Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

A Sequential Friedländer and Anionic Benzannulation Strategy for the Regiodefined Assembly of Unsymmetrical Acridines

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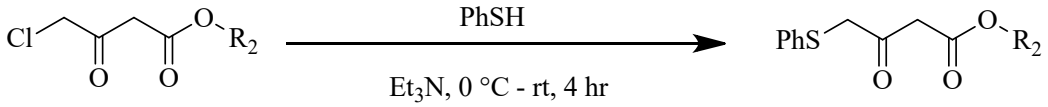
1. General Information

Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere. Solvents were dried and distilled according to the standard procedures. TLC was performed using precoated plates of silica gel 60 F254 with UV light. Column chromatography was performed on silica gel (60-120 or 230-400 mesh) using ethyl acetate as eluent. ^{1}H and ^{13}C for all the compounds were recorded at 400/500/600 and 100/125/150 MHz (Bruker) at 25 ˚C in suitable solvents and spectral data were reported in ppm relative to tetramethyl silane (TMS) as internal standard. Commercial-grade reagents were used without further purification except as indicated below. Michael acceptors used in this paper such as methyl acrylate (**4a**), ethyl acrylate (**4b**), methyl-crotonate (**4c**), dimethyl-maleate (**4d**), methyl cinnamate (**4e**) and vinyl cinnamate (**4f**) are procured from commercial suppliers and used as obtained. Few other Michael acceptors were prepared according to Horner-Wadsworth-Emmons reaction. Mass spectrometric analysis was performed in the Department of Chemistry, IIT Kharagpur (TOF analyzer).

2. General Procedures

2.1 General Procedure A: Synthesis of alkyl 3-oxo-4-(phenylthio)butanoate (2)

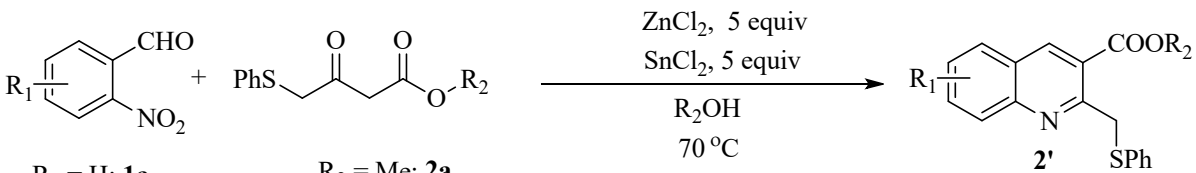


R_2 = Me, Et

2a: R_2 = Me
2b: R_2 = Et

Methyl or ethyl 4-chloroacetoacetate (1 equiv) was added slowly to an ice-cold solution of a mixture of thiophenol (1.1 equiv) and triethyl amine (1.5 equiv) with stirring. Then the reaction solution was stirred for an additional 3-4 h.[1] After that time, water was added to the reaction solution and it was extracted with ethyl acetate. The organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica column chromatography (petroleum ether: ethyl acetate = 40:1 to 20:1, volume ratio) on silica gel to afford the desired product **2a**/**2b** (85-90%) as a slightly yellow liquid.

2.2 General Procedure B: Synthesis of alkyl-2-((phenylthio)methyl)quinoline-3-carboxylate (2')



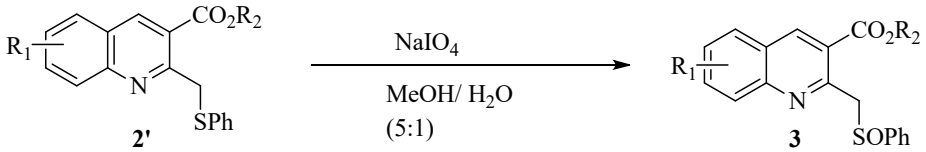
R_1 = H; **1a**
R_1 = Br; **1b**
R_1= OMe; **1c**

R_2 = Me; **2a**
R_2 = Et; **2b**

To a stirred solution of 2-nitrobenzaldehyde (**1a** or **1b** or **1c**; 5 mmol) in 30 ml of anhydrous alcohol in a flame dried two necks round bottom flask charged with 6 gm of 3A molecular sieves, 25 mmol $ZnCl_2$ and 25 mmol $SnCl_2$ was added at room temperature. The resulting mixture was heated at a refluxing temperature under an atmosphere of N_2 for 5 h. Alkyl-3-oxo-

4-(phenylthio)butanoate (5.5 mmol) was then added dropwise to the reaction mixture and again the reaction was continued at refluxing temperature for another 10 hr. After completion, as indicated by TLC analysis, the reaction solution was then allowed to cool at room temperature and made alkaline (pH = 8.0) by the drop-by-drop addition of potassium carbonate solution. After filtration and usual workup by ethyl acetate the organic phase was dried over anhydrous Na_2SO_4. The residue was purified through column chromatography to give pure compounds (**2'a-2'd)** as solid.[2]

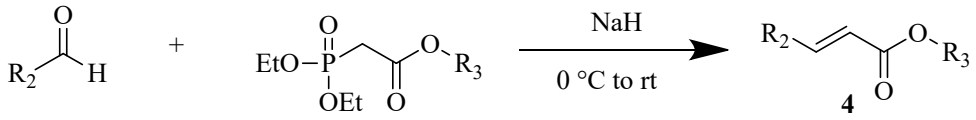
2.3 General Procedure C: Synthesis of alkyl-2-((phenylsulfinyl)methyl)quinoline-3-carboxylate (3)



R_1 = H, Br, OMe
R_2 = Me, Et

To a stirred solution of compound **2'** (1 mmol) in a mixture of methanol and water (5: 1 volume ratio), $NaIO_4$ (1.2 mmol) was added portion-wise at 30-minute intervals. Then the resulting mixture was allowed to stir at room temperature. After completion of the reaction, the methanol was removed under reduced pressure. The reaction mixture was then workup by ethyl acetate and water and the crude product was purified by flash column chromatography to furnish the desired product as a white solid.[3]

2.4 General procedure D: Horner-Wadsworth-Emmons reaction for the synthesis of Michael acceptors (4)



R_2= Alkyl, Aryl, Het-aryl R_3 = Me, Et

To a stirred solution of NaH (1.5 equiv) in THF at 0 ˚C, methyl 2-(diethoxyphosphoryl)acetate or ethyl 2-(diethoxyphosphoryl)acetate (1 equiv) was added slowly under nitrogen atmosphere and the resulting solution was stirred for 30 minutes at 0 ˚C. Then a solution of suitable aldehyde (1 equiv) in THF was added slowly to the reaction mixture. After that reaction mixture was stirred at room temperature for 2-3 hr. After completion of the reaction as indicated by TLC analysis, the solvent was evaporated under reduced pressure. The crude product was then purified by column chromatography to afford the α,β-unsaturated esters (petroleum ether: ethyl acetate = 25: 1 to 10 : 1, volume ratio).

(*E*)-methyl pent-2-enoate (**4g**): Prepared from n-propanal and methyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [4]

(*E*)-ethyl 3-(naphthalen-1-yl)acrylate (**4h**): Prepared from 1-napthaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [5]

(*E*)-ethyl 3-(4-nitrophenyl)acrylate (**4i**): Prepared from 4-nitrobenzaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [6]

(*E*)-ethyl 3-(4-(trifluoromethyl)phenyl)acrylate (**4j**): Prepared from 4-trifluoromethylbenzaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [7]

(*E*)-ethyl 3-(4-bromophenyl)acrylate (**4k**): Prepared from 4-bromobenzaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [8]

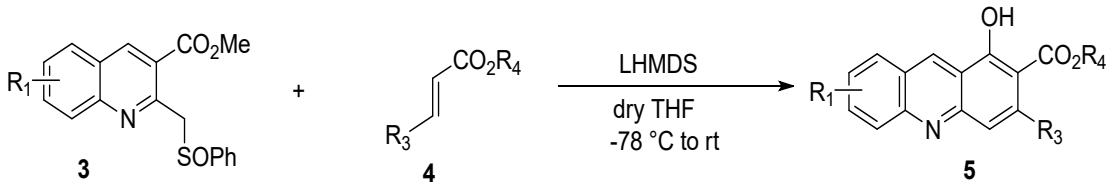
(*E*)-ethyl 3-(4-methoxyphenyl)acrylate (**4l**): Prepared from 4-methoxybenzaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [9]

(*E*)-ethyl 3-(pyridin-4-yl)acrylate (**4m**): Prepared from pyridine-4-carboxaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [10]

(*E*)-methyl 3-(furan-2-yl)acrylate (**4n**): Prepared from furan-2-carboxaldehyde and methyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [11]

(*E*)-ethyl 3-(thiophen-2-yl)acrylate (**4o**): Prepared from thiophene-2-carboxaldehyde and ethyl-2(diethoxyphosphoryl) acetate through HWE olefination as depicted above. Spectroscopic (^{1}H, ^{13}C-NMR) data matches perfectly as reported. [5]

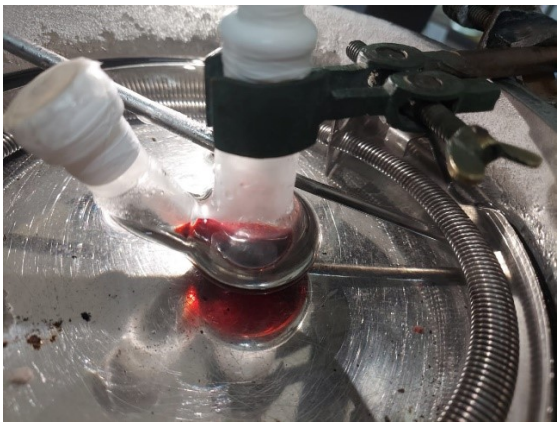
2.5 General Procedure E: Annulation between quinolone sulfoxide derivative (3) and Michael acceptors (4)



To a cooled (–78 ˚C) stirred solution of lithium bis(trimethylsilyl) amide (3 mmol) in THF (5 ml) was added to a solution of quinoline sulfoxide **3** (1 mmol) in THF (5 ml) under a nitrogen atmosphere. The resulting deep red solution (see the attached image below) was stirred at –78 ˚C for 30 min, then a solution of Michael acceptor **4** in THF (5 ml) was added slowly. After stirring at the same temperature for an additional hour the cooling bath was removed and the

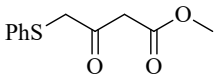
reaction mixture was settled to arrive at room temperature. Then the reaction mixture was stirred overnight at room temperature.[3a-3b] Upon completion of the reaction, 10% aq. NH_4Cl was added and the resulting solution was concentrated under vacuum. The residue was extracted with ethyl acetate, dried over Na_2SO_4 and the removal of the solvent under reduced pressure provide the crude product. Purification by flash column chromatography provides the pure product **5a** to **5v.**

Reaction color at beginning



Deep red carbanion generated after base addition

Methyl 3-oxo-4-(phenylthio)butanoate (2a)

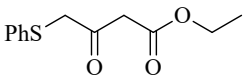


2a

Following the general procedure as described in **A** using the thiophenol (4.03 gm, 0.36 mol), methyl 4-chloro-3-oxobutanoate (5 gm, 0.33 mol), and triethyl amine (0.5 mol), the title compound **2a** was obtained in 80% yield as light-yellow liquid (5.54 gm). R_f = 0.5 (Hexane: EtOAc = 30:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 3.82 (s, 2H), 3.73 (s, 3H), 3.67 (s, 2H).
^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 197.8, 167.4, 134.0, 129.8, 129.27, 127.25, 52.4, 46.2, 43.9.

Ethyl 3-oxo-4-(phenylthio)butanoate (2b)



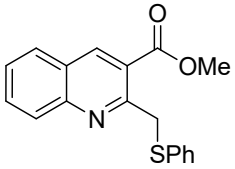
2b

Following the general procedure as described in **A** using the thiophenol (4.03 gm, 0.36 mol), ethyl 4-chloro-3-oxobutanoate (5 gm, 0.33 mol), and triethyl amine (0.5 mol), the title compound was obtained in 78 % as light-yellow liquid (5.9 gm). R_f = 0.5 (Hexane: EtOAc = 30: 1), NMR spectral data was well matched with previously reported for this compound. [12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 5H), 4.19 (q, *J* = 8.0 Hz, 2H), 3.83 (s, 2H), 3.65 (s, 2H), 1.28 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 197.8, 166.9, 134.1, 129.8, 129.2, 127.2, 61.4, 46.5, 44.0, 14.0

Methyl 2-((phenylthio)methyl)quinoline-3-carboxylate (2'a)



Following the general procedure as described in **B**, using the 2-nitro benzaldehyde (**1a**) (1 gm, 6.6 mmol) and **2a** (1.632 gm, 6.6 mmol), the title compound was obtained in 77% yield as white solid (1.24 gm). R_f = 0.4 (Hexane: EtOAc = 10: 1). M.pt (°C): 70-72.

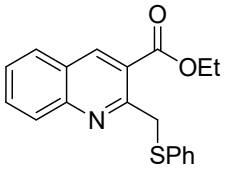
IR (KBr, cm $^{-1}$), 3057, 2935, 1708, 1419, 1261, 1052, 938, 749.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.2 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 8.1, 6.7 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 4.88 (s, 2H), 3.98 (s, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 166.6, 157.6, 147.9, 140.7, 136.1, 131.8, 130.2, 128.8, 128.6, 128.4, 127.2, 126.3, 126.1, 123.1, 52.5, 40.6.

HRMS (ESI-TOF) m/z: [M + H] $^{+}$ calcd. for $C_{18}H_{16}NO_2S$ 310.0902; Found 310.0883

Ethyl 2-((phenylthio)methyl)quinoline-3-carboxylate (2'b)



Following the general procedure as described in **B**, using the 2-nitro benzaldehyde (**1a**) (1 gm, 6.6 mmol) and **2b** (1.632 gm, 6.6 mmol), the title compound was obtained in 80% yield as white solid (1.25 gm). R_f = 0.4 (Hexane: EtOAc = 10:1). M.pt (°C): 74-76.

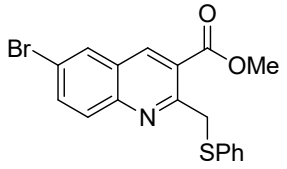
IR (KBr, cm $^{-1}$), 3062, 2930, 1710, 1420, 1261, 1050, 936, 759.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 4.90 (s, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.47 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 166.1, 157.5, 147.7, 140.7, 136.1, 134.4, 131.8, 130.2, 128.6, 128.4, 127.2, 126.3, 126.1, 123.6, 61.7, 40.5, 14.2

HRMS (ESI-TOF) m/z: [M + H] $^{+}$ calcd. for $C_{18}H_{16}NO_2S$ 324.1058; Found 324.1052

Methyl 6-bromo-2-((phenylthio)methyl)quinoline-3-carboxylate (2'c)



Following the general procedure as described in **B**, using the 5-bromo-2-nitrobenzaldehyde (**1b**) (5 gm, 21.73 mmol) and **2a** (5.36 gm, 23.91 mmol) title compound was obtained as white solid (4.97 gm, yield 73 %). R_f = 0.3 (Hexane: EtOAc = 10: 1). M.pt (°C): 102-104.

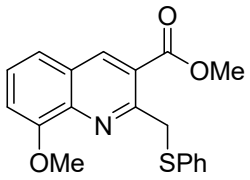
IR (KBr, cm $^{-1}$), 3057, 2935, 1708, 1419, 1261, 1052, 938, 749.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.76 (dd, *J* = 9.0 Hz, 2.5 Hz, 1H), 7.31 (d, *J* = 7.0 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 4.77 (s, 2H), 3.90 (s, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 166.2, 158.0, 146.4, 139.5, 135.7, 135.2, 133.6, 130.5, 130.3, 128.7, 127.2, 126.5, 124.1, 121.1, 52.7, 40.5.

HRMS (ESI-TOF) m/z: [M + H] $^+$ calcd. for $C_{18}H_{15}BrNO_2S$ 388.0007; Found 388.0011

Methyl-8-methoxy-2--((phenylthio)methyl)quinoline-3-carboxylate (2'd)



Following the general procedure as described in **B**, using the 3-methoxy-2-nitrobenzaldehyde (**1c**) (1 gm, 5.52 mmol) and **2a** (1.072 gm, 4.782 mmol) title compound was obtained in 75% yield as white solid (1.04 gm). R_f = 0.35 (Hexane: EtOAc = 10:1). M.pt (°C): 74-76.

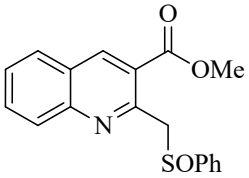
IR (KBr, cm $^{-1}$), 3050, 2938, 1712, 1422, 1260, 1050, 938, 749.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.48 (dd, *J* = 13.0, 6.9 Hz, 4H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 6.6 Hz, 2H), 4.96 (s, 2H), 4.09 (s, 3H), 3.96 (s, 3H).

^{13}C NMR {^{1}H} (126 MHz, $CDCl_3$) δ 165.7, 155.3, 154.2, 139.4, 138.9, 135.5, 128.9, 127.6, 126.4, 126.34, 125.1, 122.8, 119.1, 109.4, 55.3, 51.5, 39.6.

HRMS (ESI-TOF) m/z: [M + H] $^+$ calcd. for $C_{19}H_{18}NO_3S$ 340.1007; Found 340.1007.

Methyl 2-((phenylsulfinyl)methyl)quinoline-3-carboxylate (3a)



Following the general procedure as described in **C**, using the compound **2'a** (1 gm, 3.232 mmol) and $NaIO_4$ (0.83 gm, 3.88 mmol) title compound **3a** was obtained in 92 % yield as white solid (0.968 gm). R_f = 0.2 (Hexane: EtOAc = 3: 1). M.pt (°C): 149-151.

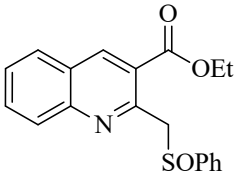
IR (KBr, cm $^{-1}$), 3033, 2932, 1700, 1426, 1274, 1201, 1042,753.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 8.4 Hz, 1H), 7.65 – 7.61 (m, 3H), 7.46 – 7.42 (m, 3H), 5.13 (d, *J* = 12.4 Hz, 1H), 4.91 (d, *J* = 12.4 Hz, 1H), 3.99 (s, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 166.3, 151.0, 148.5, 144.1, 140.5, 132.2, 130.9, 129.1, 128.9, 128.5, 127.7, 126.2, 124.4, 123.7, 64.8, 52.6.

HRMS (ESI-TOF) m/z: [M + H] $^+$ calcd. for $C_{18}H_{16}NO_3S$ 326.0851; Found 326.0828

Ethyl 2-((phenylsulfinyl)methyl)quinoline-3-carboxylate (3b)



Following the general procedure as described in **C**, using the compound **2'a** (1 gm, 3.23 mmol) and $NaIO_4$ (0.83 gm, 3.88 mmol) title compound **3b** was obtained in 92 % yield as white solid (0.98 gm). R_f = 0.2 (Hexane: EtOAc = 3: 1). M.pt (°C): 80-82.

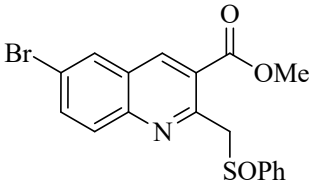
IR (KBr, cm $^{-1}$), 3038, 2930, 1708, 1420, 1265, 1200, 1040,753.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.83 (t, *J* = 7.7 Hz, 1H), 7.68 – 7.61 (m, 3H), 7.50 – 7.43 (m, 3H), 5.12 (d, *J* = 12.3 Hz, 1H), 4.92 (d, *J* = 12.3 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 165.8, 151.1, 148.6, 144.2, 140.3, 132.0, 130.9, 129.1, 128.9, 128.5, 127.6, 126.3, 124.4, 123.9, 65.0, 61.7, 14.2.

HRMS (ESI-TOF) m/z: [M + H] $^+$ calcd. for $C_{18}H_{18}NO_3S$ 340.1002; Found 340.1018

Methyl 6-bromo-2-((phenylsulfinyl)methyl)quinoline-3-carboxylate (3c)



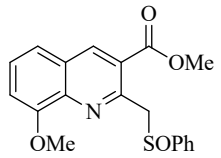
Following the general procedure as described in **C**, using the compound **2'b** (1 gm, 2.57 mmol) and $NaIO_4$ (0.66 gm, 3.09 mmol), title compound **3b** was obtained in 87% yield as white solid (0.92 gm). R_f = 0.2 (Hexane: EtOAc = 3: 1). M.pt (°C): 178-180.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.10 (s, 1H), 8.02 (d, *J* = 9.2 Hz, 1H), 7.91 (d, *J* = 9.2 Hz, 1H), 7.62 (d, *J* = 4.4 Hz, 2H), 7.47 (m, 3H), 5.18 (d, *J* = 12.4 Hz, 1H), 4.91 (d, *J* = 12.4 Hz, 1H), 4.02 (s, 3H).

^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 165.9, 151.4, 147.1, 143.8, 139.2, 135.5, 131.0, 130.8, 130.4, 128.9, 127.3, 124.6, 124.3, 121.7, 64.5, 52.7.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{18}H_{15}BrNO_3S$ 403.9956; Found 403.9952

Methyl 8-methoxy-2-((phenylsulfinyl)methyl)quinoline-3-carboxylate (3d)



Following the general procedure as described in **C**, using the compound **2'c** (1 gm, 2.94 mmol) and $NaIO_4$ (0.66 gm, 3.09 mmol), title compound **3c** was obtained in 87% yield as a white solid (0.9 gm). R_f = 0.2 (Hexane: EtOAc = 2:1). M.pt (°C): 172-174.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.67 (d, *J* = 4.4 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 10.8 Hz, 4H), 7.18 (d, *J* = 7.6 Hz, 1H), 5.13 (d, *J* = 12.4 Hz, 1H), 5.06 (d, *J* = 12.4 Hz, 1H), 4.09 (s, 3H), 3.99 (s, 3H).

^{13}C NMR {^{1}H} (126 MHz, $CDCl_3$) δ 166.4, 155.2, 149.8, 144.13, 144.11, 140.5, 140.2, 130.9, 128.9, 128.0, 127.5, 124.5, 120.1, 110.5, 64.4, 56.3, 52.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{19}H_{18}NO_4S$ 356.0957; Found 356.0947

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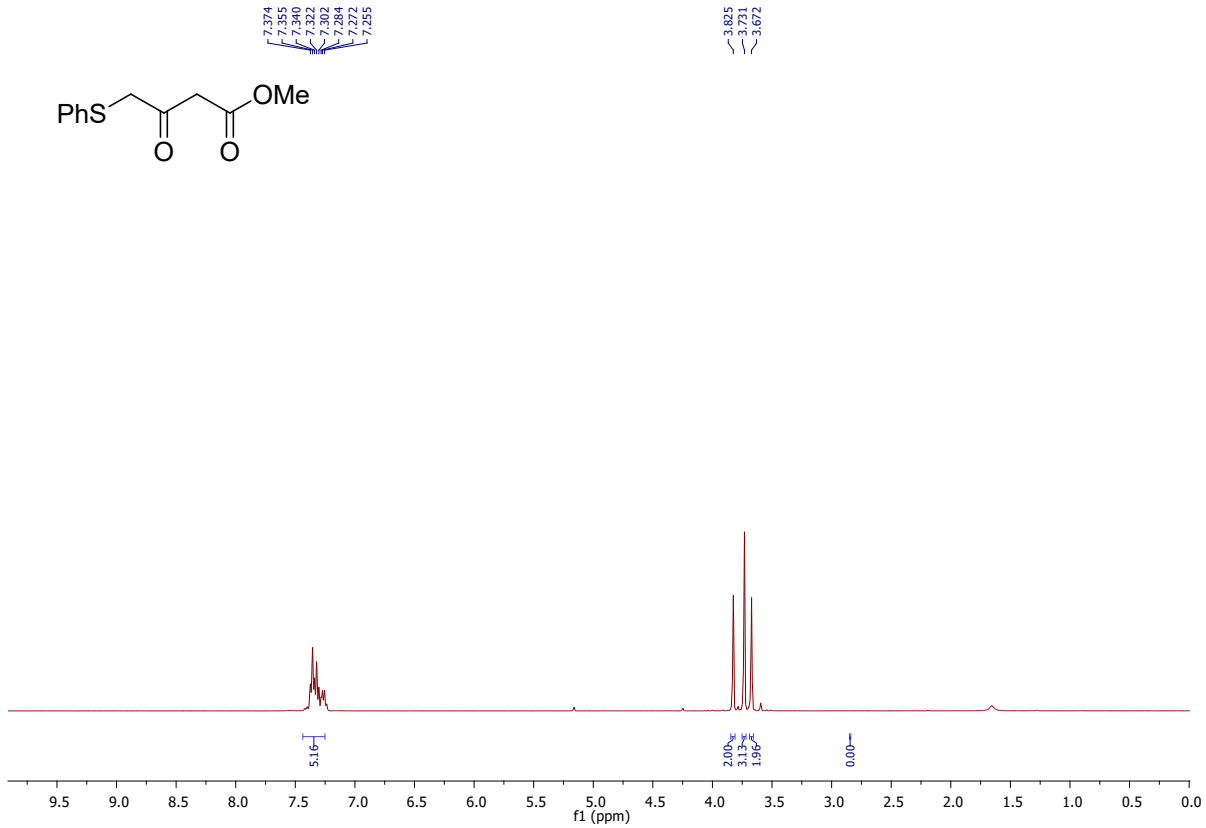
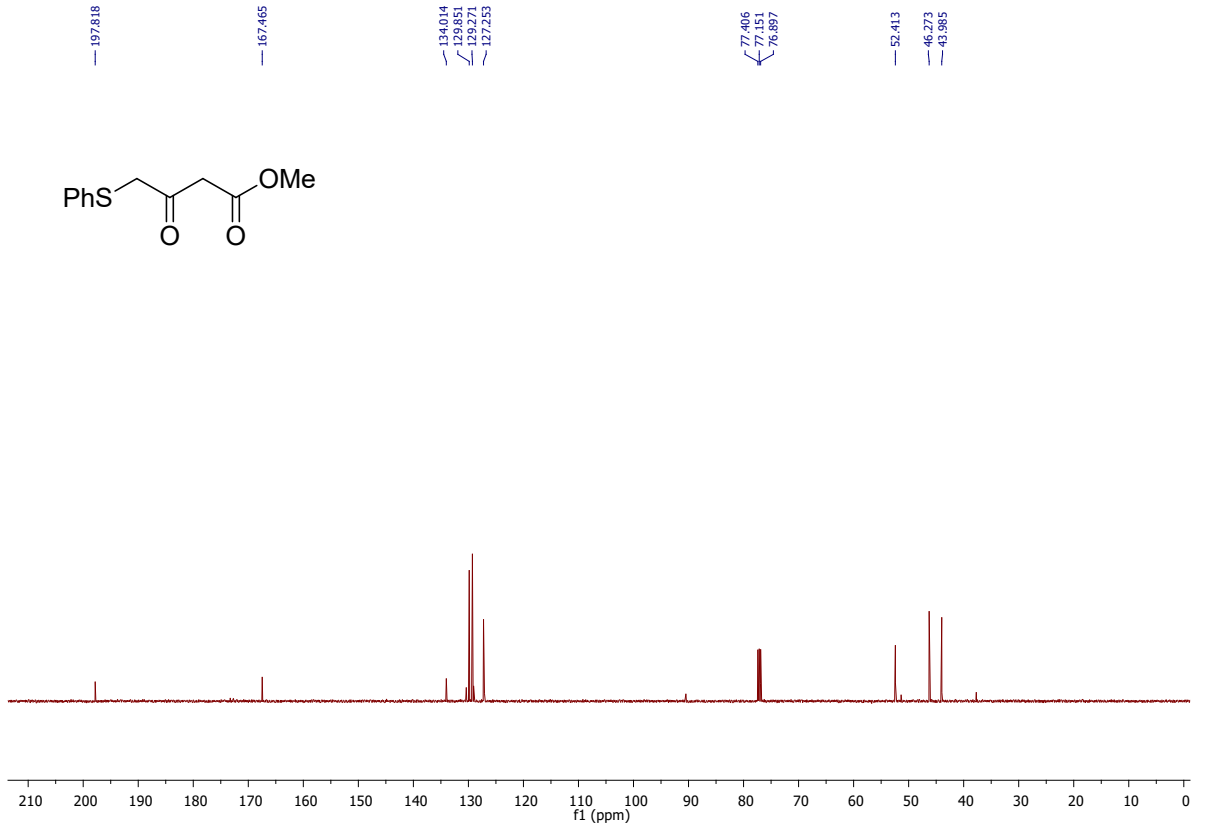
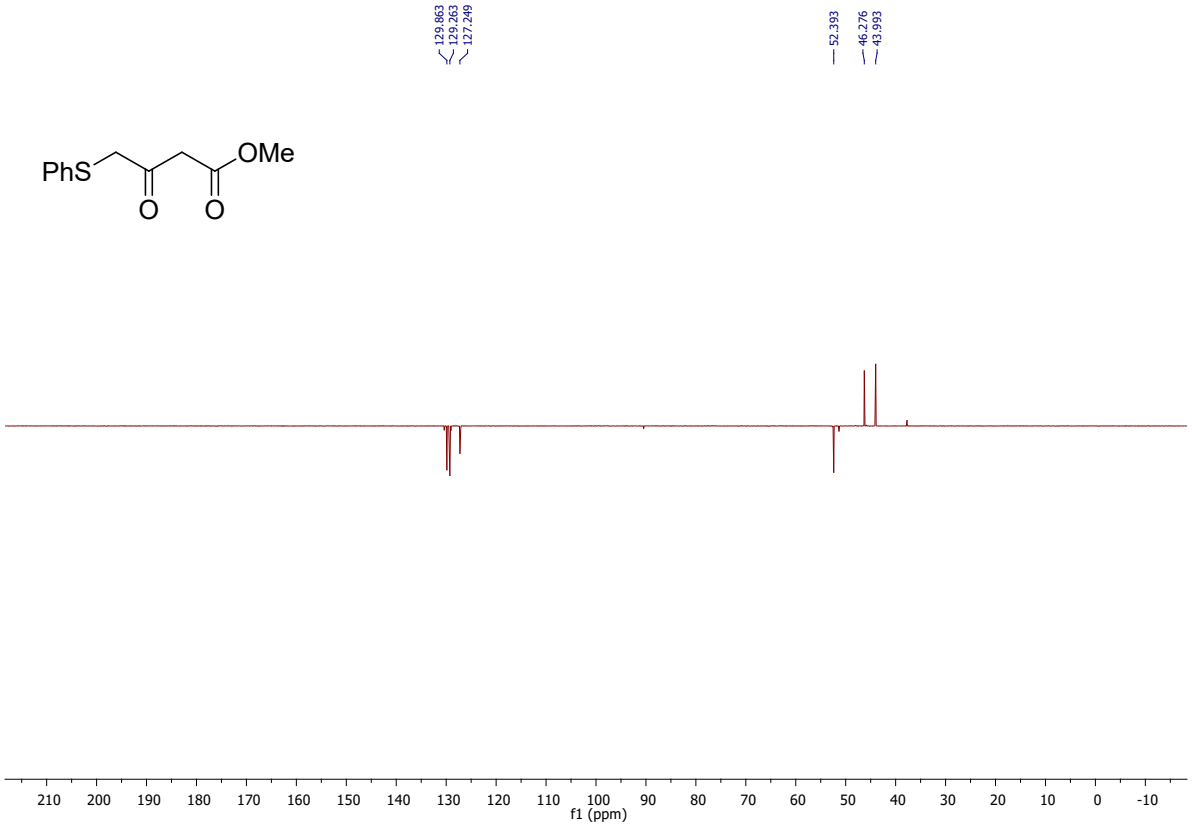
^{1}H NMR (400 MHz) of compound **2a** in $CDCl_3$



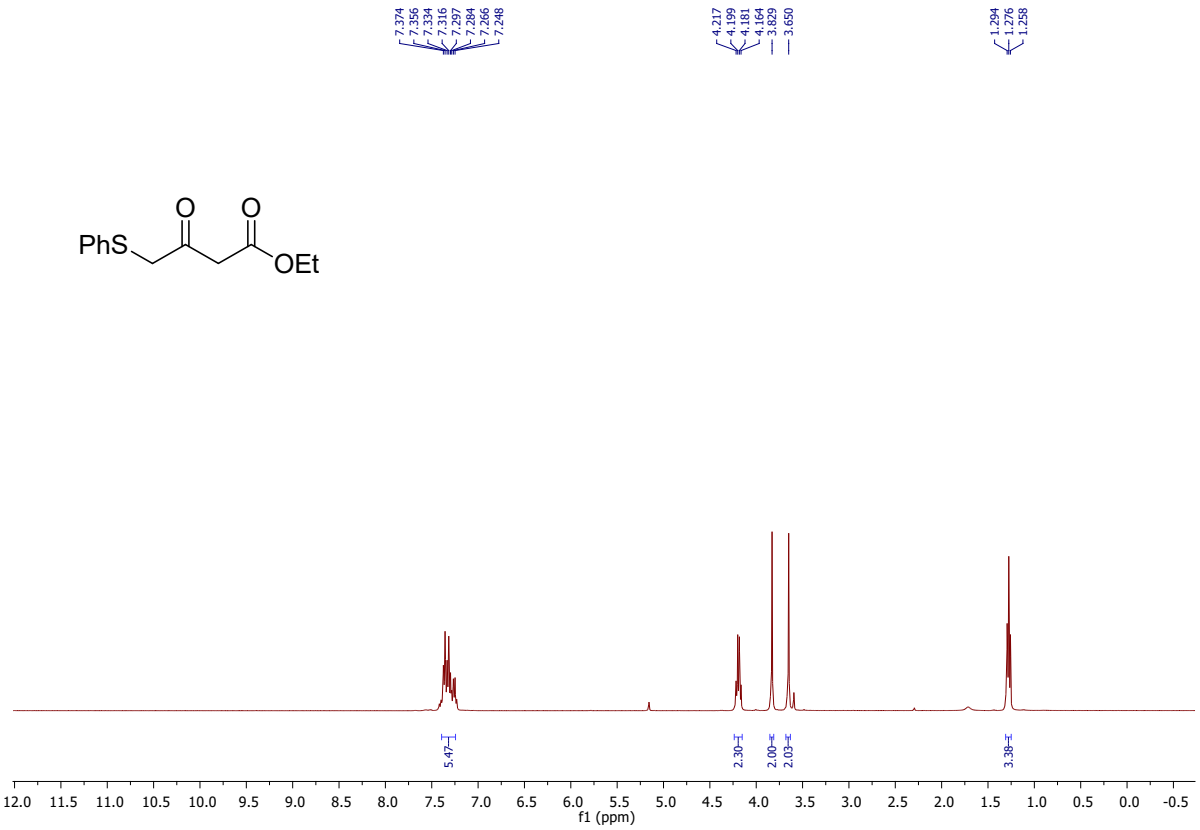
^{13}C NMR **{^{1}H}** (125 MHz) of compound **2a** in $CDCl_3$



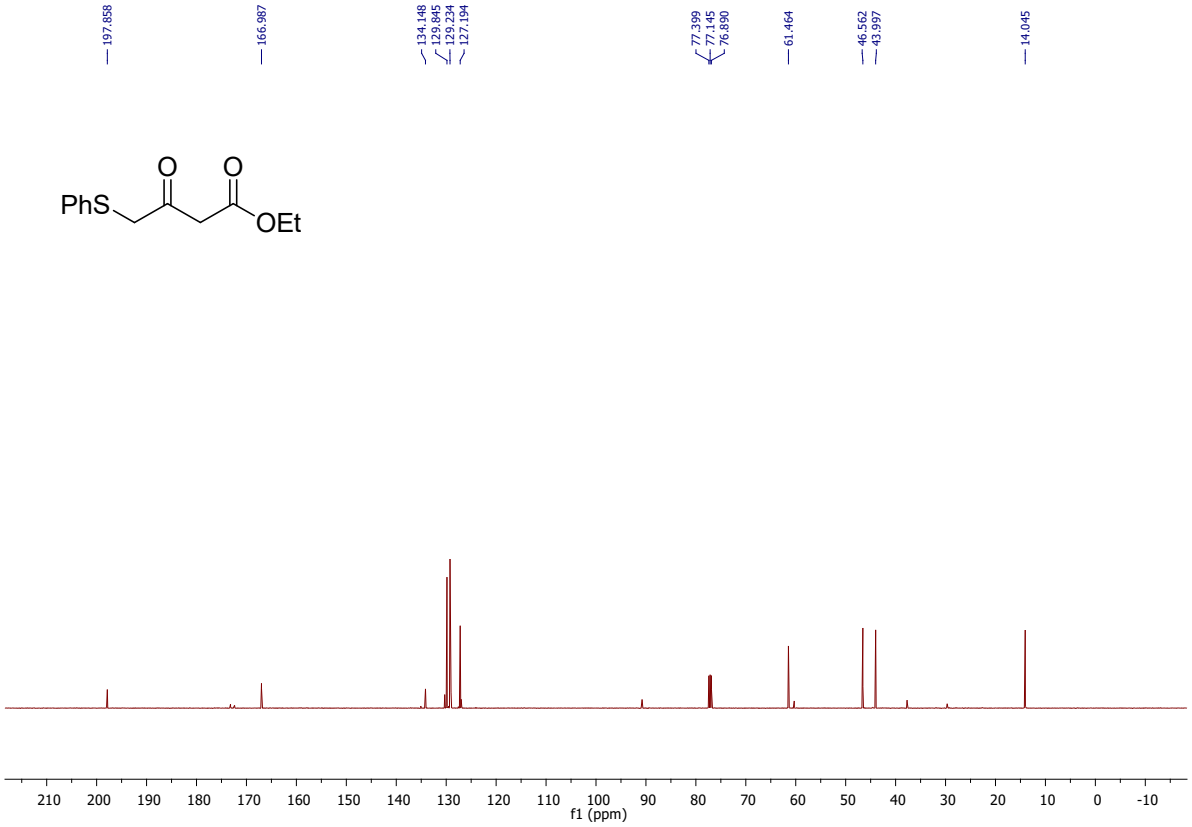
DEPT NMR (125 MHz) of compound **2a** in $CDCl_3$



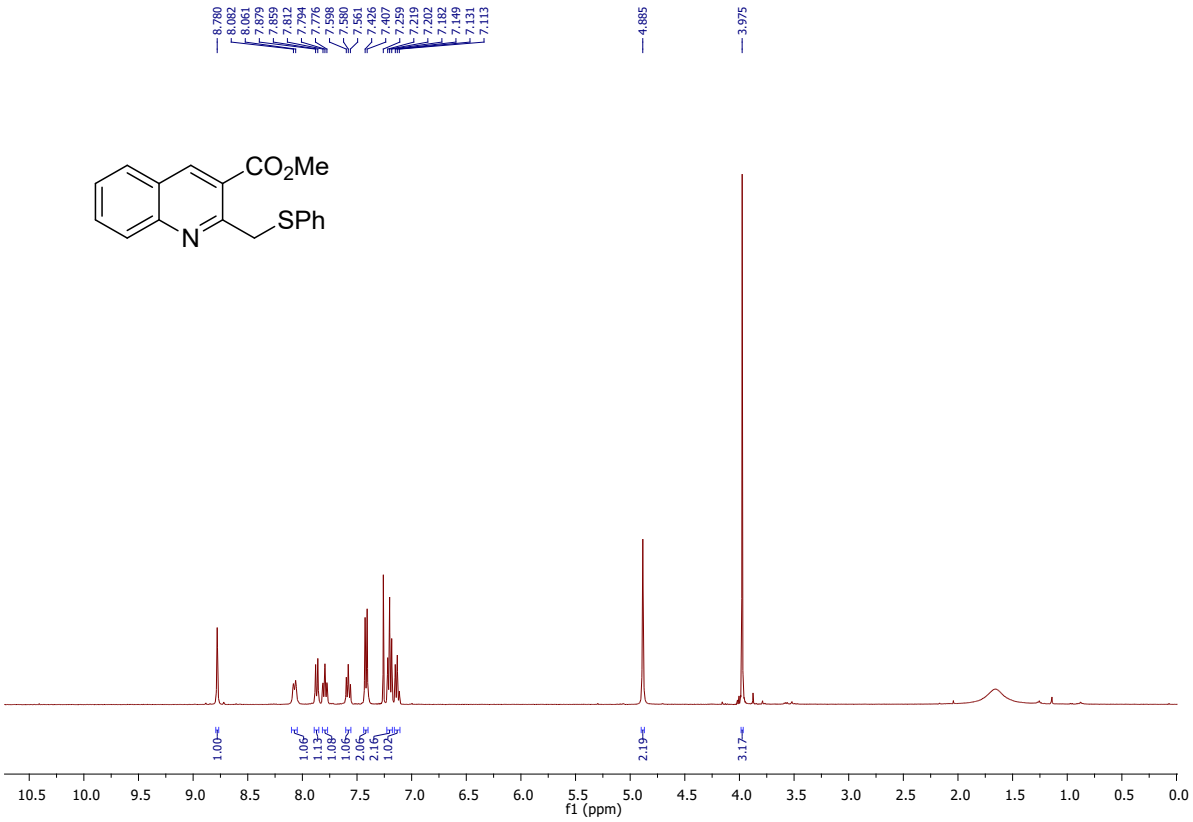
^{1}H NMR (400 MHz) of compound **2b** in $CDCl_3$



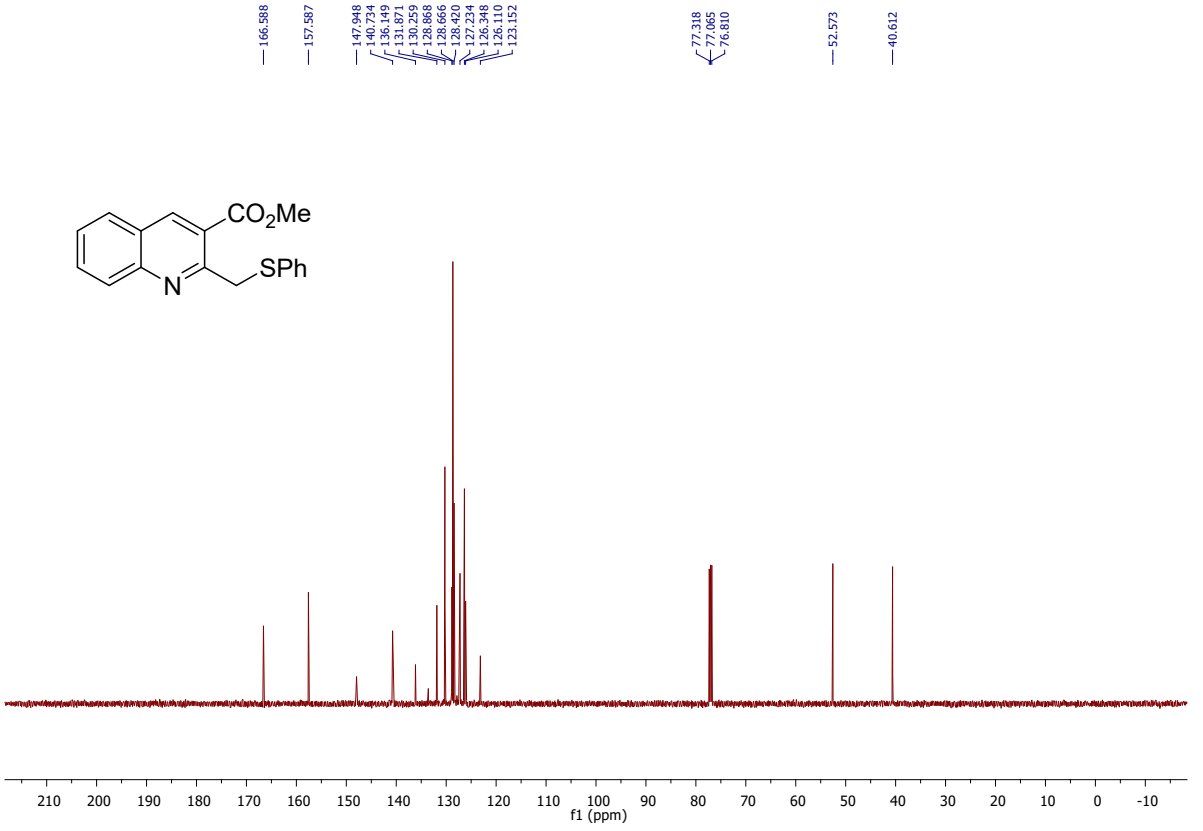
^{13}C NMR **{^{1}H}** (125 MHz) of compound **2b** in $CDCl_3$



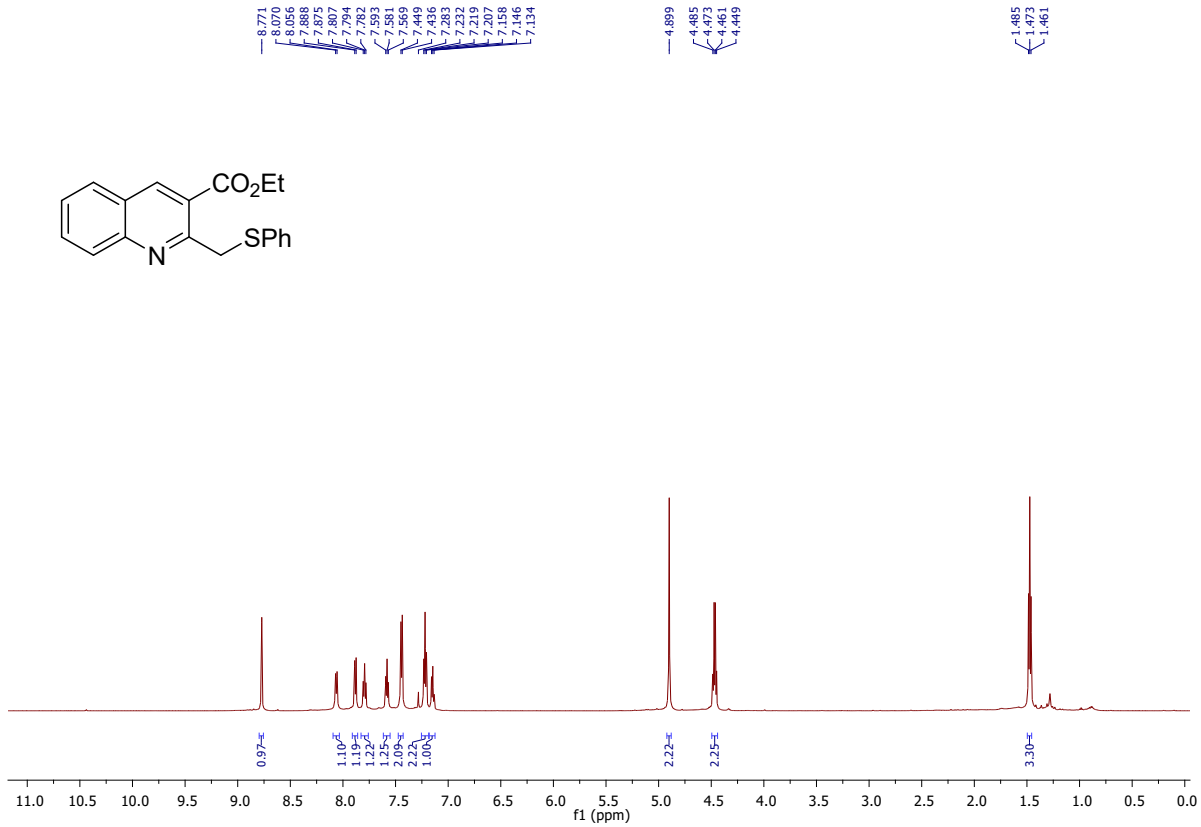
^{1}H NMR (400 MHz) of compound **2'a** in $CDCl_3$



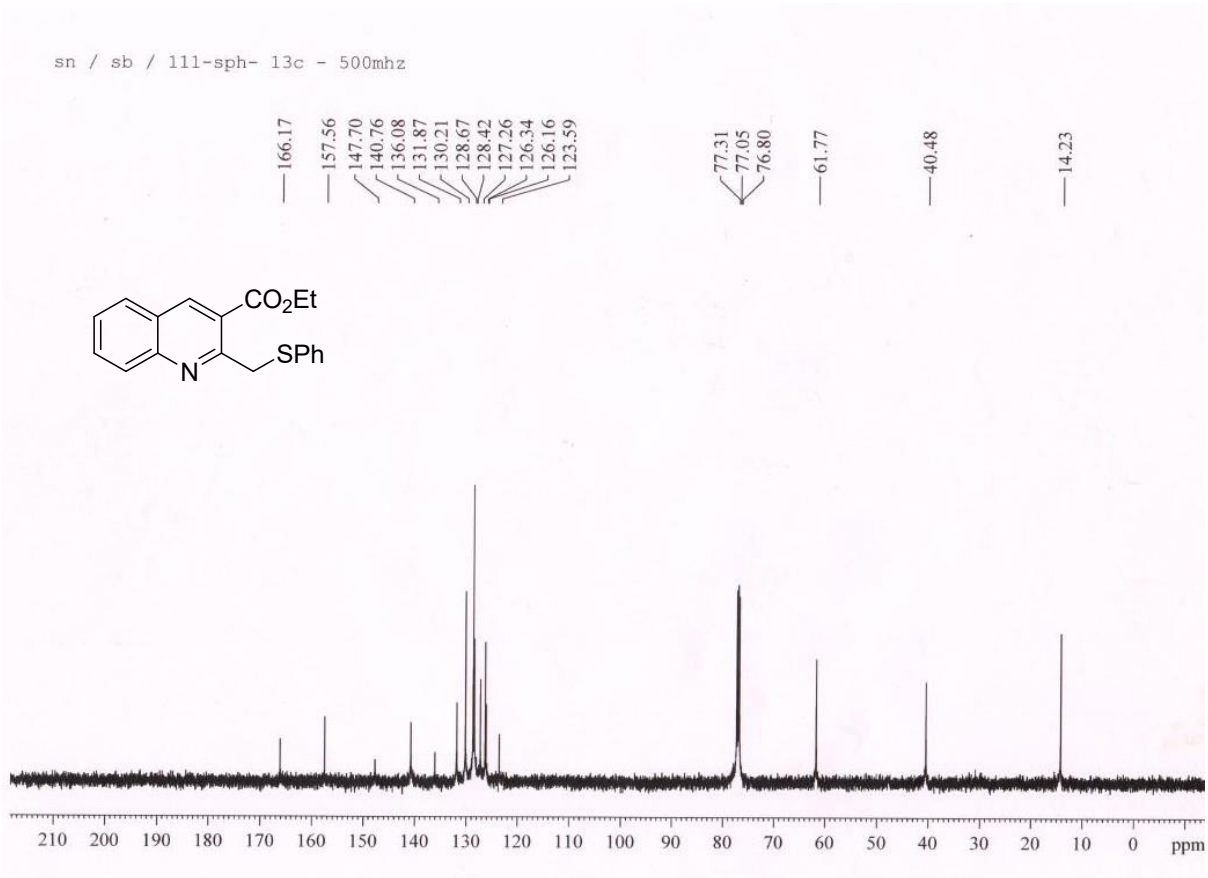
^{13}C NMR **{^{1}H}** (125 MHz) of compound **2'a** in $CDCl_3$



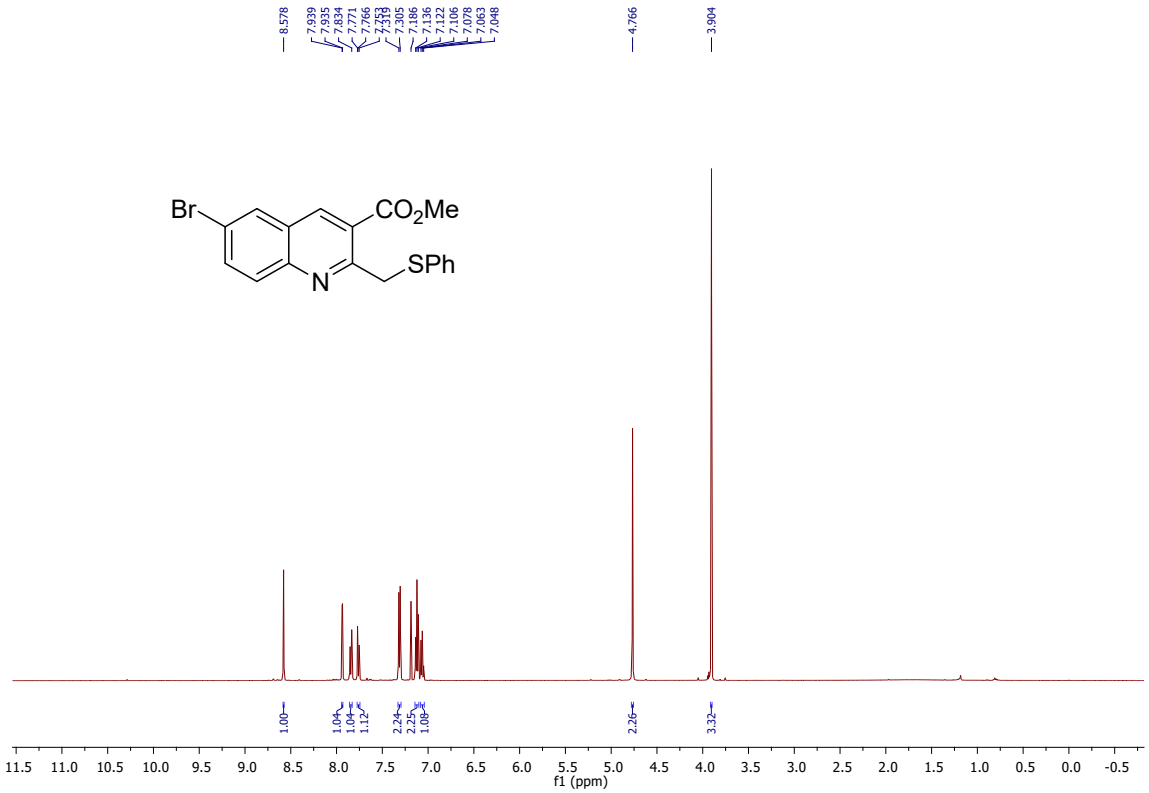
^{1}H NMR (400 MHz) of compound **2'b** in $CDCl_3$



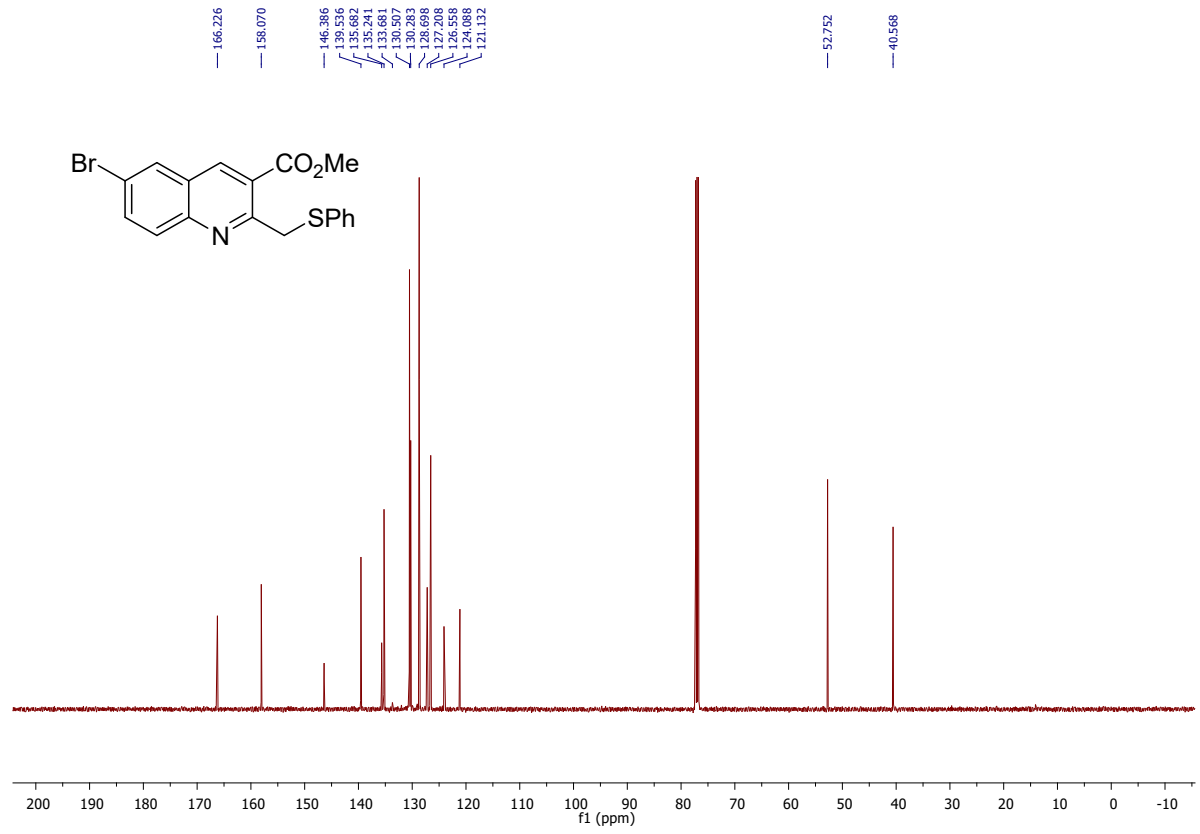
^{13}C NMR {^{1}**H**} (100 MHz) of compound **2'b** in $CDCl_3$



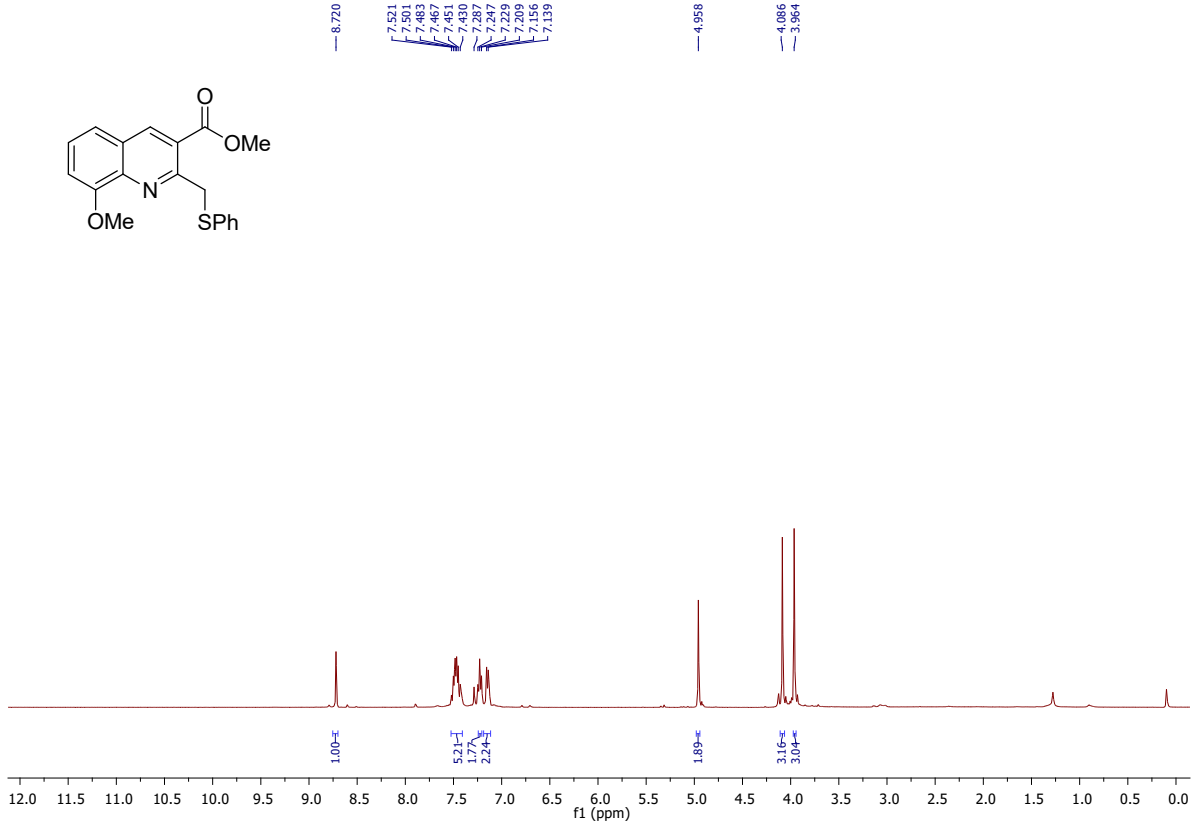
^{1}H NMR (400 MHz) of compound **2'c** in $CDCl_3$



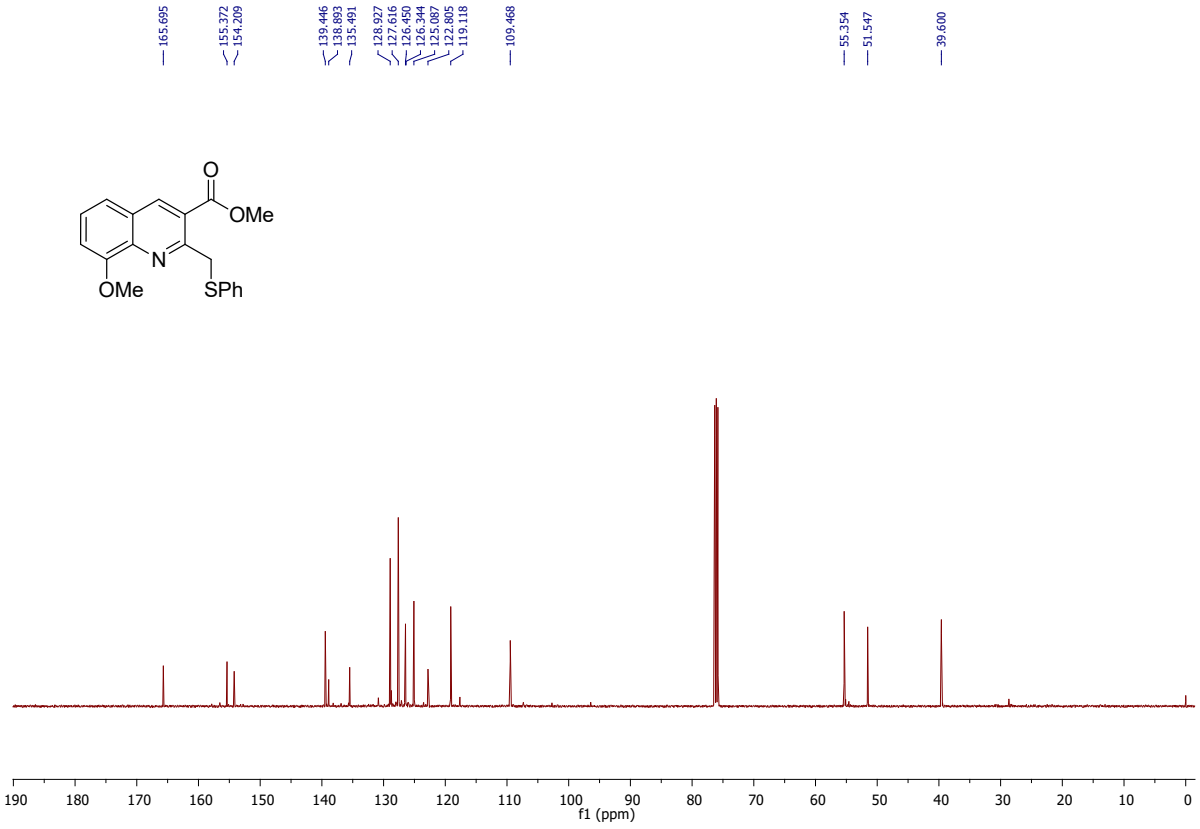
^{13}C NMR **{^{1}H}** (125 MHz) of compound **2'c** in $CDCl_3$



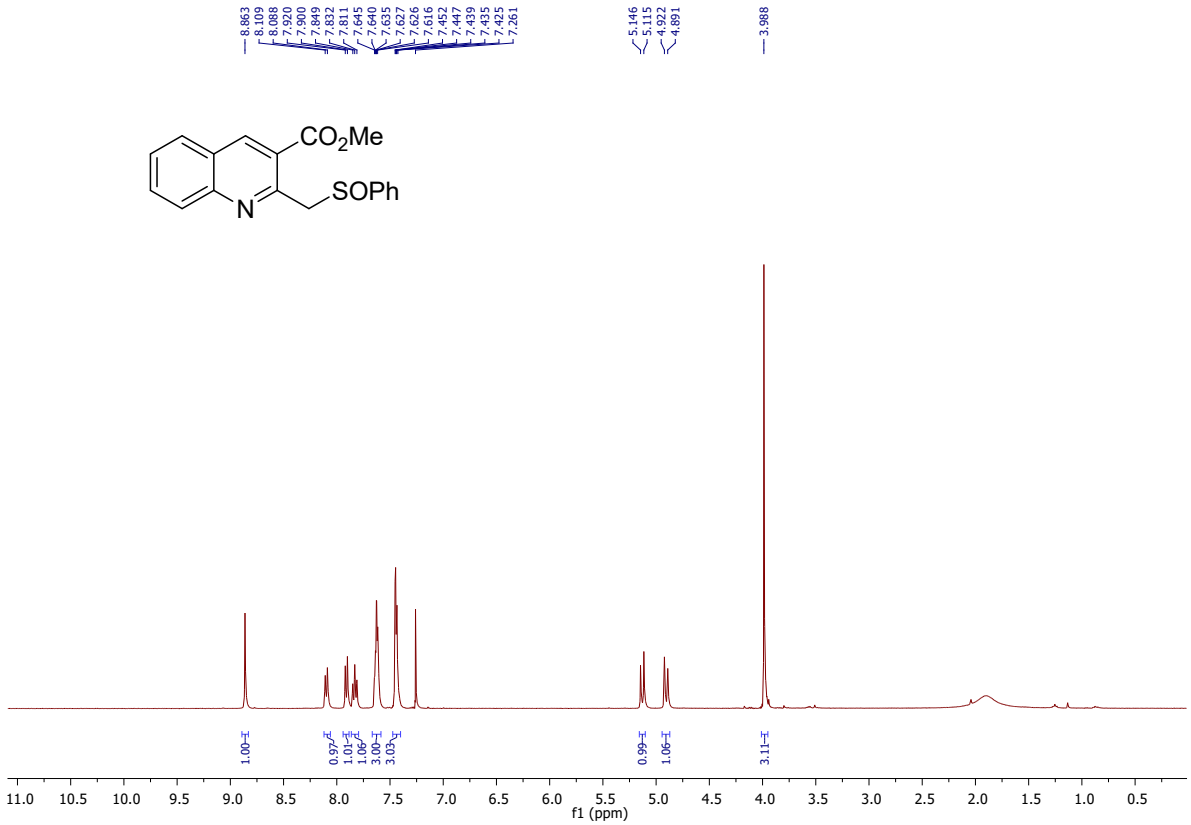
^{1}H NMR (400 MHz) of compound **2'd** in $CDCl_3$



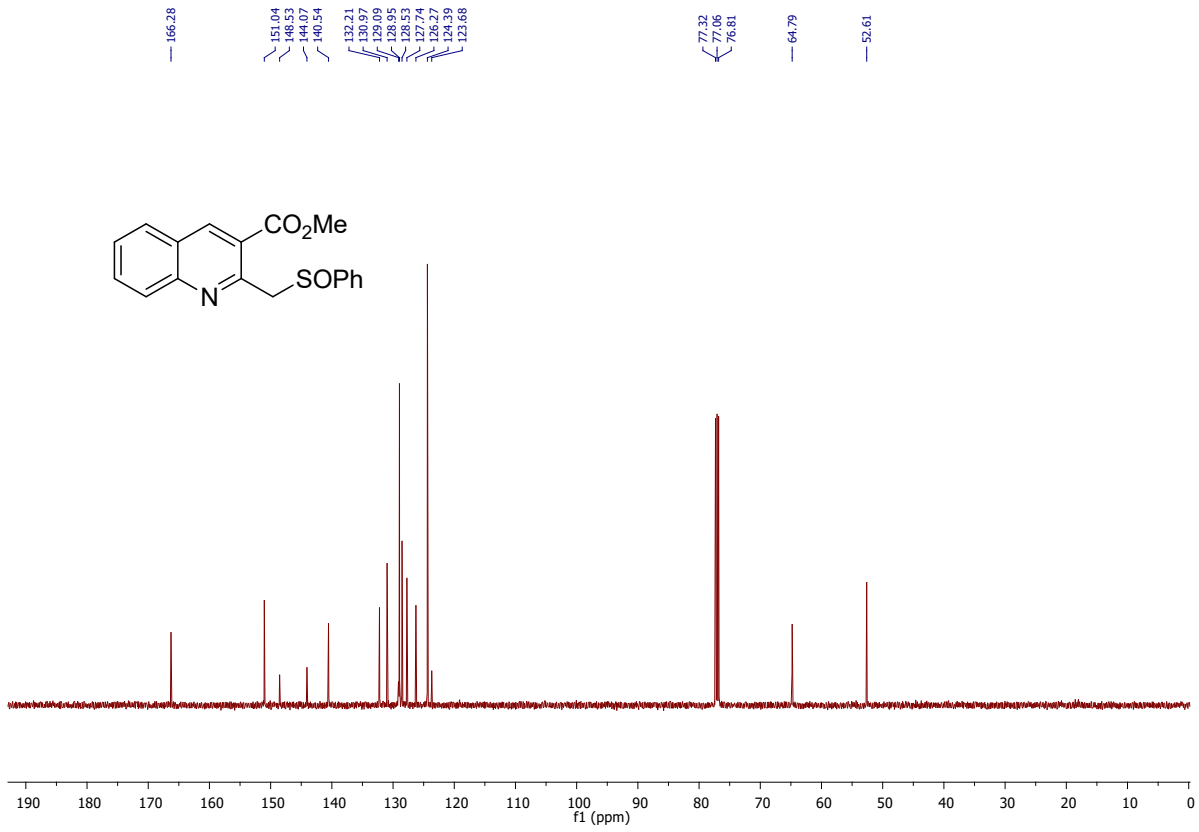
^{13}C NMR **{^{1}H}** (125 MHz) of compound **2'd** in $CDCl_3$



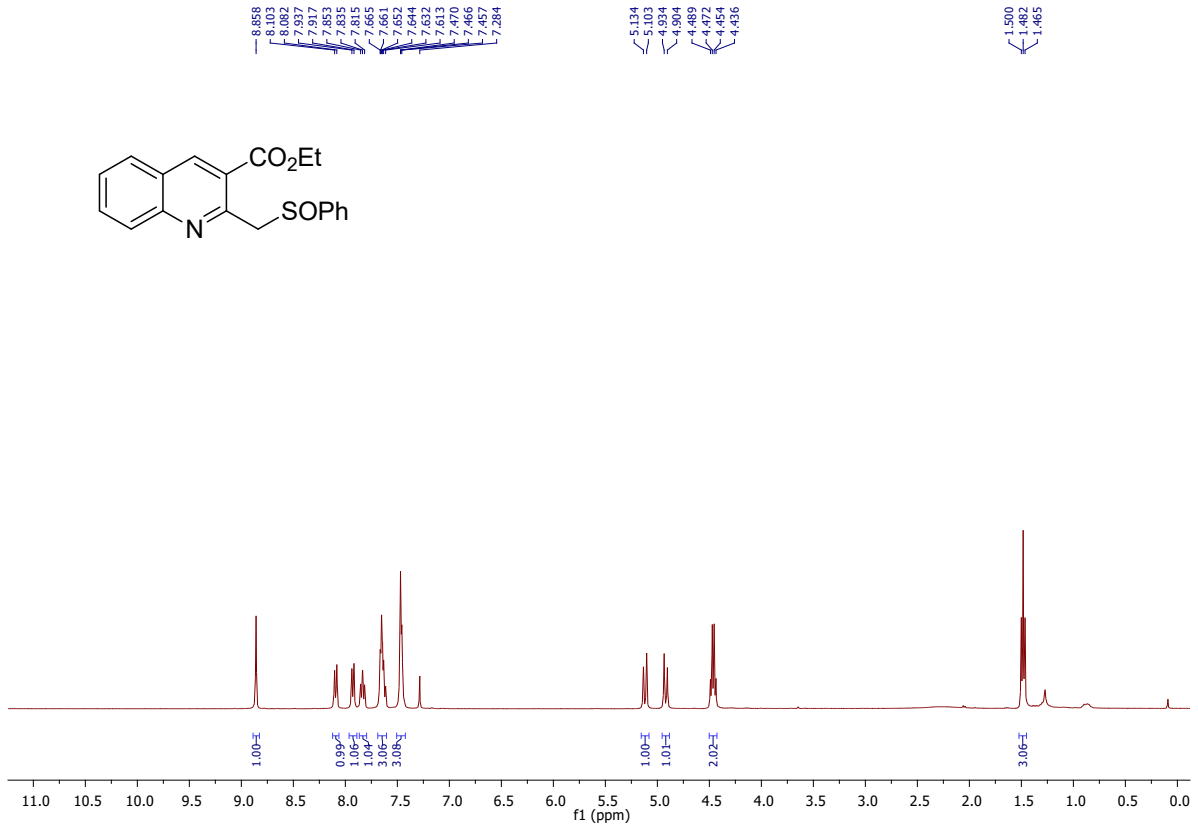
^{1}H NMR (400 MHz) of compound **3a** in $CDCl_3$



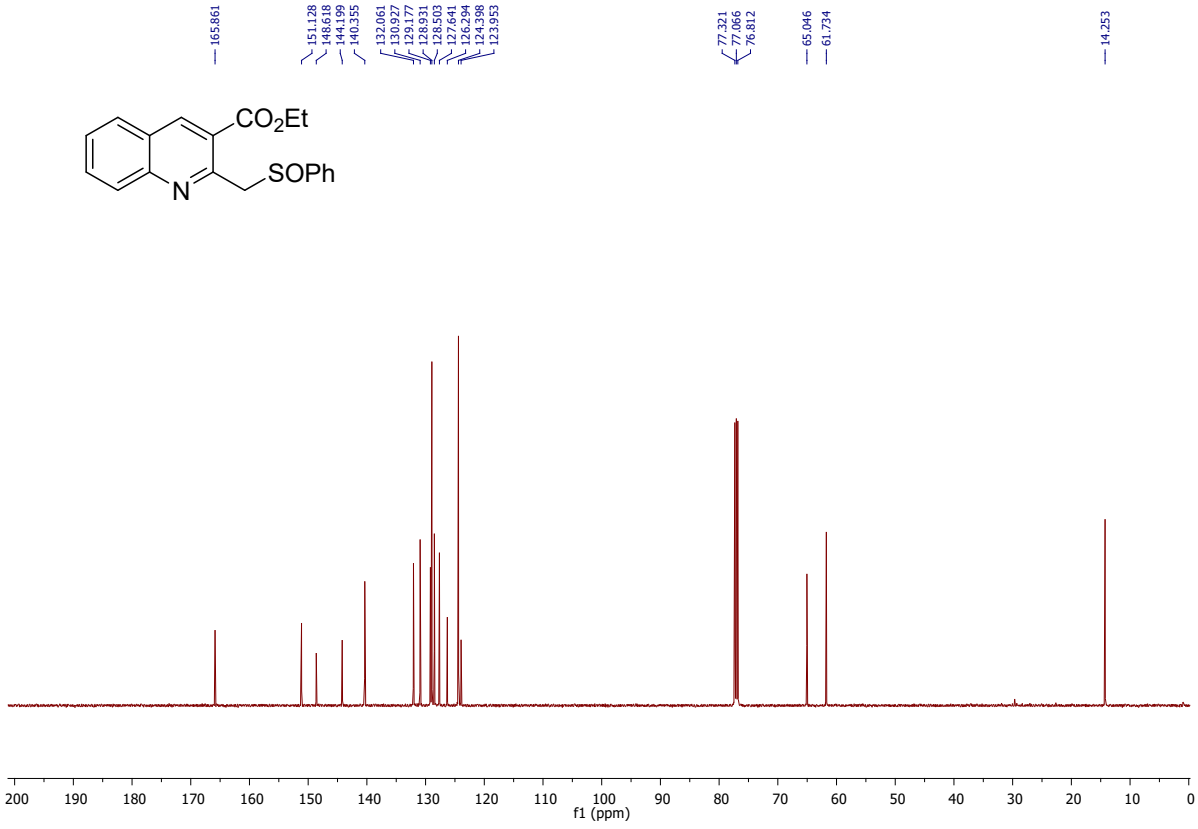
^{13}C NMR **{^{1}H}** (125 MHz) of compound **3a** in $CDCl_3$



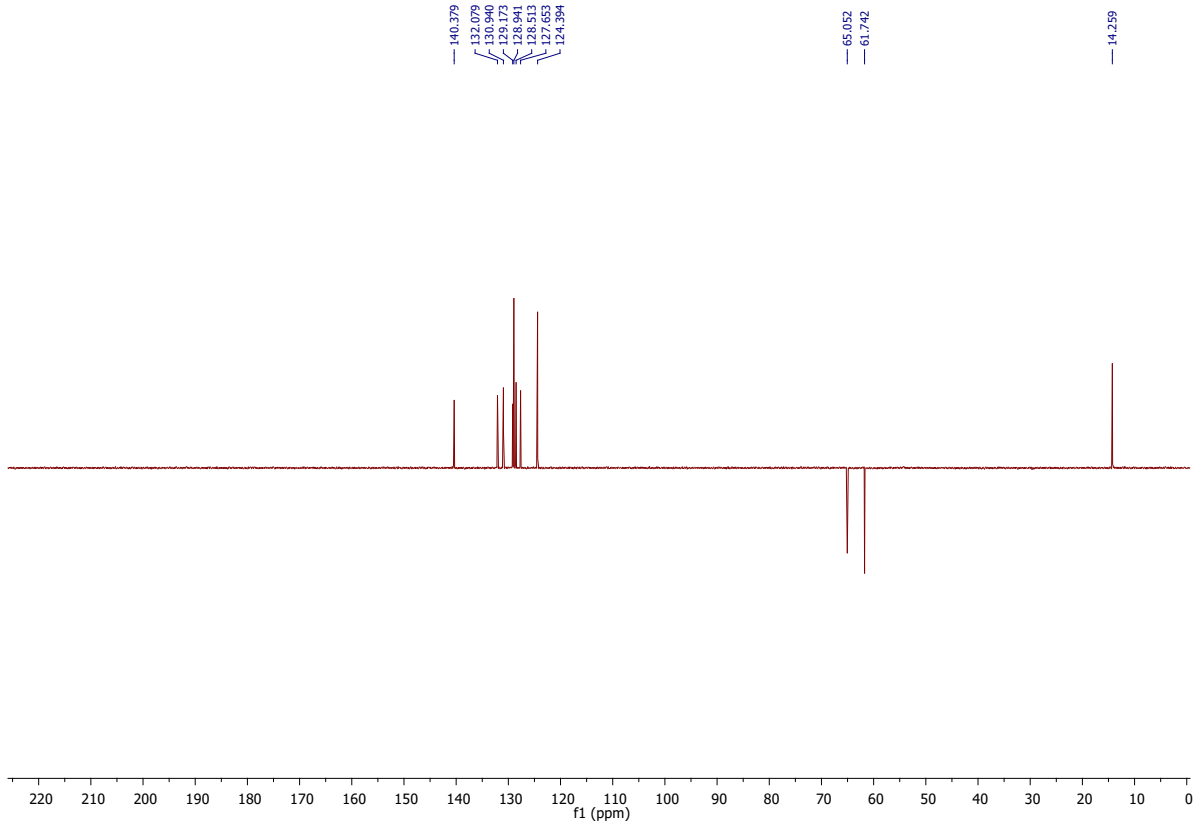
^{1}H NMR (400 MHz) of compound **3b** in $CDCl_3$



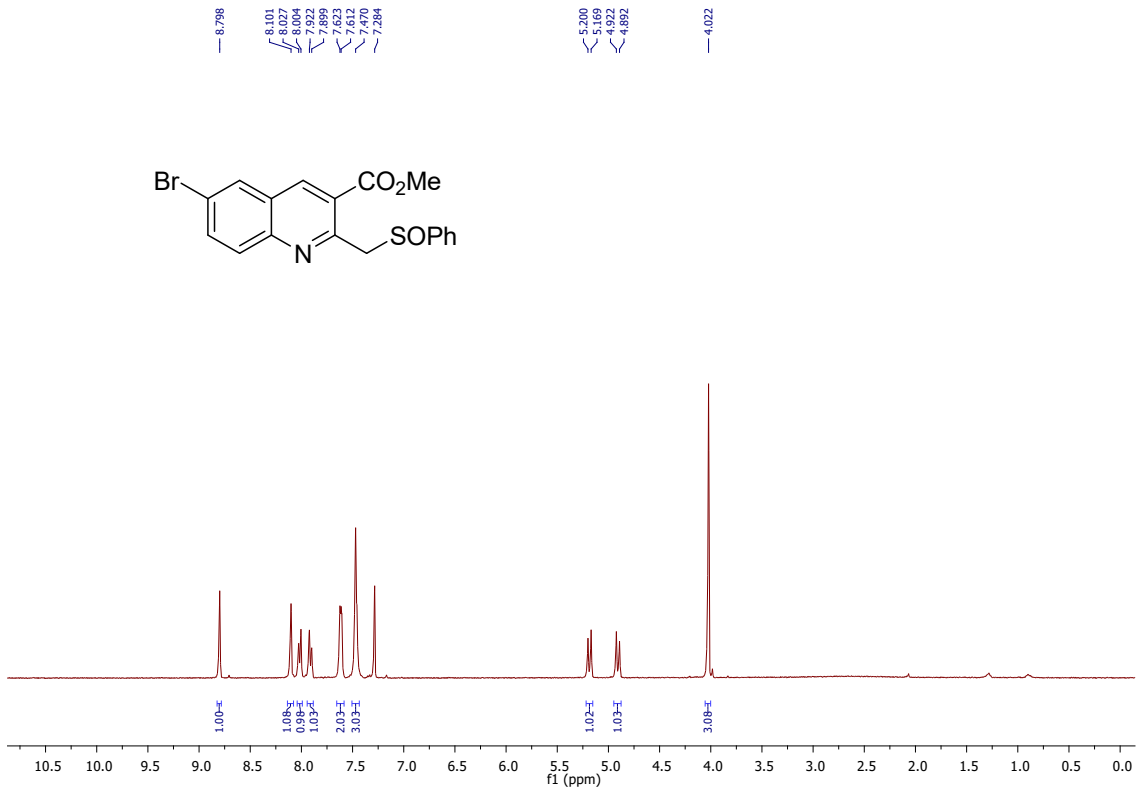
^{13}C NMR {^{1}**H**} (125 MHz) of compound **3b** in $CDCl_3$



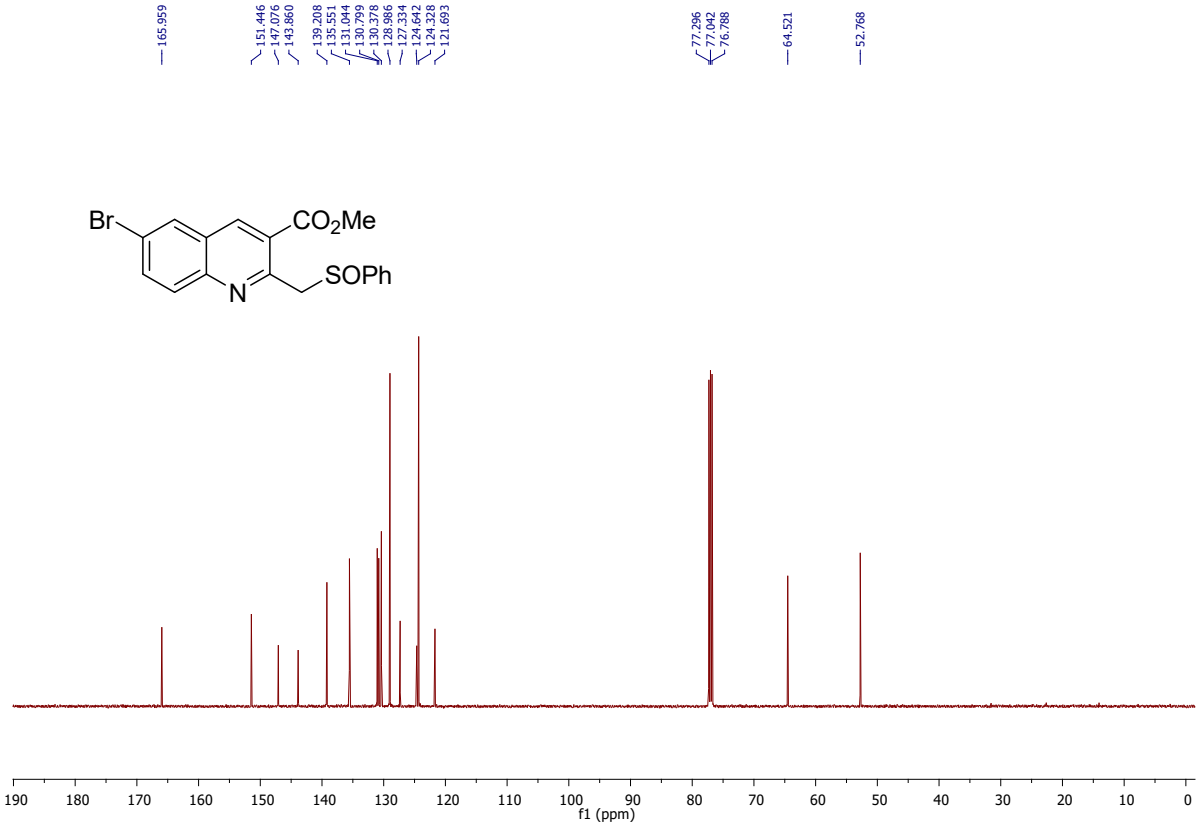
DEPT NMR (125 MHz) of compound **3b** in $CDCl_3$



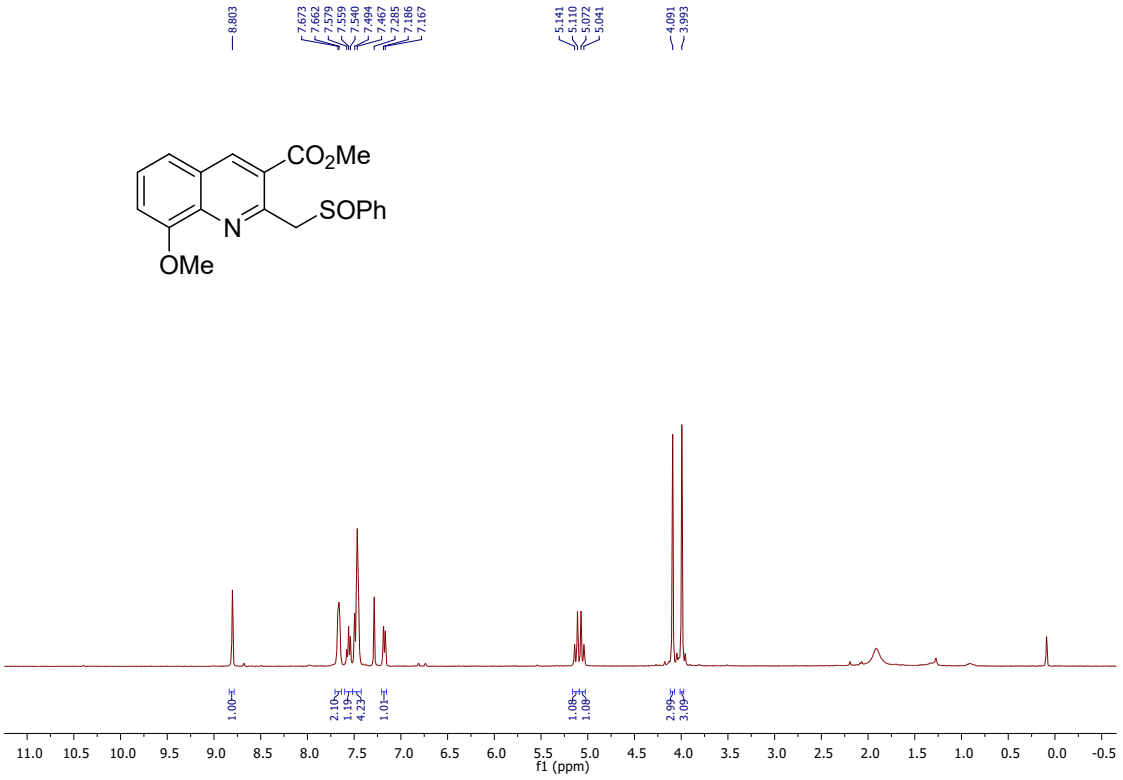
^{1}H NMR (125 MHz) of compound **3c** in $CDCl_3$



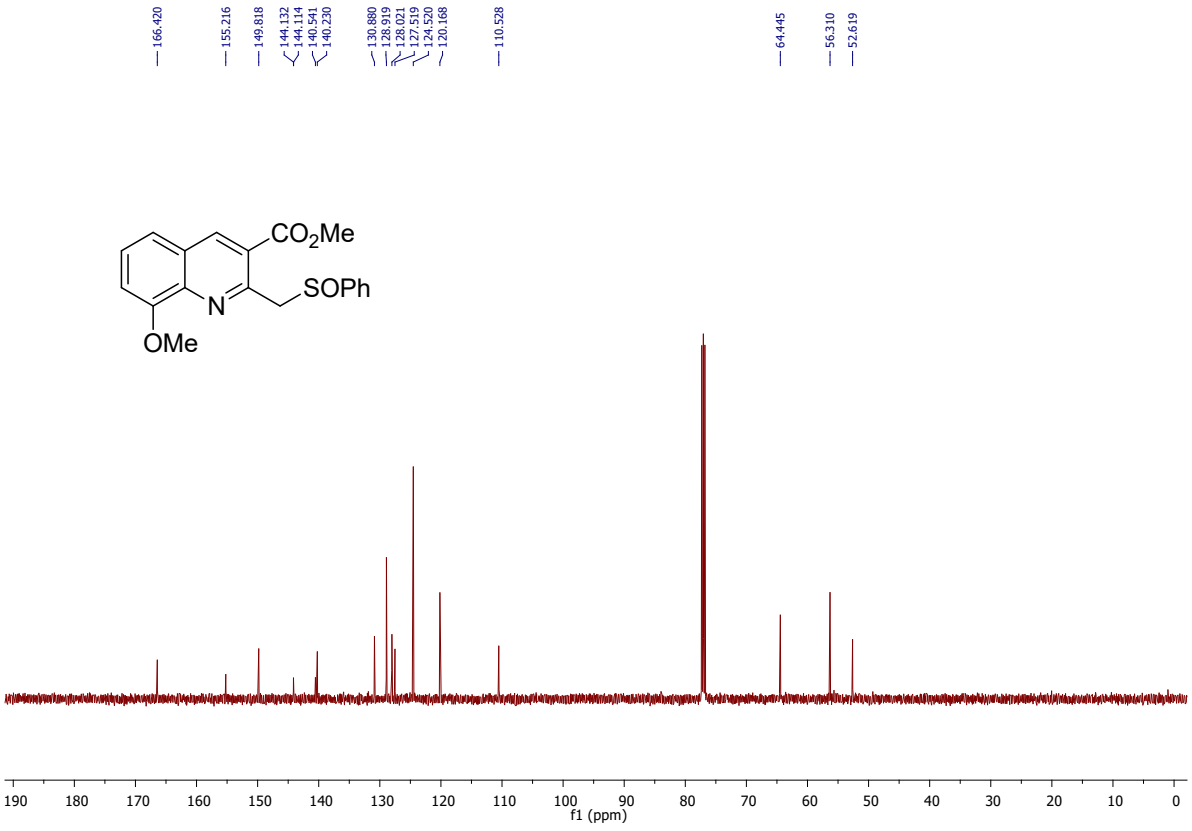
^{13}C NMR **{^{1}H}** (125 MHz) of compound **3c** in $CDCl_3$



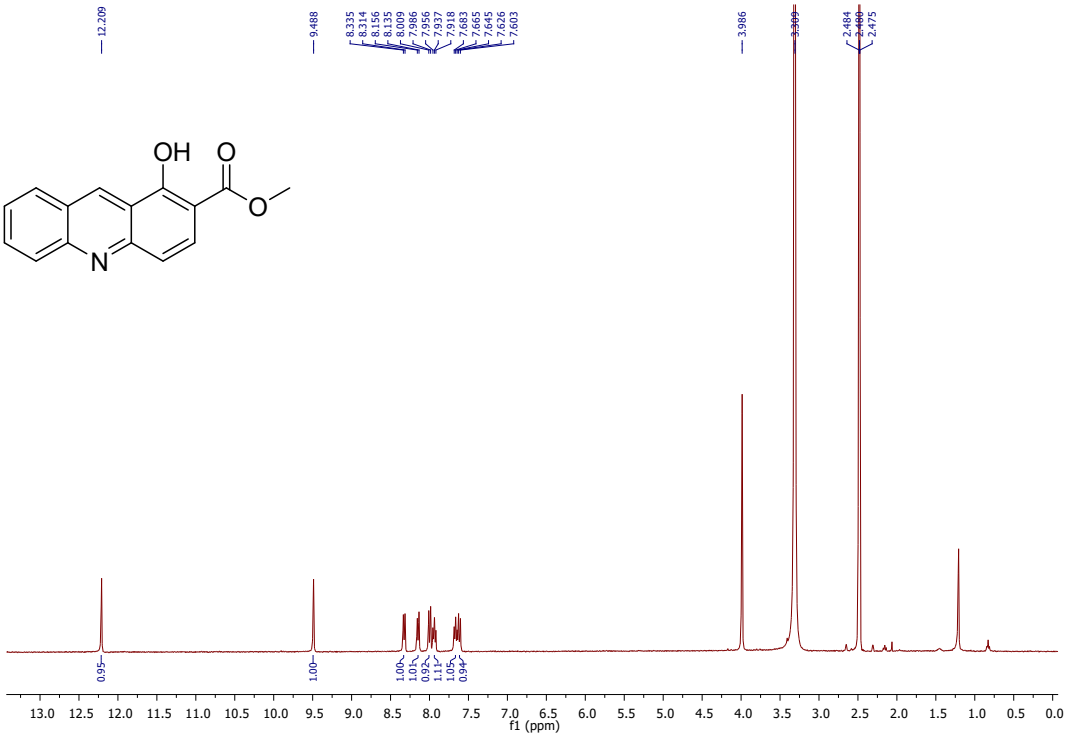
^{1}H NMR (500 MHz) of compound **3d** in $CDCl_3$



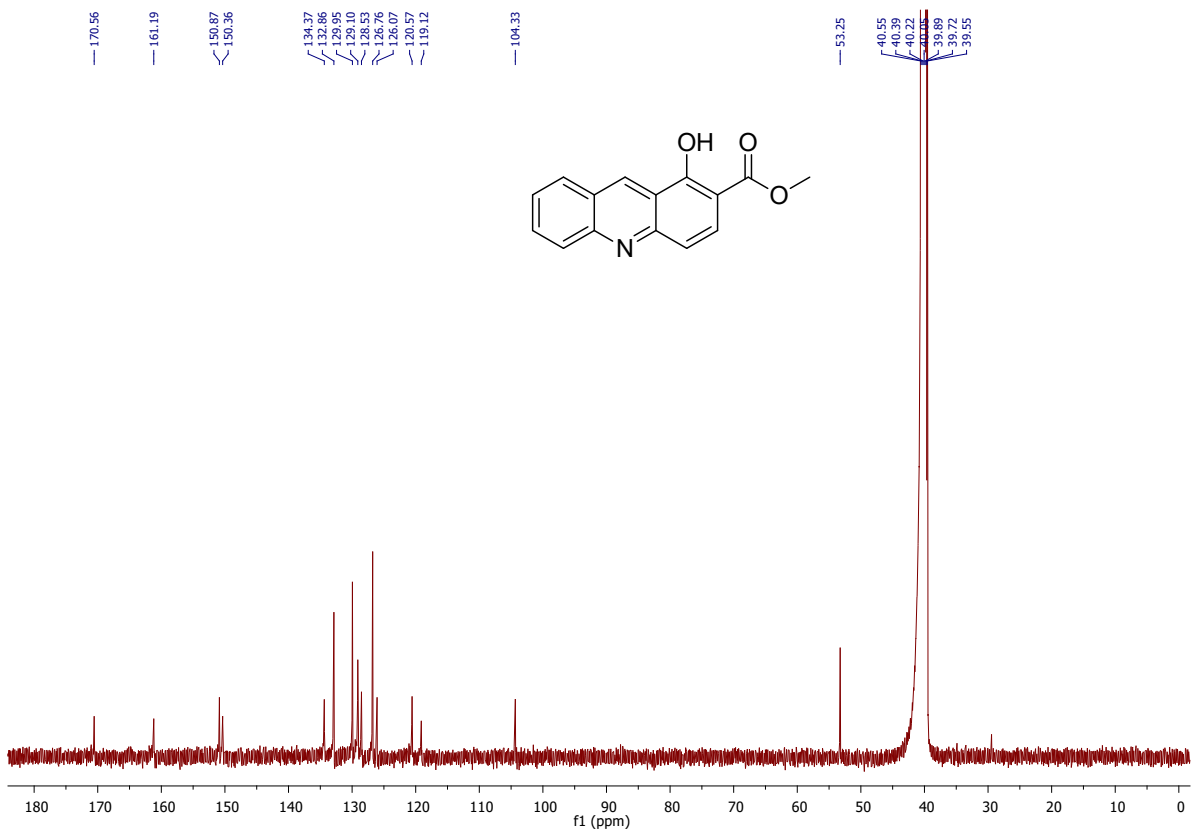
^{13}C NMR {^{1}**H**} (125 MHz) of compound **3d** in $CDCl_3$



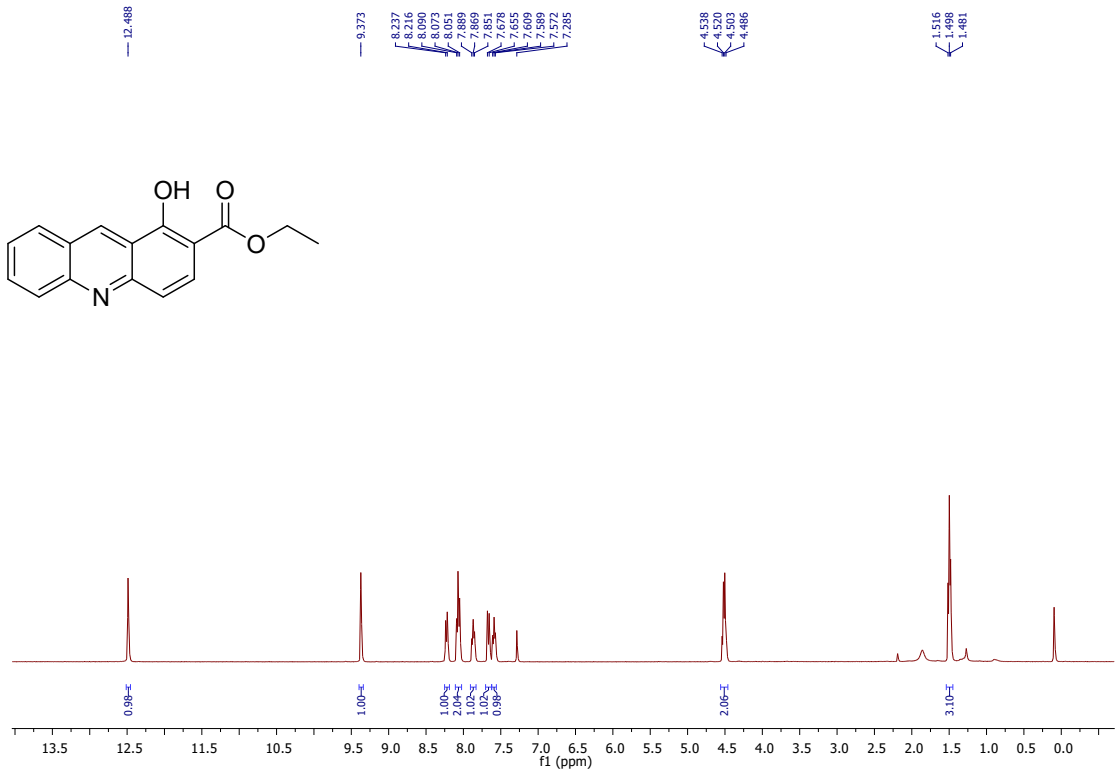
^{1}H NMR (400 MHz) of compound **5a** in DMSO-d_6



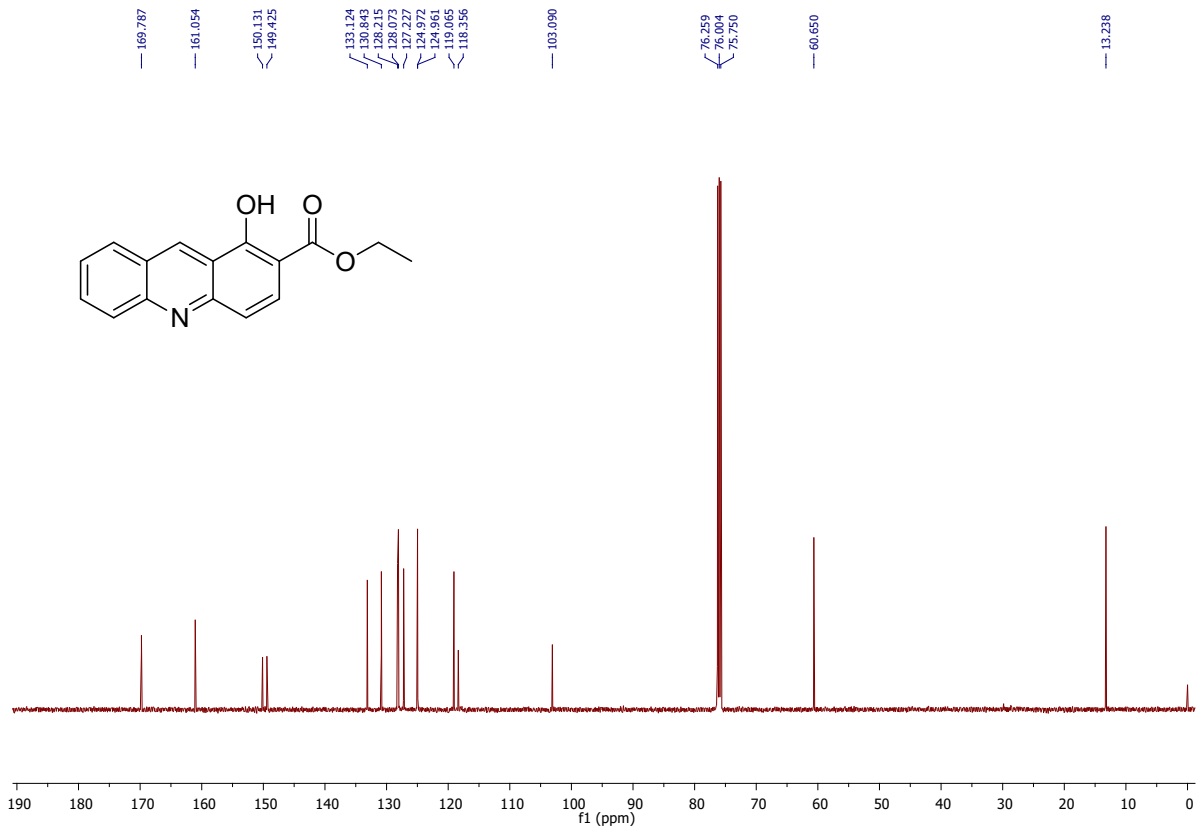
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5a** in DMSO-d_6



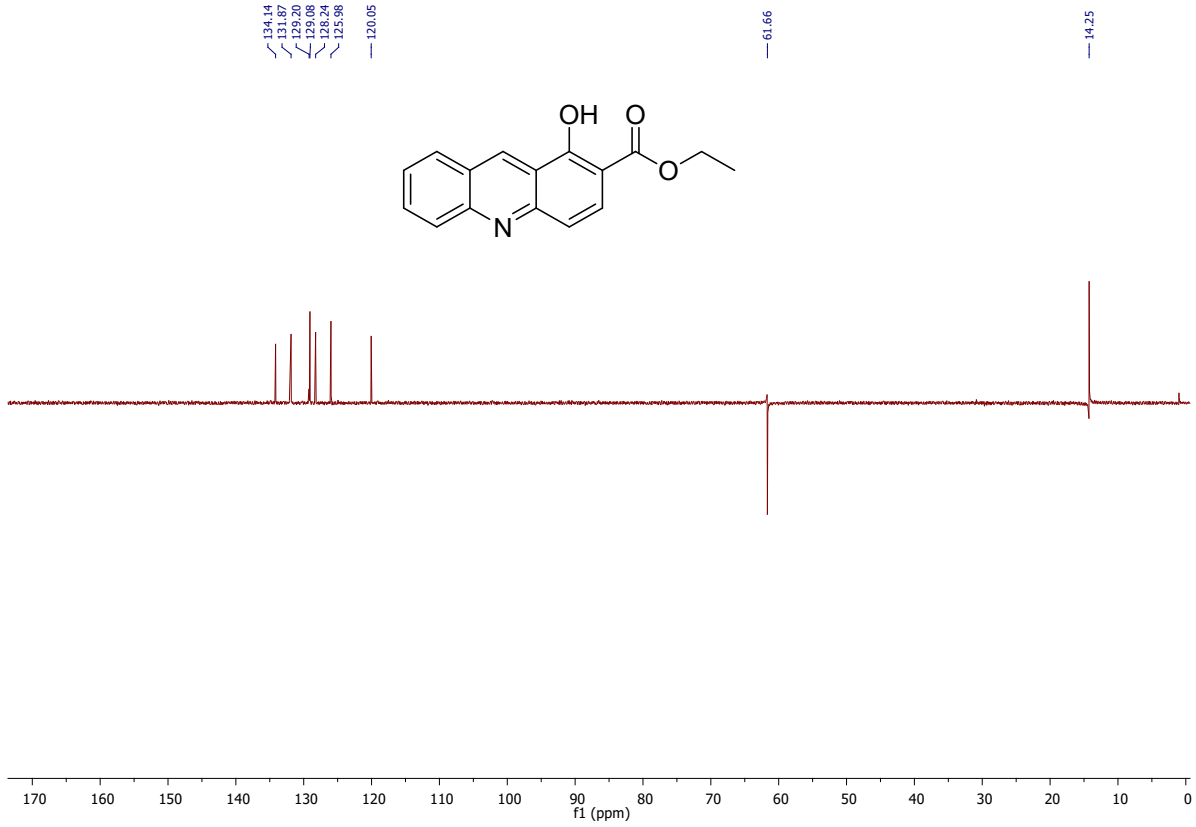
^{1}H NMR (400 MHz) of compound **5b** in $CDCl_3$



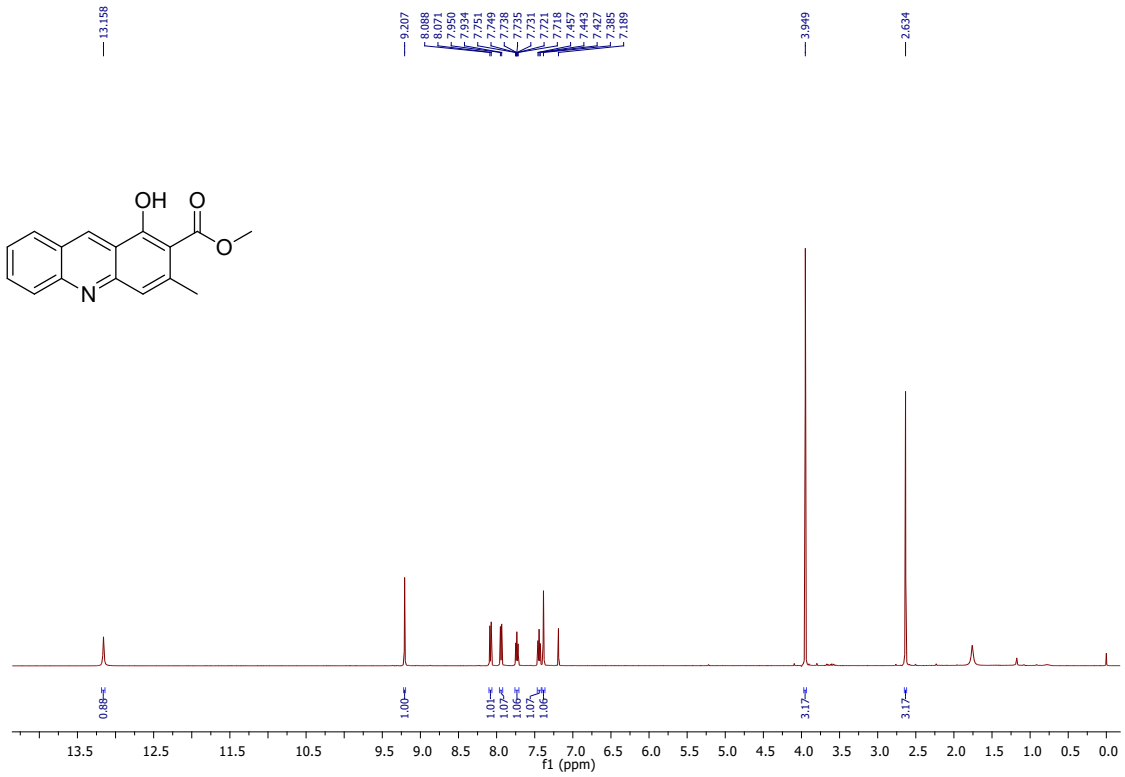
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5b** in $CDCl_3$



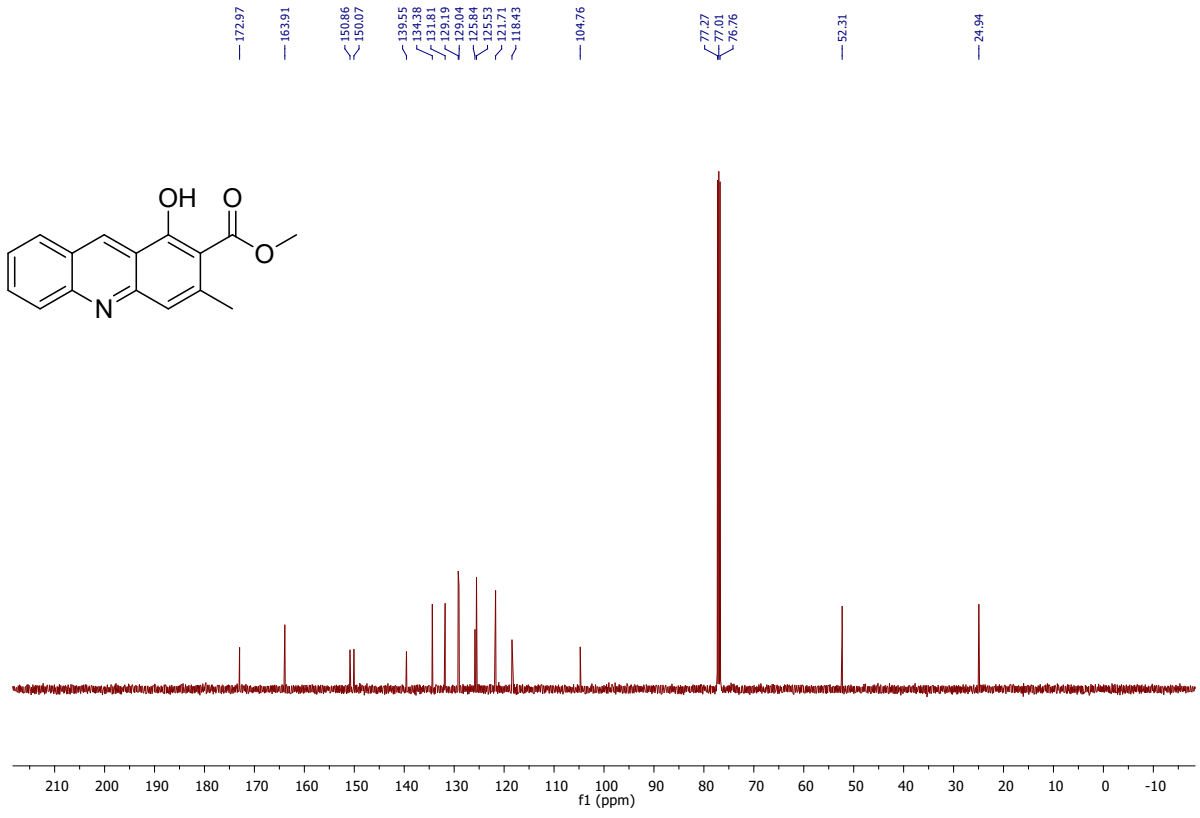
DEPT NMR (125 MHz) of compound **5b** in $CDCl_3$



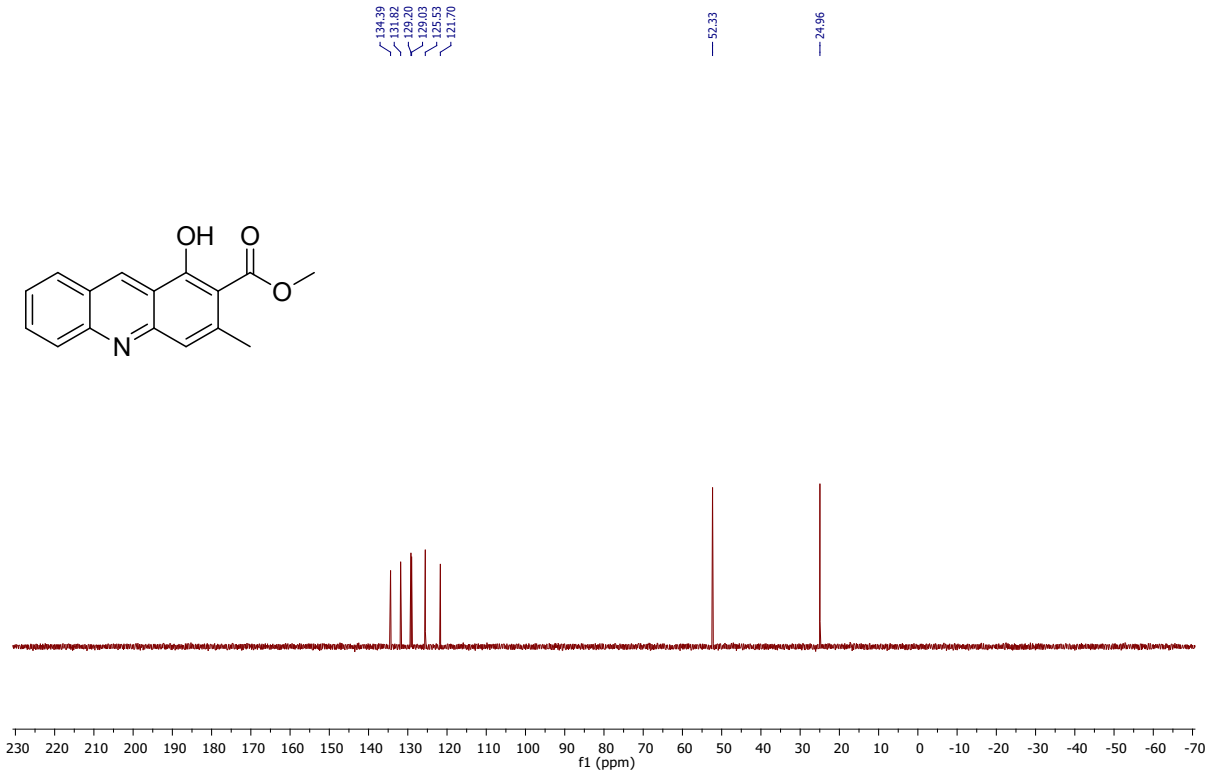
^{1}H NMR (500 MHz) of compound **5c** in $CDCl_3$



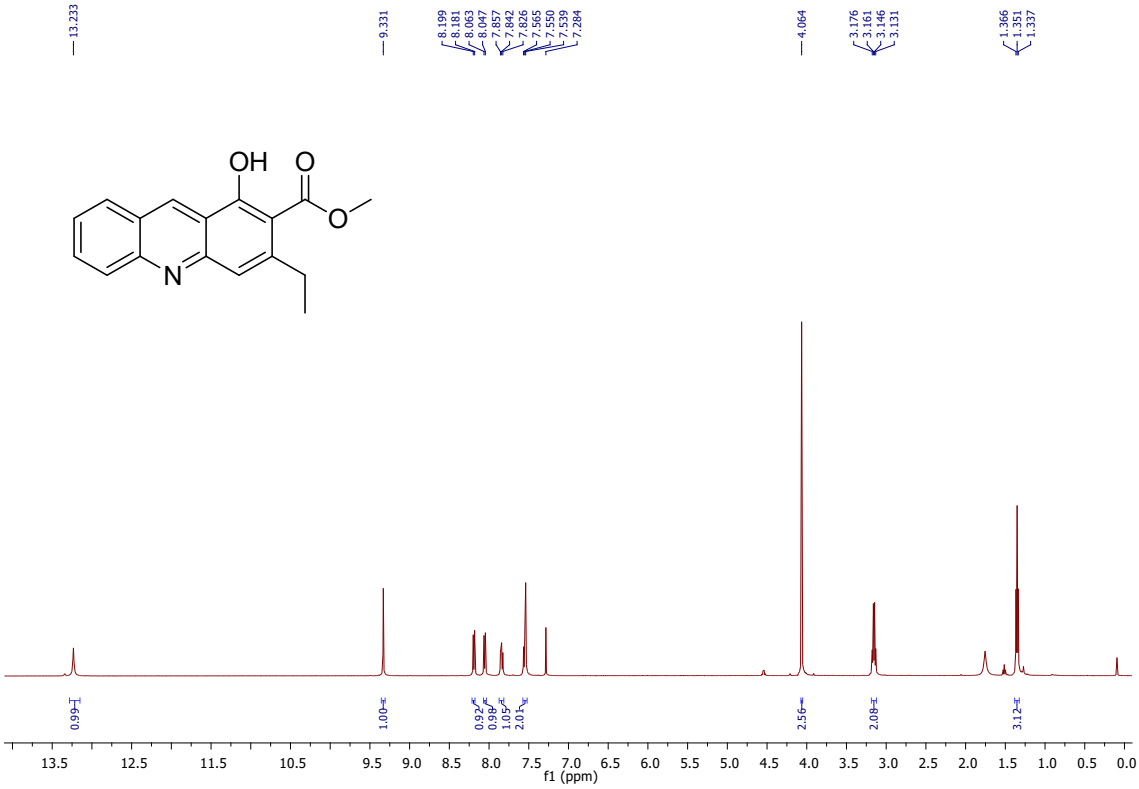
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5c** in $CDCl_3$



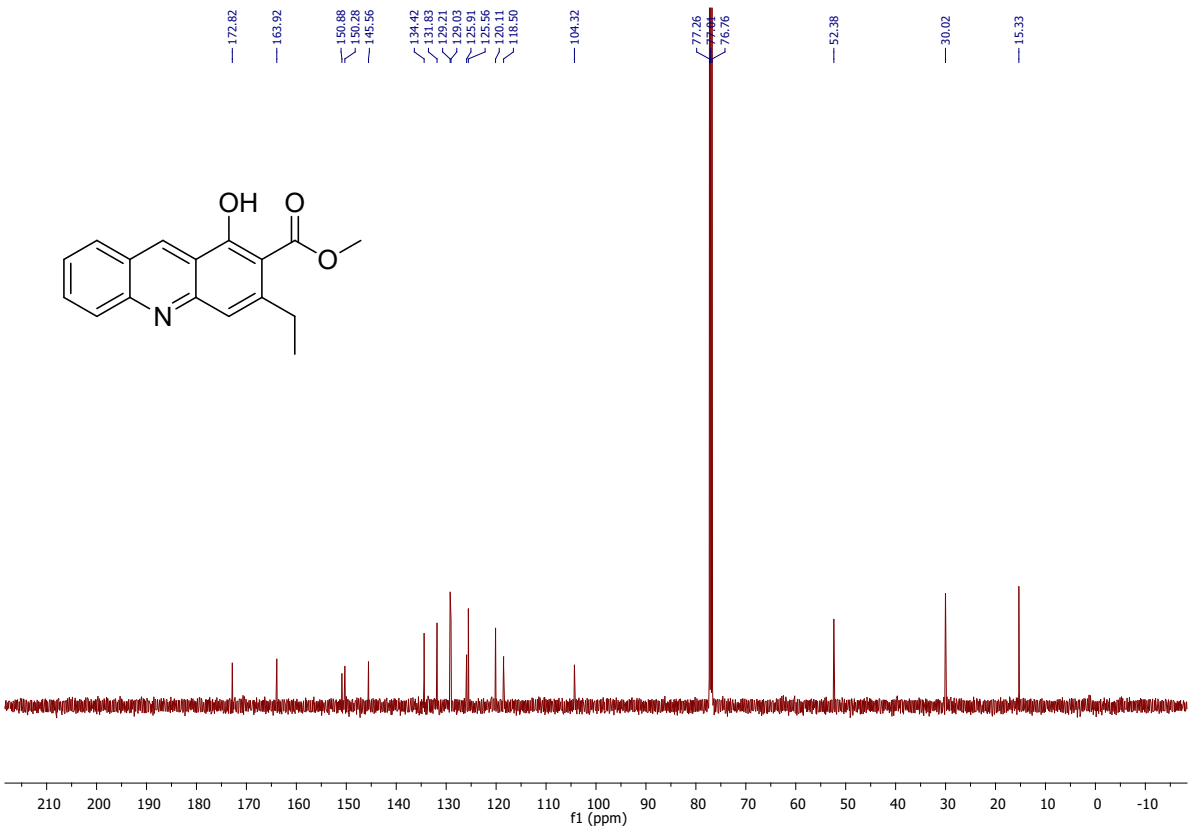
DEPT NMR (125 MHz) of compound **5c** in $CDCl_3$



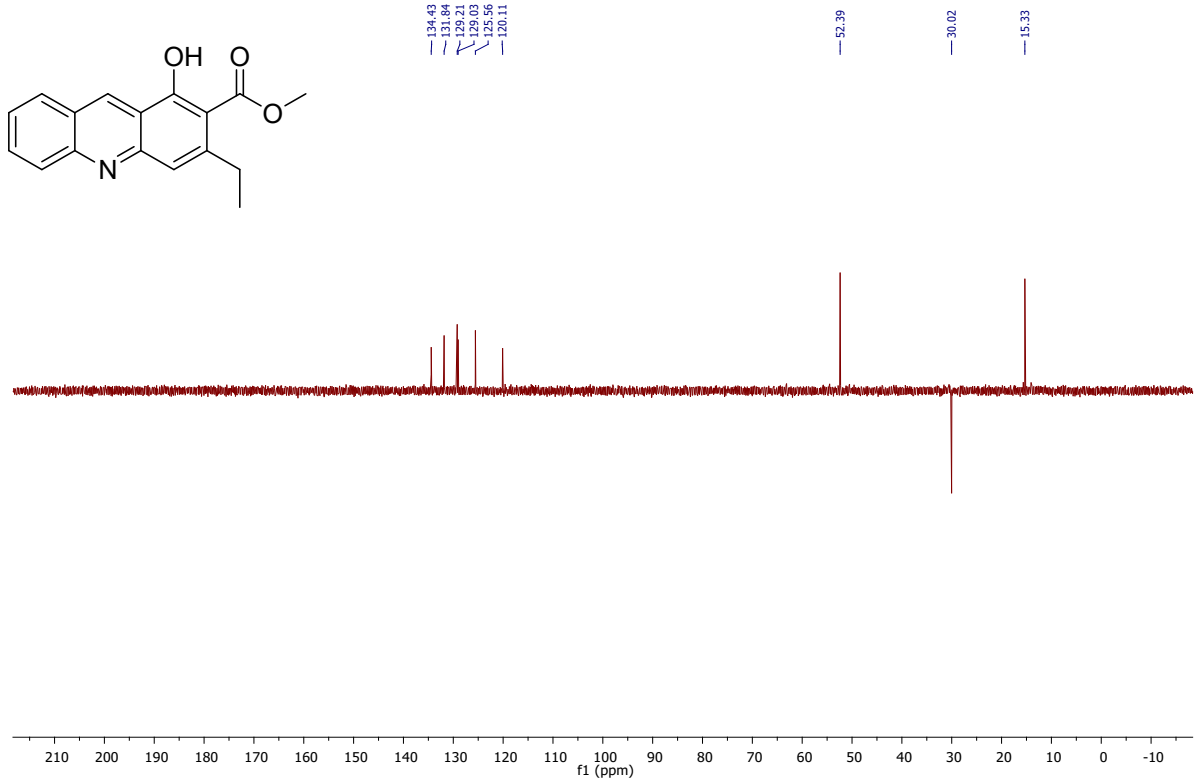
^{1}H NMR (500 MHz) of compound **5d** in $CDCl_3$



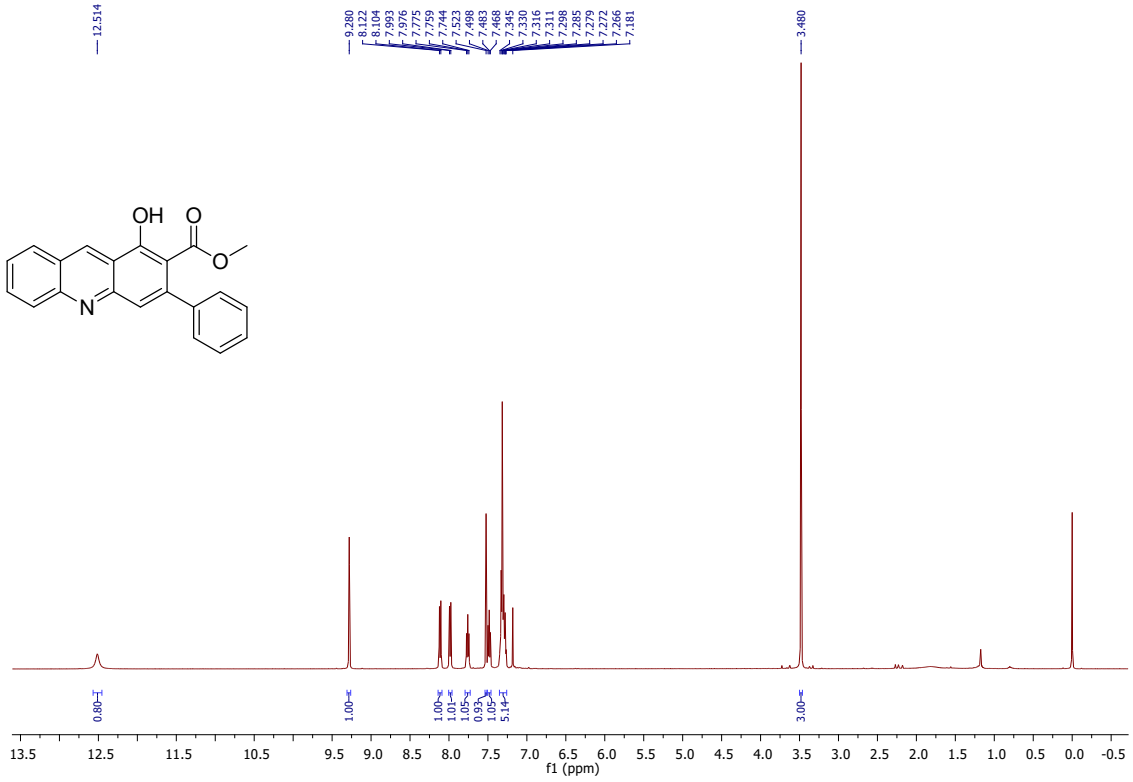
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5d** in $CDCl_3$



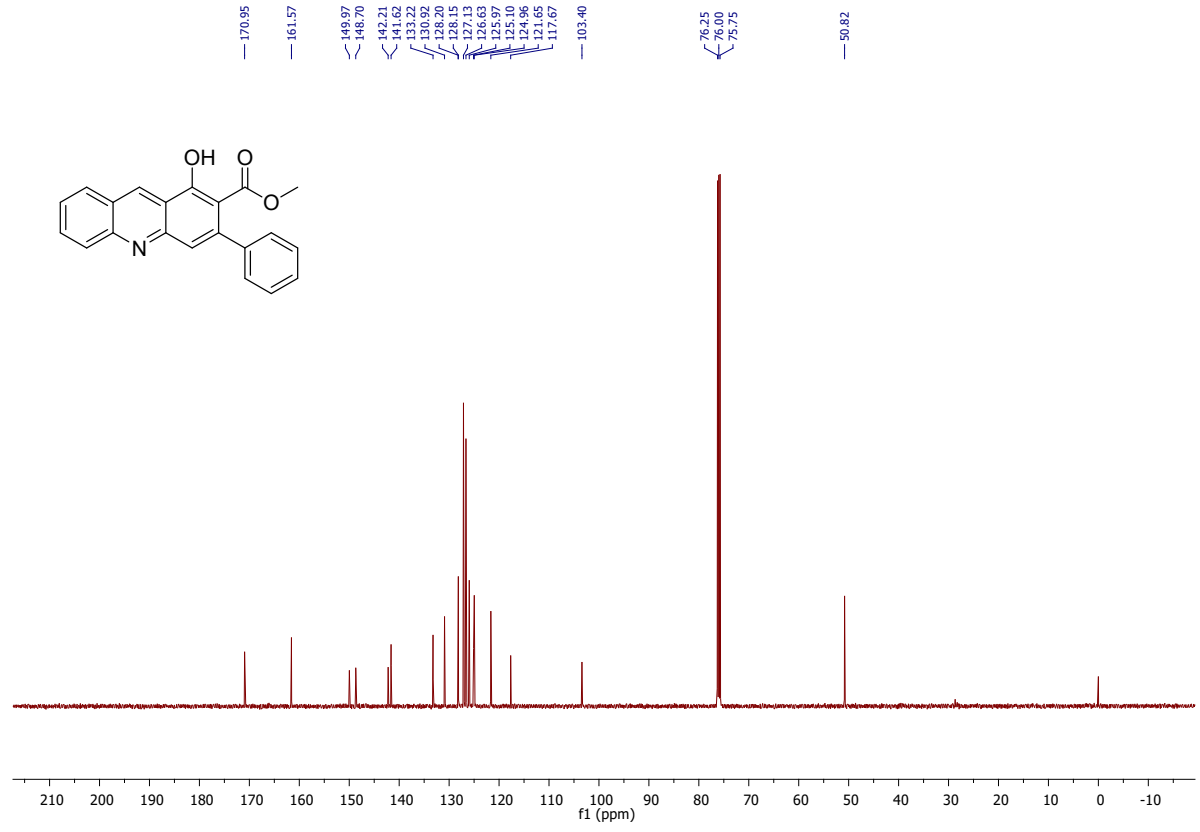
DEPT NMR (125 MHz) of compound **5d** in $CDCl_3$



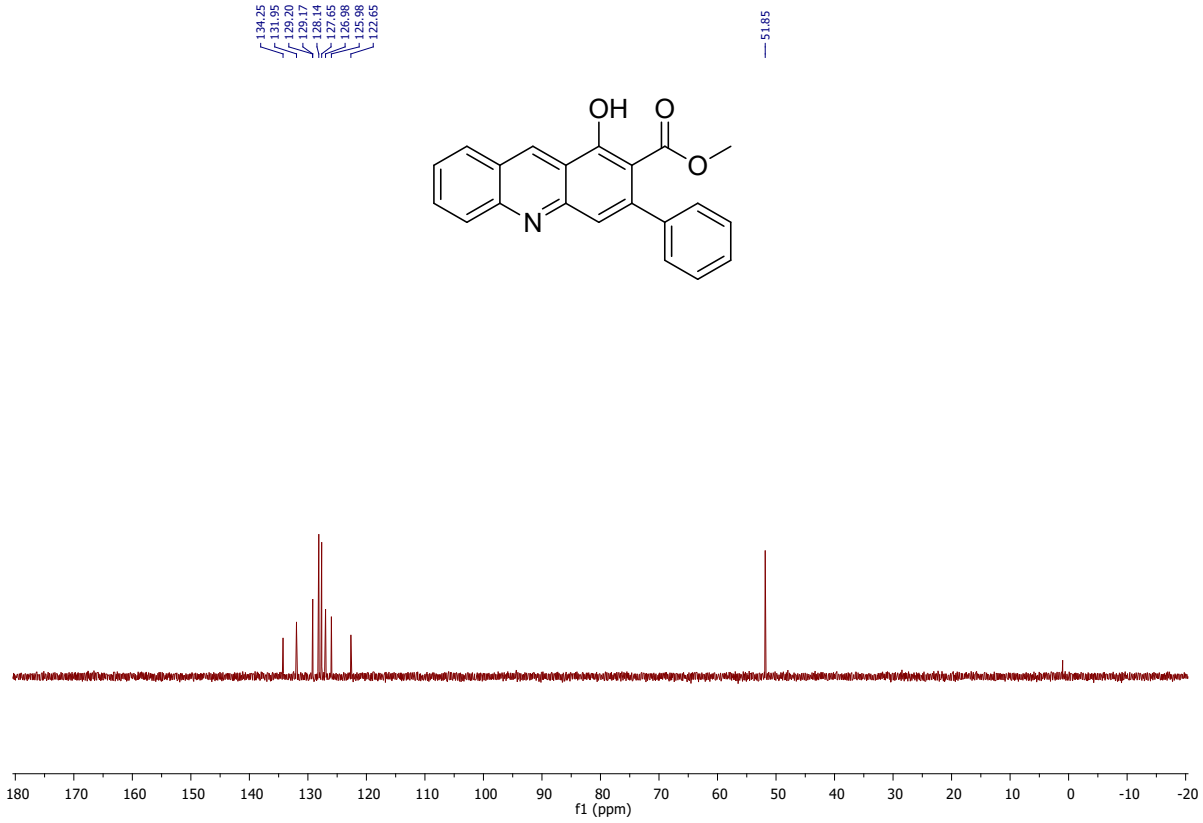
^{1}H NMR (500 MHz) of compound **5e** in $CDCl_3$



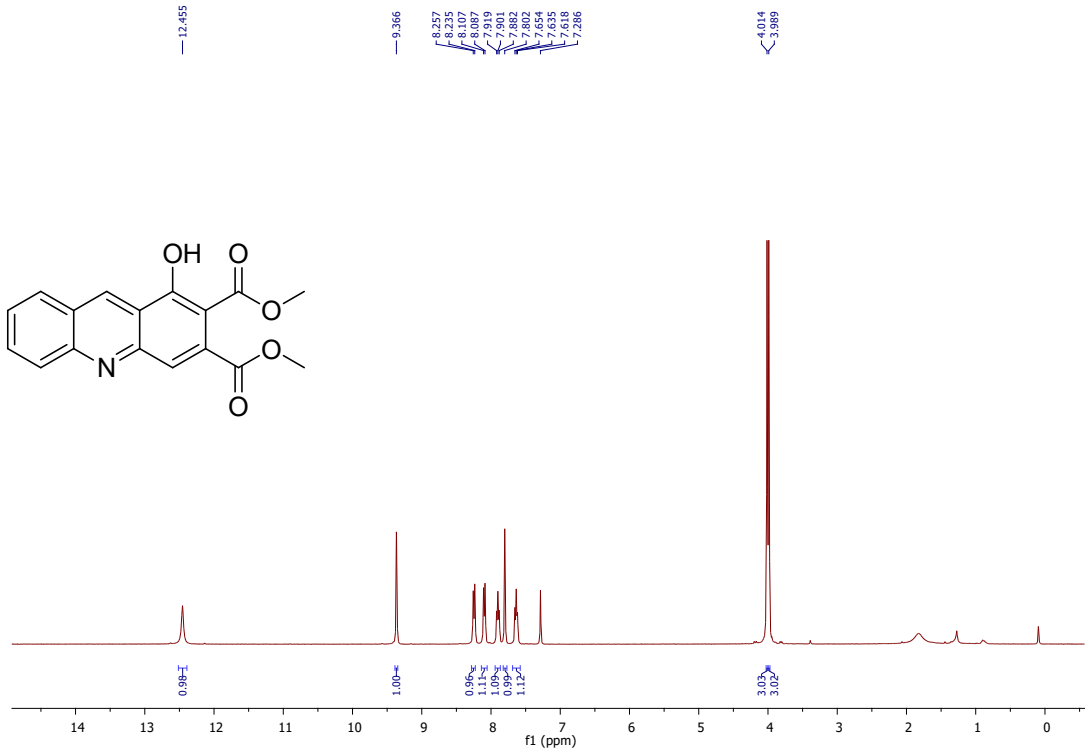
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5e** in $CDCl_3$



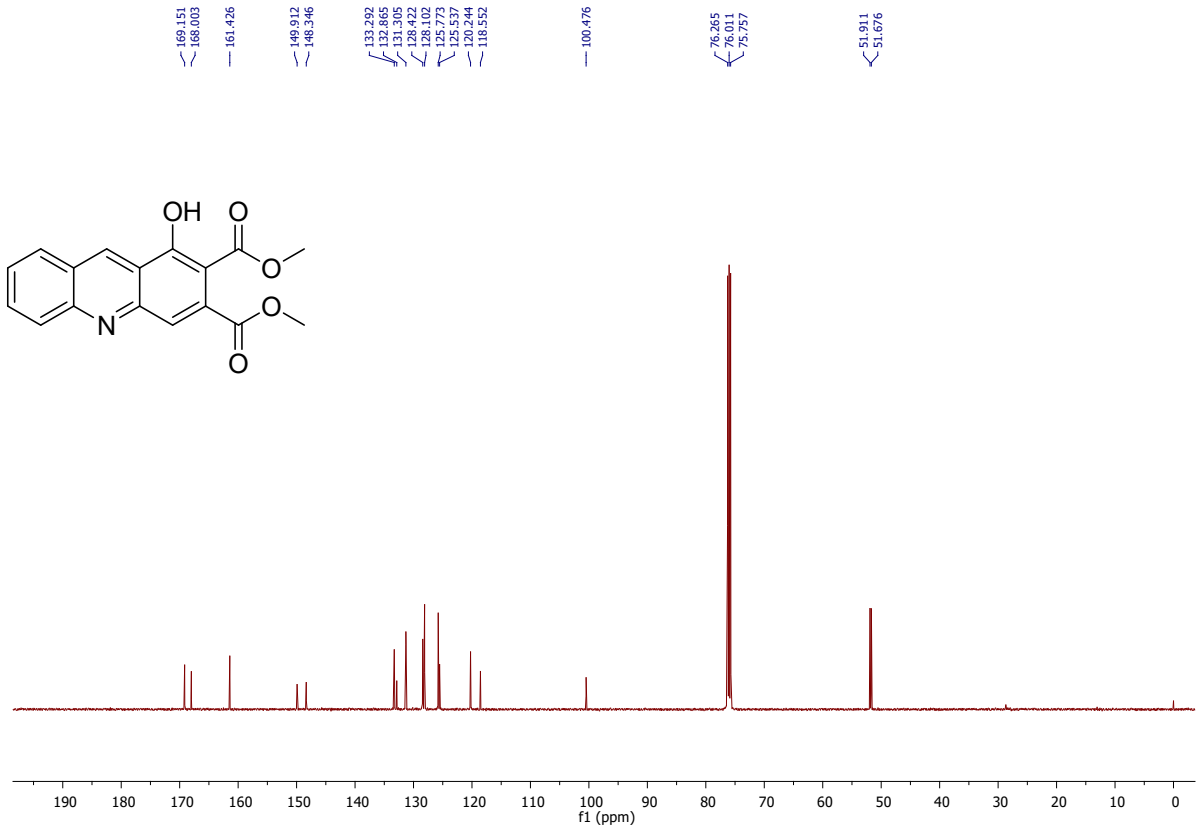
DEPT NMR (125 MHz) of compound **5e** in $CDCl_3$



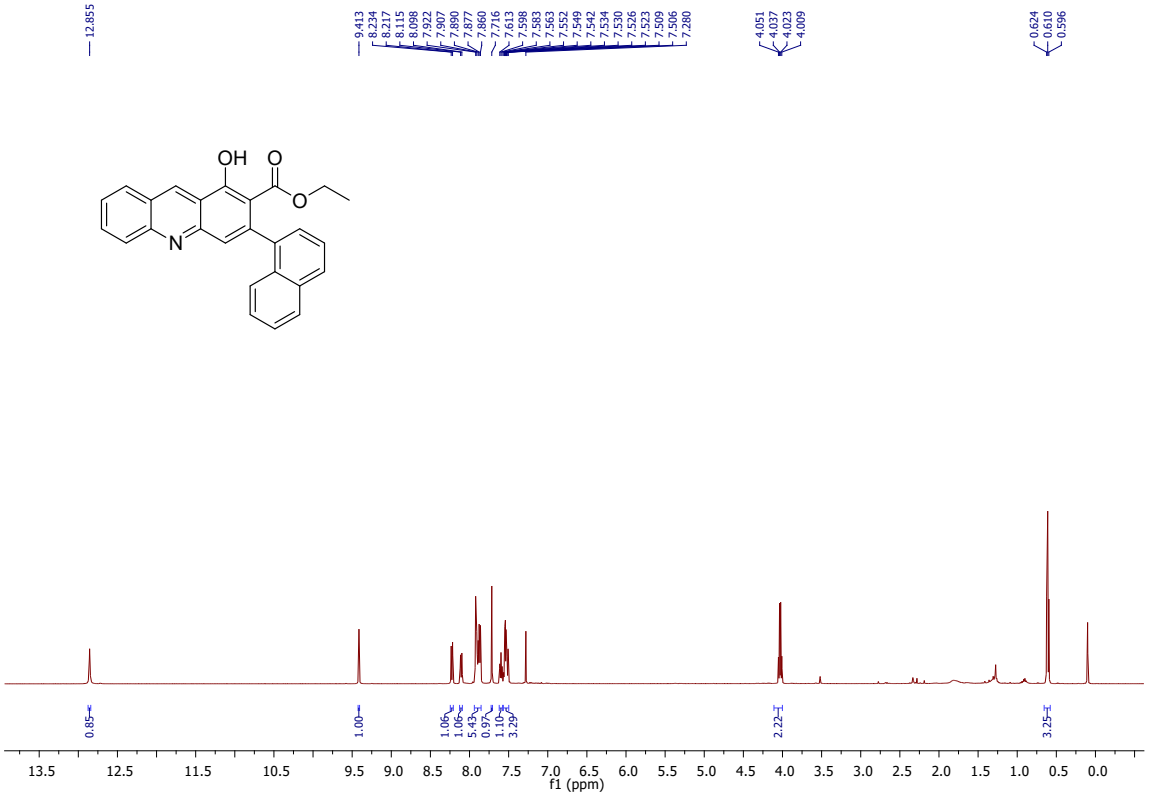
^{1}H NMR (400 MHz) of compound **5f** in $CDCl_3$



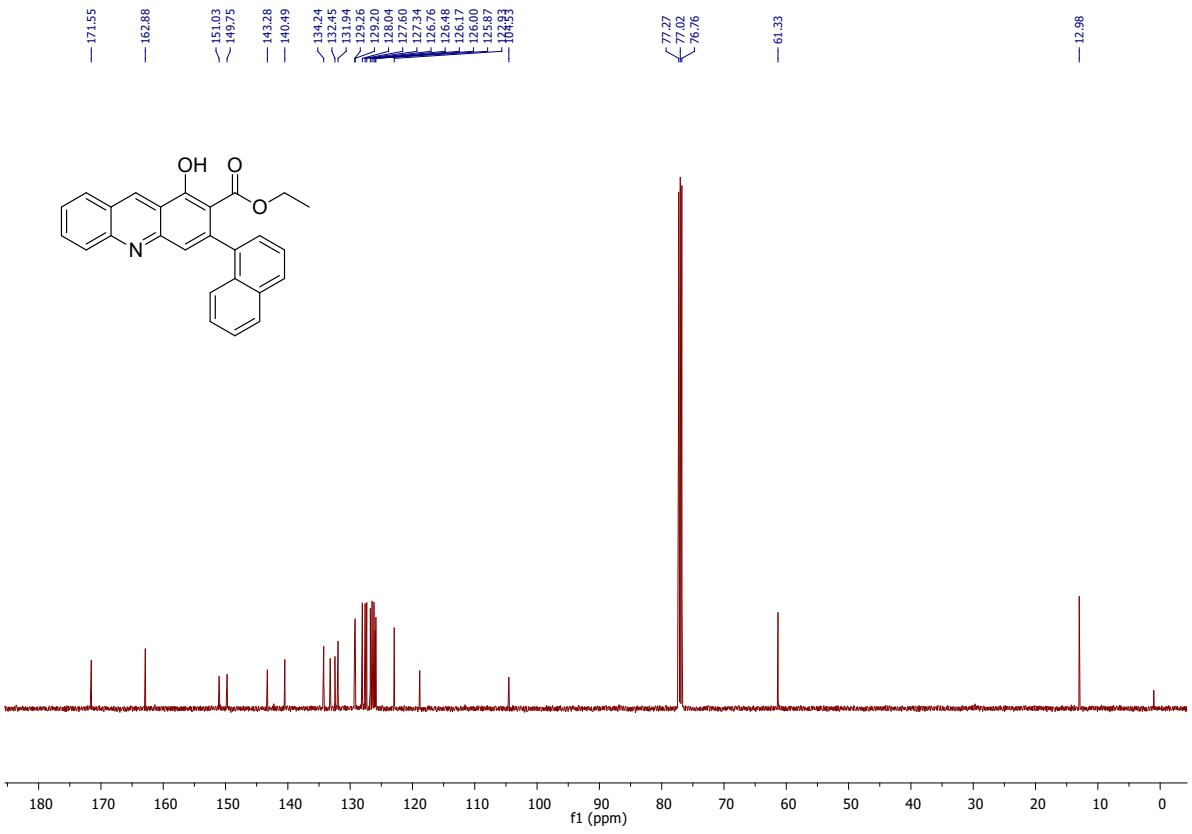
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5f** in $CDCl_3$



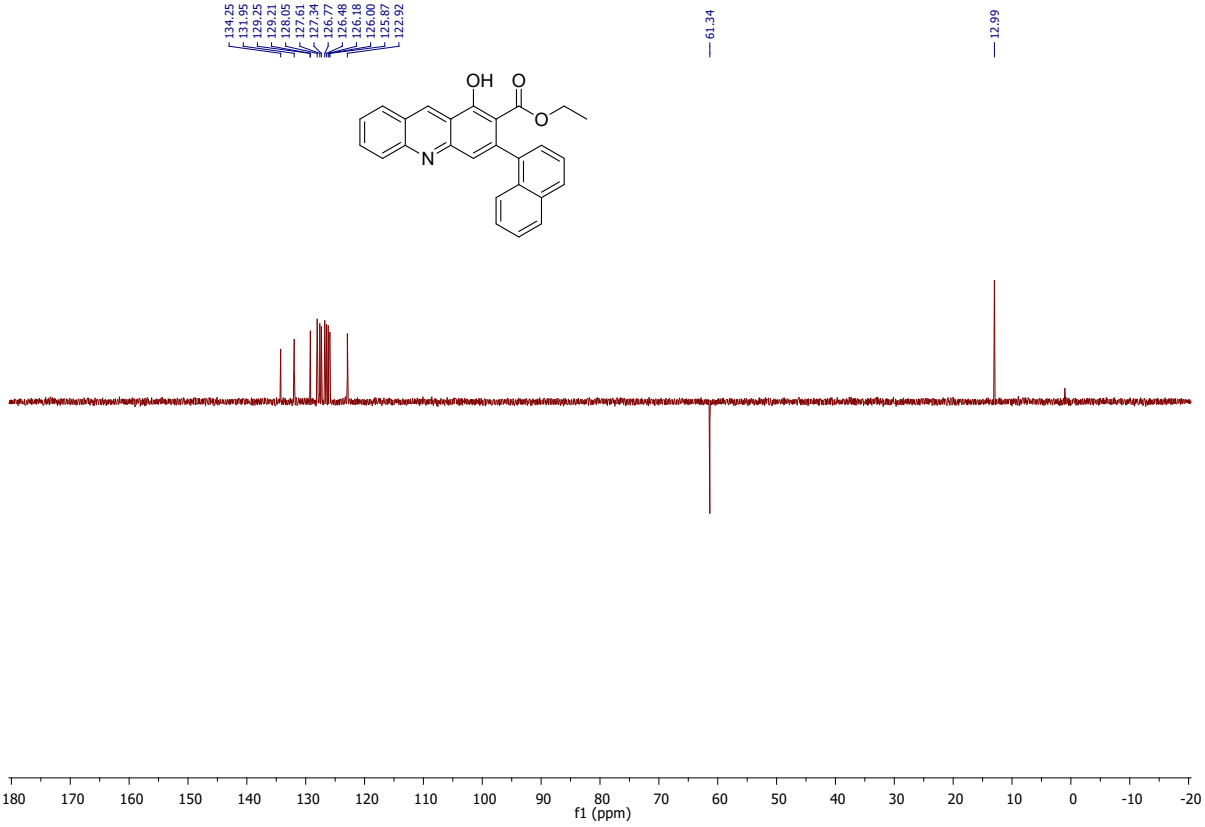
^{1}H NMR (500 MHz) of compound **5g** in $CDCl_3$



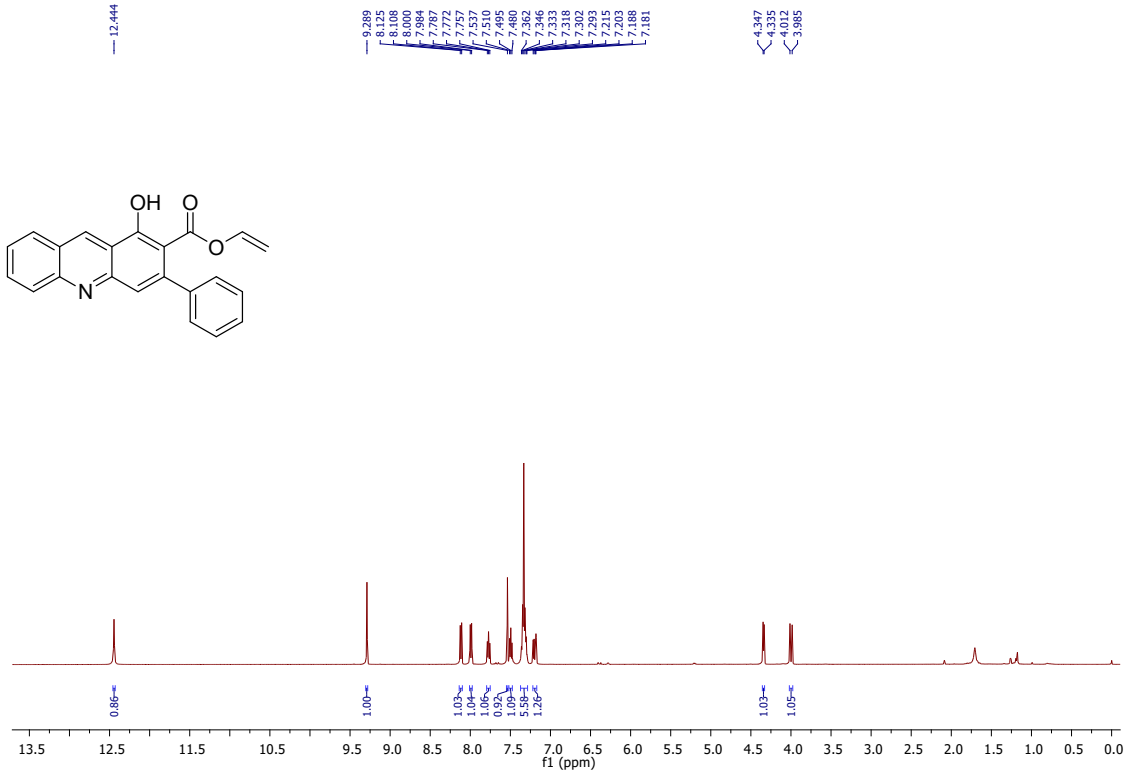
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5g** in $CDCl_3$



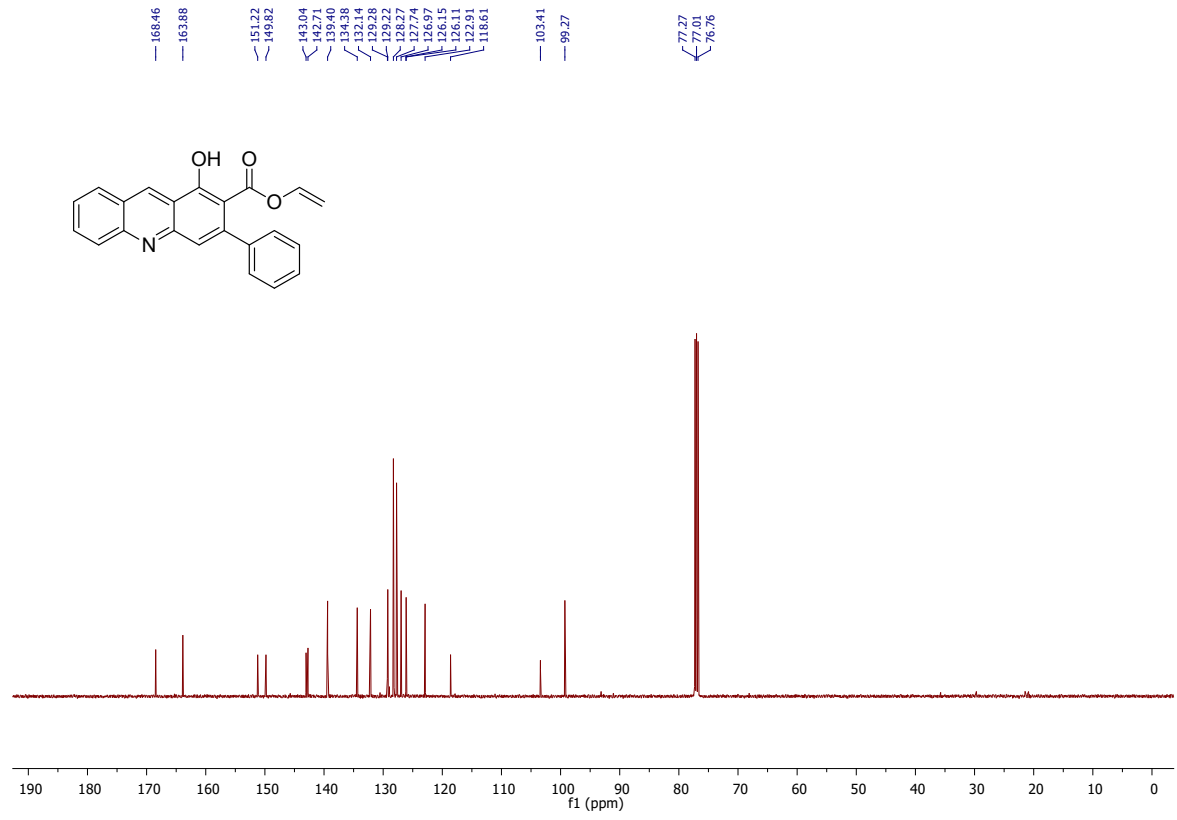
DEPT NMR (125 MHz) of compound **5g** in $CDCl_3$



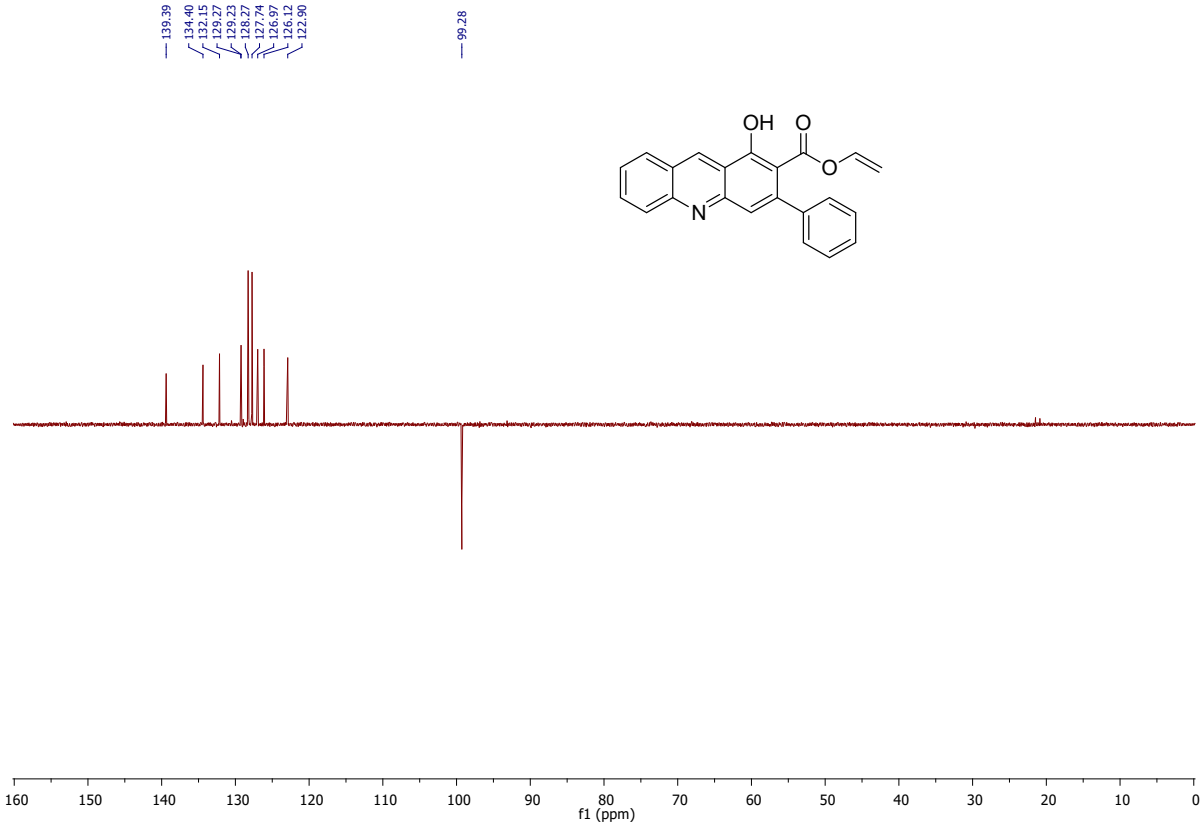
^{1}H NMR (500 MHz) of compound **5h** in $CDCl_3$



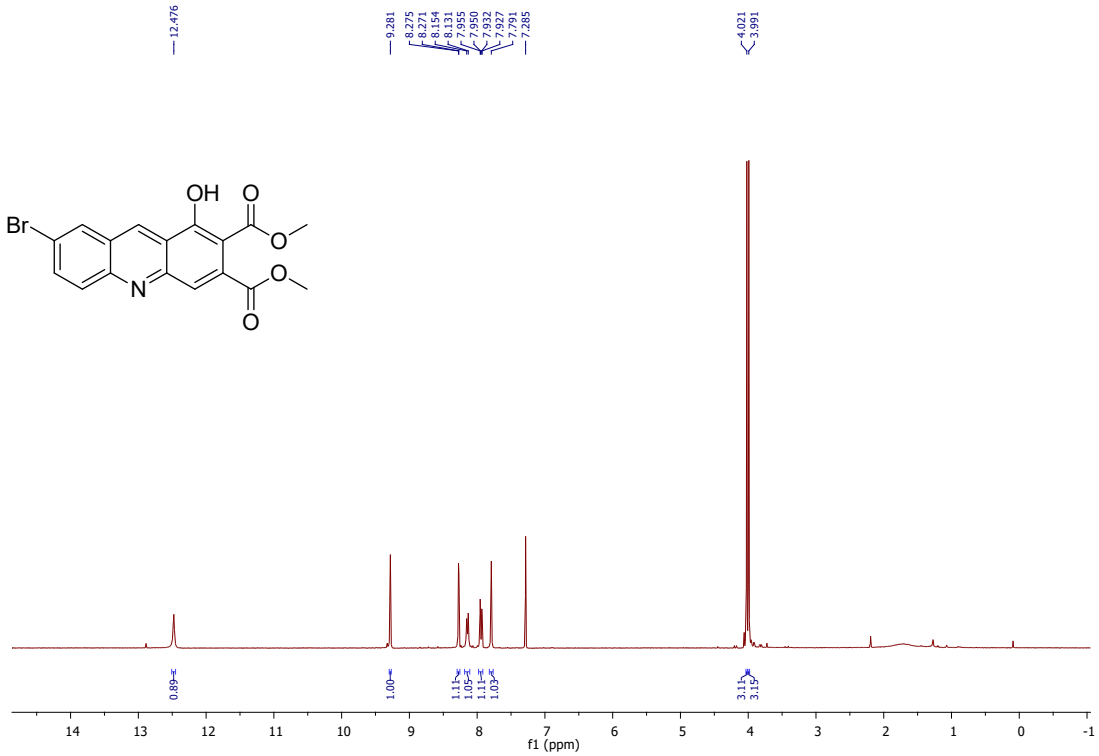
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5h** in $CDCl_3$



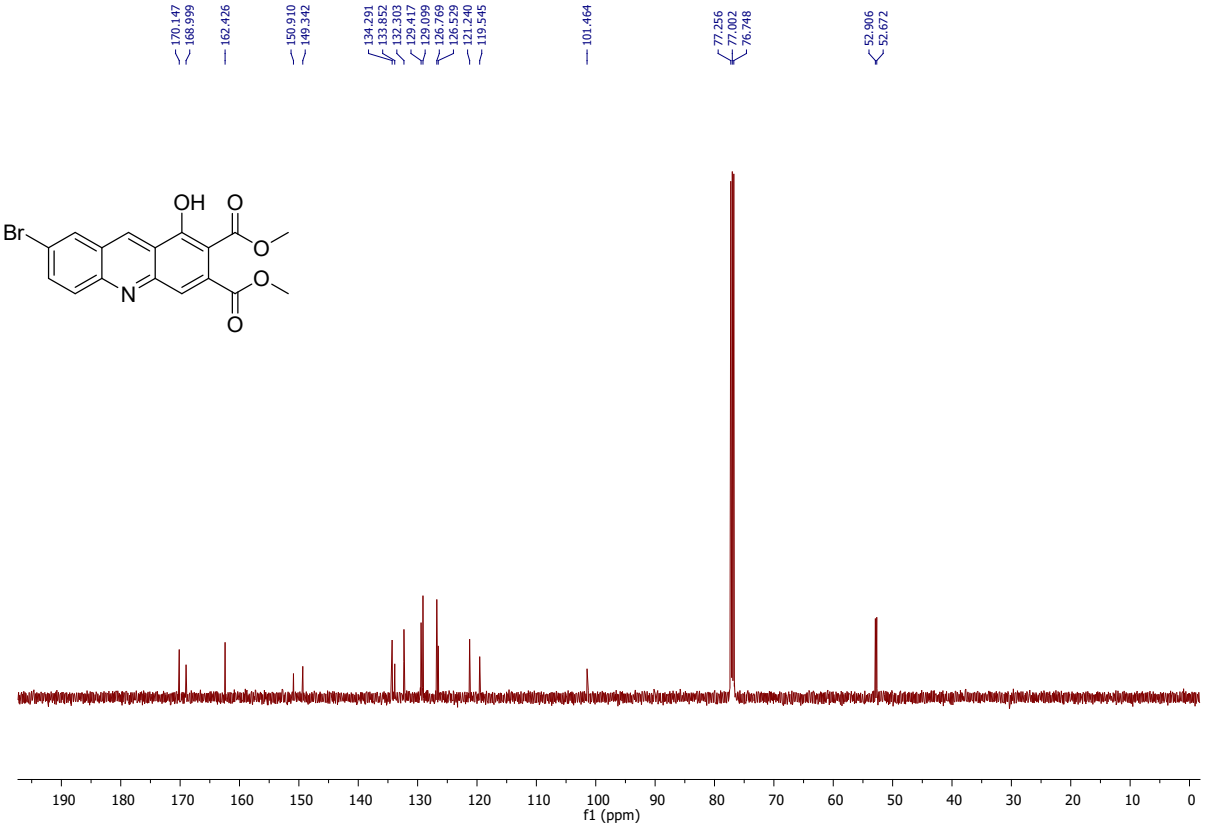
DEPT NMR (125 MHz) of compound **5h** in $CDCl_3$



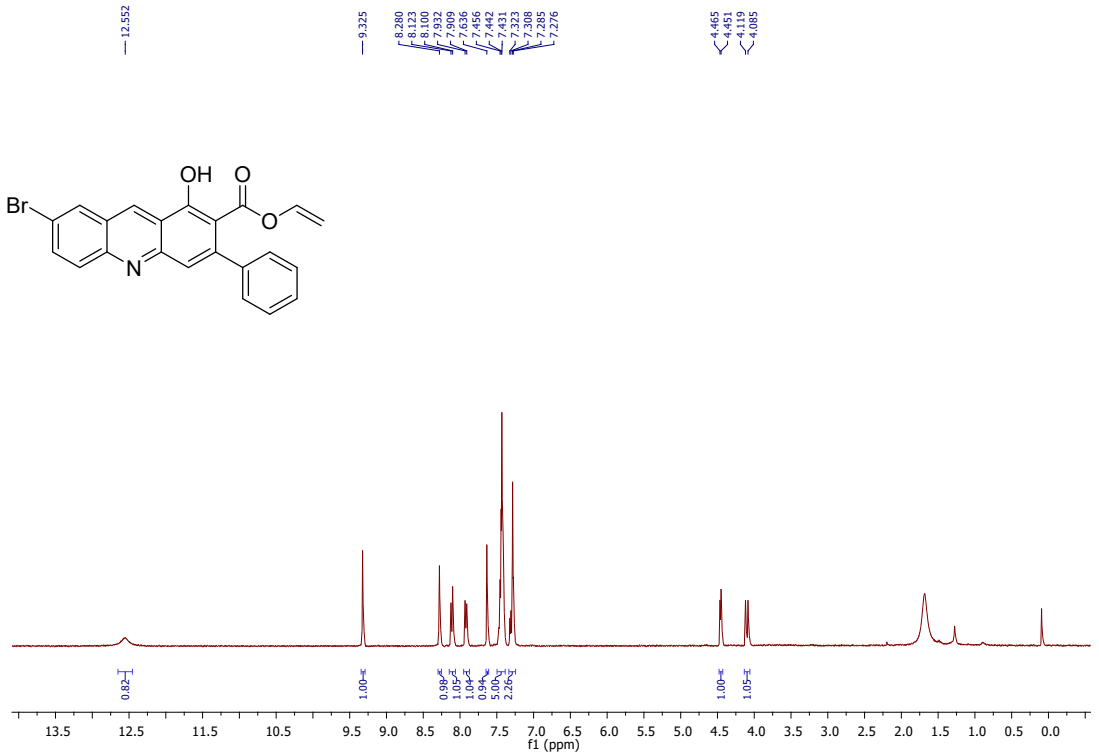
^{1}H NMR (400 MHz) of compound **5i** in $CDCl_3$



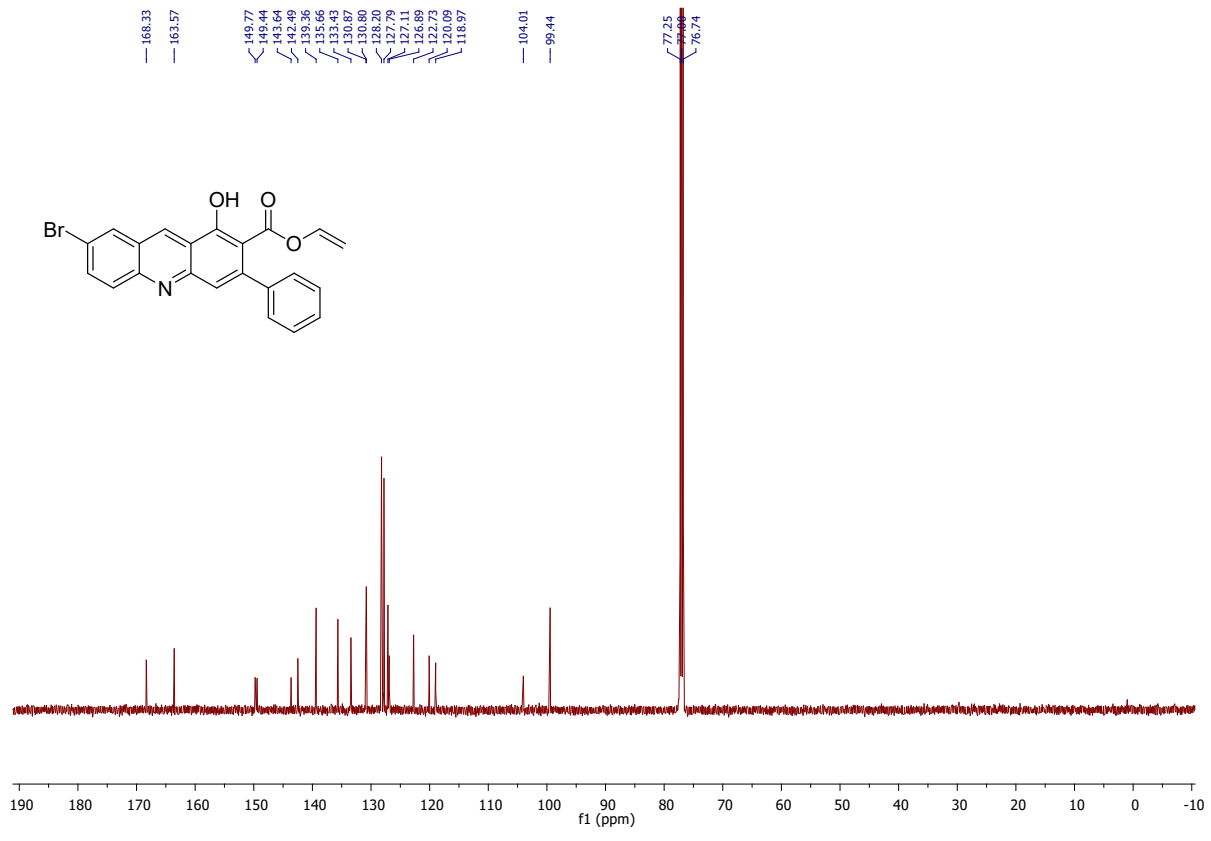
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5i** in $CDCl_3$



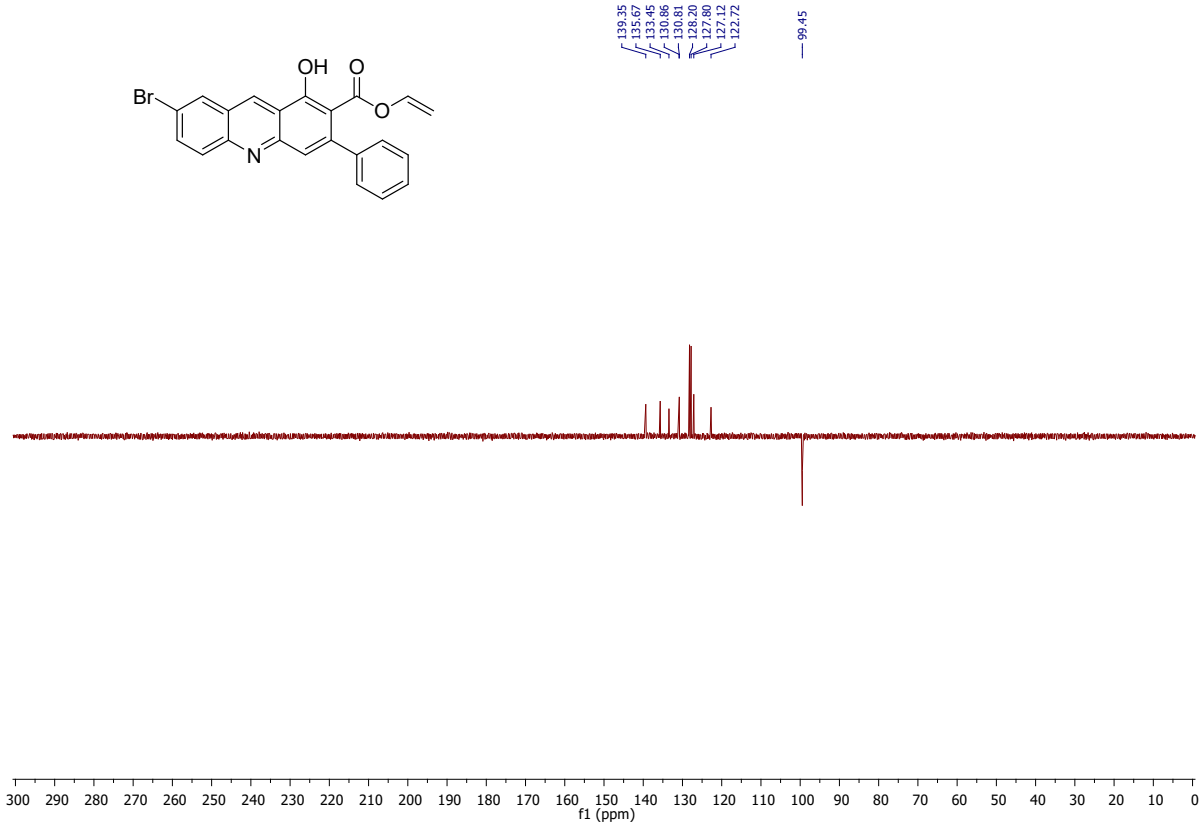
^{1}H NMR (500 MHz) of compound **5j** in $CDCl_3$



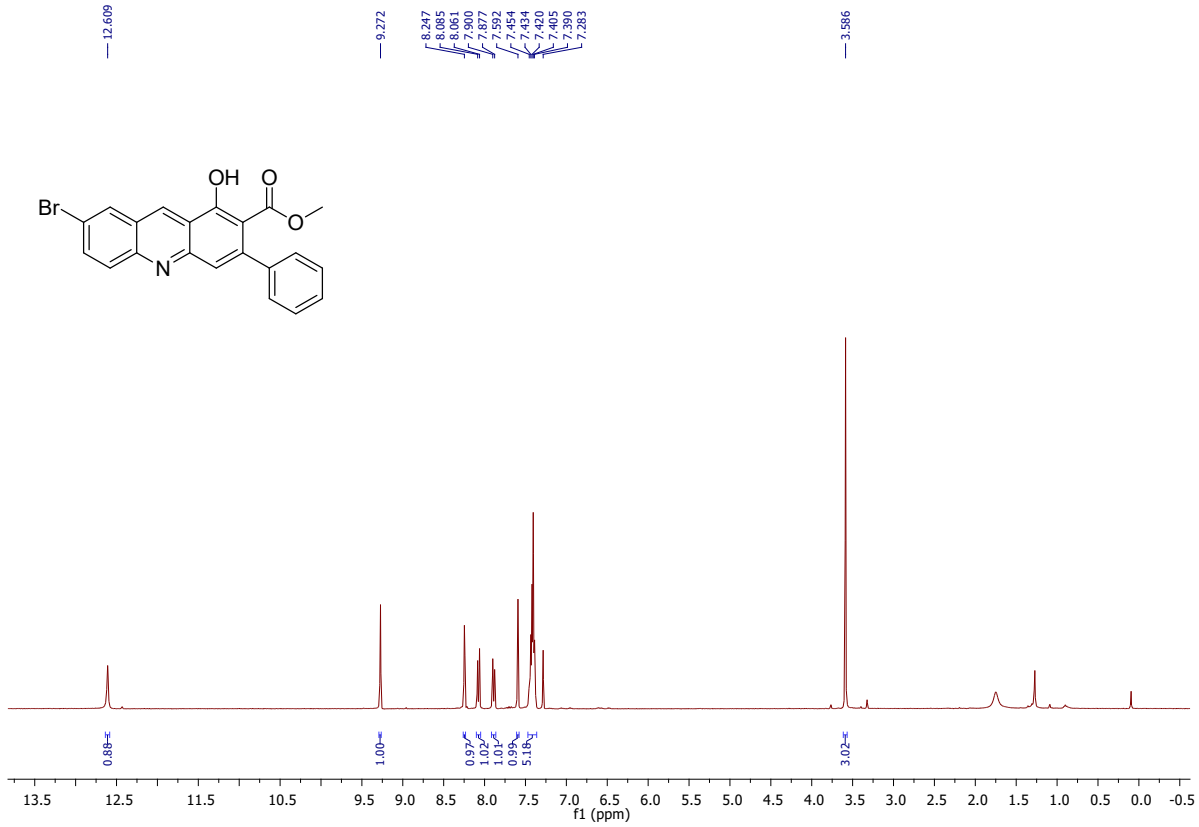
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5j** in $CDCl_3$



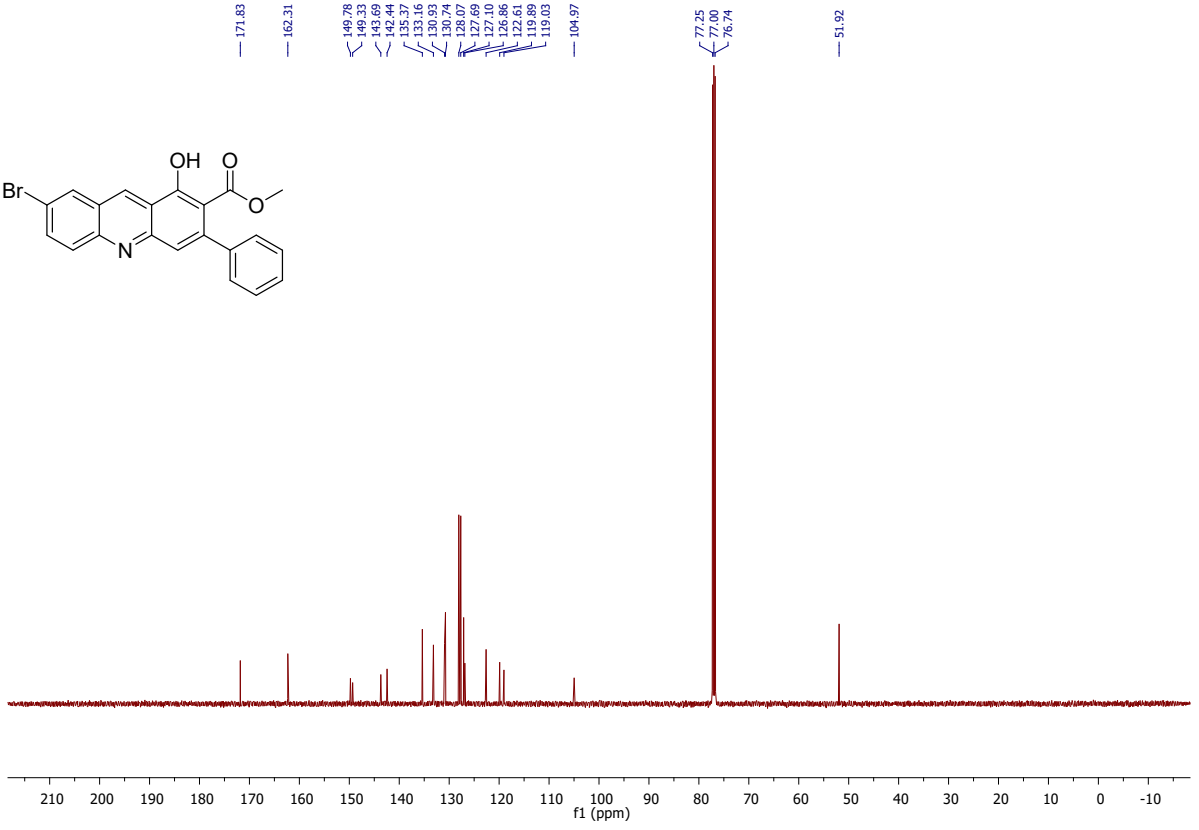
DEPT NMR (125 MHz) of compound **5j** in $CDCl_3$



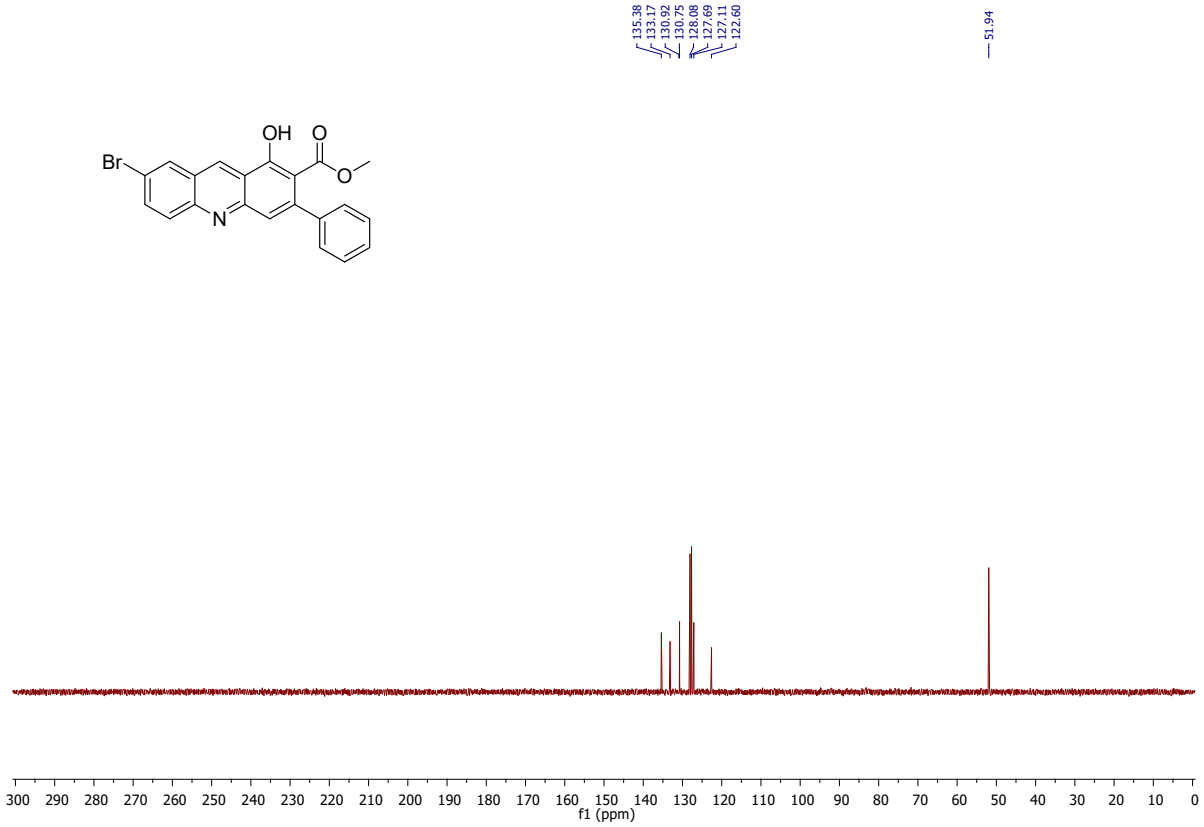
^{1}H NMR (500 MHz) of compound **5k** in $CDCl_3$



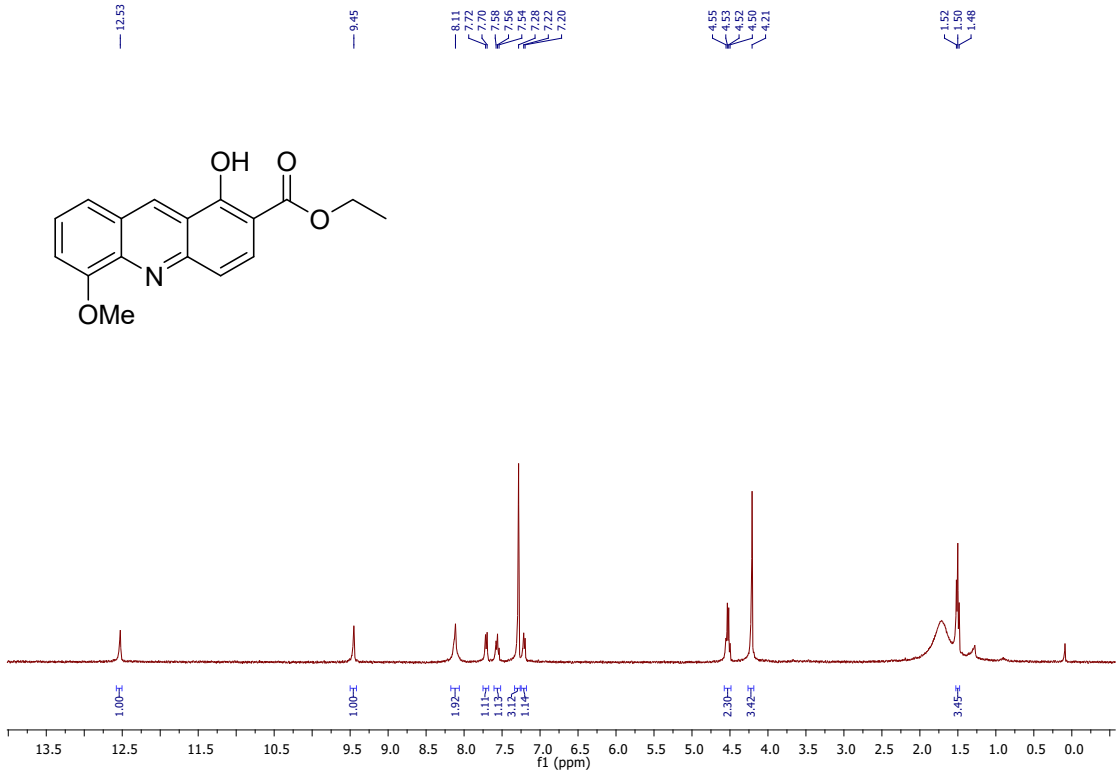
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5k** in $CDCl_3$



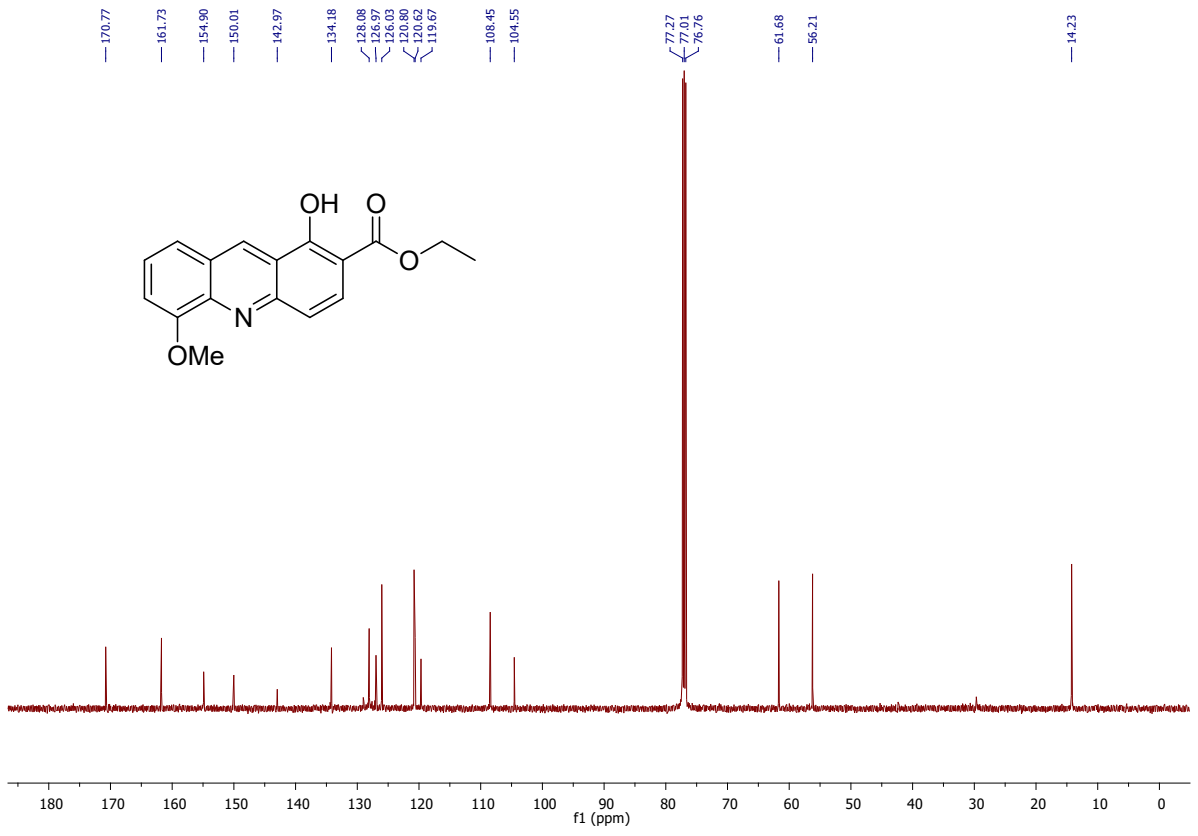
DEPT NMR (125 MHz) of compound **5k** in $CDCl_3$



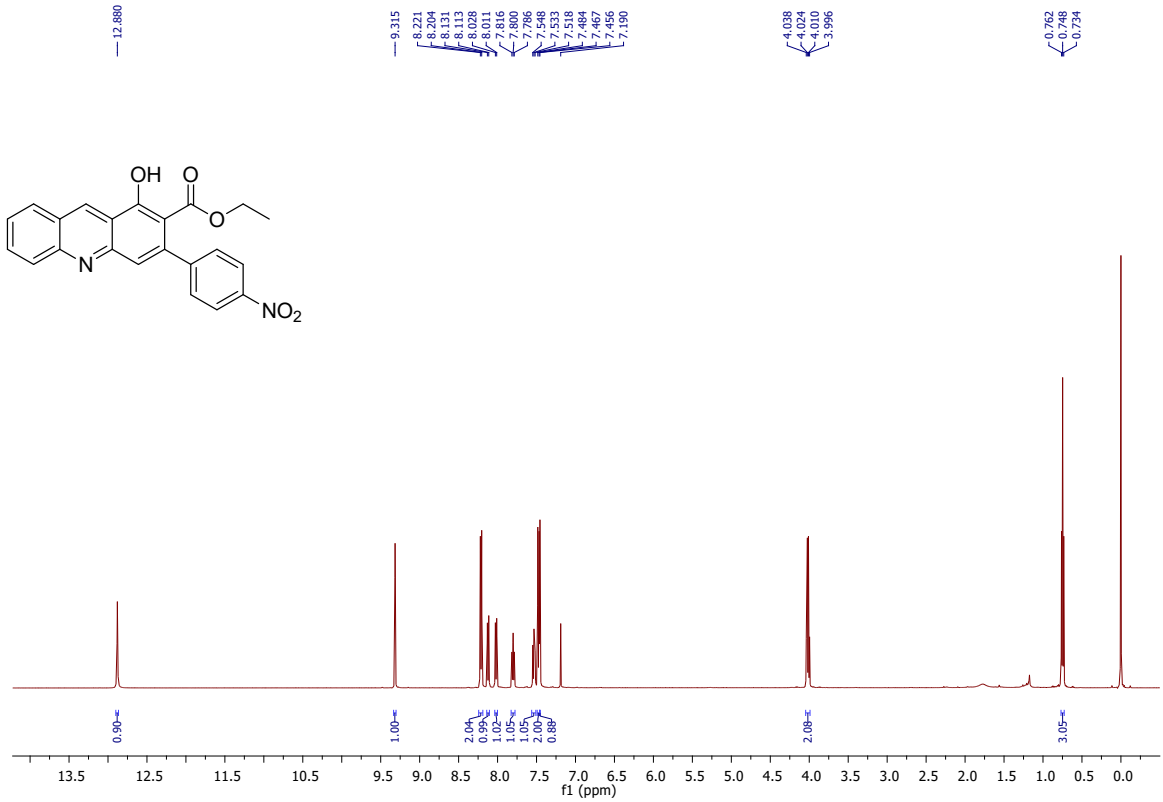
^{1}H NMR (500 MHz) of compound **5l** in $CDCl_3$



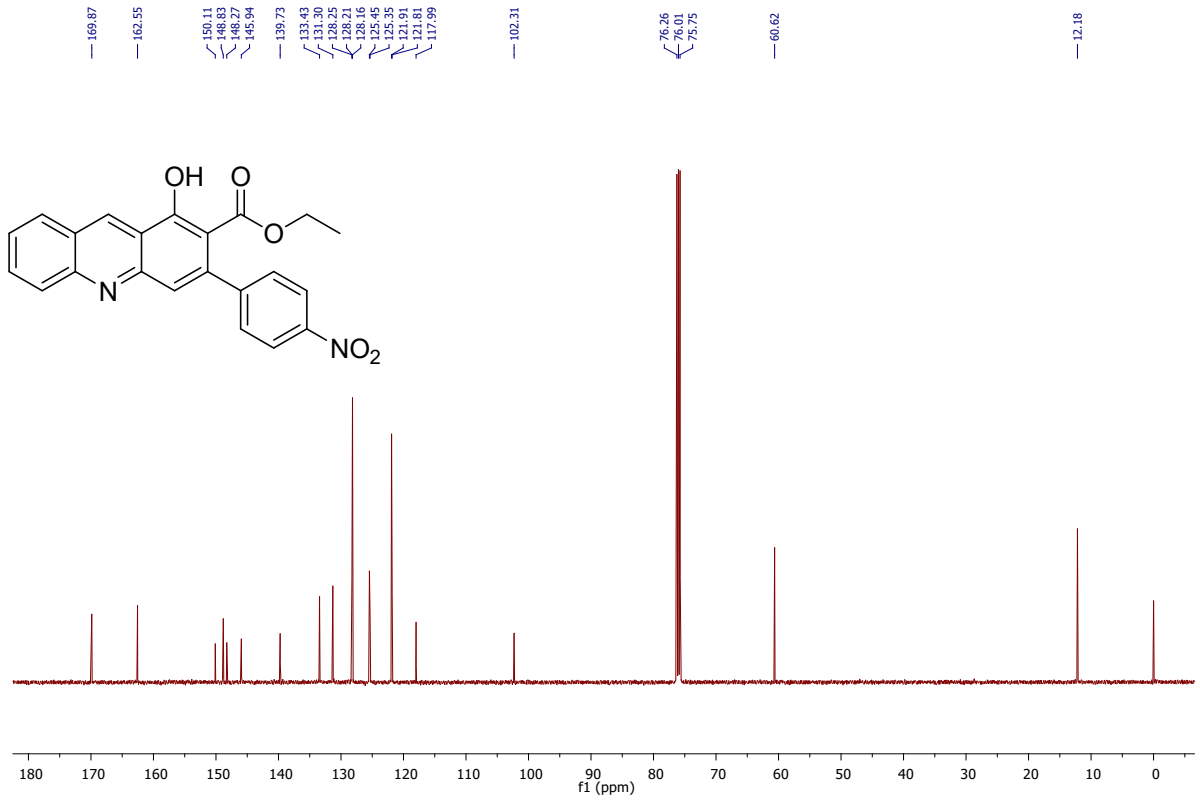
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5l** in $CDCl_3$



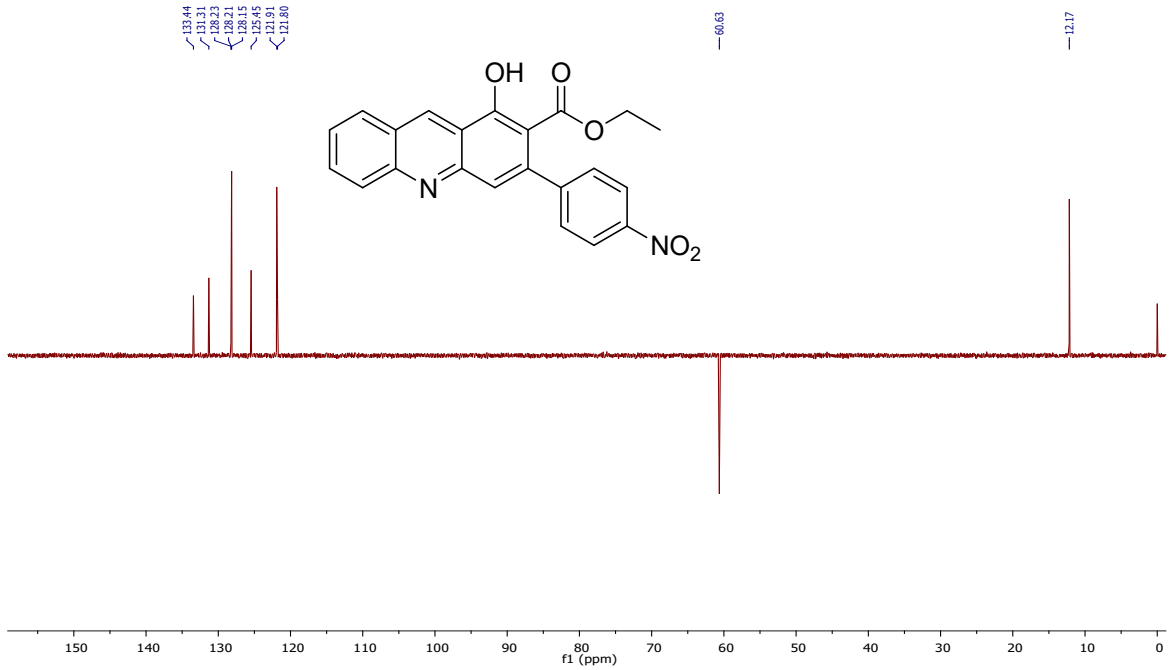
^{1}H NMR (500 MHz) of compound **5m** in $CDCl_3$



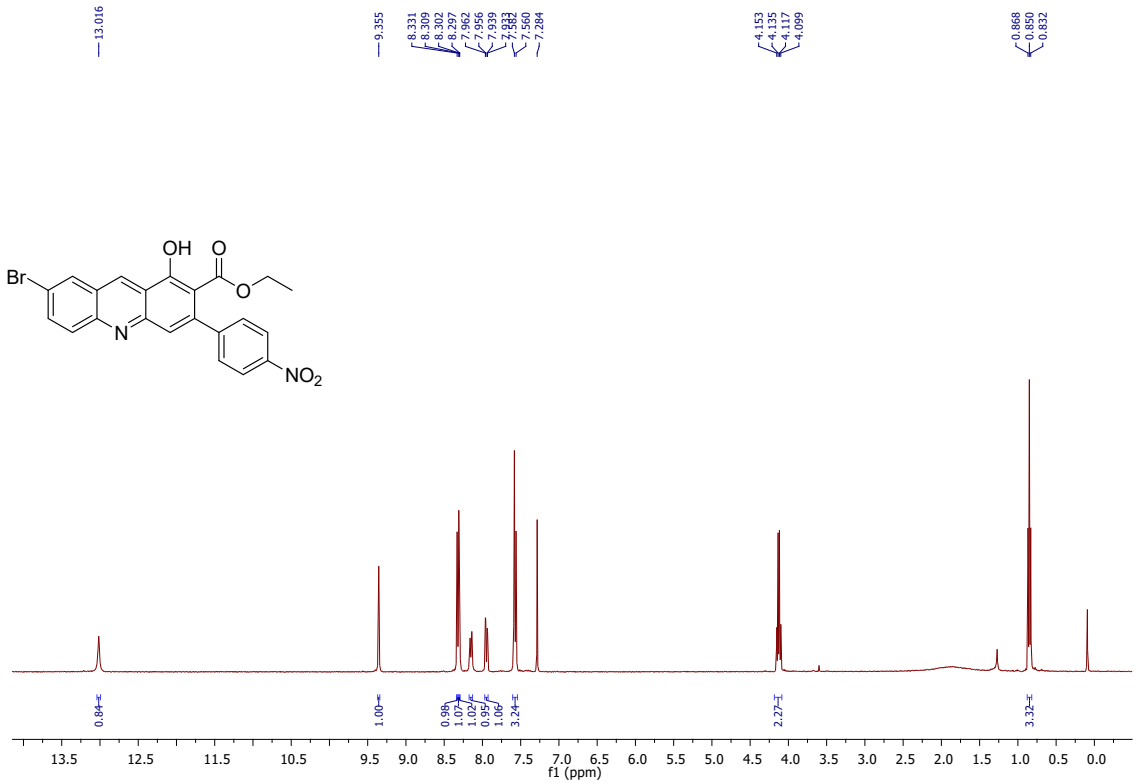
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5m** in $CDCl_3$



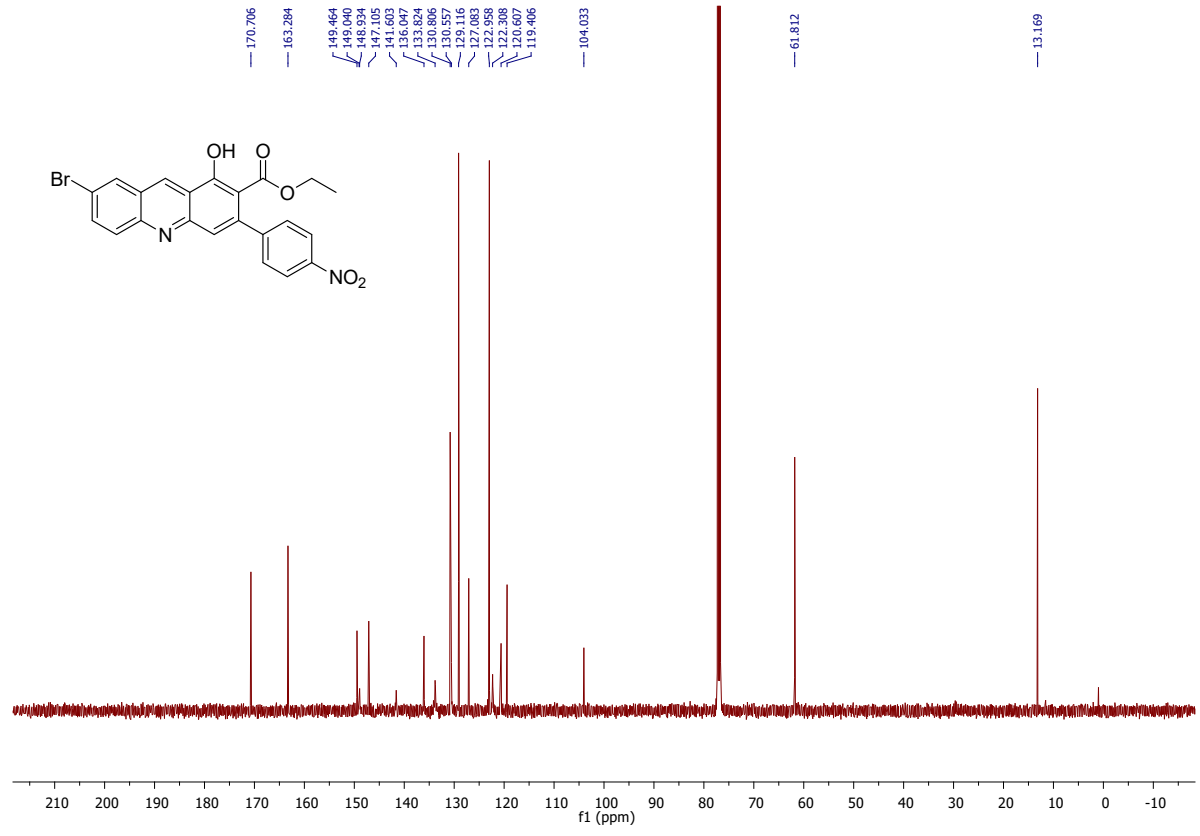
DEPT NMR (125 MHz) of compound **5m** in $CDCl_3$



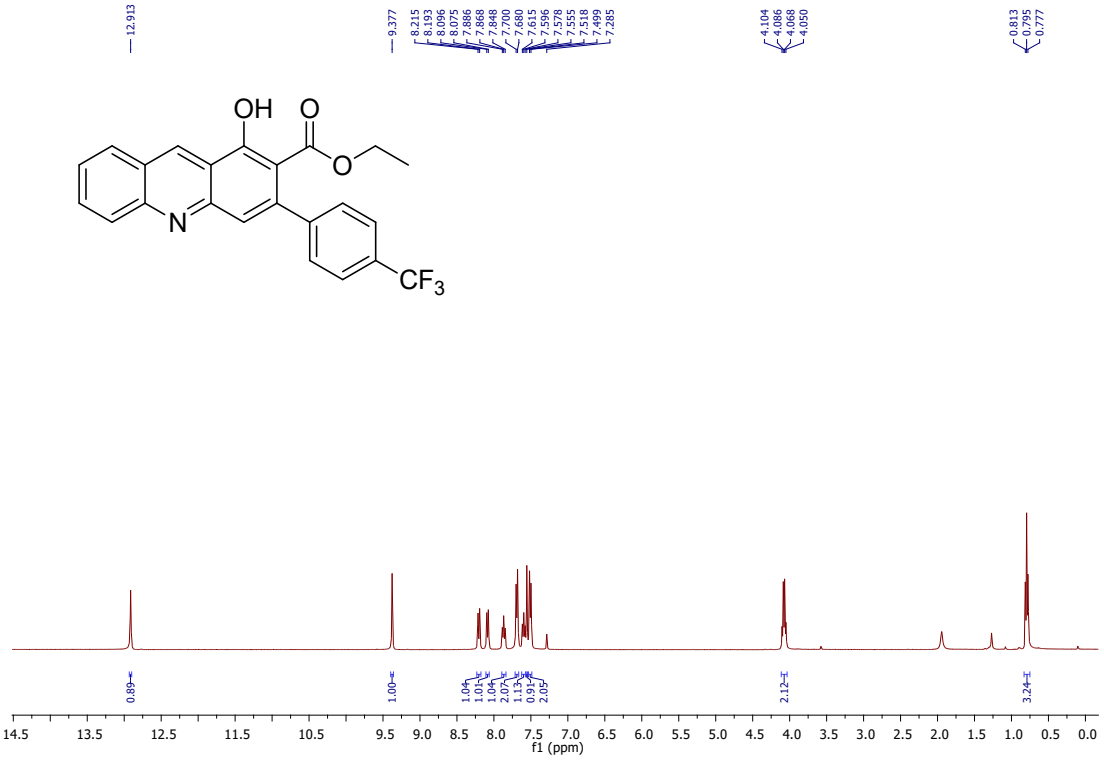
^{1}H NMR (500 MHz) of compound **5n** in $CDCl_3$



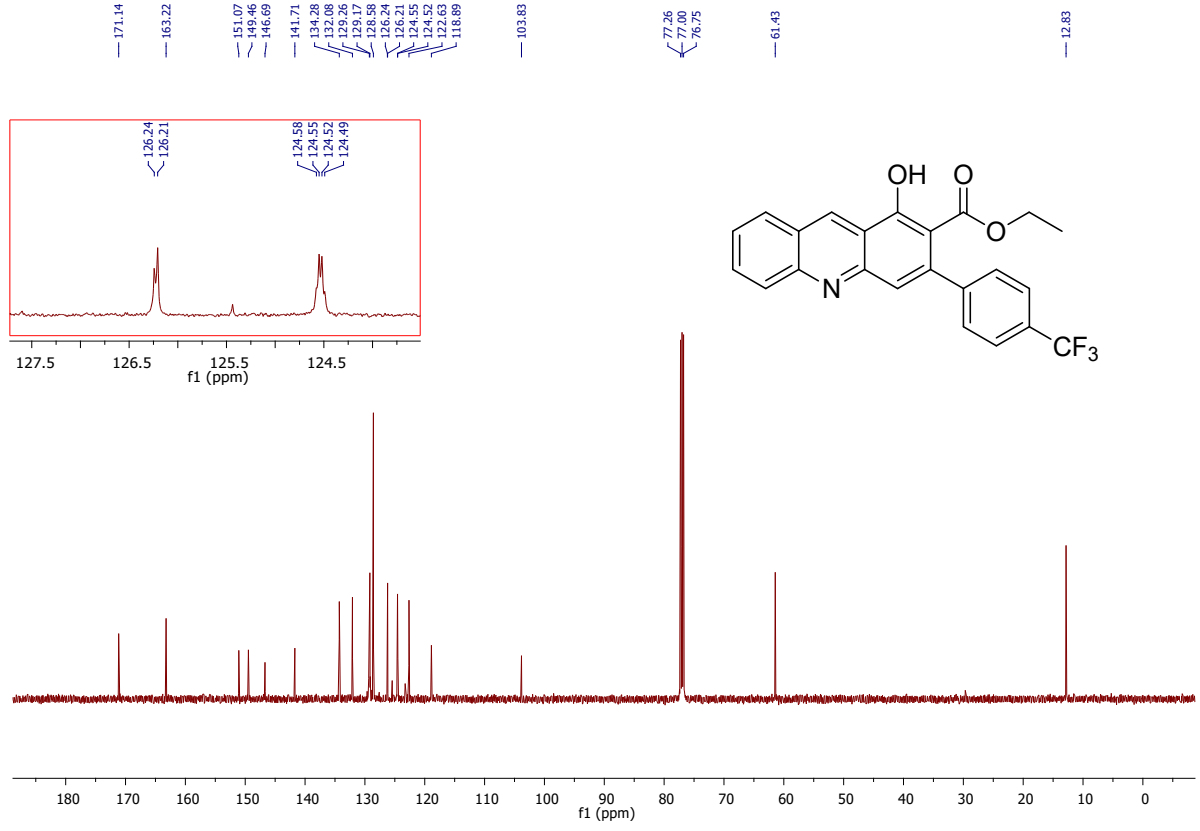
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5n** in $CDCl_3$



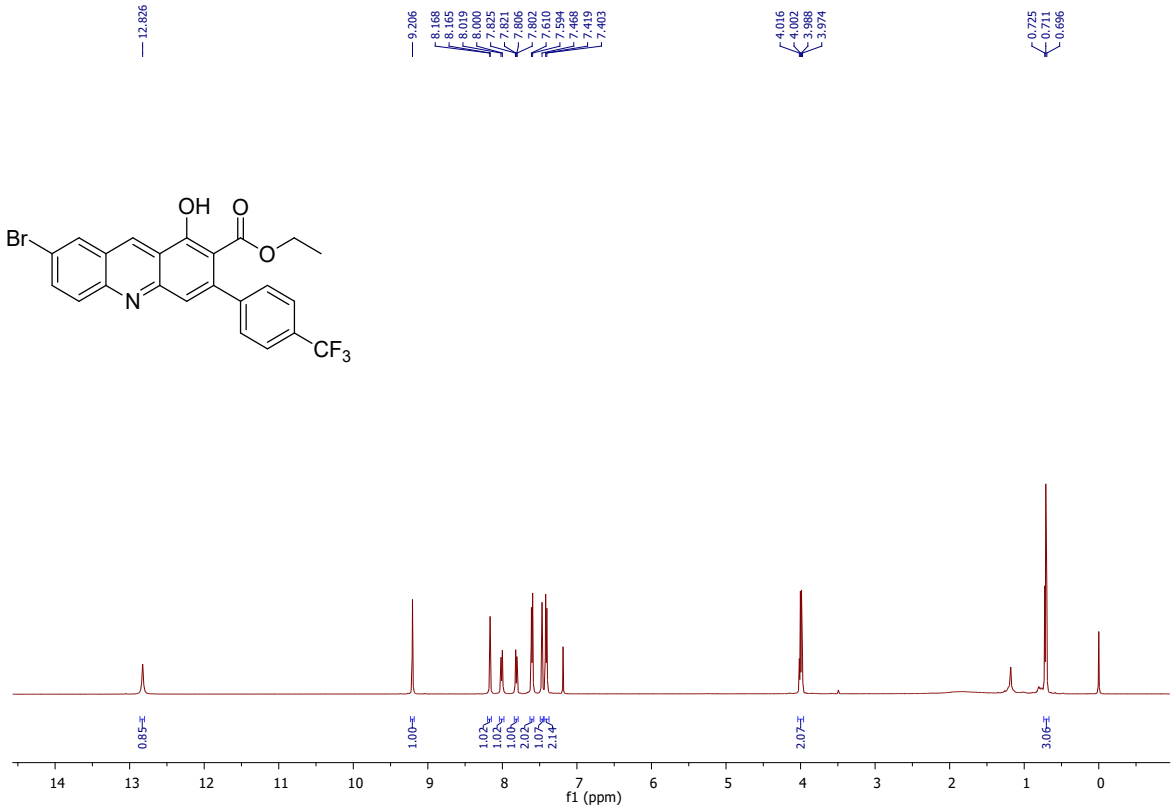
^{1}H NMR (500 MHz) of compound **5o** in $CDCl_3$



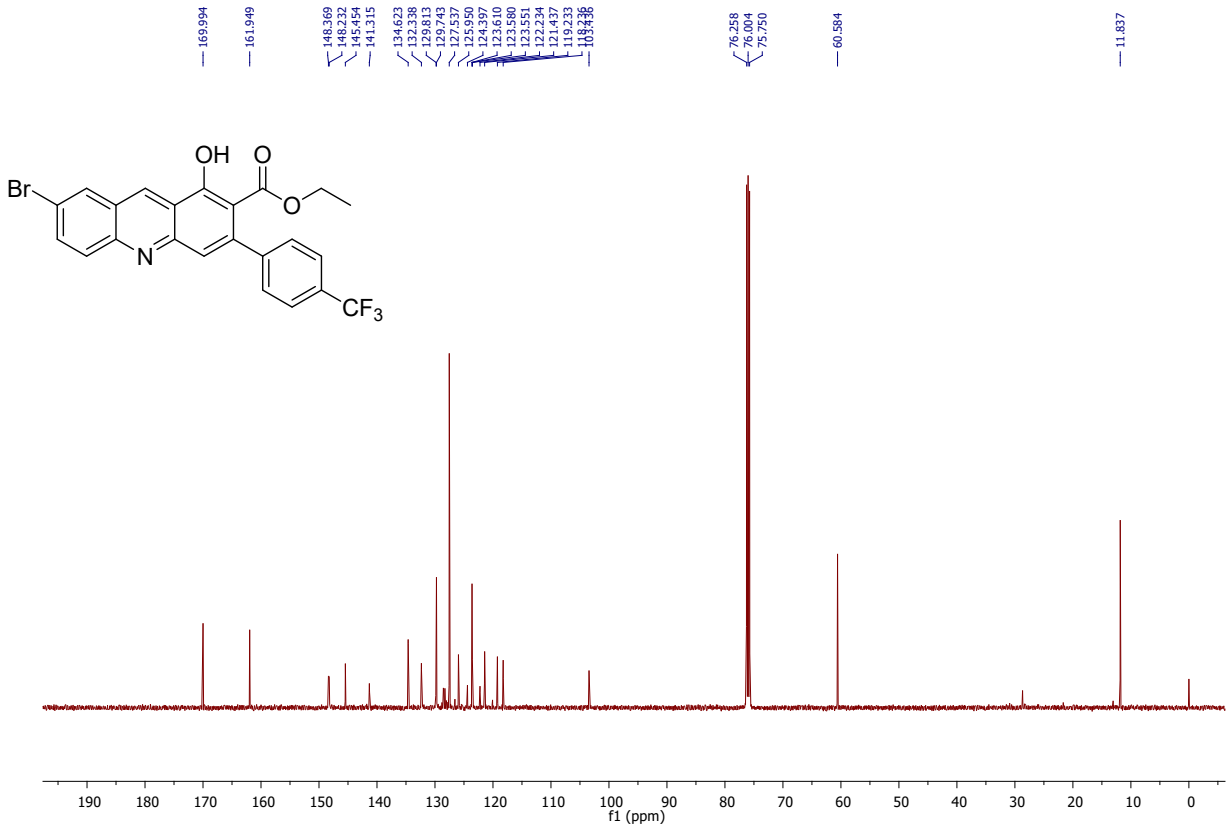
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5o** in $CDCl_3$



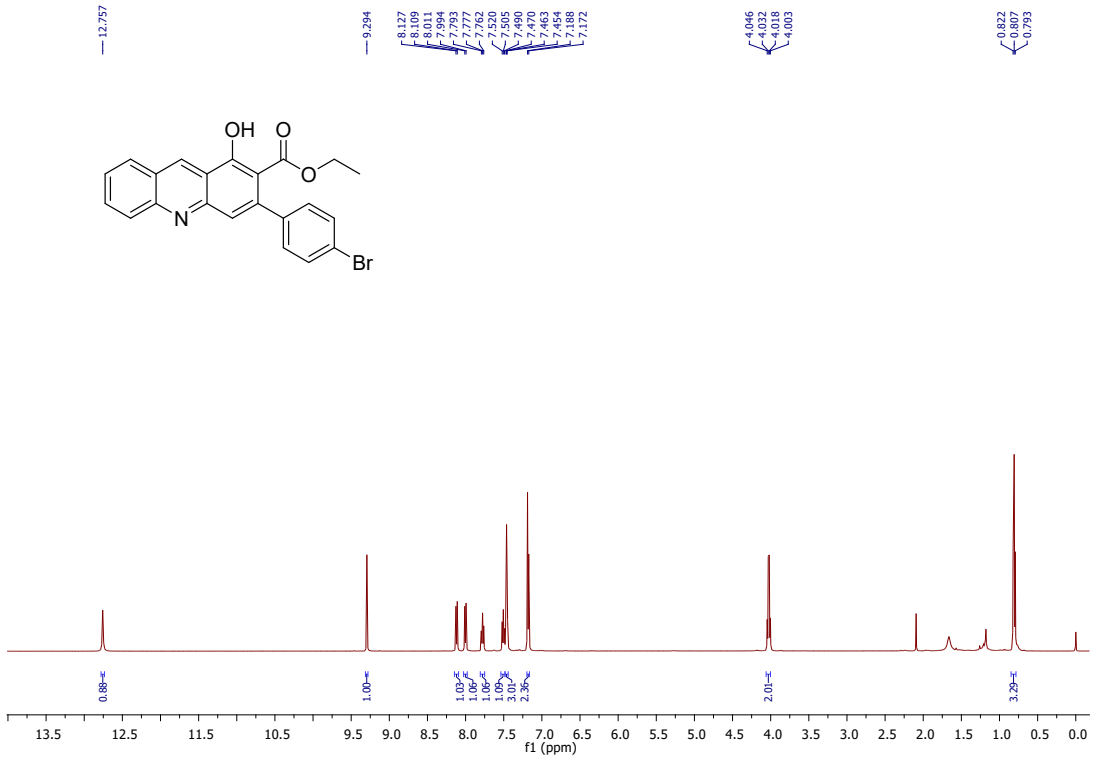
^{1}H NMR (500 MHz) of compound **5p** in $CDCl_3$



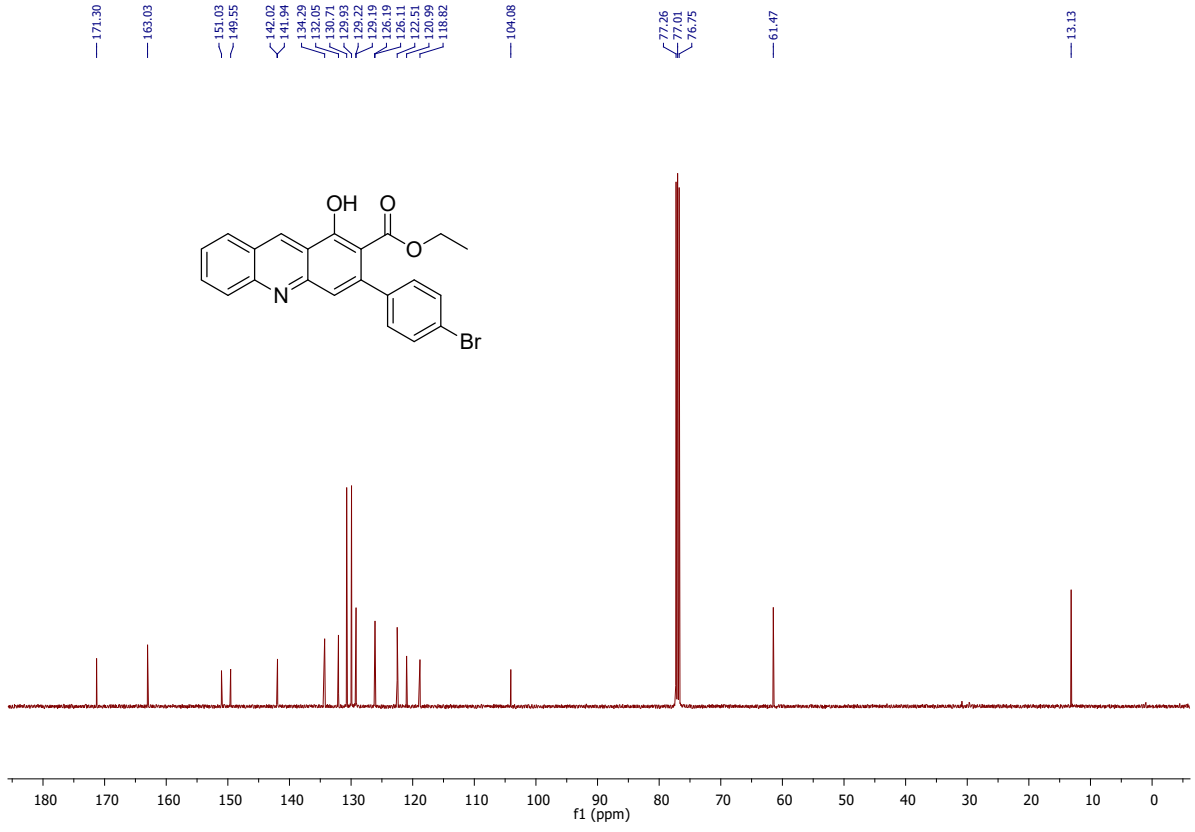
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5p** in $CDCl_3$



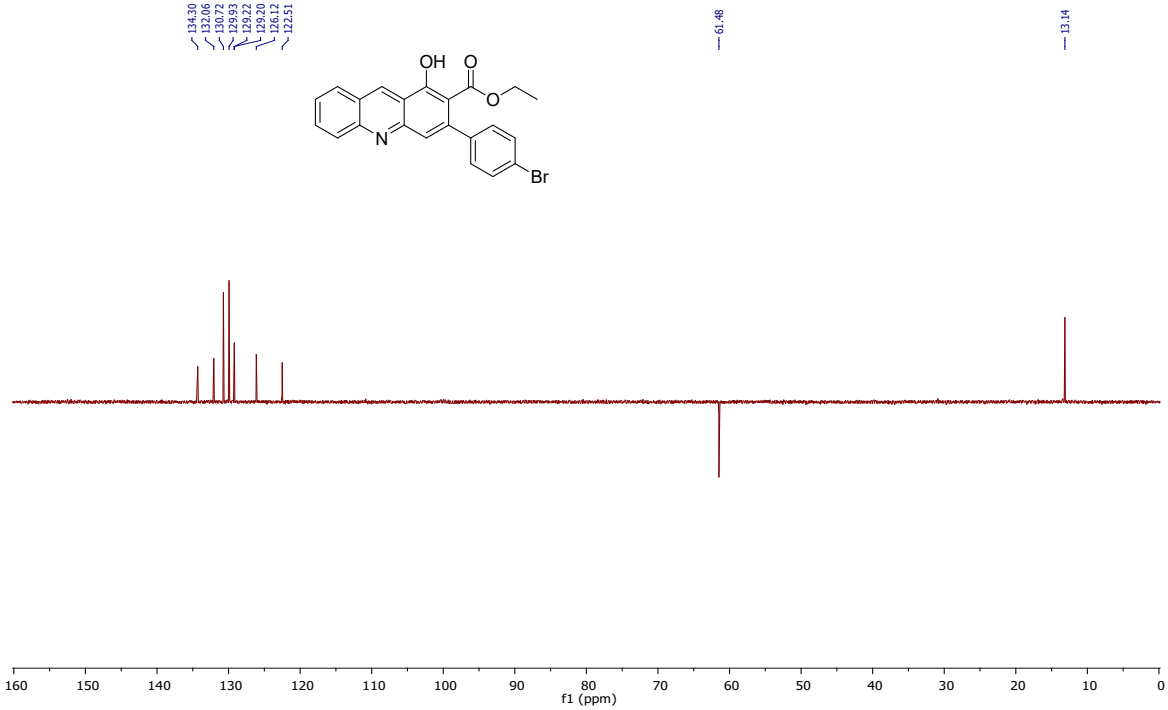
^{1}H NMR (500 MHz) of compound **5q** in $CDCl_3$



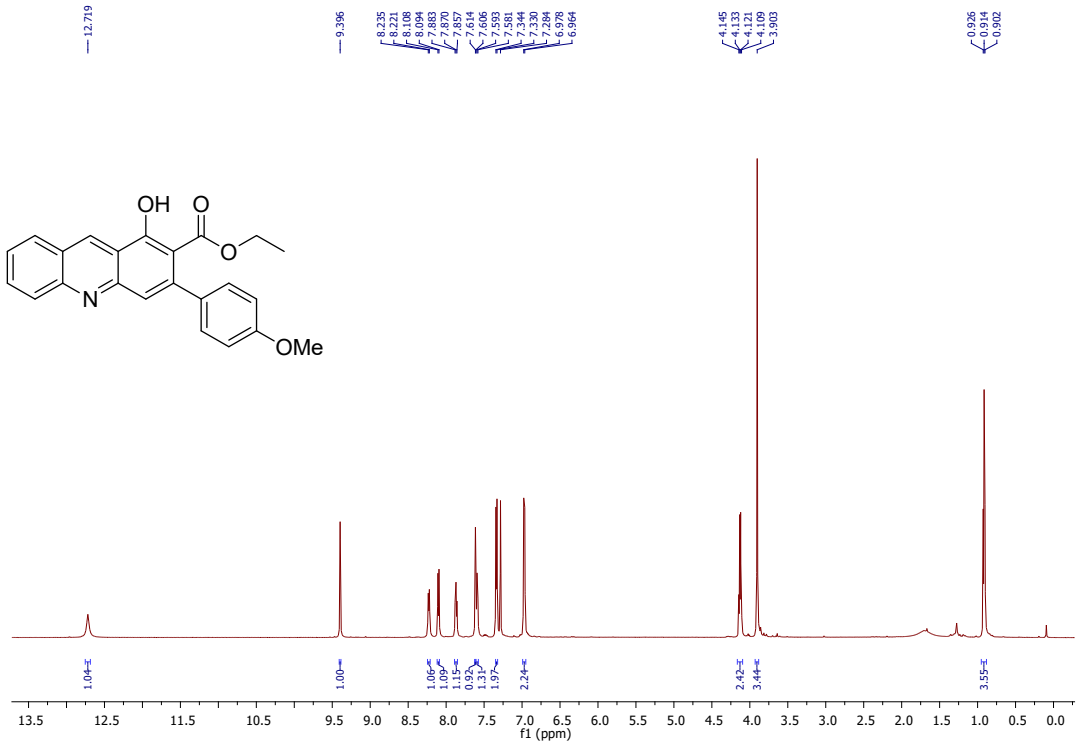
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5q** in $CDCl_3$



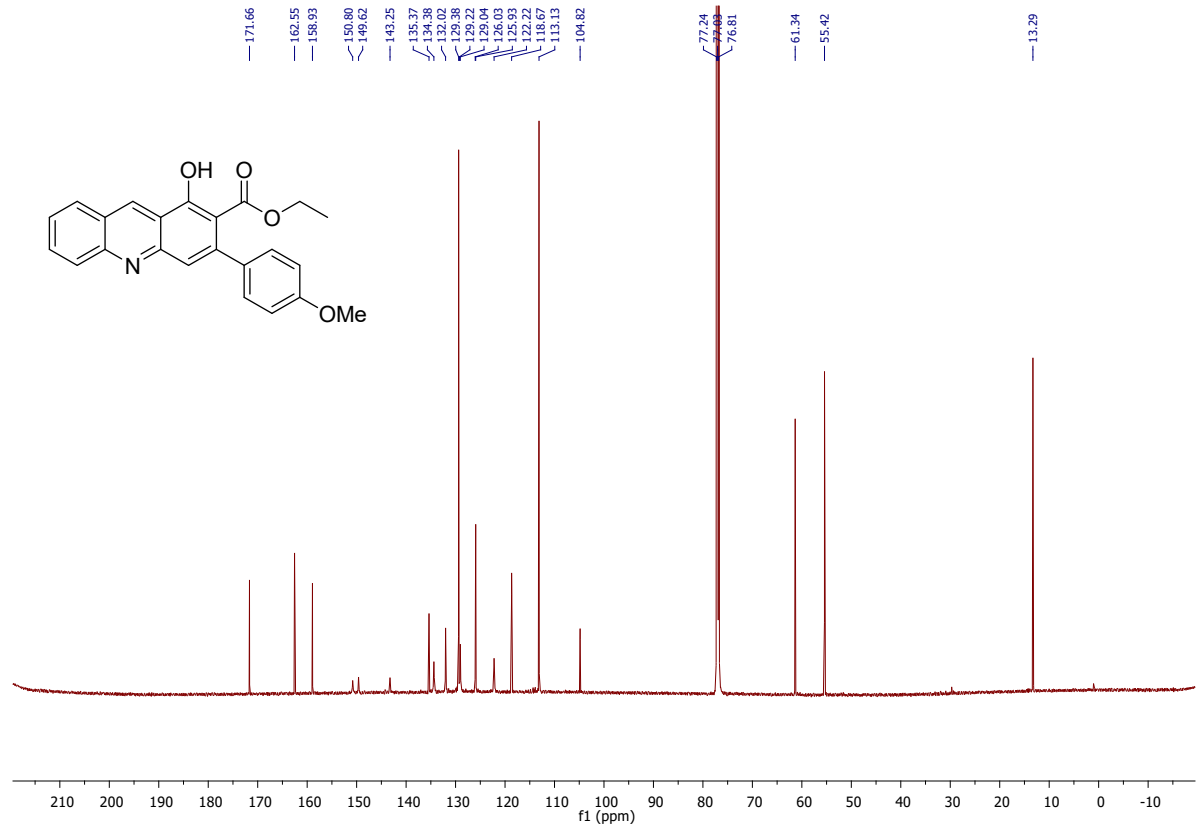
DEPT NMR (125 MHz) of compound **5q** in $CDCl_3$



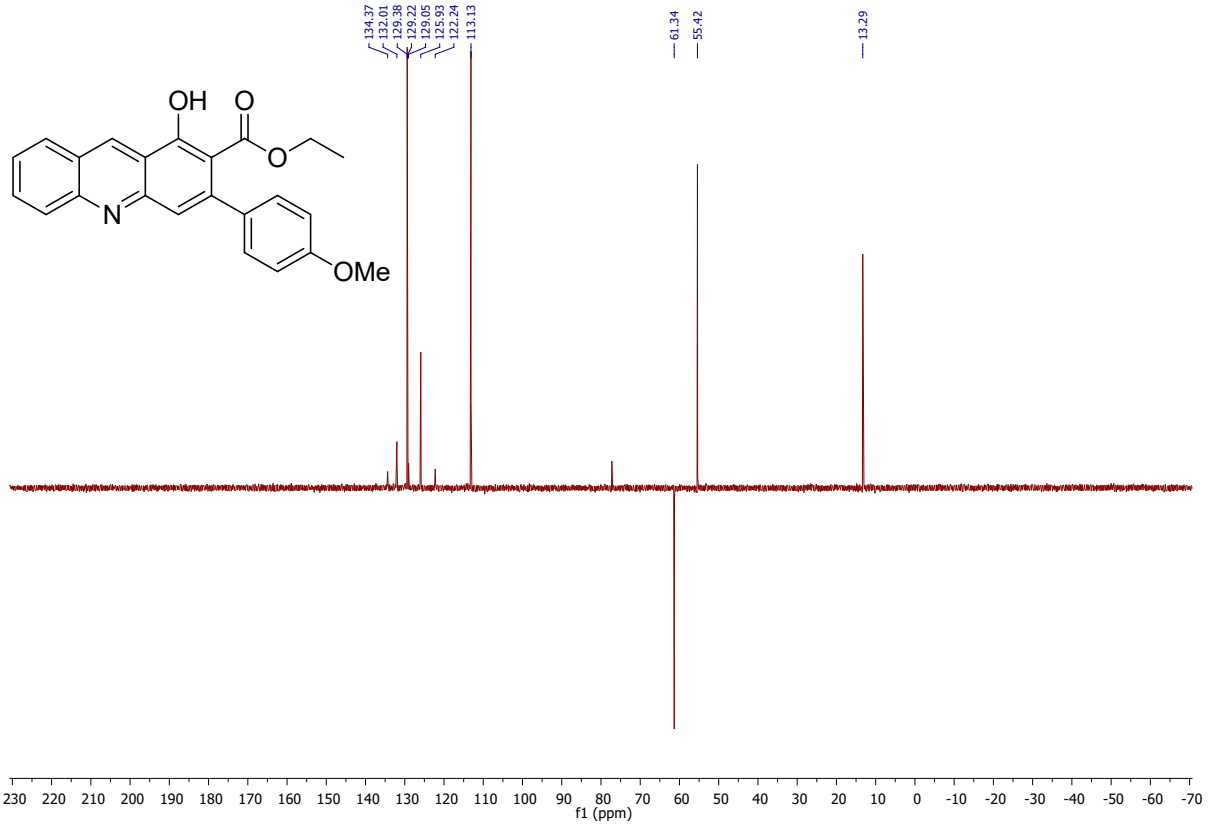
^{1}H NMR (600 MHz) of compound **5r** in $CDCl_3$



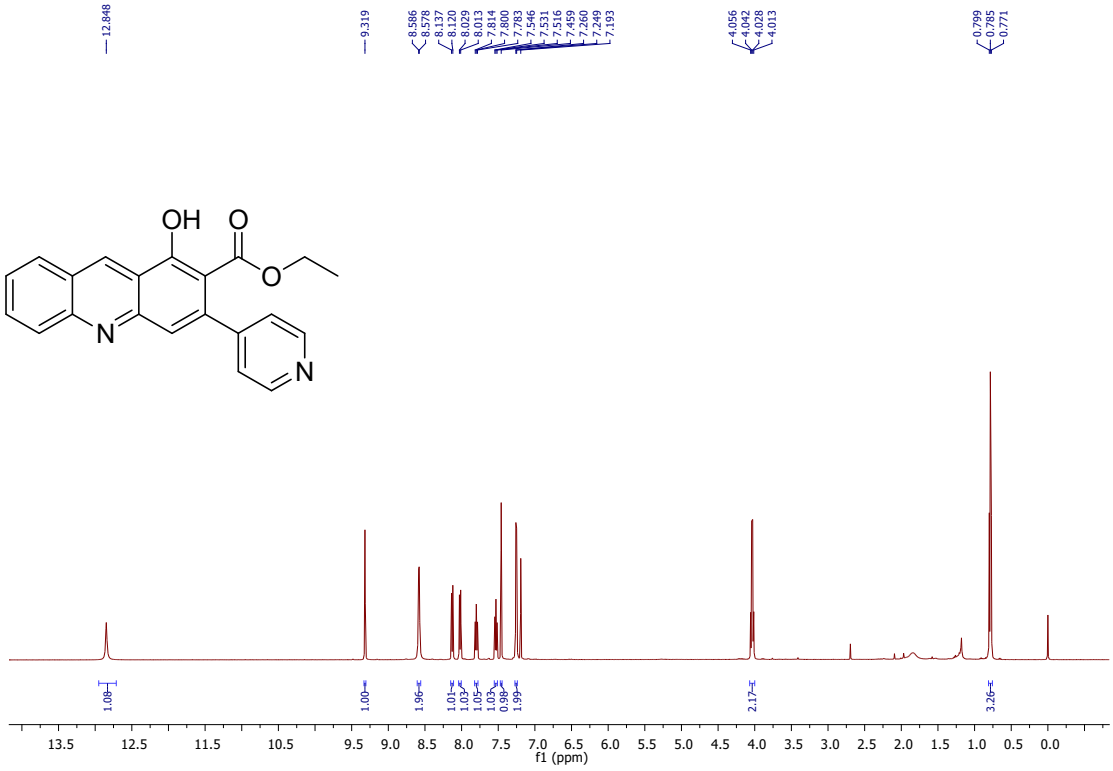
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5r** in $CDCl_3$



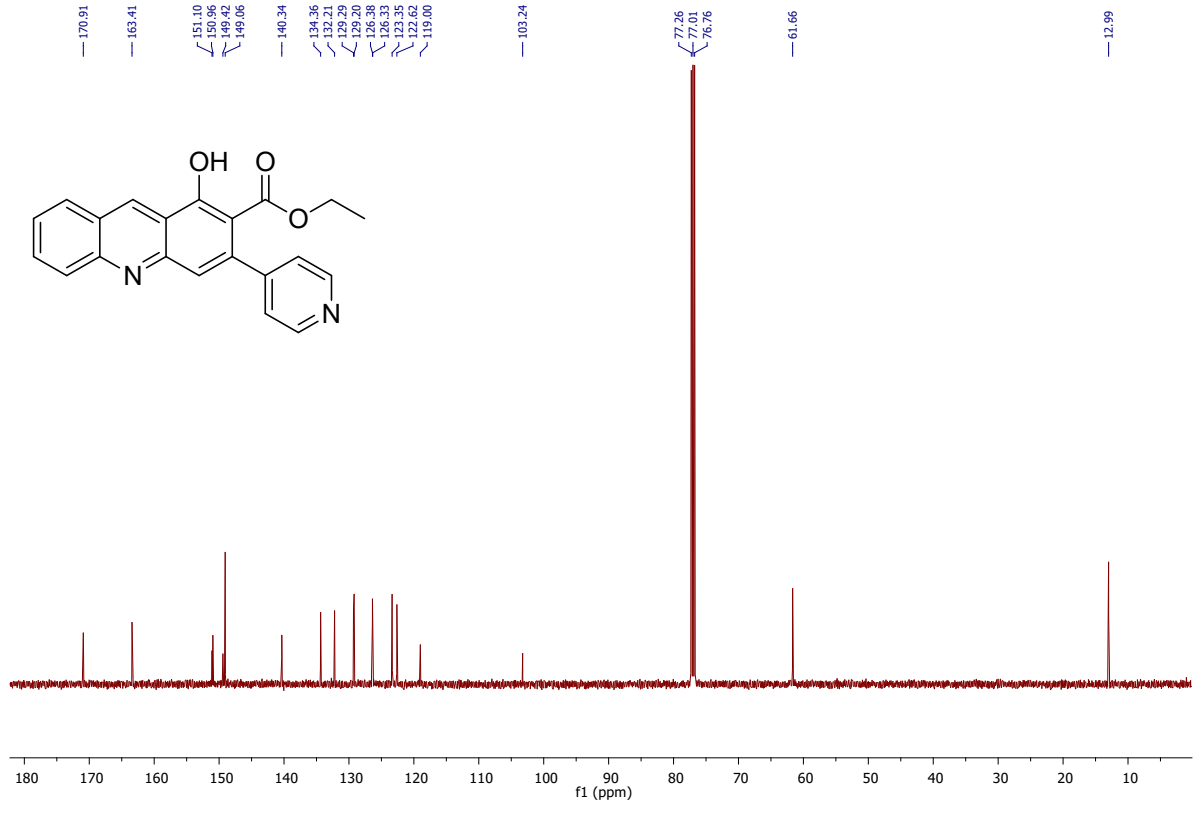
DEPT (150 MHz) of compound **5r** in $CDCl_3$



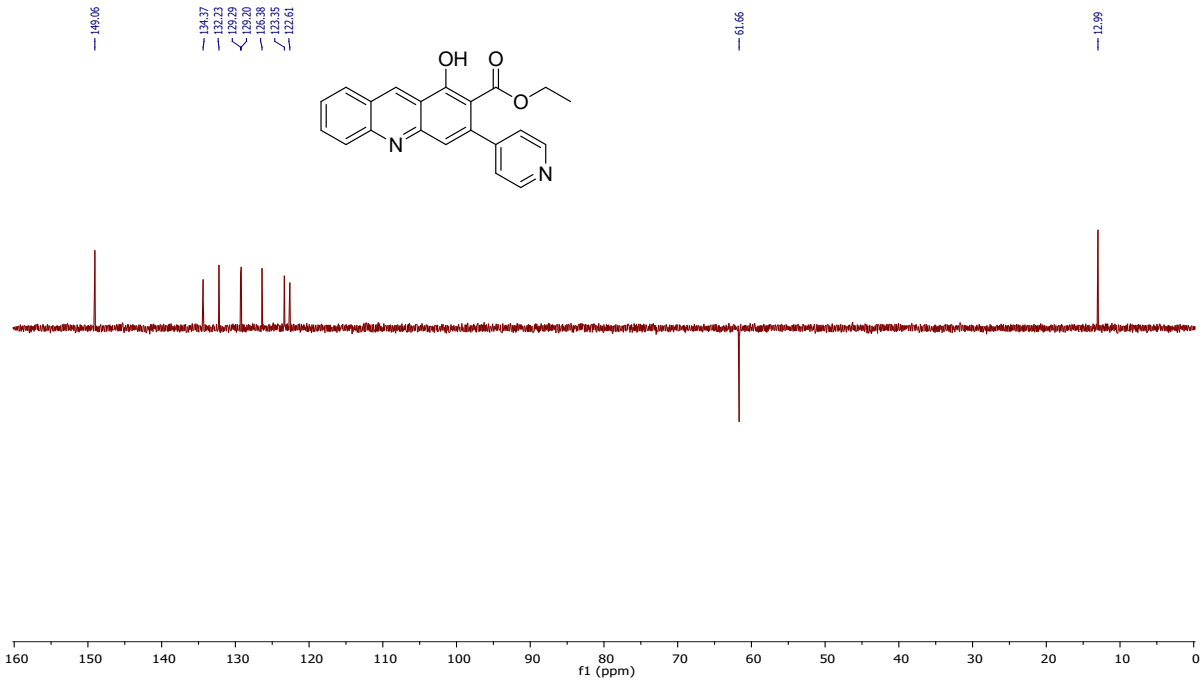
^{1}H NMR (500 MHz) of compound **5s** in $CDCl_3$



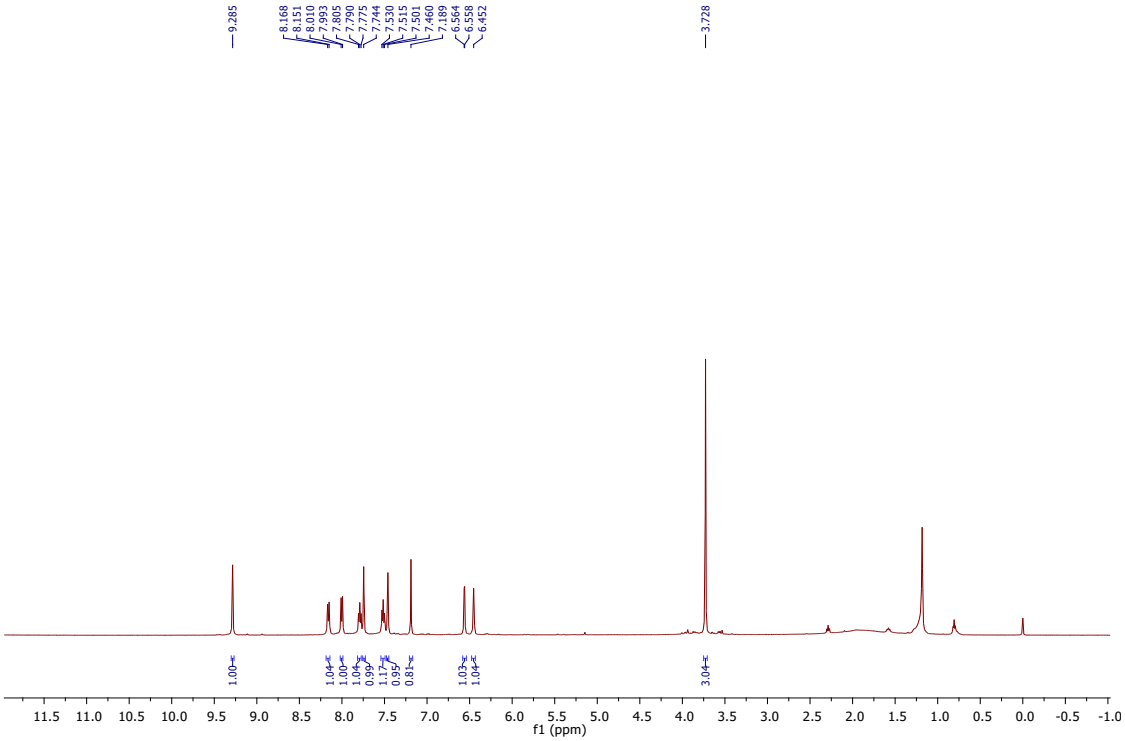
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5s** in $CDCl_3$



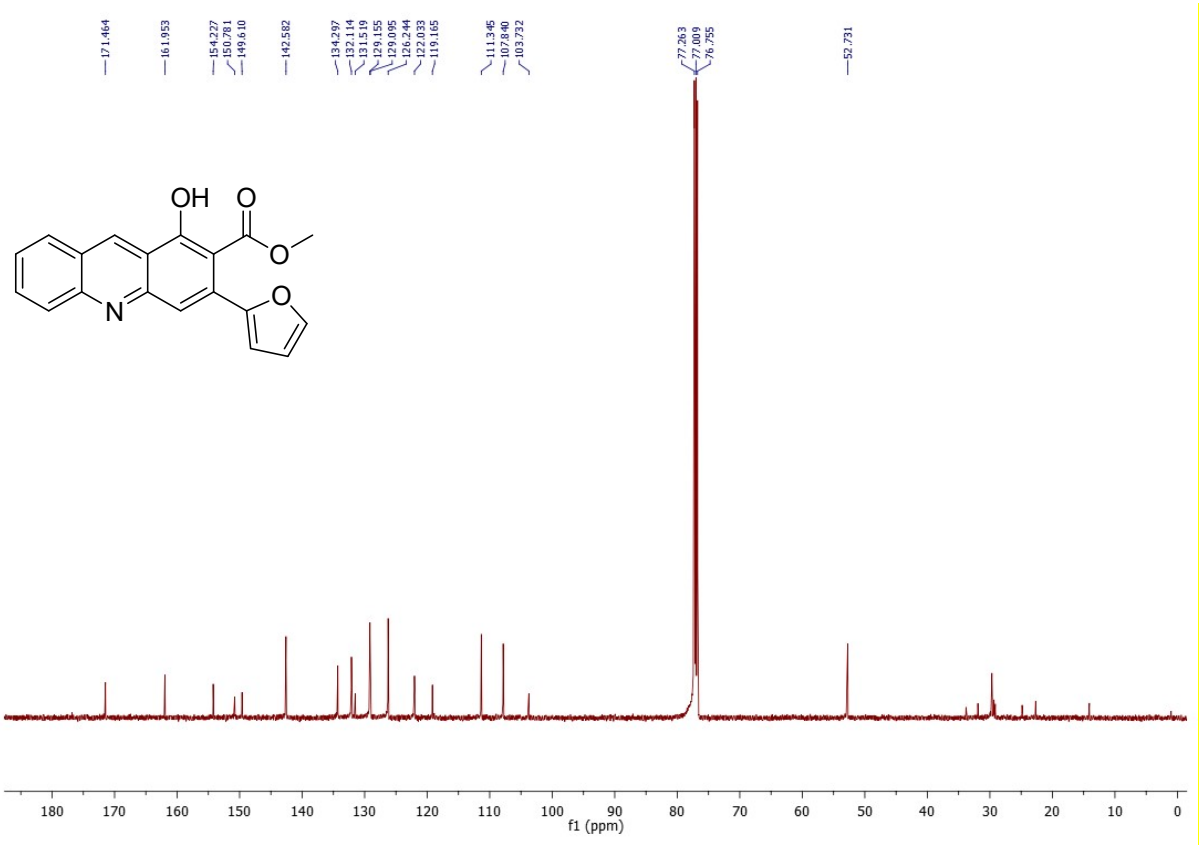
DEPT NMR (125 MHz) of compound **5s** in $CDCl_3$



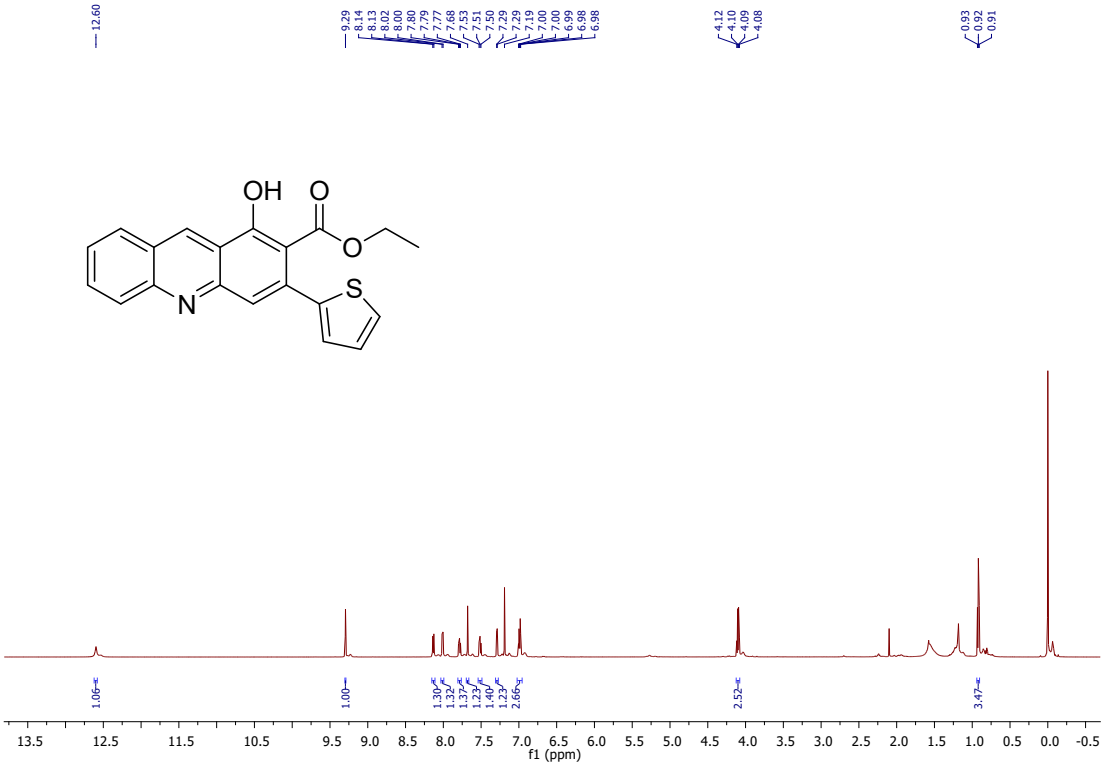
^{1}H NMR (500 MHz) of compound **5t** in $CDCl_3$



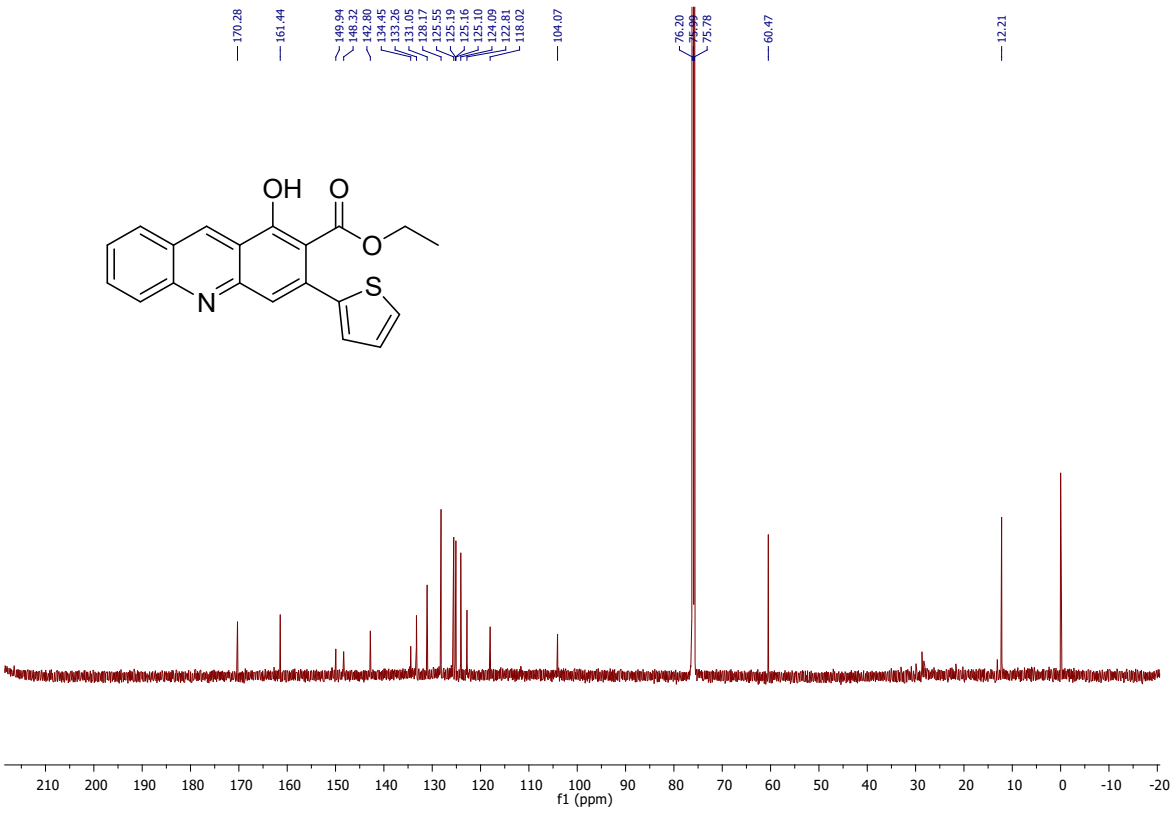
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5t** in $CDCl_3$



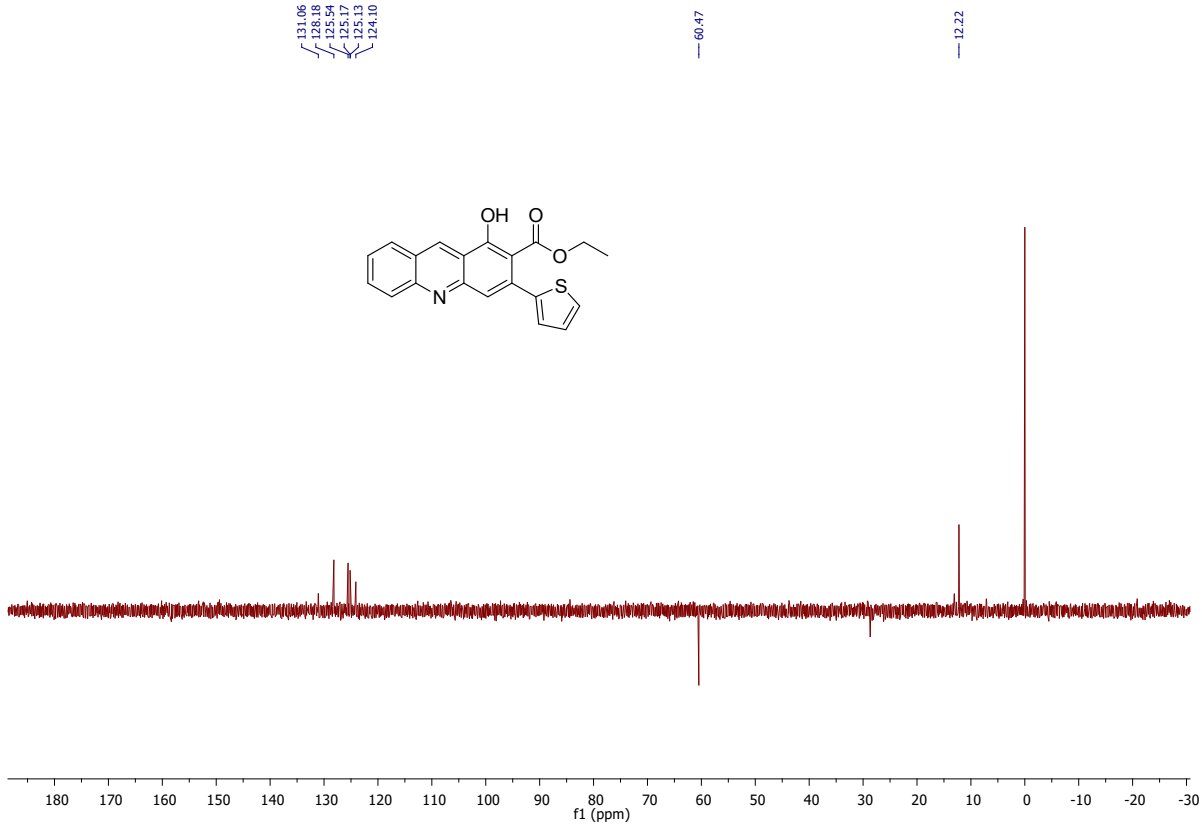
^{1}H NMR (500 MHz) of compound **5u** in $CDCl_3$



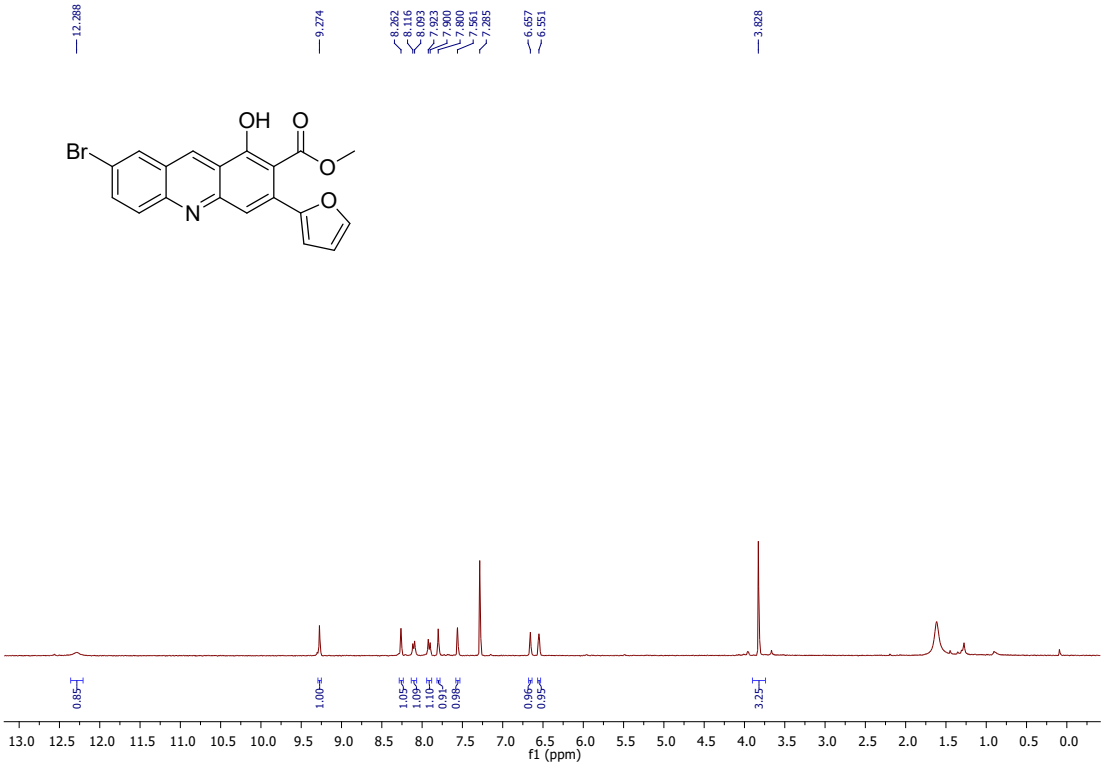
^{13}C NMR {^{1}**H**} (125 MHz) of compound **5u** in $CDCl_3$



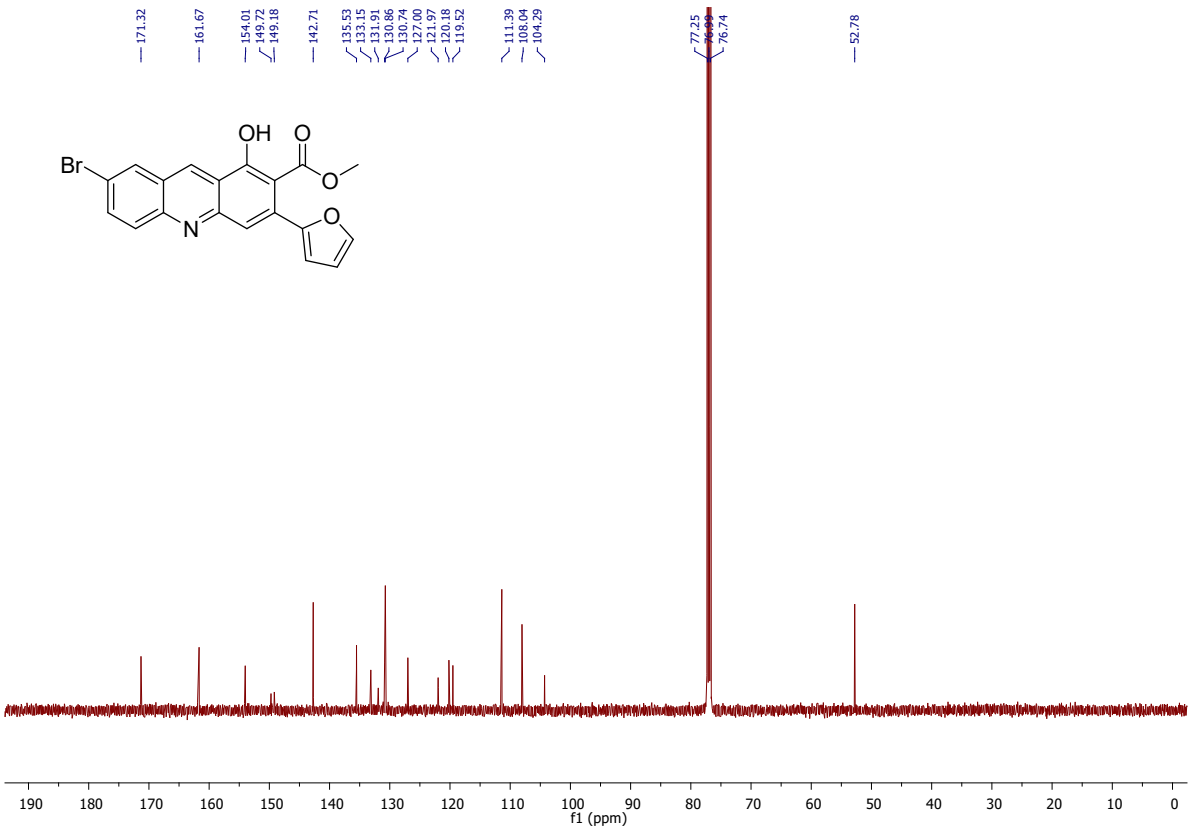
DEPT NMR (125 MHz) of compound **5u** in $CDCl_3$



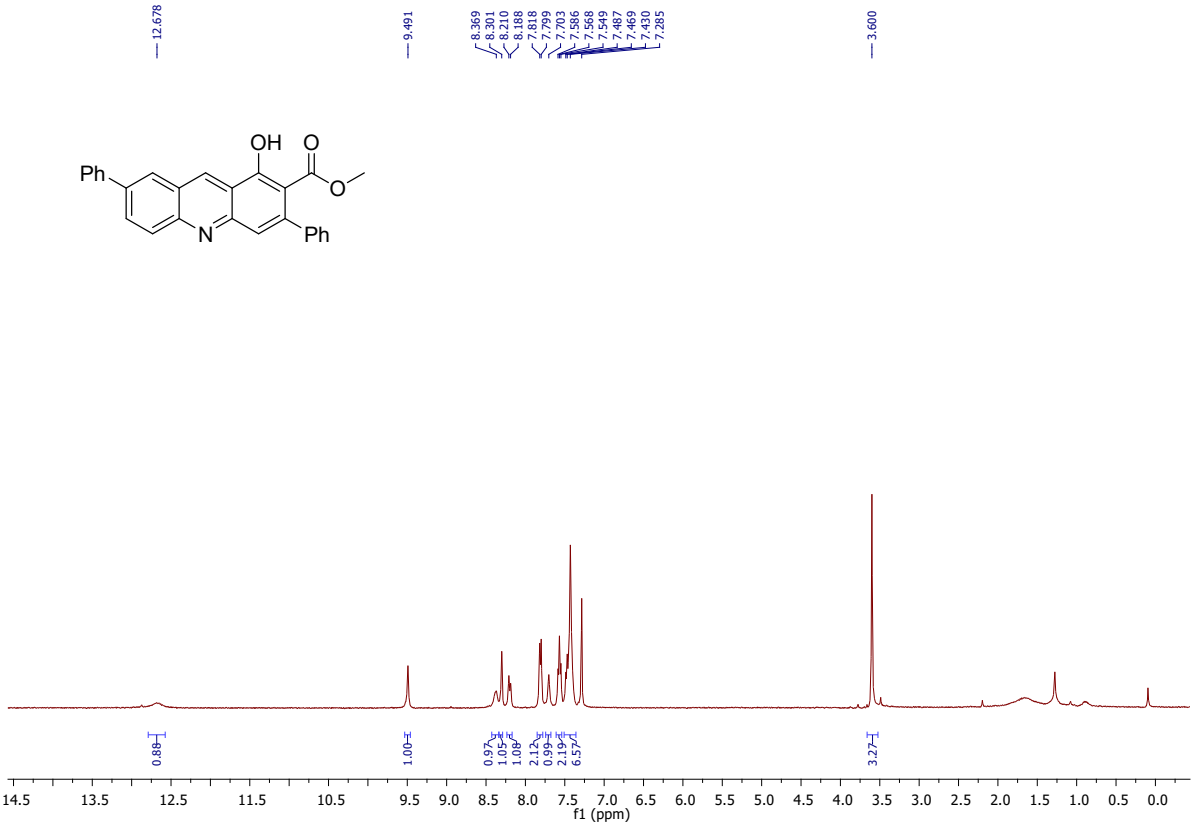
^{1}H NMR (500 MHz) of compound **5v** in $CDCl_3$



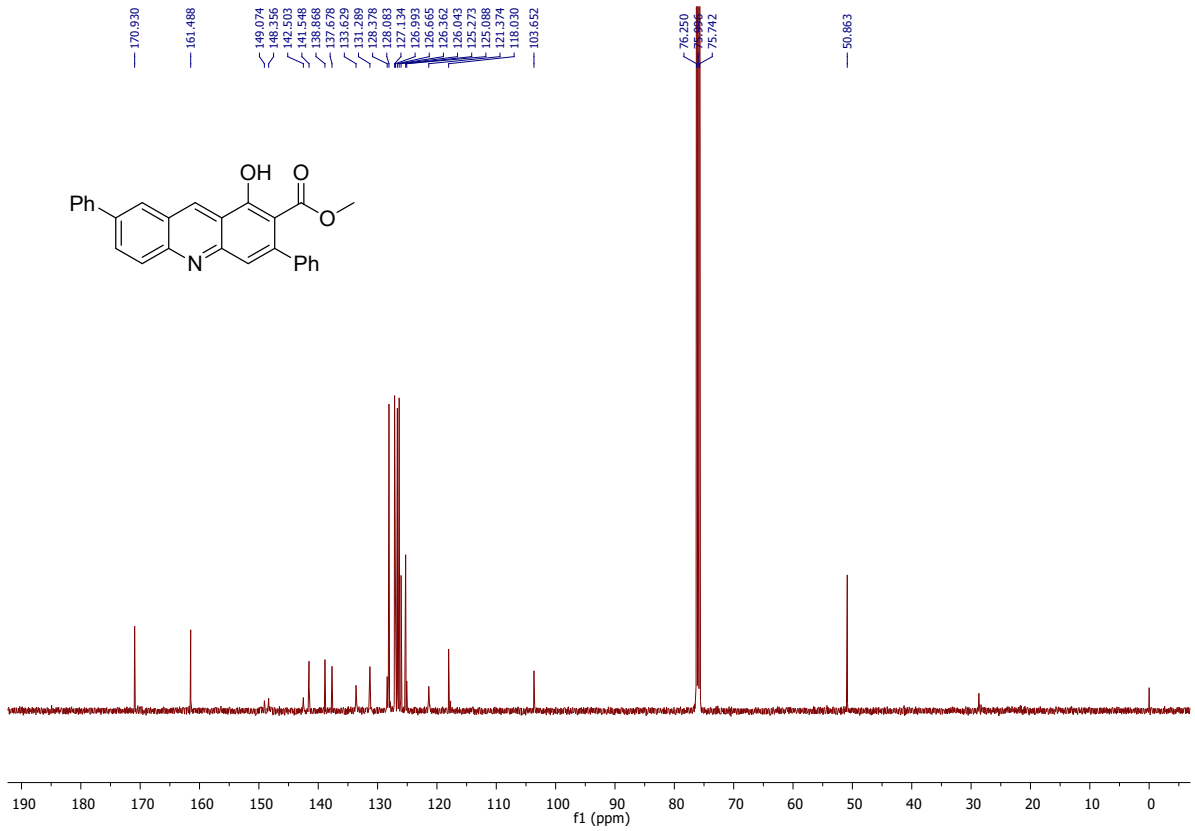
^{13}C NMR **{^{1}H}** (125 MHz) of compound **5v** in $CDCl_3$



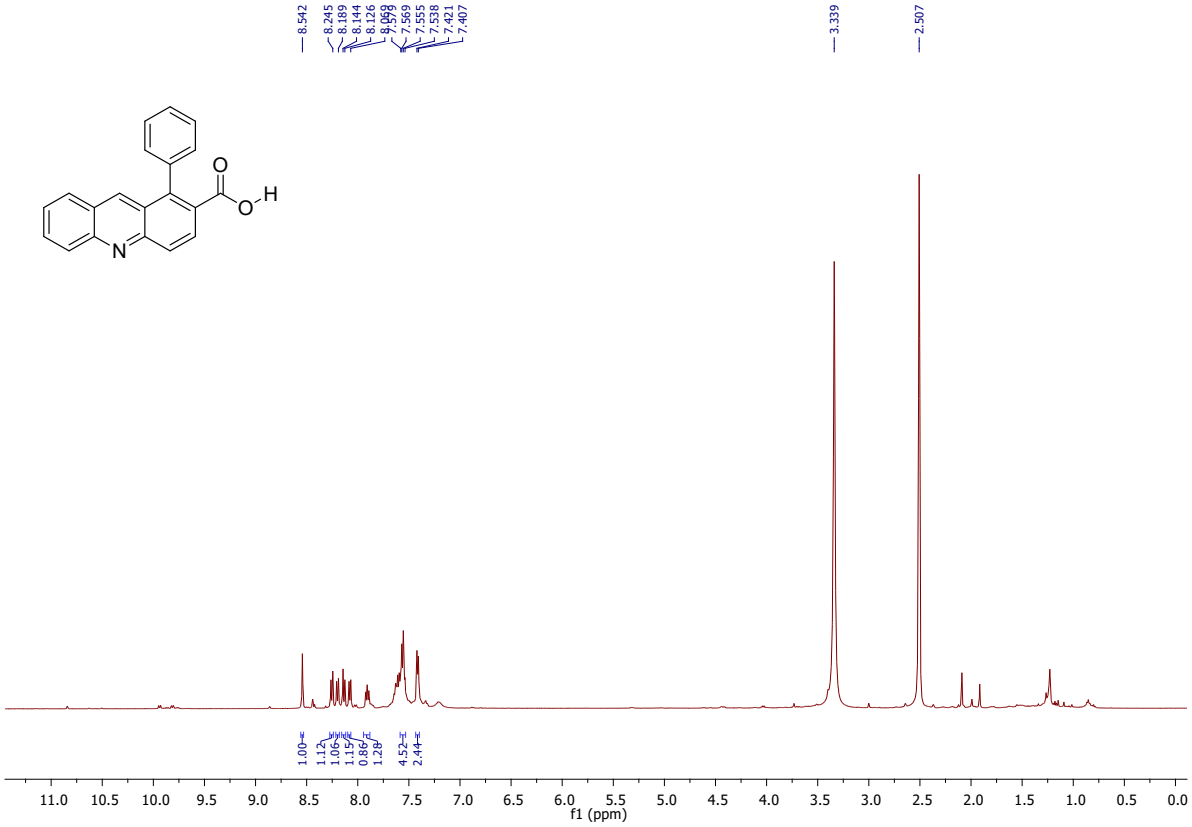
^{1}H NMR (500 MHz) of compound **8a** in $CDCl_3$



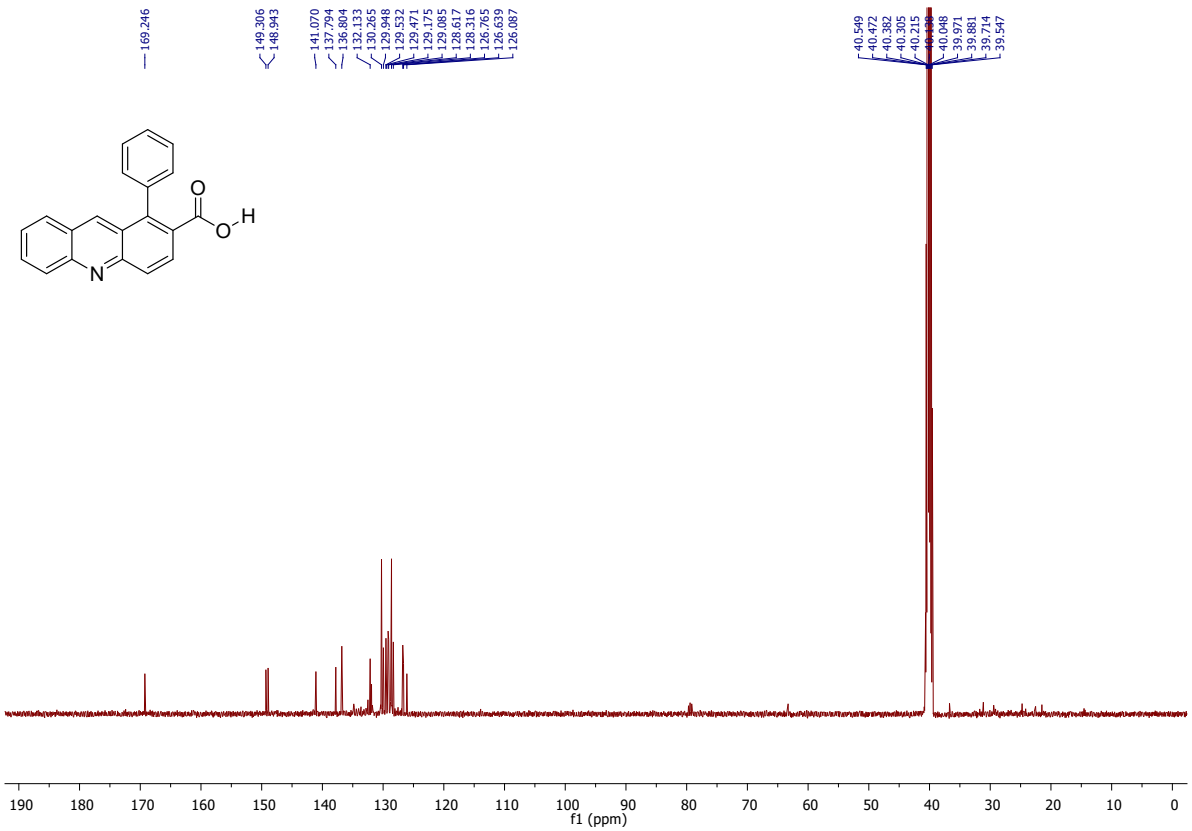
^{13}C NMR **{^{1}H}** (125 MHz) of compound **8a** in $CDCl_3$



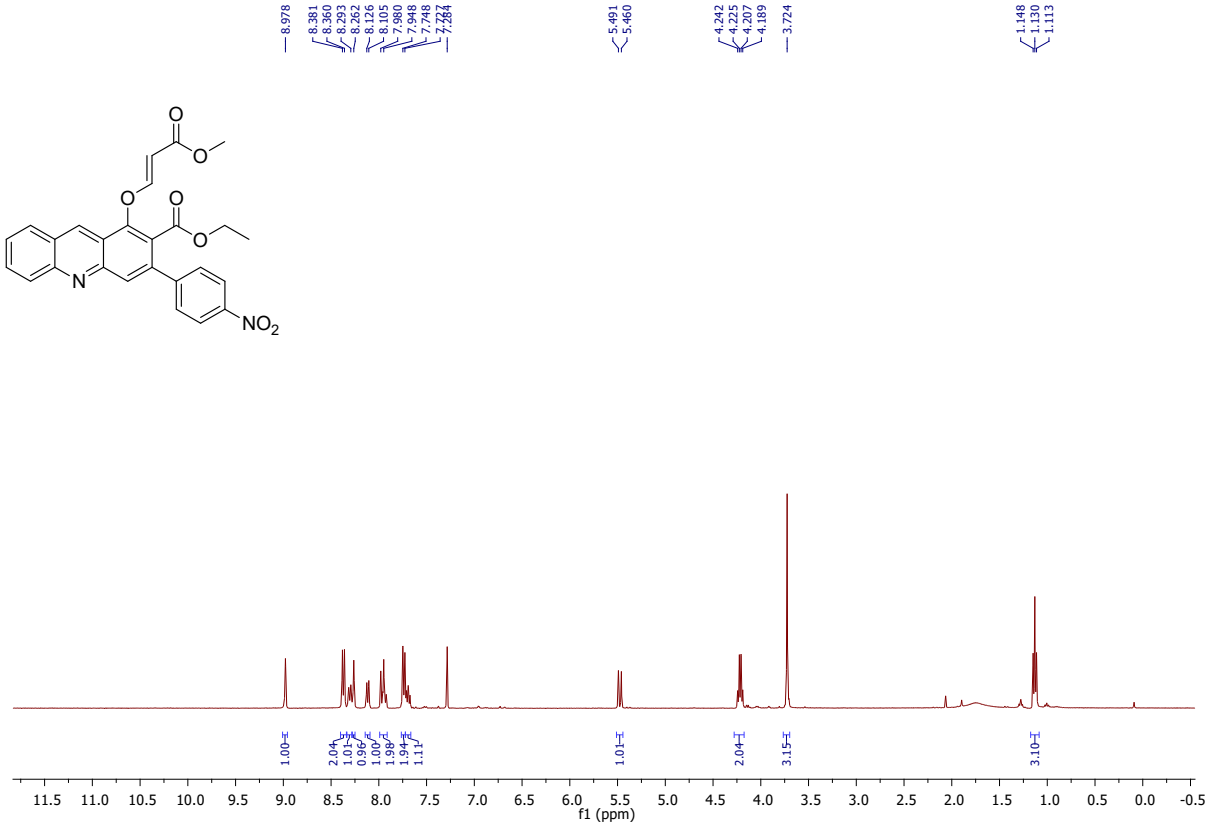
^{1}H NMR (500 MHz) of compound **8b in** DMSO-d_6



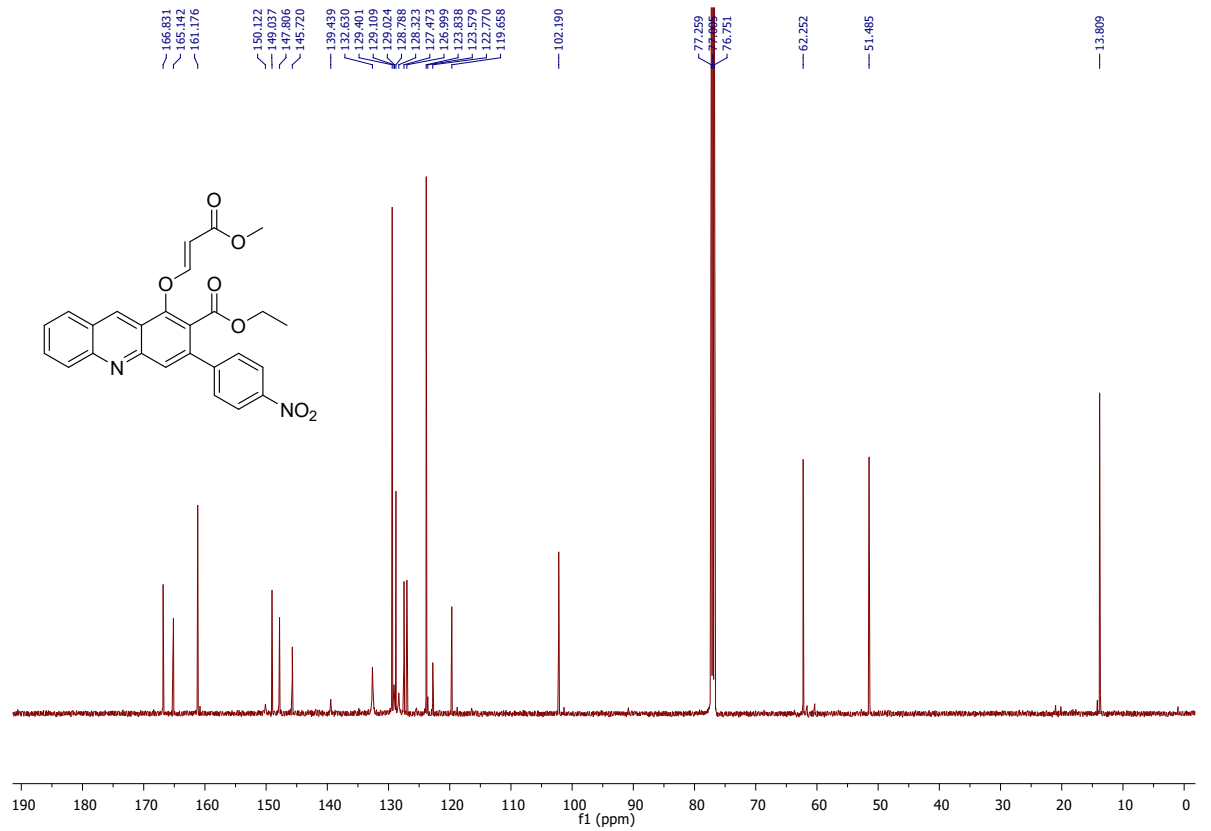
^{13}C NMR **{^{1}H}** (125 MHz) of compound **8b** in DMSO-d_6



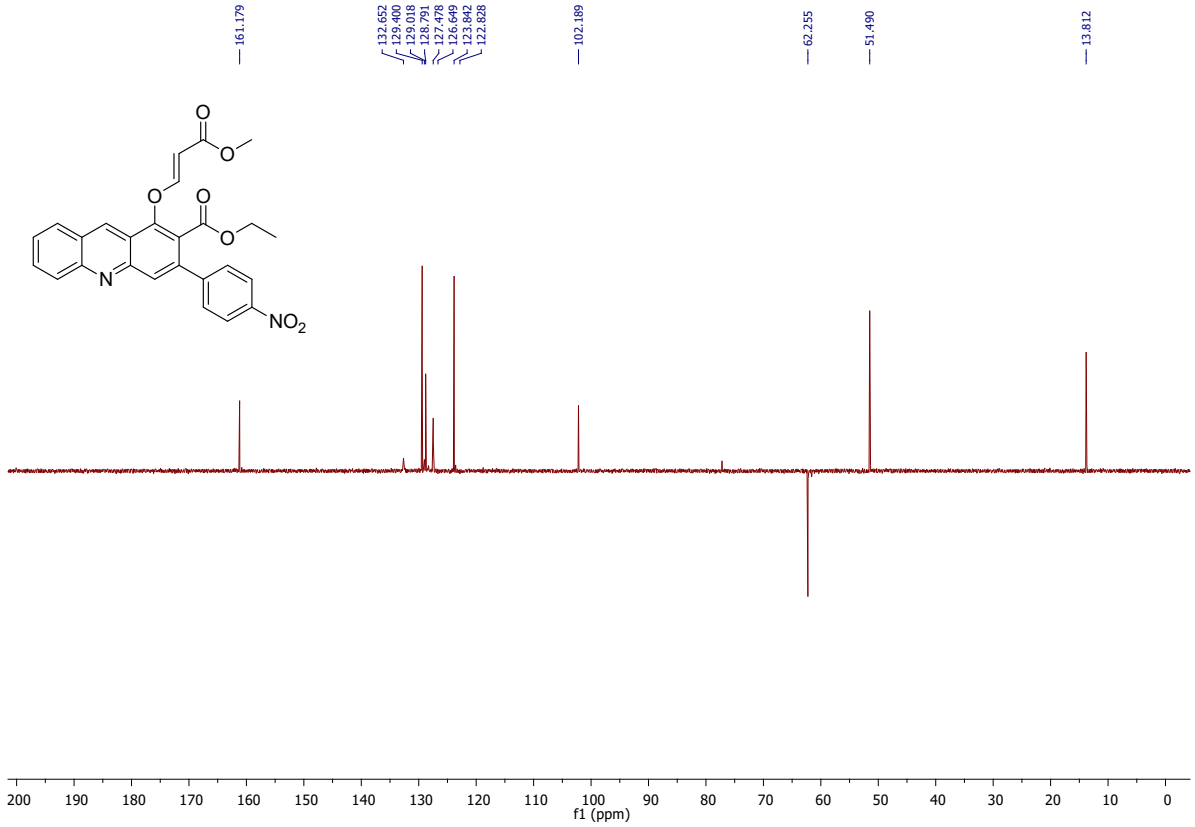
^{1}H NMR (400 MHz) of compound **8c** in $CDCl_3$



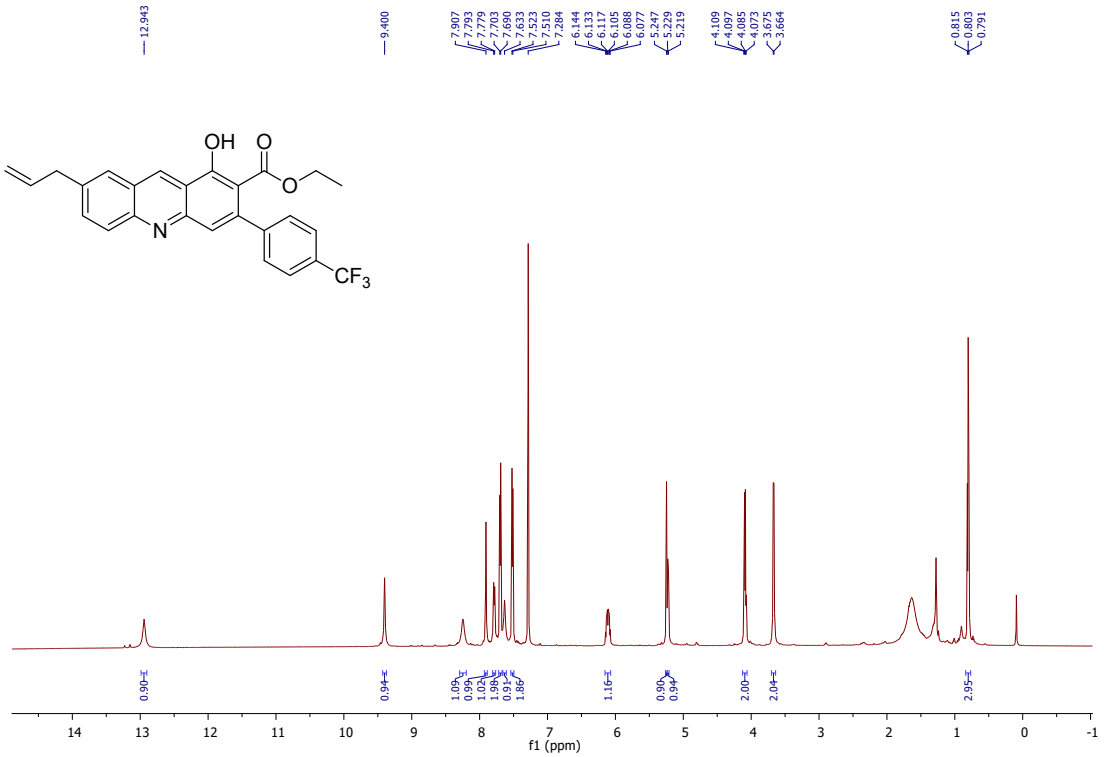
^{13}C NMR **{^{1}H}** (125 MHz) of compound **8c** in $CDCl_3$



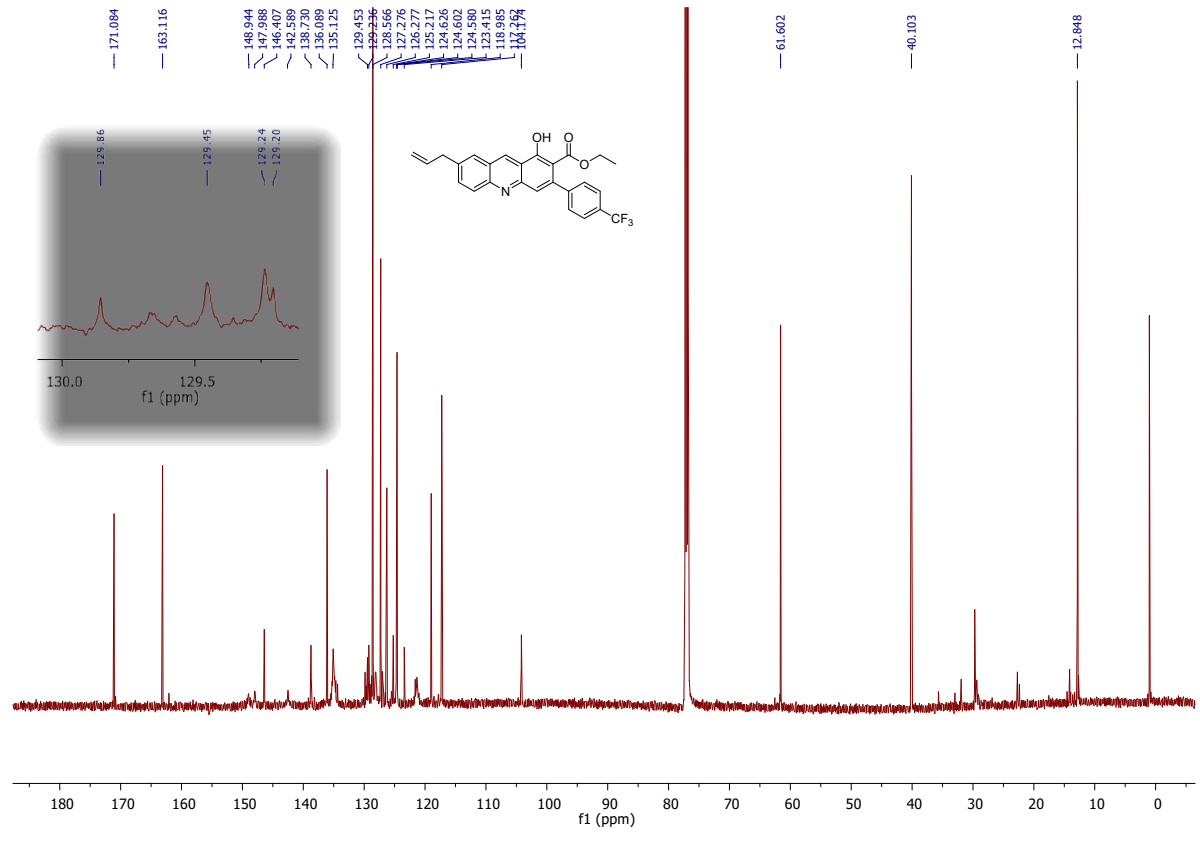
DEPT NMR (125 MHz) of compound **8c** in $CDCl_3$



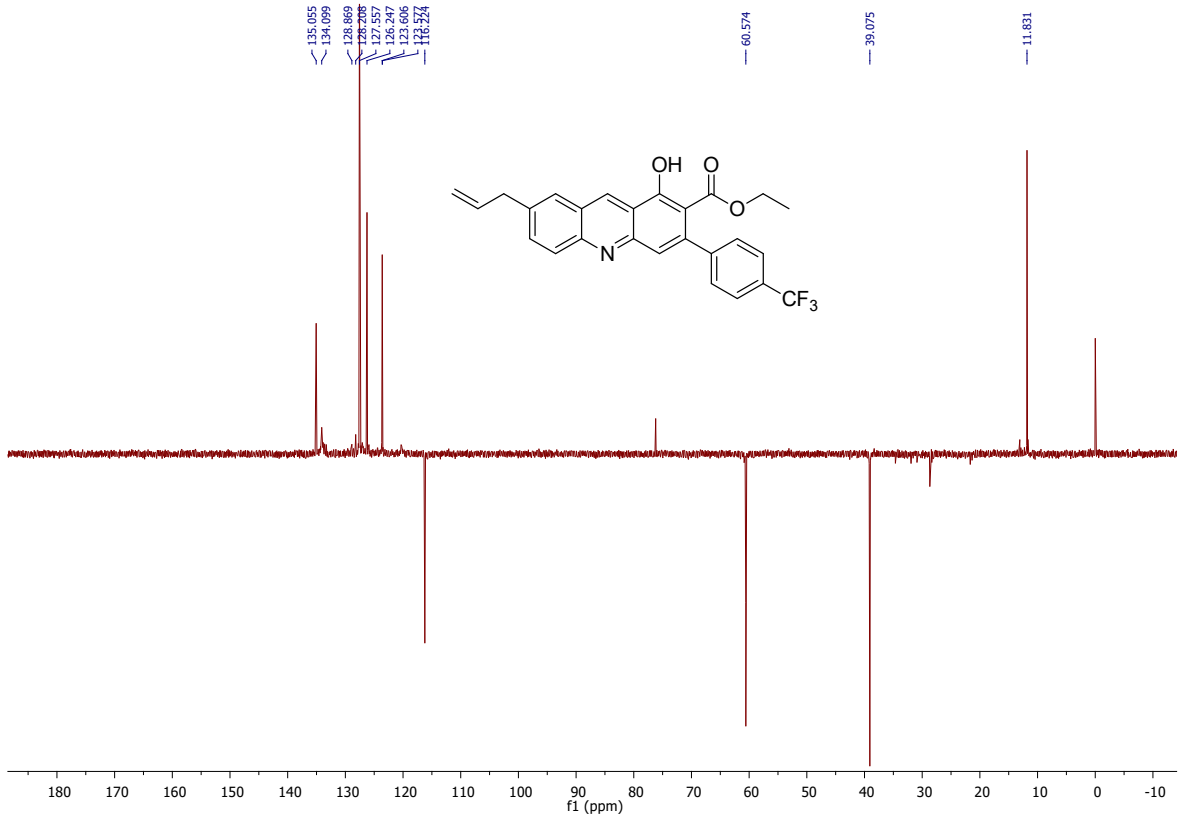
^{1}H NMR (600 MHz) of compound **8d** in $CDCl_3$



^{13}C NMR {^{1}**H**} (150 MHz) of compound **8d** in $CDCl_3$

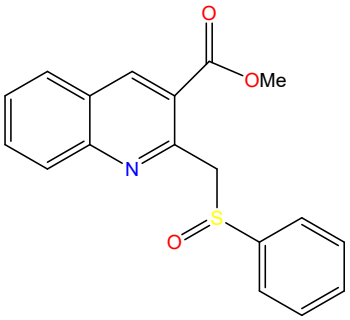


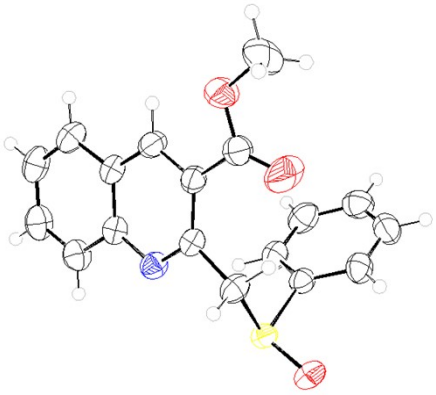
DEPT NMR (125 MHz) of compound **8d** in $CDCl_3$



Crystal data and structure refinement for compound 3a.

X-ray crystal data of compound **3a** (the following crystal has been deposited at the Cambridge Crystallographic Data Centre and has the deposition number CCDC 2248017).





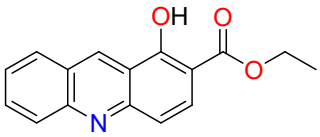
ORTEP presentation (drawn at 50% probability)

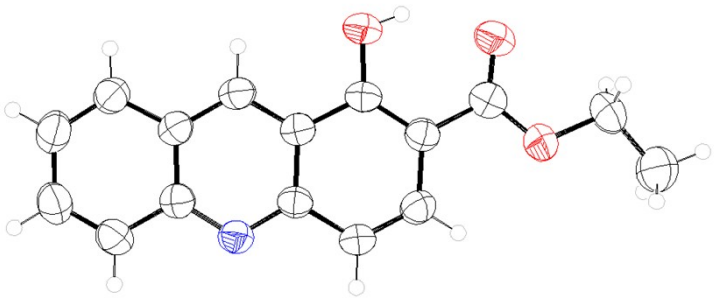
Empirical formula	$C_{17}H_{13}NO_3S$
Formula weight	311.36
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 10.5598(5) Å α = 90 °
	b = 10.2814(4)Å β = 108.9780(10)
	c = 15.2307(6)Å γ = 90 °
Volume	1563.71(11)Å^3
Z, Calculated density	4, 1.382 Mg/m^3
Absorption coefficient	0.221 mm^{-1}
F(000)	680
Crystal size	0.25 x 0.20 x 0.20 mm^3
Theta range for data collection	2.43 to 27.09 °
Reflections collected/independent/observed [I > 2σ(I)]	59766/3445/2996
No. of variables	209
Goodness-of-fit on F^2	1.087
Final R indices [I>2sigma(I)][a]	R1 = 0. 0370, wR2 = 0.1003
R indices (all data)[a]	R1 = 0. 0443, wR2 = 0.1084

[a]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]$

Crystal data and structure refinement for compound 5b

X-ray crystal data of compound **5b** (the following crystal has been deposited at the Cambridge Crystallographic Data Centre and has the deposition number CCDC 2248019)





O

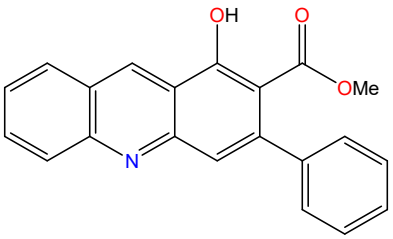
RTEP presentation (drawn at 50% probability)

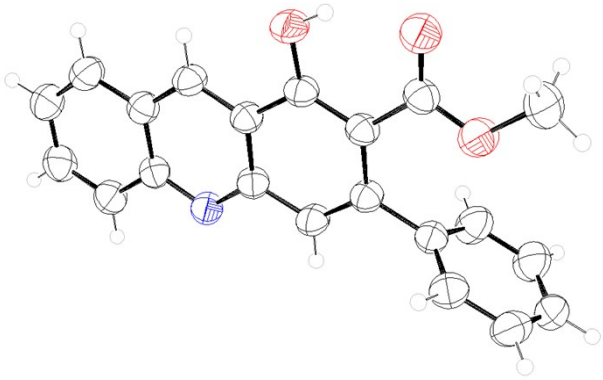
Empirical formula	$C_{16}H_{13}NO_3$
Formula weight	267.27
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.110(2) Å α = 82.026(13)°
	b = 7.857(3) Å β = 79.905(13)°
	c = 11.773(4) Å γ = 85.894(13)°
Volume	640.5(4) $Å^3$
Z, Calculated density	2, 1.386 Mg/m^3
Absorption coefficient	0.097mm^{-1}
F(000)	280
Crystal size	0.30 x 0.20 x 0.20 mm^3
Theta range for data collection	2.62 to 33.09°
Reflections collected/independent/observed [I > 2σ(I)]	12012/3997/1643
No. of variables	183
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)][a]	R1 = 0.0652, wR2 = 0.1617
R indices (all data)[a]	R1 = 0.1764, wR2 = 0.2081

[a]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]$

Crystal data and structure refinement for compound 5e

X-ray crystal data of compound **5e** (the following crystal has been deposited at the Cambridge Crystallographic Data Centre and has the deposition number CCDC 2248020).





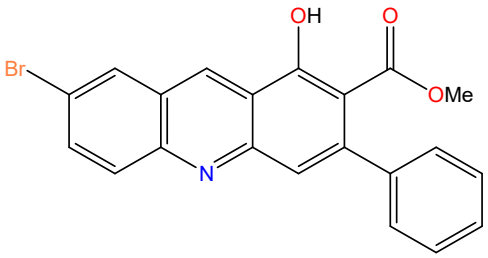
ORTEP presentation (drawn at 50% probability)

Empirical formula	$C_{21}H_{15}NO_3$
Formula weight	329.34
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 6.384(4) Å α = 75.635(12)°
	b = 11.473(5) Å β = 88.166(16)°
	c = 11.661(6) Å γ = 74.104(13)°
Volume	795.2(7) $Å^3$
Z, Calculated density	2, 1.375 Mg/m^3
Absorption coefficient	0.093 mm^{-1}
F(000)	344
Crystal size	0.30 x 0.20 x 0.20 mm^3
Theta range for data collection	3.32 to 27.89°
Reflections collected/independent/observed [I > 2σ(I)]	46112/3797/2883
No. of variables	228
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)][a]	R1 = 0.0509, wR2 = 0.1452
R indices (all data)[a]	R1 = 0.0681, wR2 = 0.1628

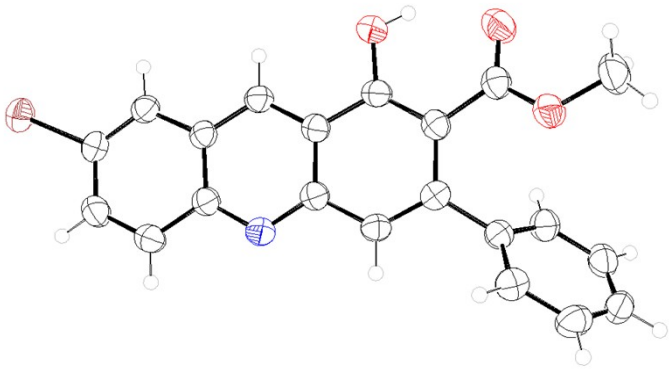
[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]$

Crystal data and structure refinement for compound 5k

X-ray crystal data of compound **5k** (the following crystal has been deposited at the Cambridge Crystallographic Data Centre and has the deposition number CCDC 2248021)



ORTEP presentation (drawn at 50% probability)

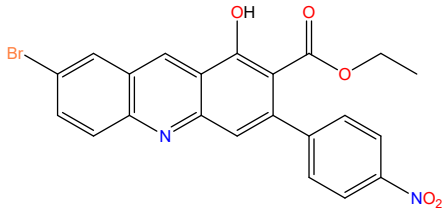


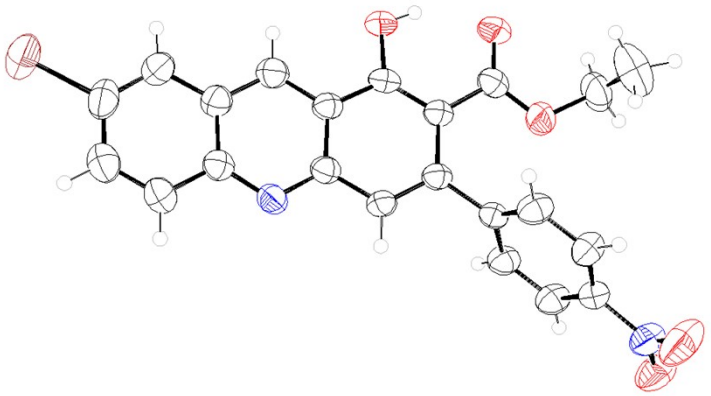
Empirical formula	$C_{21}H_{14}BrNO_3$
Formula weight	408.24
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 5.315(2) Å α = 90.03(3)°
	b = 14.209(3) Å β = 91.78(3)°
	c = 22.732(5) Å γ = 90.00(3)°
Volume	1716.0(8) $Å^3$
Z, Calculated density	1, 1.580 Mg/m^3
Absorption coefficient	2.417 mm^{-1}
F(000)	824
Crystal size	0.30 x 0.20 x 0.20 mm^3
Theta range for data collection	2.29 to 27.93°
Reflections collected/independent/observed [I > 2σ(I)]	28932/3785/2913
No. of variables	237
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)][a]	R1 = 0.0386, wR2 = 0.0752
R indices (all data)[a]	R1 = 0.0579, wR2 = 0.0816

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]$

Crystal data and structure refinement for compound 5n

X-ray crystal data of compound **5n** (the following crystal has been deposited at the Cambridge Crystallographic Data Centre and has the deposition number CCDC 2248018)





ORTEP presentation (drawn at 50% probability)

Empirical formula	$C_{22}H_{15}BrNO_5$
Formula weight	467.27
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 8.0568(9) Å α = 90.00°
	b = 10.5478(11) Å β = 90.00°
	c = 23.068(3) Å γ = 90.00°
Volume	1960.4(4)Å^3
Z, Calculated density	5, 1.583Mg/m^3
Absorption coefficient	2.135 mm^{-1}
F(000)	944
Crystal size	0.20 x 0.20 x 0.15 mm^3
Theta range for data collection	2.12 to 26.84°
Reflections collected/independent/observed [I > 2σ(I)]	41669/4204/3235
No. of variables	273
Goodness-of-fit on F^2	1.044
Final R indices [I>2sigma(I)][a]	R1 = 0.0604, wR2 = 0.1451
R indices (all data)[a]	R1 = 0.0824, wR2 = 0.1592

[a]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]$