# Supporting Information

## Concise Total Synthesis of (±)- Applanatumol Y

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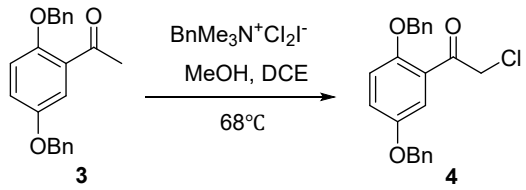
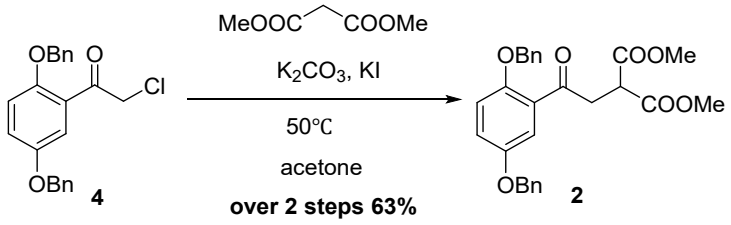
**General Experimental Procedures:** All reactions were performed with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF) was distilled over sodium. Dichloromethane were distilled over calcium hydride. Reagents were used as received without further purification, unless otherwise stated. Silica gel (200-300 mesh, Qingdao Marine Chemical Ltd., China), light petroleum ether (bp 60–90 ºC) and ethyl acetate were used for product purification by flash column chromatography. Melting Point (MP)was determined with a X-4 Taike micro melting point apparatus and was uncorrected. Proton nuclear magnetic resonance ($^{1}$H-NMR) spectra were recorded on Bruker Avance 400 spectrometer at 400 MHz. Carbon-13 nuclear magnetic resonance ($^{13}$C-NMR) was recorded on Bruker Avance 400 at 100 MHz. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. Mass spectra were recorded on a VG-Auto-Spec-3000 spectrometer. High-resolution mass spectral analysis (HRMS) data were recorded via electron impact mass spectrometry using a time of flight analyzer.

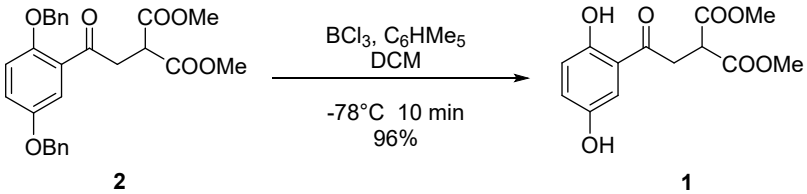



**Synthesis of compound 4**：To a solution of **3** (8.00 g, 24.07 mmol, 1.0 equiv.) in DCE (15 mL) and MeOH (15 mL) was added $BnMe_3N^+Cl_2I^-$ (16.75 g, 48.14 mmol, 2 equiv.). After stirring for 12 h at reflux temperature (68 °C), the reaction mixture was quenched with $Na_2S_2O_3$ aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (70 mL), and washed with brine (3×10 mL). The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The compound **4** as a white solid that was used in the next step without further purification.




**Synthesis of compound 2:** To a solution of **4** (7.10 g, 19.41 mmol, 1.0 equiv.) in acetone (50 mL) was added KI (4.83 g, 29.11 mmol, 1.5 equiv.) and $K_2CO_3$ (5.36 g, 38.81 mmol, 2 equiv.) and dimethyl malonate (2.44 mL, 21.35 mmol, 1.5 equiv.). After stirring for 10 h at reflux temperature (50 °C), the mixture was concentrated in vacuo, diluted with EtOAc (70 mL), and washed with brine (3×10 mL). The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **2** (7.01 g, 63%) as white solid.

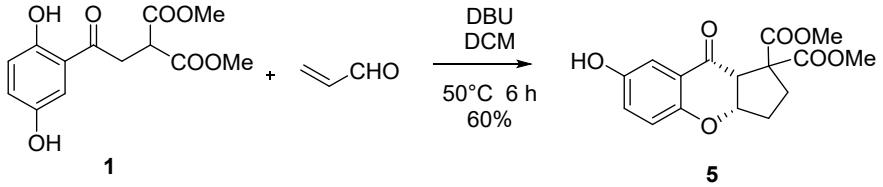
**Characterization data of 2:** Rf = 0.3 (silica gel, PE/EtOAc = 3/1). $^1$H NMR (400MHz, $CDCl_3$): δ 7.49 (d, *J* = 3.2 Hz, 1H), 7.47 – 7.30 (m, 10H), 7.11 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.98 (d, *J* = 9.1 Hz, 1H), 5.15 (s, 2H), 5.03 (s, 2H), 4.01 (t, *J* = 7.2 Hz, 1H), 3.72 (s, 6H), 3.68 (d, *J* = 7.2 Hz, 2H).$^{13}$C NMR (100MHz, $CDCl_3$): δ 197.06, 169.64, 153.20, 152.76, 136.73, 136.17, 128.71, 128.63, 128.22, 128.09, 127.71, 127.63, 126.79, 122.22, 115.02, 114.55, 71.32, 70.56, 52.77, 47.27, 43.52.




**Synthesis of compound 1:** To a solution of **2** (2.00 g, 4.32 mmol, 1.0 equiv.) in anhydrous DCM (21 mL) was added $C_6HMe_5$(3.85 g, 25.95 mmol, 6 equiv.) and

$BCl_3$(10.37 mL, 1M in DCM, 10.37 mmol, 2.4 equiv.). Then stirring for 10 min at -78 °C, quenched by MeOH (0.5 mL), stirred for additional 5 min. The reaction mixture was diluted with EtOAc (100 mL), and washed with brine (5×20 mL). The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **1** (1.17 g 96%) as yellow solid.

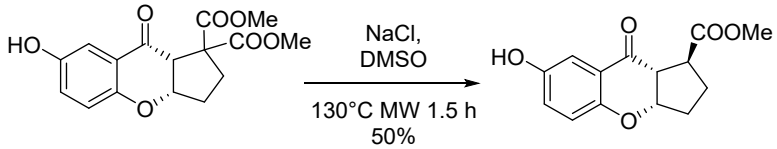
**Characterization data of 1:** Rf = 0.4 (silica gel, PE/EtOAc = 1/1). $^1$H NMR (400 MHz, $CDCl_3$) δ 11.34 (s, 1H), 7.20 (d, *J* = 3.0 Hz, 1H), 7.02 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.85 (d, *J* = 8.9 Hz, 1H), 5.51 (d, *J* = 2.9 Hz, 1H), 4.05 (t, *J* = 7.1 Hz, 1H), 3.80 (s, 6H), 3.62 (d, *J* = 7.2 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ201.56, 169.60, 156.10, 147.98, 125.54, 119.30, 118.30, 114.43, 53.27, 46.46, 37.57. **HRMS** (EIMS) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}O_7$ 283.0812; Found 283.0804.




**1** **5**

**Synthesis of compound 5:** To a solution of **4** (1.00 g, 3.54 mmol, 1.0 equiv.) in anhydrous DCM (12 mL) was added acrolein (0.36 mL, 5.31 mmol, 1.5 equiv.) and DBU (1.08 g, 7.08 mmol, 2 equiv.). Then stirring for 6 h at 50 °C, and evaporated. The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **5** (0.68 g, 60%) as yellow amorphous.

**Characterization data of 5:** Rf = 0.3 (silica gel, PE/EtOAc = 1/1). $^1$H NMR (400 MHz, $CD_3OD$) δ 7.14 (d, *J* = 3.1 Hz, 1H), 6.97 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.79 (d, *J* = 8.9 Hz, 1H), 4.92 – 4.89 (m, 1H), 3.75 (s, 3H), 3.48 (d, *J* = 5.0 Hz, 1H), 3.28 (s, 3H), 2.91 – 2.82 (m, 1H), 2.23 – 2.08 (m, 3H). $^{13}$C NMR (100 MHz, $CD_3OD$) δ 190.49, 170.57, 168.77, 153.46, 151.00, 123.22, 120.85, 117.96, 108.92, 81.37, 62.44, 55.29, 51.60, 50.62, 32.10, 30.17. **HRMS** (EIMS) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}O_7$ 321.0969; Found 321.0957.

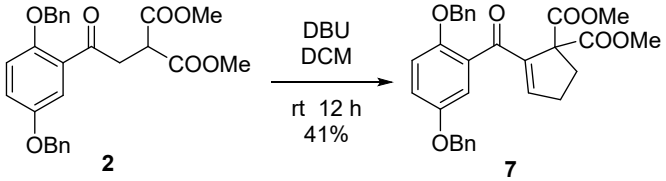



**5** **applanatumols Y (6)**

**Synthesis of compound 6:** An oven-dried 10-mL microwave reaction vial containing a teflon-coated magnetic stir bar was charged with **5** (0.50 g, 1.56 mmol, 1.0 equiv.) in anhydrous DMSO (5 mL) and NaCl (182 mg, 3.12 mmol, 2 equiv.). The vessel was sealed with a plastic microwave septum, stirred at room temperature for 1 min and then placed into the MW cavity for 130°C and 1.5 h. After completion of reaction (TLC), the mixture was cooled to room temperature. The reaction mixture was diluted with

EtOAc (100 mL), and washed with brine (5×20 mL). The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **6** (205 mg, 50%) as yellow amorphous.

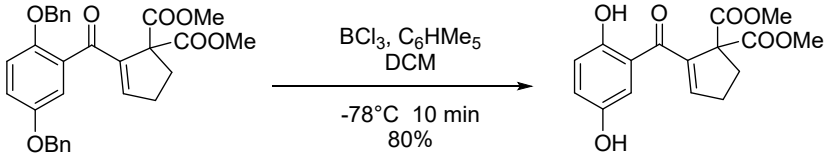
**Characterization data of 6:** Rf = 0.4 (silica gel, PE/EtOAc = 1/1). $^1$H NMR (400 MHz, $CD_3OD$) δ 7.14 (d, *J* = 3.1 Hz, 1H), 7.01 (dd, *J* = 8.9, 3.1 Hz, 1H), 6.82 (d, *J* = 8.9 Hz, 1H), 4.96 – 4.92 (m, 1H), 3.69 (s, 3H), 3.10 – 2.98 (m, 2H), 2.34 – 2.23 (m, 1H), 2.14 – 2.07 (m, 2H), 2.00 (dt, *J* = 13.5, 6.8 Hz, 1H). $^{13}$C NMR (100 MHz, $CD_3OD$) δ 194.35, 176.48, 155.61, 153.08, 126.25, 120.47, 120.23, 111.29, 84.44, 55.35, 52.65, 46.66, 32.96, 28.68.




**2** **7**

**Synthesis of compound 7:** To a solution of **3** (1.00g, 2.16 mmol, 1.0 equiv.) in anhydrous DCM (7 mL) was added acrolein (0.22 mL, 3.24 mmol, 1.5 equiv.) and DBU (0.33 g, 2.16 mmol, 1 equiv.). Then stirring for 12 h at rt, and evaporated. The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **7** (0.44 g, 41%) as yellow viscous liquid.

**Characterization data of 7:** Rf = 0.5 (silica gel, PE/EtOAc = 2/1). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.26 (m, 11H), 6.99 (dd, *J* = 6.9, 3.0 Hz, 2H), 6.95 – 6.91 (m, 1H), 6.54 (t, *J* = 2.6 Hz, 1H), 5.00 (d, *J* = 5.5 Hz, 4H), 3.68 (s, 6H), 2.70 – 2.63 (m, 2H), 2.60 – 2.53 (m, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.58, 171.45, 152.75, 150.40, 150.37, 144.21, 136.91, 136.81, 130.35, 128.63, 128.43, 128.08, 127.84, 127.59, 127.23, 118.20, 115.79, 115.22, 71.50, 70.70, 65.18, 52.86, 35.23, 32.25.

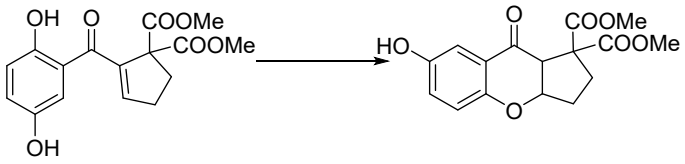



**7** **8**

**Synthesis of compound 8:** To a solution of **7** (1.00 g, 2.00 mmol, 1.0 equiv.) in anhydrous DCM (10 mL) was added $C_6HMe_5$ (1.78 g,12.00 mmol, 6 equiv.) and $BCl_3$(4.8 mL, 1M in DCM, 4.8 mmol, 2.4 equiv.). Then stirring for 10 min at -78 °C, quenched by MeOH (0.5 mL), stirred for additional 5 min. The reaction mixture was diluted with EtOAc (100 mL), and washed with brine (5×20 mL). The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **8** (0.51 g, 80%) as yellow viscous liquid.

**Characterization data of 8:** Rf = 0.4 (silica gel, PE/EtOAc = 1/1). $^1$H NMR (400 MHz, $CDCl_3$) δ 11.21 (s, 1H), 7.19 (d, *J* = 3.0 Hz, 1H), 7.00 (dd, *J* = 8.9, 3.1 Hz, 1H), 6.83

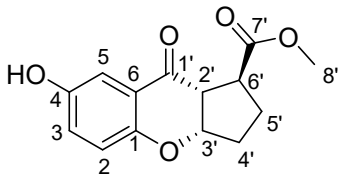
(d, $J$ = 8.9 Hz, 1H), 6.57 (t, $J$ = 2.5 Hz, 1H), 5.94 (s, 1H), 3.76 (s, 6H), 2.75 (td, $J$ = 7.3, 2.4 Hz, 2H), 2.61 (dd, $J$ = 7.8, 6.3 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.98, 171.85, 153.14, 150.81, 150.76, 144.59, 137.28, 137.19, 130.74, 118.60, 116.16, 115.61, 71.91, 71.10, 65.56, 53.25, 35.61, 32.64. **HRMS** (EIMS) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}O_7$ 321.0969; Found 321.0961.




**8** **5**

**Synthesis of compound 5:** To a solution of **8** (0.06 g, 0.19 mmol, 1.0 equiv.) in anhydrous DCM (1 mL) was added DBU (0.03 g, 0.19 mmol, 1.0 equiv.). Then stirring for 6 h at 50 °C, and evaporated. The organic phase was dried over $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **5** (0.04 g, 67%) as yellow amorphous.

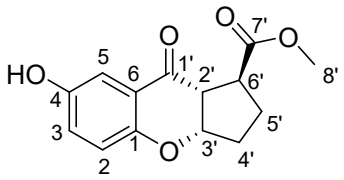
Comparison of the $^{1}$H NMR Data Recorded for applanatumol Y Obtained by the Present Route with those Reported by Cheng.




| No. | **Synthetic product ($\delta_H$) [a]** | **No.** | **Isolated product ($\delta_H$) [b]** | **Δδ** |
|---|---|---|---|---|
| 3 | 7.15 d (3.1) | 3 | 7.15 d (2.9) | 0 |
| 5 | 7.02 dd (8.9, 3.1) | 5 | 7.03 dd (8.9, 2.9) | -0.01 |
| 6 | 6.82 d (8.9) | 6 | 6.83 d (8.9) | -0.01 |
| 2’ | 3.10 – 2.98 m | 2’ | 3.03 m | -- |
| 3’a | 4.97 – 4.93 m | 3’a | 4.95 dd (6.3, 3.2) | -- |
| 4’a | 2.11 m | 4’a | 2.12 m | -0.01 |
| 5’a | 2.30 m | 5’a | 2.31 m | -0.01 |
| 5’b | 2.01 m | 5’b | 2.02 m | -0.01 |
| 6’a | 3.05 m | 6’a | 3.07 m | -0.02 |
| 8’ | 3.69 s | 8’ | 3.66 s | +0.03 |

[a] spectrum recorded in $CD_3OD$ at 400 MHz; b data obtained from Cheng., spectrum recorded in $CD_3OD$ at 600 MHz.

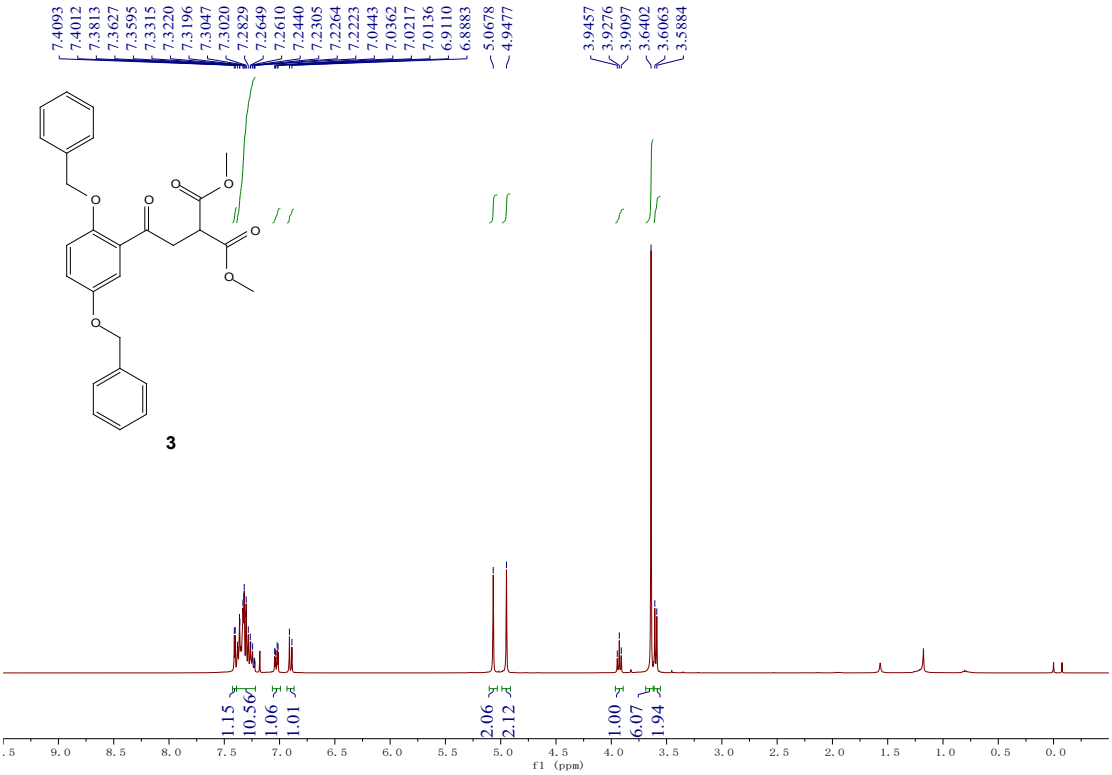
Comparison of the $^{13}C$ NMR Data Recorded for applanatumol Y Obtained by the Present Route with Those Reported by Dong.



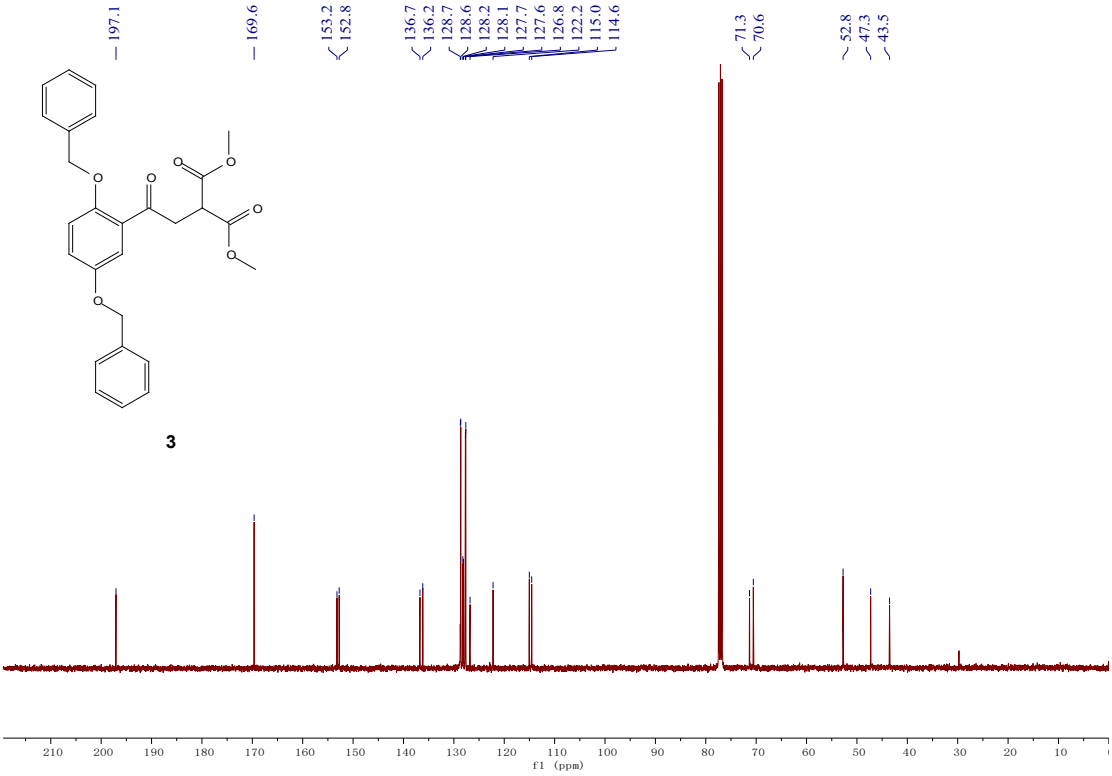

| No. | **Synthetic product** ($\delta_C$) [a] | No. | **Isolated product** ($\delta_C$) [b] | $\Delta\delta$ |
|---|---|---|---|---|
| 1 | 155.6 | 1 | 155.7 | -0.1 |
| 2 | 120.5 | 2 | 120.5 | 0 |
| 3 | 111.3 | 3 | 111.3 | 0 |
| 4 | 153.1 | 4 | 153.1 | 0 |
| 5 | 126.2 | 5 | 126.3 | -0.1 |
| 6 | 120.2 | 6 | 120.3 | -0.1 |
| 1’ | 194.4 | 1’ | 194.5 | -0.1 |
| 2’ | 55.4 | 2’ | 55.4 | 0 |
| 3’ | 84.4 | 3’ | 84.5 | -0.1 |
| 4’ | 33.0 | 4’ | 33.0 | 0 |
| 5’ | 28.7 | 5’ | 28.7 | 0 |
| 6’ | 46.7 | 6’ | 46.7 | 0 |
| 7’ | 176.5 | 7’ | 176.6 | -0.1 |
| 8’ | 52.7 | 8’ | 52.7 | 0 |

[a] spectrum recorded in $CD_3OD$ at 100 MHz; [b] data obtained from Cheng., spectrum recorded in $CD_3OD$ at 150 MHz.

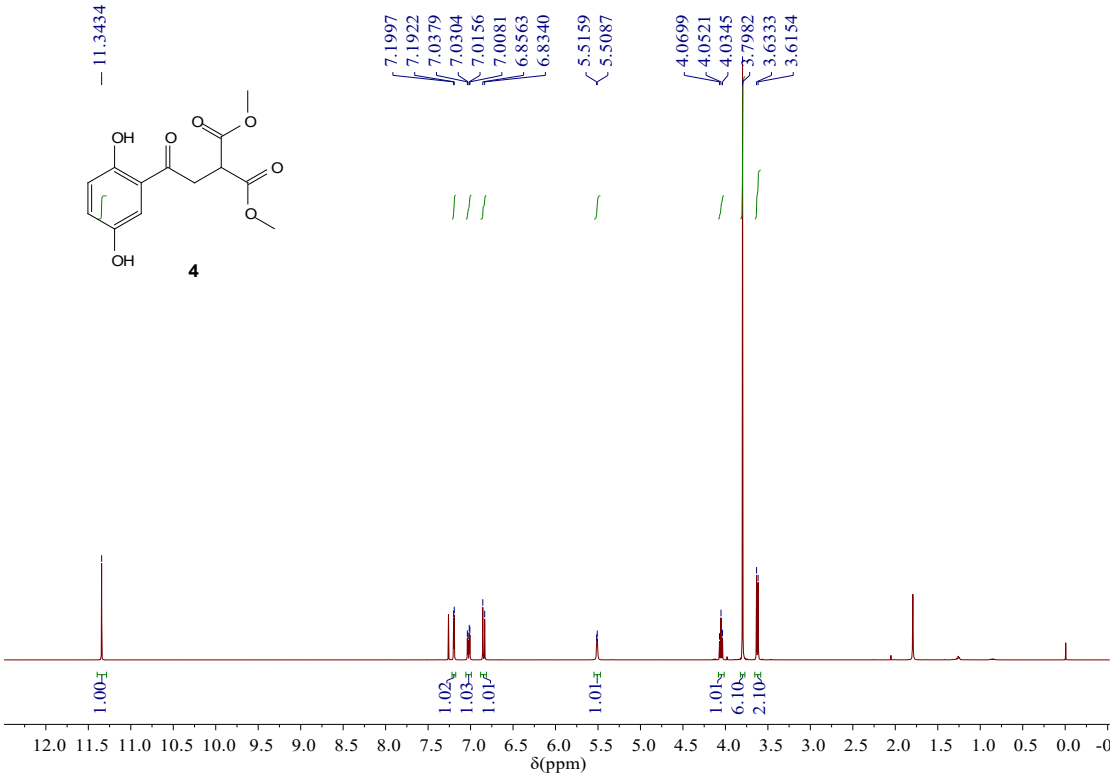
NMR Spectra for the Synthesized Compounds



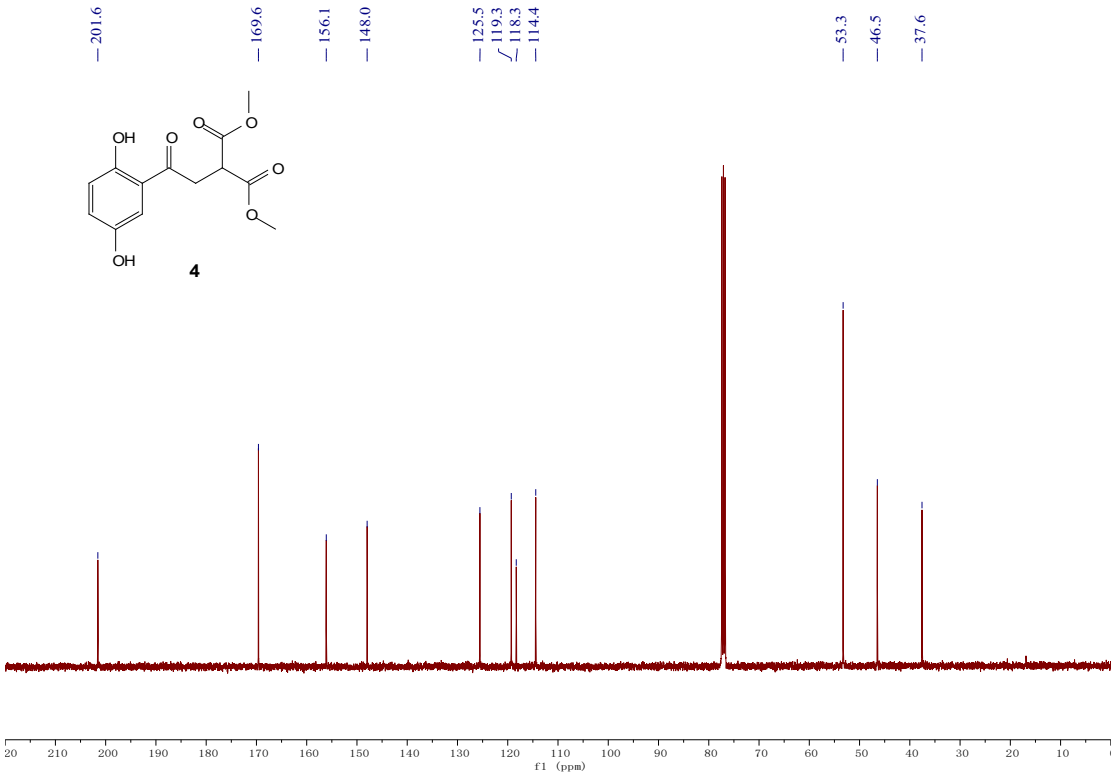

$^{1}$H NMR (400MHz,$CDCl_3$) of compound **2**



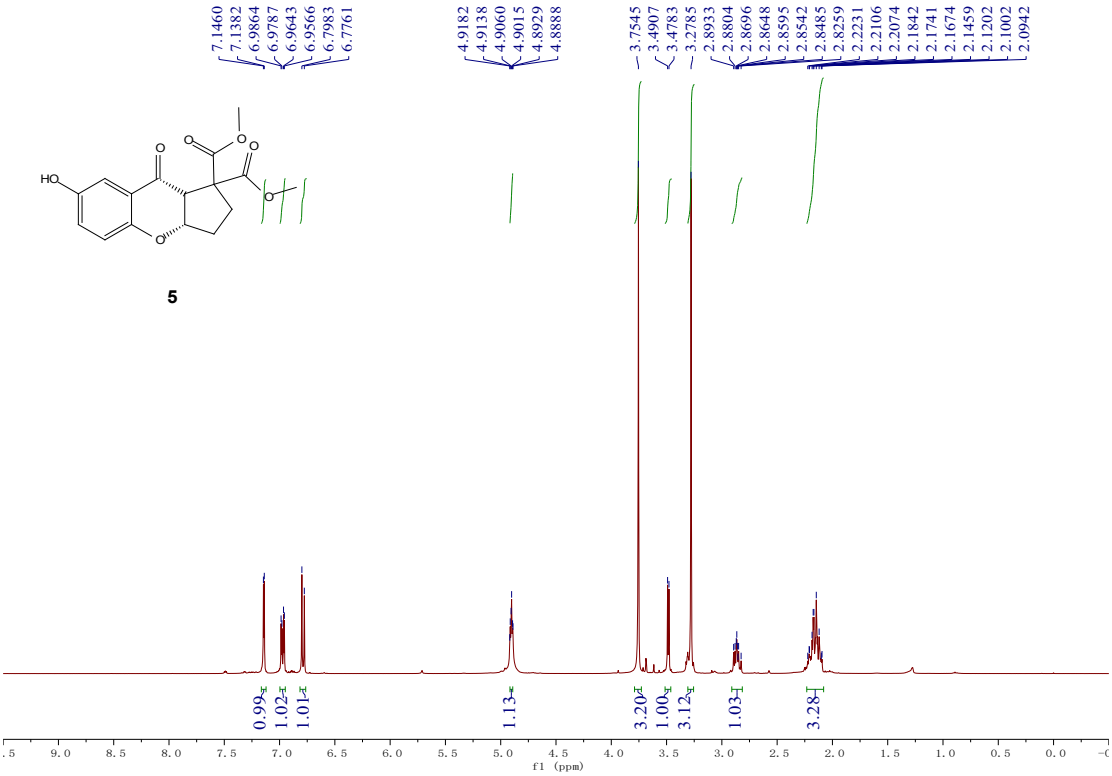

$^{13}$C NMR (100MHz, $CDCl_3$) of compound **2**



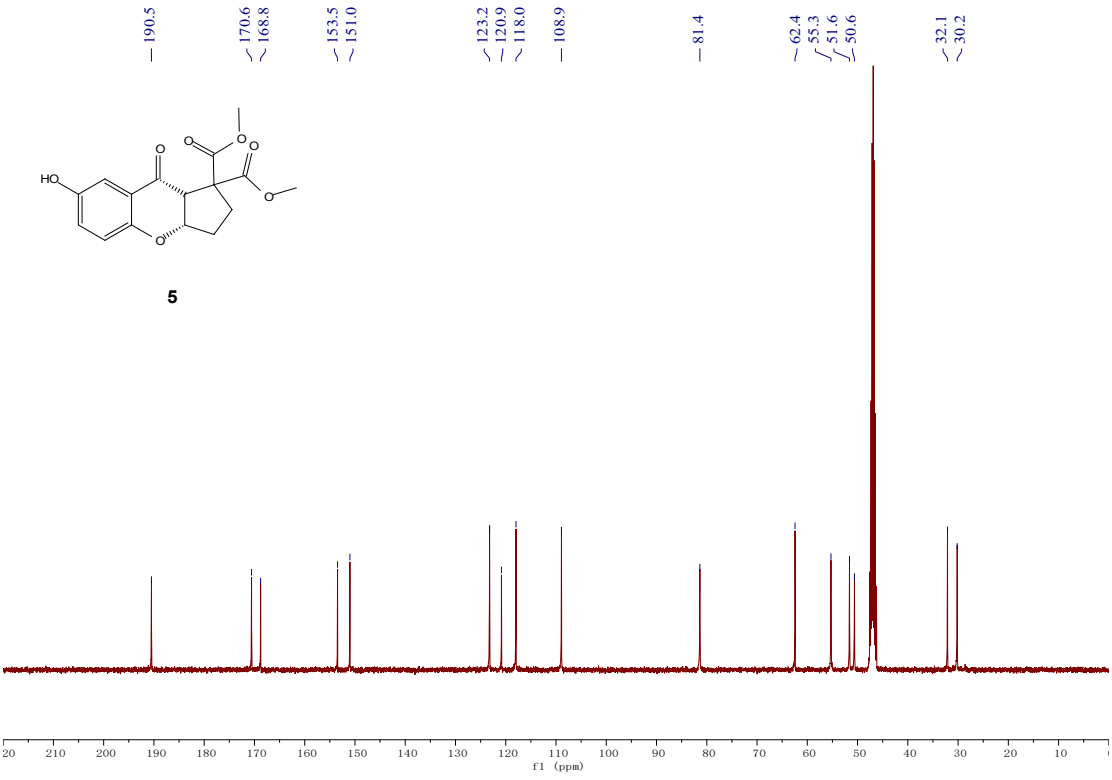

$^{1}$H NMR (400MHz,$CDCl_3$) of compound **1**



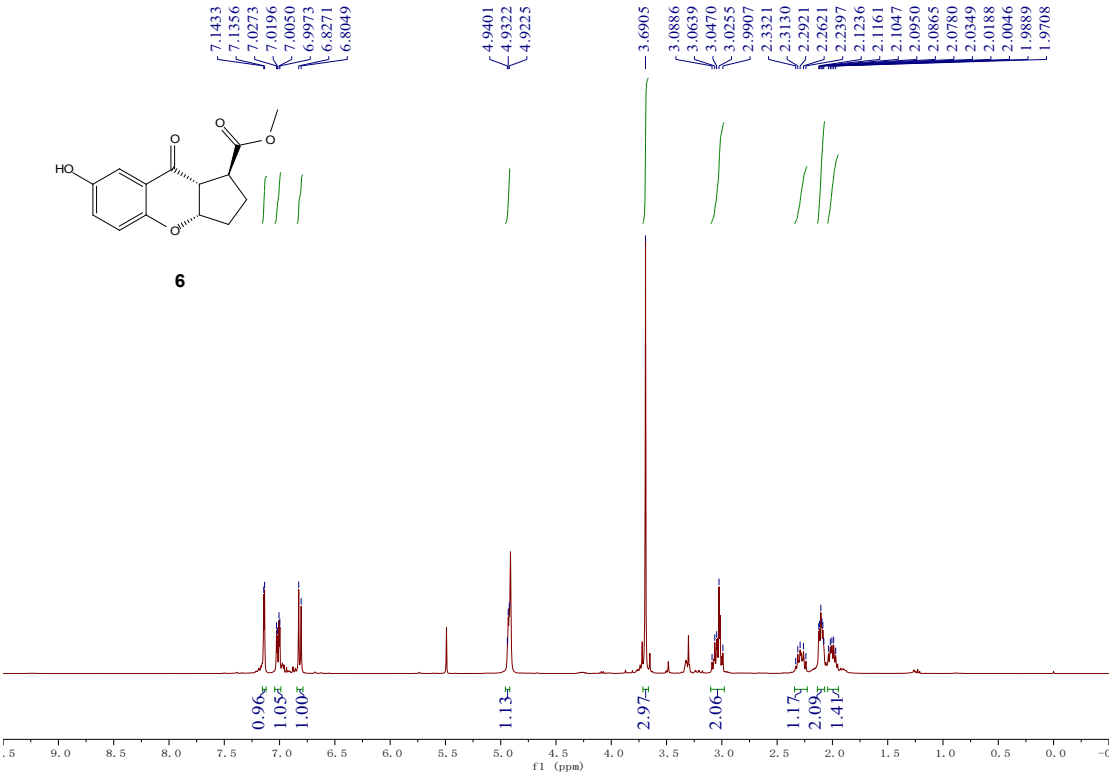

$^{13}$C NMR (100MHz, $CDCl_3$) of compound **1**



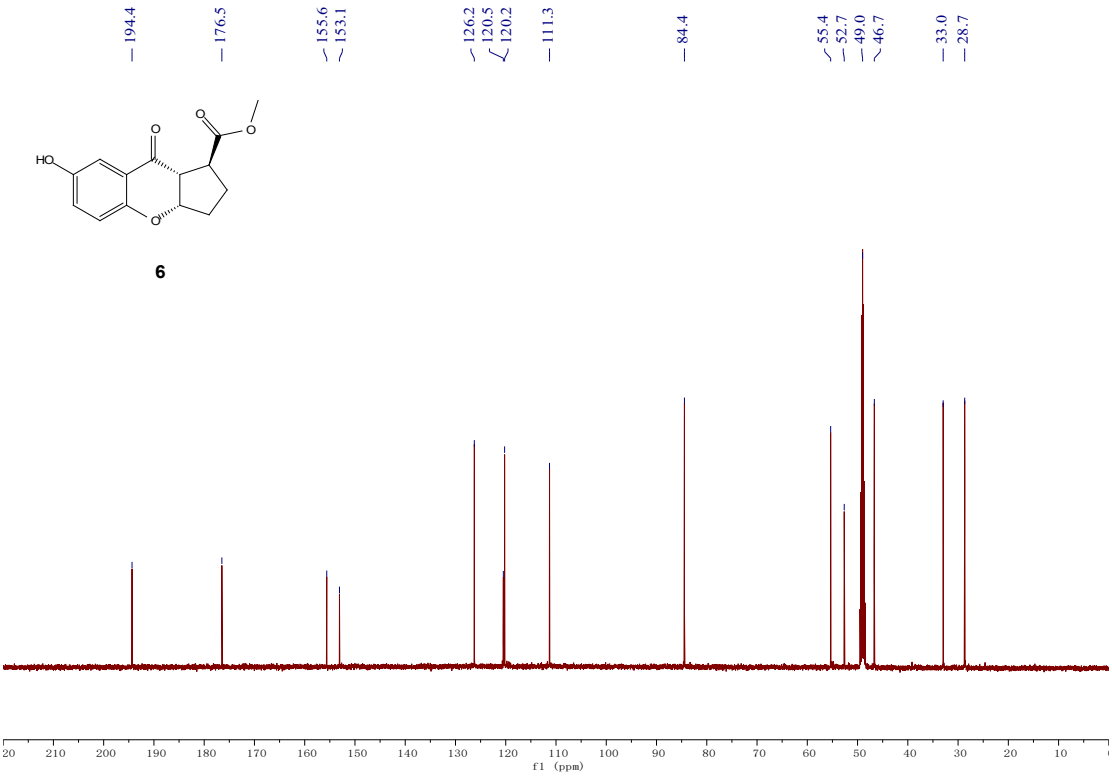

$^{1}$H NMR (400MHz, $CD_3OD$) of compound **5**



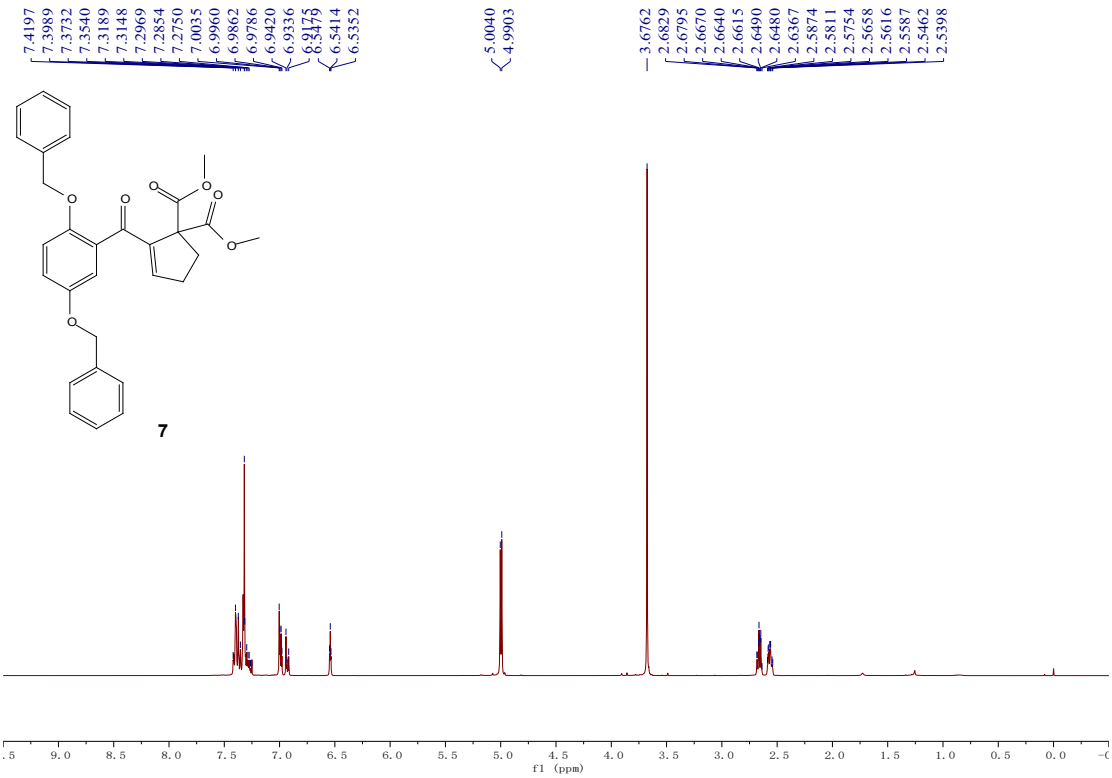

$^{13}$C NMR (100MHz, $CD_3OD$) of compound **5**



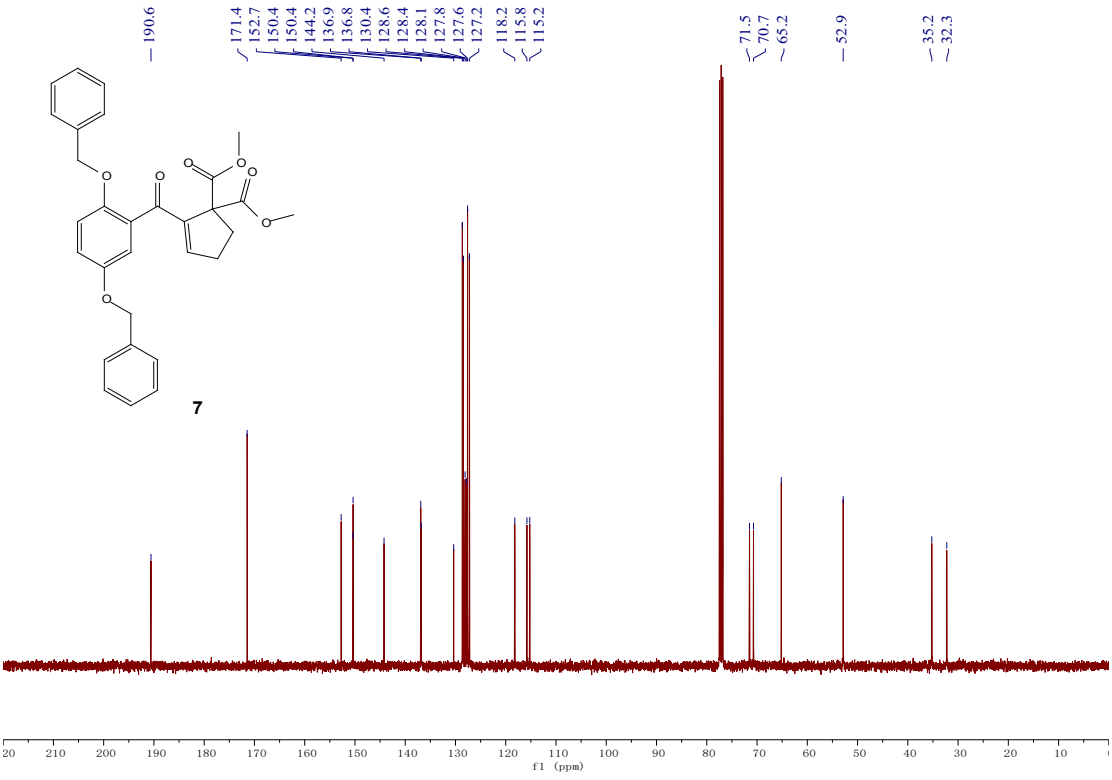

$^{1}$H NMR (400MHz,$CD_3OD$) of compound **6**



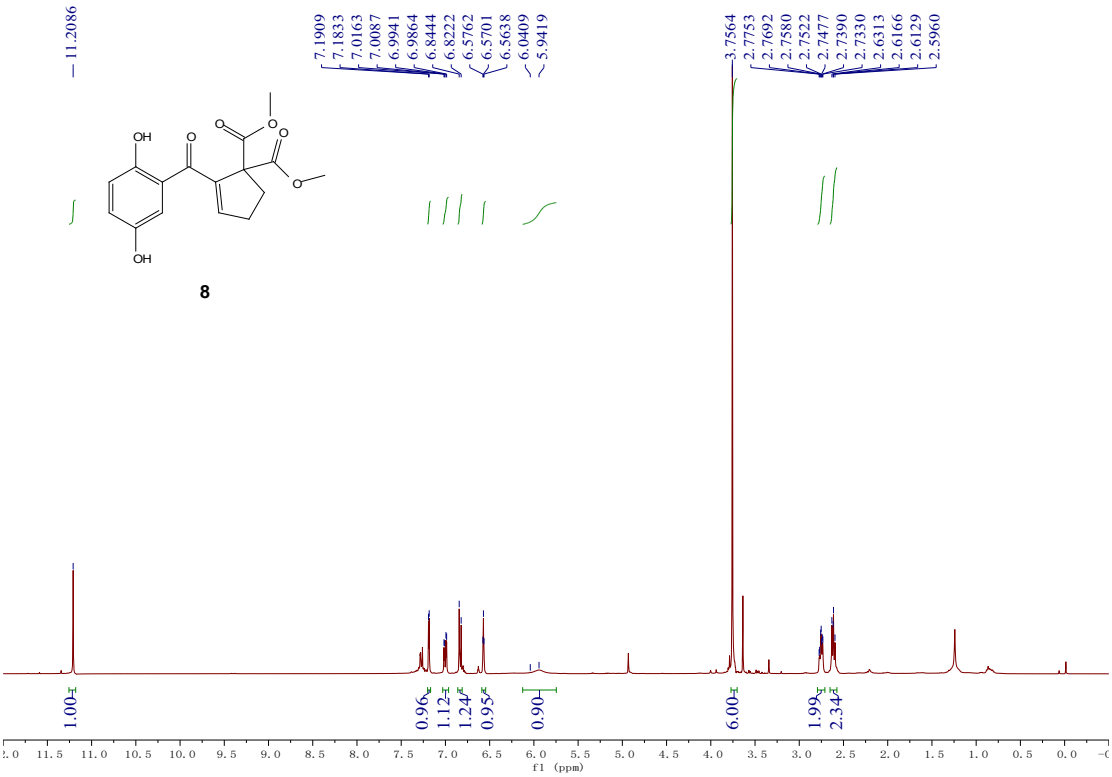

$^{13}$C NMR (100MHz, $CD_3OD$) of compound **6**



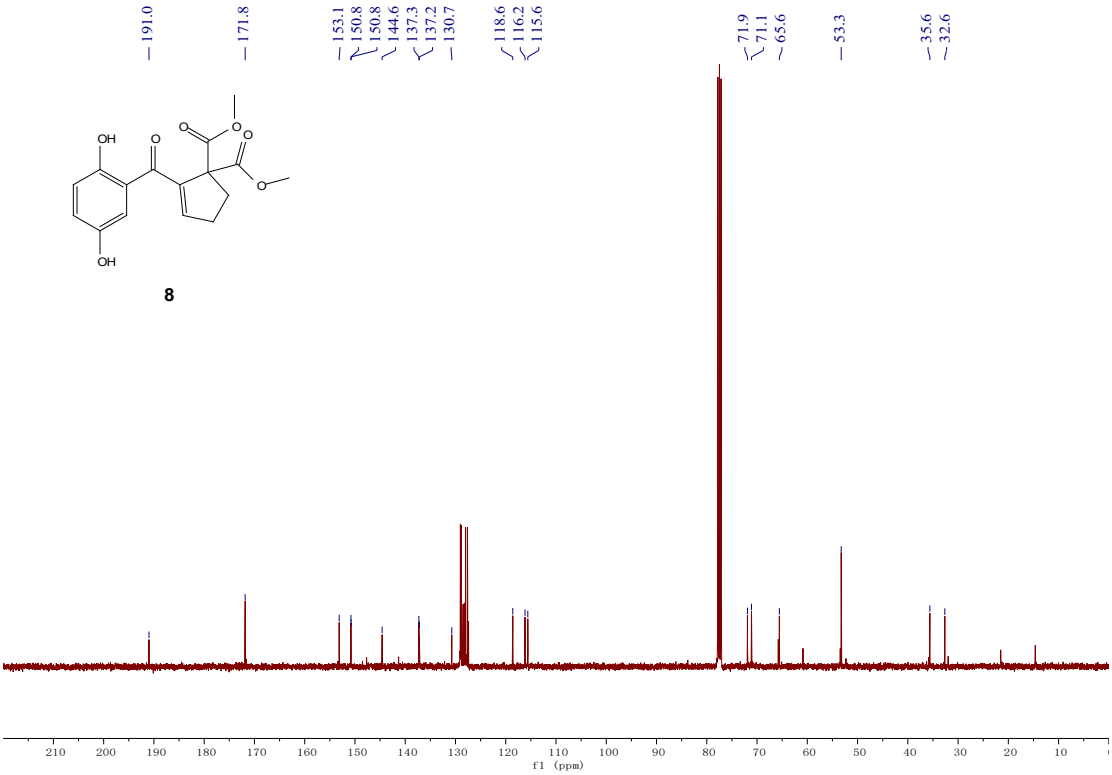

$^{1}$H NMR (400MHz,$CDCl_3$) of compound **7**




$^{13}$C NMR (100MHz, $CDCl_3$) of compound **7**




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




$^{13}$C NMR (100MHz, $CDCl_3$) of compound **8**

## H-H ROESY NMR spectrum of applanatumol Y