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Copper(I)-Catalyzed Radical Carboamination Reaction of 8-Aminoquinoline-Oriented Buteneamides with Chloroform: Synthesis of-β-Lactams

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1. General information.

Unless otherwise noted, all reactions were carried out in the oven-dried glass tubes with magnetic stirring. All reagents and solvents were purchased for commercial suppliers. Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F 254 aluminum plates and visualized with UV light (254 nm). The pure products were obtained by means of column chromatography which was performed on silica gel (200-300 mesh).

2. Instrumentation.

The ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and ^{19}F NMR (376 MHz) spectra were recorded at 23 ^{o}C with $CDCl_3$ as solvent on a Bruker 400 spectrometer or Varian Inova 400 spectrometer and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in ppm from internal TMS (δ), all coupling constants (J values) were reported in Hertz (Hz). High resolution mass spectra (HRMS) were obtained on a TOF machine (ESI-TOF).

3. Synthetic procedures.

3.1 General procedure for synthesis of substrate 1a [1]

A oven-dried 100 mL RB flask charged with a magnetic stirring bar was added vinyl acetic acid (12 mmol, 1.0 equiv.), 8-aminoquinoline (1.44 g, 10 mmol), pyridine (2.6 mL, 20 mmol), HATU (4.94 g, 13 mmol), DCM (30 mL), and the flask was evacuated and backfilled with argon (3 times). The reaction mixture was stirred at 25 ^{o}C for 16 h. After removal of DCM, The reaction mixture was extracted with EtOAc (200 mL), washed with $NaHCO_3$ saturated solution (100 mL) and 10% HCl solution (100 mL), then the solvent was removed under vacuum, and the residue **1a** was purified by regular column chromatography (hexanes: ethyl acetate: =6:1).

3.2 General procedure for synthesis of α-substituted vinyl acetic acids [2]

A solution of LDA 2 M in THF (11.8 mL, 23.5 mmol) was cooled to 0℃ in ice-water, 3-butenoic acid (1 mL, 11.77 mmol) dissolved in THF (10 mL) was added to cooled LDA solution slowly over a period of 15 min. The reaction mixture was stirred at the same temperature for 45 min to obtain a deep yellow solution. A total of 1.1 eq. (12.9 mmol) of the alkylating agent was added, whereupon the reaction mixture immediately

turned colorless. After 30 min at the same temperature and 1 h at room temperature, the pH of the solution was adjusted to 2.5 with 10% HCl. The reaction mixture was extracted with EtOAc, and washed with NaCl saturated solution for 2 times. The organic phase was dried by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated in vacuo to afford crude product. The resulting residue was purified by column chromatography on silica gel (10-20% ethyl acetate/hexanes) to produce the targeted molecules (28%-78% yield).

3.3 General procedure for synthesis of γ-substituted vinylacetic acids [3]

A mixture of aldehyde in DMSO (1M), malonic acid (1.1 equiv), acetic acid (6 μL) and piperidine (10 μL) were added in a 10 mL RB flask. The mixture was heated at 100ºC for 8 h and then quenched with saturated saline. After extraction with EtOAc for several times, the concentrated organic phase was dried over Na_2SO_4. The crude product was purified by column chromatography to give the target carboxylic acid (56%-82% yield).

3.4 General procedure for Synthesis of β-lactam 2

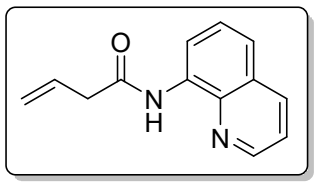
A mixture of **1** (0.2 mmol), DTBP (220 μL, 1.2 mmol), $Cu(CH_3CN)_4PF_6$ (7.5 mg, 0.02 mmol), and $CHCl_3$ (2 mL) in a 15 mL glass vial sealed under air atmosphere was heated at 110℃ for 6 hours. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography (PE / EA = 30 / 1) on silica gel to give the product **2**.

3.5 Gram-scale reaction

A mixture of **1a** (1.05 g, 5 mmol), DTBP (6.6 mL, 30 mmol), $Cu(CH_3CN)_4PF_6$ (185 mg, 0.5 mmol), and $CHCl_3$ (15 mL) in a 50 mL glass vial sealed under air atmosphere was heated at 110℃ for 6 hours. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography (PE / EA = 30 / 1) on silica gel to give the product 2a (1.28 g, 78%).

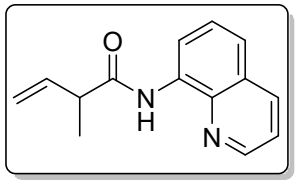
4. Characterization data.

4.1 N-(quinolin-8-yl)but-3-enamide (1a)



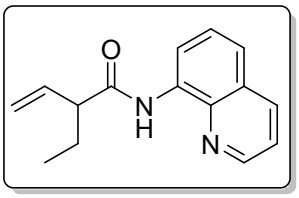
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 – 9.83 (m, 1H), 8.78 – 8.73 (m, 2H), 8.11 – 8.07 (m, 1H), 7.51 – 7.42 (m, 2H), 7.41 – 7.36 (m, 1H), 6.18 – 6.07 (m, 1H), 5.40 – 5.32 (m, 2H), 3.33 (d, *J* = 7.1 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.30, 148.24, 138.44, 136.30, 134.34, 130.98, 127.90, 127.31, 121.64, 121.59, 120.06, 116.45, 43.16. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{13}H_{13}N_2O^+$: 213.1028, found: 213.1029.

4.2 2-methyl-N-(quinolin-8-yl)but-3-enamide (1b)



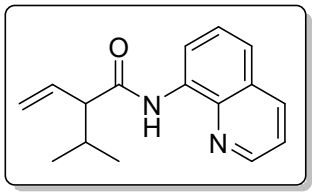
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.81 – 8.76 (m, 2H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.48 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.16 – 6.05 (m, 1H), 5.39 (dt, *J* = 17.2, 1.2 Hz, 1H), 5.33 – 5.28 (m, 1H), 3.40 – 3.32 (m, 1H), 1.45 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.56, 148.25, 138.60, 137.99, 136.30, 134.52, 127.94, 127.38, 121.57, 121.51, 117.30, 116.37, 47.01, 16.97. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{14}H_{14}N_2ONa^+$: 249.1004, found: 249.1004.

4.3 2-ethyl-N-(quinolin-8-yl)but-3-enamide (1c)



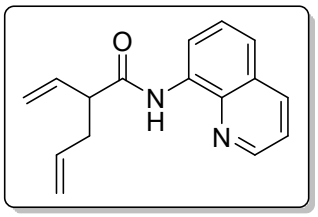
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.79 (m, 2H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.47 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.09 – 5.96 (m, 1H), 5.38 – 5.32 (m, 1H), 5.30 (dd, *J* = 10.2, 1.0 Hz, 1H), 3.10 (dd, *J* = 15.2, 7.7 Hz, 1H), 2.09 – 1.98 (m, 1H), 1.79 – 1.67 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.15, 148.23, 138.54, 136.83, 136.31, 134.51, 127.93, 127.38, 121.57, 121.49, 118.16, 116.41, 55.11, 25.11, 11.82. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{15}H_{17}N_2O^+$: 241.1341, found: 241.1334.

4.4 2-isopropyl-N-(quinolin-8-yl)but-3-enamide (1d)



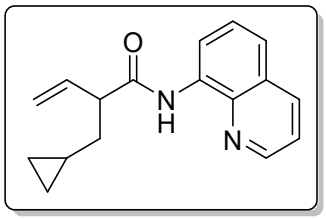
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.81 (d, *J* = 1.6 Hz, 1H), 8.80 (dd, *J* = 2.9, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.48 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.04 (dt, *J* = 17.1, 9.8 Hz, 1H), 5.34 – 5.27 (m, 2H), 2.91 – 2.83 (m, 1H), 2.33 – 2.23 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.12, 148.20, 138.50, 136.32, 135.74, 134.47, 127.93, 127.39, 121.55, 121.46, 118.75, 116.43, 61.41, 30.30, 21.04, 19.72. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{16}H_{19}N_2O^+$: 255.1497, found: 255.1486.

4.5 N-(quinolin-8-yl)-2-vinylpent-4-enamide (1e)



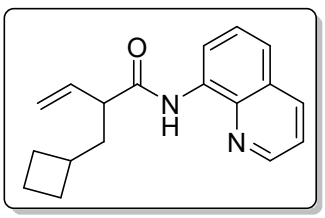
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.81 – 8.74 (m, 2H), 8.14 – 8.07 (m, 1H), 7.53 – 7.44 (m, 2H), 7.43 – 7.38 (m, 1H), 6.09 – 5.97 (m, 1H), 5.91 – 5.80 (m, 1H), 5.35 (dd, *J* = 19.5, 13.7 Hz, 2H), 5.19 – 5.12 (m, 1H), 5.08 – 5.03 (m, 1H), 3.29 (dd, *J* = 15.2, 7.5 Hz, 1H), 2.81 – 2.70 (m, 1H), 2.53 – 2.44 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.31, 148.25, 138.52, 136.36, 136.30, 135.37, 134.41, 127.92, 127.34, 121.59, 118.51, 117.10, 116.44, 53.02, 36.14. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{16}H_{17}N_2O^+$:253.1341, found: 253.1342.

4.6 2-(cyclopropylmethyl)-*N*-(quinolin-8-yl)but-3-enamide (1f)



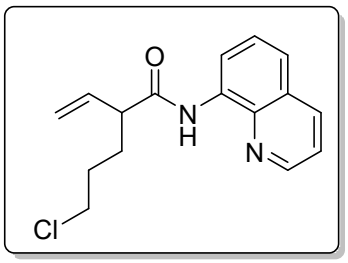
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.83 – 8.76 (m, 2H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.47 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.09 (ddd, *J* = 17.2, 10.1, 8.6 Hz, 1H), 5.41 – 5.33 (m, 1H), 5.28 (dd, *J* = 10.2, 0.9 Hz, 1H), 3.32 (dd, *J* = 15.5, 7.4 Hz, 1H), 1.88 – 1.80 (m, 1H), 1.72 – 1.64 (m, 1H), 0.87 – 0.76 (m, 1H), 0.52 – 0.39 (m, 2H), 0.18 – 0.08 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.14, 148.22, 138.53, 137.08, 136.29, 134.52, 127.93, 127.38, 121.55, 121.46, 117.76, 116.39, 53.94, 37.30, 9.04, 4.73, 4.62. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{17}H_{19}N_2O^+$: 267.1497, found: 267.1499.

4.7 2-(cyclobutylmethyl)-N-(quinolin-8-yl)but-3-enamide (1g)



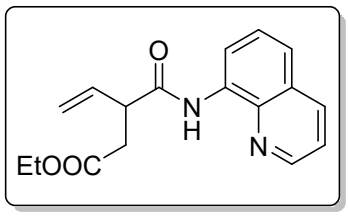
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.82 – 8.75 (m, 2H), 8.16 – 8.08 (m, 1H), 7.53 – 7.44 (m, 2H), 7.40 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.06 – 5.94 (m, 1H), 5.31 (d, *J* = 17.1 Hz, 1H), 5.25 (d, *J* = 10.1 Hz, 1H), 3.12 (q, *J* = 7.7 Hz, 1H), 2.47 – 2.34 (m, 1H), 2.14 – 2.02 (m, 3H), 1.85 – 1.63 (m, 5H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.14, 148.22, 138.50, 137.09, 136.28, 134.50, 127.91, 127.35, 121.55, 121.47, 117.67, 116.38, 51.71, 39.22, 33.93, 28.52, 28.25, 18.49. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{18}H_{21}N_2O^+$: 281.1654, found: 281.1655.

4.8 5-chloro-N-(quinolin-8-yl)-2-vinylpentanamide (1h)



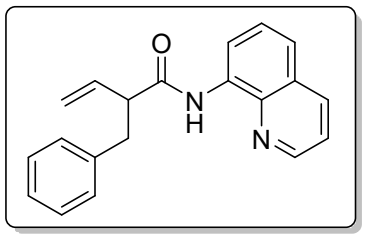
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.76 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.48 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.01 (ddd, *J* = 17.1, 10.1, 8.7 Hz, 1H), 5.42 – 5.36 (m, 1H), 5.33 (dd, *J* = 10.2, 0.8 Hz, 1H), 3.63 – 3.52 (m, 2H), 3.21 (dd, *J* = 15.1, 7.4 Hz, 1H), 2.18 – 2.08 (m, 1H), 1.95 – 1.81 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.44, 148.26, 138.44, 136.42, 134.32, 127.94, 127.36, 121.70, 121.63, 118.77, 116.52, 52.63, 44.76, 30.29, 29.07. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{16}H_{17}N_2ONa^+$: 311.0927, found: 311.0927.

4.9 ethyl 3-(quinolin-8-ylcarbamoyl)pent-4-enoate (1i)



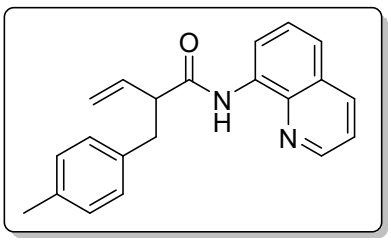
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.77 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.73 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.12 – 8.08 (m, 1H), 7.51 – 7.45 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.10 – 5.97 (m, 1H), 5.46 (d, *J* = 17.1 Hz, 1H), 5.35 (d, *J* = 10.1 Hz, 1H), 4.18 – 4.11 (m, 2H), 3.79 – 3.69 (m, 1H), 3.06 (dd, *J* = 16.5, 7.7 Hz, 1H), 2.64 (dd, *J* = 16.5, 6.3 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.77, 170.40, 148.29, 138.52, 136.25, 135.33, 134.38, 127.90, 127.26, 121.66, 121.59, 119.41, 116.41, 60.69, 48.82, 36.11, 14.18. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{17}H_{19}N_2O_3^+$: 299.1396, found: 299.1392.

4.10 2-benzyl-N-(quinolin-8-yl)but-3-enamide (1j)



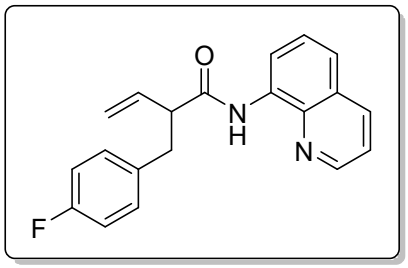
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.79 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.44 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.37 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 – 7.22 (m, 4H), 7.19 – 7.13 (m, 1H), 6.06 (ddd, *J* = 17.1, 10.2, 8.6 Hz, 1H), 5.31 – 5.23 (m, 2H), 3.50 (dd, *J* = 15.4, 7.6 Hz, 1H), 3.39 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.98 (dd, *J* = 13.7, 7.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.28, 148.22, 139.19, 138.50, 136.35, 136.28, 134.42, 129.27, 128.39, 127.92, 127.36, 126.34, 121.63, 121.59, 118.74, 116.47, 55.15, 38.16. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{20}H_{19}N_2O^+$:303.1497, found: 303.1505.

4.11 2-(4-methylphenyl)-N-(quinolin-8-yl)but-3-enamide (1k)



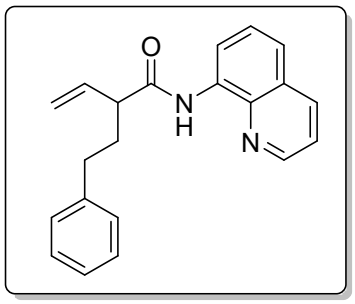
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.84 (d, *J* = 7.6 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.12 – 8.05 (m, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.46 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.16 – 6.03 (m, 1H), 5.31 (dd, *J* = 13.6, 8.4 Hz, 2H), 3.52 (dd, *J* = 15.3, 7.6 Hz, 1H), 3.39 (dd, *J* = 13.7, 6.9 Hz, 1H), 2.99 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.29 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.36, 148.18, 138.48, 136.46, 136.25, 136.05, 135.73, 134.45, 129.12, 129.09, 127.89, 127.33, 121.59, 121.56, 118.63, 116.45, 55.24, 37.77, 21.08. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{21}H_{21}N_2O^+$: 317.1654, found: 317.1654.

4.12 2-(4-fluorophenyl)-N-(quinolin-8-yl)but-3-enamide (1l)



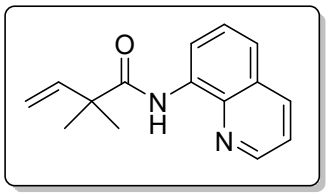
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.79 (d, *J* = 7.2 Hz, 1H), 8.74 (d, *J* = 2.9 Hz, 1H), 8.09 (d, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.38 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.21 (dd, *J* = 8.1, 5.6 Hz, 2H), 6.93 (t, *J* = 8.6 Hz, 2H), 6.12 – 5.99 (m, 1H), 5.33 – 5.25 (m, 2H), 3.46 (dd, *J* = 15.4, 7.5 Hz, 1H), 3.34 (dd, *J* = 13.7, 7.0 Hz, 1H), 2.96 (dd, *J* = 13.7, 7.4 Hz, 1H). **^{19}F NMR (377 MHz, $CDCl_3$)** δ -117.00 (s). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.04,161.55 (d, *J* = 244.0 Hz), 148.23, 138.48, 136.31, 136.12, 134.78, 134.32, 130.70, 130.62, 127.93, 127.35, 121.67, 121.60, 118.85, 116.47, 115.24, 115.03, 55.27, 37.32. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{20}H_{18}FN_2O^+$: 321.1403, found: 321.1409.

4.13 2-phenethyl-N-(quinolin-8-yl)but-3-enamide (1m)



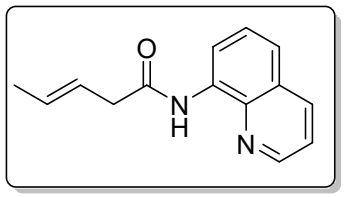
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.79 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.44 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.22 – 7.14 (m, 3H), 6.03 (ddd, *J* = 17.2, 10.1, 8.7 Hz, 1H), 5.39 – 5.29 (m, 2H), 3.18 (dd, *J* = 15.4, 7.6 Hz, 1H), 2.77 – 2.66 (m, 2H), 2.41 – 2.30 (m, 1H), 2.03 – 1.93 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.79, 148.28, 141.58, 138.57, 136.83, 136.35, 134.50, 128.63, 128.48, 127.98, 127.41, 126.01, 121.63, 118.58, 116.50, 52.62, 33.36, 33.32. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{21}H_{21}N_2O^+$: 317.1654, found: 317.1645.

4.14 2,2-dimethyl-N-(quinolin-8-yl)but-3-enamide (1n)



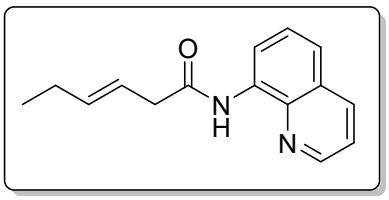
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.80 – 8.74 (m, 2H), 8.07 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.49 (dd, *J* = 10.0, 5.8 Hz, 1H), 7.43 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.37 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.23 (dd, *J* = 17.5, 10.6 Hz, 1H), 5.40 (ddd, *J* = 14.0, 11.5, 0.8 Hz, 2H), 1.48 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.82, 148.31, 142.86, 138.85, 136.20, 134.67, 127.91, 127.32, 121.51, 121.43, 116.18, 115.02, 46.83, 24.89. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{15}H_{17}N_2O^+$: 241.1341, found: 241.1341.

4.15 N-(quinolin-8-yl)pent-3-enamide (1o)



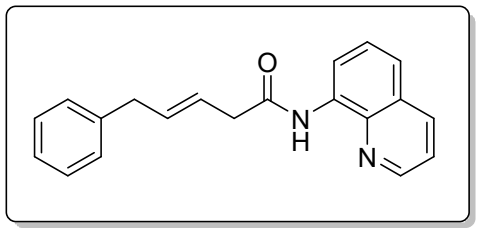
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.79 – 8.73 (m, 2H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.46 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.85 – 5.70 (m, 2H), 3.27 – 3.23 (m, 2H), 1.83 – 1.78 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.08, 148.22, 138.50, 136.28, 134.46, 131.31, 127.91, 127.36, 123.50, 121.55, 121.49, 116.33, 42.09, 18.12. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{14}H_{15}N_2O^+$:227.1184, found: 227.1182.

4.16. N-(quinolin-8-yl)hex-3-enamide (1p)



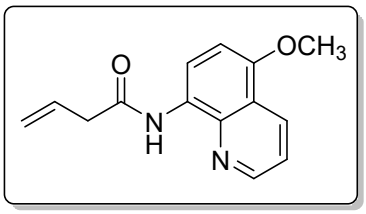
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.78 – 8.72 (m, 2H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.45 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.39 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.89 – 5.80 (m, 1H), 5.76 – 5.67 (m, 1H), 3.25 (dd, *J* = 7.0, 0.9 Hz, 2H), 2.21 – 2.13 (m, 2H), 1.11 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.11, 148.12, 138.68, 138.52, 136.23, 134.44, 127.89, 127.33, 121.53, 121.48, 121.36, 116.27, 42.07, 25.79, 13.57. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{15}H_{17}N_2O^+$: 241.1341, found: 241.1344.

4.17 5-phenyl-N-(quinolin-8-yl)pent-3-enamide (1q)



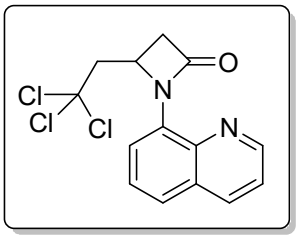
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.80 (dd, *J* = 7.3, 1.6 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.49 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.34 – 7.29 (m, 4H), 7.26 – 7.20 (m, 1H), 6.03 – 5.93 (m, 1H), 5.89 – 5.79 (m, 1H), 3.52 (d, *J* = 6.5 Hz, 2H), 3.33 (dd, *J* = 7.1, 0.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.79, 148.21, 139.94, 138.53, 136.34, 135.40, 134.44, 128.76, 128.52, 127.96, 127.40, 126.22, 123.75, 121.61, 116.42, 42.05, 39.12. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{20}H_{19}N_2O^+$: 303.1497, found: 303.1496.

4.18 *N*-(5-methoxyquinolin-8-yl)but-3-enamide (1r)



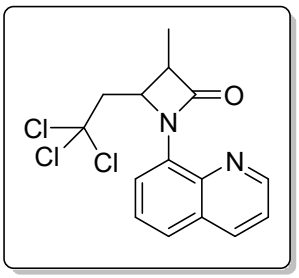
^{1}H NMR (400 MHz, CDCl3) δ 9.62 (s, 1H), 8.68 (dd, J = 4.2, 1.7 Hz, 1H), 8.60 (d, J = 8.5 Hz, 1H), 8.42 (dd, J = 8.4, 1.7 Hz, 1H), 7.29 (dd, J = 8.4, 4.2 Hz, 1H), 6.68 (d, J = 8.6 Hz, 1H), 6.22 – 5.98 (m, 1H), 5.38 – 5.24 (m, 2H), 3.85 (s, 3H), 3.27 (d, J = 7.1 Hz, 2H). **^{13}C NMR (100 MHz, CDCl3)** δ 168.67, 150.18, 148.57, 139.06, 131.23, 131.04, 127.76, 120.57, 120.25, 119.76, 116.51, 104.13, 55.61, 43.03. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{14}H_{15}N_2O_2^+$: 243.1134, found: 243.1143.

4.19 1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2a)



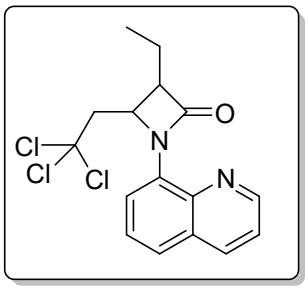
yellow oil, 60 mg (92% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.33 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.42 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.70 – 5.62 (m, 1H), 3.66 (dd, *J* = 14.3, 1.6 Hz, 1H), 3.57 (dd, *J* = 15.6, 5.2 Hz, 1H), 3.29 (dd, *J* = 15.6, 2.6 Hz, 1H), 2.91 (dd, *J* = 14.3, 10.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.82, 149.13, 140.06, 136.13, 132.86, 128.97, 126.82, 124.12, 121.58, 121.17, 96.68, 57.07, 54.23, 45.56. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{14}H_{12}Cl_3N_2O^+$: 329.0015, found:329.0013.

4.20 3-methyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2b)



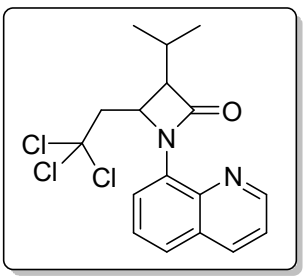
yellow oil, 40 mg (59% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.83 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.33 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, J = 8.4, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.42 (dd, *J* = 8.4, 4.1 Hz, 1H), 5.28 (dt, *J* = 10.2, 2.0 Hz, 1H), 3.64 (dd, *J* = 14.3, 1.8 Hz, 1H), 3.47 – 3.40 (m, 1H), 2.93 (dd, *J* = 14.3, 10.2 Hz, 1H), 1.57 (d, *J* = 7.3 Hz, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.54, 149.11, 140.12, 136.12, 132.77, 129.00, 126.82, 124.03, 121.54, 121.43, 96.62, 62.25, 56.97, 53.02, 13.40. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{15}H_{14}Cl_3N_2O^+$: 343.0172, found:343.0169.

4.21 3-ethyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2c)



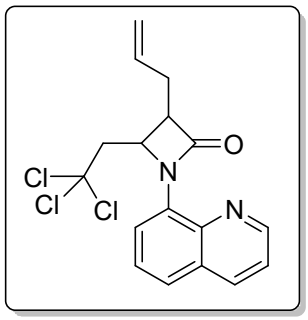
yellow oil, 43 mg (61% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.35 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.39 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.63 (dd, *J* = 14.3, 1.9 Hz, 1H), 3.46 – 3.41 (m, 1H), 2.94 (dd, *J* = 14.3, 10.1 Hz, 1H), 2.09 – 1.97 (m, 2H), 1.19 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.09, 149.12, 140.16, 136.09, 132.76, 128.99, 126.82, 123.98, 121.52, 121.35, 96.67, 59.65, 59.01, 56.97, 21.89, 11.22. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{16}H_{16}Cl_3N_2O^+$: 357.0328, found:357.0321.

4.22 3-isopropyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2d)



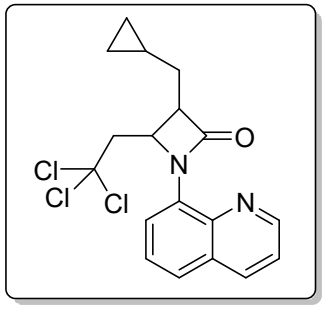
yellow oil, 37 mg (50% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.36 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.45 (dt, *J* = 9.8, 2.0 Hz, 1H), 3.59 (dd, *J* = 14.4, 2.1 Hz, 1H), 3.38 (dd, *J* = 5.6, 2.0 Hz, 1H), 2.93 (dd, *J* = 14.4, 9.9 Hz, 1H), 2.35 – 2.26 (m, 1H), 1.21 (dd, *J* = 9.6, 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.40, 149.14, 140.24, 136.06, 132.65, 128.96, 126.80, 123.99, 121.50, 121.37, 96.63, 63.75, 58.41, 57.03, 28.22, 21.52, 18.91. **HRMS(ESI- TOF)**: $[M+H]^+$ m/z calcd for $C_{17}H_{18}Cl_3N_2O^+$: 371.0485, found:371.0491.

4.23 3-allyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2e)



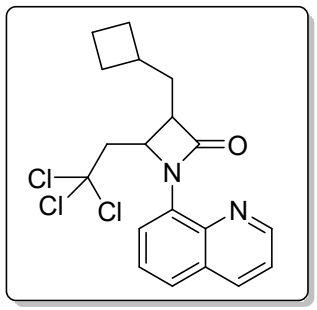
yellow oil, 35 mg (47% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.34 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.42 (dd, *J* = 8.4, 4.1 Hz, 1H), 6.04 – 5.97 (m, 1H), 5.42 (dt, *J* = 10.1, 2.1 Hz, 1H), 5.28 – 5.23 (m, 1H), 5.16 – 5.12 (m, 1H), 3.65 (dd, *J* = 14.3, 1.9 Hz, 1H), 3.56 – 3.51 (m, 1H), 2.95 (dd, *J* = 14.3, 10.1 Hz, 1H), 2.79 – 2.67 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.28, 149.15, 140.11, 136.08, 133.89, 132.70, 128.98, 126.81, 124.05, 121.53, 121.35, 118.12, 96.59, 59.24, 57.23, 56.84, 32.68. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{17}H_{15}Cl_3N_2ONa^+$: 391.0148, found: 391.0140.

4.24 3-(cyclopropylmethyl)-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2f)



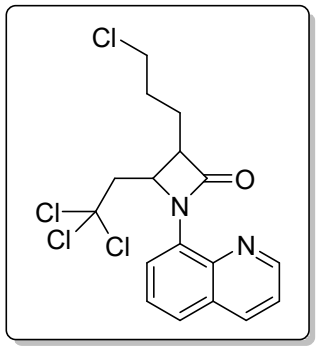
yellow oil, 38 mg (50% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.36 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.54 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.64 (dd, *J* = 14.3, 1.9 Hz, 1H), 3.58 – 3.52 (m, 1H), 2.94 (dd, *J* = 14.3, 10.1 Hz, 1H), 1.95 – 1.83 (m, 2H), 1.08 – 0.98 (m, 1H), 0.57 – 0.47 (m, 2H), 0.23 – 0.12 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.14, 149.11, 140.17, 136.08, 132.80, 128.99, 126.83, 123.98, 121.52, 121.34, 96.72, 59.62, 58.08, 57.04, 33.62, 8.42, 5.25, 4.65. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{18}H_{18}Cl_3N_2O^+$: 383.0485, found:383.0481.

4.25 3-(cyclobutylmethyl)-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2g)



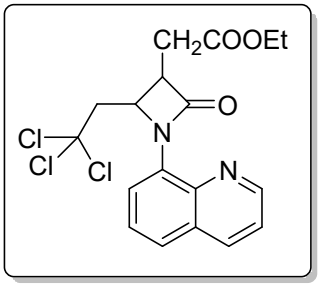
yellow oil, 37 mg (47% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.83 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.34 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.37 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.60 (dd, *J* = 14.3, 1.9 Hz, 1H), 3.40 – 3.34 (m, 1H), 2.90 (dd, *J* = 14.3, 10.1 Hz, 1H), 2.75 – 2.65 (m, 1H), 2.20 – 2.12 (m, 2H), 2.09 (t, *J* = 7.2 Hz, 2H), 1.86 – 1.67 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.18, 149.07, 140.12, 136.07, 132.77, 128.96, 126.81, 123.93, 121.50, 121.29, 96.70, 59.97, 57.06, 56.33, 35.95, 33.52, 29.02, 28.35, 18.44. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{19}H_{20}Cl_3N_2O^+$: 397.0641, found:397.0638.

4.26 3-(3-chloropropyl)-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2h)



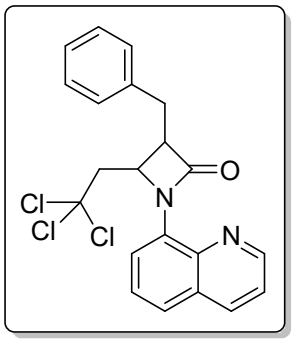
yellow oil, 38.6 mg (48% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.32 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 5.38 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.66 – 3.59 (m, 3H), 3.50 – 3.44 (m, 1H), 2.94 (dd, *J* = 14.4, 10.1 Hz, 1H), 2.27 – 2.16 (m, 2H), 2.12 – 2.00 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.50, 149.21, 140.16, 136.14, 132.54, 128.99, 126.79, 124.23, 121.60, 121.46, 96.52, 60.22, 56.89, 56.87, 44.75, 29.71, 26.36. **HRMS(ESI-TOF)**:$[M+H]^+$ m/z calcd for $C_{17}H_{17}Cl_4N_2O^+$: 405.0095, found:405.0087.

4.27 ethyl 2-(2-oxo-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-3-yl)acetate (2i)



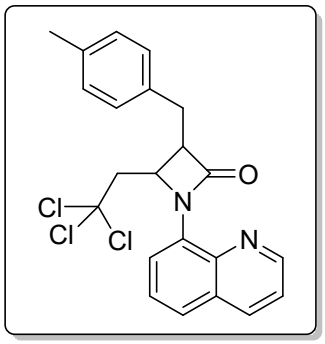
yellow oil, 51.1 mg (62% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.83 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.30 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 1H), 5.51 (dt, *J* = 9.9, 2.2 Hz, 1H), 4.19 – 4.12 (m, 2H), 3.78 – 3.73 (m, 1H), 3.69 (dd, *J* = 14.4, 2.0 Hz, 1H), 3.04 – 2.93 (m, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.62, 167.09, 149.20, 140.21, 136.13, 132.53, 128.98, 126.79, 124.28, 121.63, 121.57, 96.40, 61.01, 59.83, 57.03, 53.51, 32.85, 14.08. **HRMS(ESI- TOF)**: $[M+Na]^+$ m/z calcd for $C_{18}H_{17}Cl_3N_2O_3Na^+$: 437.0202, found: 437.0201.

4.28 3-benzyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2j)



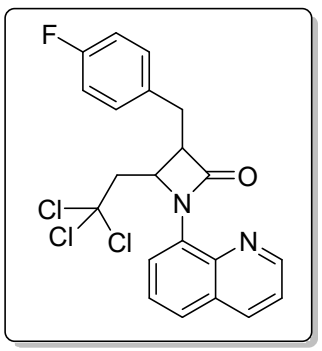
yellow oil, 58 mg (70% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.79 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.27 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.14 – 8.09 (m, 1H), 7.58 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.42 – 7.35 (m, 3H), 7.32 – 7.25 (m, 2H), 7.22 – 7.17 (m, 1H), 5.40 (dt, *J* = 10.0, 2.0 Hz, 1H), 3.74 – 3.67 (m, 1H), 3.60 (dd, *J* = 14.4, 1.9 Hz, 1H), 3.37 – 3.24 (m, 2H), 2.95 (dd, *J* = 14.4, 10.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.30, 149.11, 140.19, 137.93, 136.03, 132.59, 129.51, 128.94, 128.51, 126.76, 126.64, 124.19, 121.52, 121.49, 96.51, 59.44, 58.91, 56.85, 34.73. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{21}H_{18}Cl_3N_2O^+$: 419.0485, found: 419.0485.

4.29 3-(4-methylbenzyl)-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2k)



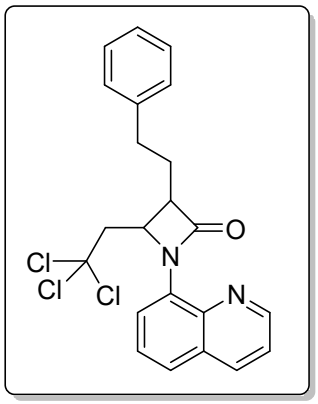
yellow oil, 44.9 mg (52% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.80 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.28 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.39 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.39 (dt, *J* = 10.0, 2.0 Hz, 1H), 3.71 – 3.65 (m, 1H), 3.61 (dd, *J* = 14.4, 1.9 Hz, 1H), 3.33 – 3.20 (m, 2H), 2.94 (dd, *J* = 14.4, 10.1 Hz, 1H), 2.28 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.41, 149.09, 140.18, 136.06, 136.02, 134.81, 132.65, 129.34, 129.18, 128.94, 126.76, 124.12, 121.50, 121.46, 96.54, 59.48, 59.04, 56.88, 34.29, 21.07. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{22}H_{19}Cl_3N_2ONa^+$: 455.0461, found:455.0461.

4.30 3-(4-fluorobenzyl)-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2f)



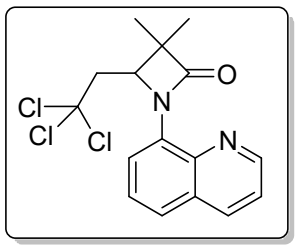
yellow oil, 52.9 mg (61% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.78 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.26 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.00 – 6.93 (m, 2H), 5.38 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.70 – 3.65 (m, 1H), 3.59 (dd, *J* = 14.4, 1.9 Hz, 1H), 3.32 (dd, *J* = 14.3, 5.0 Hz, 1H), 3.23 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.95 (dd, *J* = 14.4, 10.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.08 , 161.77 (d, *J* = 244.3 Hz),149.14, 140.17, 136.05, 133.52, 132.42, 131.05, 130.97, 128.95, 126.73, 124.28, 121.55, 121.50, 115.40, 115.19, 96.52, 59.16, 58.81, 56.74, 33.73. **^{19}F NMR (377 MHz, $CDCl_3$)** δ -116.53 (s). **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{21}H_{17}Cl_3FN_2O^+$: 437.0390, found: 437.0388.

4.31 3-phenethyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2m)



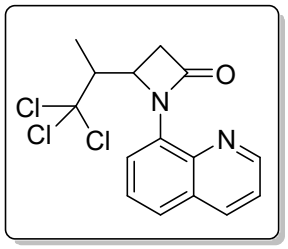
yellow oil, 53 mg (61% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.82 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.35 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.28 – 7.24 (m, 4H), 7.22 – 7.15 (m, 1H), 5.39 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.61 (dd, *J* = 14.3, 1.9 Hz, 1H), 3.50 – 3.42 (m, 1H), 3.11 – 3.01 (m, 1H), 2.94 – 2.84 (m, 2H), 2.38 – 2.26 (m, 2H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.88, 149.14, 141.38, 140.16, 136.12, 132.72, 129.00, 128.56, 128.42, 126.83, 126.03, 124.08, 121.56, 121.37, 96.59, 60.20, 57.01, 56.90, 32.98, 30.74. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{22}H_{20}Cl_3N_2O^+$: 433.0641, found: 433.0646.

4.32 3,3-dimethyl-1-(quinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2n)



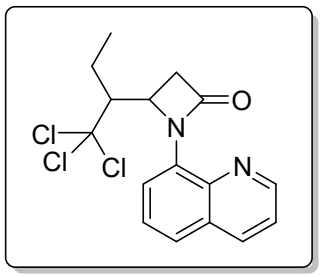
yellow oil, 30.7 mg (43% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.11 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.32 (dd, *J* = 9.4, 1.5 Hz, 1H), 3.28 (dd, *J* = 15.1, 1.5 Hz, 1H), 3.15 (dd, *J* = 15.1, 9.4 Hz, 1H), 1.59 (s, 3H), 1.52 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.94, 149.41, 141.43, 136.02, 132.17, 129.03, 126.61, 125.05, 123.52, 121.60, 96.82, 65.61, 54.19, 52.55, 22.11, 18.76. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{16}H_{15}Cl_3N_2ONa^+$: 379.0148, found:379.0149.

4.33 1-(quinolin-8-yl)-4-(1,1,1-trichloropropan-2-yl)azetidin-2-one (2o)



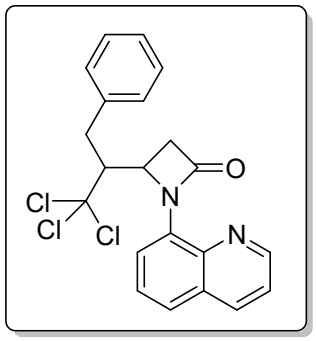
yellow oil, 28 mg (41% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.89 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.68 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.80 (ddd, *J* = 6.7, 5.6, 2.6 Hz, 1H), 3.64 (dd, *J* = 15.5, 5.5 Hz, 1H), 3.27 (dd, *J* = 15.5, 2.6 Hz, 1H), 3.08 (p, *J* = 6.8 Hz, 1H), 1.22 (d, *J* = 6.8 Hz, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.79, 149.40, 142.64, 136.18, 133.70, 129.14, 126.50, 125.90, 124.59, 121.59, 102.98, 59.01, 57.35, 45.70, 14.60. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{15}H_{14}Cl_3N_2O^+$: 343.0172, found: 343.0168.

4.34 1-(quinolin-8-yl)-4-(1,1,1-trichlorobutan-2-yl)azetidin-2-one (2p)



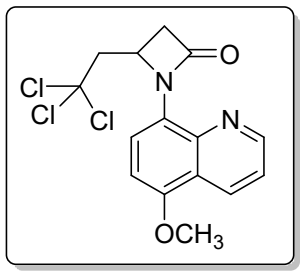
yellow oil, 23.4 mg (33% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.01 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.66 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.83 (dd, *J* = 8.6, 4.8 Hz, 1H), 3.57 – 3.47 (m, 2H), 2.94 – 2.88 (m, 1H), 1.97 – 1.82 (m, 1H), 1.63 – 1.52 (m, 1H), 1.13 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.62, 149.19, 141.95, 136.24, 133.22, 129.10, 126.65, 125.24, 123.97, 121.51, 102.53, 62.31, 57.22, 42.94, 24.11, 14.02. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{16}H_{16}Cl_3N_2O^+$: 357.0328, found: 357.0320.

4.35 1-(quinolin-8-yl)-4-(1,1,1-trichloro-3-phenylpropan-2-yl)azetidin-2-one (2q)



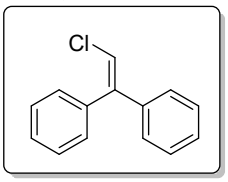
yellow oil, 17.3 mg (21% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.89 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.58 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.37 – 7.27 (m, 4H), 7.24 – 7.19 (m, 2H), 5.83 (dt, *J* = 6.4, 3.3 Hz, 1H), 3.61 – 3.53 (m, 2H), 3.49 – 3.38 (m, 2H), 2.84 (dd, *J* = 14.7, 9.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.04, 148.90, 141.45, 138.55, 135.98, 133.23, 128.98, 128.84, 128.71, 126.77, 126.59, 124.76, 123.33, 121.23, 102.07, 60.87, 56.80, 41.27, 36.48. **HRMS(ESI-TOF)**: $[M+H]^+$ m/z calcd for $C_{21}H_{18}Cl_3N_2O^+$: 419.0485, found: 419.0485.

4.36 1-(5-methoxyquinolin-8-yl)-4-(2,2,2-trichloroethyl)azetidin-2-one (2r)



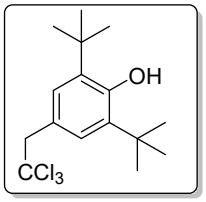
yellow oil, 59.4 mg (83% yield); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.84 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.57 (dd, *J* = 8.5, 1.8 Hz, 1H), 8.15 – 8.09 (m, 1H), 7.41 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.86 – 6.81 (m, 1H), 5.59 – 5.49 (m, 1H), 4.00 (s, 3H), 3.55 (dd, *J* = 15.4, 5.0 Hz, 1H), 3.49 (dd, *J* = 14.3, 1.7 Hz, 1H), 3.25 (dd, *J* = 15.4, 2.5 Hz, 1H), 2.90 (dd, *J* = 14.3, 10.2 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.63, 152.54, 149.74, 141.55, 130.92, 125.65, 122.47, 120.92, 120.76, 104.17, 96.71, 56.91, 55.94, 53.71, 45.28. **HRMS(ESI-TOF)**: $[M+Na]^+$ m/z calcd for $C_{15}H_{13}Cl_3N_2O_2Na^+$: 380.9940, found: 380.9943.

4.37 (2-chloroethene-1,1-diyl)dibenzene (3)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.29 (m, 8H), 7.24 – 7.19 (m, 2H), 6.61 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 143.9, 140.1, 137.6, 129.9, 128.4, 128.2, 128.1, 128.0, 127.7, 115.9. **HRMS(ESI-TOF)**: $[M + H]^+$ m/z calcd for $C_{14}H_{12}Cl^+$: 215.0628, found: 215.0633.

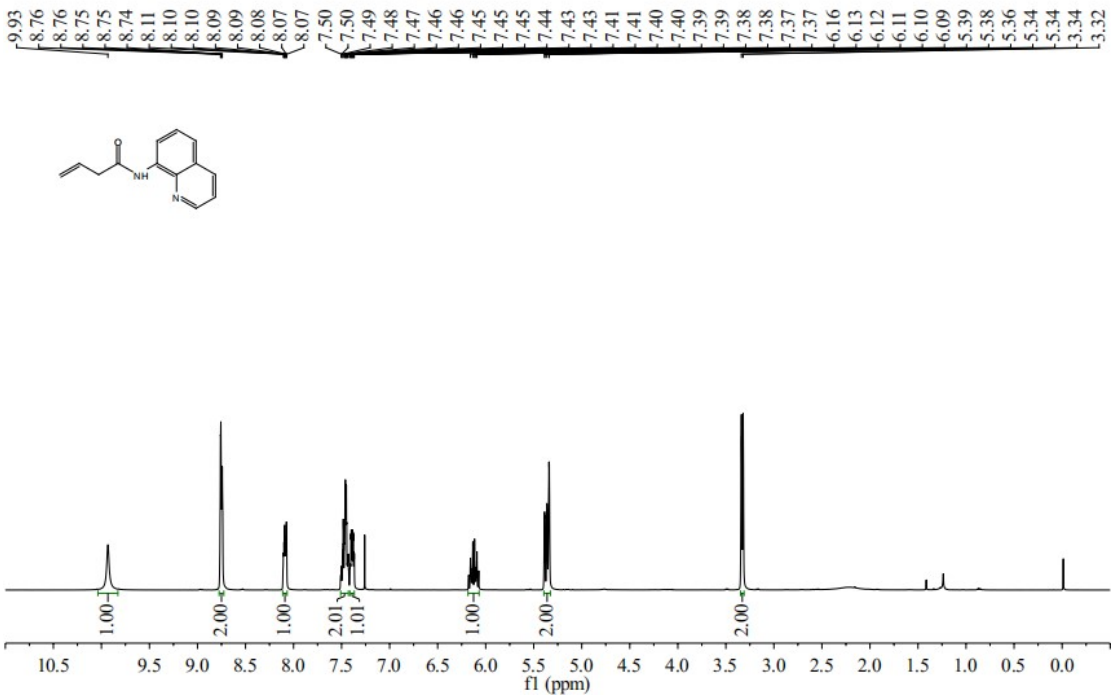
4.38 2,6-di-tert-butyl-4-(2,2,2-trichloroethyl)phenol (4)



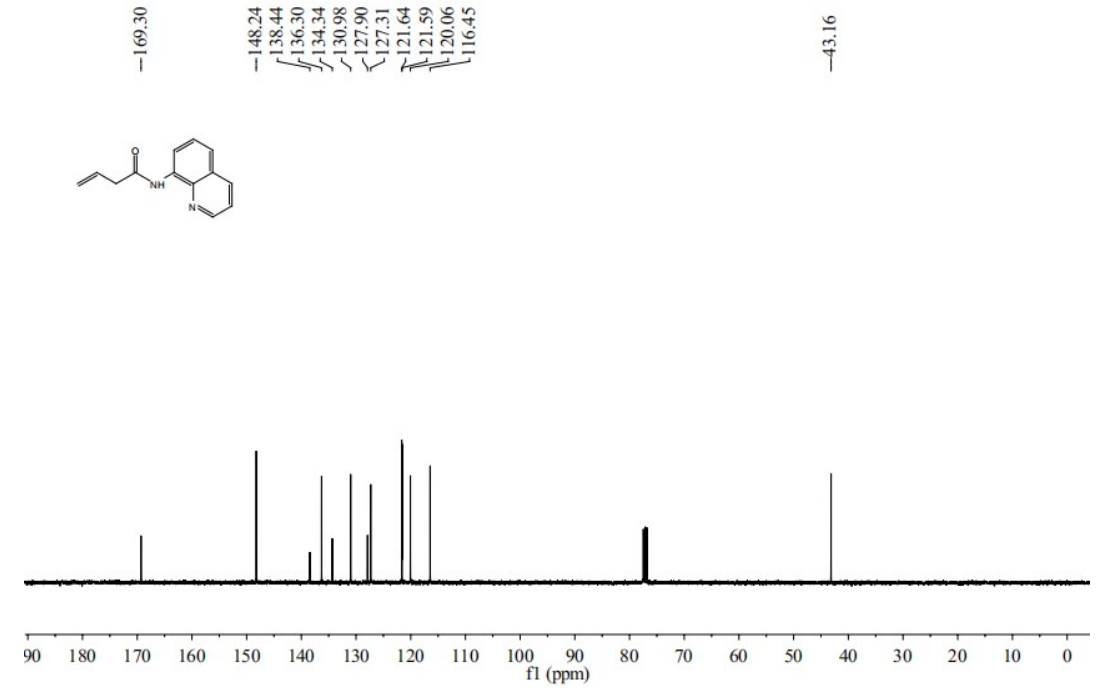
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 2H), 5.27 (s, 1H), 3.84 (s, 2H), 1.46 (s, 18H). **^{13}C NMR (100 MHz, $CDCl_3$)**: *δ* 153.2, 135.5, 128.5, 124.2, 100.0, 59.9, 34.3, 30.3. **HRMS(ESI-TOF)**: $[M]^+$ Calcd for $C_{16}H_{23}Cl_3O^+$: 336.0814, found: 336.0813.

5. NMR spectra

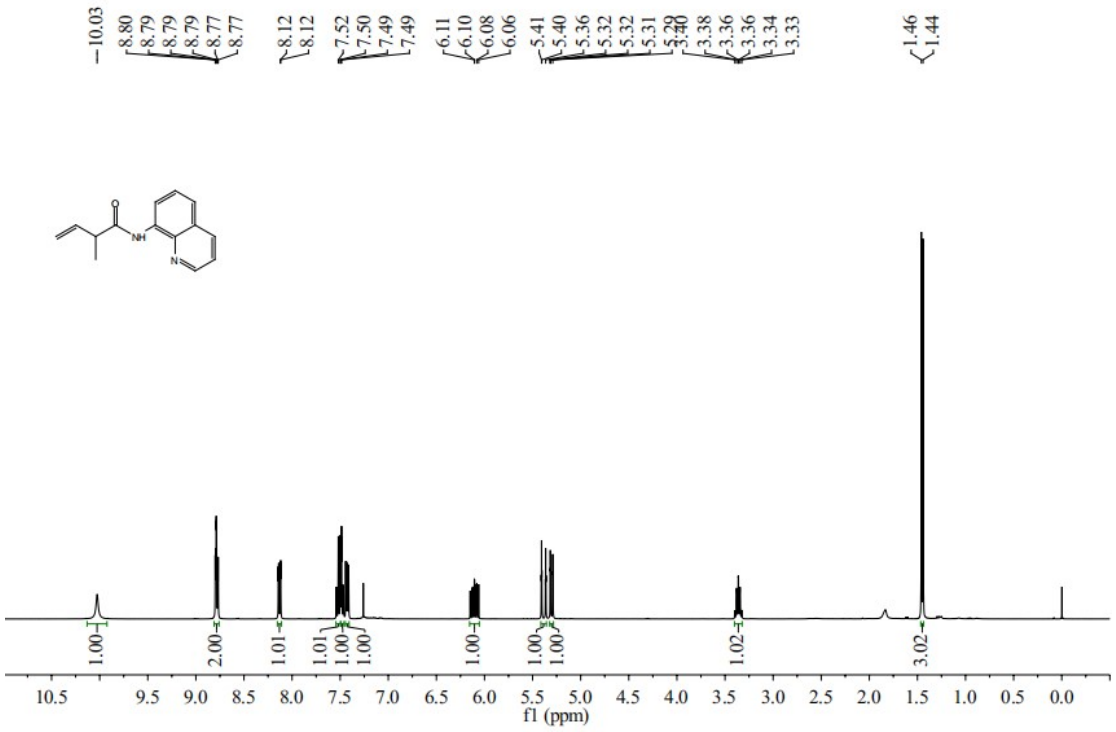
^{1}H NMR of 1a



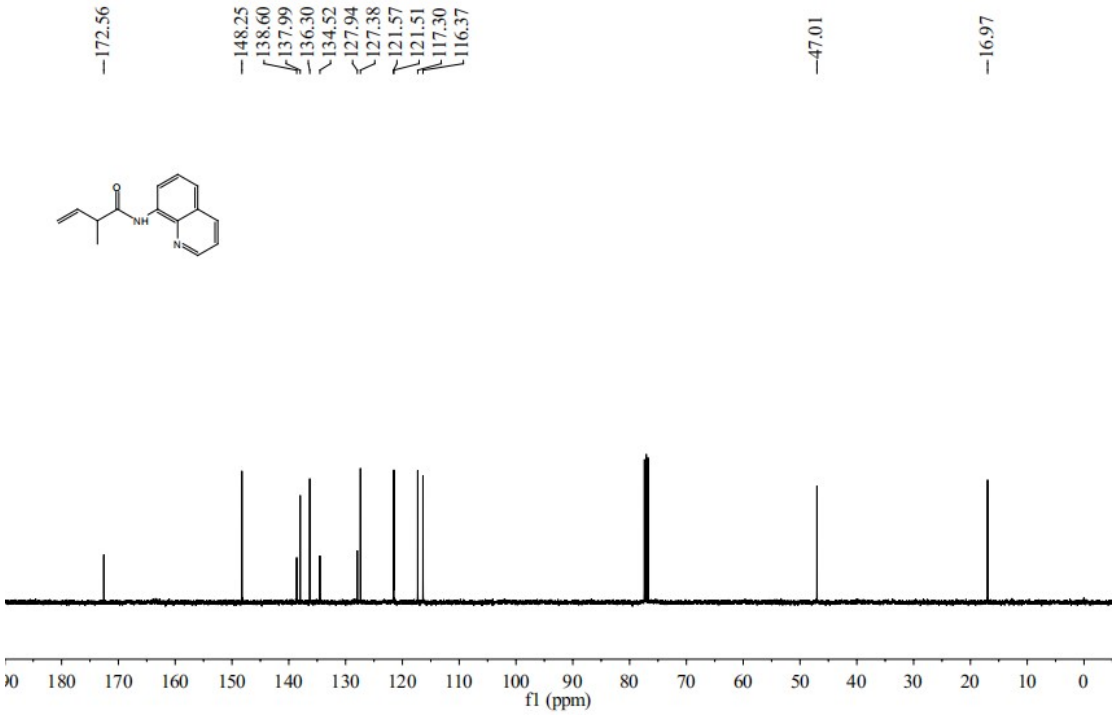
^{13}C NMR of 1a



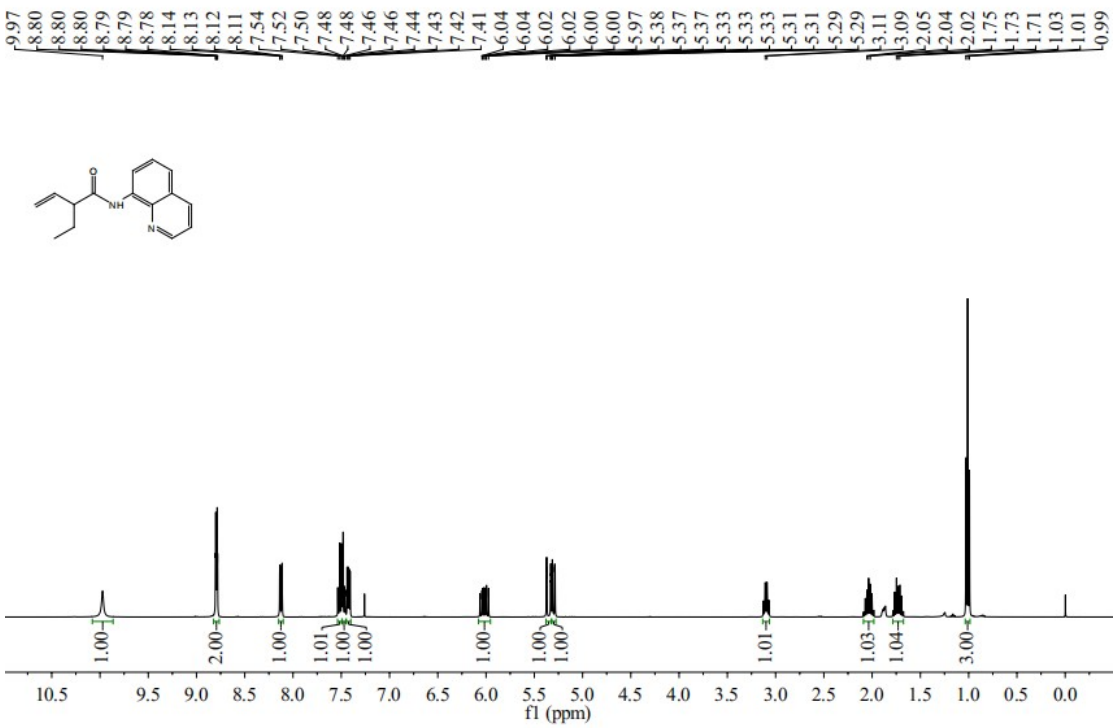
^{1}H NMR of 1b



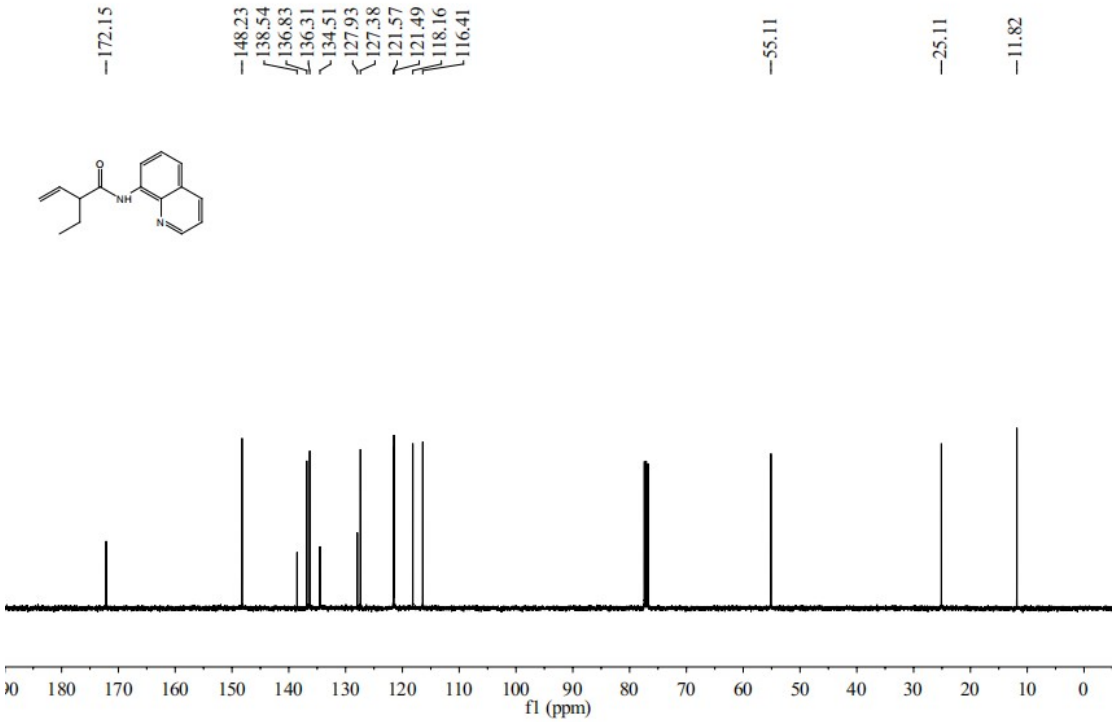
^{13}C NMR of 1b



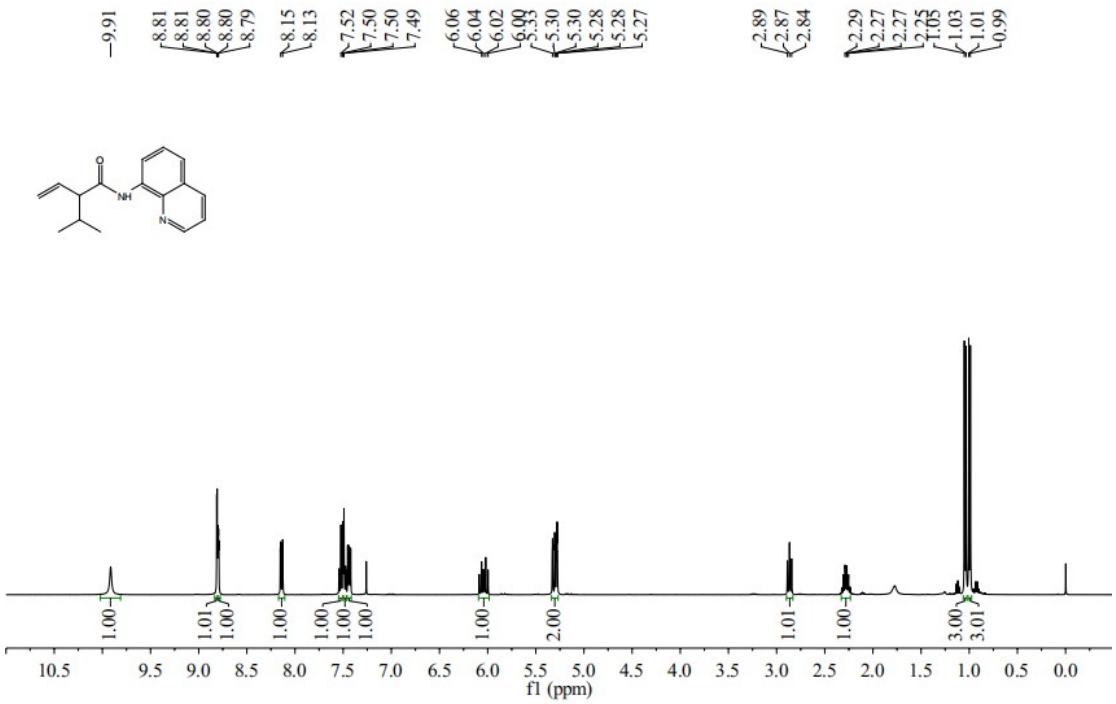
^{1}H NMR of 1c


9.97
8.80
8.80
8.80
8.79
8.79
8.78
8.14
8.13
8.12
8.11
7.54
7.52
7.50
7.48
7.48
7.46
7.46
7.44
7.43
7.42
7.41
6.04
6.04
6.02
6.02
6.00
6.00
5.97
5.38
5.37
5.37
5.33
5.33
5.33
5.31
5.31
5.29
5.29
3.11
3.09
2.05
2.04
2.02
1.75
1.73
1.71
1.03
1.01
0.99
O
NH
N
1.00
2.00
1.00
1.01
1.00
1.00
1.00
1.00
1.00
1.01
1.03
1.04
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

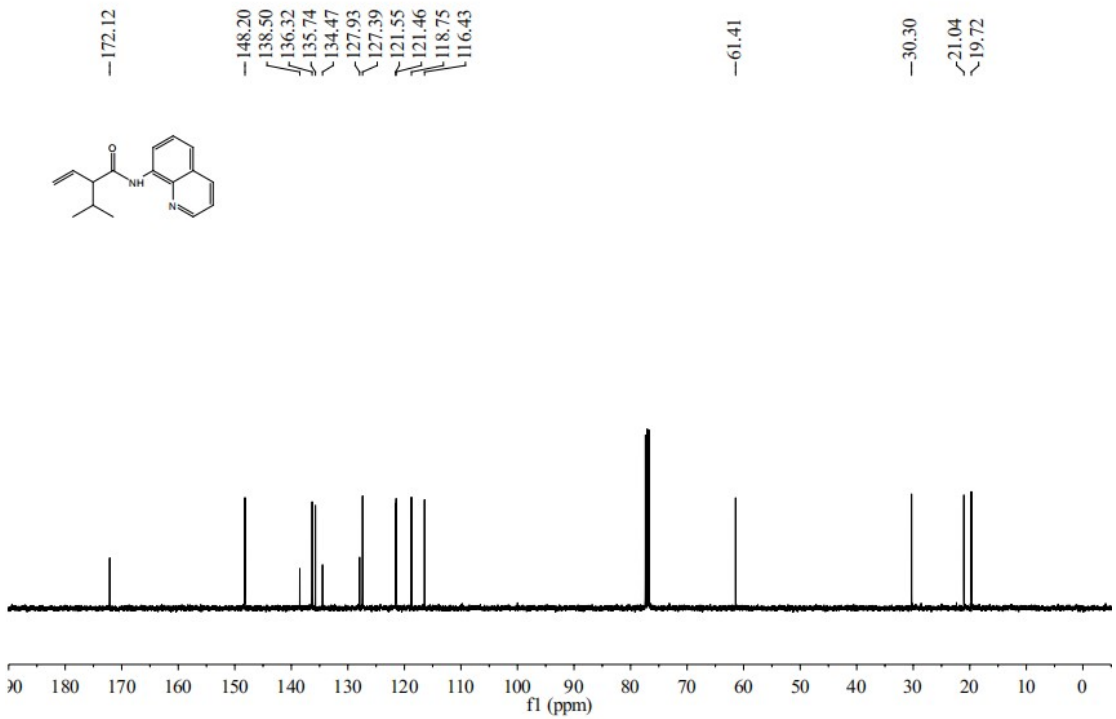
^{13}C NMR of 1c


172.15
148.23
138.54
136.83
136.31
134.51
127.93
127.38
121.57
121.49
118.16
116.41
55.11
25.11
11.82
O
NH
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

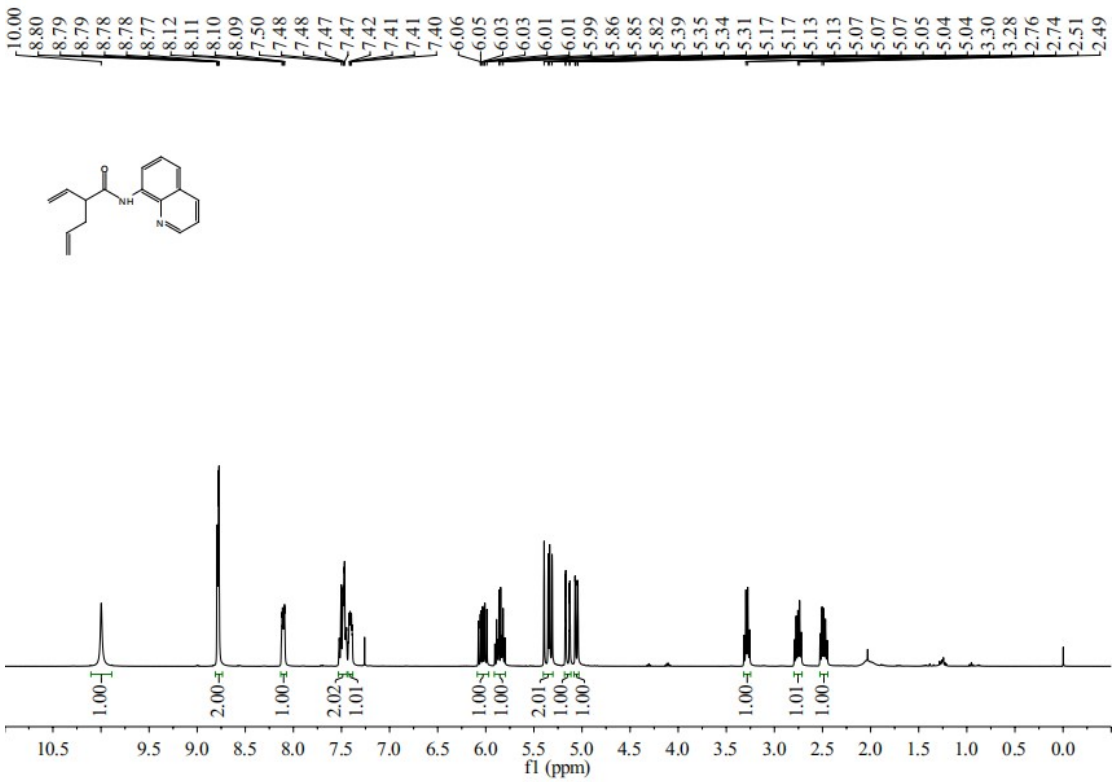
^{1}H NMR of 1d



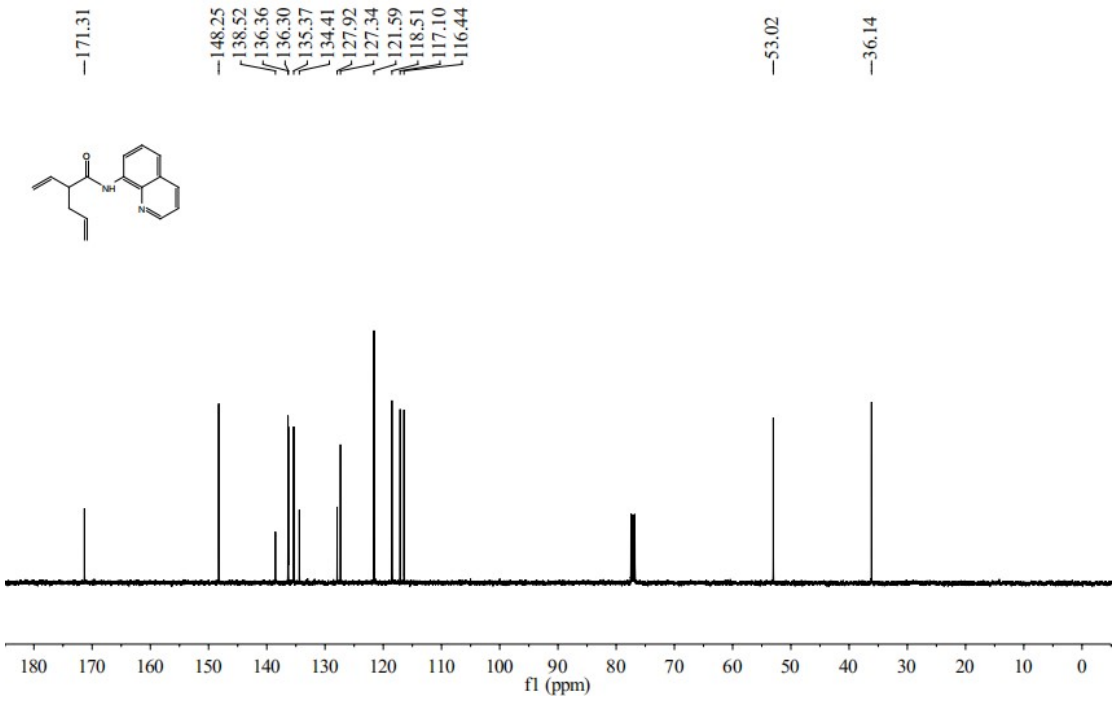
^{13}C NMR of 1d



^{1}H NMR of 1e



^{13}C NMR of 1e



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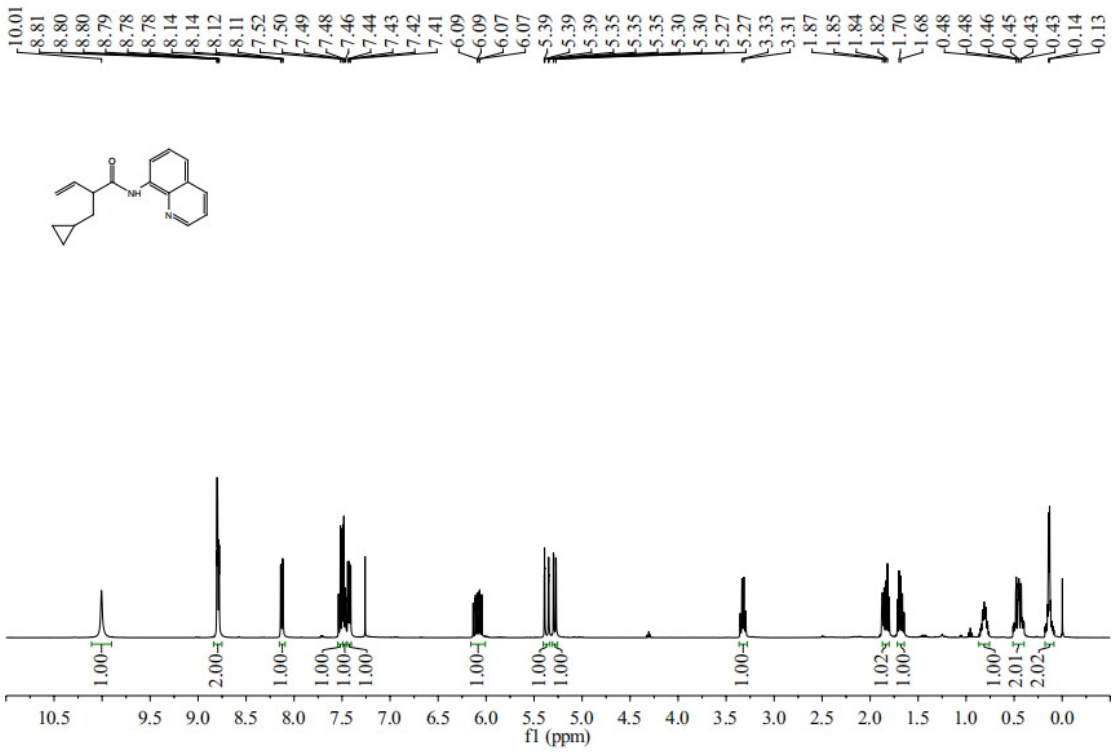

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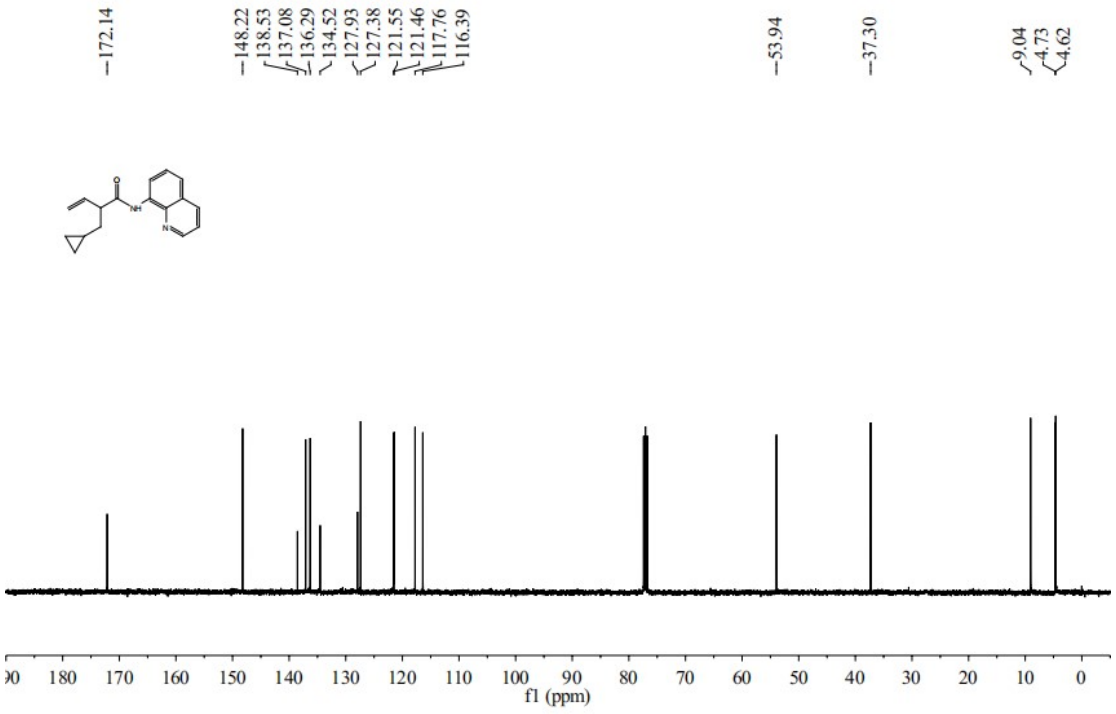

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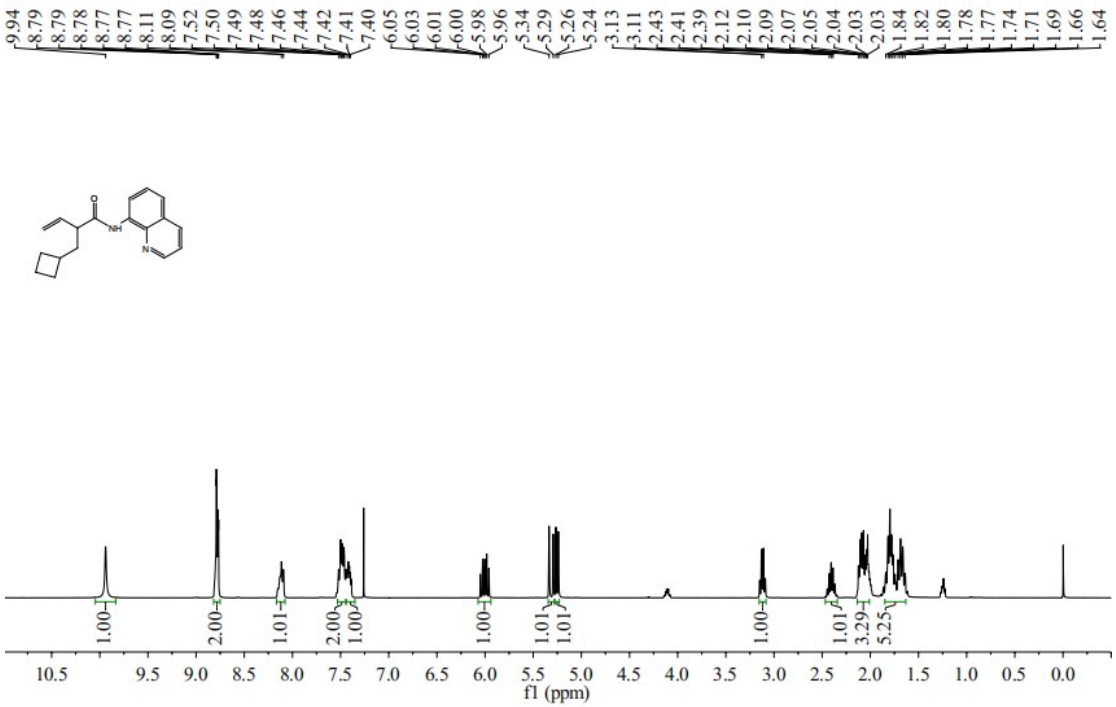

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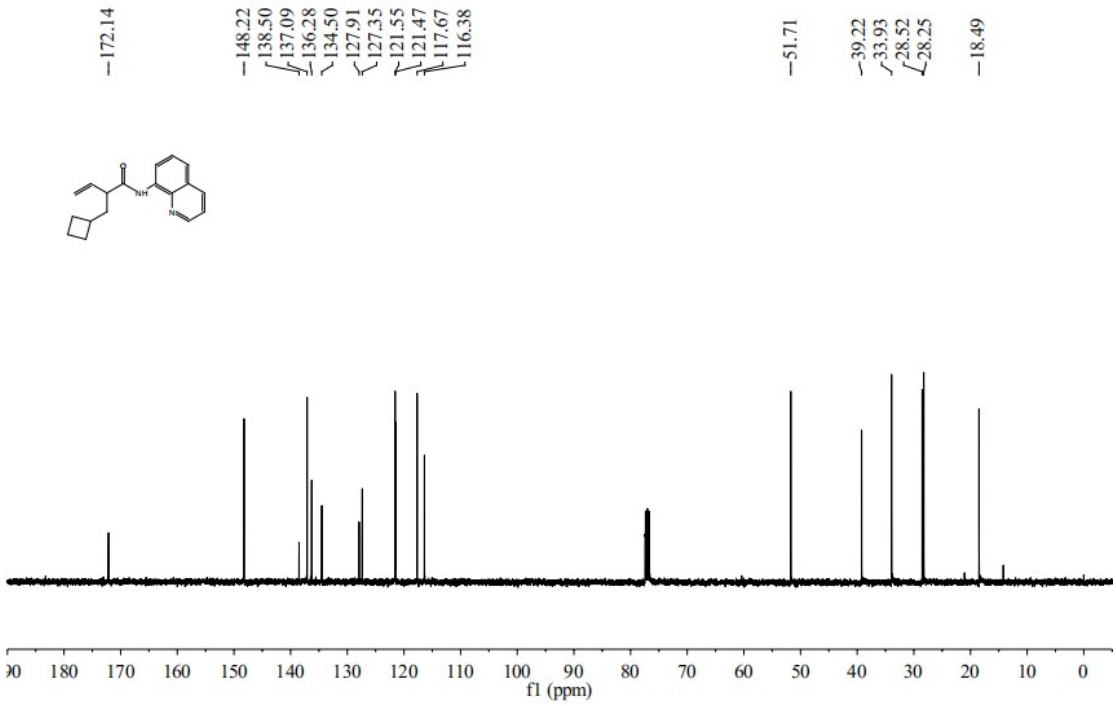

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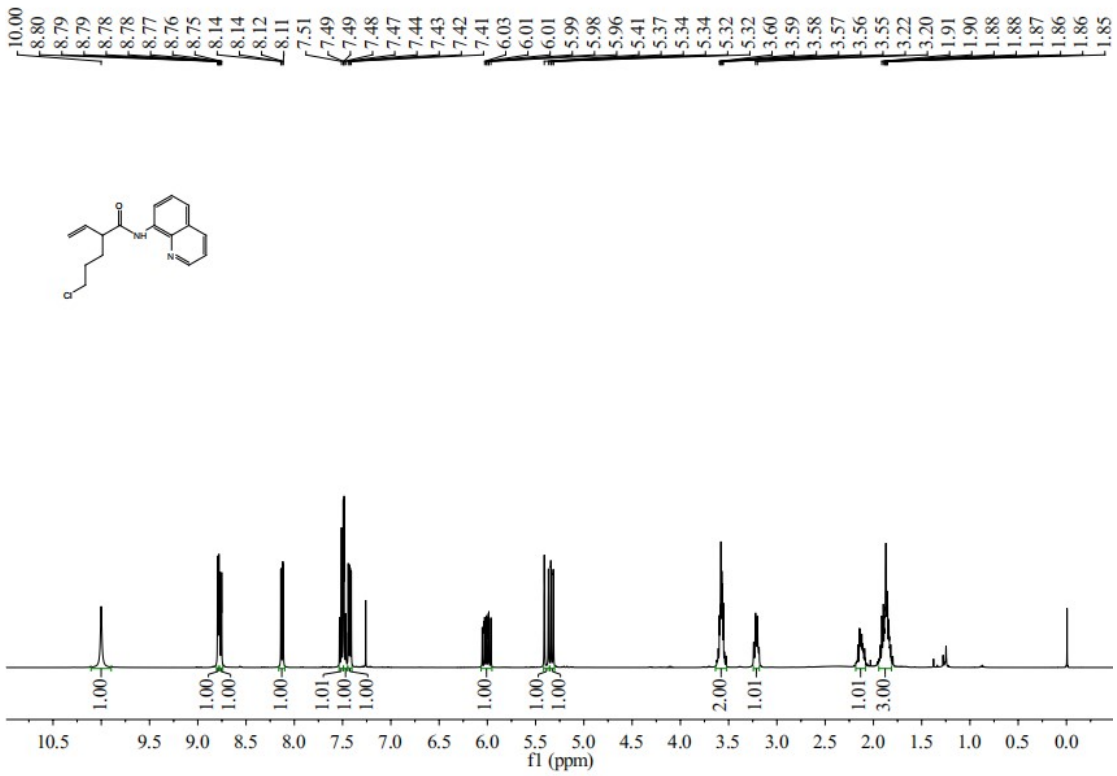

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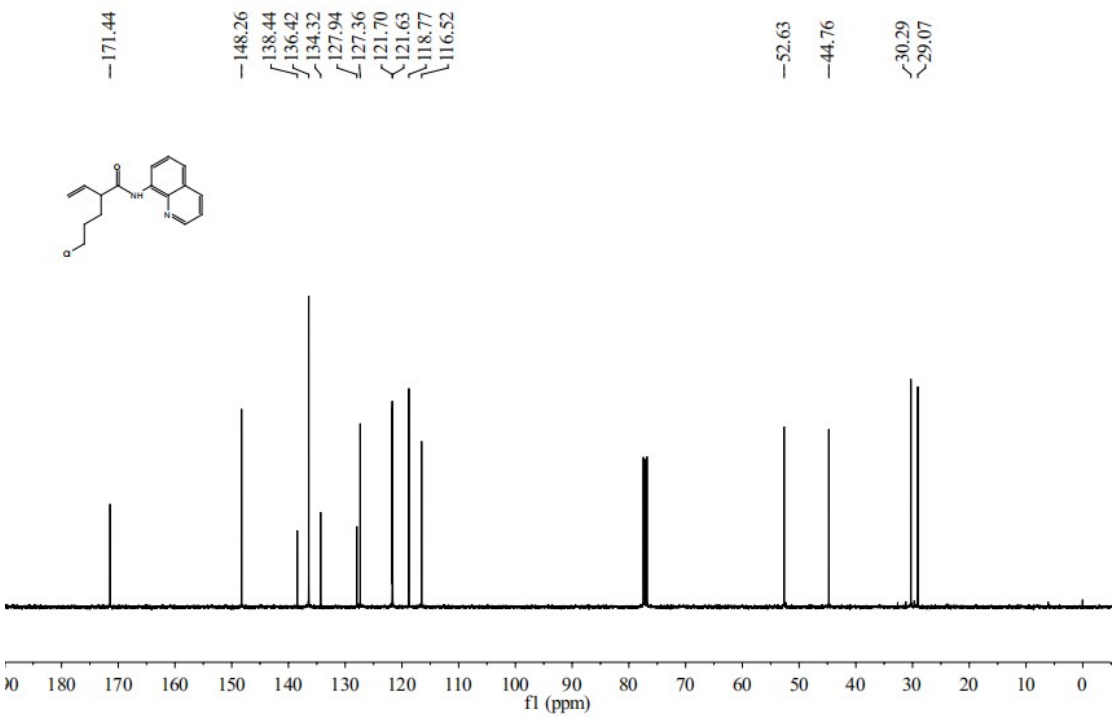
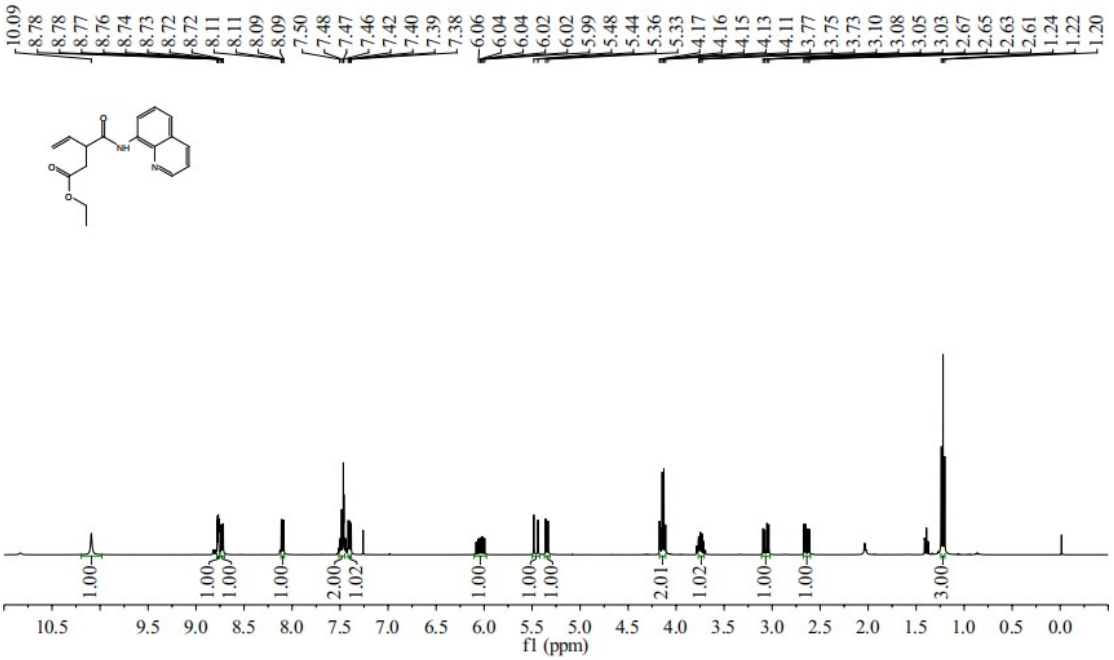


^{1}H NMR of 1i



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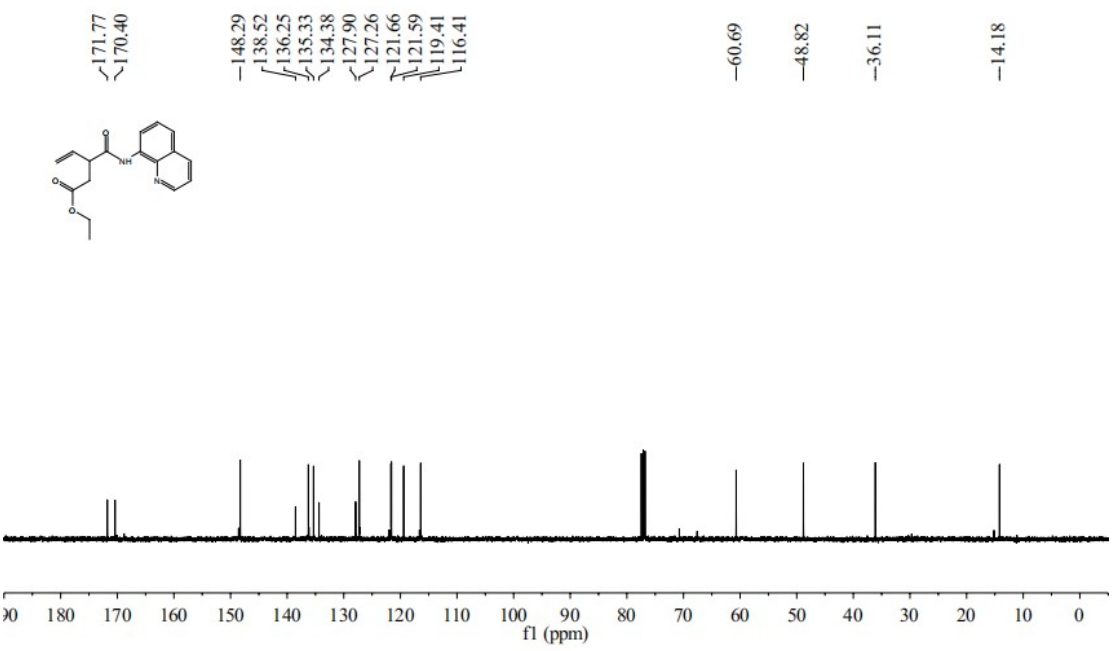

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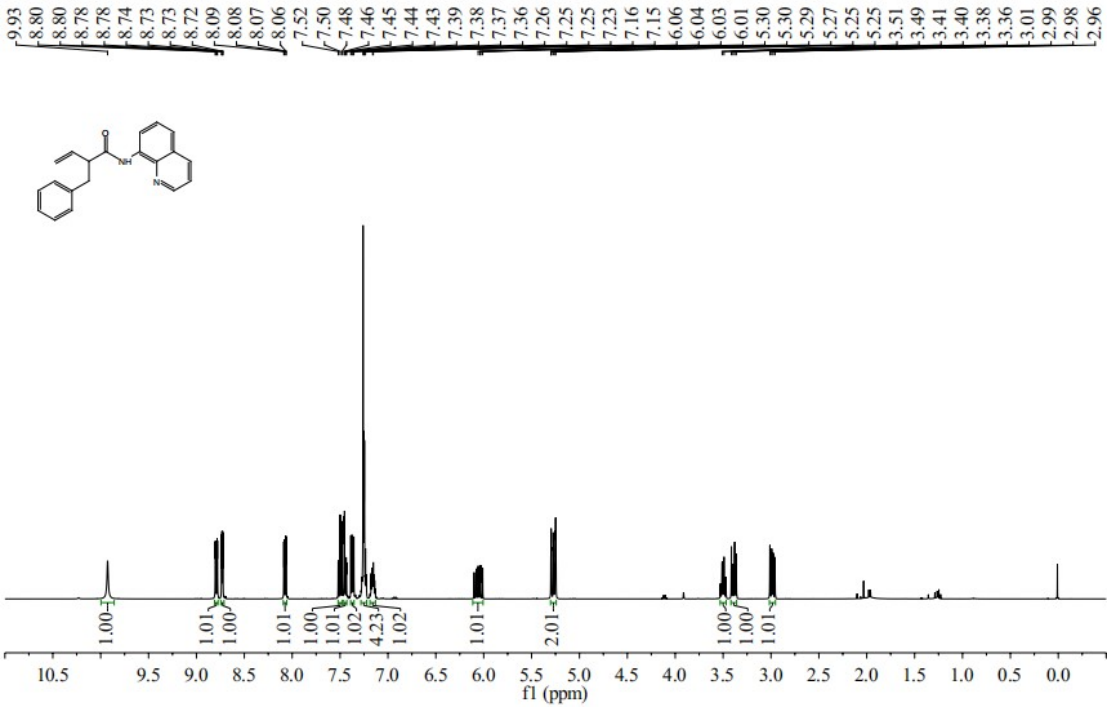

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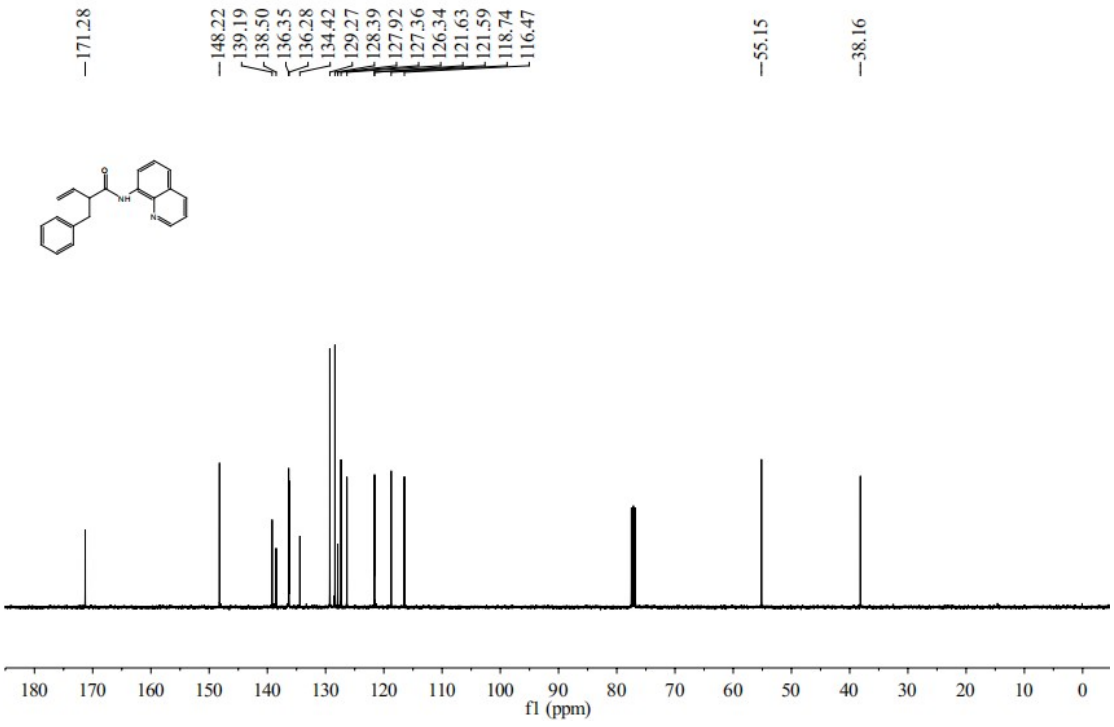
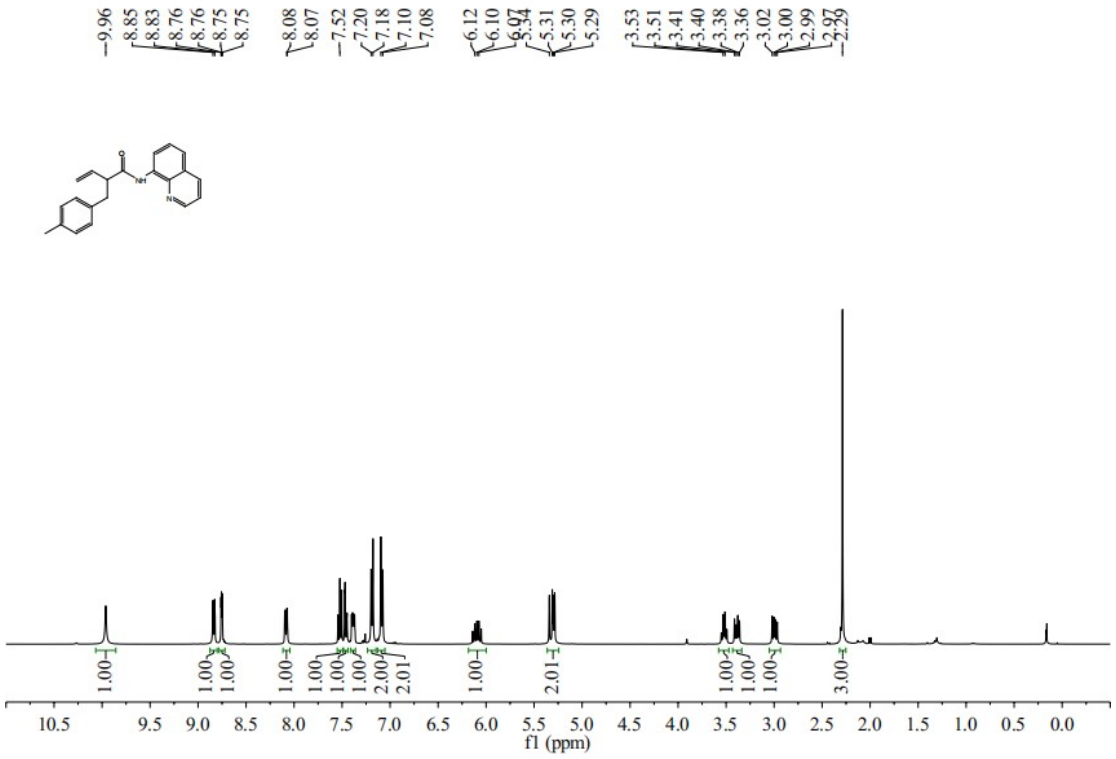


^{1}H NMR of 1k



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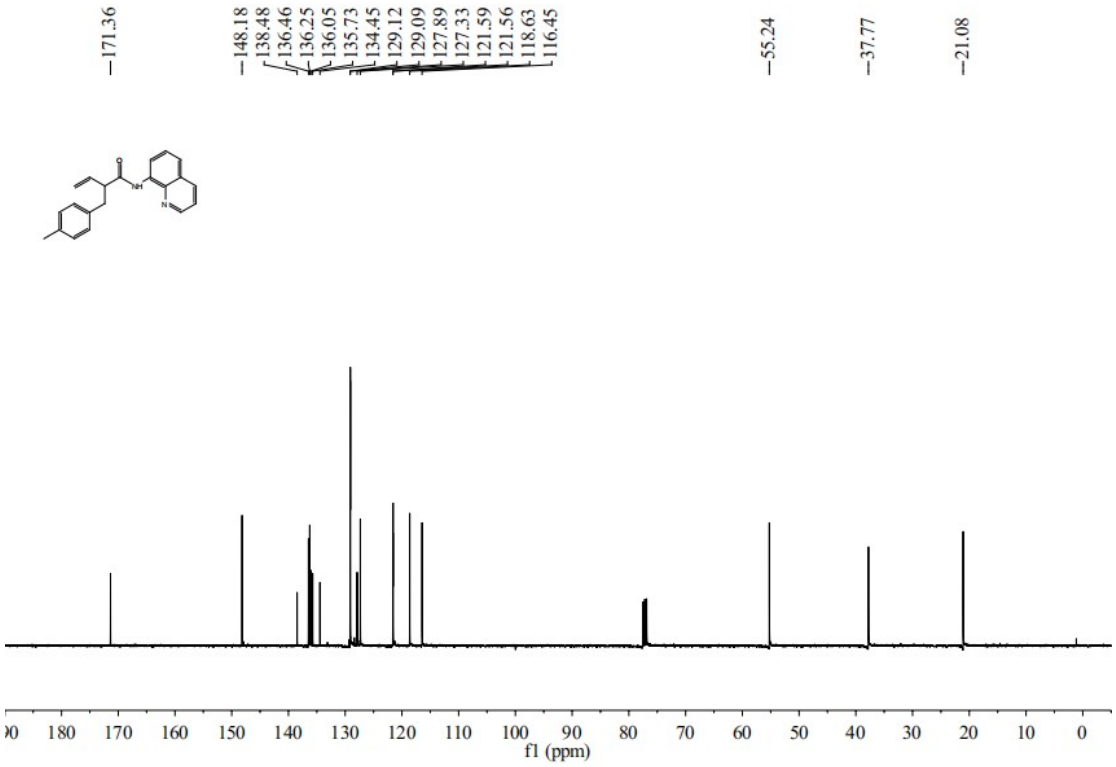
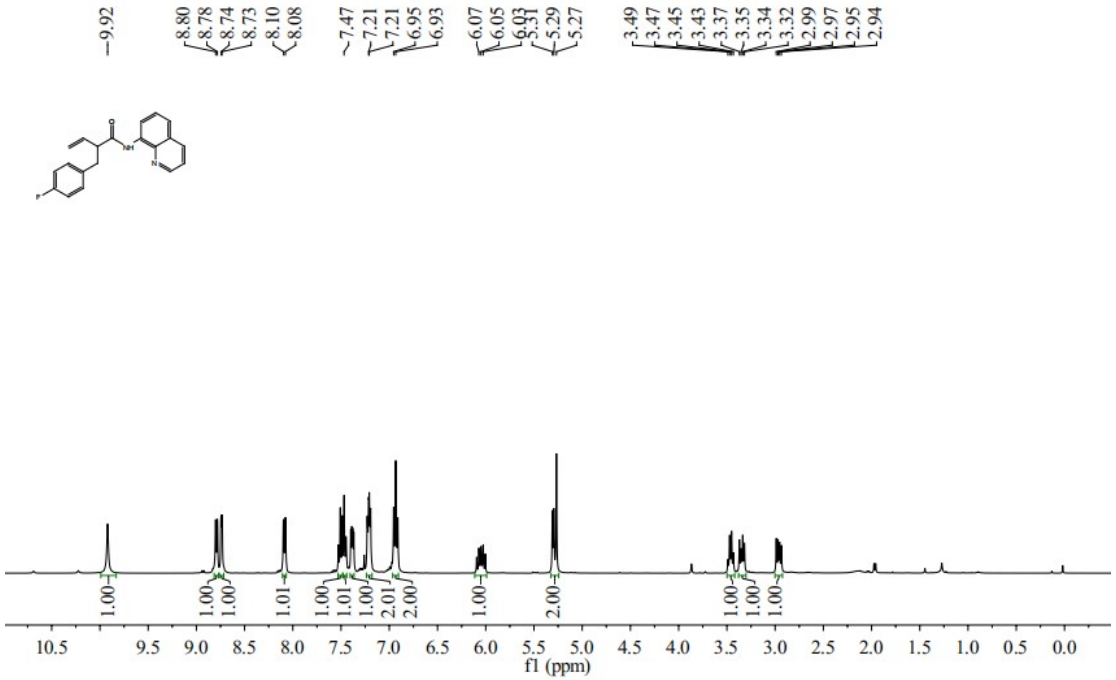
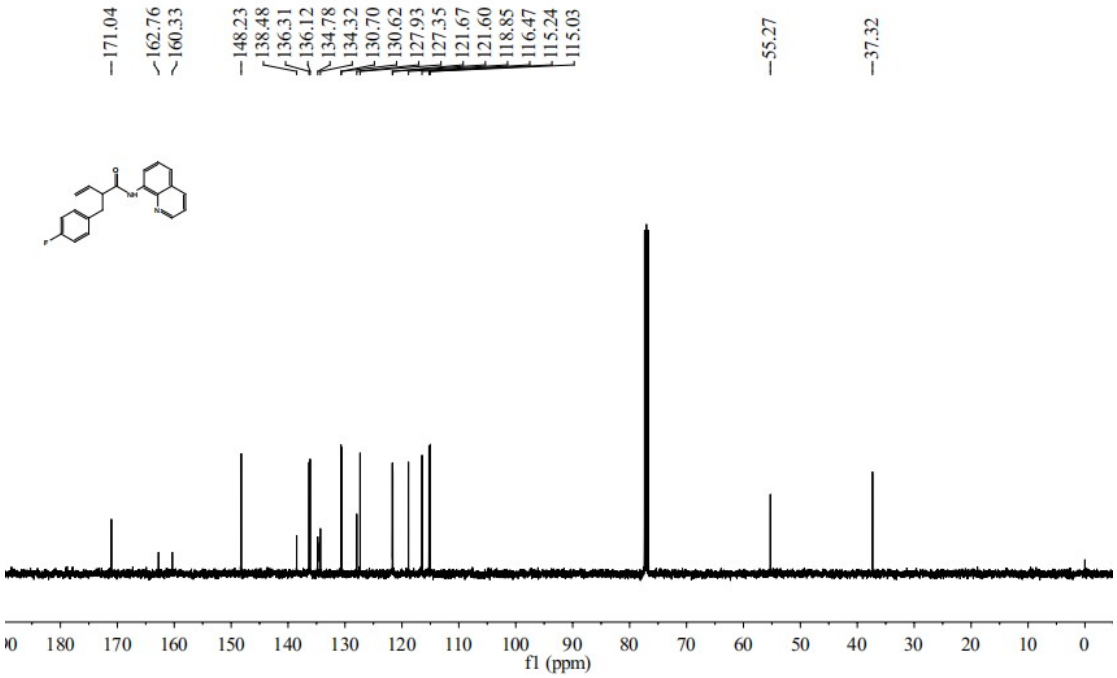


^{1}H NMR of 1l



^{13}C NMR of 1l



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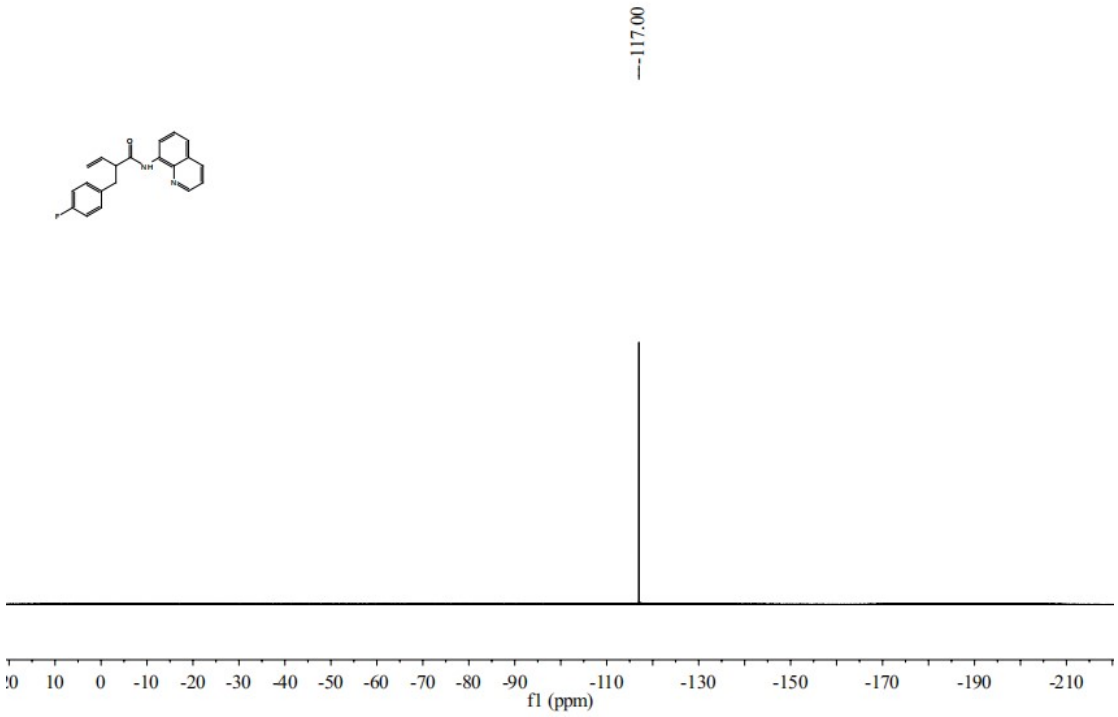
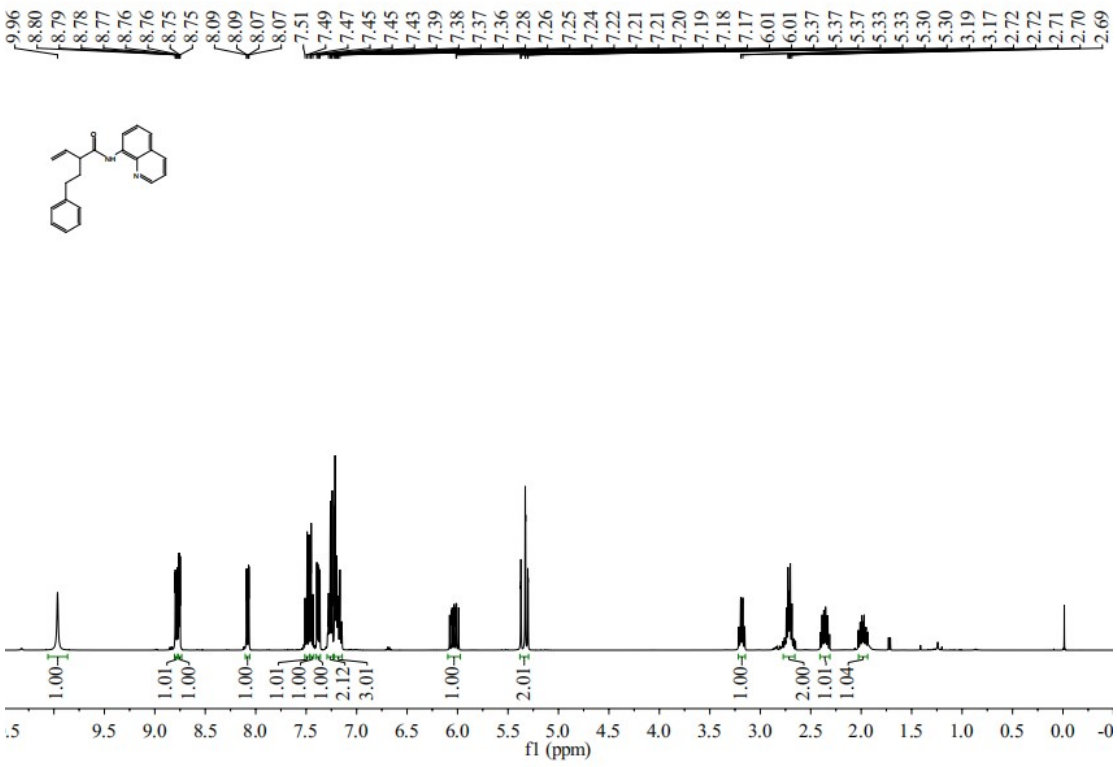


^{1}H NMR of 1m



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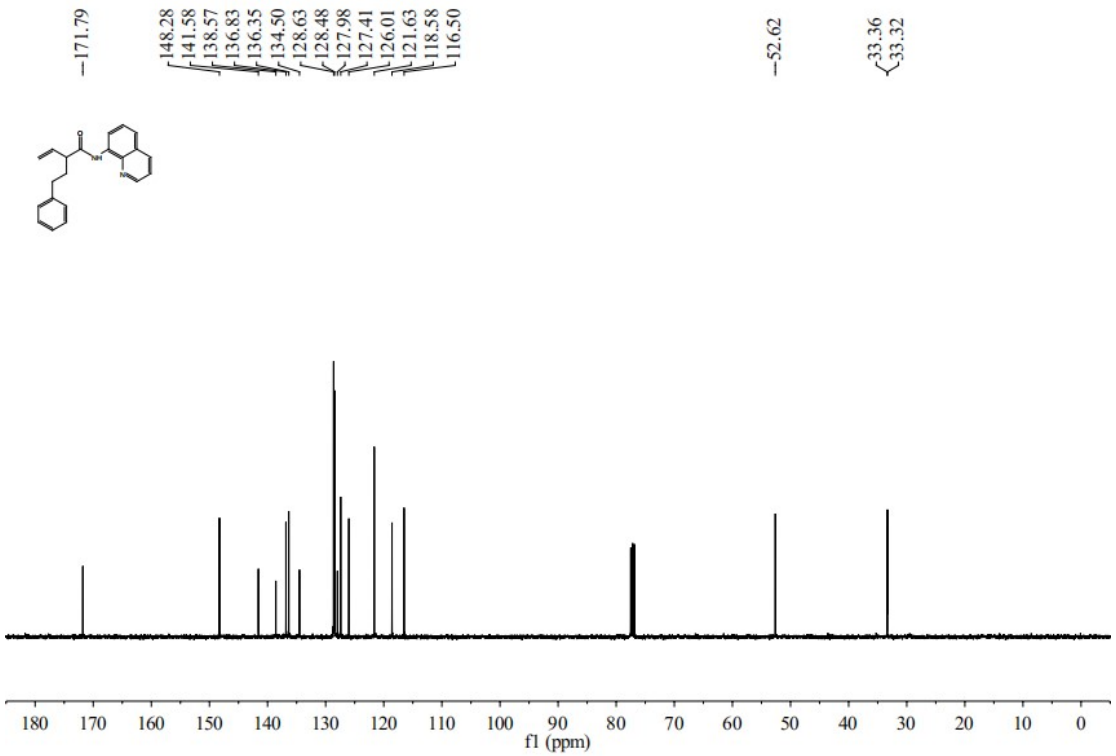
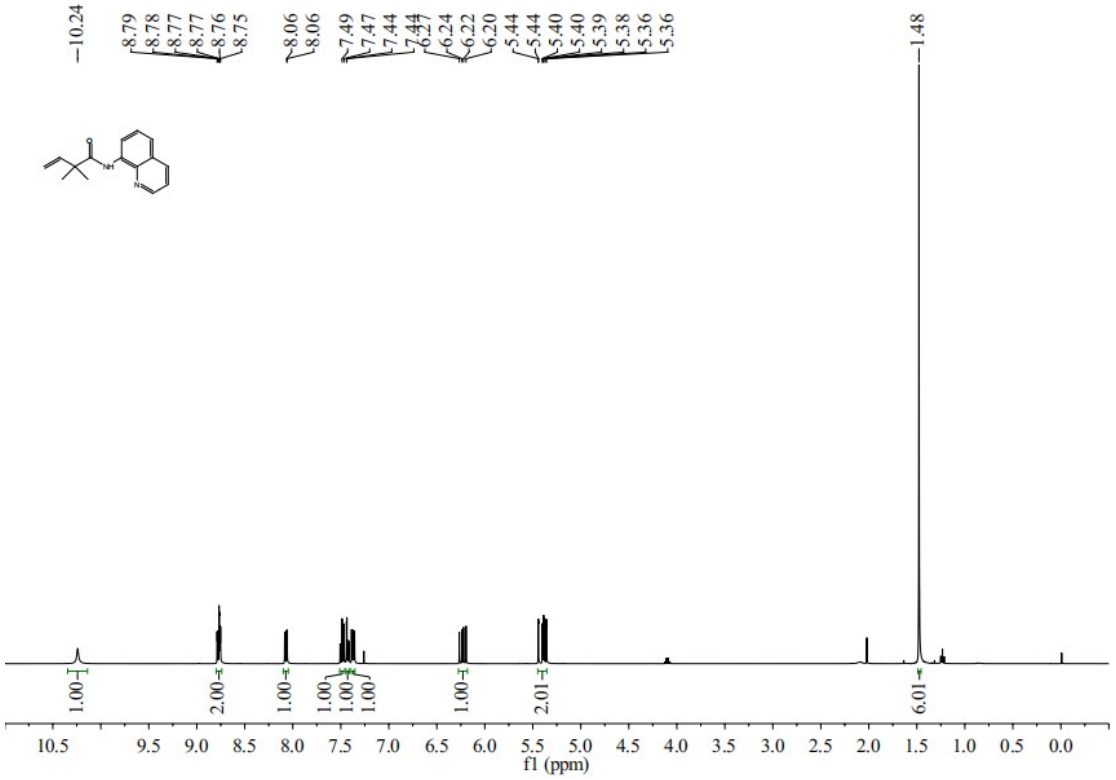


^{1}H NMR of 1n



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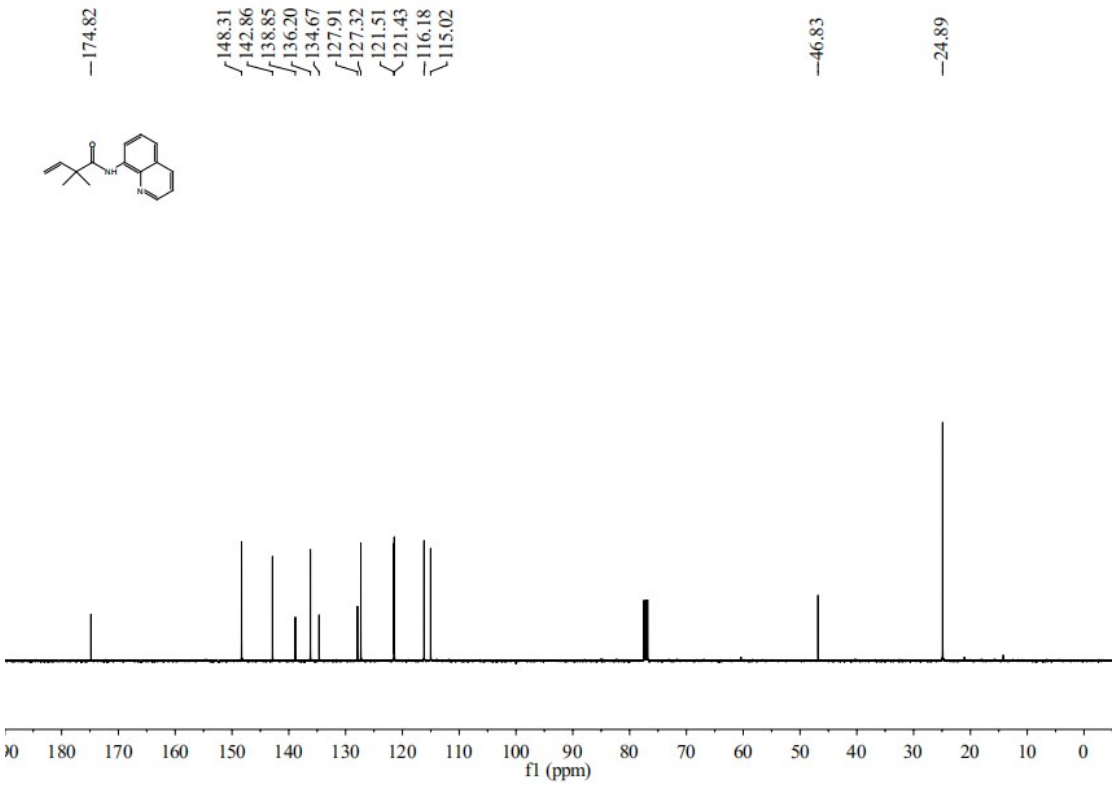
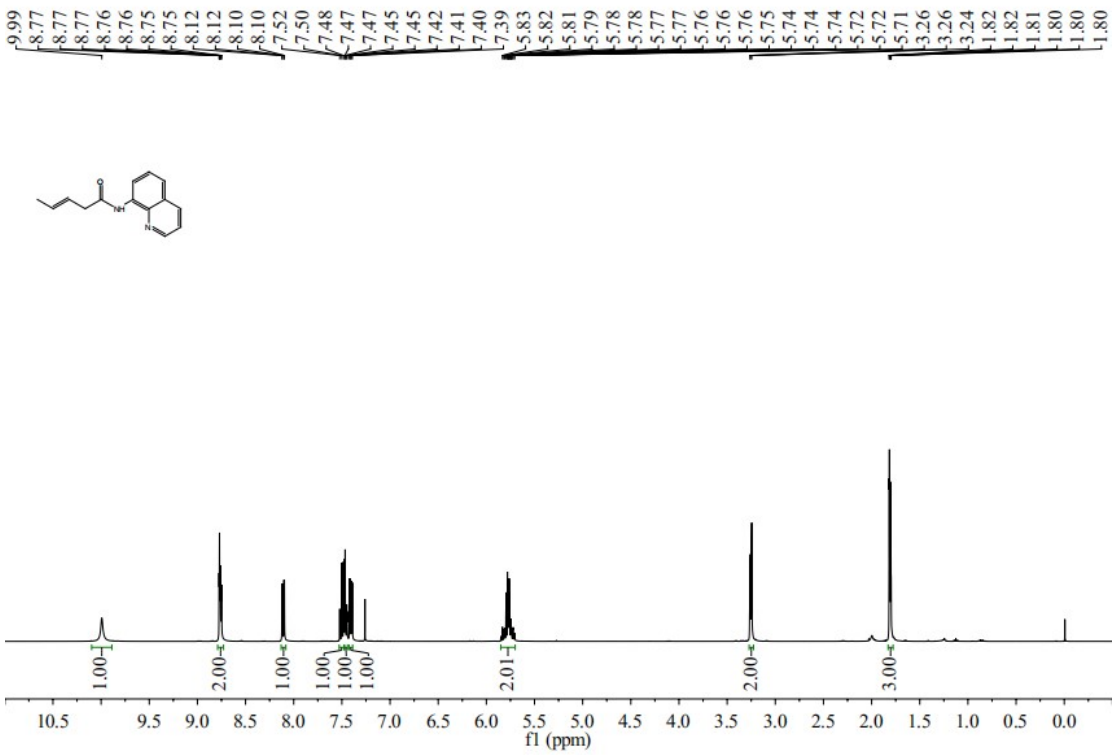


^{1}H NMR of 1o



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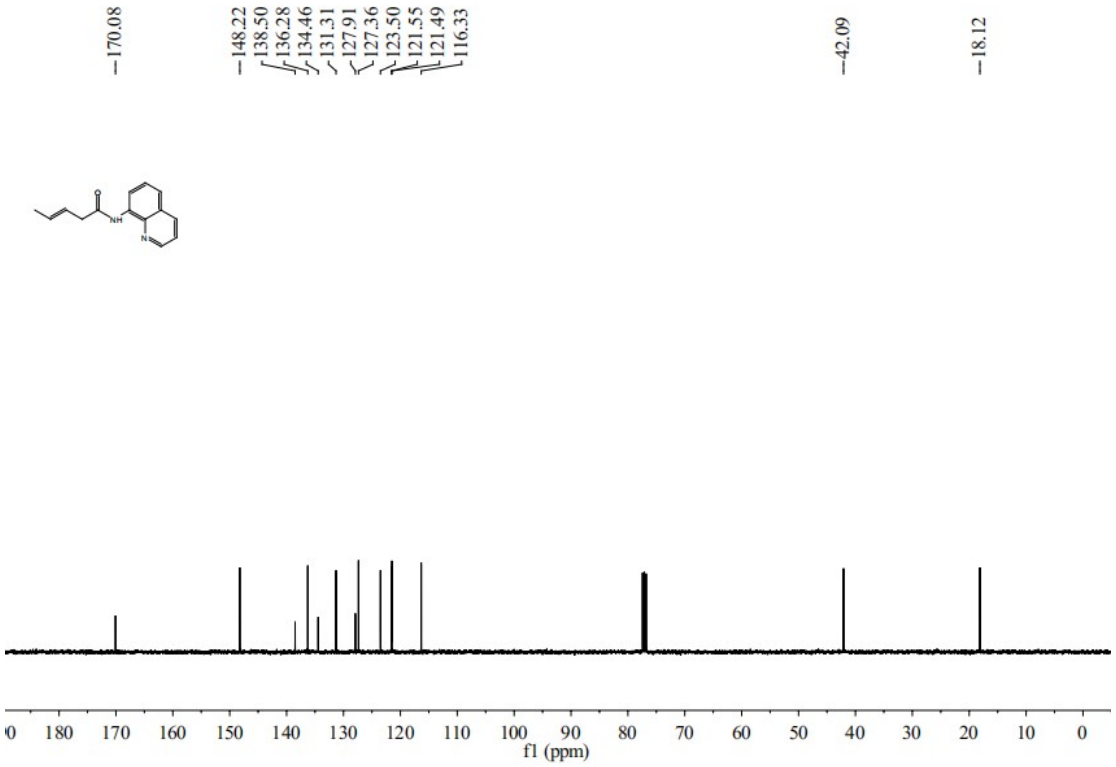
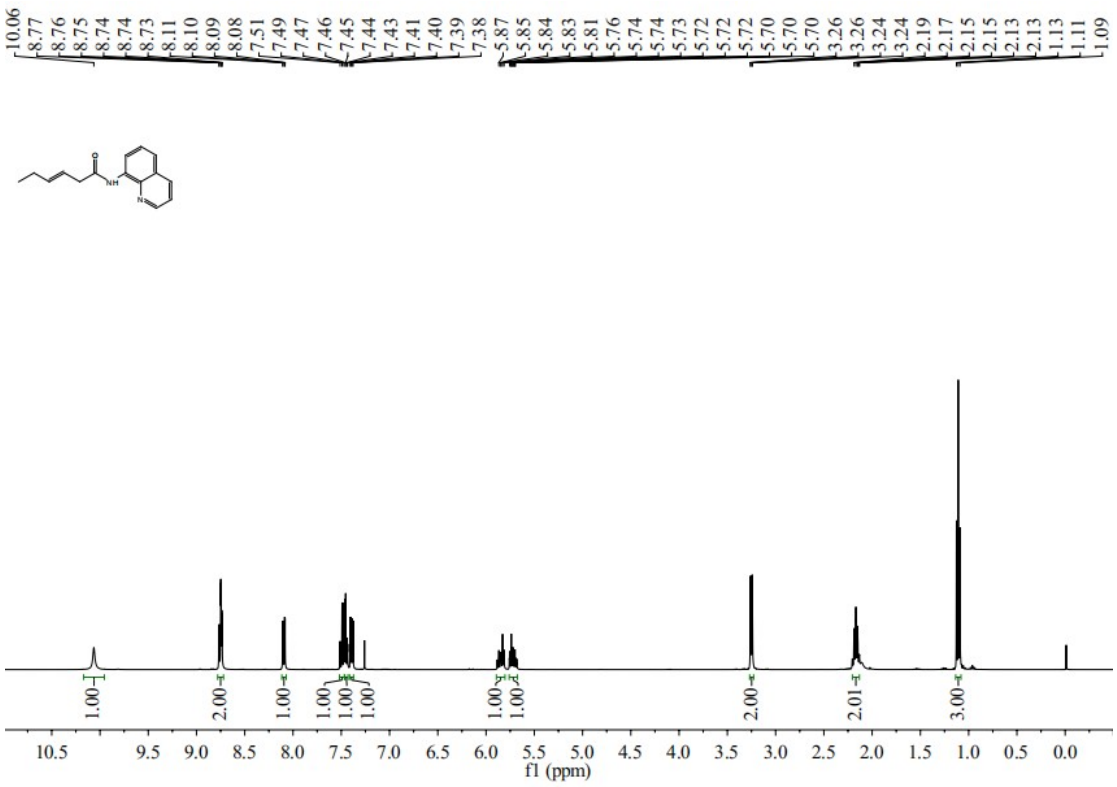
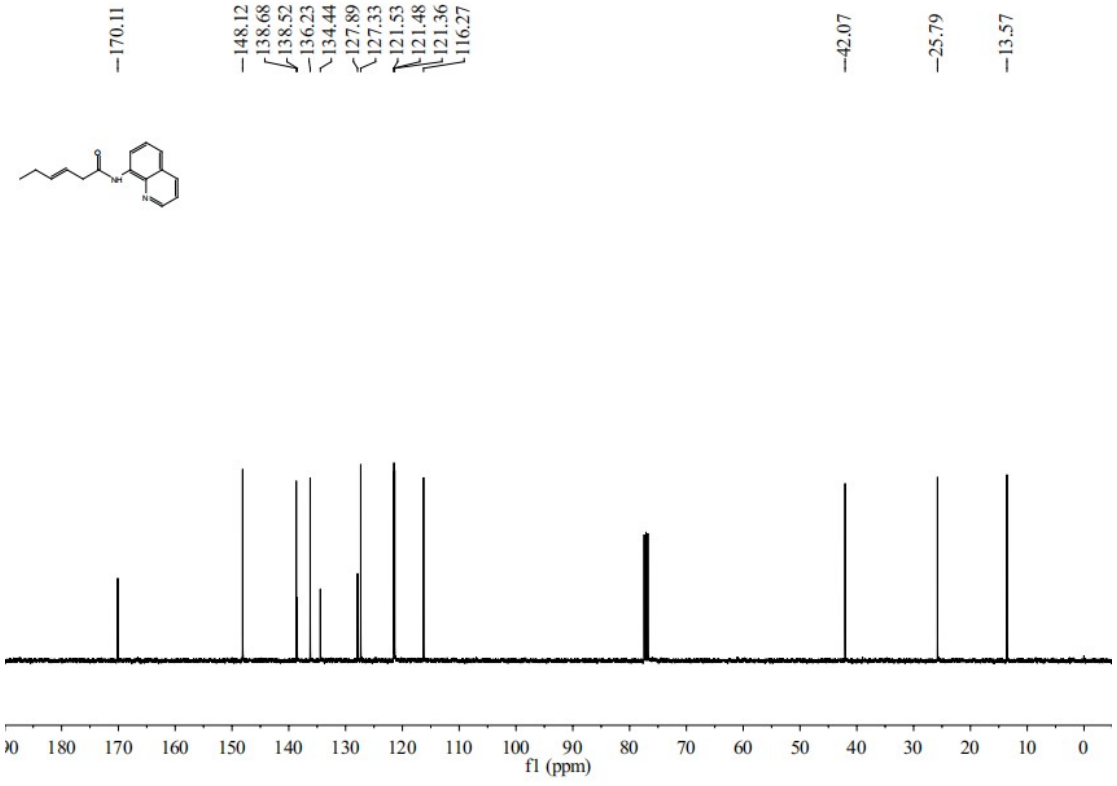


^{1}H NMR of 1p



^{13}C NMR of 1p



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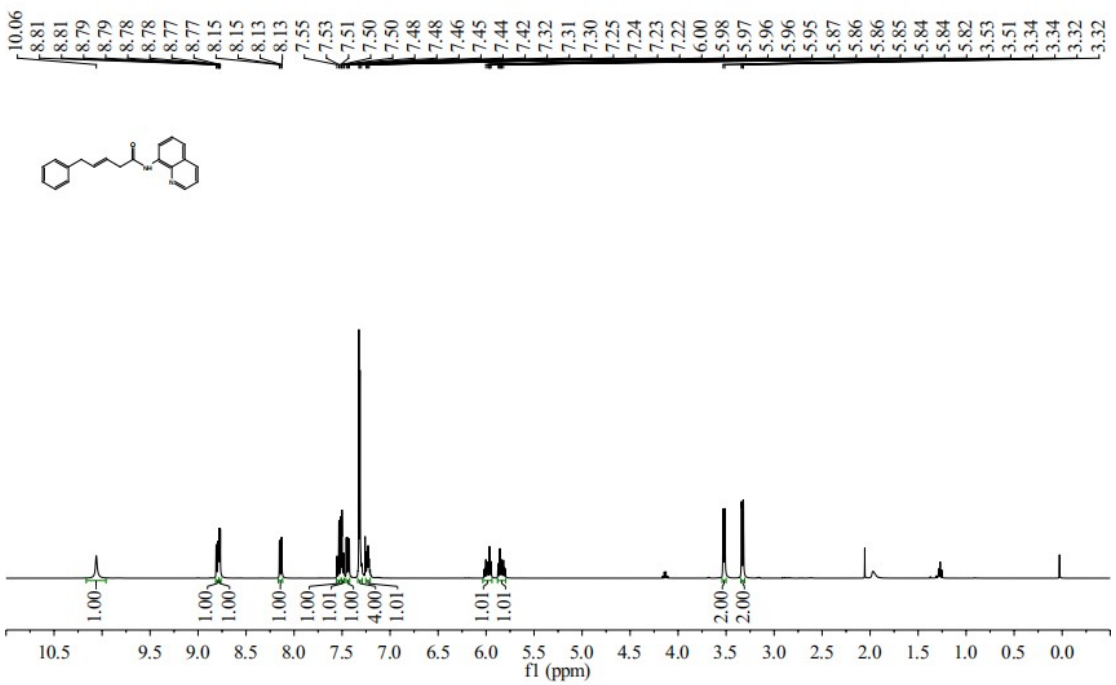

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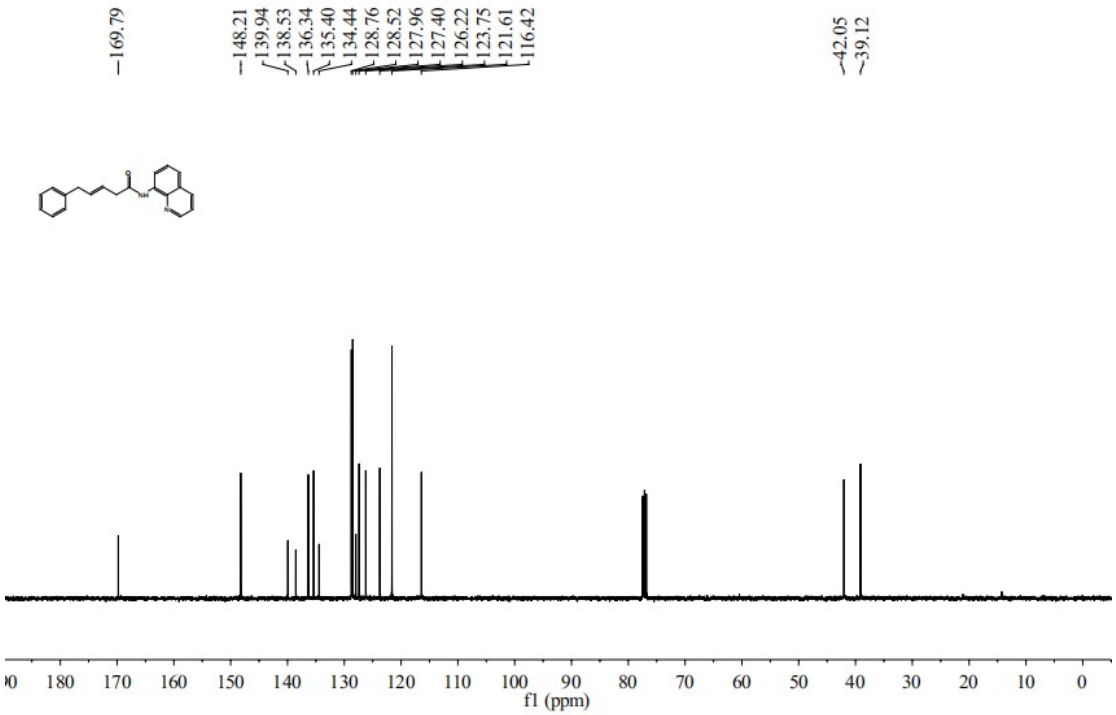
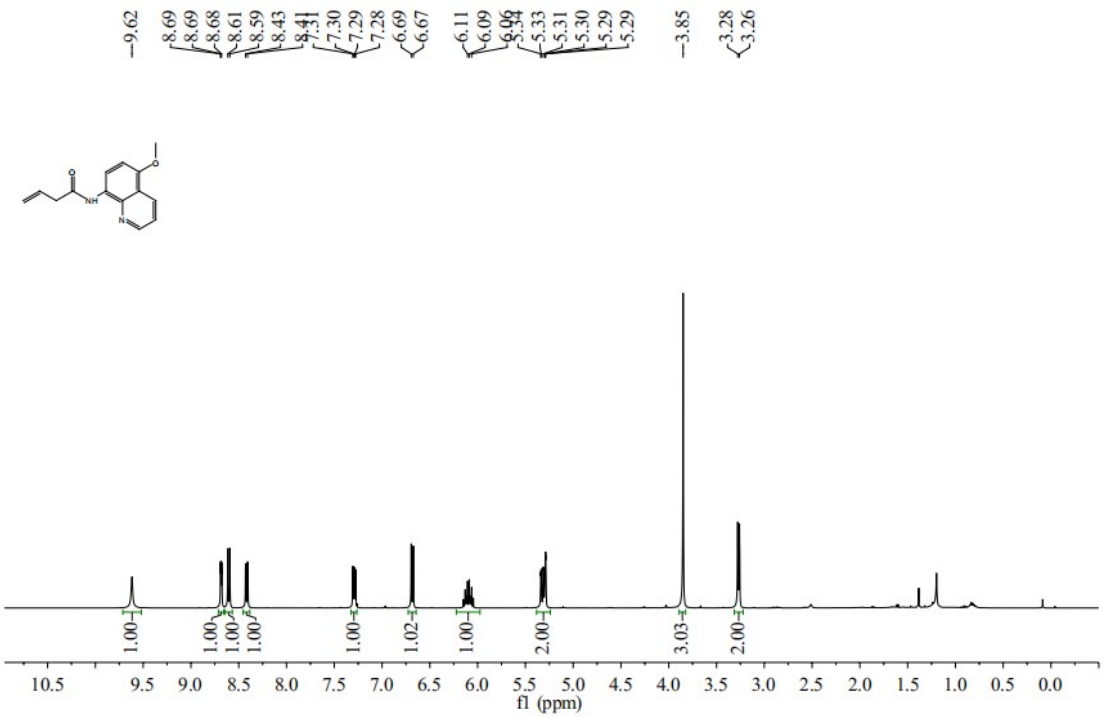


^{1}H NMR of 1r



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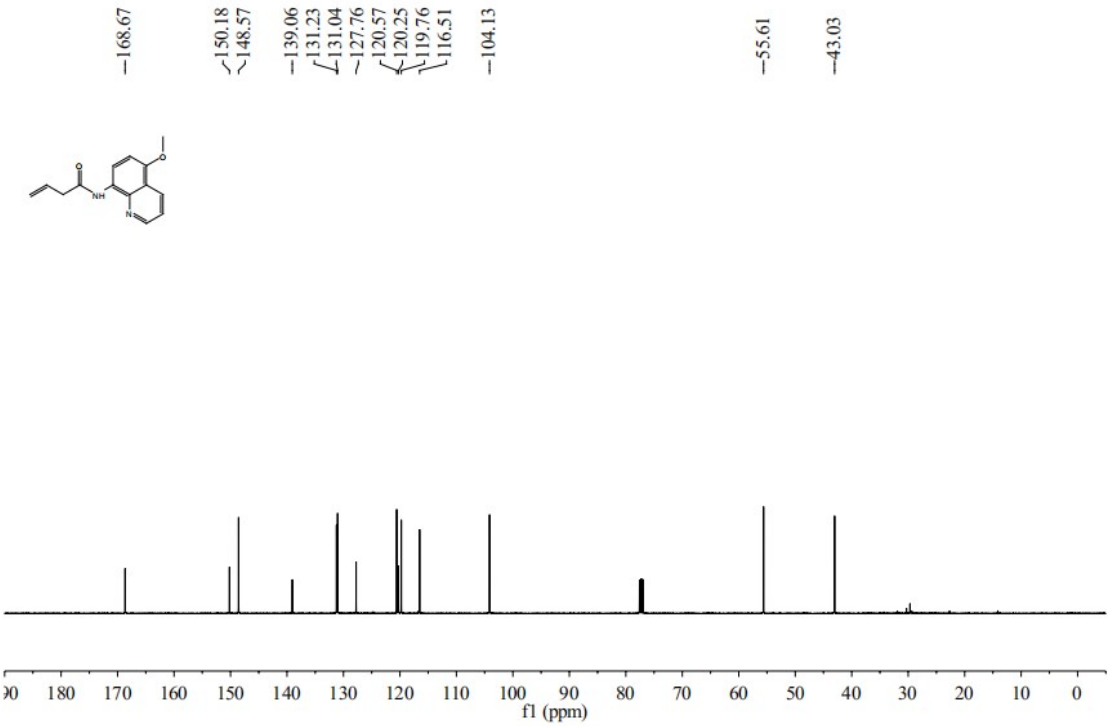
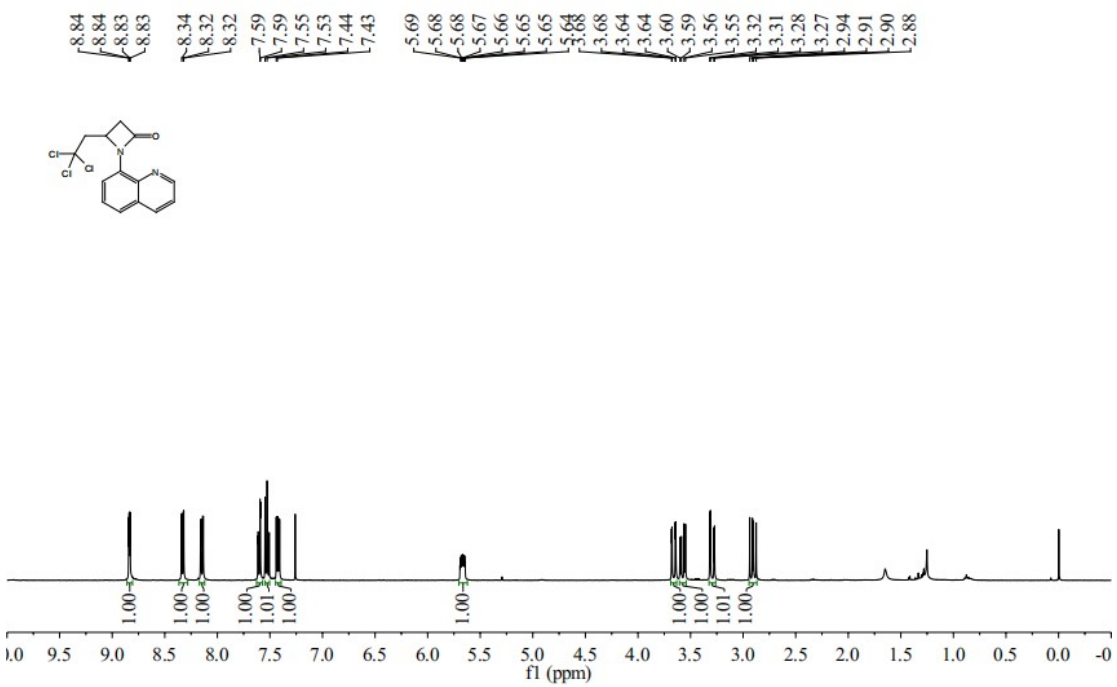
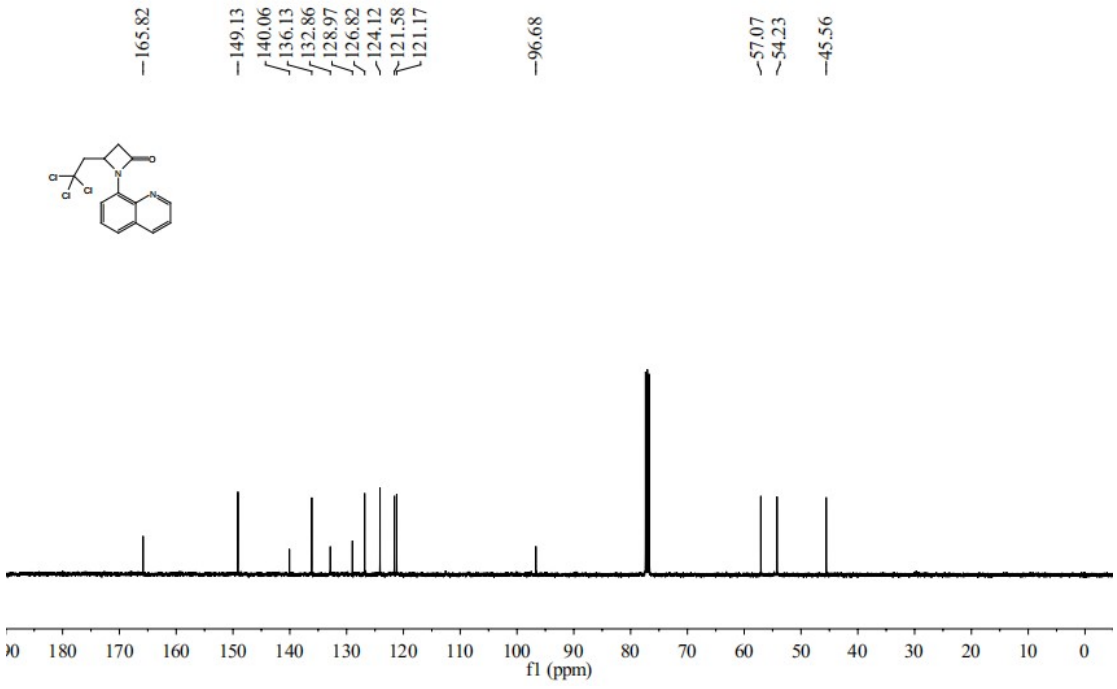


^{1}H NMR of 2a



^{13}C NMR of 2a



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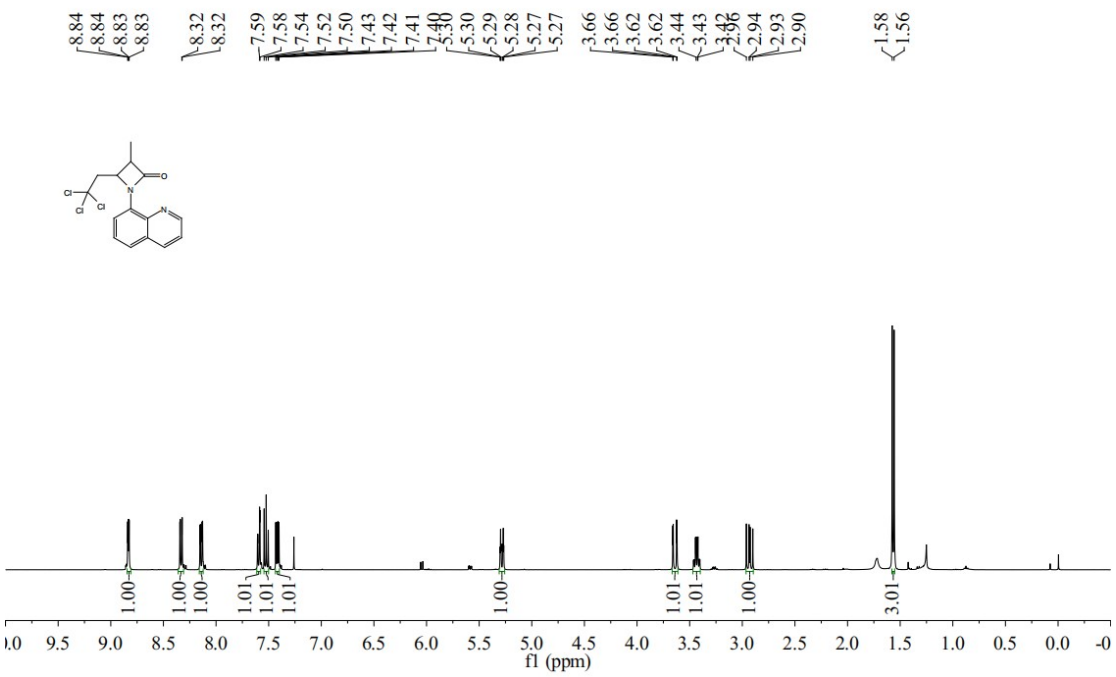
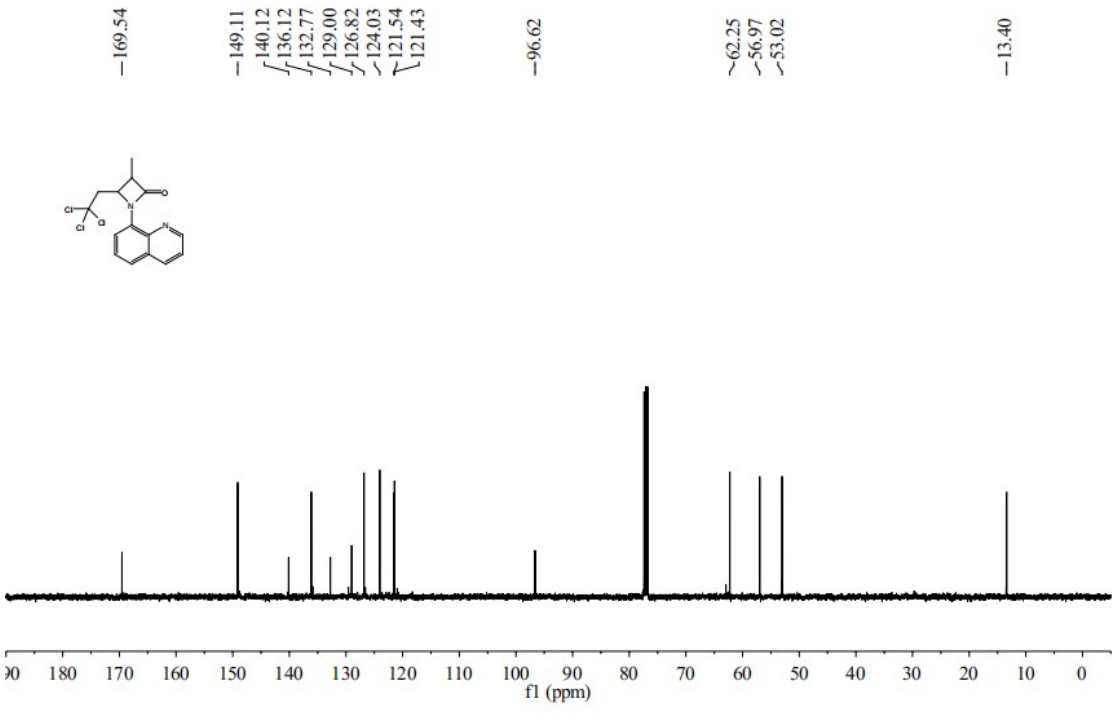


^{13}C NMR of 2b



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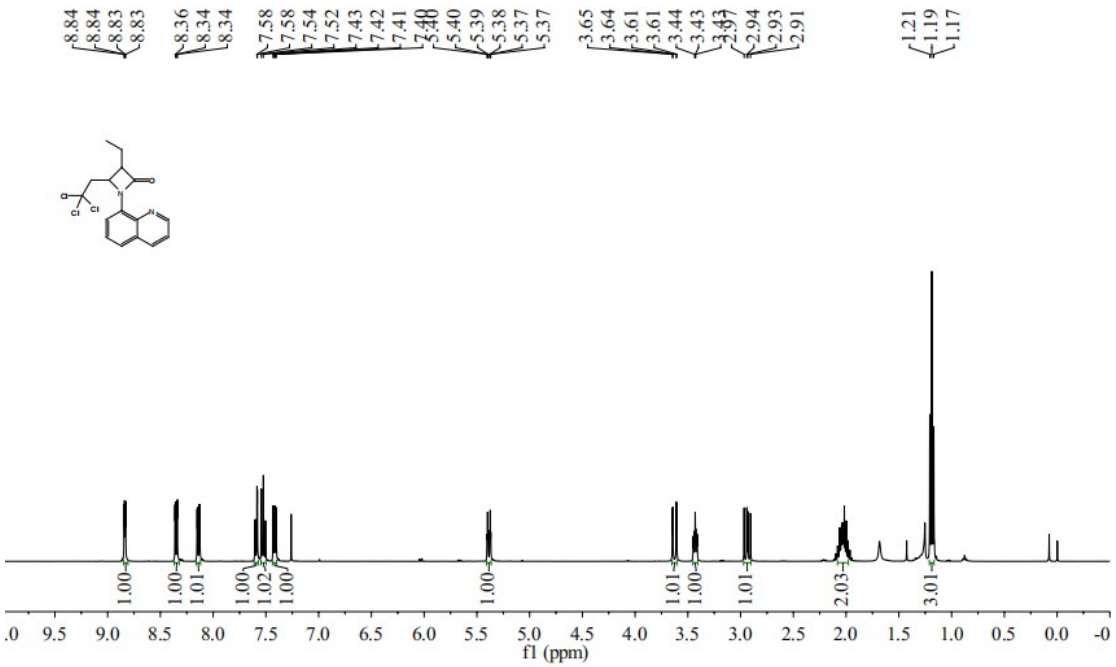
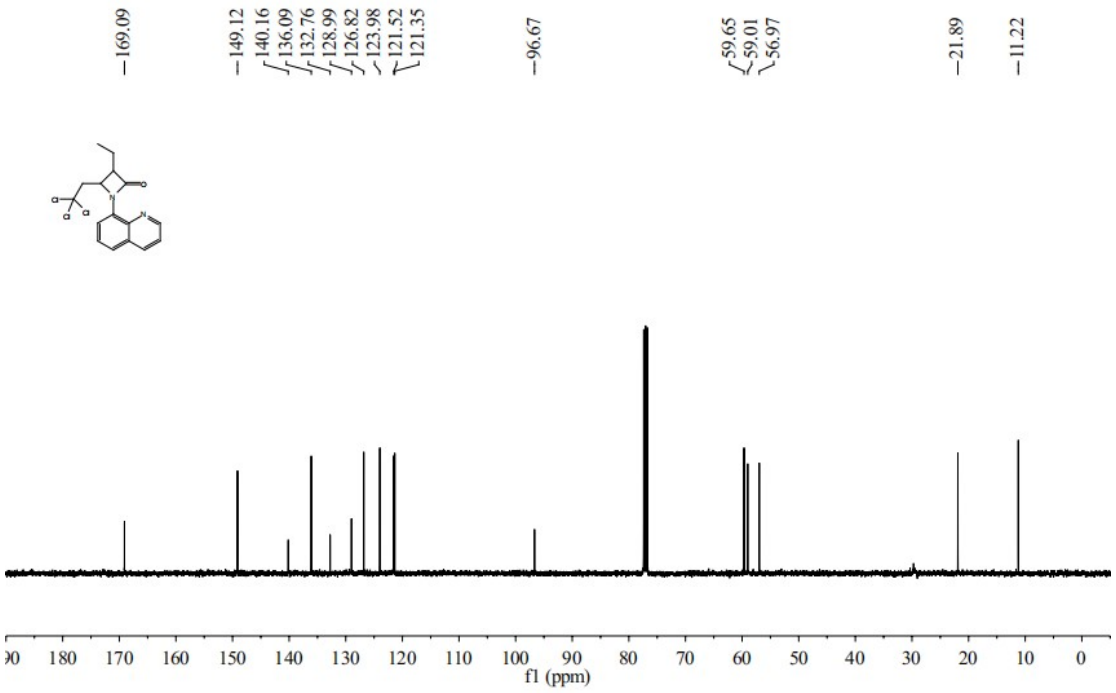


^{13}C NMR of 2c



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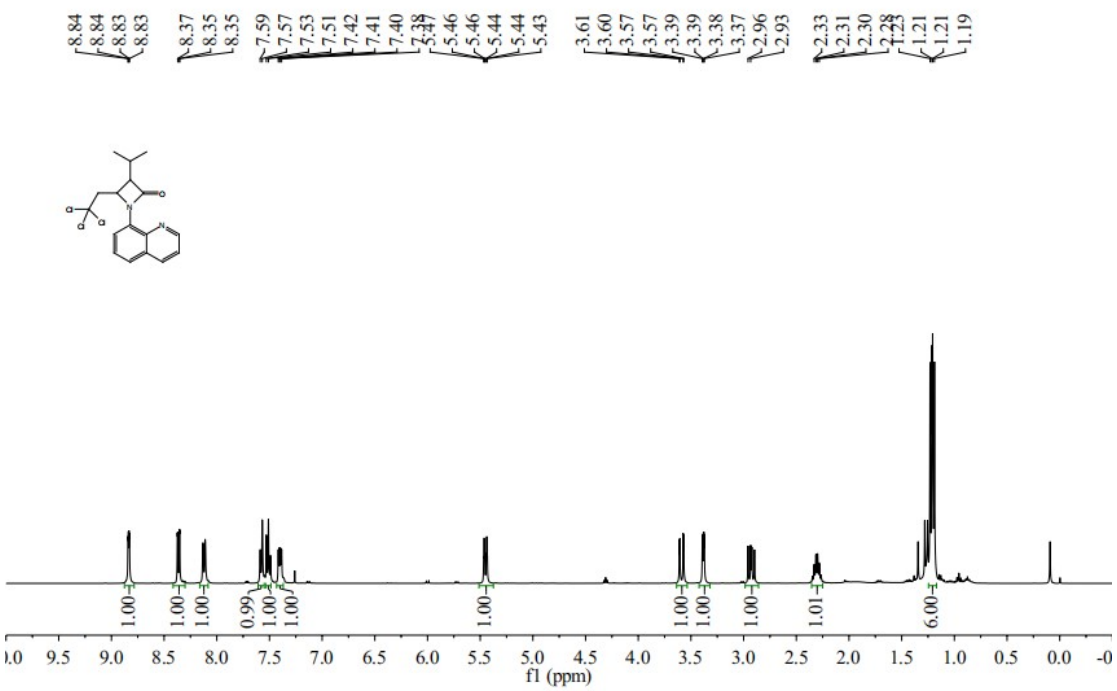
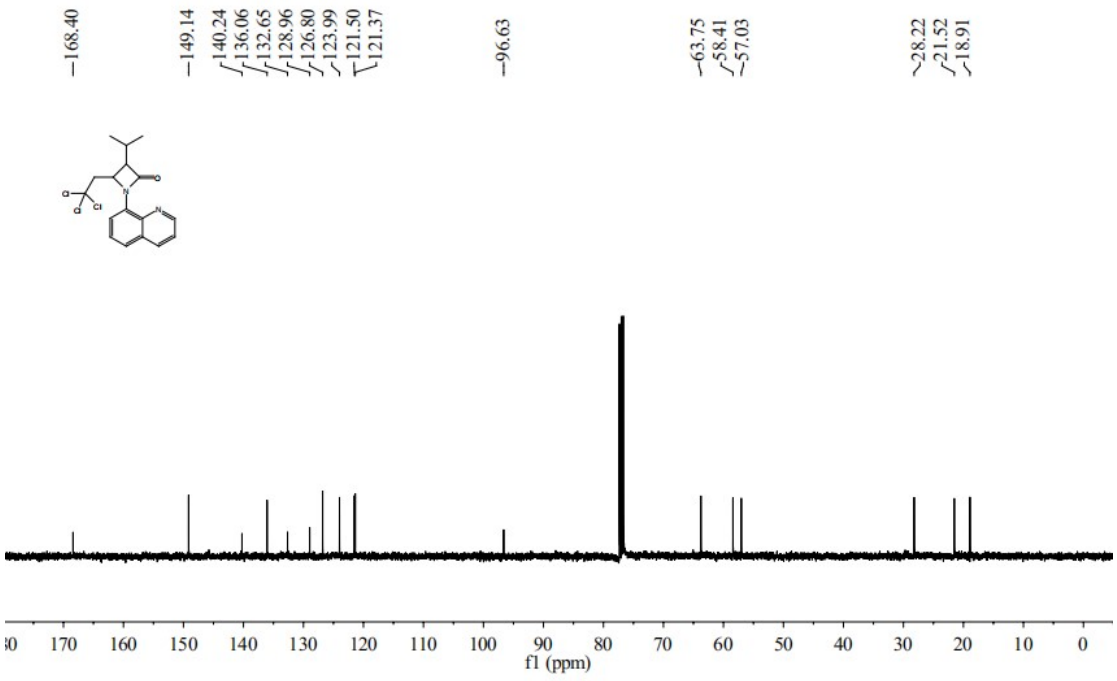


^{13}C NMR of 2d



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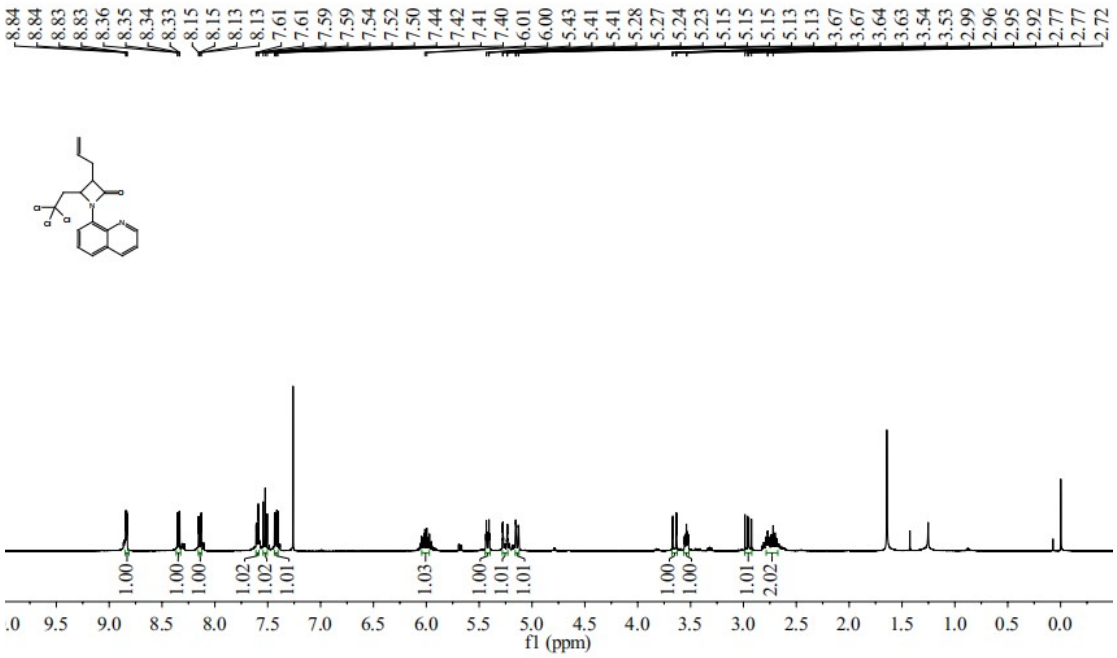

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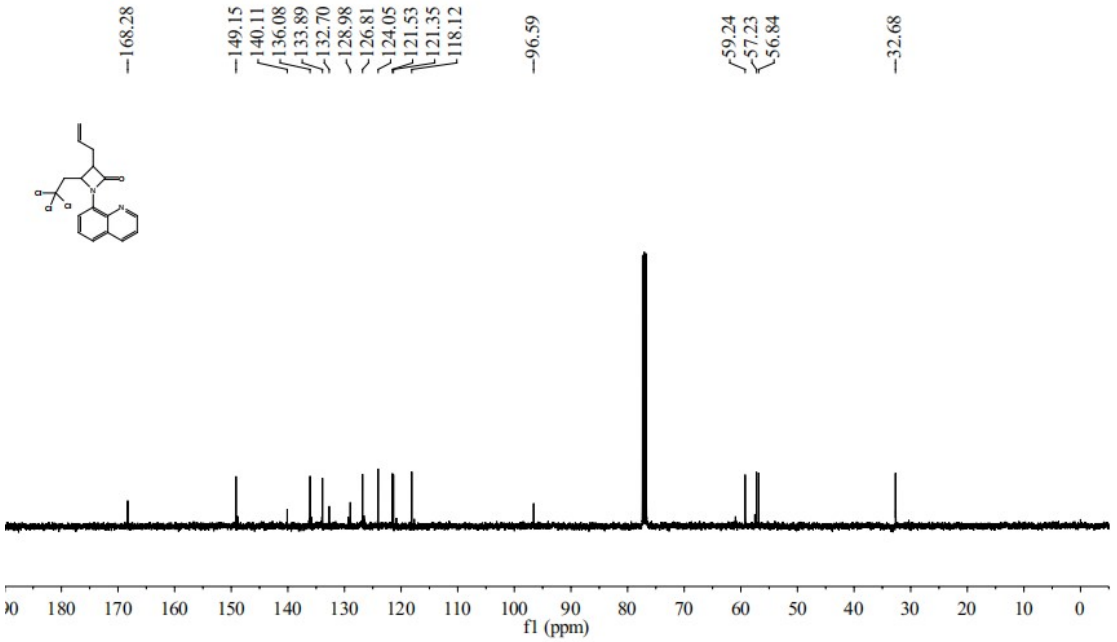

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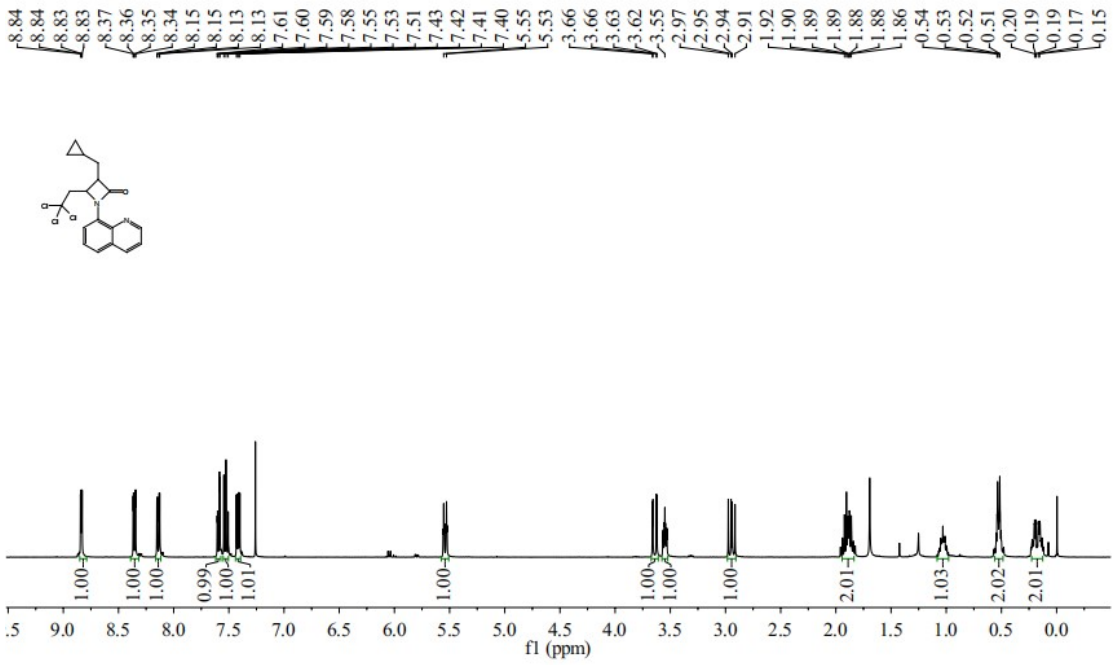

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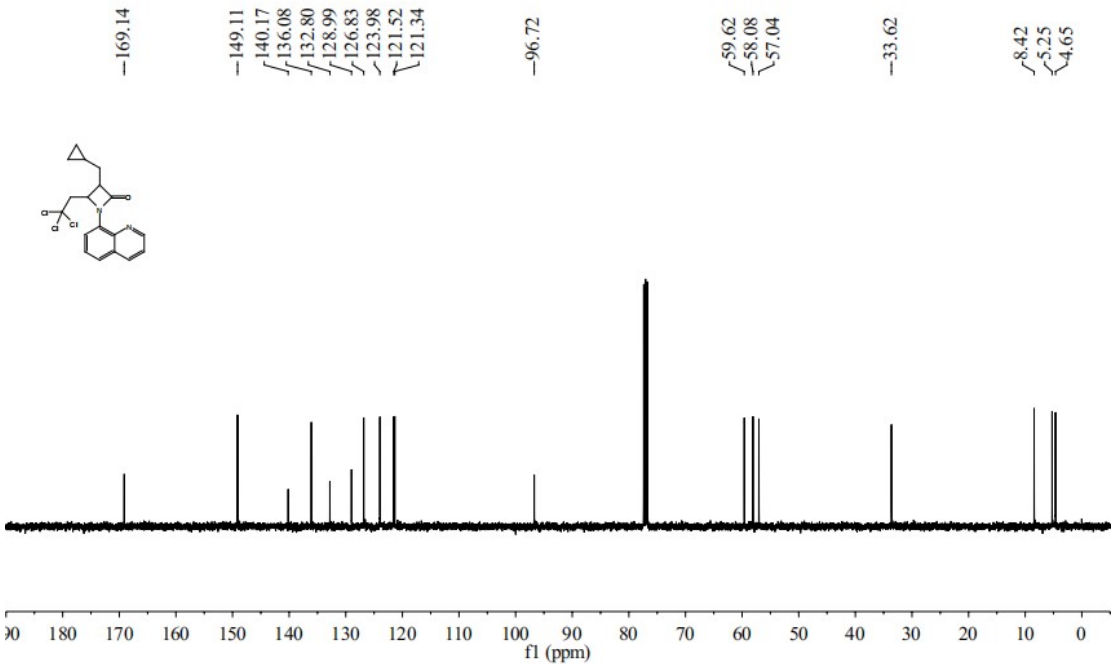

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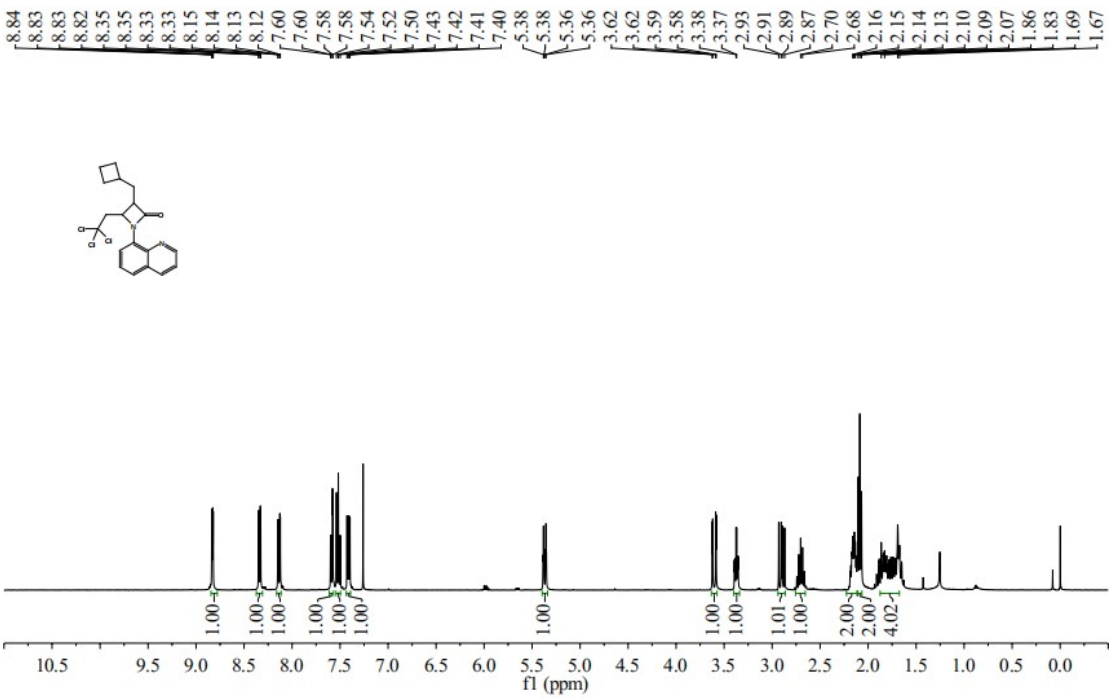

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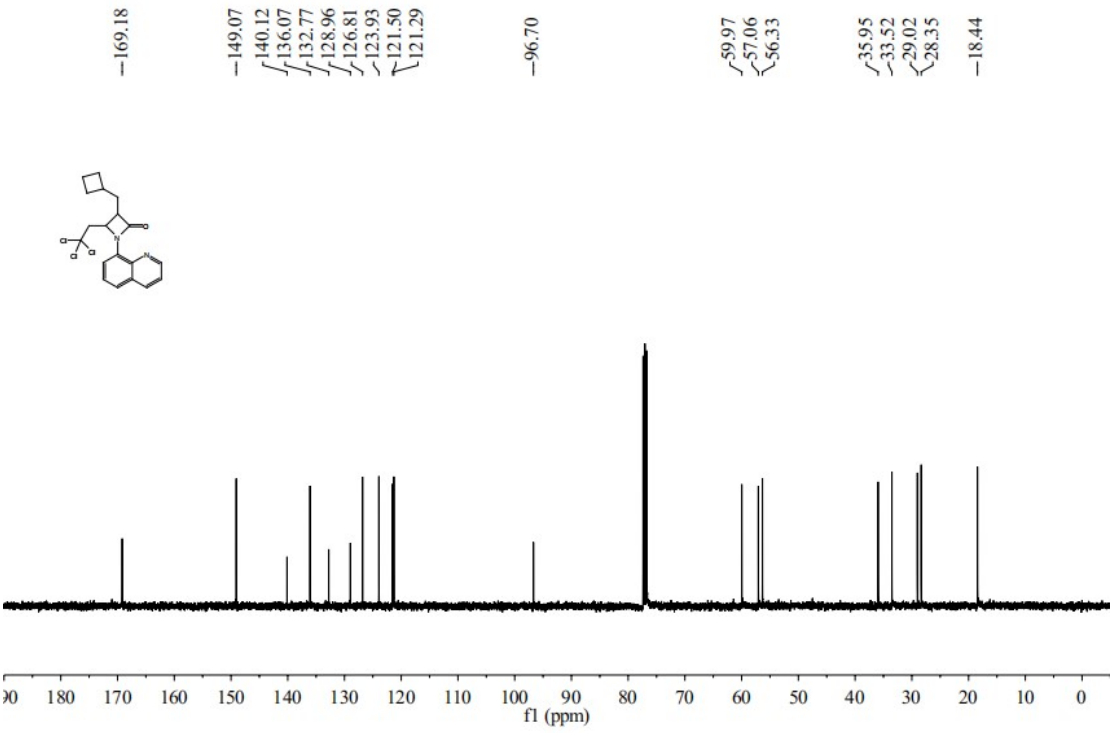

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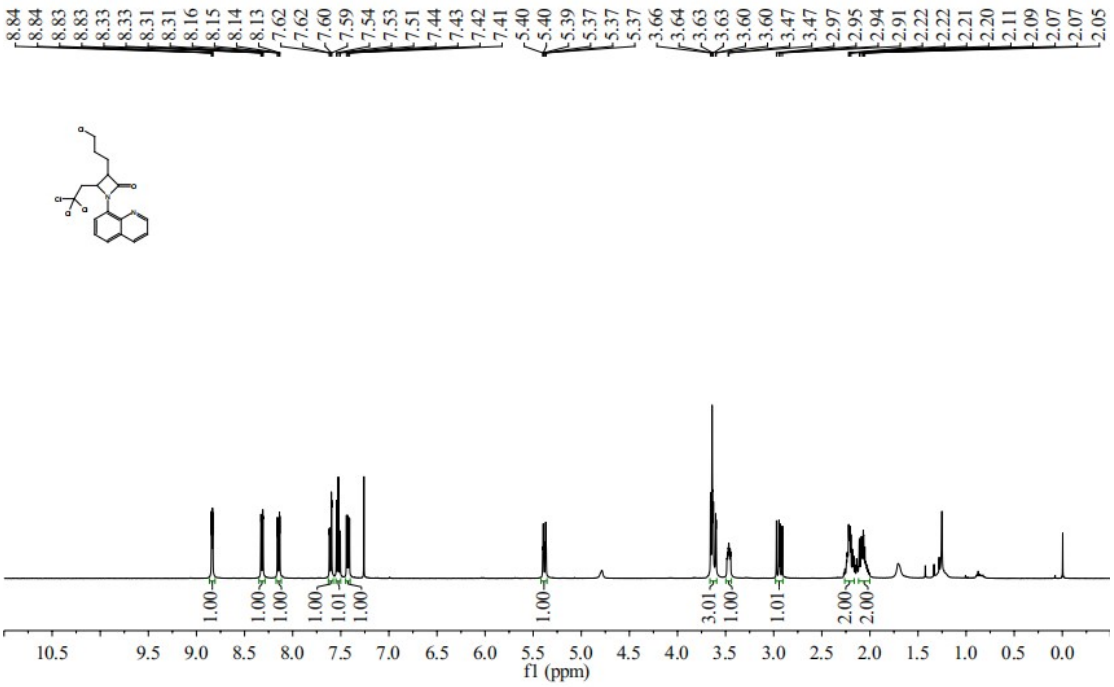

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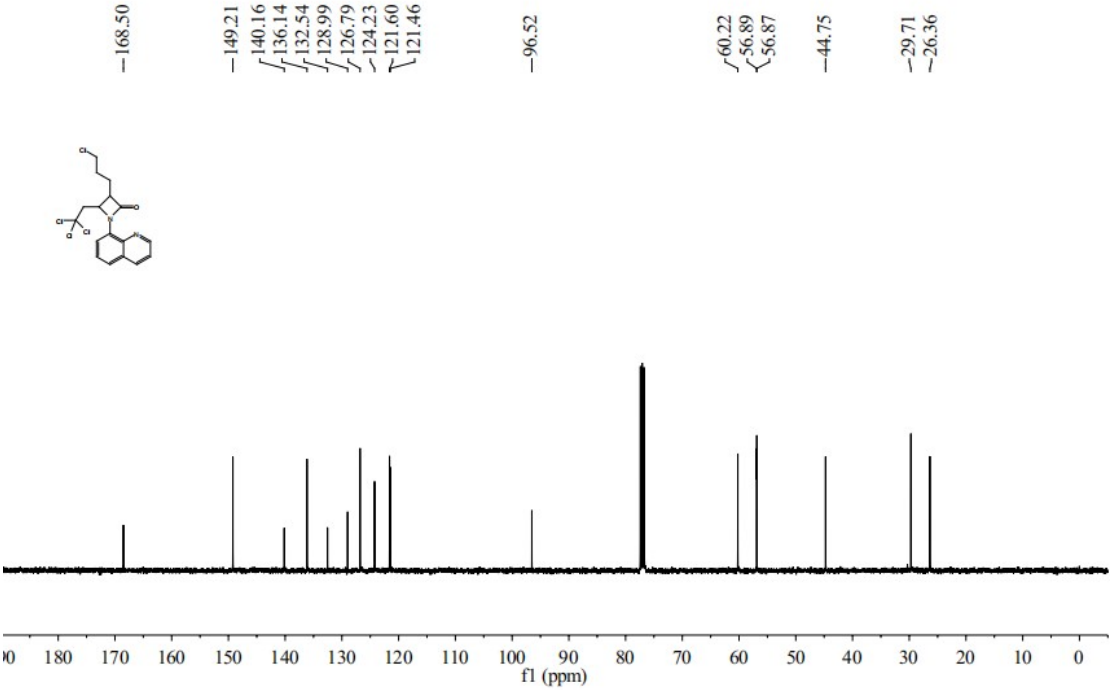

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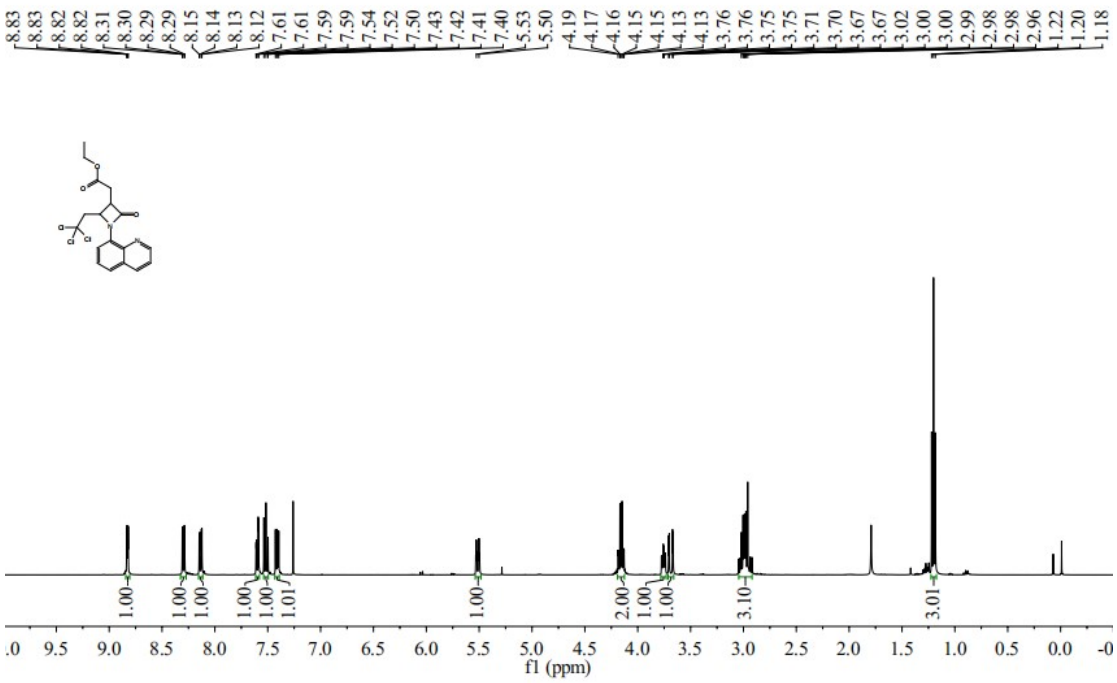

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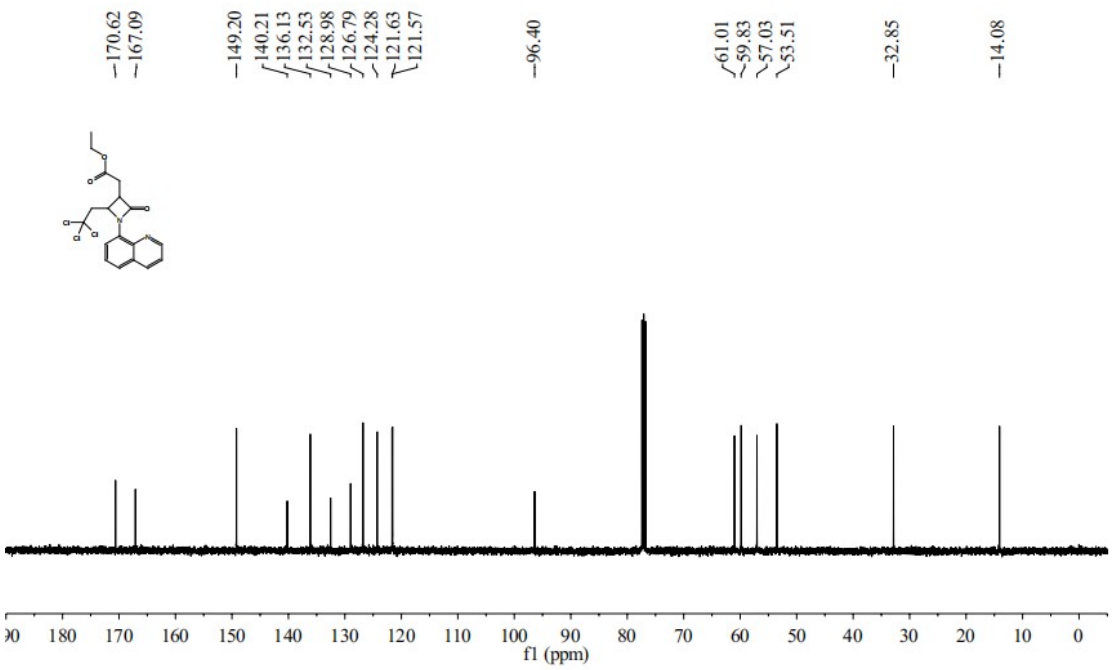

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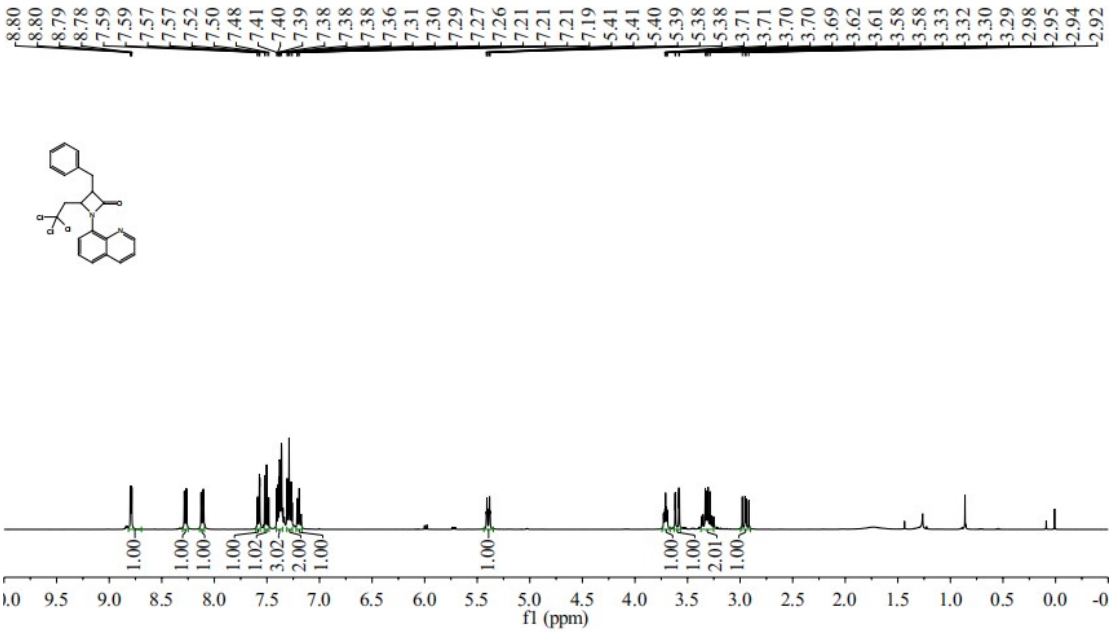

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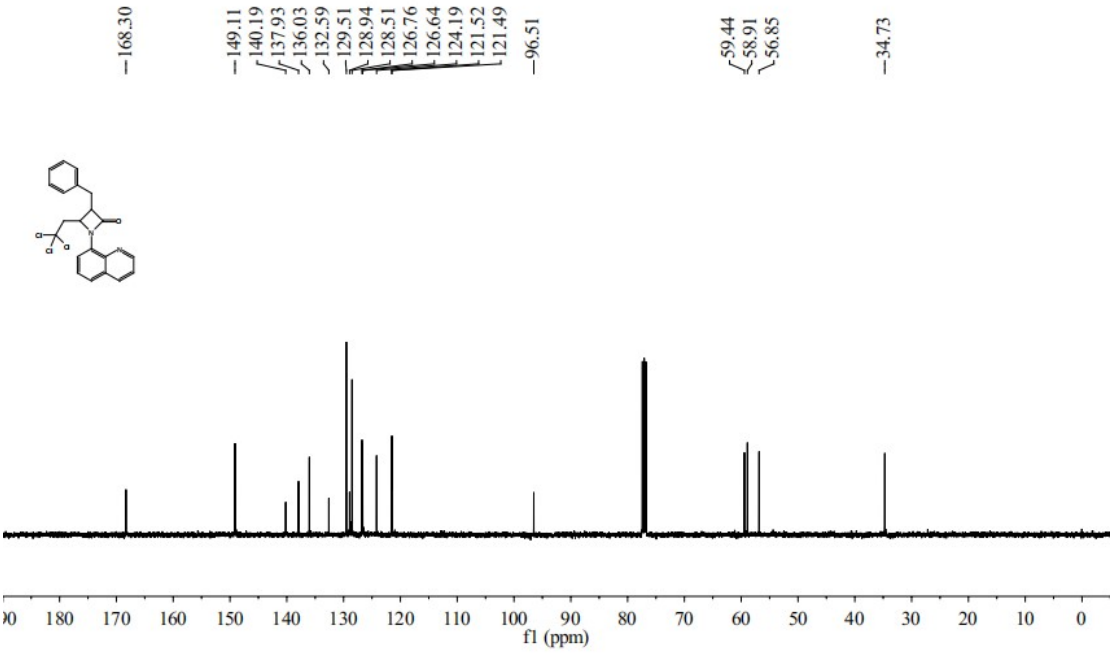

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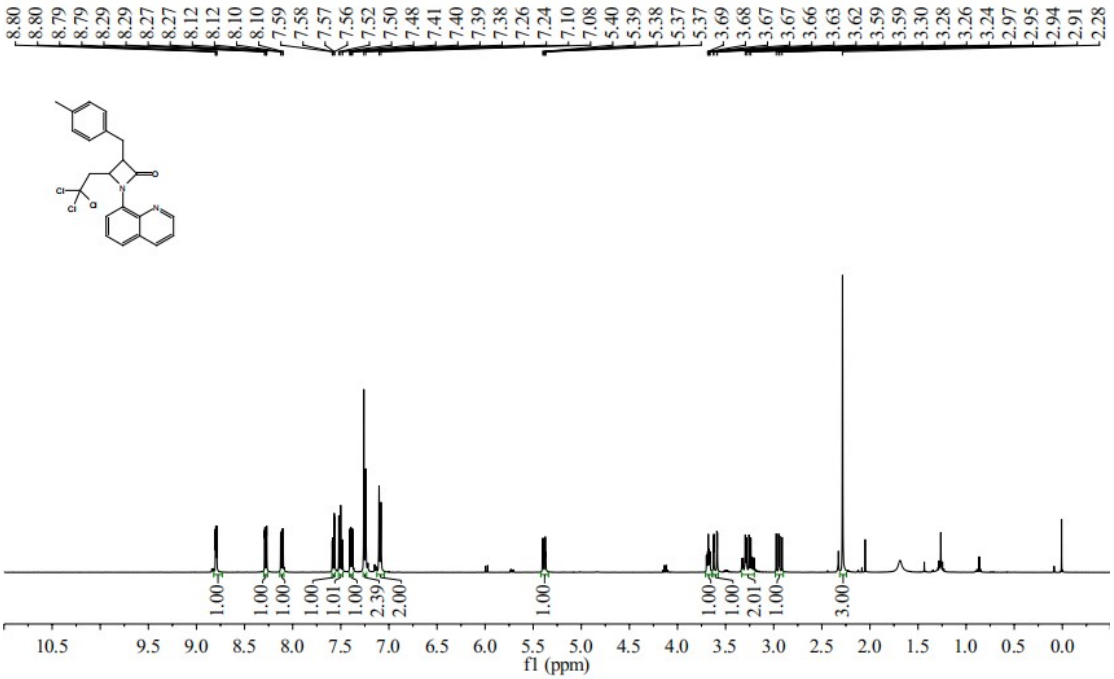

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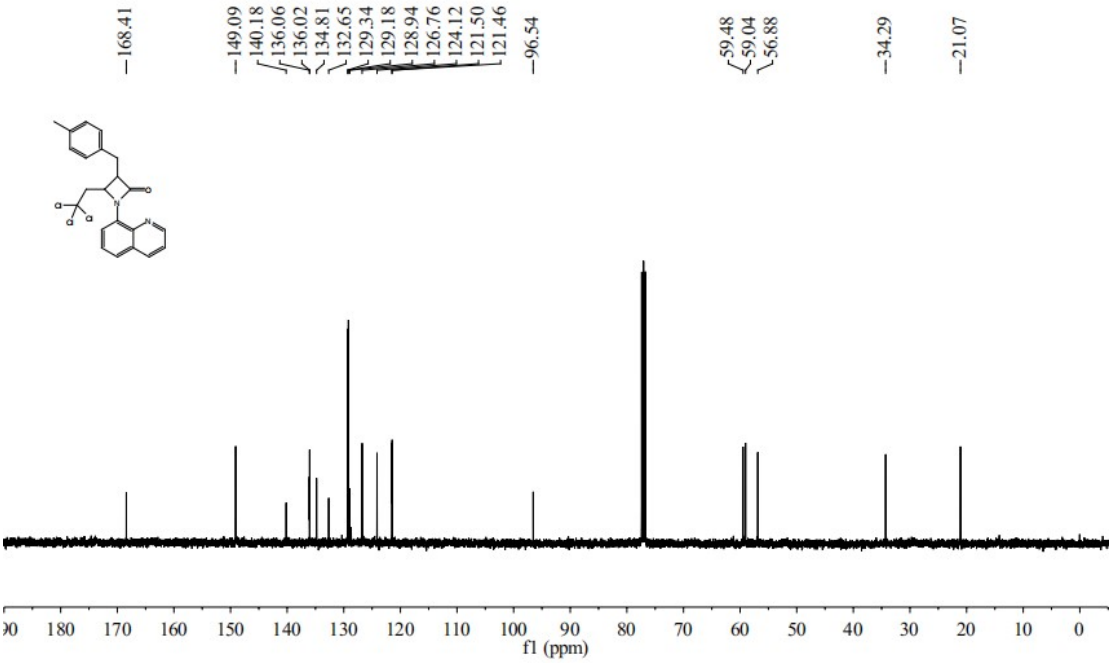

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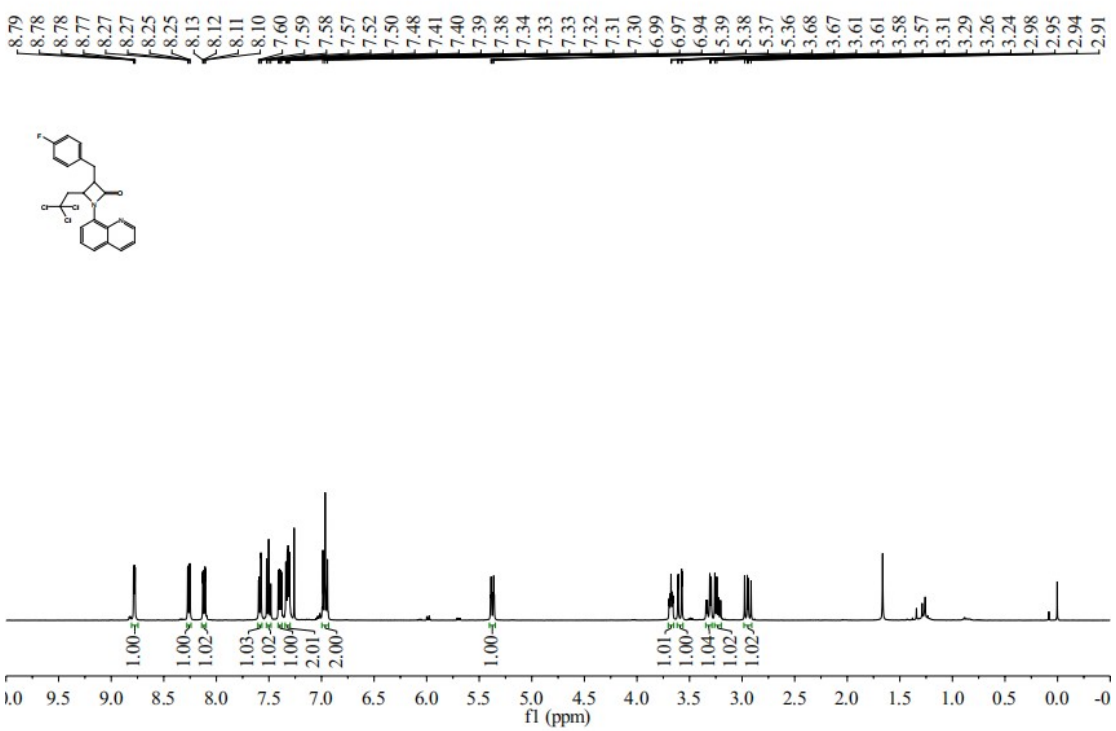

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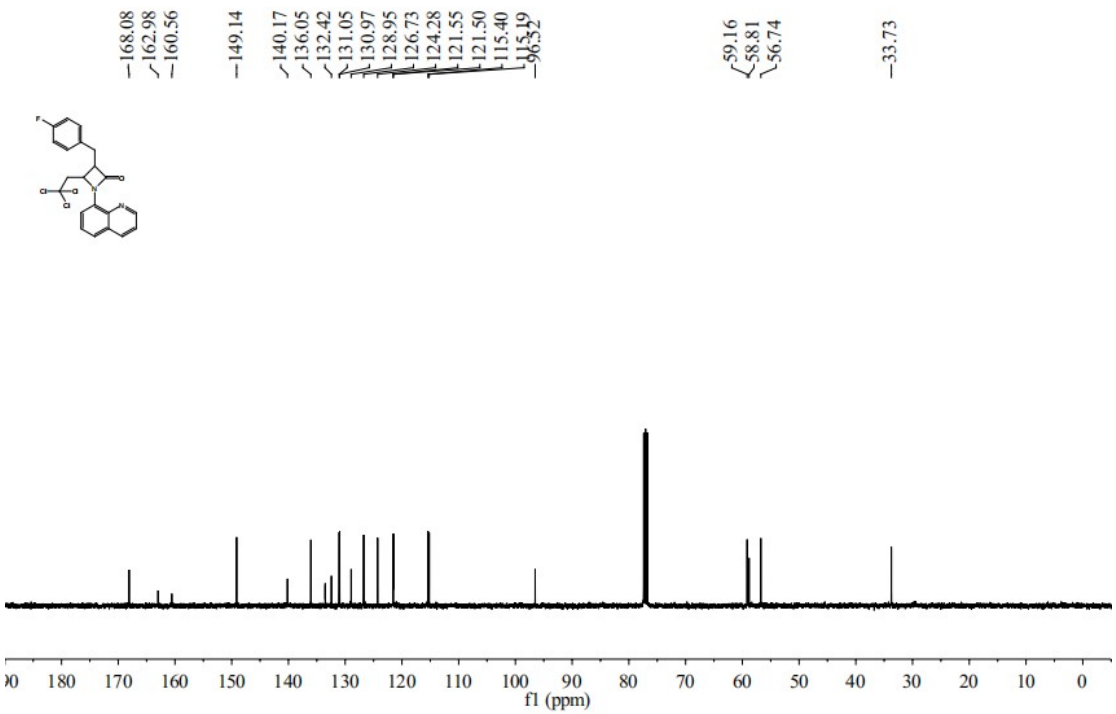

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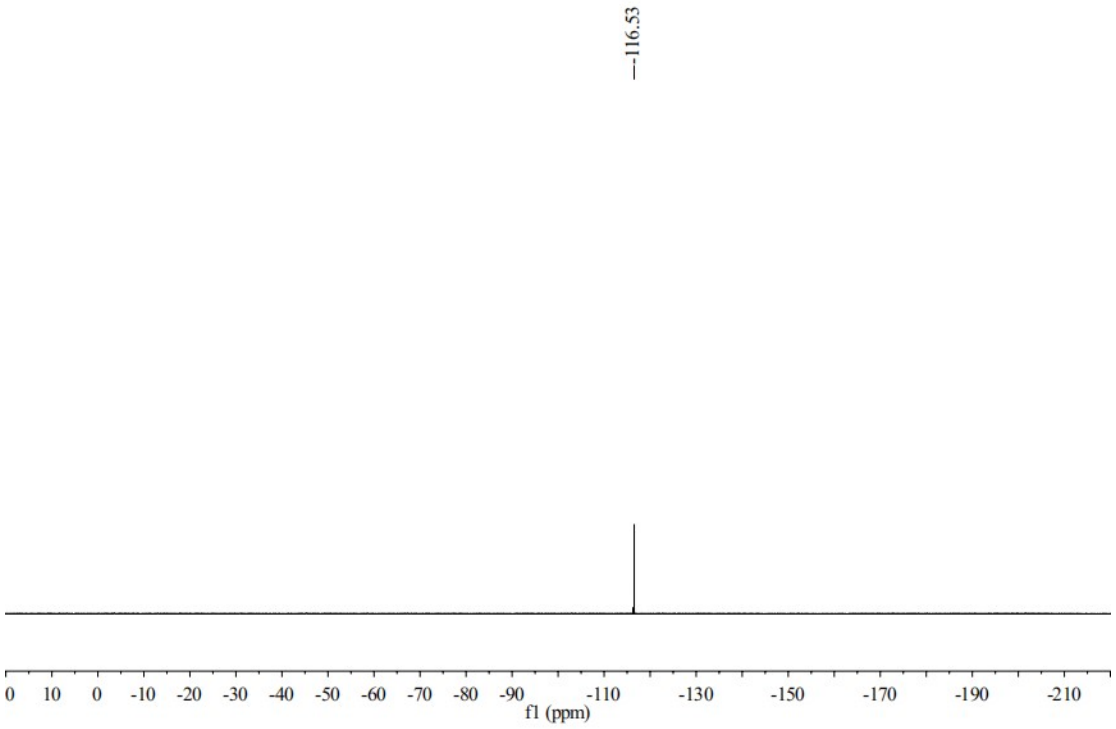
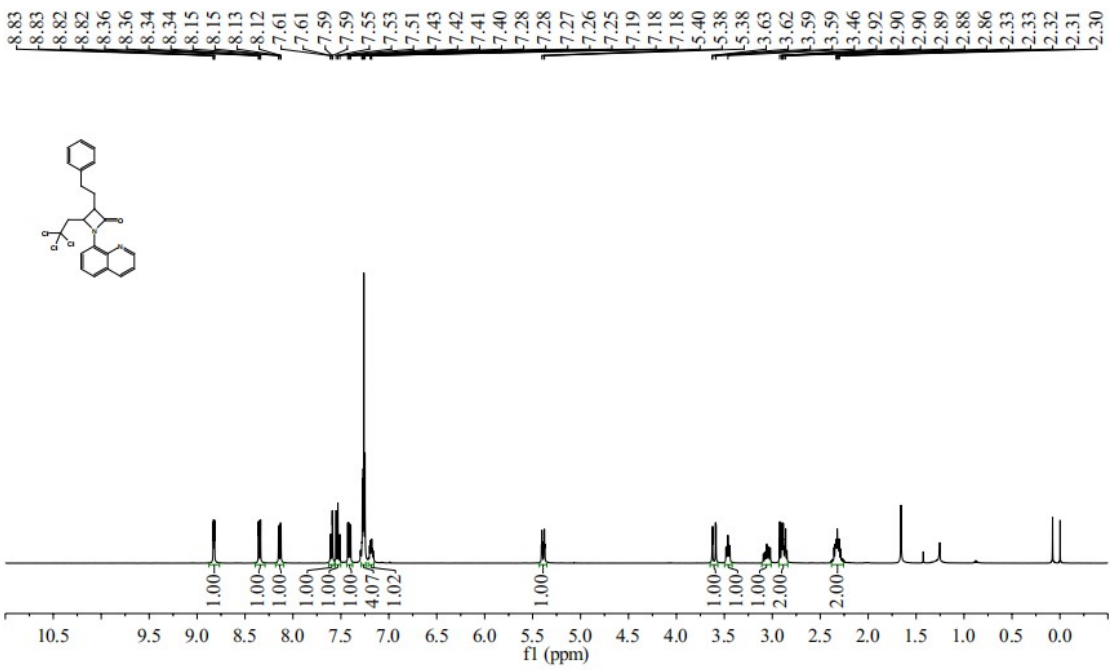

116.53
0 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)

^{1}H NMR of 2m



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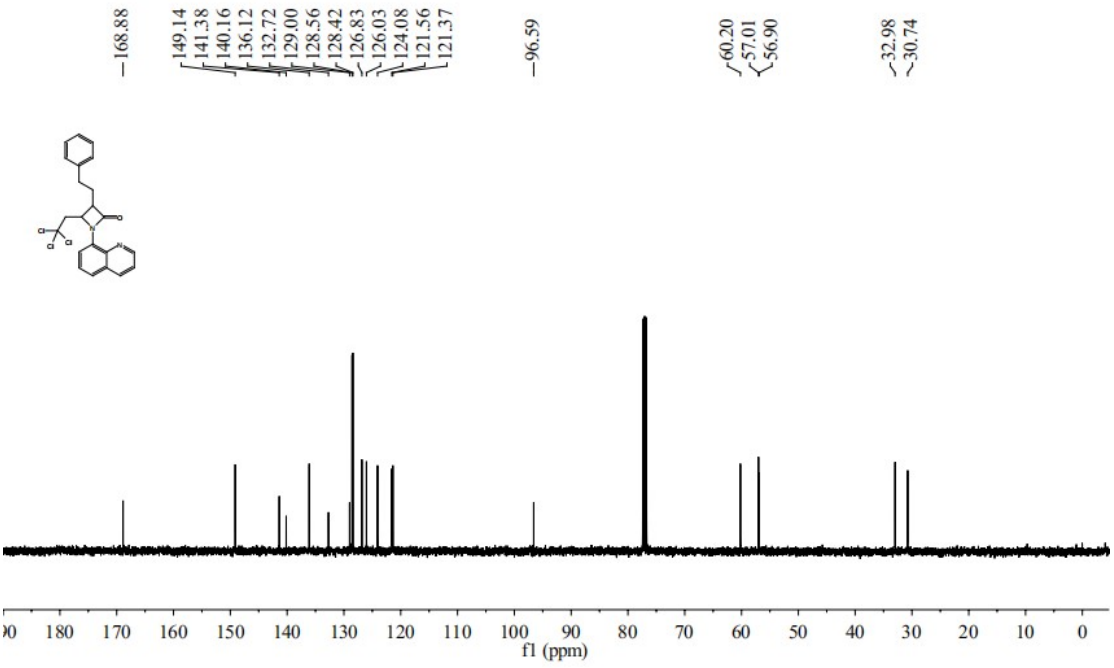
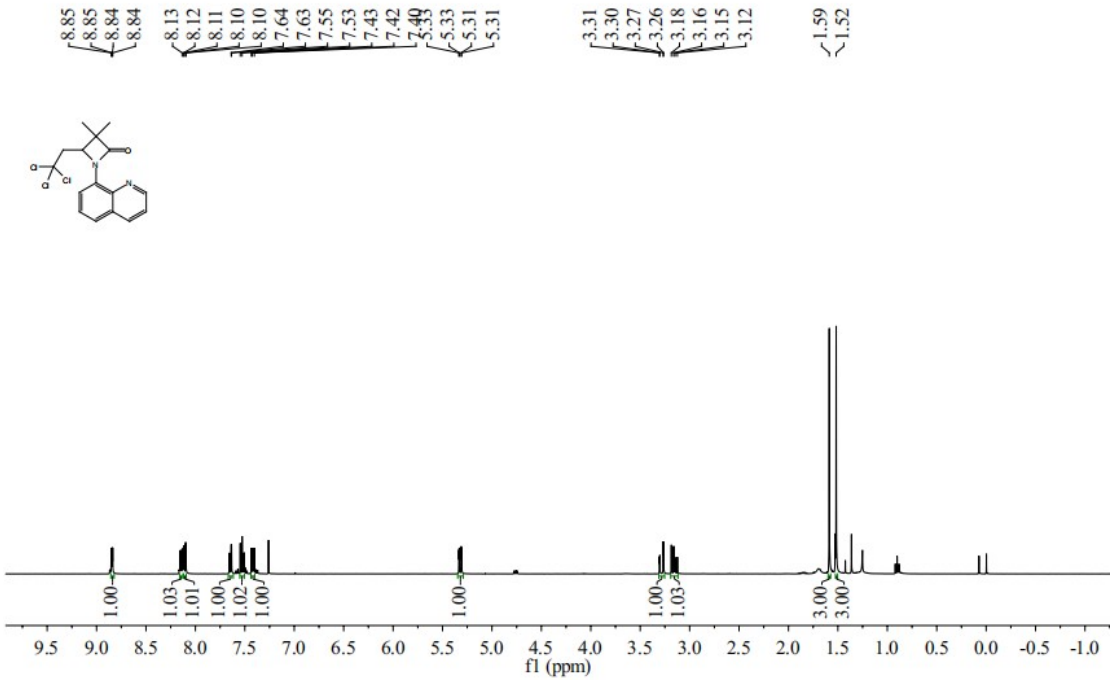
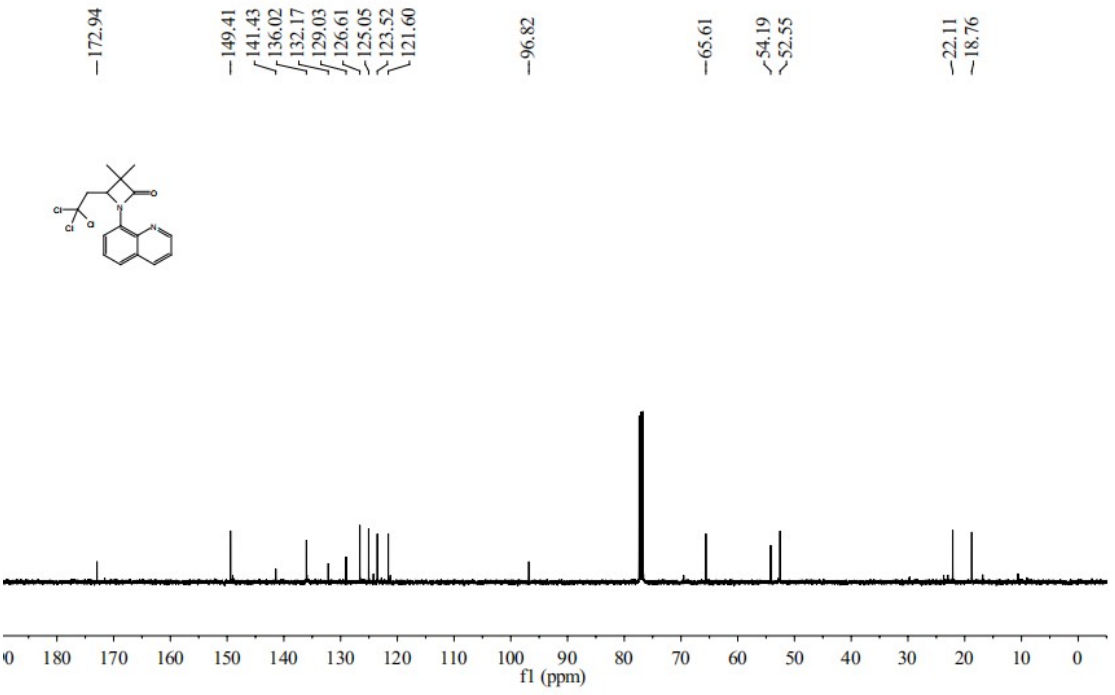


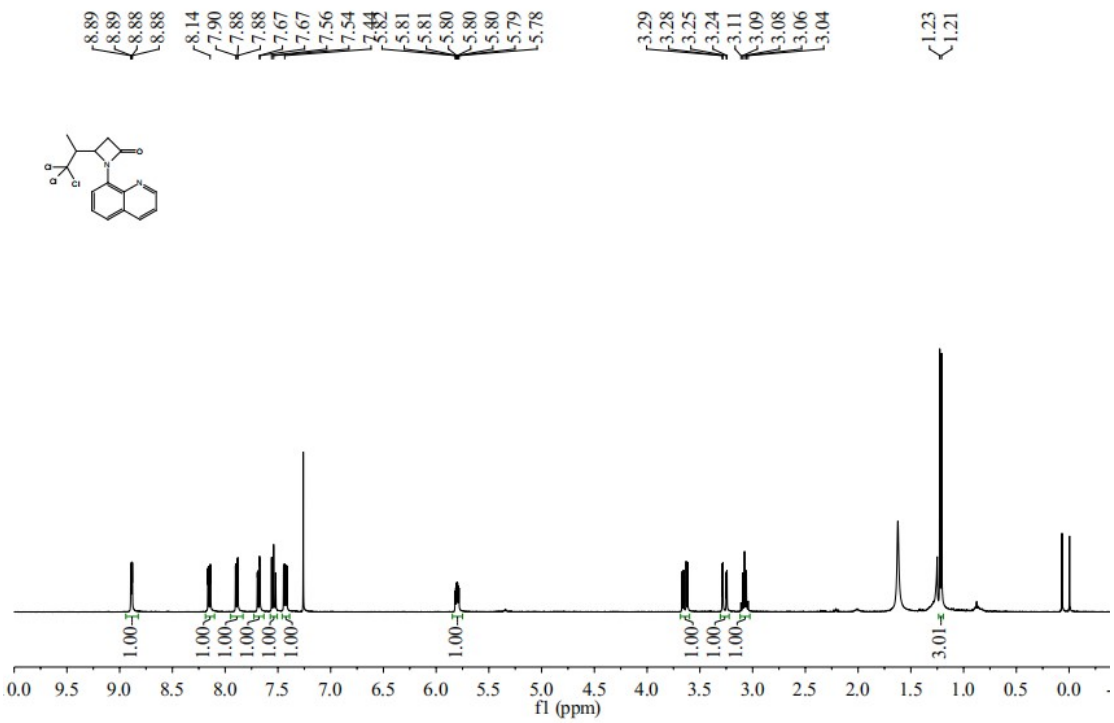
^{1}H NMR of 2n



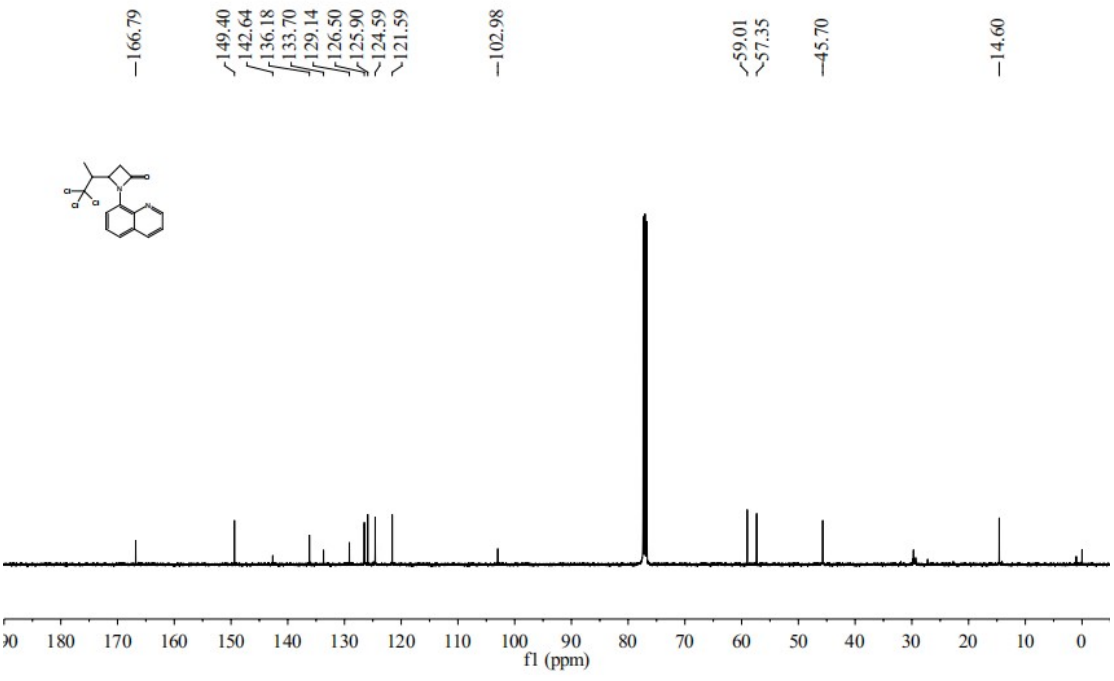
^{13}C NMR of 2n



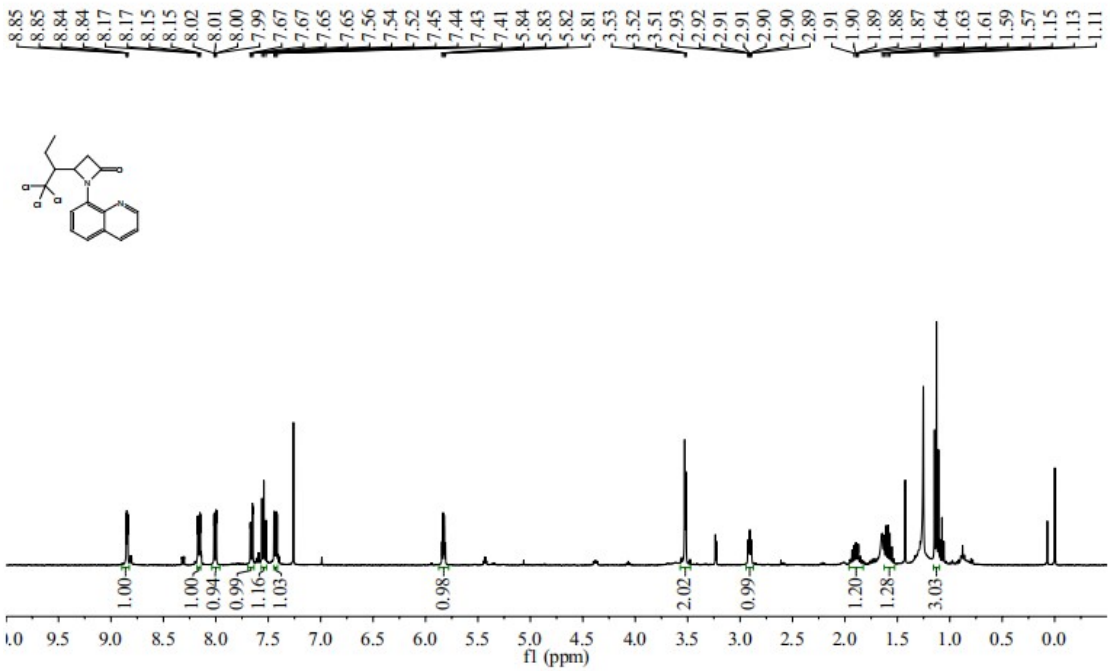
^{1}H NMR of 2o



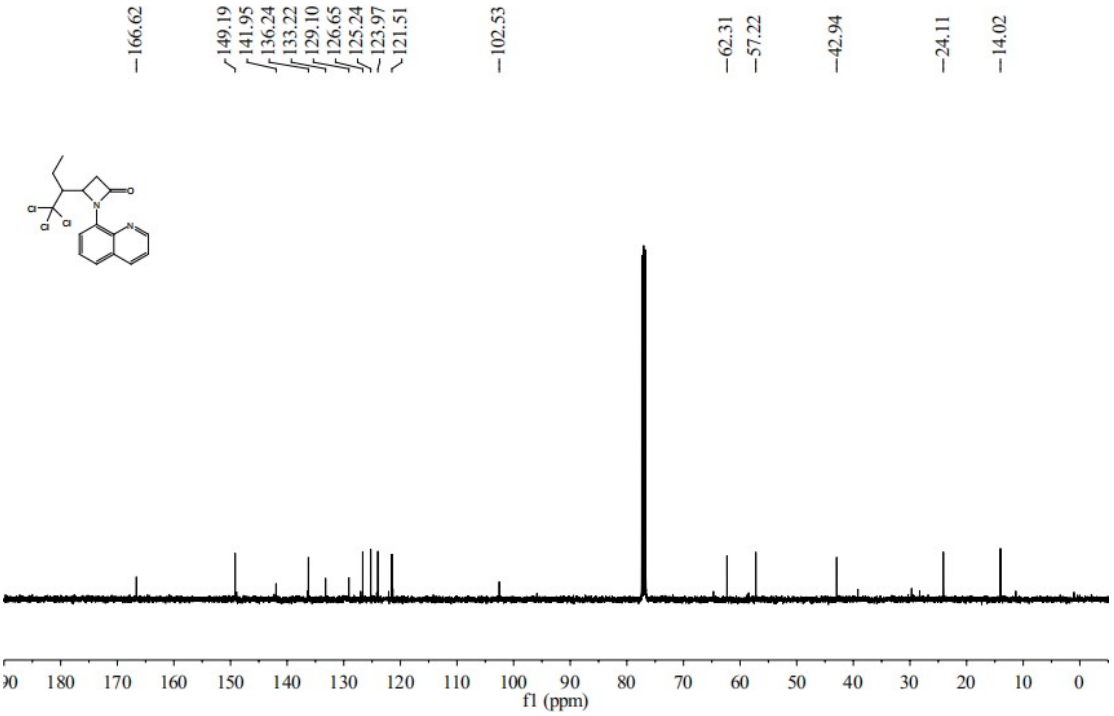
^{13}C NMR of 2o



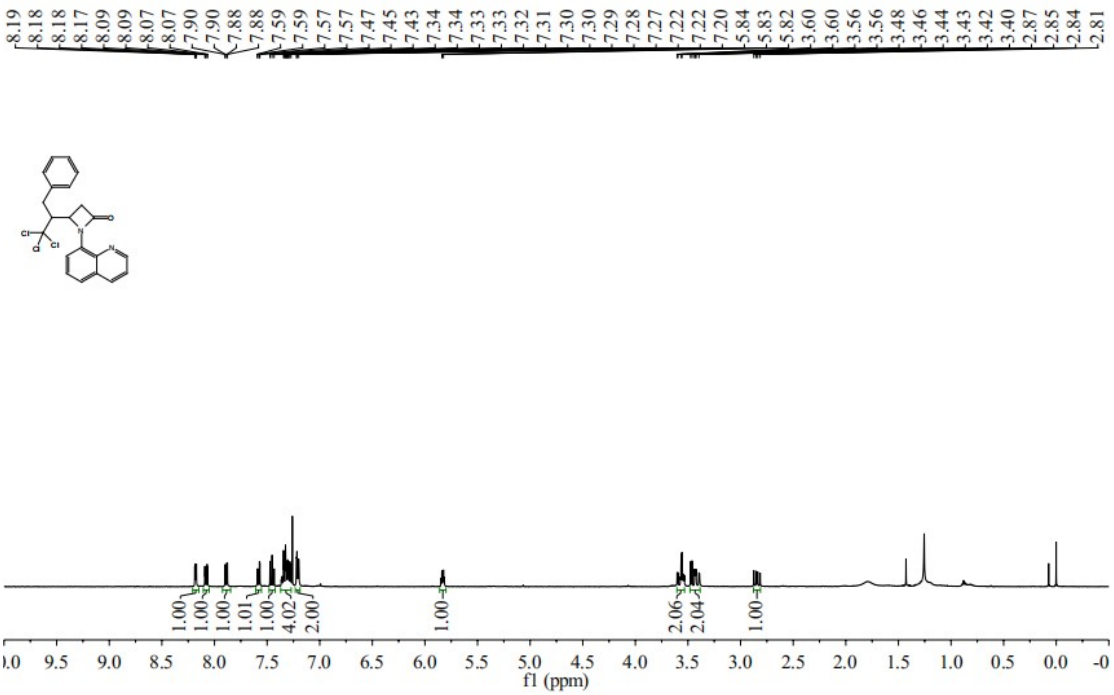
^{1}H NMR of 2p



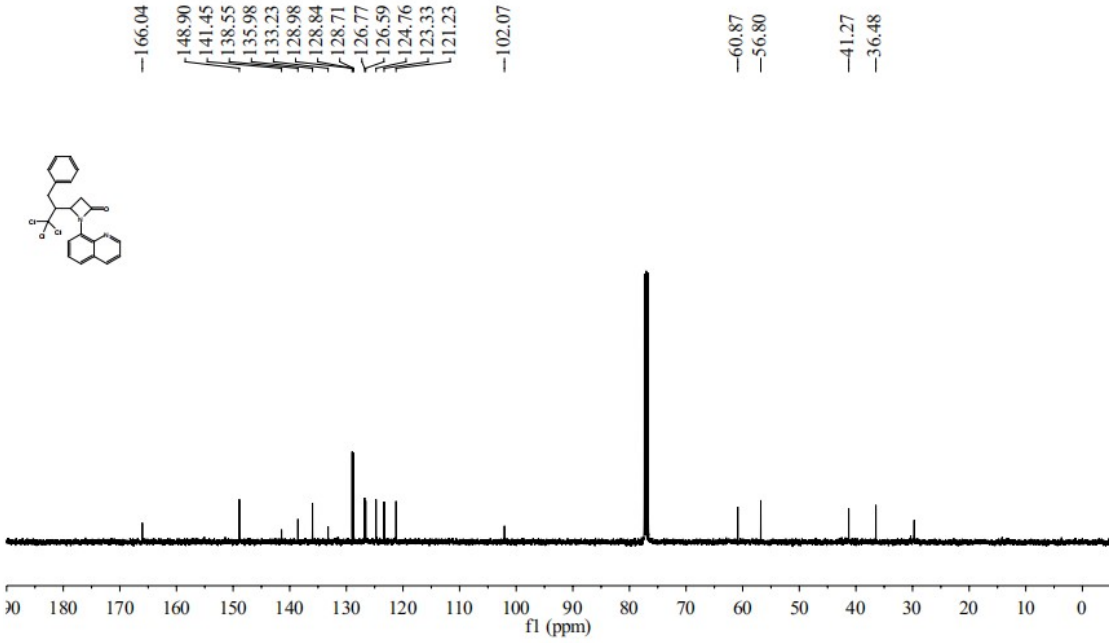
^{13}C NMR of 2p



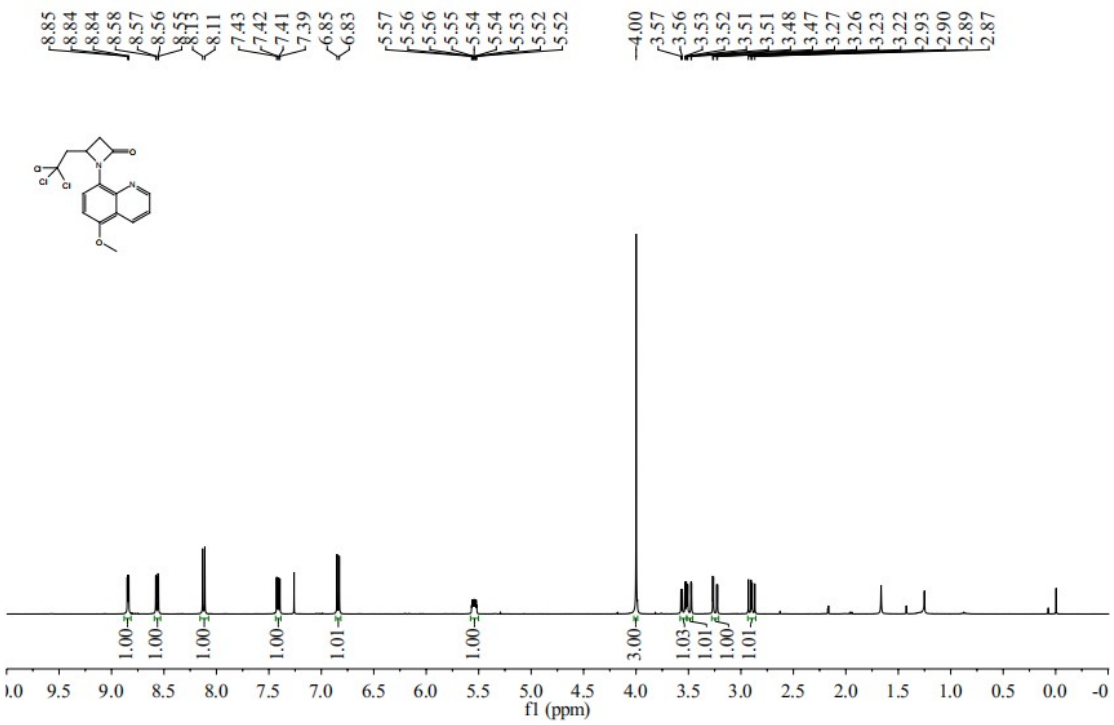
^{1}H NMR of 2q


8.19
8.18
8.18
8.17
8.09
8.09
8.07
8.07
7.90
7.90
7.88
7.88
7.59
7.59
7.57
7.57
7.47
7.45
7.43
7.34
7.34
7.33
7.33
7.32
7.31
7.30
7.30
7.29
7.28
7.27
7.22
7.22
7.20
5.84
5.83
5.82
3.60
3.60
3.56
3.56
3.48
3.46
3.44
3.43
3.42
3.40
2.87
2.85
2.84
2.81
1.00
1.00
1.00
1.01
1.00
4.02
2.00
1.00
2.06
2.04
1.00
f1 (ppm)

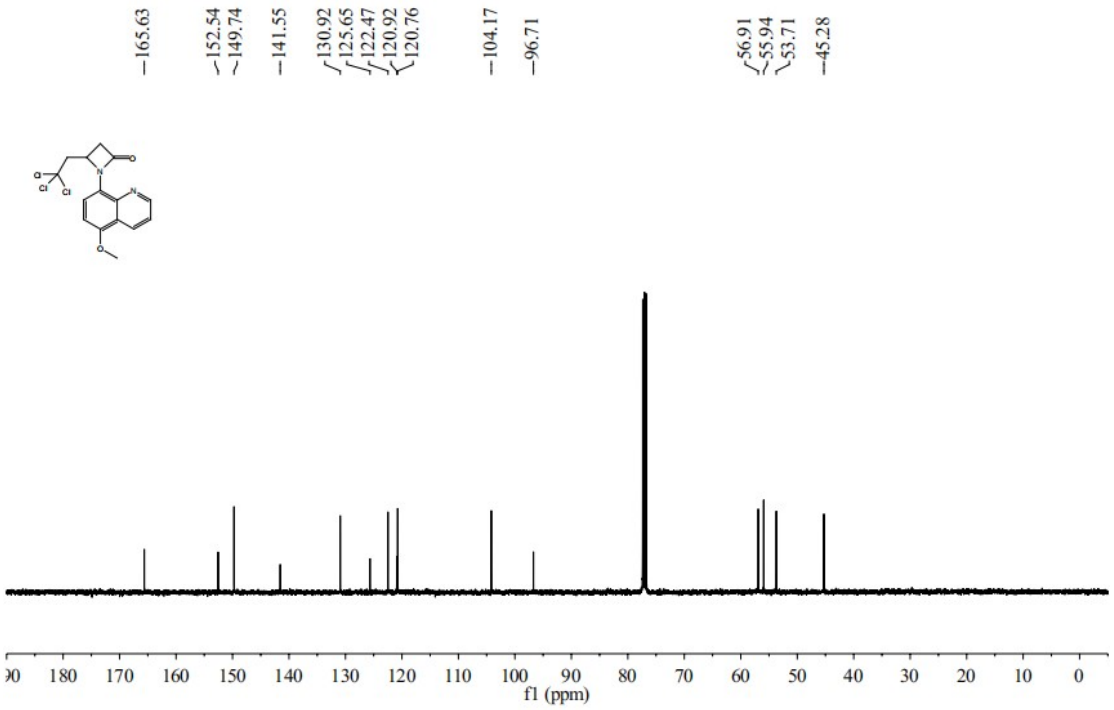
^{13}C NMR of 2q


166.04
148.90
141.45
138.55
135.98
133.23
128.98
128.84
128.71
126.77
126.59
124.76
123.33
121.23
102.07
60.87
56.80
41.27
36.48
f1 (ppm)

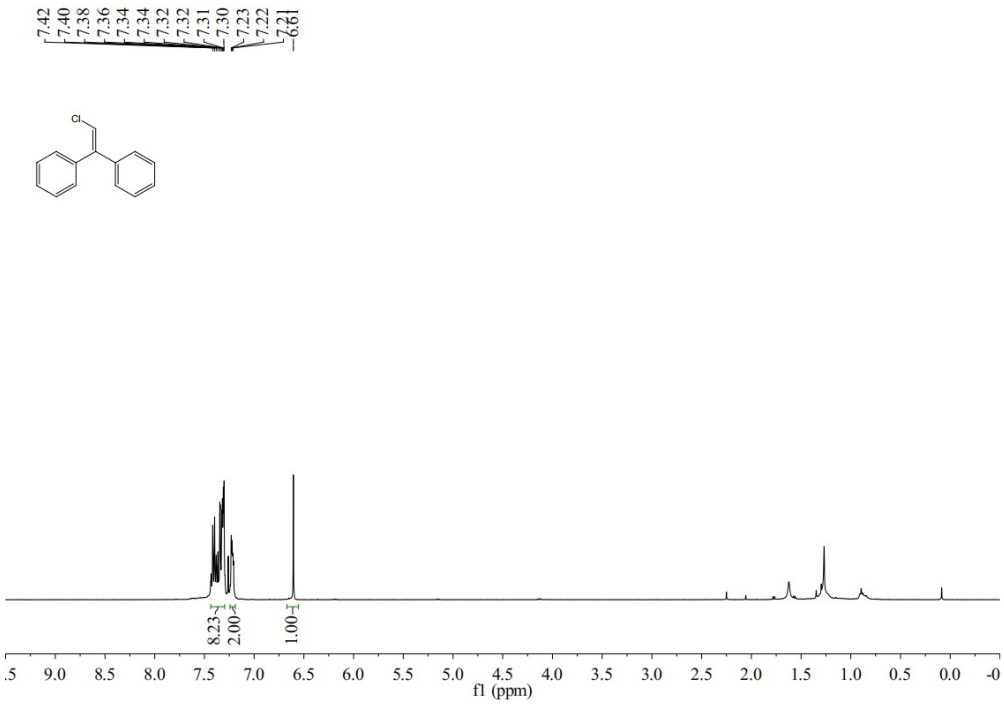
^{1}H NMR of 2r



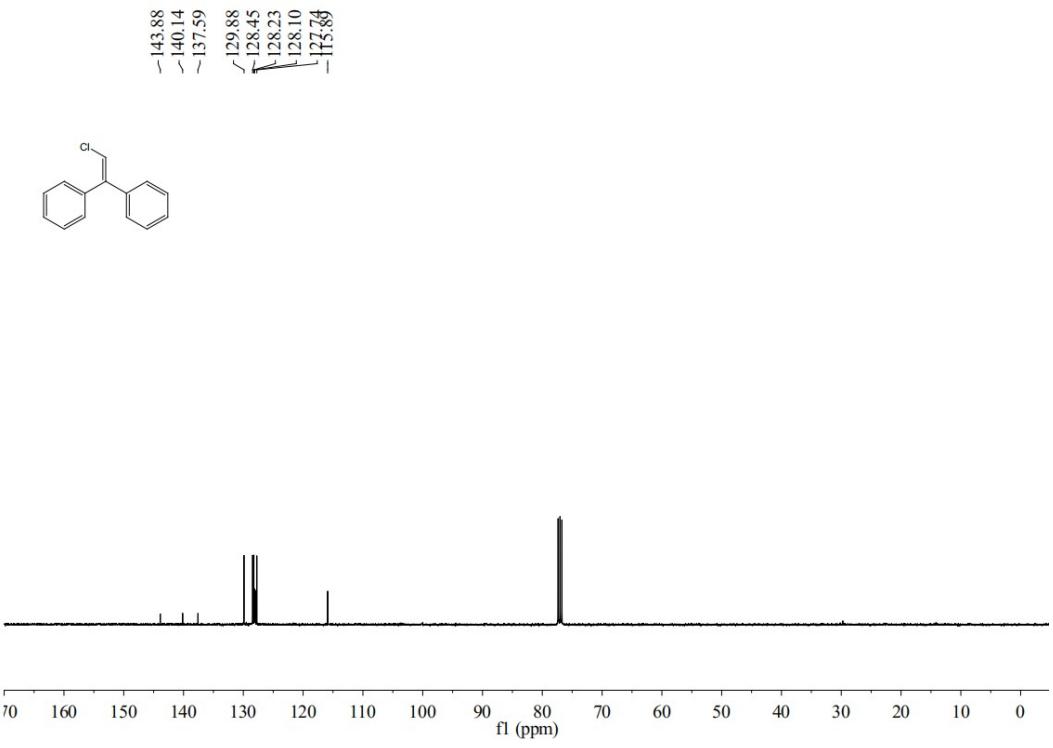
^{13}C NMR of 2r



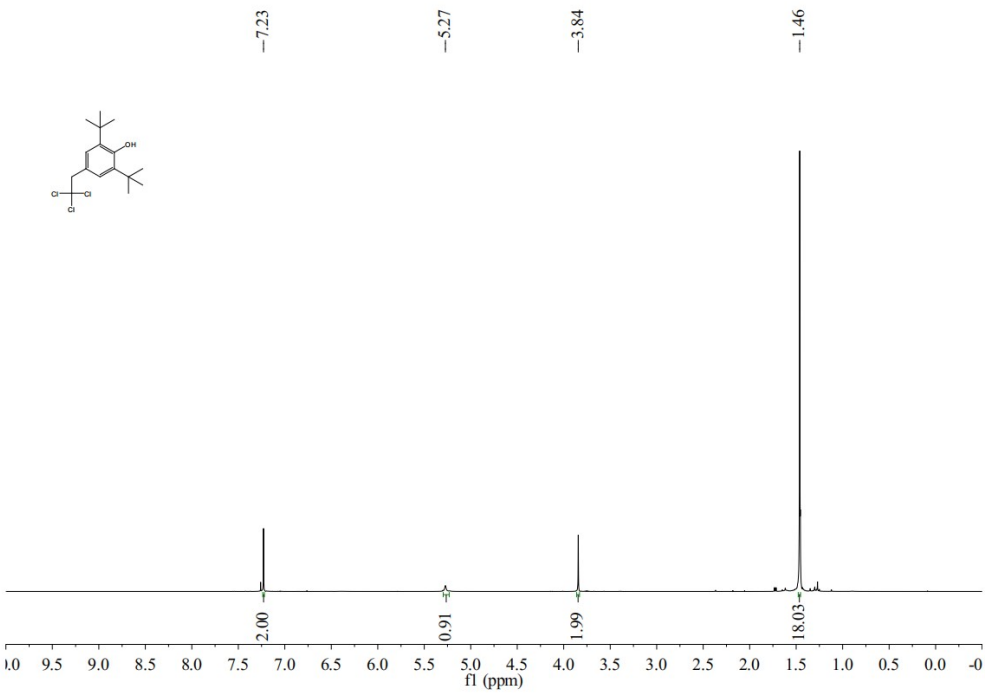
^{1}H NMR of 3



^{13}C NMR of 3



^{1}H NMR of 4



^{13}C NMR of 4