Electronic Supplementary Information (ESI)

Lipase-catalyzed regioselective domino reaction for the synthesis of chromenone derivatives

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Experimental Section

Materials and methods

Trypsin (Bovine pancreas, ≥2500 u/mg), Lipase from *Candida antarctia* B (CAL-B, 2 U/mg), Lipase from *Mucor miehei* (MML, 102.5 u/g), Lipase from Bovine pancreas (BPL, 15-35 u/g), Amano Lipase from *Mucor jaranicus* (MJL, 10 U/mg), Lipase from *Pseudomonas fluorescens* (PFL, ≥600 u/g), Lipase from *Candida rugosa* (CRL, 739 u/mg) were purchased from Sigma-Aldrich. Bovine Serum Albumin (BSA), Lipase from *Candida cylindrucea* (CCL, 7.29 u/mg) was purchased from Aladdin Co., Ltd. (Shanghai, China). Unless otherwise mentioned, all reagents were obtained from commercial suppliers and used without further purification. The NMR spectra were recorded on a Bruker 400 MHz instrument using $CDCl_3$ as solvents. Chemical shifts (δ) were expressed in ppm with TMS as internal standard, and coupling constants (*J*) were reported in Hz. HPLC was carried out on Waters instrument (Waters 2695, 2998) using a C18 column (250 mm × 4.6 mm) from Dikma Technologies. Elution was performed with a mixture of CH_3OH/H_2O (10/90-70/30, v/v) by gradient elution method at 0.8 mL/min at 30 °C. HRMS were performed on Bruker Daltonics Bio TOF mass spectrometer. Column chromatography was carried on silica gel (200-300 mesh) using ethyl acetate-petroleum ether as mobile phase.

General procedure for the synthesis of 7,8-dihydro-2H-chromen-5(6H)-ones

1,3-dione (2 mmol), *α,β*-unsaturated aldehyde (10 mmol), BPL (100 mg), acetonitrile (5 mL) were added to a round-bottom flask, and shaken at 200 rpm at 30 °C. Reactions were monitored by thin-layer chromatography and visualized by UV light. After completion of the reaction, the solid residue was filtered off and the solvent was evaporated. In the end, the products were obtained by flash chromatography with petroleum ether/ethyl acetate (2:1).

General procedure for the synthesis of 3,4,7,8-tetrahydro-2H-chromen-5(6H)-ones

1,3-dione (2 mmol), *α,β*-unsaturated aldehyde (10 mmol), PFL (100 mg), dichloromethane (4.75 mL) and deionized water (0.25 mL) were added to a round-bottom flask, and shaken at 200 rpm at 30 °C. After finishing the reaction, the products were purified by flash chromatography with petroleum ether/ethyl acetate (5:1).

Supplementary Information about optimization of reaction conditions

Table S1 The effect of molar ratio on the BPL-catalyzed domino reaction[a]

entry	Molar ratio (**1a : 2a**)	Yield of **3a**[b] [%]	Yield of **4a**[c] [%]
1	1:1	21	trace
2	1:2	40	trace
3	1:5	91	trace
4	1:10	73	trace
5	1:20	46	trace
6	1:40	10	trace
7	2:1	26	trace
8	5:1	26	trace
9	10:1	26	trace
10	20:1	35	51

[a] Reaction conditions: **1a**, **2a**, BPL (10 mg), acetonitrile (1 mL) were added to a 10 mL erlenmeyer flask, and shaken at 200 rpm at 30 °C for 24 h.

[b] Determined by HPLC.

[c] Determined by HPLC.

Table S2 The effect of molar ratio on the PFL-catalyzed domino reaction[a]

entry	Molar ratio (**1a: 2a**)	Yield of **3a**[b] [%]	Yield of **4a**[c] [%]
1	1:1	9	44
2	1:2	9	60
3	1:5	10	63
4	1:10	10	62
5	1:20	11	60
6	1:40	11	58
7	2:1	16	37
8	5:1	40	21
9	10:1	78	21
10	20:1	91	10

[a]Reaction conditions: **1a**, **2a**, PFL (10 mg), dichloromethane (950 μL), and H_2O (50 μL)were added to a 10 mL erlenmeyer flask, and shaken at 200 rpm at 30 °C for 24 h.

[b] Determined by HPLC.

[c] Determined by HPLC.

Figure S1 Complementary HPLC traces for Table 1 entries 2 and 3

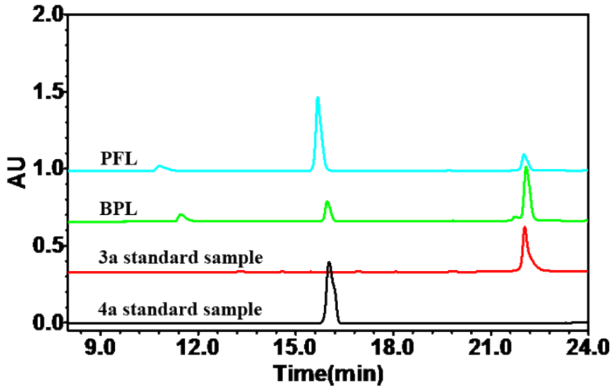


Figure S1 *Blue*: the crude HPLC traces of PFL-catalyzed domino reaction, reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol), PFL (10 mg), DMSO (1 mL), 200 rpm, 30°C, 24 h; *green*: the crude HPLC trace of BPL-catalyzed domino reaction, reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol), BPL (10 mg), DMSO (1 mL), 200 rpm, 30 °C, 24 h.

Figure S2 Complementary HPLC traces for Fig. 3

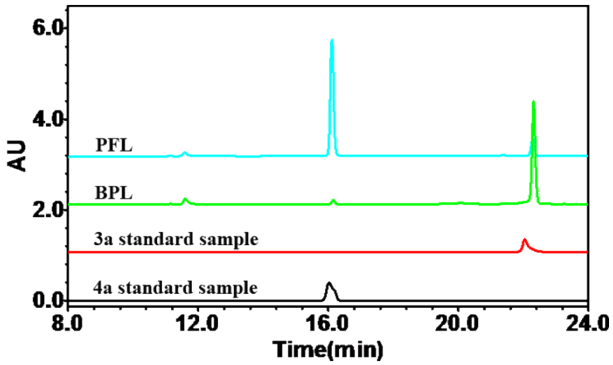


Figure S2 *Blue*: the crude HPLC traces of PFL-catalyzed domino reaction, reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol), PFL (20 mg), dichloromethane (950 μL), H_2O (50 μL), 200 rpm, 30°C, 24 h; *green*: the crude HPLC trace of BPL-catalyzed domino reaction, reaction conditions: **1a** (0.1 mmol), **2a** (0.5 mmol), BPL (20 mg), CH_3CN (1 mL), 200 rpm, 30 °C, 24 h.

Figure S3 The effect of temperature on the BPL- and PFL-catalyzed domino reaction

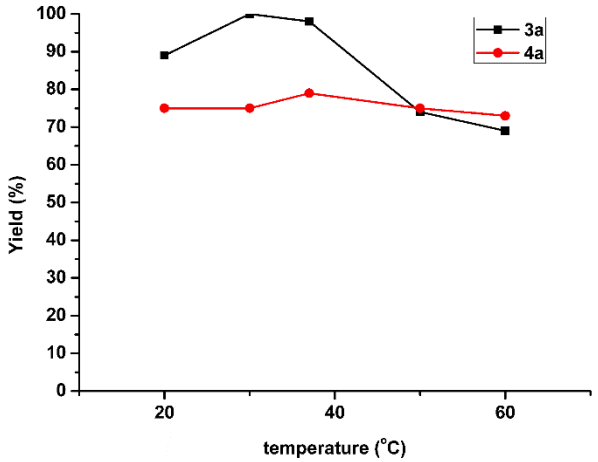


Figure S3 The effect of temperature on the BPL-catalyzed domino reaction (in black)[a] and PFL-catalyzed (in red)[b] domino reaction. Reaction conditions: (a) **1a** (0.1 mmol), **2a** (0.5 mmol), BPL (20 mg), acetonitrile (1 mL),

200 rpm, 24 h; (b) **1a** (0.1 mmol), **2a** (0.5 mmol), PFL (20 mg), dichloromethane (950 μL), and H_2O (50 μL), 200 rpm, 24 h. All yields were determined by HPLC.

^{1}H-NMR, ^{13}C-NMR and HRMS data of chromenone derivatives

2-methyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3a**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.51–6.36(m, 1H), 5.27 (dd, *J* = 10.0, 3.1 Hz, 1H), 5.00 (qdd, *J* = 6.5, 3.1, 1.7 Hz, 1H), 2.38 (ddd, *J* = 9.1, 7.4, 4.3 Hz, 4H), 1.98 – 1.93 (m, 2H), 1.40 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.87, 172.29, 118.86, 117.30, 111.33, 77.41, 77.09, 76.77, 73.92, 36.42, 28.32, 21.67, 20.62. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{10}H_{12}O_2$, 165.0915; found 165.0915.

2-ethyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3b**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (dd, *J* = 10.1, 1.7 Hz, 1H), 5.35 – 5.19 (m, 1H), 4.83 (dtd, *J* = 7.6, 3.1, 1.6 Hz, 1H), 2.45 – 2.30 (m, 4H), 2.01 – 1.89 (m, 2H), 1.79 – 1.65 (m, 2H), 1.00 – 0.90 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.99, 172.82, 117.71, 117.50, 111.33, 78.77, 77.43, 77.11, 76.79, 36.34, 28.78, 28.24, 20.58, 8.55. HRMS (ESI, m/z): $[M-H]^+$ calcd. for $C_{11}H_{14}O_2$, 177.0916; found 177.0911.

2-propyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3c**)

Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 – 6.35 (m, 1H), 5.25 (dd, *J* = 10.0, 3.2 Hz, 1H), 4.92 – 4.81 (m, 1H), 2.42 – 2.29 (m, 4H), 1.97 – 1.88 (m, 2H), 1.76 – 1.65 (m, 1H), 1.64 – 1.54 (m, 1H), 1.42 (dddt, *J* = 17.3, 13.3, 10.0, 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.71, 172.45, 117.81, 117.52, 111.37, 77.44, 77.42, 77.13, 76.81, 37.83, 36.37, 28.24, 20.59, 17.53, 13.84. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{12}H_{16}O_2$, 193.1228; found 193.1225.

2,2-dimethyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3d**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (d, *J* = 10.0 Hz, 1H), 5.19 (d, *J* = 10.0 Hz, 1H), 2.34 (dt, *J* = 9.1, 6.7 Hz, 4H), 1.93 (dd, *J* = 13.0, 6.5 Hz, 2H), 1.35 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.78, 171.56, 122.82, 115.75, 110.47, 79.66, 77.49, 77.17, 76.85, 36.36, 28.58, 28.35, 20.60. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{11}H_{14}O_2$, 179.1073; found 179.1072.

2,7,7-trimethyl-7,8-dihydro-2H-chromen-5(6H)-one (**3e**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (d, *J* = 9.9 Hz, 1H), 5.36 – 5.18 (m, 1H), 4.97 (ddd, *J* = 6.5, 3.2, 1.6 Hz, 1H), 2.30 – 2.18 (m, 4H), 1.43 – 1.34 (m, 3H), 1.06 – 1.01 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.55, 170.81, 118.61, 117.13, 110.22, 73.94, 50.34, 42.07, 32.20, 28.43, 28.34, 21.62. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{12}H_{16}O_2$, 193.1228; found 193.1229.

2-ethyl-7,7-dimethyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3f**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (dd, *J* = 10.0, 1.4 Hz, 1H), 5.25 (dd, *J* = 10.0, 3.2 Hz, 1H), 4.95 – 4.78 (m, 1H), 2.30 – 2.20 (m, 4H), 1.69 (ddd, *J* = 13.0, 7.4, 4.6 Hz, 2H), 1.03 (d, *J* = 3.8 Hz, 6H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.51, 171.18, 117.55, 117.24, 110.18, 78.80, 77.42, 77.10, 76.78, 50.31, 42.03, 32.14, 28.77, 28.40, 28.35, 8.52. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{13}H_{18}O_2$, 207.1385; found 207.1382.

7,7-dimethyl-2-propyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3g**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (dd, J = 10.0, 1.2 Hz, 1H), 5.26 (dd, J = 10.0, 3.2 Hz, 1H), 4.99 – 4.79 (m, 1H), 2.28 – 2.20 (m, 4H), 1.76 – 1.67 (m, 1H), 1.64 – 1.56 (m, 1H), 1.49 – 1.35 (m, 2H), 1.03 (d, J = 2.2 Hz, 6H), 0.92 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.70, 170.90, 118.65, 117.18, 110.29, 74.01, 50.37, 42.12, 32.25, 30.10, 28.47, 28.38, 21.66. HRMS (ESI, m/z): [M+H]+ calcd. for $C_{14}H_{20}O_2$, 221.1541; found 221.1515.

2,2,7,7-tetramethyl-7,8-dihydro-2*H*-chromen-5(6*H*)-one (**3h**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.39 (d, *J* = 9.9 Hz, 1H), 5.22 (d, *J* = 9.9 Hz, 1H), 2.24 (s, 4H), 1.38 (s, 6H), 1.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.50, 170.10, 122.68, 115.75, 109.54, 79.76, 50.41, 42.44, 32.24, 28.43, 28.34. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{13}H_{18}O_2$, 207.1385; found 207.1384.

2-hydroxy-4-methyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4a**)

White solid; ^{1}H NMR (400 MHz, DMSO) δ 7.34 (dd, *J* = 37.4, 6.3 Hz, 1H), 5.36 – 5.24 (m, 1H), 2.71 – 2.54 (m, 1H), 2.41 – 2.13 (m, 4H), 1.95 – 1.49 (m, 4H), 1.07 (dd, *J* = 40.6, 6.9 Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 196.78, 169.55, 115.28, 93.17, 40.37, 40.16, 39.95, 39.74, 39.53, 37.13, 35.90, 28.58, 23.40, 21.23, 21.07. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}O_3$, 183.1021; found 183.1025.

4-ethyl-2-hydroxy-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4b**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (s, 1H), 5.39 (dd, *J* = 9.6, 2.2 Hz, 1H), 2.66 – 2.54 (m, 1H), 2.37 (dt, *J* = 14.2, 6.4 Hz, 4H), 2.08 (dd, *J* = 17.6, 6.2 Hz, 1H), 1.97 – 1.90 (m, 2H), 1.79 – 1.35 (m, 2H), 1.13 (ddd, *J* = 13.8, 10.0, 7.1 Hz, 1H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.84, 170.60, 115.19, 93.36, 36.90, 31.19, 29.72, 28.79, 26.94, 20.86, 11.61. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{11}H_{16}O_3$, 197.1177; found 197.1176.

2-hydroxy-4-propyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4c**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 – 5.68 (m, 1H), 5.38 (d, *J* = 9.3 Hz, 1H), 2.67 (d, *J* = 4.0 Hz, 1H), 2.46 – 2.23 (m, 4H), 2.02 (dd, *J* = 7.5, 6.1 Hz, 1H), 1.96 – 1.82 (m, 2H), 1.60 (d, *J* = 14.2 Hz, 2H), 1.38 (s, 1H), 1.23 (d, *J* = 7.2 Hz, 1H), 1.09 (s, 1H), 0.86 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.78, 170.60,

115.29, 93.40, 36.87, 36.55, 31.77, 28.93, 28.78, 27.96, 27.83, 20.85, 20.24, 19.86, 14.10, 14.02. HRMS (ESI, m/z): $[M-H]^+$ calcd. for $C_{12}H_{18}O_3$, 209.1177; found 209.1179.

2-hydroxy-4,7,7-trimethyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4d**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (d, *J* = 9.6 Hz, 2H), 2.29 – 2.18 (m, 4H), 1.87 (dd, *J* = 9.1, 6.7 Hz, 1H), 1.82 – 1.70 (m, 1H), 1.26 – 1.21 (m, 1H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 12.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.34, 168.34, 114.62, 93.26, 50.80, 42.37, 35.57, 32.14, 28.83, 27.69, 23.04, 20.98. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{12}H_{18}O_3$, 211.1334; found 211.1336.

4-ethyl-2-hydroxy-7,7-dimethyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4e**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (s, 1H), 5.34 (dd, *J* = 7.2, 2.3 Hz, 1H), 2.54 (s, 1H), 2.24 – 2.07 (m, 4H), 2.06 – 1.95 (m, 1H), 1.86 – 1.52 (m, 2H), 1.23 – 1.03 (m, 1H), 1.00 – 0.91 (m, 6H), 0.88 – 0.78 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.67, 169.12, 113.80, 93.44, 50.66, 42.43, 32.09, 31.18, 29.55, 28.58, 27.84, 26.98, 11.62. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{13}H_{20}O_3$, 225.1490; found 225.1488.

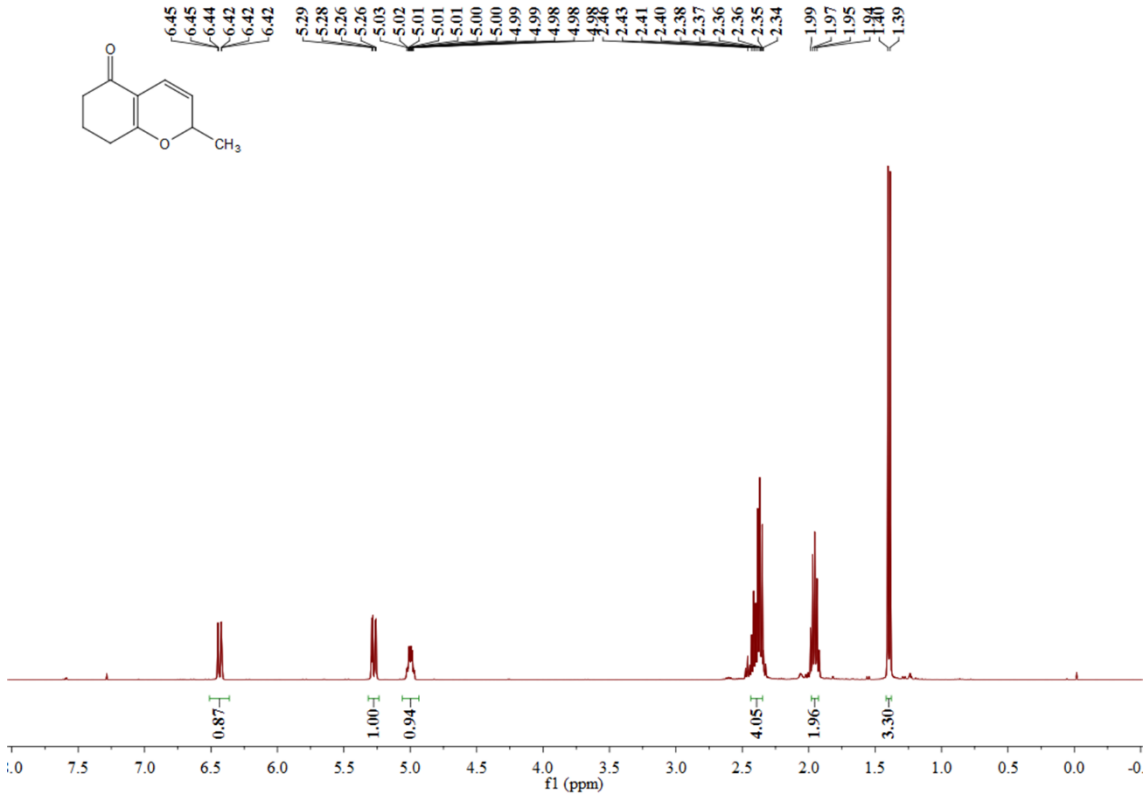
2-hydroxy-7,7-dimethyl-4-propyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4f**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (dd, *J* = 9.7, 2.0 Hz, 1H), 2.67 (dd, *J* = 21.6, 16.6 Hz, 1H), 2.33 – 2.13 (m, 4H), 2.11 – 1.99 (m, 1H), 1.99 – 1.55 (m, 2H), 1.55 – 1.06 (m, 4H), 1.02 (d, *J* = 10.7 Hz, 6H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.43, 168.62, 114.07, 93.46, 50.78, 42.46, 36.64, 32.15, 31.85, 28.66, 27.87, 20.29, 14.08. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}O_3$, 239.1647; found 239.1648.

2-hydroxy-7,7-dimethyl-4-pentyl-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (**4g**)

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (dd, *J* = 9.8, 2.4 Hz, 1H), 2.77 – 2.60 (m, 1H), 2.29 – 2.16 (m, 4H), 2.10 (d, *J* = 13.6 Hz, 1H), 1.63 (ddd, *J* = 13.6, 9.8, 5.6 Hz, 2H), 1.54 – 1.16 (m, 8H), 1.05 (dd, *J* = 9.8, 3.7 Hz, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.09, 168.03, 114.20, 93.39, 50.86, 42.42, 34.30, 32.15, 31.91, 31.78, 28.72, 28.07, 27.86, 26.81, 22.61, 14.07. HRMS (ESI, m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}O_3$, 267.1960; found 267.1959.

^{1}H-NMR, ^{13}C-NMR and HRMS spectra of chromenone derivatives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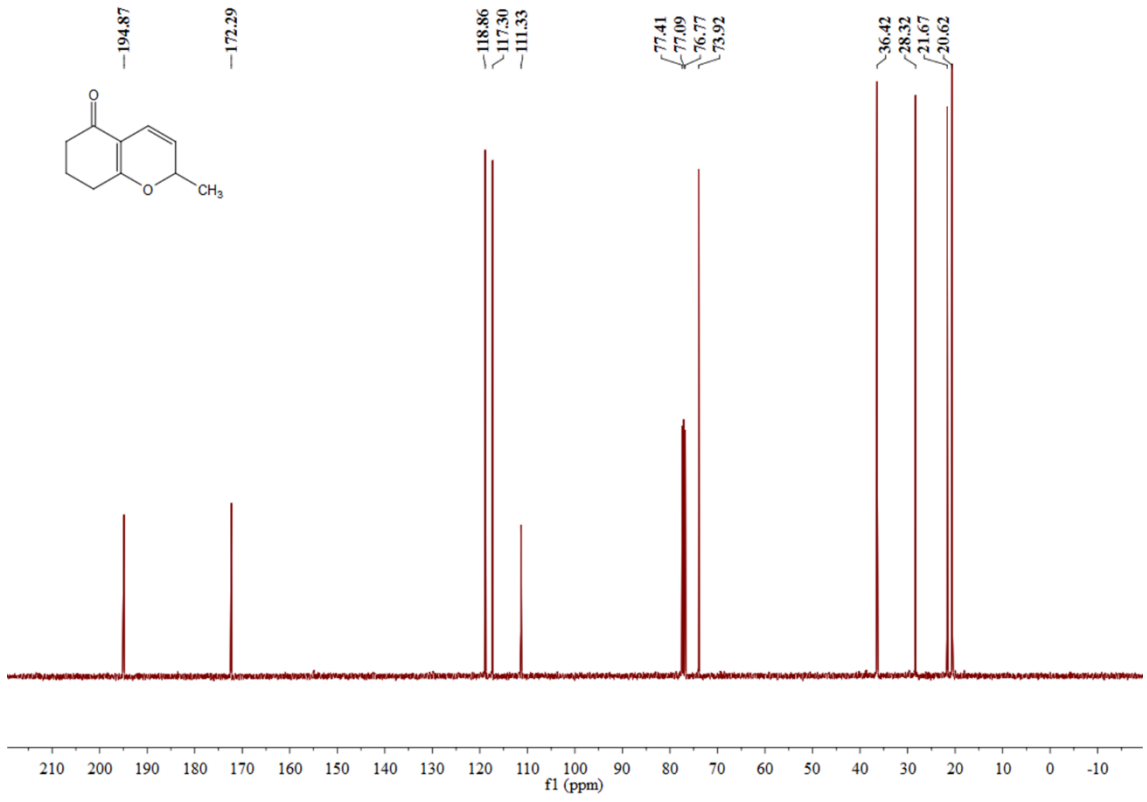
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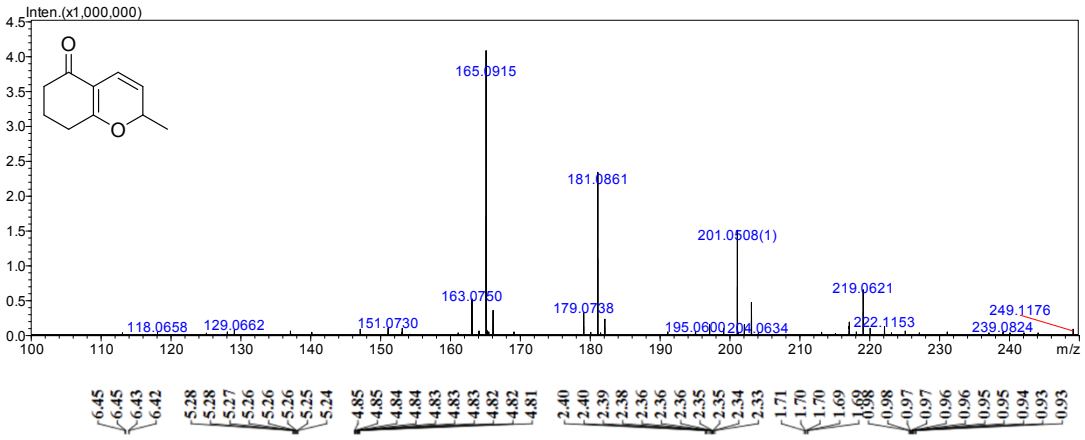
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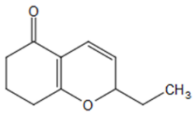
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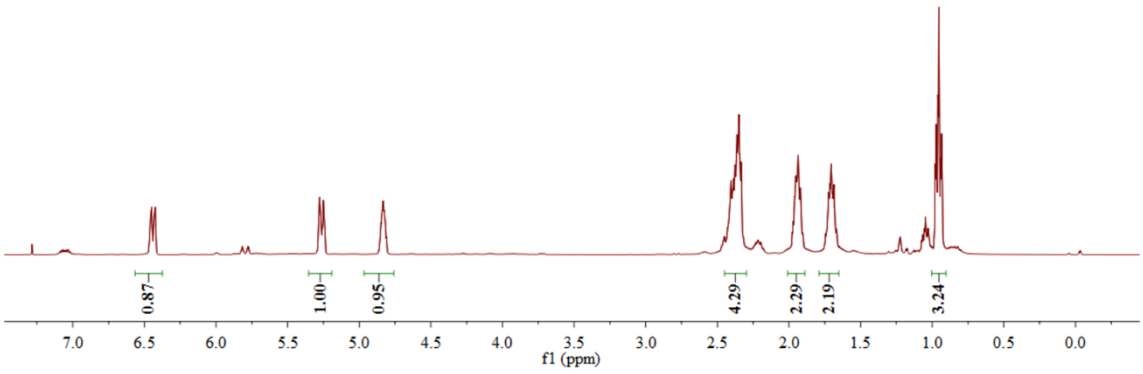
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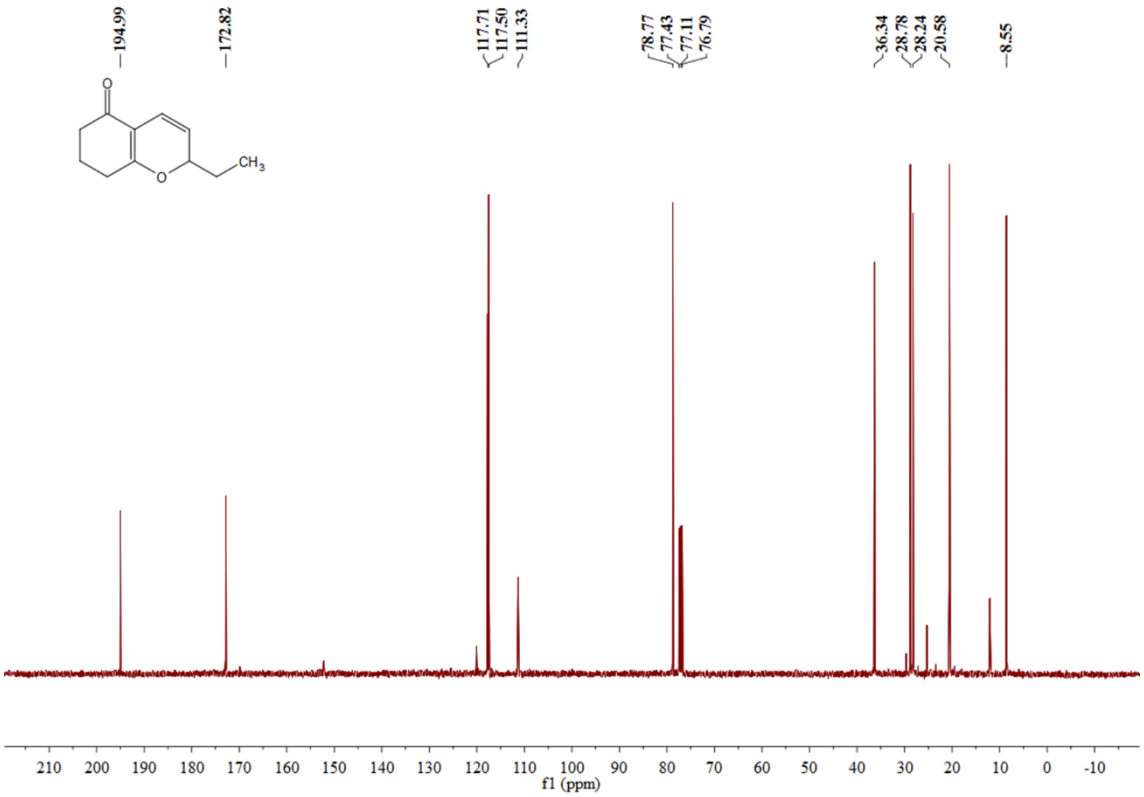
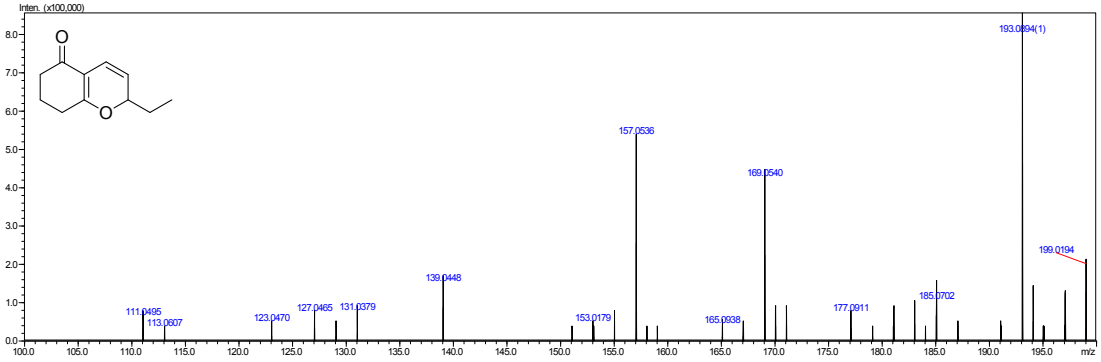
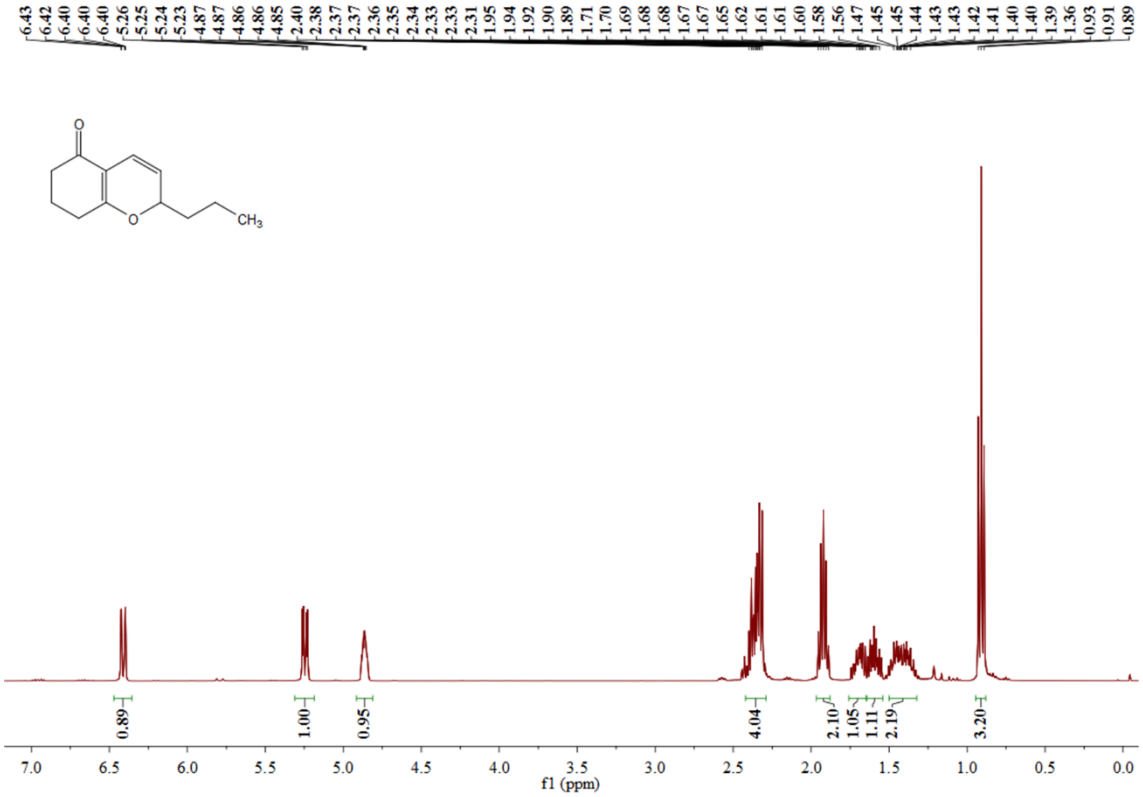
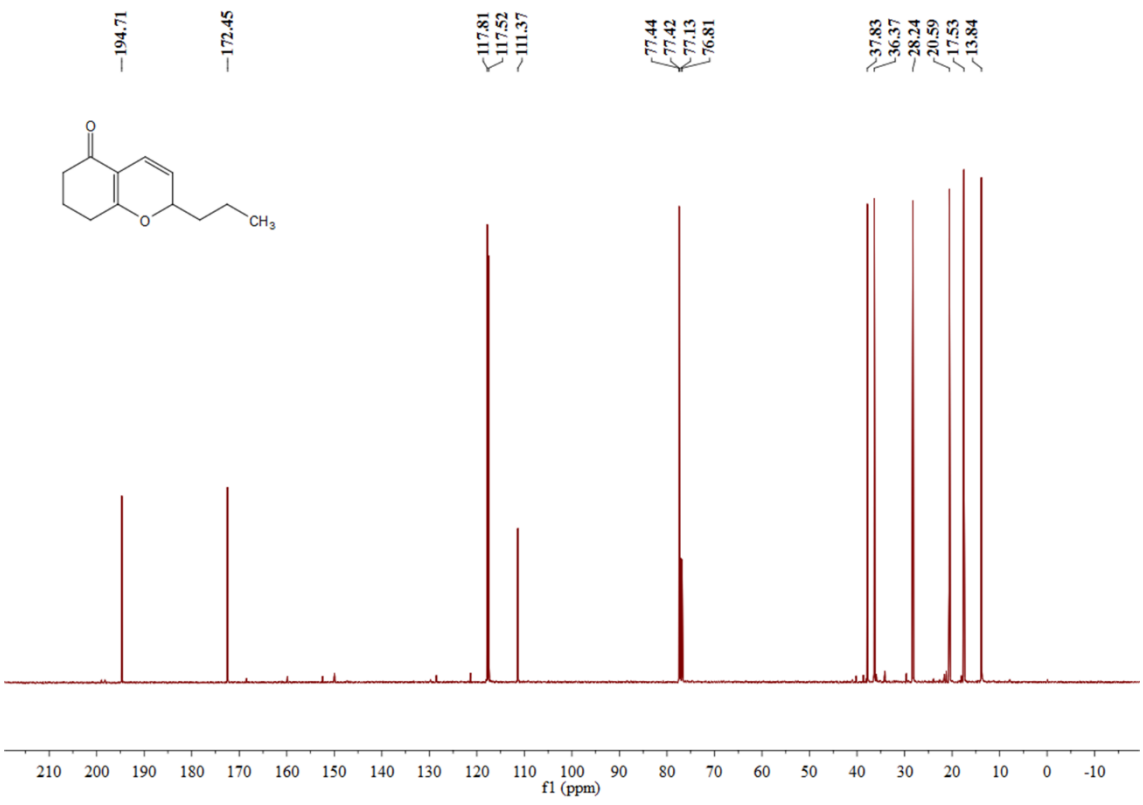
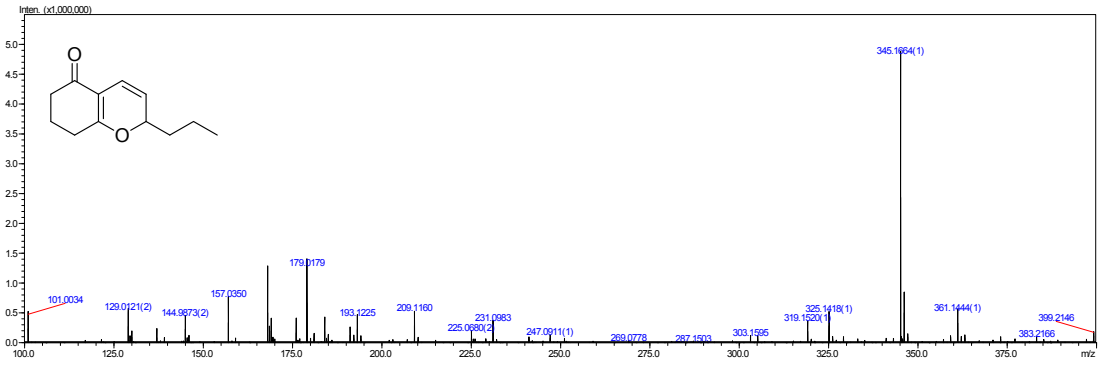
3.24
f1 (ppm)

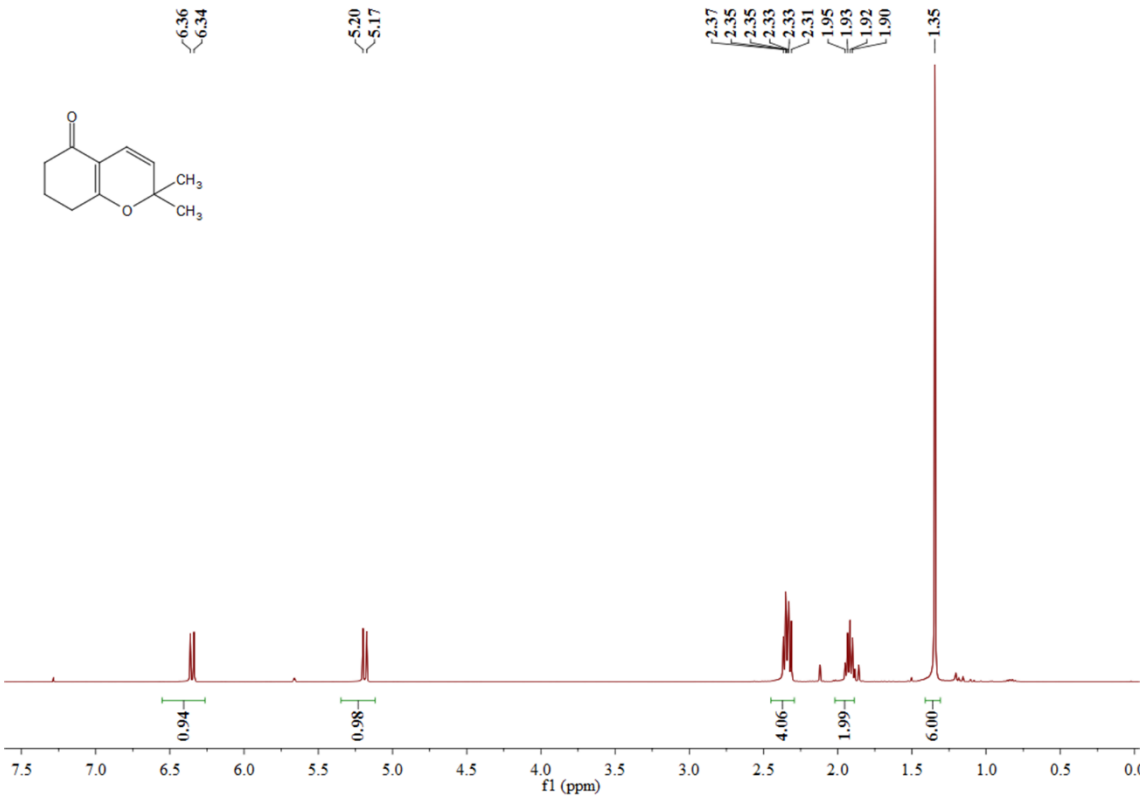

194.99
172.82
117.71
117.50
111.33
78.77
77.43
77.11
76.79
36.34
28.78
28.24
20.58
8.55
O
O
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

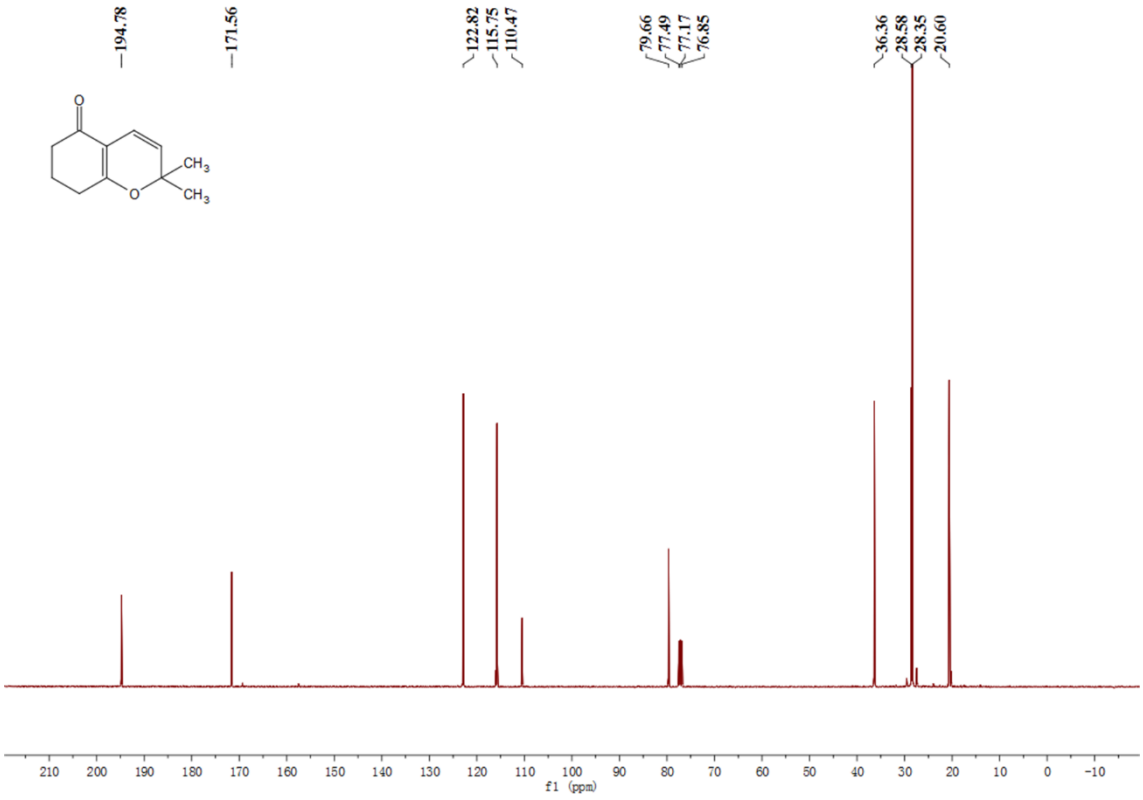

Inten. (x100,000)
O
O
193.0494(1)
157.0536
169.0540
199.0194
139.0448
111.0495
113.0607
123.0470
127.0465
131.0379
153.0179
165.0338
177.0911
185.0702
mz

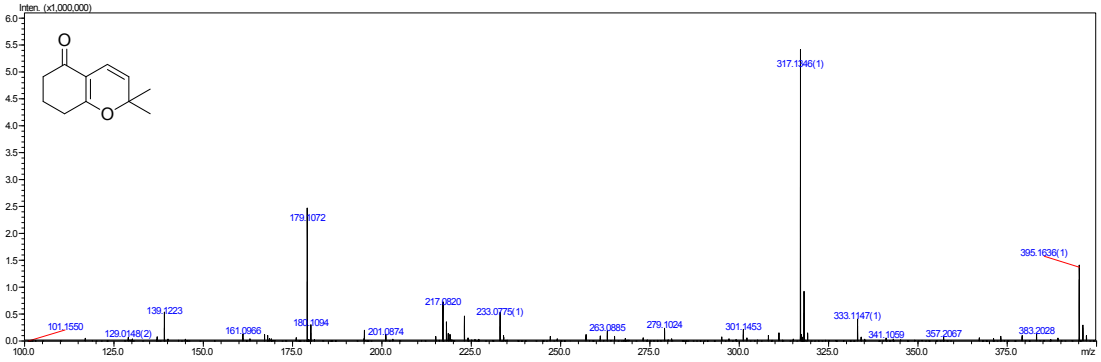

6.43 6.42 6.40 6.40 6.40 5.26 5.25 5.24 5.23 4.87 4.87 4.86 4.86 4.85 2.40 2.38 2.37 2.37 2.36 2.35 2.34 2.33 2.33 2.31 1.95 1.94 1.92 1.90 1.89 1.71 1.70 1.69 1.68 1.68 1.67 1.67 1.65 1.62 1.61 1.61 1.60 1.58 1.56 1.47 1.45 1.45 1.44 1.43 1.43 1.42 1.41 1.40 1.40 1.39 1.36 0.93 0.91 0.89
O
O
CH3
0.89
1.00
0.95
4.04
2.10
1.05
1.11
2.19
3.20
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

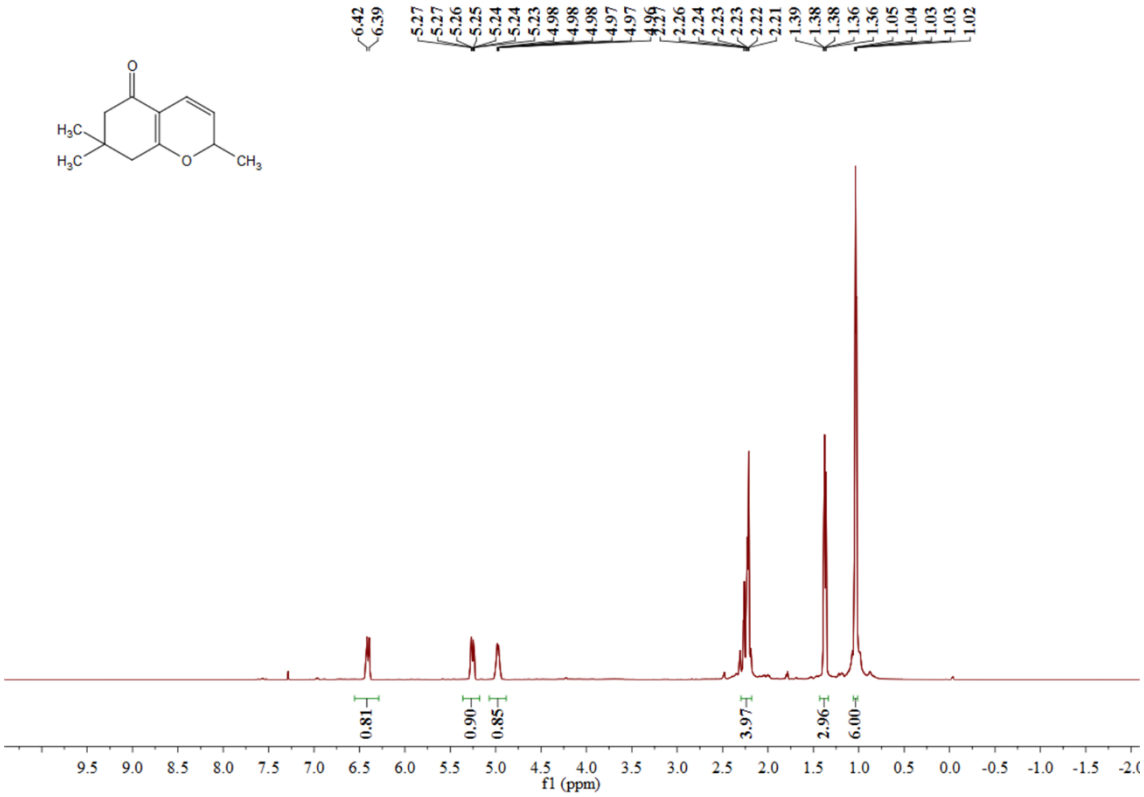

194.71
172.45
117.81
117.52
111.37
77.44
77.42
77.13
76.81
37.83
36.37
28.24
20.59
17.53
13.84
O
O
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

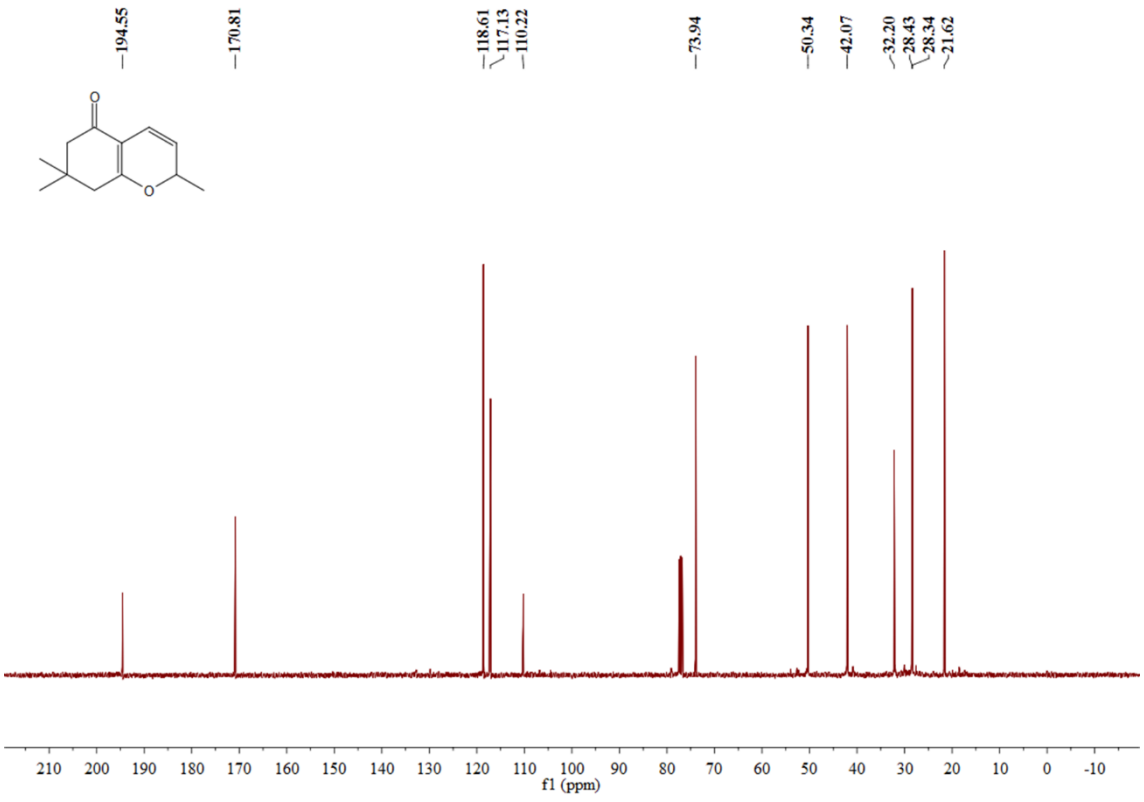

Inten. (x1,000,000)
O
O
345.1964(1)
179.0179
101.0034
129.0121(2)
144.9873(2)
157.0350
193.1225
209.1160
231.0983
225.0680(2)
247.0911(1)
269.0778
287.1503
303.1595
319.1520(1)
325.1418(1)
361.1444(1)
399.2146
383.2166
100.0
125.0
150.0
175.0
200.0
225.0
250.0
275.0
300.0
325.0
350.0
375.0
m/z

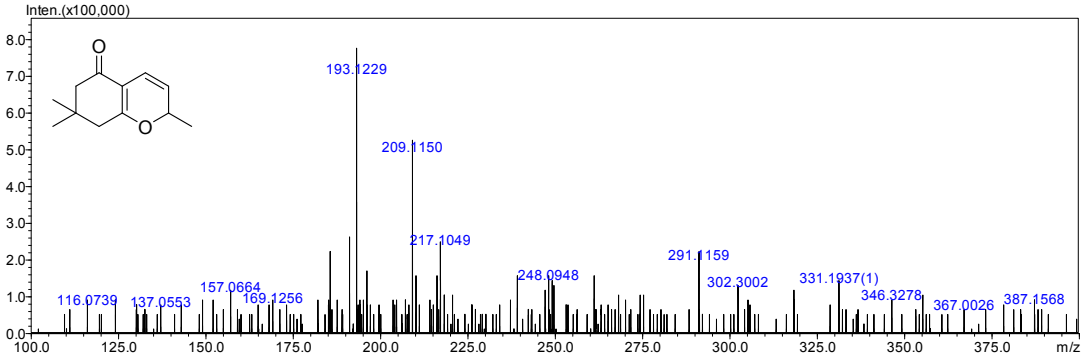

6.36
6.34
5.20
5.17
2.37
2.35
2.35
2.33
2.33
2.31
1.95
1.93
1.92
1.90
1.35
O
CH3
O
CH3
0.94
0.98
4.06
1.99
6.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

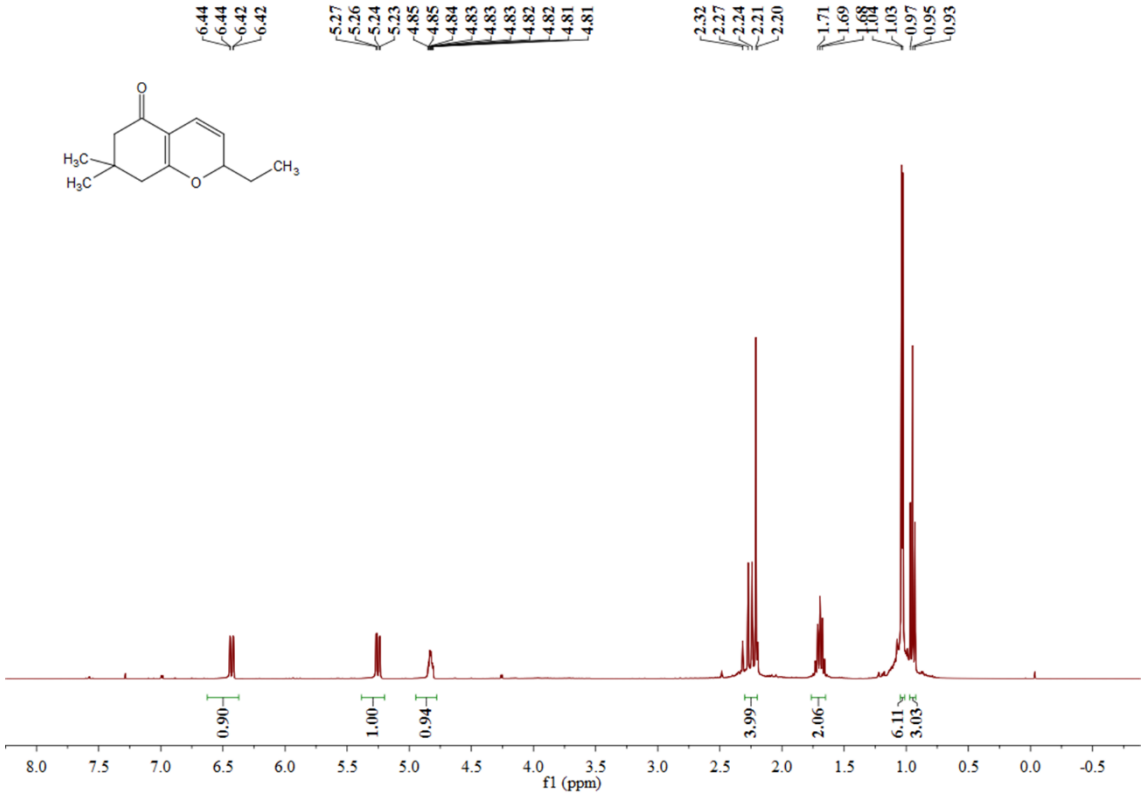

194.78
171.56
122.82
115.75
110.47
79.66
77.49
77.17
76.85
36.36
28.58
28.35
20.60
O
CH3
CH3
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

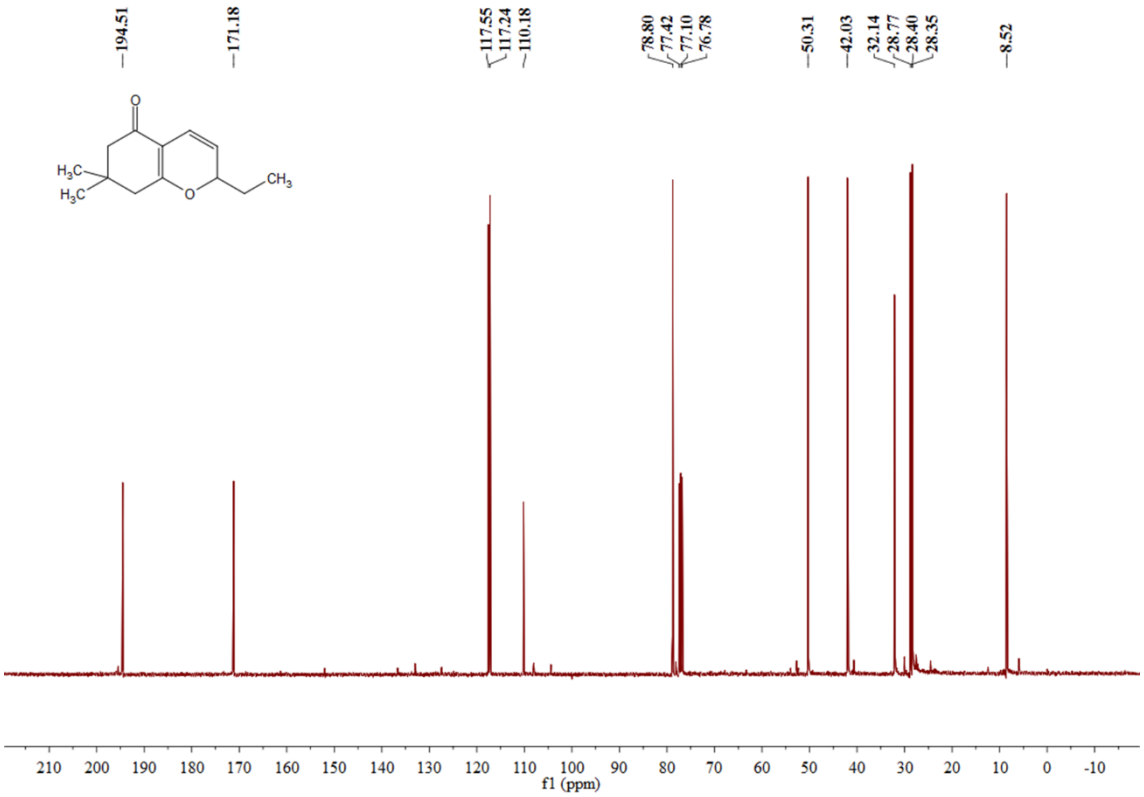

Inten. (x1,000,000)
O
O
317.1346(1)
179.1072
395.1636(1)
139.1223
217.0820
233.0775(1)
101.1550
129.0148(2)
161.0966
180.1094
201.0874
263.0885
279.1024
301.1453
333.1147(1)
341.1059
357.2067
383.2028
m/z

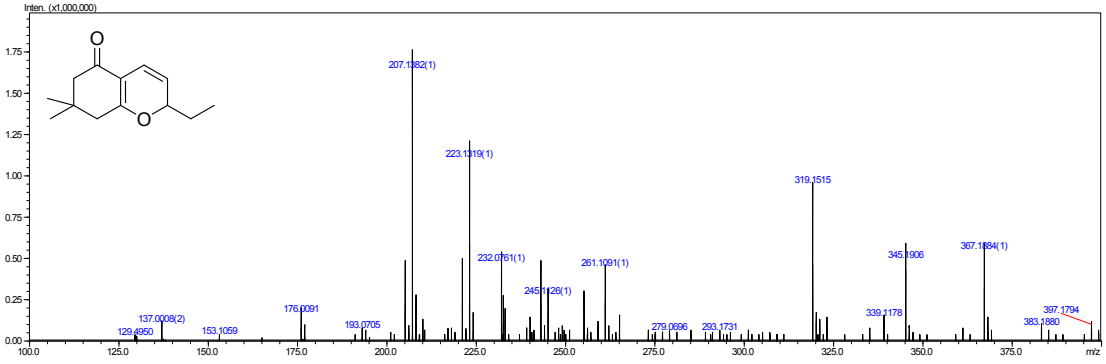

6.42
6.39
5.27
5.27
5.26
5.25
5.24
5.24
5.23
4.98
4.98
4.98
4.97
4.97
4.96
2.27
2.26
2.24
2.23
2.23
2.22
2.21
1.39
1.38
1.38
1.36
1.36
1.05
1.04
1.03
1.03
1.02
O
H3C
H3C
O
CH3
0.81
0.90
0.85
3.97
2.96
6.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

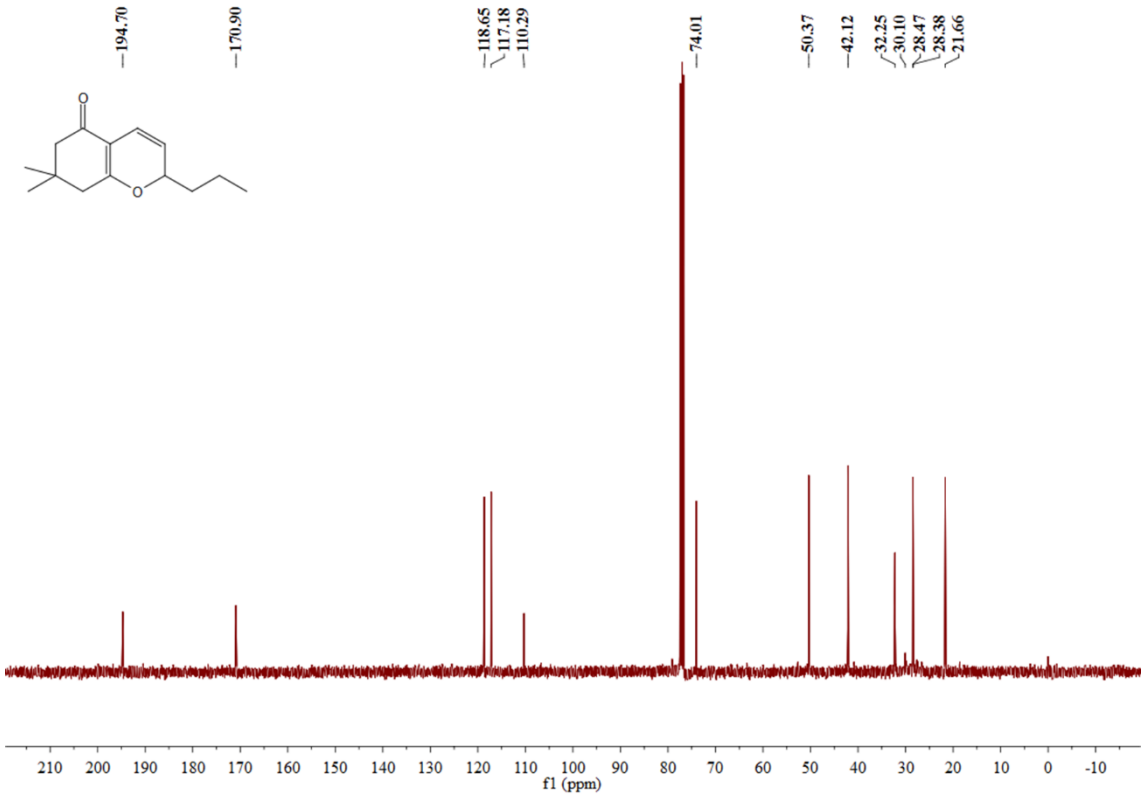

194.55
170.81
118.61
117.13
110.22
73.94
50.34
42.07
32.20
28.43
28.34
21.62
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

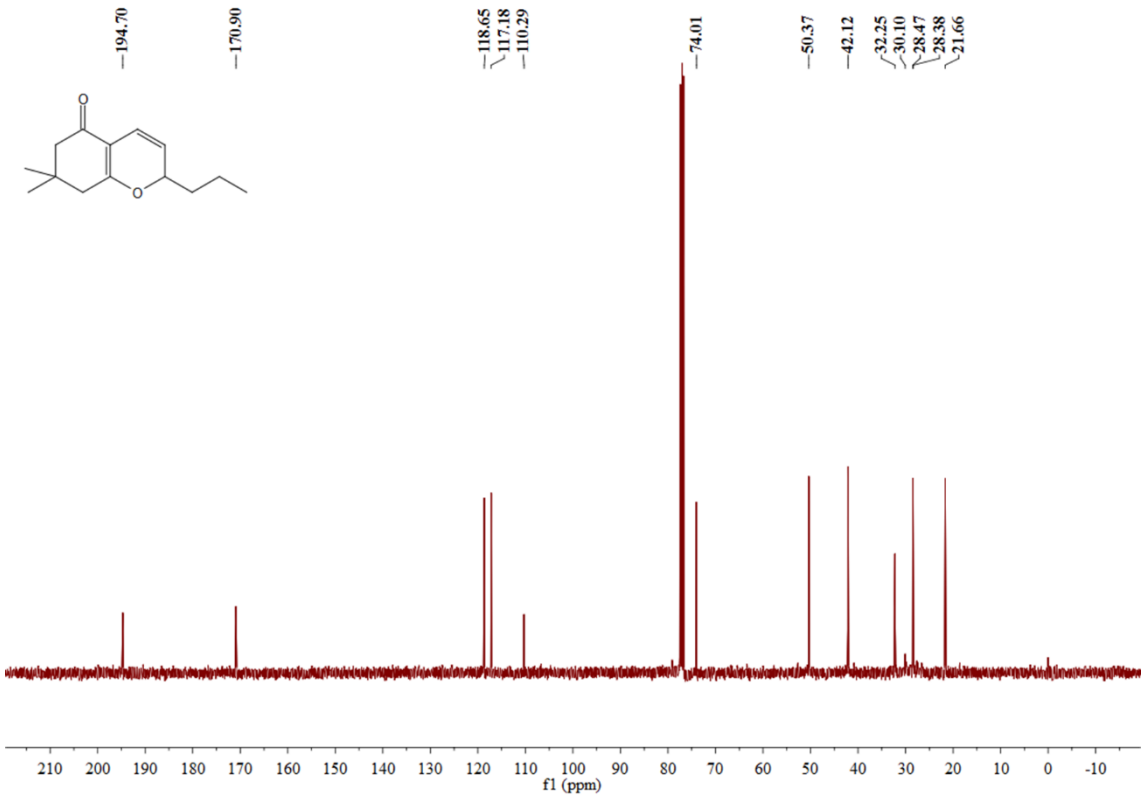

Inten.(x100,000)
193.1229
209.1150
217.1049
291.1159
248.0948
302.3002
331.1937(1)
346.3278
367.0026
387.1568
116.0739
137.0553
157.0664
169.1256
m/z

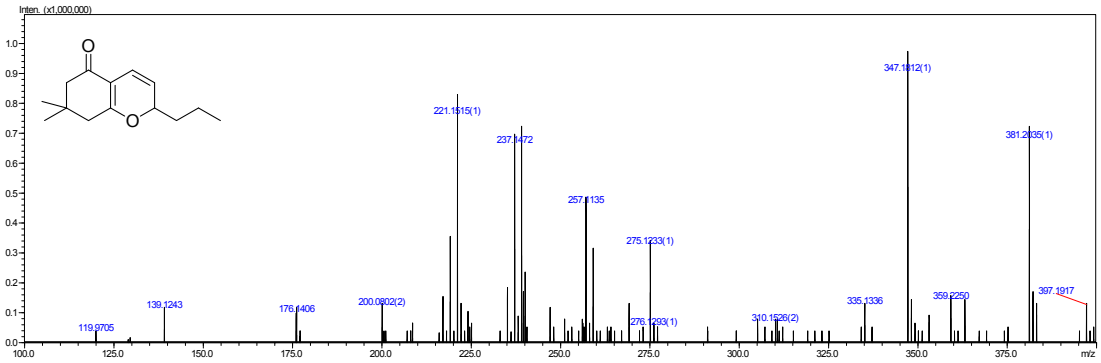

6.44
6.44
6.42
6.42
5.27
5.26
5.24
5.23
4.85
4.85
4.84
4.83
4.83
4.83
4.82
4.82
4.81
4.81
2.32
2.27
2.24
2.21
2.20
1.71
1.69
1.03
0.97
0.95
0.93
0.90
1.00
0.94
3.99
2.06
6.11
3.03
f1 (ppm)

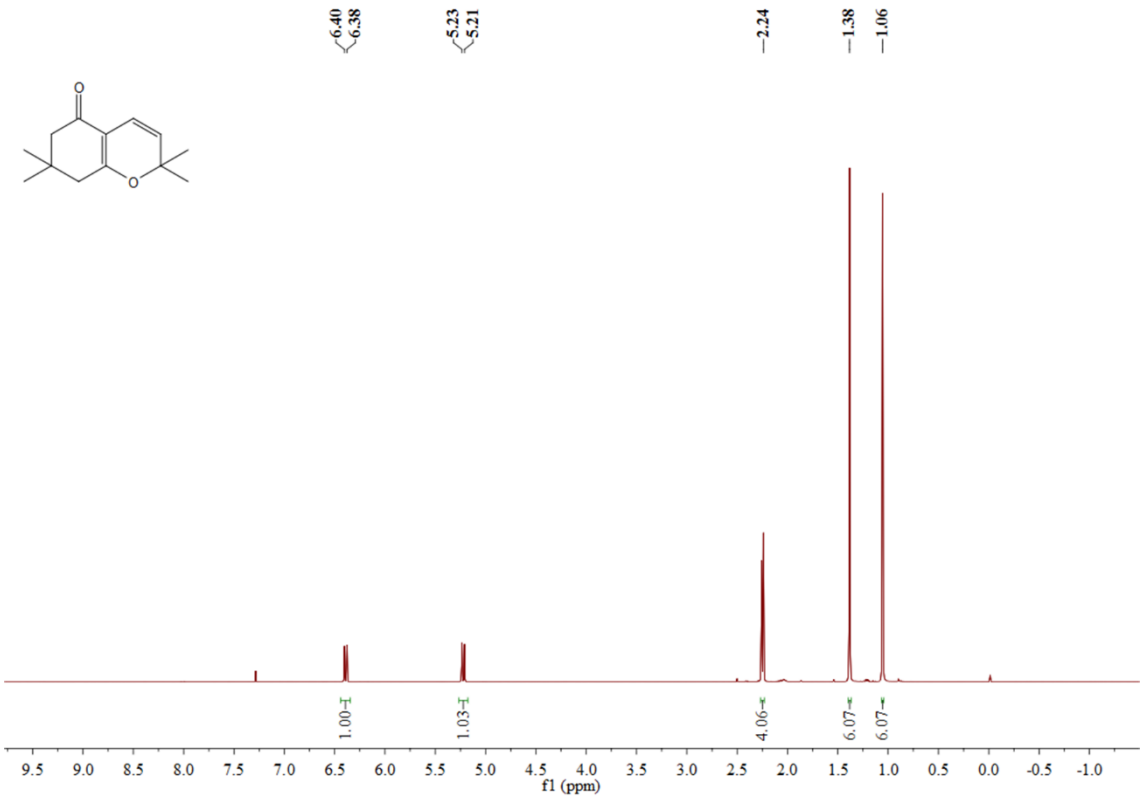

194.51
171.18
117.55
117.24
110.18
78.80
77.42
77.10
76.78
50.31
42.03
32.14
28.77
28.40
28.35
8.52
O
H3C
H3C
O
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

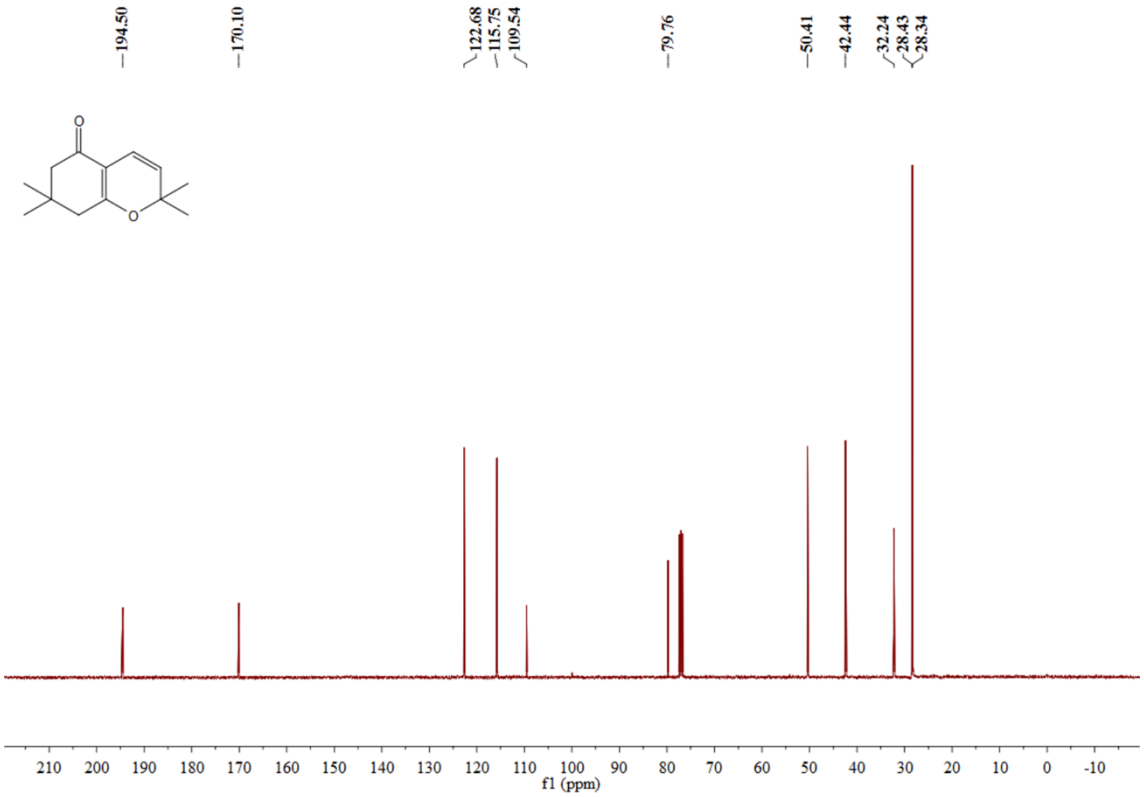

Inten. (x1,000,000)
O
O
207.1382(1)
223.1319(1)
319.1515
232.0761(1)
261.1091(1)
345.1906
367.1884(1)
245.1126(1)
137.0008(2)
129.4950
153.1059
176.0091
193.0705
270.0696
293.1731
339.1178
397.1794
383.1880
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
100.0
125.0
150.0
175.0
200.0
225.0
250.0
275.0
300.0
325.0
350.0
375.0
m/z

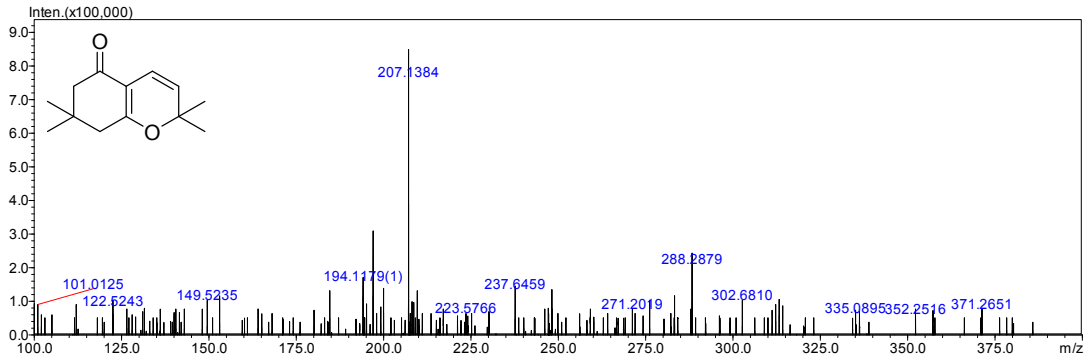

194.70
170.90
118.65
117.18
110.29
74.01
50.37
42.12
32.25
30.10
28.47
28.38
21.66
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

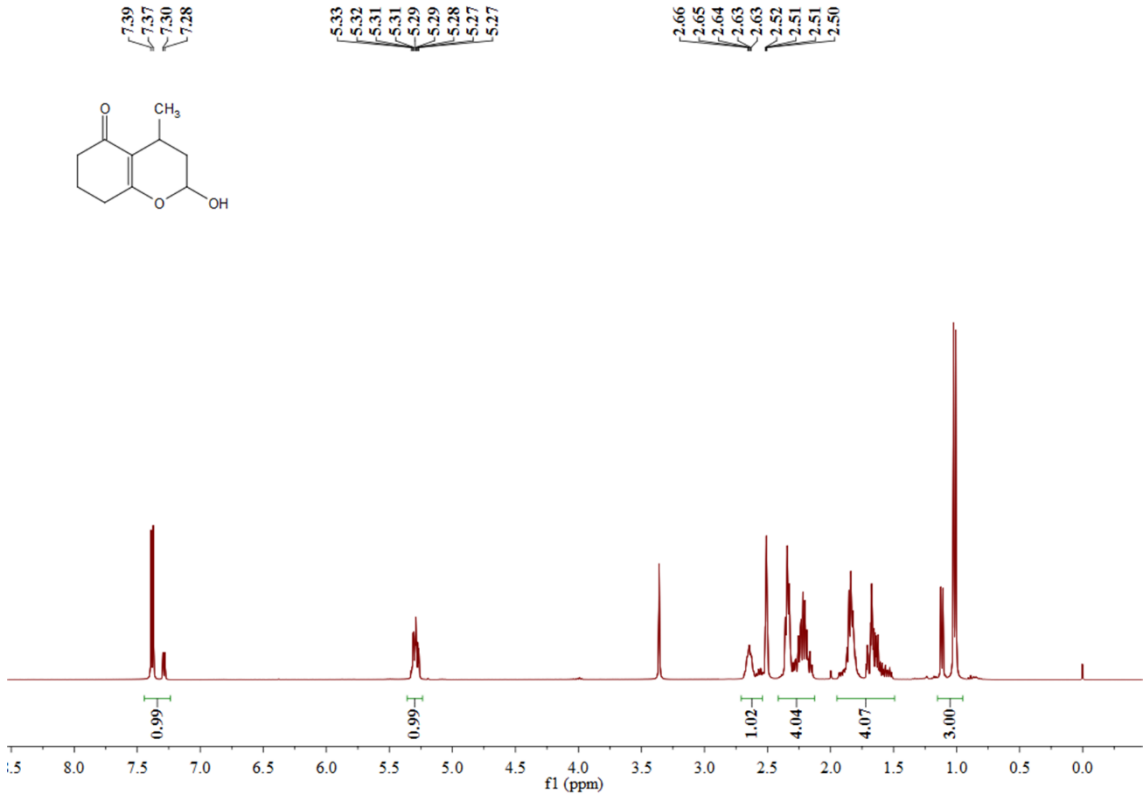

194.70
170.90
118.65
117.18
110.29
74.01
50.37
42.12
32.25
30.10
28.47
28.38
21.66
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

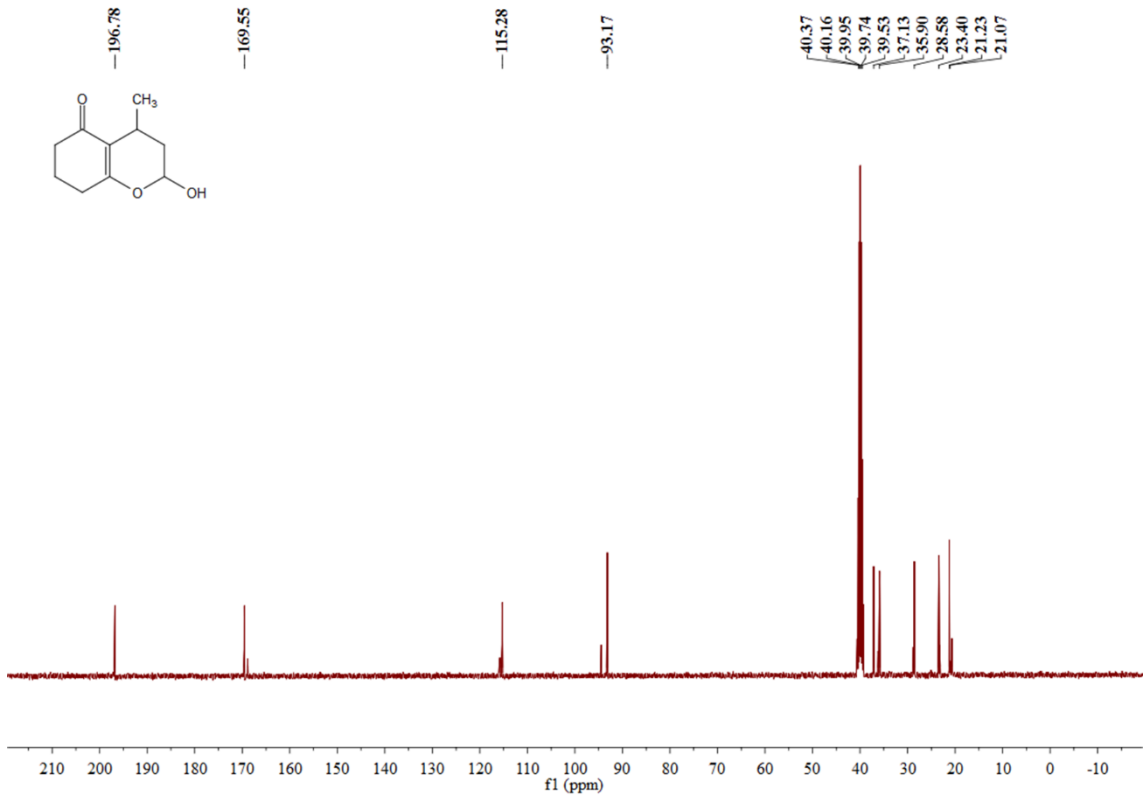

Inten. (x1,000,000)
O
O
221.1515(1)
237.1472
257.1135
275.1233(1)
347.1812(1)
381.2035(1)
397.1917
359.2250
335.1336
310.1526(2)
276.1293(1)
200.0802(2)
176.1406
139.1243
119.0705
m/z

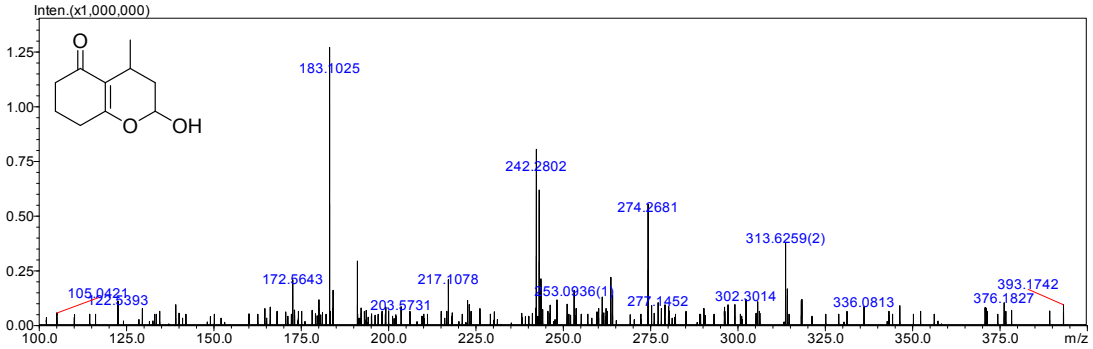

6.40
6.38
5.23
5.21
2.24
1.38
1.06
O
O
1.00
1.03
4.06
6.07
6.07
f1 (ppm)

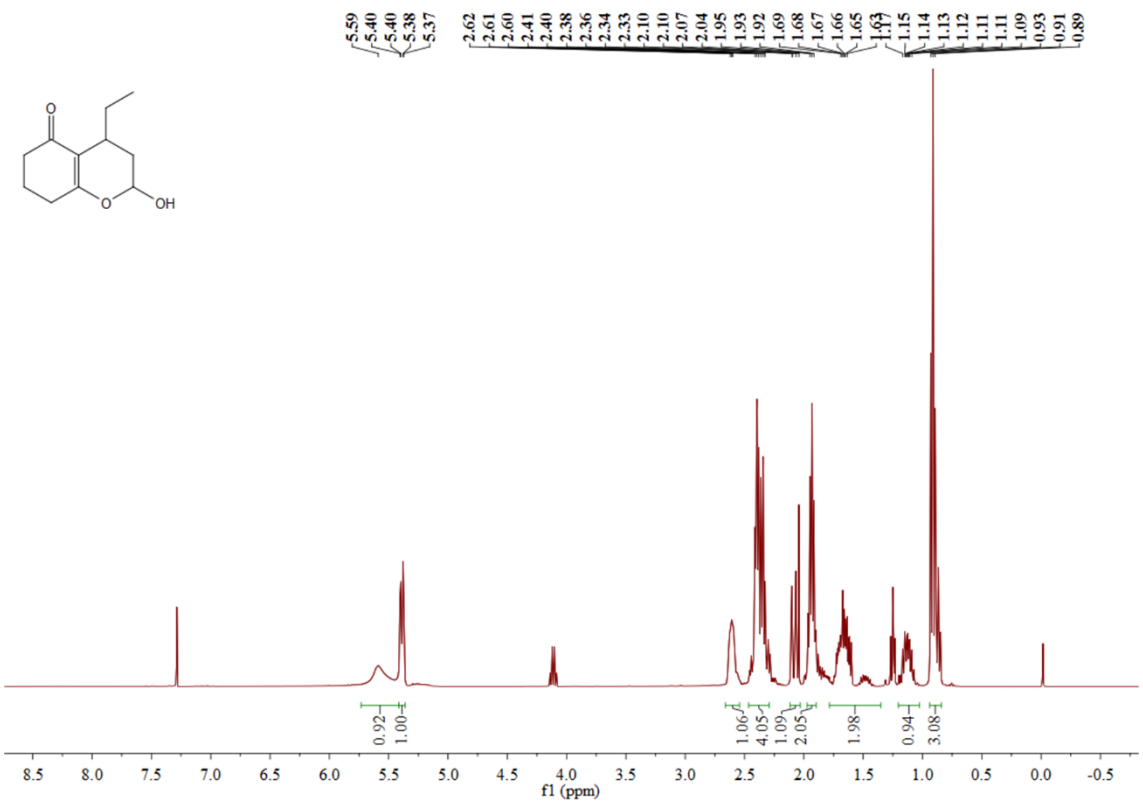

194.50
170.10
122.68
115.75
109.54
79.76
50.41
42.44
32.24
28.43
28.34
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

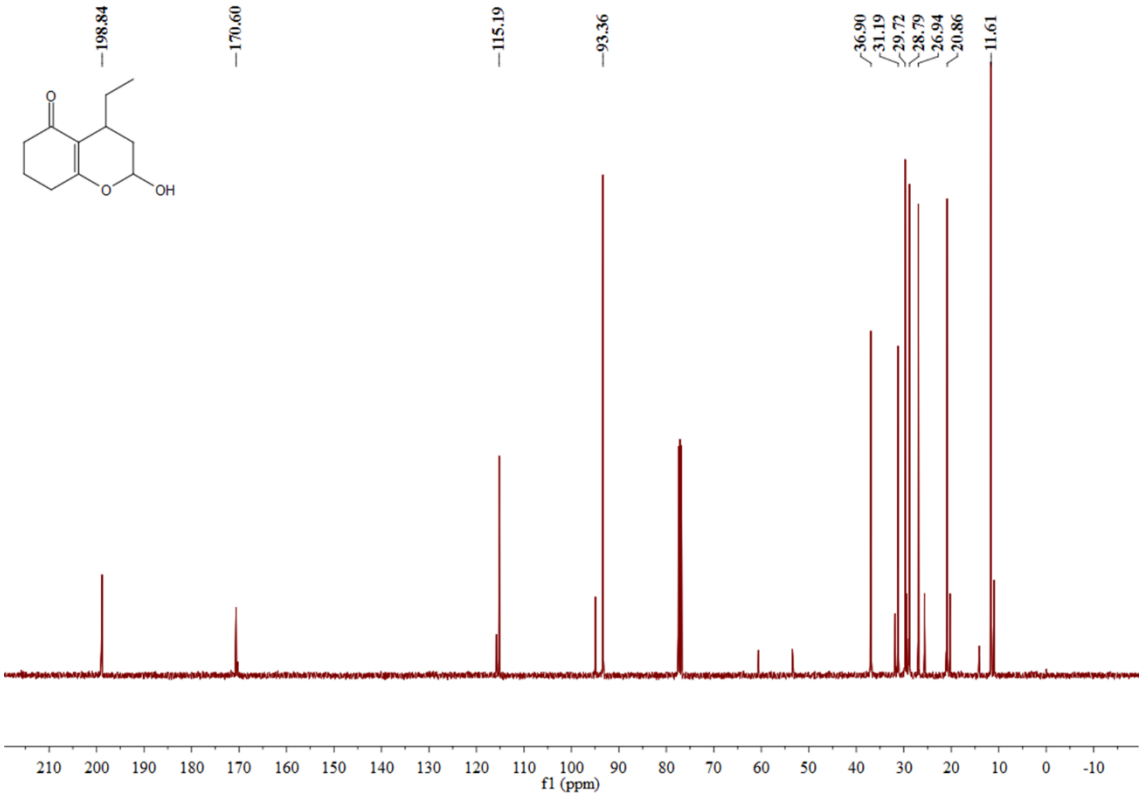

Inten.(x100,000)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
O
O
207.1384
288.2879
194.1179(1)
237.6459
101.0125
122.5243
149.5235
223.5766
271.2019
302.6810
335.0895
352.2516
371.2651
100.0 125.0 150.0 175.0 200.0 225.0 250.0 275.0 300.0 325.0 350.0 375.0
m/z

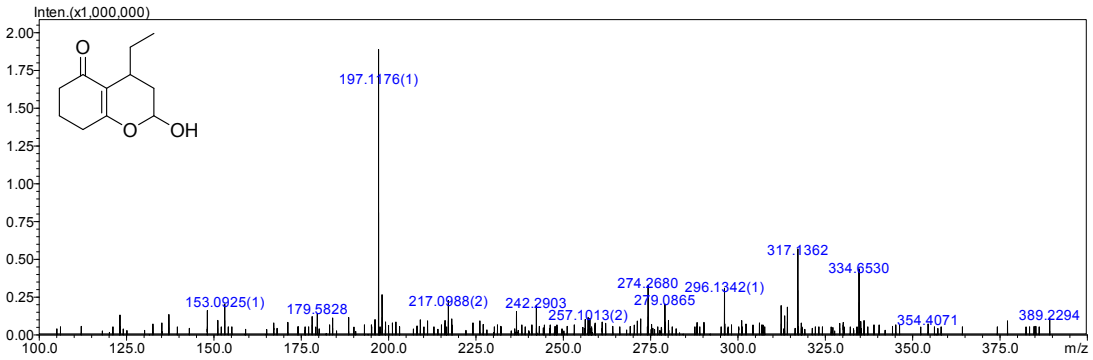

7.39
7.37
7.30
7.28
5.33
5.32
5.31
5.31
5.29
5.29
5.28
5.27
5.27
2.66
2.65
2.64
2.63
2.63
2.52
2.51
2.51
2.50
O
CH3
O
OH
0.99
0.99
1.02
4.04
4.07
3.00
f1 (ppm)

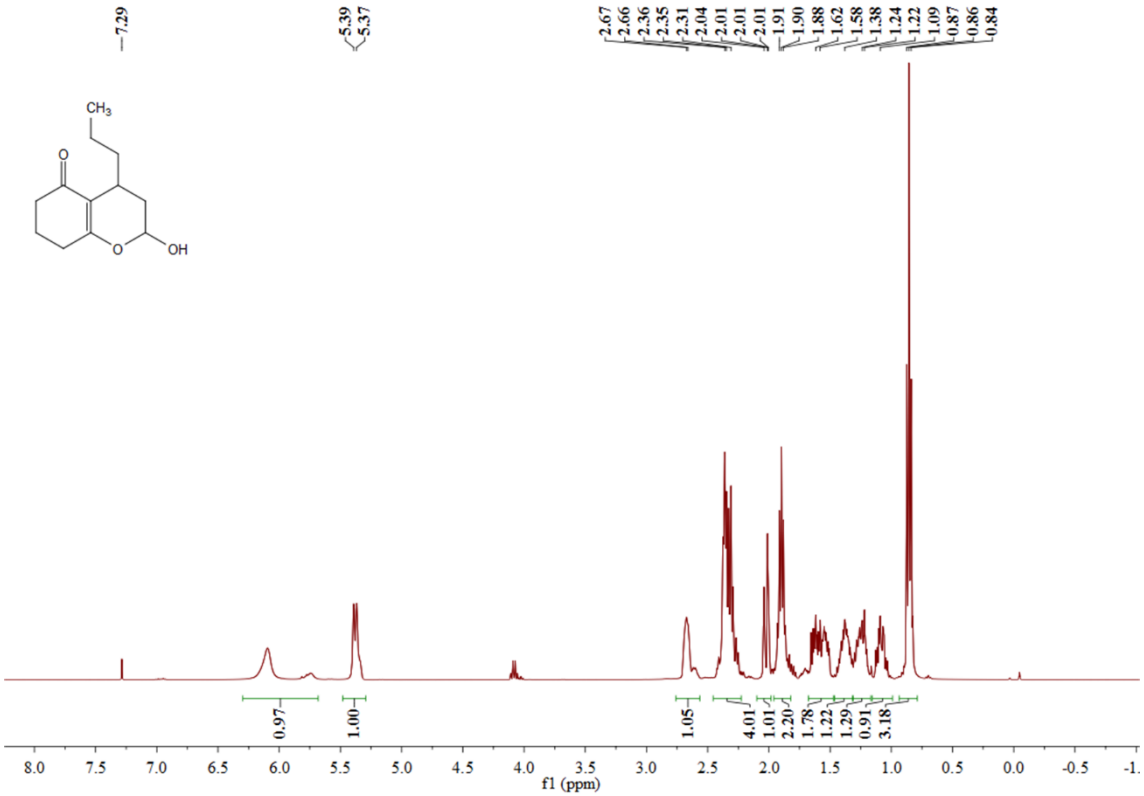

196.78
169.55
115.28
93.17
40.37
40.16
39.95
39.74
39.53
37.13
35.90
28.58
23.40
21.23
21.07
O
CH3
O
OH
f1 (ppm)

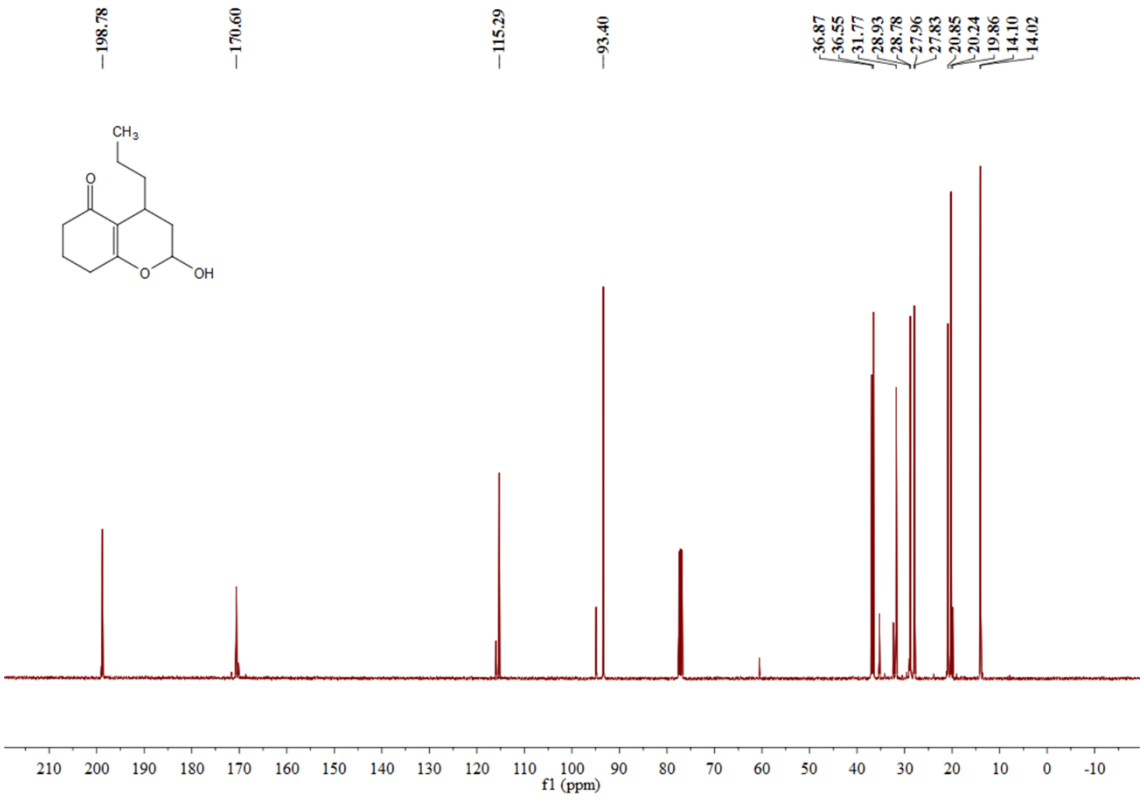

Inten.(x1,000,000)
O
OH
183.1025
242.2802
274.2681
313.6259(2)
105.0421
122.0393
172.0643
203.5731
217.1078
253.0936(1)
277.1452
302.3014
336.0813
376.1827
393.1742
m/z

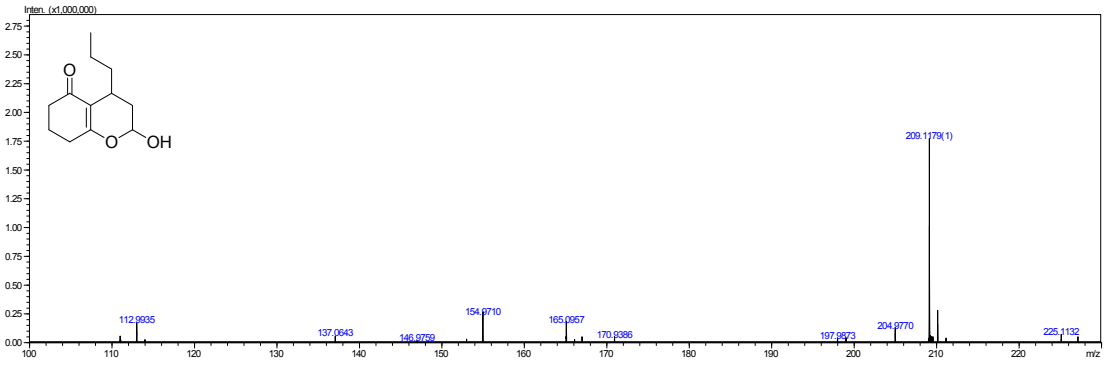

O
OH
5.59
5.40
5.40
5.38
5.37
2.62
2.61
2.60
2.41
2.40
2.38
2.36
2.34
2.33
2.10
2.10
2.07
2.04
1.95
1.93
1.92
1.69
1.68
1.67
1.66
1.65
1.63
1.17
1.15
1.14
1.13
1.12
1.11
1.11
1.09
0.93
0.91
0.89
0.92
1.00
1.06
4.05
1.09
2.05
1.98
0.94
3.08
f1 (ppm)

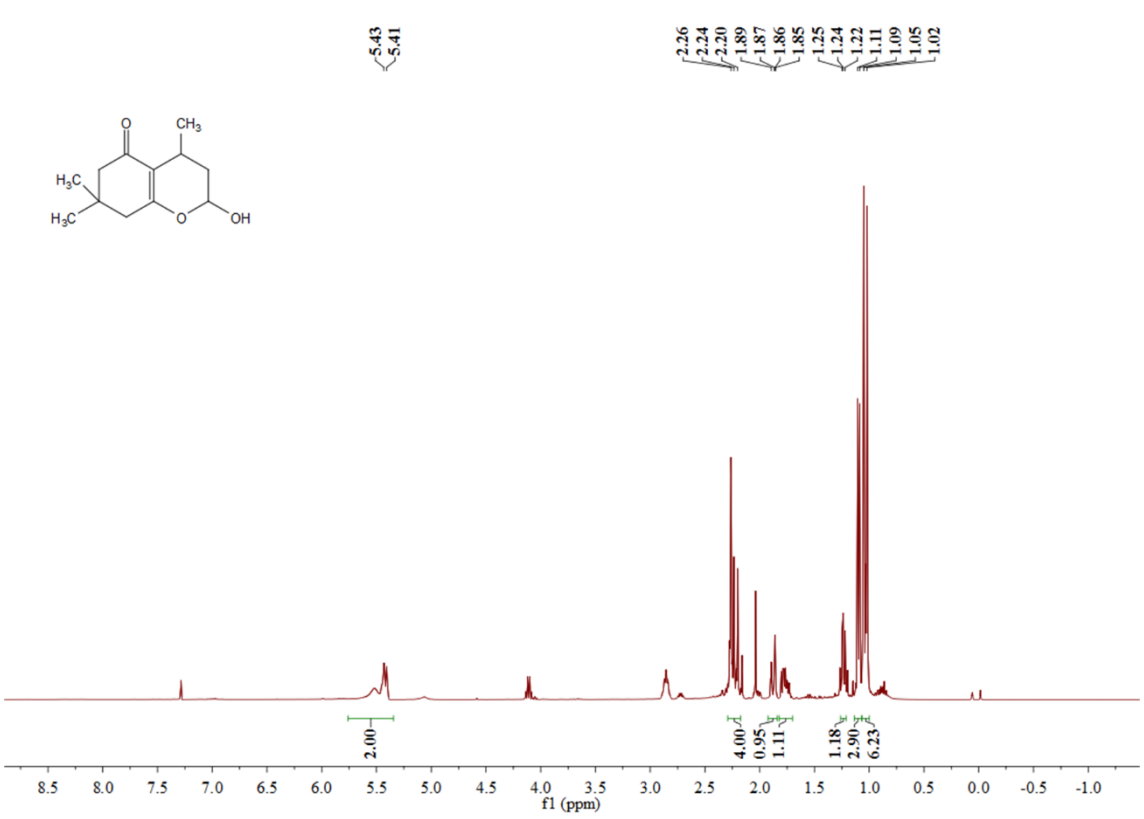

198.84
170.60
115.19
93.36
36.90
31.19
29.72
28.79
26.94
20.86
11.61
O
O
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

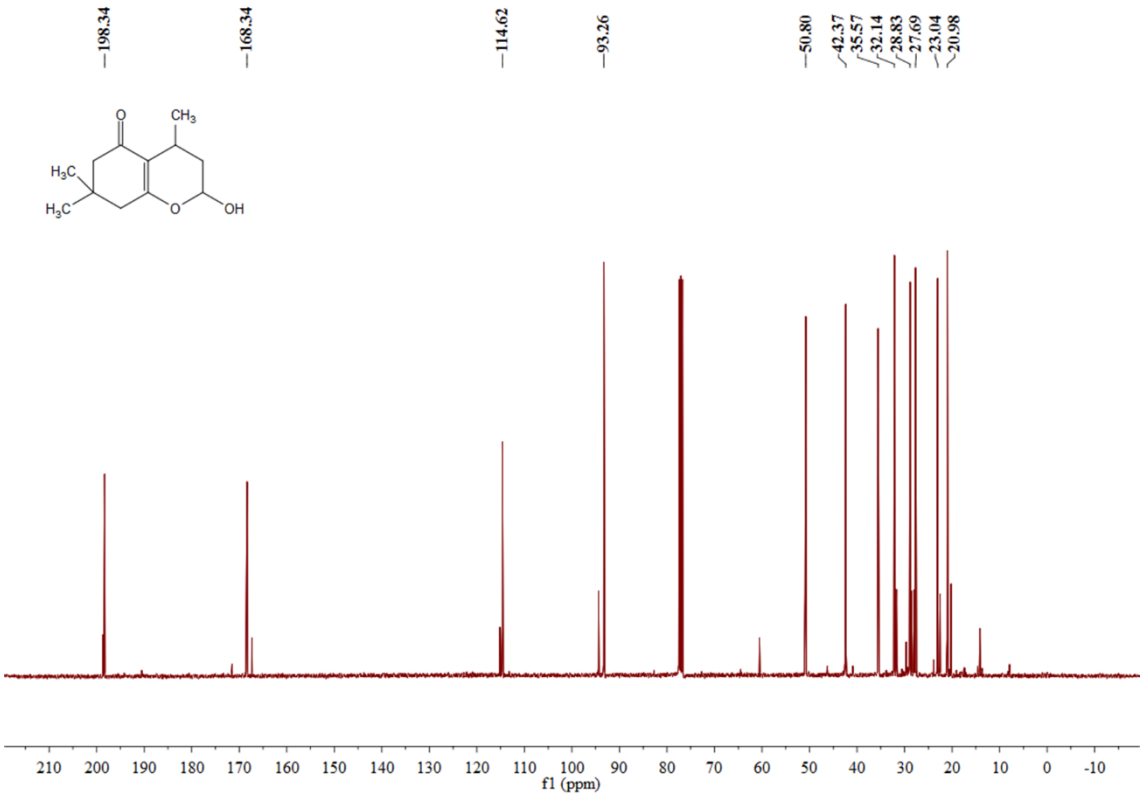

Inten.(x1,000,000)
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
O
O
OH
197.1176(1)
317.1362
334.6530
274.2680
296.1342(1)
279.0865
153.0925(1)
179.5828
217.0988(2)
242.2903
257.1013(2)
354.4071
389.2294
100.0 125.0 150.0 175.0 200.0 225.0 250.0 275.0 300.0 325.0 350.0 375.0 m/z

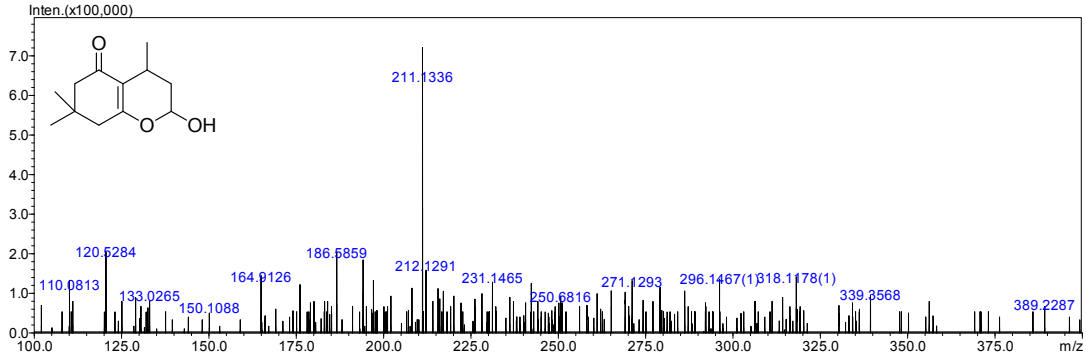

7.29
5.39
5.37
2.67
2.66
2.36
2.35
2.31
2.04
2.01
2.01
2.01
1.91
1.90
1.88
1.62
1.58
1.38
1.24
1.22
1.09
0.87
0.86
0.84
CH3
O
O
OH
0.97
1.00
1.05
4.01
1.01
2.20
1.78
1.22
1.29
0.91
3.18
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

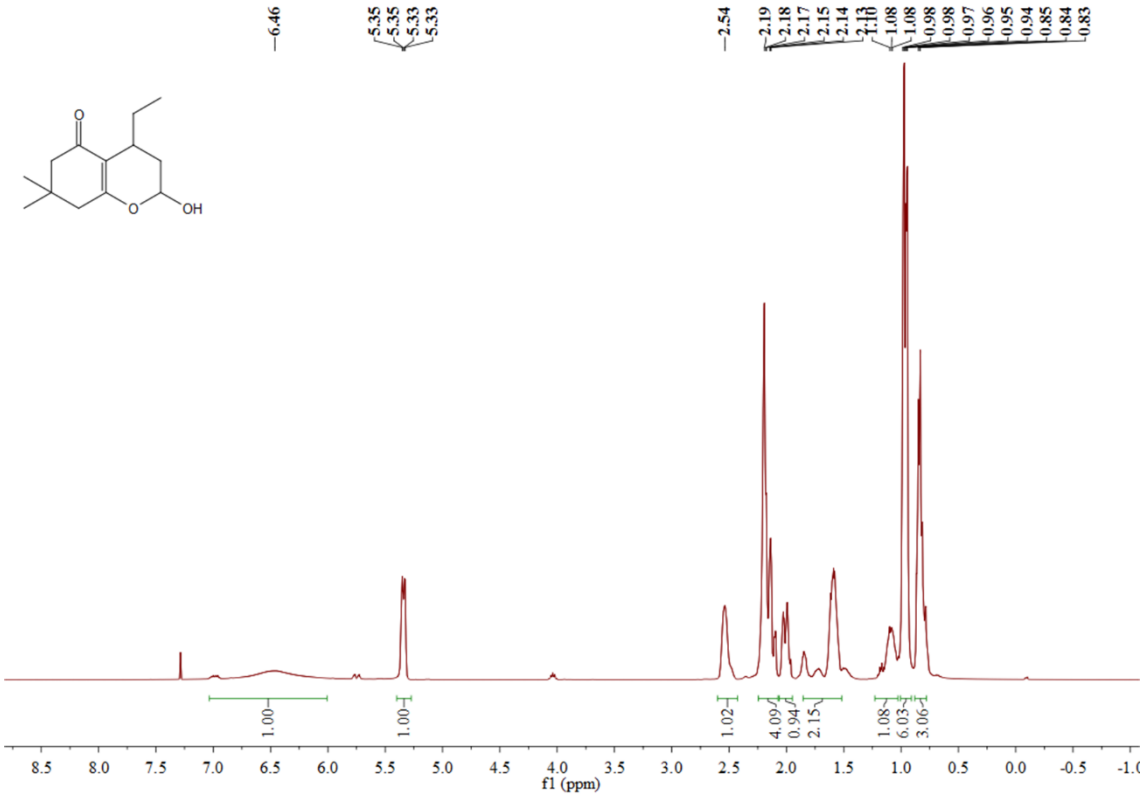

198.78
170.60
115.29
93.40
36.87
36.55
31.77
28.93
28.78
27.96
27.83
20.85
20.24
19.86
14.10
14.02
CH3
O
O
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

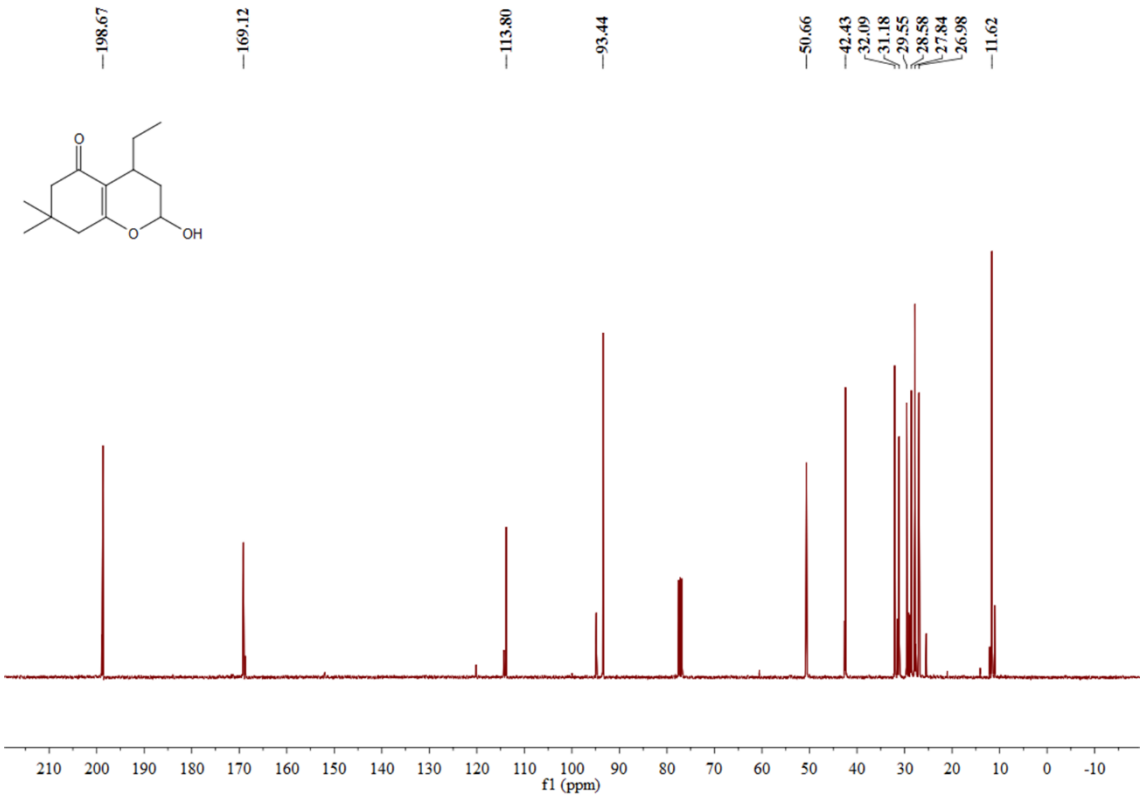

Inten. (x1,000,000)
209.1179(1)
112.9935
137.0643
146.9759
154.9710
165.0957
170.9386
197.9873
204.9770
225.1132
m/z

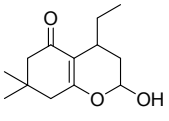

5.43
5.41
2.26
2.24
2.20
1.89
1.87
1.86
1.85
1.25
1.24
1.22
1.11
1.09
1.05
1.02
2.00
4.00
0.95
1.11
1.18
2.90
6.23
f1 (ppm)

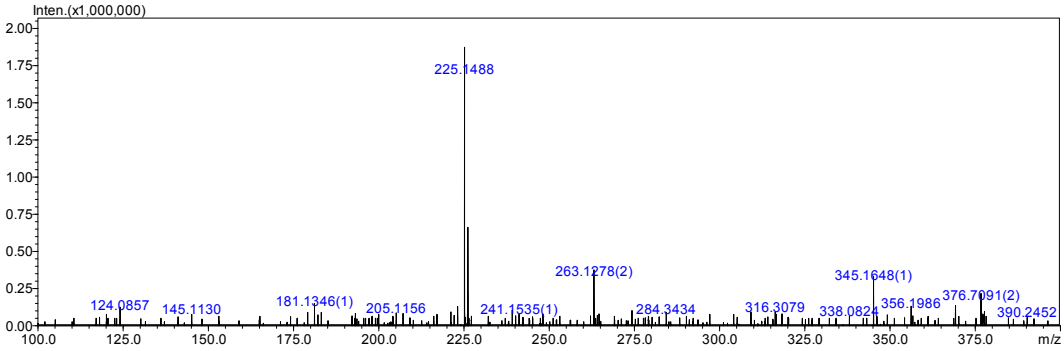

198.34
168.34
114.62
93.26
50.80
42.37
35.57
32.14
28.83
27.69
23.04
20.98
O
CH3
H3C
H3C
O
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

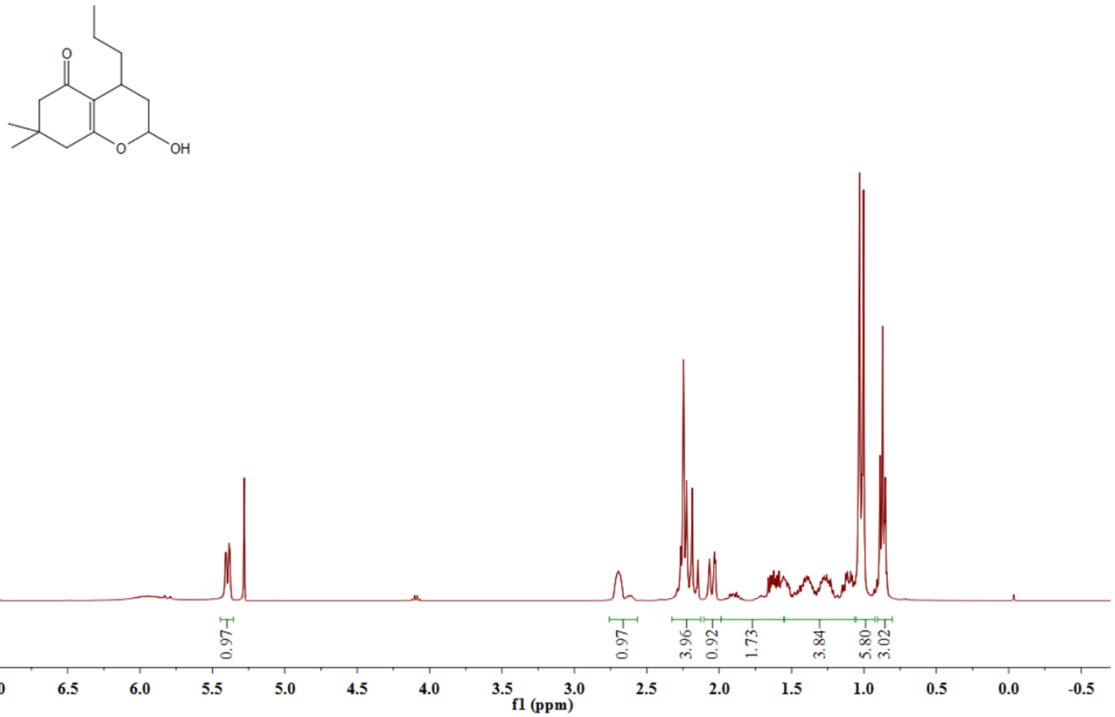

Inten.(x100,000)
O
OH
211.1336
120.0284
110.0813
133.0265
150.1088
164.0126
186.0859
212.1291
231.1465
250.0816
271.1293
296.1467(1)
318.1178(1)
339.0568
389.2287
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
100.0 125.0 150.0 175.0 200.0 225.0 250.0 275.0 300.0 325.0 350.0 375.0 m/z

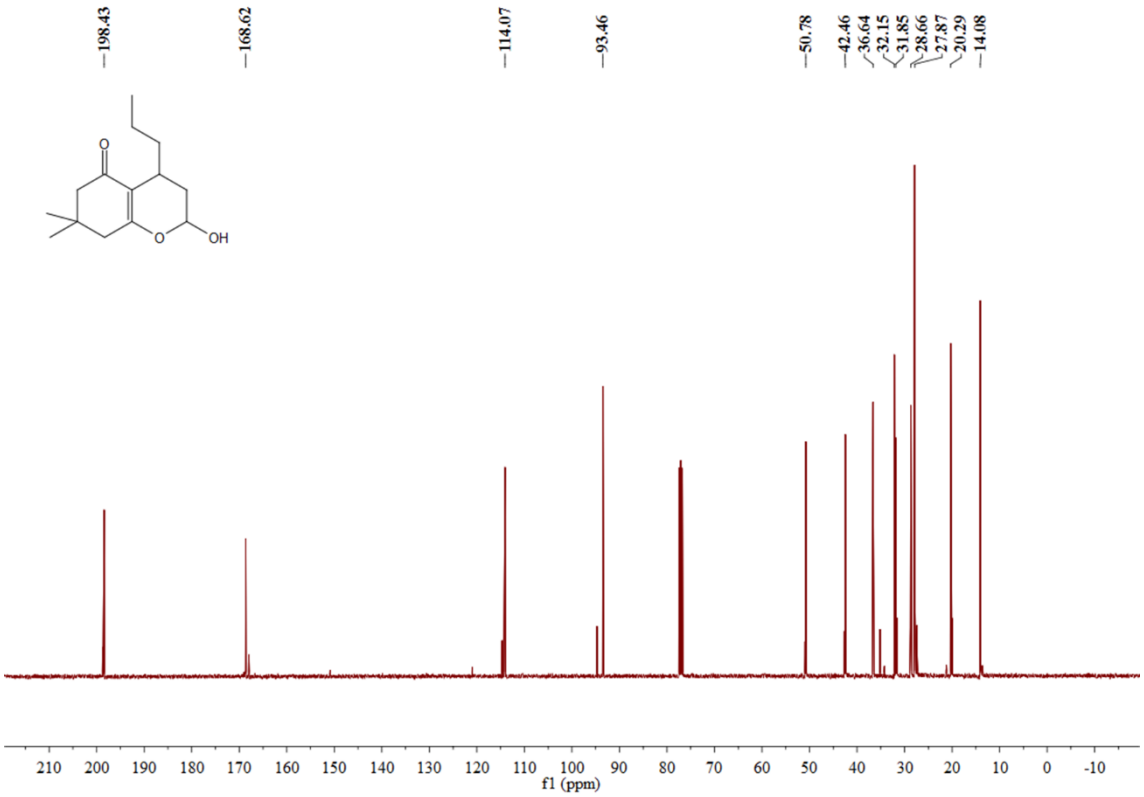

6.46
5.35
5.35
5.33
5.33
2.54
2.19
2.18
2.17
2.15
2.14
1.10
1.08
1.08
0.98
0.98
0.97
0.96
0.95
0.94
0.85
0.84
0.83
O
OH
1.00
1.00
1.02
4.09
0.94
2.15
1.08
6.03
3.06
f1 (ppm)

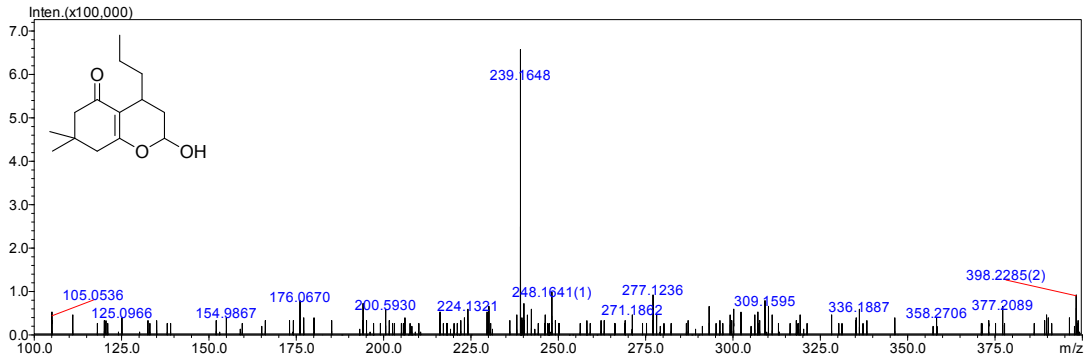

198.67
169.12
113.80
93.44
50.66
42.43
32.09
31.18
29.55
28.58
27.84
26.98
11.62
O
OH
f1 (ppm)

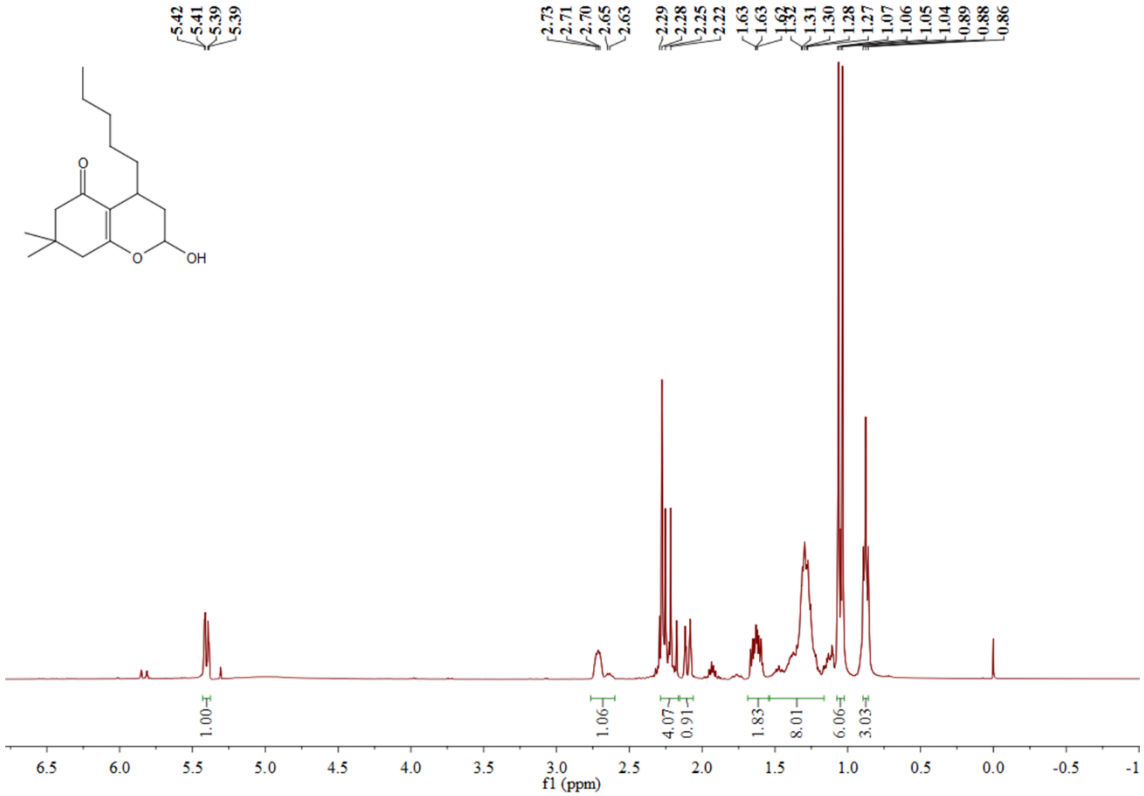

O
O
OH

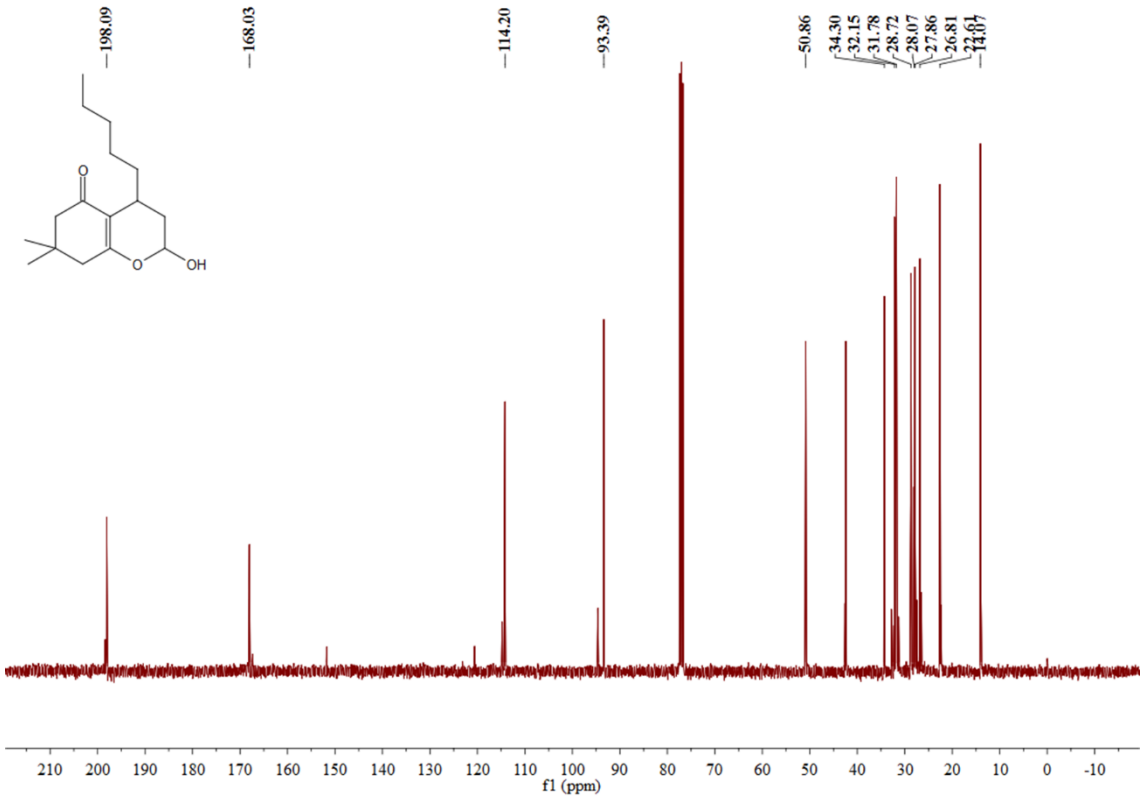

Inten.(x1,000,000)
225.1488
263.1278(2)
345.1648(1)
124.0857
145.1130
181.1346(1)
205.1156
241.1535(1)
284.3434
316.3079
338.0824
356.1986
376.7091(2)
390.2452
m/z

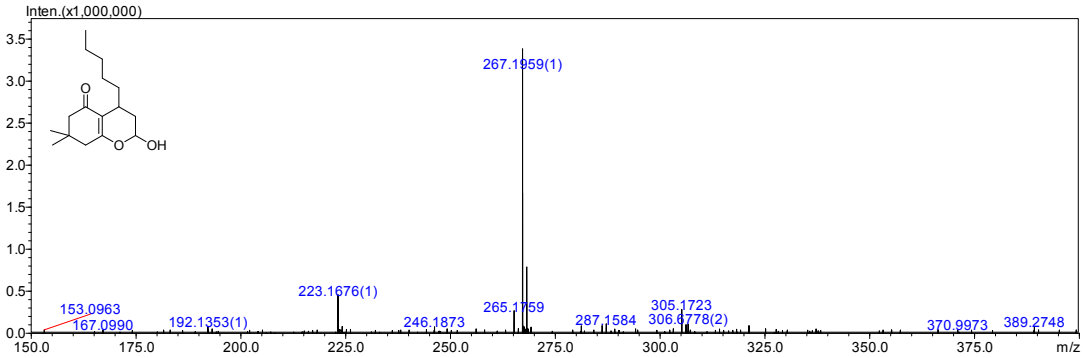

O
O
OH
0.97
0.97
3.96
0.92
1.73
3.84
5.80
3.02
f1 (ppm)


198.43
168.62
114.07
93.46
50.78
42.46
36.64
32.15
31.85
28.66
27.87
20.29
14.08
O
O
OH
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)


Inten.(x100,000)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
O
O
OH
239.1648
105.0536
125.0966
154.9867
176.0670
200.5930
224.1321
248.1641(1)
271.1862
277.1236
309.1595
336.1887
358.2706
377.2089
398.2285(2)
100.0 125.0 150.0 175.0 200.0 225.0 250.0 275.0 300.0 325.0 350.0 375.0 m/z


5.42
5.41
5.39
5.39
2.73
2.71
2.70
2.65
2.63
2.29
2.28
2.25
2.22
1.63
1.63
1.32
1.31
1.30
1.28
1.27
1.07
1.06
1.05
1.04
0.89
0.88
0.86
O
O
OH
1.00
1.06
4.07
0.91
1.83
8.01
6.06
3.03
6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


198.09
168.03
114.20
93.39
50.86
34.30
32.15
31.78
28.72
28.07
27.86
26.81
22.61
14.07
O
O
OH
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)


Inten.(x1,000,000)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
O
O
OH
267.1959(1)
223.1676(1)
153.0963
167.0990
192.1353(1)
246.1873
265.1759
287.1584
305.1723
306.6778(2)
370.9973
389.2748
150.0
175.0
200.0
225.0
250.0
275.0
300.0
325.0
350.0
375.0
m/z