Access to Acridones by Tandem Copper(I)-Catalyzed Electrophilic Amination/Ag(I)-mediated Oxidative Annulation of Anthranils with Arylboronic Acids

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Supporting Information

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1. General information

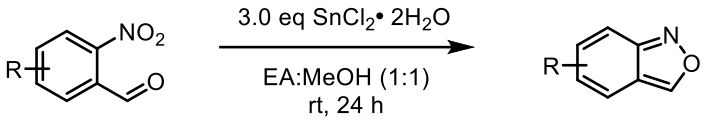
Unless otherwise noted, all reactions were carried out at room temperature under an atmosphere of nitrogen with flame-dried glassware. If reaction was not conducted at room temperature, reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The dry solvents used were purified by distillation over the drying agents indicated in parentheses and were transferred under nitrogen: THF (Na, benzophenone), Toluene (Na, benzophenone), Et_2O (Na, benzophenone), dichloromethane CaH_2). Anhydrous DMF was purchased from Acros Organics and stored under nitrogen atmosphere. Commercially available chemicals were obtained from commercial suppliers and used without further purification unless otherwise stated.

Proton NMR (^1H) were recorded at 400 MHz, and Carbon NMR (^{13}C) at 101 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, br s: broad singlet for proton spectra. Coupling constants (J) are reported in Hertz (Hz).

Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short wave UV light, or $KMnO_4$ staining solutions followed by heating. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

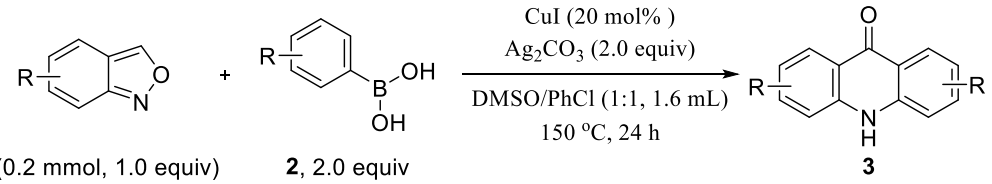
No attempts were made to optimize yields for substrate synthesis.

2. General procedure and characterization of products



To a solution of 2-nitroacylbenzene (2.0 mmol) in Ethyl acetate/Methanol 1:1 (10 mL) was added $SnCl_2 \cdot 2H_2O$ (1.35 g, 6.0 mmol). The reaction mixture was stirred at room temperature for 24 h. The reaction was quenched by saturated $NaHCO_3$, and filtered and washed with DCM. Organic layer was then washed with water and saturated brine solution, dried over MgSO4 and concentrated. Crude product was then purified by flash chromatography on silica gel using (EA/Hexane = 1:50) to give substituted anthranils **1**.[9]

General procedure A

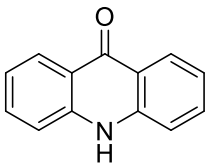


1, (0.2 mmol, 1.0 equiv) **2**, 2.0 equiv **3**

In an oven-dried Schlenk tube under air, a mixture of the substrates **1** (0.2 mmol, 1.0 equiv), boronic acid **2** (0.2 mmol, 2.0 equiv), CuI (20 mol%), Ag_2CO_3 (2.0 equiv), and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **3**.

Characterization of products

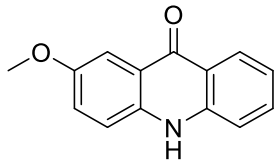
acridin-9(*10H*)-one (3aa)



Following the general procedure A, the product **3aa** was obtained in 78% yield (30.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.73 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 2H), 7.73 (t, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 177.0, 141.0, 133.7, 126.2,

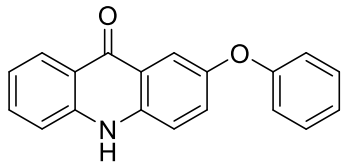
121.2, 120.6, 117.5. spectroscopic data matched those previously reported in the literature.[1]

2-methoxyacridin-9(*10H*)-one (3ab)



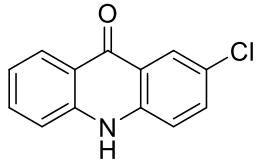
Following the general procedure A, the product **3ab** was obtained in 34% yield (15.3 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.72 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.63 (d, *J* = 2.2 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.41 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.3, 154.2, 140.6, 135.9, 133.2, 126.1, 124.5, 121.1, 120.9, 119.8, 119.4, 117.5, 105.0, 55.9. spectroscopic data matched those previously reported in the literature.[1]

2-phenoxyacridin-9(*10H*)-one (3ac)



Following the general procedure A, the product **3ac** was obtained in 84% yield (48.5 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.86 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 7.1 Hz, 1H), 7.65 (dd, *J* = 9.0, 5.8 Hz, 2H), 7.55 (dd, *J* = 8.9, 3.2 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.3, 157.1, 151.2, 140.9, 137.4, 133.65, 130.4, 126.6, 126.1, 123.8, 121.3, 121.2, 119.9, 119.9, 118.9, 117.6, 112.9. ESI-MS: calculated $C_{19}H_{14}NO_2$ $[M+H]^+$ 288.1019; Found 288.1017.

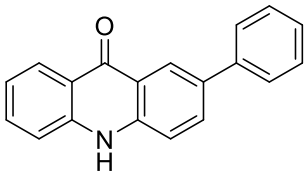
2-chloroacridin-9(*10H*)-one (3ad)



Following the general procedure A, the product **3ad** was obtained in 58% yield (26.6 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.92 (s, 1H), 8.22 (dd, *J* = 8.1, 1.1 Hz, 1H), 8.15 (d, *J* = 2.5 Hz, 1H), 7.75 (dd, *J* = 8.8, 2.6 Hz, 2H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.25 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 175.9, 140.9, 139.6, 133.9, 133.6, 126.1, 125.5,

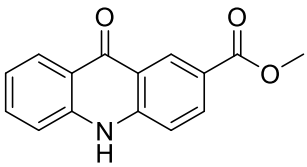
124.8, 121.6, 121.3, 120.4, 119.9, 117.7. spectroscopic data matched those previously reported in the literature.[3]

2-phenylacridin-9(*10H*)-one (3ae)



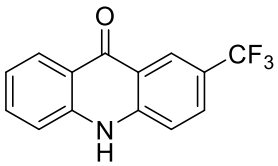
Following the general procedure A, the product **3ae** was obtained in 43% yield (23.2 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.86 (s, 1H), 8.48 (d, *J* = 2.2 Hz, 1H), 8.32 – 8.21 (m, 1H), 8.09 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.79 – 7.73 (m, 3H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.32 – 7.25 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.9, 140.9, 140.4, 139.5, 133.7, 133.0, 132.3, 129.2, 127.4, 126.6, 126.2, 123.4, 121.3, 120.8, 120.6, 118.4, 117.6. spectroscopic data matched those previously reported in the literature.[1]

methyl 9-oxo-9,10-dihydroacridine-2-carboxylate (3af)



Following the general procedure A, the product **3af** was obtained in 88% yield (45 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 12.06 (s, 1H), 8.84 (d, *J* = 2.0 Hz, 1H), 8.22 (ddd, *J* = 10.8, 8.4, 1.6 Hz, 2H), 7.78 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.59 (dd, *J* = 14.7, 8.5 Hz, 2H), 7.36 – 7.29 (m, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.7, 165.9, 143.8, 140.9, 134.2, 133.1, 128.8, 126.2, 122.2, 121.9, 121.0, 119.8, 118.0, 117.8, 52.2. spectroscopic data matched those previously reported in the literature.[4]

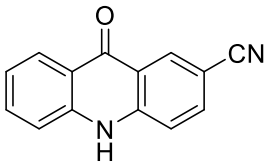
2-(trifluoromethyl)acridin-9(*10H*)-one (3ag)



Following the general procedure A, the product **3ag** was obtained in 38% yield (20.5 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.11 (s, 1H), 8.48 (s, 1H), 8.25 (d, *J* = 7.9 Hz, 1H), 8.00 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H),

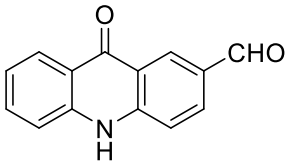
7.34 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 176.5, 143.0, 140.9, 134.4, 129.3 (q, *J* = 3.1 Hz), 126.1, 124.5 (q, *J* = 269.2 Hz), 123.8 (q, *J* = 4.2 Hz), 122.3, 121.2 (q, *J* = 32.6 Hz), 120.9, 119.5, 119.1, 117.8. ^{19}F NMR (376 MHz, DMSO-*d*6) δ -60.2. spectroscopic data matched those previously reported in the literature.[3]

9-oxo-9,10-dihydroacridine-2-carbonitrile (3ah)



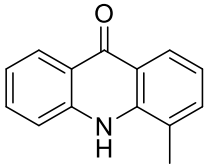
Following the general procedure A, the product **3ah** was obtained in 49% yield (21.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 12.19(s, 1H), 8.56 (s, 1H), 8.24 (d, *J* = 8.1 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.1, 143.3, 140.8, 135.2, 134.6, 132.3, 126.3, 122.7, 121.1, 120.1, 119.1, 119.1, 118.0, 103.1. spectroscopic data matched those previously reported in the literature.[1]

9-oxo-9,10-dihydroacridine-2-carbaldehyde (3ai)



Following the general procedure A, the product **3ai** was obtained in 45% yield (20.1 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 12.16 (s, 1H), 10.04 (s, 1H), 8.78 (s, 1H), 8.26 (d, *J* = 8.1 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 191.9, 177.0, 144.8, 140.8, 134.4, 132.2, 131.2, 129.5, 126.3, 122.6, 121.3, 120.0, 118.6, 118.0.

4-methylacridin-9(10*H*)-one (3aj)

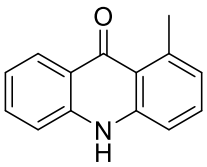


Following the general procedure A, the product **3aj** was obtained in 48% yield (20.8 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 10.59 (s, 1H), 8.22 (dd, *J* = 8.1, 1.4 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.73 (ddd, *J* = 8.5, 6.9, 1.6 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 1H), 7.29 – 7.25 (m, 1H),

7.19 – 7.15 (m, 1H), 2.60 (s, 3H).[13]C NMR (101 MHz, DMSO-*d*6) δ 177.2, 141.2, 139.6, 134.2, 133.3, 125.8, 125.4, 124.0, 121.4, 120.8, 120.8, 120.4, 118.3, 17.9. spectroscopic data matched those previously reported in the literature.[4]

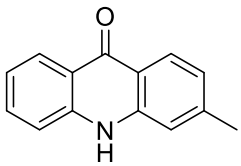
1-methylacridin-9(10*H*)-one (3ak) and 3-methylacridin-9(10*H*)-one (3ak')

1-methylacridin-9(10*H*)-one (3ak)



Following the general procedure A, the product **3ak** was obtained in 56% yield (23.5 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). [1]H NMR (500 MHz, DMSO-*d*6) δ 11.55 (s, 1H), 8.17 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.67 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.52 (dd, *J* = 8.2, 7.3 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.22 – 7.18 (m, 1H), 6.95 (d, *J* = 7.1 Hz, 1H), 2.87 (s, 3H). [13]C NMR (101 MHz, DMSO-*d*6) δ 179.0, 142.7, 140.6, 140.3, 133.2, 132.6, 126.3, 123.7, 121.9, 120.9, 119.1, 116.9, 115.6, 23.9. spectroscopic data matched those previously reported in the literature.[1]

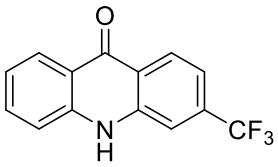
3-methylacridin-9(10*H*)-one (3ak')



Following the general procedure A, the product **3ak'** was obtained in 25% yield (10.6 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). [1]H NMR (400 MHz, DMSO-*d*6) δ 11.61 (s, 1H), 8.21 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.30 (s, 1H), 7.23 (t, *J* = 7.0 Hz, 1H), 7.08 (dd, *J* = 8.3, 1.1 Hz, 1H), 2.46 (s, 3H). [13]C NMR (101 MHz, DMSO-*d*6) δ 176.6, 144.0, 141.2, 141.0, 133.4, 126.2, 126.1, 123.0, 121.0, 120.7, 118.7, 117.4, 116.7, 21.7. spectroscopic data matched those previously reported in the literature.[1]

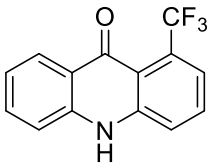
1-(trifluoromethyl)acridin-9(10*H*)-one (3al) and 3-(trifluoromethyl)acridin-9(10*H*)-one (3al')

3-(trifluoromethyl)acridin-9(10*H*)-one (3al)



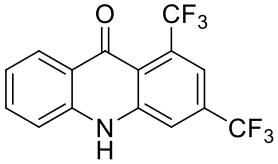
Following the general procedure A, the product **3al** was obtained in 41% yield (21.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.04 (s, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 7.88 (s, 1H), 7.79 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.52 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.37 – 7.25 (m, 1H). ^{3}C NMR (101 MHz, DMSO) δ 176.4, 141.0, 140.5, 134.3, 132.8 (q, *J* = 31.9 Hz), 128.0, 126.1, 123.8 (q, *J* = 272.8 Hz), 122.3, 122.0, 120.9, 117.7, 116.5 (q, *J* = 3.3 Hz), 114.9 (q, *J* = 4.4 Hz). ^{19}F NMR (376 MHz, DMSO-*d*6) δ -61.81. ESI-MS: calculated $C_{14}H_9F_3NO$ $[M+H]^+$ 264.0631; Found 264.0639.

1-(trifluoromethyl)acridin-9(10*H*)-one (3al')



Following the general procedure A, t the product **3al'** was obtained in 16% yield (8.2 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 11.87 (s, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 7.90 – 7.82 (m, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.64 (dd, *J* = 12.7, 3.8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 175.0, 142.9, 139.8, 133.8, 132.4, 127.4 (q, *J* = 31.9 Hz), 126.3, 124.2 (q, *J* = 272.9 Hz), 123.3, 121.9, 120.9 (q, *J* = 7.9 Hz), 119.2, 117.1, 116.5. ^{19}F NMR (376 MHz, DMSO-*d*6) δ -56.69. ESI-MS: calculated $C_{14}H_9F_3NO$ $[M+H]^+$ 264.0631; Found 264.0640.

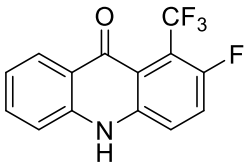
1,3-bis(trifluoromethyl)acridin-9(10*H*)-one (3am)



Following the general procedure A, the product **3am** was obtained in 40% yield (17.9 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.32 (s, 1H), 8.26 – 8.19 (m, 2H), 7.82 (dd, *J* = 14.5, 5.9 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 174.5, 142.8, 139.8, 134.4, 131.5 (q, *J* = 33.2 Hz), 129.5 (q, *J* = 33.1 Hz), 126.3, 125.7 (q, *J* = 272.8 Hz), 122.96 (q, *J* = 272.6 Hz), 122.8, 122.3, 120.9 (q, *J* = 5.2 Hz), 118.4, 117.4, 115.7 (q, *J* = 7.3 Hz). ^{19}F NMR (376 MHz, DMSO-*d*6) δ -57.3, -62.4. ESI-MS: calculated $C_{15}H_8F_6NO$ $[M+H]^+$ 332.0505; Found 332.0501.

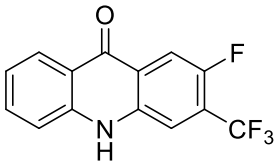
2-fluoro-1-(trifluoromethyl)acridin-9(10*H*)-one (3an) and 2-fluoro-3-(trifluoromethyl)acridin-9(10*H*)-one (3an')

2-fluoro-1-(trifluoromethyl)acridin-9(10*H*)-one (3an)



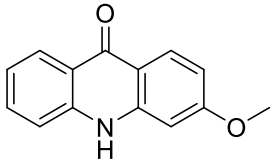
Following the general procedure A, the product **3an** was obtained in 26% yield (14.8 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.03 (s, 1H), 8.16 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.87 (dd, *J* = 9.3, 4.3 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.27 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 175.3, 155.3 (d, *J* = 254.5 Hz), 139.6, 139.5, 133.9, 126.2, 125.7 (d, *J* = 10.5 Hz), 123.9, 123.6, 123.3 (d, *J* = 273.2 Hz), 122.2, 121.6, 117.1, 116.7. ^{19}F NMR (376 MHz, DMSO-*d*6) δ -51.7 (d, *J* = 41.8 Hz), -115.9 (m, *J* = 46.8, 41.6, 12.1, 4.6 Hz). ESI-MS: calculated $C_{14}H_8F_4NO$ $[M+H]^+$ 282.0537; Found 282.0544.

2-fluoro-3-(trifluoromethyl)acridin-9(10*H*)-one (3an')



Following the general procedure A, the product **3an'** was obtained in 18% yield (10.2 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.14 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 11.0 Hz, 1H), 7.95 (d, *J* = 5.8 Hz, 0H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 175.7, 141.0, 136.9, 134.5, 126.0, 123.2, 122.2, 120.0, 119.5 (q, *J* = 269.8 Hz), 117.9 (d, *J* = 5.1 Hz), 117.8, 116.4 (q, *J* = 36.2 Hz), 113.8 (d, *J* = 261.3 Hz), 112.6 (d, *J* = 21.0 Hz). ESI-MS: calculated $C_{14}H_8F_4NO$ $[M+H]^+$ 282.0537; Found 282.0546.

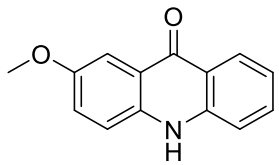
3-methoxyacridin-9(10*H*)-one (3ba)



Following the general procedure A, the product **3ba** was obtained in 52% yield (23.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.60 (s, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.9 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.92 – 6.83 (m, 2H).

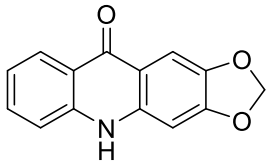
^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.0, 163.5, 143.0, 141.1, 133.2, 128.2, 126.1, 121.1, 120.8, 117.2, 115.1, 111.7, 98.0, 55.6. spectroscopic data matched those previously reported in the literature.[2]

2-methoxyacridin-9(10*H*)-one (3ab)



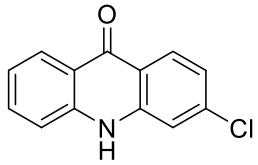
Following the general procedure A, the product **3ab** was obtained in 40% yield (17.9 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.72 (s, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.63 (d, *J* = 2.2 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.41 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.3, 154.2, 140.6, 135.9, 133.2, 126.1, 124.5, 121.1, 120.9, 119.8, 119.4, 117.5, 105.0, 55.9. spectroscopic data matched those previously reported in the literature.[1]

[1,3]dioxolo[4,5-b]acridin-10(5*H*)-one (3ca)



Following the general procedure A, the product **3ca** was obtained in 30% yield (14.5 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.68 (s, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 6.15 (s, 2H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 175.2, 152.8, 143.9, 140.3, 138.6, 132.7, 125.9, 121.2, 120.1, 117.2, 115.5, 102.2, 102.2, 95.9. spectroscopic data matched those previously reported in the literature.[1]

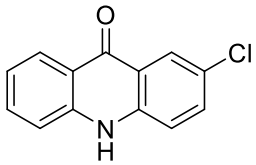
3-chloroacridin-9(*10H*)-one (3da)



Following the general procedure A, the product **3da** was obtained in 45% yield (20.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.81 (s, 1H), 8.21 (d, *J* = 8.6 Hz, 2H), 7.77 – 7.73 (m, 1H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.31 – 7.24 (m, 2H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.3, 141.7, 140.9, 138.2, 134.0, 128.5, 126.1, 121.7, 121.5, 120.8, 119.2, 117.6, 116.4.

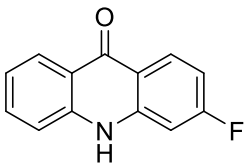
spectroscopic data matched those previously reported in the literature.[4]

2-chloroacridin-9(*10H*)-one (3ad)



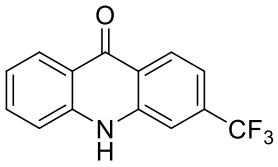
Following the general procedure A, the product **3ad** was obtained in 57% yield (26.4 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (400 MHz, DMSO-*d*6) δ 11.92 (s, 1H), 8.22 (dd, *J* = 8.1, 1.1 Hz, 1H), 8.15 (d, *J* = 2.5 Hz, 1H), 7.75 (dd, *J* = 8.8, 2.6 Hz, 2H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.25 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 175.9, 140.9, 139.6, 133.9, 133.6, 126.1, 125.5, 124.8, 121.6, 121.3, 120.4, 119.9, 117.7. spectroscopic data matched those previously reported in the literature.[3]

3-fluoroacridin-9(*10H*)-one (3ea)



Following the general procedure A, the product **3ea** was obtained in 47% yield (20 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 11.81 (s, 1H), 8.28 (dd, *J* = 8.7, 6.7 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.31 – 7.21 (m, 2H), 7.10 (dd, *J* = 8.6, 6.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.1, 165.2 (d, *J* = 249.6 Hz), 142.5 (d, *J* = 13.1 Hz), 141.1, 133.8, 129.7 (d, *J* = 11.4 Hz), 126.1, 121.6, 120.6, 117.7, 117.3, 110.1 (d, *J* = 23.7 Hz), 102.3 (d, *J* = 24.9 Hz). ^{19}F NMR (376 MHz, DMSO-*d*6) δ -60.2. spectroscopic data matched those previously reported in the literature.[2]

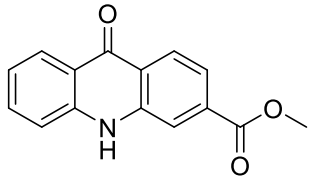
3-(trifluoromethyl)acridin-9(10*H*)-one (3al)



Following the general procedure A, the product **3al** was obtained in 45% yield (23.6 mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 12.03 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.29 – 8.21 (m, 1H), 7.88 (s, 1H), 7.83 – 7.76 (m, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.51 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.32 (dd, *J* = 11.1, 4.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 176.4, 141.0, 140.5, 134.3, 132.8 (q, *J* = 31.8

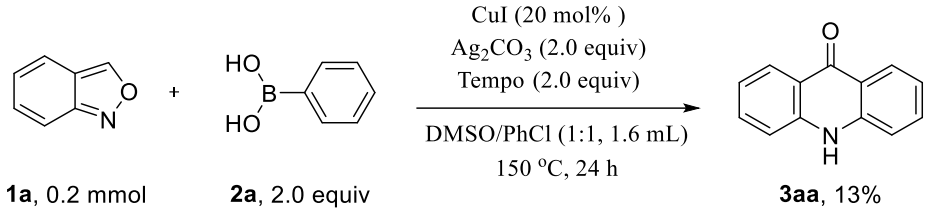
Hz), 128.1, 126.2, 123.8 (q, J = 272.9 Hz), 122.4, 122.0, 120.9, 117.7, 116.5 (q, 3.2 Hz), 114.9 (q, J = 4.3 Hz). ^{19}F NMR (376 MHz, DMSO-*d*6) δ -61.8. ESI-MS: calculated $C_{14}H_9F_3NO$ $[M+H]^+$ 264.0631; Found 264.0640.

methyl 9-oxo-9,10-dihydroacridine-3-carboxylate (3fa)



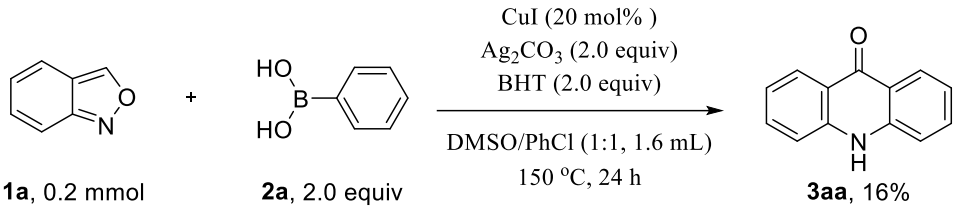
Following the general procedure A, the product **3fa** was obtained in 23% yield (12.2mg, 0.20 mmol) as a yellow solid after chromatography on silica gel (eluent = etroleum ether/EtOAc 4:1 v/v). ^{1}H NMR (500 MHz, DMSO-*d*6) δ 11.96 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.25 – 8.22 (m, 1H), 8.19 (d, J = 1.2 Hz, 1H), 7.77 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.72 (dd, J = 8.4, 1.5 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.32 – 7.26 (m, 1H), 3.93 (s, 5H). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.8, 165.9, 141.3, 140.7, 134.3, 133.7, 127.1, 126.3, 122.9, 121.9, 121.0, 120.5, 119.4, 117.8, 52.9. spectroscopic data matched those previously reported in the literature.[5]

3. Mechanistic Studies



1a, 0.2 mmol **2a**, 2.0 equiv **3aa**, 13%

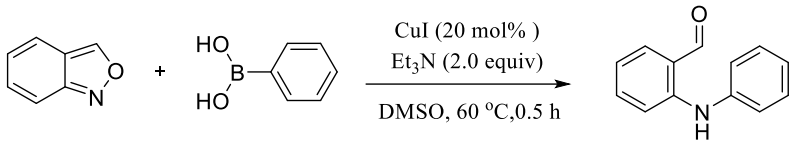
In an oven-dried Schlenk tube under air, a mixture of the substrates **1a** (0.2 mmol, 1.0 equiv), boronic acid **2a** (2.0 mmol, 2.0 equiv), CuI (20 mol%), Ag_2CO_3 (2.0 equiv), Tempo (2.0 equiv) and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was then diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 4:1) to give **3aa** (5.1 mg, 13%).



1a, 0.2 mmol **2a**, 2.0 equiv **3aa**, 16%

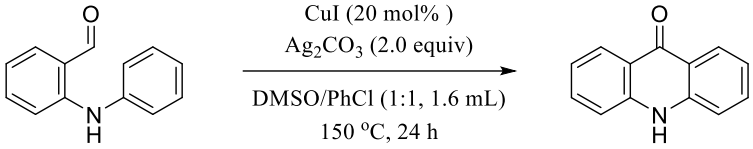
In an oven-dried Schlenk tube under air, a mixture of the substrates **1a** (0.2 mmol, 1.0 equiv), boronic acid **2a** (2.0 mmol, 2.0 equiv), CuI (20 mol%), Ag_2CO_3 (2.0 equiv), BHT (2.0 equiv) and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was then diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 4:1) to give **3aa** (6.2 mg, 16%).

4. Control experiment



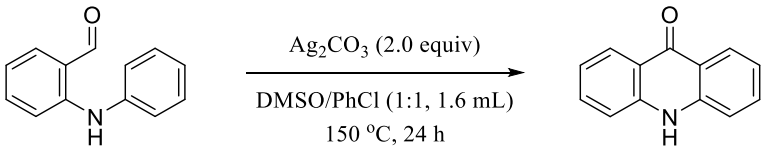
1a, 5.0 mmol **2a**, 2.0 equiv **4a**, 476.5 mg, 48%

In an oven-dried Schlenk tube under air, a mixture of the substrates **1a** (5.0 mmol, 1.0 equiv), boronic acid **2a** (10.0 mmol, 2.0 equiv), CuI (20 mol%), Et_3N (2.0 equiv), and DMSO was stirred at 60 °C for 0.5 h. Then the reaction mixture was then diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 100:1) to give **4a** (476.5 mg, 48%).



4a, 0.2 mmol **3aa**, 75%

In an oven-dried Schlenk tube under air, a mixture of the substrates **4a** (0.2 mmol, 1.0 equiv), CuI (20 mol%), Ag_2CO_3 (2.0 equiv), and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was then diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 4:1) to give **3aa** (29.3 mg, 75%).



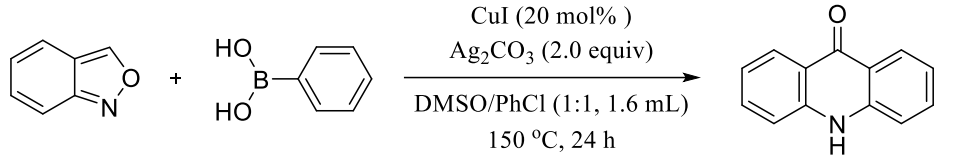
4a, 0.2 mmol **3aa**, 79%

In an oven-dried Schlenk tube under air, a mixture of the substrates **4a** (0.2 mmol, 1.0 equiv), Ag_2CO_3 (2.0 equiv), and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was then diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The

pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 4:1) to give **3aa** (30.9 mg, 79%).

5. Synthetic application of the product

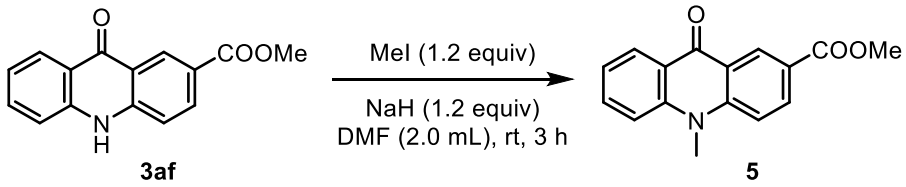
5.1 Gram- Scale Synthesis



1a, 1.0 mmol **2a**, 2.0 equiv **3aa**, 100.8 mg, 52%

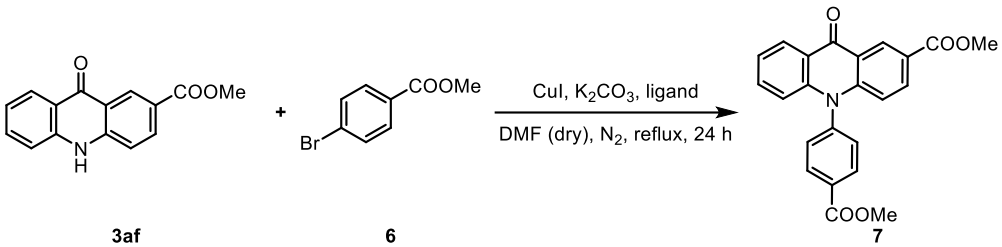
In an oven-dried Schlenk tube under air, a mixture of the substrates **1a** (1.0 mmol, 1.0 equiv), boronic acid **2a** (2.0 mmol, 2.0 equiv), CuI (20 mol%), Ag_2CO_3 (2.0 equiv), and DMSO/PhCl (1:1, 1.6 mL) was stirred at 150 °C for 24 h. Then the reaction mixture was diluted with CH_2Cl_2 and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 again. The organic layers were combined, washed with brine and dried over Na_2SO_4. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product (petroleum ether : ethyl acetate = 4:1) to give **3aa** (100.8 mg, 52%).

5.2 Synthetic application of the product



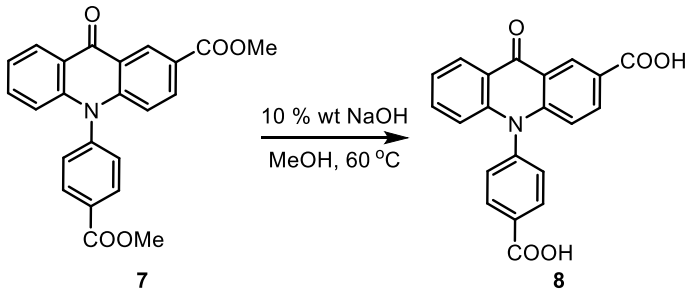
3af **5**

To a solution of methyl 9-oxo-9,10-dihydroacridine-2-carboxylate (101.3 mg, 0.4 mmol) and DMF (2 mL) was added NaH (1.2 eq, 60% oil dispersion) at 0 °C under the nitrogen atmosphere, then the temperature rose to rt, the mixture was stirred for 30 min. MeI (1.2 eq) was added, and the mixture was continuously stirred at rt for 3 h. Finally, the reaction was quenched with water, and the solid was filtered. The filtrate was extracted with DCM, dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate 4:1) to give a yellow solid **5** in 92% yield (98.4 mg).[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.53 (d, J = 7.9 Hz, 1H), 8.30 (d, J = 9.0 Hz, 1H), 7.74 (t, J = 7.7 Hz, 1H), 7.52 (d, J = 8.9 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9, 166.6, 145.3, 142.6, 134.4, 134.2, 130.5, 128.0, 123.0, 122.9, 122.4, 121.9, 115.2, 115.1, 52.3, 34.1. ESI-MS: calculated $C_{16}H_{14}NO_3$ $[M+H]^+$ 268.0968; Found 268.0961.



3af **6** **7**

Compounds **7** were synthesized by adapting a previously reported procedure[7]: methyl 4-bromobenzoate **6** (1.1 eq.), methyl 9-oxo-9,10-dihydroacridine-2-carboxylate (0.2 mmol, 1 eq.), K_2CO_3 (1.1 eq.), CuI (0.1 eq.), 2,2,6,6- tetramethyl-3,5-heptanedione (ligand, 0.2 eq.) were dissolved in anhydrous DMF (6 mL) into a three-necked round flask. The mixture was degassed and refluxed under nitrogen atmosphere for 24 h. After cooling to room temperature, the reaction mixture was quenched with H_2O and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were collected, dried over sodium sulfate, and evaporated under vacuum. Then, the crude product **7** was purified by flash chromatography (petroleum ether/ethyl acetate 4:1) to give a yellow solid in 45% yield (34.9 mg). ^{1}H NMR (400 MHz, DMSO) δ 8.91 (s, 1H), 8.42 – 8.28 (m, 3H), 8.08 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 8.1 Hz, 2H), 7.67 (t, J = 7.7 Hz, 1H), 7.38 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 9.0 Hz, 1H), 6.73 (d, J = 8.6 Hz, 1H), 3.96 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 176.7, 165.6, 145.0, 142.5, 142.2, 134.5, 133.5, 132.3, 131.2, 130.6, 128.7, 126.6, 122.8, 122.6, 121.5, 120.4, 117.6, 117.3, 52.7, 52.3. ESI-MS: calculated $C_{23}H_{18}NO_5$ $[M+H]^+$ 388.1180; Found 388.1178.

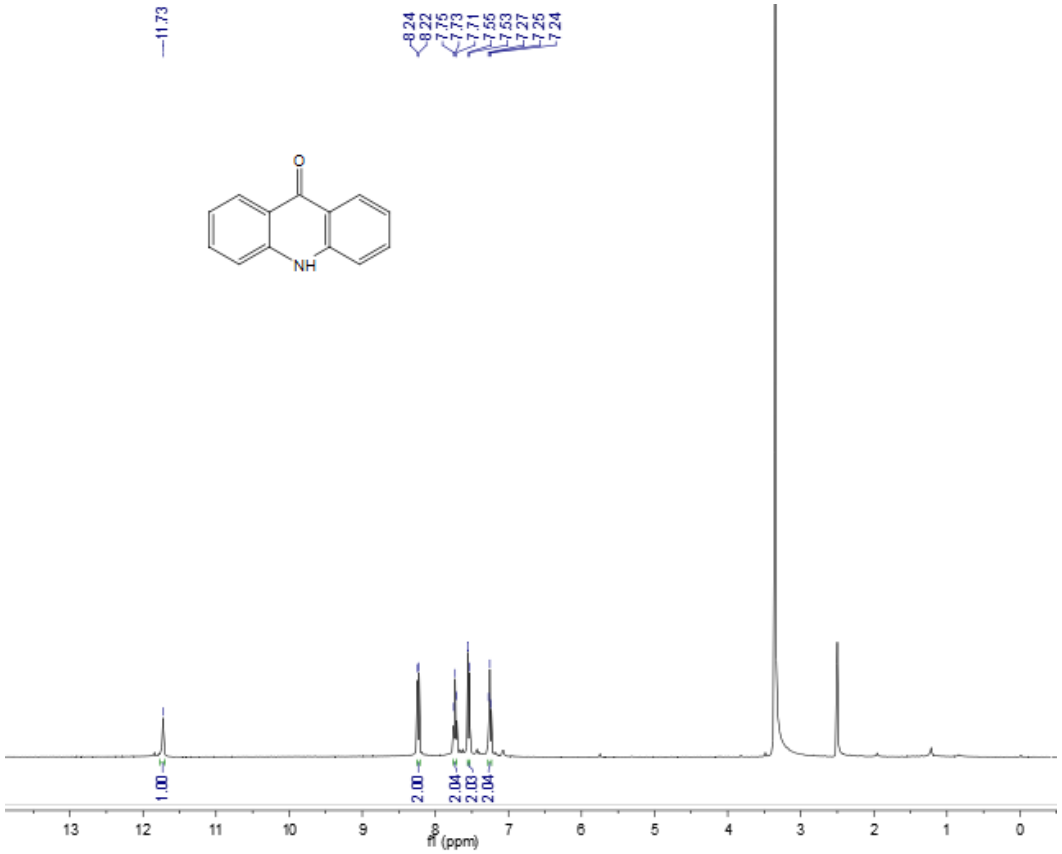


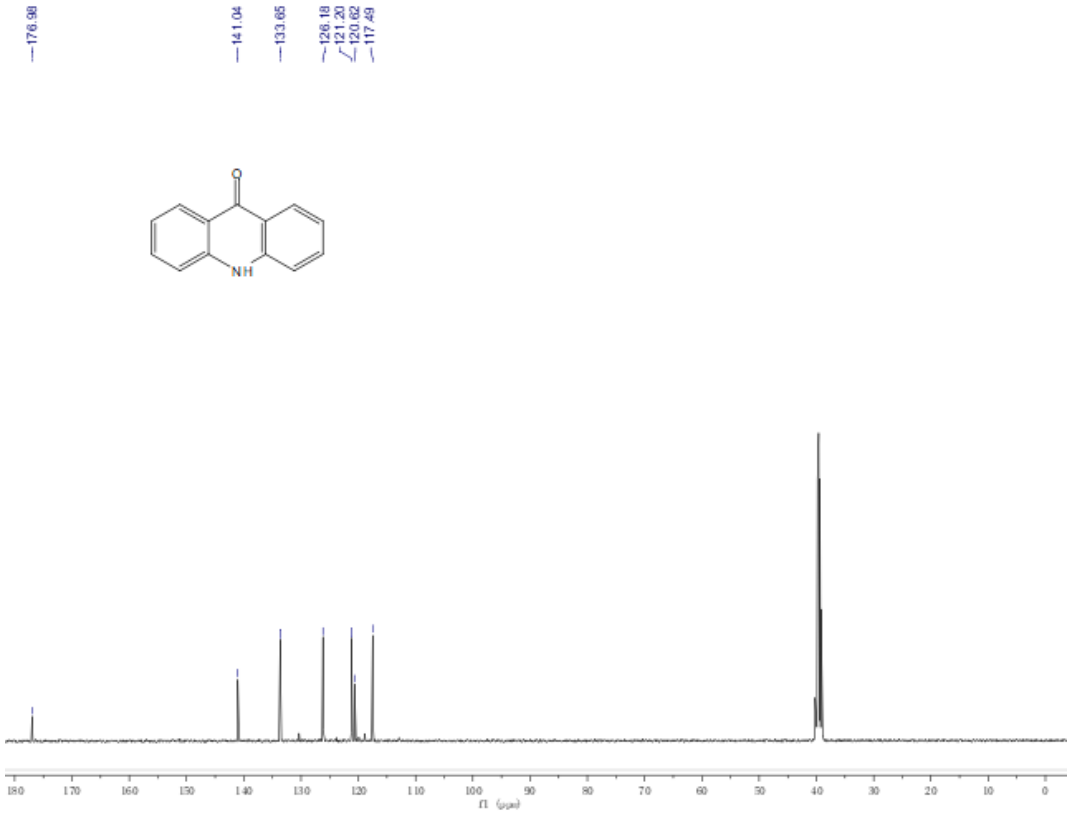
7 **8**

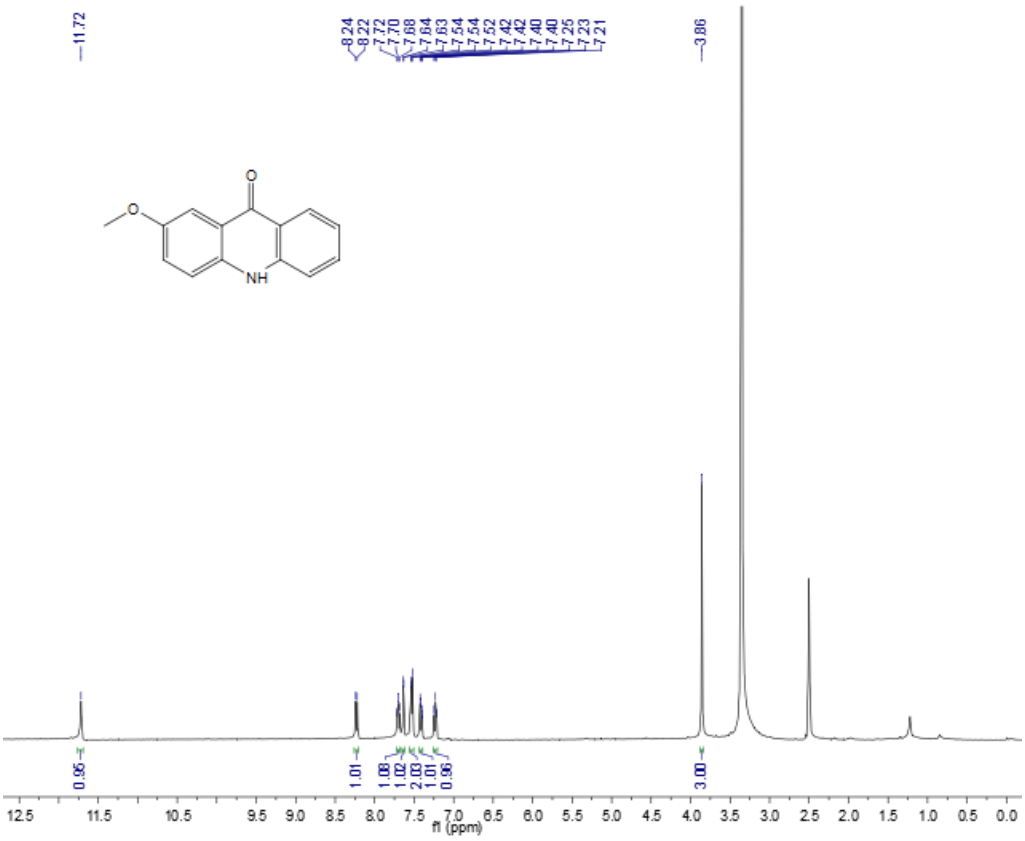
Following the procedure[8]: to a solution of **7** (38.8 mg, 0.1 mmol) in MeOH (3 mL), was added 0.5 mL 10% sodium hydroxide solution.. The mixture was stirred at 60 °C for 3 hour until TLC indicated completion of reaction. After cooling down, the mixture was concentrated and 10 mL ice water was added. The residue was stirred and pH was adjusted to 5 - 6. The mixture was filtered

and the solid was washed with H_2O, dried to give **8** as a light-yellow solid (yield, 87 %).^{1}H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.32 (d, *J* = 8.2 Hz, 2H), 8.08 (d, *J* = 8.9 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 176.8, 166.7, 144.9, 142.6, 141.9, 134.5, 133.9, 132.6, 132.4, 130.4, 128.8, 126.6, 123.9, 122.7, 121.5, 120.4, 117.4, 117.3. ESI-MS: calculated $C_{21}H_{13}NO_5$ $[M-H]^-$ 358.0721; Found 358.0721.

6. NMR Spectra for New Compounds



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7.68
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7.63
7.54
7.54
7.52
7.42
7.42
7.40
7.40
7.25
7.23
7.21
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O
NH
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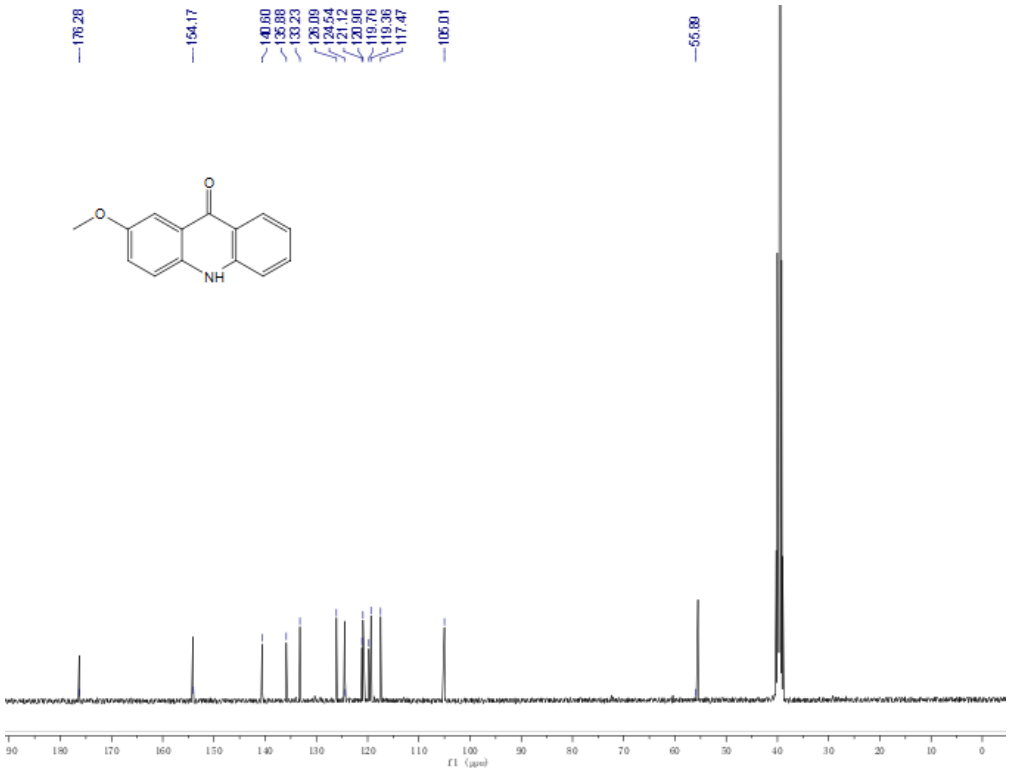
1.08
1.02
2.03
1.01
0.96
3.00
f1 (ppm)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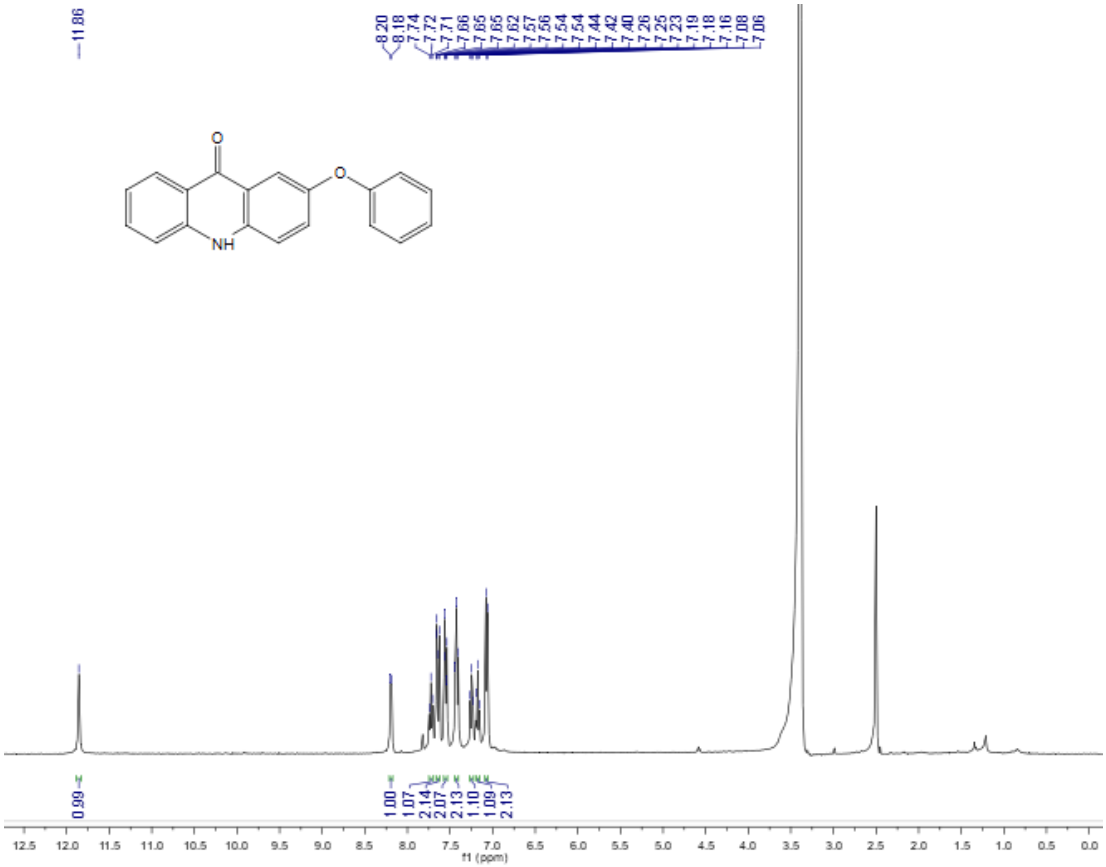
O
NH
f1 (ppm)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7.54
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7.42
7.40
7.26
7.25
7.23
7.19
7.18
7.16
7.08
7.06
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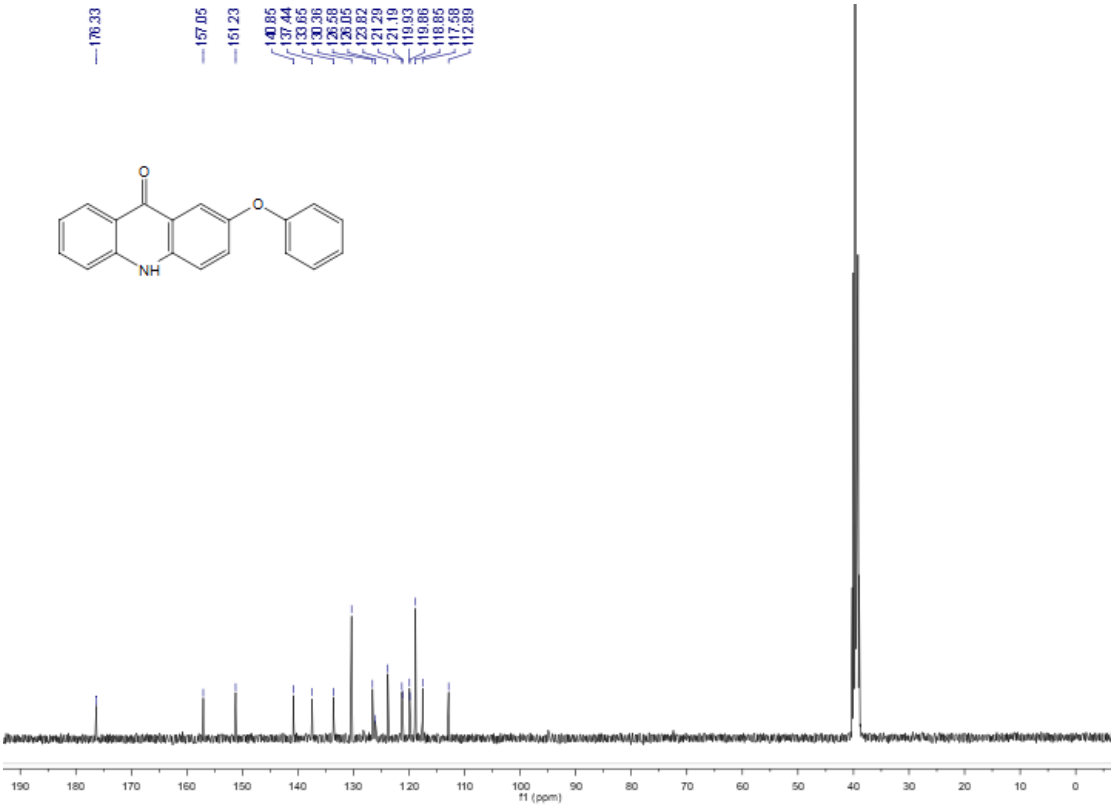
2.13
f1 (ppm)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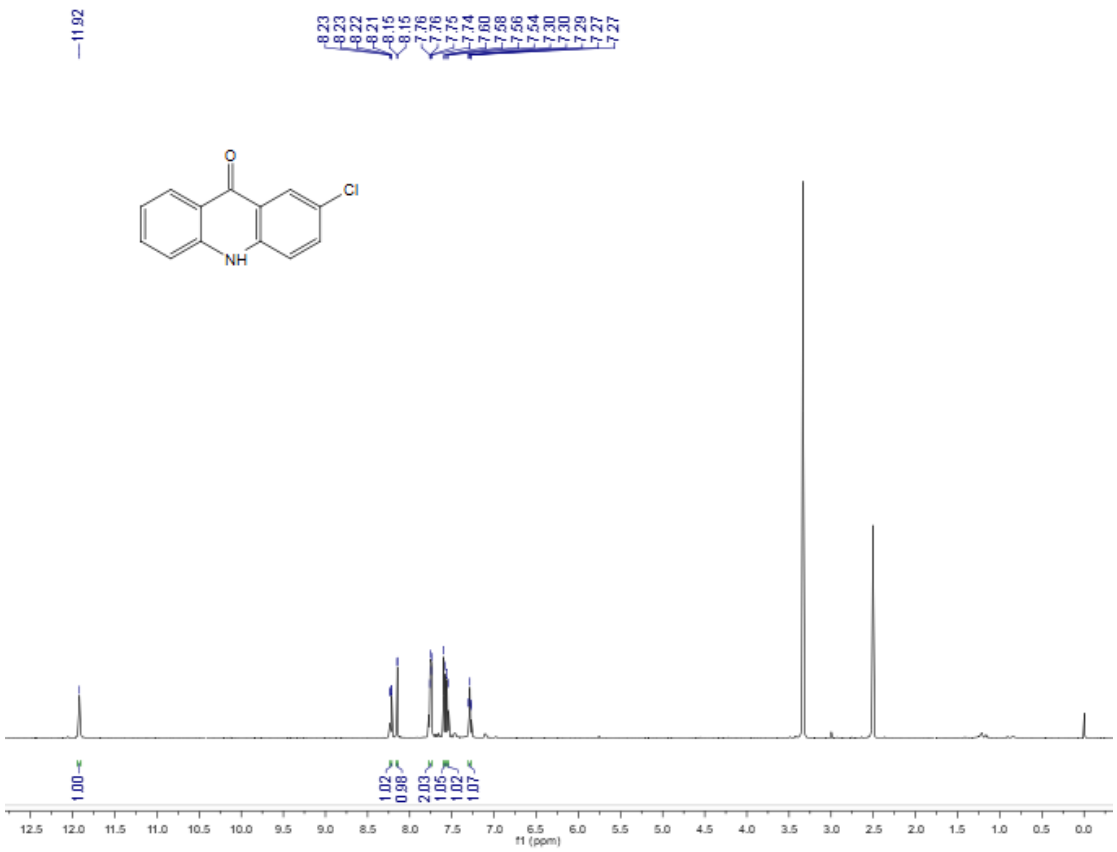
O
NH
f1 (ppm)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7.30
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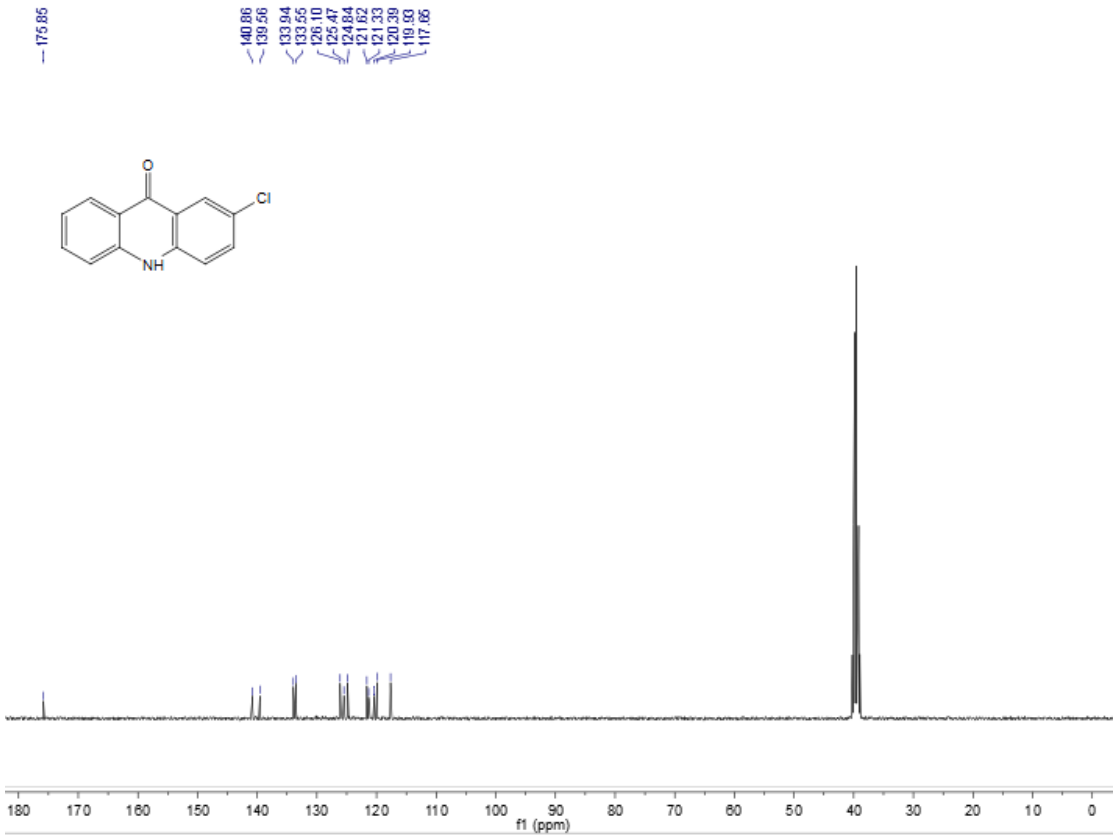
f1 (ppm)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124.84
121.62
121.33
120.39
119.93
117.66
O
Cl
NH
f1 (ppm)


11.86
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8.48
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8.26
8.10
8.09
8.08
8.08
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7.77
7.76
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7.75
7.75
7.74
7.74
7.67
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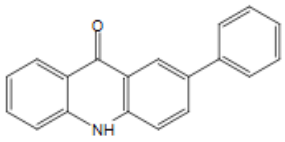
7.27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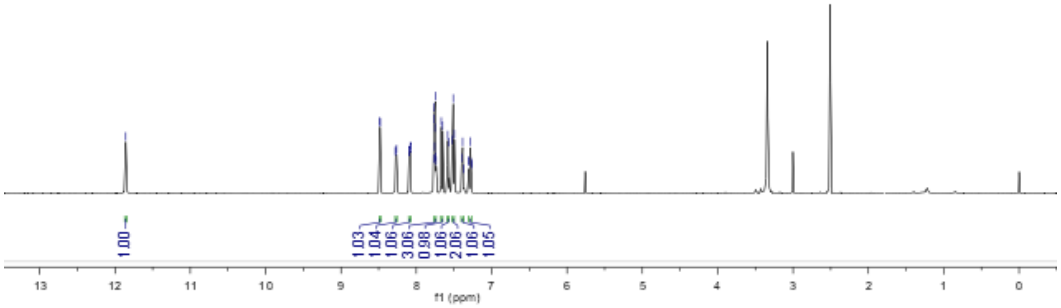
NH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5
4
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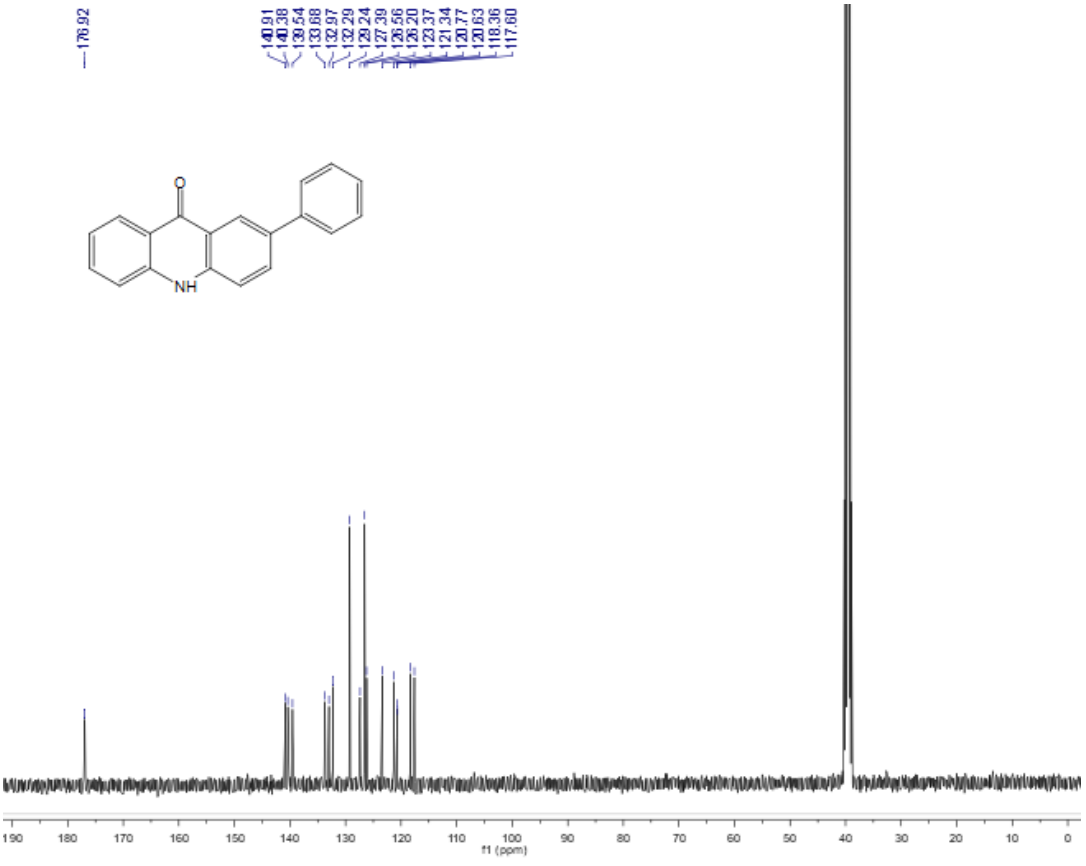
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117.60
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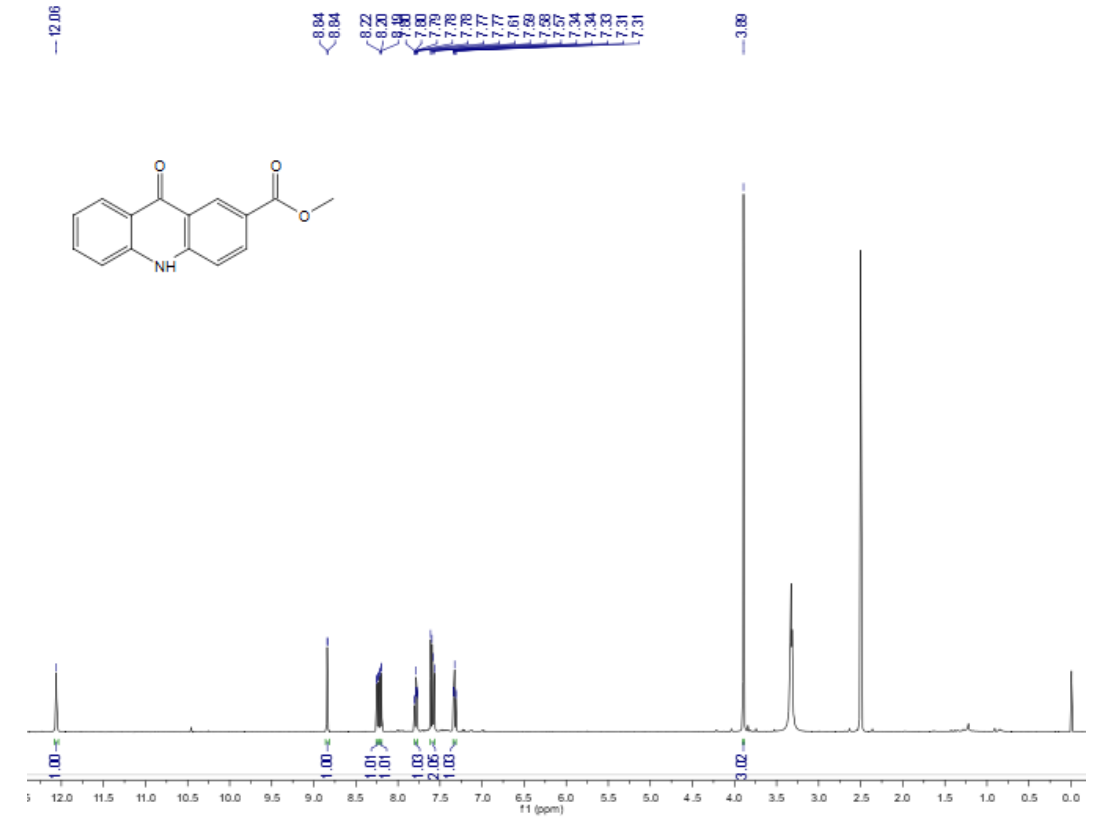
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7.57
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7.31
7.31
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O
O
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1.03
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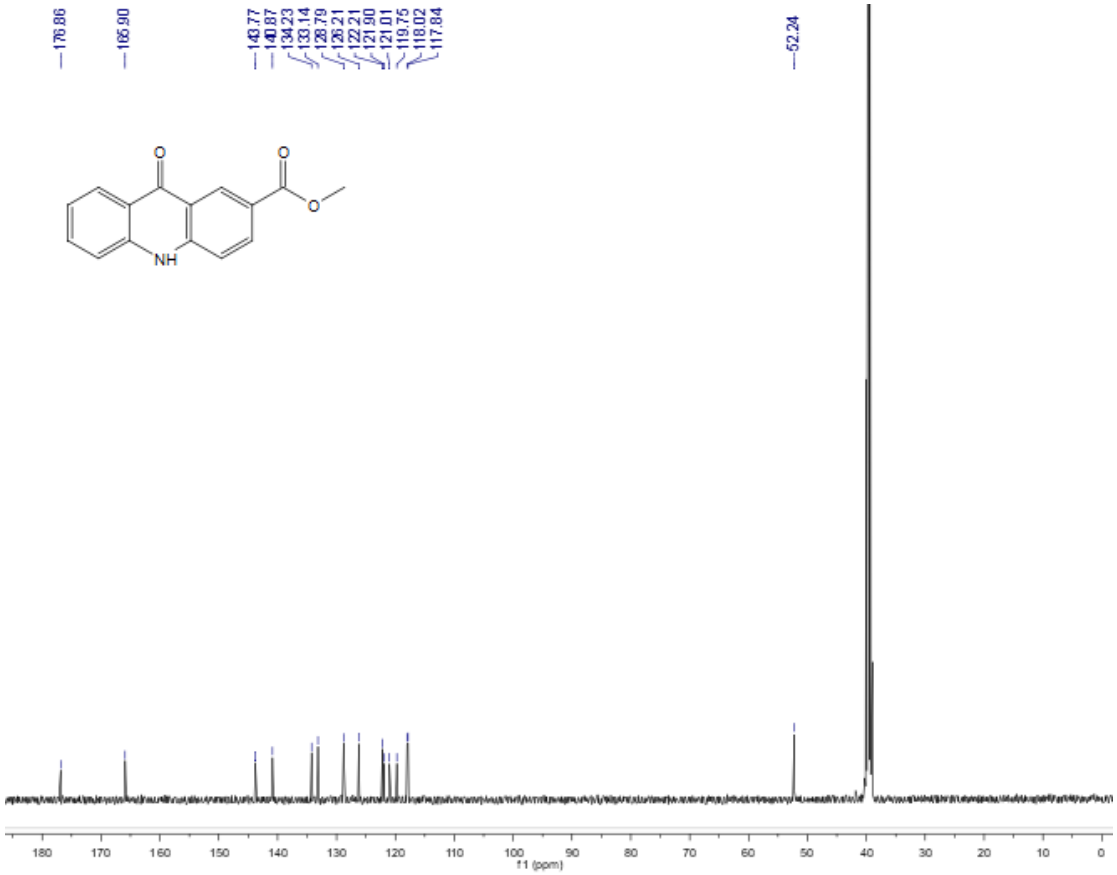
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O
NH
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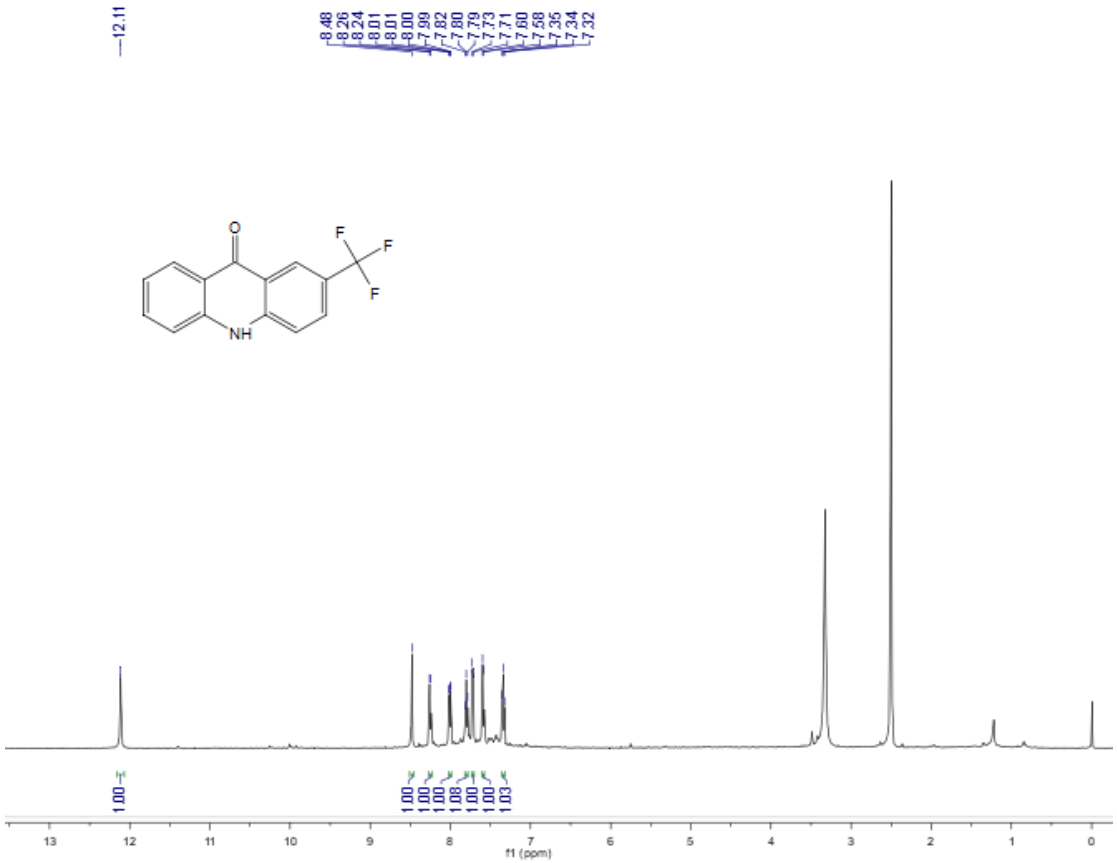
f1 (ppm)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7.35
7.34
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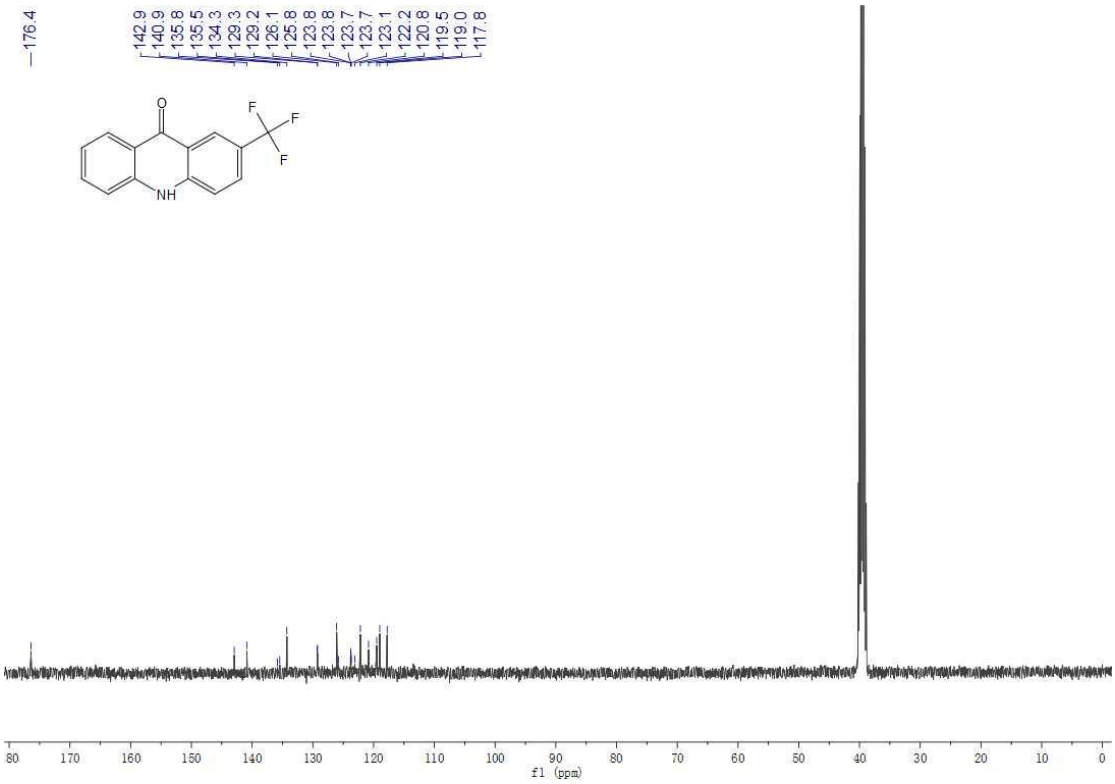
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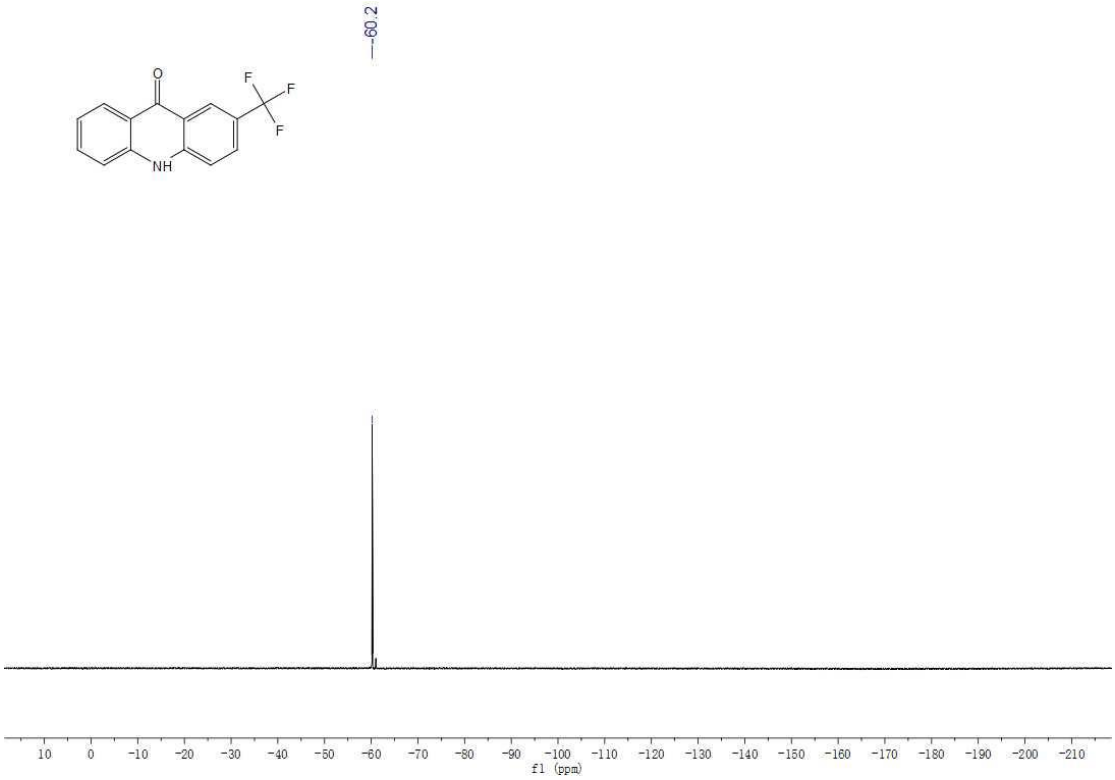
f1 (ppm)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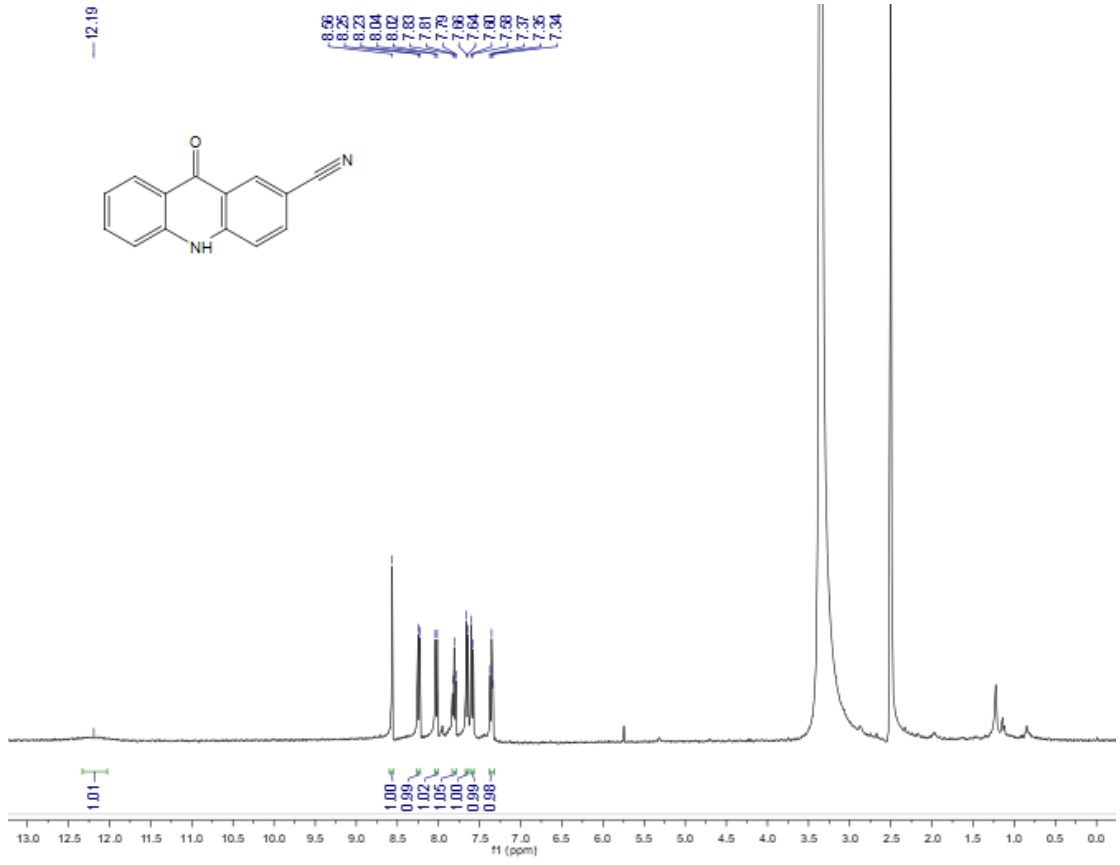
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7.37
7.35
7.34
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N
NH
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1.00
0.99
1.02
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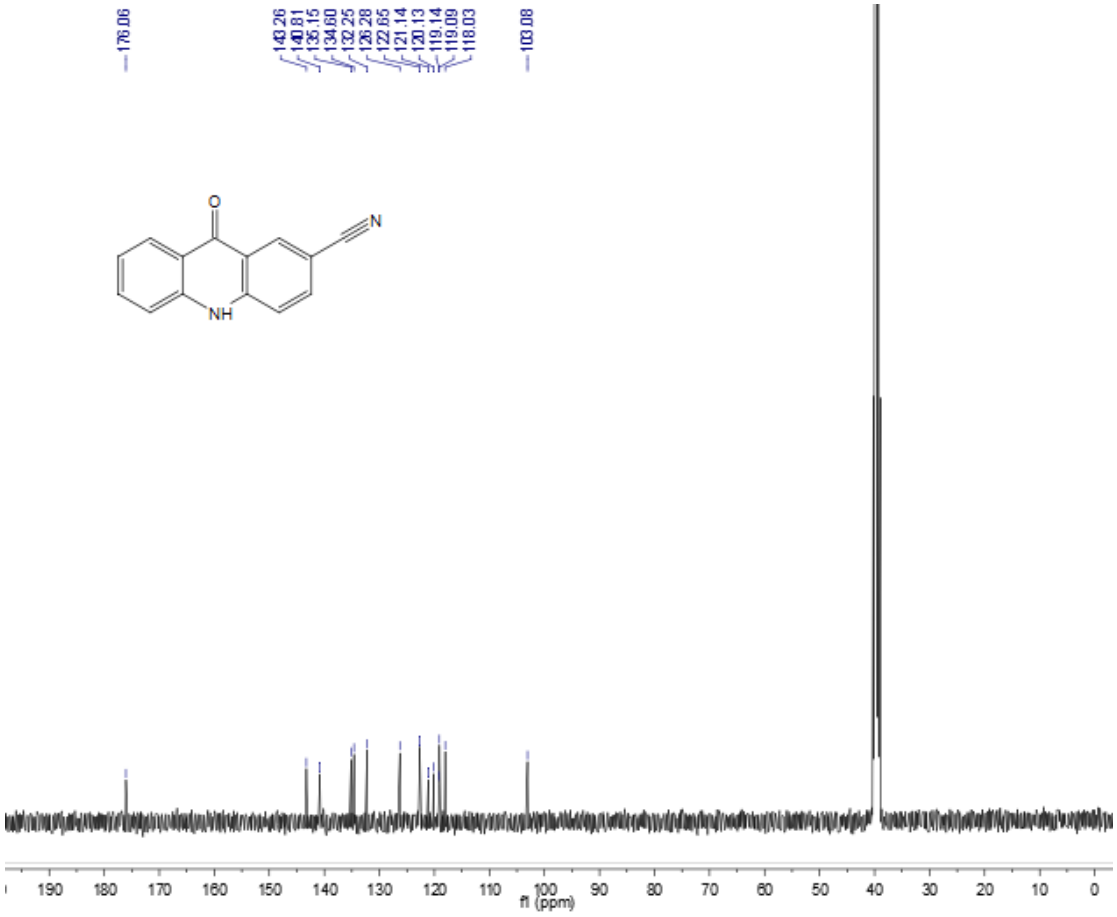
1.00
0.99
0.98
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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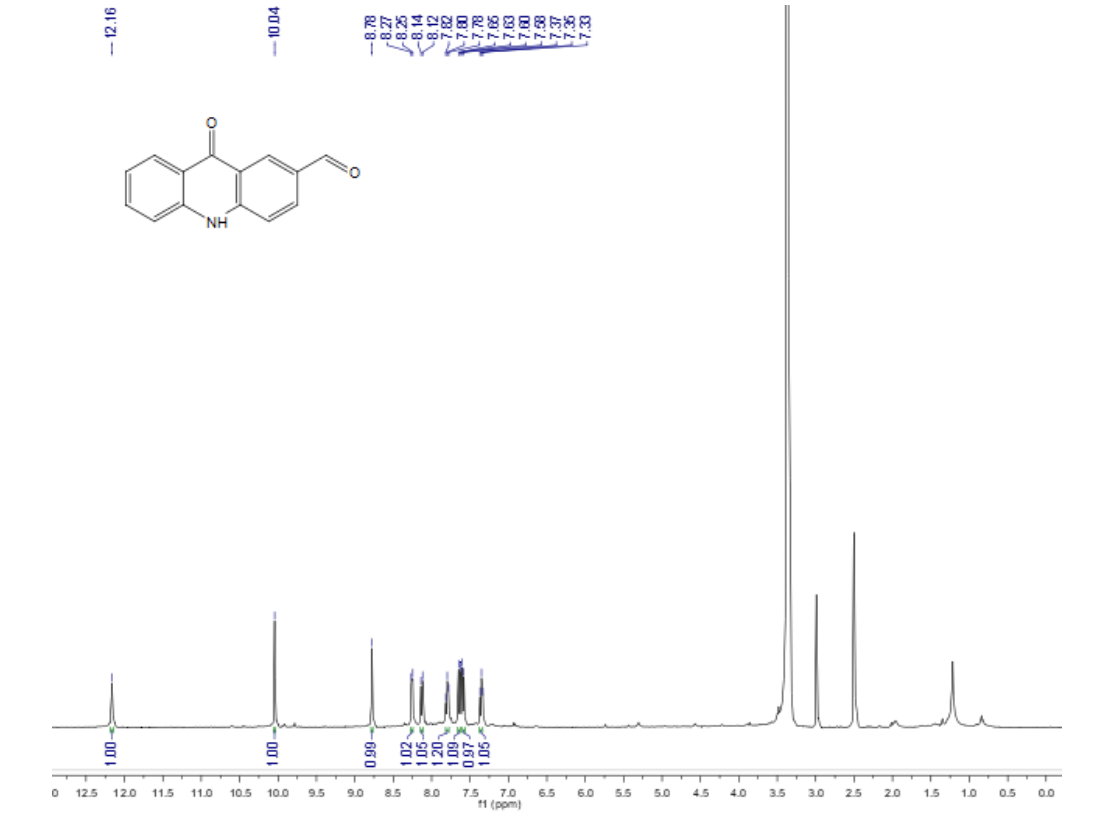
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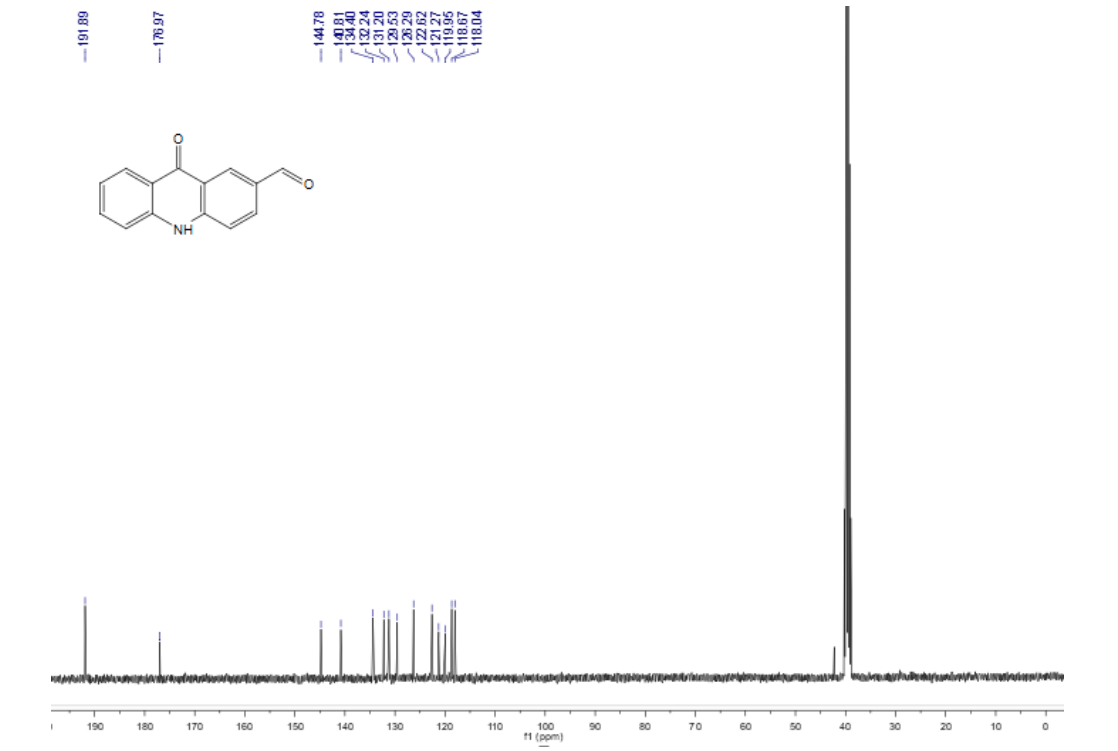
f1 (ppm)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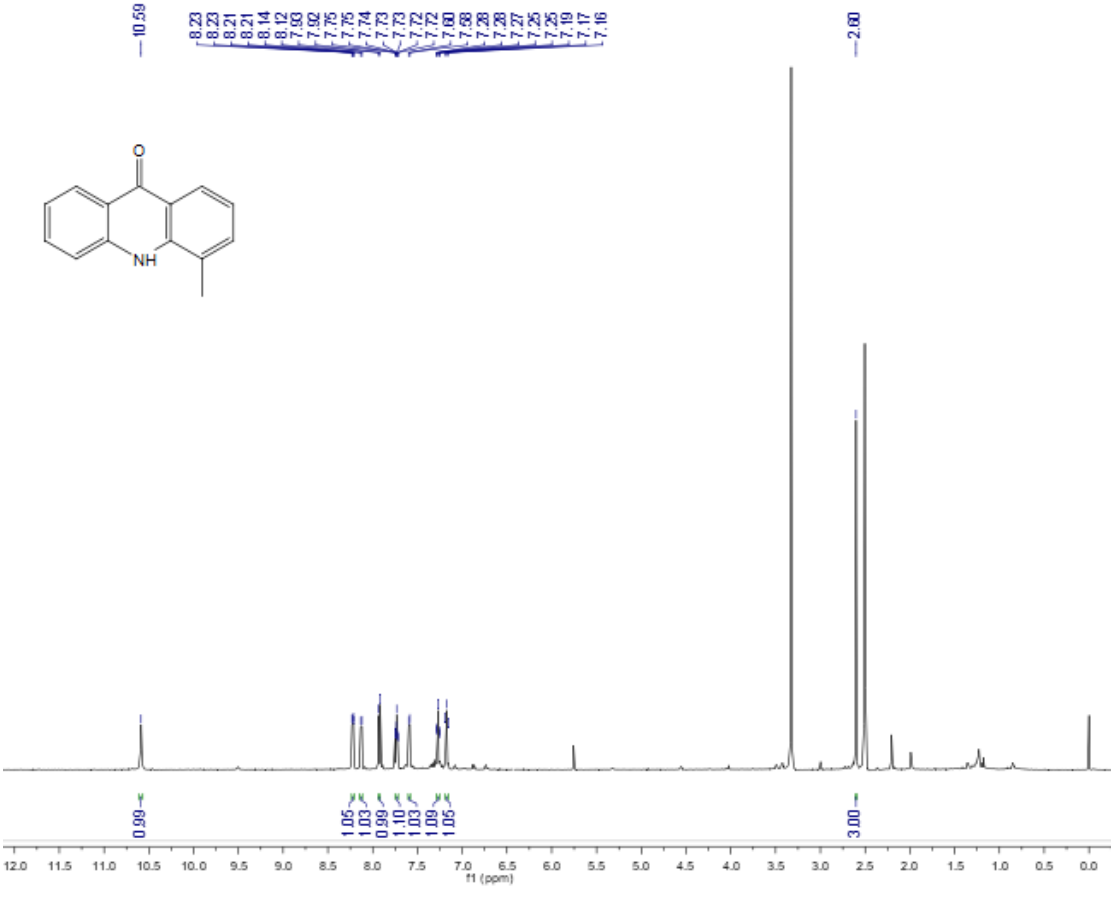
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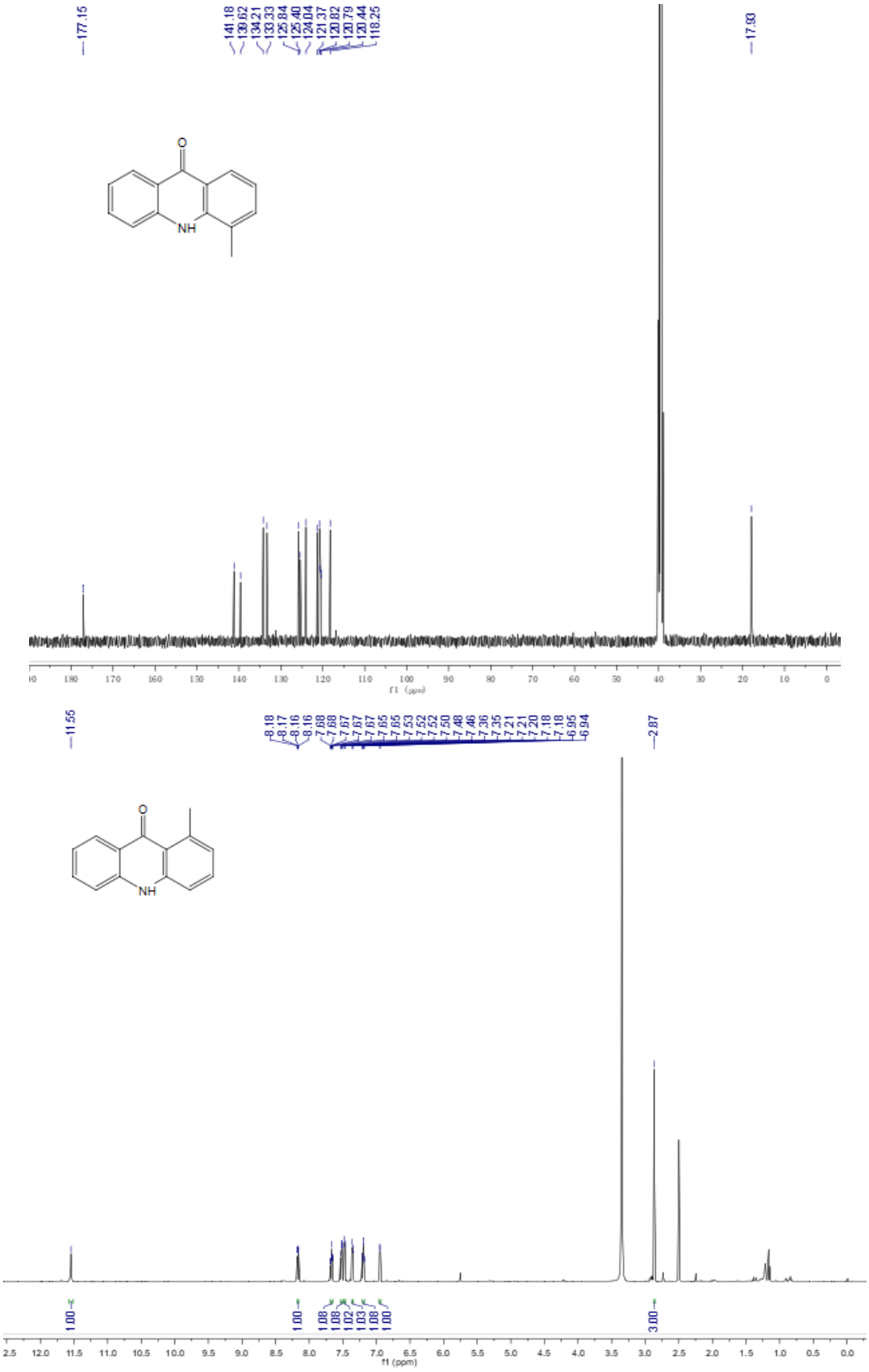
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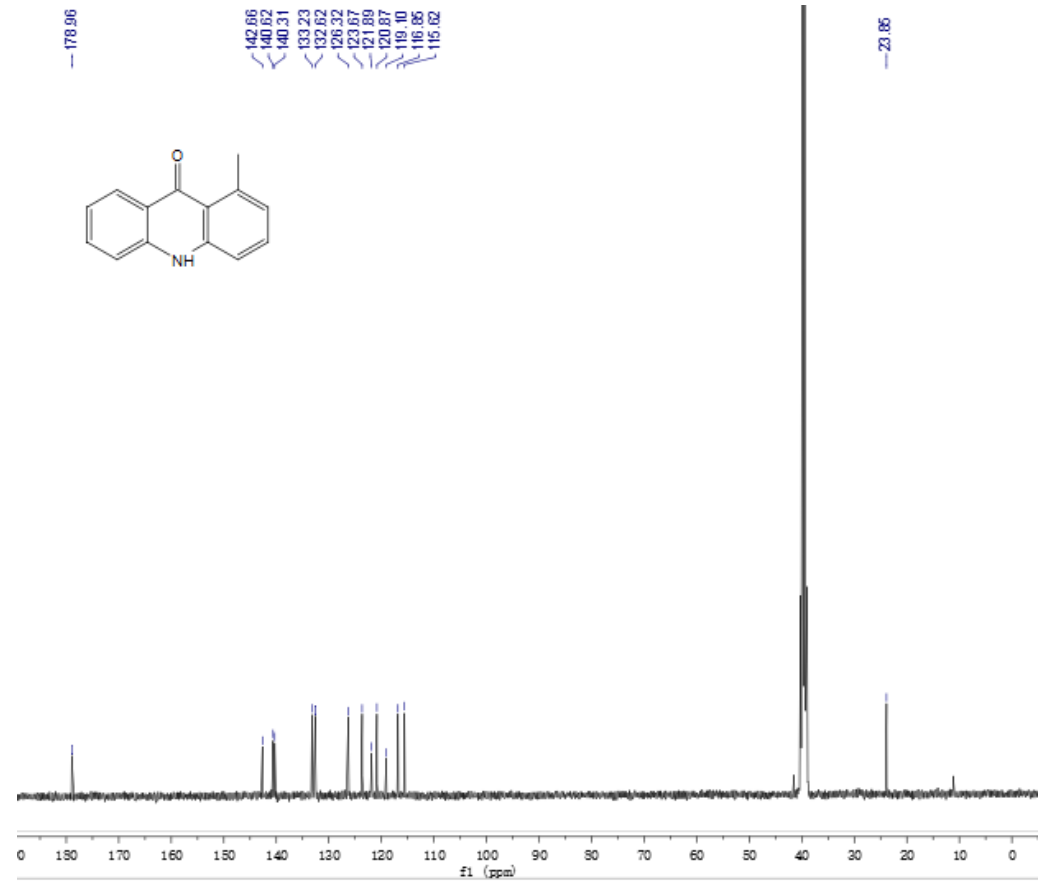
3.00
f1 (ppm)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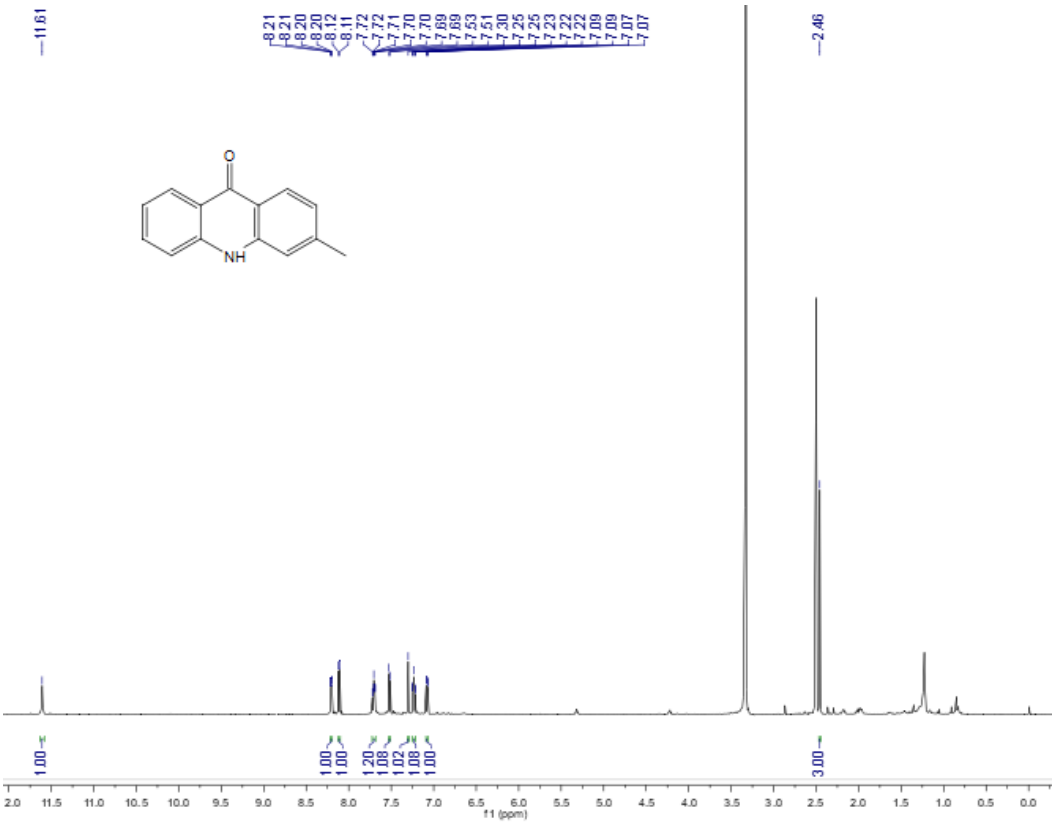
NH
f1 (ppm)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7.07
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3.00
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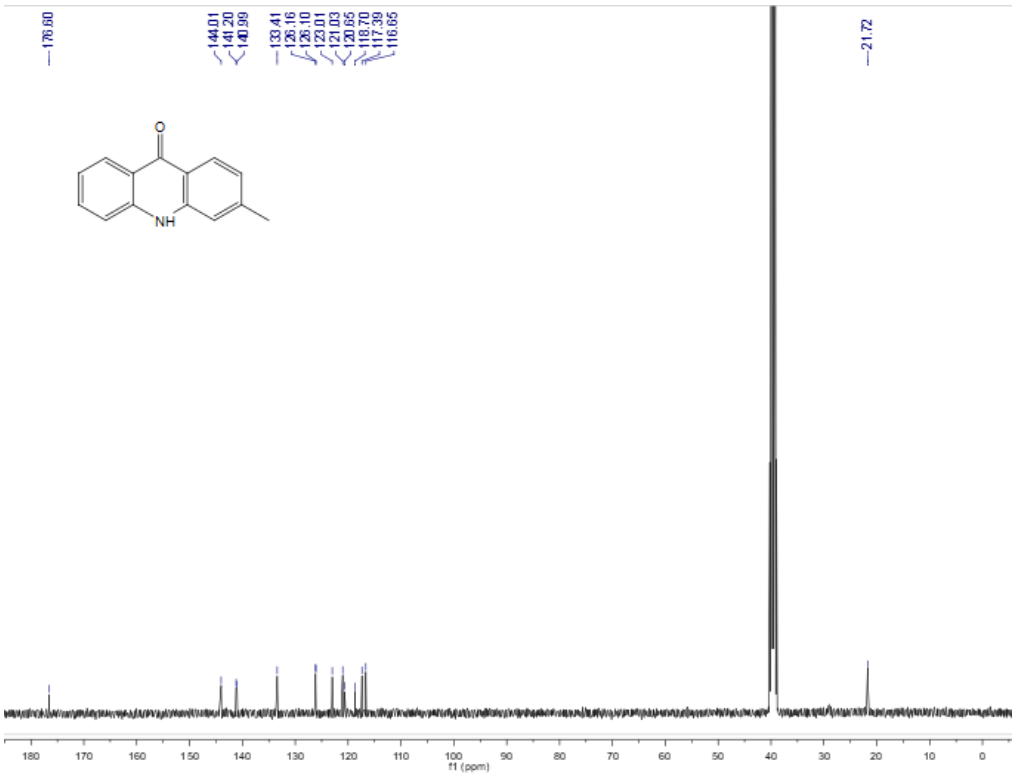
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116.65
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NH
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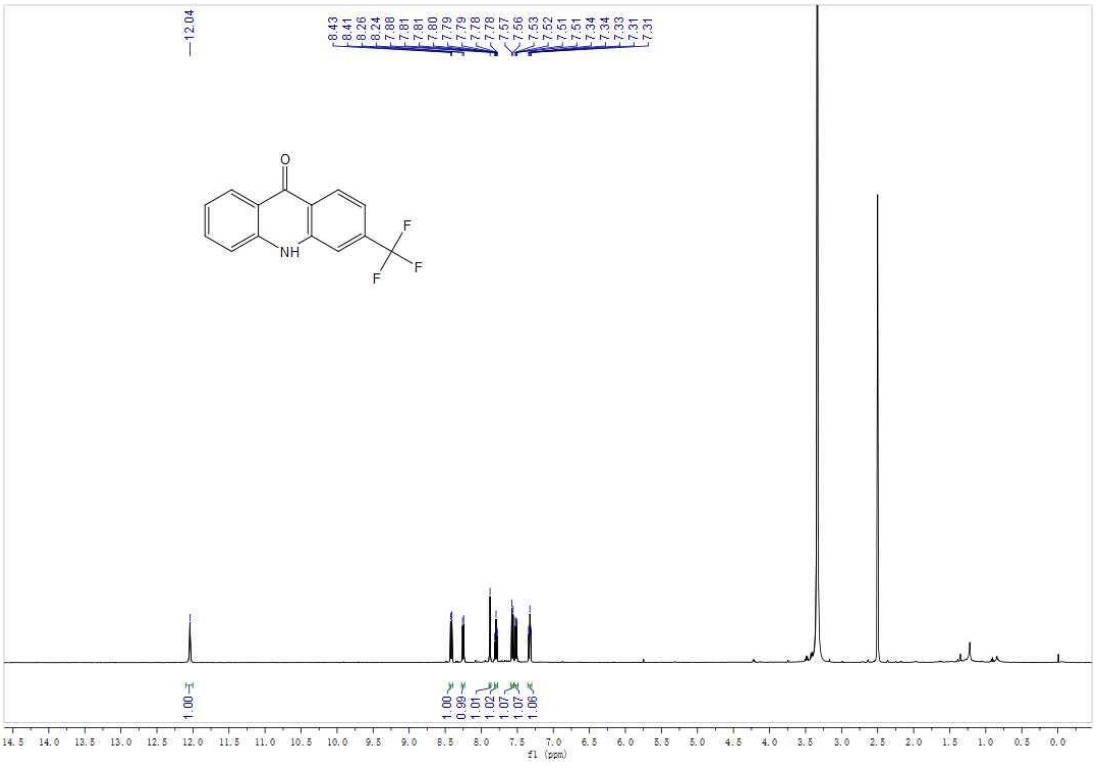
f1 (ppm)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7.34
7.34
7.33
7.31
7.31
O
NH
F
F
F
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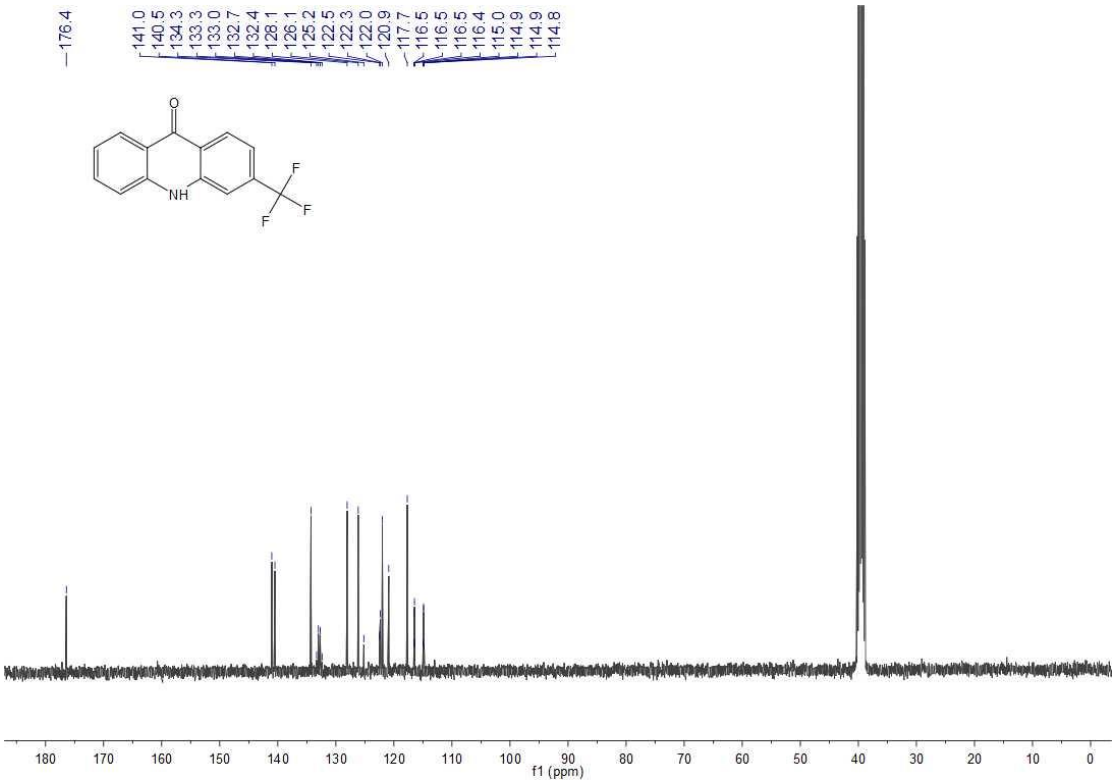
1.00
0.99
1.01
1.02
1.07
1.07
1.06
14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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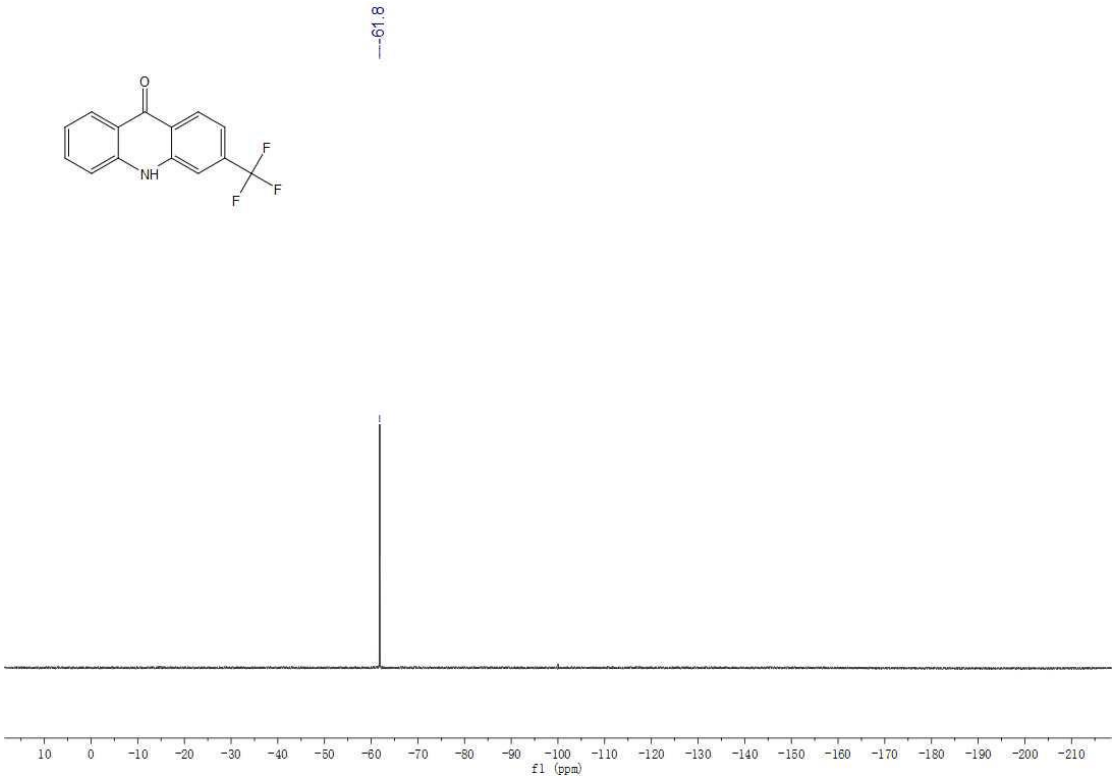
140.5
134.3
133.3
133.0
132.7
132.4
128.1
126.1
125.2
122.5
122.3
122.0
120.9
117.7
116.5
116.5
116.5
116.4
115.0
114.9
114.9
114.8
O
NH
F
F
F
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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O
NH
F
F
F
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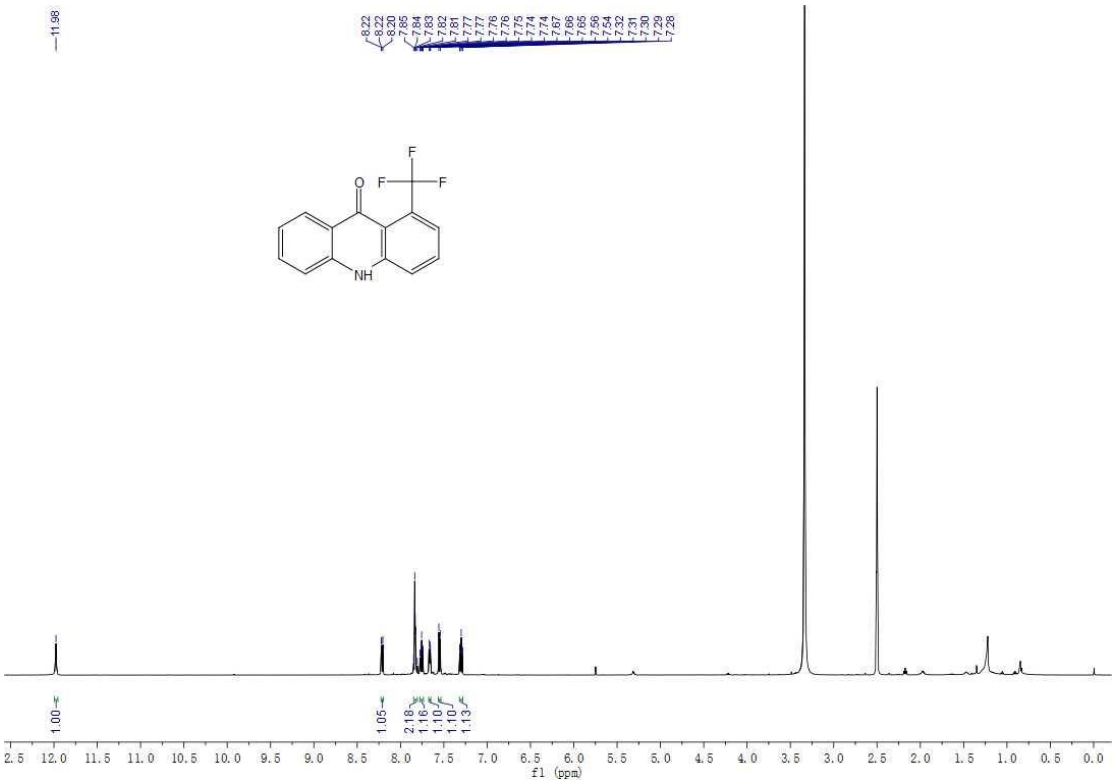
f1 (ppm)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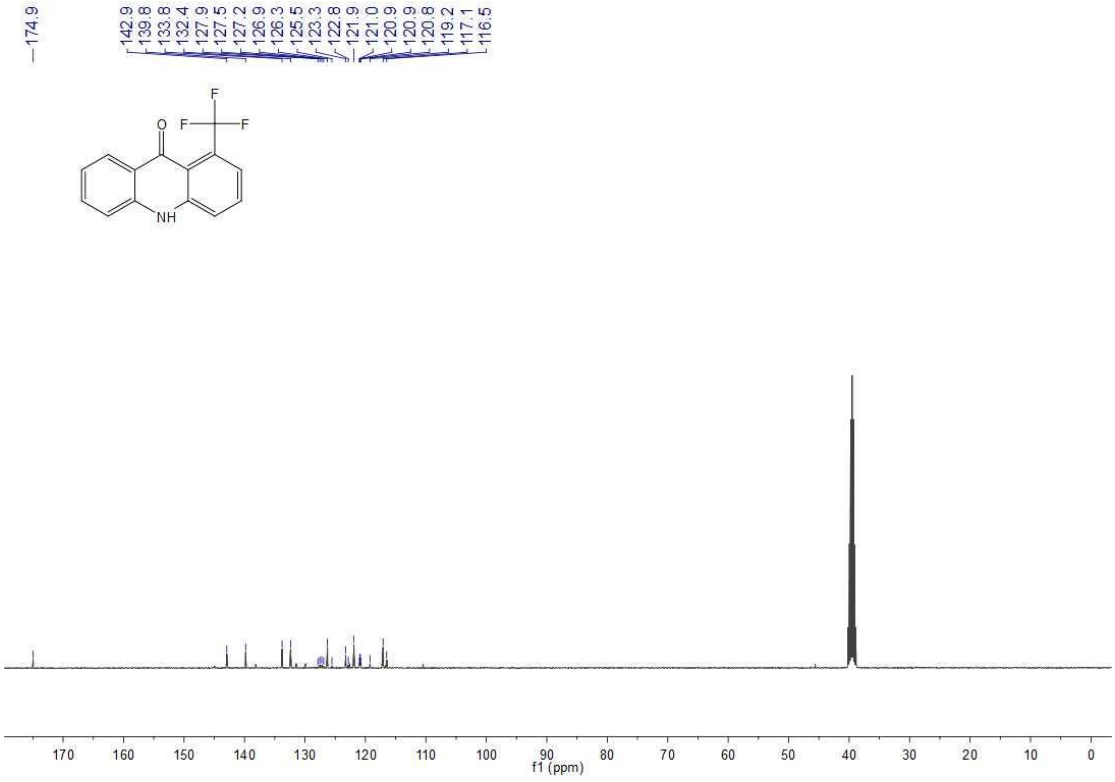
8.22
8.20
7.85
7.84
7.83
7.82
7.81
7.77
7.77
7.77
7.76
7.76
7.75
7.74
7.74
7.67
7.66
7.65
7.56
7.54
7.32
7.31
7.30
7.29
7.28
F
F
F
O
NH
1.00
1.05
2.18
1.16
1.10
1.10
1.13
f1 (ppm)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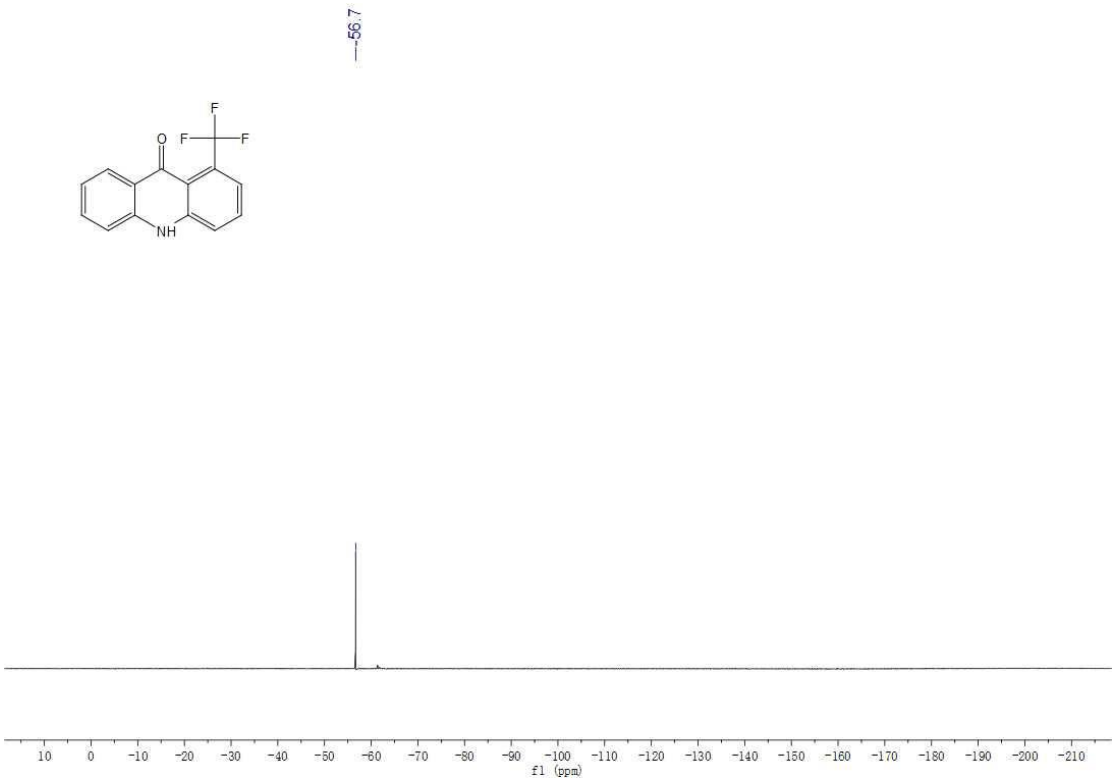
142.9
139.8
133.8
132.4
127.9
127.5
127.2
126.9
126.3
125.5
123.3
122.8
121.9
121.0
120.9
120.9
120.8
119.2
117.1
116.5
F
F
F
O
NH
f1 (ppm)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F
O
F
F
NH
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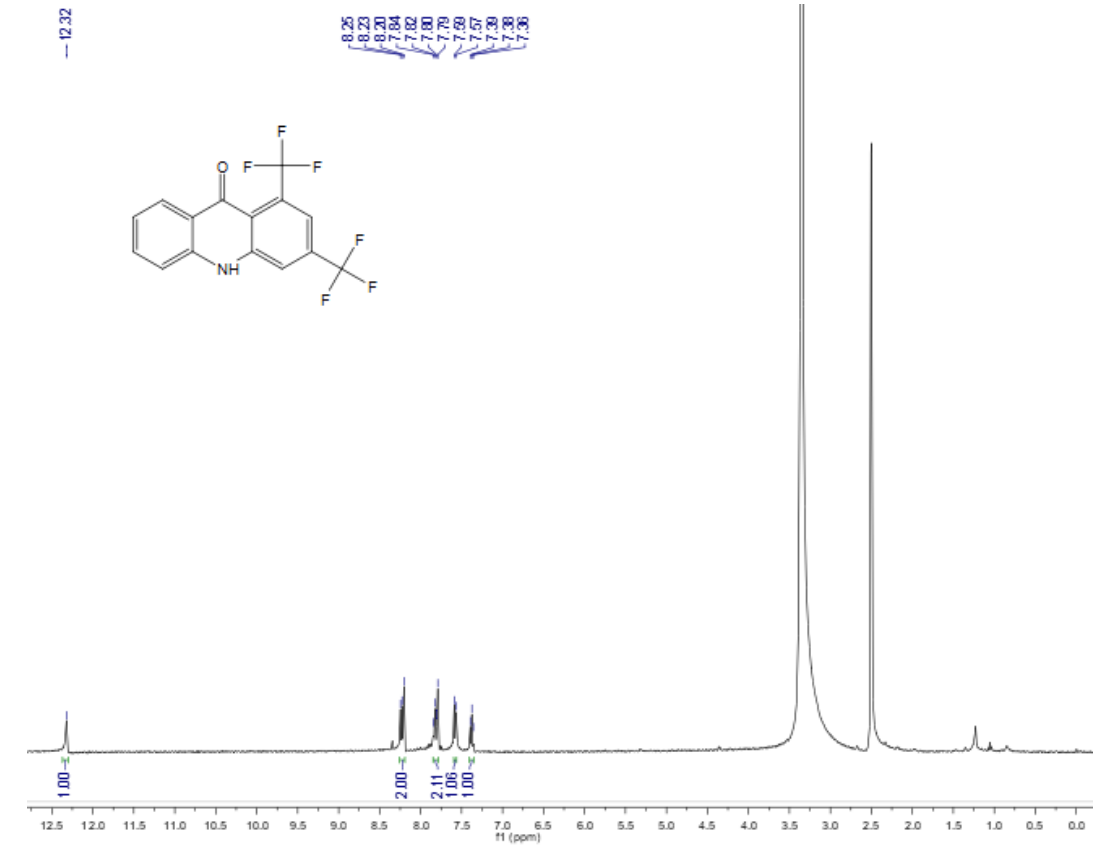
f1 (ppm)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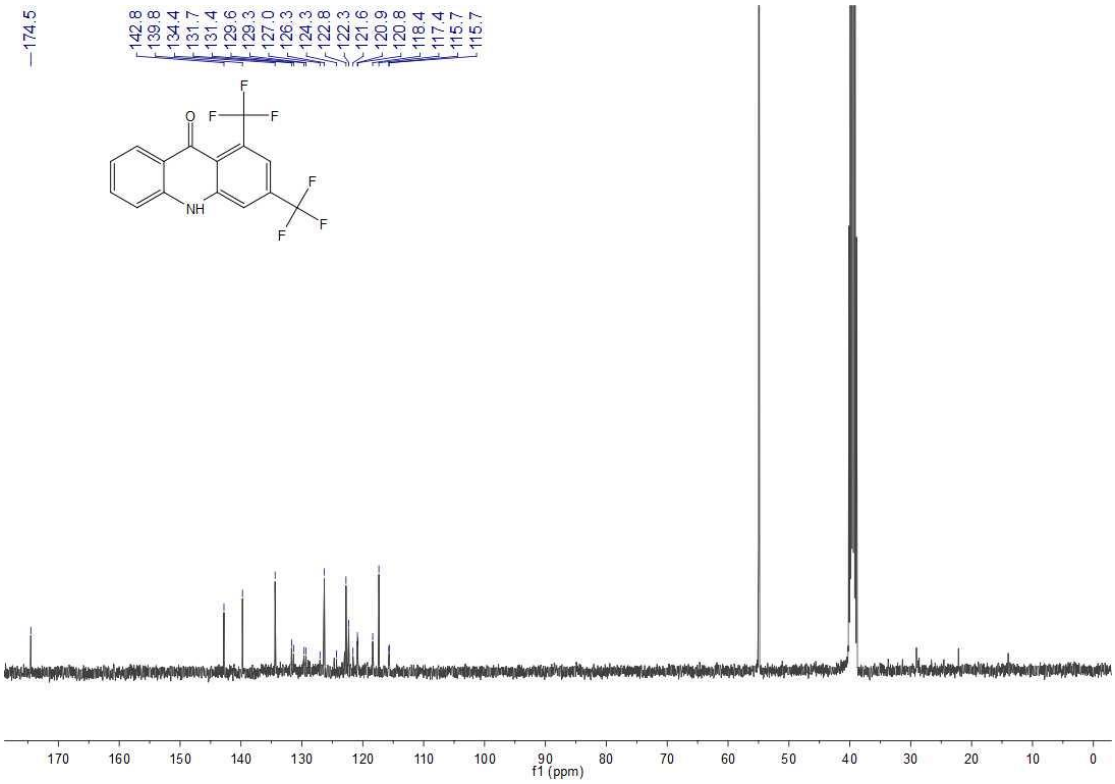
8.25
8.23
8.20
8.03
7.84
7.82
7.80
7.79
7.69
7.67
7.39
7.38
7.36
F
O
F
F
NH
F
F
F
1.00
2.00
2.11
1.06
1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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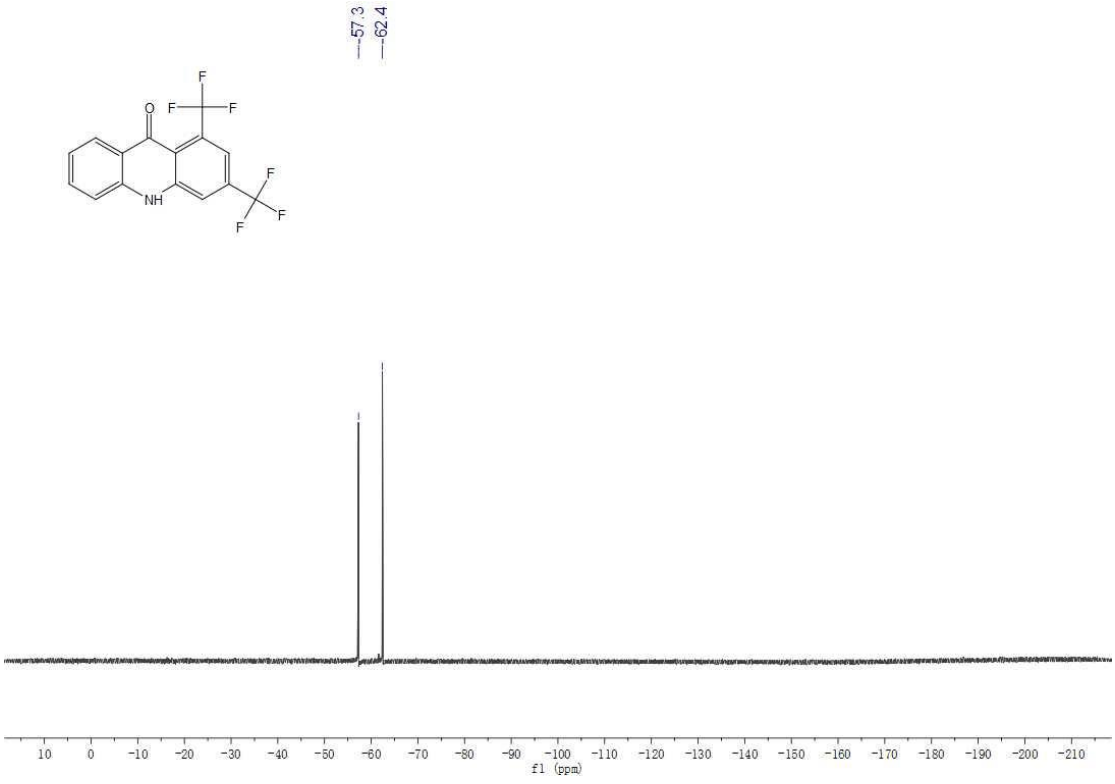
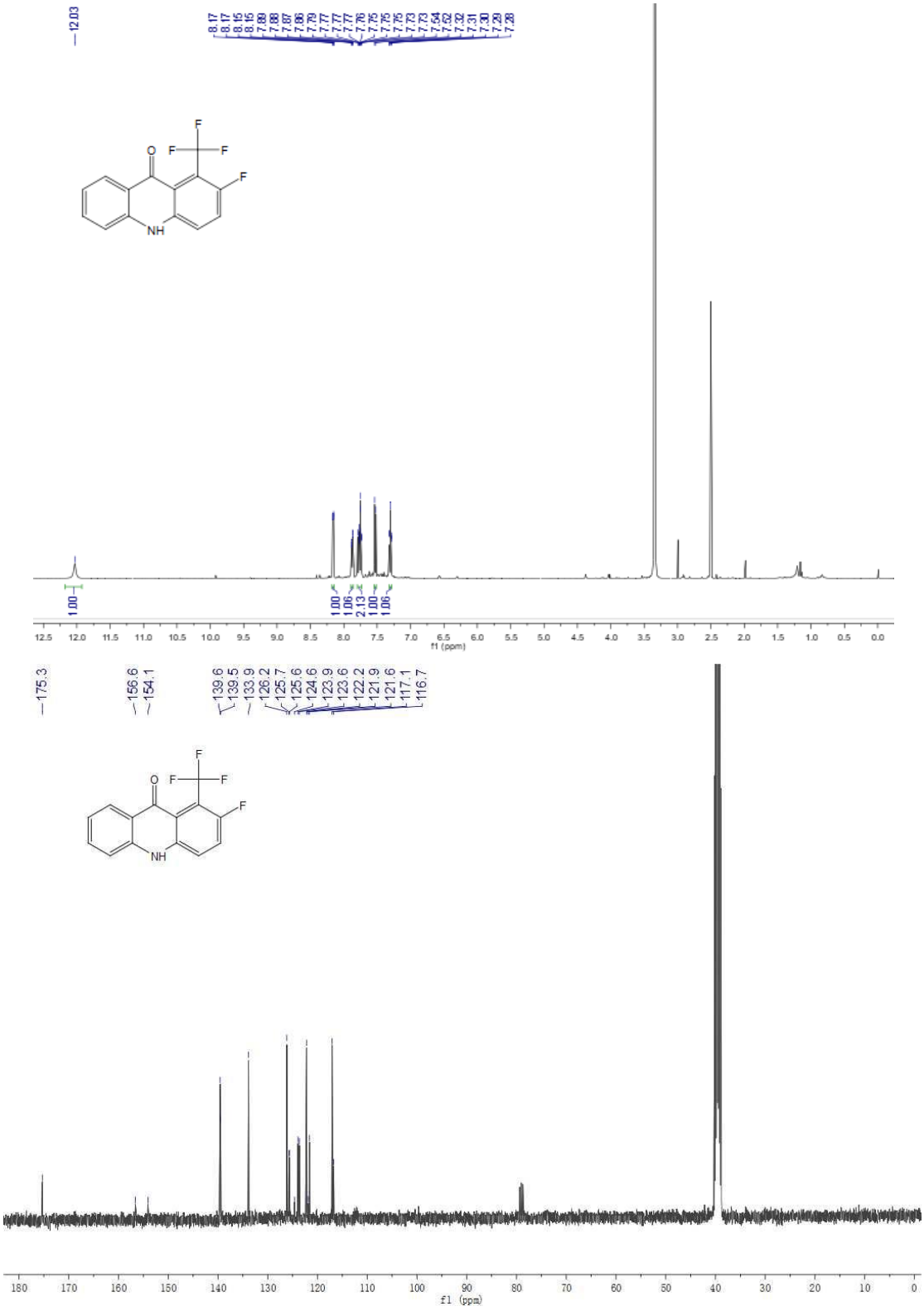
142.8
139.8
134.4
131.7
131.4
129.6
129.3
127.0
126.3
124.3
122.8
122.3
121.6
120.9
120.8
118.4
117.4
115.7
115.7
O
F
F
F
NH
F
F
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


57.3
62.4
O
F
F
F
NH
F
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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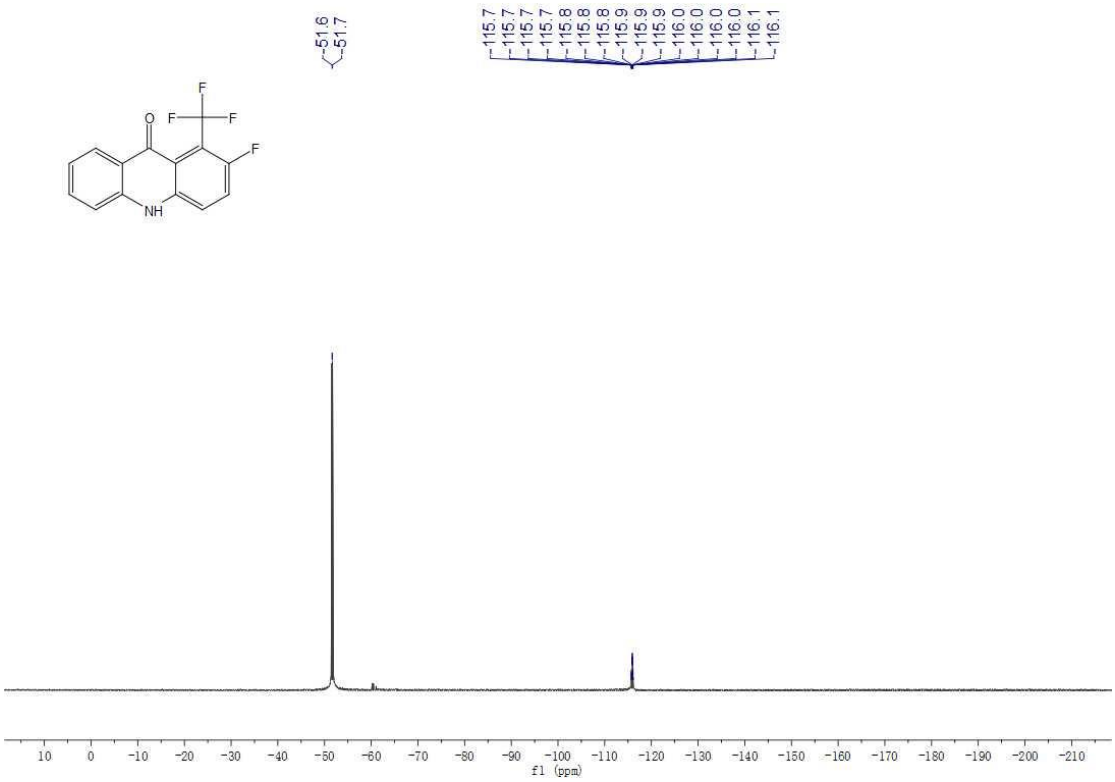
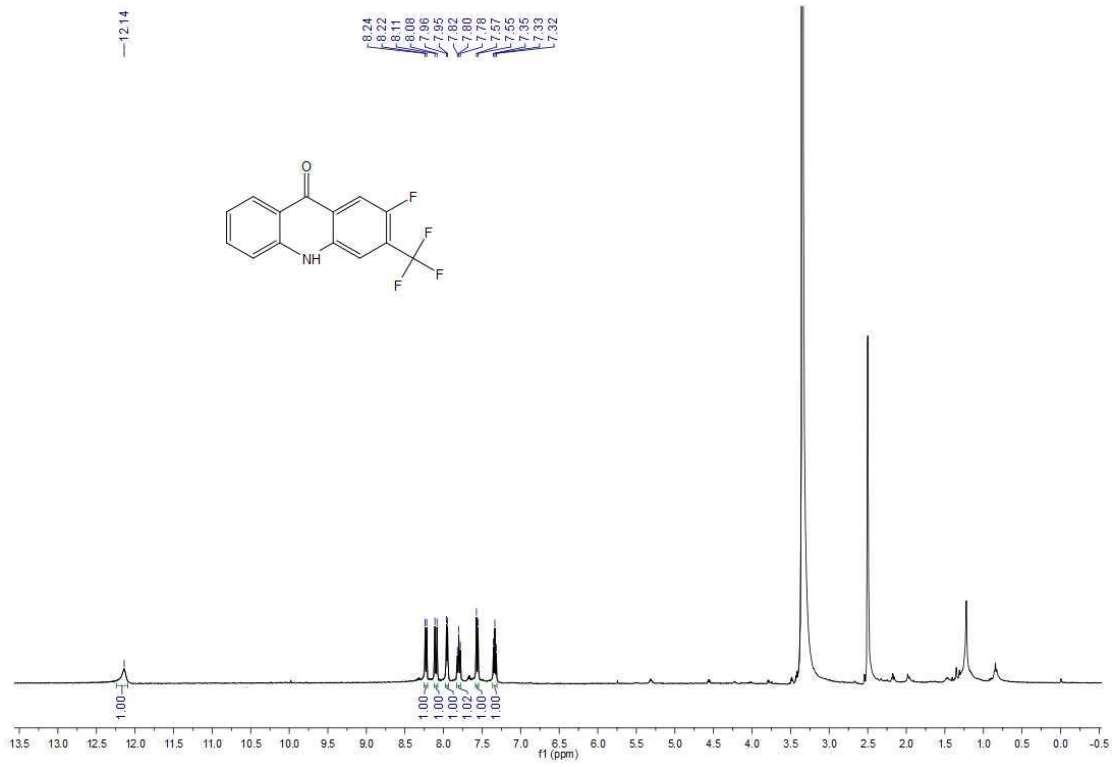
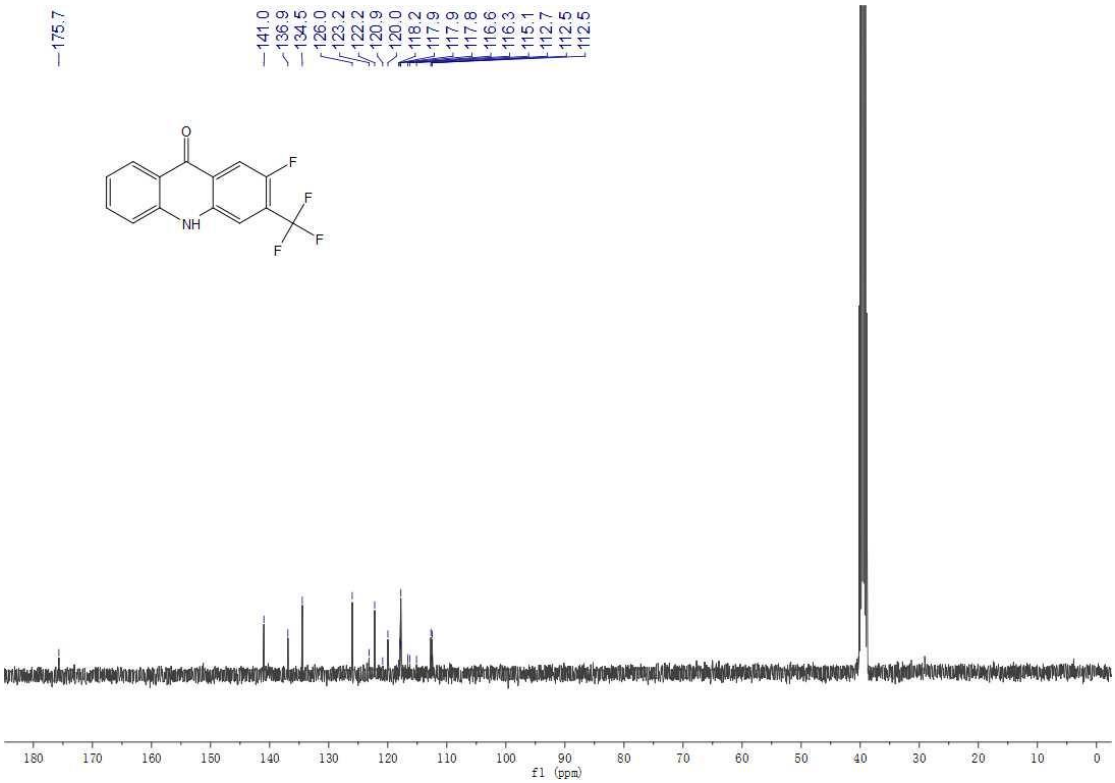
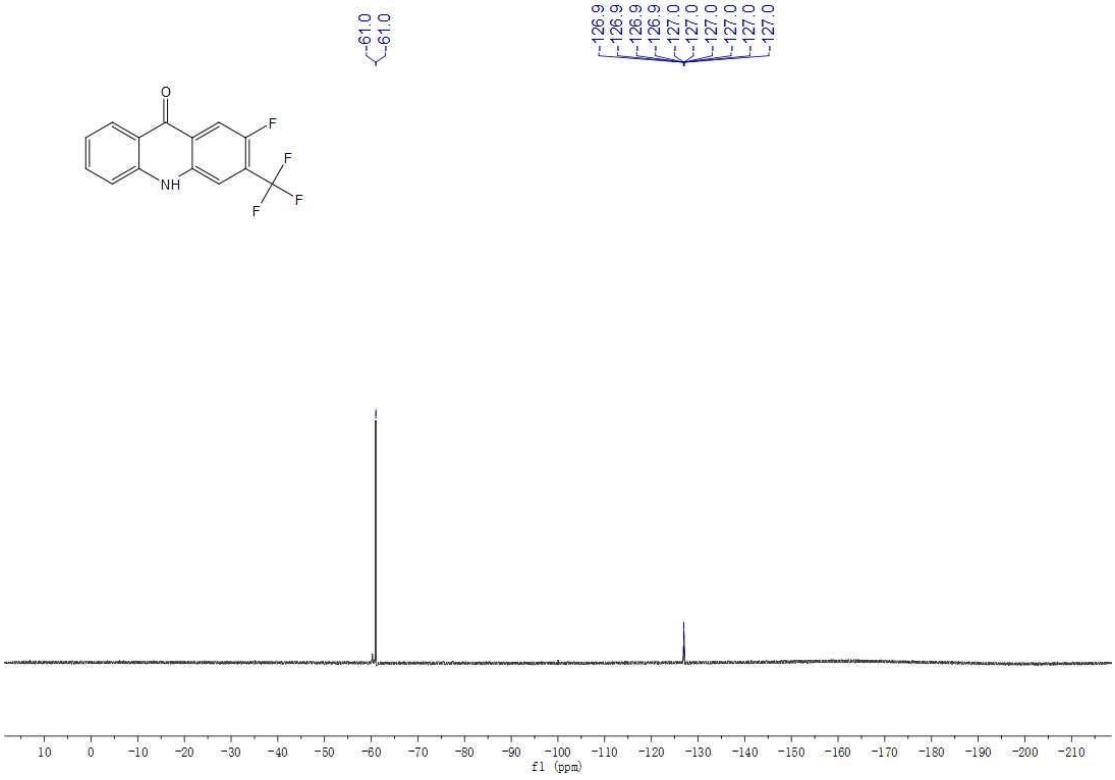
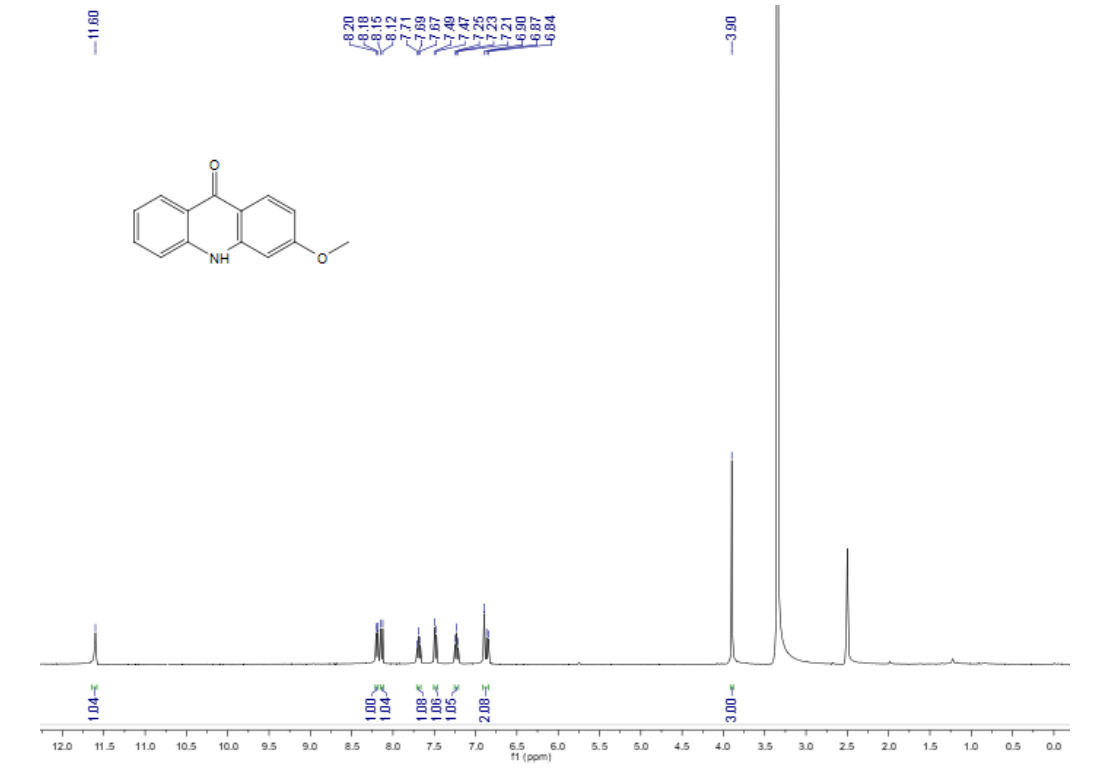
8.17
8.17
8.15
8.15
7.89
7.88
7.87
7.86
7.79
7.77
7.77
7.77
7.76
7.75
7.75
7.75
7.73
7.54
7.52
7.32
7.31
7.30
7.29
7.28
F
F
F
O
NH
1.00
1.00
1.06
2.13
1.00
1.06
f1 (ppm)
175.3
156.6
154.1
139.6
139.5
133.9
126.2
125.7
125.6
124.6
123.9
123.6
122.2
121.9
121.6
117.1
116.7
f1 (ppm)


51.6
51.7
115.7
115.7
115.7
115.7
115.8
115.8
115.8
115.9
115.9
115.9
116.0
116.0
116.0
116.0
116.1
116.1
F
F
F
F
O
NH
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


12.14
8.24
8.22
8.11
8.08
7.96
7.95
7.82
7.80
7.78
7.57
7.55
7.35
7.33
7.32
O
F
F
F
NH
1.00
1.00
1.00
1.00
1.02
1.00
1.00
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 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 -0.5
f1 (ppm)


175.7
141.0
136.9
134.5
126.0
123.2
122.2
120.9
120.0
118.2
117.9
117.9
117.8
116.6
116.3
115.1
112.7
112.5
112.5
O
NH
F
F
F
F
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


61.0
61.0
126.9
126.9
126.9
126.9
127.0
127.0
127.0
127.0
127.0
127.0
O
NH
F
F
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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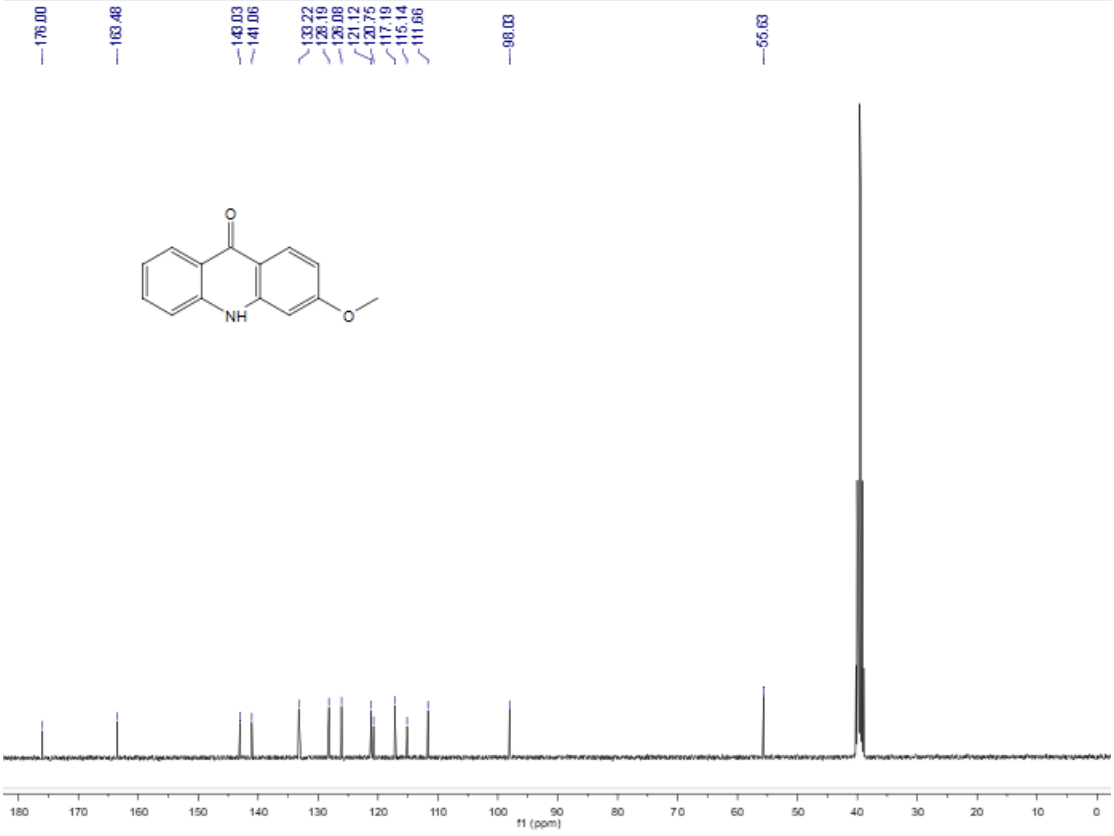
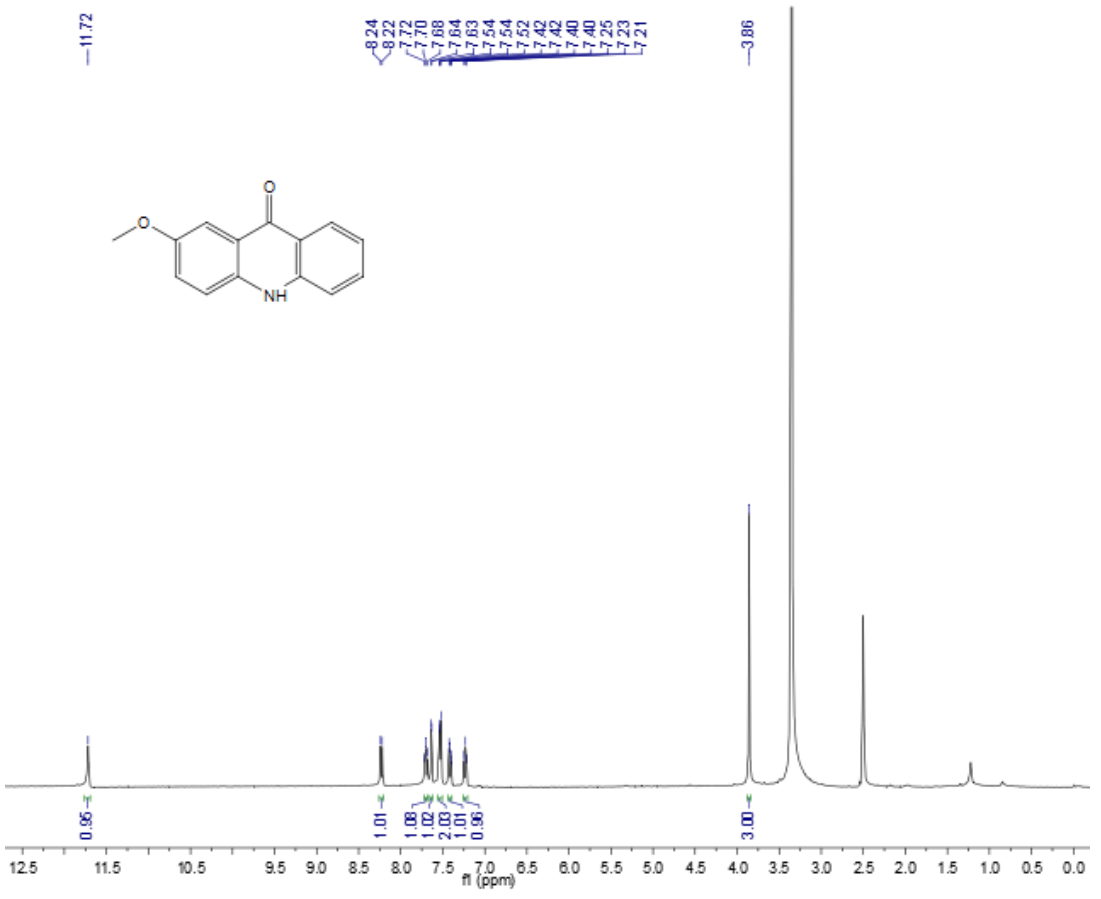
8.20
8.18
8.15
8.12
7.71
7.69
7.67
7.49
7.47
7.25
7.23
7.21
6.90
6.87
6.84
3.90
O
NH
O
1.04
1.00
1.04
1.08
1.06
1.05
2.08
3.00
f1 (ppm)


176.00
163.48
143.03
141.06
133.22
128.19
126.08
121.12
120.75
117.19
115.14
111.66
98.03
55.63
O
NH
O
f1 (ppm)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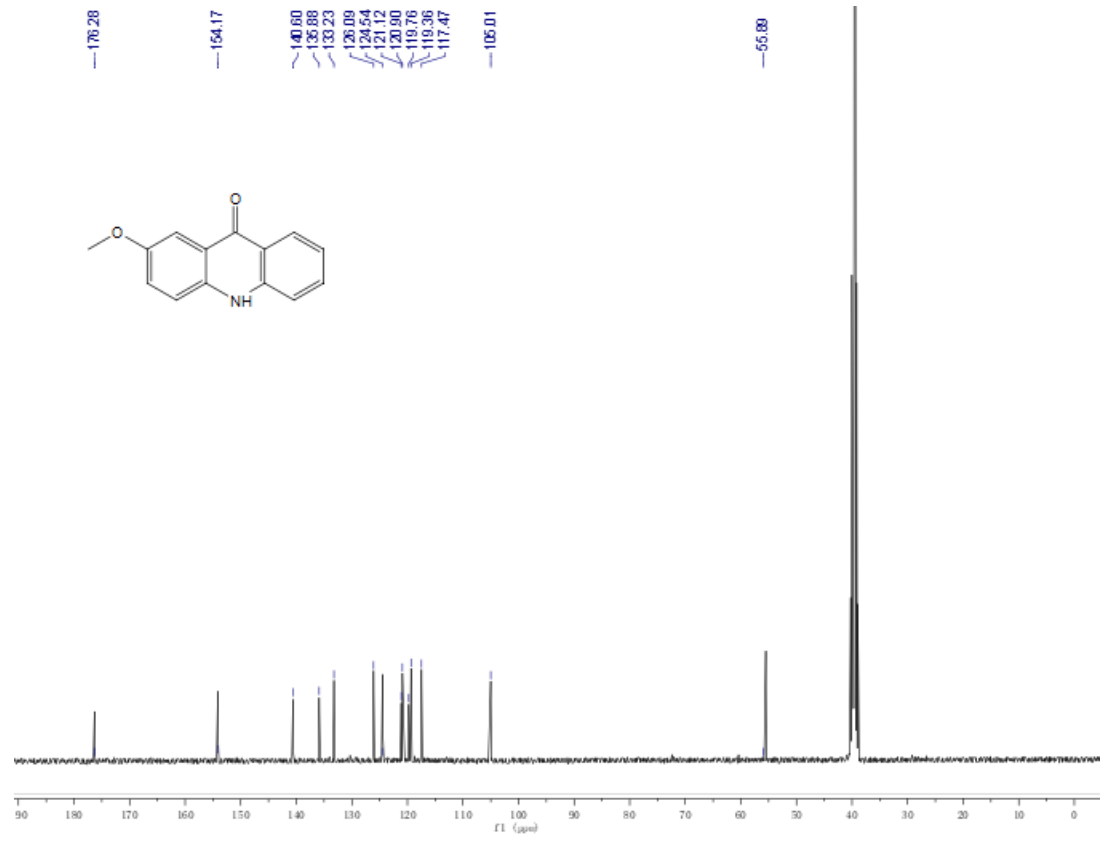
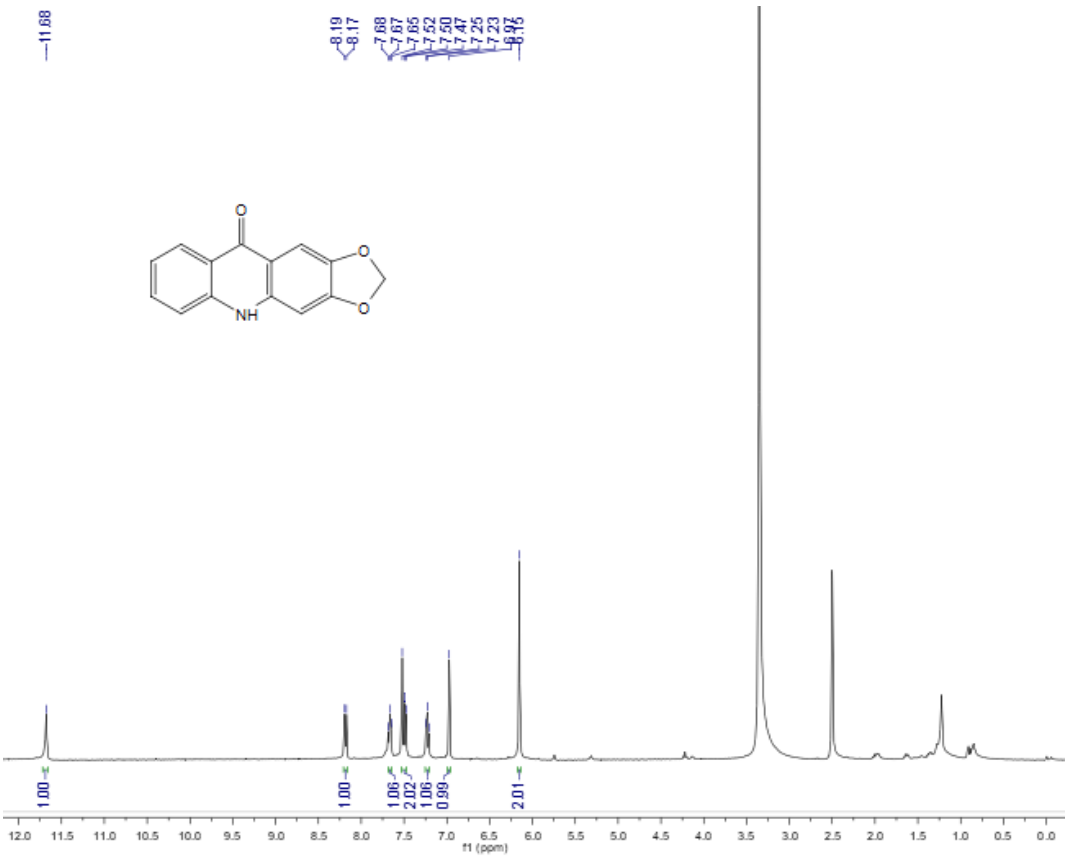
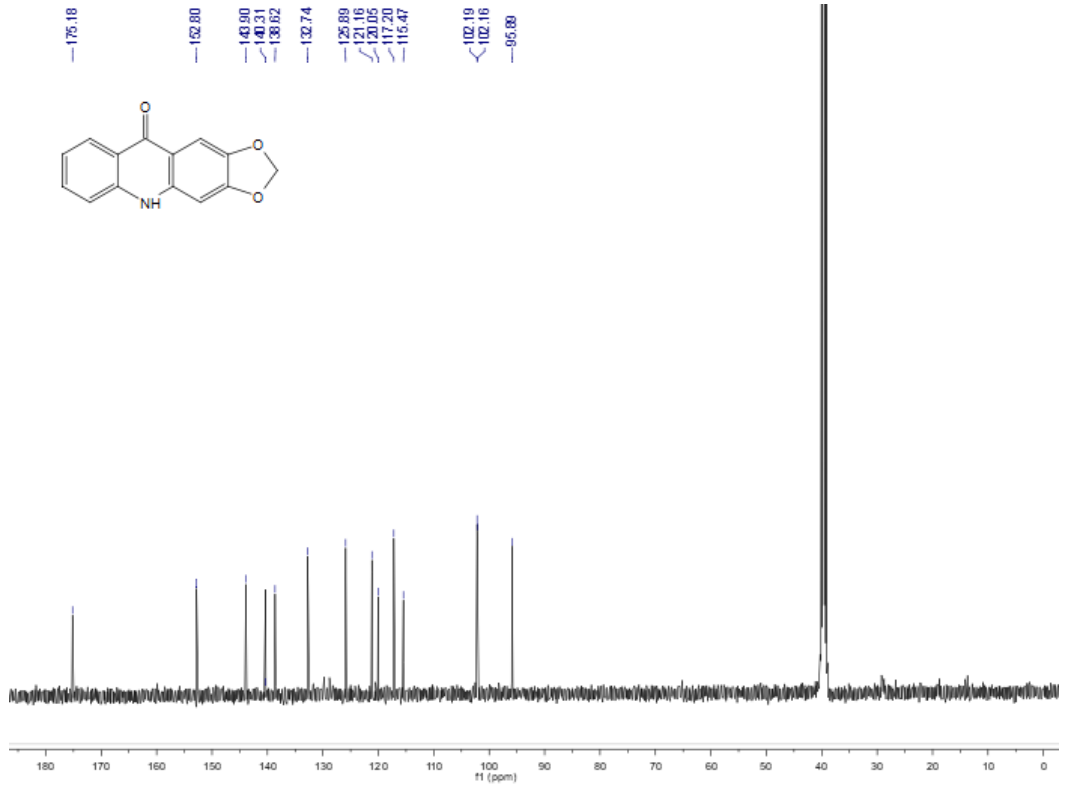
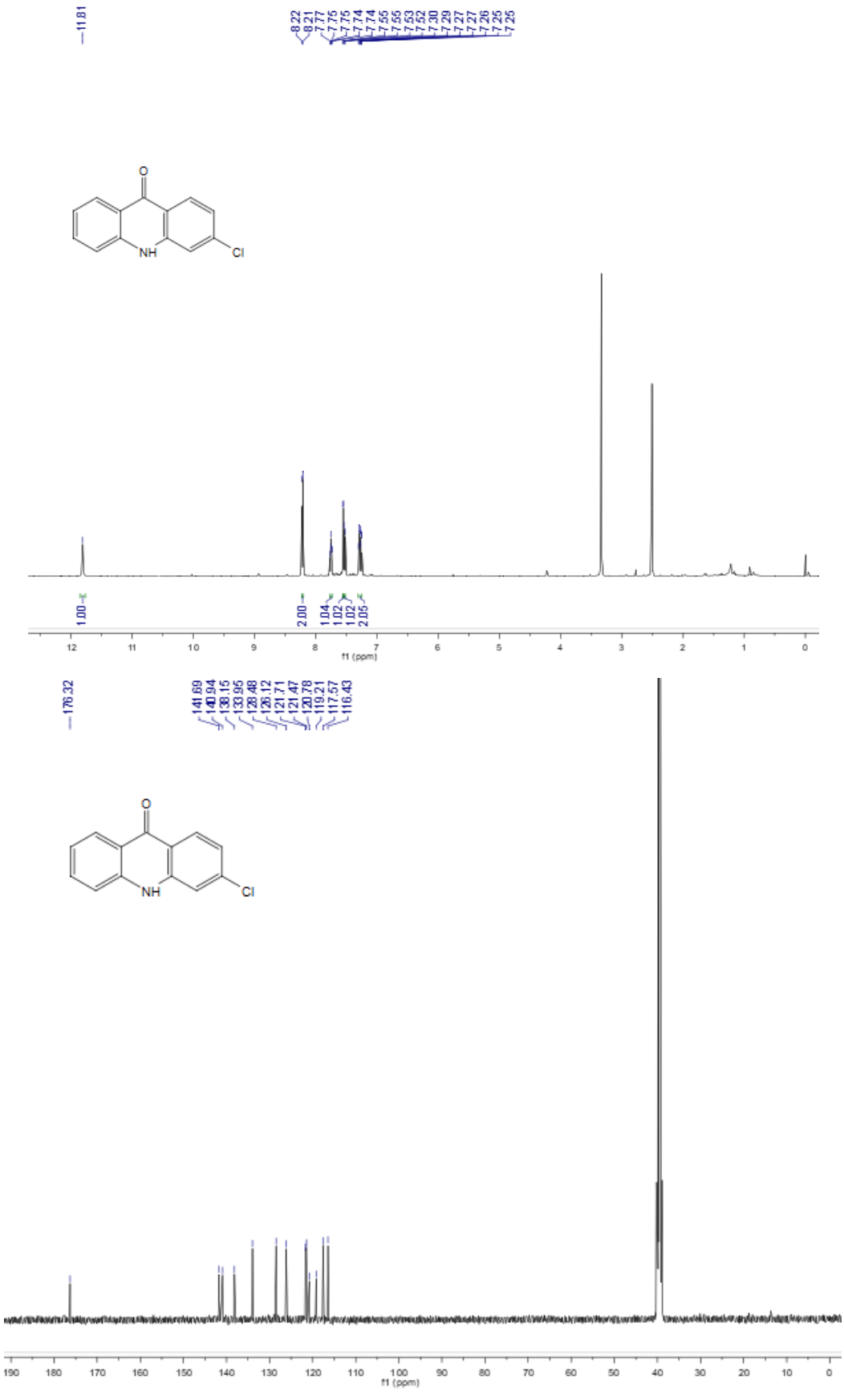
8.22
7.72
7.70
7.68
7.64
7.63
7.54
7.54
7.52
7.42
7.42
7.40
7.40
7.25
7.23
7.21
3.86
O
O
NH
0.95
1.01
1.08
1.02
2.03
1.01
0.96
3.00
f1 (ppm)


176.28
154.17
140.60
135.88
133.23
126.09
124.54
121.12
120.90
119.76
119.36
117.47
105.01
55.89
O
O
NH
f1 (ppm)


11.68
8.19
8.17
7.68
7.67
7.65
7.52
7.50
7.47
7.25
7.23
O
O
O
NH
1.00
1.00
1.06
2.02
1.06
0.99
2.01
f1 (ppm)


175.18
152.80
143.90
140.31
138.62
132.74
125.89
121.16
120.05
117.20
115.47
102.19
102.16
95.89
O
O
O
NH
f1 (ppm)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7.75
7.74
7.74
7.55
7.55
7.53
7.52
7.30
7.29
7.27
7.27
7.26
7.25
7.25
O
NH
Cl
1.00
2.00
1.04
1.02
1.02
2.05
f1 (ppm)
176.32
141.69
140.94
130.15
133.95
128.48
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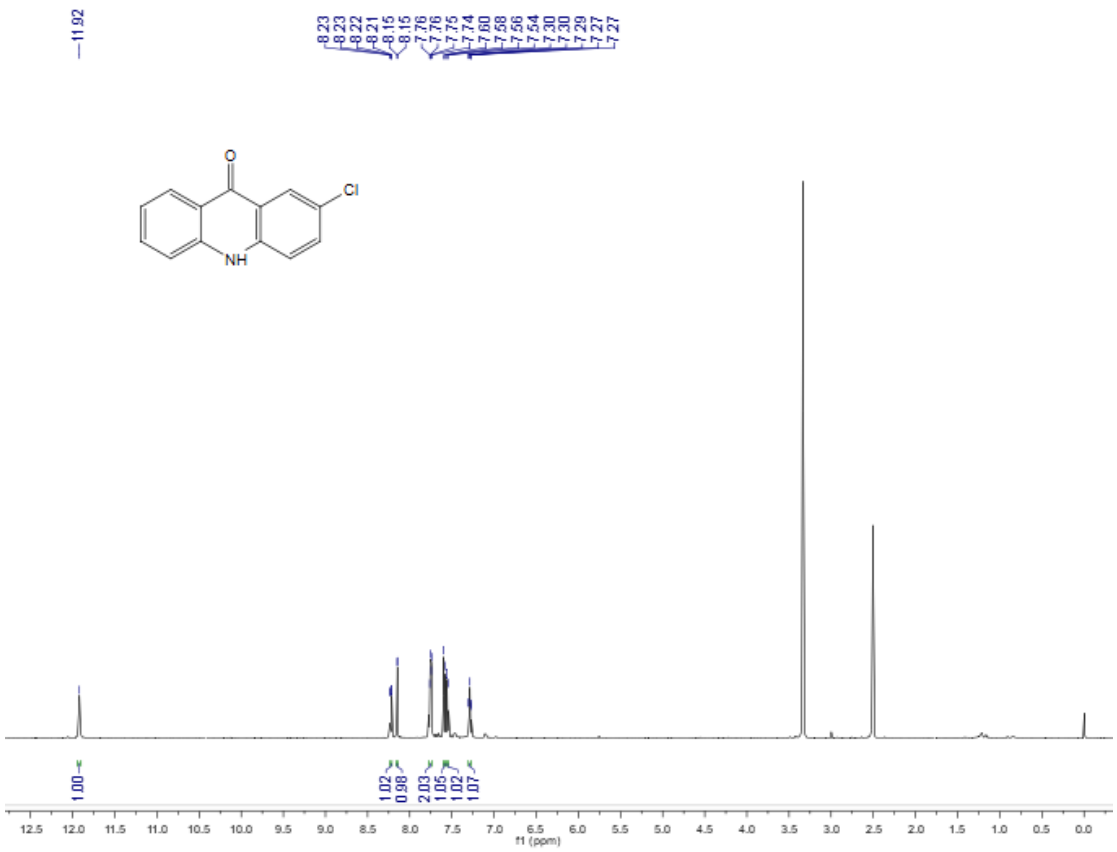
121.71
121.47
120.78
119.21
117.57
116.43
O
NH
Cl
f1 (ppm)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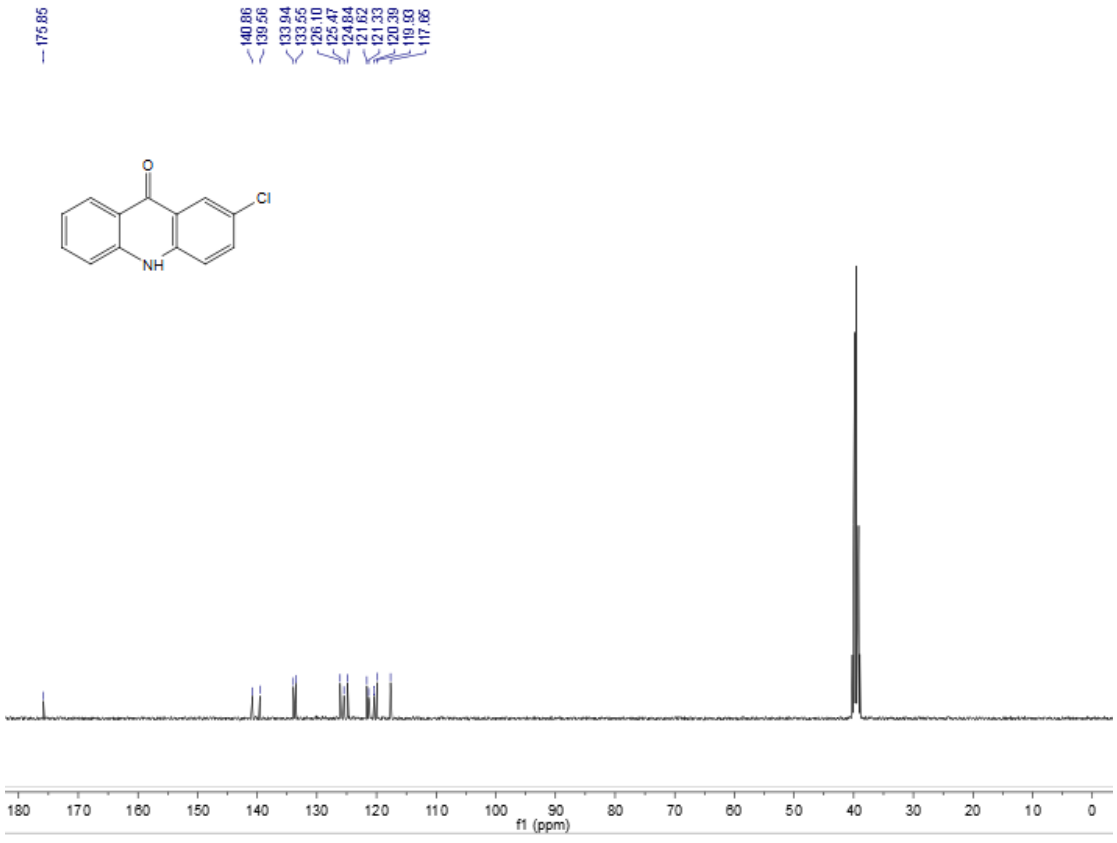
8.23
8.23
8.22
8.21
8.15
8.15
7.76
7.76
7.75
7.74
7.60
7.58
7.56
7.54
7.30
7.30
7.29
7.27
7.27
O
Cl
NH
1.00
1.02
0.98
2.03
1.05
1.02
1.07
f1 (ppm)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140.86
139.56
133.94
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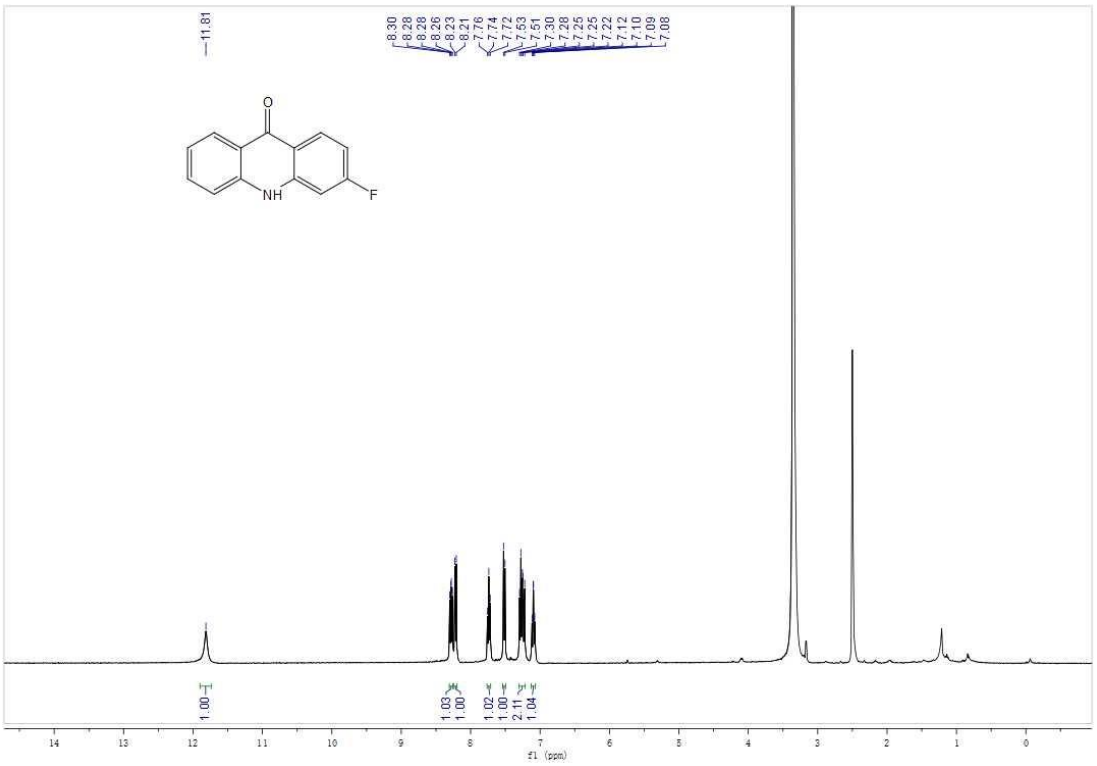
124.84
121.62
121.33
120.39
119.93
117.66
O
Cl
NH
f1 (ppm)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8.28
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8.23
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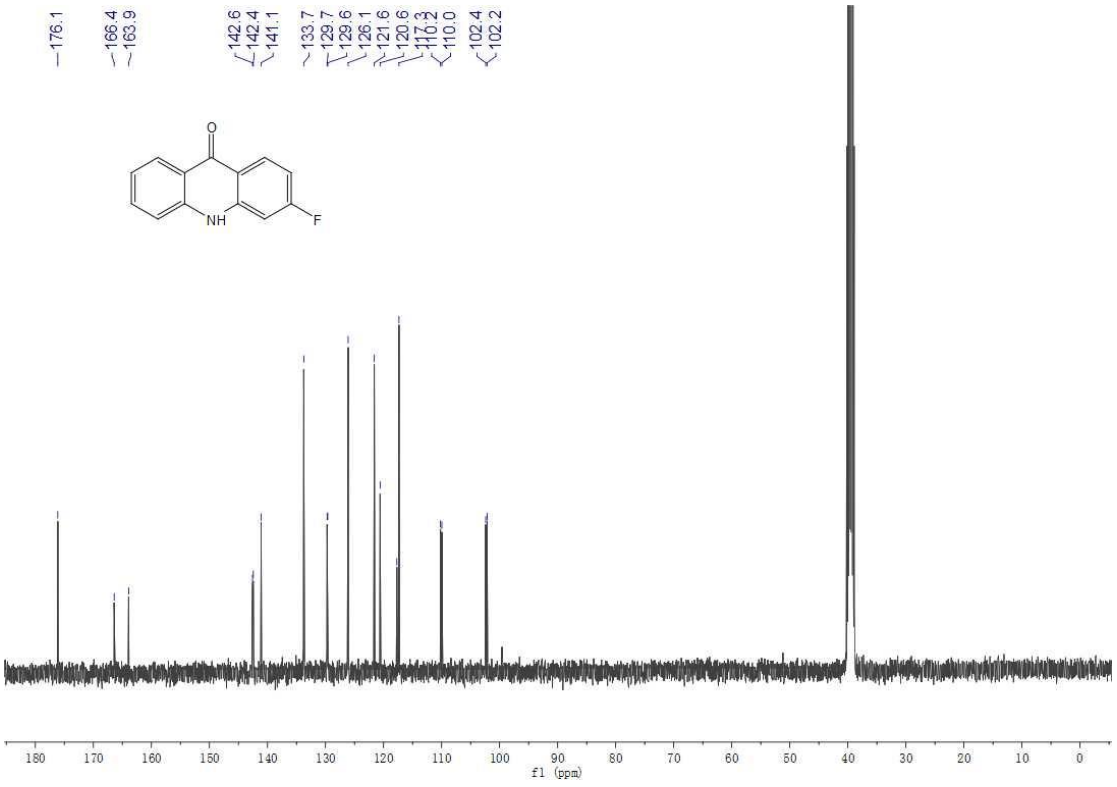
7.76
7.74
7.72
7.53
7.51
7.30
7.28
7.25
7.25
7.22
7.12
7.10
7.09
7.08
O
NH
F
1.00
1.03
1.00
1.02
1.00
2.11
1.04
f1 (ppm)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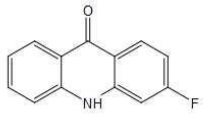
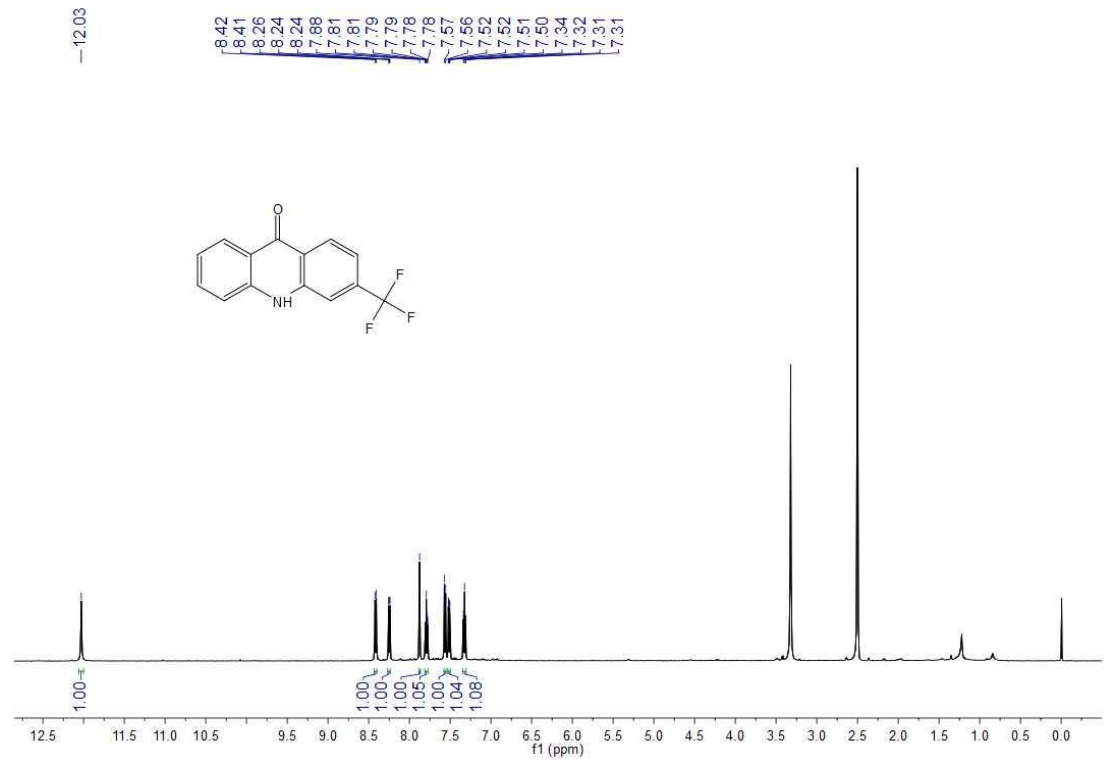
166.4
163.9
142.6
142.4
141.1
133.7
129.7
129.6
126.1
121.6
120.6
117.3
117.2
110.0
102.4
102.2
O
NH
F
f1 (ppm)


O
NH
F

-105.2
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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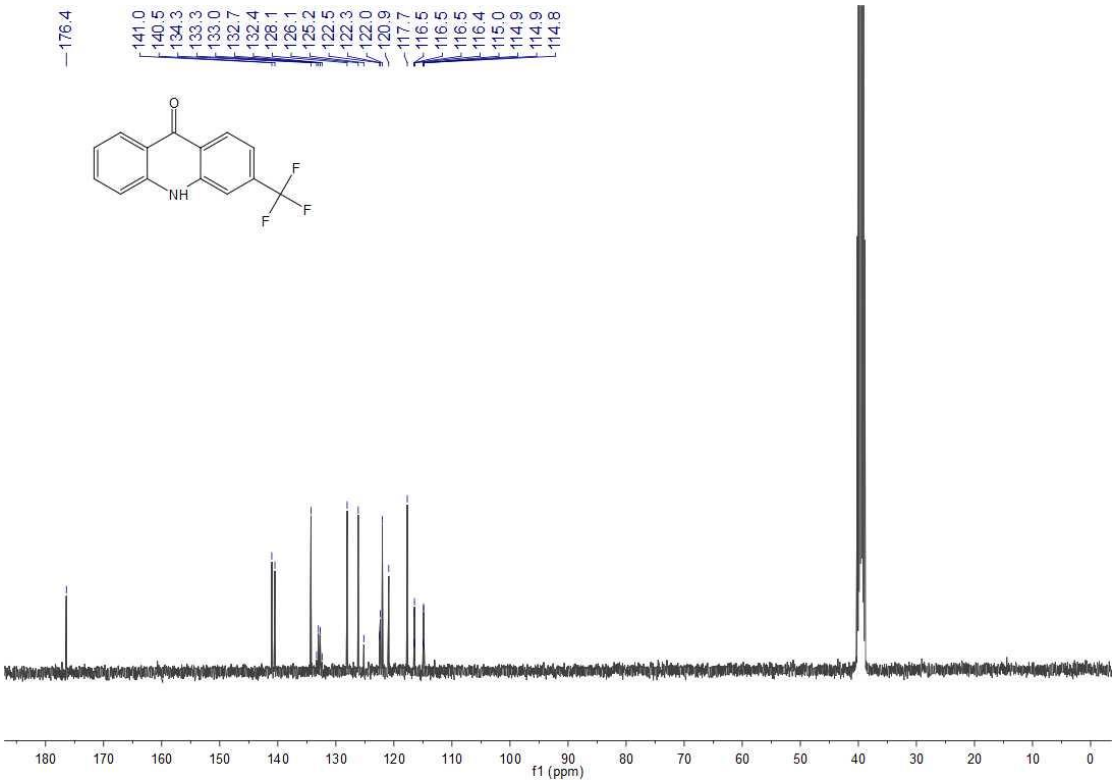
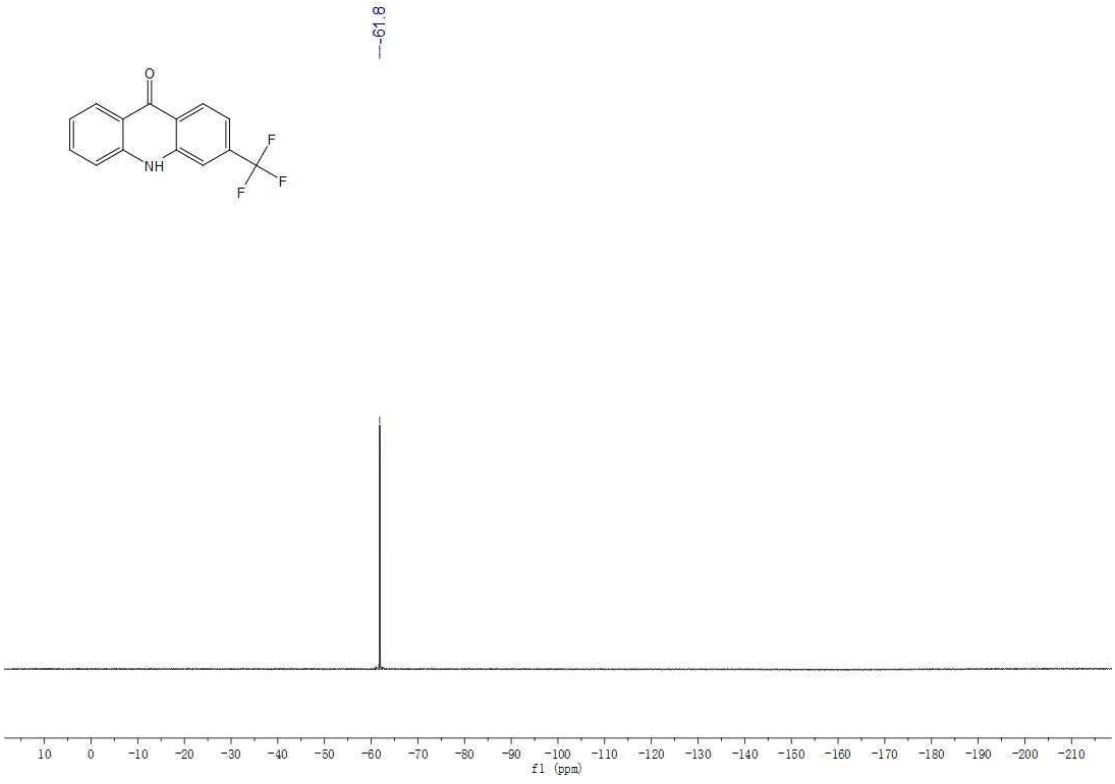
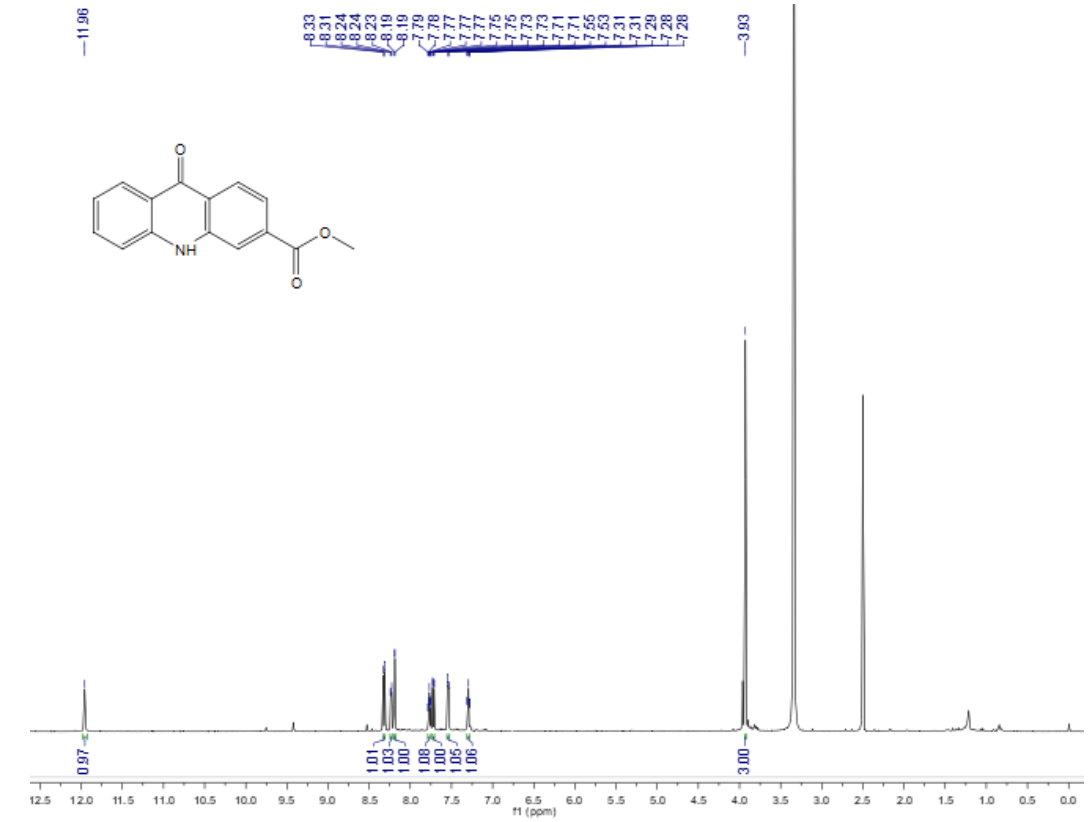
8.26
8.24
8.24
7.88
7.81
7.81
7.79
7.79
7.78
7.78
7.57
7.56
7.52
7.52
7.51
7.50
7.34
7.32
7.31
7.31
O
NH
F
F
F
1.00
1.00
1.00
1.00
1.05
1.00
1.04
1.08
12.5 11.5 11.0 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


176.4
141.0
140.5
134.3
133.3
133.0
132.7
132.4
128.1
126.1
125.2
122.5
122.3
122.0
120.9
117.7
116.5
116.5
116.5
116.4
115.0
114.9
114.9
114.8
O
NH
F
F
F
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-61.8
O
NH
F
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


11.96
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8.24
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8.19
8.19
7.79
7.78
7.77
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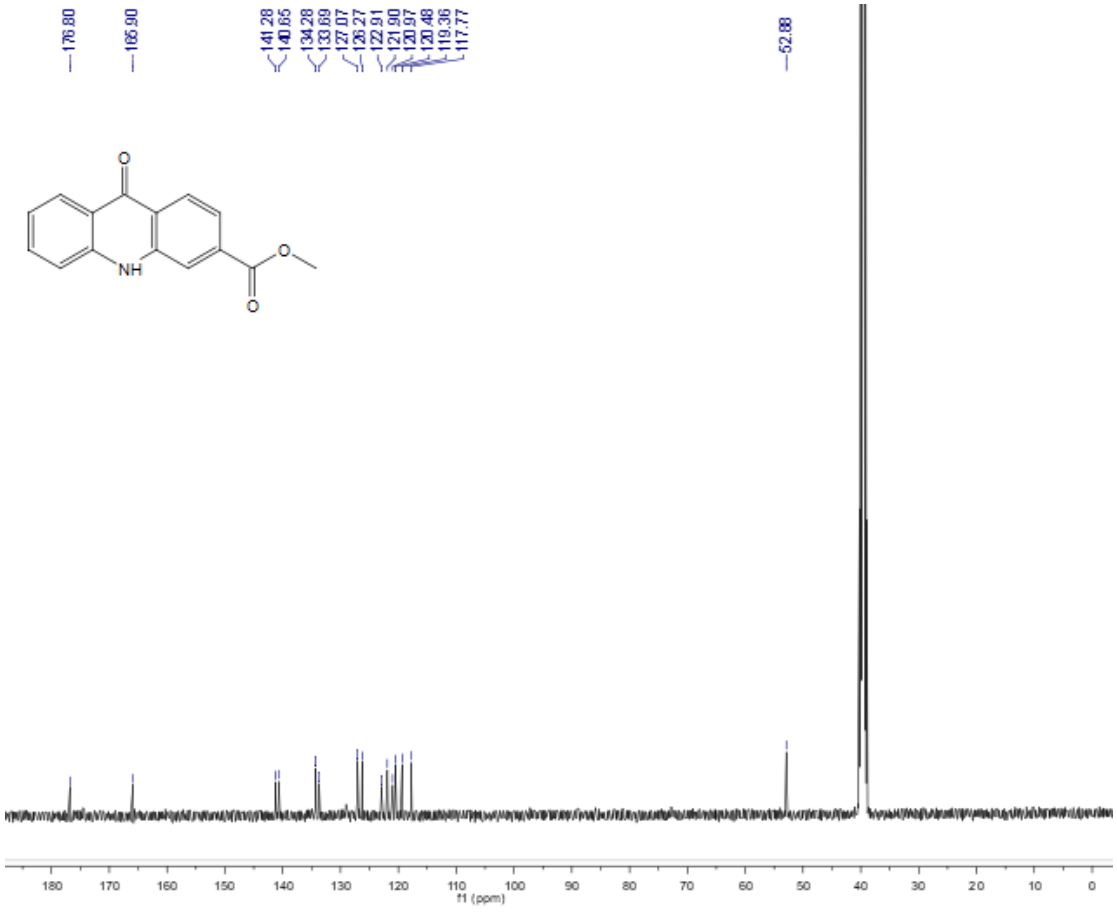
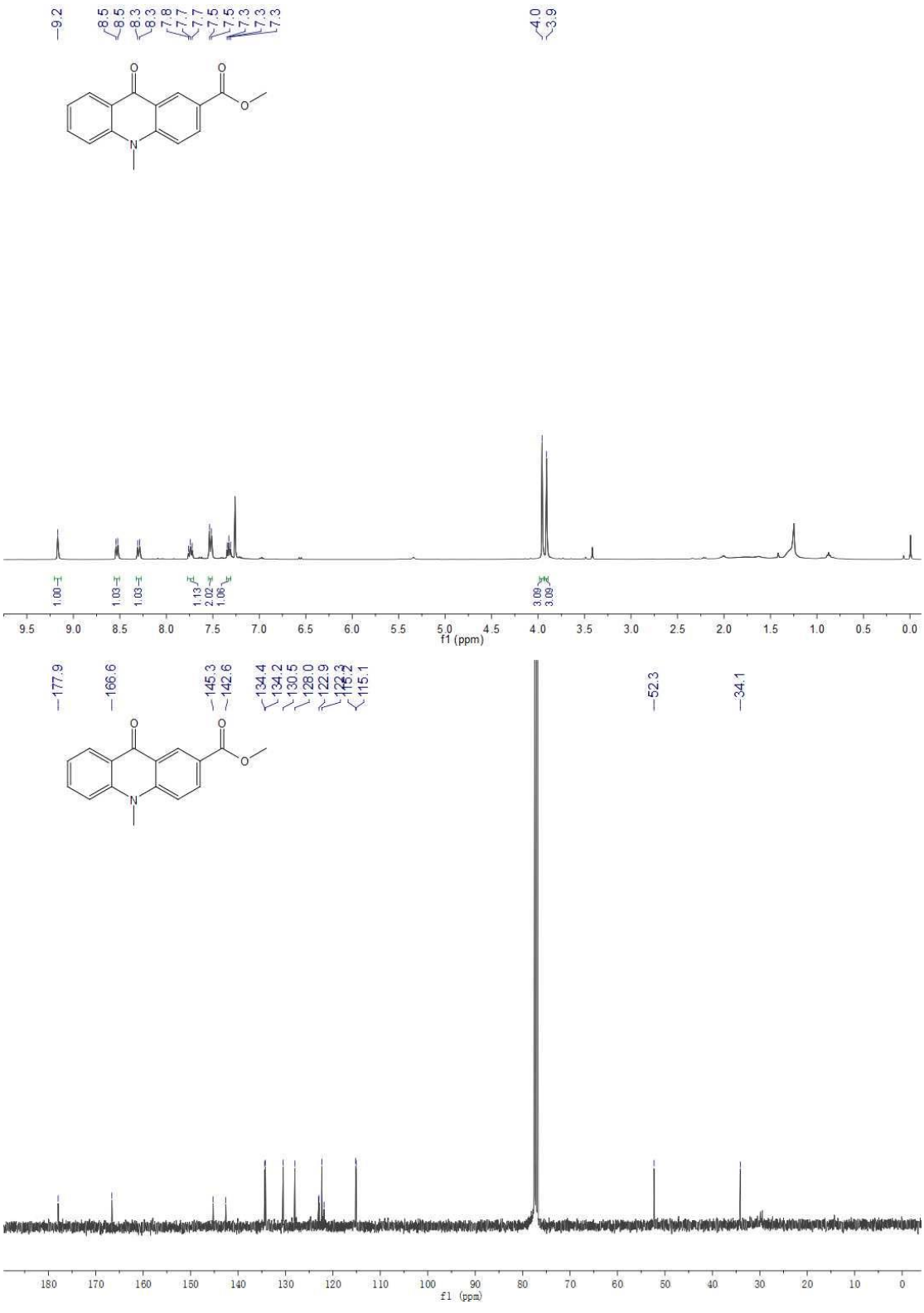
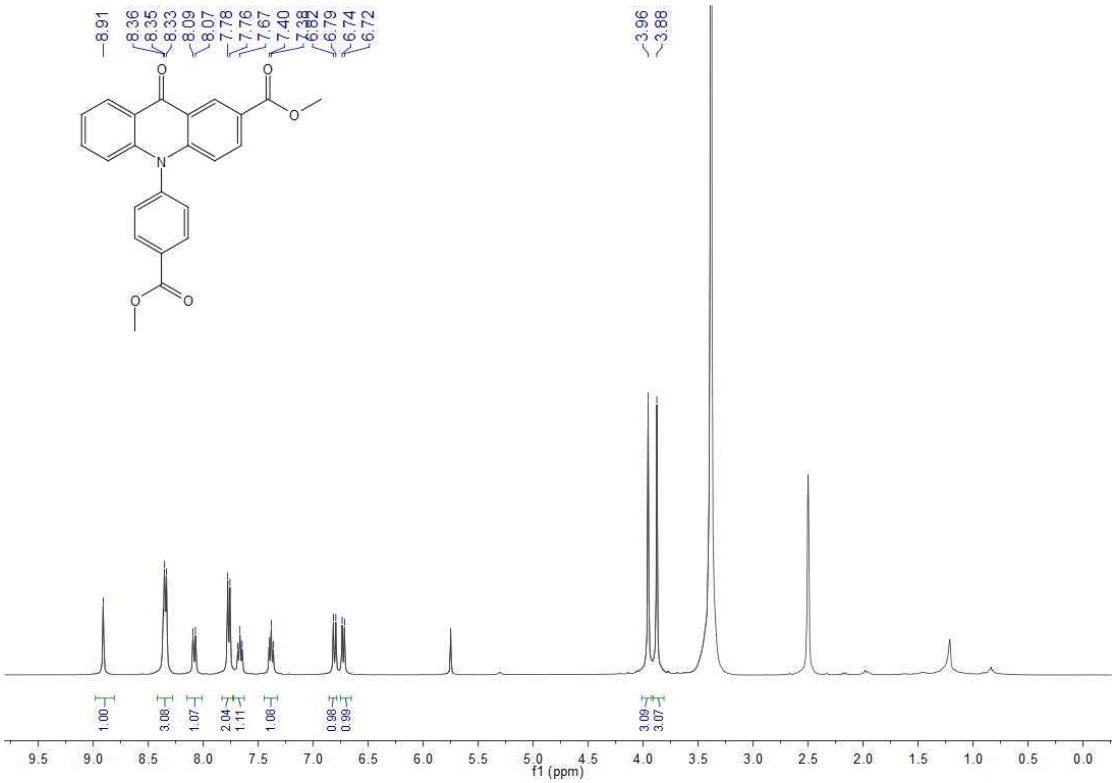
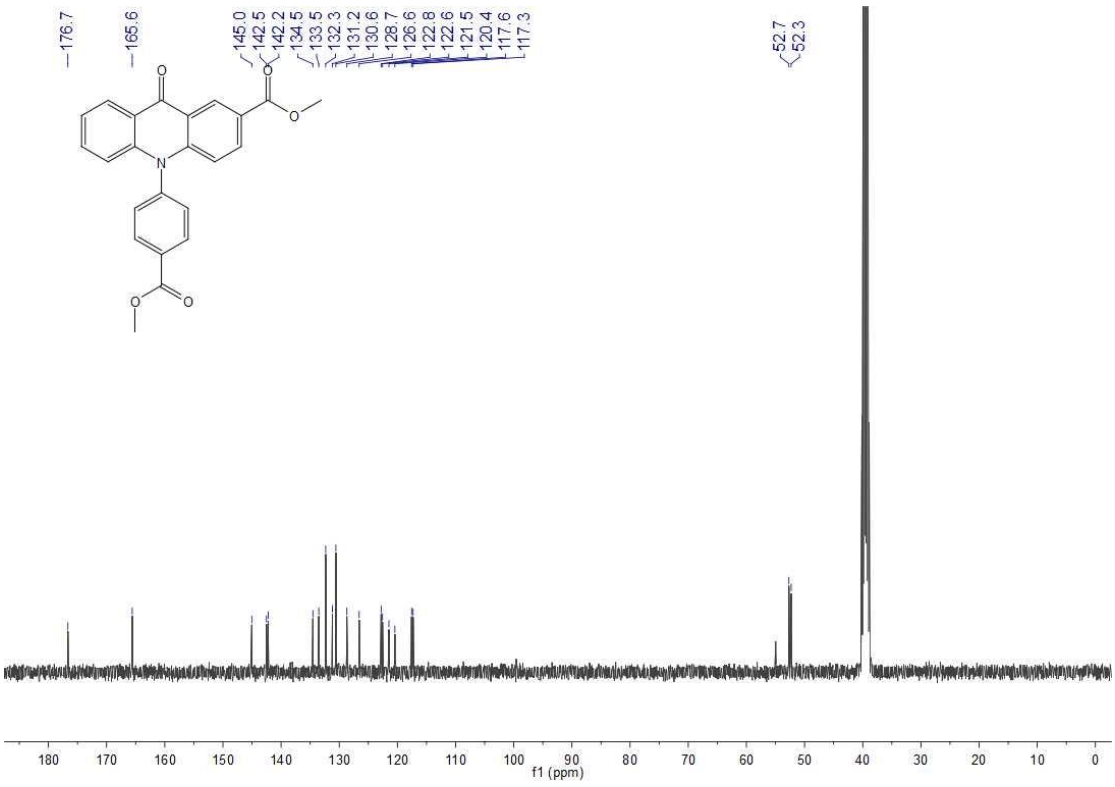
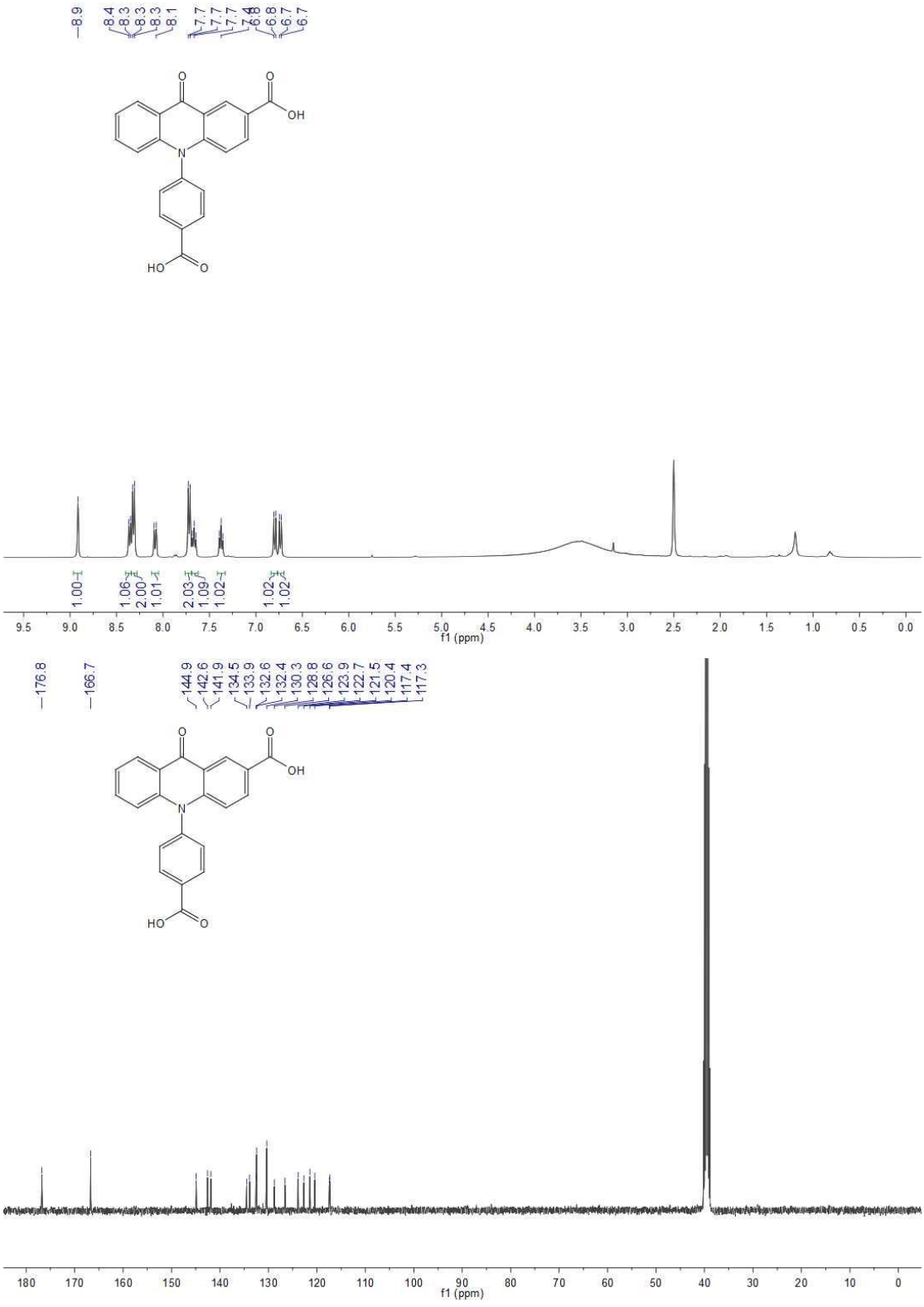
7.75
7.75
7.73
7.73
7.71
7.71
7.55
7.53
7.31
7.31
7.29
7.28
7.28
3.93
O
NH
O
O
0.97
1.01
1.03
1.00
1.08
1.00
1.05
1.06
3.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


176.80
165.90
141.28
140.65
134.28
133.69
127.07
126.27
122.91
121.90
120.97
120.48
119.36
117.77
52.88
O
NH
O
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.2
8.5
8.5
8.3
8.3
7.8
7.7
7.7
7.5
7.5
7.3
7.3
7.3
4.0
3.9
O
O
O
N
1.00
1.03
1.03
1.13
2.02
1.06
3.09
3.09
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)
177.9
166.6
145.3
142.6
134.4
134.2
130.5
128.0
122.9
52.3
34.1
115.1
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.91
8.36
8.35
8.33
8.09
8.07
7.78
7.76
7.67
7.40
6.79
6.74
6.72
3.96
3.88
1.00
3.08
1.07
2.04
1.11
1.08
0.98
0.99
3.09
3.07
f1 (ppm)


176.7
165.6
145.0
142.5
142.2
134.5
133.5
132.3
131.2
130.6
128.7
126.6
122.8
122.6
121.5
120.4
117.6
117.3
52.7
52.3
f1 (ppm)


8.9
8.4
8.3
8.3
8.3
8.1
7.7
7.7
7.7
7.4
6.8
6.7
6.7
O
O
OH
N
HO
O
1.00
1.06
2.00
1.01
2.03
1.09
1.02
1.02
1.02
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)
176.8
166.7
144.9
142.6
141.9
134.5
133.9
132.6
132.4
130.3
128.8
126.6
123.9
122.7
121.5
120.4
117.4
117.3
O
O
OH
N
HO
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

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