Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Cascade Approach to Fused Indolizinones through Lewis Acid/Copper(I) Relay Catalysis

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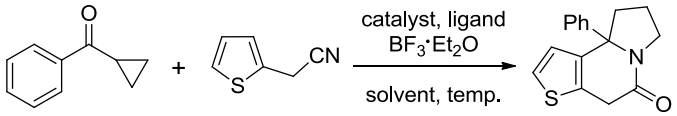
1. General methods.

Melting points were measured with a melting point instrument and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts were referenced to signals at 7.26 and 77.0 ppm, respectively, and $CDCl_3$ was used as the solvent with TMS as the internal standard. IR spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide pellets. High-resolution mass spectra were obtained with a LCMS-IT-TOF mass spectrometer. TLC was performed by using commercially prepared 100–400 mesh silica gel plates (GF_{254}) and visualization was effected at 254 nm. Unless otherwise noted, all commercial materials and solvents were used without further purification.

2. Optimization of reaction conditions.

Table 1. Screening the reaction conditions.[a]



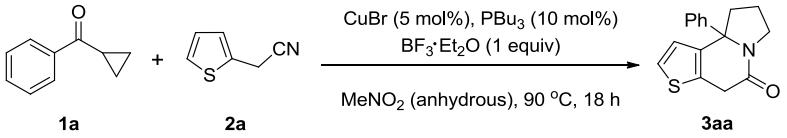
1a **2a** **3aa**

entry	catalyst (mol%), ligand (mol%)	temp. (^{o}C)	solvent	yield (%)
1	–	90	$MeNO_2$	np
2	$PdCl_2$(5)	90	$MeNO_2$	np
3	$FeCl_3$(5)	90	$MeNO_2$	np
4	AgOAc(5)	90	$MeNO_2$	24
5	$Ni(COD)_2$(5)	90	$MeNO_2$	np
6	CuI(5)	90	$MeNO_2$	40
7	CuCl(5)	90	$MeNO_2$	31
8	CuBr(5)	90	$MeNO_2$	46
9	$CuCl_2$(5)	90	$MeNO_2$	<5
10	CuBr(5), 1,10-phenanthroline(5)	90	$MeNO_2$	40
11	CuBr(5), 2,2'-bipyridine(5)	90	$MeNO_2$	32
12	CuBr(5), PPh_3(10)	90	$MeNO_2$	51
13	CuBr(5), PBu_3(10)	90	$MeNO_2$	80
14	CuBr(5), PCy_3(10)	90	$MeNO_2$	70
15	CuBr(5), (*S*)-(–)-BINAP(5)	90	$MeNO_2$	66
16	CuBr(5), PBu_3(10)	90	toluene	np
17	CuBr(5), PBu_3(10)	90	DMF	np
18	CuBr(5), PBu_3(10)	90	DCE	20
19	CuBr(5), PBu_3(10)	90	THF	np
20	CuBr(5), PBu_3(10)	70	$MeNO_2$	40
21	CuBr(5), PBu_3(10)	80	$MeNO_2$	77
22	CuBr(5), PBu_3(10)	100	$MeNO_2$	80

23[b]	CuBr(5), PBu_3(10)	90	$MeNO_2$	0

[a] *Reaction conditions*: **1a** (0.2 mmol), **2a** (1.2 equiv), $BF_3{\cdot}Et_2O$ (1 equiv), catalyst (5 mol%), and ligand (10 mol%) in solvent (1.5 mL) under air at 90 °C for 18 h. [b] Without $BF_3{\cdot}Et_2O$.

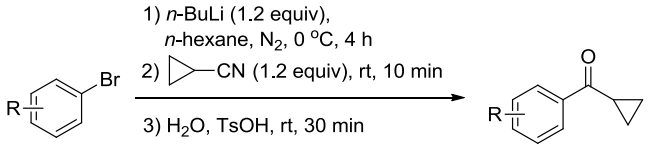
Table 2. The effects of water and the atmosphere on the generation of the product **3aa**.



1a **2a** **3aa**

entry	conditions	yield (%)
1	under N_2	20
2	under air	76
3	under air (dried)	21
4	under O_2	17
5	adding 5 mol% of H_2O, under N_2	79
6	adding 10 mol% of H_2O, under N_2	78
7	adding 15 mol% of H_2O, under N_2	75
8	adding 50 mol% of H_2O, under N_2	42

3. General method for preparation of aryl cyclopropyl ketones.



To a solution of aryl bromide (2 mmol) in *n*-hexane (5 mL) was added *n*-BuLi (1.2 equiv, 2.4 M in n-hexane) with an ice bath under nitrogen atmosphere. The mixture was stirred for 4 h at room temperature. Then cyclopropanecarbonitrile (1.2 equiv) was added dropwise, and the mixture was stirred for 10 min. The reaction was quenched by an aqueous solution of TsOH (5 M). The mixture was extracted with diethyl ether (3×10 mL) and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed and the crude product was separated by flash column chromatography on silica gel to give the pure product.

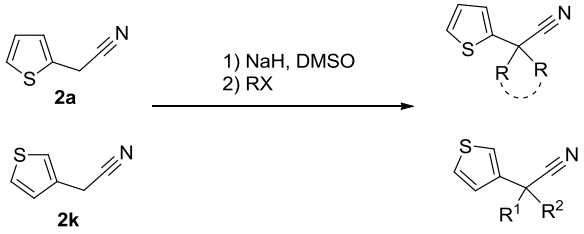
Cyclopropyl(*p*-tolyl)methanone (1d). 179 mg, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 2.69–2.61 (m, 1H), 2.41 (s, 3H), 1.22 (dt, *J* = 7.5, 3.6 Hz, 2H), 1.01 (td, *J* = 7.0, 3.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.2, 143.4, 135.5, 129.2, 128.1, 21.6, 16.9, 11.4.

Cyclopropyl(3-(trifluoromethyl)phenyl)methanone (1e). 334 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 2.70–2.62 (m, 1H), 1.24–1.24 (m, 2H), 1.09 (td, *J* = 6.9, 3.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 138.5, 131.1, 131.0, 129.2, 129.1, 124.8, 123.8, 17.3, 12.1.

Cyclopropyl(3-chlorophenyl)methanone (1g). 245 mg, 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.94 (m, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 2.65–2.57 (m, 1H), 1.25 (dt, *J* = 7.7, 3.7 Hz, 2H), 1.06 (td, *J* = 7.1, 3.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 139.6, 134.8, 132.6, 129.8, 128.2, 126.1, 17.33, 12.0.

Cyclopropyl(naphthalen-1-yl)methanone (1h). 274 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.4 Hz, 1H), 7.99–7.86 (m, 3H), 7.60–7.49 (m, 3H), 2.63–2.55 (m, 1H), 1.42–1.36 (m, 2H), 1.12 (td, *J* = 7.1, 3.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.7, 137.8, 133.8, 131.8, 129.8, 128.3, 127.4, 127.1, 126.3, 125.7, 124.5, 21.5, 12.3.

4. General method for preparation of substituted thiophenyl-acetonitriles.



The mixture of thiophenyl acetonitrile (1.0 mmol, 1 equiv), and NaH (2.5 equiv) was stirred in DMSO (4 mL) at room temperature under nitrogen atmosphere for 30 min. Then corresponding halogenated alkane (1-3 equiv) was added dropwise, and the mixture was stirred for 2 h. The reaction was quenched by the addition of 10 mL water. The aqueous solution was extracted with diethyl ether (3×10 mL) and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed and the crude product was separated by flash column chromatography on silica gel to give the pure product.

1-(Thiophen-2-yl)cyclopropanecarbonitrile (2b). Resulted from **2a** and 1,2-dibromoethane (2 equiv), 120 mg, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.06 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.6 Hz, 1H), 1.75 (q, *J* = 5.0 Hz, 2H), 1.44 (q, *J* = 5.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 127.2, 126.2, 124.8, 121.8, 19.2, 10.0.

1-(Thiophen-2-yl)cyclobutanecarbonitrile (2c). Resulted from **2a** and 1,3-diiodopropane (2 equiv), 127 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.09 (dd, *J* = 3.5, 1.1 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.93–2.86 (m, 2H), 2.67–2.58 (m, 2H), 2.41–2.29 (m, 1H), 2.20–2.09 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 127.1, 125.2, 124.8, 123.1, 37.1, 36.9, 17.0.

1-(Thiophen-2-yl)cyclopentanecarbonitrile (2d). Resulted from **2a** and 1,4-diiodobutane (2 equiv), 150 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.11 (dd, *J* = 3.5, 1.1 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.55–2.48 (m, 2H), 2.18–2.10 (m, 2H), 2.05–1.90 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 126.9, 125.1, 124.8, 123.4, 44.3, 41.8, 23.9.

1-(Thiophen-2-yl)cyclohexanecarbonitrile (2e). Resulted from **2a** and 1,5-diiodopentane (2 equiv), 149 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.24 (m, 1H), 7.13 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.35–2.30 (d, *J* = 8.3 Hz, 2H), 1.89–1.74 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 126.8, 124.5, 124.1, 121.9, 40.8, 38.8, 24.8, 23.4.

2-Benzyl-3-phenyl-2-(thiophen-2-yl)propanenitrile (2f). Resulted from **2a** and (chloromethyl)benzene (3 equiv), 209 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.16 (m, 8H), 7.12–7.08 (m, 3H), 6.80–6.77 (m, 1H), 6.72–6.69 (m, 1H), 3.26 (q, *J* = 13.5 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 134.6, 130.2, 128.1, 127.4, 127.1, 126.6, 125.0, 120.4, 48.1, 47.8.

2-Allyl-2-(thiophen-2-yl)pent-4-enenitrile (2g). Resulted from **2a** and allyl bromide (3 equiv), 179 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.10 (d, *J* = 3.6 Hz, 1H), 6.96 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.74 (ddt, *J* = 17.1, 9.5, 7.3 Hz, 2H), 5.21–5.16 (m, 4H), 2.71 (qd, *J* = 13.9, 7.2 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 131.2, 126.6, 126.0, 125.2, 120.8, 120.5, 45.2, 44.6.

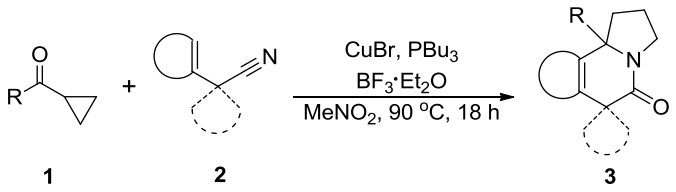
2-(Prop-2-yn-1-yl)-2-(thiophen-2-yl)pent-4-ynenitrile (2h). Resulted from **2a** and propargyl bromide (3 equiv), 159 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.31 (m, 1H), 7.26–7.24 (m, 1H), 7.00 (dd, *J* = 5.0, 3.8 Hz, 1H), 3.11–2.99 (m, 4H), 2.23 (t, *J* = 2.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 126.8, 126.5, 126.0, 119.9, 77.0, 73.7, 42.9, 30.5.

2-(Thiophen-3-yl)propanenitrile (2k). Resulted from **2j** and iodomethane (1 equiv), 75 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 5.1, 3.1 Hz, 1H), 7.30 (dd, *J* = 3.0, 1.6 Hz, 1H), 7.08 (dd, *J* = 5.1, 1.6 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 1H), 1.68 (d, *J* = 7.5 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 128.2, 126.4, 122.2, 120.3, 29.2, 20.5.

2-Methyl-2-(thiophen-3-yl)propanenitrile (2l). Resulted from **2j** and iodomethane (3 equiv), 119 mg, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.25 (dd, *J* = 2.9, 1.4 Hz, 1H), 7.11 (dd, *J* = 5.1, 1.4 Hz, 1H), 1.69 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 127.0, 125.0, 124.1, 120.4, 33.9, 28.7.

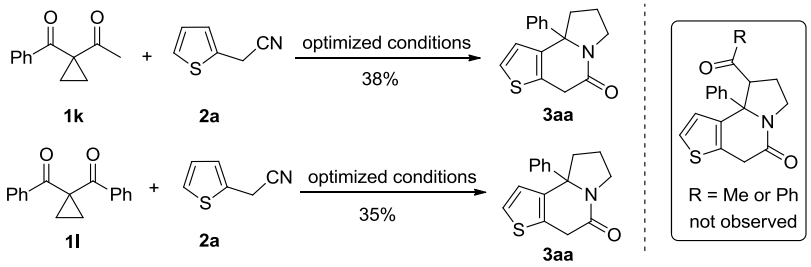
2-Allyl-2-(thiophen-3-yl)pent-4-enenitrile (2m). Resulted from **2j** and allyl bromide (3 equiv), 172 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.28 (dd, *J* = 2.8, 1.5 Hz, 1H), 7.06 (dd, *J* = 5.1, 1.3 Hz, 1H), 5.77–5.65 (m, 2H), 5.20–5.15 (m, 4H), 2.74–2.62 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 131.5, 127.0, 124.9, 122.2, 121.7, 120.1, 44.3, 43.7.

5. General method for preparation of ring-fused indolizinones.



1 2 3

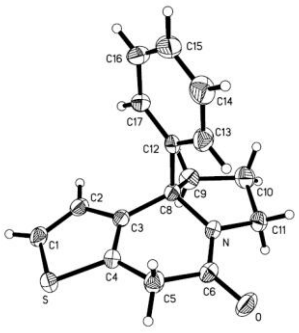
To a 10 mL tube were added a mixture of cyclopropyl ketone **1** (0.2 mmol, 1.0 equiv), nitrile **2** (1.2 equiv), CuBr (5 mol%), $MeNO_2$ (1.5 mL), $BF_3{\cdot}Et_2O$ (1.0 equiv), and PBu_3 (10 mol%) successively. The mixture was stirred at 90 °C for 18 h. Upon completion, the crude product was cooled to room temperature and then separated directly by flash column chromatography on silica gel to give the pure product **3**. Reaction with 10 mmol scale was performed in a flask.



1k 2a 3aa

1l 2a 3aa

9a-Phenyl-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3aa).



(X-ray structure, CCDC number: 873749)

White solid, 43 mg, 80% yield, m.p. 136–138 °C. IR (KBr): 2929, 1647, 1449, 1404, 1213, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.17 (m, 6H), 7.12 (d, *J* = 5.2 Hz, 1H), 3.86–3.53 (m, 4H), 2.77 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.33–2.24 (m, 1H), 2.04–1.96 (m, 1H), 1.76–1.63 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 143.2, 139.9, 130.3, 128.7, 127.1, 124.7, 124.7, 123.4, 69.8, 45.0, 39.6, 33.5, 20.7. HRMS (ESI) calc. $C_{16}H_{15}NOS$ $[M+H]^+$: 270.0947, found: 270.0936.

9a-(4-Fluoro-phenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ba). White solid, 49 mg, 85% yield, m.p. 166–168 °C. IR (KBr): 2934, 1647, 1507, 1399, 1230, 1160, 832, 648 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.16 (m, 3H), 7.08

(d, *J* = 5.2 Hz, 1H), 6.96 (t, *J* = 8.6 Hz, 2H), 3.81–3.49 (m, 4H), 2.70 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.30–2.22 (m, 1H), 2.03–1.95 (m, 1H), 1.69–1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 161.6, 139.7, 139.0, 130.2, 126.3, 124.9, 123.2, 115.5, 69.3, 44.9, 39.6, 33.4, 20.6. HRMS (ESI) calc. $C_{16}H_{14}FNOS$ $[M+H]^+$: 288.0853, found: 288.0840.

9a-(4-Chloro-phenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ca). White solid, 51 mg, 84% yield, m.p. 164–166 °C. IR (KBr): 2968, 1647, 1402, 1243, 1095, 1009, 824, 728 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2H), 7.20–7.17 (m, 3H), 7.09 (d, *J* = 5.2 Hz, 1H), 3.85–3.51 (m, 4H), 2.72 (dd, *J* = 12.0, 6.4 Hz, 1H), 2.31–2.25 (m, 1H), 2.05–1.98 (m, 1H), 1.70–1.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 141.9, 139.4, 133.0, 130.4, 128.8, 126.1, 125.0, 123.1, 69.4, 45.0, 39.5, 33.4, 20.6. HRMS (ESI) calc. $C_{16}H_{14}ClNOS$ $[M+H]^+$: 304.0557, found: 304.0551.

9a-(*p*-Tolyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3da). White solid, 41 mg, 72% yield, m.p. 177–179 °C. IR (KBr): 2974, 1647, 1428, 1355, 1245, 977, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.09 (m, 6H), 3.82–3.53 (m, 4H), 2.75 (dd, *J* = 11.8, 6.5 Hz, 1H), 2.34–2.19 (m, 4H), 2.02–1.93 (m, 1H), 1.77–1.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 140.2, 140.1, 136.8, 130.0, 129.4, 124.7, 124.5, 123.4, 69.7, 44.9, 39.5, 33.4, 20.8, 20.7. HRMS (ESI) calc. $C_{17}H_{17}NOS$ $[M+H]^+$: 284.1104, found: 284.1090.

9a-(3-(Trifluoromethyl)phenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ea). White solid, 57 mg, 85% yield, m.p. 171–172 °C. IR (KBr): 2933, 1640, 1388, 1209, 986, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.36 (m, 4H), 7.20 (d, *J* = 4.8 Hz, 1H), 7.12 (d, *J* = 5.0 Hz, 1H), 3.90–3.46 (m, 4H), 2.75 (dd, *J* = 11.9, 6.3 Hz, 1H), 2.31 (td, *J* = 12.4, 7.4 Hz, 1H), 2.05–1.98 (m, 1H), 1.72–1.58 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 144.6, 139.0, 131.1, 130.6, 129.3, 128.0, 125.2, 124.1, 123.8, 123.1, 121.4, 69.6, 45.0, 39.6, 33.4, 20.9. HRMS (ESI) calc. $C_{17}H_{14}F_3NOS$ $[M+H]^+$: 338.0821, found: 338.0825.

9a-(3-Fluorophenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3fa). White solid, 40 mg, 70% yield, m.p. 155–157 °C. IR (KBr): 2938, 1643, 1500, 1241, 1149, 835, 656 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–6.88 (m, 6H), 3.85–3.53 (m, 4H), 2.74 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.29 (td, *J* = 12.5, 7.3 Hz, 1H), 2.07–1.97 (m, 1H), 1.76–1.64 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 163.0, 146.1, 139.3, 130.6, 130.3, 125.0, 123.3, 120.3, 114.1, 112.1, 69.6, 45.0, 39.6, 33.4, 20.7. HRMS (ESI) calc. $C_{16}H_{14}FNOS$ $[M+H]^+$: 288.0853, found: 288.0843.

9a-(3-Chlorophenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ga). White solid, 40 mg, 66% yield, m.p. 158–160 °C. IR (KBr): 2957, 1646, 1410, 1240, 1001, 832, 722 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.09 (m, 6H), 3.86–3.53 (m, 4H), 2.73 (dd, *J* = 12.0, 6.4 Hz, 1H), 2.28 (td, *J* = 12.5, 7.3 Hz, 1H), 2.06–1.98 (m, 1H), 1.76–1.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 145.5, 139.2, 134.8, 130.6, 130.0, 127.4, 125.1, 125.0, 123.3, 122.9, 69.5, 45.0, 39.6, 33.5, 20.7. HRMS (ESI) calc. $C_{16}H_{14}ClNOS$ $[M+H]^+$: 304.0557, found: 304.0542.

9a-(Naphthalen-1-yl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ha). White solid, 35 mg, 55% yield, m.p. 202–204 °C. IR (KBr): 2957, 1649, 1408, 1244, 998, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.51–7.39 (m, 4H), 7.34 (d, *J* = 6.8 Hz, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 3.76–3.48 (m, 4H), 3.28 (dd, *J* = 12.0, 5.7 Hz, 1H), 2.64 (td, *J* = 12.1, 7.4 Hz, 1H), 2.09–1.96 (m, 1H), 1.75–1.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 140.6, 136.7, 135.2, 133.3, 129.5, 129.5, 129.2, 125.4, 125.4, 125.4, 125.0, 124.9, 123.2, 123.2, 70.8, 44.7, 38.2, 34.5, 21.6. HRMS (ESI) calc. $C_{20}H_{17}NOS$ $[M+H]^+$: 320.1104, found: 320.1107.

9a'-Phenyl-7',8',9',9a'-tetrahydro-5'*H*-spiro[cyclopropane-1,4'-thieno[2,3-g]indolizin]-5'-one (3ab). White solid, 19 mg, 32% yield, m.p. 189–191 °C. IR (KBr): 2919, 1624, 1420, 1375, 1244, 970, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 4H), 7.24–7.18 (m, 1H), 7.01 (s, 2H), 3.85 (dt, *J* = 12.2, 8.8 Hz, 1H), 3.58–3.51 (m, 1H), 2.88 (dd, *J* = 11.9, 6.7 Hz, 1H), 2.31 (td, *J* = 12.3, 7.7 Hz, 1H), 2.16 (ddd, *J* = 10.0, 7.4, 4.5 Hz, 1H), 2.06–1.96 (m, 1H), 1.74–1.65 (m, 1H), 1.57–1.51 (m, 1H), 1.19 –1.13 (m, 1H), 1.01–0.95 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 143.8, 139.4, 138.0, 128.7, 127.0, 124.6, 124.0, 122.5, 69.6, 44.8, 39.0, 24.1, 22.8, 20.6, 17.5. HRMS (ESI) calc. $C_{18}H_{17}NOS$ $[M+H]^+$: 296.1104, found: 296.1102.

9a'-Phenyl-7',8',9',9a'-tetrahydro-5'*H*-spiro[cyclobutane-1,4'-thieno[2,3-g]indolizin]-5'-one (3ac). White solid, 41 mg, 66% yield, m.p. 199-201 °C. IR (KBr): 2937, 1634, 1445, 1404, 1242, 755, 701 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.11

(m, 7H), 3.86–3.77 (m, 1H), 3.66 (t, *J* = 11.0 Hz, 1H), 3.32 (dd, *J* = 19.8, 8.8 Hz, 1H), 2.68 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.58–2.50 (m, 1H), 2.28–2.06 (m, 4H), 2.00–1.90 (m, 1H), 1.74–1.62 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 144.2, 141.6, 138.8, 128.4, 126.8, 124.8, 123.9, 123.8, 69.2, 46.0, 45.2, 39.8, 36.3, 31.1, 20.5, 15.9. HRMS (ESI) calc. $C_{19}H_{19}NOS$ $[M+H]^+$: 310.1260, found: 310.1257.

9a'-Phenyl-7',8',9',9a'-tetrahydro-5'*H*-spiro[cyclopentane-1,4'-thieno[2,3-g]indolizin]-5'-one (3ad). White solid, 39 mg, 60% yield, m.p. 197-199 °C. IR (KBr): 2924, 1637, 1446, 1379, 971, 699, 669 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.27 (m, 4H), 7.24–7.13 (m, 3H), 3.89–3.81 (m, 1H), 3.71–3.65 (m, 1H), 2.93–2.85 (m, 1H), 2.66 (dd, *J* = 11.7, 6.5 Hz, 1H), 2.25 (td, *J* = 12.4, 7.3 Hz, 1H), 2.02– 1.86 (m, 5H), 1.78–1.63 (m, 3H), 1.40–1.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 144.2, 143.4, 138.2, 128.4, 126.9, 125.1, 123.9, 123.7, 69.2, 52.1, 45.6, 42.4, 40.6, 38.9, 26.3, 25.9, 20.4. HRMS (ESI) calc. $C_{20}H_{21}NOS$ $[M+H]^+$: 324.1417, found: 324.1409.

9a'-Phenyl-7',8',9',9a'-tetrahydro-5'*H*-spiro[cyclohexane-1,4'-thieno[2,3-g]indolizin]-5'-one (3ae). White solid, 34 mg, 50% yield, m.p. 210-212 °C. IR (KBr): 2927, 1639, 1446, 1379, 1207, 912, 749, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.17 (m, 7H), 3.88–3.82 (m, 1H), 3.69 (t, *J* = 10.5 Hz, 1H), 2.61–2.47 (m, 2H), 2.23–2.12 (m, 2H), 1.92–1.80 (m, 2H), 1.76–1.66 (m, 3H), 1.53–1.42 (m, 3H), 1.36–1.27 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 144.4, 142.3, 138.8, 128.4, 126.9, 125.2, 124.1, 124.0, 68.8, 46.1, 45.8, 41.6, 37.2, 34.2, 25.2, 23.0, 21.8, 20.2. HRMS (ESI) calc. $C_{21}H_{23}NOS$ $[M+H]^+$: 338.1573, found: 338.1558.

4,4-Dibenzyl-9a-phenyl-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3af). White solid, 42 mg, 47% yield, m.p. 200-202 °C. IR (KBr): 2918, 1634, 1454, 1415, 1228, 1071, 753, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.09 (m, 9H), 6.97 (t, *J* = 7.2 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 4H), 6.44 (d, *J* = 5.2 Hz, 1H), 6.27 (d, *J* = 7.6 Hz, 2H), 3.90–3.75 (m, 3H), 3.14 (dd, *J* = 65.0, 12.7 Hz, 2H), 2.74–2.64 (m, 1H), 2.29 (dd, *J* = 12.1, 7.3 Hz, 1H), 1.45–1.19 (m, 2H), 0.09–0.01 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 141.7, 139.0, 137.3, 137.1, 135.6, 130.8, 129.6, 128.3, 128.2, 127.6, 126.6, 126.5, 126.4, 125.0, 124.9, 124.5, 69.1, 54.9, 51.5, 47.2, 42.6, 35.4, 20.4. HRMS (ESI) calc. $C_{30}H_{27}NOS$ $[M+H]^+$: 450.1886, found: 450.1873.

4,4-Diallyl-9a-phenyl-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ag). White solid, 38 mg, 55% yield, m.p. 142-144 °C. IR (KBr): 2977, 1640, 1409, 1237, 995, 917, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.17 (m, 6H), 7.04 (d, *J* = 5.2 Hz, 1H), 5.69–5.58 (m, 1H), 5.49–5.39 (m, 1H), 5.06–4.90 (m, 4H), 3.91 (dt, *J* = 12.2, 8.7 Hz, 1H), 3.53–3.39 (m, 1H), 3.10 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.77 (dd, *J* = 11.7, 6.8 Hz, 1H), 2.64–2.58 (m, 1H), 2.48–2.35 (m, 2H), 2.06 (td, *J* = 12.1, 8.0 Hz, 1H), 1.97–1.88 (m, 1H), 1.66–1.52 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 143.5, 138.4, 138.2, 133.6, 133.4, 128.4, 127.0, 125.3, 125.2, 123.8, 118.6, 118.2, 69.2, 50.3, 45.8, 45.0, 44.5, 40.1, 20.4. HRMS (ESI) calc. $C_{22}H_{23}NOS$ $[M+H]^+$: 350.1573, found: 350.1565.

9a-Phenyl-4,4-di(prop-2-yn-1-yl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ah). White solid, 29 mg, 42% yield, m.p. 209-211 °C. IR (KBr): 2927, 2360, 1637, 1419, 1382, 1239, 924, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.21 (m, 6H), 7.15 (d, *J* = 5.2 Hz, 1H), 3.99 (dt, *J* = 12.4, 8.9 Hz, 1H), 3.65–3.58 (m, 1H), 3.11 (ddd, *J* = 72.1, 16.5, 2.5 Hz, 2H), 2.79 (dd, *J* = 11.7, 6.6 Hz, 1H), 2.65 (ddd, *J* = 52.3, 16.7, 2.6 Hz, 2H), 2.24 (td, *J* = 12.2, 7.7 Hz, 1H), 2.08–1.97 (m, 2H), 1.90 (t, *J* = 2.5 Hz, 1H), 1.74–1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 143.4, 139.4, 136.1, 128.7, 127.2, 126.2, 125.0, 123.5, 80.6, 79.1, 73.1, 70.7, 69.4, 48.8, 45.2, 40.4, 29.9, 29.3, 20.4. HRMS (ESI) calc. $C_{22}H_{19}NOS$ $[M+H]^+$: 346.1260, found: 346.1262.

2-Bromo-9a-phenyl-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3ai). White solid, 48 mg, 69% yield, m.p. 156–158 °C. IR (KBr): 2925, 1738, 1648, 1513, 1457, 1380, 1252, 1031, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 2H), 7.24–7.20 (m, 3H), 7.08 (s, 1H), 3.84–3.76 (m, 1H), 3.66–3.43 (m, 3H), 2.71 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.27-2.19 (m, 1H), 2.03–1.96 (m, 1H), 1.73–1.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 142.6, 140.2, 131.2, 128.8, 127.3, 126.2, 124.5, 111.3, 69.6, 44.9, 39.3, 33.3, 20.6. HRMS (ESI) calc. $C_{16}H_{14}BrNOS$ $[M+H]^+$: 348.0052, found: 348.0049.

2-Bromo-9a-(4-fluorophenyl)-7,8,9,9a-tetrahydrothieno[2,3-g]indolizin-5(4*H*)-one (3bi). White solid, 51 mg, 70% yield, m.p. 180–182 °C. IR (KBr): 2956, 1649, 1506, 1404, 1228, 1161, 826 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.20–7.15 (m, 2H), 7.05 (s, 1H), 7.02–6.97 (m, 2H), 3.84–3.76 (m, 1H), 3.65–3.55 (m, 2H), 3.43 (d, *J* = 19.8 Hz, 1H), 2.66 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.27–2.19 (m, 1H), 2.04–1.96 (m, 1H), 1.73–1.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 161.8, 140.0, 138.5, 131.3, 126.3, 126.0, 115.7, 111.6, 69.2, 44.9, 39.4, 33.2, 20.5. HRMS (ESI) calc. $C_{16}H_{13}BrFNOS$ $[M+Na]^+$: 387.9777, found: 387.9765.

9a-Phenyl-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3aj). White solid, 45 mg, 84% yield, m.p. 140–142 °C. IR (KBr): 2925, 1738, 1646, 1521, 1404, 1242, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.28 (m, 4H), 7.24–7.18 (m, 1H), 7.16 (d, *J* = 5.0 Hz, 1H), 6.70 (d, *J* = 5.0 Hz, 1H), 3.86–3.78 (m, 1H), 3.69–3.57 (m, 2H), 3.41 (d, *J* = 19.4 Hz, 1H), 2.75 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.40-2.31 (m, 1H), 2.03–1.95 (m, 1H), 1.73–1.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 142.5, 138.8, 131.5, 128.7, 127.2, 125.6, 124.9, 124.3, 69.5, 44.9, 40.9, 34.2, 20.9. HRMS (ESI) calc. $C_{16}H_{15}NOS$ $[M+H]^+$: 270.0947, found: 270.0940.

9a-(4-Fluorophenyl)-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3bj). White solid, 52 mg, 90% yield, m.p. 169–171 °C. IR (KBr): 2923, 1647, 1519, 1407, 1361, 755, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.7, 5.1 Hz, 2H), 7.19 (d, *J* = 5.0 Hz, 1H), 7.00 (t, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 5.0 Hz, 1H), 3.86–3.78 (m, 1H), 3.68–3.57 (m, 2H), 3.40 (d, *J* = 19.4 Hz, 1H), 2.71 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.41–2.32 (m, 1H), 2.06–1.98 (m, 1H), 1.74–1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 161.6, 138.6, 138.5, 131.5, 126.6, 125.6, 124.3, 115.5, 69.0, 44.8, 40.9, 34.2, 20.8. HRMS (ESI) calc. $C_{16}H_{14}FNOS$ $[M+H]^+$: 288.0853, found: 288.0847.

9a-(4-Chlorophenyl)-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3cj). White solid, 51 mg, 84% yield, m.p. 167–169 °C. IR (KBr): 2926, 1648, 1488, 1402, 1093, 820, 705 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (q, *J* = 8.8 Hz, 4H), 7.19 (d, *J* = 5.0 Hz, 1H), 6.73 (d, *J* = 5.0 Hz, 1H), 3.86–3.78 (m, 1H), 3.68–3.58 (m, 2H), 3.39 (d, *J* = 19.4 Hz, 1H), 2.70 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.41–2.32 (m, 1H), 2.06–1.99 (m, 1H), 1.74–1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 141.3, 138.3, 133.2, 131.7, 128.9, 126.4, 125.7, 124.5, 69.1, 45.0, 40.9, 34.2, 20.9. HRMS (ESI) calc. $C_{16}H_{14}ClNOS$ $[M+H]^+$: 304.0557, found: 304.0544.

4-Methyl-9a-phenyl-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3ak). White solid, 43 mg, 76% yield, m.p. 164-166 °C. IR (KBr): 2972, 1643, 1407, 1290, 1187, 834, 758, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.18 (m, 6H), 6.72 (d, *J* = 5.0 Hz, 1H), 3.90 (dt, *J* = 12.1, 9.0 Hz, 1H), 3.68 –3.57 (m, 2H), 2.72 (dd, *J* = 11.7, 6.5 Hz, 1H), 2.28 (td, *J* = 12.3, 7.4 Hz, 1H), 2.01–1.93 (m, 1H), 1.68–1.54 (m, 1H), 1.30 (d, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 143.6, 137.8, 137.1, 128.6, 127.1, 125.2, 125.0, 124.8, 69.4, 44.9, 41.7, 39.7, 20.6, 20.1. HRMS (ESI) calc. $C_{17}H_{17}NOS$ $[M+H]^+$: 284.1104, found: 284.1101.

4,4-Dimethyl-9a-phenyl-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3al). White solid, 42 mg, 71% yield, m.p. 155-157 °C. IR (KBr): 2971, 1642, 1397, 1207, 1084, 834, 757, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.28 (m, 4H), 7.23–7.17 (m, 2H), 6.80 (d, *J* = 5.2 Hz, 1H), 3.90 (dt, *J* = 12.2, 9.0 Hz, 1H), 3.65–3.58 (m, 1H), 2.70 (dd, *J* = 11.6, 6.6 Hz, 1H), 2.29 (td, *J* = 12.3, 7.5 Hz, 1H), 2.01–1.92 (m, 1H), 1.64–1.54 (m, 4H), 1.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 143.4, 141.4, 137.1, 128.5, 127.1, 125.3, 124.4, 124.3, 68.8, 45.2, 42.2, 41.6, 28.9, 26.1, 20.5. HRMS (ESI) calc. $C_{18}H_{19}NOS$ $[M+H]^+$: 298.1260, found: 298.1242.

4,4-Diallyl-9a-phenyl-7,8,9,9a-tetrahydrothieno[3,2-g]indolizin-5(4*H*)-one (3am). White solid, 42 mg, 60% yield, m.p. 149-151 °C. IR (KBr): 2976, 1641, 1405, 1206, 995, 917, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.22–7.16 (m, 2H), 6.74 (d, *J* = 5.2 Hz, 1H), 5.52 (ddt, *J* = 17.2, 10.0, 7.4 Hz, 1H), 5.35 (ddt, *J* = 17.2, 10.1, 7.0 Hz, 1H), 4.98–4.84 (m, 4H), 3.93 (dt, *J* = 12.3, 8.8 Hz, 1H), 3.51–3.44 (m, 1H), 3.06 (dd, *J* = 13.7, 7.0 Hz, 1H), 2.76 (dd, *J* = 11.7, 6.7 Hz, 1H), 2.58–2.40 (m, 3H), 2.19–2.10 (m, 1H), 1.96–1.88 (m, 1H), 1.61–1.48 (m, 1H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 171.4, 143.3, 138.4, 136.3, 134.0, 133.6, 128.4, 127.1, 125.3, 124.9, 124.2, 118.2, 117.6, 68.8, 50.0, 44.7, 44.5, 42.7, 42.0, 20.6. HRMS (ESI) calc. $C_{22}H_{23}NOS$ $[M+H]^+$: 350.1573, found: 350.1566.

11b-Phenyl-1,2,3,11b-tetrahydrobenzo[4,5]thieno[3,2-g]indolizin-5(6*H*)-one (3an). White solid, 46 mg, 72% yield, m.p. 175–177 °C. IR (KBr): 2923, 1646, 1508, 1407, 1231, 1160, 833, 671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.42–7.28 (m, 6H), 7.23 (t, *J* = 7.2 Hz, 1H), 3.95–3.82 (m, 2H), 3.67 (t, *J* = 10.7 Hz, 1H), 3.55 (d, *J* = 19.5 Hz, 1H), 2.85 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.45–2.36 (m, 1H), 2.08–2.01 (m, 1H), 1.78–1.65 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 142.1, 139.3, 139.0, 136.9, 128.8, 127.4, 125.5, 124.9, 124.7, 124.6, 122.6, 121.2, 69.9, 44.7, 40.1, 32.4, 20.8. HRMS (ESI) calc. $C_{20}H_{17}NOS$ $[M+Na]^+$: 342.0923, found: 342.0913.

11b-(4-Chlorophenyl)-1,2,3,11b-tetrahydrobenzo[4,5]thieno[3,2-g]indolizin-5(6*H*)-one (3cn). White solid, 42 mg, 60% yield, m.p. 196–198 °C. IR (KBr): 2924, 1647, 1404, 1093, 820, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.39–7.28 (m, 6H), 3.94–3.82 (m, 2H), 3.65 (t, *J* = 10.7 Hz, 1H), 3.53 (d, *J* = 19.7 Hz, 1H), 2.79 (dd, *J* = 11.9, 6.4 Hz, 1H), 2.45–2.37 (m, 1H), 2.10–2.03 (m, 1H), 1.77–1.64 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 140.8, 139.3, 138.4, 136.9, 133.5, 129.0, 126.4, 125.7, 124.9, 124.8, 122.7, 121.4, 69.5, 44.7, 40.1, 32.4, 20.8. HRMS (ESI) calc. $C_{20}H_{16}ClNOS$ $[M+H]^+$: 354.0714, found: 354.0704.

10-Chloro-11b-phenyl-1,2,3,11b-tetrahydrobenzo[4,5]thieno[3,2-g]indolizin-5(6*H*)-one (3ao). White solid, 39 mg, 55% yield, m.p. 207–209 °C. IR (KBr): 2935, 1736, 1647, 1540, 1404, 1240, 1075, 857, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.6 Hz, 1H), 7.49 (s, 1H), 7.40–7.32 (m, 4H), 7.26–7.22 (m, 2H), 3.94–3.49 (m, 4H), 2.84 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.44–2.36 (m, 1H), 2.09–2.01 (m, 1H), 1.78–1.64 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 141.8, 141.1, 138.1, 137.3, 131.1, 128.9, 127.6, 125.1, 125.0, 124.9, 123.6, 121.0, 69.8, 44.7, 40.1, 32.2, 20.8. HRMS (ESI) calc. $C_{20}H_{16}ClNOS$ $[M+H]^+$: 354.0714, found: 354.0710.

9a-Phenyl-7,8,9,9a-tetrahydrofuro[3,2-g]indolizin-5(4*H*)-one (3ap). White solid, 29 mg, 57% yield, m.p. 137–139 °C. IR (KBr): 2956, 1652, 1522, 1403, 1232, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 5.0 Hz, 1H), 7.32–7.28 (m, 4H), 7.24–7.18 (m, 1H), 6.26 (d, *J* = 5.0 Hz, 1H), 3.88–3.79 (m, 1H), 3.71–3.58 (m, 2H), 3.42 (d, *J* = 19.4 Hz, 1H), 2.76 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.42-2.33 (m, 1H), 2.04–1.97 (m, 1H), 1.72–1.61 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 143.3, 138.2, 131.3, 128.7, 127.2, 125.6, 124.9, 123.9, 67.6, 45.7, 40.4, 35.1, 22.3. HRMS (ESI) calc. $C_{16}H_{15}NO_2$ $[M+H]^+$: 254.1176, found: 254.1167.

8,9-Dimethoxy-10b-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-a]isoquinolin-5(6*H*)-one (3ar). White solid, 43 mg, 66% yield, m.p. 135–137 °C. IR (KBr): 2948, 1644, 1505, 1463, 1229, 834, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.17 (m, 5H), 7.07 (s, 1H), 6.59 (s, 1H), 4.00 (s, 3H), 3.90–3.81 (m, 4H), 3.69 (dd, *J* = 19.1, 11.0 Hz, 1H), 3.37 (q, *J* = 18.2 Hz, 2H), 2.69 (dd, *J* = 11.6, 6.1 Hz, 1H), 2.52–2.44 (m, 1H), 2.04–1.98 (m, 1H), 1.86–1.71 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 148.5, 147.8, 142.8, 133.1, 128.4, 126.9, 125.1, 124.9, 110.5, 108.3, 71.1, 56.4, 55.9, 45.4, 40.4, 38.3, 20.9. HRMS (ESI) calc. $C_{20}H_{21}NO_3$ $[M+H]^+$: 324.1594, found: 324.1601.

***N*-[4-(4-Chloro-phenyl)-4-oxo-butyl]-2-thiophen-3-yl-acetamide (7).** White solid, 29 mg, 45% yield, m.p. 86–88 °C. IR (KBr): 2927, 1646, 1607, 1543, 1456, 1357, 1238, 835, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.32 (dd, *J* = 4.6, 2.8 Hz, 1H), 7.14 (s, 1H), 6.98 (d, *J* = 4.8 Hz, 1H), 6.01 (s, 1H), 3.60 (s, 2H), 3.33 (q, *J* = 6.2 Hz, 2H), 2.95 (t, *J* = 6.7 Hz, 2H), 1.91 (p, *J* = 6.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5, 171.2, 139.7, 134.9, 134.5, 129.4, 129.0, 128.4, 126.8, 123.6, 39.4, 37.9, 35.8, 23.5. HRMS (ESI) calc. $C_{16}H_{16}ClNO_2S$ $[M+H]^+$: 322.0663, found: 322.0659.

***N*-(4-Oxo-4-phenyl-butyl)-benzamide (8).** White solid, 47 mg, 88% yield, m.p. 118–120 °C. IR (KBr): 2970, 1643, 1406, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.7 Hz, 2H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.46–7.36 (m, 5H), 6.90 (br, 1H), 3.53 (q, *J* = 6.5 Hz, 2H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.08 (p, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

200.3, 167.5, 136.6, 134.4, 133.2, 131.2, 128.5, 128.4, 128.0, 126.8, 39.8, 36.2, 23.5. HRMS (ESI) calc. $C_{17}H_{17}NO_2$ $[M+H]^+$: 268.1332, found: 268.1337.

6. Procedure for synthesis of crispine A.

To a reaction tube was added cyclopropyl aldehyde (**1m**, 0.5 mmol, 35 mg), benzylamine (0.5 mmol, 53.5 mg), TsOH (5 mol%, 4.3 mg), 4A molecular sieve (100 mg), and toluene (3 mL).The mixture was allowed to stir under reflux for 4 hours, and then cooled to room temperature. The molecular sieve was removed by filter and the solvent was removed under reduced pressure to give the crude product aldimine **5** (92% GC yield). The aldimine without further purification was directly subjected to the cascade reaction under standard conditions to afford 3,4-dimethoxyphenyl indolizinone **6**.

8,9-Dimethoxy-1,2,3,10b-tetrahydropyrrolo[2,1-a]isoquinolin-5(6*H*)-one[1] **(6).** Light yellow solid, 34 mg, 28% yield for two steps, m.p. 159–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.66 (s, 1H), 4.60 (t, *J* = 5.2 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.69 (t, *J* = 10.2 Hz, 1H), 3.63–3.49 (m, 3H), 2.61 (dd, *J* = 12.0, 6.4 Hz, 1H), 2.16 (td, *J* = 12.4, 7.3 Hz, 1H), 2.09–1.98 (m, 1H), 1.95–1.82 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 148.6, 147.9, 127.9, 124.9, 110.3, 107.4, 59.6, 56.1, 56.0, 44.6, 37.9, 31.7, 23.1. HRMS (ESI) calc. $C_{14}H_{17}NO_3$ $[M+H]^+$: 248.1281, found: 248.1287.

To a reaction flask containing a mixture of $LiAlH_4$ (19 mg, 0.5 mmol, 5.0 equiv) and $Et_3NH{\cdot}Cl$ (69 mg, 0.5 mmol, 5.0 equiv) in an ice bath, was added THF (2 mL) via a syringe under nitrogen. The suspension was allowed to stir in an ice bath for 15 min. Then, product **6** (25 mg, 0.1 mmol) was added directly. The reaction mixture was allowed to stir overnight, and then the reaction was cooled in an ice bath. The reaction was quenched by slow addition of aqueous 10% NaOH solution (2 mL), with stirring for 30 min. The reaction mixture was extracted with ether (3×5 mL). The combined organic layer was dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure to give the crude product. Purification of the crude product by flash chromatography on silica gel afforded the corresponding crispine A

8,9-Dimethoxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-a]isoquinoline (crispine A).[2] White solid, 21 mg, 90% yield, m.p. 86–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (s, 1H), 6.56 (s, 1H), 3.84(s, 3H), 3.83 (s, 3H), 3.41 (t, *J* = 8.0 Hz, 1H), 3.21–3.16 (m, 1H), 3.10–2.97 (m, 2H), 2.76–2.52 (m, 3H), 2.37–2.28 (m, 1H), 1.96–1.76 (m, 2H), 1.71–1.67 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 147.1, 130.7, 126.1, 111.3, 108.7, 62.8, 55.9, 55.8, 53.0, 48.2, 30.4, 28.0, 22.1. HRMS (ESI) calc. $C_{14}H_{19}NO_2$ $[M+H]^+$: 234.1489, found: 234.1499.

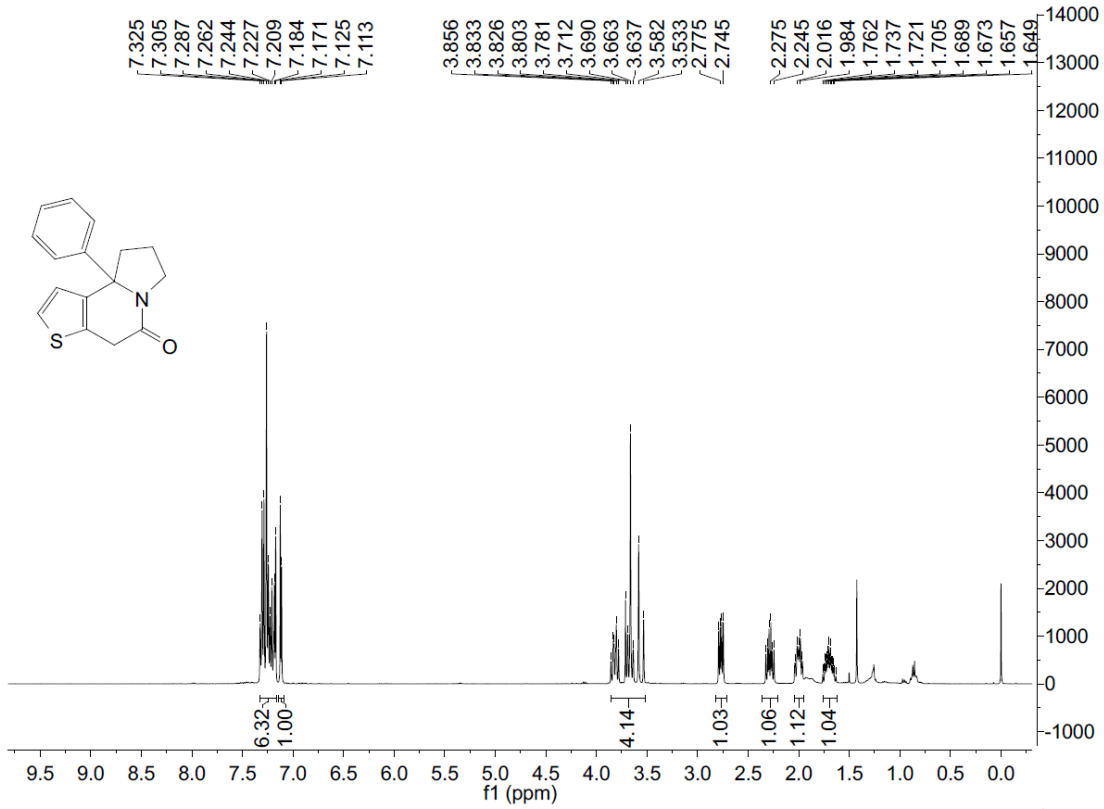
Reference

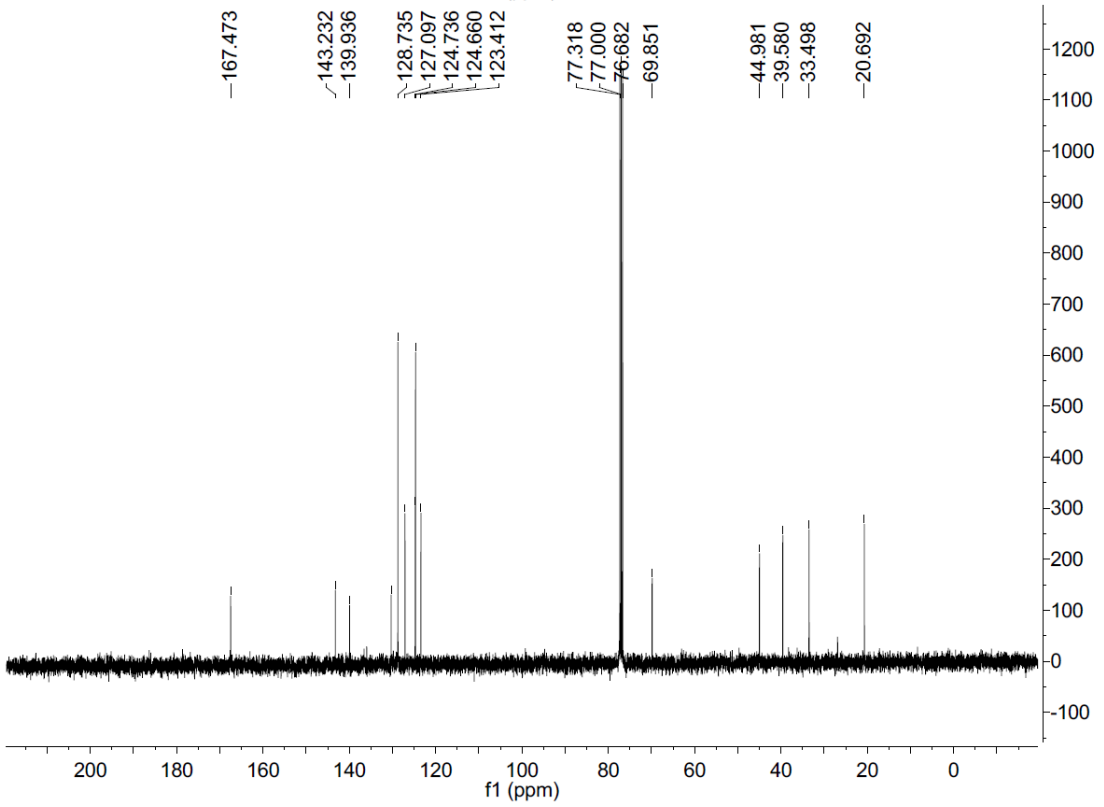
(1) F. D. King, *Tetrahedron* **2007**, *63*, 2053-2056.

(2) Q. Zhang, G. Tu, Y. Zhao, T. Cheng, *Tetrahedron* **2002**, *58*, 6795-6798.

^{1}H and ^{13}C NMR spectra

3aa





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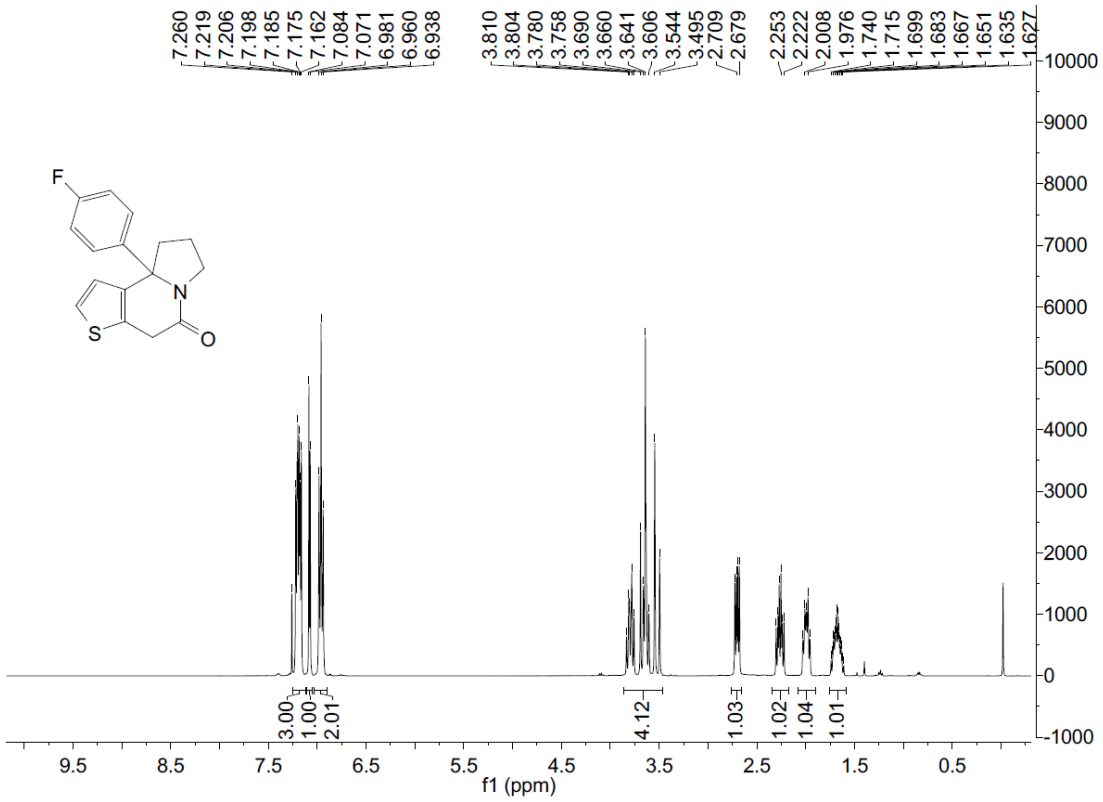
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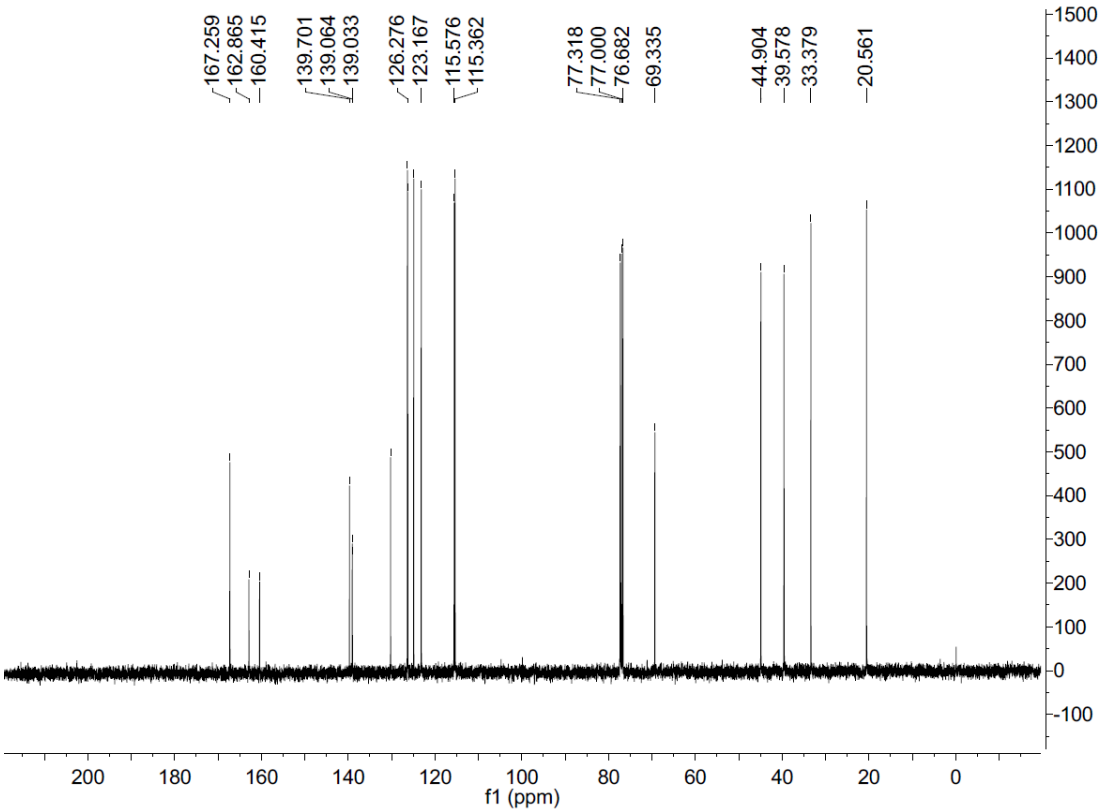
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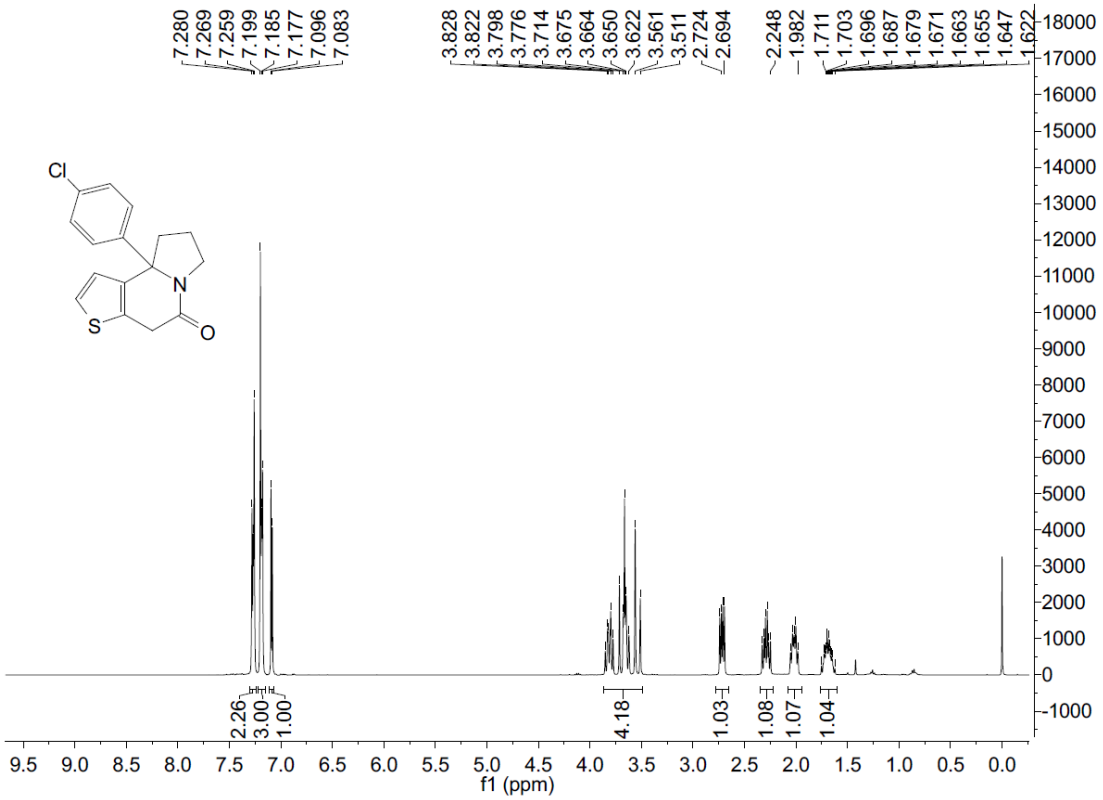

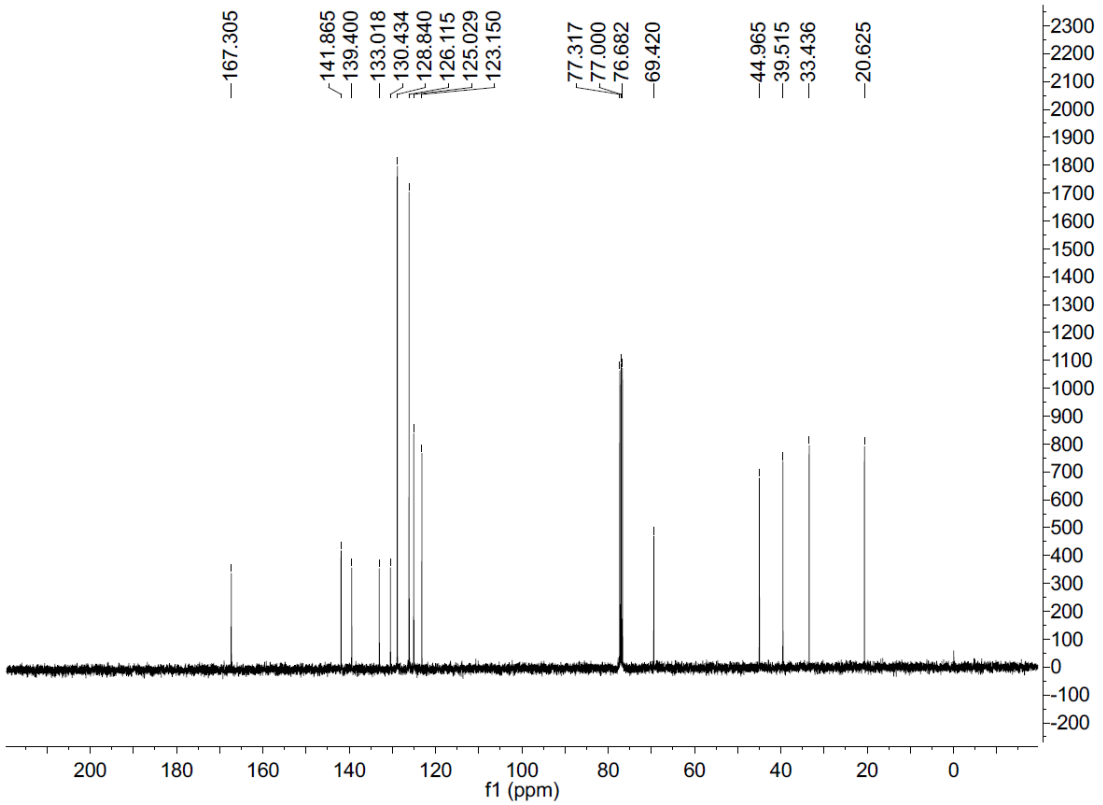

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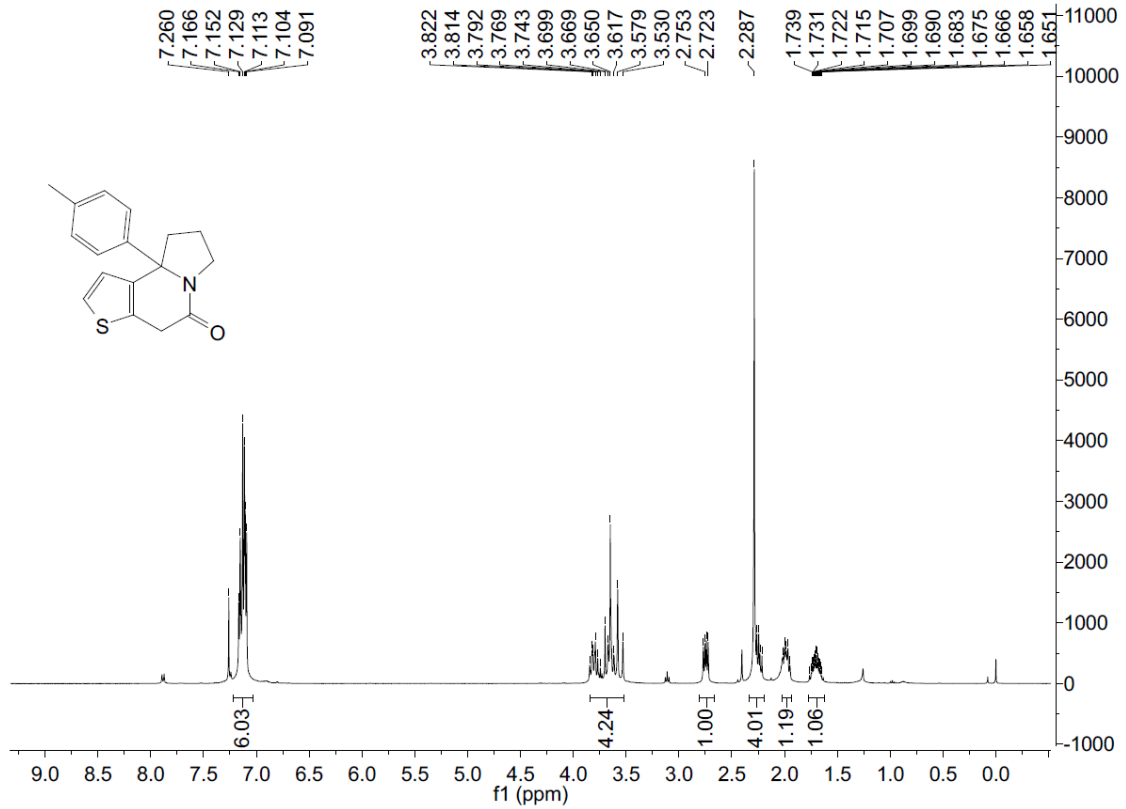
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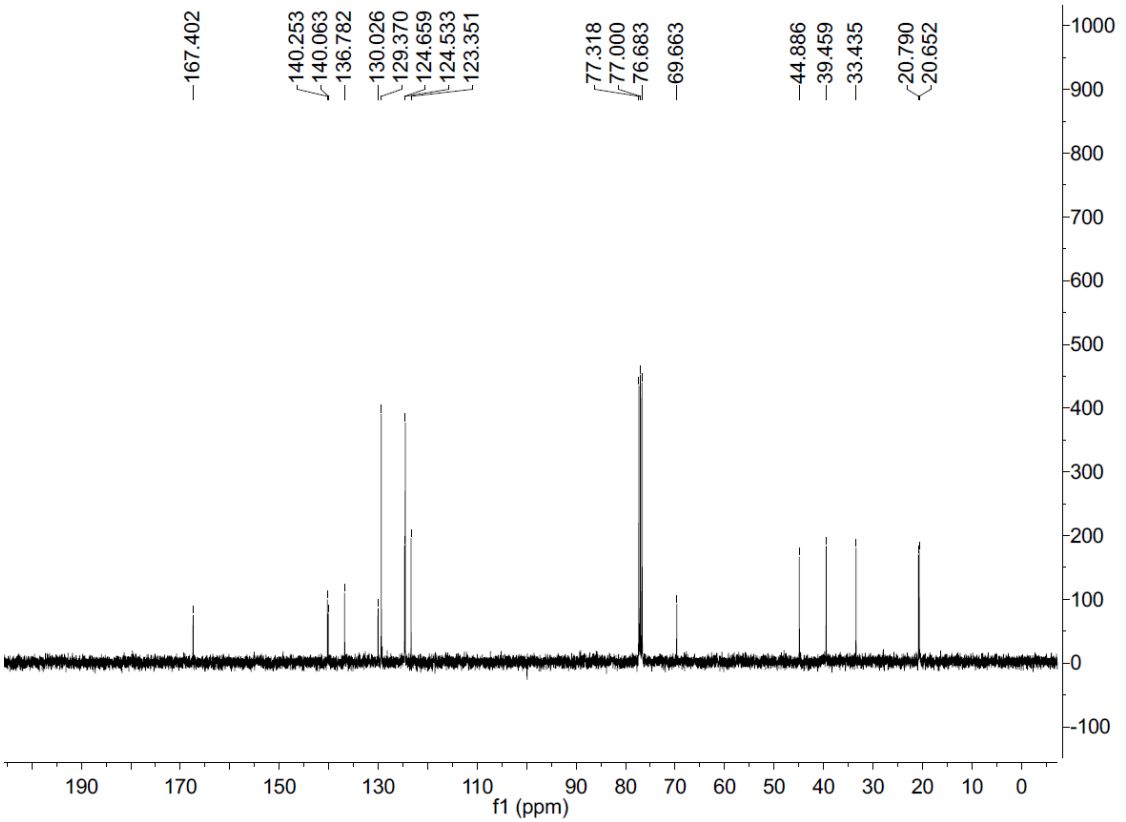
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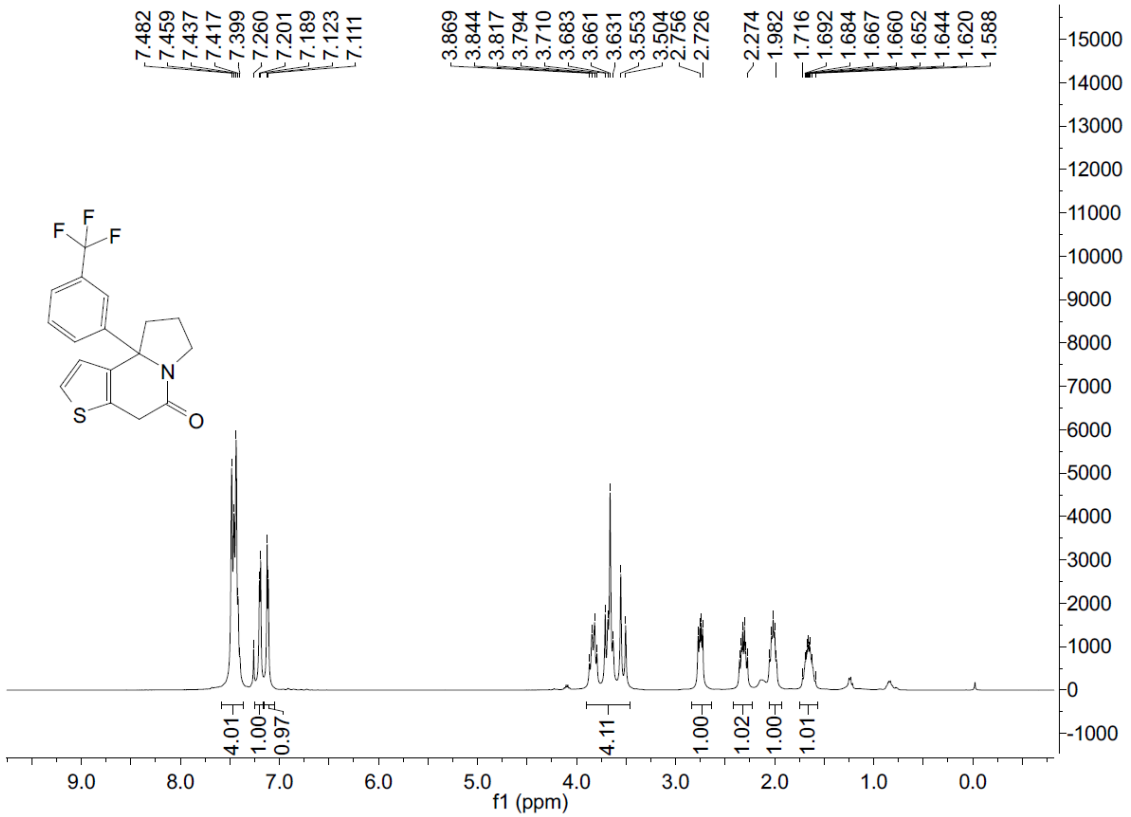

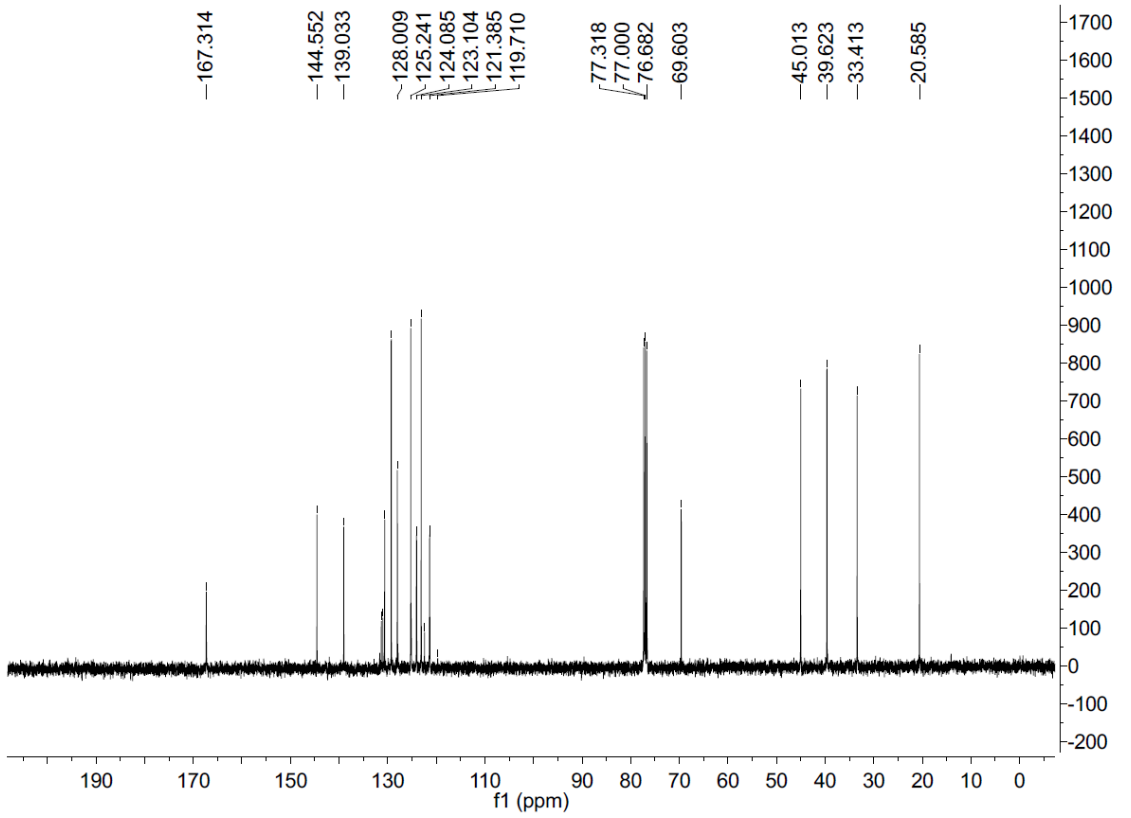

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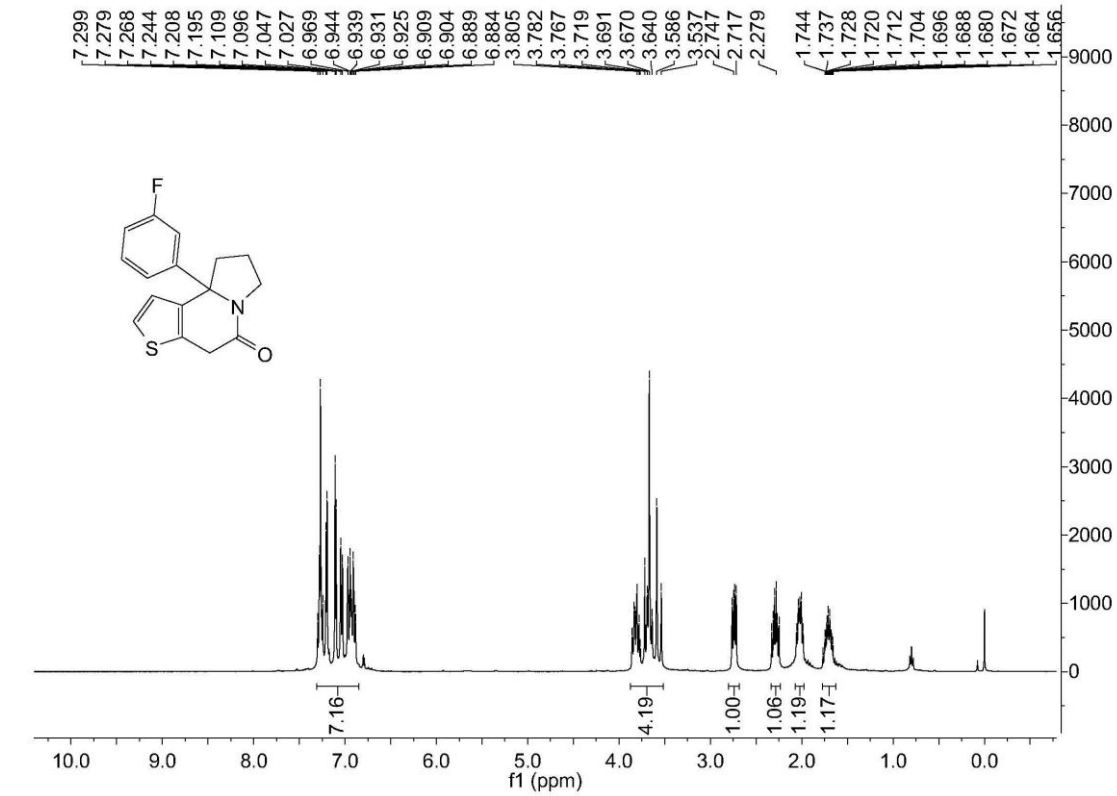
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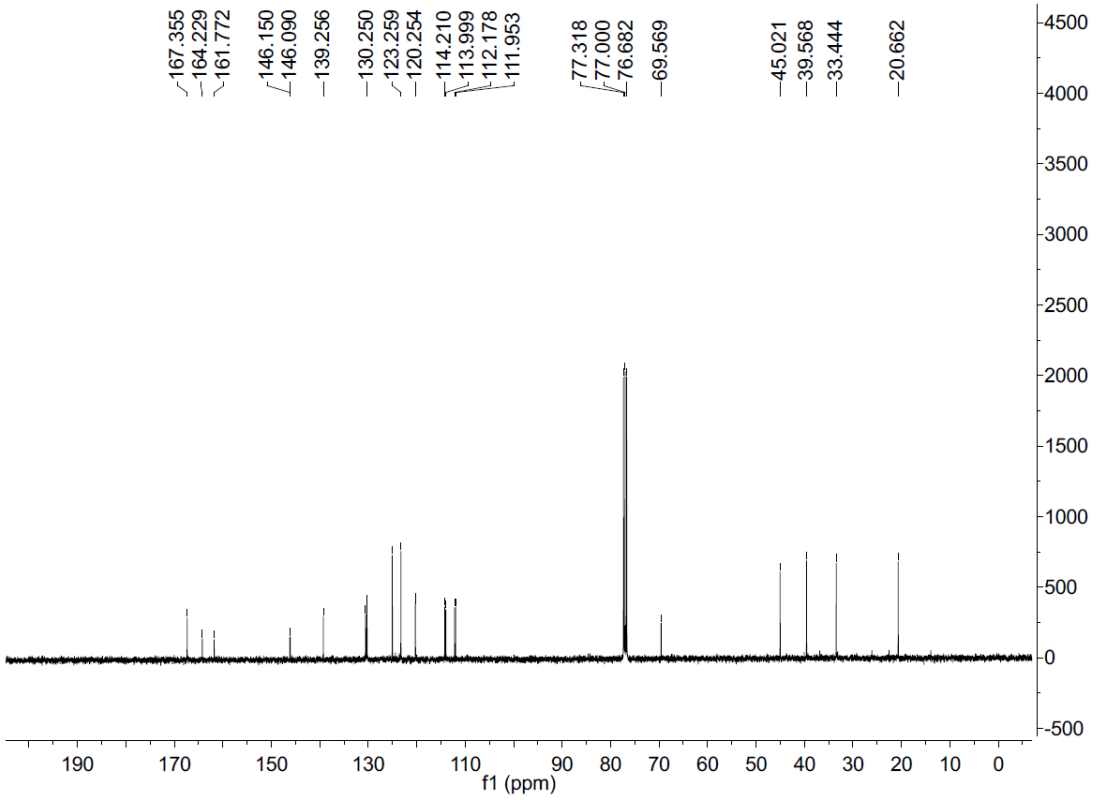
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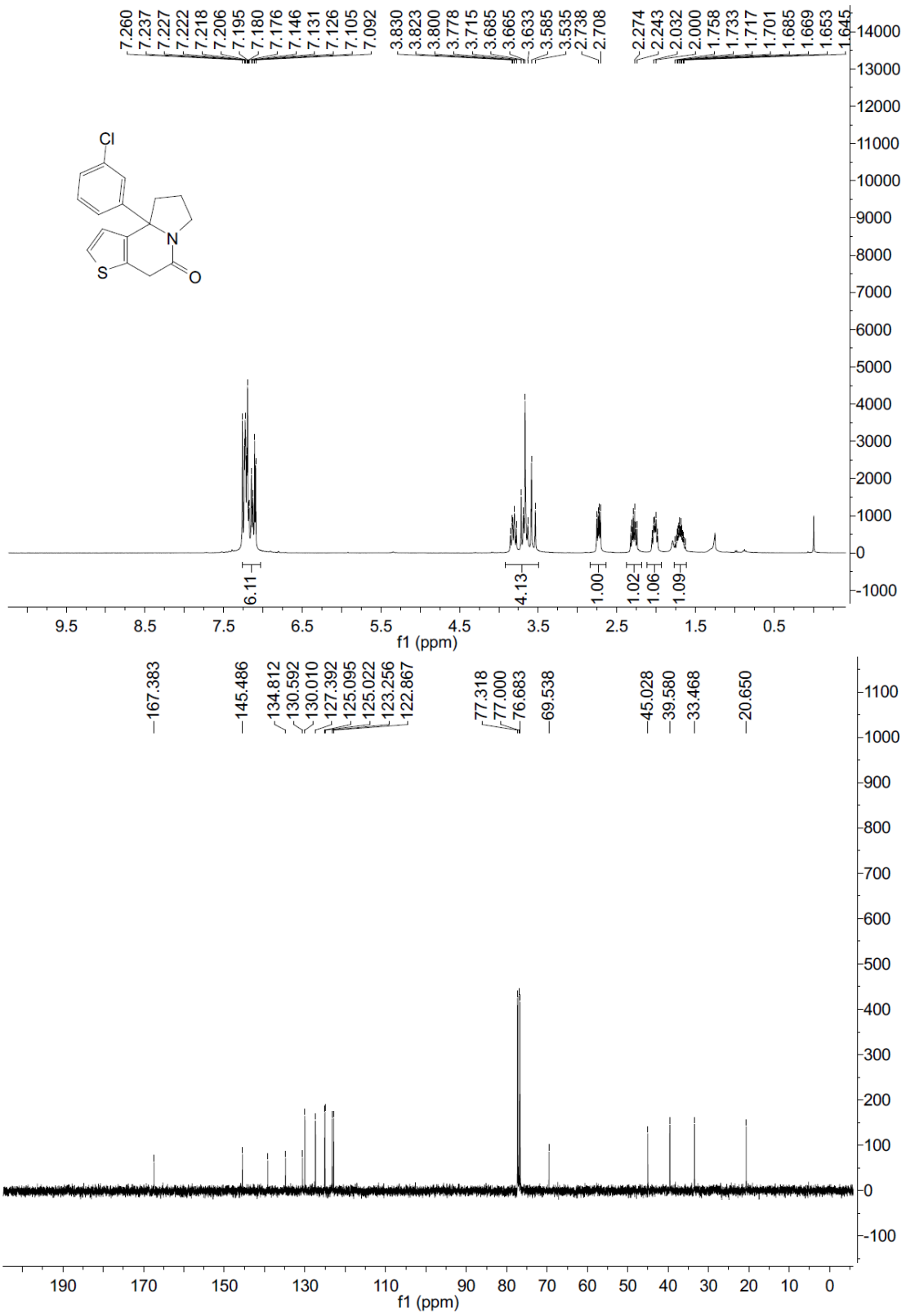

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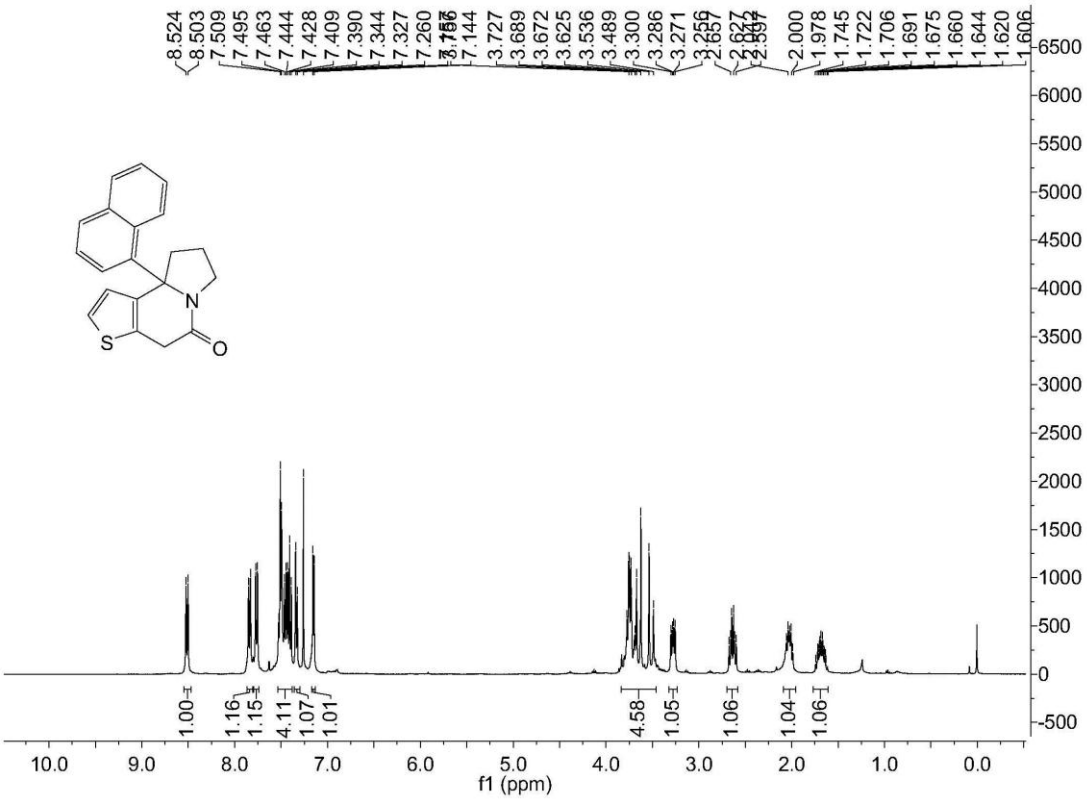

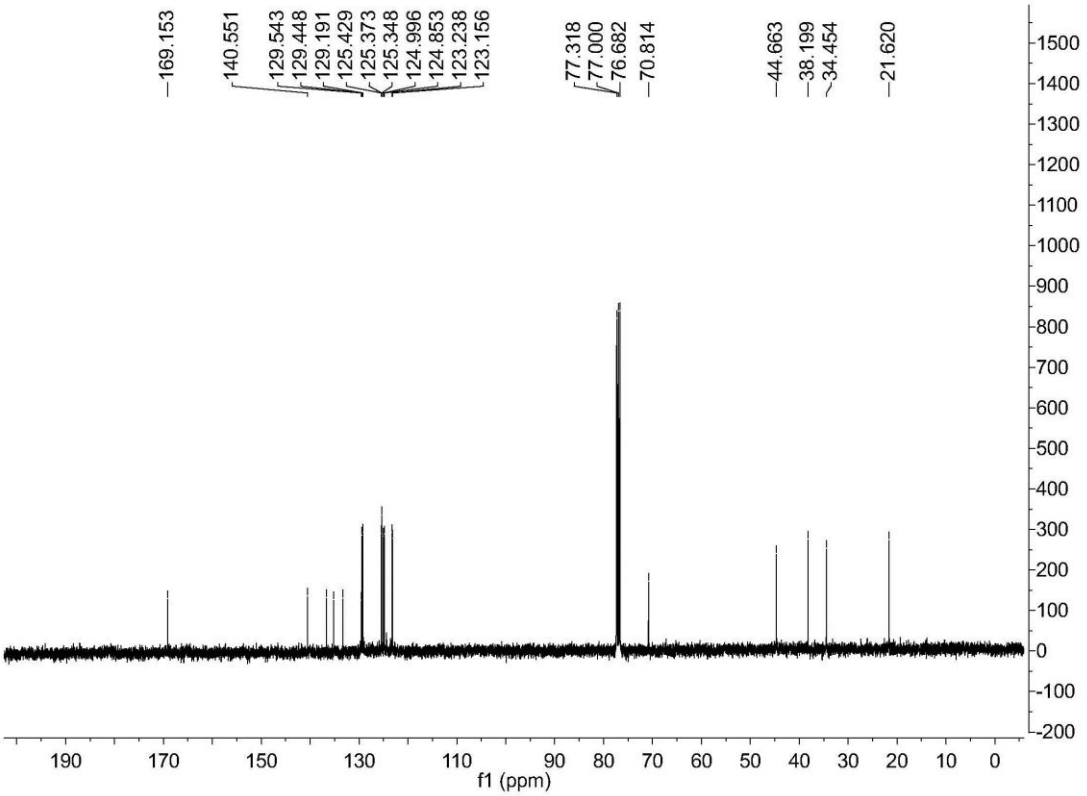

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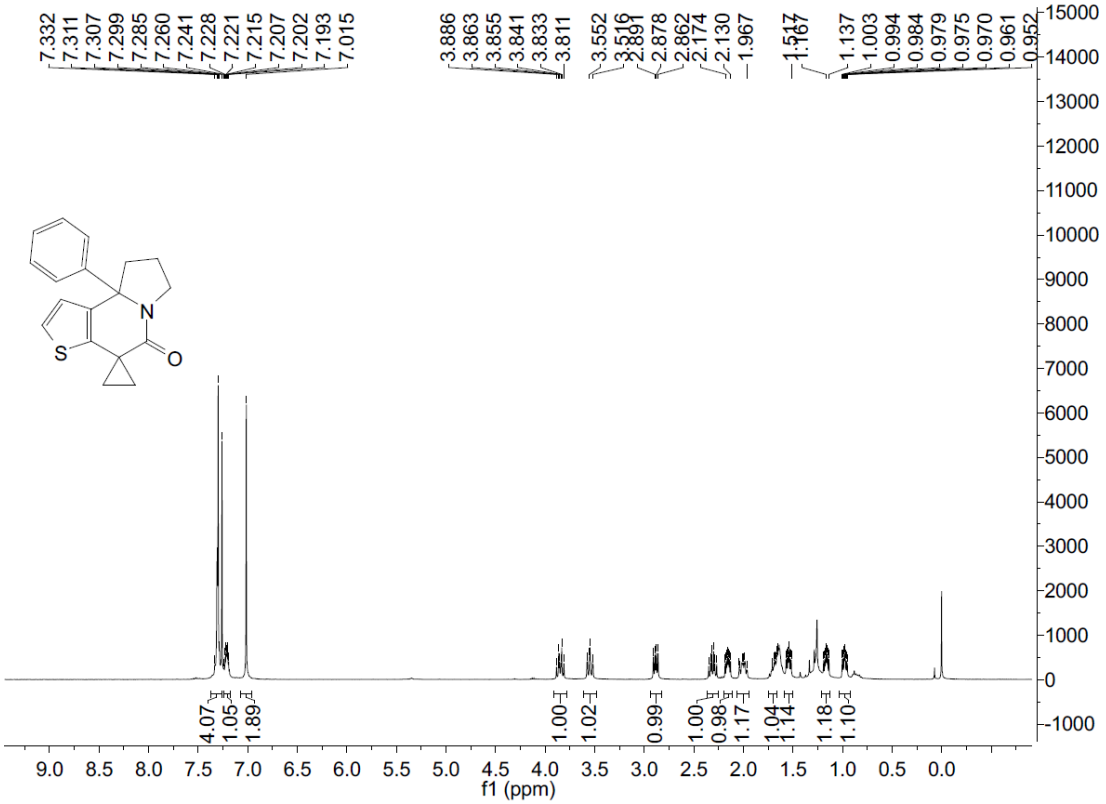

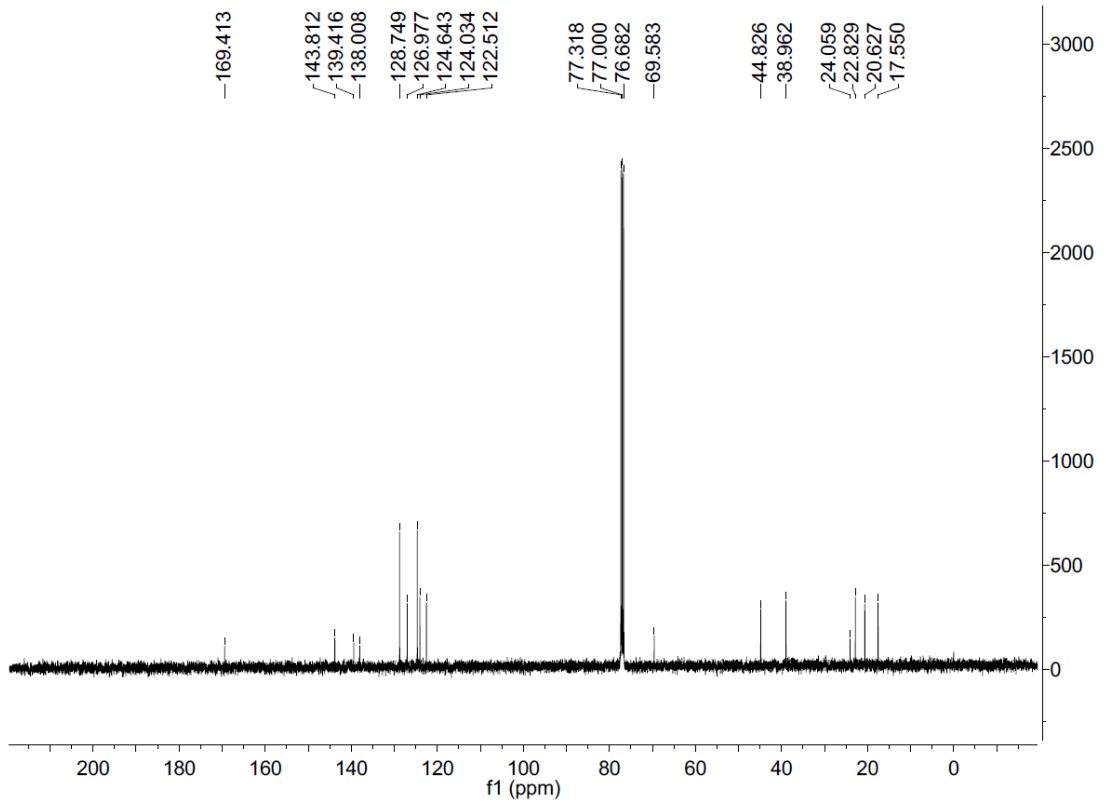

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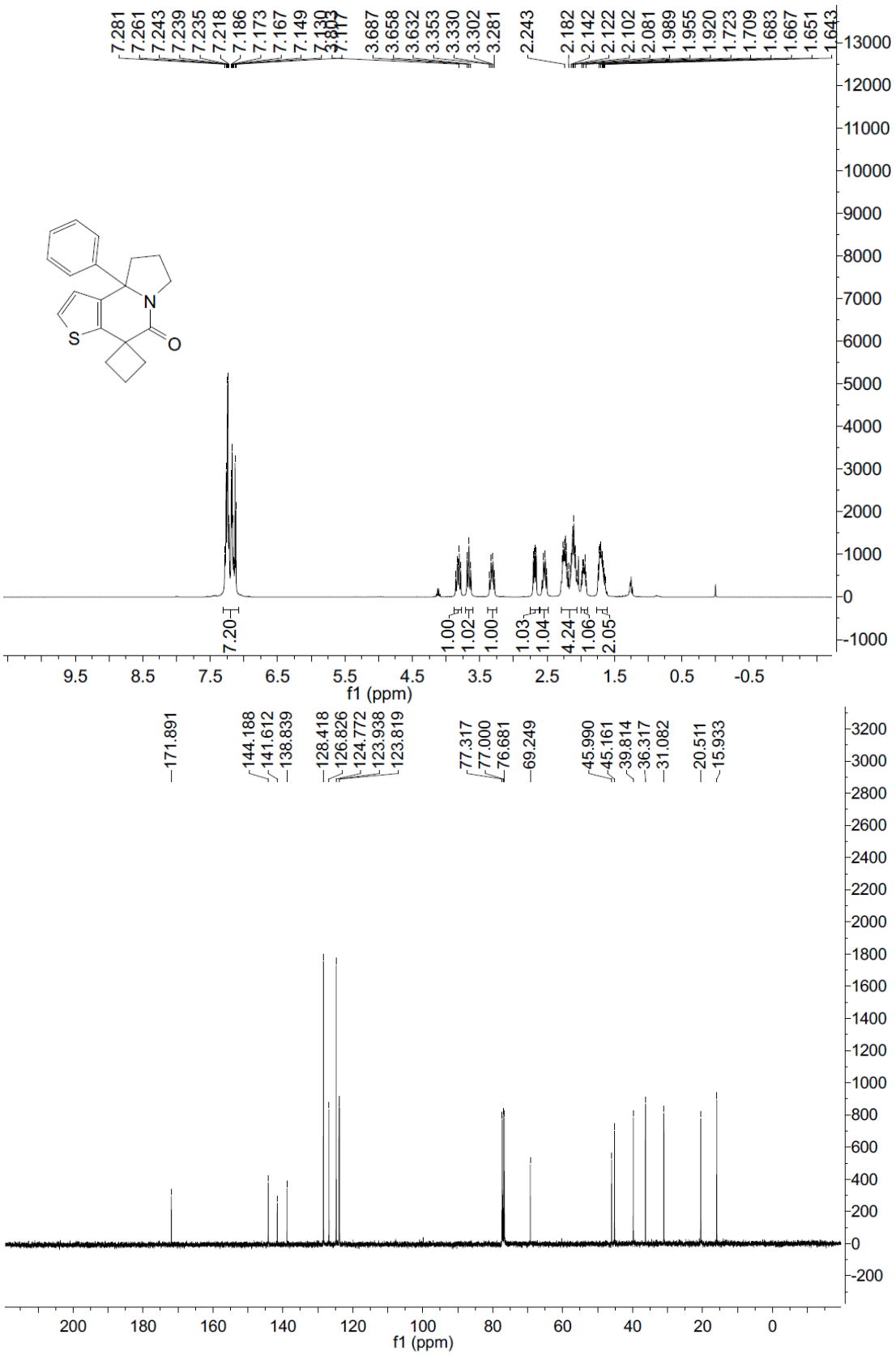

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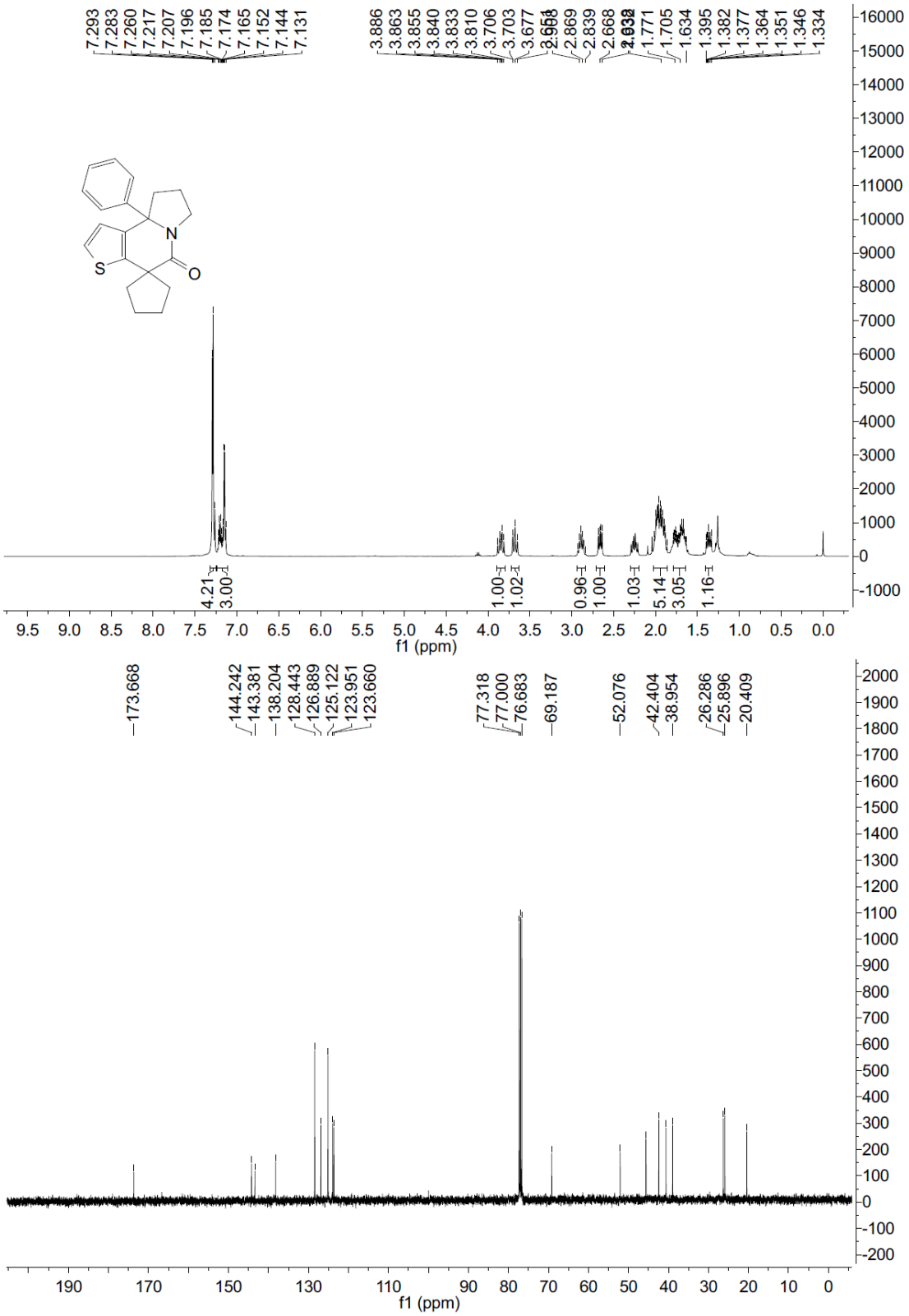

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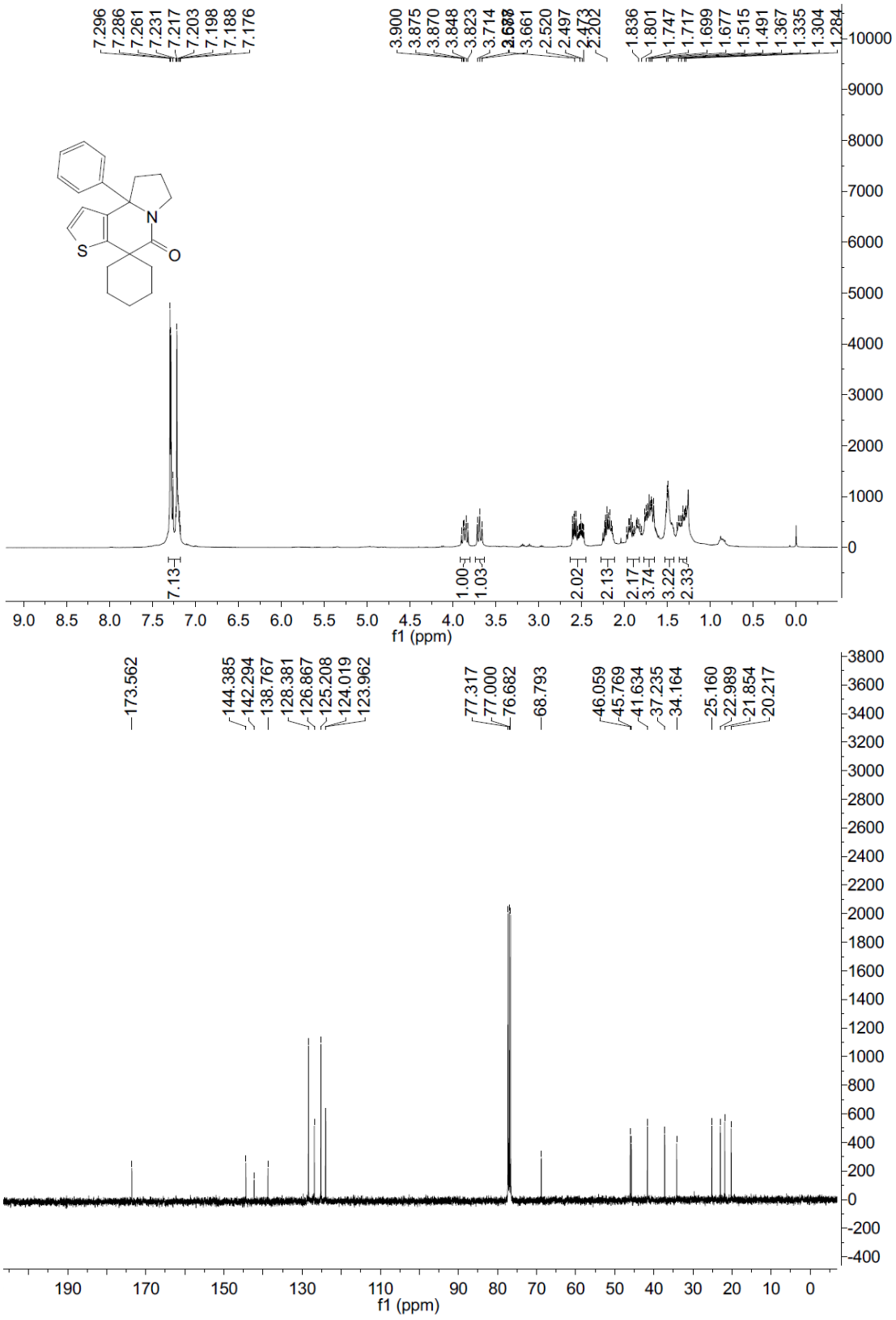

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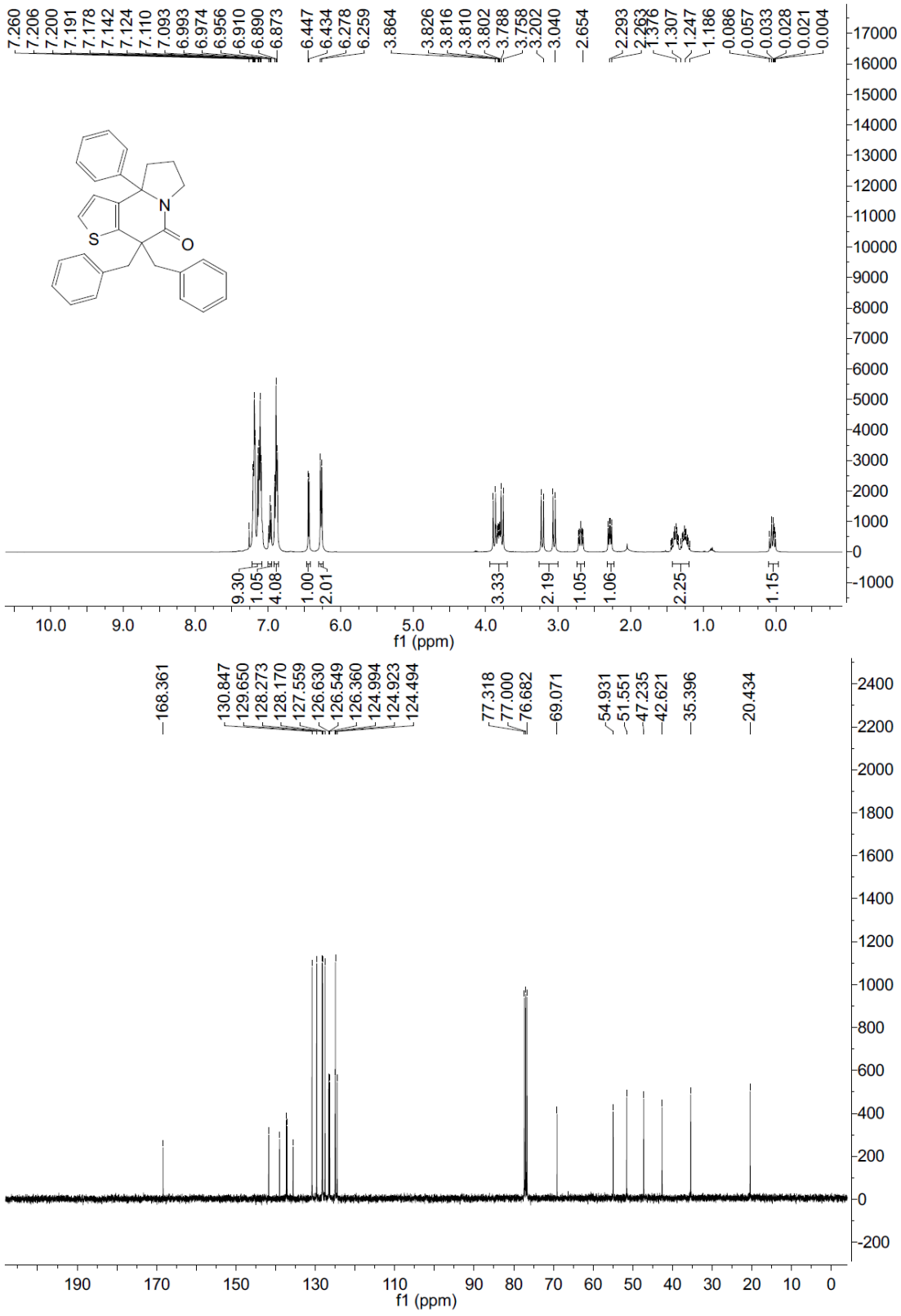

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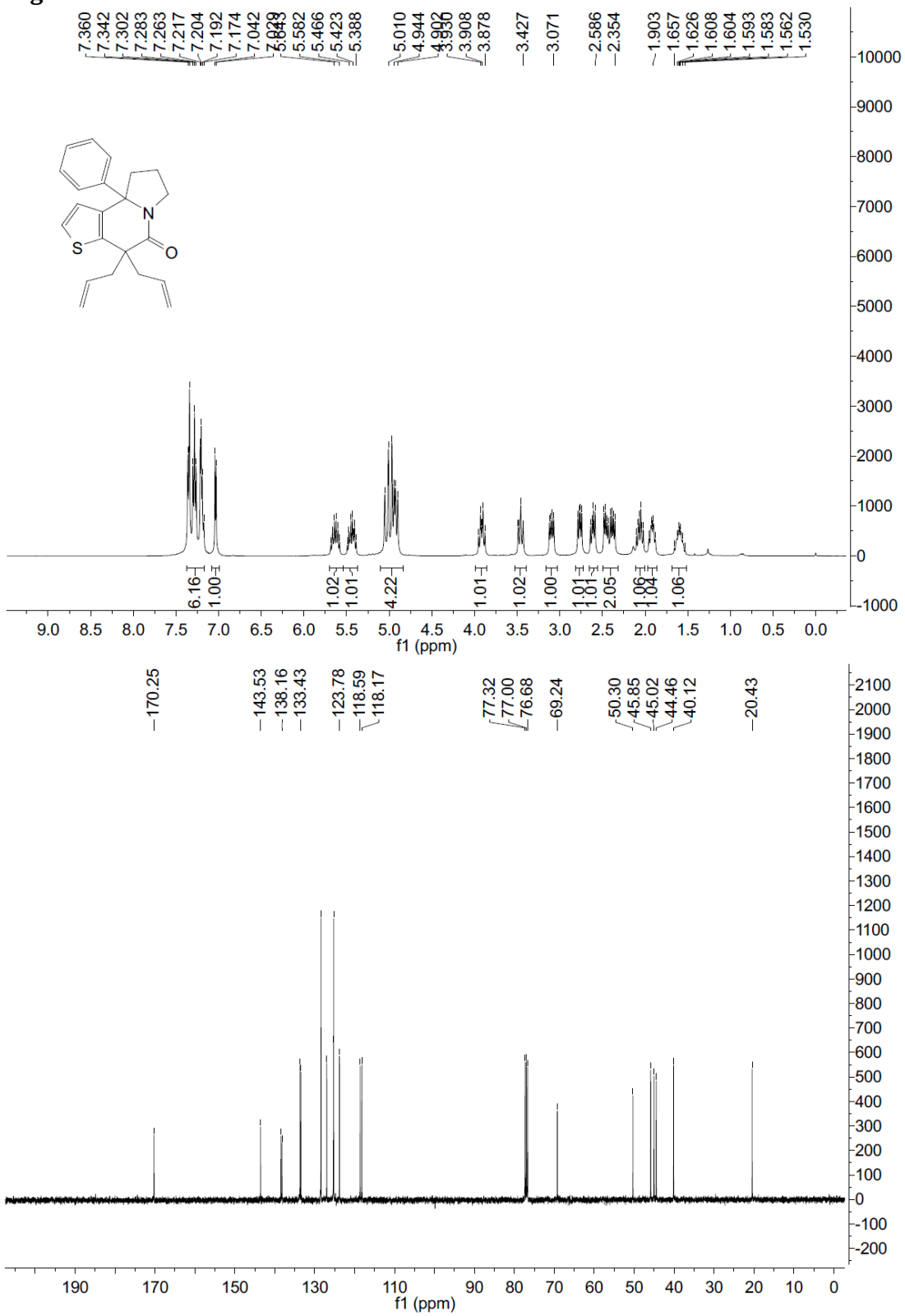

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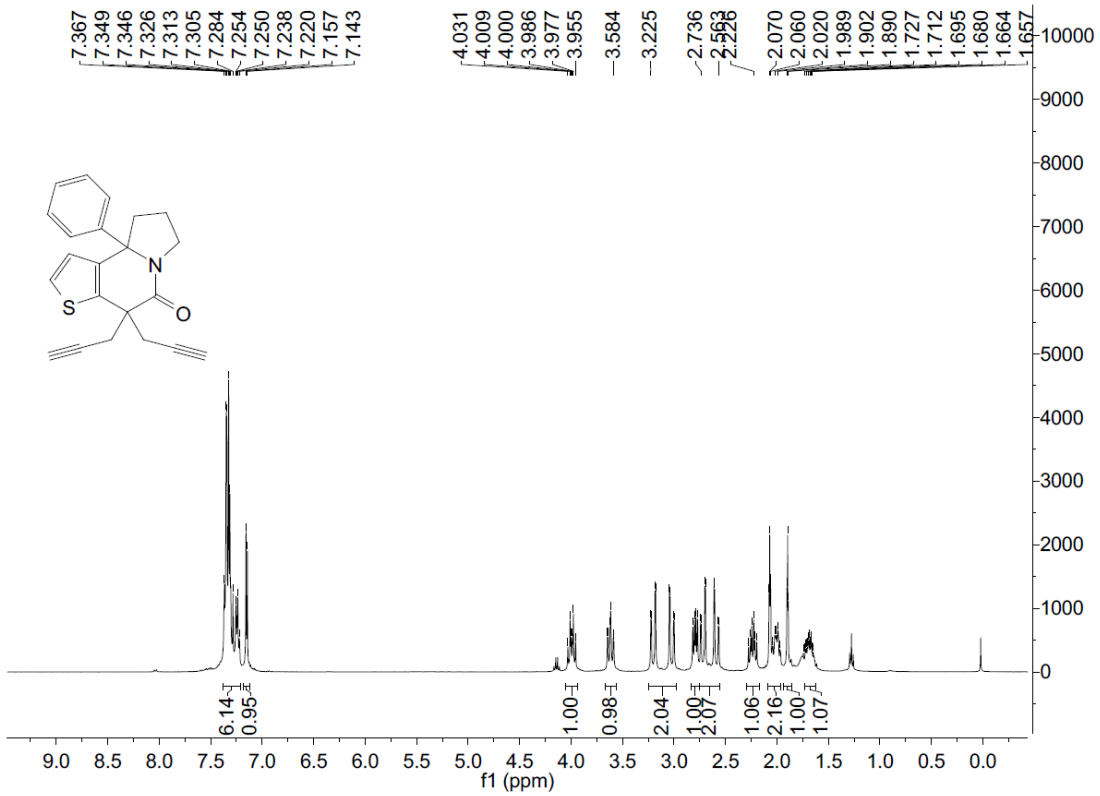

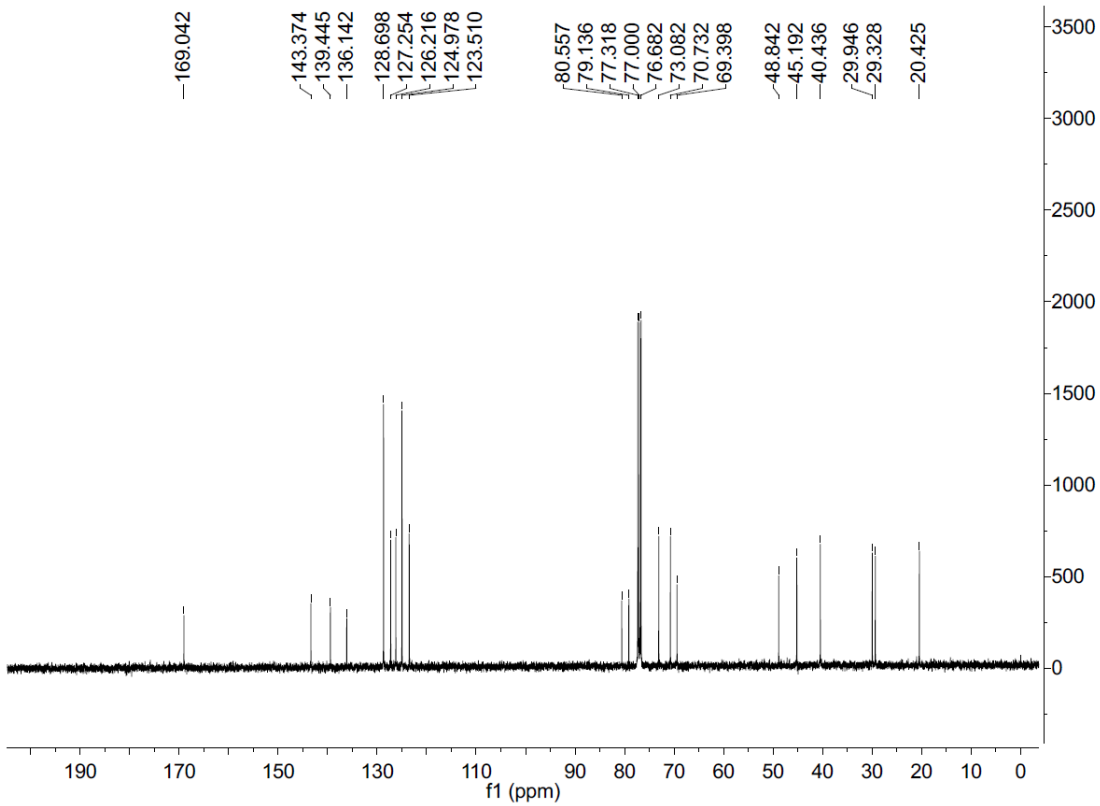

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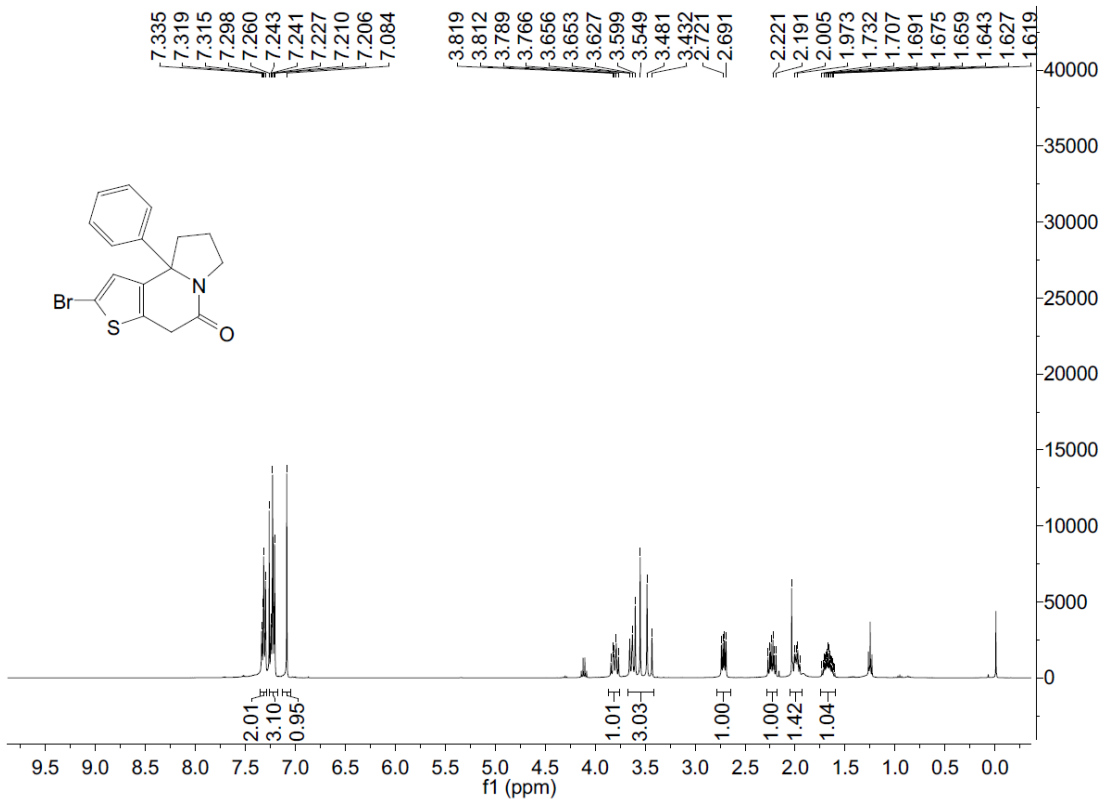
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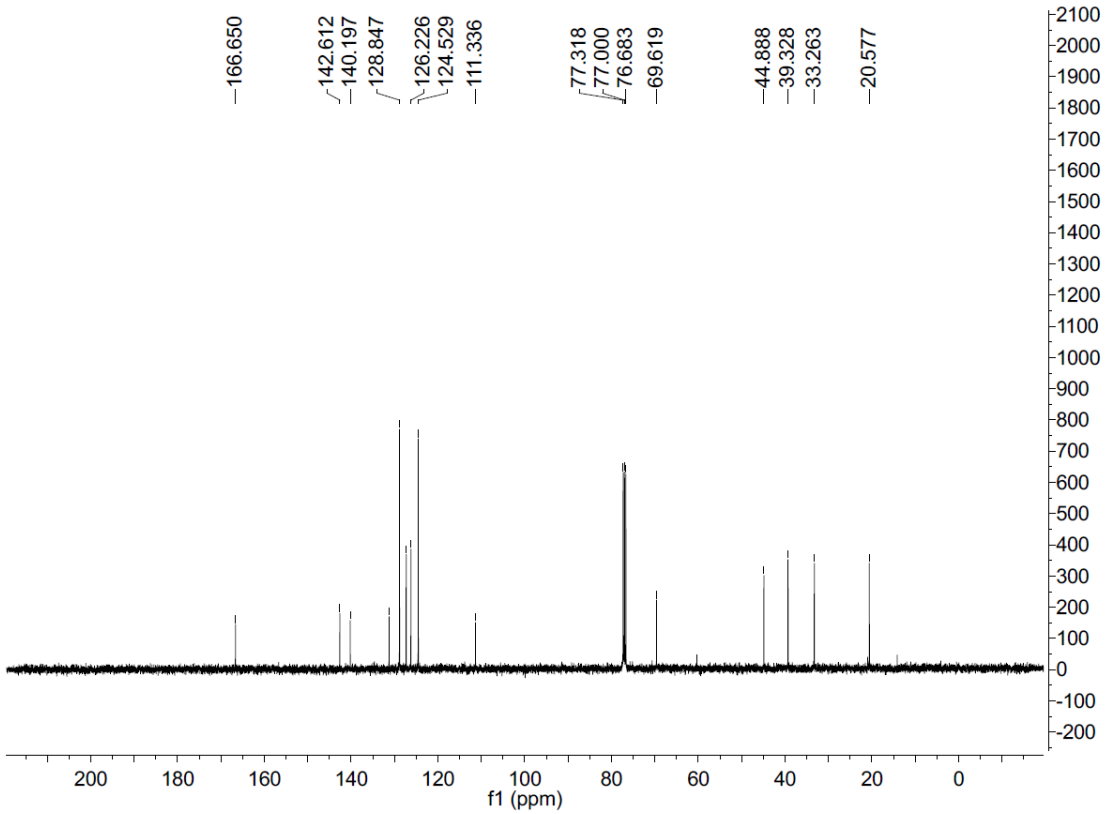
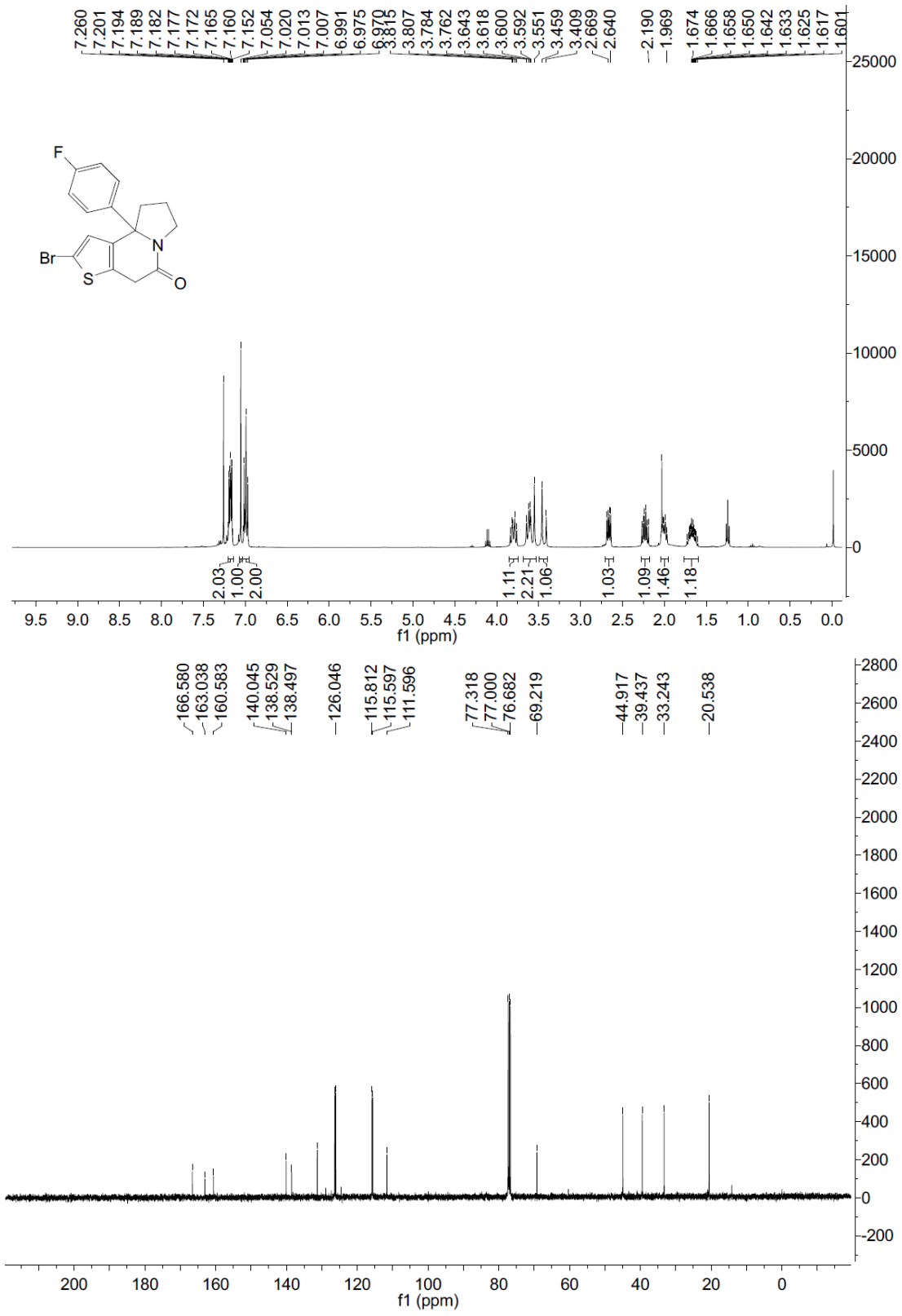
7.319
7.315
7.298
7.260
7.243
7.241
7.227
7.210
7.206
7.084
3.819
3.812
3.789
3.766
3.656
3.653
3.627
3.599
3.549
3.481
3.432
2.721
2.691
2.221
2.191
2.005
1.973
1.732
1.707
1.691
1.675
1.659
1.643
1.627
1.619
Br
S
N
O
2.01
3.10
0.95
1.01
3.03
1.00
1.00
1.42
1.04
f1 (ppm)


166.650
142.612
140.197
128.847
126.226
124.529
111.336
77.318
77.000
76.683
69.619
44.888
39.328
33.263
20.577
f1 (ppm)

3bi



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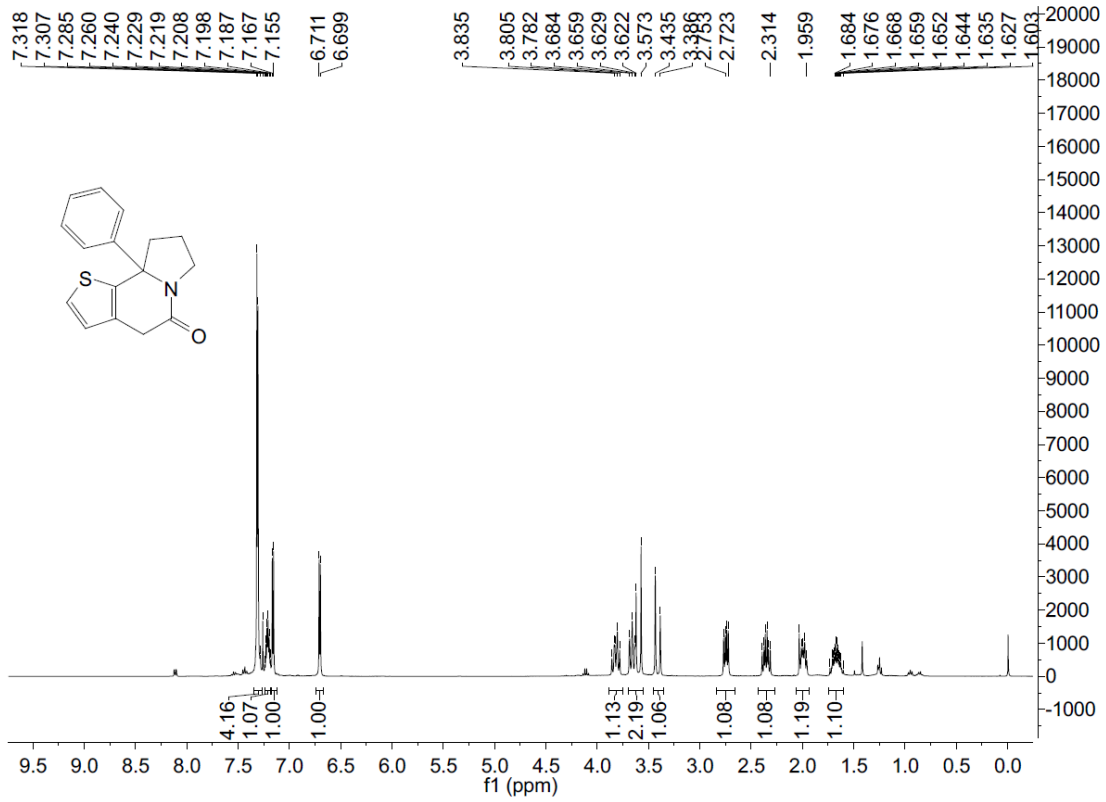

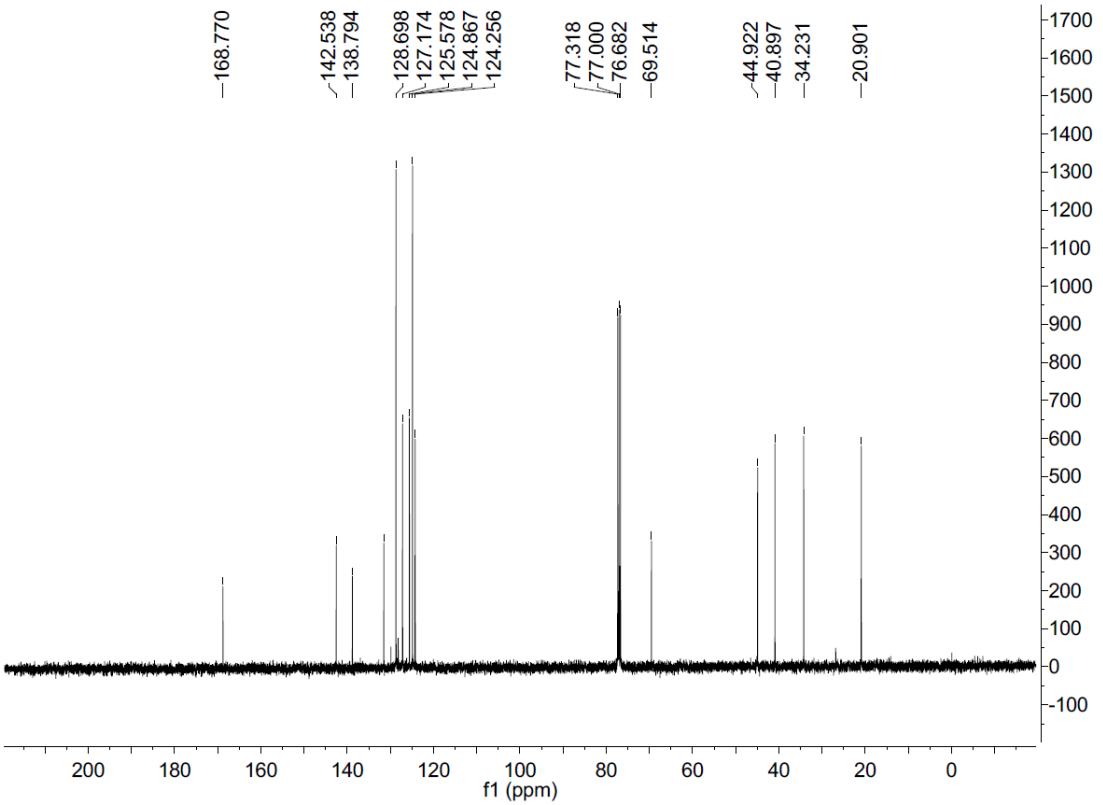

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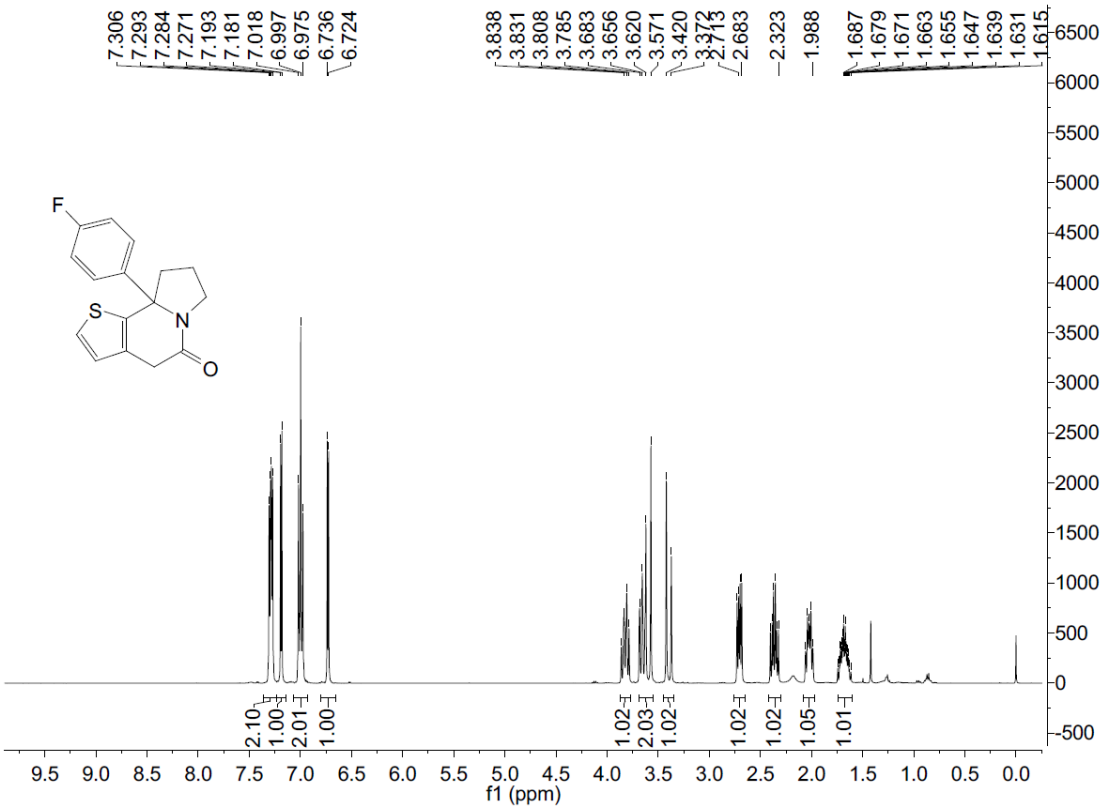

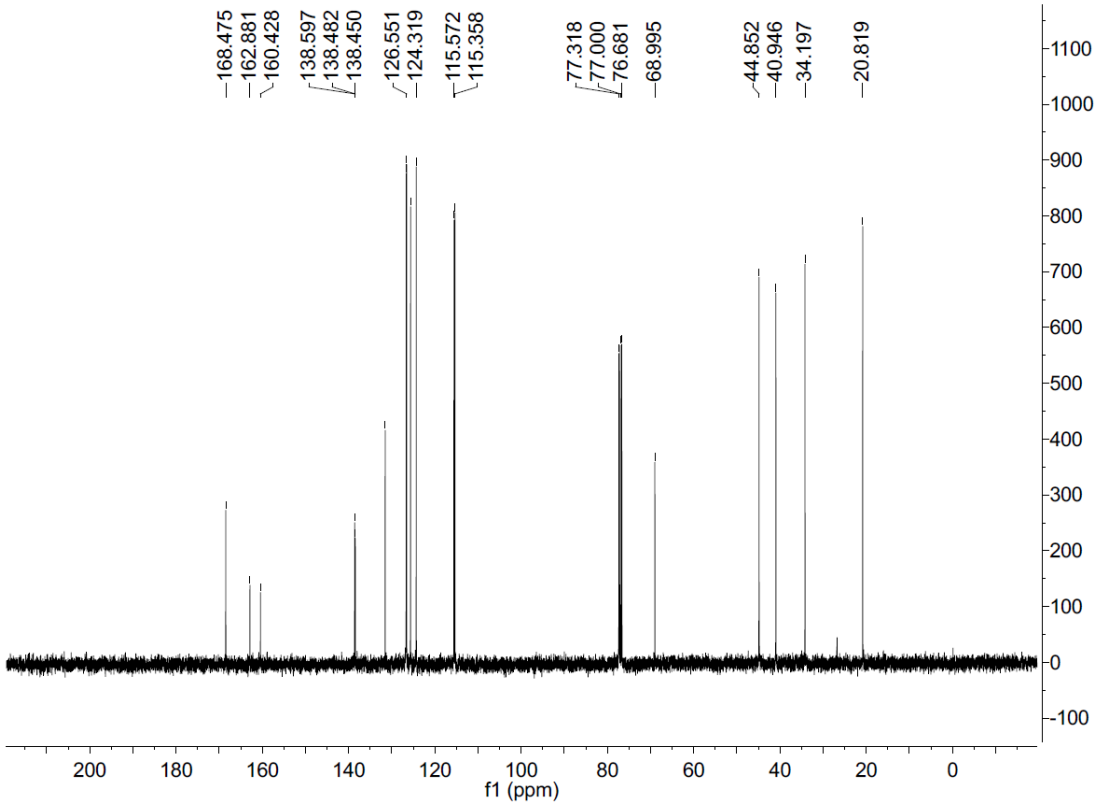

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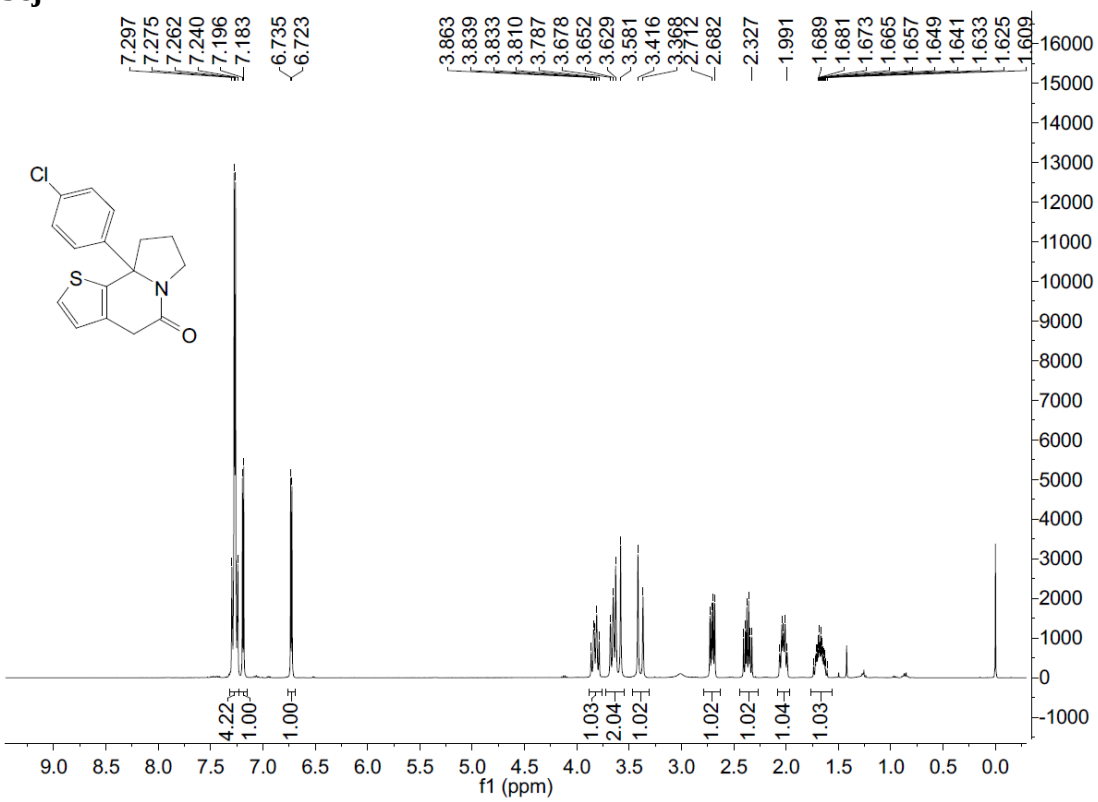
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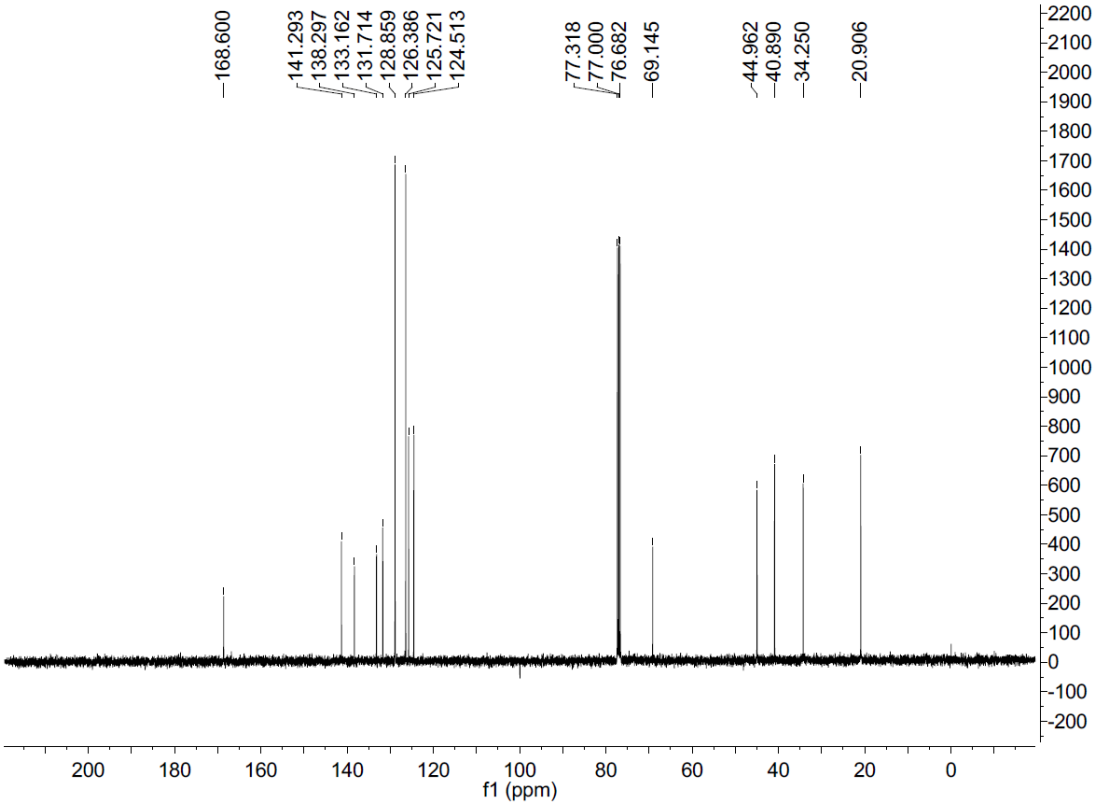
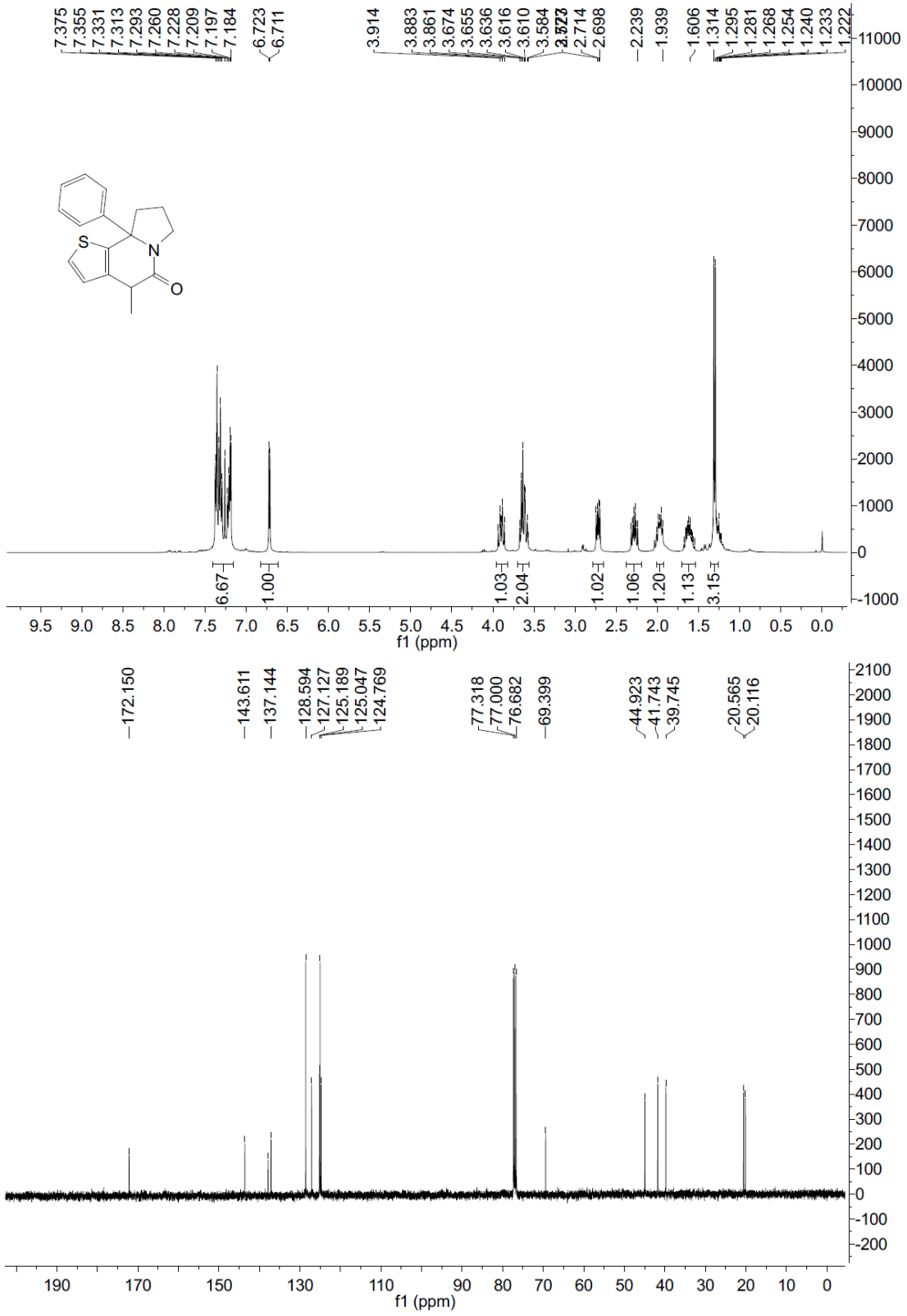
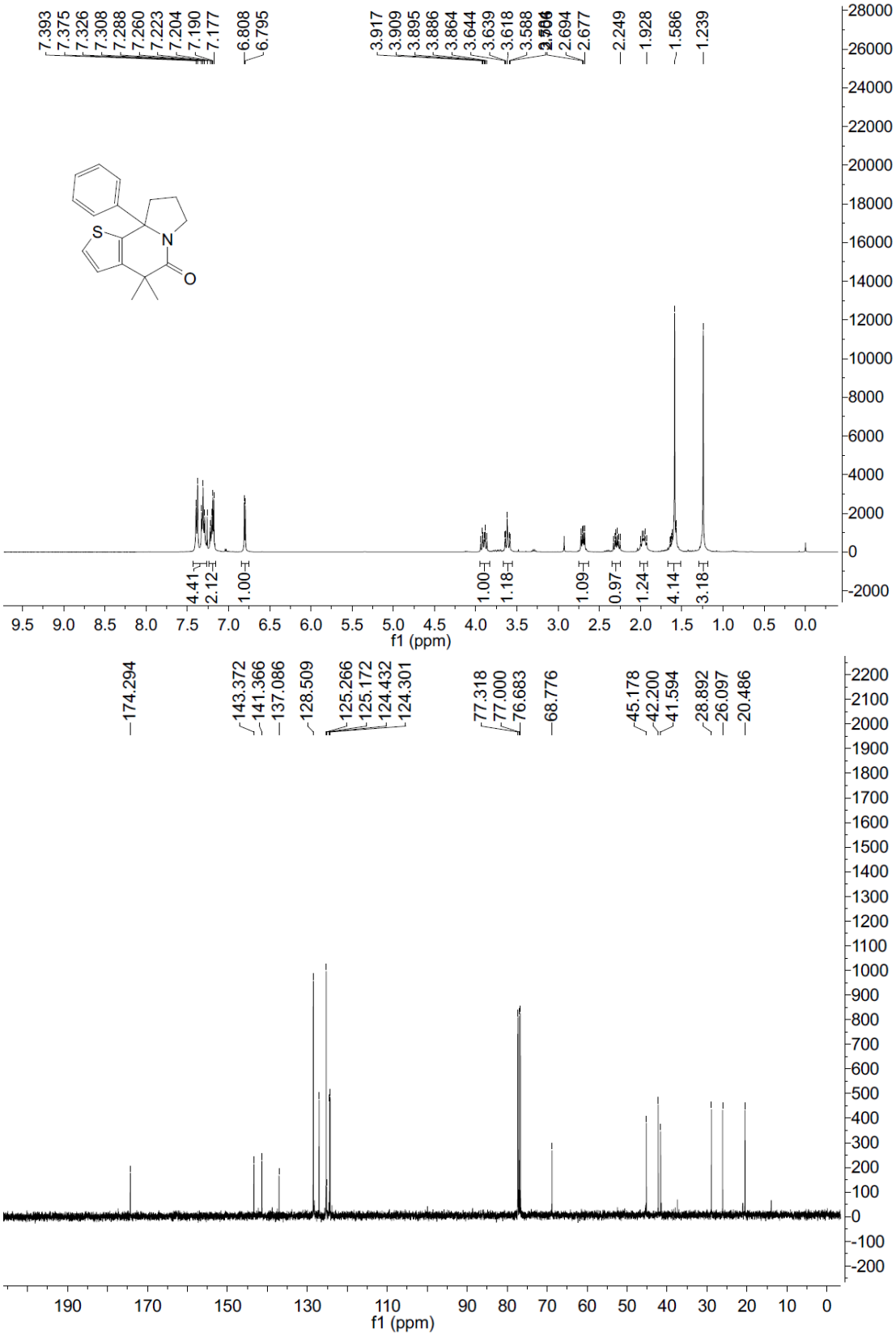
7.275
7.262
7.240
7.196
7.183
6.735
6.723
3.863
3.839
3.833
3.810
3.787
3.678
3.652
3.629
3.581
3.416
3.368
2.712
2.682
2.327
1.991
1.689
1.681
1.673
1.665
1.657
1.649
1.641
1.633
1.625
1.609
Cl
S
N
O
4.22
1.00
1.00
1.03
2.04
1.02
1.02
1.02
1.04
1.03
f1 (ppm)


168.600
141.293
138.297
133.162
131.714
128.859
126.386
125.721
124.513
77.318
77.000
76.682
69.145
44.962
40.890
34.250
20.906
f1 (ppm)

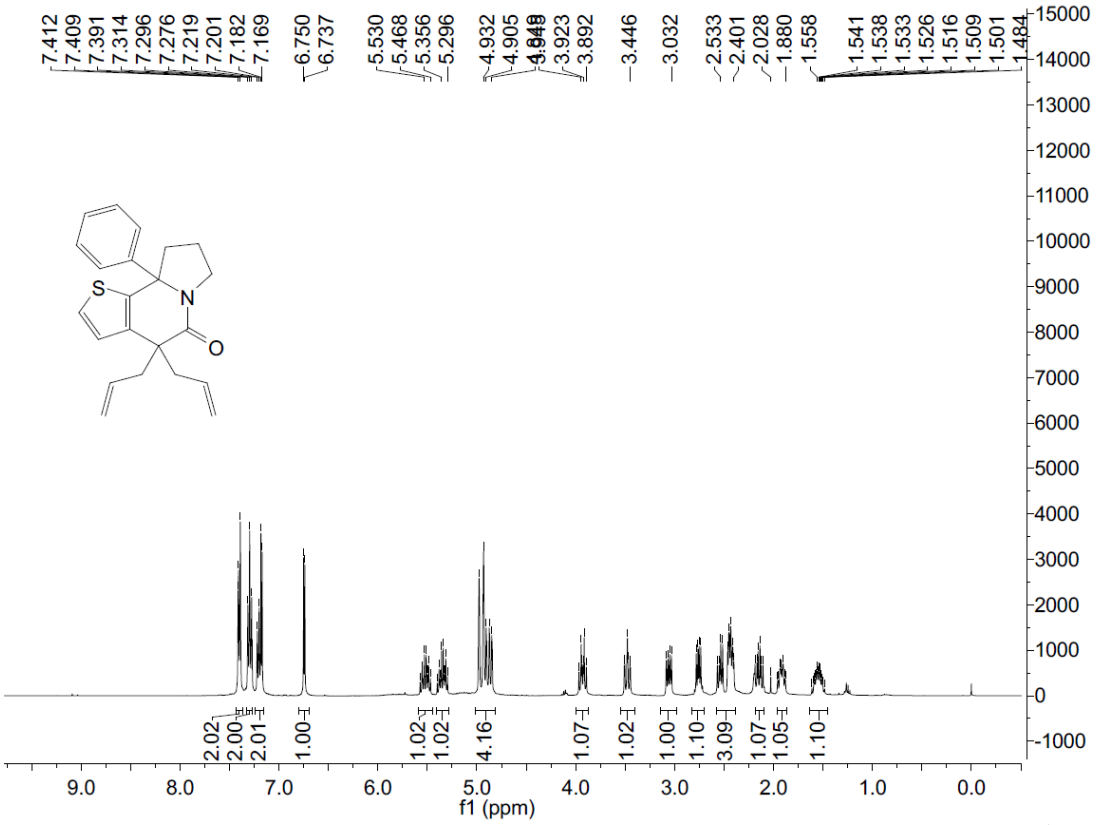
3ak

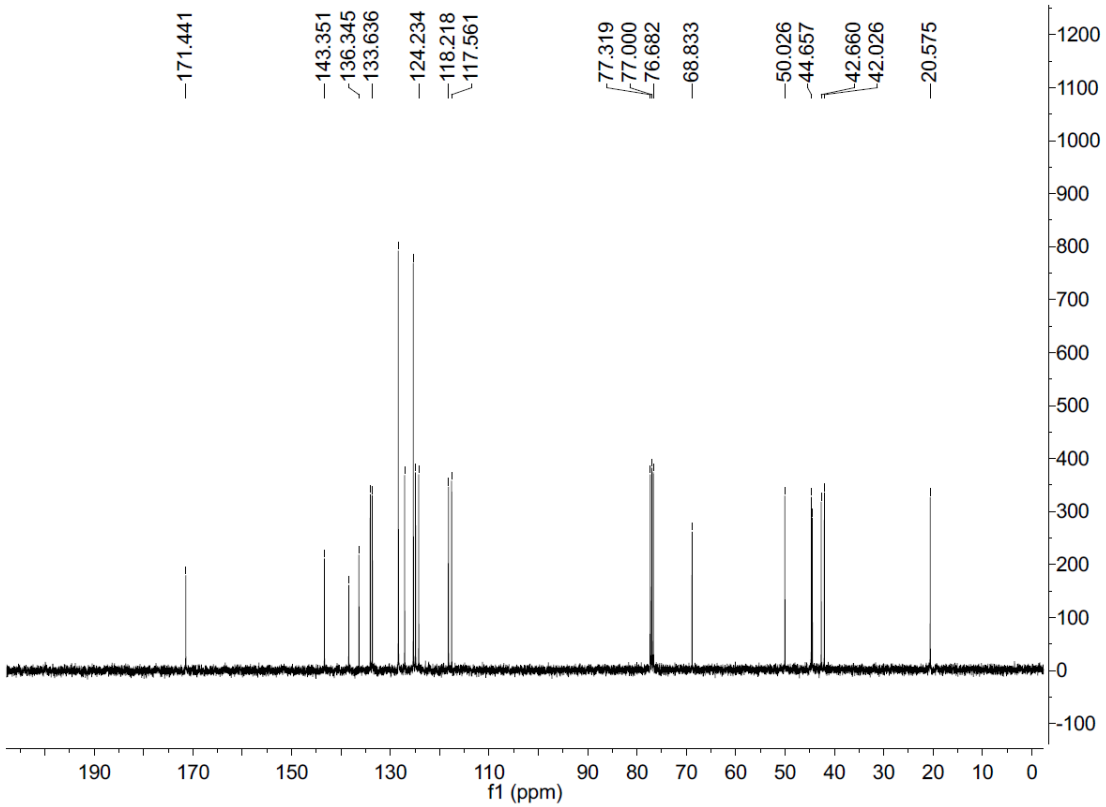


3al

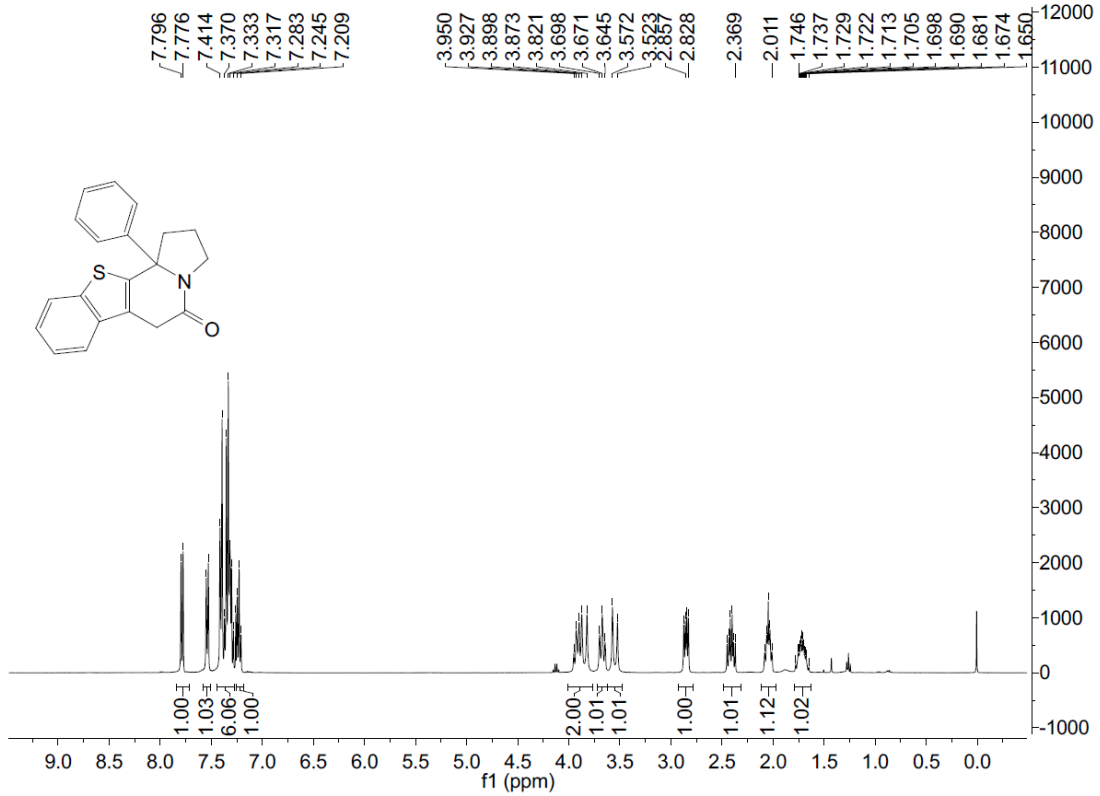


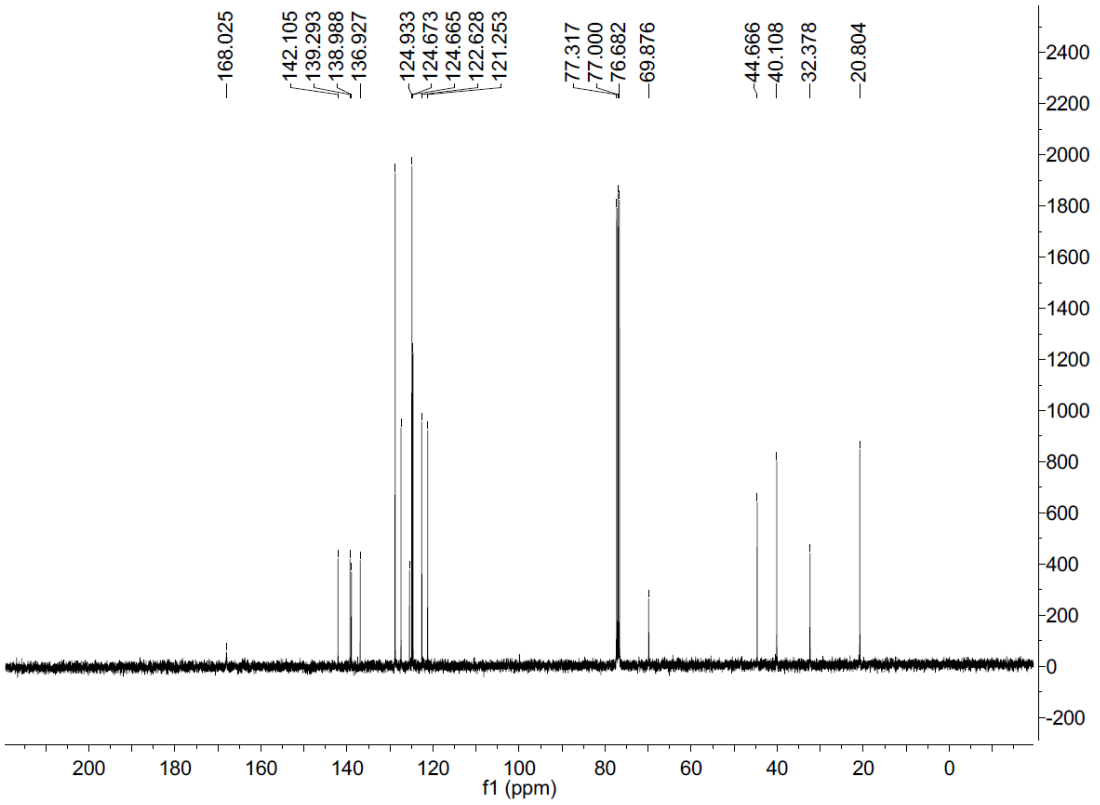
3am


7.412
7.409
7.391
7.314
7.296
7.276
7.219
7.201
7.182
7.169
6.750
6.737
5.530
5.468
5.356
5.296
4.932
4.905
3.923
3.892
3.446
3.032
2.533
2.401
2.028
1.880
1.558
1.541
1.538
1.533
1.526
1.516
1.509
1.501
1.484
S
N
O
2.02
2.00
2.01
1.00
1.02
1.02
4.16
1.07
1.02
1.00
1.10
3.09
1.07
1.05
1.10
f1 (ppm)


171.441
143.351
136.345
133.636
124.234
118.218
117.561
77.319
77.000
76.682
68.833
50.026
44.657
42.660
42.026
20.575
f1 (ppm)

3an





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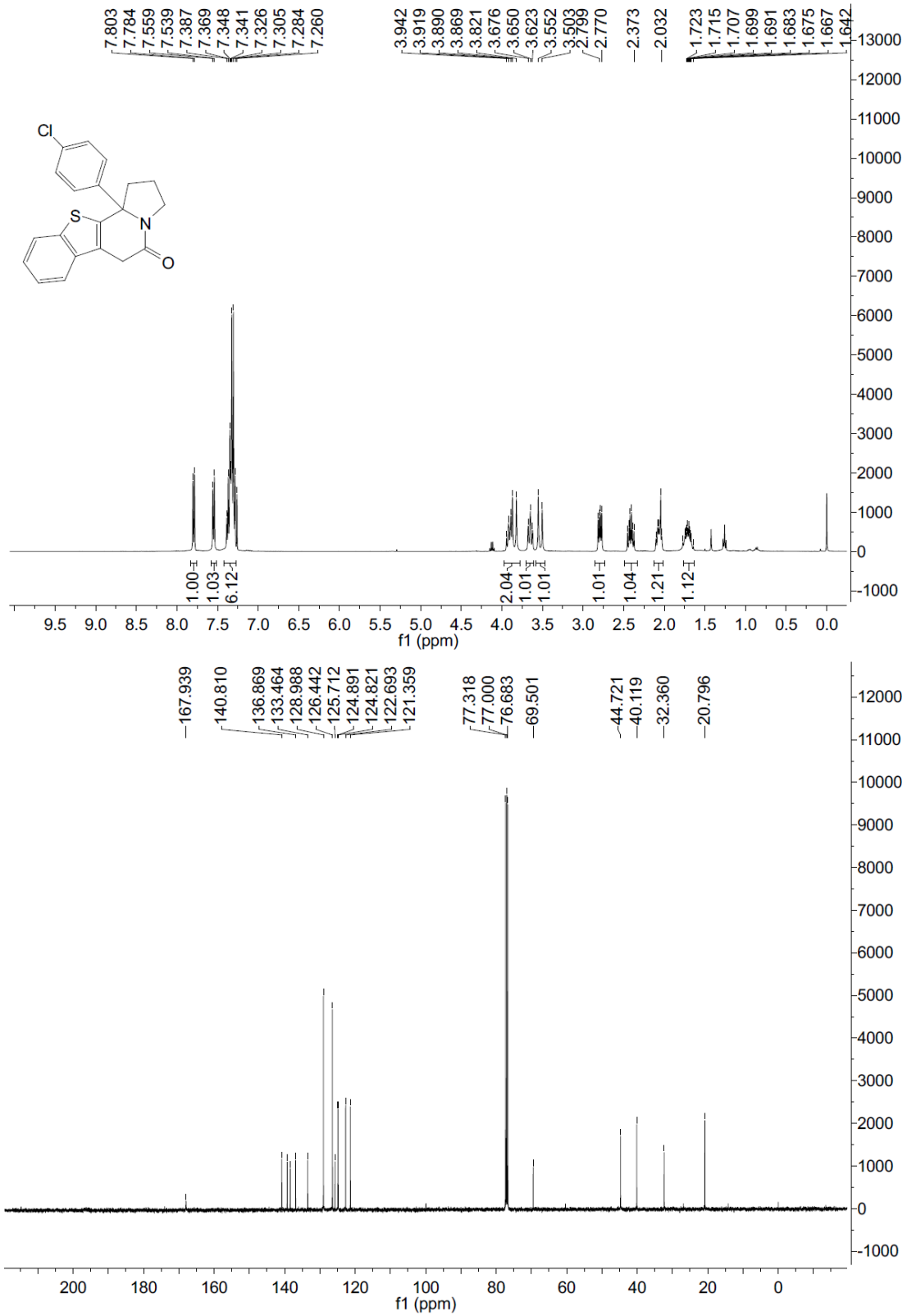
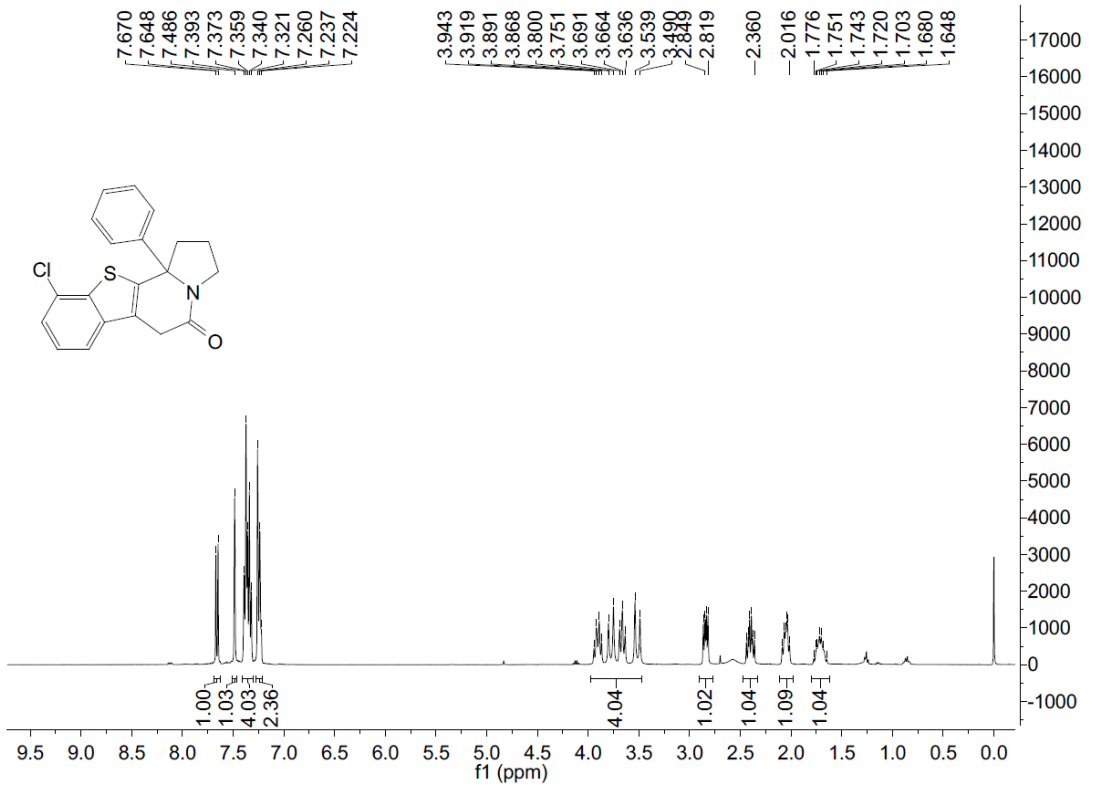
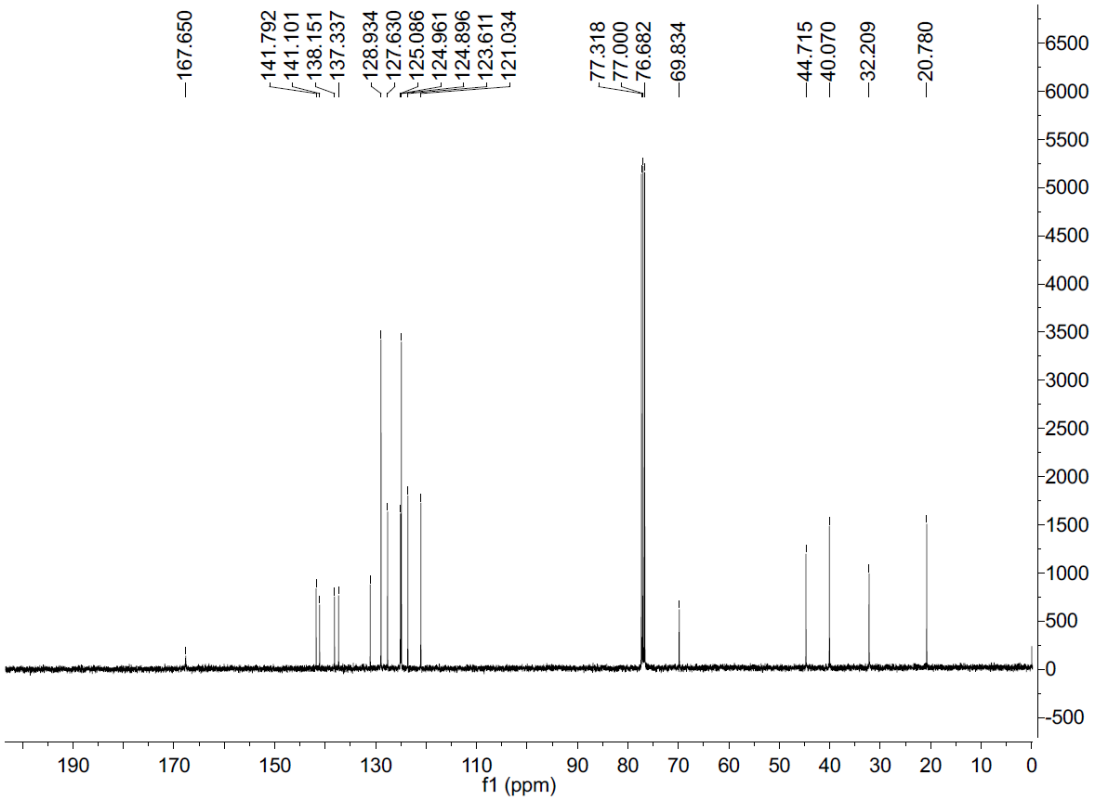


3ao





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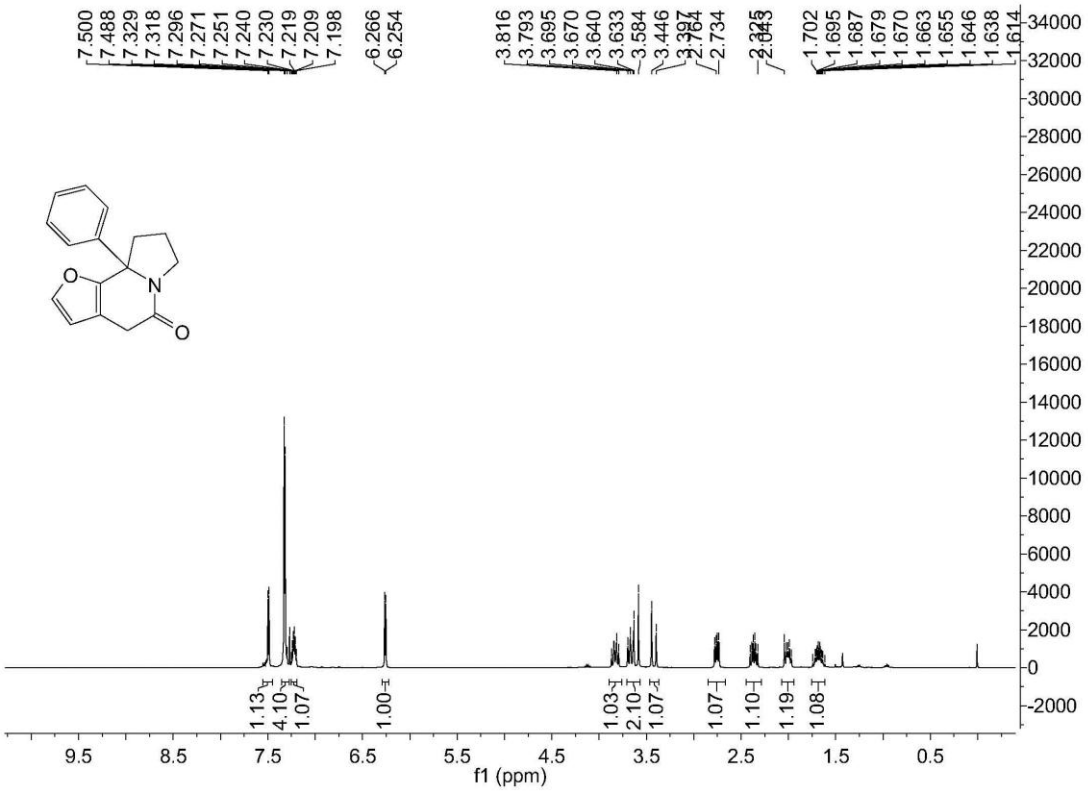
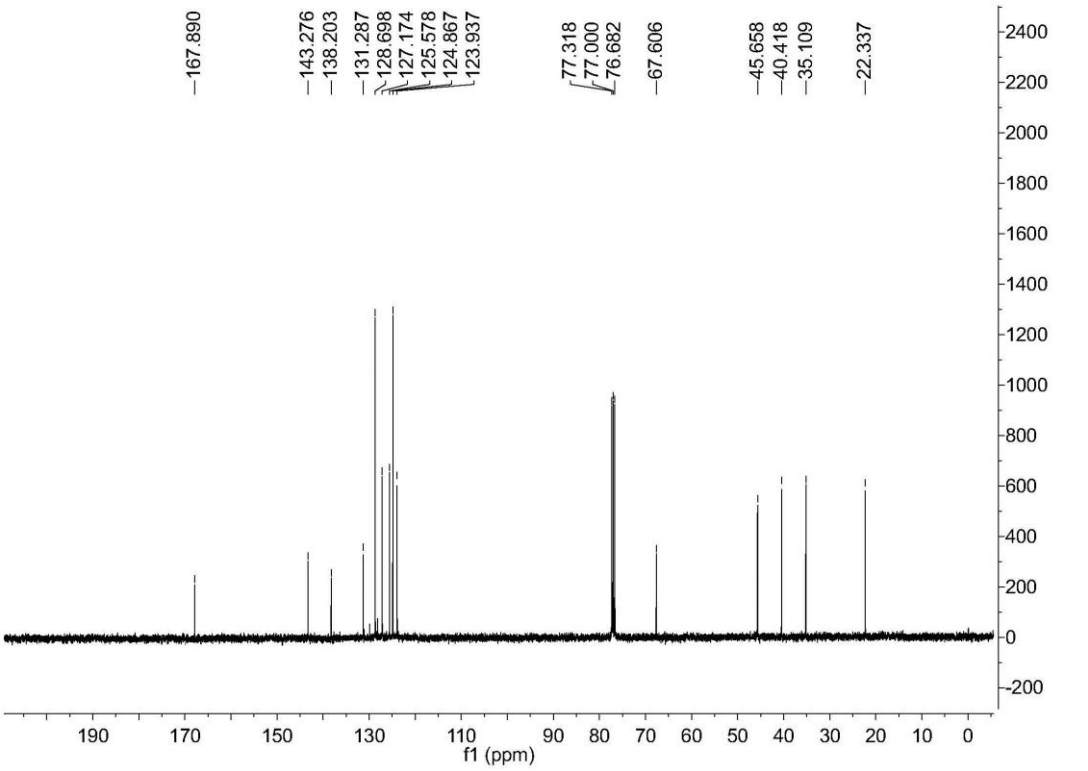
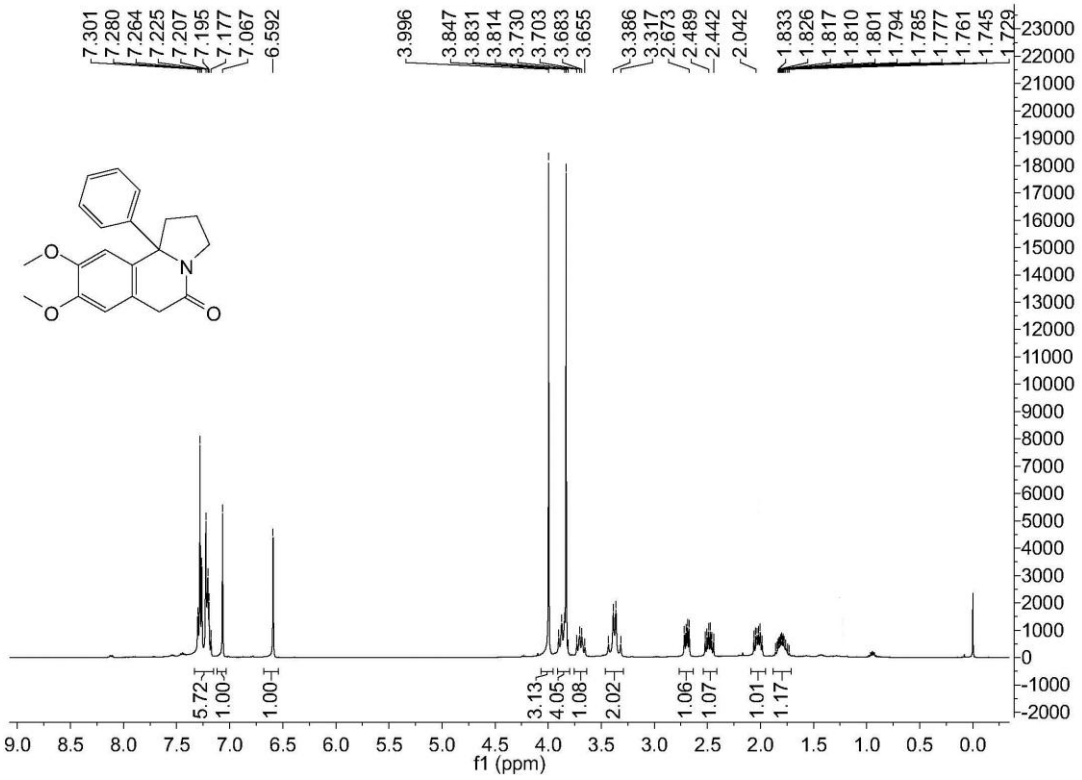
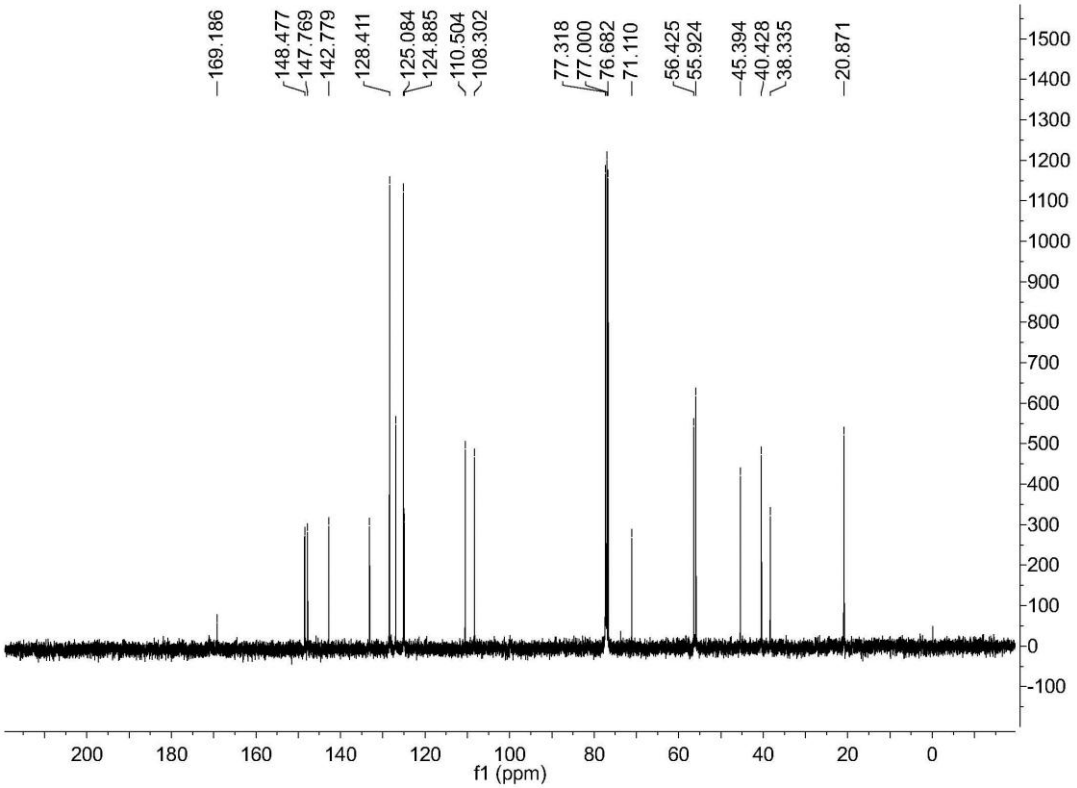


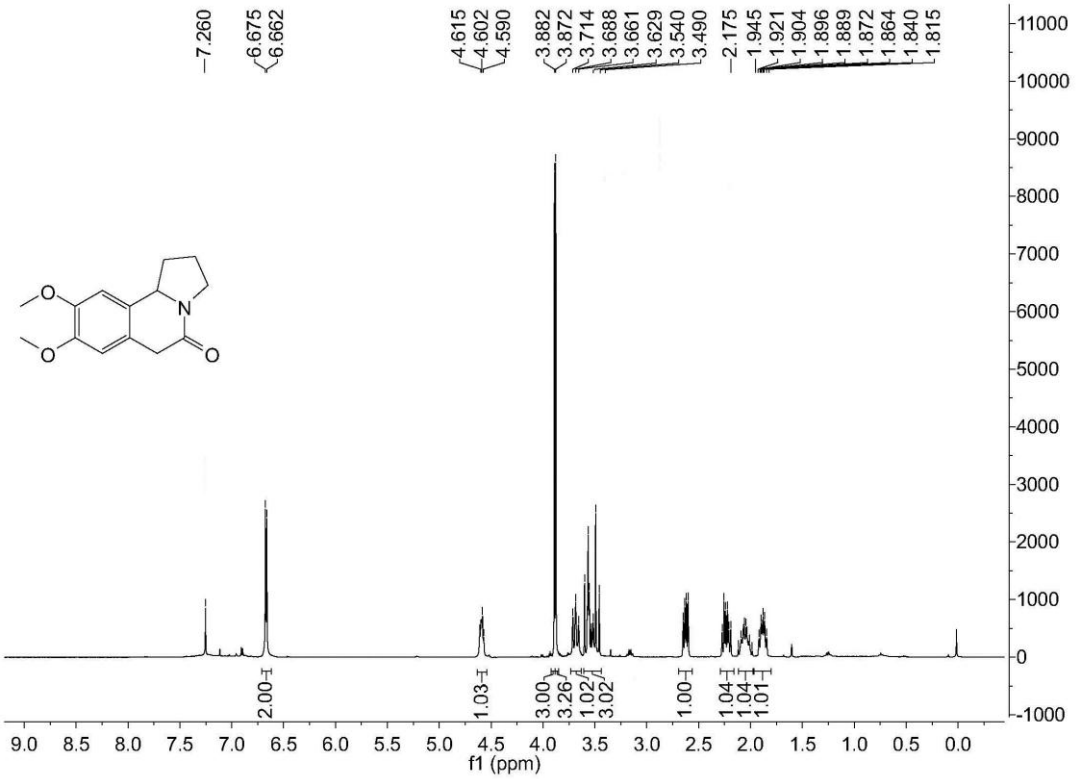


3ar





6


7.260
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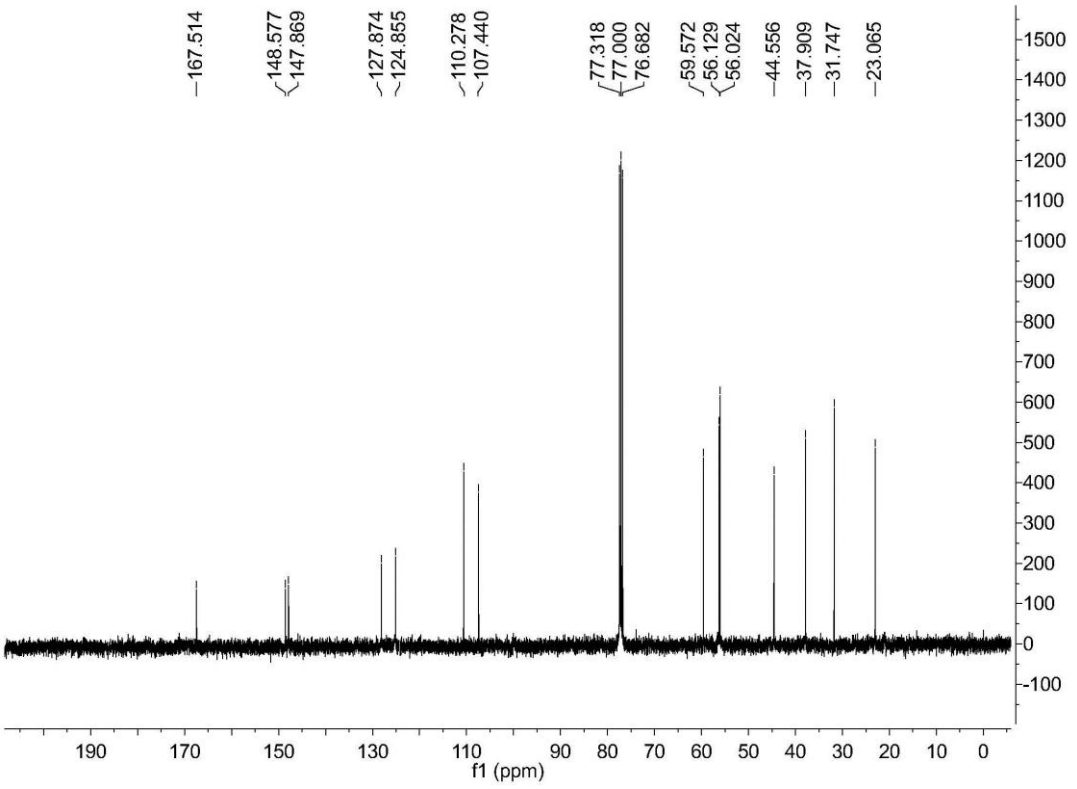
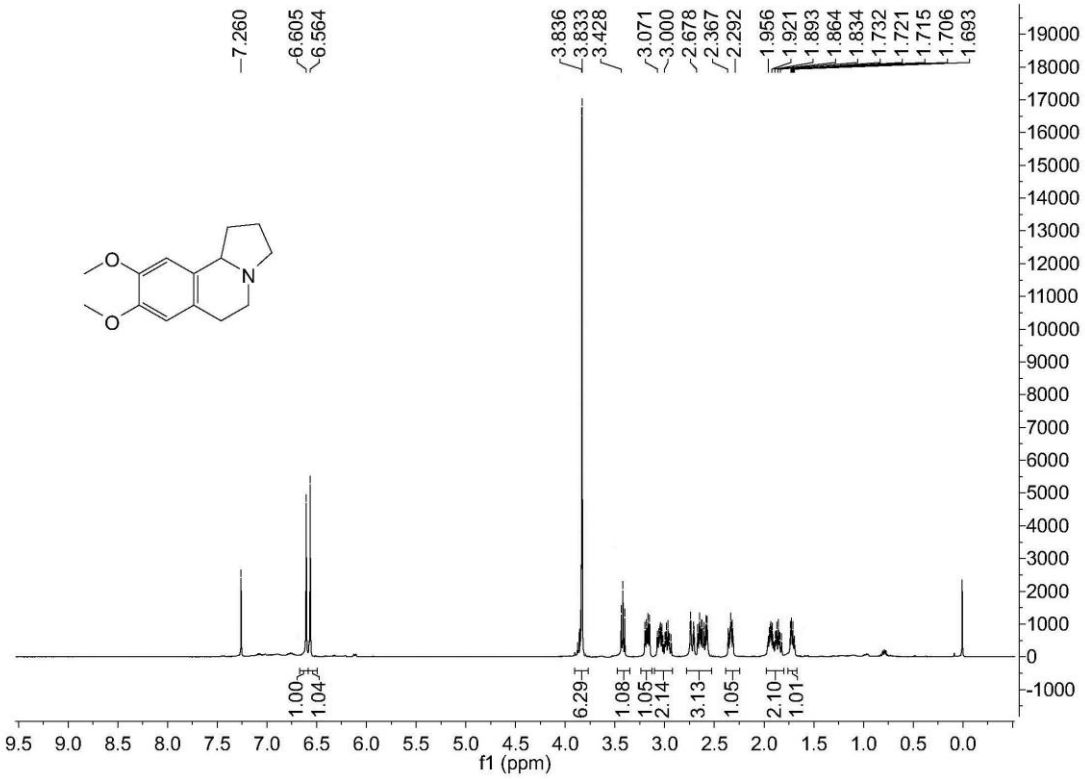
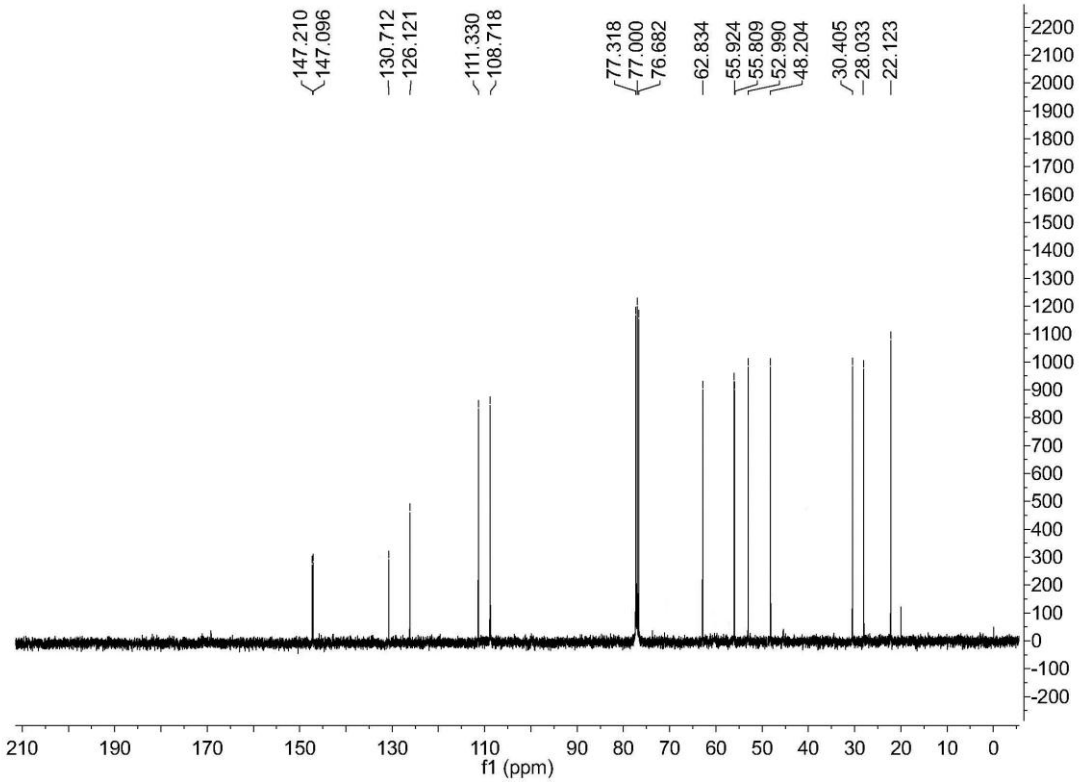
6.662
4.615
4.602
4.590
3.882
3.872
3.714
3.688
3.661
3.629
3.540
3.490
2.175
1.945
1.921
1.904
1.896
1.889
1.872
1.864
1.840
1.815
2.00
1.03
3.00
3.26
1.02
3.02
1.00
1.04
1.04
1.01
f1 (ppm)

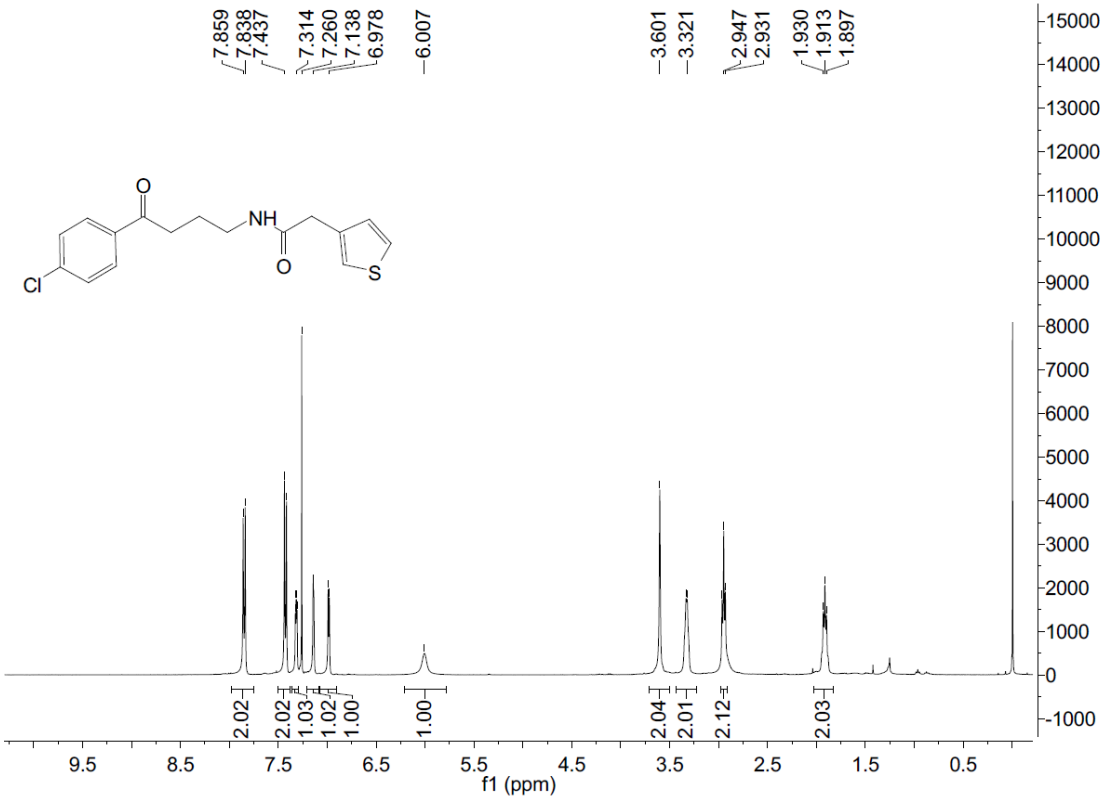

167.514
148.577
147.869
127.874
124.855
110.278
107.440
77.318
77.000
76.682
59.572
56.129
56.024
44.556
37.909
31.747
23.065
f1 (ppm)

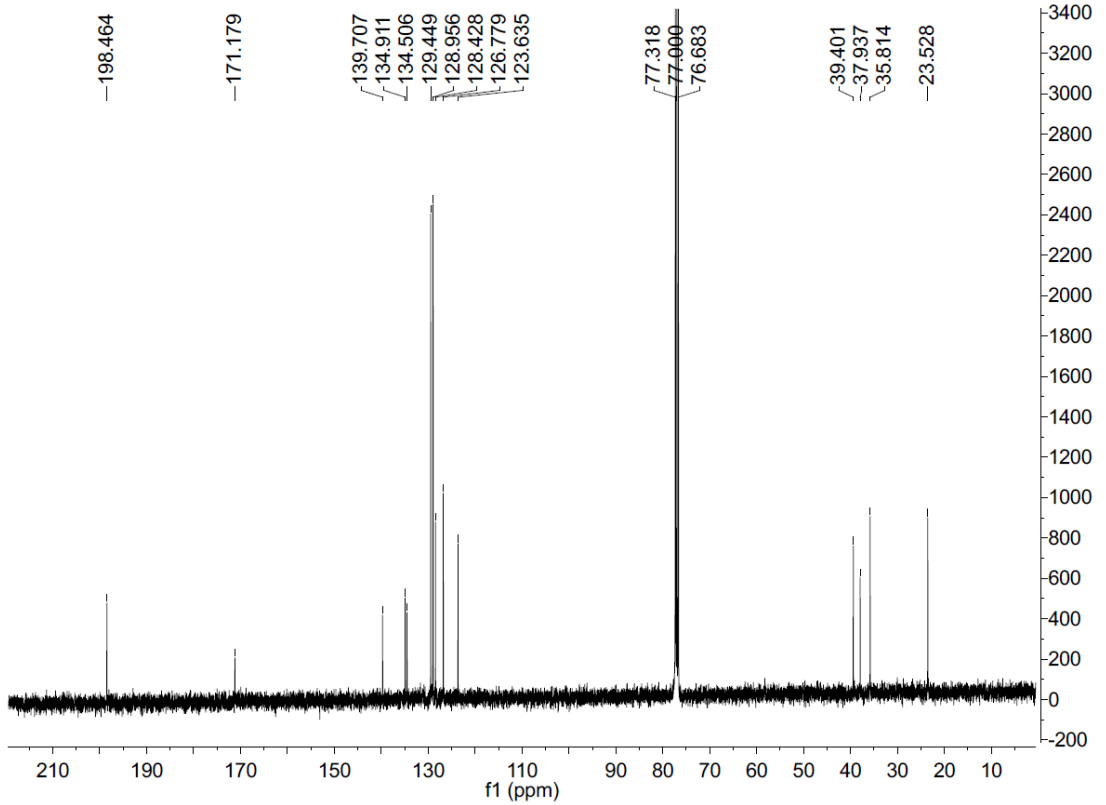
Crispine A



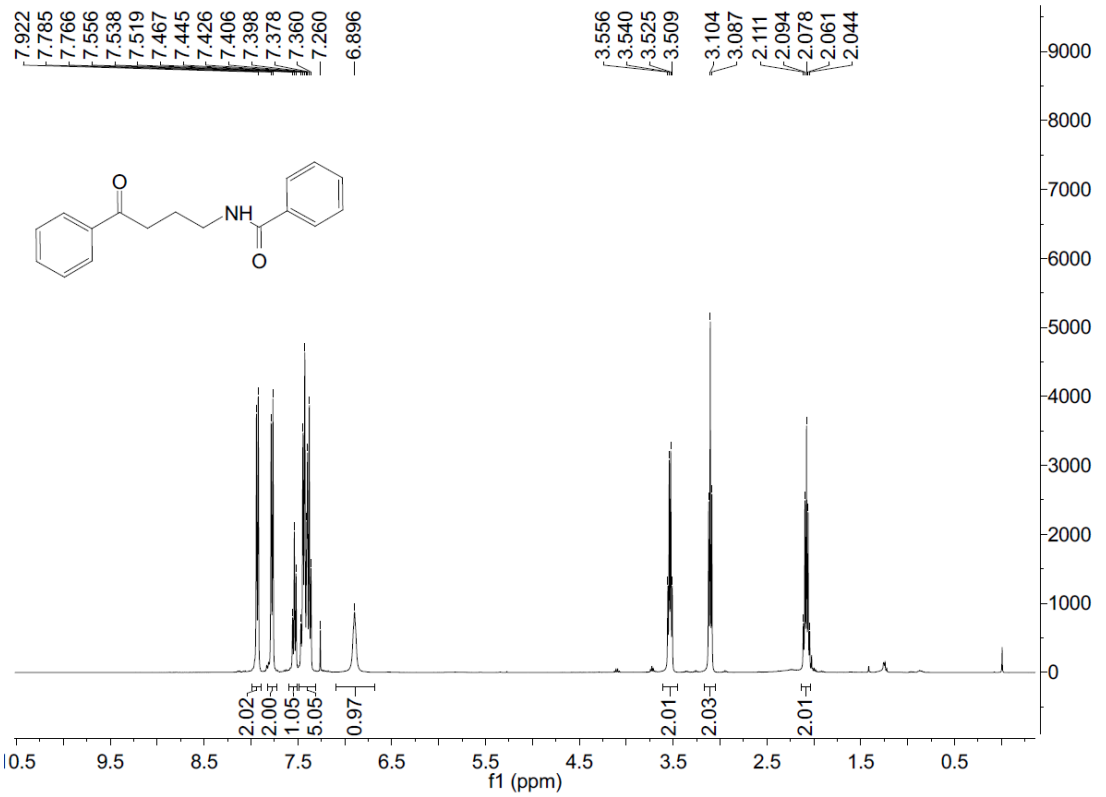


7





8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7.519
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7.445
7.426
7.406
7.398
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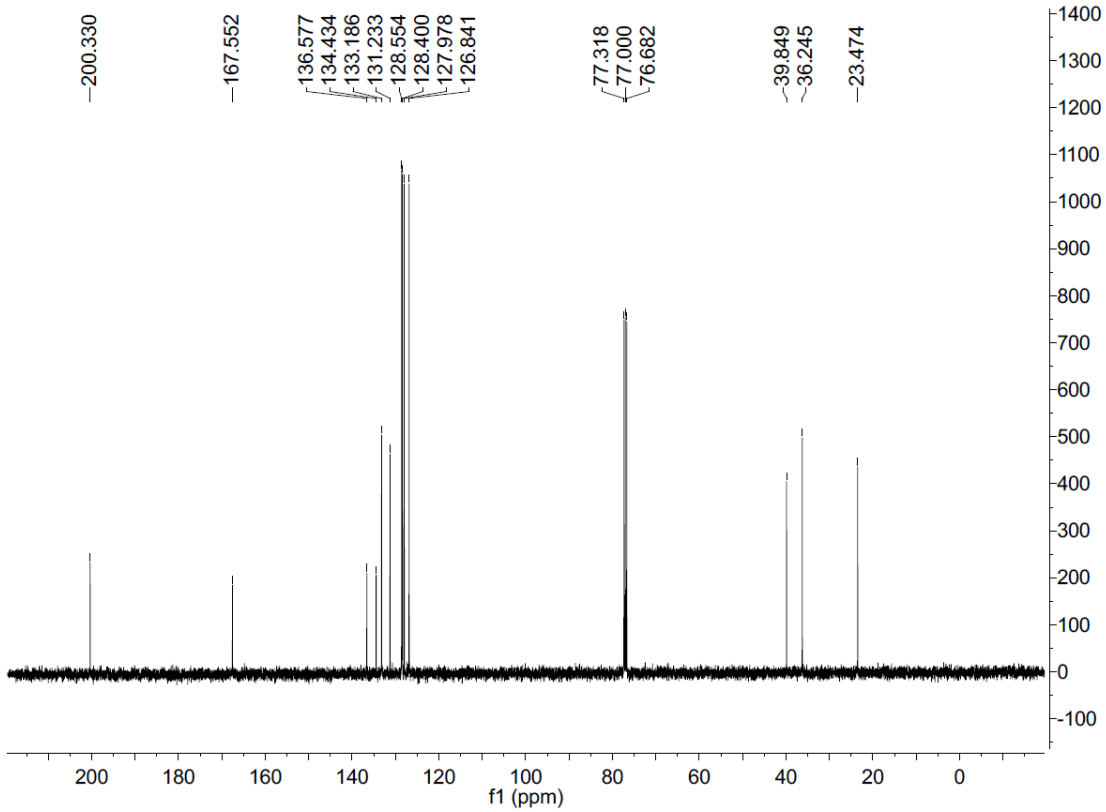
7.260
6.896
3.556
3.540
3.525
3.509
3.104
3.087
2.111
2.094
2.078
2.061
2.044
O
NH
O
2.02
2.00
1.05
5.05
0.97
2.01
2.03
2.01
f1 (ppm)


200.330
167.552
136.577
134.434
133.186
131.233
128.554
128.400
127.978
126.841
77.318
77.000
76.682
39.849
36.245
23.474
f1 (ppm)