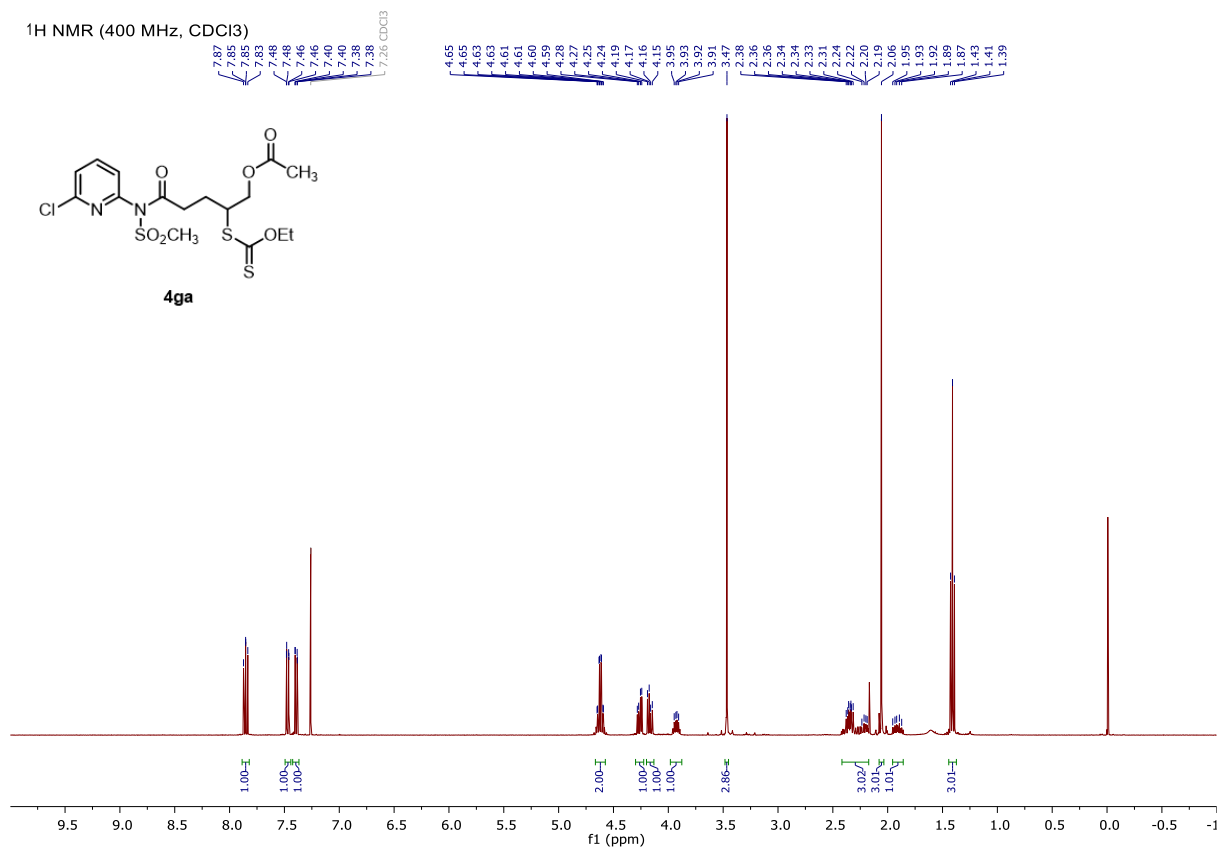
25.1
24.8
18.4
17.6
13.9
13.8



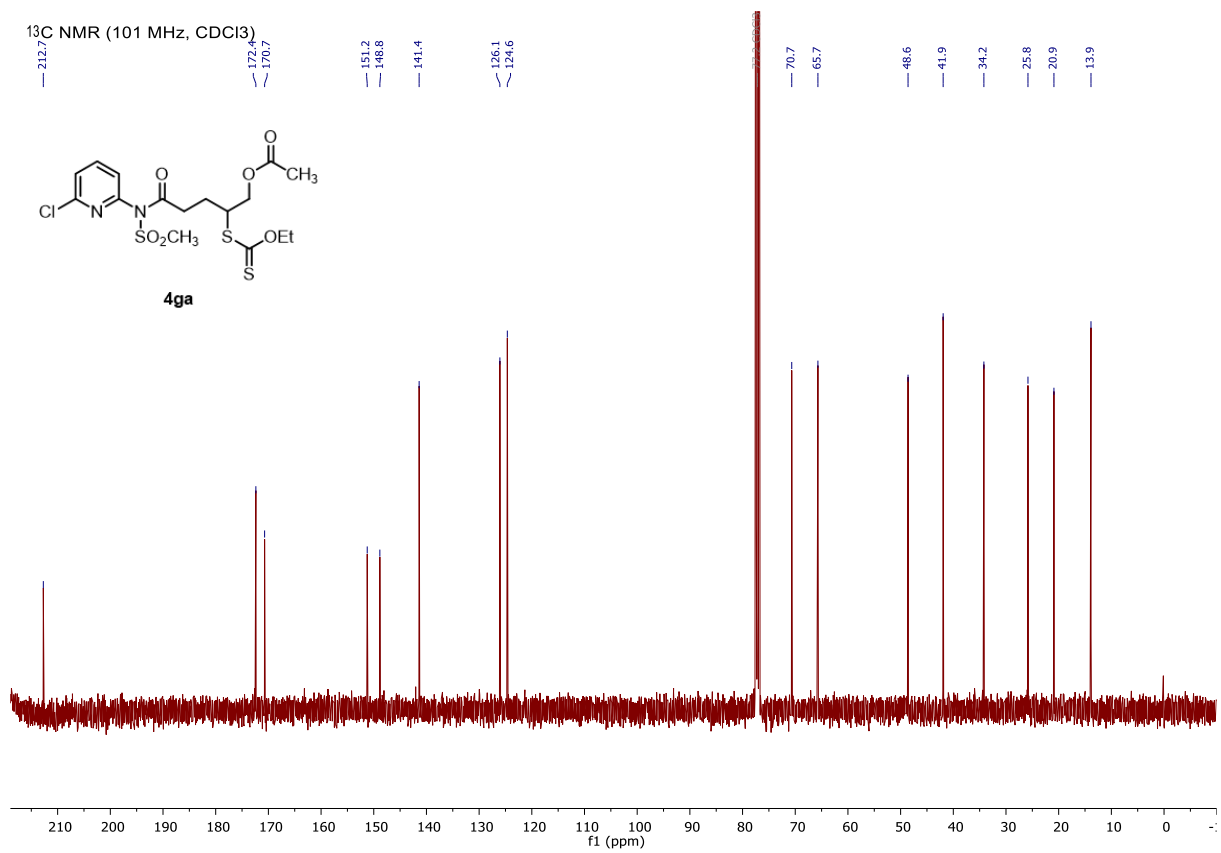




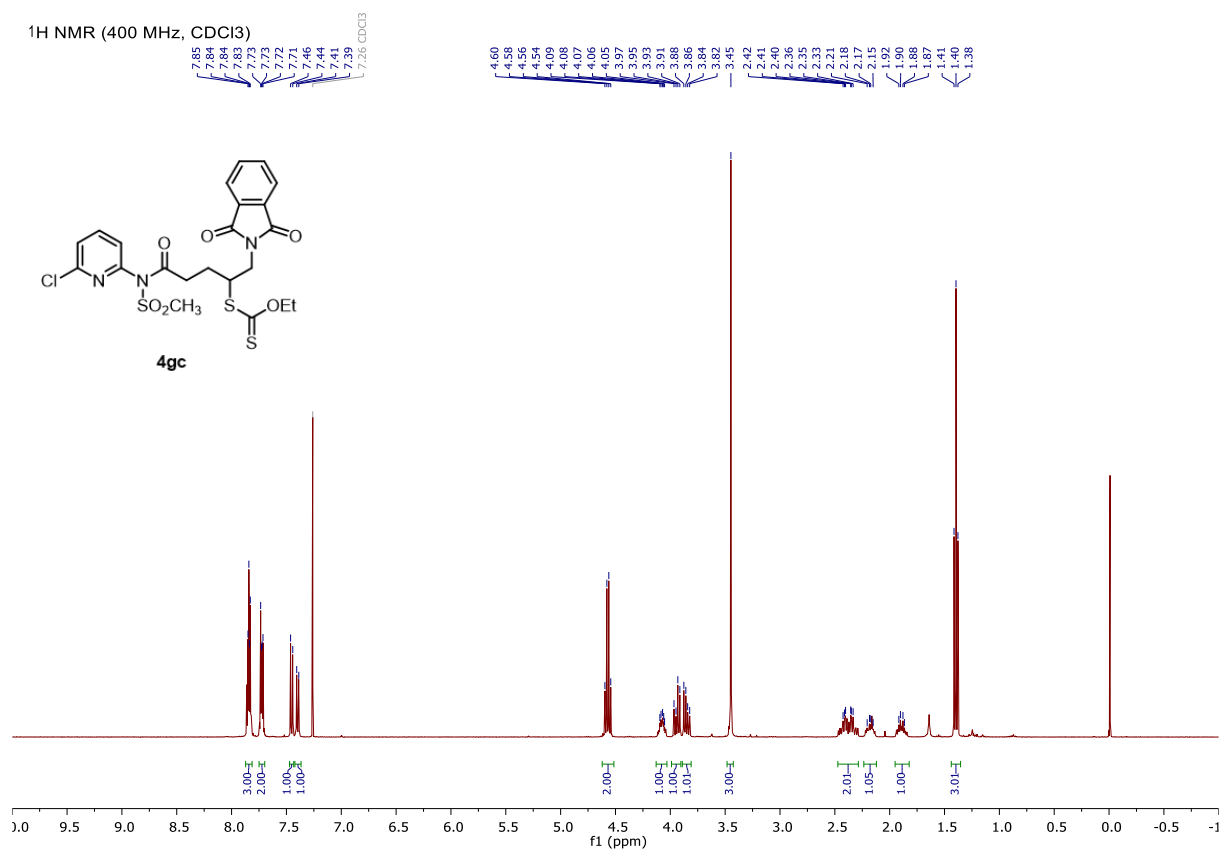
¹H NMR (400 MHz, CDCl₃)



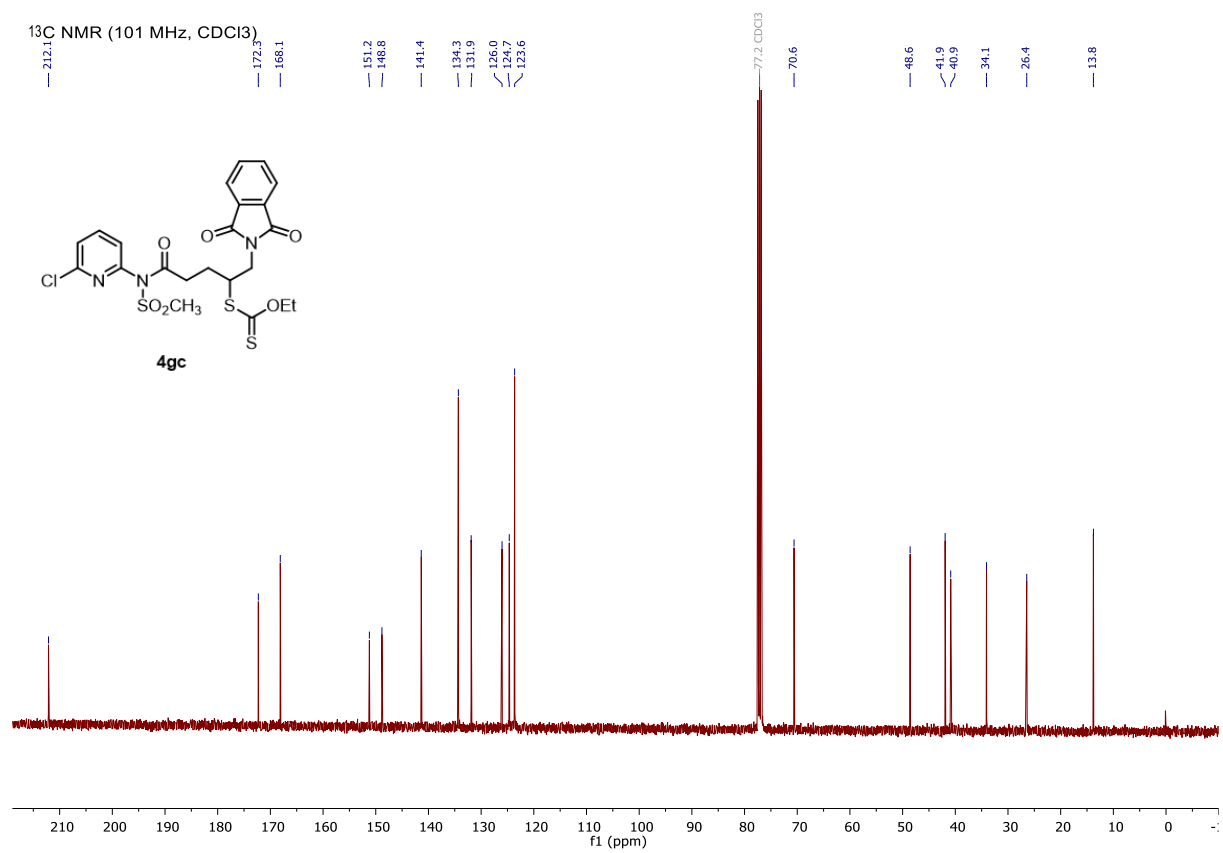
¹³C NMR (101 MHz, CDCl₃)



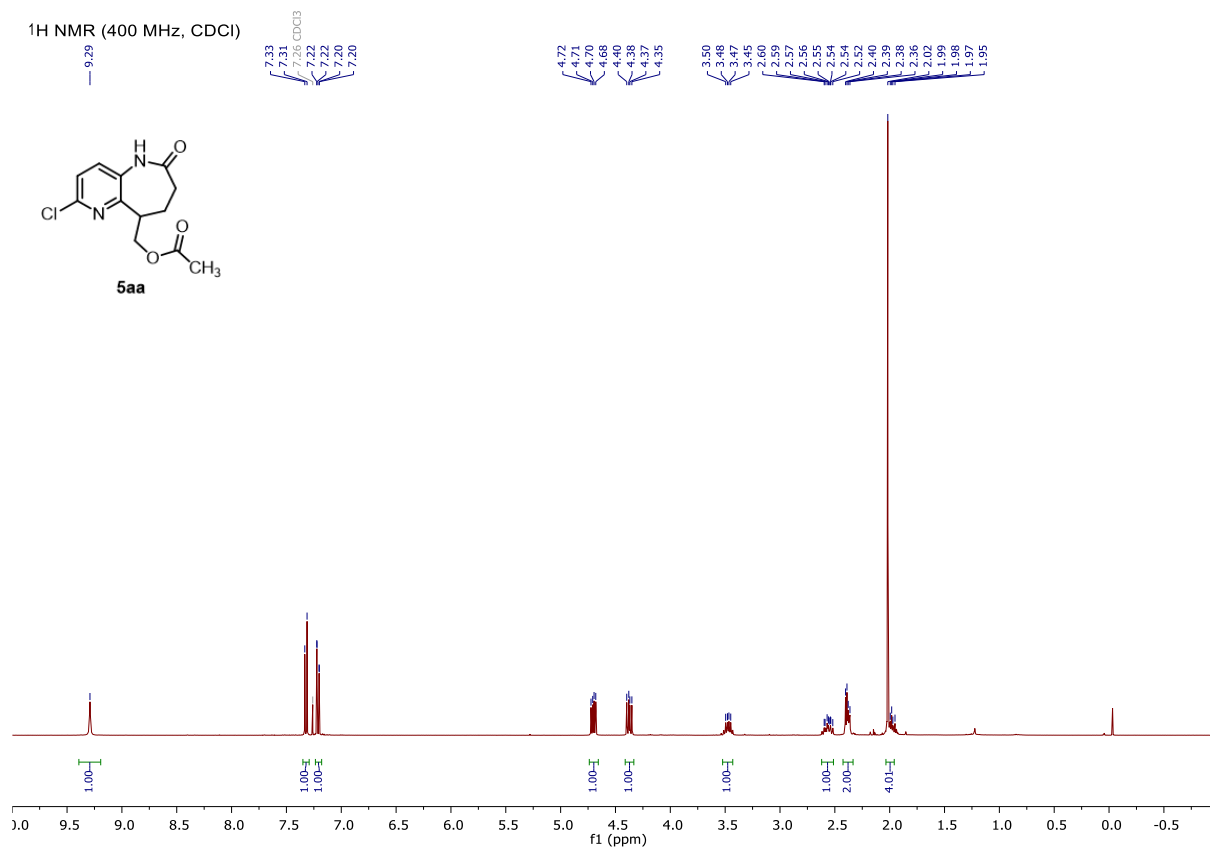
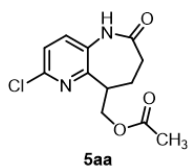
¹H NMR (400 MHz, CDCl₃)



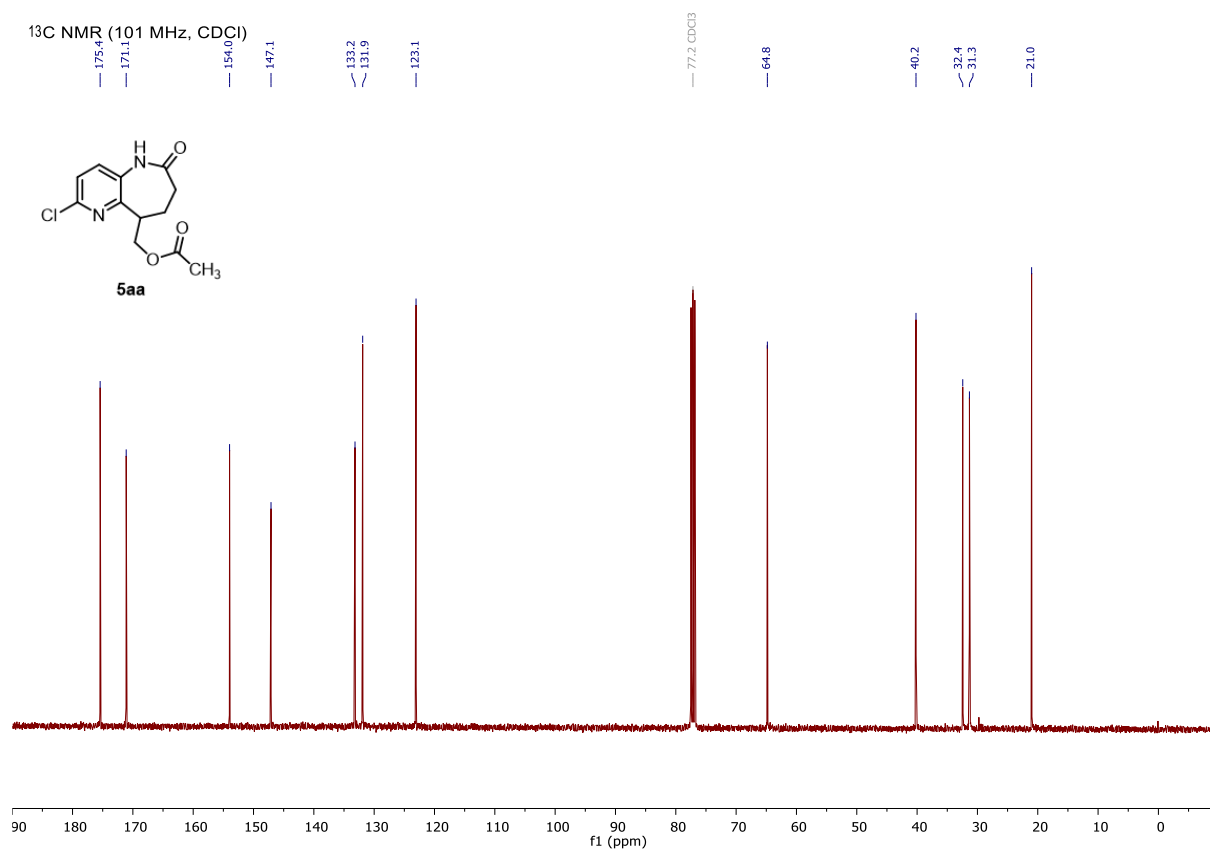
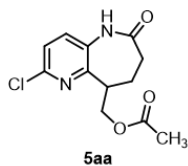
¹³C NMR (101 MHz, CDCl₃)



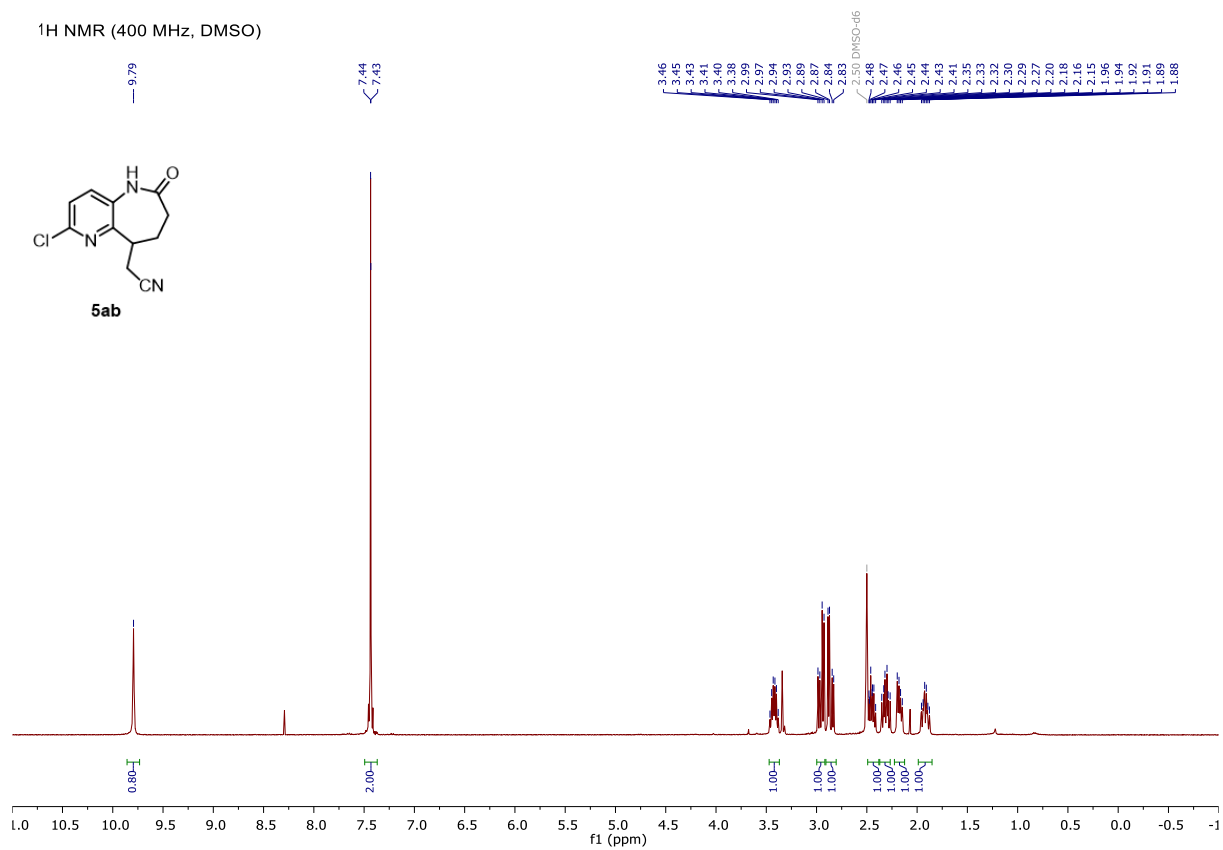
¹H NMR (400 MHz, CDCl₃)



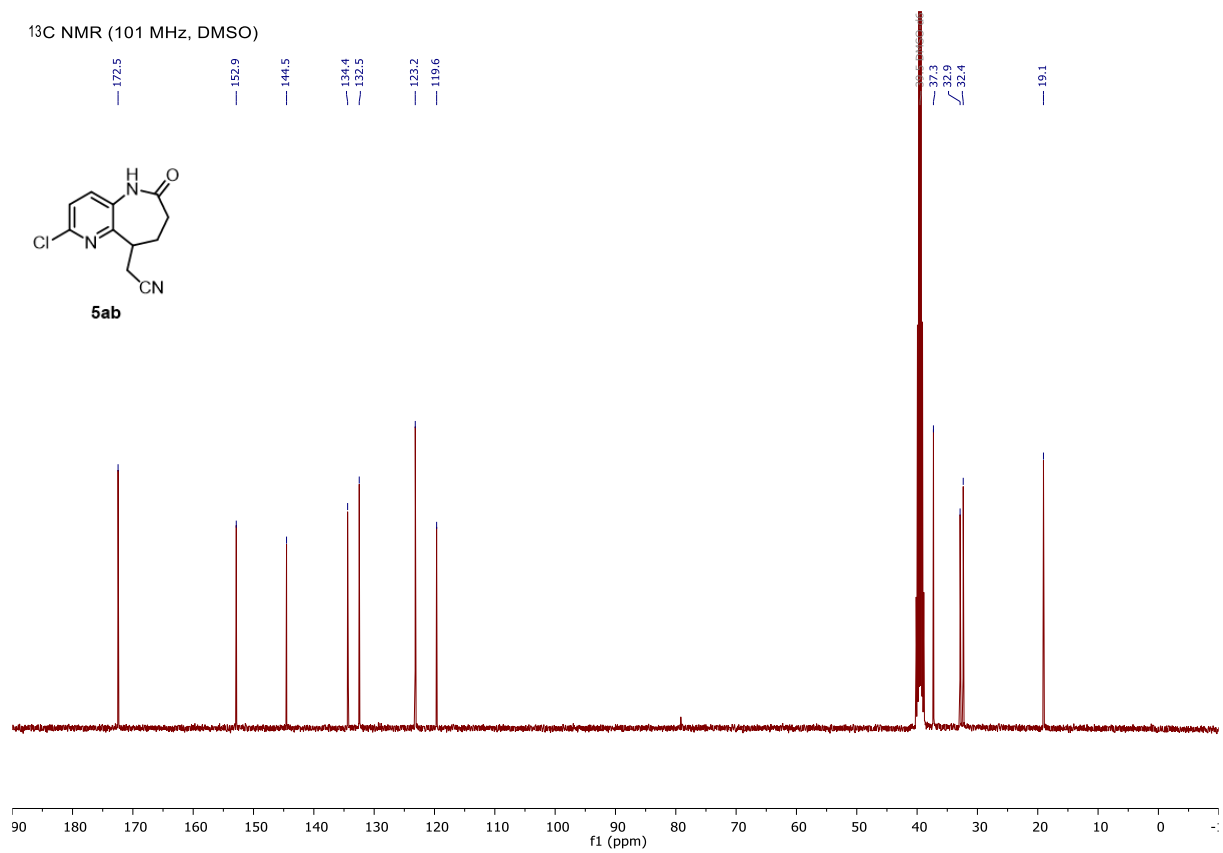
¹³C NMR (101 MHz, CDCl₃)



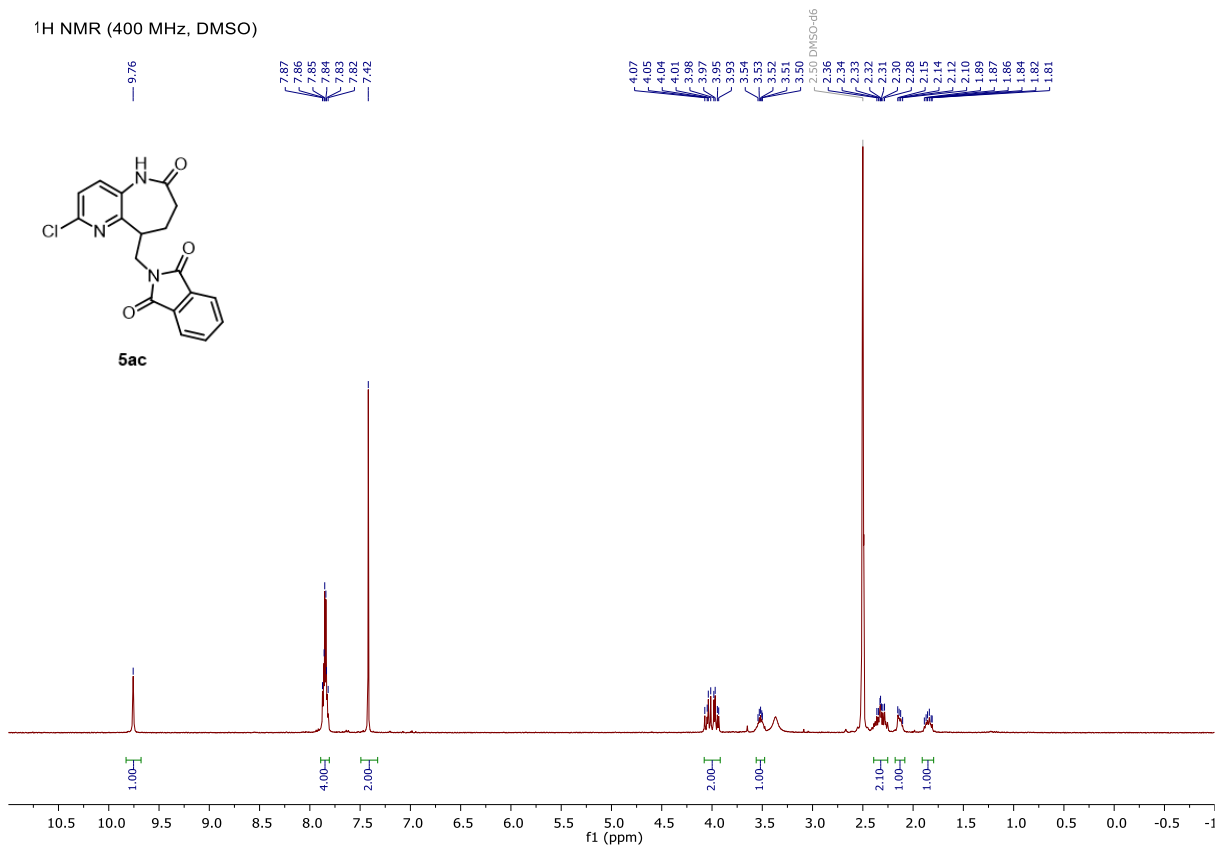
¹H NMR (400 MHz, DMSO)



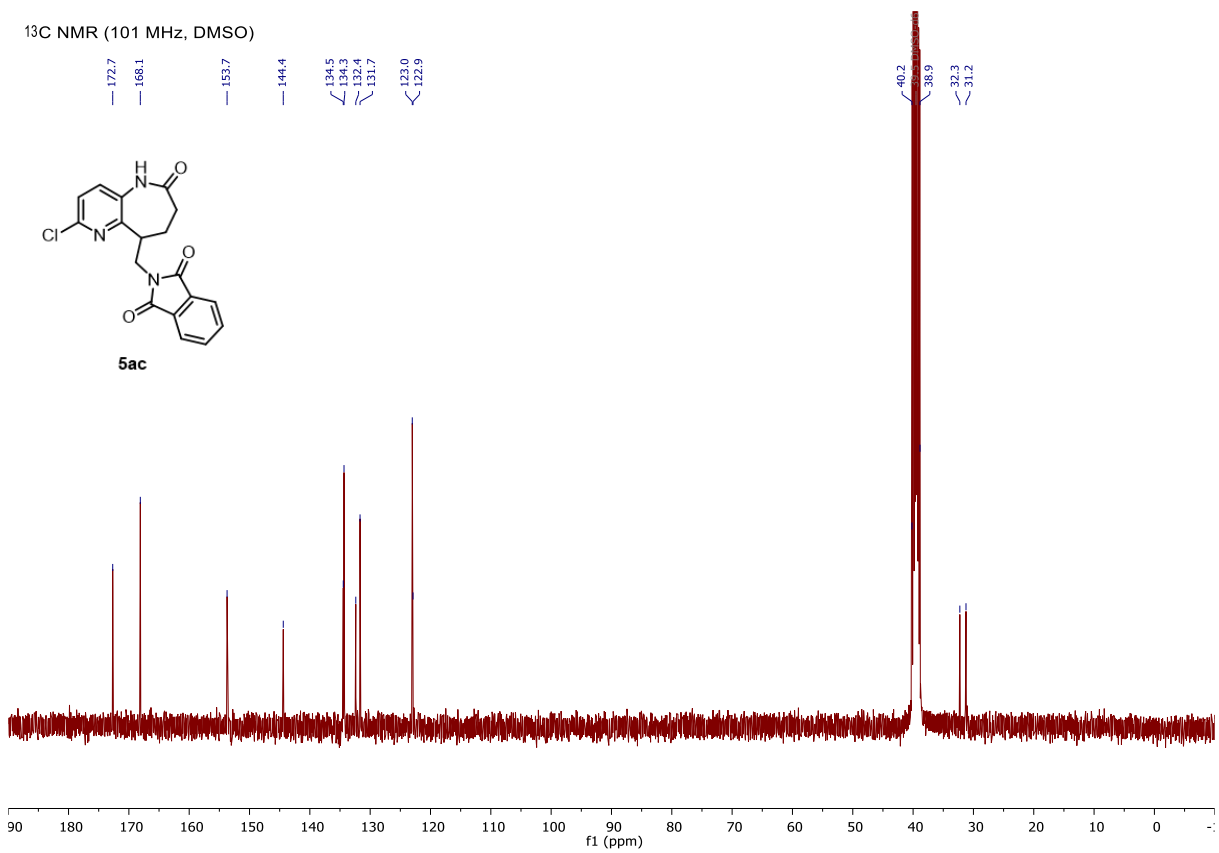
¹³C NMR (101 MHz, DMSO)

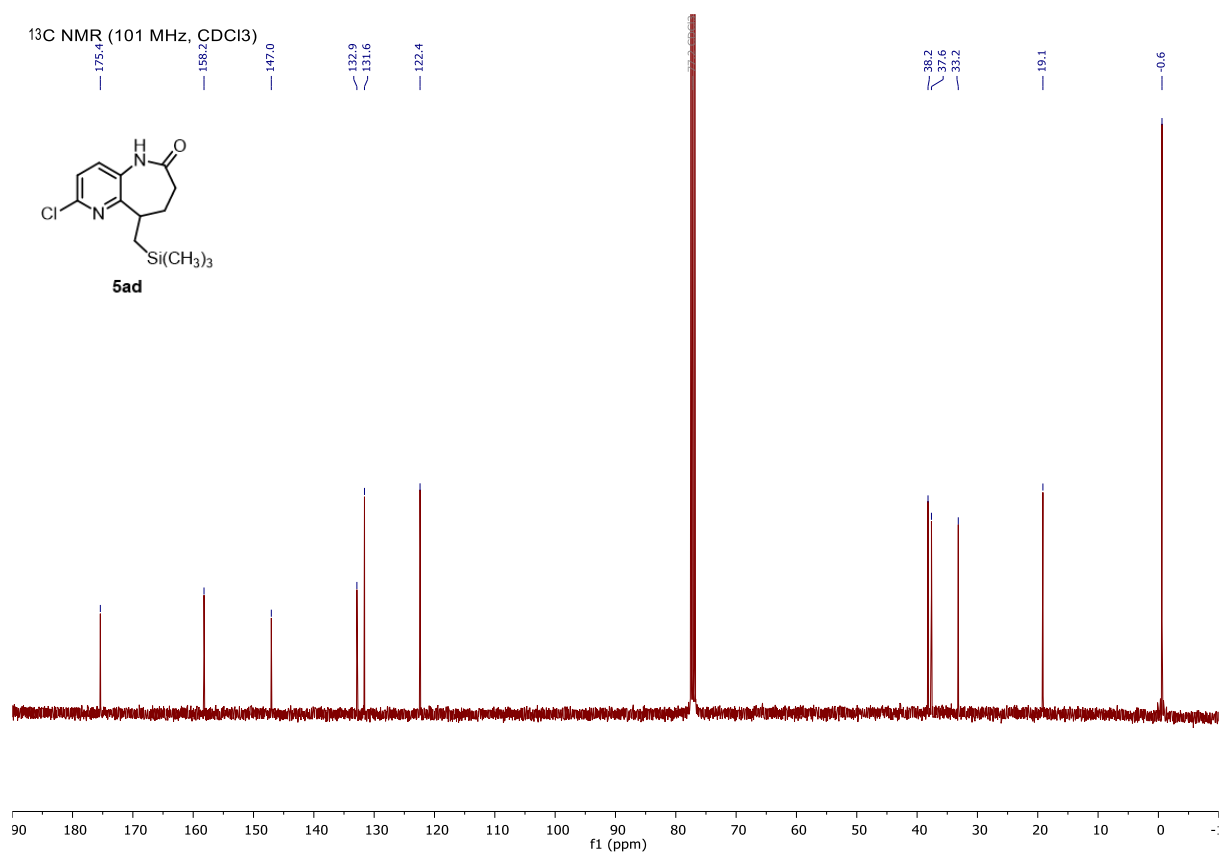
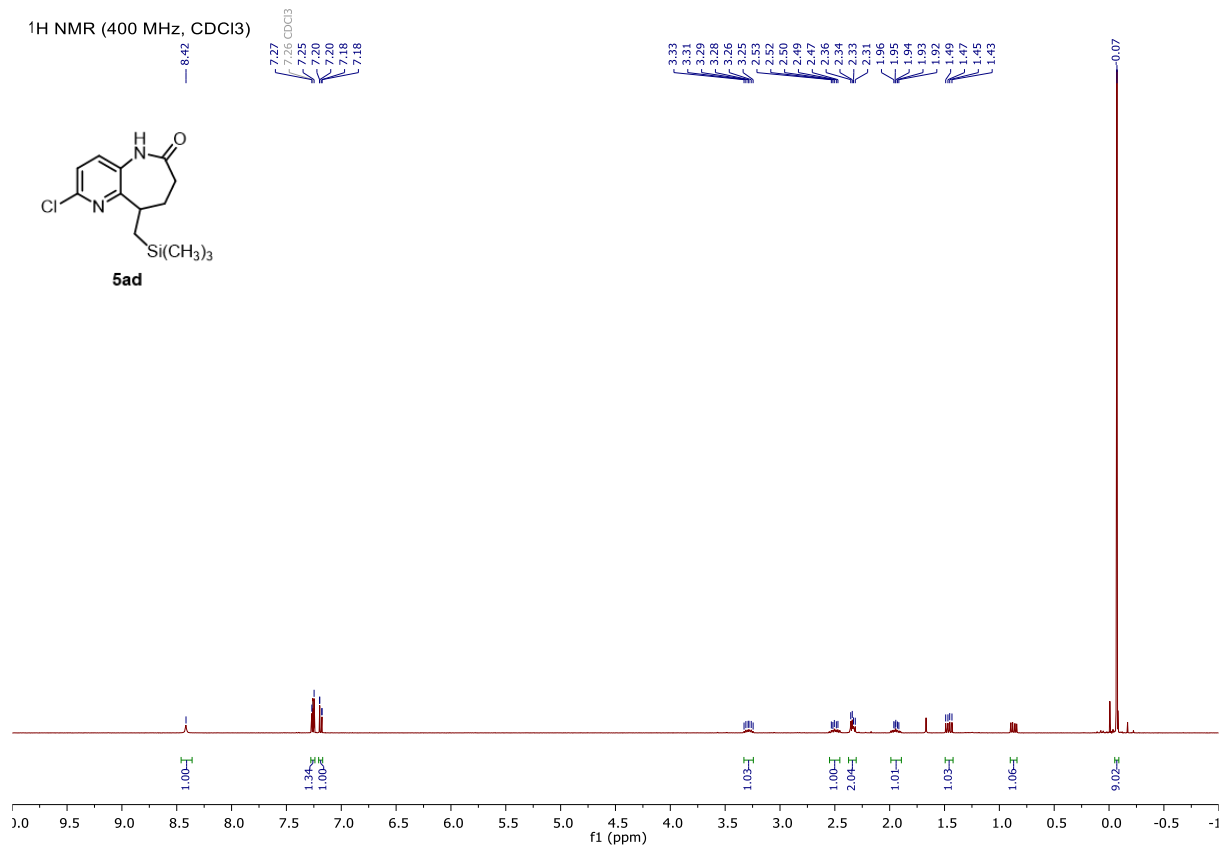


1H NMR (400 MHz, DMSO)

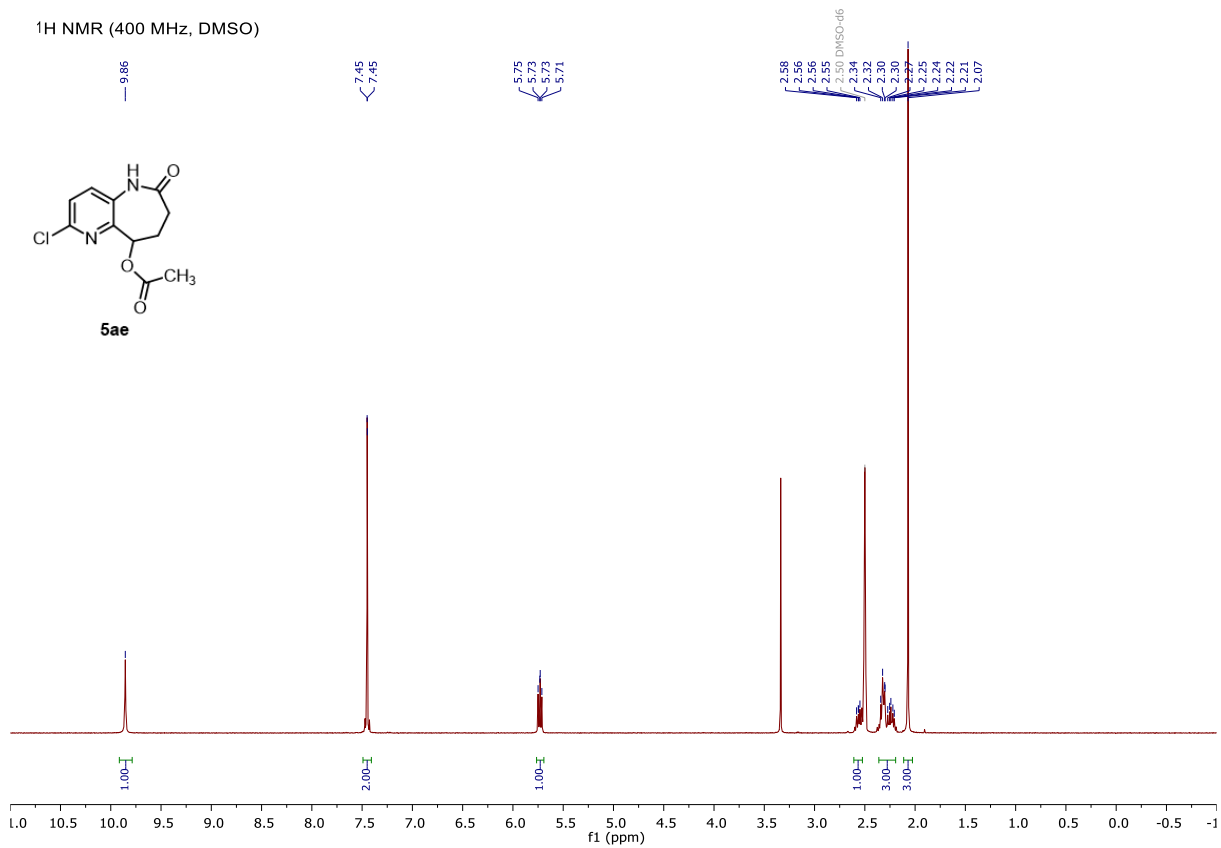


13C NMR (101 MHz, DMSO)

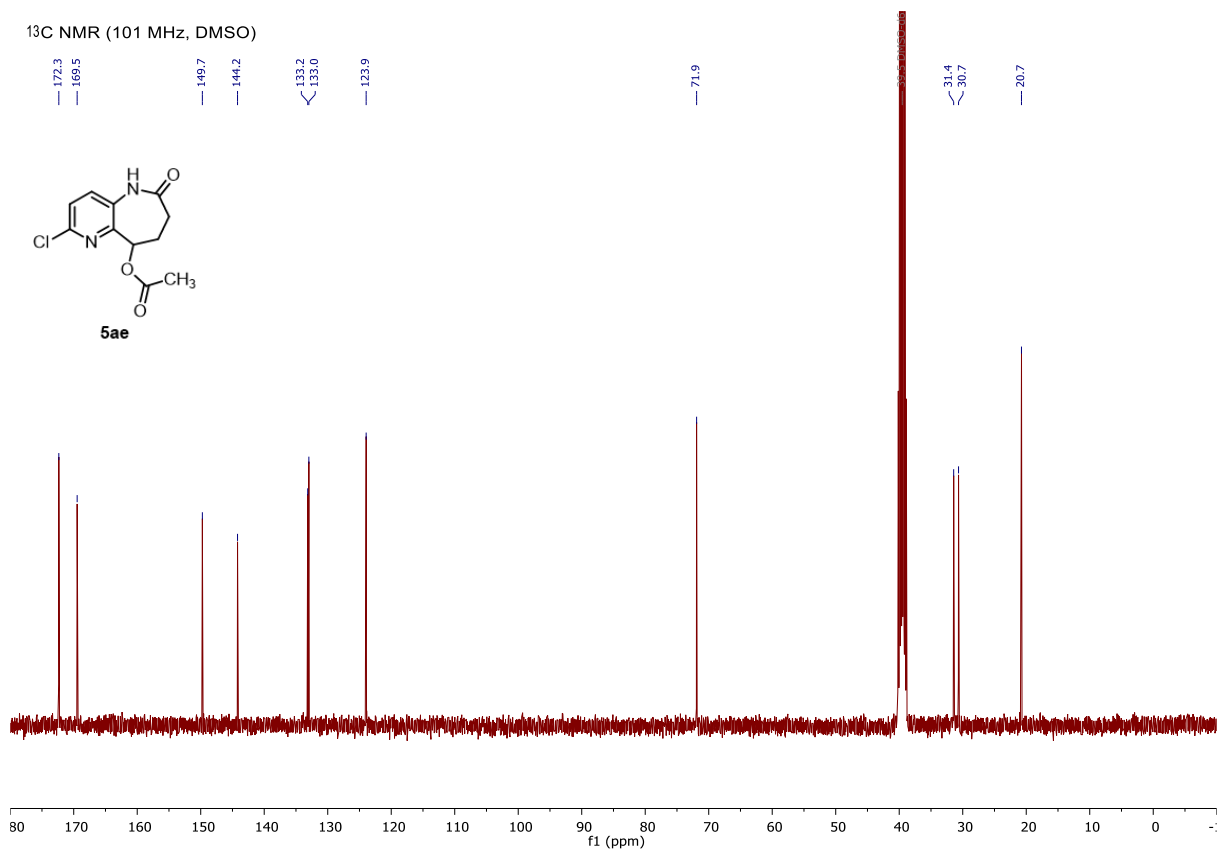




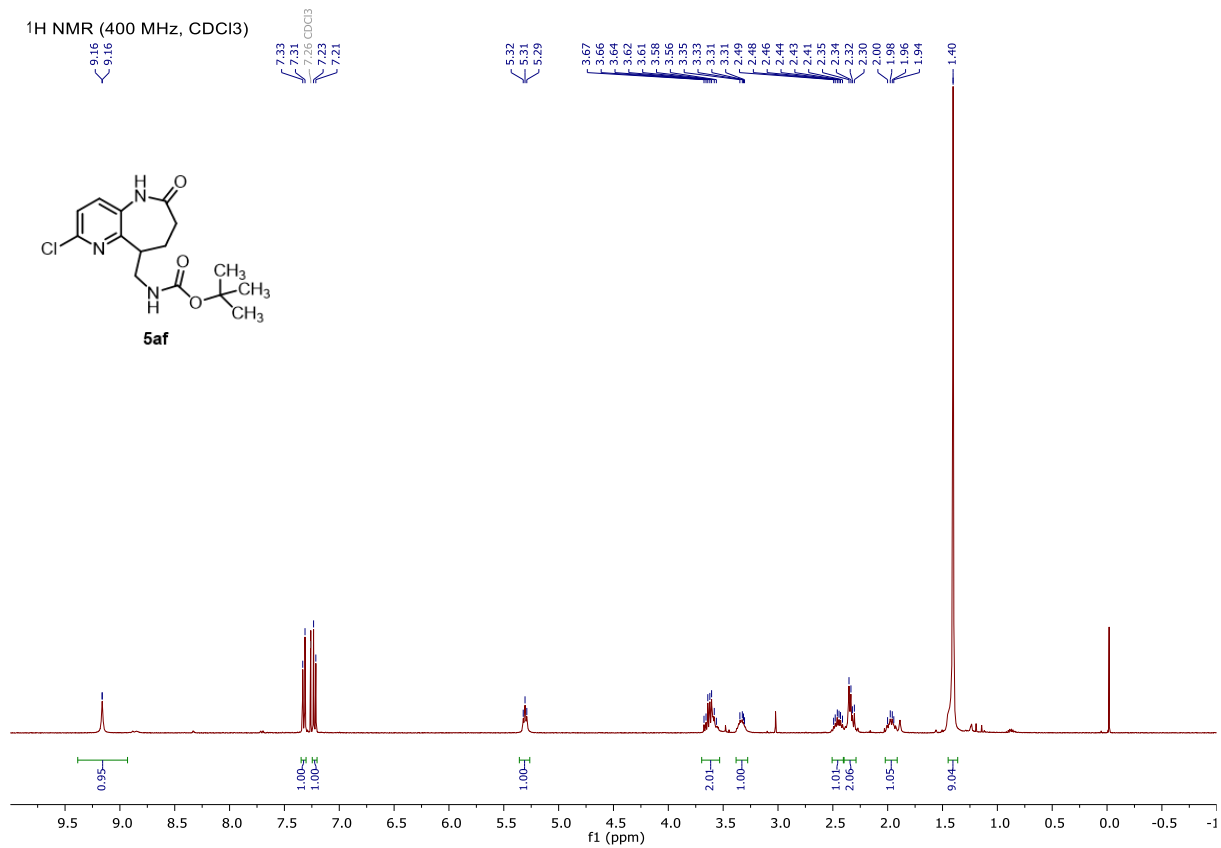
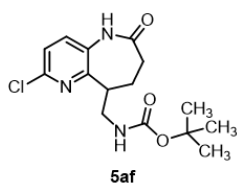
1H NMR (400 MHz, DMSO)



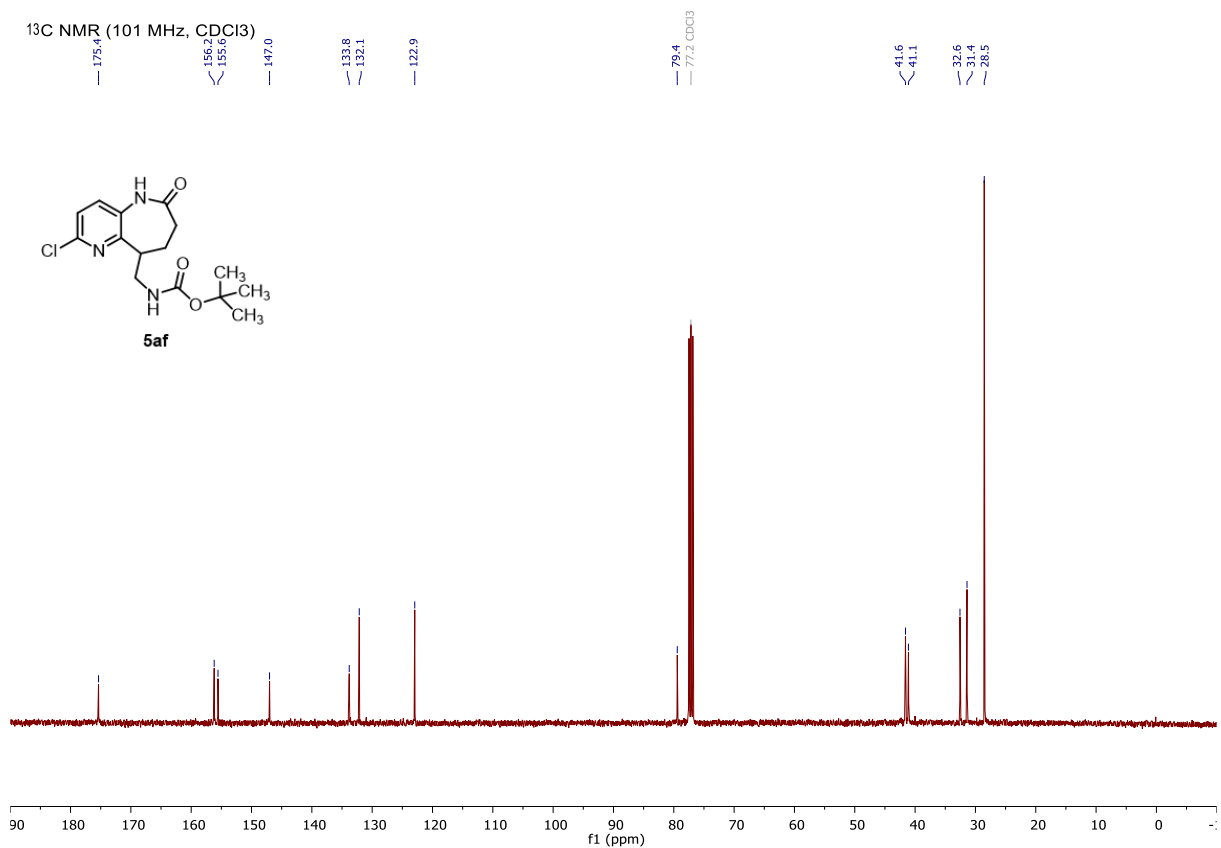
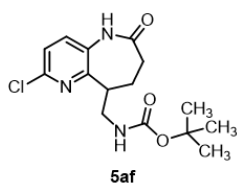
13C NMR (101 MHz, DMSO)



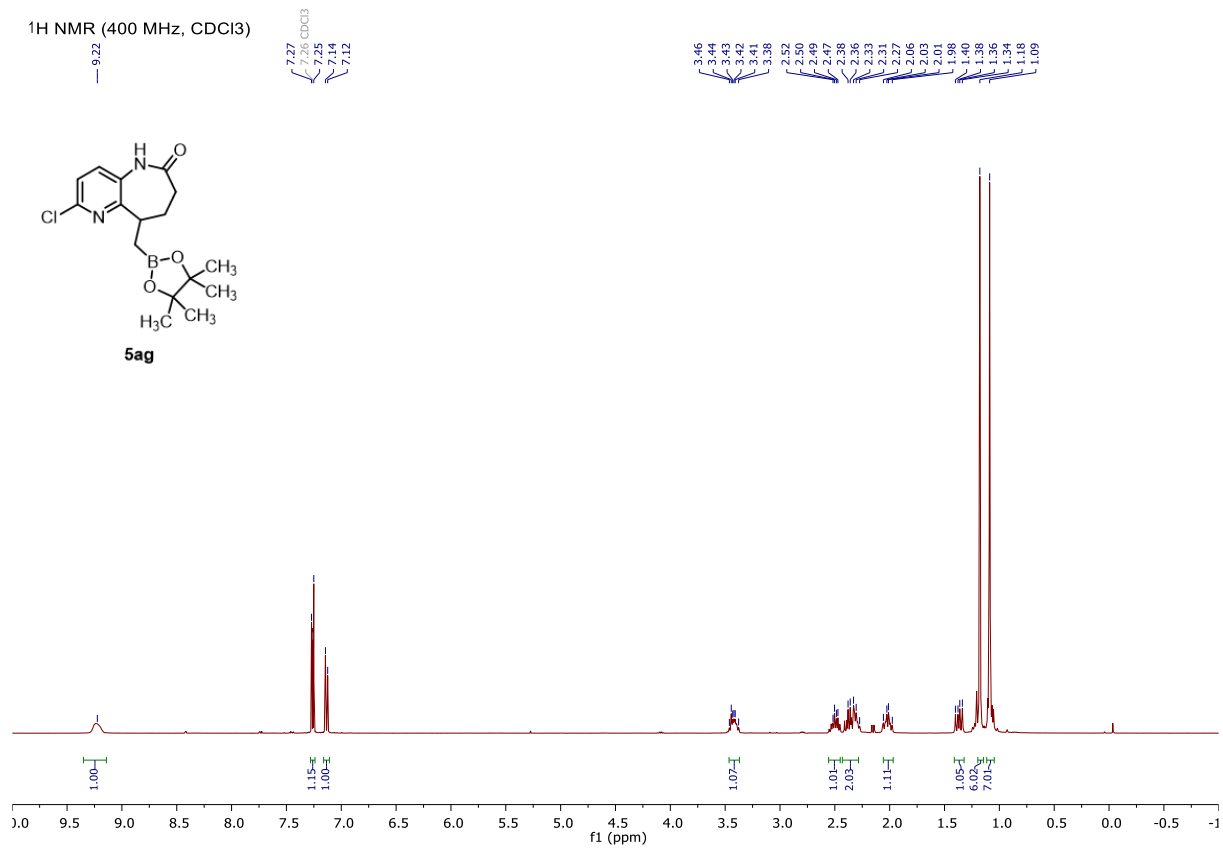
¹H NMR (400 MHz, CDCl₃)



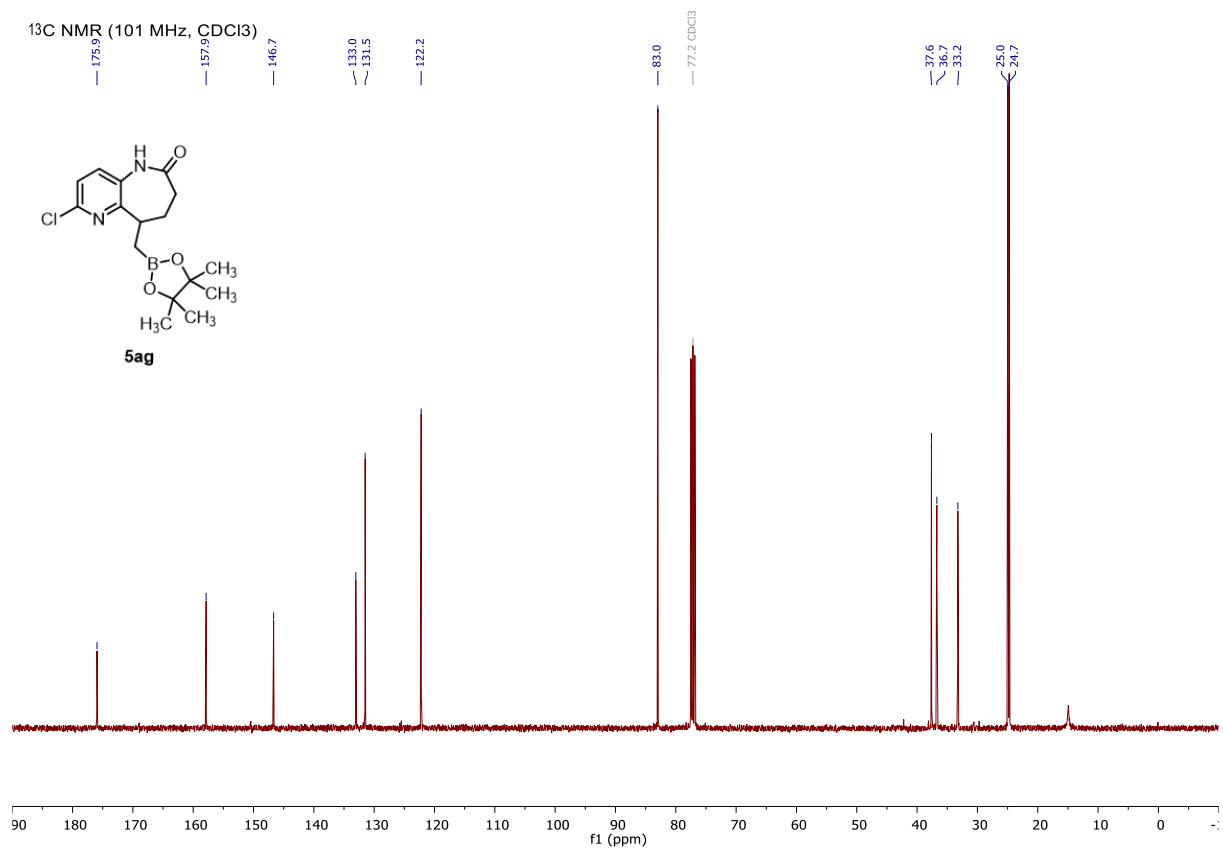
¹³C NMR (101 MHz, CDCl₃)

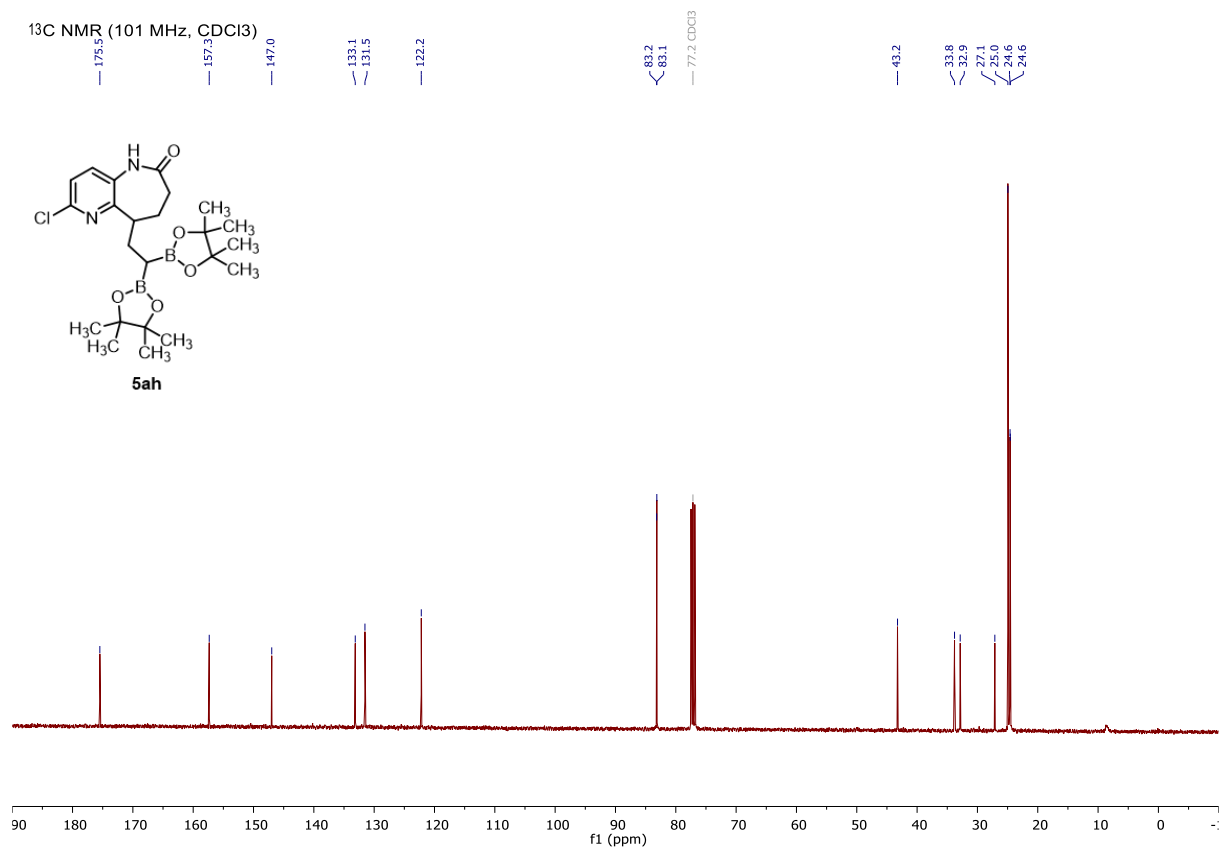
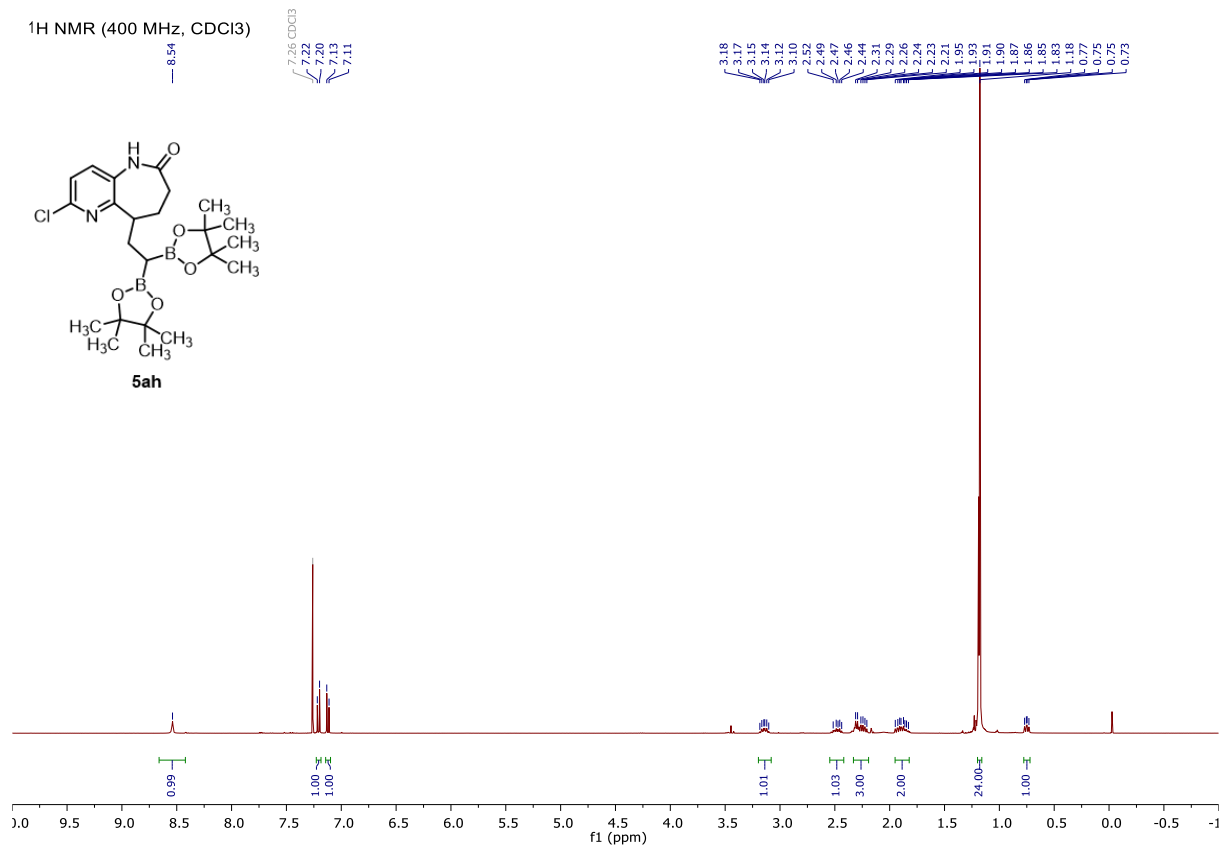


¹H NMR (400 MHz, CDCl₃)

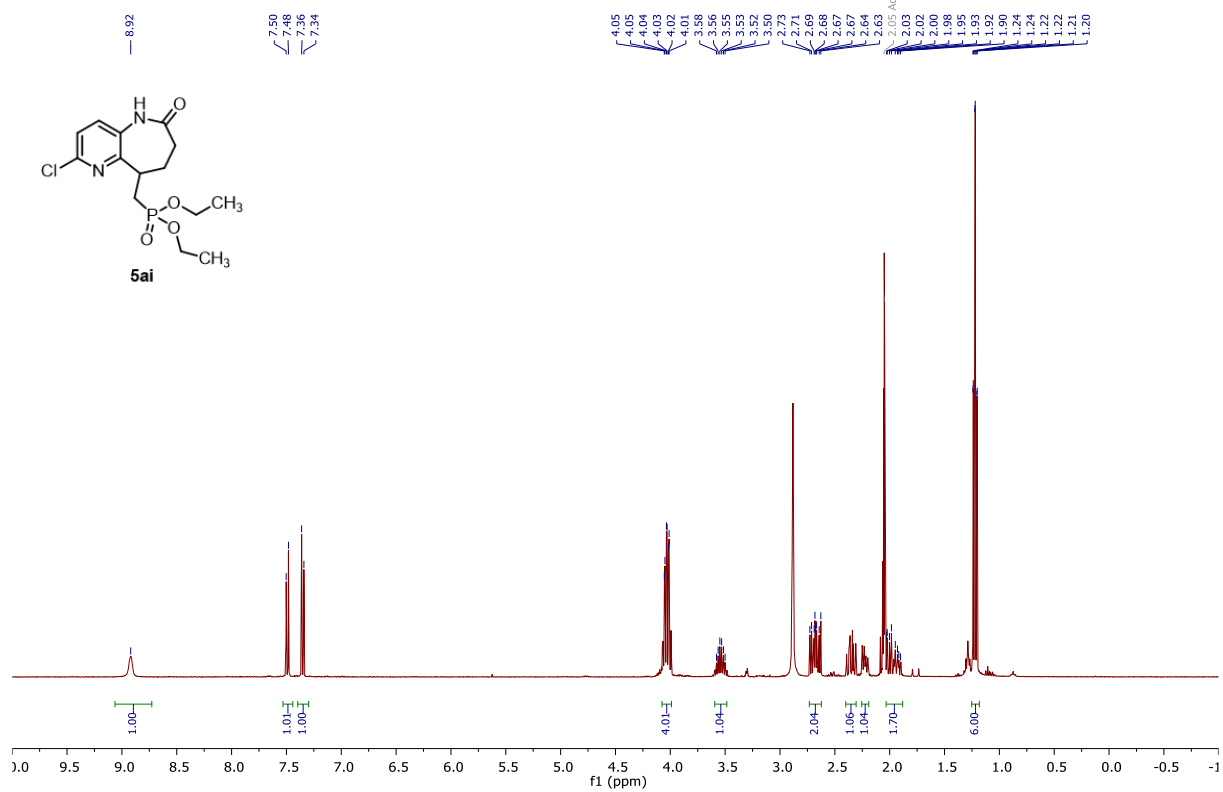


¹³C NMR (101 MHz, CDCl₃)

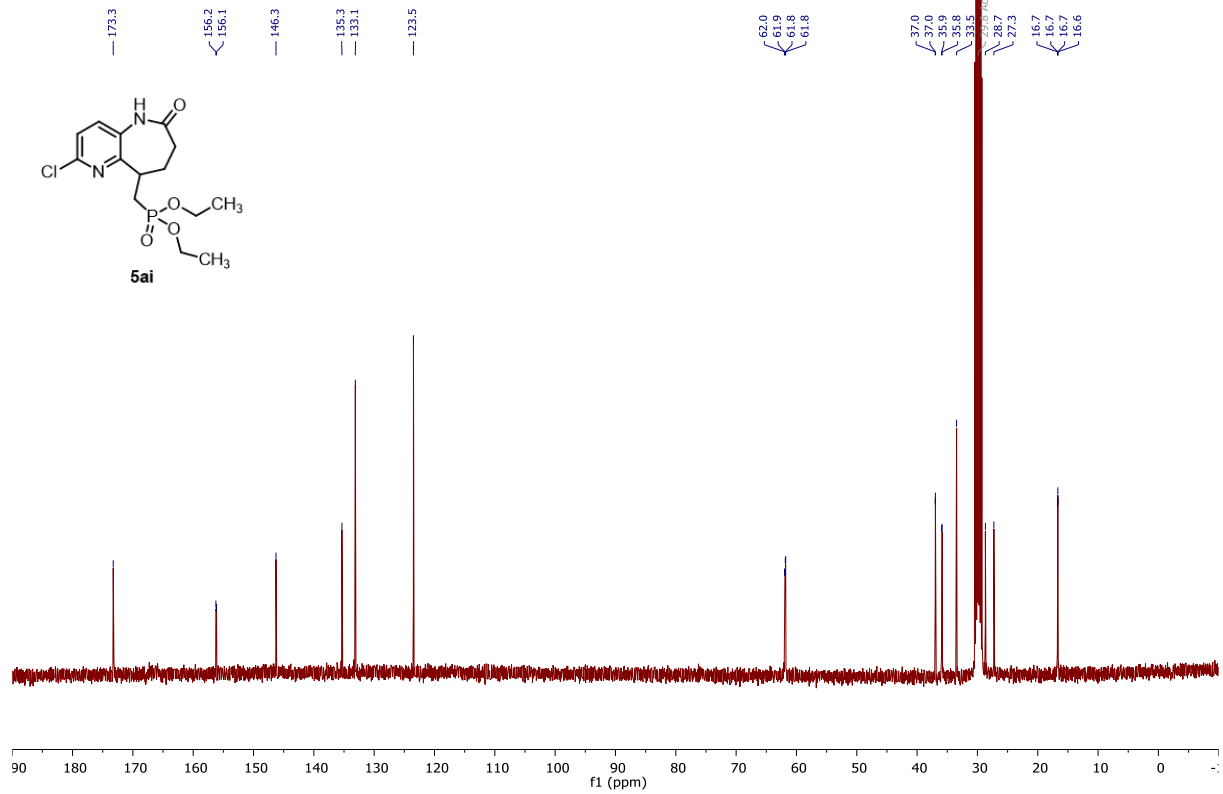




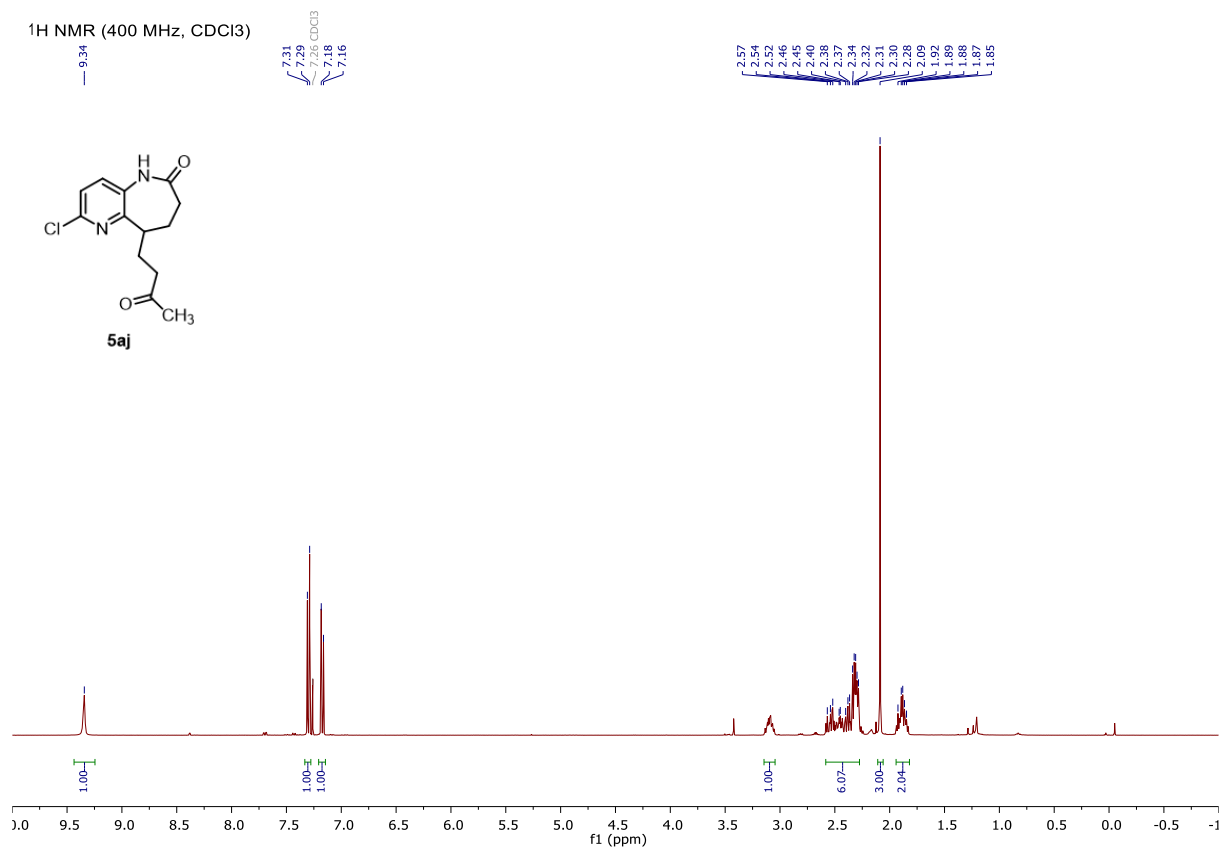
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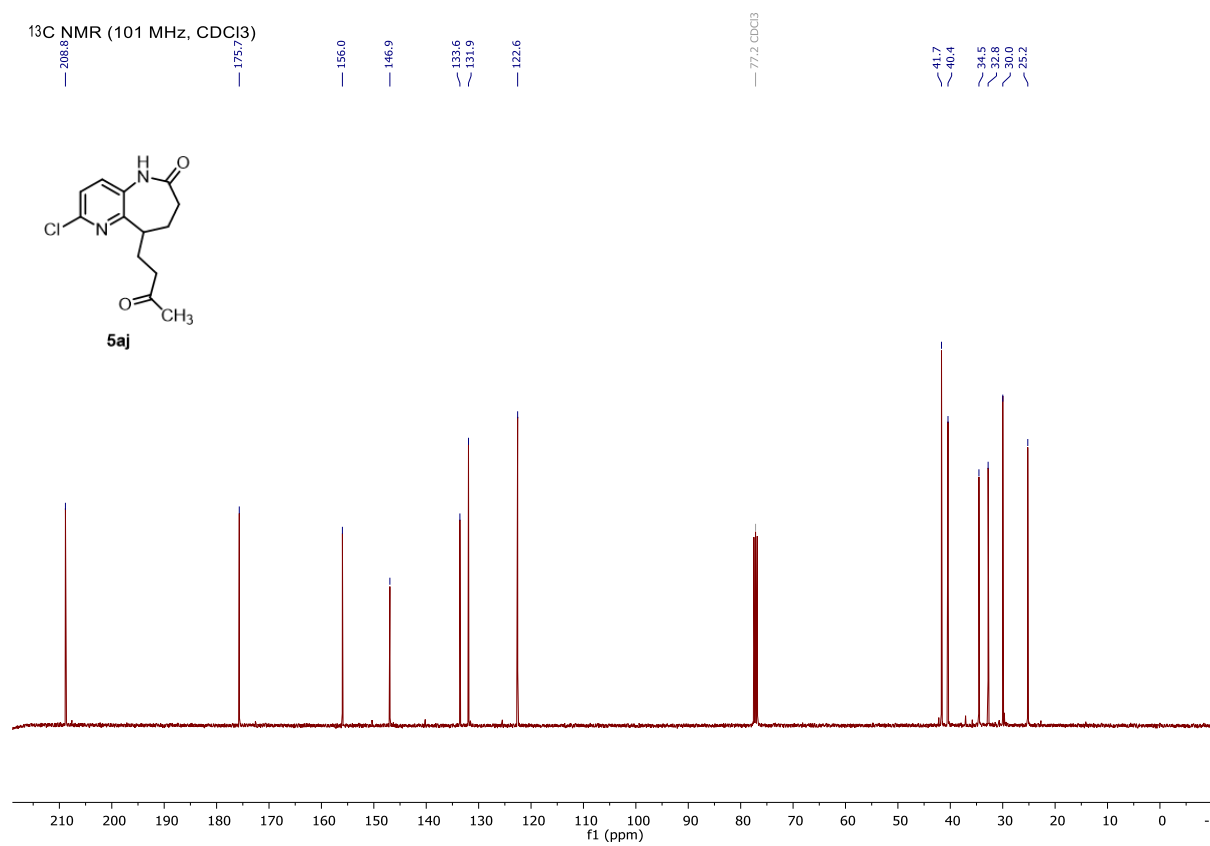
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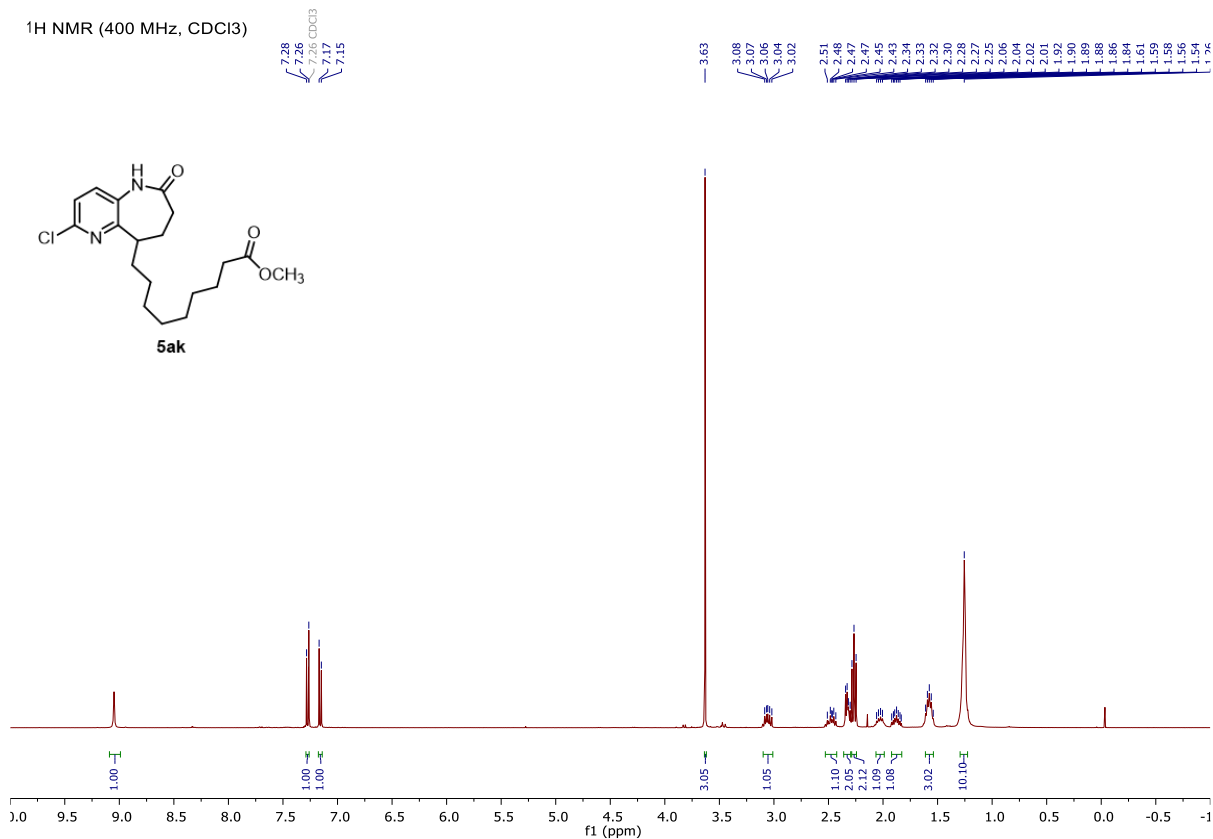
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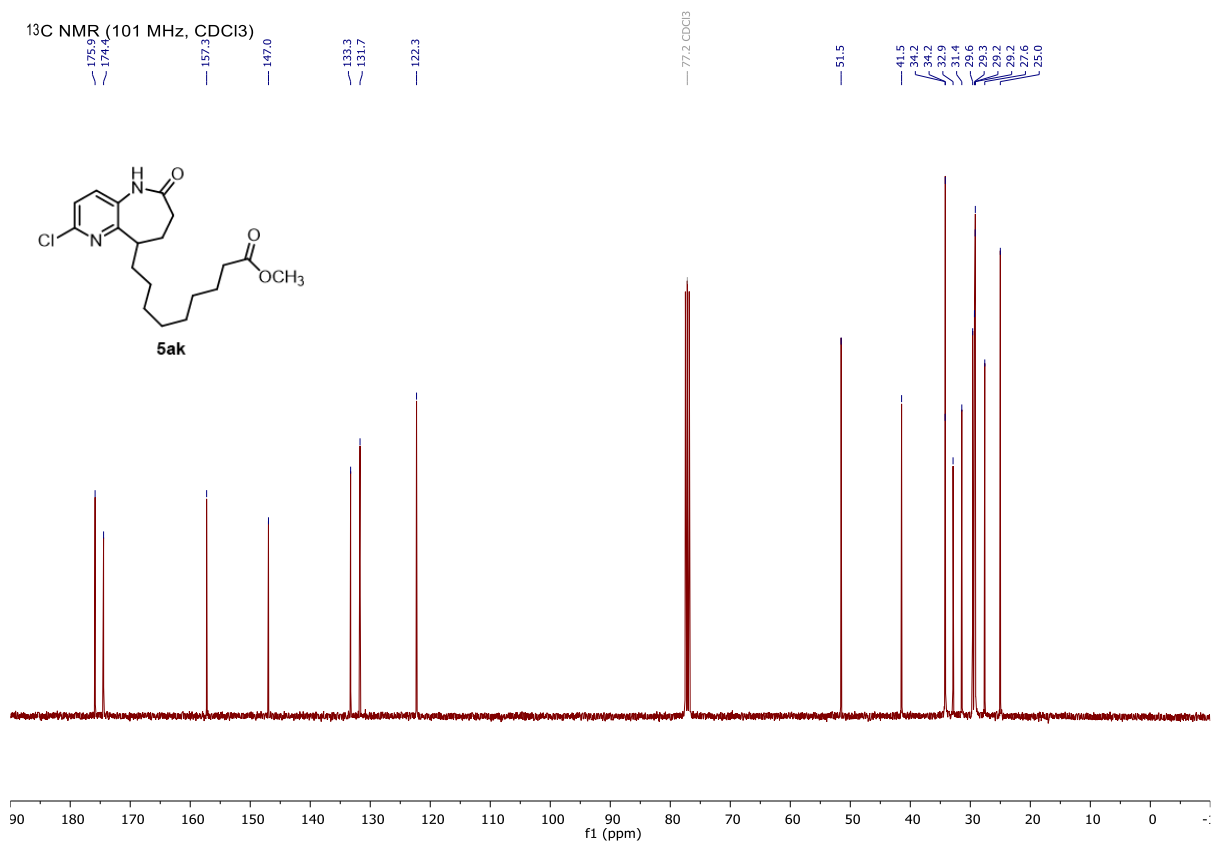
¹³C NMR (101 MHz, CDCl₃)

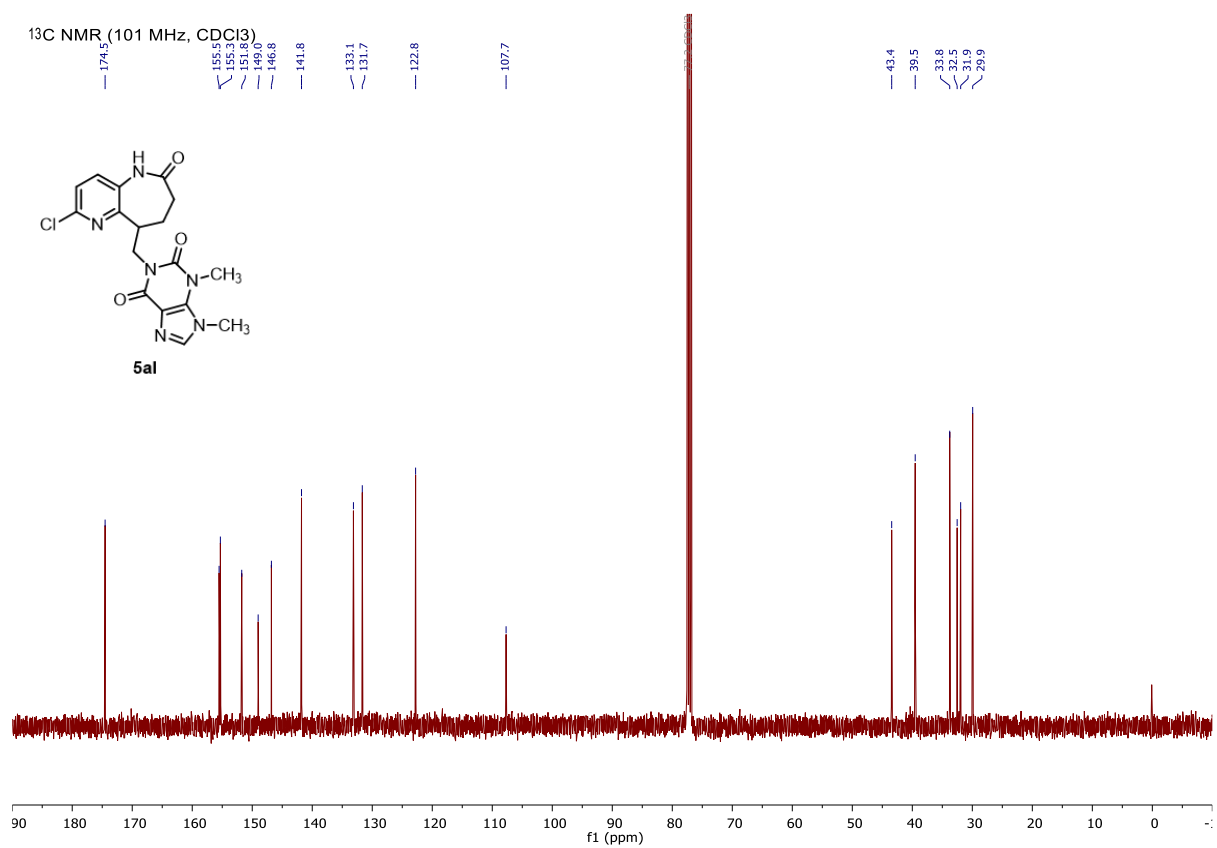
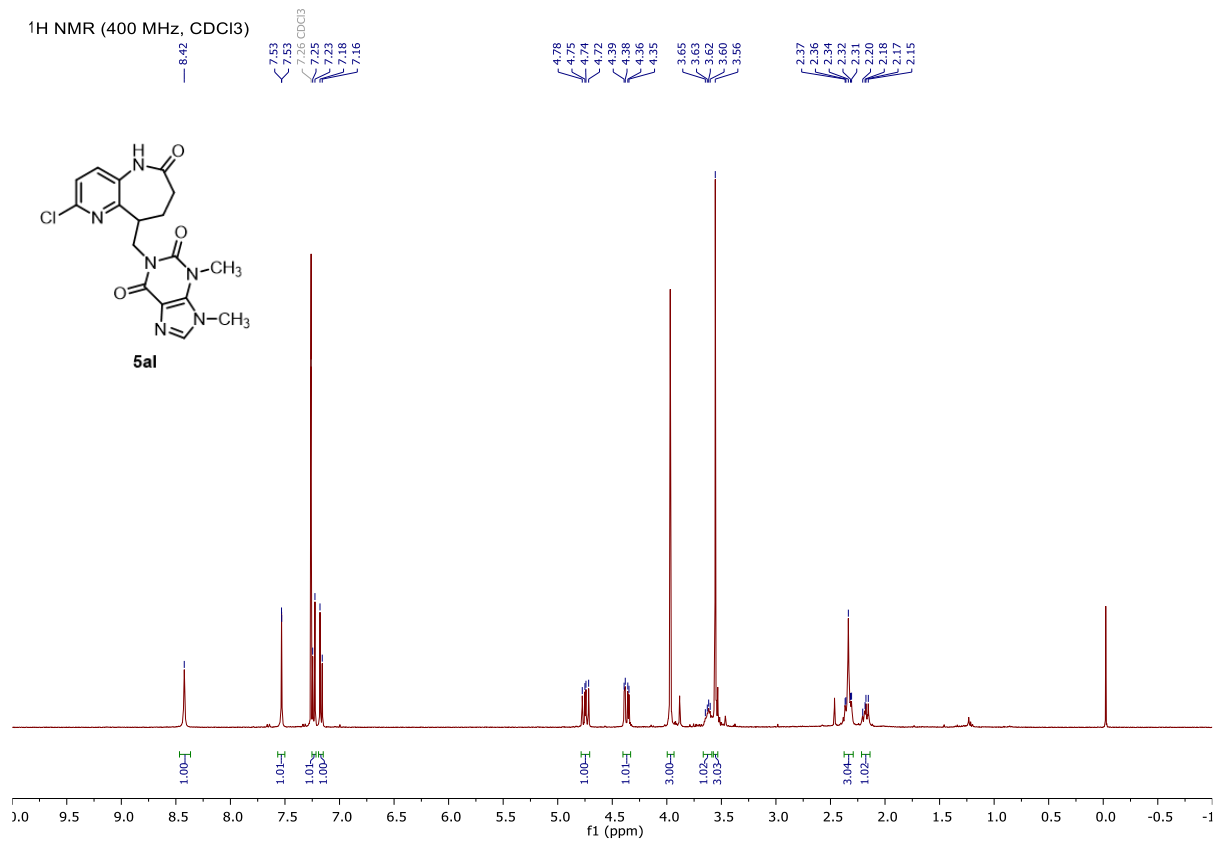


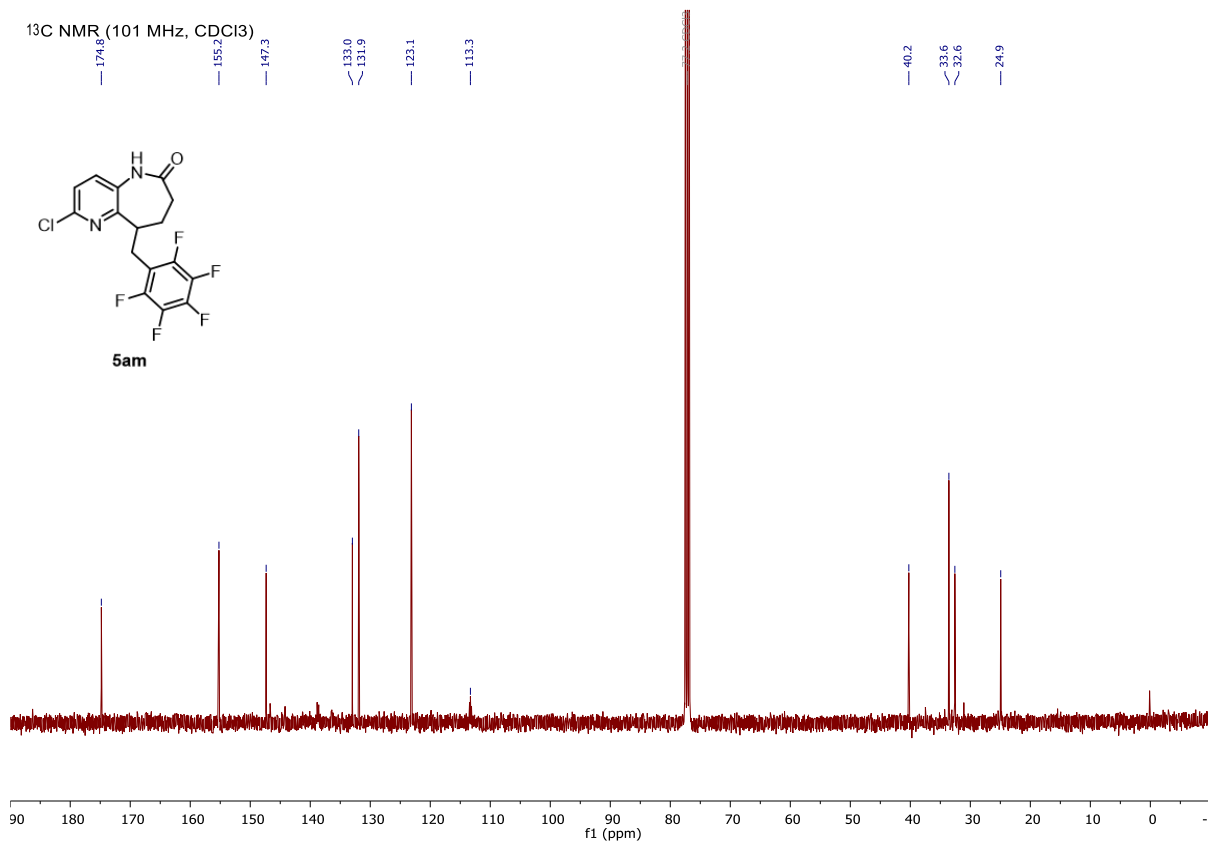
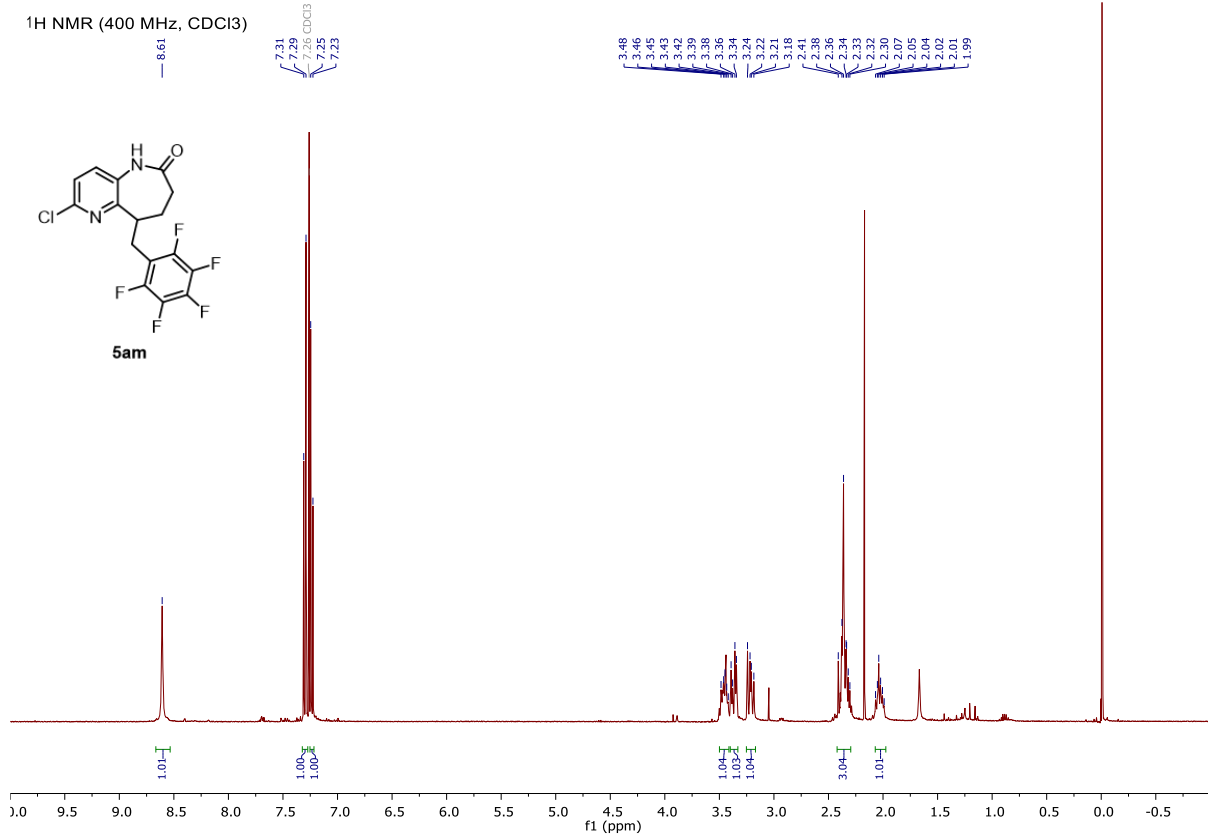
¹H NMR (400 MHz, CDCl₃)

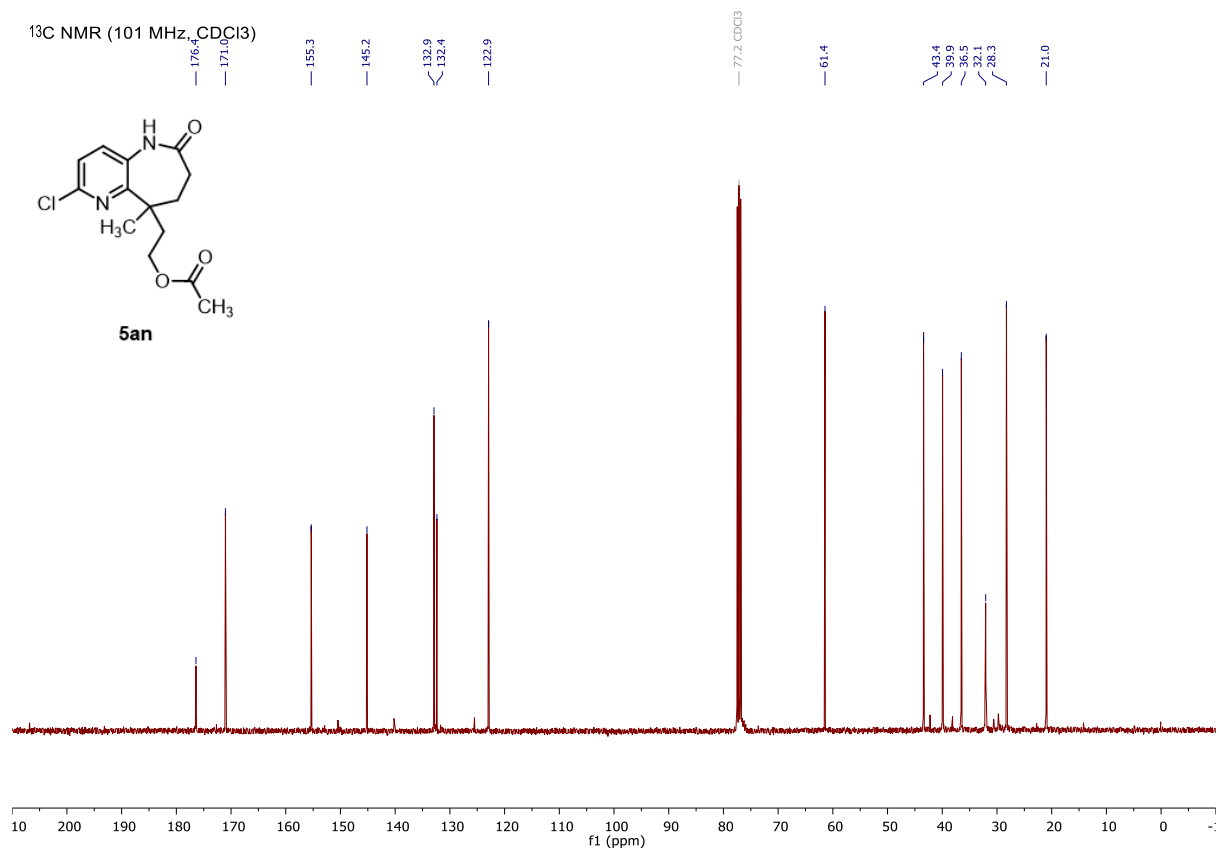
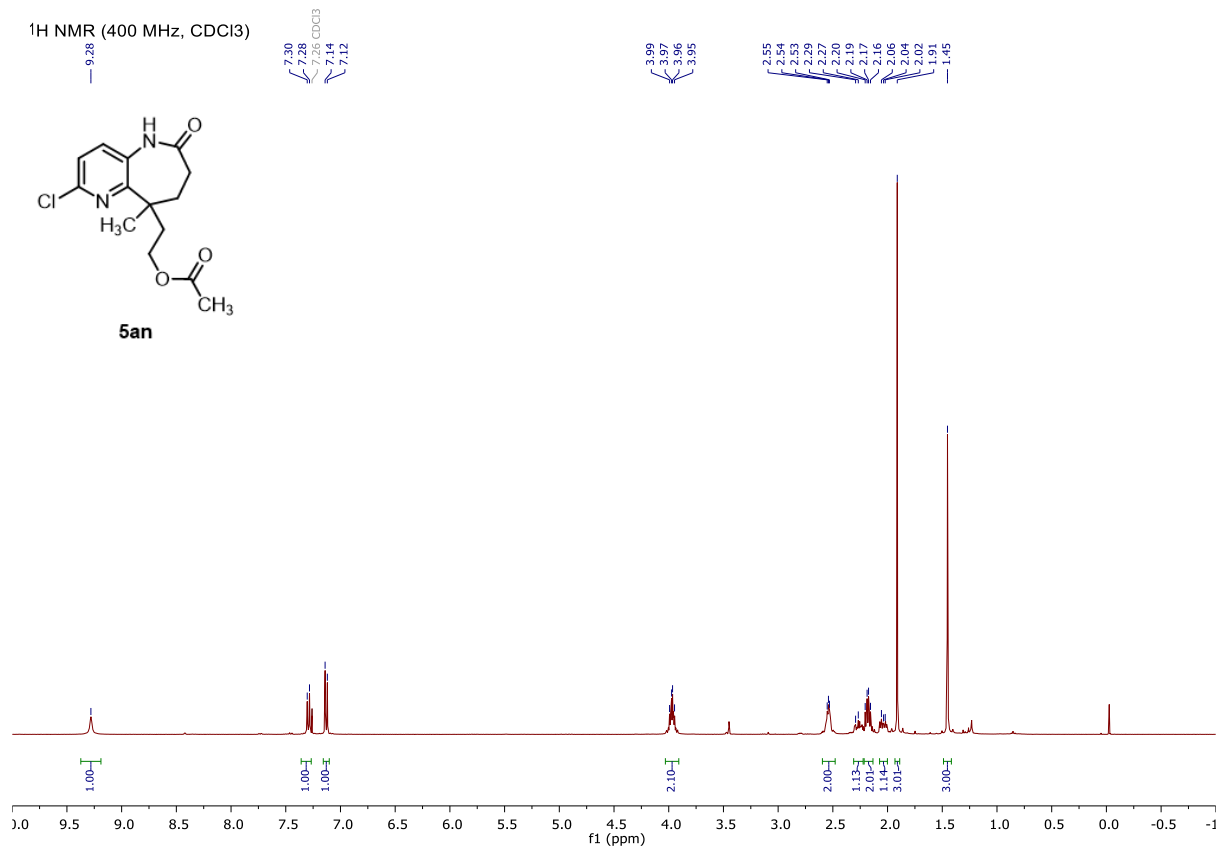


¹³C NMR (101 MHz, CDCl₃)

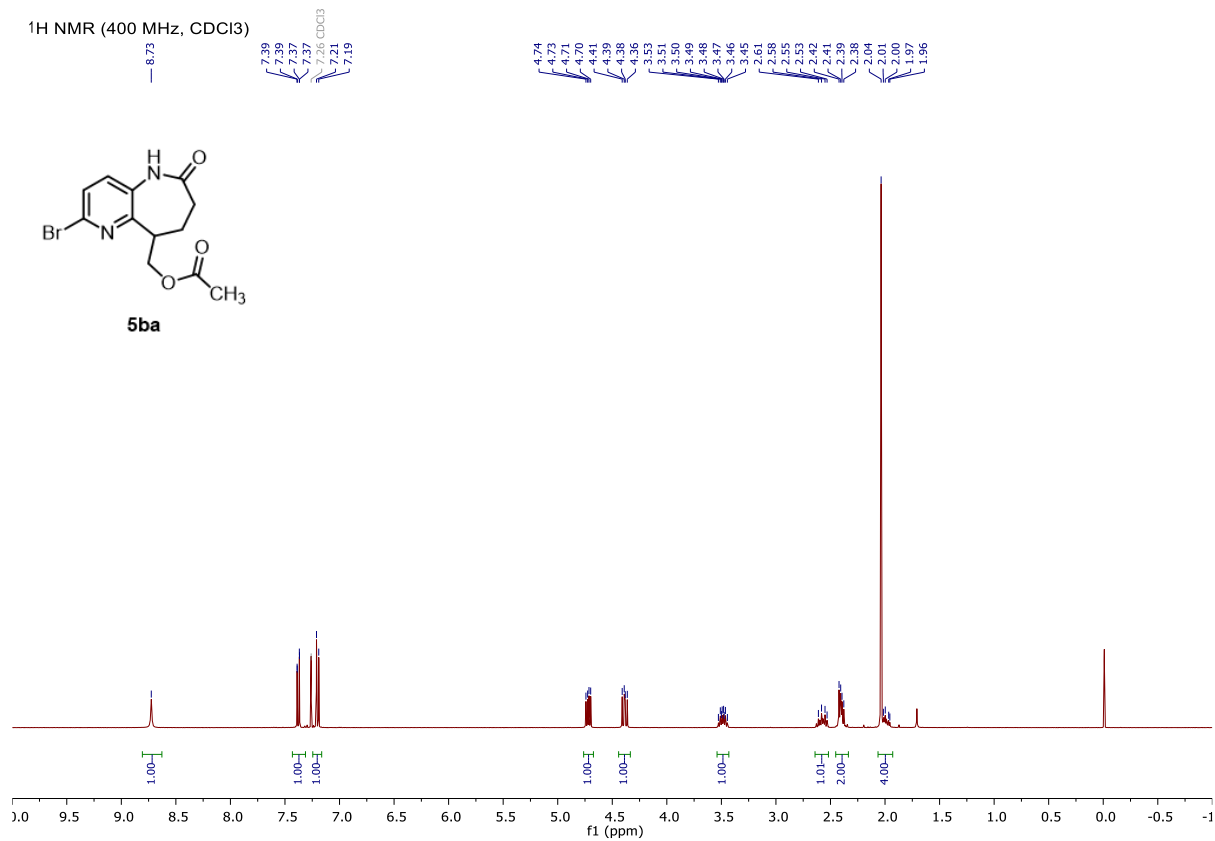
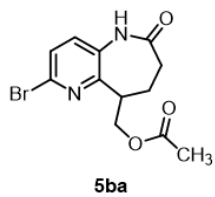




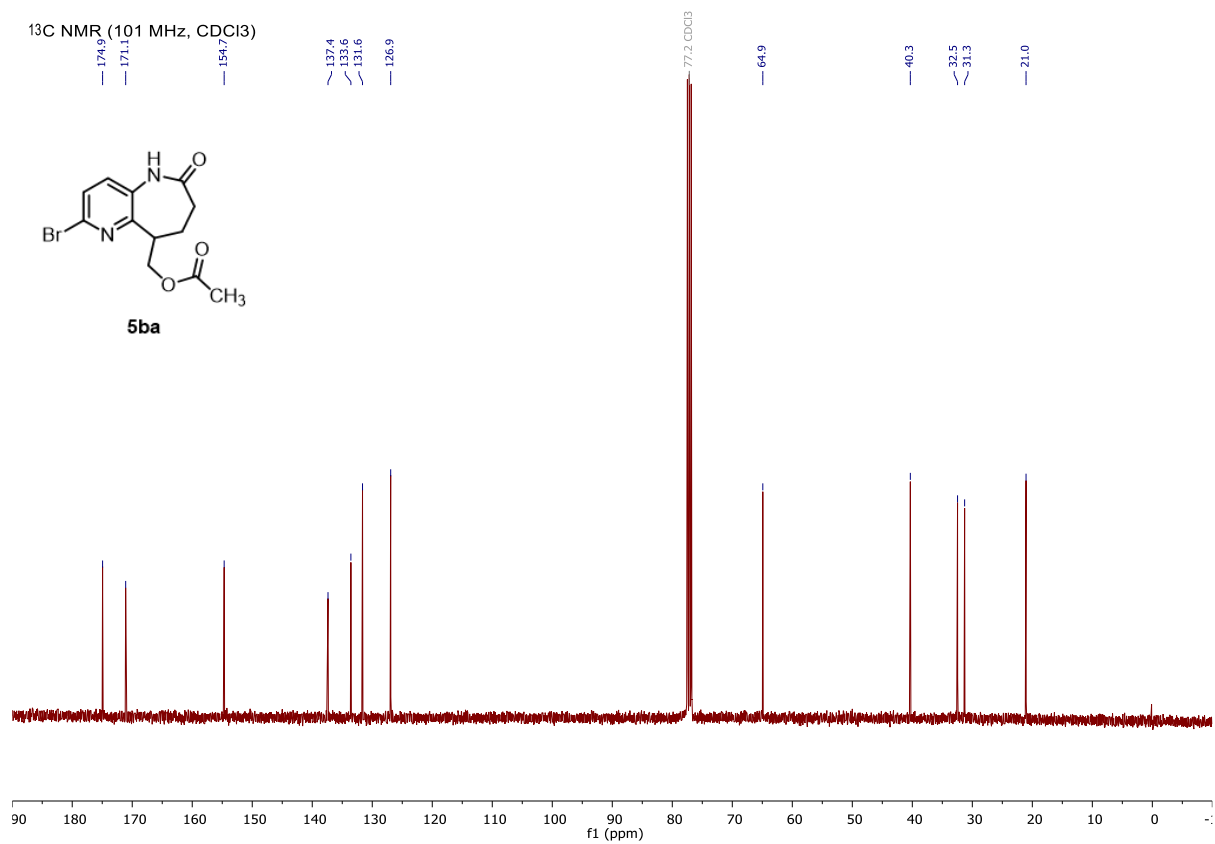
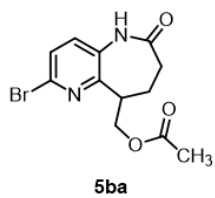




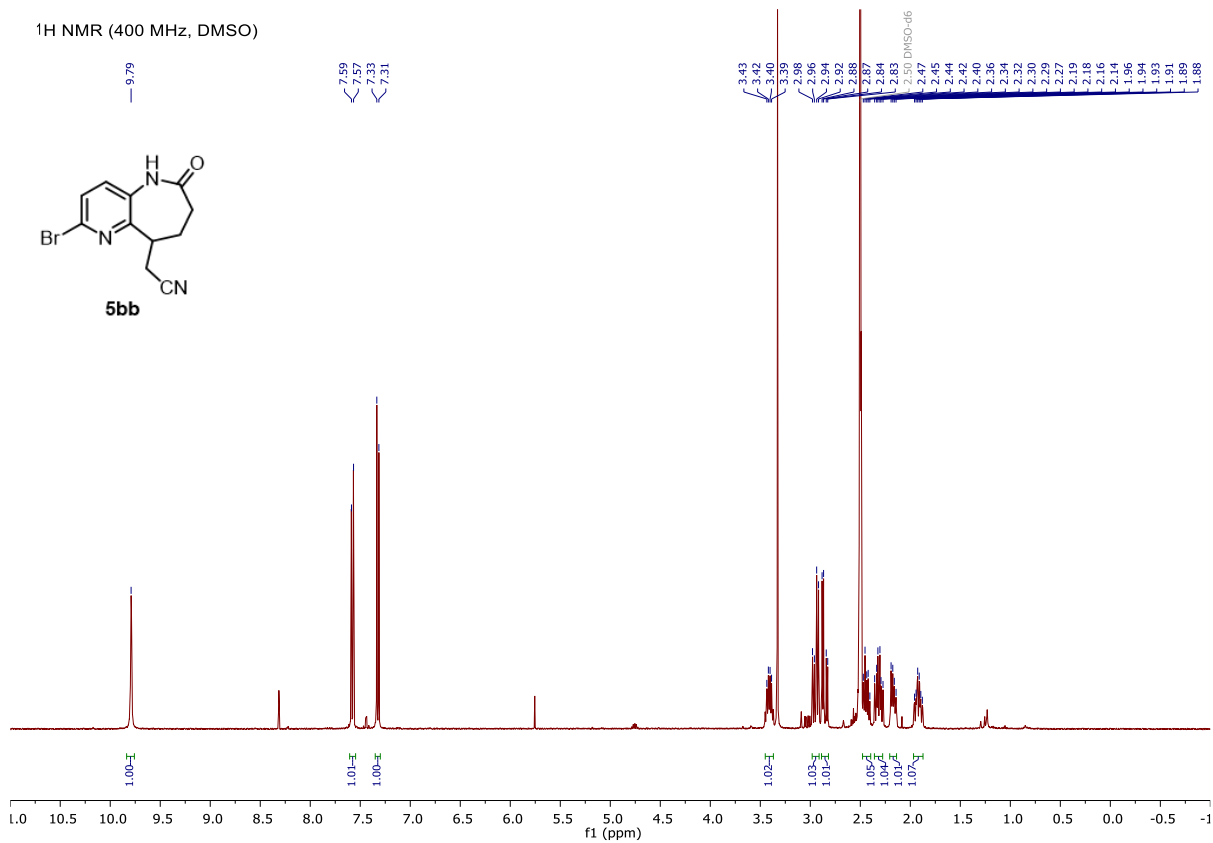
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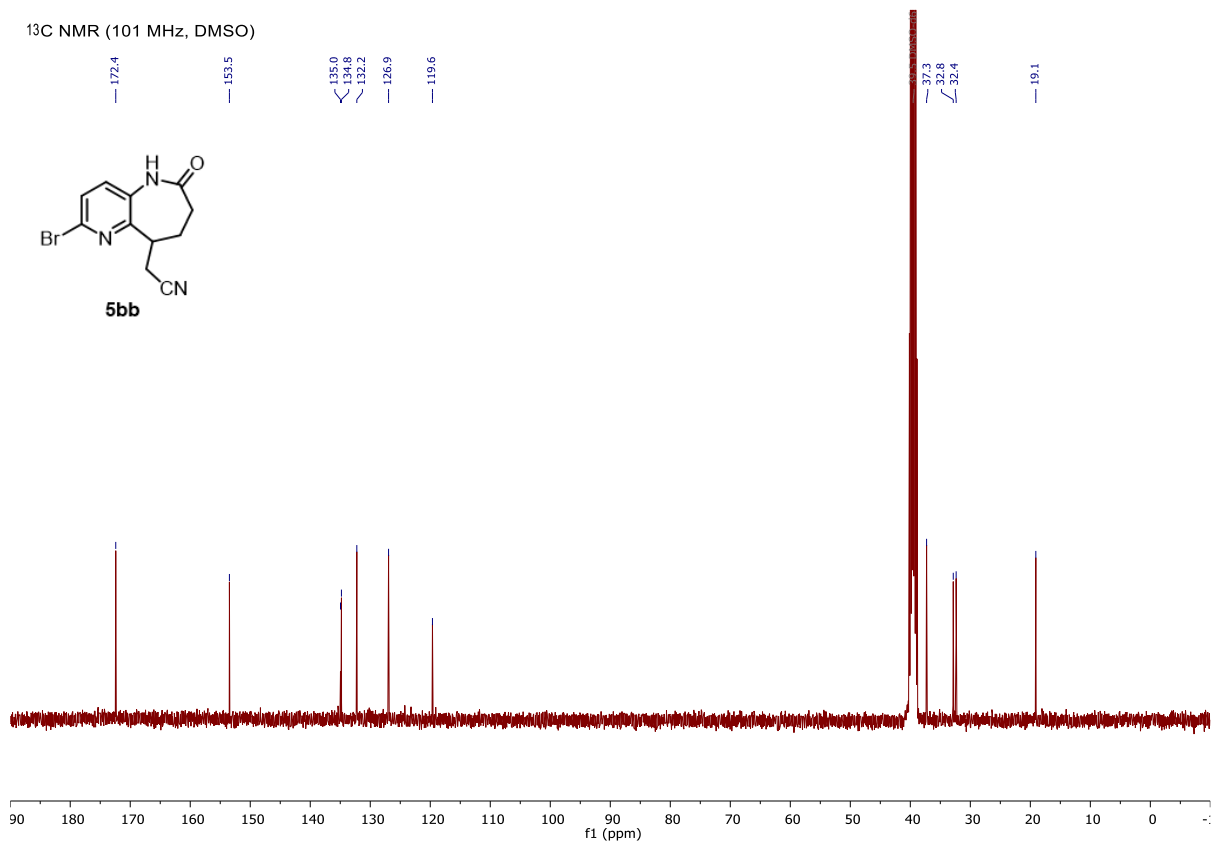
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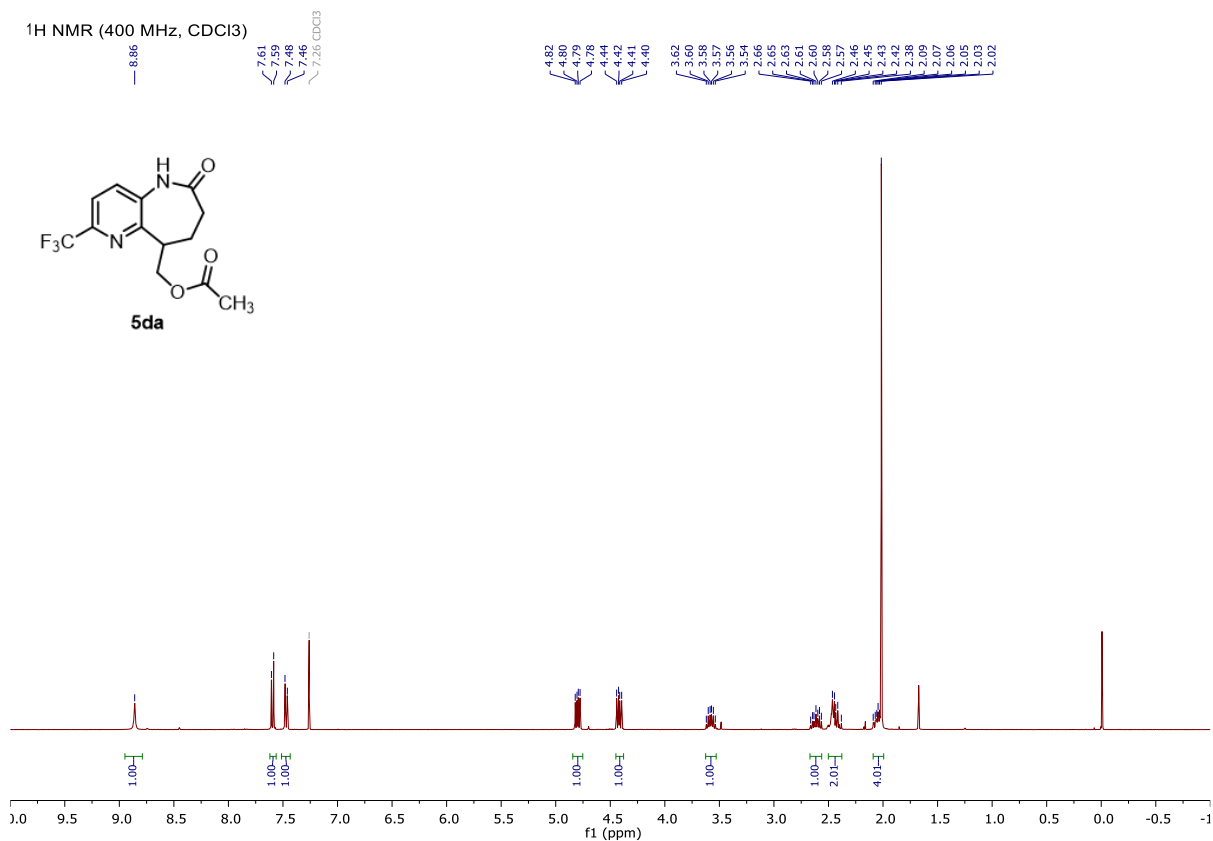
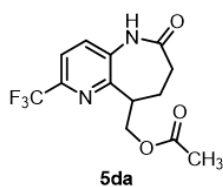
¹H NMR (400 MHz, DMSO)



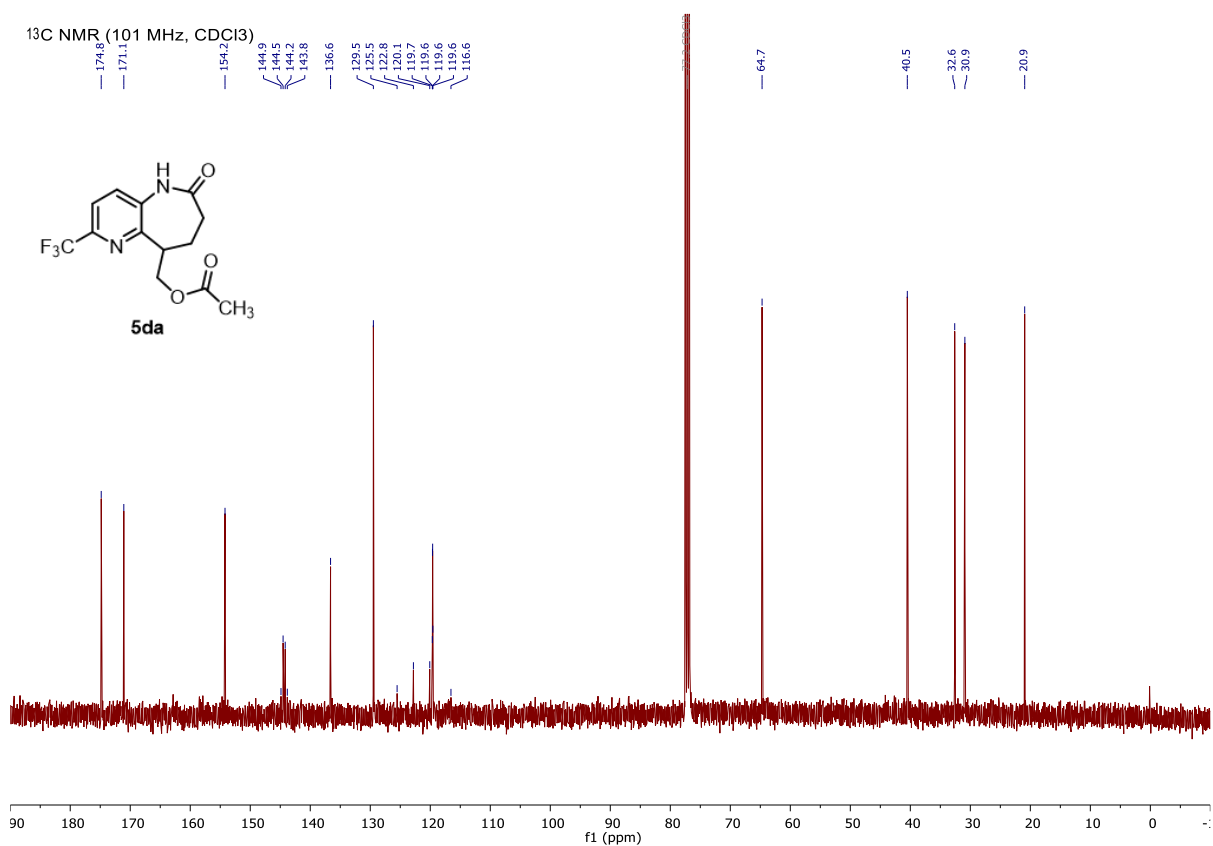
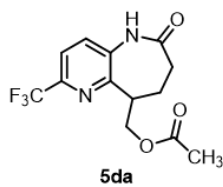
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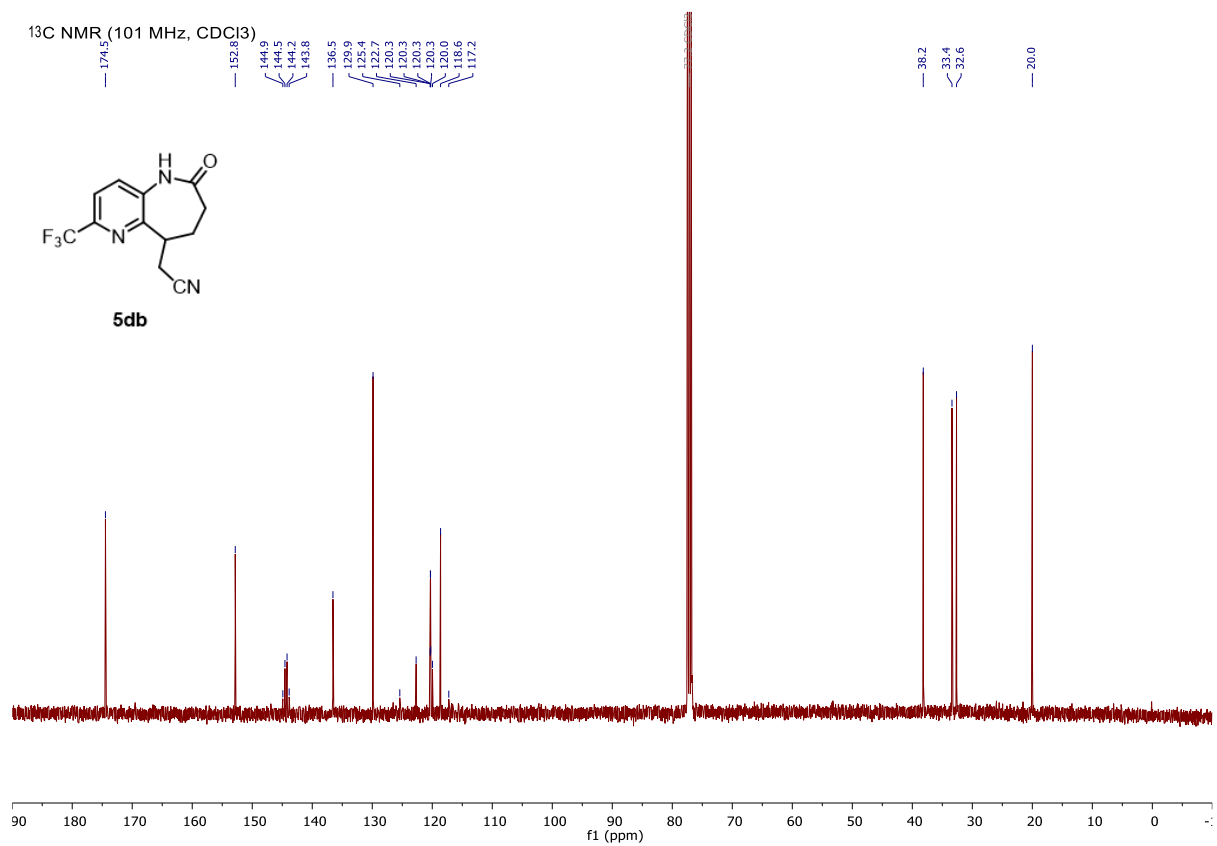
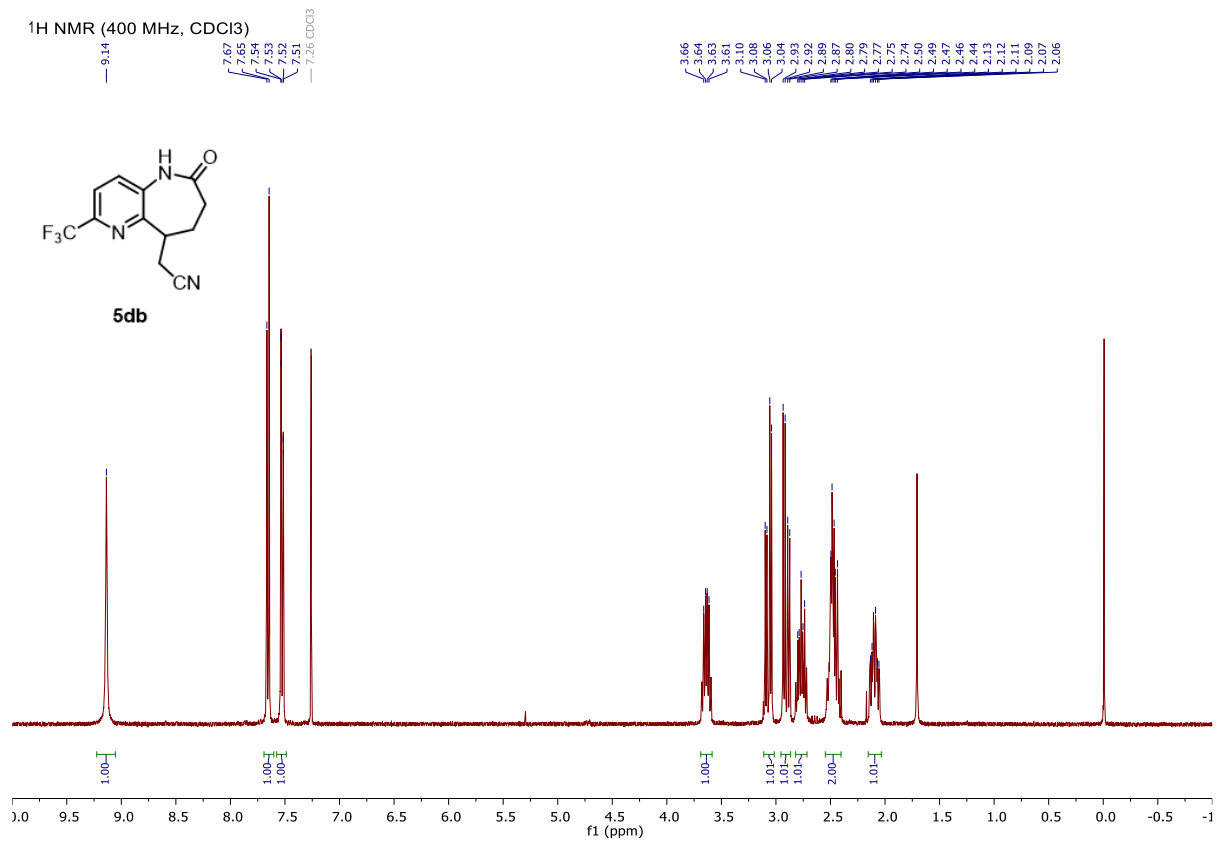


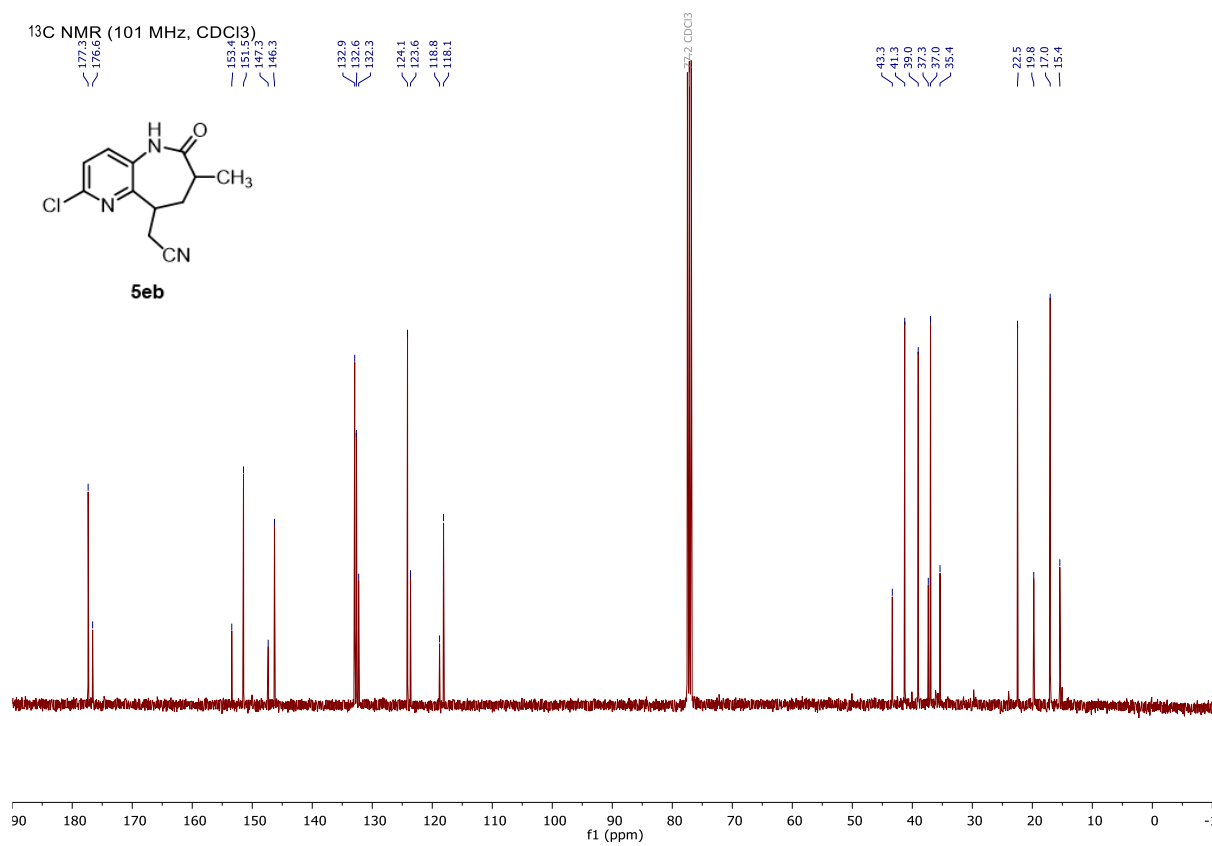
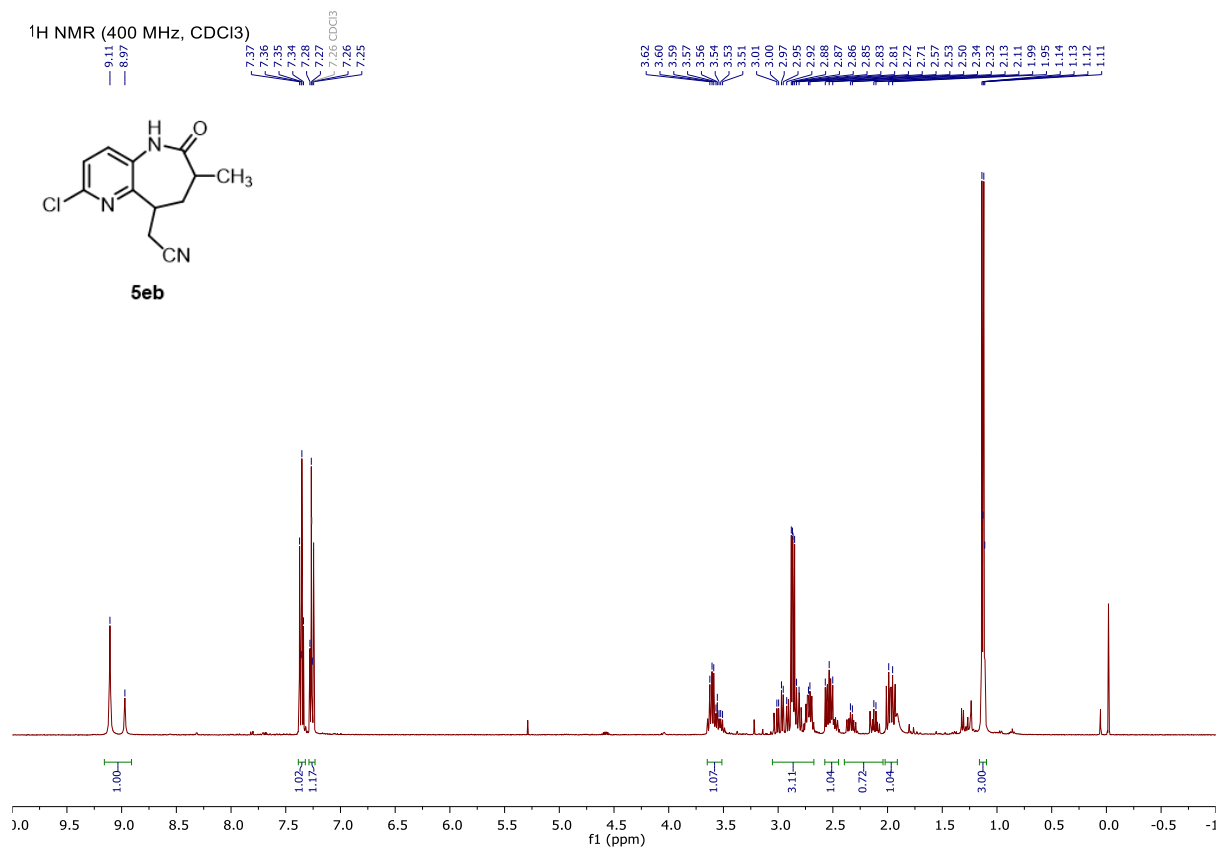
¹H NMR (400 MHz, CDCl₃)



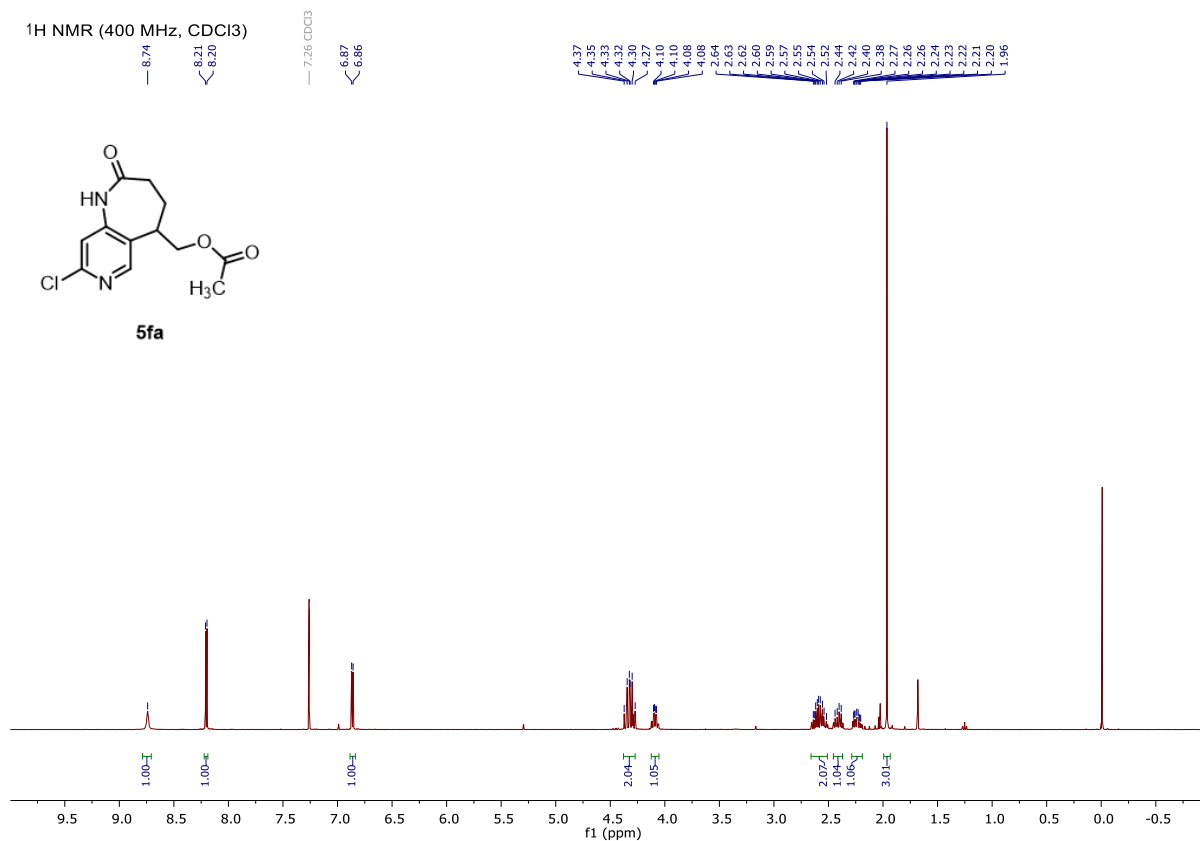
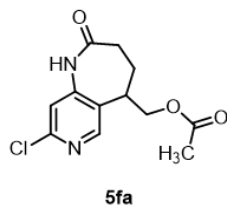
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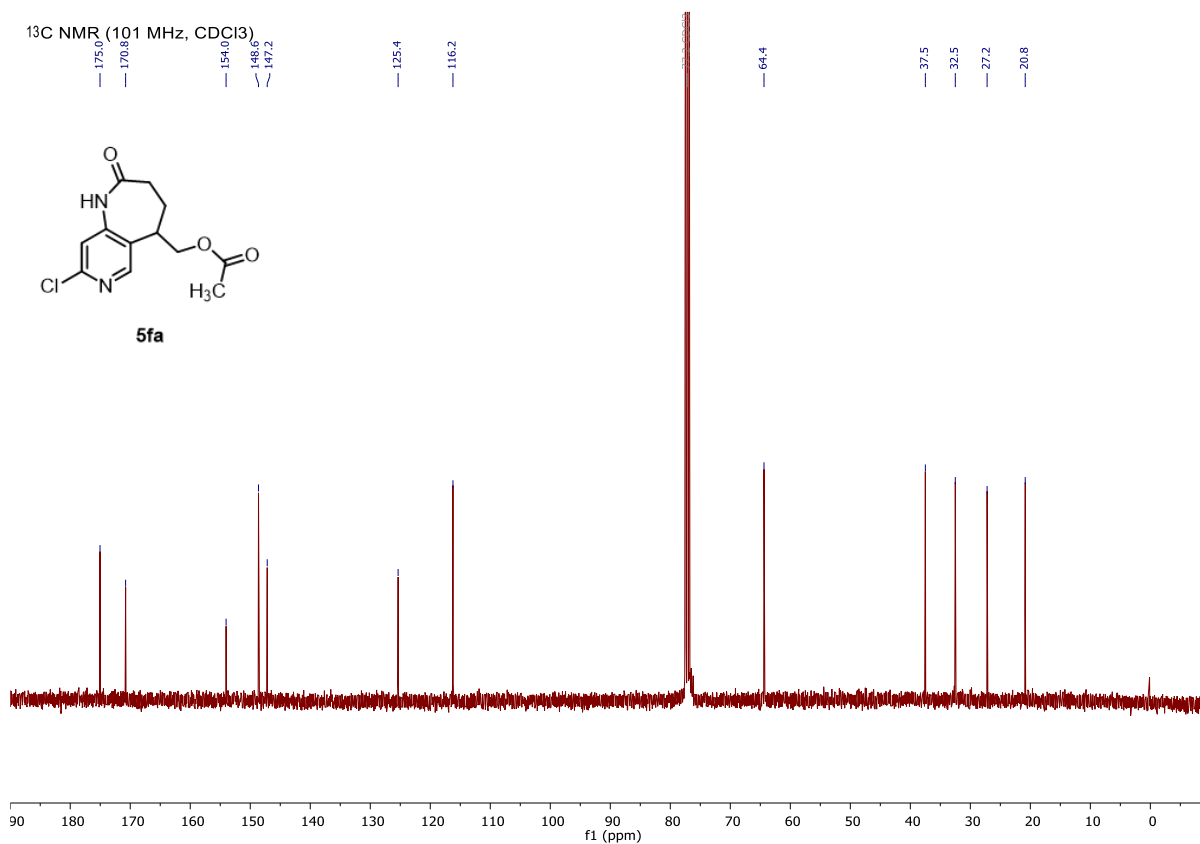
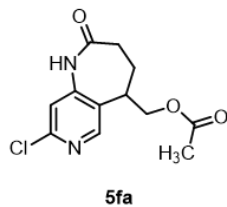




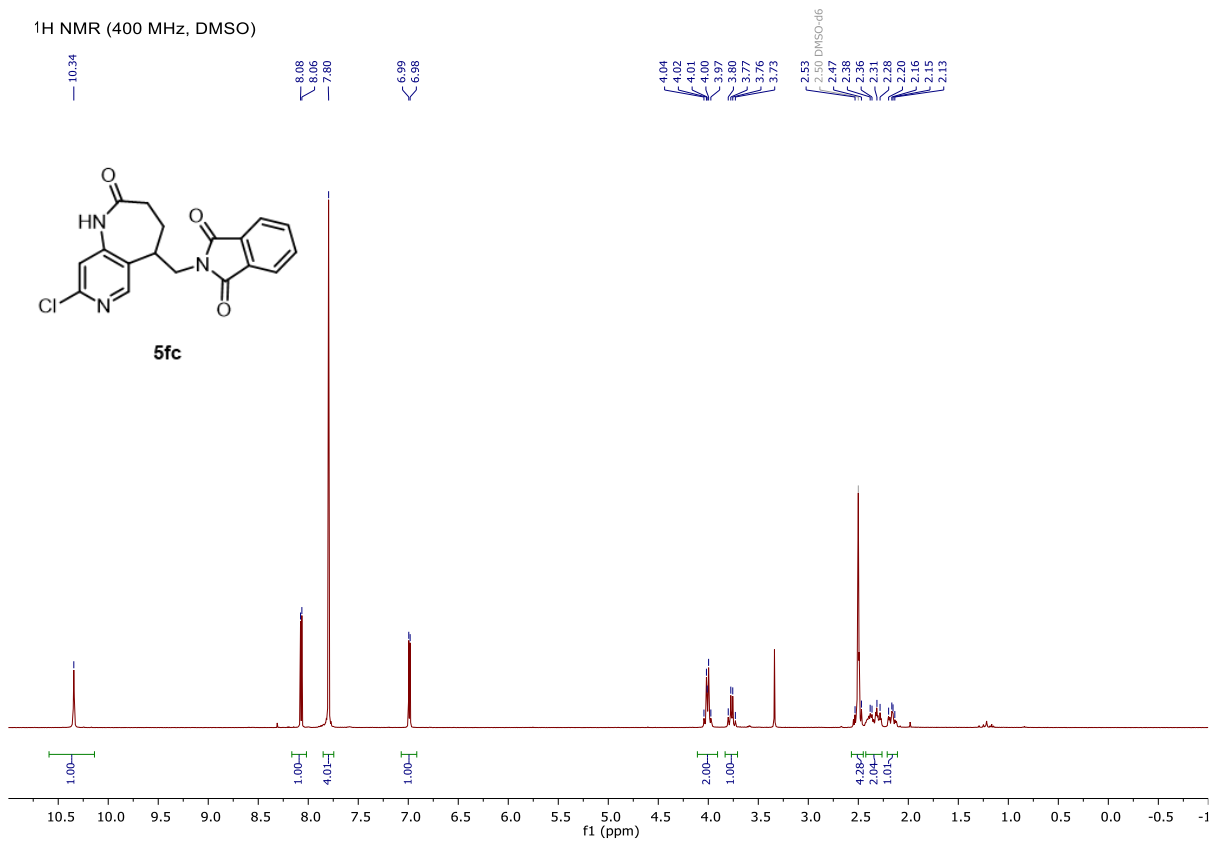
¹H NMR (400 MHz, CDCl₃)



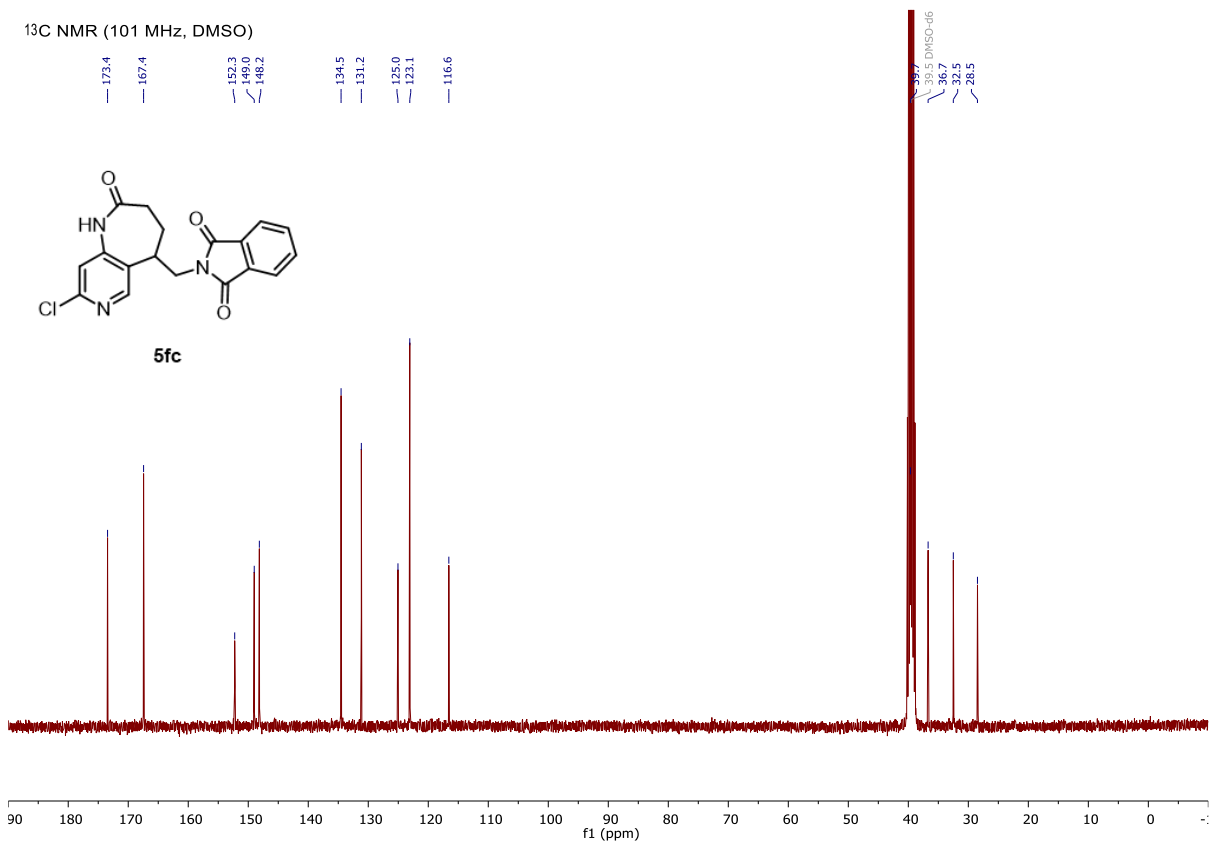
¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, DMSO)



¹³C NMR (101 MHz, DMSO)

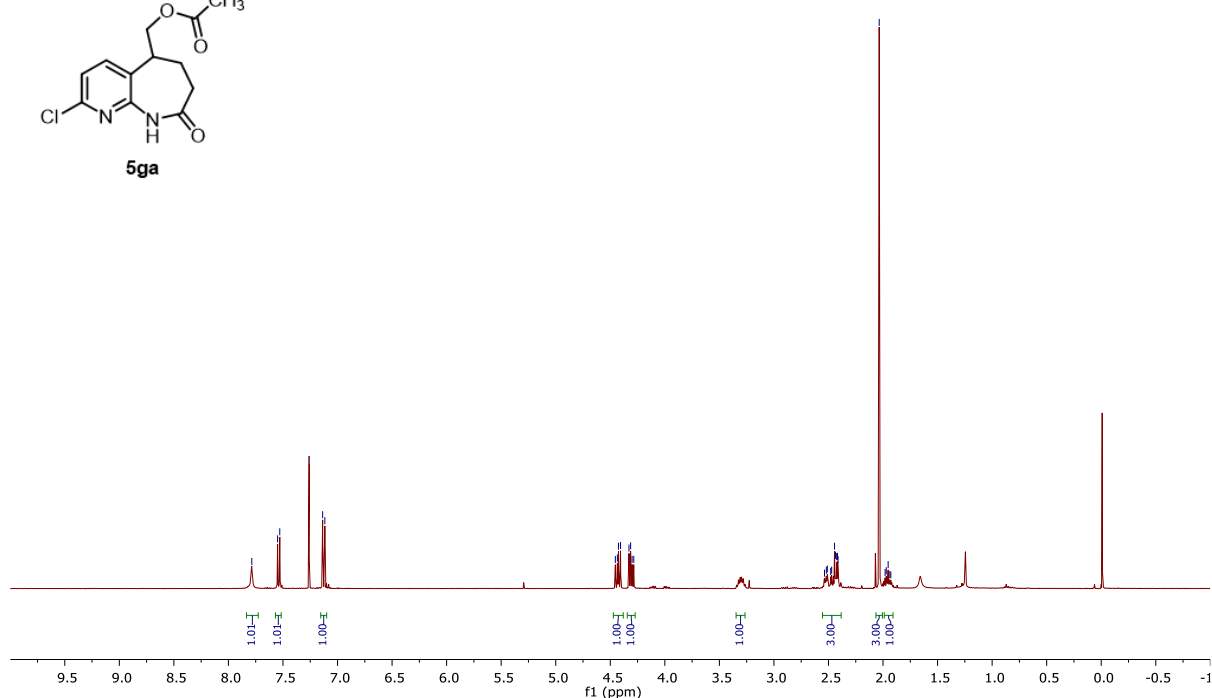
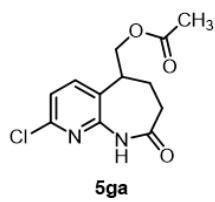


¹H NMR (400 MHz, CDCl₃)

7.79
7.55
7.53
7.26 CDCl₃
7.14
7.12

4.45
4.43
4.42
4.41
4.33
4.31
4.30
4.28

2.54
2.52
2.51
2.48
2.47
2.44
2.42
2.41
2.03
1.98
1.97
1.95
1.94
1.93



¹³C NMR (101 MHz, CDCl₃)

173.3
170.8

151.1
148.5

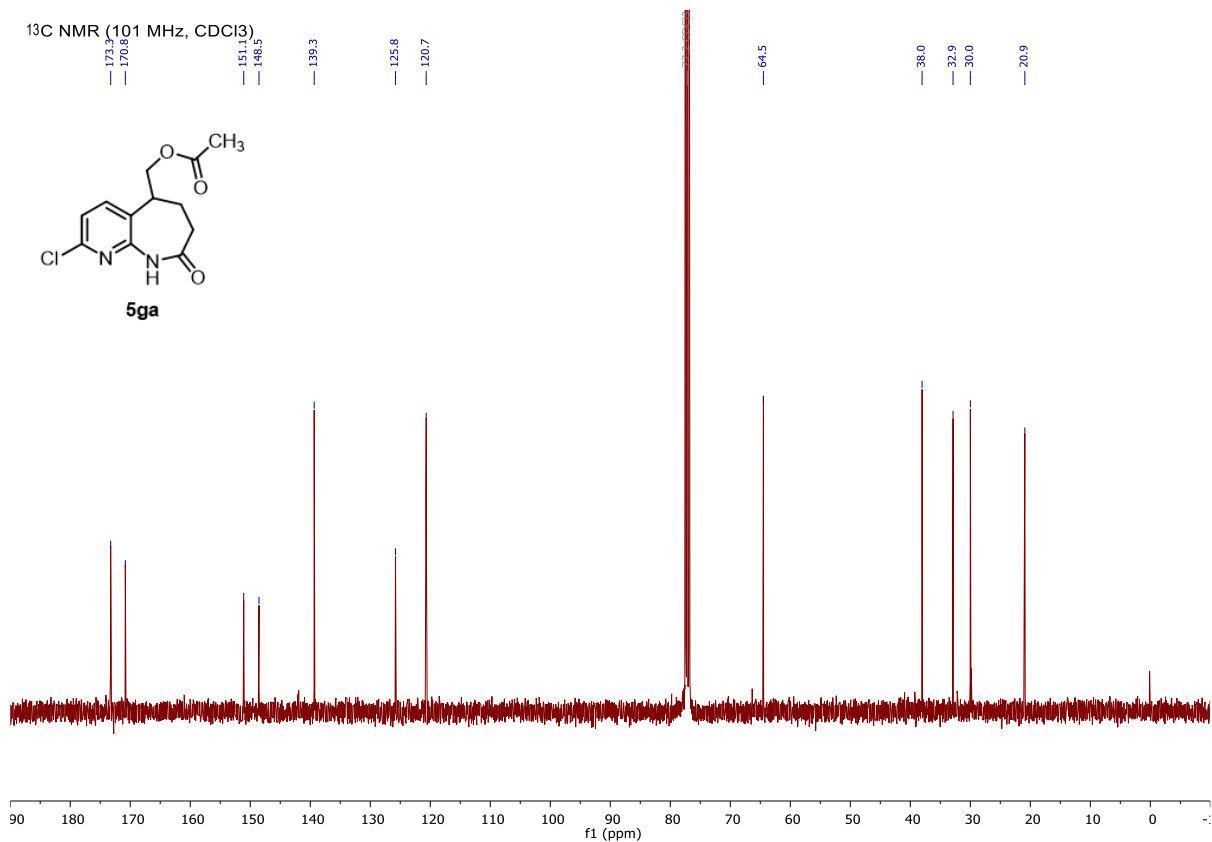
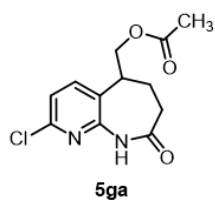
139.3

125.8
120.7

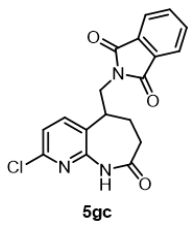
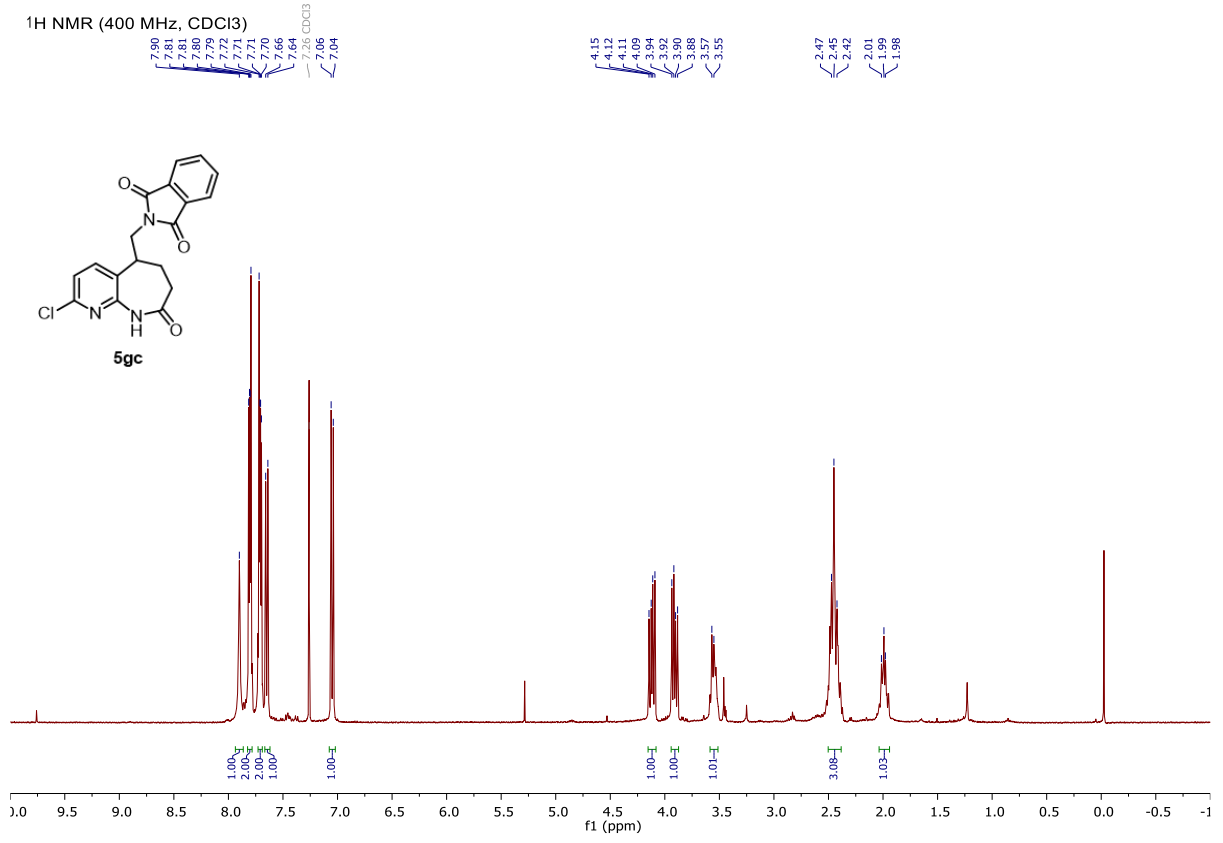
64.5

38.0
32.9
30.0

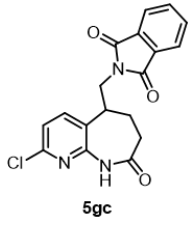
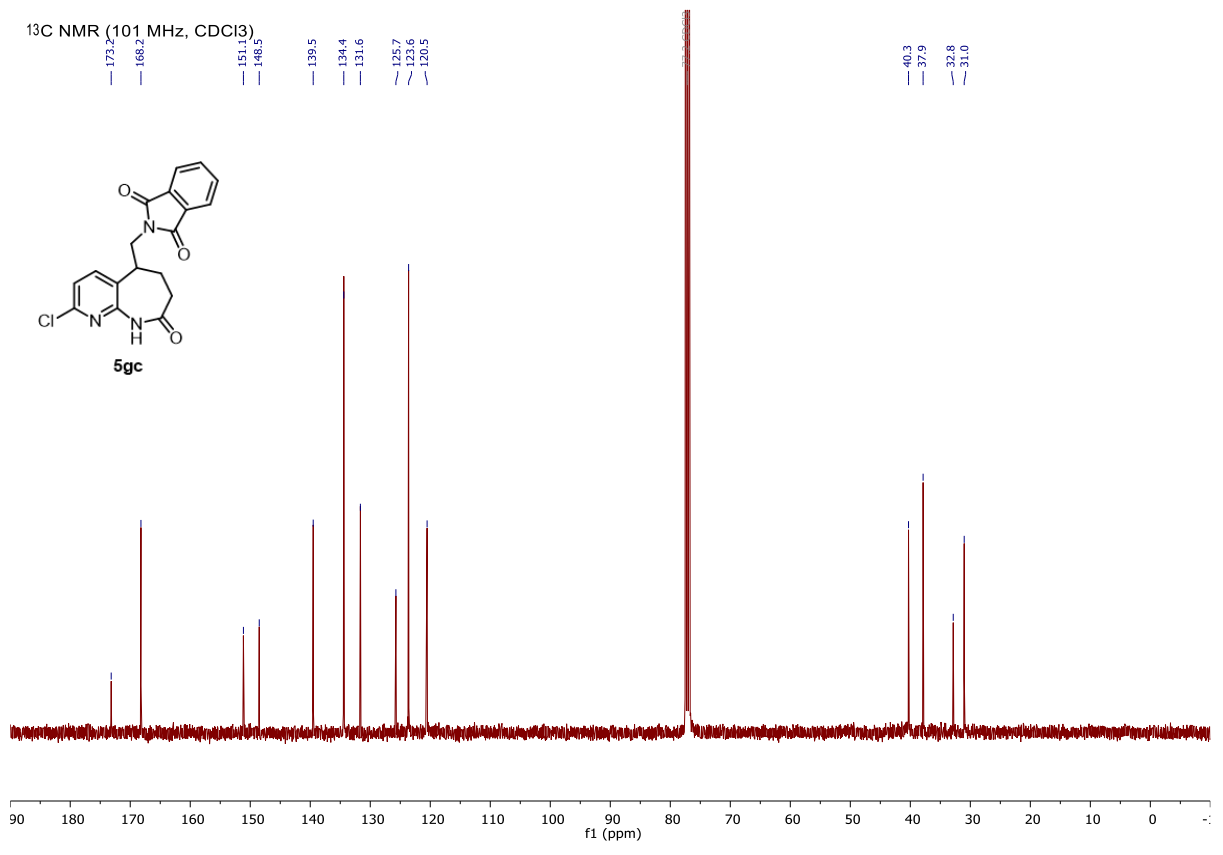
20.9



¹H NMR (400 MHz, CDCl₃)



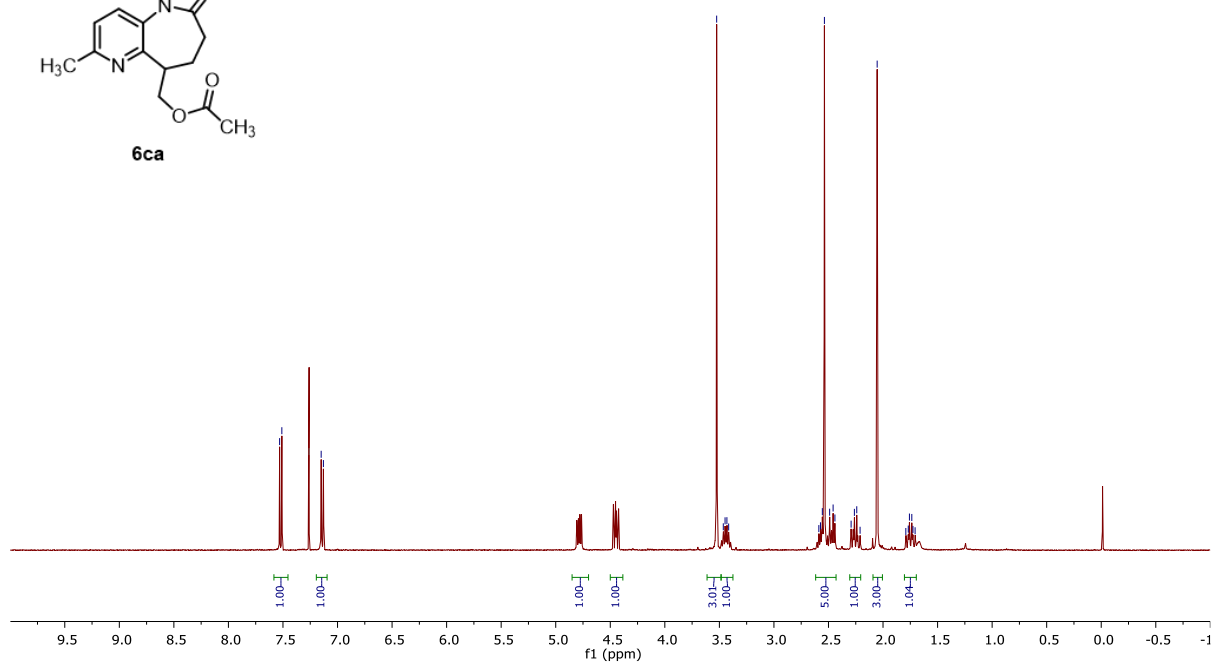
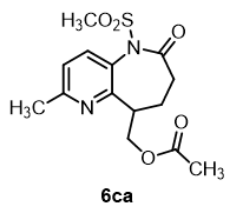
¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)

7.53
7.51
7.26 CDCl₃
7.15
7.13

3.52
3.46
3.43
3.41
2.57
2.56
2.54
2.46
2.44
2.29
2.26
2.24
2.21
2.16
1.99
1.77
1.76
1.74
1.73
1.71



¹³C NMR (101 MHz, CDCl₃)

173.2
171.2

159.2
154.1

135.7

129.1

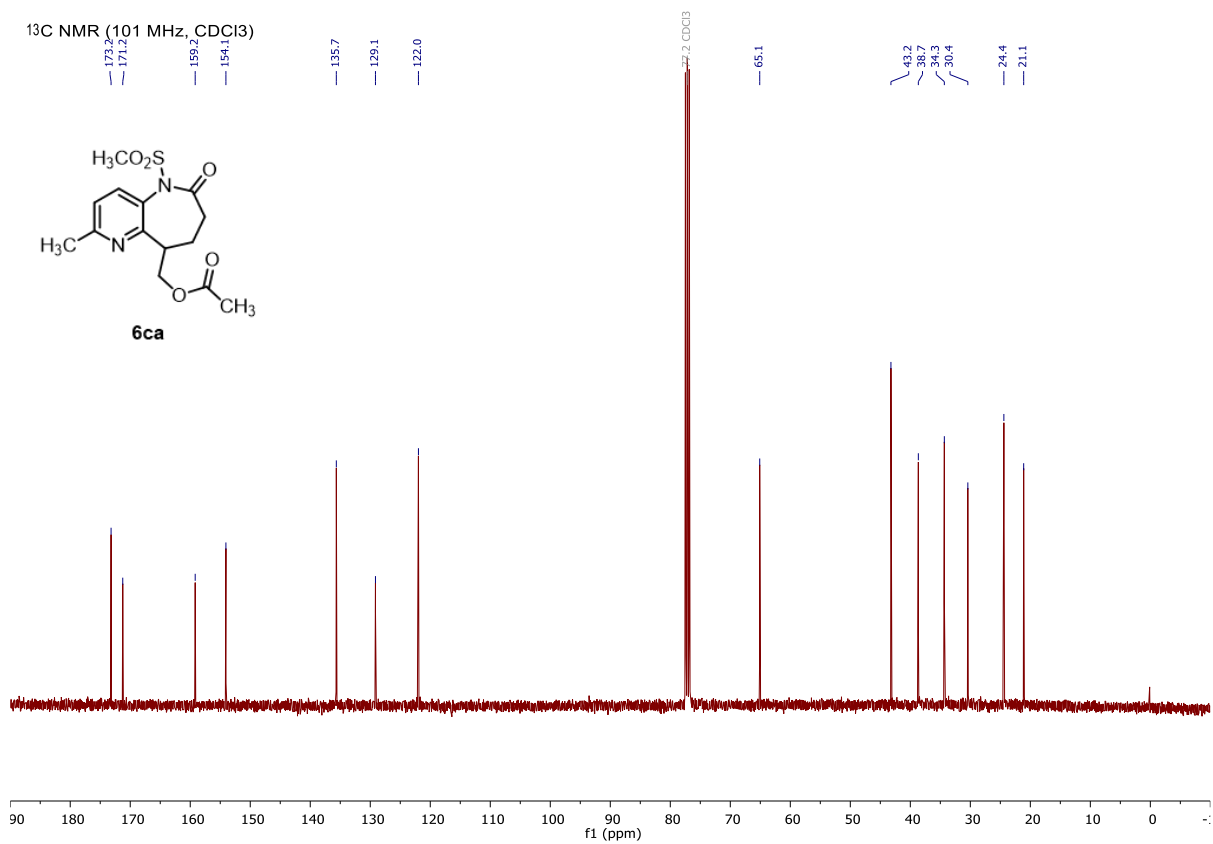
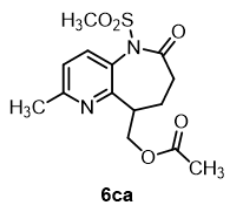
122.0

77.2 CDCl₃

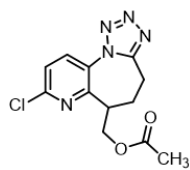
65.1

43.2
38.7
34.3
30.4

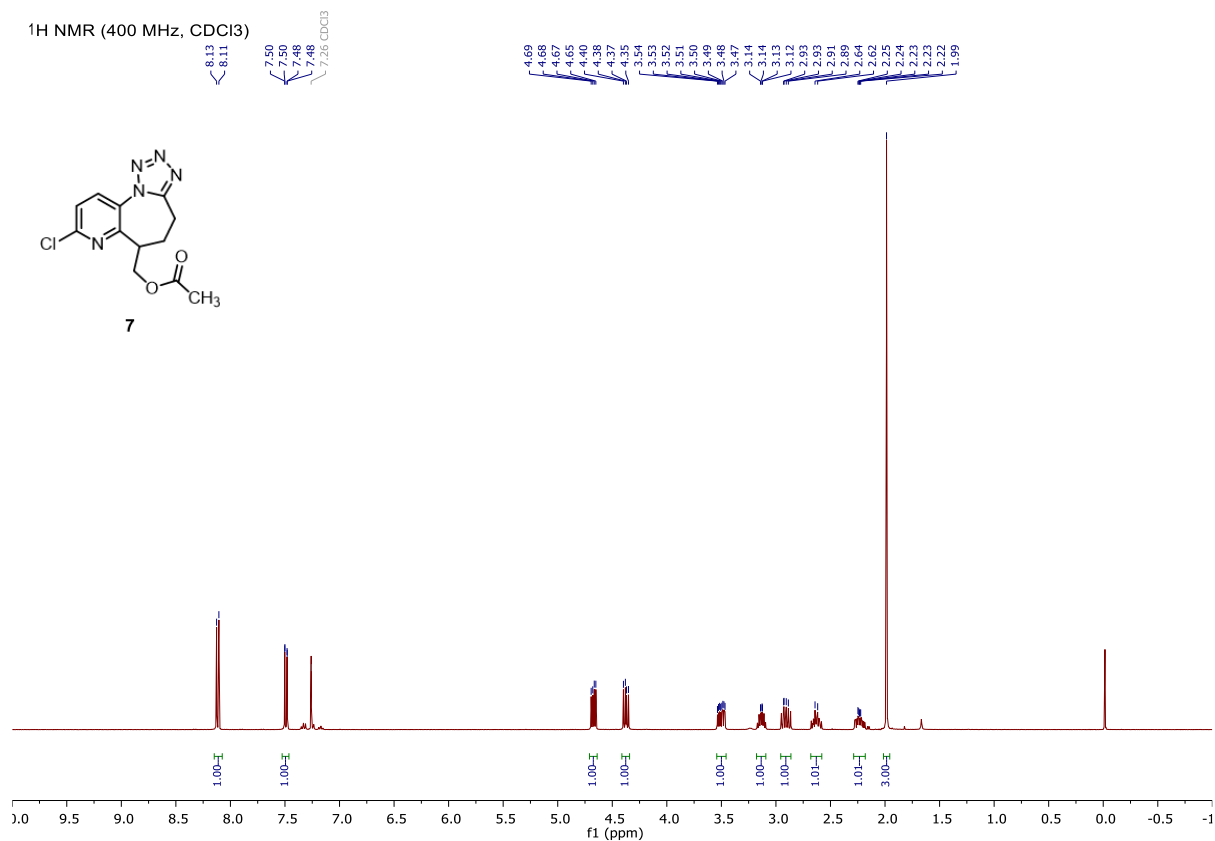
24.4
21.1



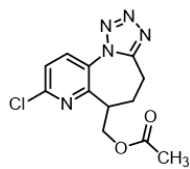
¹H NMR (400 MHz, CDCl₃)



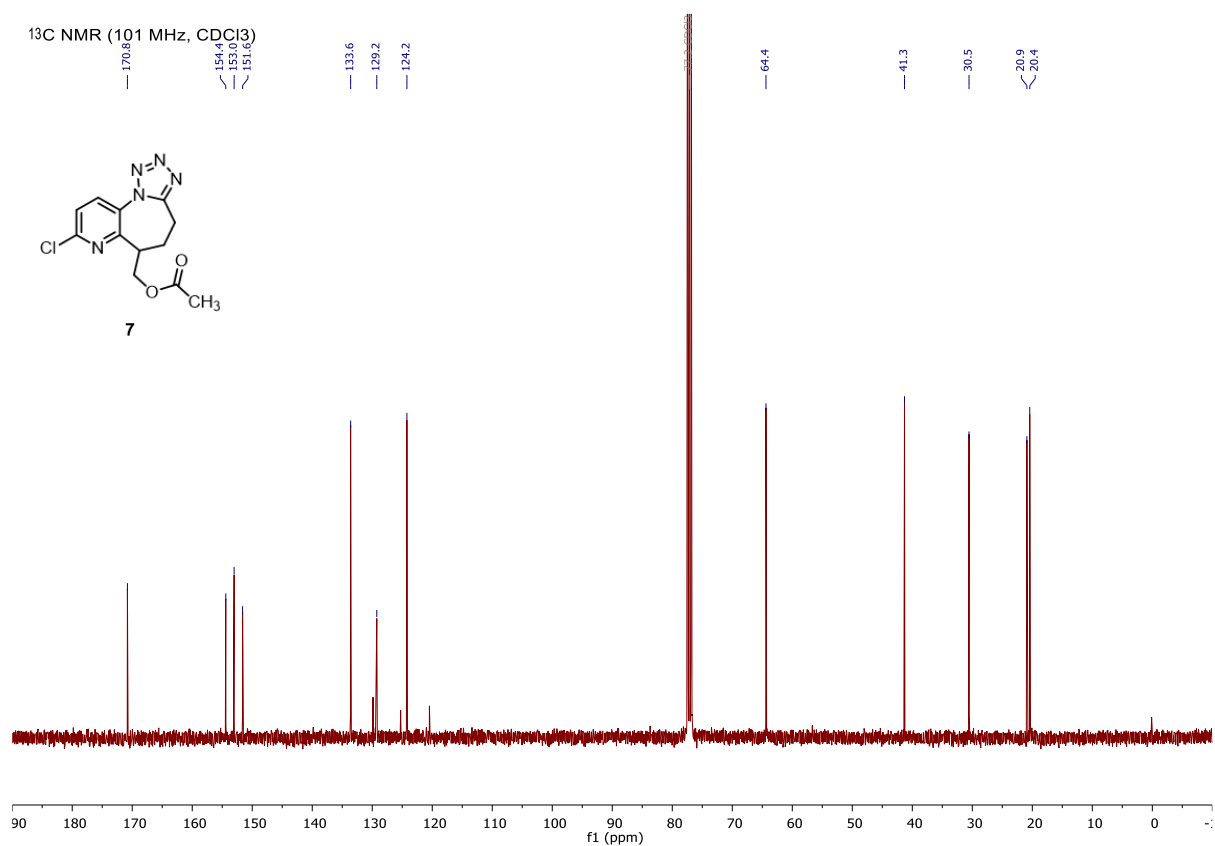
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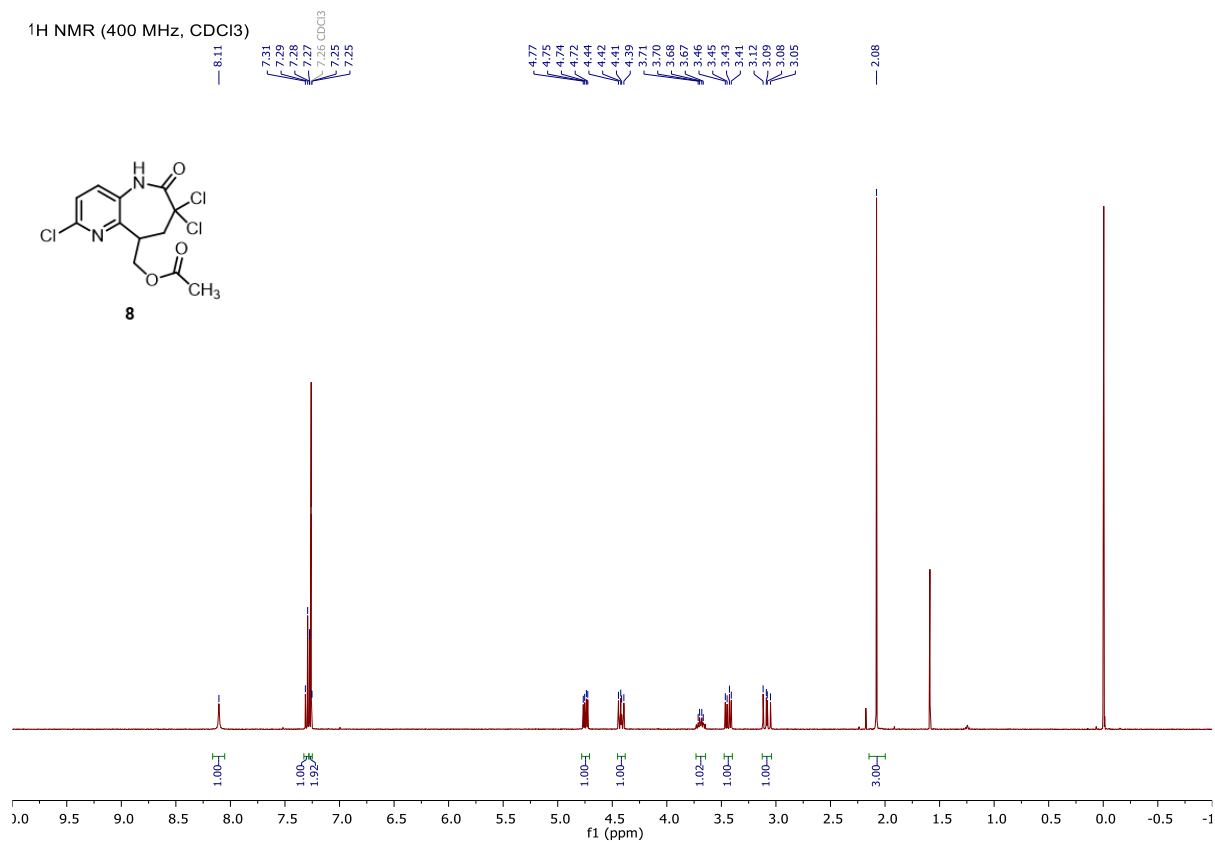
¹³C NMR (101 MHz, CDCl₃)



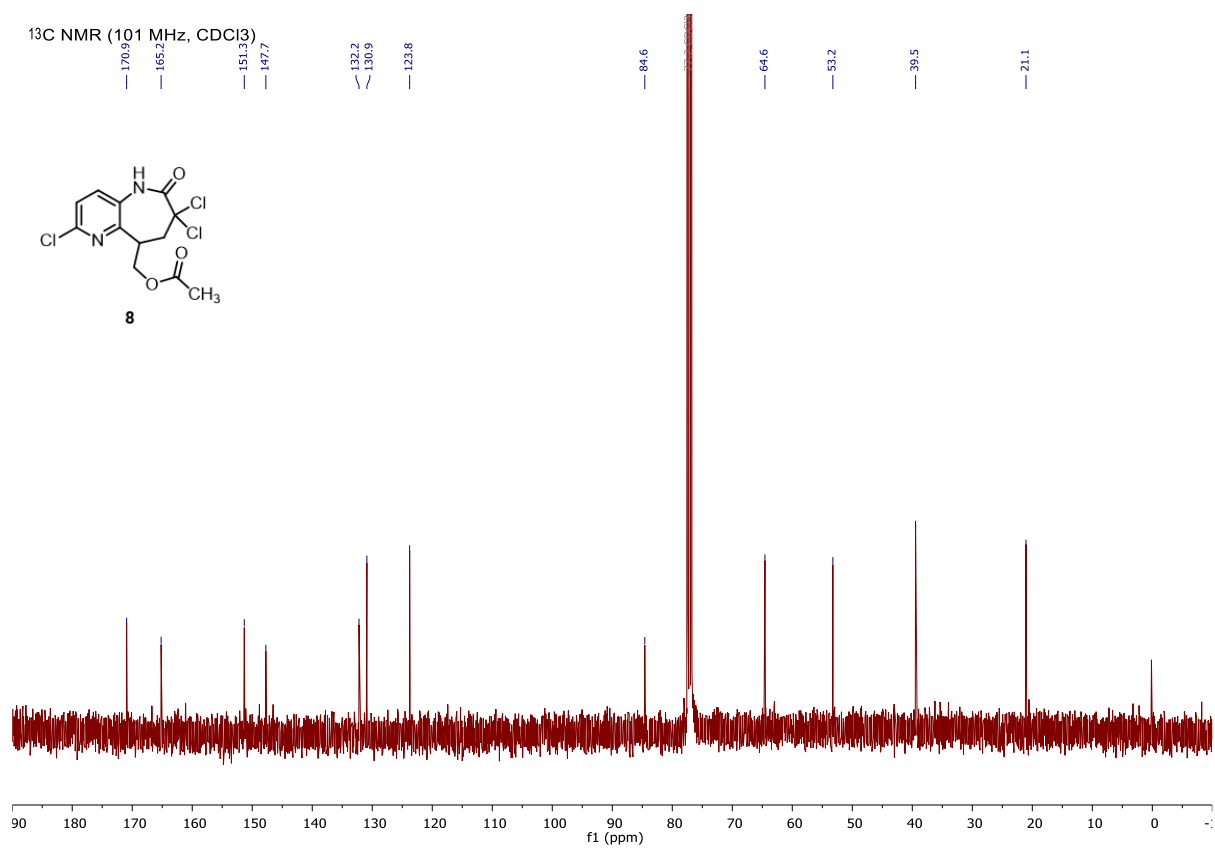
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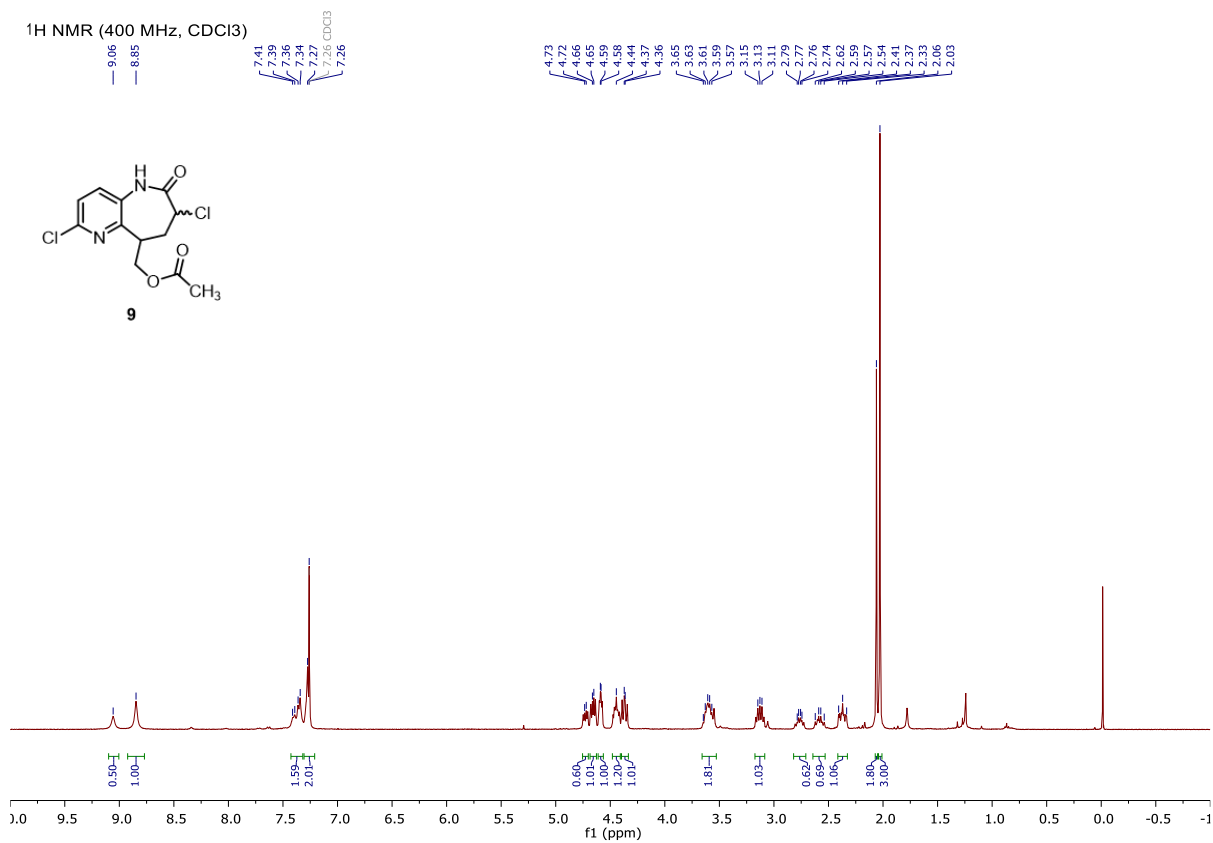
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)



¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)

