

Functionalization of Photochromic Dithienylmaleimides

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Supporting Information

Non-hydrolytic methyl ester deprotection of 12	S-2
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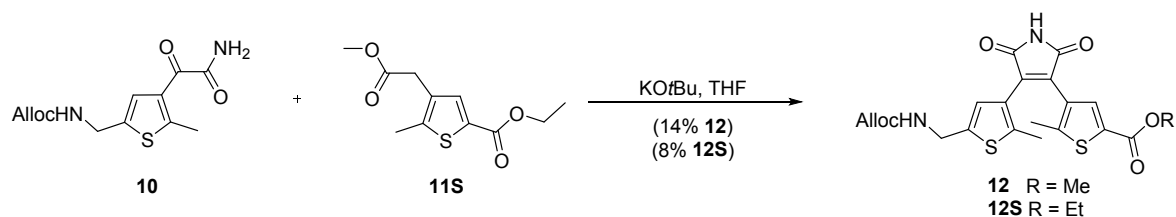
Non-hydrolytic methyl ester deprotection of **12**

Table S1. Non-hydrolytic methyl ester deprotection of **12**.

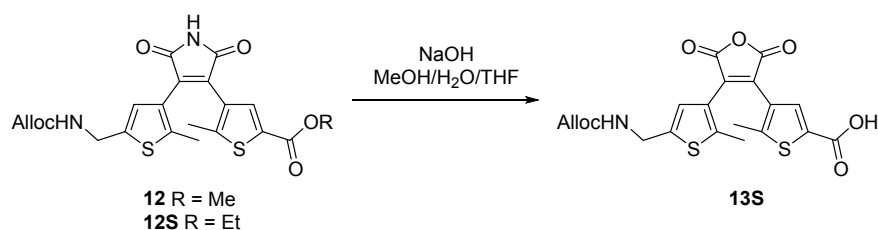
Entry	LiI [eq]	Solvent	T [°C]	Isolated yield ^[a]
1	3.0	EtOAc	r.t.	--
2	3.0	EtOAc	reflux	--
3	30	EtOAc	reflux	26%
4	3.0	acetone	reflux	--
5	30	acetone	reflux	35%
6	30	MeCN	reflux	--
7	30	DMSO	100 °C	--

^[a] If conversion was too low the product **13b** was not isolated.

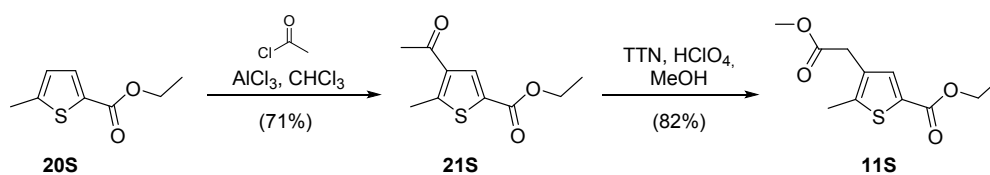
Synthesis of compounds **11S**, **12S**, **13S** and **21S**



Scheme S1. Perkin condensation of **10** and **11S** yielding dithienylmaleimide **12** and **12S**.



Scheme S2. Hydrolytic ester cleavage yielding maleic anhydride **13S**.



Scheme S3. Synthesis of ethyl ester **11S**.

Ethyl 4-(2-methoxy-2-oxoethyl)-5-methylthiophene-2-carboxylate (11S): Thallium trinitrate (2.20 g, 4.94 mmol) and 70% HClO₄ (2 mL) were added to a suspension of **21S** (875 mg, 4.12 mmol) in MeOH (10 mL) at room temperature. After stirring for 24 h the mixture was concentrated under reduced pressure and diluted with water (10 mL). The aqueous phase was extracted with chloroform (3 x 15 mL) and the combined organic layers were dried over MgSO₄. The solvent was evaporated and purification of the crude product by automated flash column chromatography (PE/EtOAc, 3% - 15% EtOAc) yielded compound **11S** (816 mg, 82%) as yellowish oil. *R*_f: 0.23 (PE/EtOAc: 9/1); IR (neat) ν_{\max} : 3081, 2987, 2922, 1730, 1705, 1460, 1254, 1201, 1172, 1061; ¹H-NMR (400 MHz, CDCl₃): δ = 1.35 (t, *J* = 7.1 Hz, 3H, O-CH₂-CH₃), 2.42 (s, 3H, thiophene-CH₃), 3.54 (s, 2H, C-CH₂-CO), 3.70 (s, 3H, CO-O-CH₃), 4.31 (q, *J* = 7.1 Hz, 2H, O-CH₂-CH₃), 7.60 (s, 1H, thiophene-*H*); ¹³C-NMR (75 MHz, CDCl₃): δ = 13.8 (+), 14.4 (+), 33.8 (-), 52.2 (+), 61.0 (-), 129.6 (q), 130.6 (q), 135.4 (+), 143.8 (q), 162.2 (q), 171.0 (q); HR-MS (ESI): calcd. for C₁₁H₁₄NaO₄S (M+Na)⁺ 265.0505; found 265.0502.

Methyl/Ethyl 4-(4-(5-(((allyloxy)carbonyl)amino)methyl)-2-methyl-thiophen-3-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-5-methylthiophene-2-carboxylate (12/12S): KO^tBu (1 M in THF, 1.34 mL, 1.34 mmol) was added to a solution of **10** (316 mg, 1.12 mmol) in anhydrous THF (6 mL) at 0 °C under nitrogen atmosphere. After stirring for 90 min at 0 °C, diester **11S** (326 mg, 1.34 mmol) was added and stirred for 15 h at room temperature. Then the reaction was heated to 60 °C for 1 h, quenched with 1 M HCl solution (4 mL) and diluted with EtOAc (10 mL). The organic phase was washed with water (3 x 5 mL), brine (5 mL) and dried over MgSO₄. The solvent was removed under reduced pressure and purification of the crude product by automated reversed phase flash column chromatography (H₂O/EtOH, 20% - 45% EtOH) yielded **12S** (40 mg, 8%) as orange foam, **12** (74 mg, 14%) as yellow foam and a mixed fraction of both (65 mg). Analytical data of **12S**: *R*_f: 0.25 (PE/EtOAc: 2/1); IR (neat) ν_{\max} : 3288, 3071, 2980, 1710, 1541, 1458, 1252, 995, 916, 760; UV/Vis (50 μ M in MeOH): open isomer: λ_{\max} = 250 nm; closed isomer: λ_{\max} = 232 nm, 378 nm, 554 nm; ¹H-NMR (400 MHz, CDCl₃): δ = 1.36 (t, *J* = 7.1 Hz, 3H, O-CH₂-CH₃), 1.91 (s, 3H, thiophene-CH₃), 1.97 (s, 3H, thiophene-CH₃), 4.33 (q, *J* = 7.1 Hz, 2H, O-CH₂-CH₃), 4.45 (d, *J* = 5.9 Hz, 2H, C-CH₂-NH), 4.60 (d, *J* = 4.8 Hz, 2H, O-CH₂-CH), 5.14 -5.26 (m, 2H, CH₂=CH-CH₂ and CH₂-NH-CO), 5.31 (dd, *J* = 17.2, 1.1 Hz, 1H, CH₂=CH-CH₂), 5.92 (ddt, *J* = 16.3, 10.8, 5.6 Hz, 1H, CH₂=CH-CH₂), 6.90 (s, 1H, thiophene-*H*), 7.75 (s, 1H, thiophene-*H*), 7.97 (bs, 1H, CO-NH-CO); ¹³C-NMR (101 MHz, CDCl₃): δ = 14.3 (+), 15.0 (+), 15.3 (+), 39.9 (-),

61.4 (-), 65.9 (-), 117.9 (-), 125.8 (q), 126.7 (+), 127.4 (q), 131.4 (q), 132.7 (+), 132.8 (q), 134.7 (+), 139.4 (q), 142.1 (q), 148.4 (q), 156.0 (q), 161.7 (q), 170.0 (q), 170.1 (q); HR-MS (ESI): calcd. for C₂₂H₂₃N₂O₆S₂ (M+H)⁺ 475.0993; found 475.0992.

4-(4-(5-(((Allyloxy)carbonyl)amino)methyl)-2-methylthiophen-3-yl)-2,5-dioxo-2,5-dihydrofuran-3-yl)-5-methylthiophene-2-carboxylic acid (13S): A mixture of **12** and **12S** (62 mg) in 10 mL of H₂O/MeOH/THF (2:5:3, v/v/v) was stirred for 20 h with NaOH (78 mg, 1.95 mmol) at room temperature. After addition of water (10 mL) the reaction mixture was washed with EtOAc (2 x 10 mL) and then acidified with conc. HCl to pH 1. The aqueous phase was extracted with EtOAc (3 x 10 mL) and the combined organic phases were dried over MgSO₄. Evaporation of the solvent and purification of the crude product by automated reversed phase flash column chromatography (H₂O/MeCN, 20% - 55% MeCN) yielded **13S** (29 mg)^A as green solid. R_f: 0.02 (PE/EtOAc: 1/1); m.p.: 84 °C; IR (neat) ν_{max}: 3327, 3164, 3020, 2925, 1764, 1702, 1541, 1458, 1254, 931, 750; UV/Vis (50 μM in MeOH): open isomer: λ_{max} = 246 nm; closed isomer: λ_{max} = 384 nm, 568 nm; ¹H-NMR (400 MHz, DMSO-*d*₆): δ = 1.90 (s, 3H, thiophene-CH₃), 1.96 (s, 3H, thiophene-CH₃), 4.28 (d, *J* = 6.1 Hz, 2H, thiophene-CH₂NH), 4.49 (d, *J* = 5.3 Hz, 2H, CH₂=CHCH₂O), 5.17 (dd, *J* = 10.5, 1.4 Hz, 1H, CH₂=CHCH₂), 5.27 (dd, *J* = 17.2, 1.5 Hz, 1H, CH₂=CHCH₂), 5.90 (ddt, *J* = 17.2, 10.6, 5.3 Hz, 1H, CH₂=CHCH₂), 6.86 (s, 1H, thiophene-*H*), 7.65 (s, 1H, thiophene-*H*), 7.92 (t, *J* = 6.0 Hz, 1H, CH₂NHCO), 13.30 (bs, 1H, COOH); ¹³C-NMR (75 MHz, DMSO-*d*₆): δ = 14.1 (+), 14.5 (+), 38.8 (-), 64.4 (-), 116.9 (-), 124.9 (q), 125.5 (+), 126.8 (q), 131.6 (q), 133.5 (+), 133.9 (q), 134.1 (+), 135.6 (q), 140.8 (q), 141.4 (q), 148.6 (q), 155.9 (q), 162.2 (q), 164.9 (q), 164.9 (q); HR-MS (ESI): calcd. for C₂₀H₁₈NO₇S₂ (M+H)⁺ 448.0519; found 448.0516.

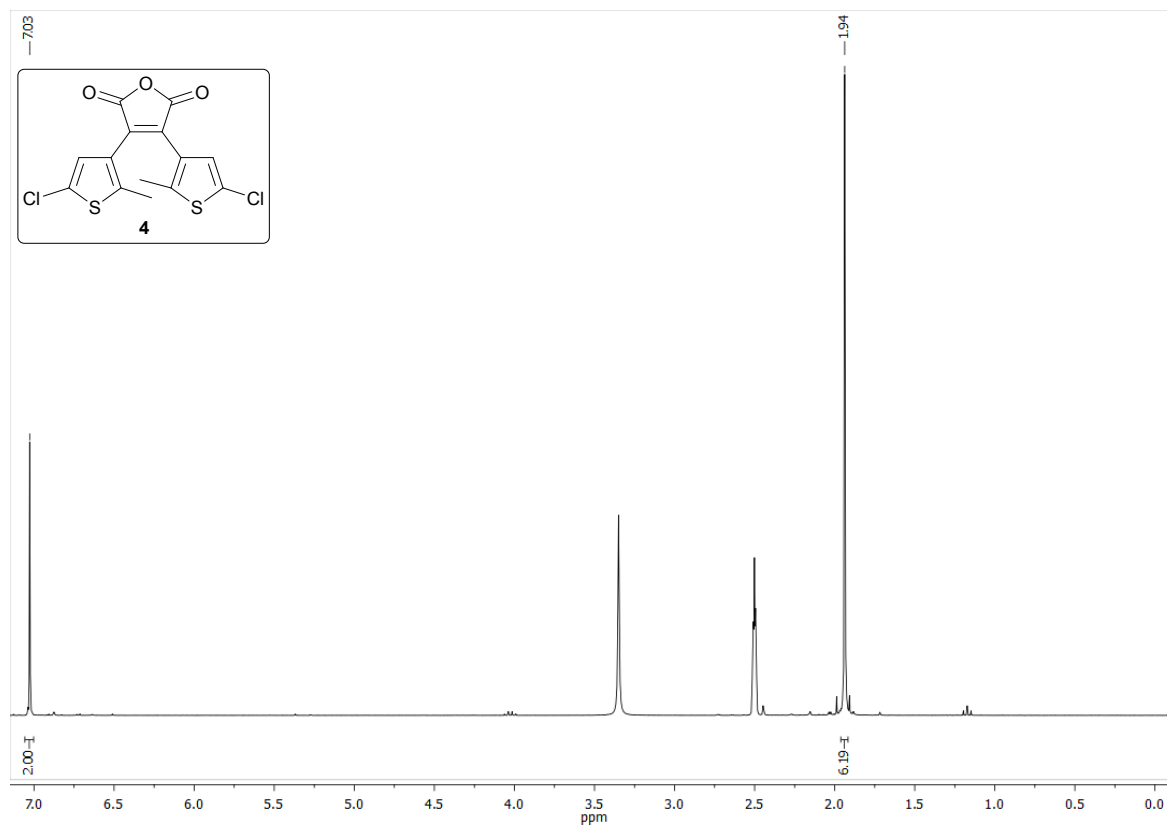
Ethyl 4-acetyl-5-methylthiophene-2-carboxylate (21S): A solution of acetyl chloride (128 μL, 1.80 mmol) in anhydrous chloroform (2 mL) was added to AlCl₃ (480 mg, 3.60 mmol) at room temperature under nitrogen atmosphere. After stirring for 10 min a solution of **20S** (204 mg, 1.20 mmol) in anhydrous chloroform (2 mL) was dropped to the suspension. The mixture was heated to 60 °C for 9 h, then the reaction was quenched with ice/water and the aqueous phase was extracted with chloroform (2 x 30 mL). The combined organic phases were washed with saturated aqueous solution of NaHCO₃ (50 mL) and brine

^A Yield could not be determined because the ratio of **12** to **12S** in the mixture was not calculated.

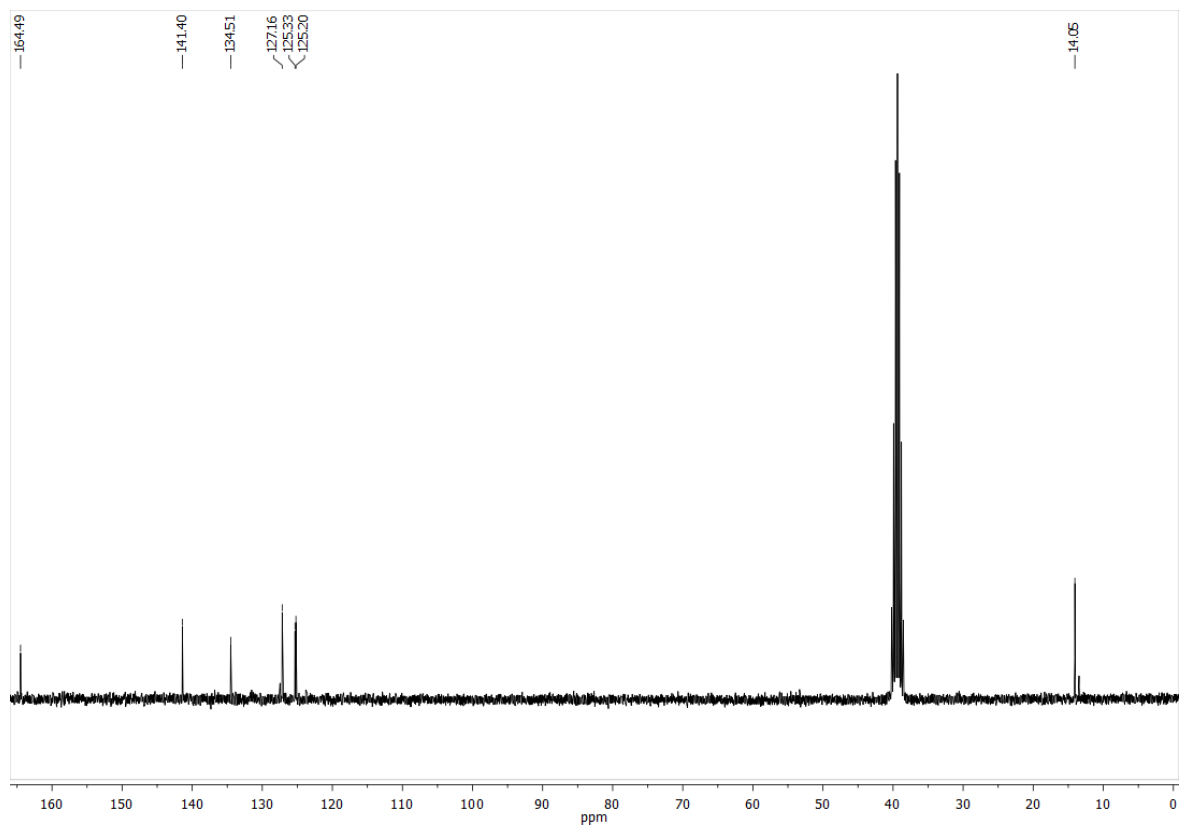
(50 mL). The organic phase was dried over MgSO_4 and the solvent was evaporated. The crude product was purified by automated flash column chromatography (PE/EtOAc, 8% - 30% EtOAc) and **21S** (180 mg, 71%) was obtained as colorless solid. R_f : 0.15 (PE/EtOAc: 9/1); m.p.: 103 °C; IR (neat) ν_{max} : 3008, 2985, 2944, 1713, 1670, 1540, 1452, 1250, 1236, 1082, 1021, 747; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.37 (t, J = 7.1 Hz, 3H, O- CH_2 - CH_3), 2.52 (s, 3H, thiophene- CH_3), 2.75 (s, 3H, acetyl- CH_3), 4.34 (q, J = 7.1 Hz, 2H, O- CH_2 - CH_3), 8.02 (s, 1H, thiophene- H); $^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ = 14.3 (+), 16.8 (+), 29.6 (+), 61.4 (-), 129.0 (q), 134.7 (+), 136.3 (q), 155.6 (q), 161.6 (q), 193.7 (q); HR-MS (ESI): calcd. for $\text{C}_{10}\text{H}_{13}\text{O}_3\text{S}$ ($\text{M}+\text{H}$) $^+$ 213.0580; found 213.0581.

¹H- and ¹³C-NMR spectra of all prepared compounds

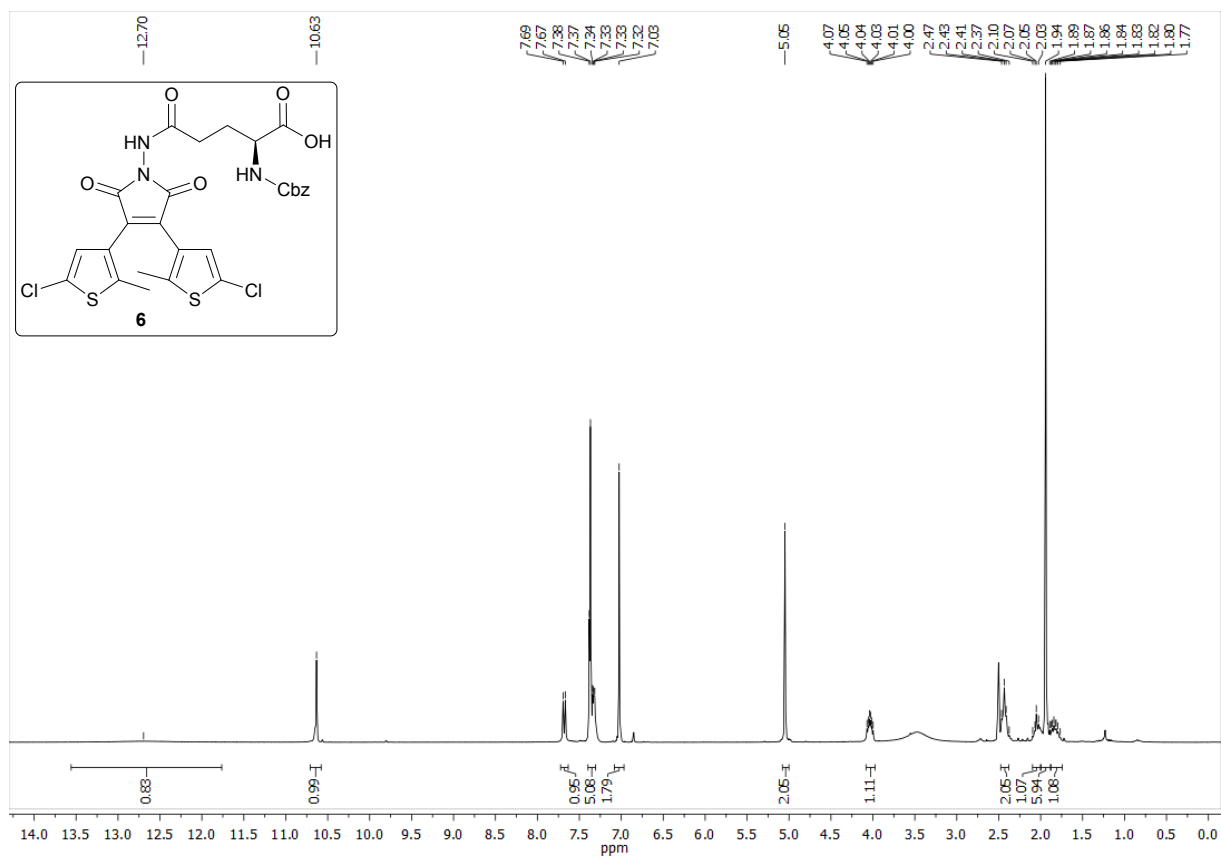
¹H-NMR (300 MHz, DMSO-*d*₆) for compound **4**:



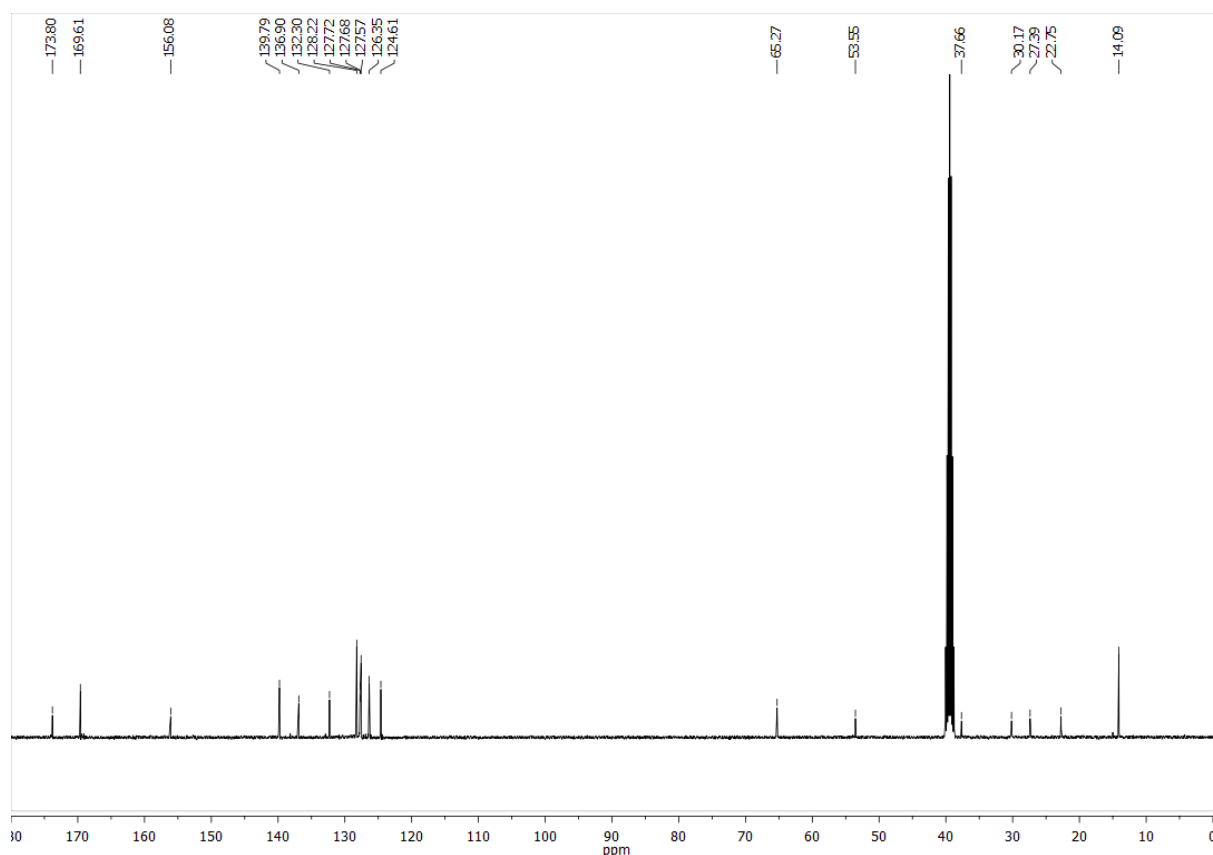
¹³C-NMR (75 MHz, DMSO-*d*₆) for compound **4**:



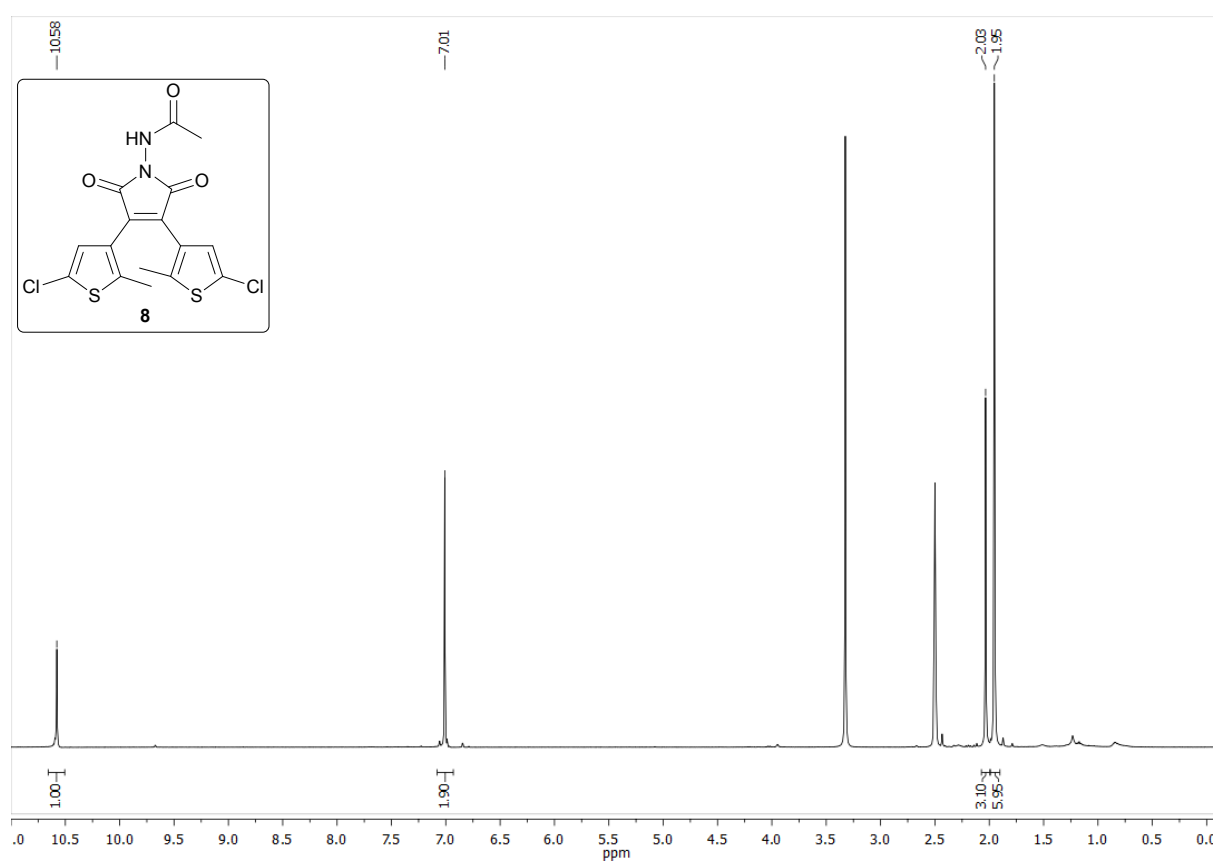
$^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **6**:



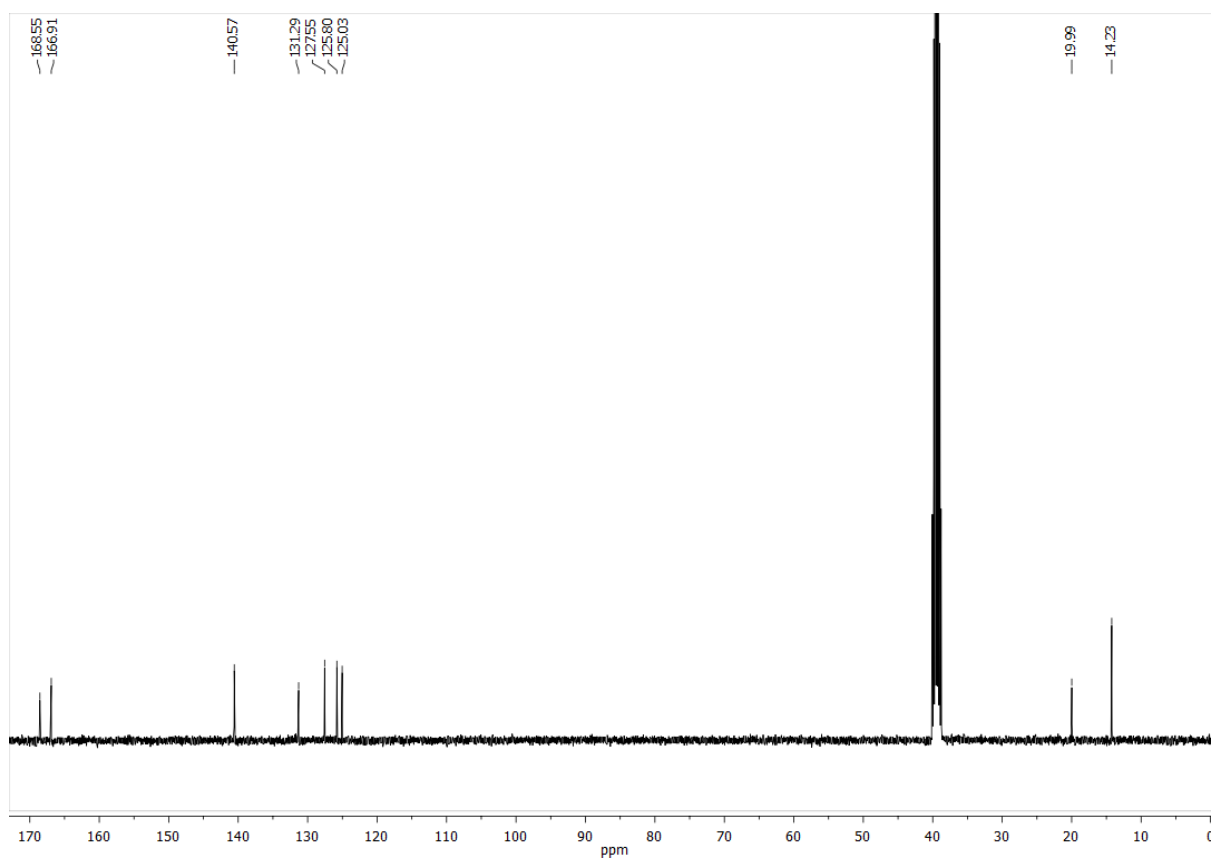
$^{13}\text{C-NMR}$ (75 MHz, $\text{DMSO-}d_6$) for compound **6**:



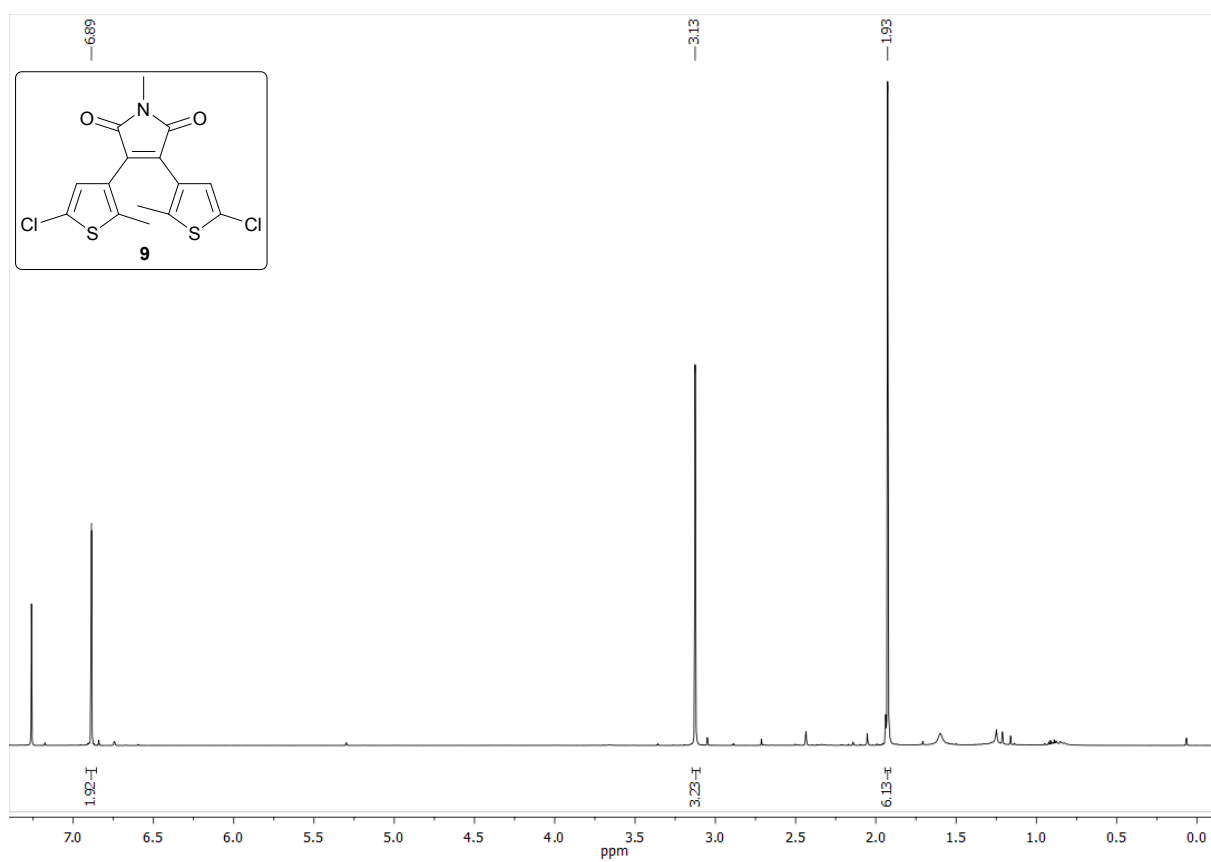
^{13}C -NMR (101 MHz, $\text{DMSO-}d_6$) for compound **8**:



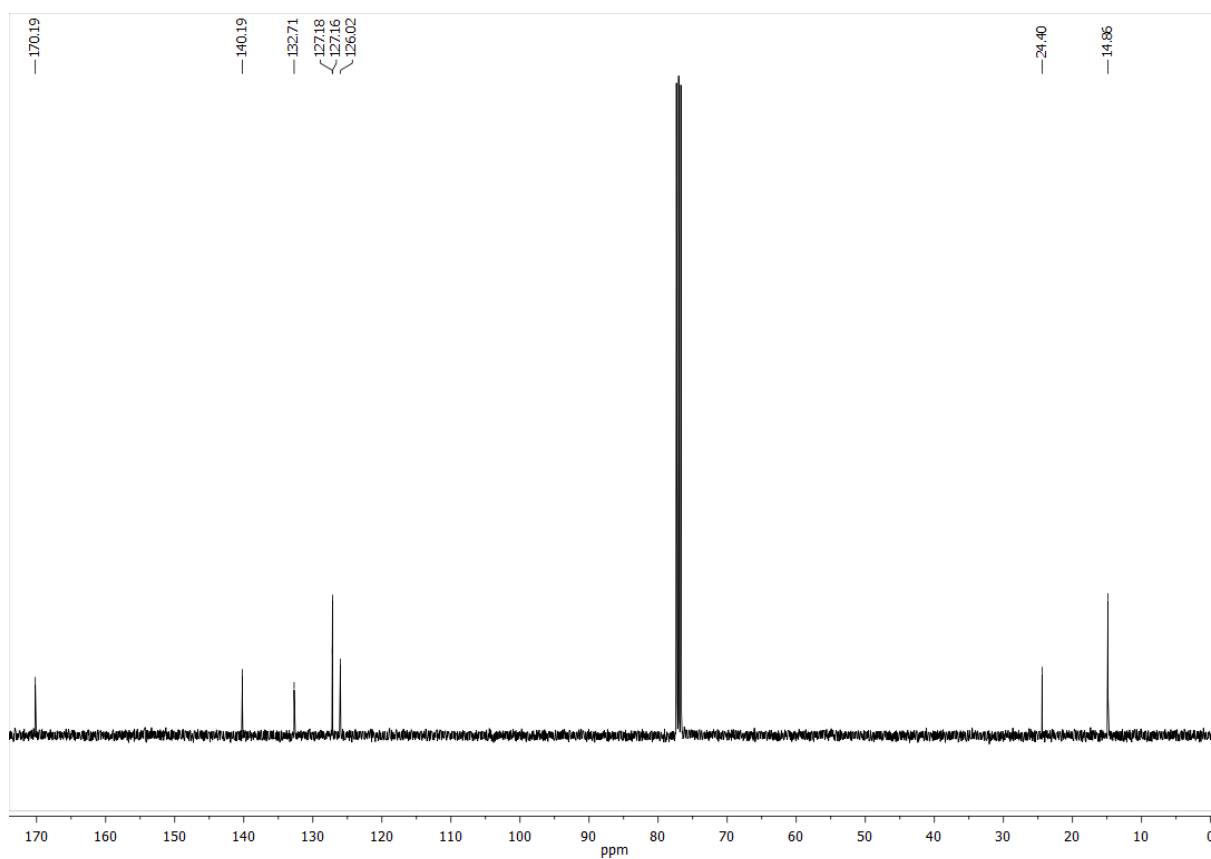
^1H -NMR (400 MHz, $\text{DMSO-}d_6$) for compound **8**:



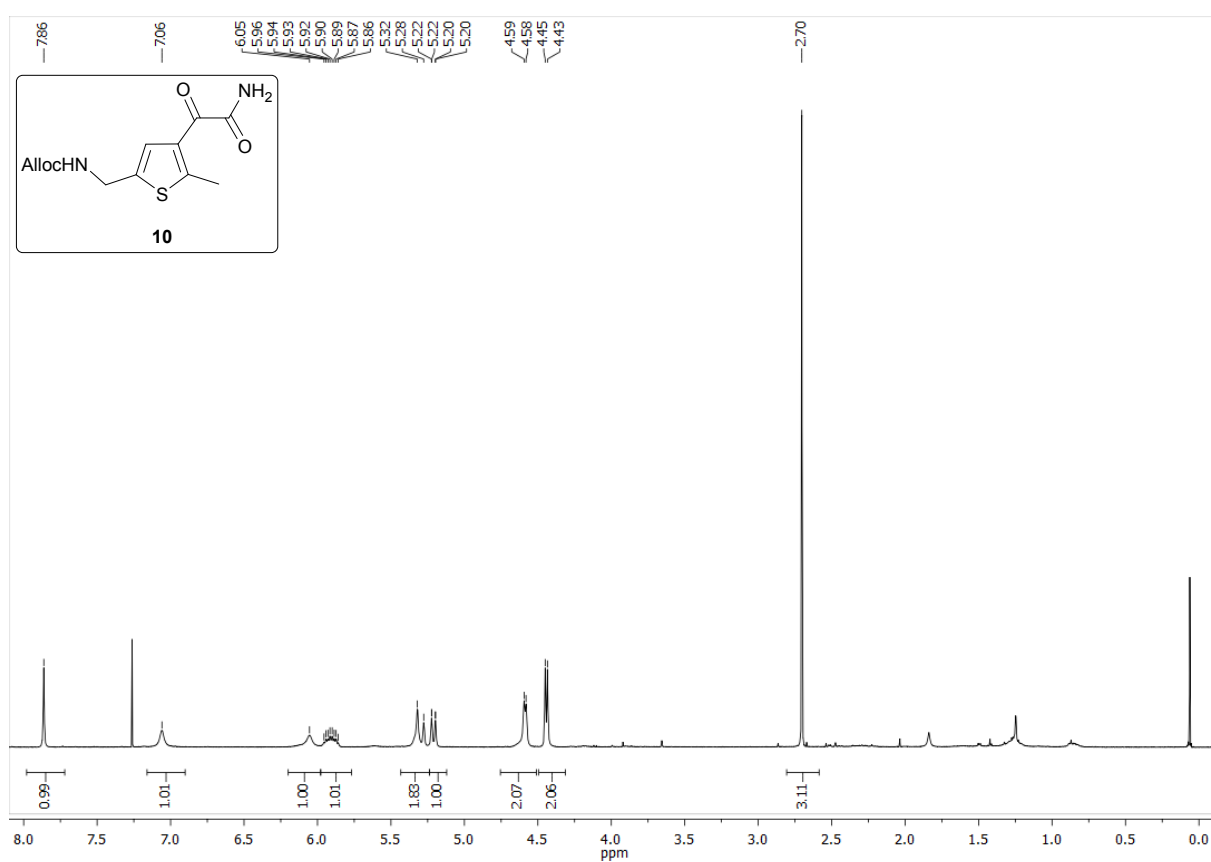
^{13}C -NMR (75 MHz, CDCl_3) for compound **9**:



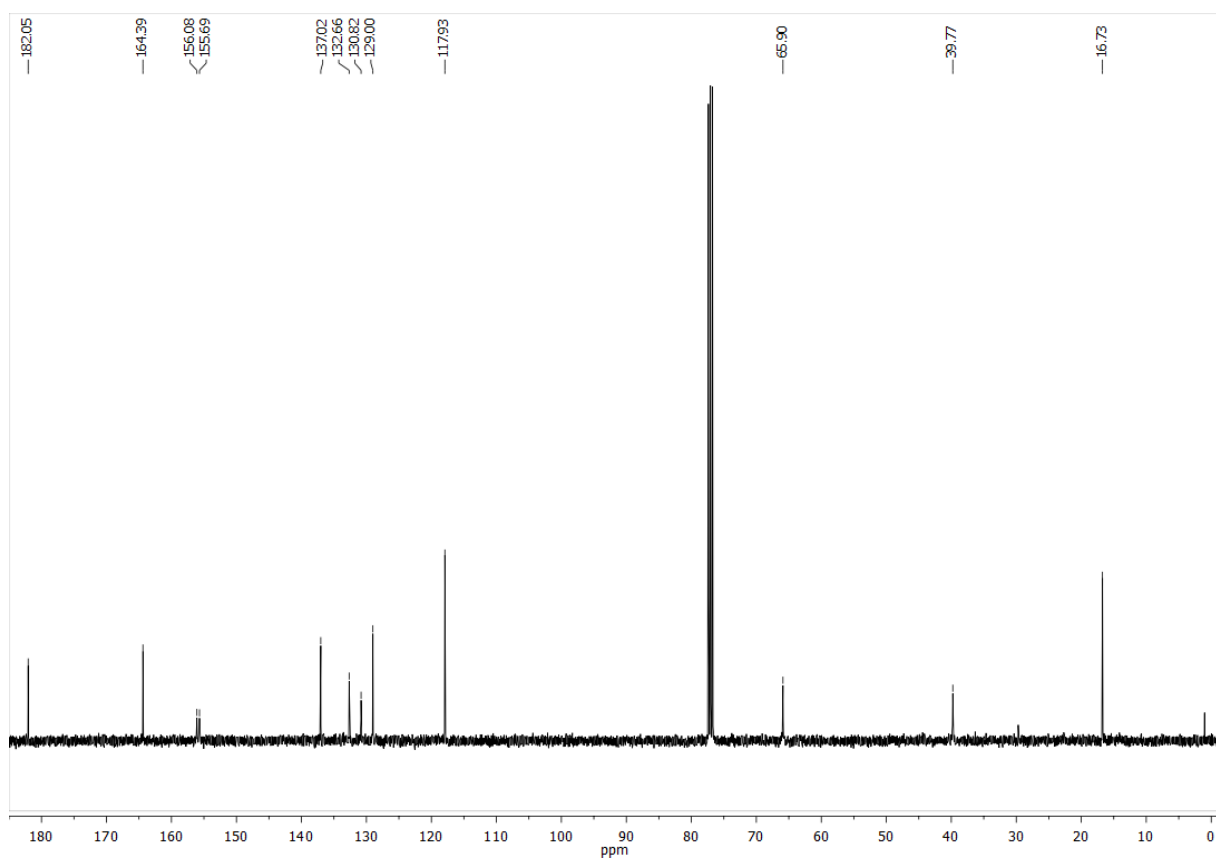
^1H -NMR (300 MHz, CDCl_3) for compound **9**:



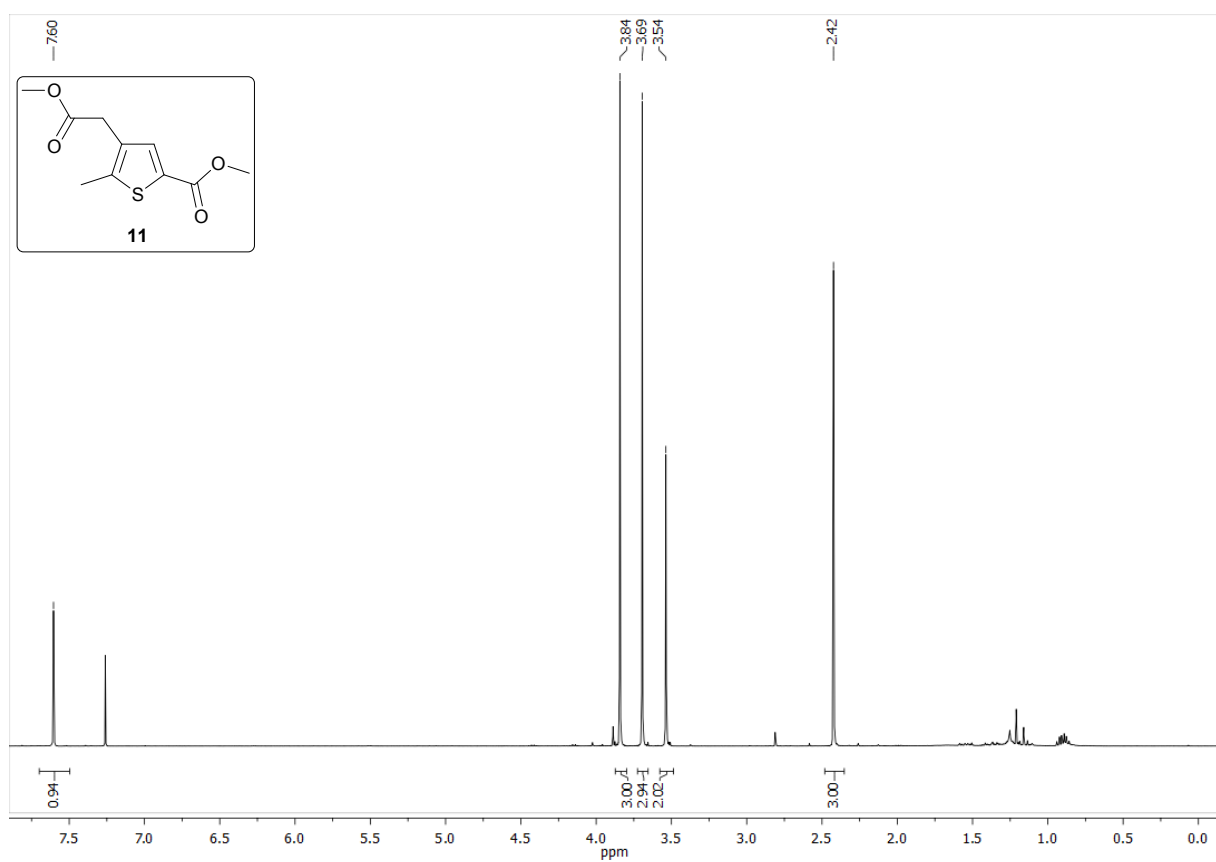
^{13}C -NMR (101 MHz, CDCl_3) for compound **10**:



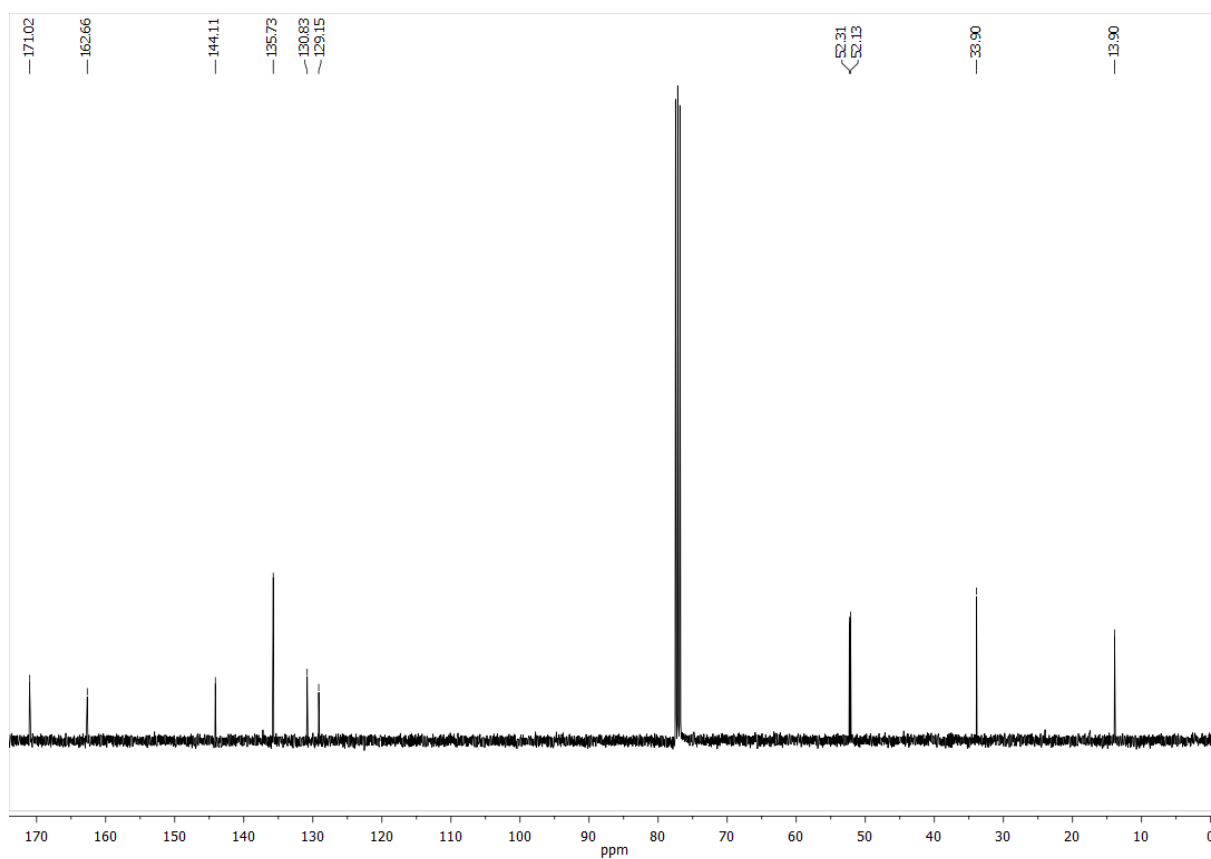
^1H -NMR (400 MHz, CDCl_3) for compound **10**:



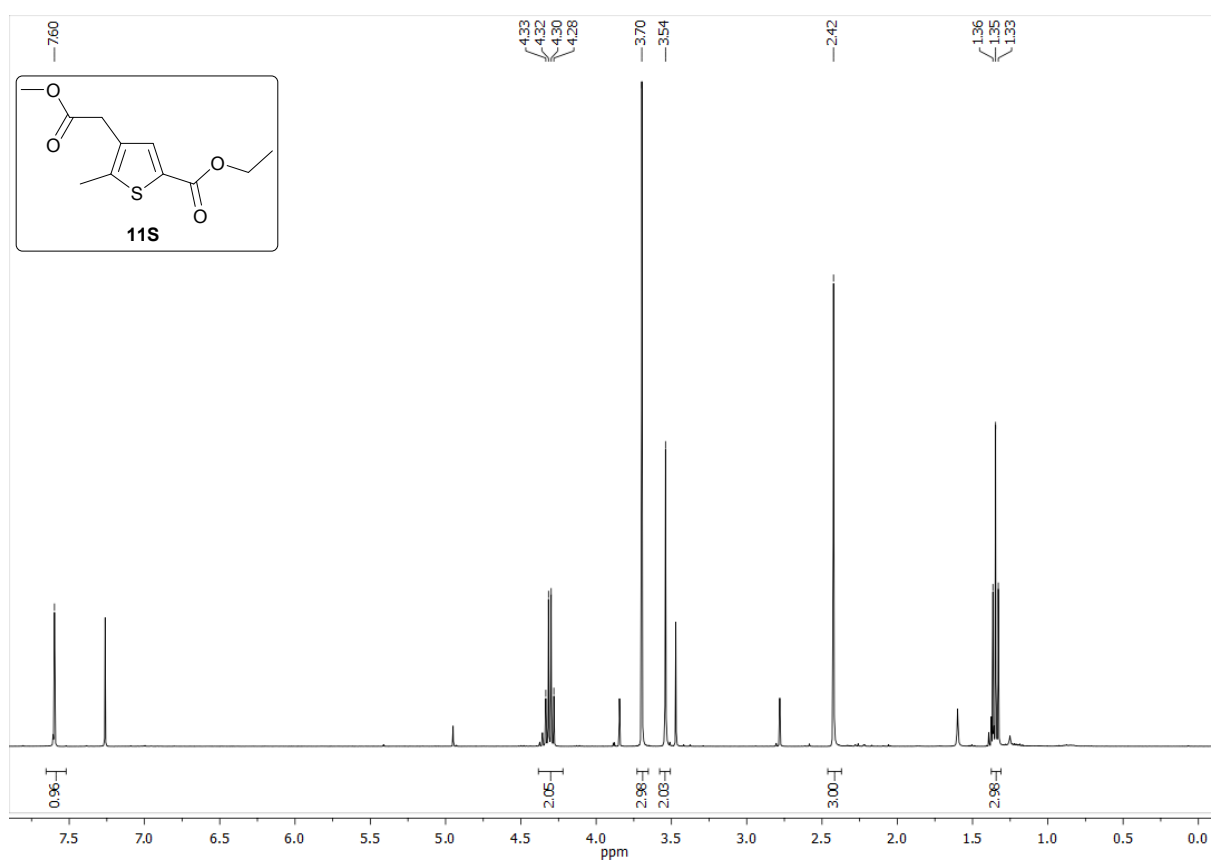
^{13}C -NMR (101 MHz, CDCl_3) for compound **11**:



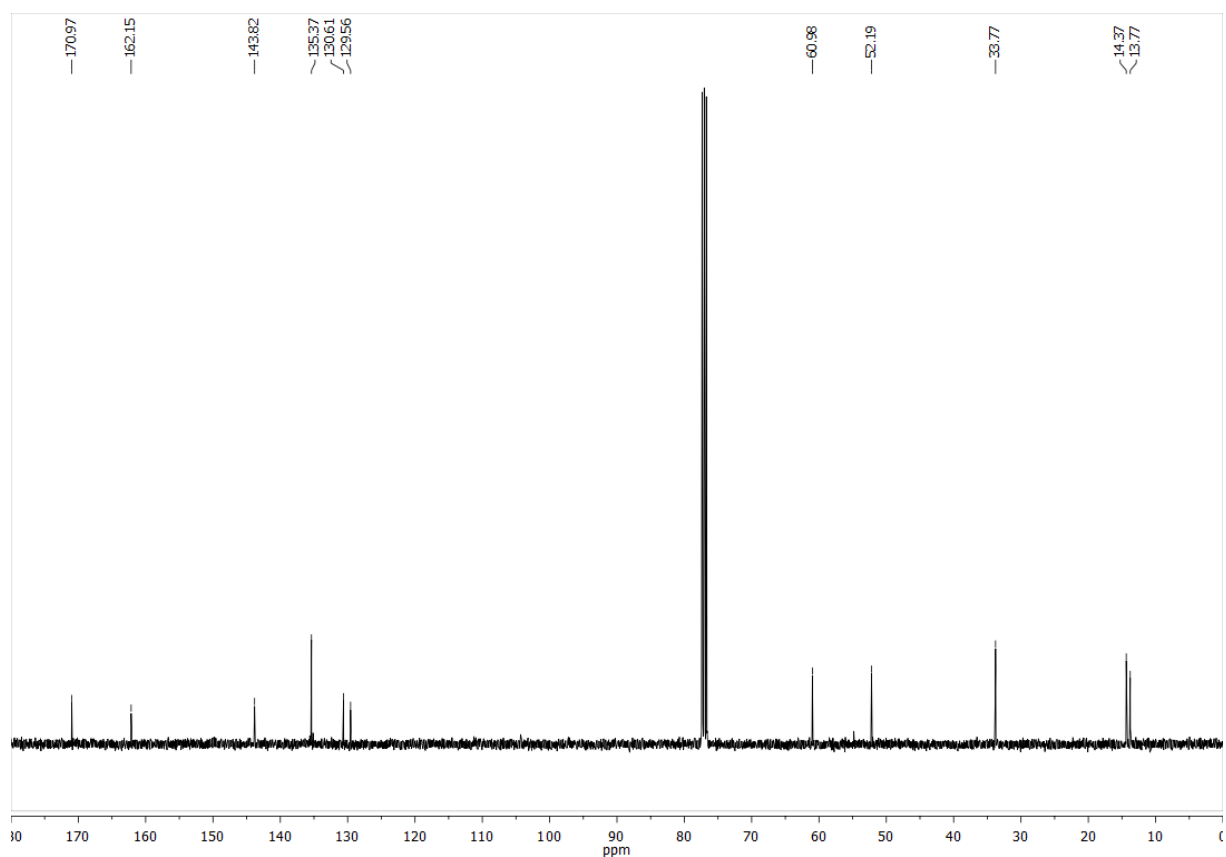
^1H -NMR (400 MHz, CDCl_3) for compound **11**:



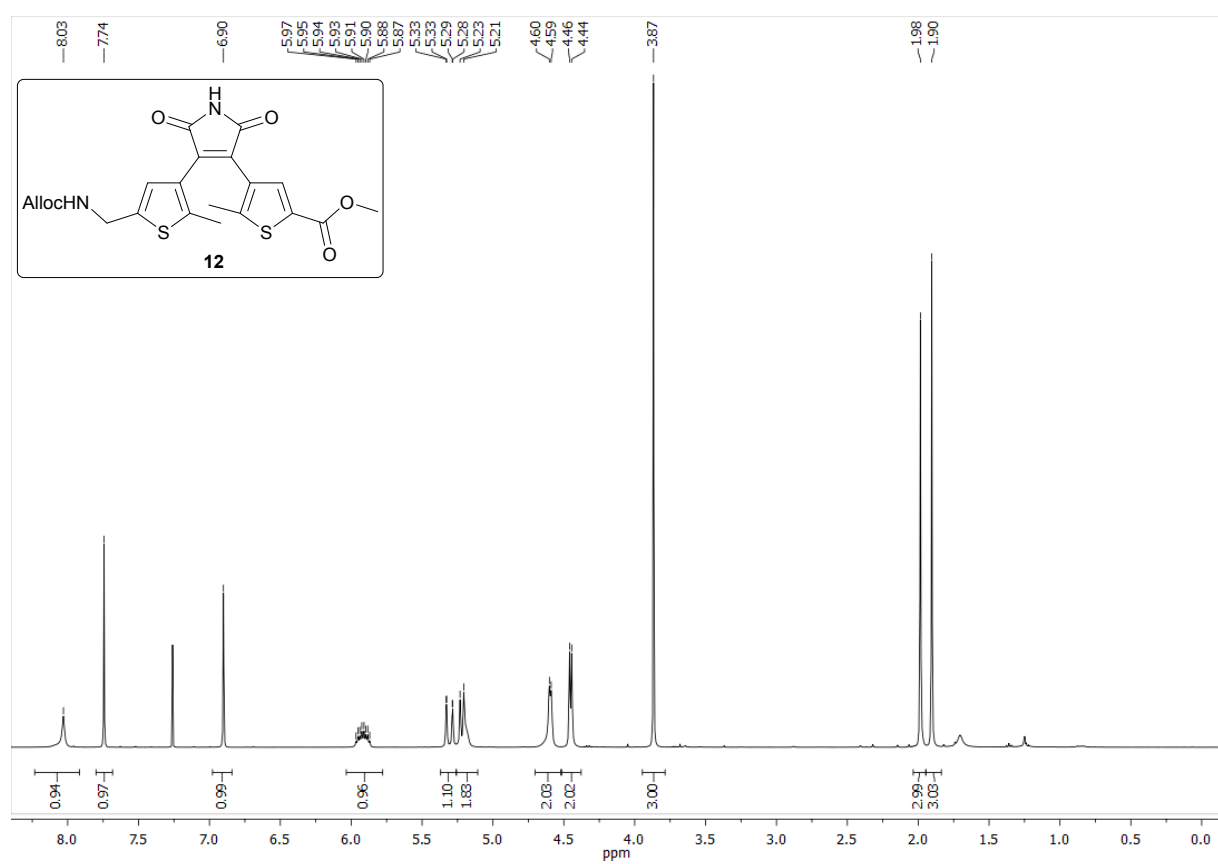
$^1\text{H-NMR}$ (400 MHz, CDCl_3) for compound **11S**:



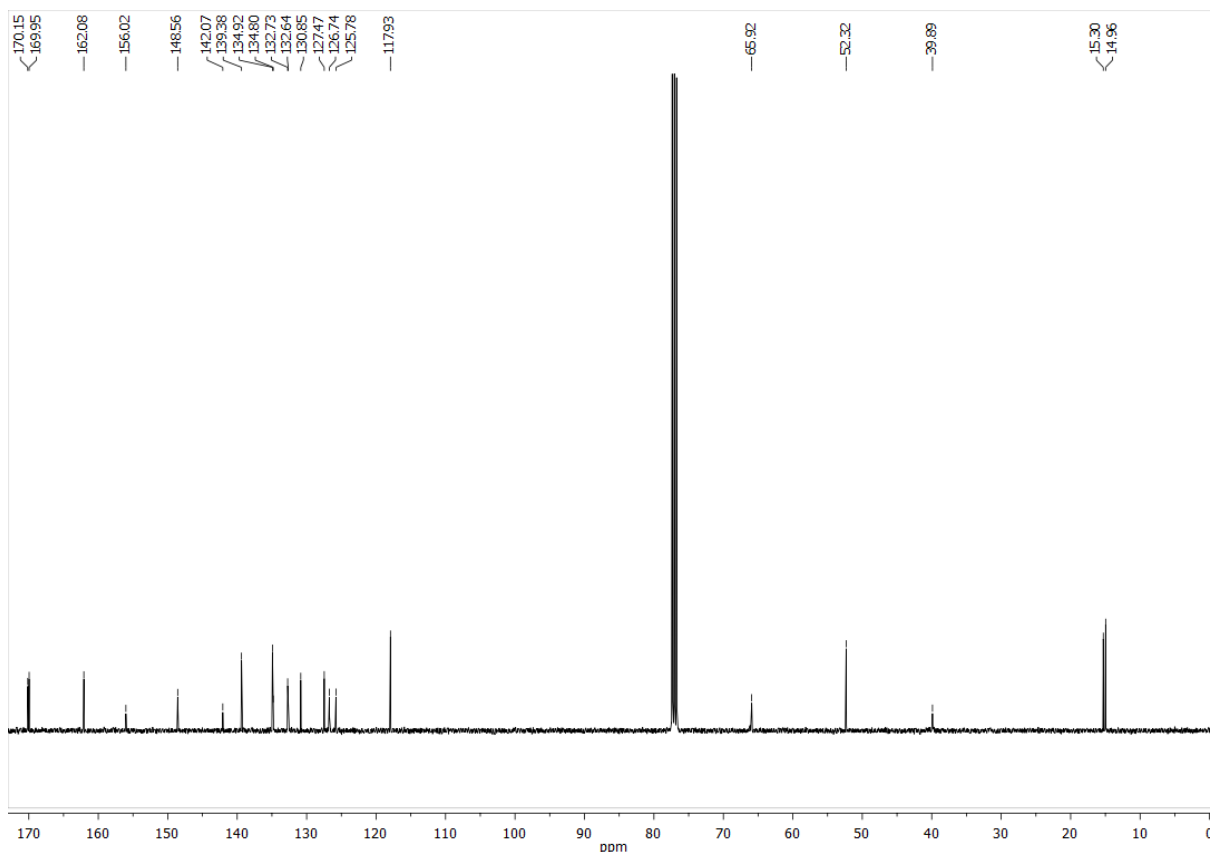
$^{13}\text{C-NMR}$ (101 MHz, CDCl_3) for compound **11S**:



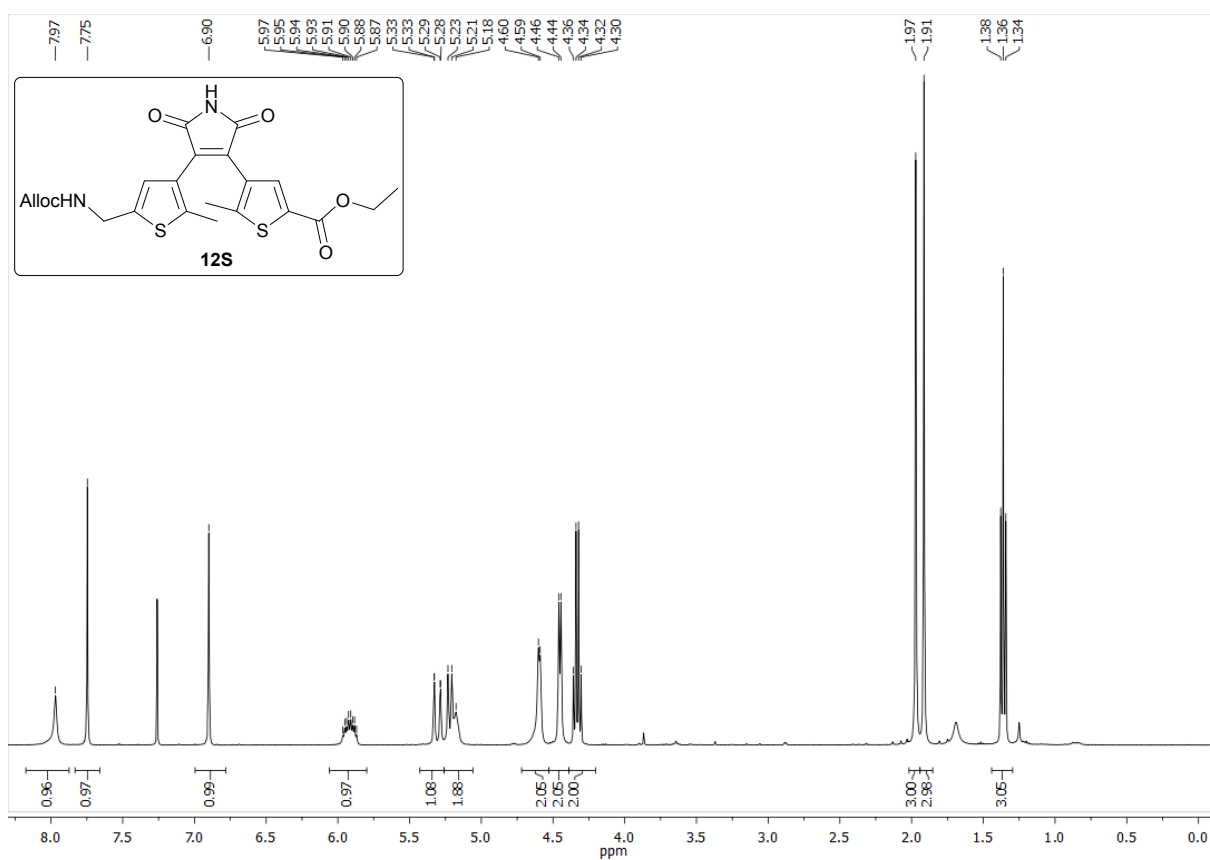
$^1\text{H-NMR}$ (400 MHz, CDCl_3) for compound **12**:



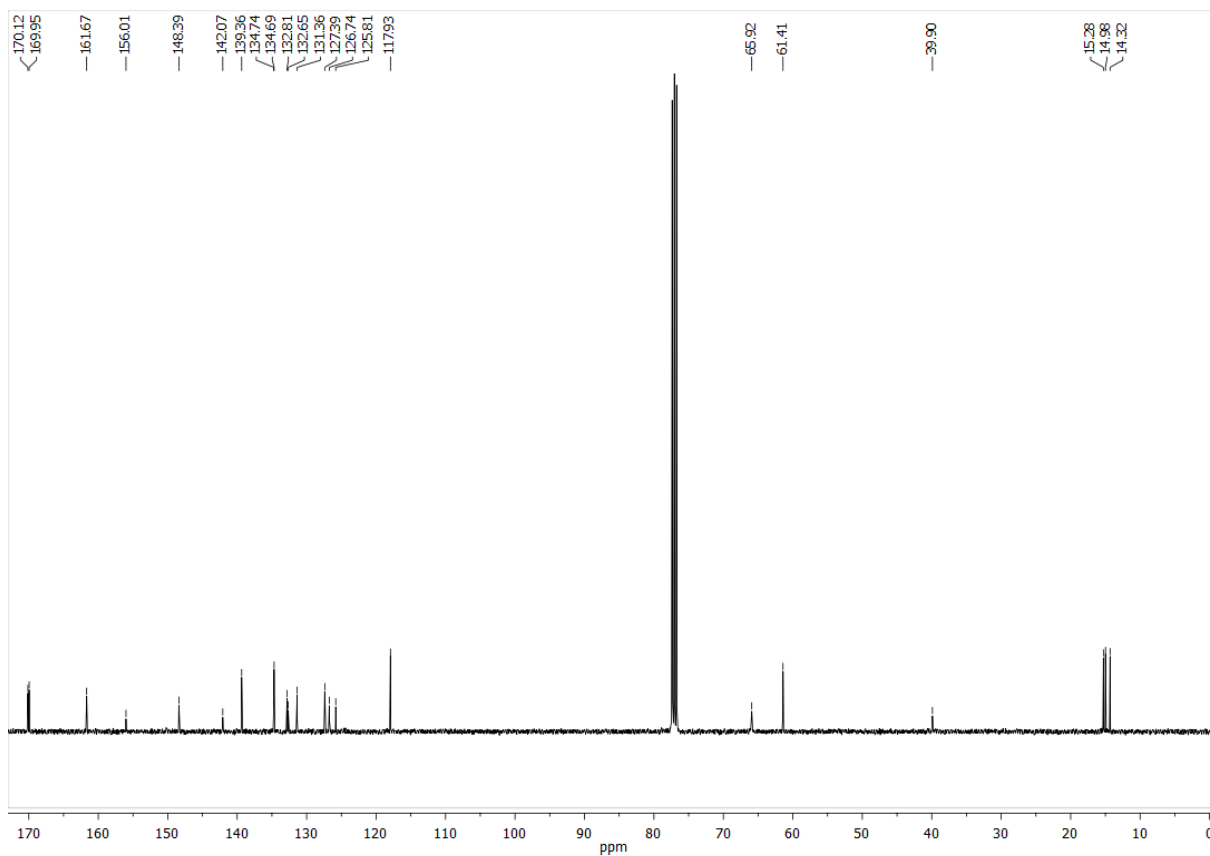
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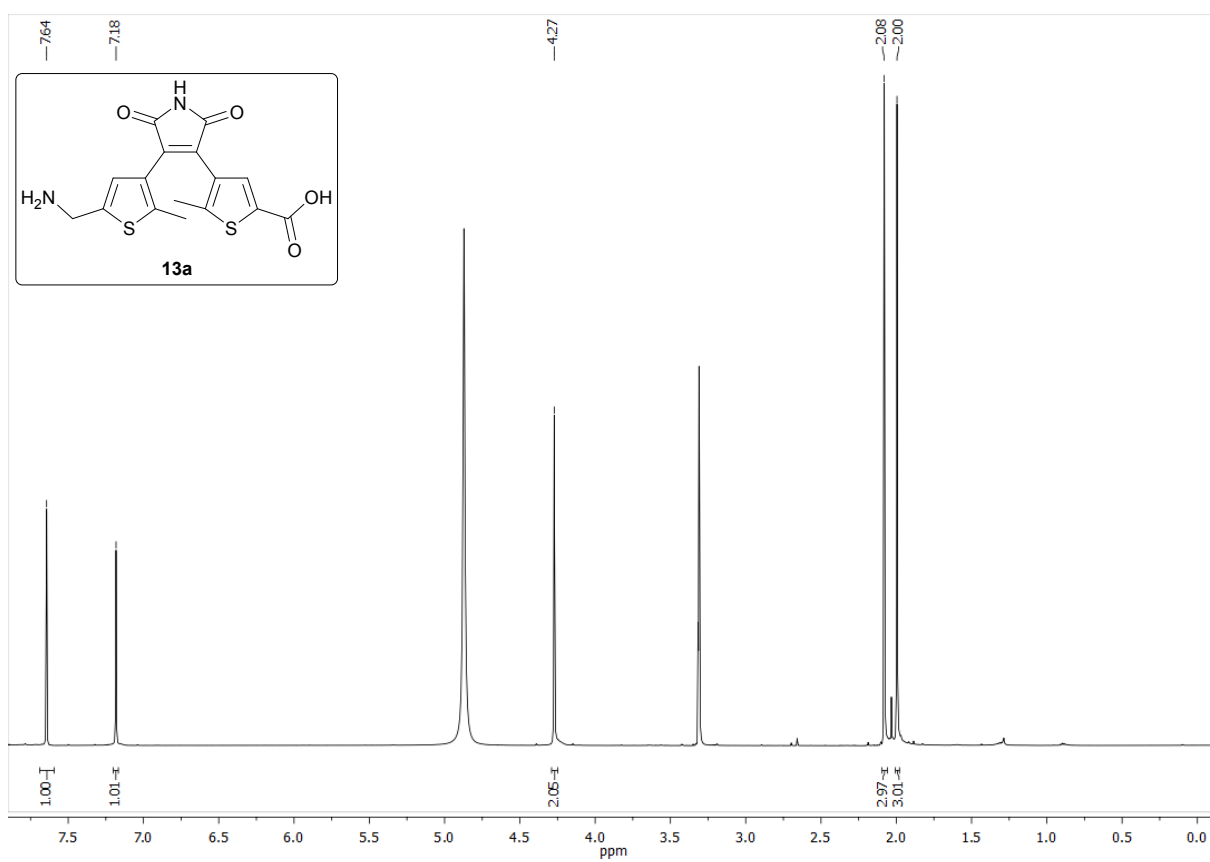
^{13}C -NMR (101 MHz, CDCl_3) for compound **12S**:



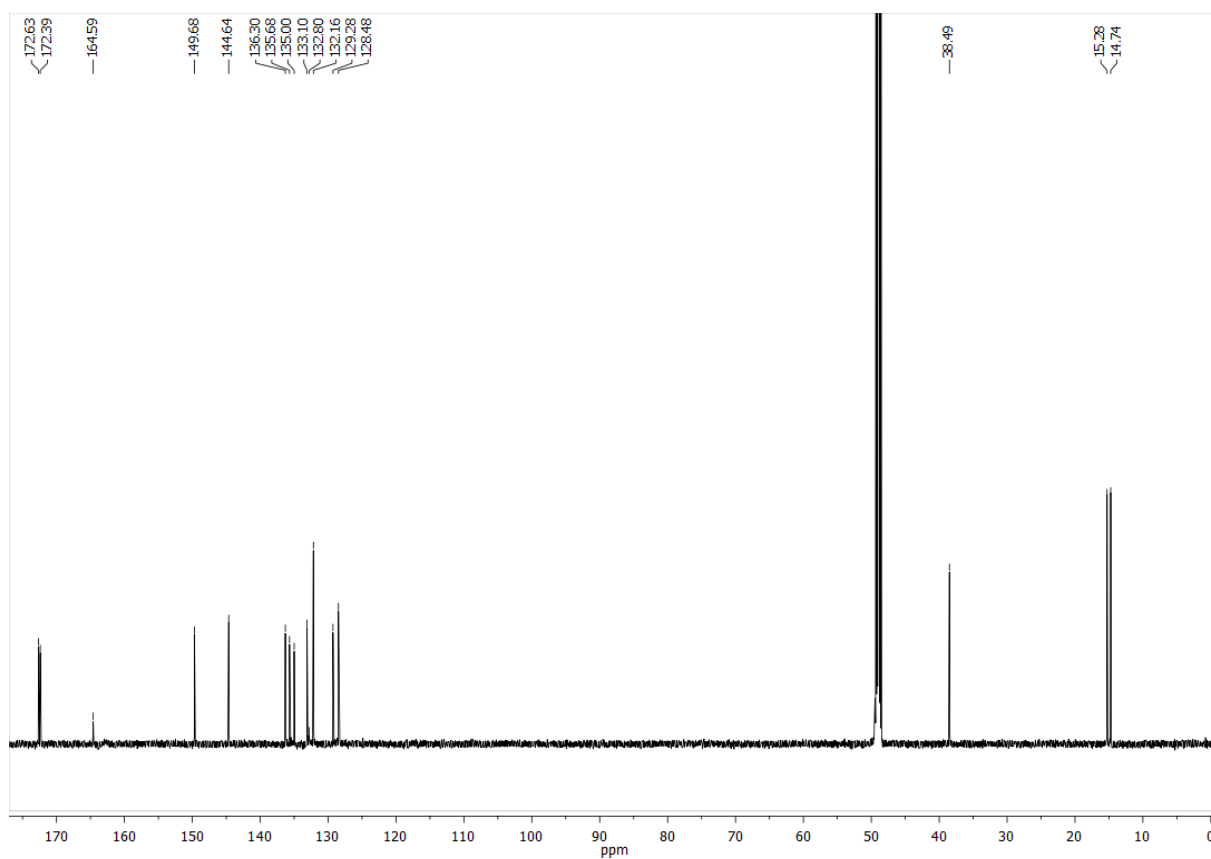
^1H -NMR (400 MHz, CDCl_3) for compound **12S**:



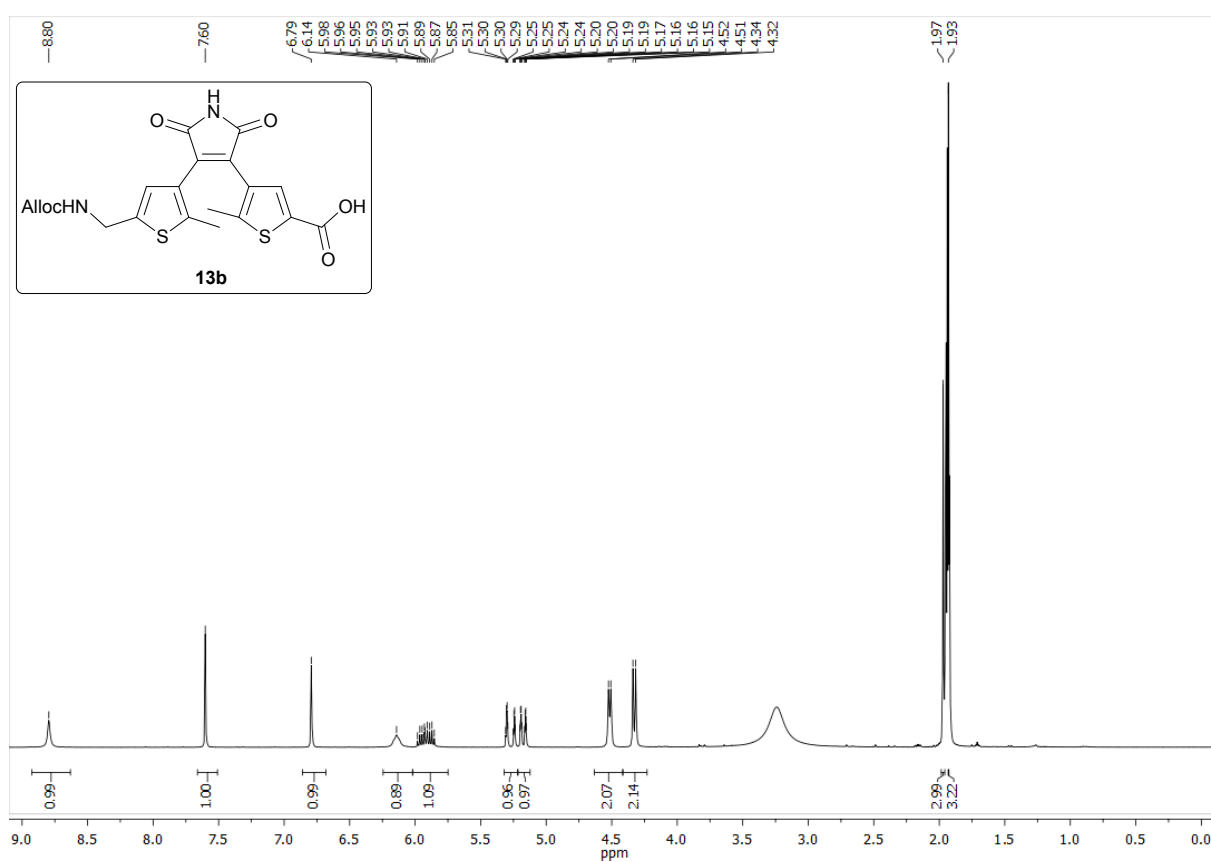
^{13}C -NMR (151 MHz, MeOD) for compound **13a**:



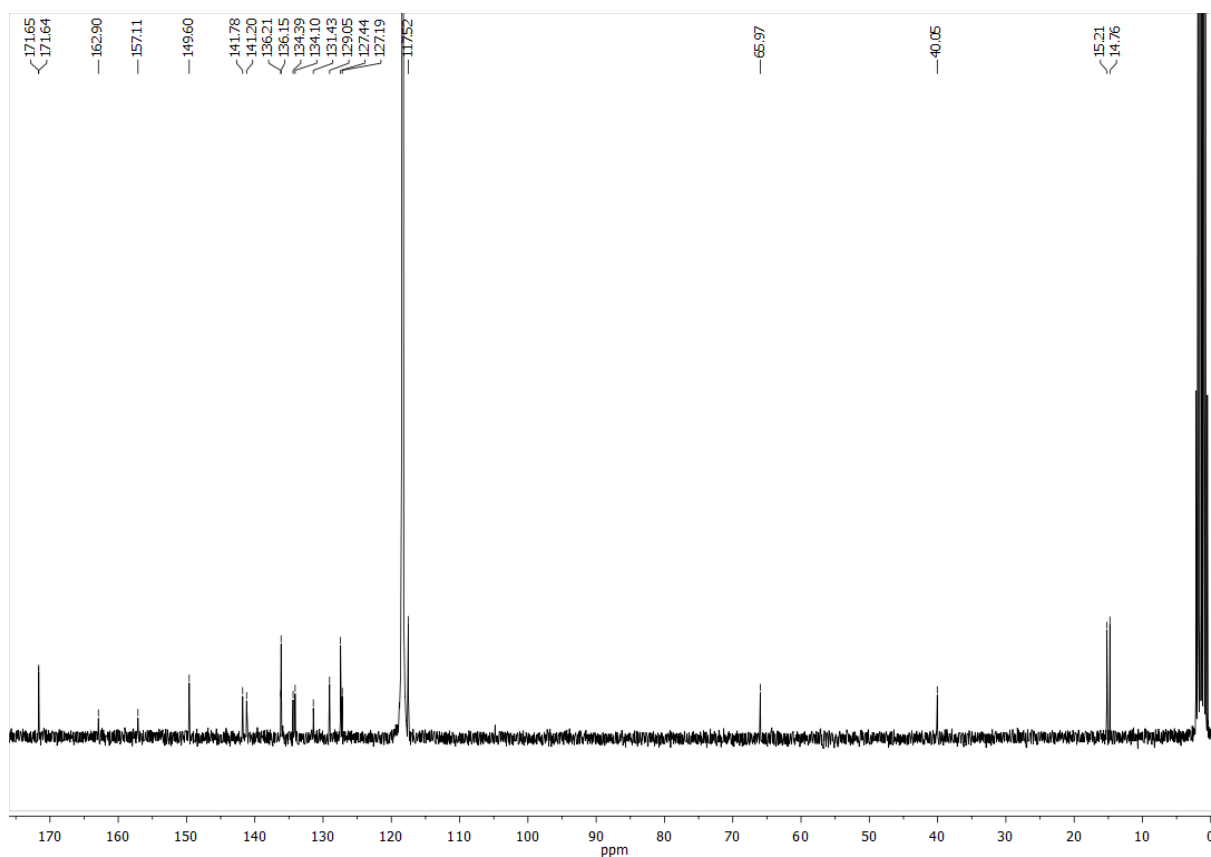
^1H -NMR (600 MHz, MeOD) for compound **13a**:



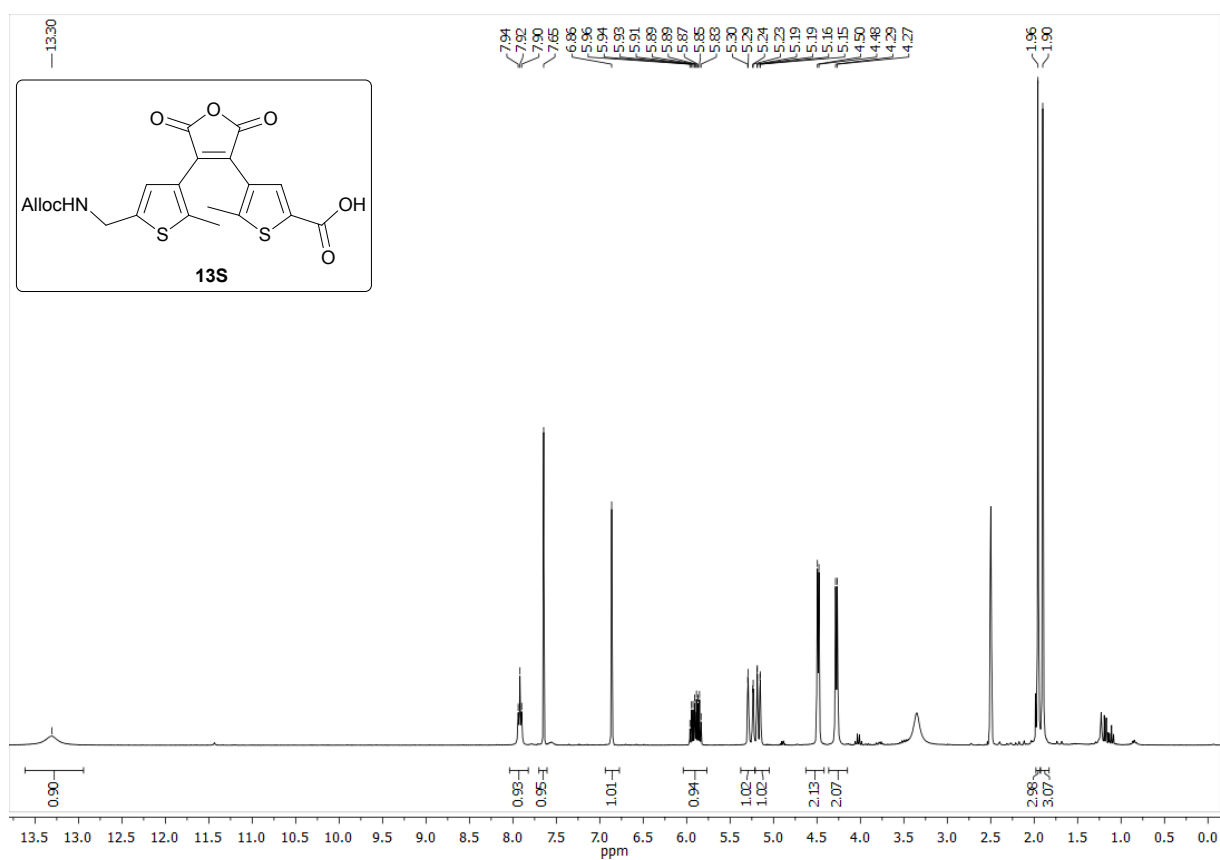
^{13}C -NMR (75 MHz, CD_3CN) for compound **13b**:



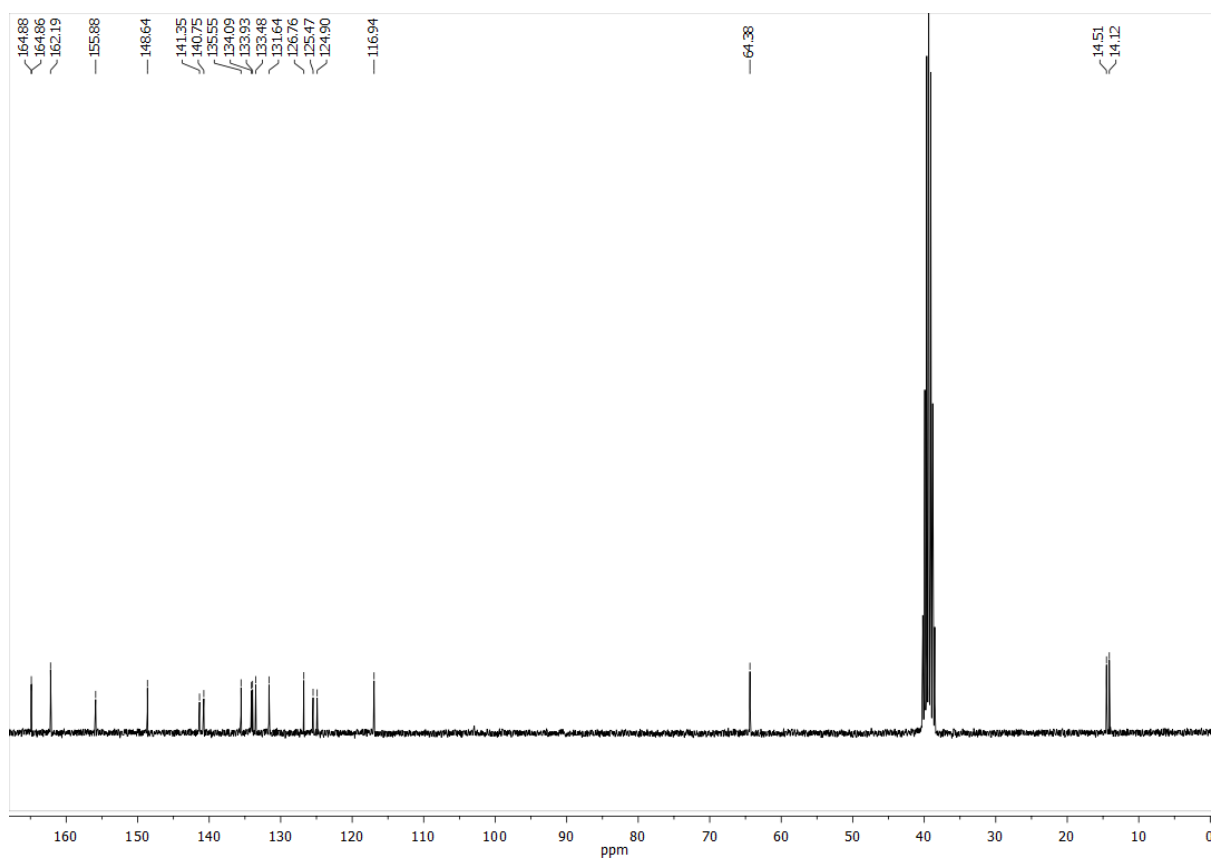
^1H -NMR (300 MHz, CD_3CN) for compound **13b**:



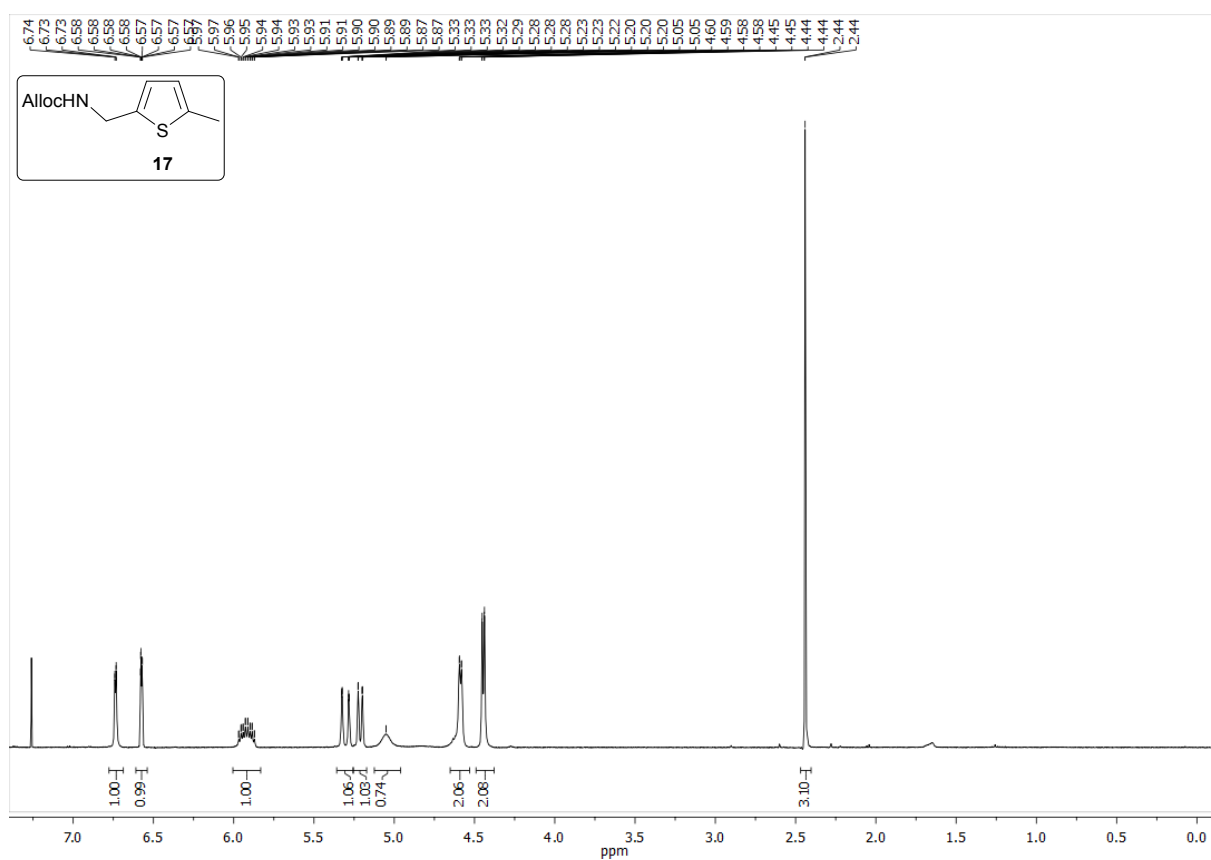
$^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **13S**:



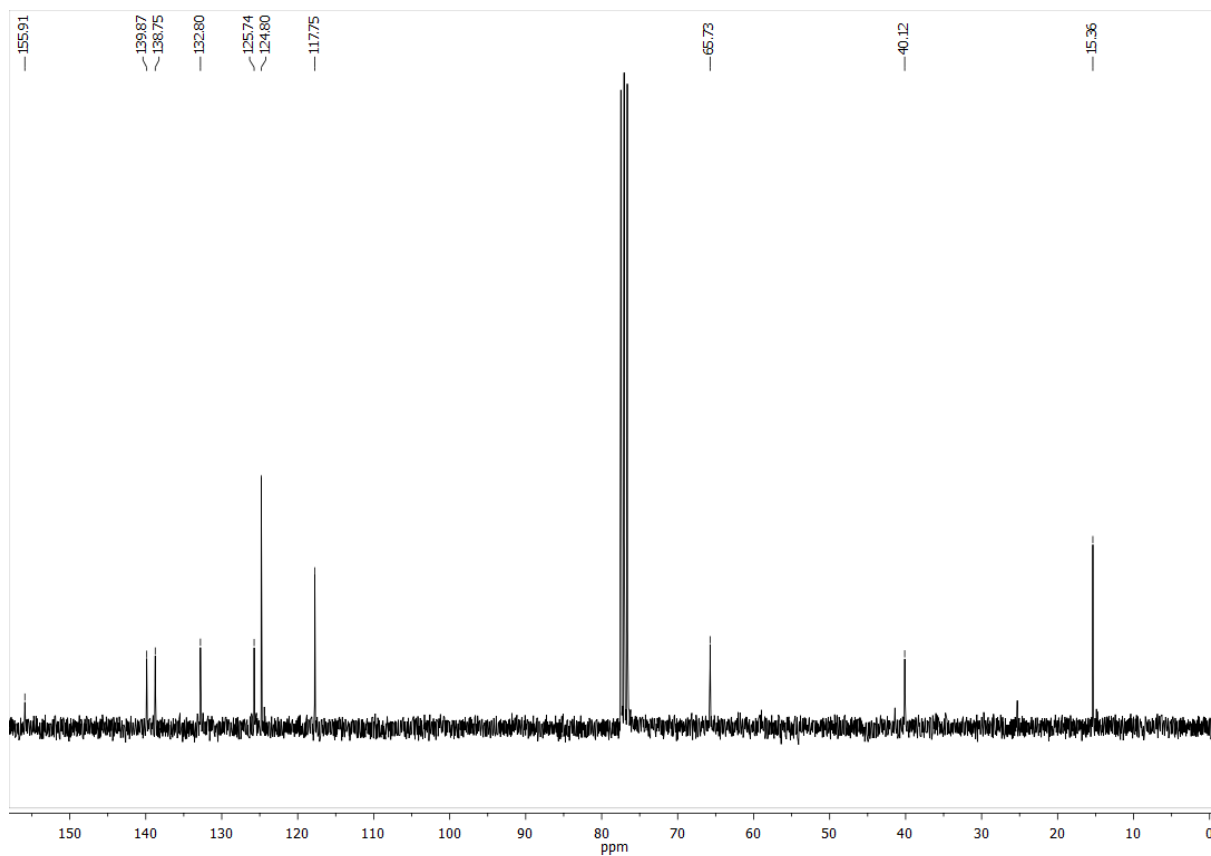
$^{13}\text{C-NMR}$ (75 MHz, $\text{DMSO-}d_6$) for compound **13S**:



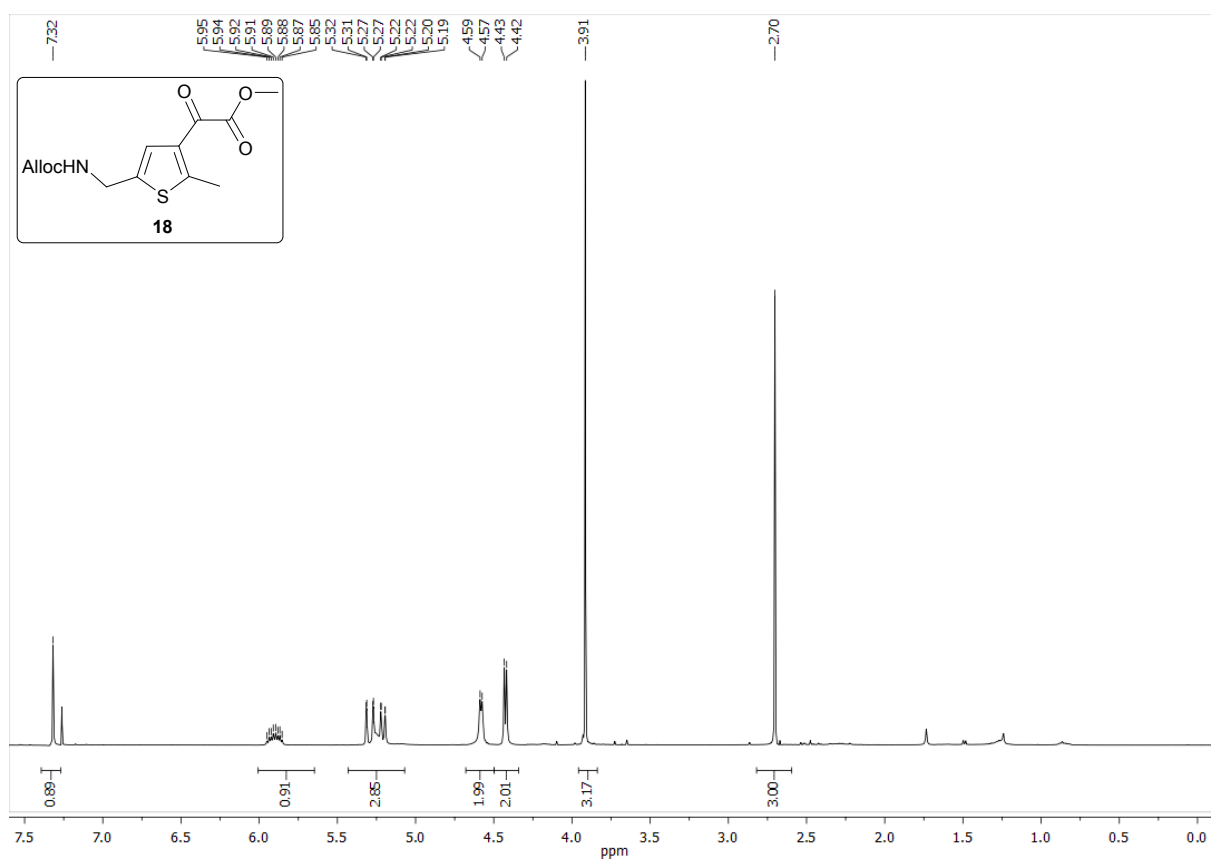
¹H-NMR (400 MHz, CDCl₃) for compound **17**:



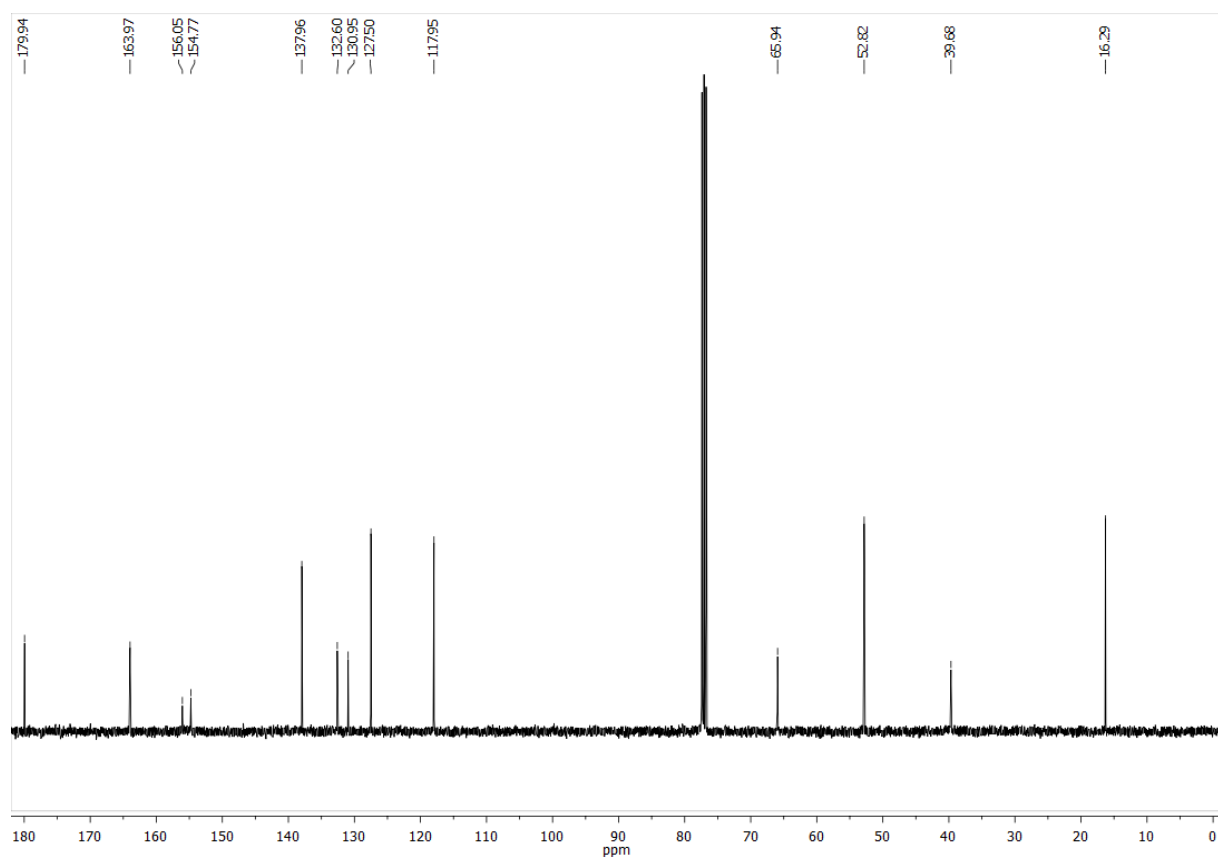
¹³C-NMR (101 MHz, CDCl₃) for compound **17**:



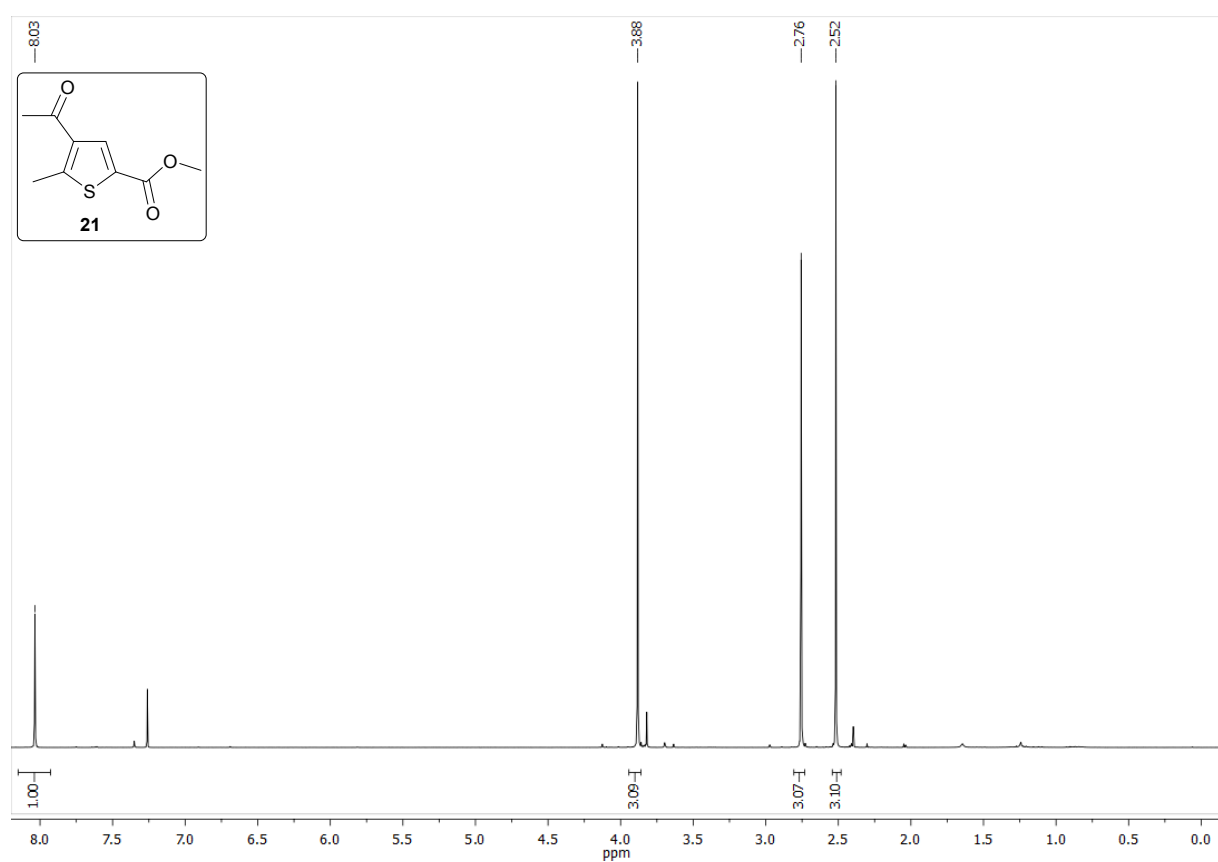
^{13}C -NMR (101 MHz, CDCl_3) for compound **18**:



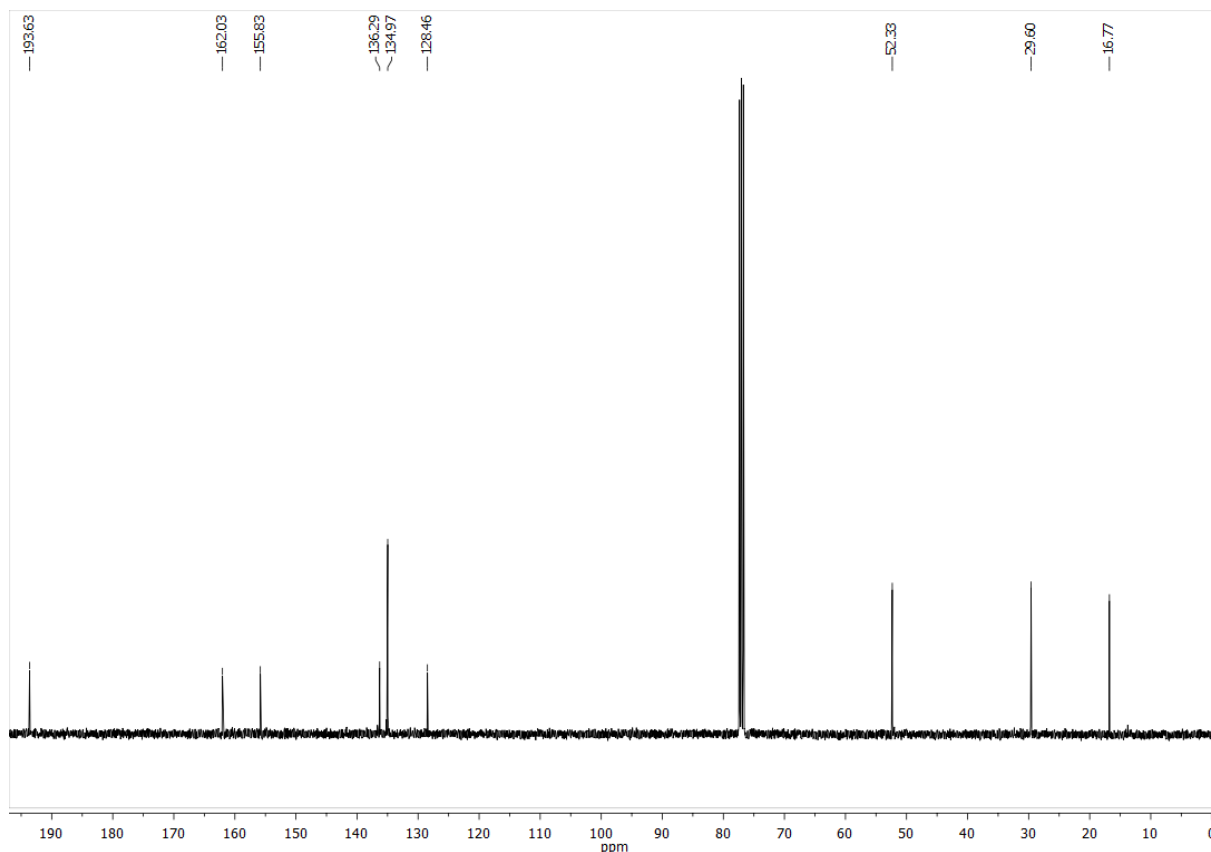
^1H -NMR (400 MHz, CDCl_3) for compound **18**:



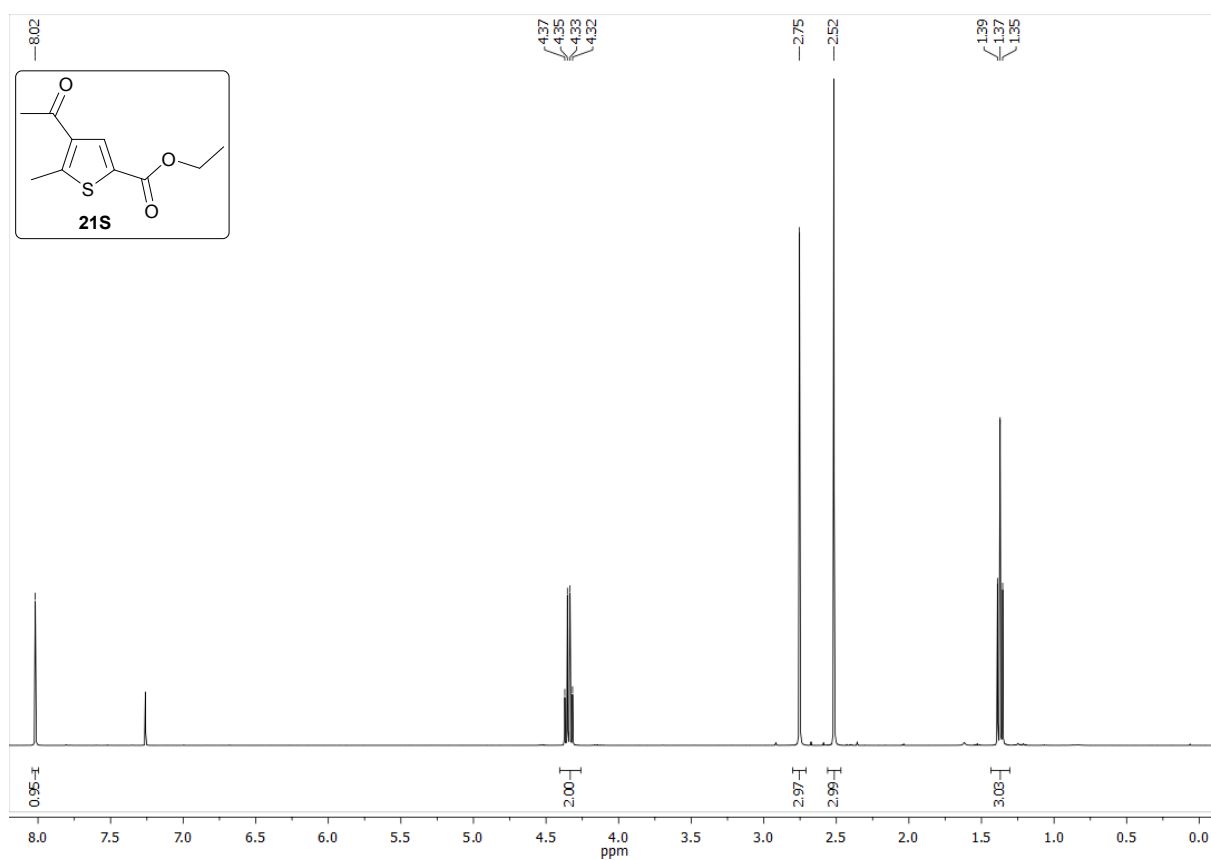
^{13}C -NMR (75 MHz, CDCl_3) for compound **21**:



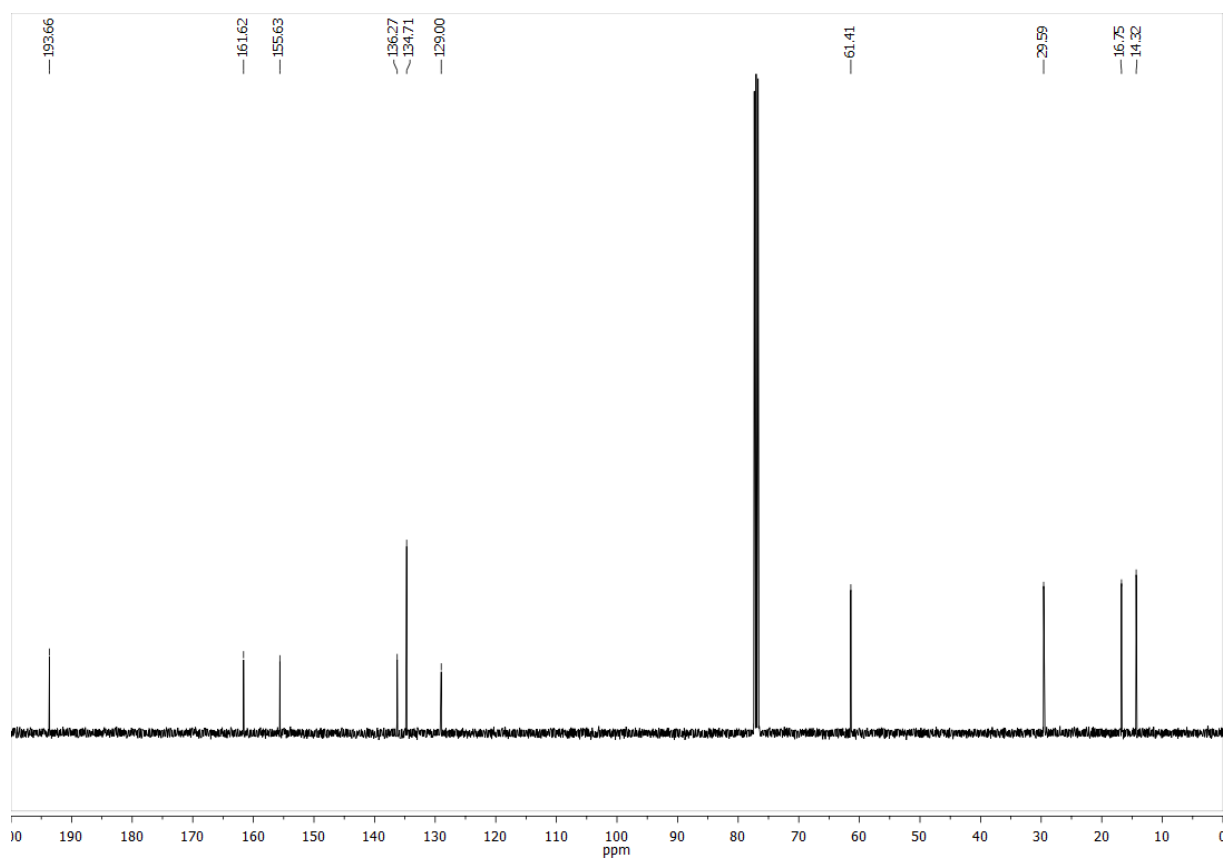
^1H -NMR (300 MHz, CDCl_3) for compound **21**:



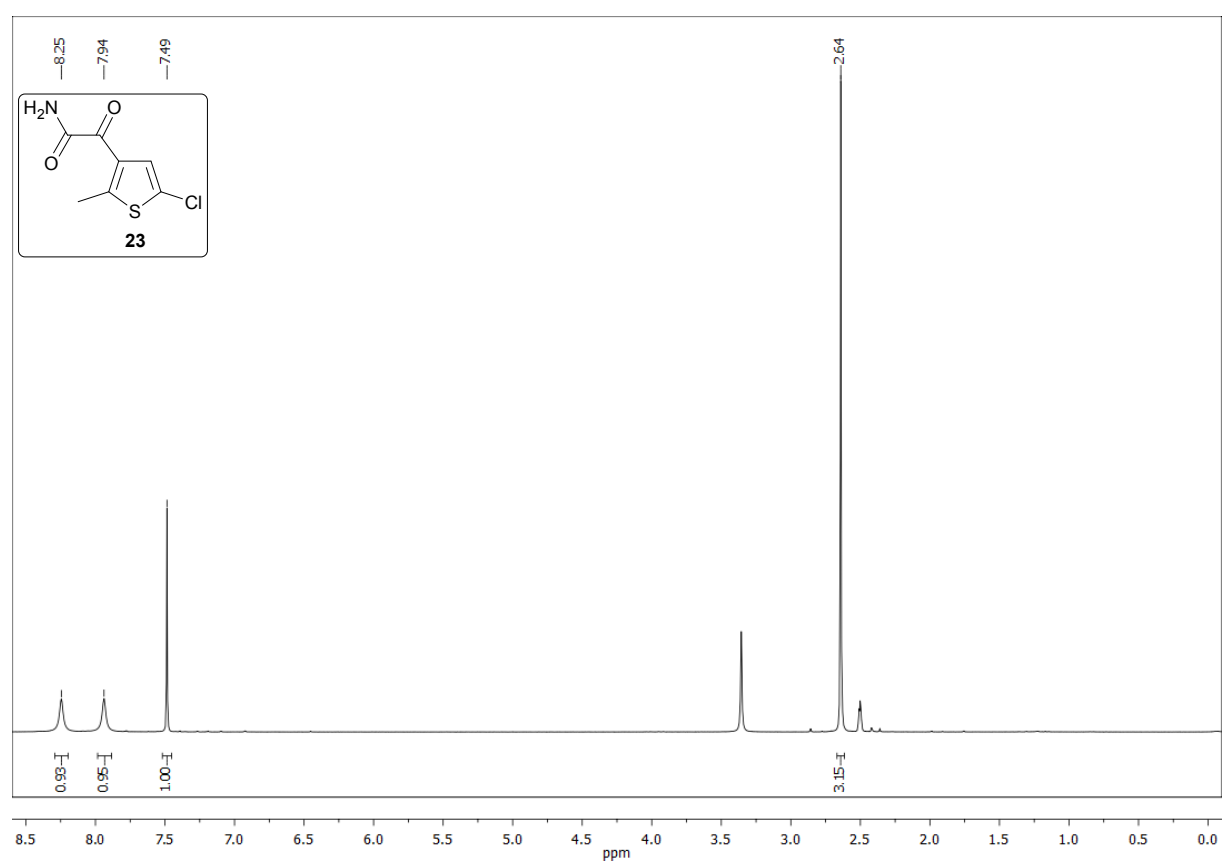
^{13}C -NMR (101 MHz, CDCl_3) for compound **21S**:



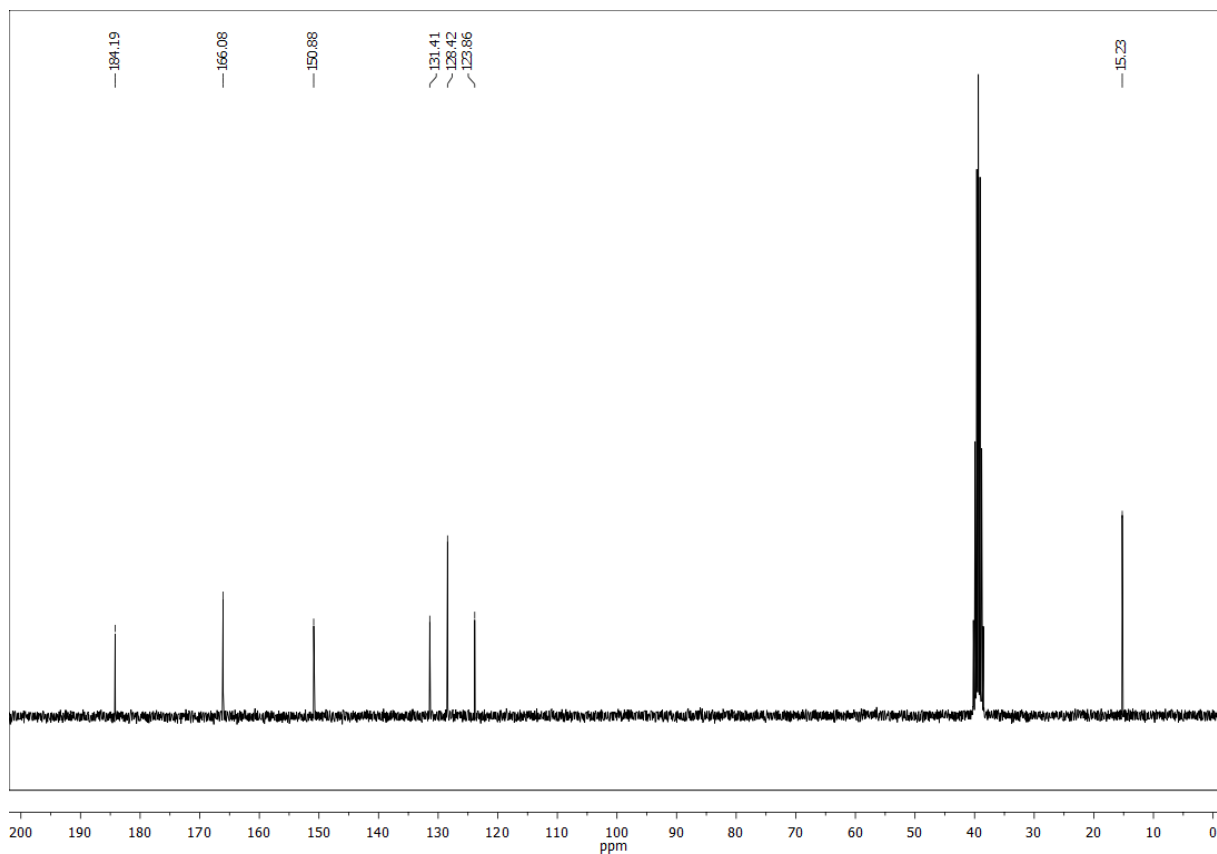
^1H -NMR (400 MHz, CDCl_3) for compound **21S**:



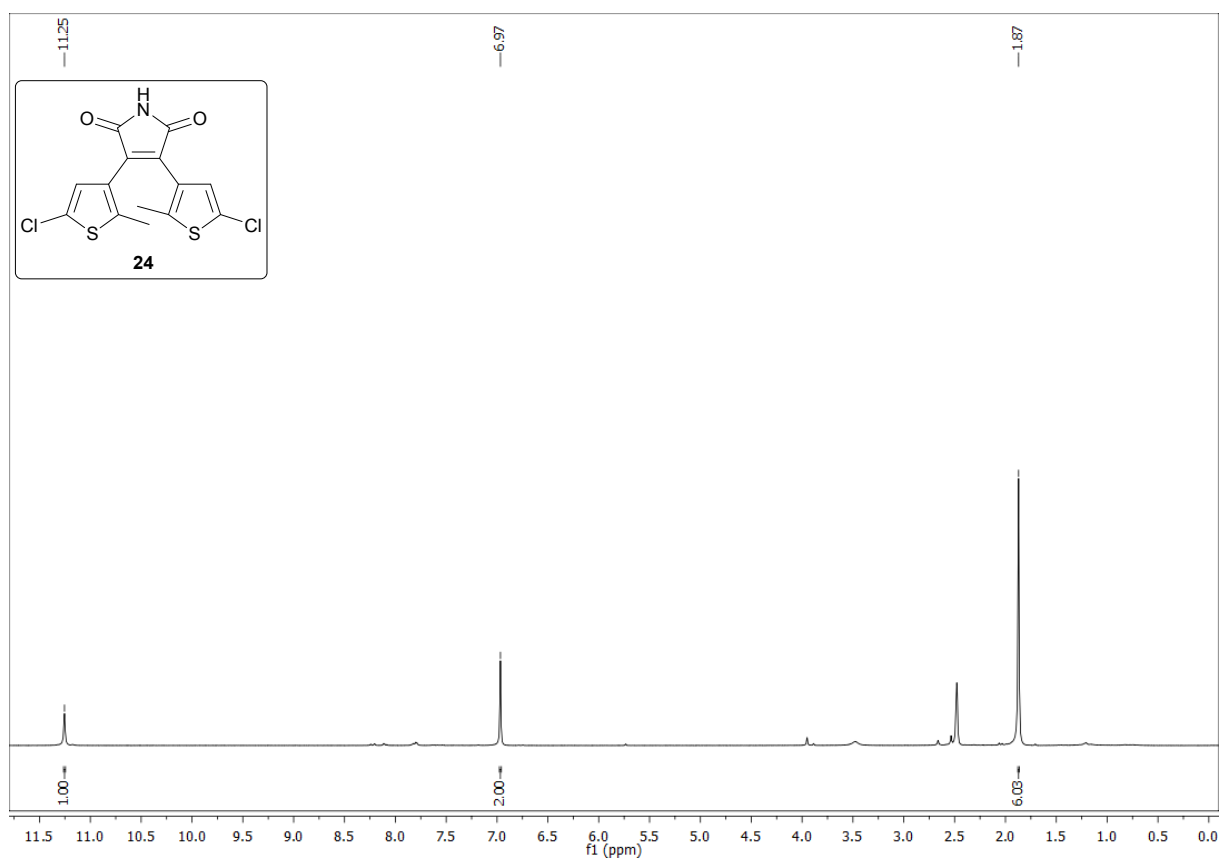
^{13}C -NMR (75 MHz, $\text{DMSO}-d_6$) for compound **23**:



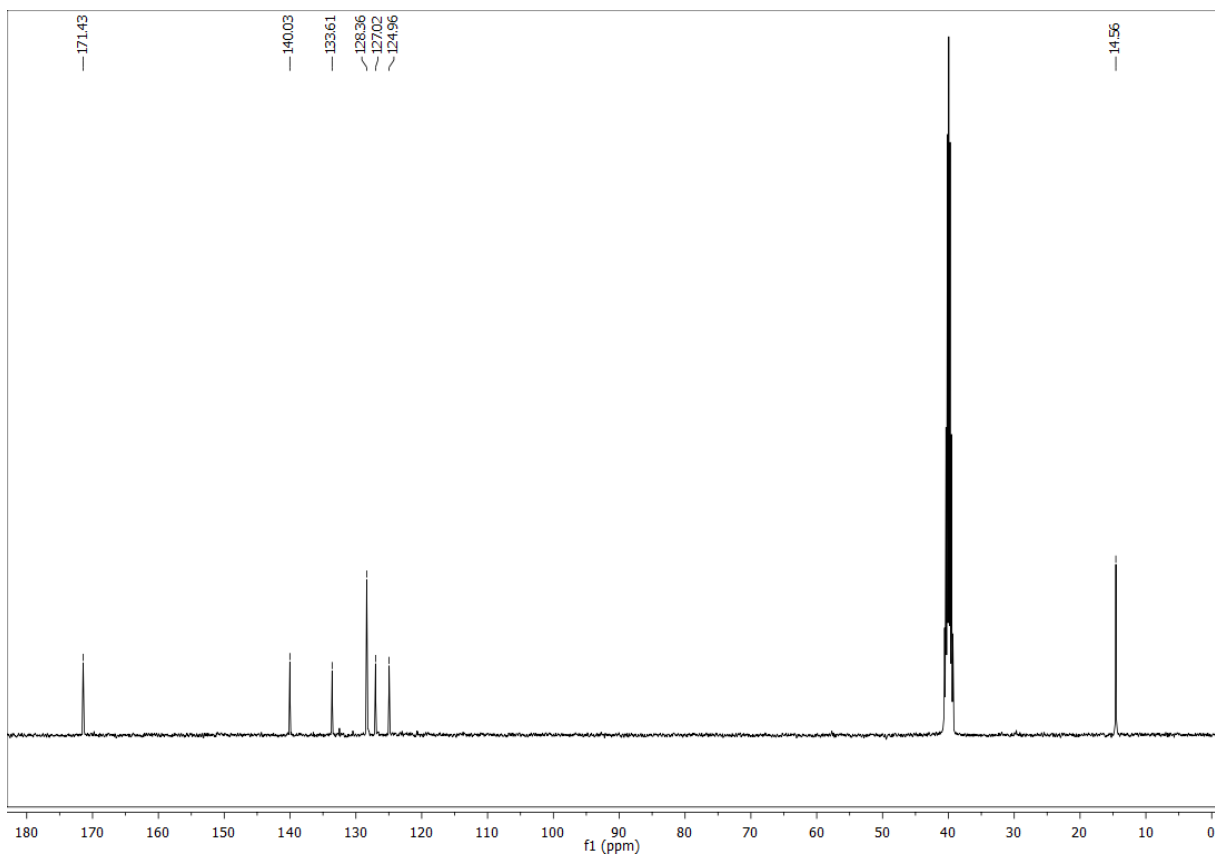
^1H -NMR (300 MHz, $\text{DMSO}-d_6$) for compound **23**:



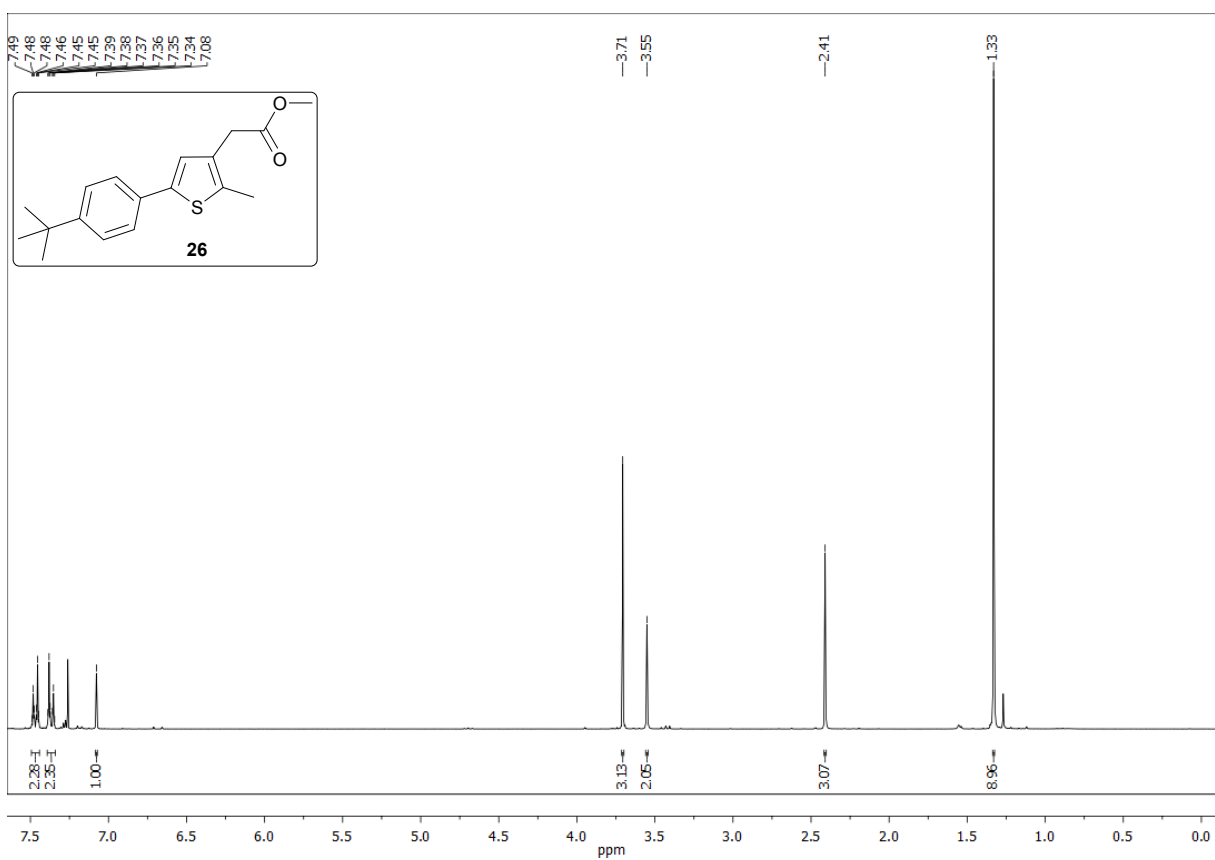
^1H -NMR (400 MHz, $\text{DMSO-}d_6$) for compound **24**:



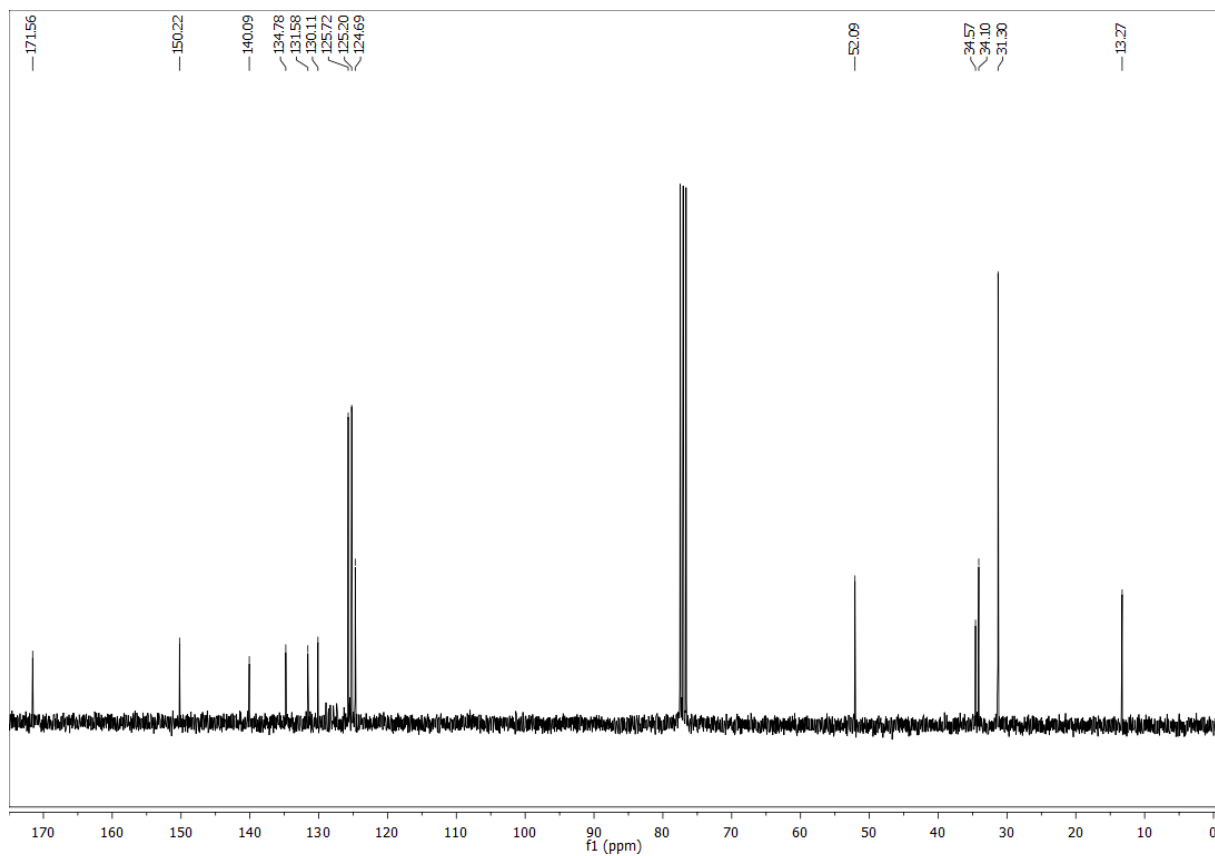
^{13}C -NMR (101 MHz, $\text{DMSO-}d_6$) for compound **24**:



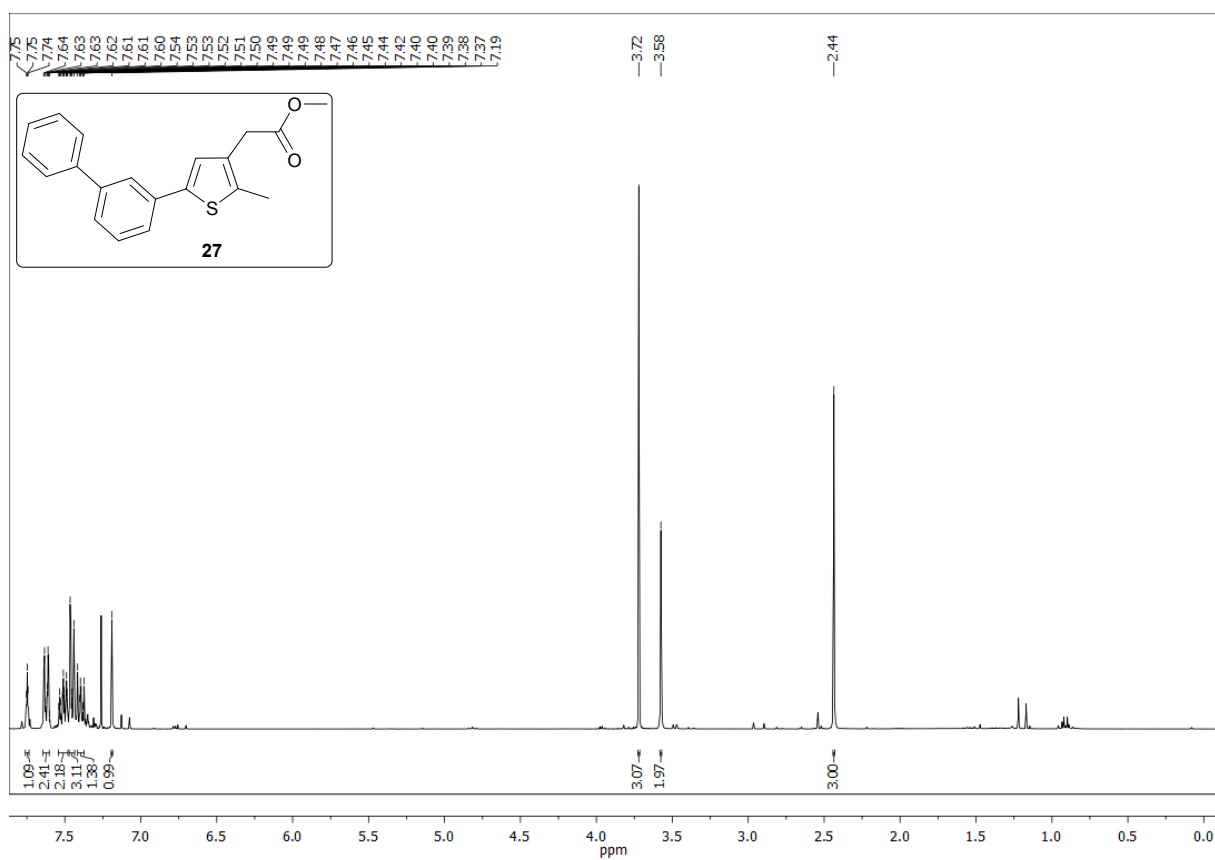
¹H-NMR (300 MHz, CDCl₃) for compound **26**:



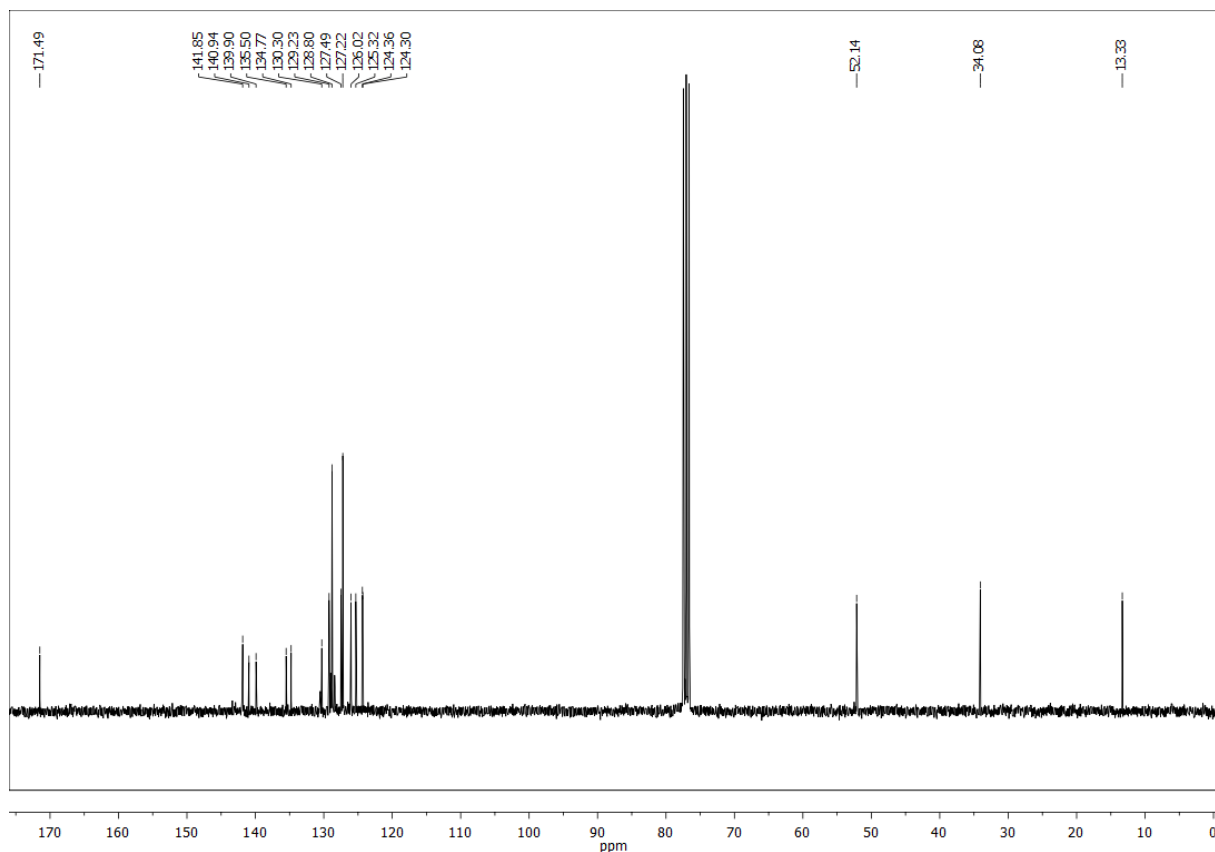
¹³C-NMR (75 MHz, CDCl₃) for compound **26**:



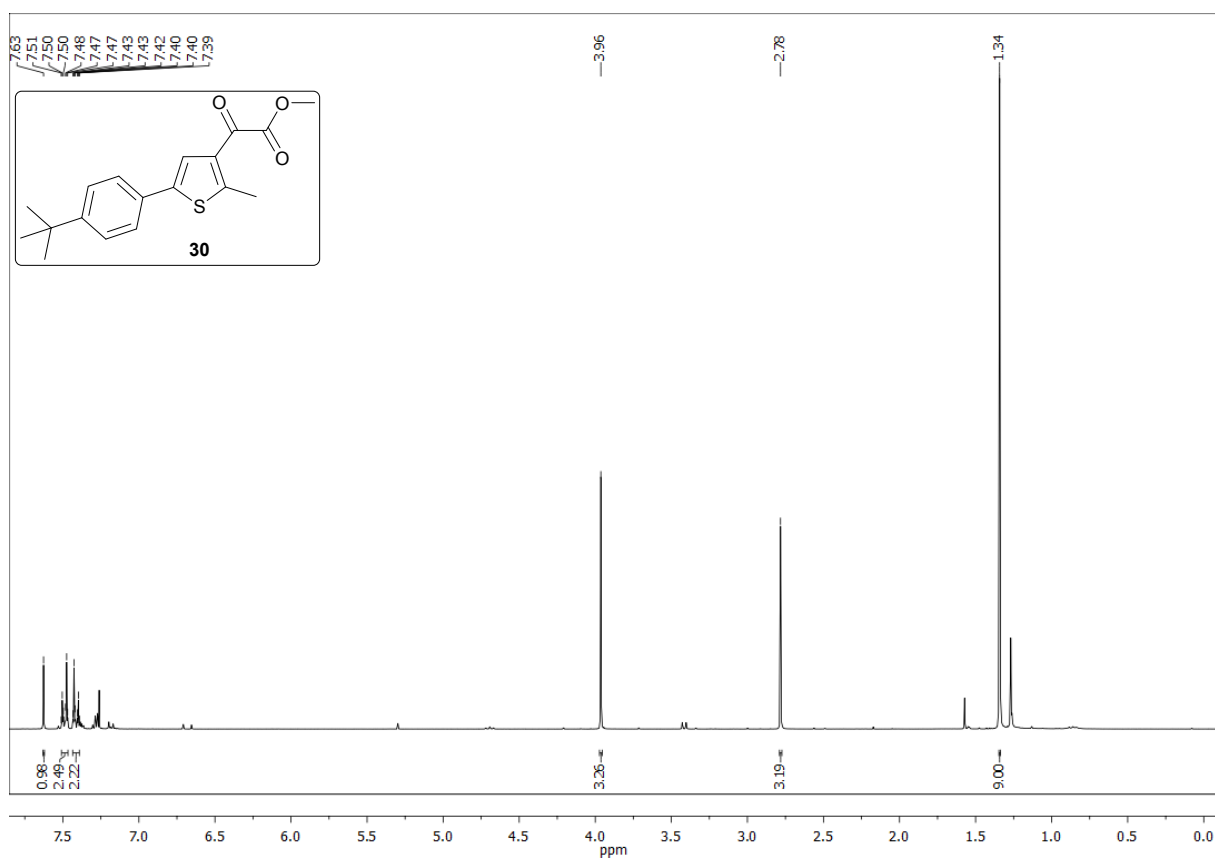
$^1\text{H-NMR}$ (300 MHz, CDCl_3) for compound **27**:



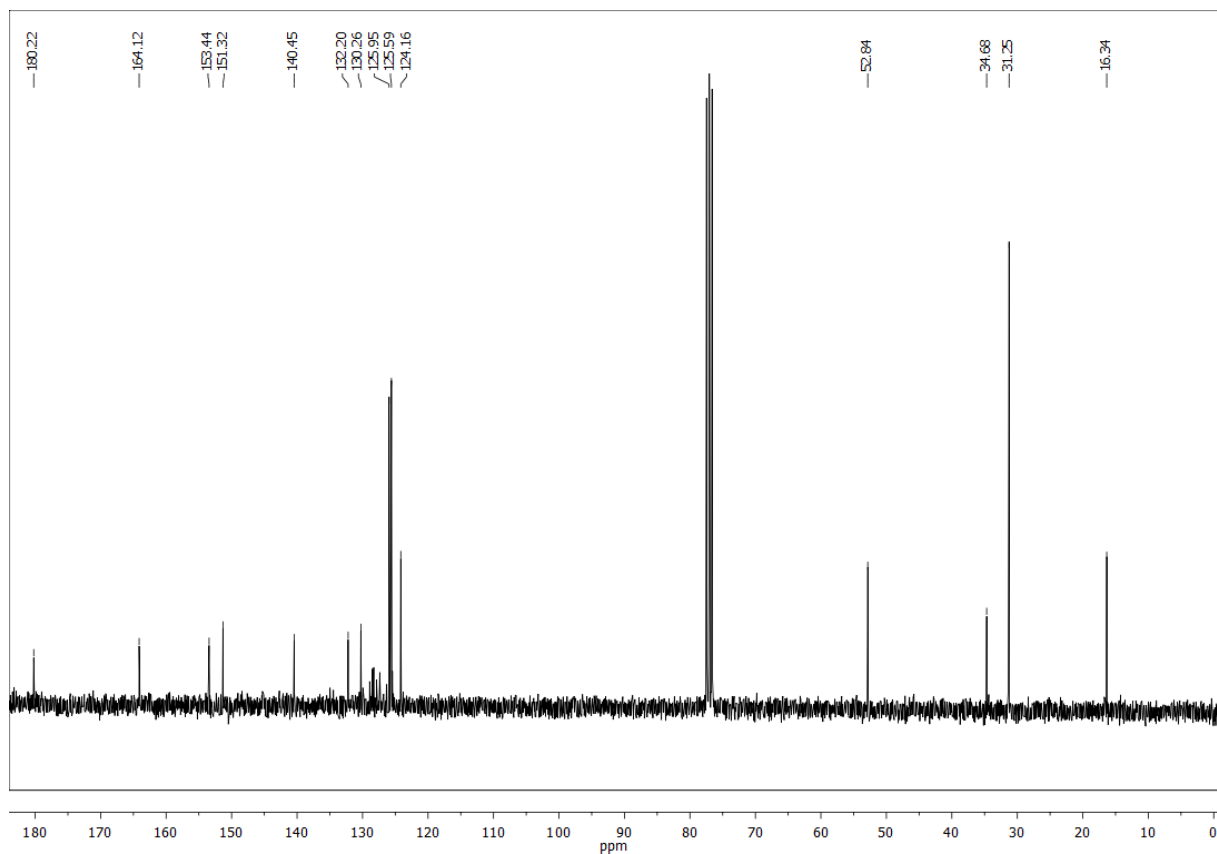
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) for compound **27**:



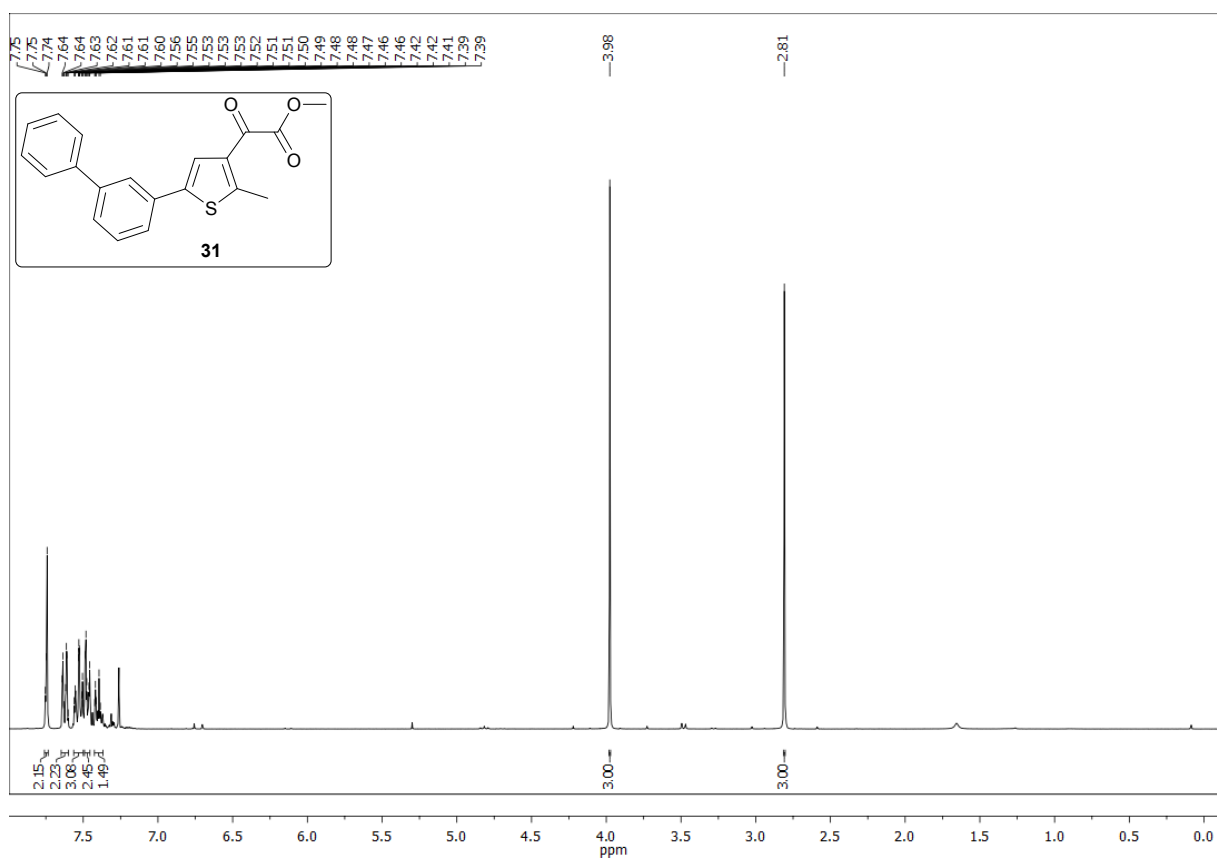
^{13}C -NMR (75 MHz, CDCl_3) for compound **30**:



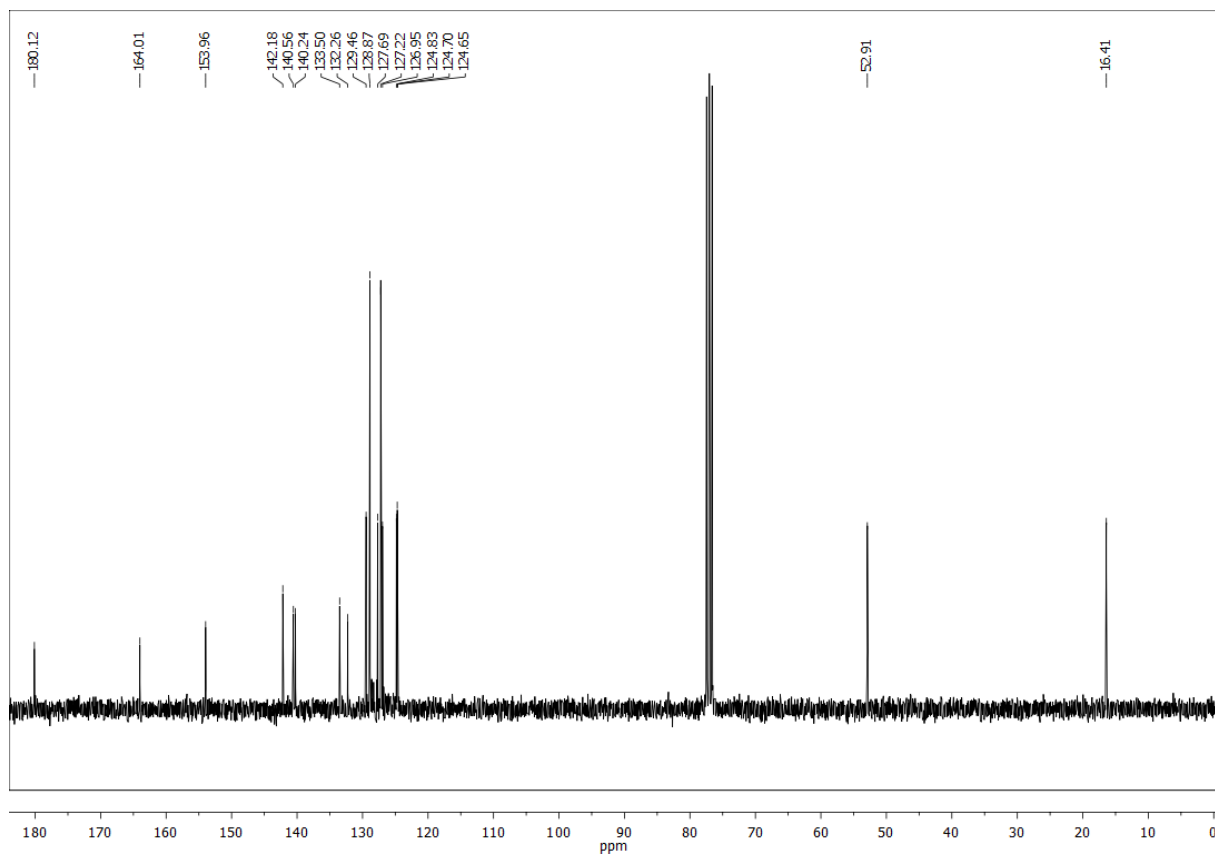
^1H -NMR (300 MHz, CDCl_3) for compound **30**:



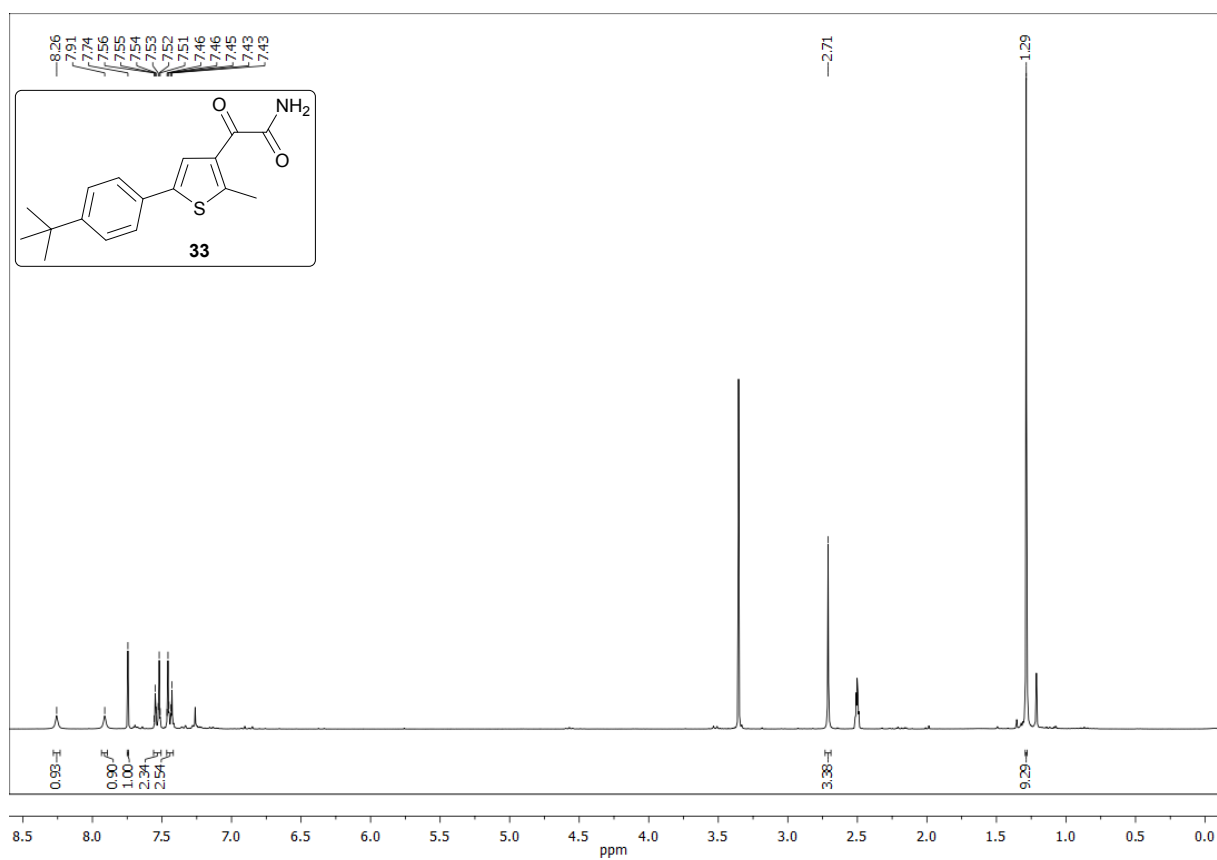
$^1\text{H-NMR}$ (300 MHz, CDCl_3) for compound **31**:



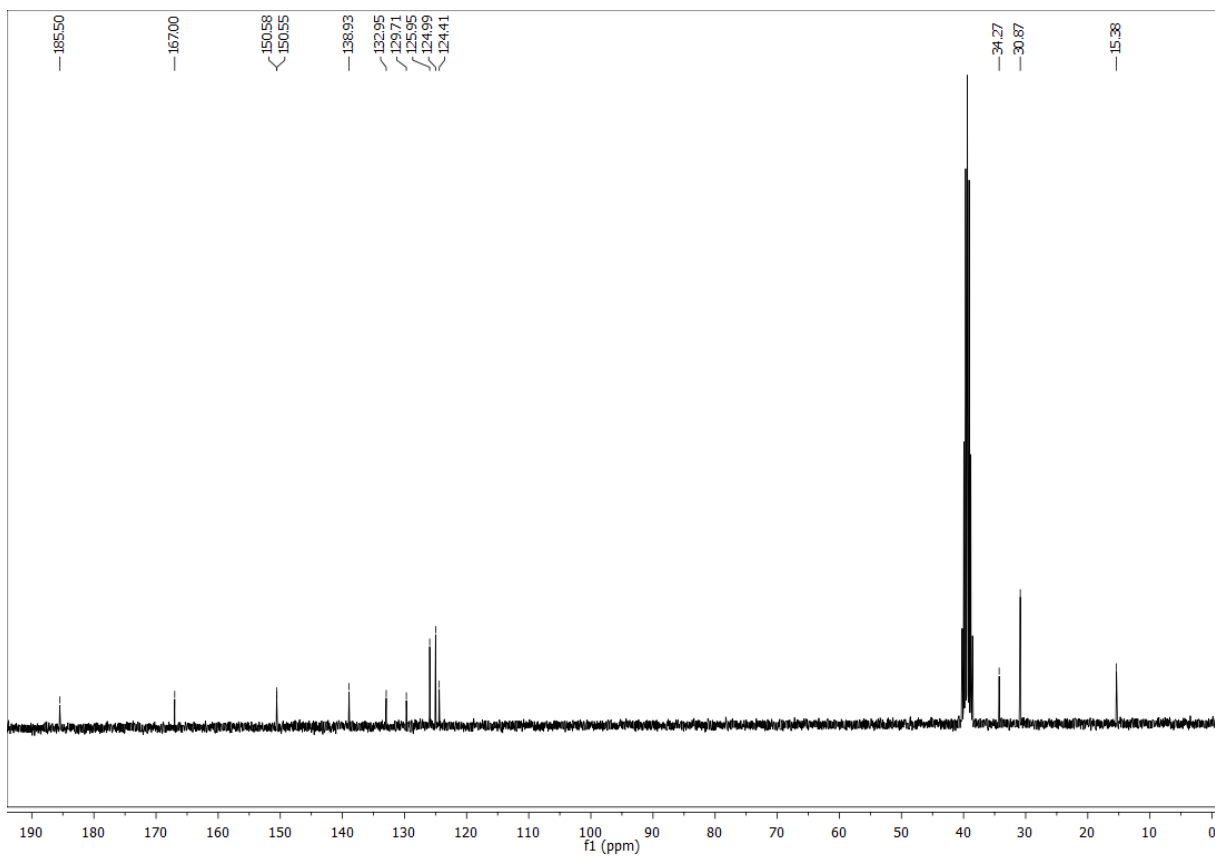
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3) for compound **31**:



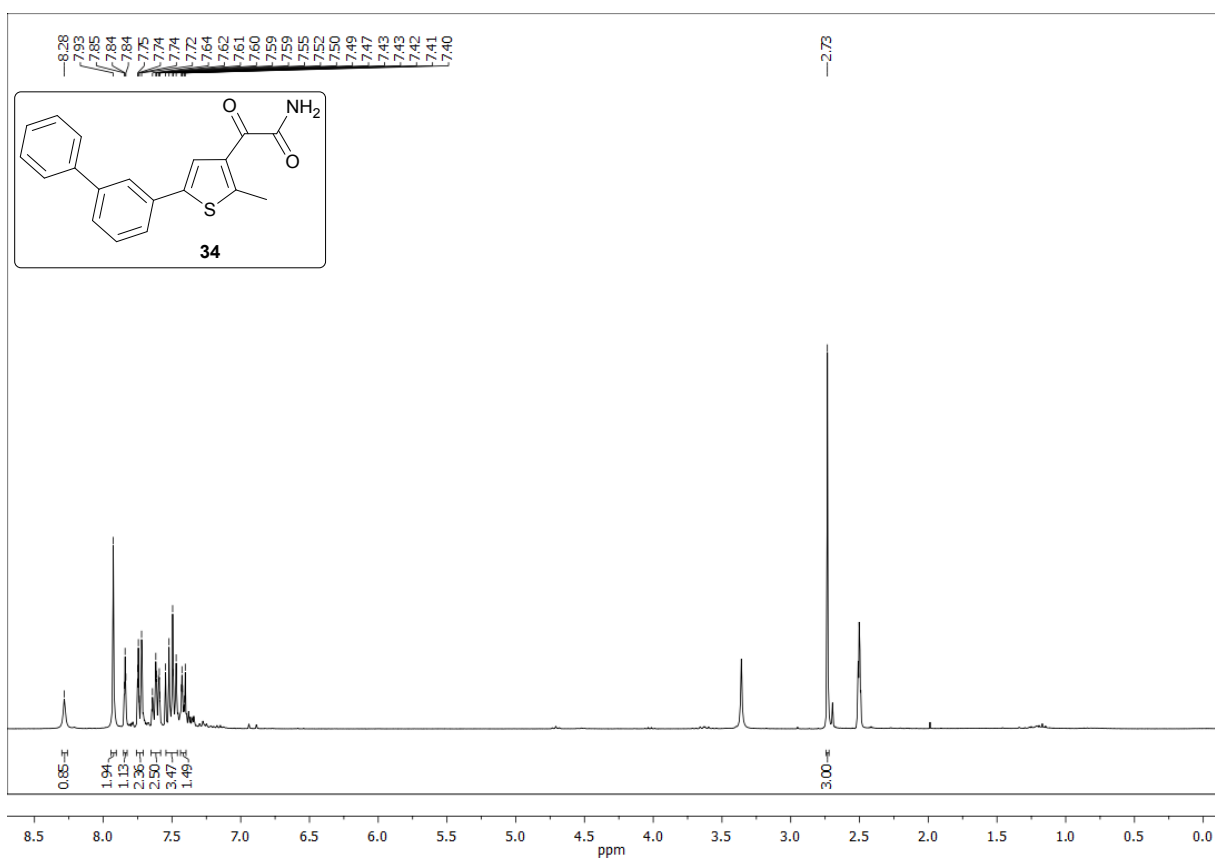
$^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **33**:



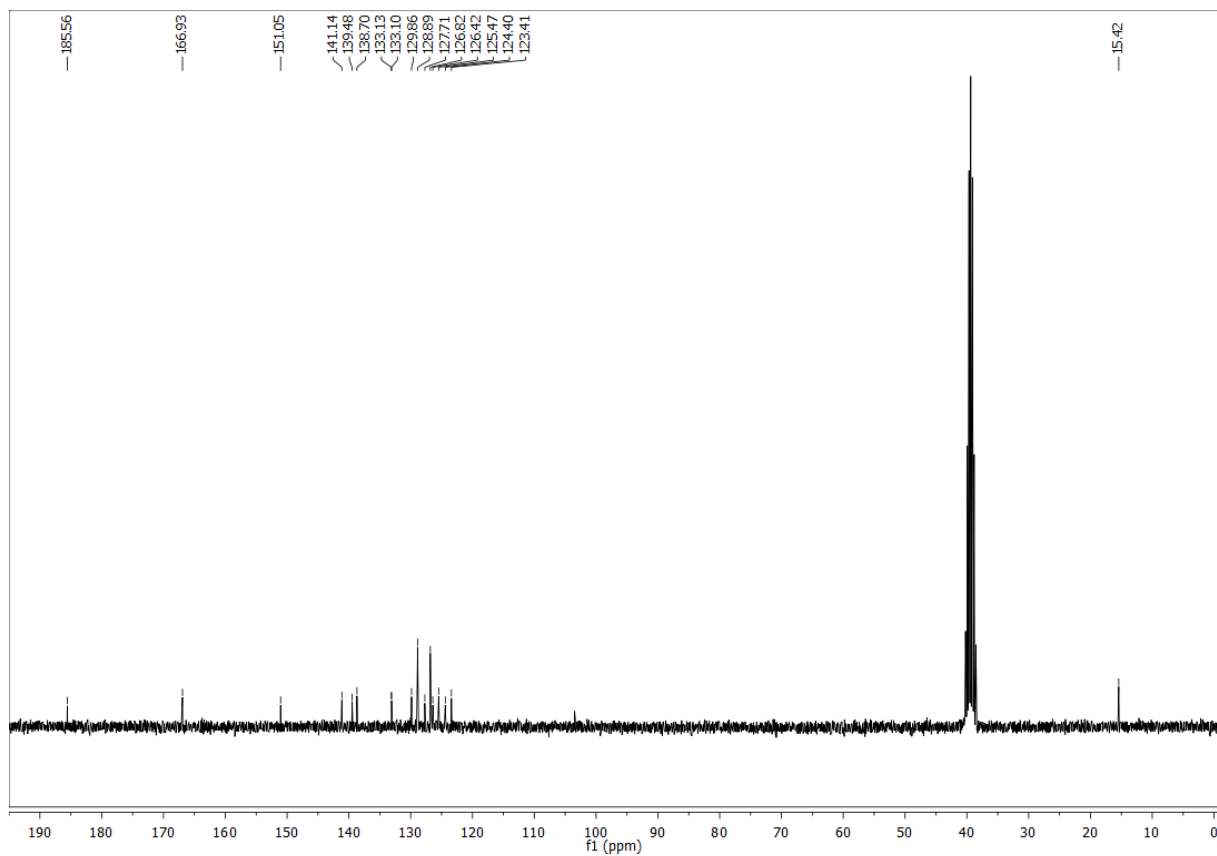
$^{13}\text{C-NMR}$ (75 MHz, $\text{DMSO-}d_6$) for compound **33**:



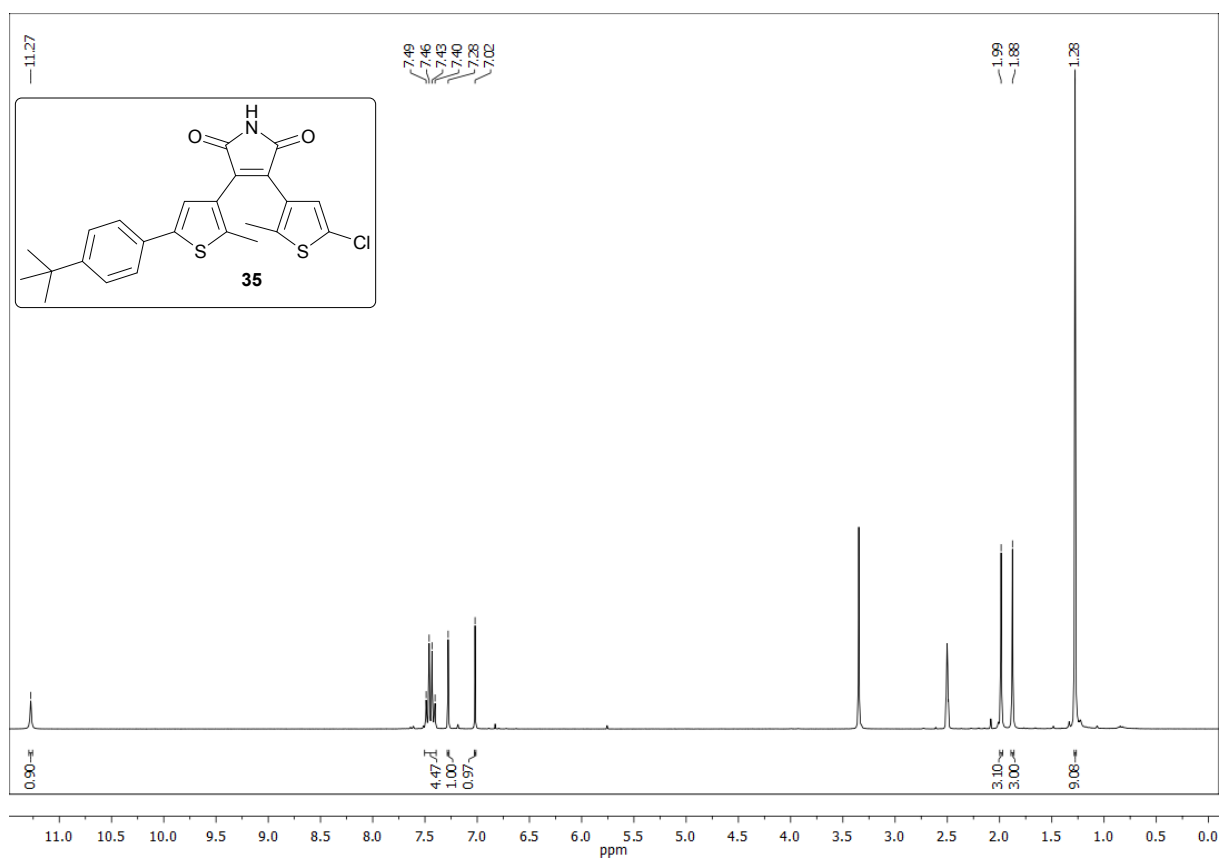
$^{13}\text{C-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **34**:



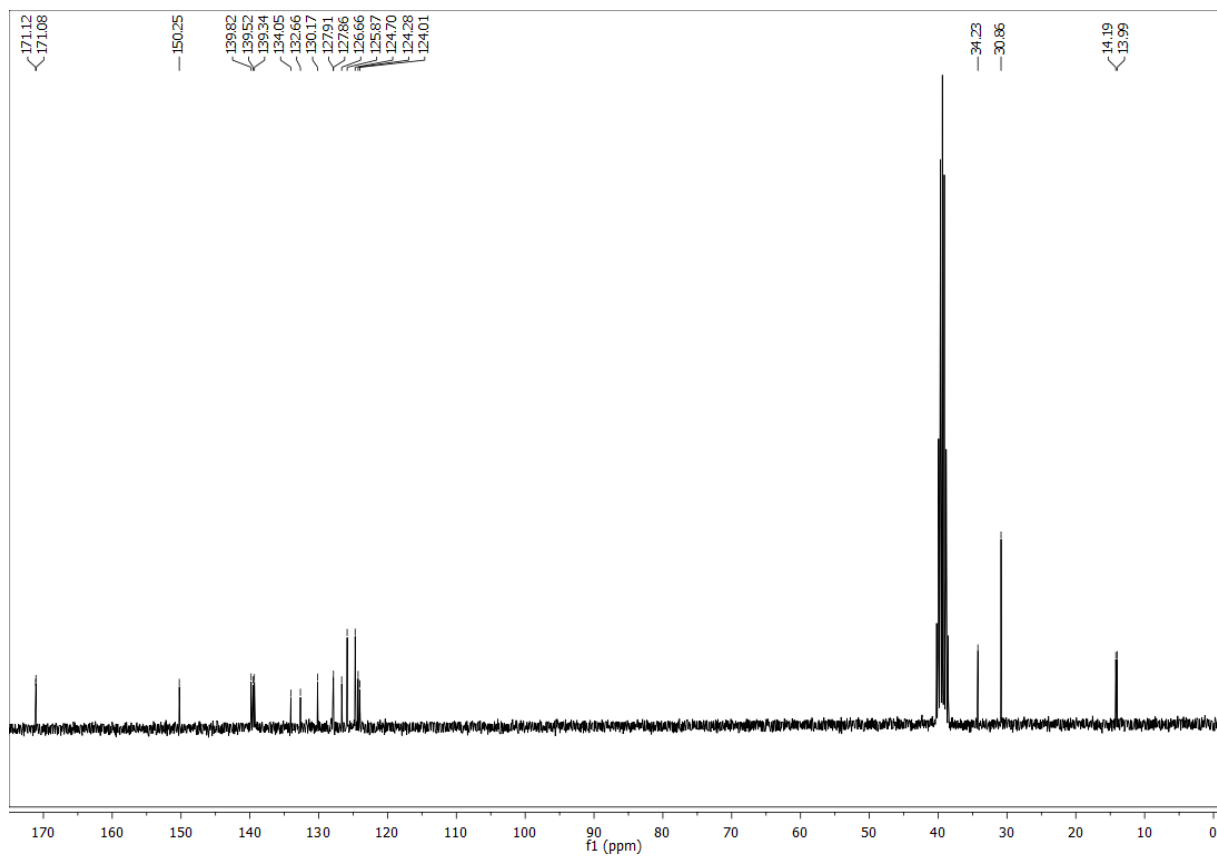
$^1\text{H-NMR}$ (75 MHz, $\text{DMSO-}d_6$) for compound **34**:



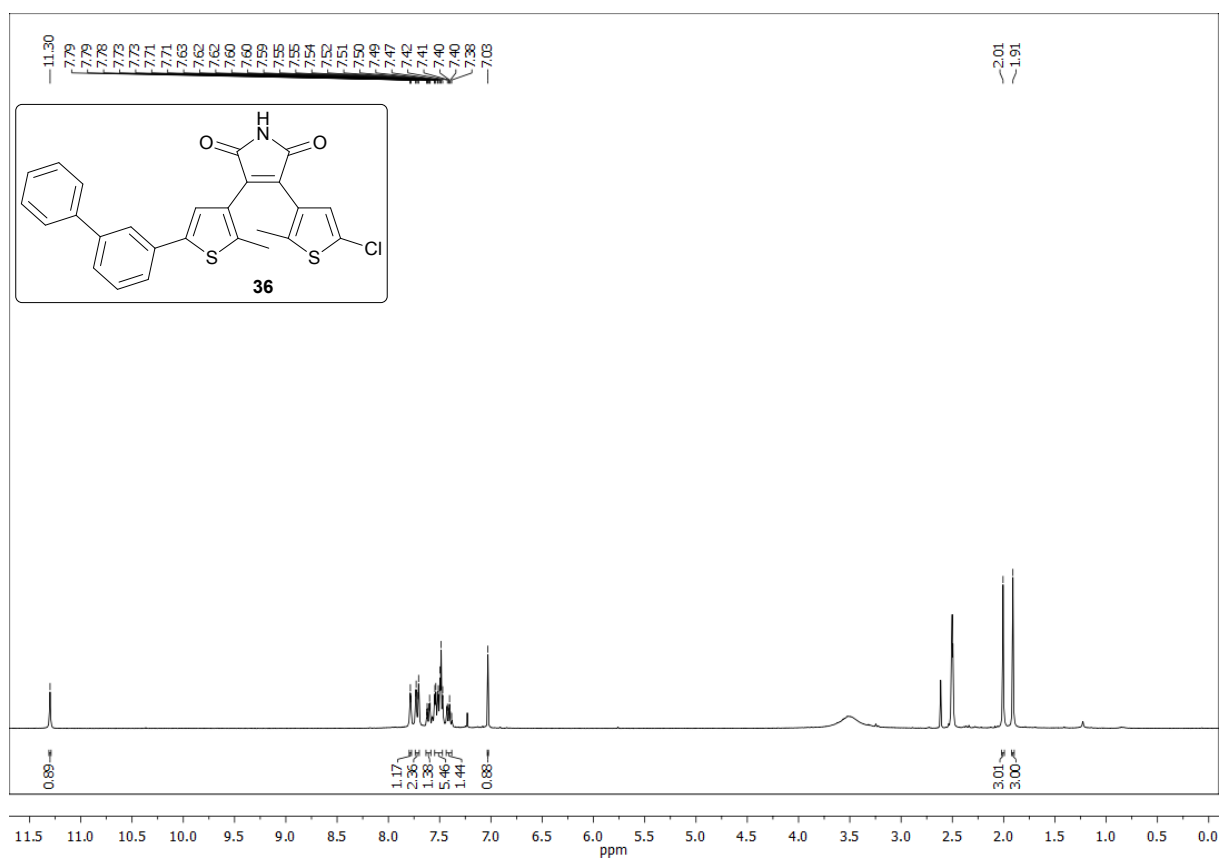
^{13}C -NMR (300 MHz, $\text{DMSO-}d_6$) for compound **35**:



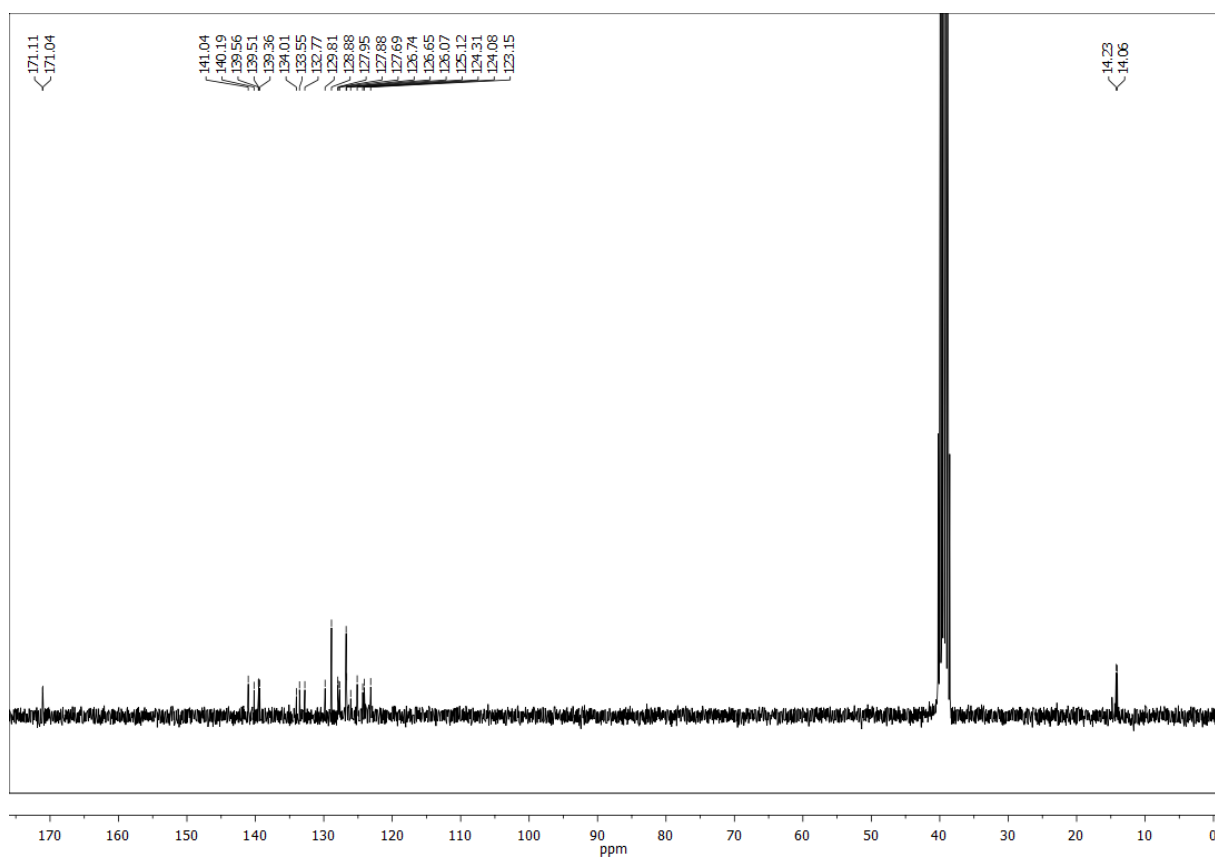
^1H -NMR (75 MHz, $\text{DMSO-}d_6$) for compound **35**:



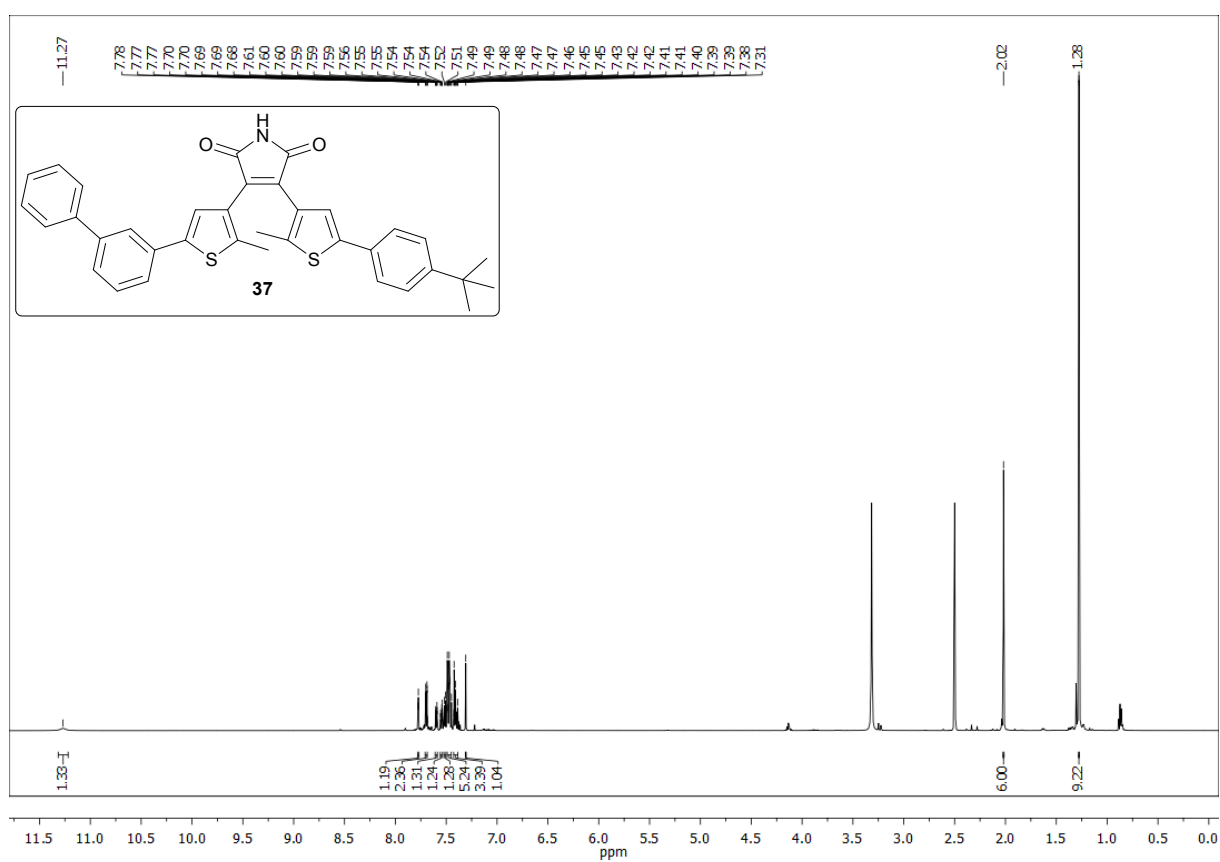
¹H-NMR (300 MHz, DMSO-*d*₆) for compound **36**:



¹³C-NMR (75 MHz, DMSO-*d*₆) for compound **36**:



$^{13}\text{C-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **37**:



$^1\text{H-NMR}$ (300 MHz, $\text{DMSO-}d_6$) for compound **37**:

