Silver catalyzed cascade cyclization of 2-(allyloxy)arylaldehydes: synthesis of chroman-4-one derivatives

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Supporting Information

Table of Contents

I. General methods and materials........SI-2
II. Synthesis of substrates........SI-2
III. General procedures for the reaction of 2-(allyloxy)benzaldehyde with different alcohols and ketones........SI-2
IV. Additional experiments........SI-2
V. Characterization of the products........SI-3
VI. References........SI-9
VII. NMR Charts........SI-10

I. General methods and materials

All reactions involving air and moisture-sensitive reagents were carried out under an argon atmosphere. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance 400 spectrometer (400 MHz or 600 MHz for ^{1}H NMR, 100 MHz or 150 MHz for ^{13}C NMR) in $CDCl_3$ (with TMS as internal standard). Chemical shifts (δ) were measured in ppm. Coupling constants *J* were reported in hertz. High resolution mass spectra were obtained on a high-resolution mass spectrometer MALDI-TOF. The starting materials were purchased from Energy Chemical or *J* & *K* scientific and used without further purification. Solvents were dried and purified according to the procedure from "*Purification of Laboratory Chemicals book*". The crude products were purified by flash column chromatography on silica gel and the reported yields are the actual isolated yields of pure products.

II. Synthesis of substrates

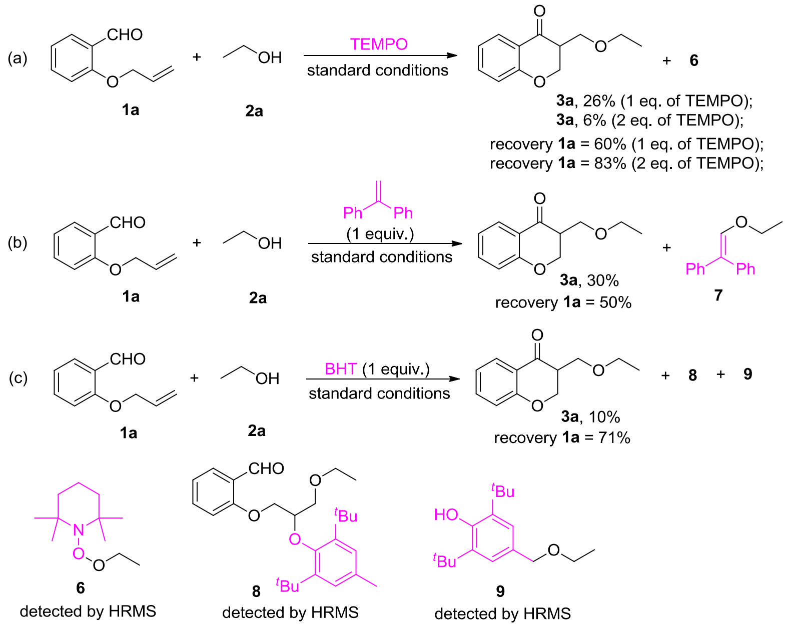
The substrates of various 2-(allyloxy) benzaldehydes in Table 2 (**1a**-**1i**) and Table 3 (**1a**-**1f**) were synthesized according to the procedures described in previous literatures [1]. The different alcohols (**2a**-**2i**) in Table 2 and the different ketones (**4a**-**4d**) in Table 3 were purchased as standard products, a magnetic stirrer was added into a 160 mL flask. Then, DMF (15 mL), salicylaldehyde (342 μL, 32.75 mmol) and K_2CO_3 (4.98 g, 36.03 mmol) were added into this reaction. After that, 3-bromopropene (3.05 mL, 36.03 mmol) was added dropwise in an ice-bath. After the dropwise addition was completed, the reaction mixture was warmed to room temperature and it was reacted for 15 h, which was monitored by TLC until it was completed. Then a saturated NH_4Cl solution was added dropwise to quench the reaction system, which was washed with 200 mL of a saturated NaCl solution followed by extracted twice with ethyl acetate. The organic phase was dried with anhydrous sodium sulfate then concentrated under reduced pressure to remove the organic solvent. The crude product was separated and purified by silica gel on column chromatography (ethyl acetate/petroleum ether (v: v) = 1:50) to obtain a colorless oily liquid (5.42 g, yield 98%).

III. General procedures for the reaction of 2-(allyloxy)benzaldehyde with different alcohols and ketones

In a Schlenk tube equipped with a magnetic stir bar, 2-(allyloxy)benzaldehyde (0.3 mmol), silver carbonate (Ag_2CO_3) (0.6 mmol, 2 equivalents), and potassium persulfate ($K_2S_2O_8$) (0.6 mmol) were added successively. then the Schlenk tube was purged with argon and perform evacuation three times in sequence. Then, EtOH/H_2O (3 mL, v: v = 5:1) mixture were added subsequently via syringe. The reaction mixture was stirred in an oil bath at 80 ℃ under an argon atmosphere. Similarly, for the reaction with ketone, acetone/H_2O (3 mL, v: v = 1:1) mixture were added and stirred in an oil bath at 80 ℃ under an argon atmosphere until the substrate was consumed (monitored by TLC, 8-10 h). The reaction was quenched with saturated sodium sulfite solution (20 mL). The mixture was washed with a saturated NaCl solution (200 mL) and then extracted twice with ethyl acetate. The combined organic phases were dried over anhydrous sodium sulfate, concentrated under reduced pressure to remove the solvent, and purified by silica gel column chromatography to afford the corresponding chroman-4-one derivatives.

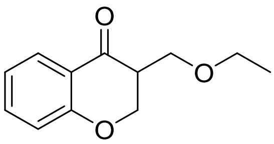
IV. Additional experiments

Under the optimal reaction conditions, three radical scavengers, TEMPO, 1,1-diphenylethylene and BHT, were separately added to the reaction system for radical trapping experiments. The research results showed that when 1 equivalent of TEMPO was additionally added to the reaction system, the radical cascade cyclization was inhibited, the yield of the desired product **3a** was dropped to 26%, and 60% of the starting material was recovered. When the amount of TEMPO increased to 2 equivalents, the reaction was almost completely inhibited and the product **3a** was obtained only in 6% yield. When 1 equivalent of 1,1-diphenylethylene was added to the reaction system, the inhibitory effect was not as good as that of TEMPO. The product **3a** was still formed in 30% yield, but only 50% of the starting material was recovered. Then, it was monitored by thin-layer chromatography (TLC), a product spot with an R_f value of 0.85 was found in the reaction system. It was speculated that the product might be trapped by 1,1-diphenylethylene. When 1 equivalent of BHT was added to the reaction system, the reaction was also inhibited, and the yield of product **3a** decreased significantly to 10%. The above-mentioned results indicate that the reaction system might proceed through the generation of radical intermediates.



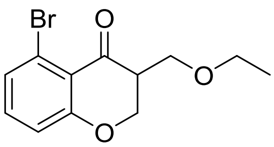
V. Characterization of the products

3a



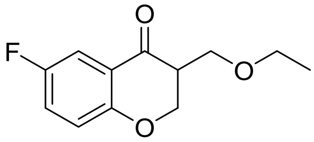
The crude product was separated and purified by silica gel on column chromatography (eluent: petroleum ether/ethyl acetate = 5:1), obtaining colorless oily liquid **3a** (37.10 mg) with a reaction yield of 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 1.8 Hz, 1H), 7.56 (d, *J* = 10.8 Hz, 1H), 7.08-7.03 (m, 2H), 4.67-4.61 (m, 1H), 4.38-4.31 (m, 1H), 4.03 (d, *J* = 8.0 Hz, 1H), 3.81-3.75 (m, 1H), 3.11-3.03 (m, 1H), 2.13-2.01 (m, 1H), 1.63-1.57 (m, 1H), 1.30 (t, *J* = 7.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.55 (d, *J* = 55.0 Hz), 161.68 (d, *J* = 9.2 Hz), 136.08 (d, *J* = 6.8 Hz), 127.49 (d, *J* = 7.6 Hz), 121.43 (d, *J* = 5.5 Hz), 120.48 (d, *J* = 17.4 Hz), 117.75 (d, *J* = 3.2 Hz), 71.05 (d, *J* = 57.4 Hz), 66.10 (d, *J* = 22.4 Hz), 43.61 (d, *J* = 73.7 Hz), 35.51 (d, *J* = 10.4 Hz), 24.02 (d, *J* = 49.0 Hz) ppm; HRMS(ESI): m/z Calcd for $C_{12}H_{14}O_3$ [M+H$^+$]: 207.1021, found 207.1027.

3b



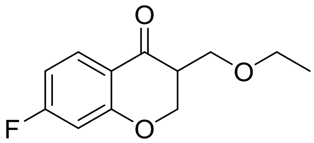
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3b** (32.38 mg) with a reaction yield of 41%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.84-7.81 (m, 1H), 7.42-7.39 (m, 1H), 6.96-6.88 (m, 1H), 4.53-4.50 (m, 1H), 4.24-4.17 (m, 1H), 3.91-3.88 (m, 1H), 2.94-2.89 (m, 1H), 2.00-1.96 (m, 1H), 1.89-1.85 (m, 1H), 1.49-1.44 (m, 1H), 1.16 (d, *J* = 6.18 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 194.62 (d, *J* = 88.7 Hz), 160.64 (d, *J* = 15.9 Hz), 135.10 (d, *J* = 11.7 Hz), 126.47 (d, *J* = 11.9 Hz), 120.48, 119.41 (d, *J* = 27.0 Hz), 116.73 (d, *J* = 6.45 Hz), 69.70 (d, *J* = 86.4 Hz), 65.08 (d, *J* = 45.3 Hz), 42.58 (d, *J* = 122.5 Hz), 34.46 (d, *J* = 13.5 Hz), 23.00 (d, *J* = 80.7 Hz) ppm; HRMS (ESI): m/z Calcd for $C_{12}H_{13}B_rO_3$ [M+H$^+$]: 285.0126, found 285.0024.

3c



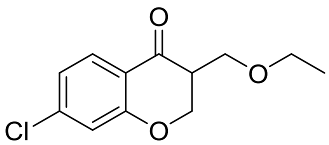
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3c** (35.63 mg) with a reaction yield of 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59-7.61 (m, 1H), 7.24-7.29 (m, 1H), 7.01 (dd, *J* = 4.1 Hz, *J* = 9.0 Hz, 1H), 4.57-4.67 (m, 1H), 4.28-4.37 (m, 1H), 4.00-4.04 (m, 1H), 3.78 (dd, *J* = 7.0 Hz, *J* = 14.0 Hz, 1H), 2.99-3.10 (m, 1H), 1.96-2.12 (m, 1H), 1.61-1.64 (m, 1H), 1.30 (t, *J* = 4.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.76 (d, *J* = 52.7 Hz), 158.44, 123.68 (d, *J* = 23.9 Hz), 119.44, 112.47 (d, *J* = 6.2 Hz), 112.24 (d, *J* = 6.1 Hz), 71.19 (d, *J* = 62.3 Hz), 66.06, 43.39 (d, *J* = 56.0 Hz), 35.33 (d, *J* = 17.2 Hz), 24.10 (d, *J* = 38.7 Hz) ppm; ^{19}F NMR (564 MHz, $CDCl_3$) δ: -121.36 (s, 1F) ppm. HRMS(ESI): m/z Calcd for $C_{12}H_{13}FO_3$ [M+H$^+$]: 227.0984, found 227.1058.

3d



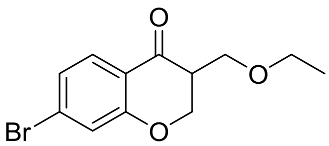
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3d** (37.65 mg) with a reaction yield of 56%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94-7.90 (m, 1H), 6.74 (t, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 9.8 Hz, 1H), 4.64-4.54 (m, 1H), 4.34-4.25 (m, 1H), 3.97 (t, *J* = 3.2 Hz, 1H), 3.02-2.96 (m, 1H), 2.08-1.91 (m, 1H), 1.56-1.50 (m, 1H), 1.42 (t, *J* = 7.0 Hz, 1H), 1.27 (t, *J* = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.05 (d, *J* = 51.9 Hz), 166.27 (t, *J* = 254.9 Hz), 130.09 (d, *J* = 11.2 Hz), 117.42 (d, *J* = 15.1 Hz), 109.94 (d, *J* = 22.5 Hz), 104.48 (d, *J* = 24.4 Hz), 71.51 (d, *J* = 59.2 Hz), 66.09 (d, *J* = 9.11 Hz), 43.31 (d, *J* = 61.0 Hz), 35.36 (d, *J* = 14.8 Hz), 24.09 (d, *J* = 41.7 Hz) ppm; ^{19}F NMR (564 MHz, $CDCl_3$) δ: -100.21 (d, *J* = 8.46 Hz, 1F) ppm. HRMS (ESI): m/z Calcd for $C_{12}H_{13}FO_3$ [M+H$^+$]: 225.0927, found 225.0941.

3e



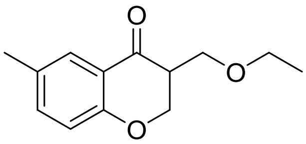
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid 3e (37.45 mg) with a reaction yield of 52%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.75 - 7.73 (m , 1H), 6.90 (s, 2H), 4.55-4.53 (m, 1H), 4.24-4.18 (m, 1H), 3.88 (s, 1H), 2.94-2.88 (m, 1H), 1.98-1.94 (m, 1H), 1.88-1.86 (m, 1H), 1.46-1.45 (m, 1H), 1.21-1.15 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 193.46 (d, *J* = 80.7 Hz), 160.95 (d, *J* = 12.3 Hz), 140.93 (d, *J* = 11.6 Hz), 127.69 (d, *J* = 8.9 Hz), 121.44 (d, *J* = 8.3 Hz), 117.99(d, *J* = 26.9 Hz), 116.87 (d, *J* = 4.2 Hz), 70.29(d, *J* = 94.4 Hz), 65.05, 42.36 (d, *J* = 88.8 Hz), 34.26 (d, *J* = 16.3 Hz), 28.67, 23.06 (d, *J* = 61.7 Hz) ppm; HRMS (ESI): m/z Calcd for $C_{12}H_{13}ClO_3$ [M+H$^+$]: 241.0631, found 241.0620.

3f



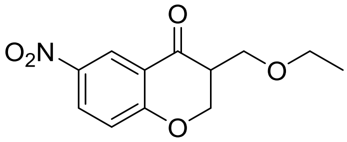
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3f** (40.90 mg) with a reaction yield of 48%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.67 (s, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 4.56-4.53 (m, 1H), 4.25-4.18 (m, 1H), 3.90-3.88 (m, 1H), 2.92-2.88 (m, 1H), 1.99-1.95 (m, 1H), 1.54 (d, *J* = 13.2 Hz, 1H), 1.46-1.42 (m, 1H), 1.17 (t, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 193.32, 160.79, 129.49 (d, *J* = 9.5 Hz), 127.67, 124.06, 119.96, 118.26, 65.06(d, *J* = 8.13 Hz), 42.12, 34.33, 28.68, 22.87 ppm; HRMS (ESI): m/z Calcd for $C_{12}H_{13}BrO_3$ [M+H$^+$]: 287.0107, found 287.0128.

3g



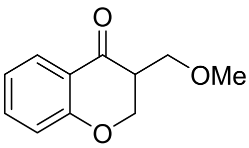
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3g** (36.98 mg) with a reaction yield of 56%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (s, 1H), 7.29 (t, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.3 Hz, 1H), 4.58-4.20 (m, 1H), 4.30-4.20 (m, 1H), 3.97 (s, 1H), 2.97-2.94 (m, 1H), 2.31 (s, 3H), 2.08-1.88 (m, 1H), 1.58-1.53 (m, 1H), 1.43 (t, *J* = 7.0 Hz, 1H), 1.27 (t, *J* = 6.3 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.63, 185.64, 136.27, 129.83, 125.94, 116.48, 70.30, 69.69, 65.23, 64.83, 43.03, 23.24, 19.38 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{16}O_3$ [M+H$^+$]: 221.1172, found 221.1184**.**

3h



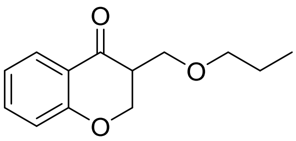
HRMS (ESI): m/z Calcd for $C_{12}H_{13}NO_5$[M+H$^+$]:252.0872, found 252.0898.

3ab



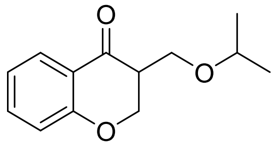
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3ab** (12.98 mg) with a reaction yield of 31%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (dd, *J* = 4.0 Hz, *J* = 7.9 Hz, 1H), 7.51-7.56 (m, 1H), 7.03-7.10 (m, 1H), 4.69 (dd, *J* = 4.9 Hz, *J* = 11.5 Hz, 1H), 4.49 (dd, *J* = 10.0 Hz, *J* = 11.3 Hz, 1H), 3.85 (dd, *J* = 4.6 Hz, *J* = 9.8 Hz, 1H), 3.76 (dd, *J* = 8.1 Hz, *J* = 9.7 Hz, 1H), 3.44 (s, 3H), 3.07-3.14 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.10, 161.85, 135.97, 127.31, 121.40, 117.89, 69.06, 68.27, 59.16, 46.40 ppm; HRMS (ESI): m/z Calcd for $C_{11}H_{12}O_3$ [M+H$^+$]: 193.0865, found 193.0864.

3ac



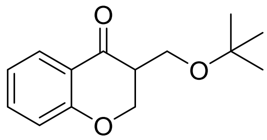
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain yellow oily liquid **3ac** (11.89 mg) with a reaction yield of 26%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.80-7.79 (m, 1H), 7.42-7.39 (m, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.48-4.45 (m, 1H), 4.18 (t, *J* = 7.6 Hz, 1H), 3.39-3.34 (m, 1H), 2.93 (dd, *J* = 4.8 Hz, 1H), 2.54-2.49 (m, 1H), 2.47-2.45 (m, 1H), 2.42-2.38 (m, 1H), 1.18 (s, 2H), 1.04 (t, *J* = 6.4 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 208.42, 193.50, 161.78, 135.99, 127.31, 121.44, 117.84, 70.33, 41.78, 37.66, 36.30, 29.70, 7.78 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{16}O_3$ [M+H$^+$]: 221.1178, found 221.1184.

3ae



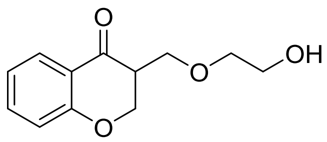
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **3ae** (31.70 mg) with a reaction yield of 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 7.9 Hz, 1H), 7.55 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 4.63 (dd, *J* = 5.4 Hz, *J* = 11.3 Hz, 1H), 4.28 (t, *J* = 11.7 Hz, 1H), 3.09-3.16 (m, 1H), 2.17-2.25 (m, 1H), 1.44 (dd, *J* = 4.5 Hz, 1H), 1.43 (s, *J* = 4.8 Hz, 3H), 1.37 (s, *J* = 4.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.17, 160.75, 135.12, 126.54, 120.37, 119.51, 116.69, 70.51, 68.53, 41.43, 37.74, 28.39 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{16}O_3$ [M+H$^+$]: 221.1178, found 221.1191.

3af



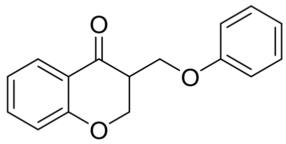
HRMS (ESI): m/z Calcd for $C_{14}H_{18}NO_3$ [M+H$^+$]: 235.1334, found 235.1362.

3ag



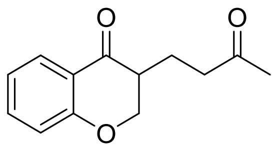
HRMS (ESI): m/z Calcd for $C_{12}H_{14}O$ [M+H$^+$]: 235.0970, found 235.0996.

3ah



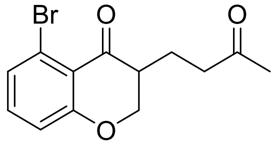
HRMS (ESI): m/z Calcd for $C_{16}H_{14}O_3$ [M+H$^+$]: 233.1178, found 233.1301.

5a



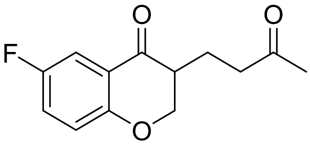
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5a** (54.30 mg) with a reaction yield of 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 4.52 (dd, *J* = 4.3 Hz, *J* = 11.4 Hz, 1H), 4.27 (dd, *J* = 8.5 Hz, *J* = 11.4 Hz, 1H), 2.63-2.76 (m, 3H), 2.17 (s, 3H), 1.99-2.09 (m, 1H), 1.80-1.89 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.86, 194.36, 161.39, 135.92, 127.30, 121.42, 120.40, 117.73, 70.86, 44.85, 40.72, 30.01, 20.71 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{14}O_3$ [M+H$^+$]: 219.1021,found 219.1019.

5b



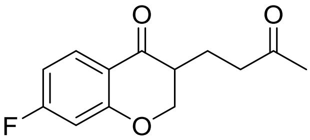
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5b** (71.04 mg) with a reaction yield of 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21-7.29 (m, 1H), 6.94 (d, *J* = 10.5 Hz, 2H), 4.51 (dd, *J* = 4.5 Hz, *J* = 11.4 Hz, 1H), 4.26 (dd, *J* = 8.4 Hz, *J* =11.4 Hz, 1H), 2.65-2.77 (m, 3H), 2.17 (s, 3H), 1.97-2.07 (m, 1H), 1.77-1.85 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.77, 192.61, 162.78, 134.91, 128.34, 121.64, 118.56, 117.55, 70.35, 45.18, 40.70, 29.97, 20.59 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{13}BrO_3$ [M+H$^+$]: 297.0126, found 297.0136.

5c



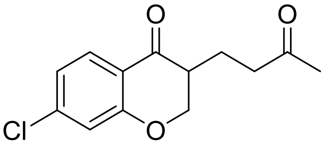
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5c** (61.62 mg) with a reaction yield of 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (dd, *J* = 3.2 Hz, *J* = 8.3 Hz, 1 H), 7.17-7.22 (m, 1H), 6.94 (dd, *J* = 4.2 Hz, *J* = 9.0 Hz, 1H), 4.50 (dd, *J* = 4.4 Hz, *J* = 11.5 Hz, 1H), 4.25 (dd, *J* = 8.5 Hz, *J* = 11.5 Hz, 1H), 2.64-2.72 (m, 3H), 2.17 (s, 3H), 1.99-2.08 (m, 1H), 1.80-1.88 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.62, 193.55, 157.67, 157.65, 156.06, 123.55, 123.30, 120.87, 120.81, 119.42, 119.37, 119.35, 112.31, 112.07, 71.05, 44.69, 40.60, 29.95, 20.62 ppm; ^{19}F NMR (564 MHz, $CDCl_3$) δ: -121.42 (s, 1F) ppm. HRMS(ESI): m/z Calcd for $C_{13}H_{13}FO_3$ [M+H$^+$]: 237.0927, found 237.0938.

5d



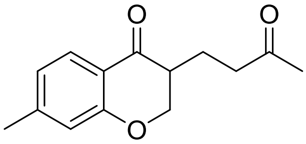
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5d** (56.66 mg) with a reaction yield of 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (dd, *J* = 6.8 Hz, *J* = 8.7 Hz, 1 H), 6.74 (dt, *J* = 2.2 Hz, *J* = 8.6 Hz, 1H), 6.64 (dd, *J* = 2.2 Hz, *J* = 9.8 Hz, 1H), 4.53 (dd, *J* = 4.4 Hz, *J* = 11.5 Hz, 1H), 4.28 (dd, *J* = 8.4 Hz, *J* = 11.4 Hz, 1H), 2.64-2.71 (m, 3H), 2.17 (s, 3H), 1.99-2.08 (m, 1H), 1.79-1.91 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.66, 192.89, 168.64, 166.10, 163.04 (d, *J* = 13.6 Hz), 129.83 (d, *J* = 11.3 Hz), 117.36, 109.85 (d, *J* = 22.6 Hz), 104.45 (d, *J* = 24.4 Hz), 71.34, 44.56, 40.65, 29.95, 20.63 ppm. ^{19}F NMR (564 MHz, $CDCl_3$) δ: -100.60 (d, *J* = 2.82 Hz, 1F) ppm. HRMS(ESI): m/z Calcd for $C_{13}H_{13}FO_3$ [M+H$^+$]: 237.0927, found 237.0937.

5e



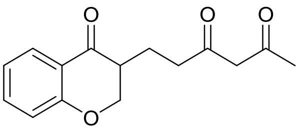
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5e** (62.01 mg) with a reaction yield of 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (dd, *J* = 7.8 Hz, *J* = 8.8 Hz, 1 H), 6.97-7.00 (m, 2H), 4.52 (dd, *J* = 4.4 Hz, *J* = 11.5 Hz, 1H), 4.27 (dd, *J* = 8.5 Hz, *J* = 11.5 Hz, 1H), 2.63-2.72 (m, 3H), 2.16 (s, 3H), 1.98-2.07 (m, 1H), 1.77-1.86 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.63, 193.26, 161.73, 141.73, 128.55, 122.23, 119.00, 117.86, 71.20, 44.69, 40.61, 30.00, 20.61 ppm; HRMS (ESI): m/z Calcd for $C_{13}H_{13}ClO_3$ [M+H$^+$]: 253.0631, found 253.0696.

5f



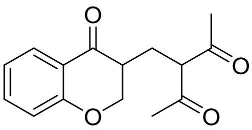
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5f** (48.74 mg) with a reaction yield of 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 8.0 Hz, 1 H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.76 (s, 1H), 4.48 (dd, *J* = 4.4 Hz, *J* = 11.5 Hz, 1H), 4.25 (dd, *J* = 8.5 Hz, *J* = 11.5 Hz, 1H), 2.60-2.67 (m, 3H), 2.35 (s, 3H), 2.16 (s, 3H), 1.98-2.07 (m, 1H), 1.77-1.88 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 207.83, 194.01, 161.43, 147.41, 127.18, 122.81, 118.18, 117.68, 70.88, 44.81, 40.76, 29.95, 21.87, 20.84 ppm; HRMS (ESI): m/z Calcd for $C_{14}H_{16}O_3$ [M+H$^+$]: 233.1178, found 233.1183.

5ab



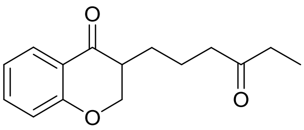
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5ab** (68.06 mg) with a reaction yield of 48%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 2H), 4.41-4.38 (m, 1H), 4.24-4.21 (m, 1H), 2.77 (dd, *J* = 4.8 Hz, 1H), 2.43-2.33 (m, 2H), 2.12 (s, 3H), 2.10 (d, *J* = 2.4 Hz, 1H), 2.02-1.99 (m, 2H), 1.99-1.97 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 193.56, 192.07, 161.41, 127.49, 127.29, 120.25, 120.21, 106.60, 68.89, 47.14, 43.57, 29.70, 27.21, 14.14 ppm; HRMS (ESI): m/z Calcd for $C_{15}H_{16}O_4$ [M+H$^+$]: 261.1127, found 261.1137.

5ab'



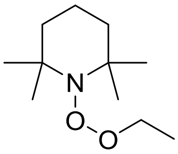
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5ab'** (68.06 mg) with a reaction yield of 48%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.78 (d, *J* = 7.8 Hz, 1H), 7.45-7.41 (m, 1H), 6.99-6.91 (m, 2H), 4.44 (dd, *J* = 4.8 Hz, 1H), 4.24-4.15 (m, 2H), 3.97 (dd, *J* = 4.8 Hz, 1H), 2.57-2.53 (m, 2H), 2.20 (s, 3H), 2.16 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 193.56, 192.07, 161.41, 127.49, 127.29, 120.25, 120.21, 106.60, 68.89, 47.14, 43.57, 29.70, 27.21, 14.14 ppm; HRMS (ESI): m/z Calcd for C15H16O4 [M+H+]: 261.1127, found 261.1137.

5ac



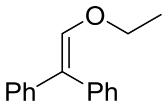
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **5ac** (59.28 mg) with a reaction yield of 32%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.80 (d, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 7.2 Hz, 1H), 4.42-4.39 (m, 1H), 4.20-4.17 (m, 1H), 4.07-4.04 (m, 1H), 2.79-2.74 (m, 1H), 2.55-2.40 (m, 3H), 1.81-1.77 (m, 1H), 1.74-1.69 (m, 1H), 1.20 (s, 2H), 1.04-1.03 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 193.38, 160.88, 135.33, 126.12, 124.36, 120.49, 119.78, 116.93, 67.59, 58.35, 46.64, 30.91, 28.68, 21.68, 13.11 ppm; HRMS (ESI): m/z Calcd for $C_{15}H_{18}O_3$ [M+H$^+$]: 270.1232, found 270.1284.

6



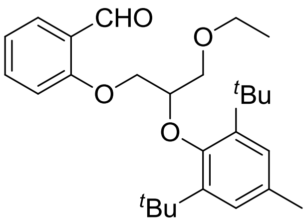
HRMS(ESI): m/z Calcd for $C_{11}H_{23}NO_2$ [M+H$^+$]: 202.1807, found 202.1810.

7



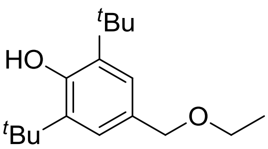
The crude product was separated and purified via silica gel on column chromatography, eluting with petroleum ether/ethyl acetate (5:1) to obtain colorless oily liquid **7** (25.02 mg) with a reaction yield of 20%. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.80 (t, *J* = 7.2 Hz, 4H), 7.60-7.58 (m, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.26 (s, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 3.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ: 196.82, 171.21, 137.60, 132.44, 130.09, 128.29, 60.63, 21.08 ppm; HRMS (ESI): m/z Calcd for $C_{16}H_{16}O$ [M+H$^+$]: 225.1279, found 225.1285.

8



HRMS (ESI): m/z Calcd for $C_{27}H_{38}O_4$ [M+H$^+$]: 427.2848, found 427.2841.

9



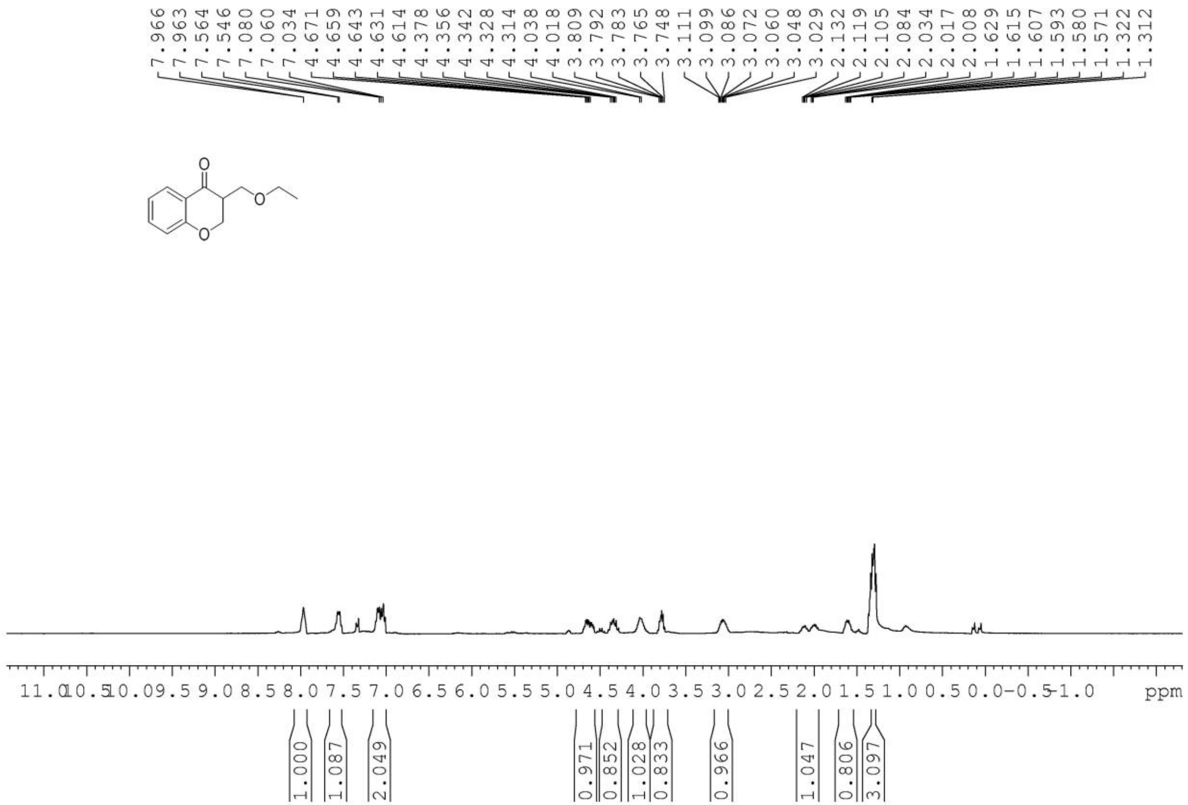
HRMS (ESI): m/z Calcd for $C_{17}H_{28}O_2$ [M+H$^+$]: 265.2168, found 265.2128.

VI. References

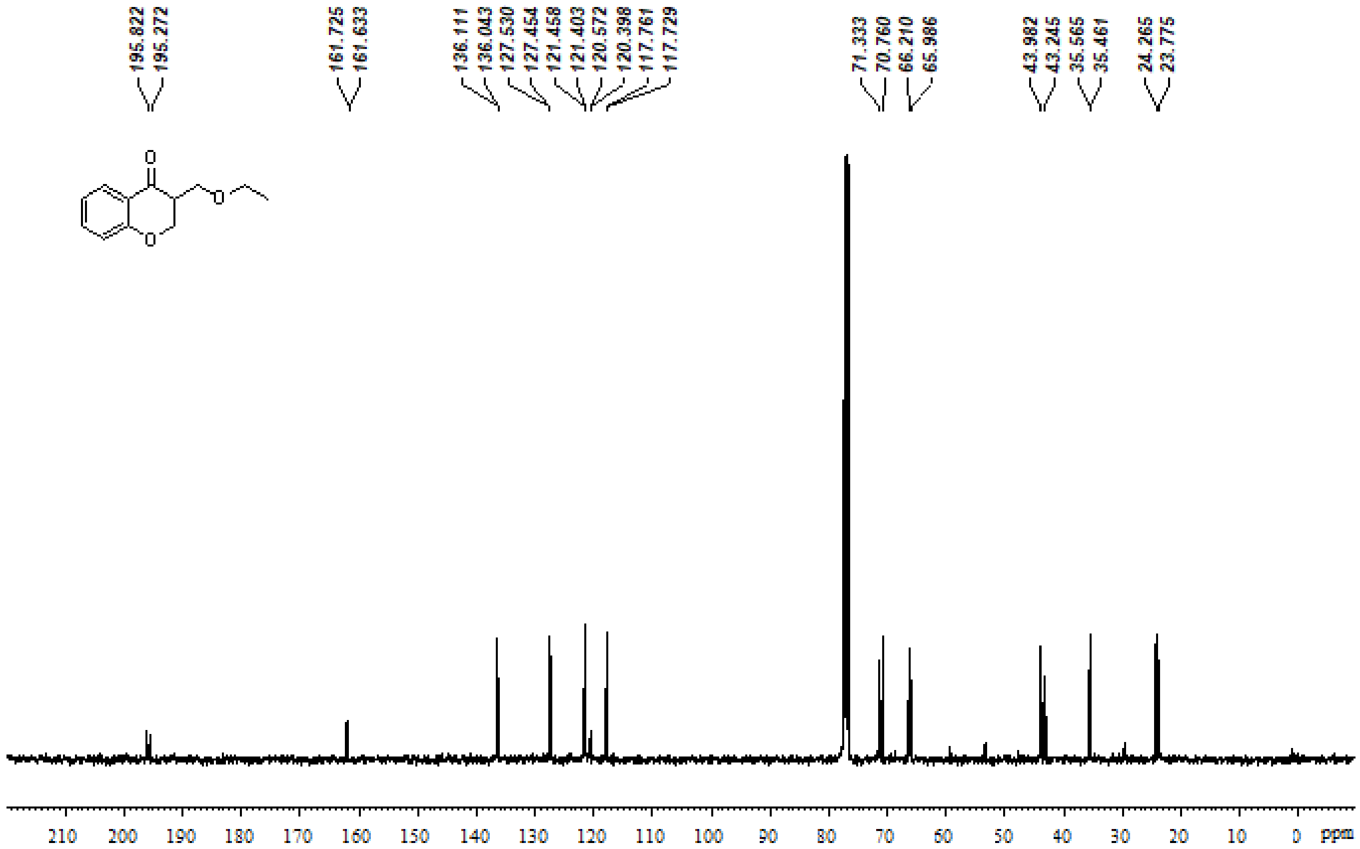
[1] Zhou, Y.; Xiong, Z.; Qiu, J.; Kong, L.; Zhu, G. *Org. Chem. Front*. **2019**, *6*, 1022-1026.

VII. NMR Charts

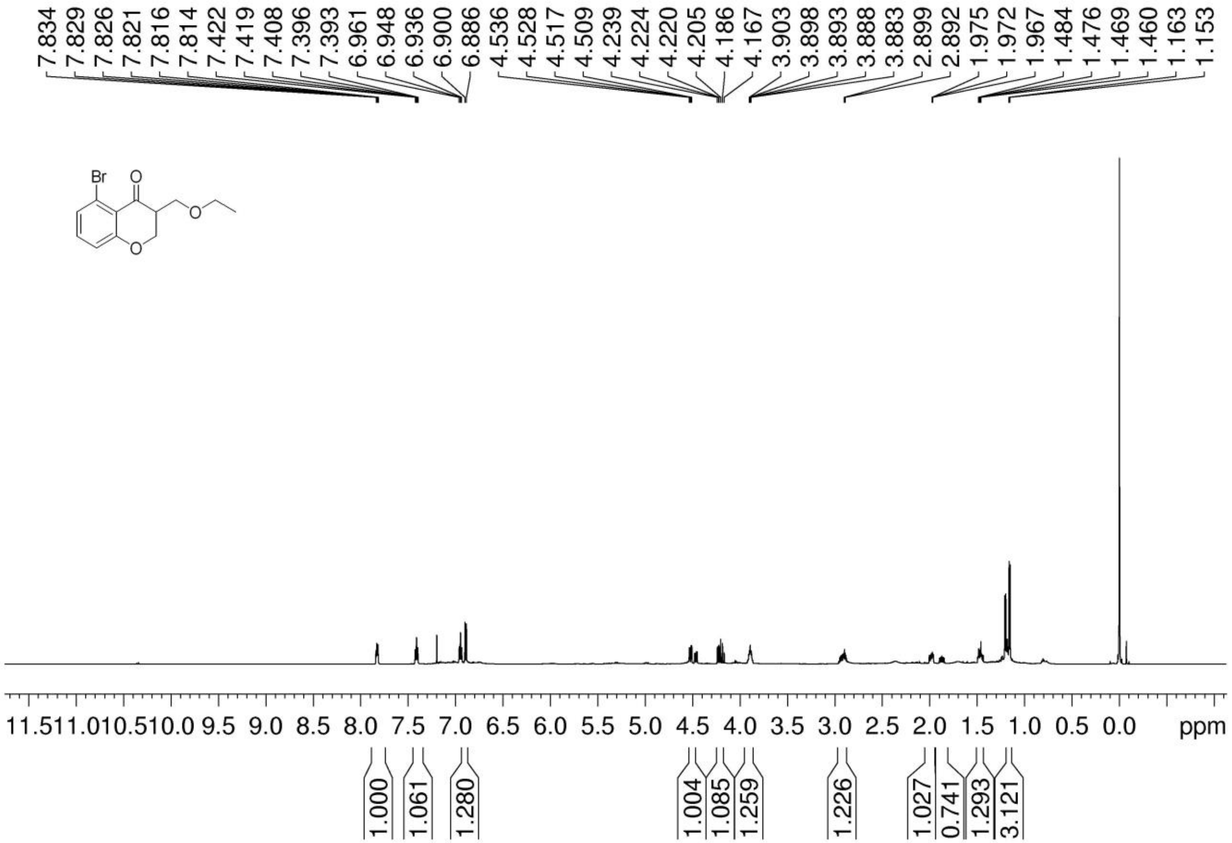
3a-^{1}H



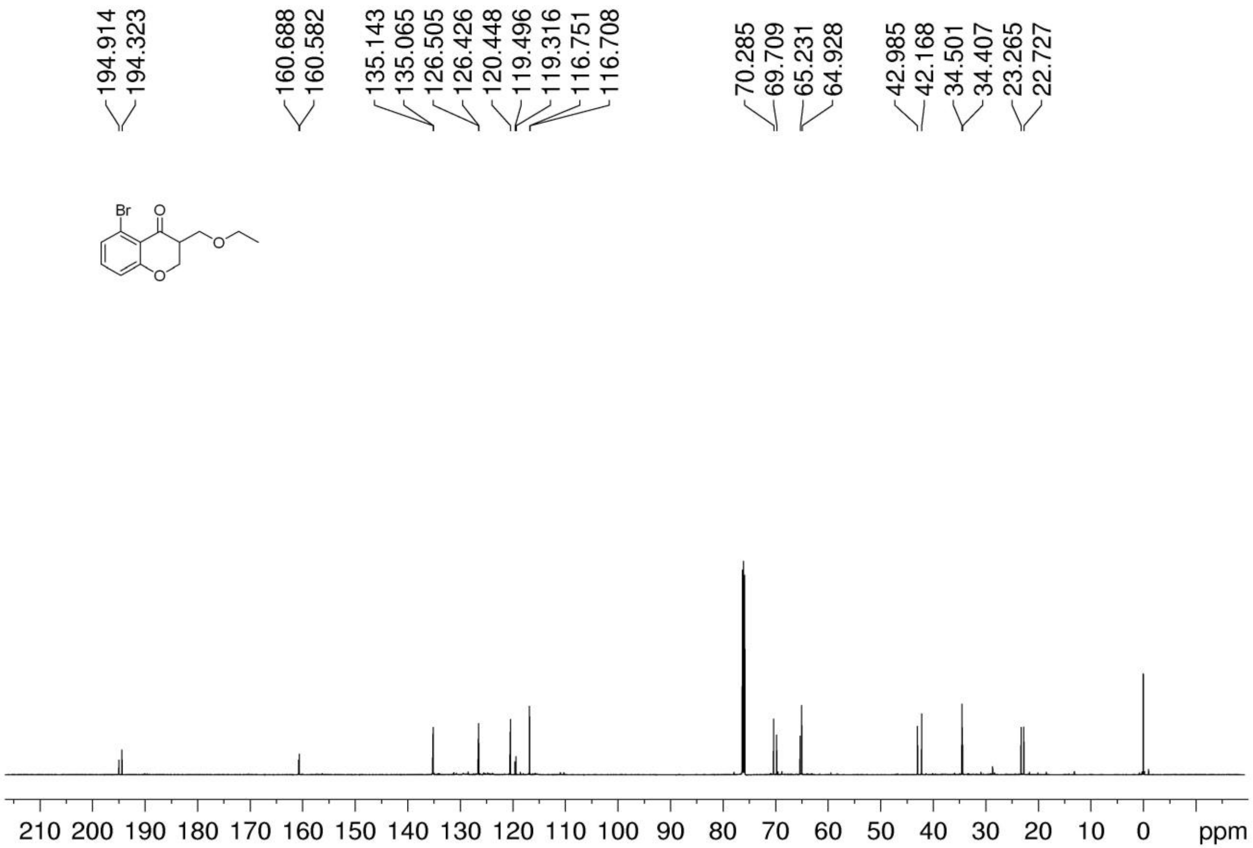
3a-^{13}C


195.822
195.272
161.725
161.633
136.111
136.043
127.530
127.454
121.458
121.403
120.572
120.398
117.761
117.729
71.333
70.760
66.210
65.986
43.982
43.245
35.565
35.461
24.265
23.775
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

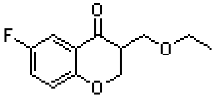
3b-[1]H

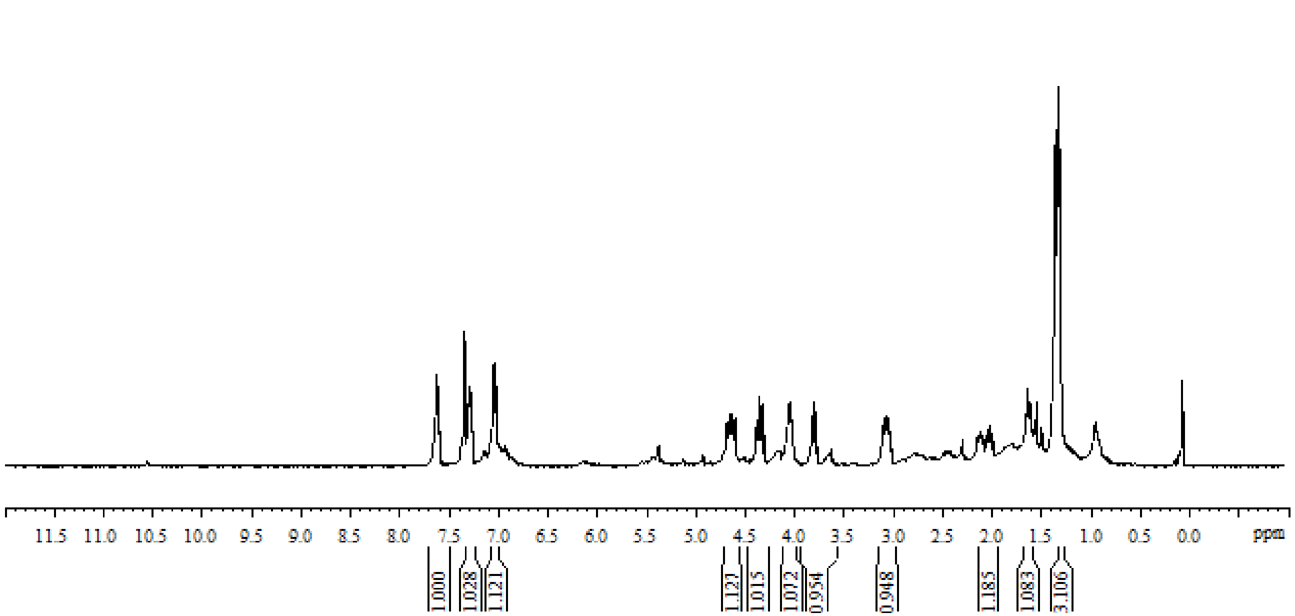

7.834
7.829
7.826
7.821
7.816
7.814
7.422
7.419
7.408
7.396
7.393
6.961
6.948
6.936
6.900
6.886
4.536
4.528
4.517
4.509
4.239
4.224
4.220
4.205
4.186
4.167
3.903
3.898
3.893
3.888
3.883
2.899
2.892
1.975
1.972
1.967
1.484
1.476
1.469
1.460
1.163
1.153
Br
O
O
O
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 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 ppm
1.000
1.061
1.280
1.004
1.085
1.259
1.226
1.027
0.741
1.293
3.121

3b-^{13}C

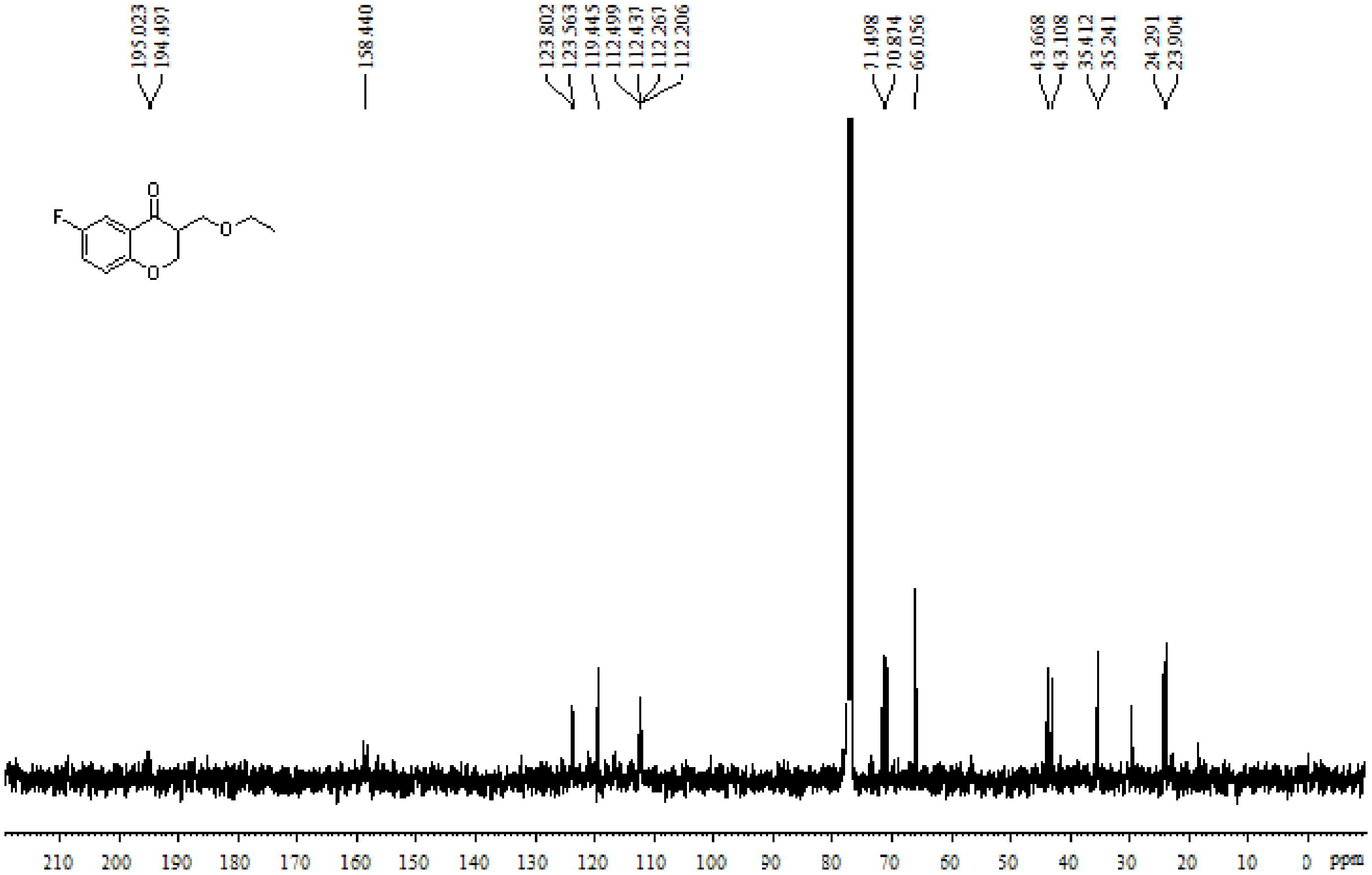

194.914
194.323
160.688
160.582
135.143
135.065
126.505
126.426
120.448
119.496
119.316
116.751
116.708
70.285
69.709
65.231
64.928
42.985
42.168
34.501
34.407
23.265
22.727
Br
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

3c-^{1}H

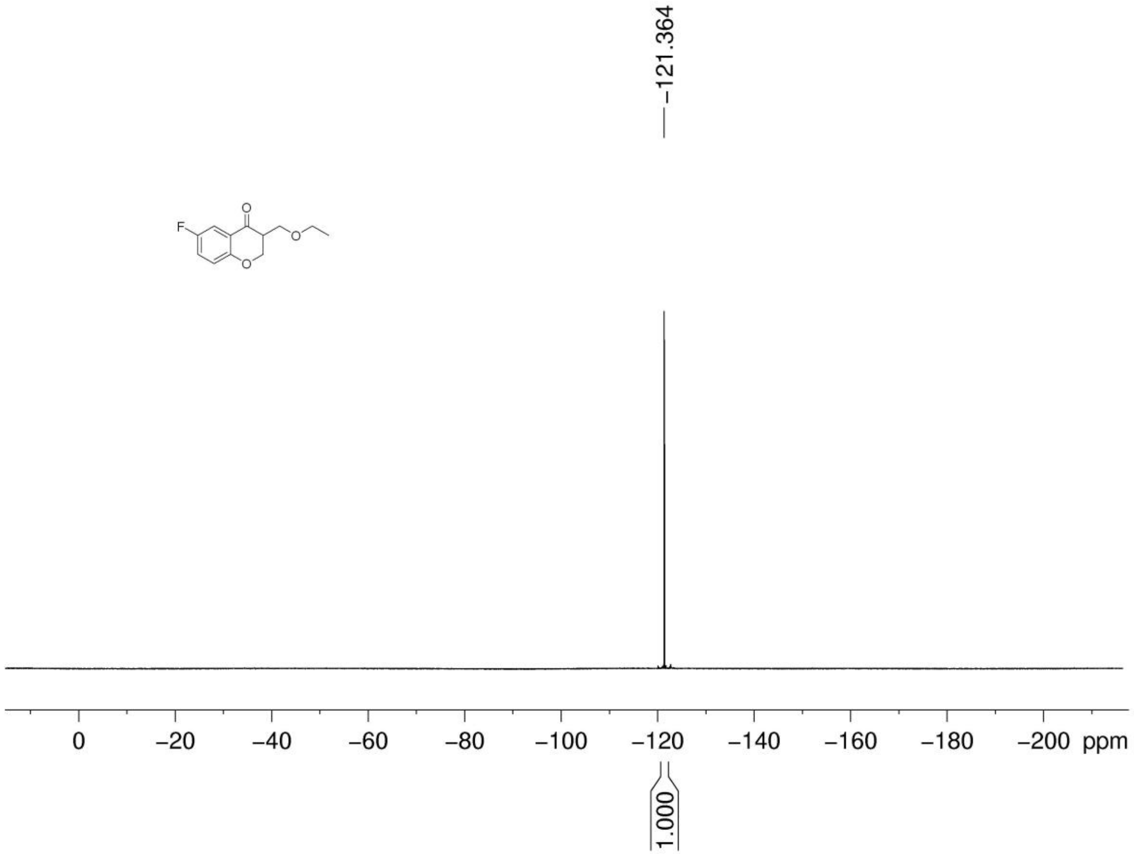




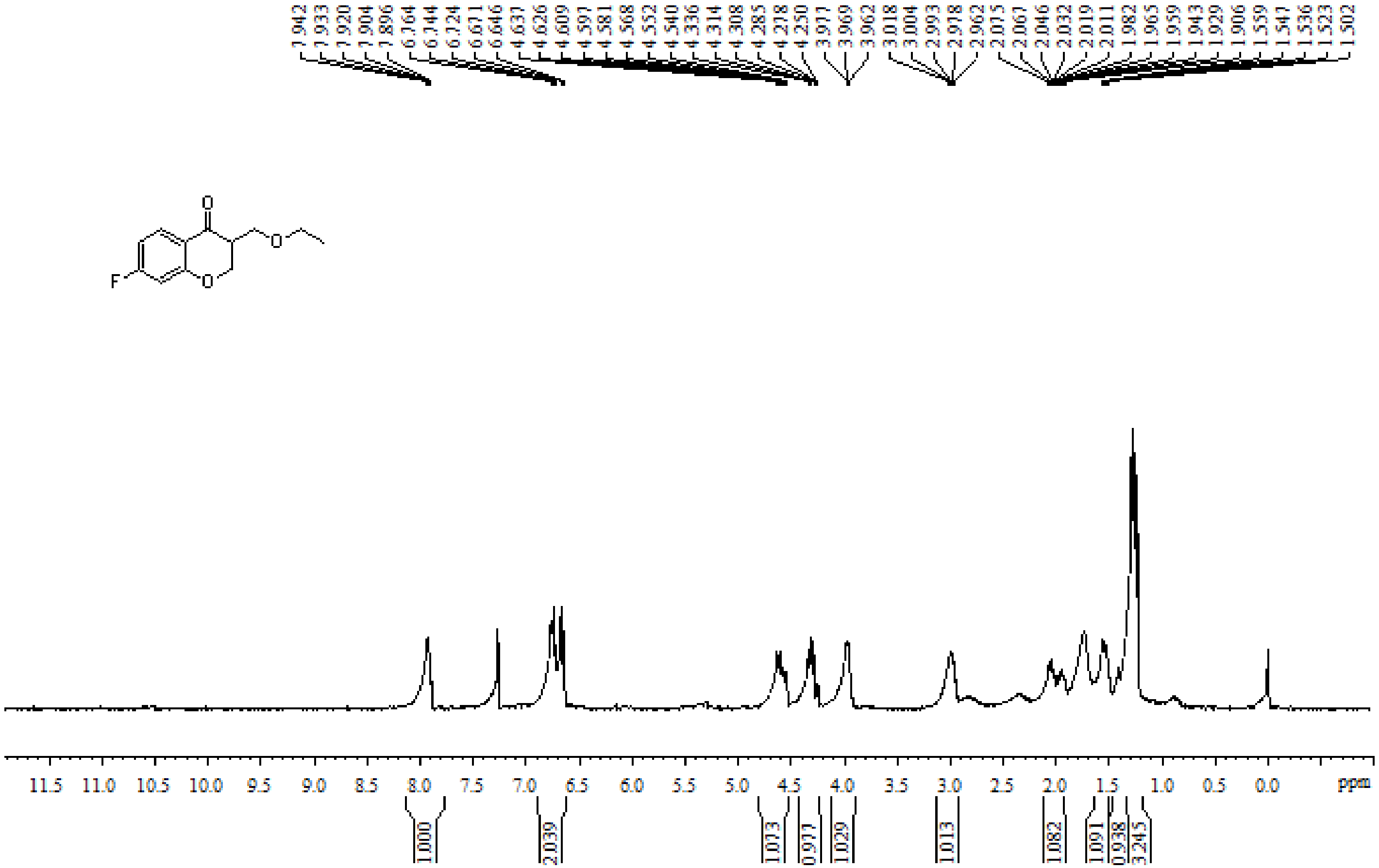
3c-^{13}C


195.023
194.497
158.440
123.802
123.563
119.445
112.499
112.437
112.267
112.206
71.498
70.874
66.056
43.668
43.108
35.412
35.241
24.291
23.904
F
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

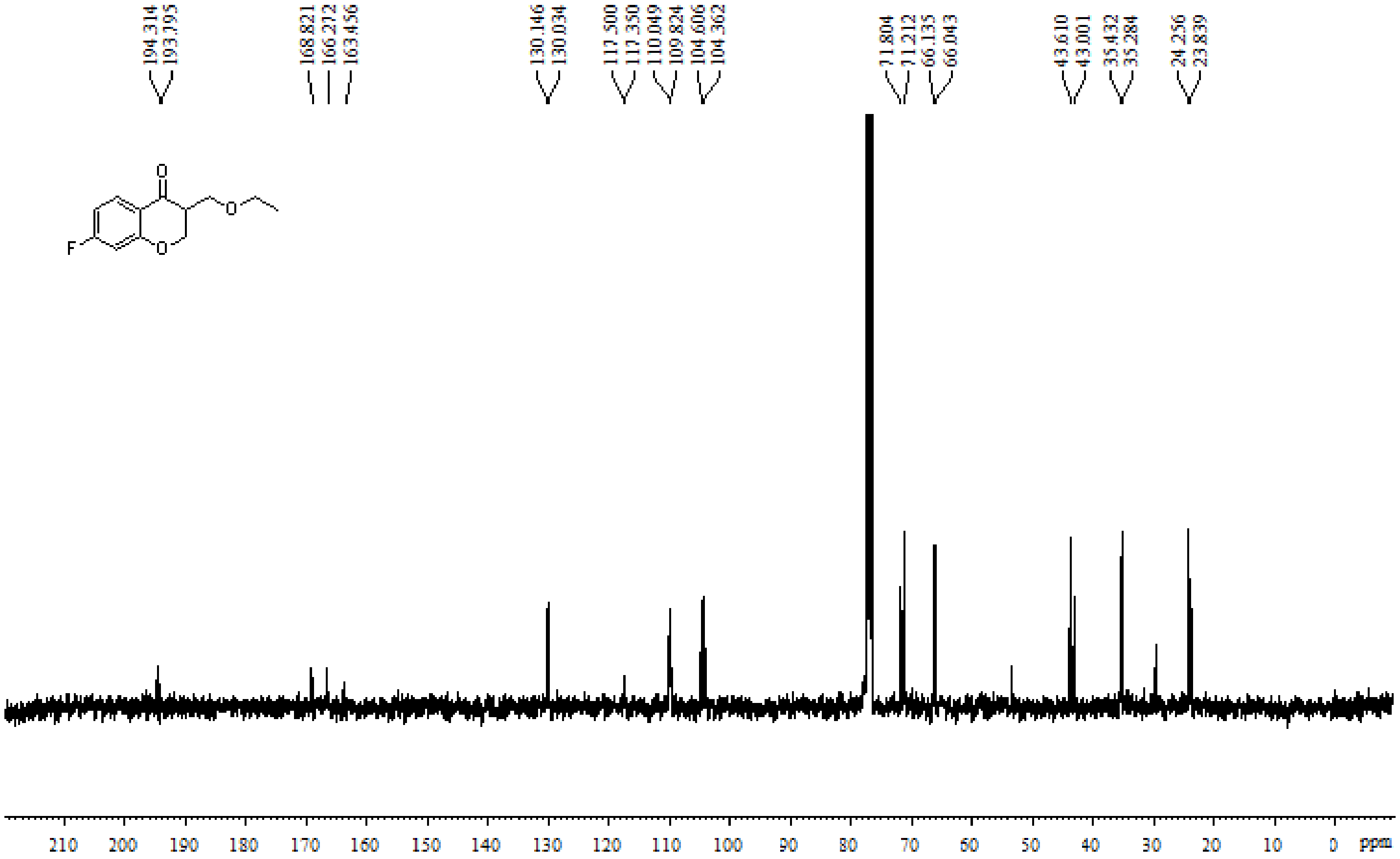
3c-[19]F



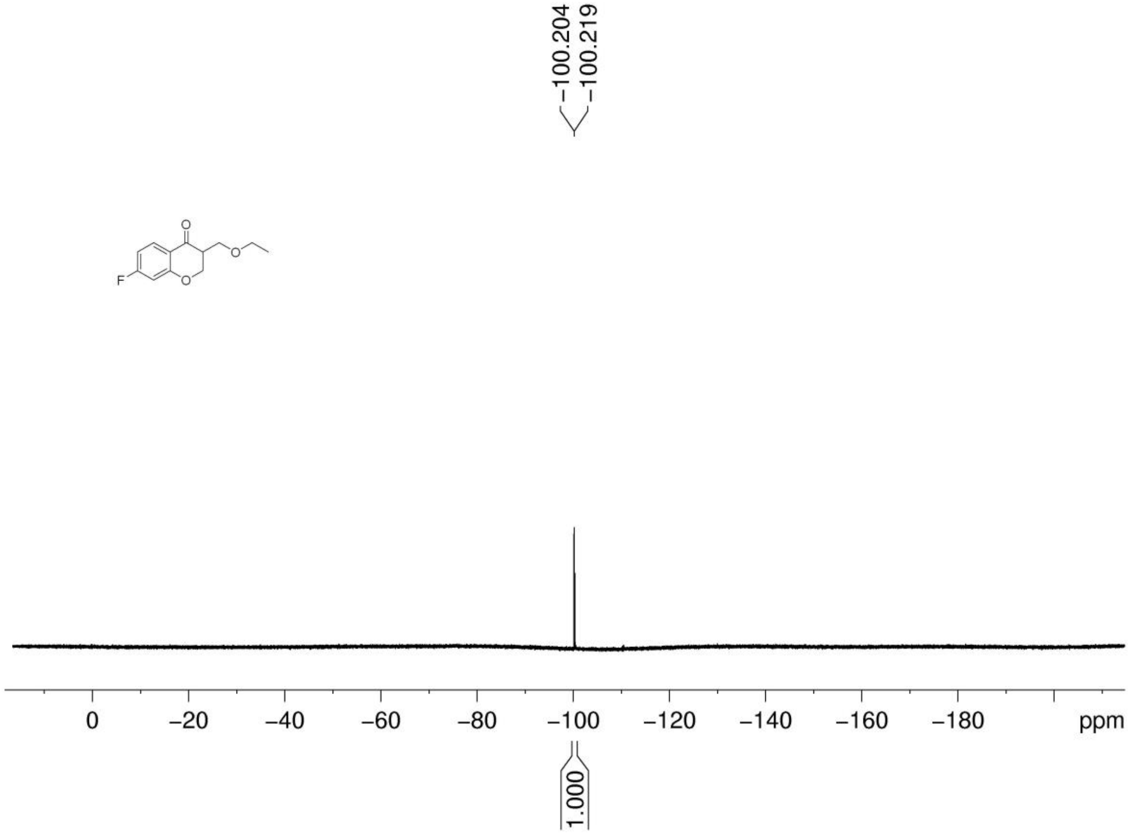
3d-^{1}H



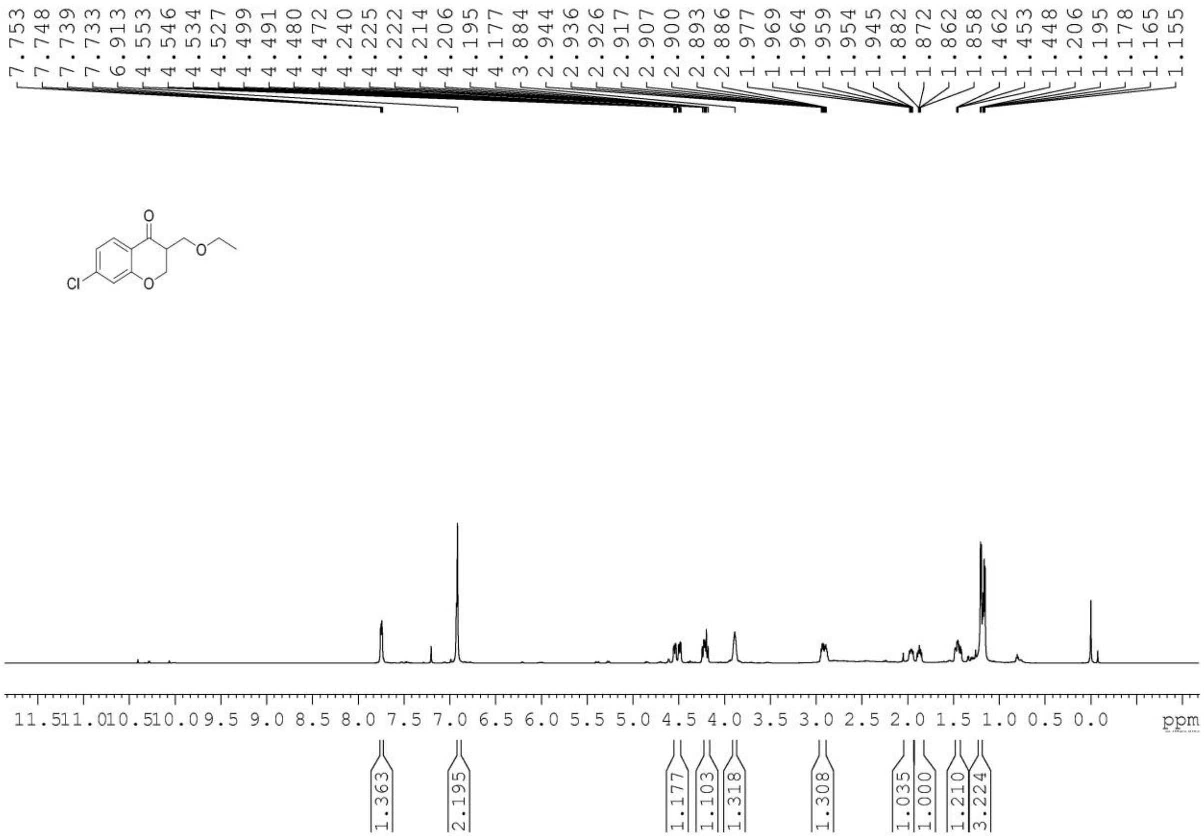
3d-^{13}C


194.314
193.195
168.821
166.212
163.456
130.146
130.034
117.500
117.350
110.049
109.824
104.606
104.362
71.804
71.212
66.135
66.043
43.610
43.001
35.432
35.284
24.256
23.839
O
O
O
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

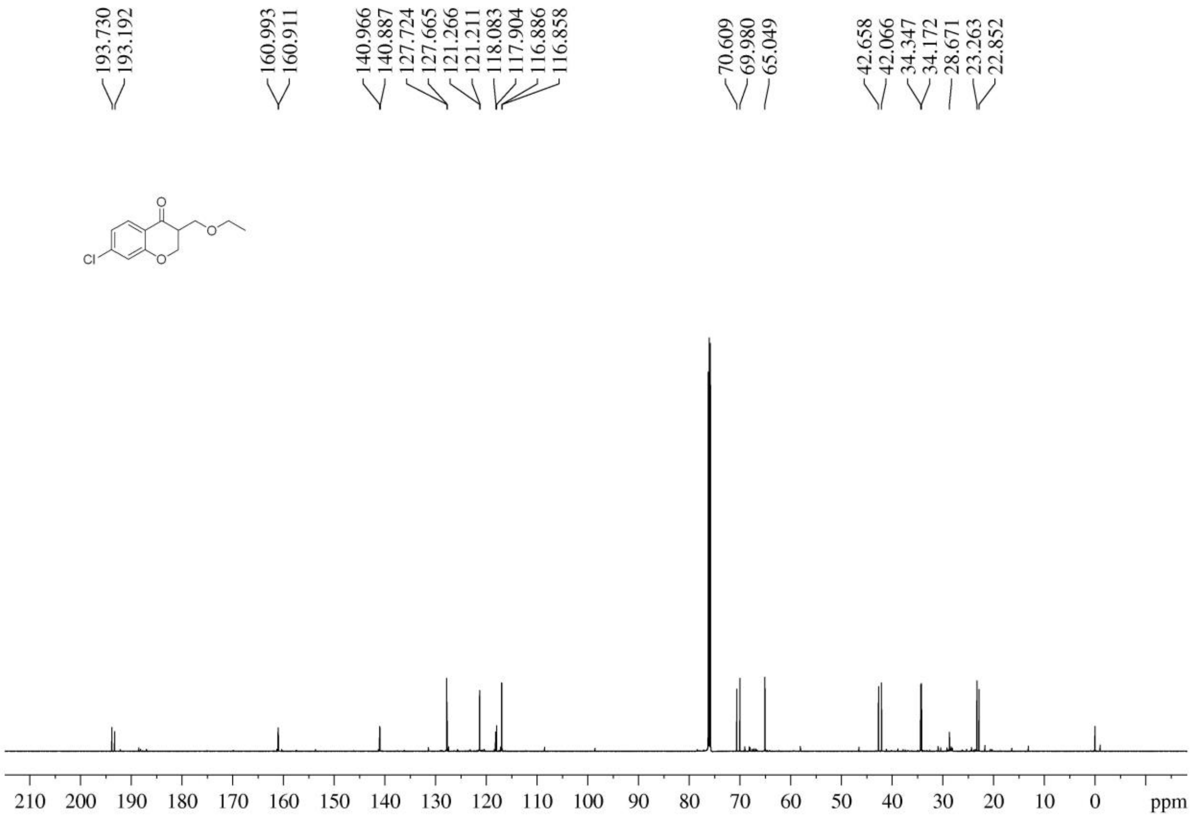
3d-^{19}F



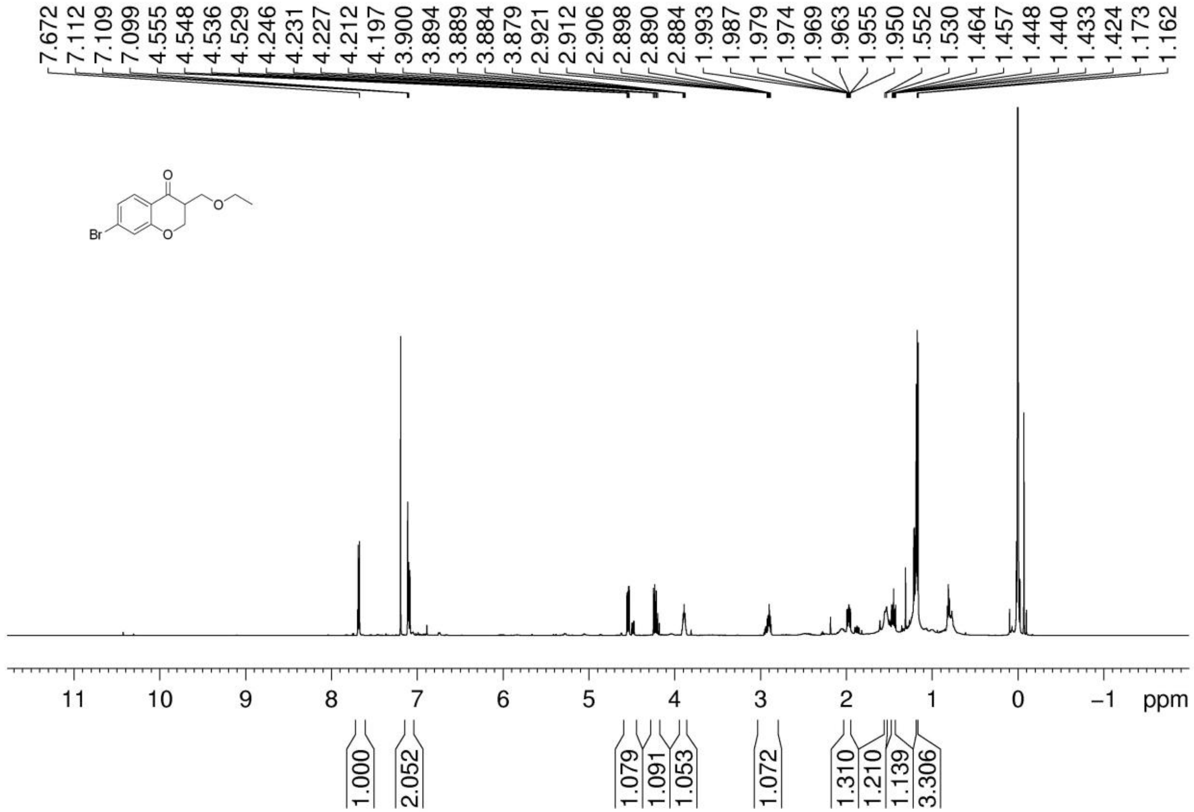
3e-1H


7.753
7.748
7.739
7.733
6.913
4.553
4.546
4.534
4.527
4.499
4.491
4.480
4.472
4.240
4.225
4.222
4.214
4.206
4.195
4.177
3.884
2.944
2.936
2.926
2.917
2.907
2.900
2.893
2.886
1.977
1.969
1.964
1.959
1.954
1.945
1.882
1.872
1.862
1.858
1.462
1.453
1.448
1.206
1.195
1.178
1.165
1.155
O
O
Cl
O
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 ppm
1.363
2.195
1.177
1.103
1.318
1.308
1.035
1.000
1.210
3.224

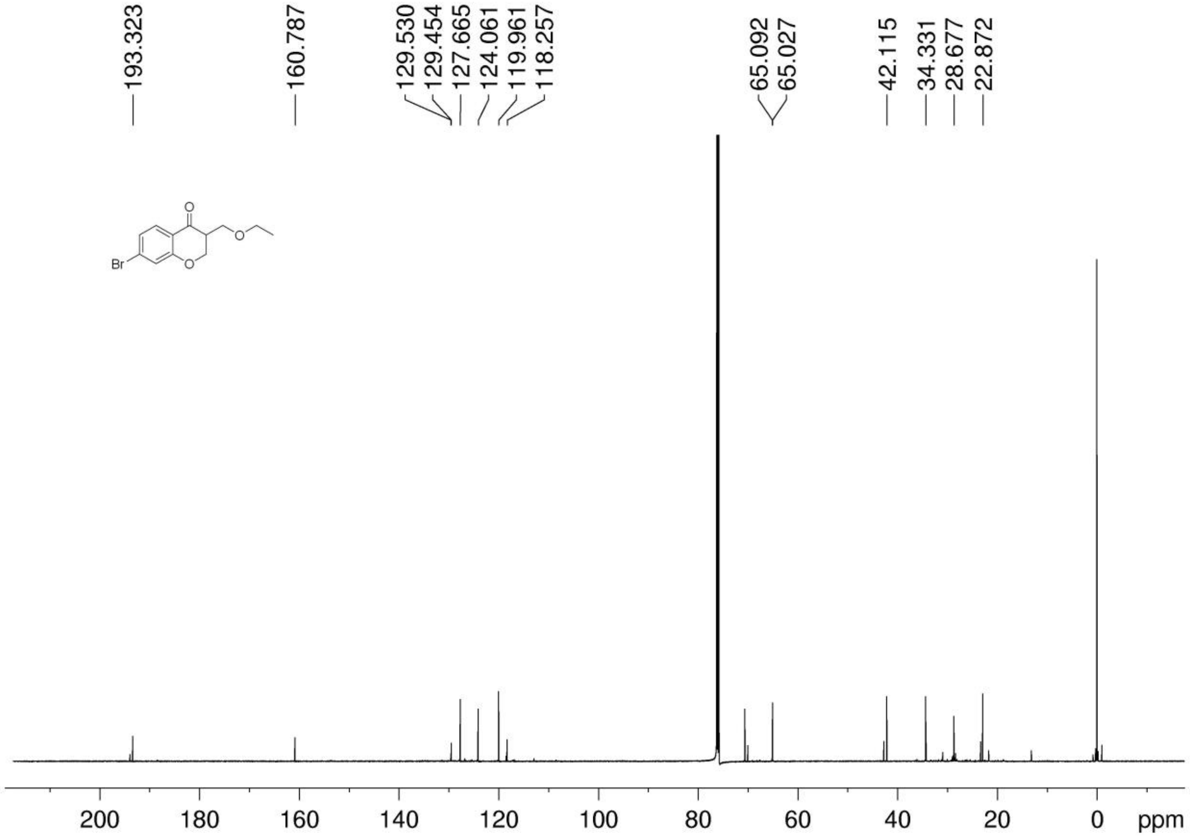
3e-^{13}C


193.730
193.192
160.993
160.911
140.966
140.887
127.724
127.665
121.266
121.211
118.083
117.904
116.886
116.858
70.609
69.980
65.049
42.658
42.066
34.347
34.172
28.671
23.263
22.852
Cl
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

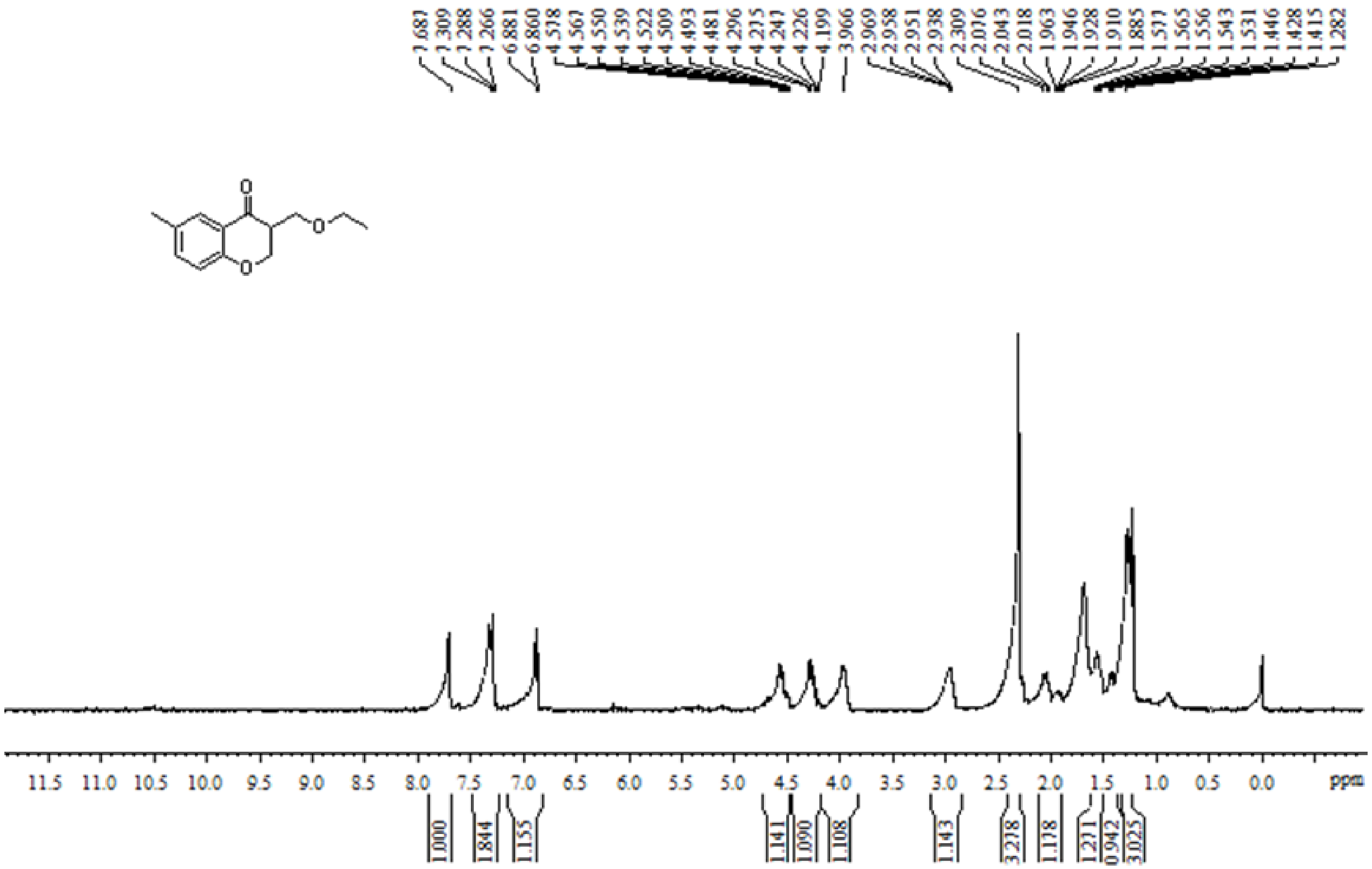
3f-[1]H


7.672
7.112
7.109
7.099
4.555
4.548
4.536
4.529
4.246
4.231
4.227
4.212
4.197
3.900
3.894
3.889
3.884
3.879
2.921
2.912
2.906
2.898
2.890
2.884
1.993
1.987
1.979
1.974
1.969
1.963
1.955
1.950
1.552
1.530
1.464
1.457
1.448
1.440
1.433
1.424
1.173
1.162
Br
O
11
10
9
8
7
6
5
4
3
2
1
0
–1
ppm
1.000
2.052
1.079
1.091
1.053
1.072
1.310
1.210
1.139
3.306

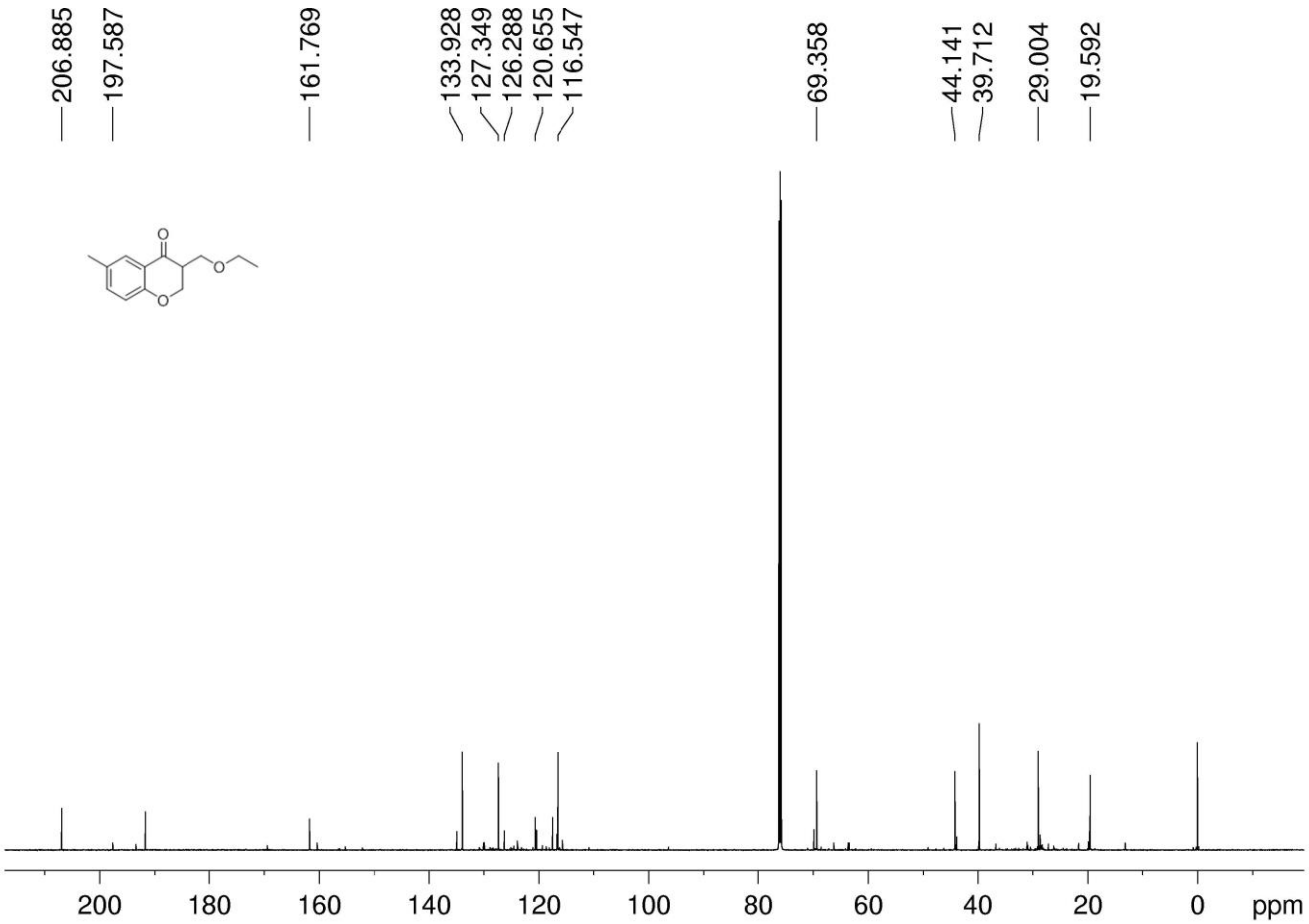
3f-^{13}C


193.323
160.787
129.530
129.454
127.665
124.061
119.961
118.257
65.092
65.027
42.115
34.331
28.677
22.872
Br
O
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

3g-^{1}H

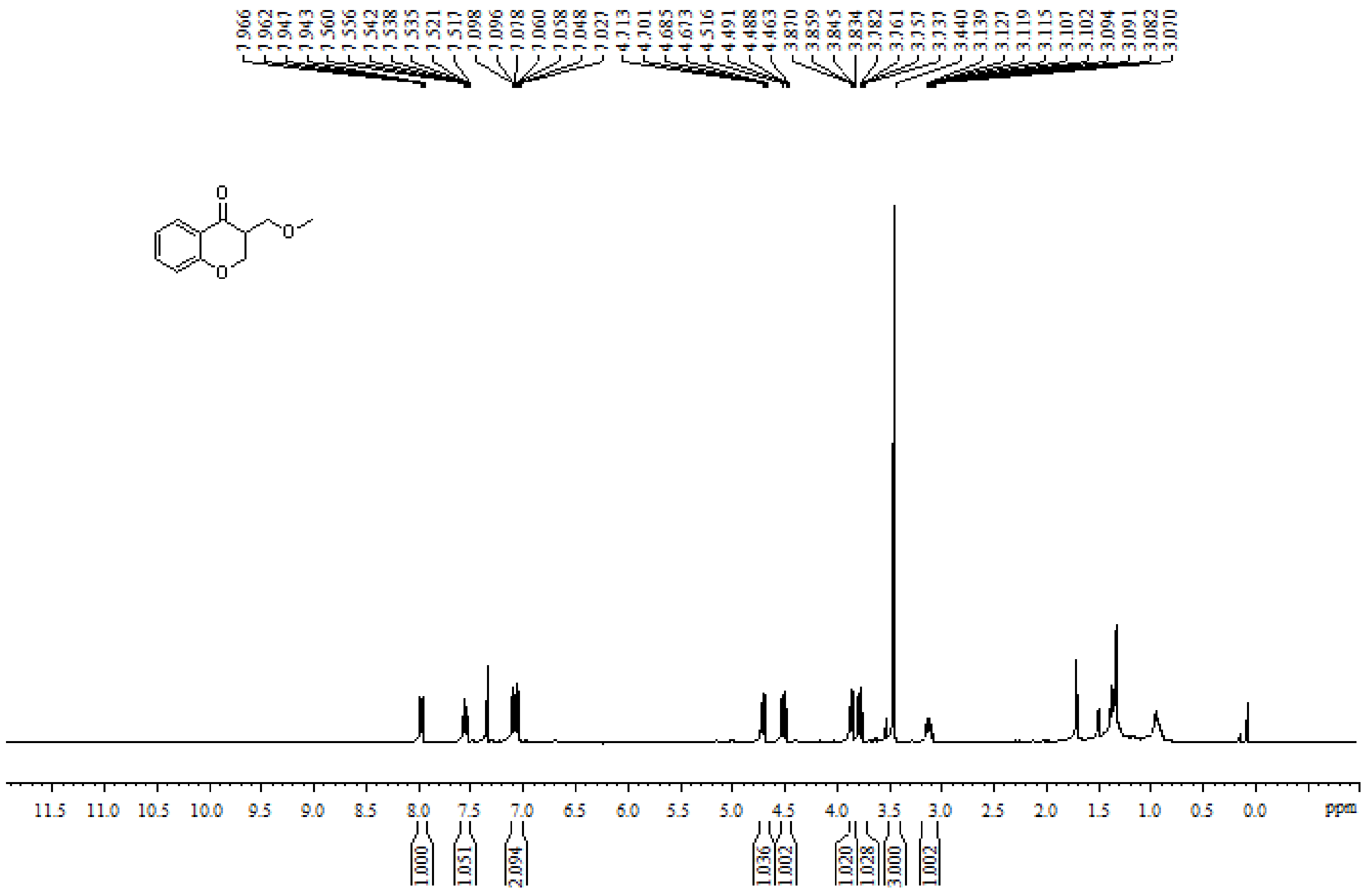


3g-^{13}C

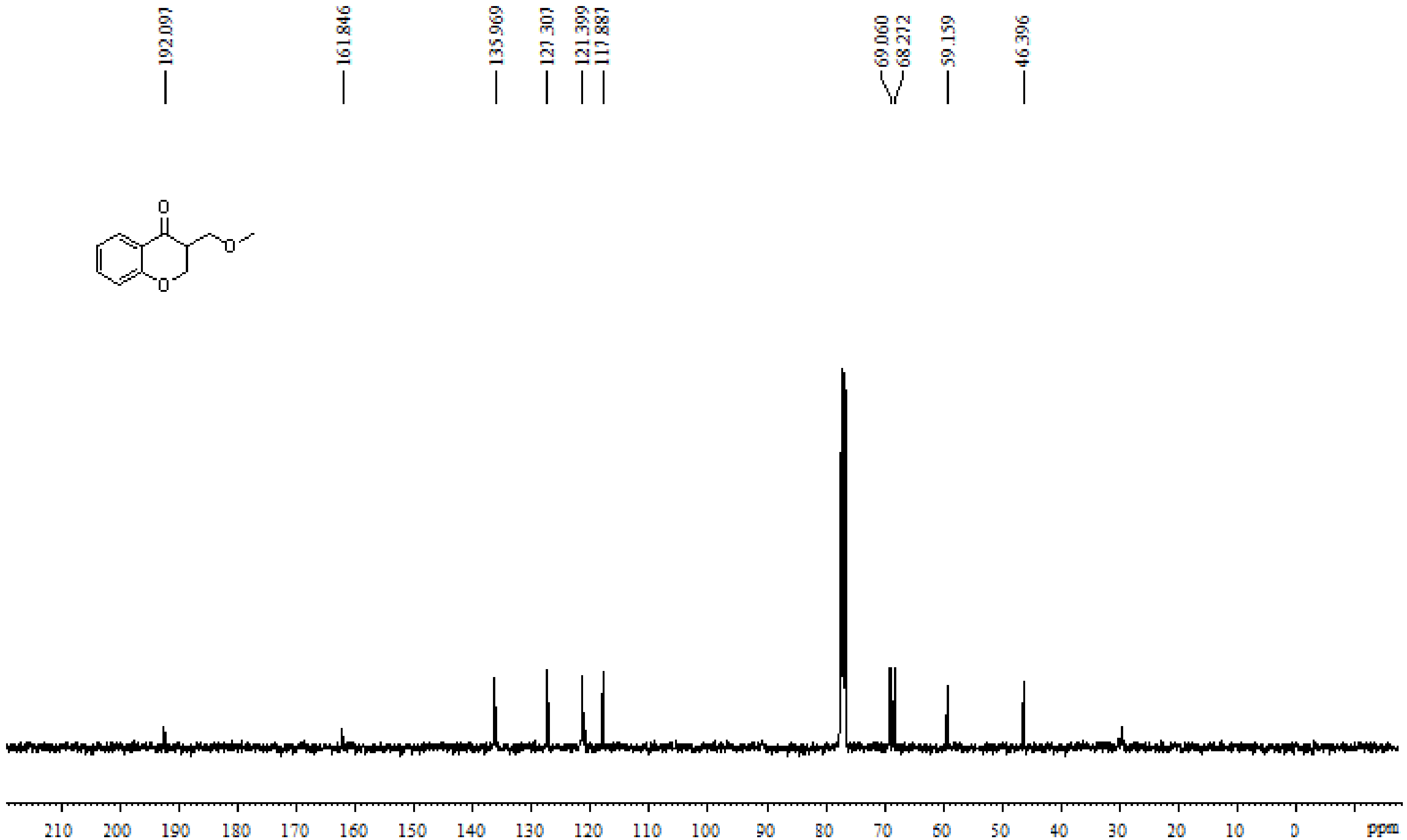


206.885
197.587
161.769
133.928
127.349
126.288
120.655
116.547
69.358
44.141
39.712
29.004
19.592
O
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

3ab-¹H

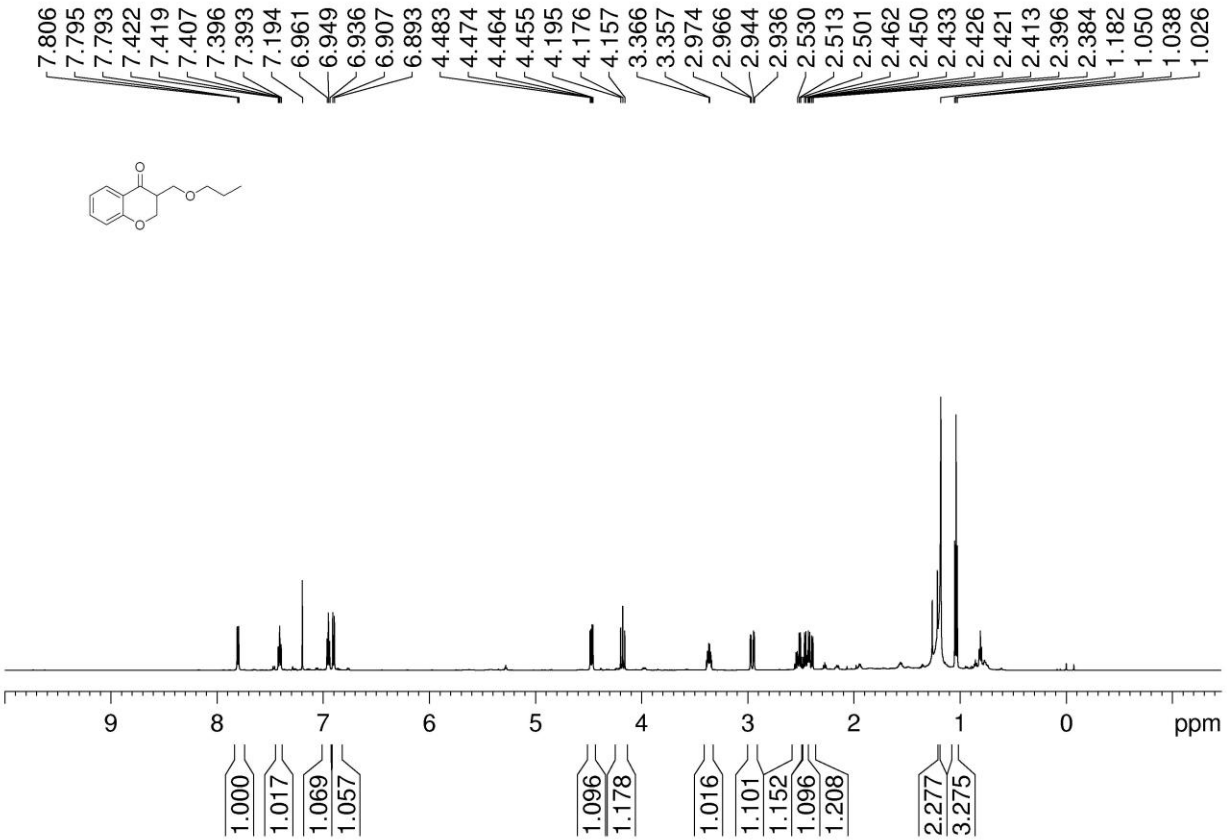


3ab-^{13}C



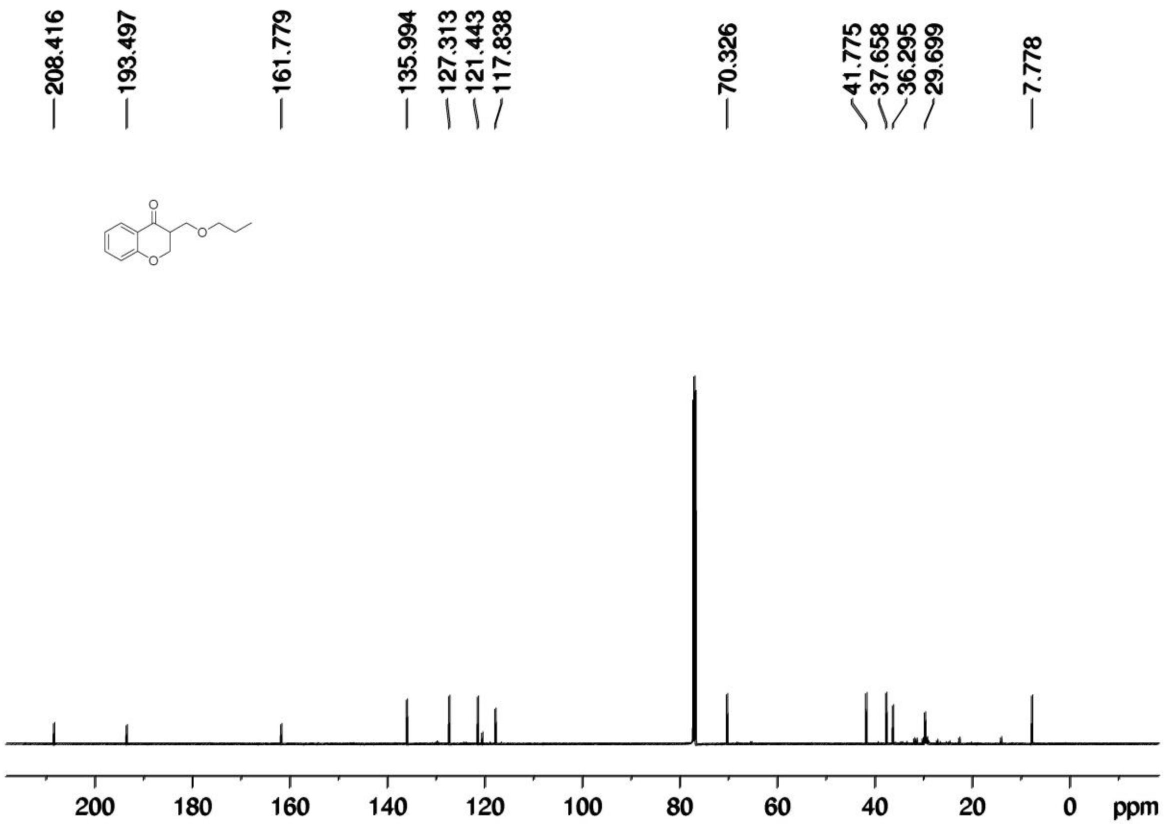
192.097
161.846
135.969
127.302
121.399
117.887
69.060
68.272
59.159
46.396
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

3ac-^{1}H



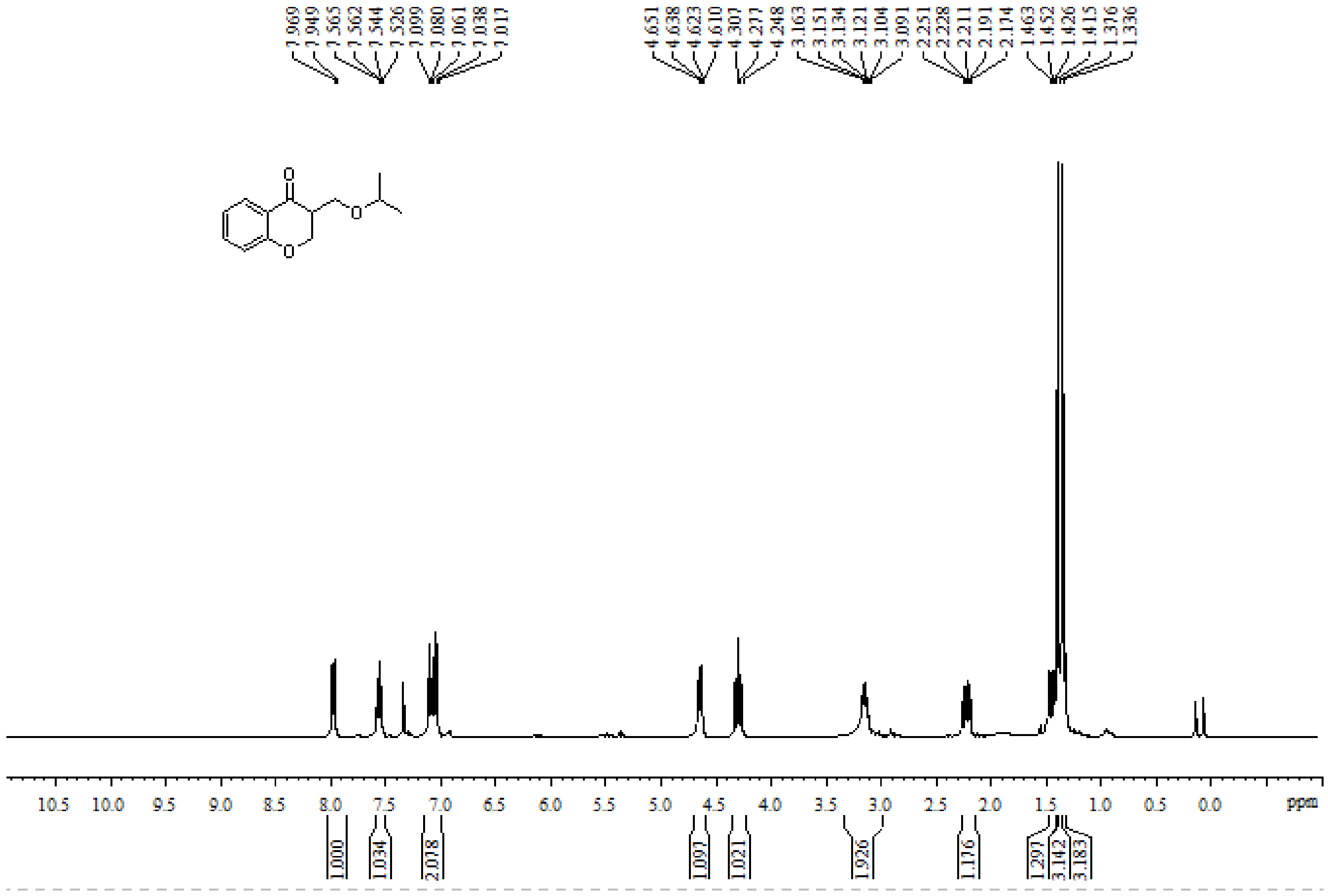
7.806
7.795
7.793
7.422
7.419
7.407
7.396
7.393
7.194
6.961
6.949
6.936
6.907
6.893
4.483
4.474
4.464
4.455
4.195
4.176
4.157
3.366
3.357
2.974
2.966
2.944
2.936
2.530
2.513
2.501
2.462
2.450
2.433
2.426
2.421
2.413
2.396
2.384
1.182
1.050
1.038
1.026
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.017
1.069
1.057
1.096
1.178
1.016
1.101
1.152
1.096
1.208
2.277
3.275

3ac-^{13}C

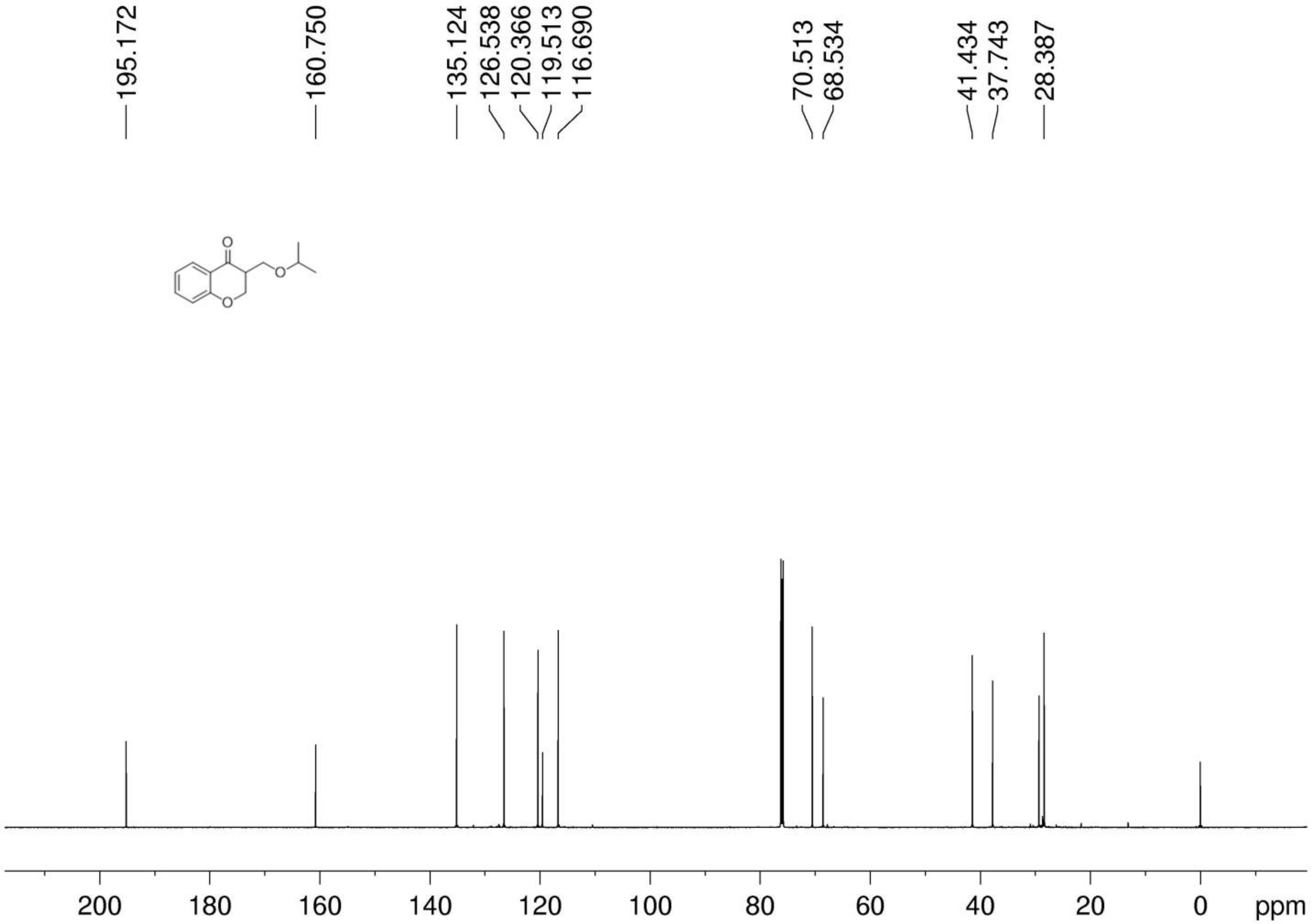


208.416
193.497
161.779
135.994
127.313
121.443
117.838
70.326
41.775
37.658
36.295
29.699
7.778
200
180
160
140
120
100
80
60
40
20
0
ppm

3ae-¹H

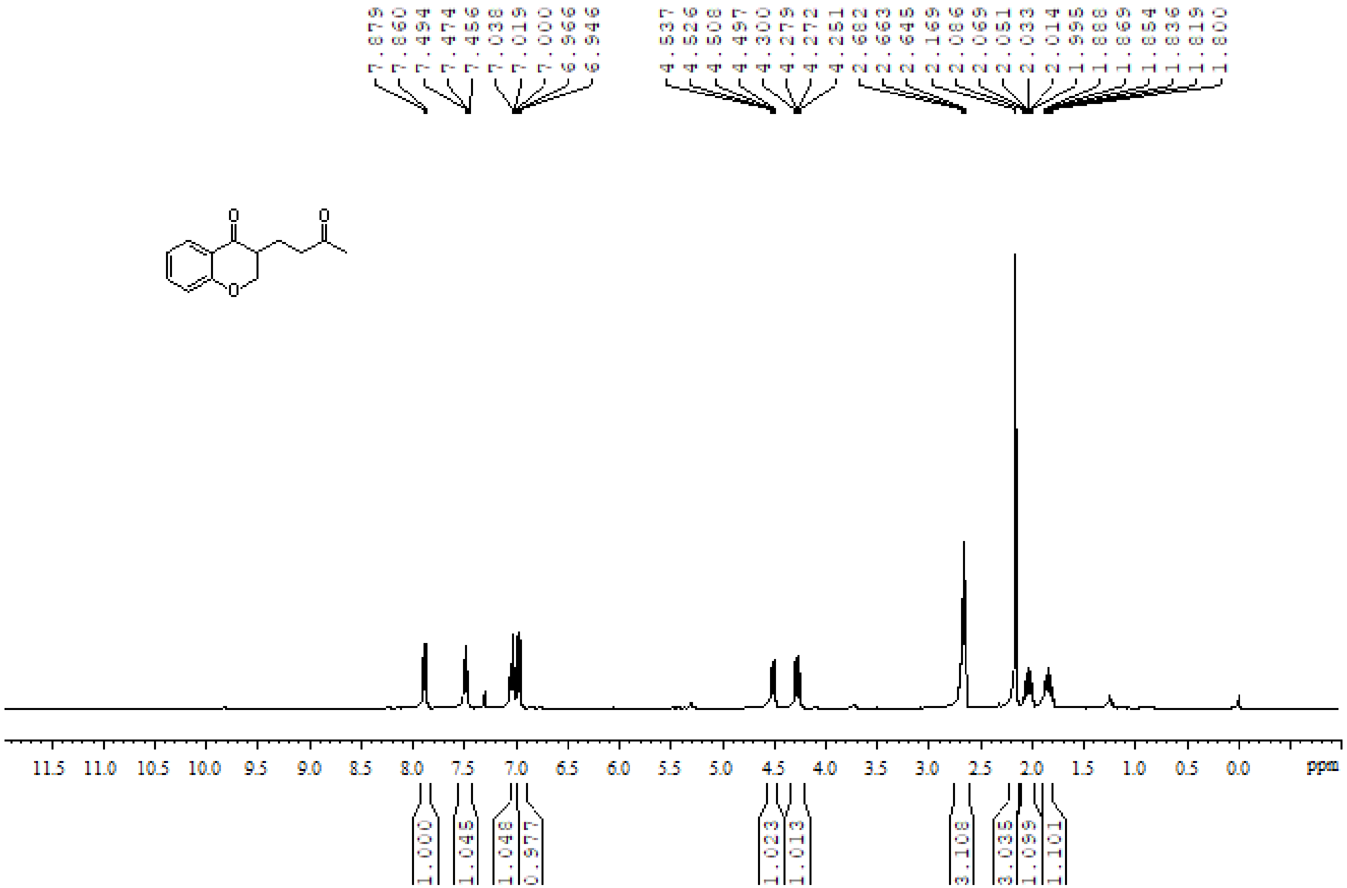


3ae-^{13}C

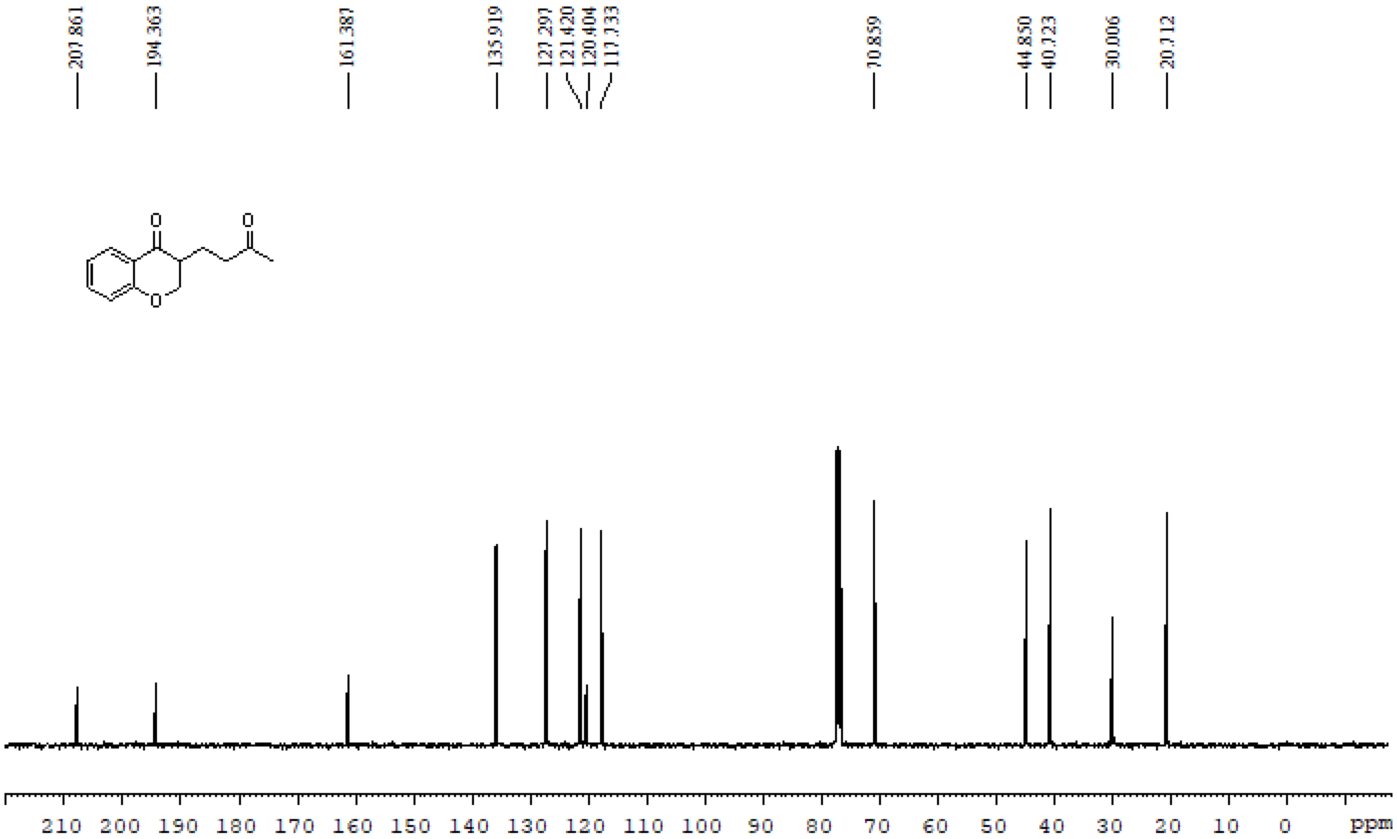


195.172
160.750
135.124
126.538
120.366
119.513
116.690
70.513
68.534
41.434
37.743
28.387
200
180
160
140
120
100
80
60
40
20
0
ppm

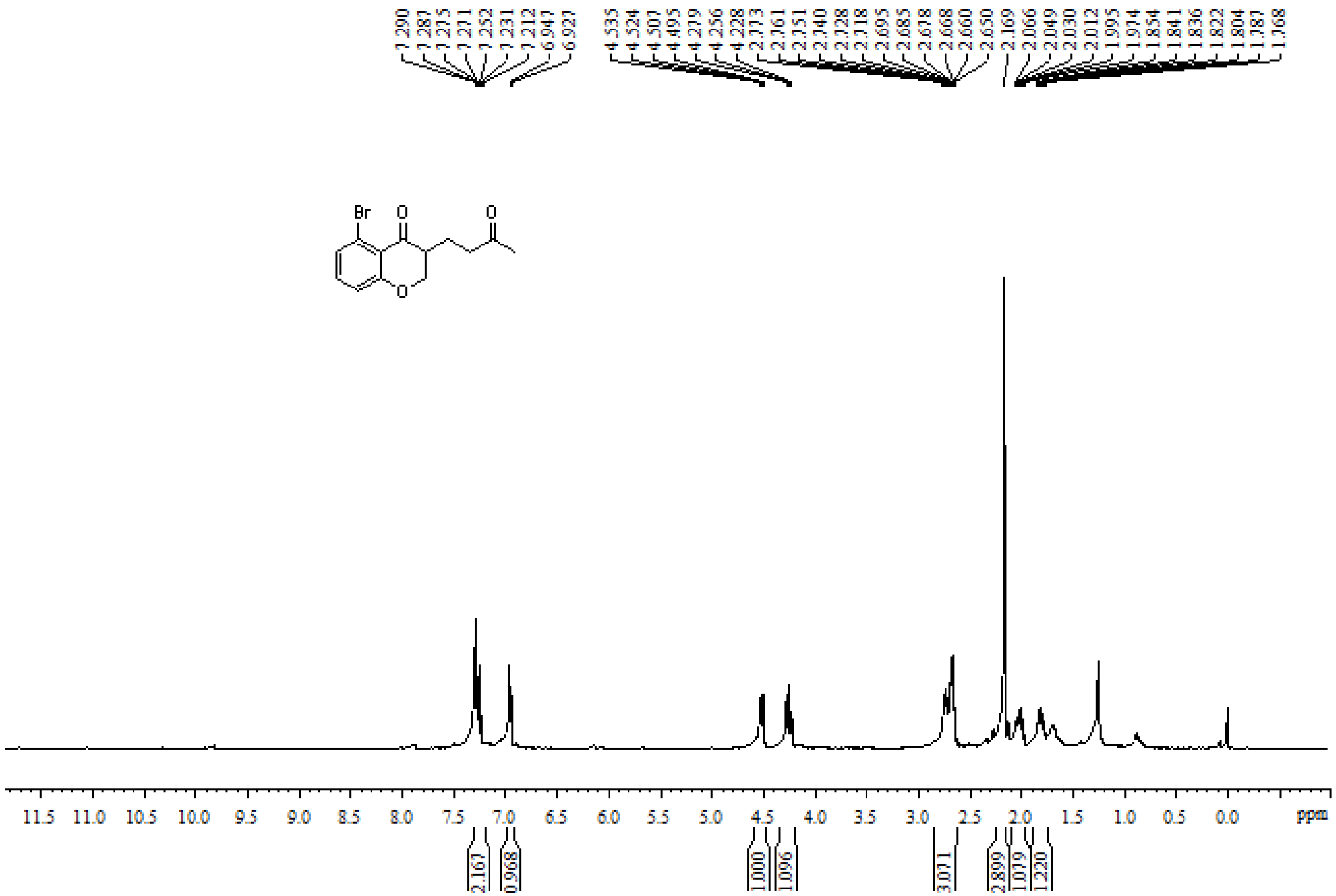
5a-¹H



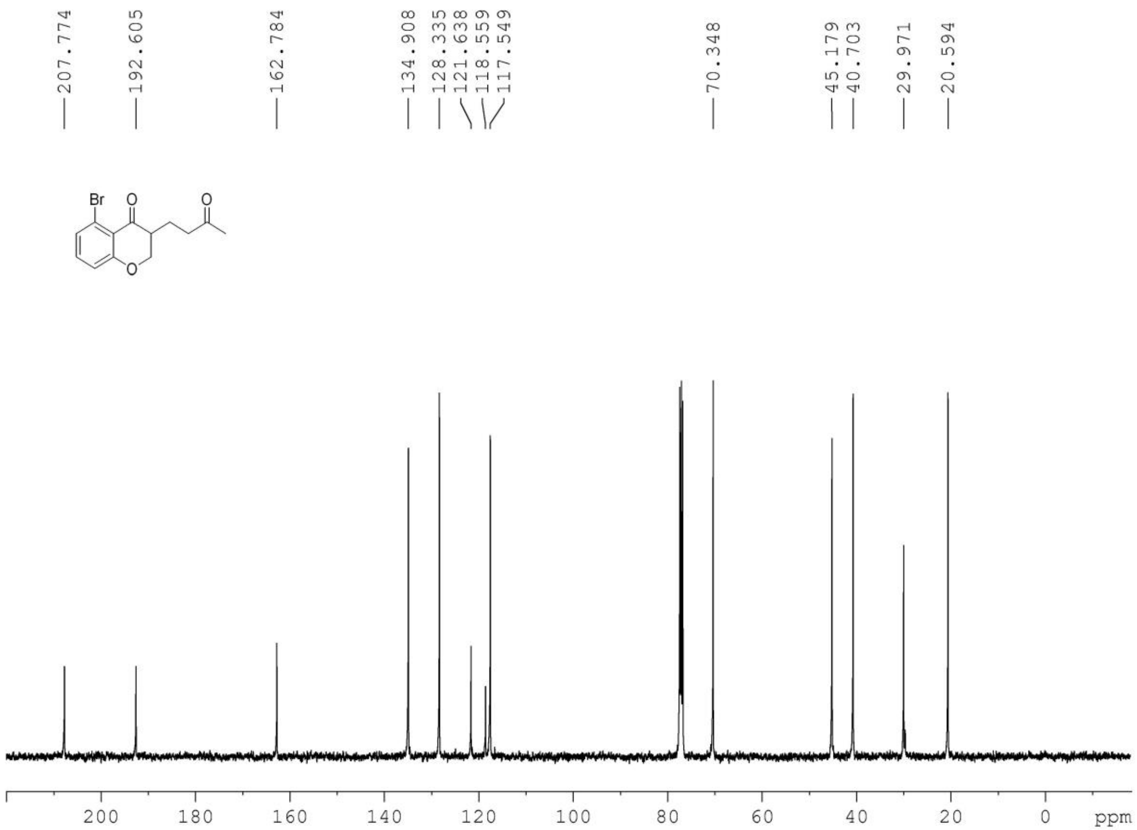
5a-^{13}C


207.861
194.363
161.387
135.919
127.293
121.420
120.404
117.733
70.859
44.850
40.723
30.006
20.712
O
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

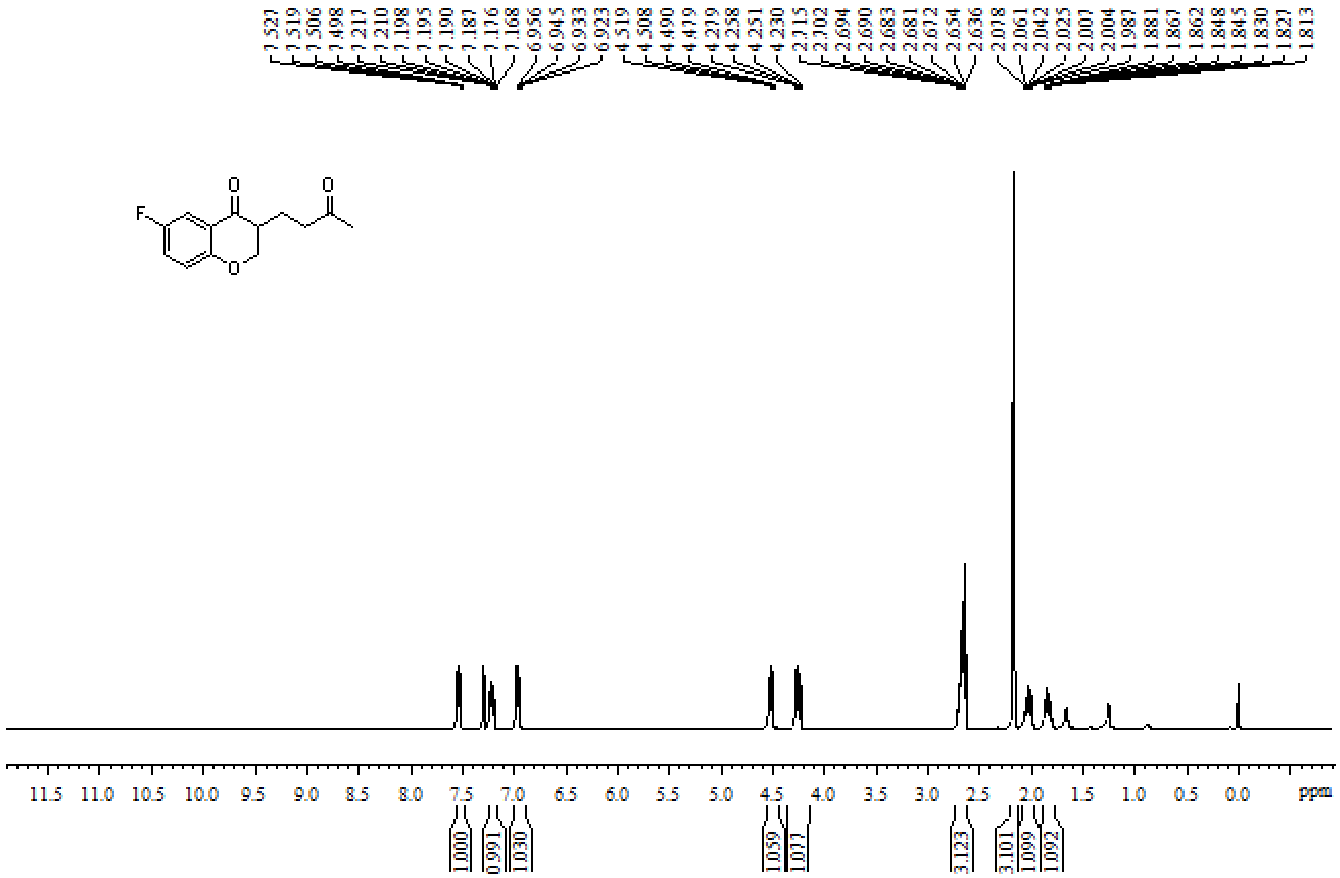
5b-[1]H



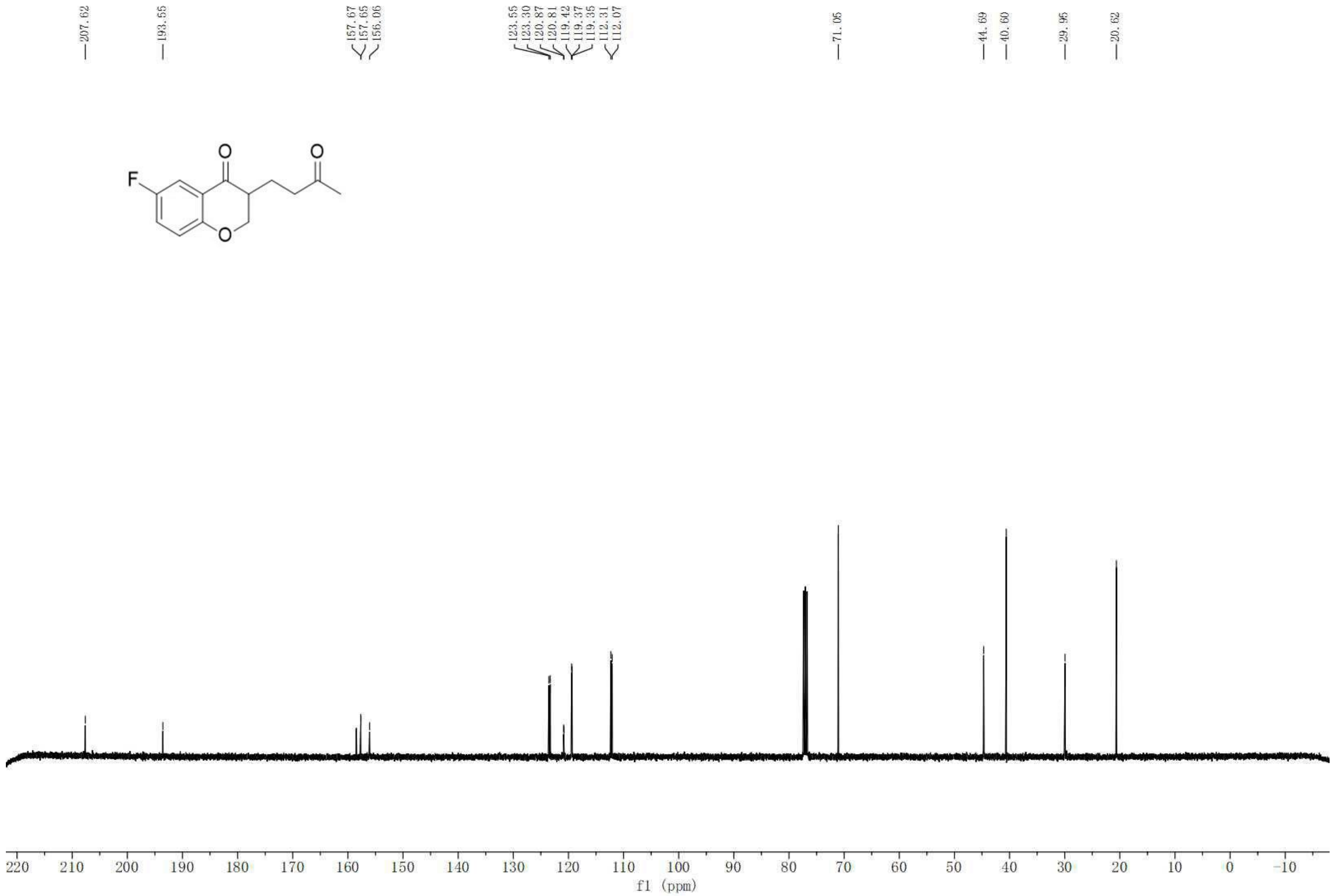
5b-^{13}C


207.774
192.605
162.784
134.908
128.335
121.638
118.559
117.549
70.348
45.179
40.703
29.971
20.594
Br
O
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

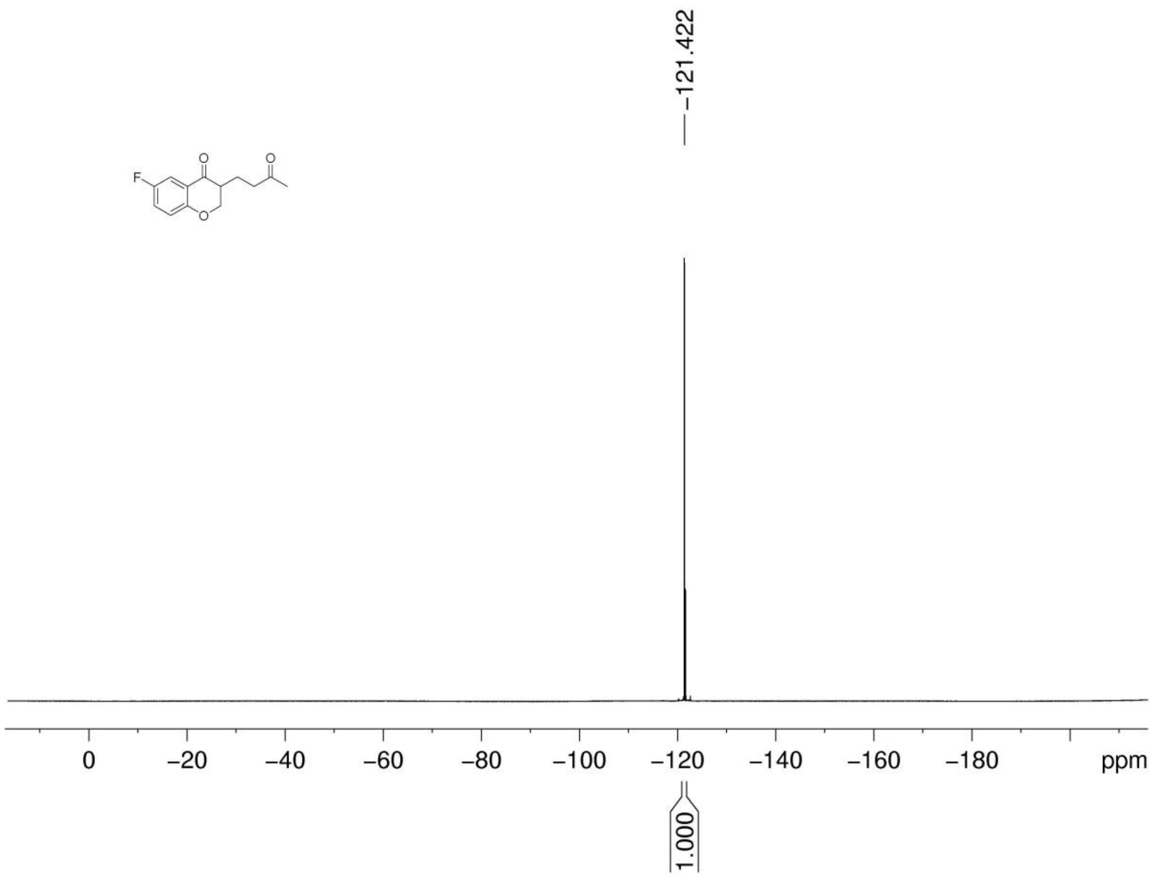
5c-¹H



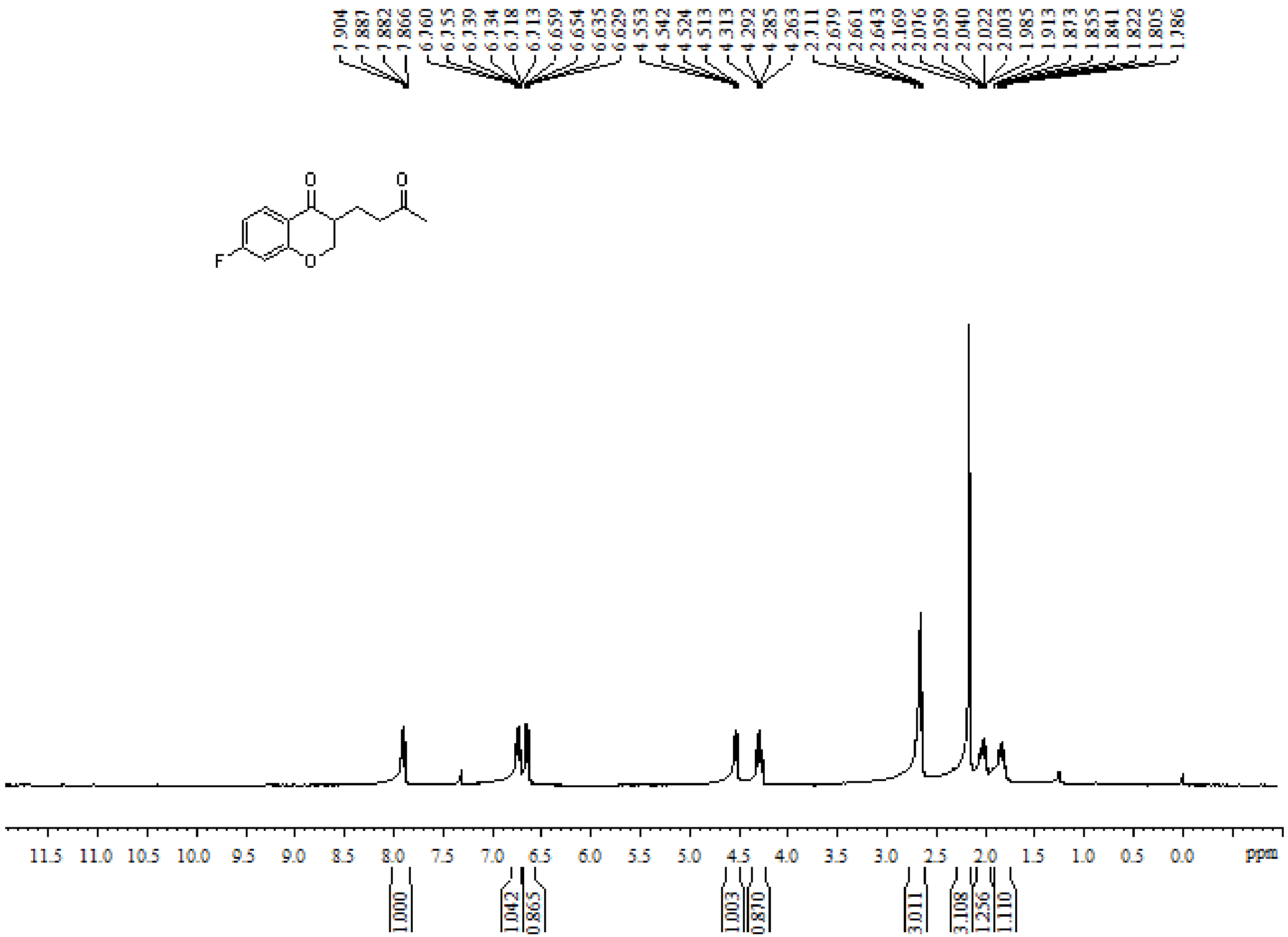
5c-^{13}C


207.62
193.55
157.67
157.65
156.06
123.55
123.30
120.87
120.81
119.42
119.37
119.35
112.31
112.07
71.05
44.69
40.60
29.95
20.62
F
O
O
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

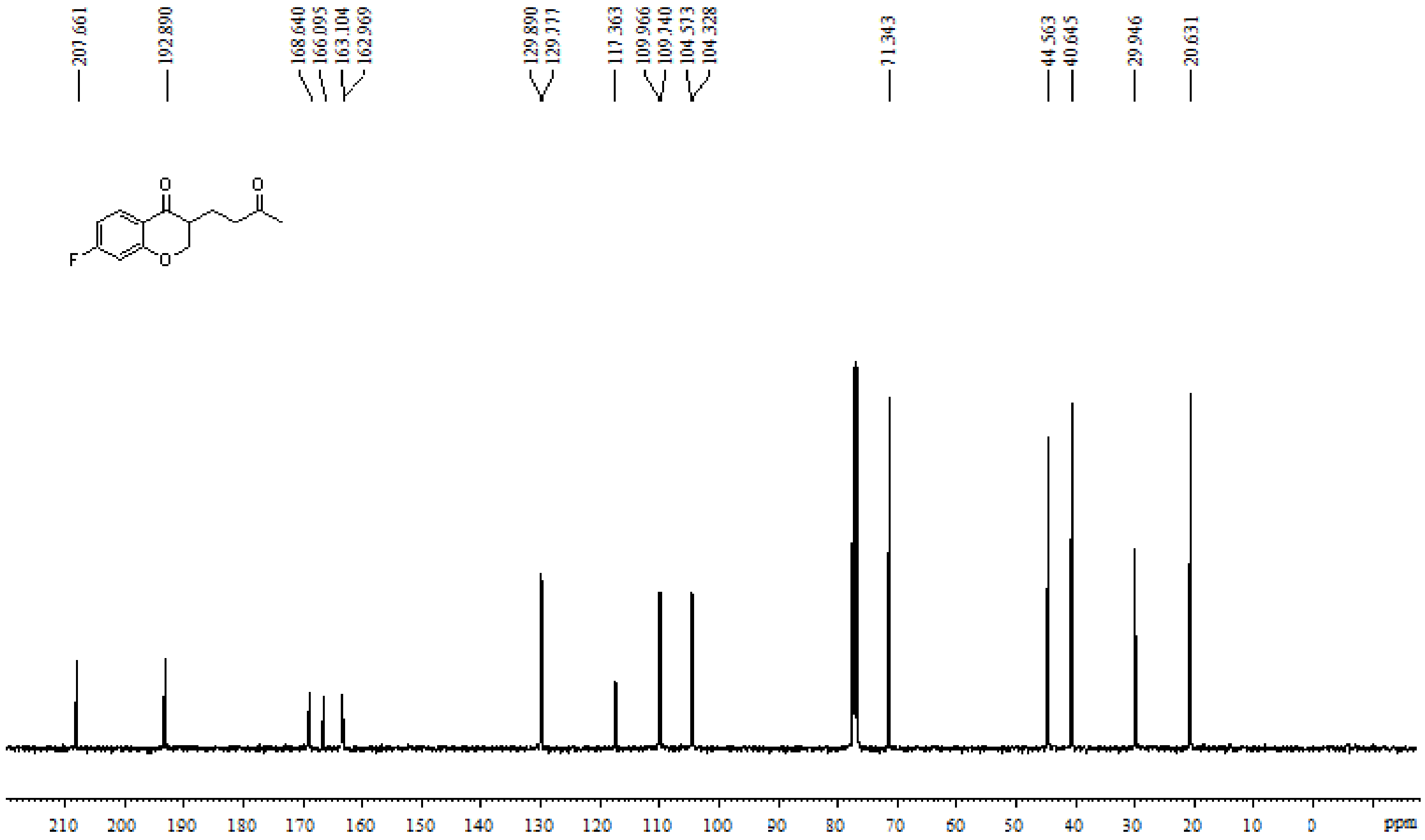
5c-^{19}F



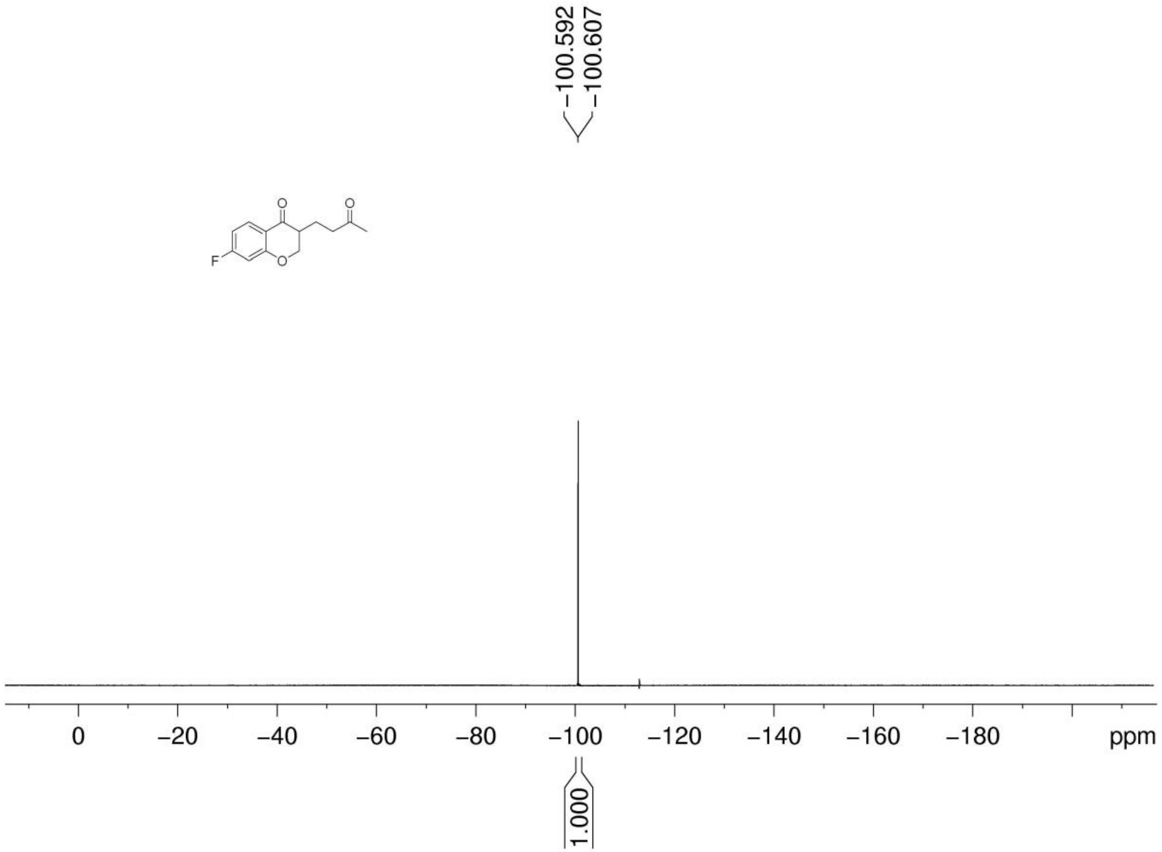
5d-¹H


F
O
O
O
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 ppm
1.000
1.042
0.865
1.003
0.870
3.011
3.108
1.256
1.110

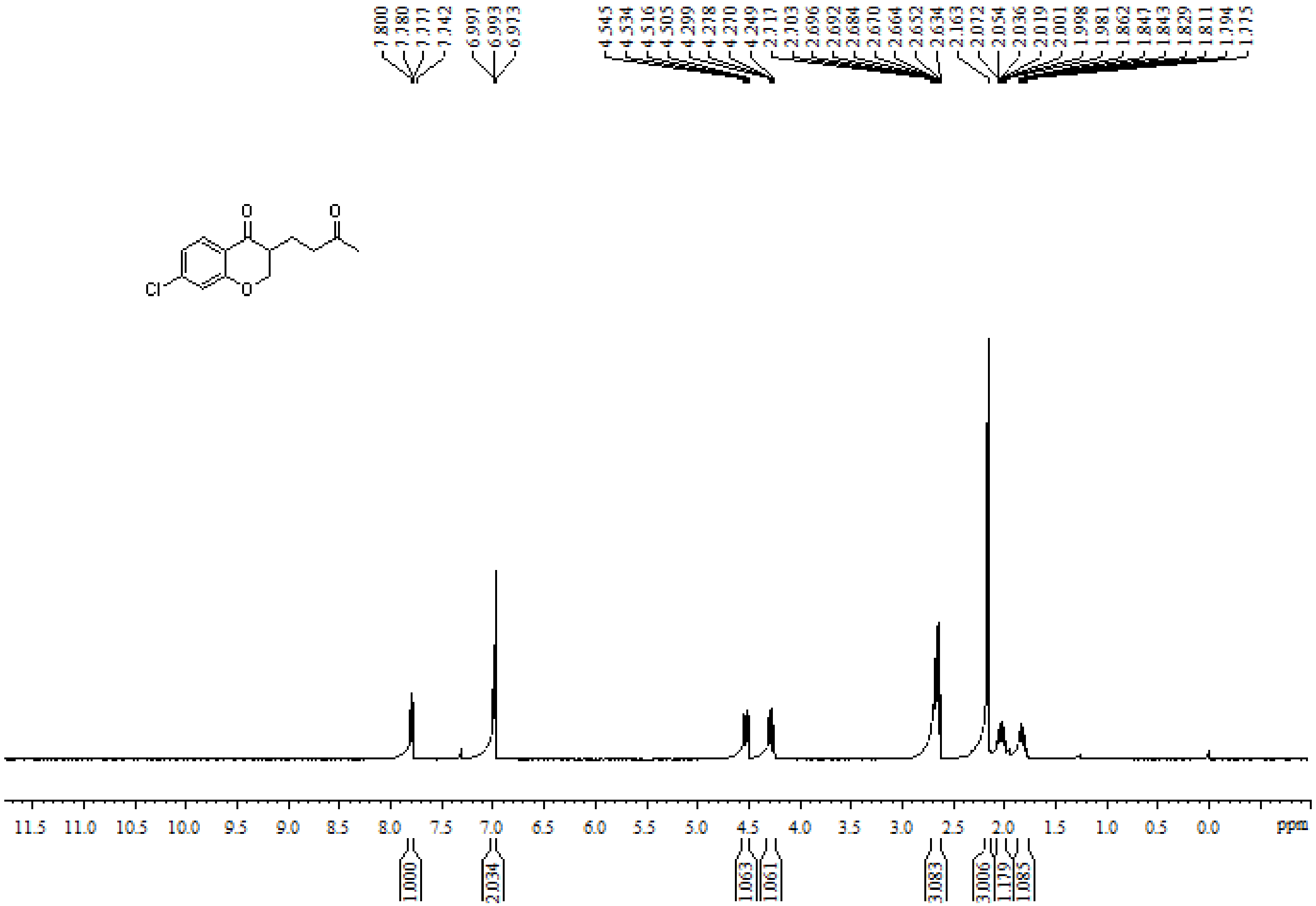
5d-^{13}C


207.661
192.890
168.640
166.095
163.104
162.969
129.890
129.777
117.363
109.966
109.740
104.573
104.328
71.343
44.563
40.645
29.946
20.631
O
O
F
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

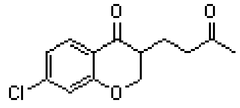
5d-^{19}F

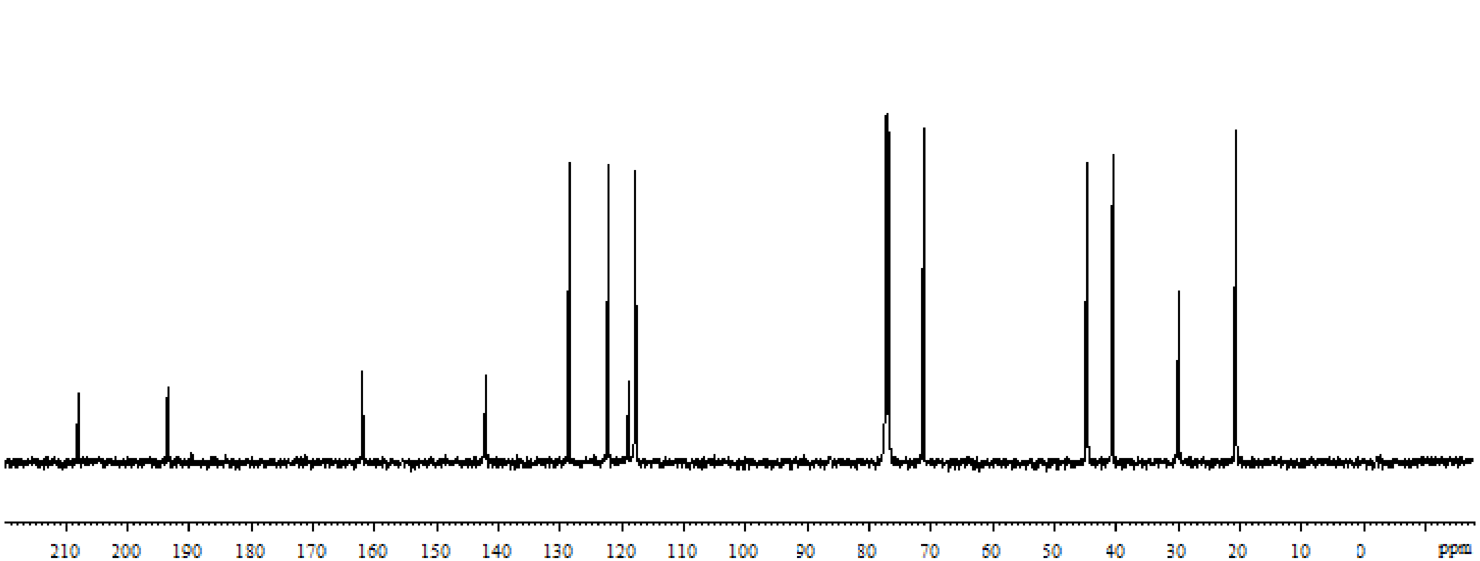


5e-[1]H

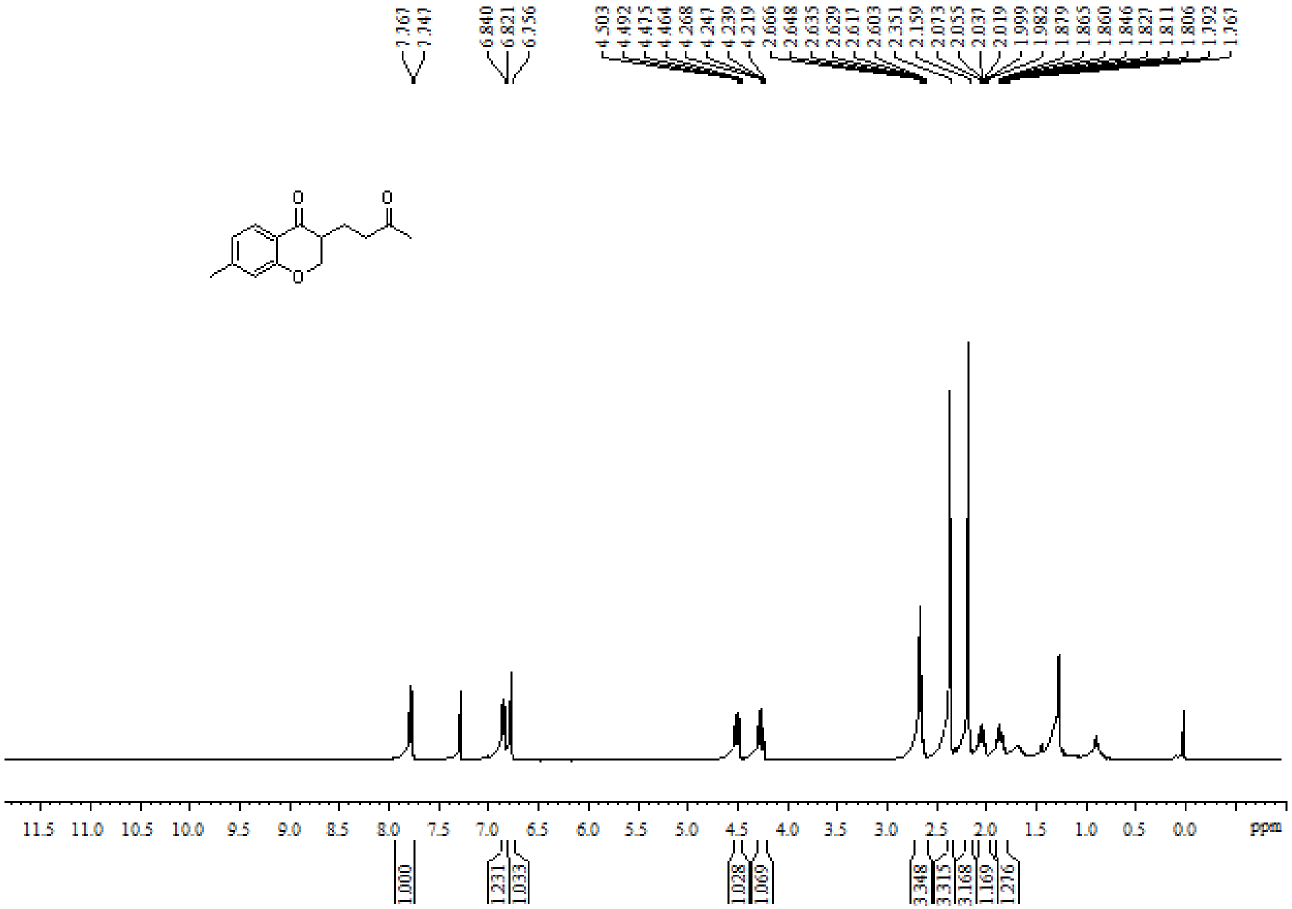


5e-^{13}C

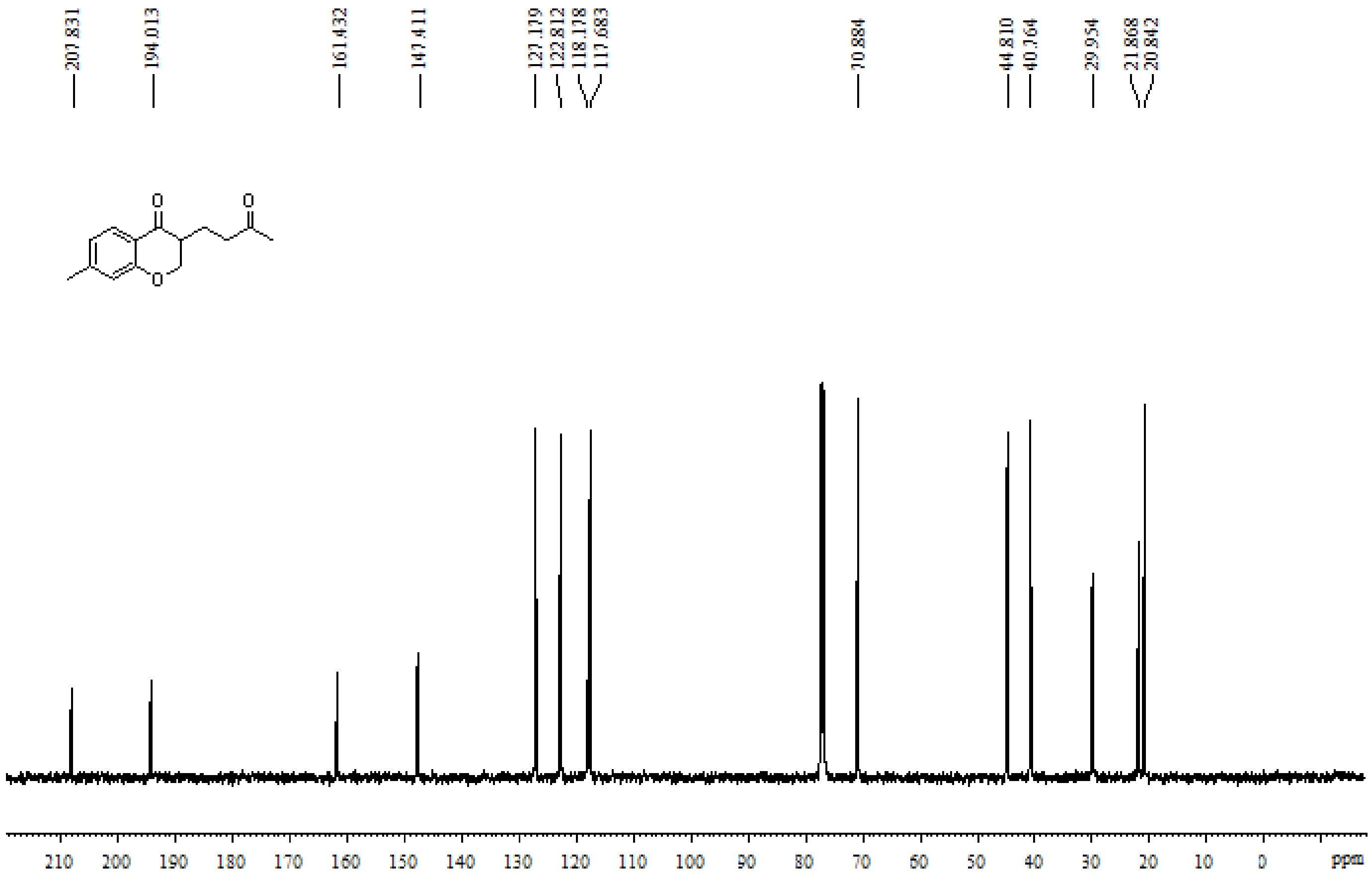



207.627
193.260
161.730
141.730
128.551
122.235
119.001
117.860
71.204
44.694
40.614
29.965
20.610
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

5f-[1]H

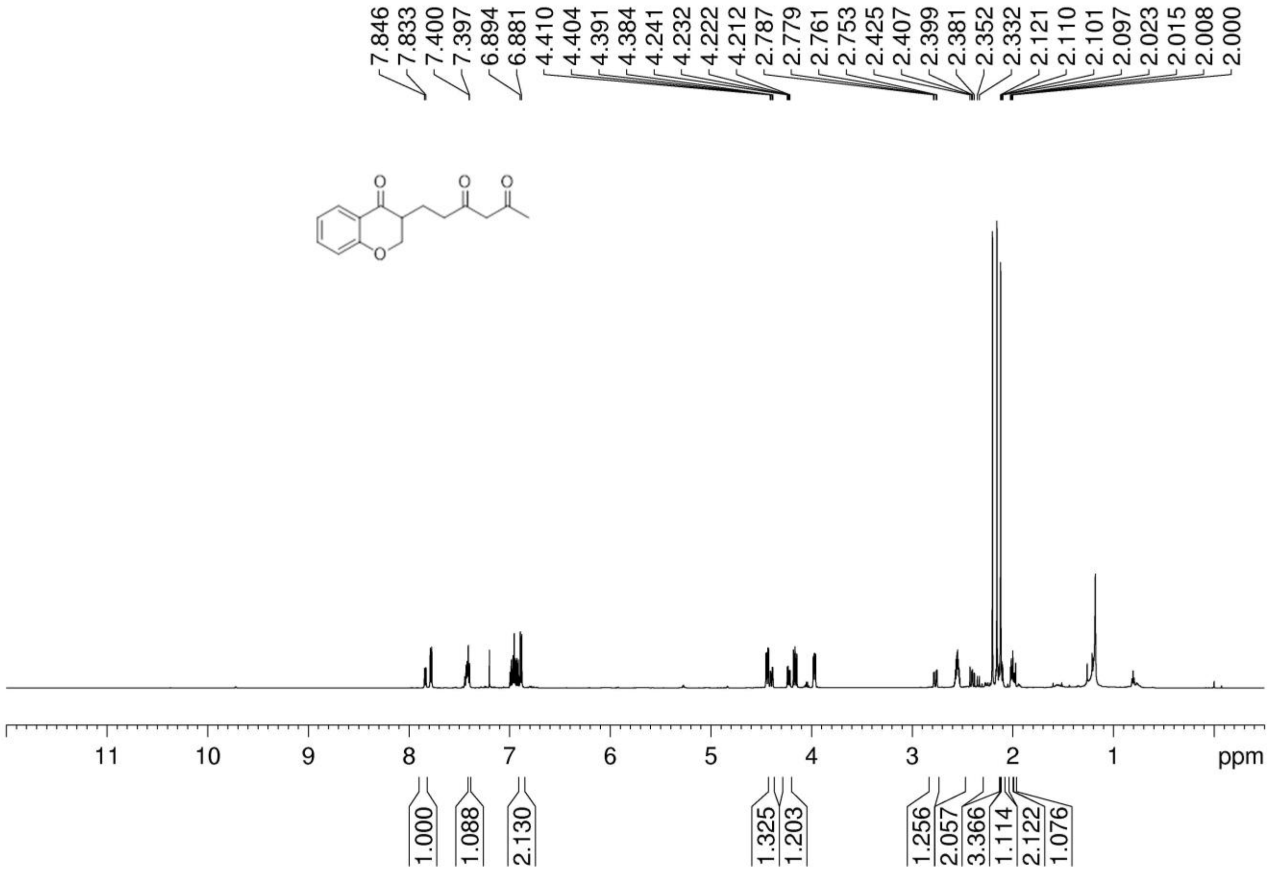


5f-^{13}C



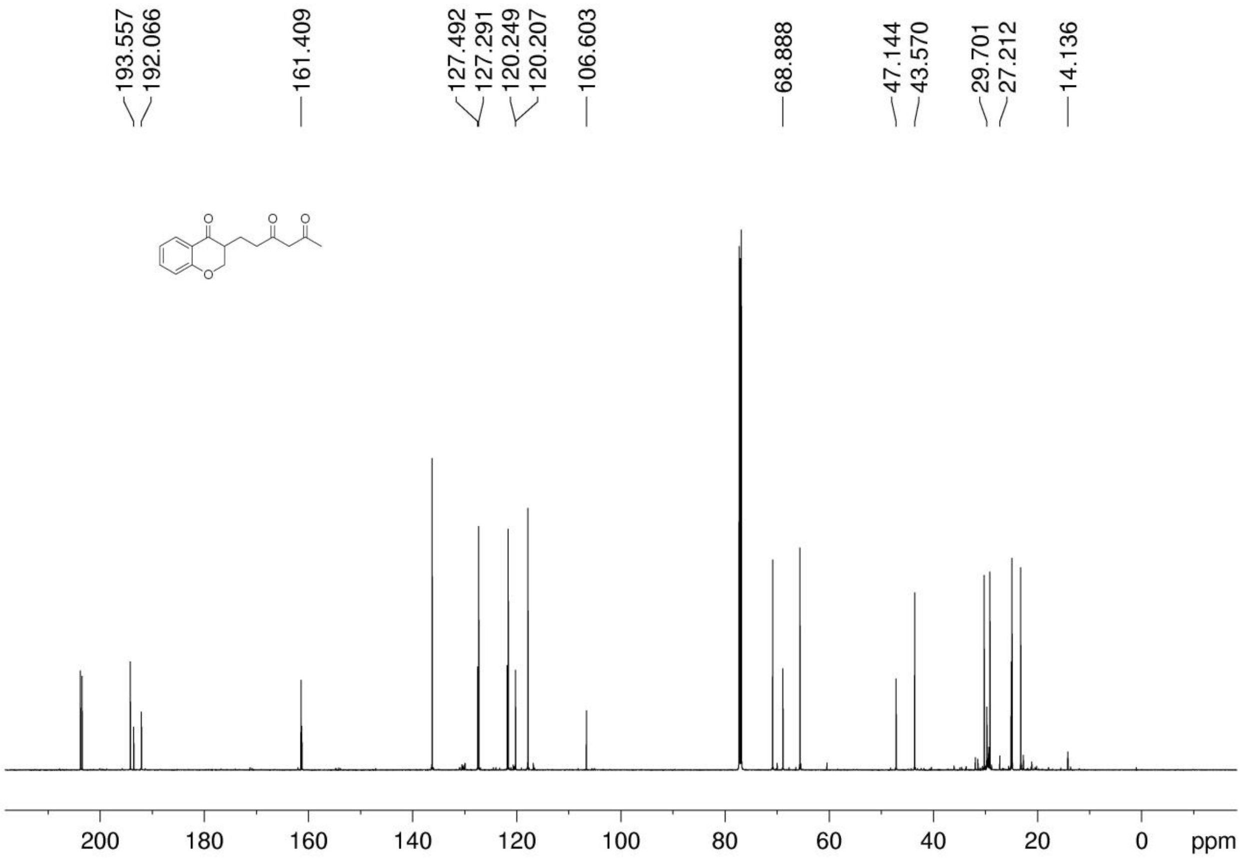
207.831
194.013
161.432
147.411
127.179
122.812
118.178
117.683
70.884
44.810
40.764
29.954
21.868
20.842
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

5ab-[1]H



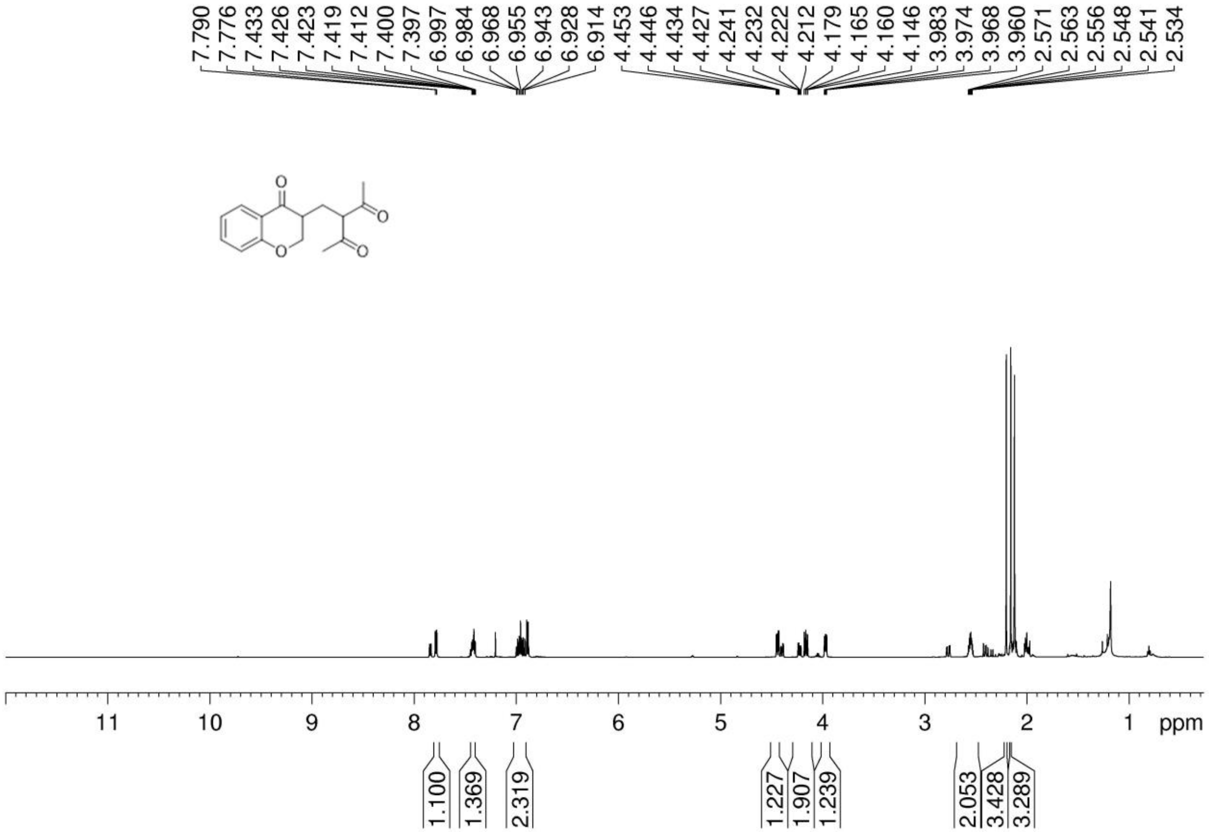
7.846
7.833
7.400
7.397
6.894
6.881
4.410
4.404
4.391
4.384
4.241
4.232
4.222
4.212
2.787
2.779
2.761
2.753
2.425
2.407
2.399
2.381
2.352
2.332
2.121
2.110
2.101
2.097
2.023
2.015
2.008
2.000
O
O
O
O
11
10
9
8
7
6
5
4
3
2
1
ppm
1.000
1.088
2.130
1.325
1.203
1.256
2.057
3.366
1.114
2.122
1.076

5ab-^{13}C

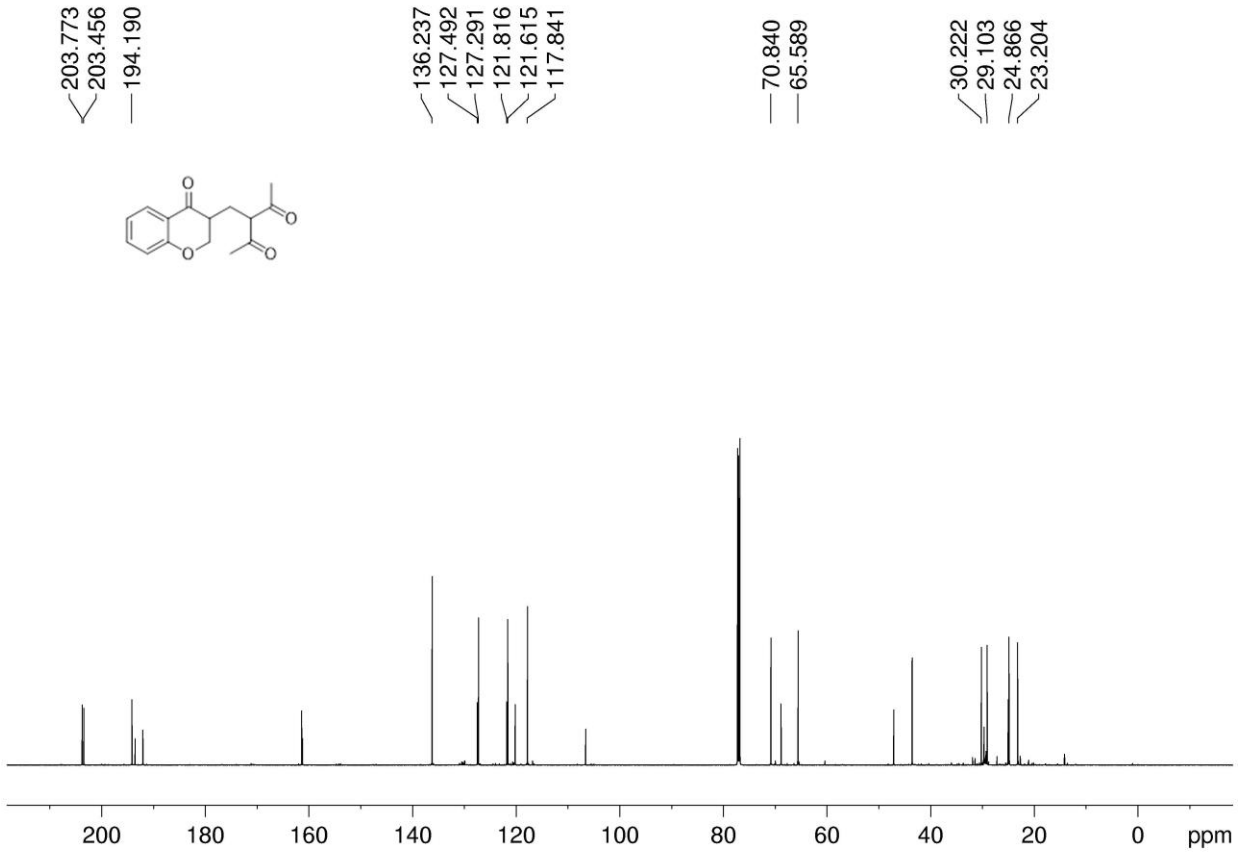


193.557
192.066
161.409
127.492
127.291
120.249
120.207
106.603
68.888
47.144
43.570
29.701
27.212
14.136
200 180 160 140 120 100 80 60 40 20 0 ppm

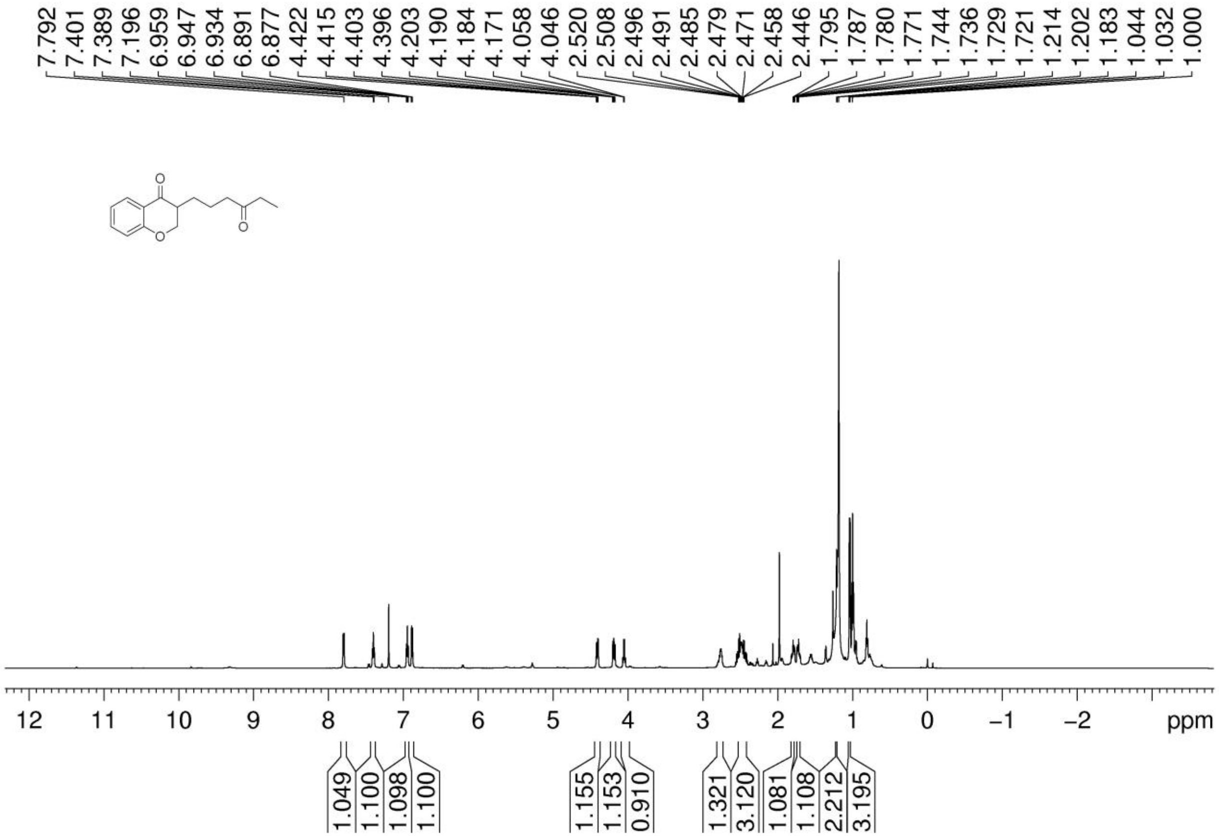
5ab'-^{1}H


7.790
7.776
7.433
7.426
7.423
7.419
7.412
7.400
7.397
6.997
6.984
6.968
6.955
6.943
6.928
6.914
4.453
4.446
4.434
4.427
4.241
4.232
4.222
4.212
4.179
4.165
4.160
4.146
3.983
3.974
3.968
3.960
2.571
2.563
2.556
2.548
2.541
2.534
11 10 9 8 7 6 5 4 3 2 1 ppm
1.100
1.369
2.319
1.227
1.907
1.239
2.053
3.428
3.289

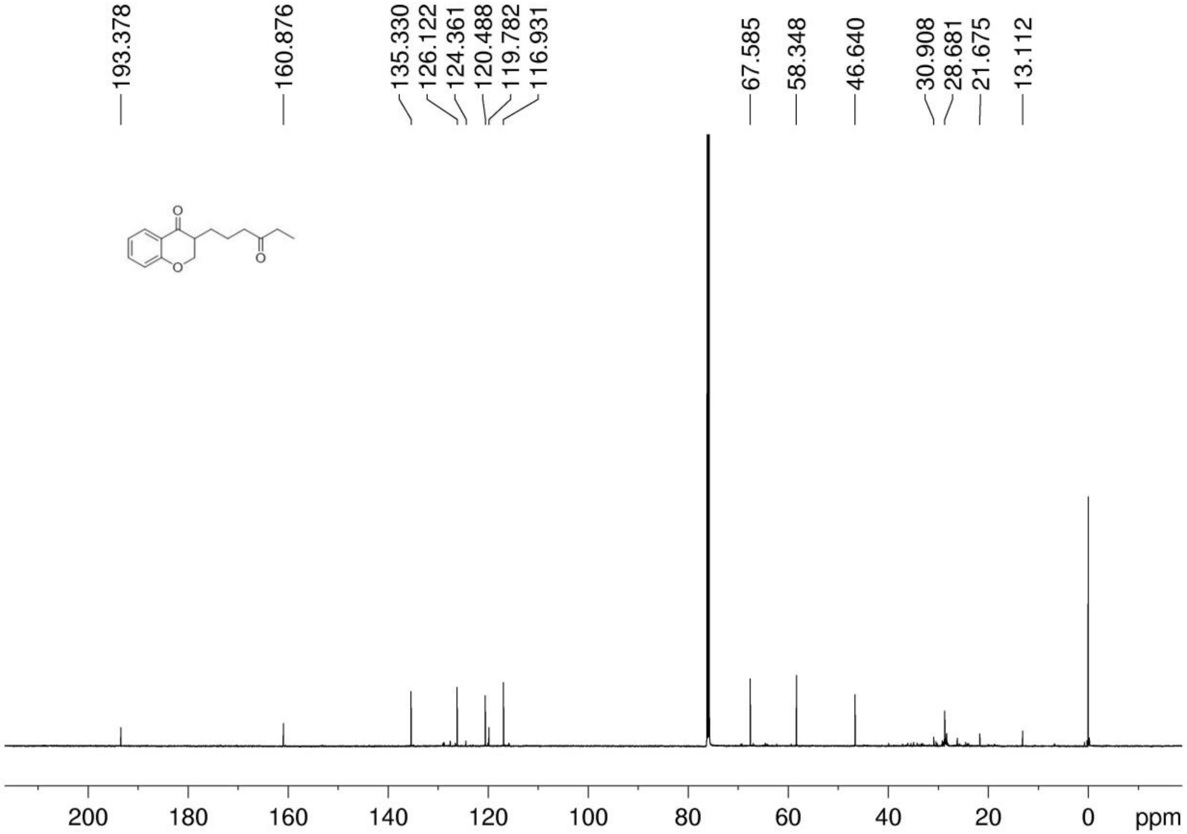
5ab'-^{13}C


203.773
203.456
194.190
136.237
127.492
127.291
121.816
121.615
117.841
70.840
65.589
30.222
29.103
24.866
23.204
O
O
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

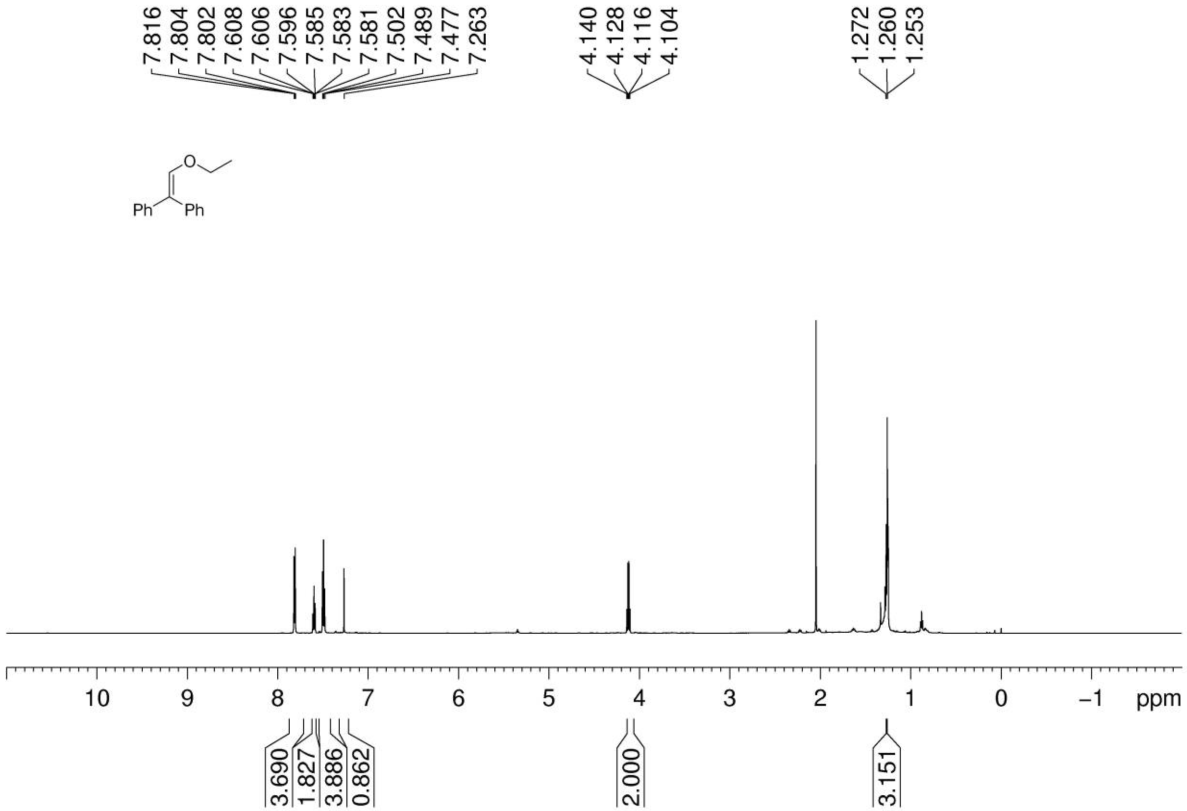
5ac-^{1}H


7.792
7.401
7.389
7.196
6.959
6.947
6.934
6.891
6.877
4.422
4.415
4.403
4.396
4.203
4.190
4.184
4.171
4.058
4.046
2.520
2.508
2.496
2.491
2.485
2.479
2.471
2.458
2.446
1.795
1.787
1.780
1.771
1.744
1.736
1.729
1.721
1.214
1.202
1.183
1.044
1.032
1.000
12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2 ppm
1.049
1.100
1.098
1.100
1.155
1.153
0.910
1.321
3.120
1.081
1.108
2.212
3.195

5ac-^{13}C

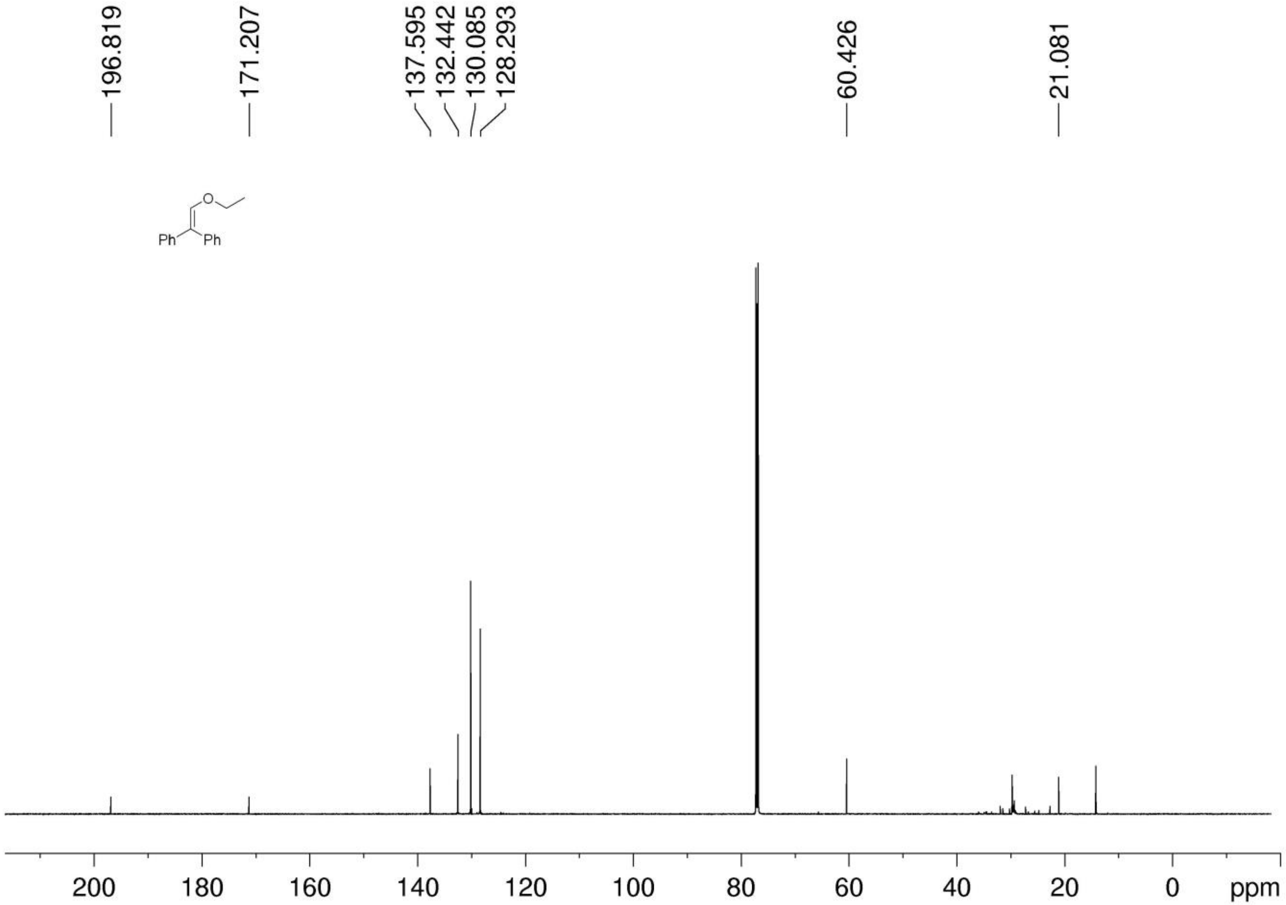

193.378
160.876
135.330
126.122
124.361
120.488
119.782
116.931
67.585
58.348
46.640
30.908
28.681
21.675
13.112
200
180
160
140
120
100
80
60
40
20
0
ppm

7-¹H



7.816
7.804
7.802
7.608
7.606
7.596
7.585
7.583
7.581
7.502
7.489
7.477
7.263
4.140
4.128
4.116
4.104
1.272
1.260
1.253
O
Ph
Ph
10
9
8
7
6
5
4
3
2
1
0
–1
ppm
3.690
1.827
3.886
0.862
2.000
3.151

7-^{13}C


196.819
171.207
137.595
132.442
130.085
128.293
60.426
21.081
O
Ph
Ph
200
180
160
140
120
100
80
60
40
20
0
ppm