A catalyst-free C-H hydroarylation of coumarin derived *ortho*-Quinone methide (*o*-QM) with electron rich arenes in glycerol

Atul Kumar,* Mukesh Kumar, Maneesh Kumar Gupta and Lalit Prakash Gupta

Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow, CSIR, Lucknow India.
Fax: 91-522-26234051; Tel: 91-522-2612411; E-mail: dratulsax@gmail.com

Supporting Information

Table of content

1.General information

Reagent grade solvents were used for extraction and flash chromatography. All the reagents and chemicals were purchased from Sigma-Aldrich Chemical Co, Lancaster and were used directly without further purification.The progress of reactions was checked by analytical thin-layer chromatography (TLC, Merck silica gel 60 F-254 plates). The plates were visualized first with UV illumination followed by iodine. Flash column chromatography was performed using silica gel (100-200 mesh). ^{1}H-NMR spectra were recorded at either 200 or 300 MHz and are reported in parts per million (ppm) on the δ scale relative to tetramethylsilane as an internal standard.^{13}C-NMR spectra were recorded at either 50 or 75 MHz and are reported in parts per million (ppm) on the δ scale relative to $CDCl_3$ (δ 77.00). Mass spectra were obtained using JEOL SX-102 (ESI) instrument.

2.General procedure for the synthesis of 3-((4-(alkylamino)-2-methylphenyl)(phenyl)methyl)-4-hydroxy-2H-chromen-2-one (4a).

4-Hydroxycumarin, **1a** (1 mmol), benzaldehyde **2a** (1 mmol) and *m*-methyl *N*,*N*-dimethylaniline **3a** (1 mmol), and 3 mL glycerol were taken in a round-bottom flask equipped with a magnetic stirrer. The reaction mixture was then stirred at room temperature for an appropriate time and the progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was washed with ethylacetate 4 to 5 times and the organic layer was seperated from glycerol, dried over anhydrous sodium sulphate and concentrate the organic layer, the crude compounds were purified by column chromatography (silica gel, ethyl acetate:hexane).

General procedure for the synthesis of 3-((4-(alkylamino)-2-methylphenyl)(phenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one (6a).

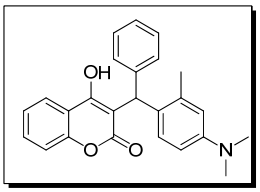
4-Hydroxypyrone, **5a** (1 mmol), benzaldehyde **2a** (1 mmol) and *m*-methyl *N*,*N*-dimethylaniline **3a** (1 mmol), and 3 mL glycerol were taken in a round-bottom flask equipped with a magnetic stirrer. The reaction mixture was then stirred at room temperature for an appropriate time and the progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was washed with ethylacetate 4 to 5 times and the organic layer was seperated from glycerol, dried over anhydrous sodium sulphate and concentrate the organic layer, the crude compounds were purified by column chromatography (silica gel, ethyl acetate:hexane).

General procedure for the synthesis of C2-alkylated dimethylamino cyclohex-2-enone (8a).

1,3 diketone, **7a** (1 mmol), benzaldehyde **2a** (1 mmol) and *m*-methyl *N*,*N*-dimethylaniline **3a** (1 mmol), and 3 mL glycerol were taken in a round-bottom flask equipped with a magnetic stirrer. The reaction mixture was then stirred at room temperature for an appropriate time and the progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was washed with ethylacetate 4 to 5 times and the organic layer was seperated from glycerol, dried over anhydrous sodium sulphate and concentrate the organic layer, the crude compounds were purified by column chromatography (silica gel, ethyl acetate:hexane).

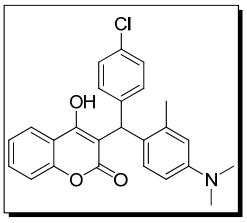
3.Spectroscopic Data of C3-benzylated 4-hydroxycoumarin,4-hydroxypyrone and C2-benzylated 1,3 diketones.

3-((4-(dimethylamino)-2-methylphenyl)(phenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4a



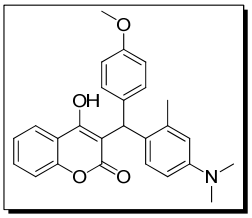
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.31(s, 3H), 2.94 (s, 6H), 5.89 (s, 1H), 6.53 (br, 1H), 6.65 (br, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 7.31-7.29 (m, 7H), 7.51 (br, 1H), 7.78 (d, *J* = 7.6 Hz, 1H).**^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 20.3, 40.5, 44.2, 105.8, 110.4, 115.3, 116.3, 117.5, 123.4, 126.6, 127.2, 128.6, 128.9, 129.1, 131.3, 138.6, 141.8, 149.8, 153.0, 163.6, 163.8; ESIMS: m/z 386 (M+H), calcd for $C_{25}H_{23}NO_3$ is C, 77.90; H, 6.01; N, 3.63. Found; C, 77.91; H, 6.03; N, 3.61.

3-((4-chlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4b



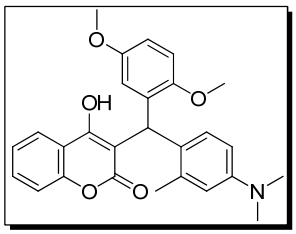
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.28(s, 3H), 2.94 (s, 6H), 5.78 (s, 1H), 6.54 (br, 1H), 6.76-6.71 (br, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 4H), 7.54-7.48 (m, 1H), 7.71 (d, *J* = 7.8 Hz, 1H).**^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 20.2, 40.1, 44.2, 105.6, 110.4, 115.5, 116.2, 116.4, 123.2, 123.8, 125.4, 128.5, 128.9, 130.2, 131.9, 132.7, 139.1, 139.4, 150.2, 152.8, 161.8, 162.9; ESIMS: m/z 420 (M+H), calcd for $C_{25}H_{22}ClNO_3$ is C, 71.51; H, 5.28; N, 3.34. Found; C, 71.50; H, 5.29; N, 3.32.

3-((4-(dimethylamino)-2-methylphenyl)(4-methoxyphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4c



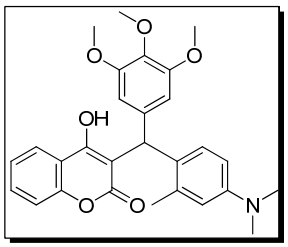
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.29(s, 3H), 2.93 (s, 6H), 3.80 (s, 3H), 5.79 (s, 1H), 6.52 (d, *J* = 7.9 Hz, 1H), 6.90-6.76 (m, 4H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.44-7.39 (m, 2H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 7.1 Hz, 1H); ESIMS: m/z 416 (M+H), calcd for $C_{26}H_{25}NO_4$ is C, 75.16; H, 6.06; N, 3.37. Found; C, 75.14; H, 6.07; N, 3.36.

3-((2,5-dimethoxyphenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4d



^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.25(s, 3H), 2.92 (s, 6H), 3.66 (s, 3H), 3.71 (s, 3H), 5.99 (s, 1H), 6.50-6.46 (m, 1H), 6.72 (br, 1H), 6.75-6.74 (br, 1H), 6.87-6.80 (m, 3H), 7.11 (br, 1H), 7.51-7.25 (m, 3H); ESIMS: m/z 456 (M+H), calcd for $C_{27}H_{27}NO_5$ is C, 72.79; H, 6.11; N, 3.14. Found; C, 72.77; H, 6.10; N, 3.16.

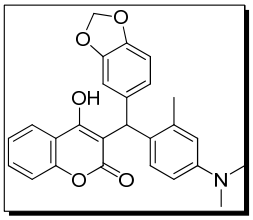
3-((4-(dimethylamino)-2-methylphenyl)(3,4,5-trimethoxyphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4e



^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.30(s, 3H), 2.96 (s, 6H), 3.77 (s, 6H), 3.86 (s, 3H), 5.80 (s, 1H), 6.49 (s, 2H), 6.55 (d, *J* = 5.9 Hz, 1H), 6.66 (br, 1H), 6.87 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H). **^{13}C NMR (75**

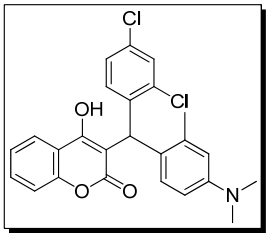
MHz, $CDCl_3$) δ (ppm): 20.2, 40.4, 44.9, 56.2, 60.8, 105.9, 106.6, 115.9, 116.4, 123.2, 123.8, 128.3, 131.9, 136.2, 137.3, 138.8, 152.7, 153.8, 161.1, 163.0; ESIMS: m/z 476 (M+H), calcd for $C_{28}H_{29}NO_6$ is C, 70.72; H, 6.15; N, 2.95. Found; C, 70.70; H, 6.16; N, 2.97

3-(benzo[d][1,3]dioxol-5-yl(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4f



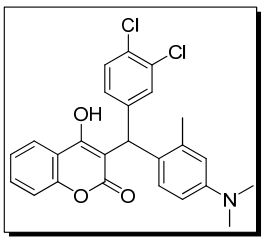
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.27(s, 3H), 2.93 (s, 6H), 5.74 (s, 1H), 5.95 (s, 2H), 6.53-6.49 (m, 1H), 6.70-6.63 (m, 2H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.54-7.49 (m, 1H), 7.70 (d, *J* = 1.2 Hz, 1H).**^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 20.2, 40.3, 44.4, 101.2, 106.6, 108.6, 109.4, 110.5, 115.6, 116.0, 116.4, 121.6, 123.1, 123.7, 125.8, 128.3, 131.8, 134.5, 138.8, 146.8, 148.4, 150.2, 152.7, 161.1, 162.9; ESIMS: m/z 430 (M+H), calcd for $C_{26}H_{23}NO_5$ is C, 72.71; H, 5.40; N, 3.26. Found; C, 72.69; H, 5.41; N, 3.27.

3-((2,4-dichlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4g



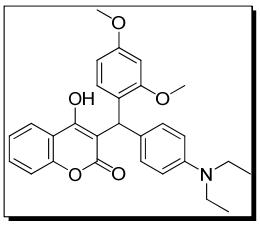
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.25(s, 3H), 2.88 (s, 6H), 5.94 (s, 1H), 6.43-6.38 (m, 1H), 6.54 (br, 1H), 6.59 (d, *J* = 3.8 Hz, 1H), 7.22-7.10 (m, 3H), 7.47-7.36 (m, 3H), 7.66-7.62 (m, 1H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 20.2, 40.2, 42.4, 104.4, 110.5, 115.7, 115.8, 116.5, 123.2, 123.3, 123.8, 127.1, 127.6, 129.9, 130.2, 132.1, 133.4, 135.6, 137.4, 139.4, 150.4, 152.8, 162.1, 162.5; ESIMS: m/z 454 (M+H), calcd for $C_{25}H_{21}Cl_2NO_3$ is C, 66.09; H, 4.66; N, 3.08. Found; C, 66.10; H, 4.64; N, 3.09.

3-((3,4-dichlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4h



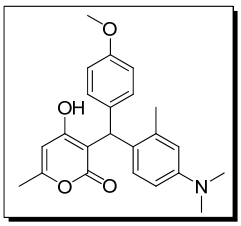
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.29(s, 3H), 2.95 (s, 6H), 5.76 (s, 1H), 6.52-6.49 (m, 1H), 6.65-6.64 (br, 1H), 6.73 (d, *J* = 8.5 Hz, 1H), 7.12-7.09 (m, 1H), 7.34-7.23 (m, 2H), 7.41 (d, *J* = 8.2 Hz, 1H),7.56-7.51 (m, 2H), 7.75 (d, *J* = 7.8 Hz, 1H); ESIMS: m/z 454 (M+H), calcd for $C_{25}H_{21}Cl_2NO_3$ is C, 66.09; H, 4.66; N, 3.08. Found; C, 66.08; H, 4.64; N, 3.09.

3-((4-(diethylamino)phenyl)(2,4-dimethoxyphenyl)methyl)-4-hydroxy-2H-chromen-2-one: 4i



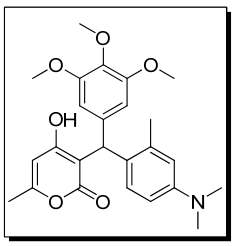
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.16 (t, *J* = 6.9 Hz, 6H), 3.35 (q, *J* = 7.2 Hz, 4H), 3.68 (s, 3H), 3.74 (s, 3H), 5.96 (s, 1H), 6.63 (d, *J* = 8.4 Hz, 2H), 6.82-6.79 (m, 2H), 6.89 (d, *J* = 8.6 Hz, 1H),7.30-6.92 (m, 4H), 7.52 (t, *J* = 8.2 Hz, 1H), 7.75 (br, 1H); ESIMS: m/z 460 (M+H), calcd for $C_{28}H_{29}NO_5$ is C, 73.18; H, 6.36; N, 3.05. Found; C, 73.17; H, 6.37; N, 3.04.

3-((4-(dimethylamino)-2-methylphenyl)(4-methoxyphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6a



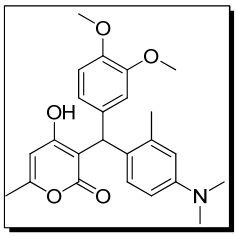
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.20(s, 3H), 2.26(s, 3H), 2.92 (s, 6H), 3.80 (s, 3H), 5.61 (s, 1H), 5.71 (s, 1H), 6.49 (q, *J* = 8.4 Hz, 1H), 6.64-6.43 (br, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 19.7, 20.1, 40.4, 43.1, 55.3, 100.9, 104.1, 110.4, 113.7, 114.3, 115.5, 126.7, 128.4, 129.7, 132.8, 138.6, 149.9, 158.6, 160.8, 165.3, 165.8; ESIMS: m/z 380 (M+H), calcd for $C_{23}H_{25}NO_4$ is C, 72.80; H, 6.64; N, 3.69. Found; C, 72.81; H, 6.62; N, 3.68.

3-((4-(dimethylamino)-2-methylphenyl)(3,4,5-trimethoxyphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6b



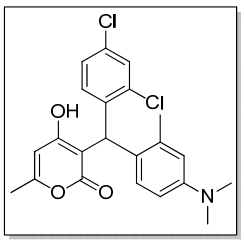
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.19 (s, 3H), 2.23 (s, 3H), 2.90 (s, 6H), 3.74 (s, 6H), 3.81 (s, 3H), 5.56 (s, 1H), 5.69 (s, 1H), 6.39 (s, 2H), 6.48-6.45 (m, 1H), 6.61-6.60 (br, 1H), 6.74 (d, J = 8.5 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 19.7, 20.1, 40.3, 44.2, 56.1, 60.8, 100.8, 103.8, 105.8, 110.4, 115.5, 126.2, 128.2, 136.6, 137.0, 138.6, 150.0, 153.5, 161.0, 165.0, 165.9; ESIMS: m/z 440 (M+H), calcd for $C_{25}H_{29}NO_6$ is C, 68.32; H, 6.65; N, 3.19. Found; C, 68.31; H, 6.64; N, 3.17.

3-((3,4-dimethoxyphenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6c



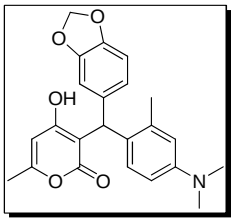
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.09 (s, 3H), 2.15 (s, 3H), 2.82 (s, 6H), 3.70 (s, 3H), 3.75 (s, 3H), 5.50 (s, 1H), 5.61 (s, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 6.8 Hz, 2H), 6.71-6.64 (m, 3H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 19.7, 20.1, 40.4, 43.5, 55.8, 100.8, 104.0, 110.4, 111.2, 112.3, 115.5, 120.1, 126.5, 128.2, 133.4, 138.6, 148.2, 149.5, 149.9, 160.9, 165.1, 165.9; ESIMS: m/z 410 (M+H), calcd for $C_{24}H_{27}NO_5$ is C, 70.40; H, 6.65; N, 3.42. Found; C, 70.42; H, 6.64; N, 3.43.

3-((2,4-dichlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6d



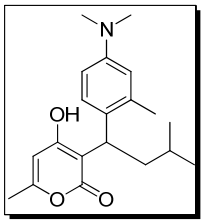
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.11 (s, 3H), 2.20 (s, 3H), 2.85 (s, 6H), 5.63 (s, 1H), 5.73 (s, 1H), 6.38-6.35 (m, 1H), 6.55 (d, *J* = 8.6 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 1H), 7.14-7.10 (m, 1H); 7.32-7.32 (br, 1H); ESIMS: m/z 418 (M+H), calcd for $C_{22}H_{21}Cl_2NO_3$ is C, 63.17; H, 5.06; N, 3.35. Found; C, 63.15; H, 5.07; N, 3.34.

3-(benzo[d][1,3]dioxol-5-yl(4-(dimethylamino)-2-methylphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6e



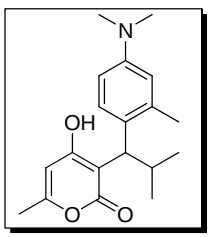
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.21 (s, 3H), 2.27 (s, 3H), 2.94 (s, 6H), 5.58 (s, 1H), 5.72 (s, 1H), 5.97 (s, 2H), 6.51-6.48 (m, 1H), 6.66 (dd, *J* = 1.2 Hz, 1.7 Hz, 2H), 6.72-6.72 (br, 1H); 6.79 (d, *J* = 8.1 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 19.6, 20.1, 40.3, 43.6, 100.8, 101.1, 103.8, 108.4, 109.4, 110.4, 115.5, 121.5, 126.3, 128.3, 134.9, 138.6, 146.6, 148.2, 149.9, 160.9, 165.0, 165.9; ESIMS: m/z 394 (M+H), calcd for $C_{23}H_{23}NO_5$ is C, 70.21; H, 5.89; N, 3.56. Found; C, 70.20; H, 5.88; N, 3.57.

3-(1-(4-(dimethylamino)-2-methylphenyl)-3-methylbutyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6f



^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.93 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.3 Hz, 3H), 1.77-1.59 (m, 3H), 2.14 (s, 3H), 2.21 (s, 3H), 2.93 (s, 6H), 4.37 (t, *J* = 6.8 Hz, 1H), 5.60 (s, 1H), 6.62 (br, 2H), 7.37 (t, *J* = 4.7 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 19.5, 20.1, 22.4, 23.1, 25.5, 34.2, 40.5, 40.9, 101.2, 105.4, 110.5, 115.9, 126.2, 126.3, 127.3, 139.2, 149.5, 160.1, 165.4, 165.7; ESIMS: m/z 330 (M+H), calcd for $C_{20}H_{27}NO_3$ is C, 72.92; H, 8.26; N, 4.25. Found; C, 72.90; H, 8.27; N, 4.23.

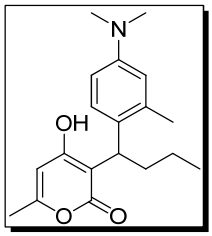
3-(1-(4-(dimethylamino)-2-methylphenyl)-2-methylpropyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6g



^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.94-0.87 (br, 6H), 1.71-1.58 (m, 1H), 2.13 (s, 3H), 2.20 (s, 3H), 2.91 (s, 6H), 4.26 (br, 1H), 5.67 (s, 1H), 6.60 (br, 2H), 7.40 (d, *J* = 7.8 Hz, 1H);

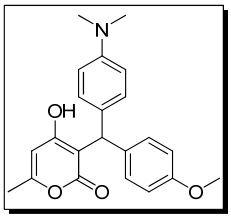
ESIMS: m/z 316 (M+H), calcd for $C_{19}H_{25}NO_3$ is C, 72.35; H, 7.99; N, 4.44. Found; C, 72.34; H, 7.98; N, 4.46.

3-(1-(4-(dimethylamino)-2-methylphenyl)butyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6h



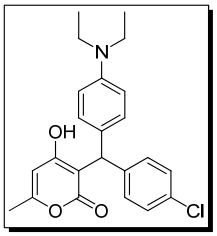
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.83 (d, *J* = 6.7 Hz, 1H), 0.89 (d, *J* = 6.2 Hz, 3H), 0.96 (d, *J* = 6.2 Hz, 3H), 2.07 (s, 3H), 2.25 (s, 3H), 2.88 (s, 6H), 3.96 (d, *J* = 10.4 Hz, 1H), 5.78 (s, 1H), 6.62 (br, 2H), 7.56 (d, *J* = 8.4 Hz, 1H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 13.7, 20.7, 21.2, 21.7, 30.5, 41.0, 43.5, 101.6, 105.2, 111.0, 115.4, 128.5, 128.8, 130.8, 130.9, 132.4, 138.3, 148.2, 159.8, 166.8, 166.9, 167.8; ESIMS: m/z 316 (M+H), calcd for $C_{19}H_{25}NO_3$ is C, 72.35; H, 7.99; N, 4.44. Found; C, 72.33; H, 7.98; N, 4.45.

3-((4-(dimethylamino)phenyl)(4-methoxyphenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6i



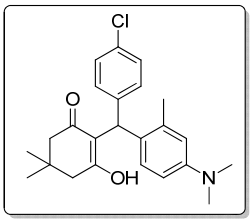
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.16 (s, 3H), 2.90 (s, 6H), 3.77 (s, 3H), 5.57 (s, 1H), 5.71 (s, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm):** 19.6, 40.7, 44.9, 55.3, 101.1, 105.5, 113.1, 114.2, 127.9, 129.3, 129.7, 132.8, 149.7, 158.6, 160.8, 165.4, 165.5; ESIMS: m/z 366 (M+H), calcd for $C_{22}H_{23}NO_4$ is C, 72.31; H, 6.34; N, 3.83. Found; C, 72.33; H, 6.32; N, 3.84.

3-((4-chlorophenyl)(4-(diethylamino)phenyl)methyl)-4-hydroxy-6-methyl-2H-pyran-2-one: 6j



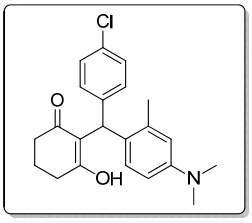
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.17 (t, *J* = 6.7 Hz, 6H), 2.16 (s, 3H), 3.36 (q, *J* = 6.9 Hz, 4H), 5.60 (s, 1H), 5.76 (s, 1H), 6.63 (d, *J* = 8.6 Hz, 2H), 7.04 (d, *J* = 8.6 Hz, 2H), 7.19 (s, Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 12.5, 19.6, 44.5, 44.7, 102.4, 104.2, 112.5, 128.1, 129.8, 130.2, 131.7, 141.3, 146.2, 160.5, 166.3, 168.8; ESIMS: m/z 398 (M+H), calcd for $C_{23}H_{24}ClNO_3$ is C, 69.43; H, 6.08; N, 3.52. Found; C, 69.44; H, 6.06; N, 3.53.

2-((4-chlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone: 8a



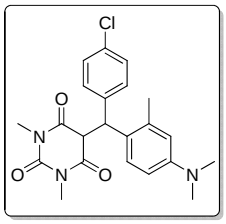
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.17 (s, 6H), 2.15 (s, 3H), 2.19 (br, 2H), 2.24 (br, 2H), 2.83 (s, 6H), 5.57 (s, 1H), 6.37 (d, *J* = 8.1 Hz, 1H), 6.53 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 7.21 (m, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 20.5, 22.6, 28.3, 31.6, 40.3, 41.6, 50.5, 110.5, 115.2, 115.6, 127.1, 128.3, 128.8, 130.2, 132.3, 138.6, 140.7, 149.8; ESIMS: m/z 398 (M+H), calcd for $C_{24}H_{28}ClNO_2$ is C, 72.44; H, 7.09; N, 3.52. Found; C, 72.42; H, 7.10; N, 3.51.

2-((4-chlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-3-hydroxycyclohex-2-enone: 8b



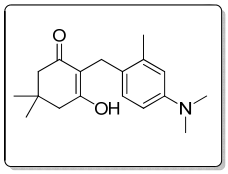
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.99 (t, *J* = 6.3 Hz, 2H), 2.22 (s, 3H), 2.46-2.37 (m, 4H), 2.90 (s, 6H), 5.66 (s, 1H), 6.44-6.41(m, 1H), 6.61(d, *J* = 10.5 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.25 (s, 1H), 7.29 (s, 1H). **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 20.1, 20.7, 31.6, 31.9, 36.8, 40.3, 110.4, 115.6, 116.2, 127.2, 128.2, 128.7, 130.2, 132.3, 138.7, 140.6, 149.8, 172.9, 197.1; ESIMS: m/z 370 (M+H), calcd for $C_{22}H_{24}ClNO_2$ is C, 71.44; H, 6.54; N, 3.79; Found; C, 71.42; H, 6.55; N, 3.77.

5-((4-chlorophenyl)(4-(dimethylamino)-2-methylphenyl)methyl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione: 8c



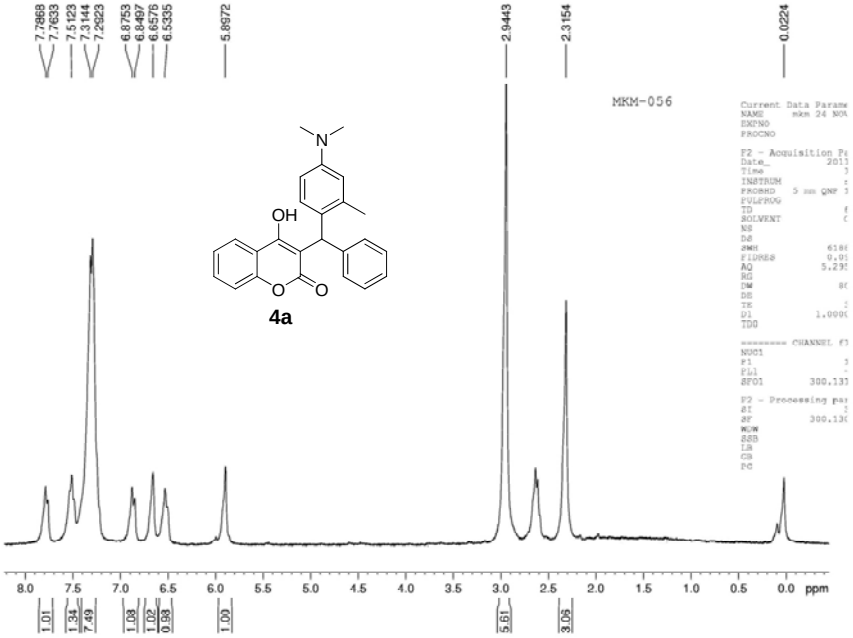
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.09 (s, 3H), 2.88 (s, 6H), 3.02 (s, 3H), 3.15 (s, 3H), 4.28 (d, *J* = 2.8 Hz, 1H), 5.04 (s, 1H), 6.44 (s, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 7.4 Hz, 3H), 7.22 (d, *J* = 8.4 Hz, 2H). **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):** 20.3, 28.5, 40.3, 49.6, 53.9, 110.2, 114.9, 124.2, 128.4, 129.1, 129.7, 132.7, 136.9, 138.9, 149.7, 168.2; ESIMS: m/z 414 (M+H), calcd for $C_{22}H_{24}ClN_3O_3$ is C, 63.84; H, 5.84; N, 10.15; Found; C, 63.82; H, 5.83; N, 10.16.

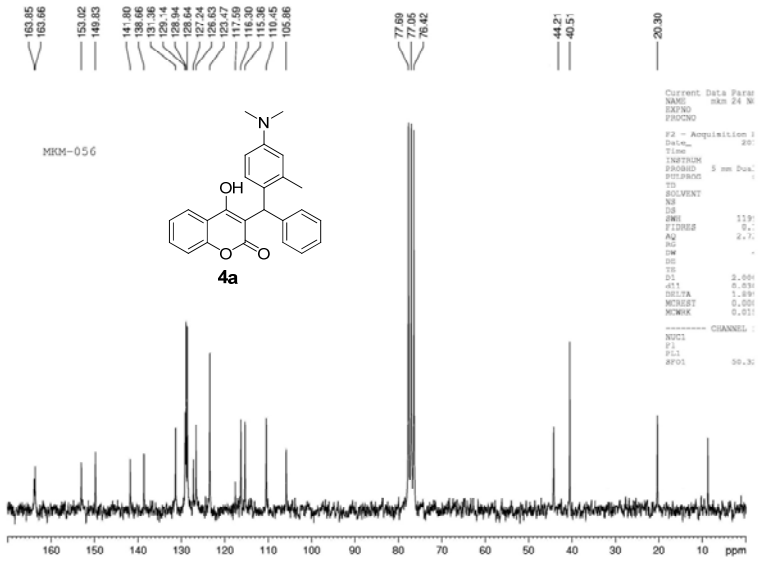
2-(4-(dimethylamino)-2-methylbenzyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone: 8d

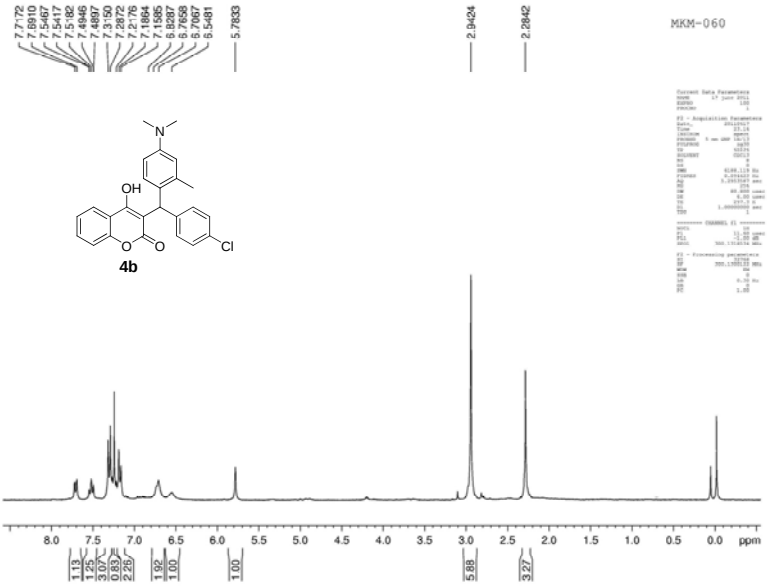


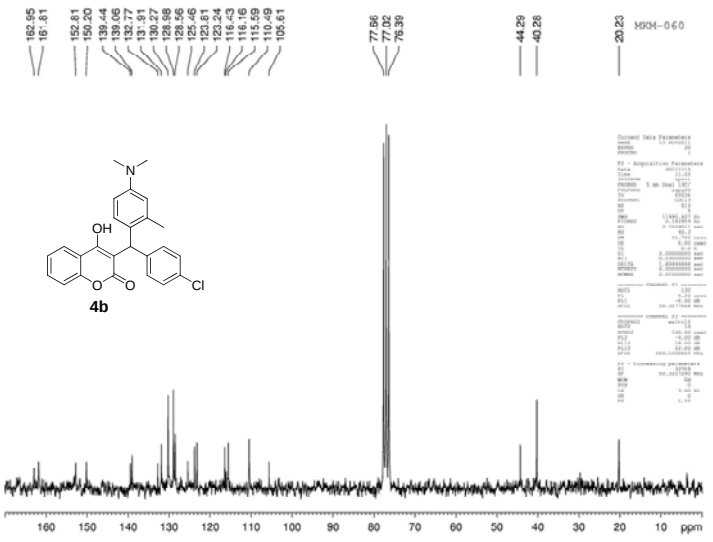
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.12 (s, 6H), 2.19 (s, 4H), 2.41 (s, 3H), 3.01 (s, 6H), 3.23 (s, 2H), 6.66-6.64 (m, 1H), 7.27-7.20 (m, 2H). ESIMS: m/z 288 (M+H), calcd for $C_{18}H_{25}NO_2$ is C, 75.22; H, 8.77; N, 4.87 Found; C, 75.20; H, 8.78; N, 4.88.

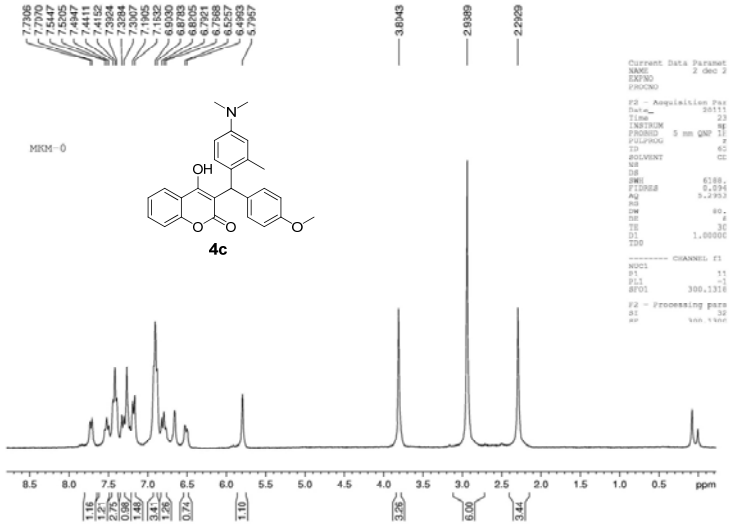
4. ^{1}H NMR and ^{13}C NMR Spectra for Spectroscopic Data of C3-benzylated 4-hydroxycoumarin, 4-hydroxypyrone and C2-benzylated 1,3 diketones.

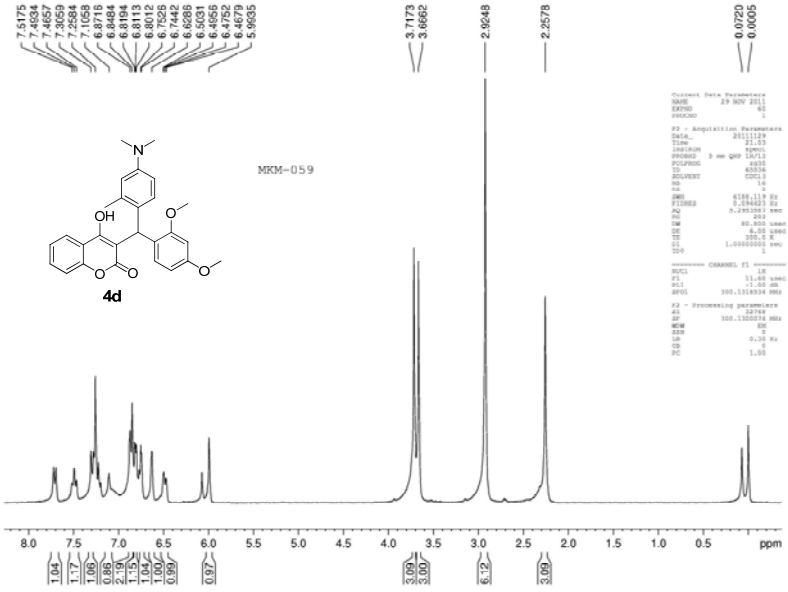

7.7868
7.7633
7.5123
7.3144
7.2923
6.8753
6.8497
6.6576
6.5335
5.8572
2.9443
2.3154
0.0224
MKM-056
OH
O
O
N
4a
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.01
1.34
7.49
1.08
1.02
0.58
1.00
5.61
3.06

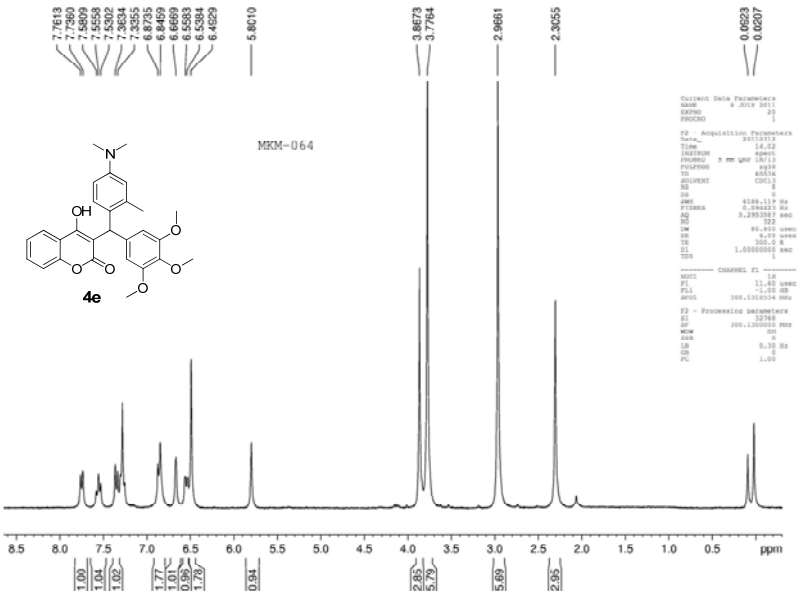

163.85
163.66
153.02
149.83
141.80
138.66
137.36
131.14
128.94
128.64
127.24
126.63
123.47
117.39
115.80
115.36
110.45
105.86
77.69
77.05
76.42
44.21
40.51
20.30
MKM-056
OH
O
O
N
4a
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

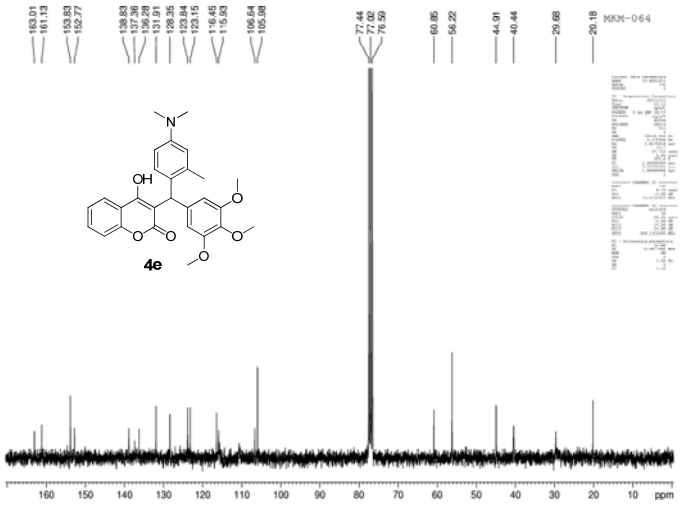

7.7172
7.6910
7.5467
7.5417
7.5182
7.4946
7.4897
7.3150
7.2872
7.2176
7.1864
7.1585
6.8287
6.7658
6.7067
6.5481
5.7833
2.9424
2.2842
MKM-060
OH
N
O
O
Cl
4b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.19
1.25
3.07
0.83
2.26
1.92
1.00
1.00
5.88
3.27

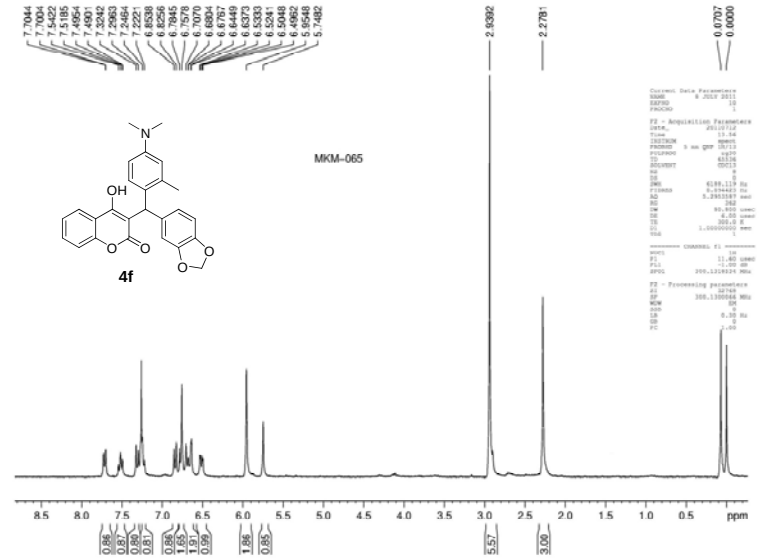

162.95
161.81
152.81
150.20
139.44
139.06
132.77
131.91
130.27
128.68
128.56
125.46
123.81
123.24
116.43
116.16
115.59
110.49
105.61
77.66
77.02
76.39
44.29
40.28
20.23
MKM-060
OH
N
O
O
Cl
4b
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

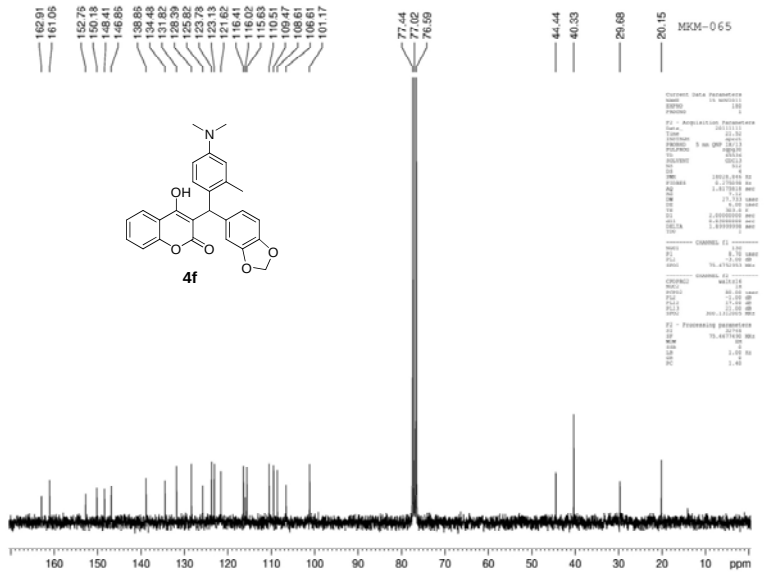

MKM-0
4c

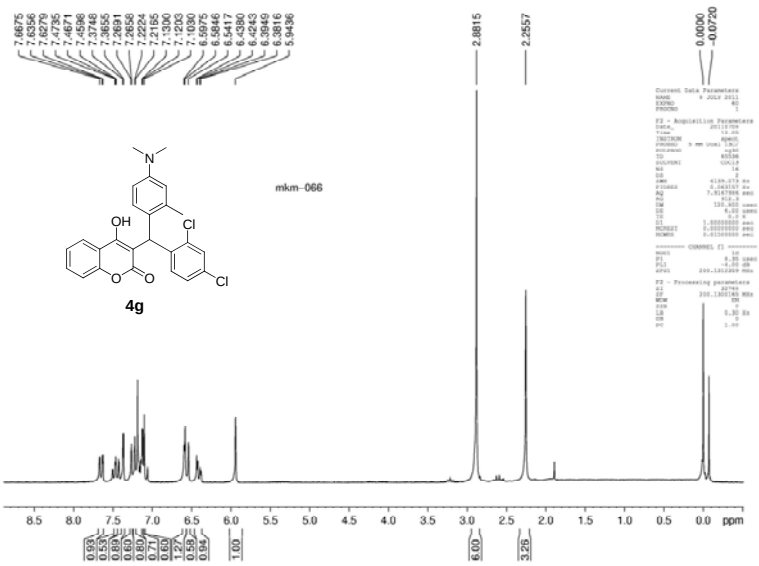

MKM-059
4d

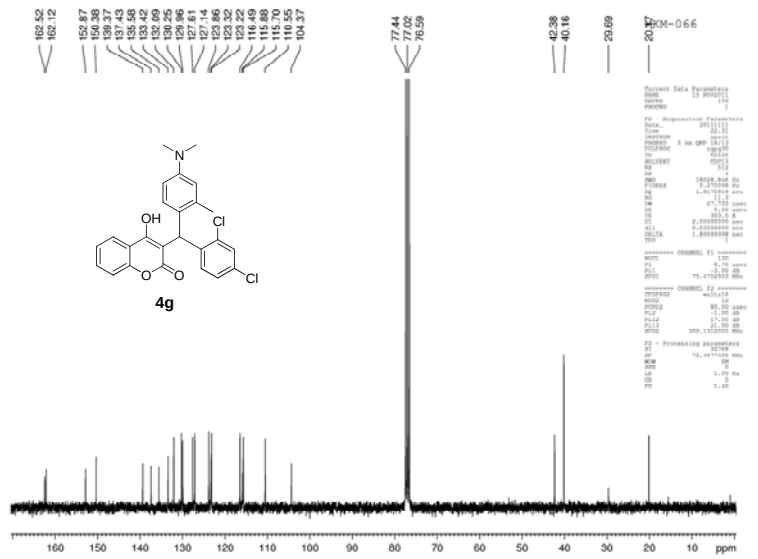

7.7613
7.7360
7.5809
7.5558
7.5302
7.3634
7.3355
6.8735
6.8459
6.6669
6.6393
6.5311
6.5084
6.4829
5.8010
3.8673
3.7764
2.9661
2.3055
0.0623
0.0207
MKM-064
OH
O
O
O
O
O
4e
N
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.04
1.02
1.77
1.01
0.98
1.76
0.94
2.85
5.79
5.69
2.95

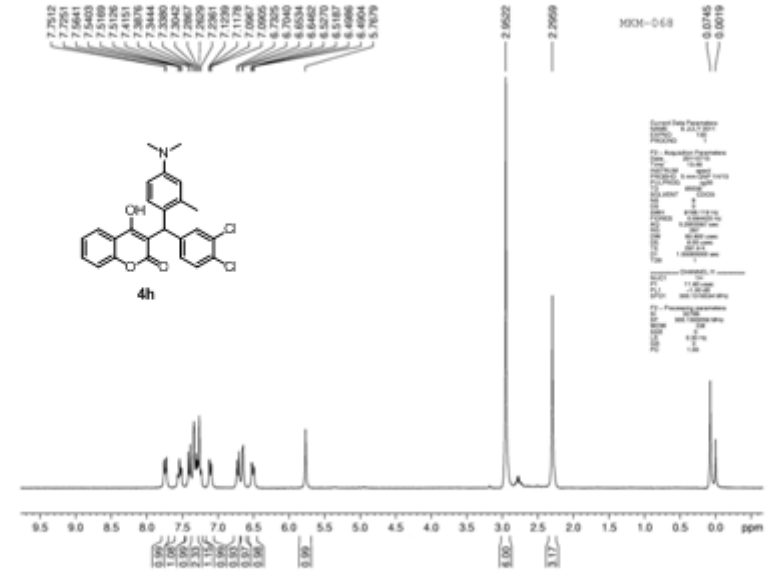

163.01
161.13
153.83
152.77
138.83
137.36
136.28
131.31
128.35
123.84
123.15
116.45
115.93
106.64
105.98
77.44
77.02
76.59
60.85
56.22
44.91
40.44
29.68
20.18
MKM-064
OH
O
O
O
O
O
4e
N
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

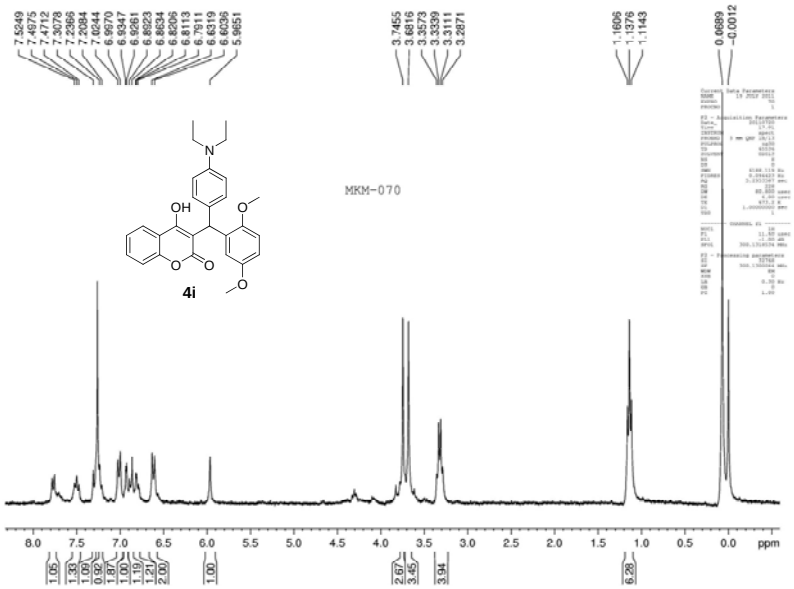

MKM-065
4f

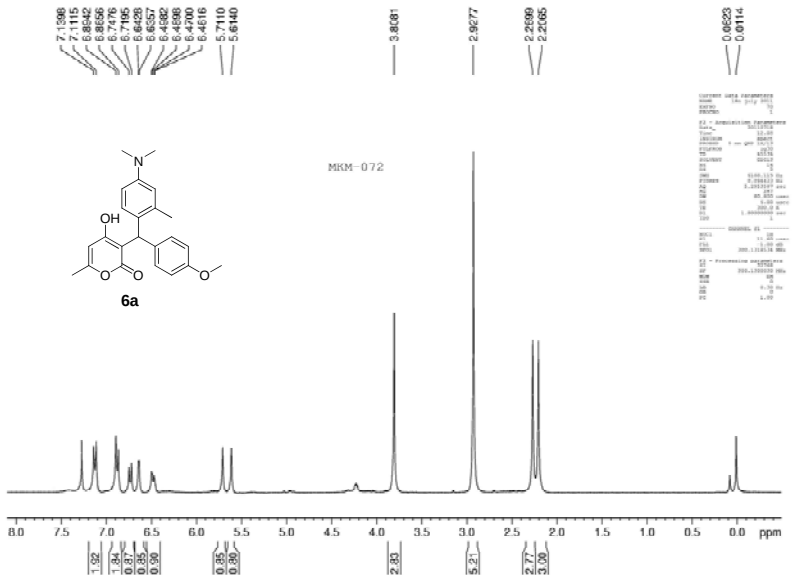

MKM-065
4f

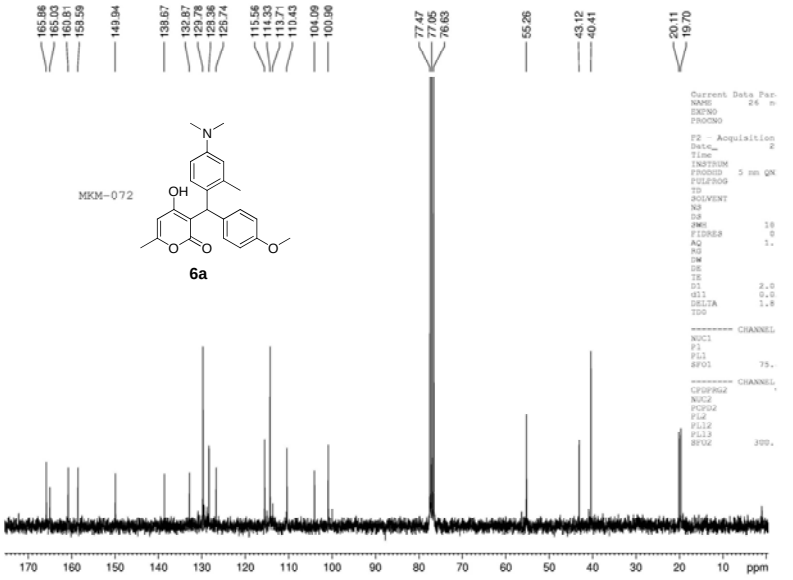

mkm-066
4g

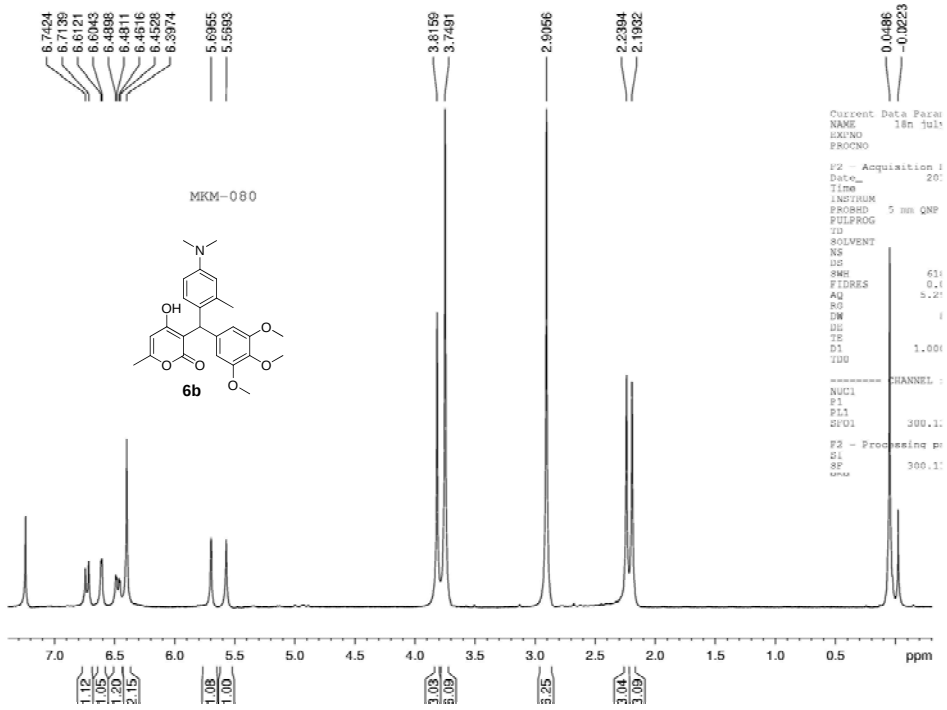

MKM-066
4g

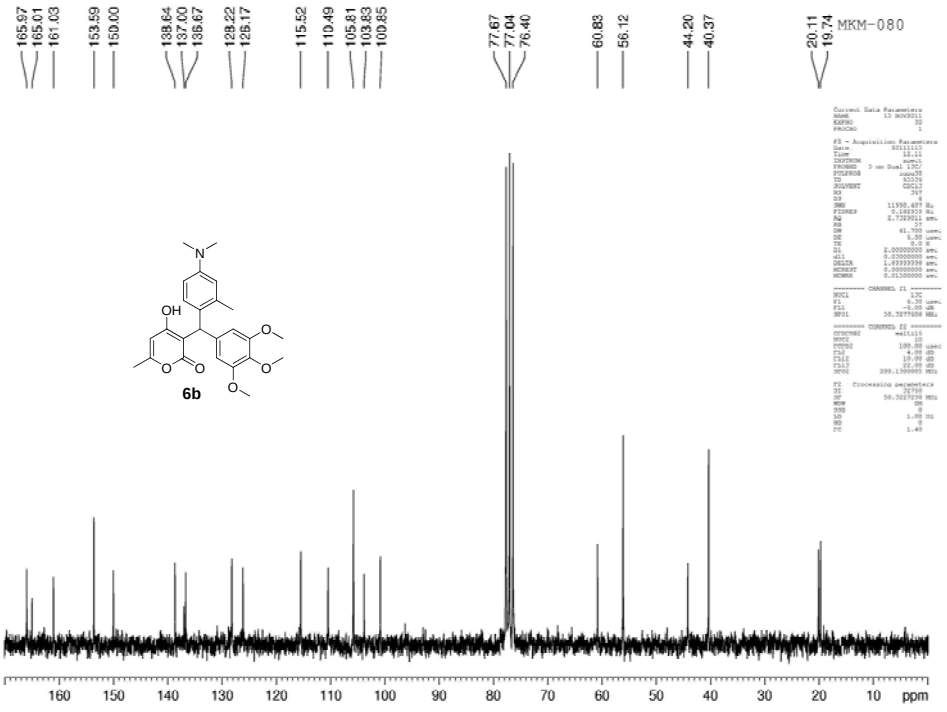

MKM-068
4h

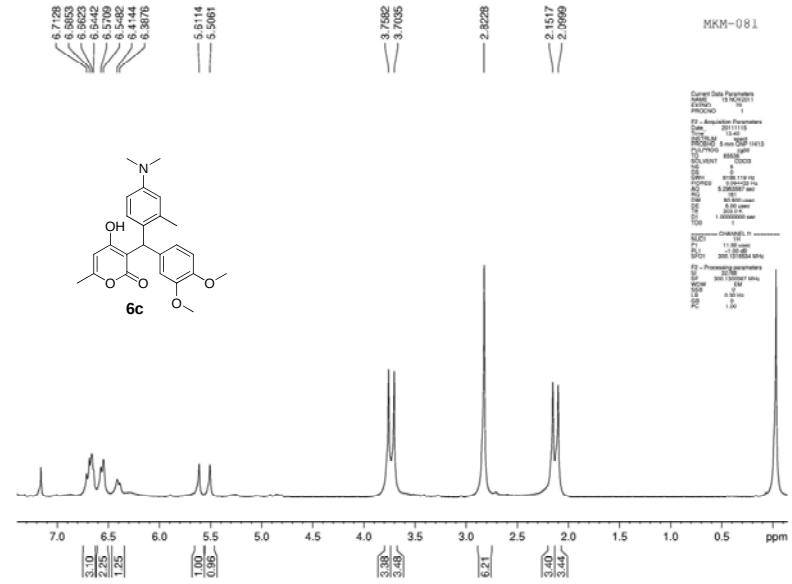

MKM-070
4i

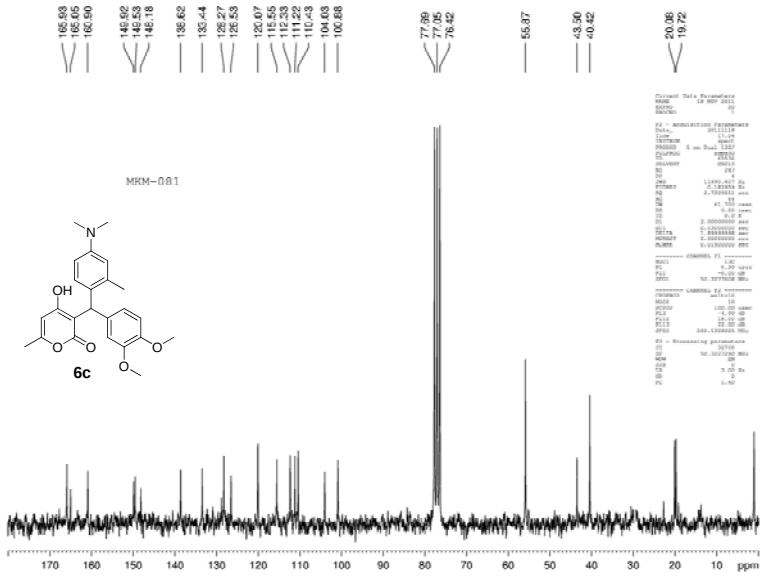

7.1596
7.1115
6.8542
6.8656
6.7476
6.7195
6.6428
6.6357
6.4382
6.4298
6.4200
6.4616
5.7110
5.6140
3.8081
2.9277
2.2699
2.2265
0.0223
0.0114
MKM-072
OH
O
O
O
6a
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.92
1.84
0.87
0.85
0.90
0.95
0.96
2.83
5.21
2.77
3.08

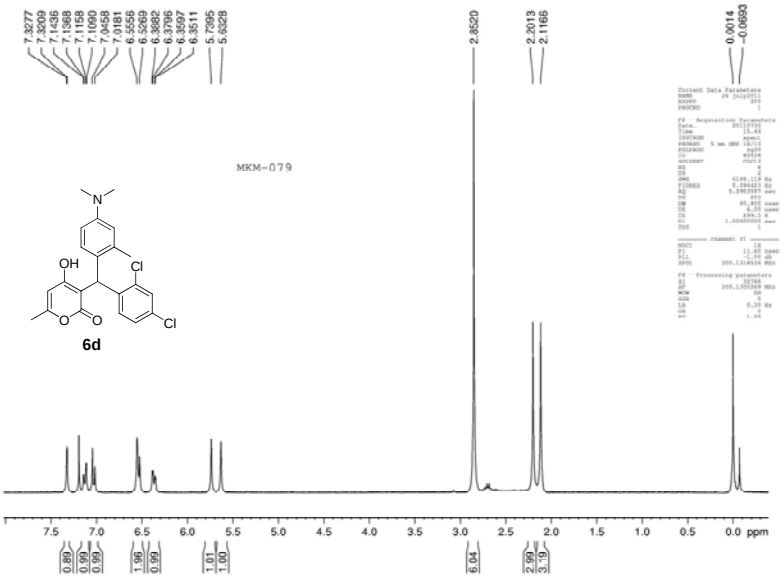

165.86
165.53
160.81
158.59
149.94
138.67
132.87
129.78
128.36
125.74
115.56
114.33
113.71
110.43
104.09
100.90
77.47
77.05
76.63
55.26
43.12
40.41
20.11
19.70
MKM-072
OH
O
O
O
6a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

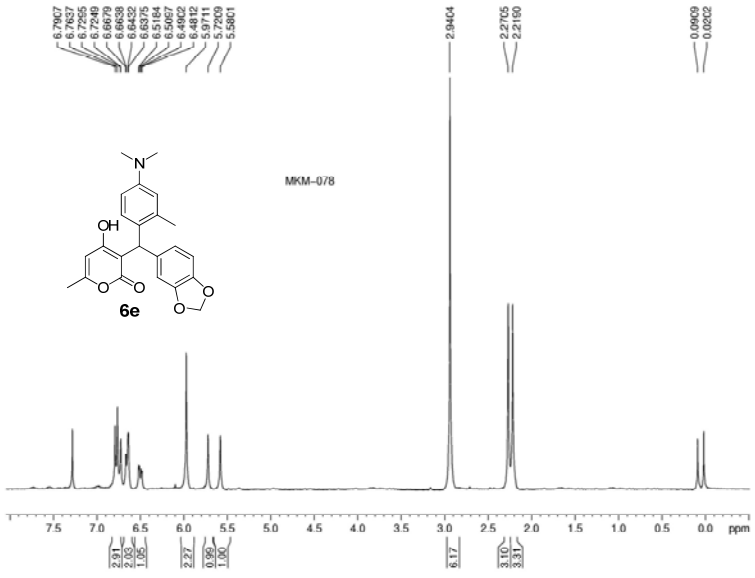

6.7424
6.7139
6.6121
6.6043
6.4898
6.4811
6.4516
6.4328
6.3974
5.6955
5.5593
3.8159
3.7491
2.9056
2.2394
2.1932
0.0486
-0.0223
MKM-080
6b
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.12
1.05
1.20
2.15
1.08
1.00
3.03
5.09
5.25
3.04
3.09

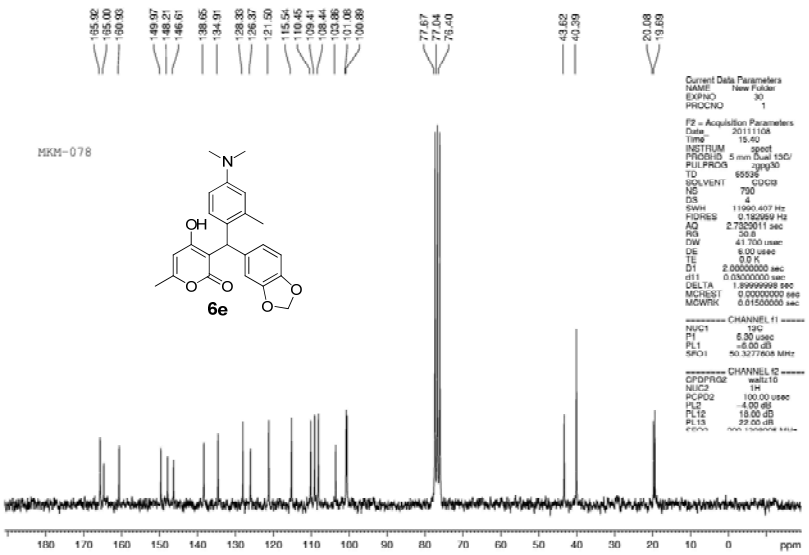

165.67
165.01
161.03
153.59
150.00
138.64
137.00
136.67
129.22
126.17
115.52
110.49
105.81
103.83
100.85
77.67
77.04
76.40
60.83
56.12
44.20
40.37
20.11
19.74
MKM-080
6b
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

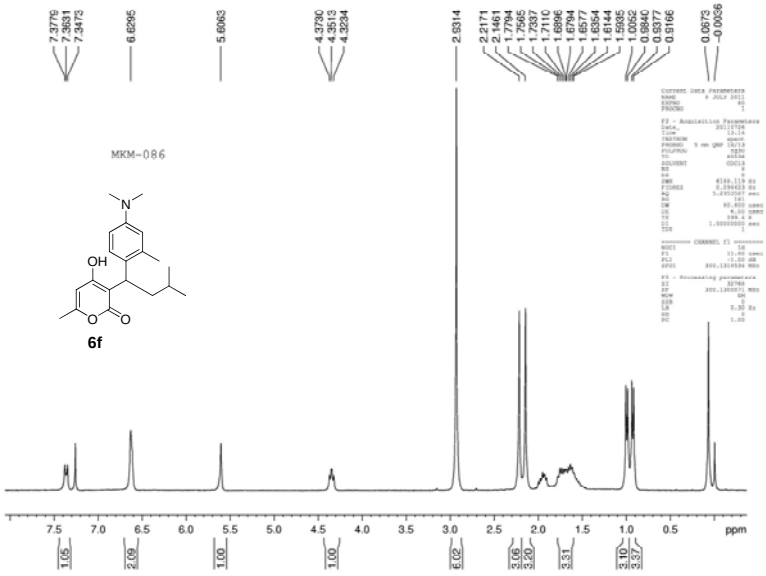

6.7128
6.6853
6.6623
6.5442
6.5709
6.5482
6.4144
6.3876
5.6114
5.5061
3.7582
3.7035
2.8228
2.1517
2.0999
MKM-081
OH
6c
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.10
2.25
1.25
1.00
0.95
3.38
3.48
6.21
2.40
3.44

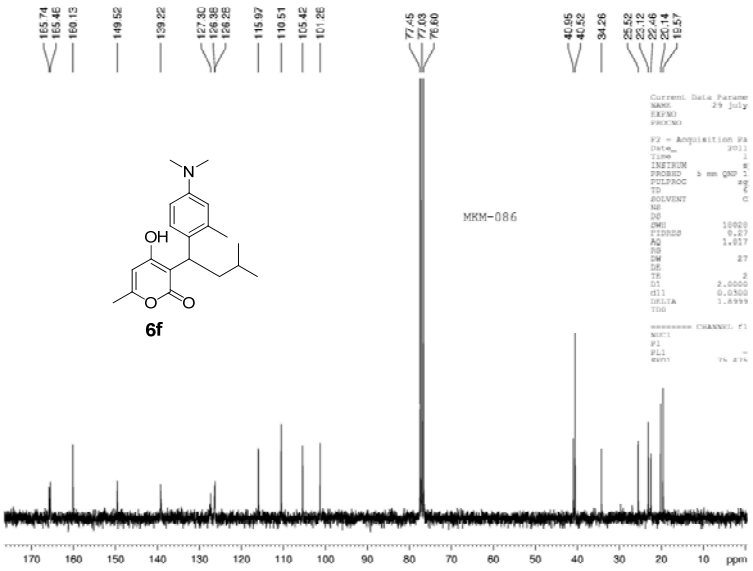

165.69
165.05
160.90
149.92
149.53
146.18
136.62
133.44
126.27
125.53
120.07
115.56
112.33
111.22
110.43
104.63
100.88
77.89
77.35
76.42
55.87
43.30
40.42
20.08
19.72
MKM-081
OH
6c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

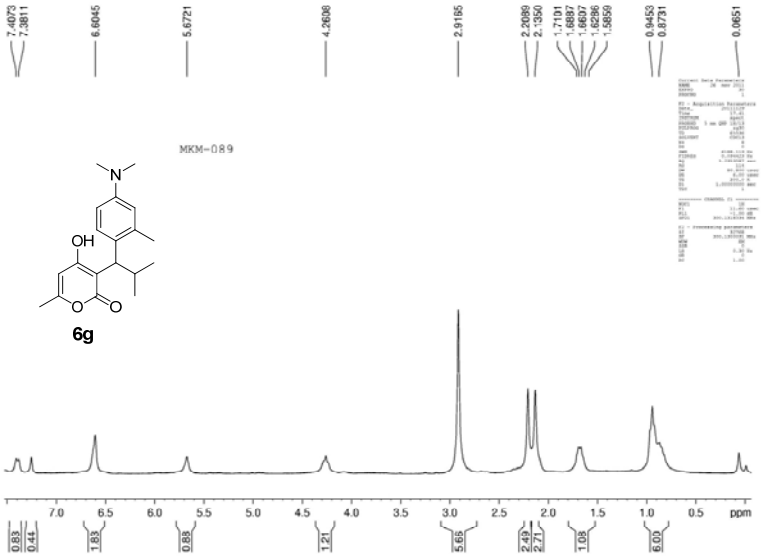

MKM-079
6d
7.3277
7.3209
7.1436
7.1368
7.1158
7.1090
7.0458
7.0181
6.5556
6.5269
6.3796
6.3511
5.7395
5.6328
2.8520
2.2013
2.1166
0.0014
-0.0683
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.89 0.99 0.99 1.96 0.99 1.01 1.00 6.04 2.99 3.19

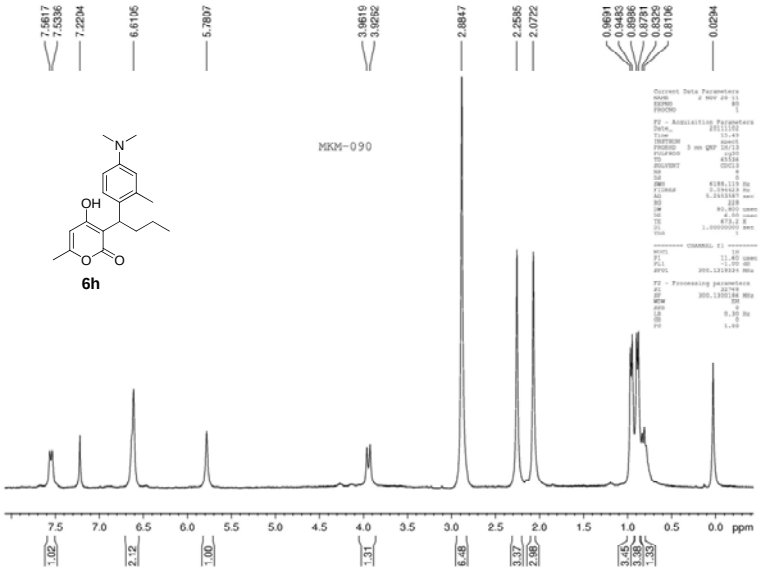

MKM-078
6e
6.7907
6.7637
6.7295
6.7249
6.6879
6.6838
6.6552
6.6375
6.5184
6.5057
6.4902
6.4812
5.9711
5.7209
5.5801
2.9404
2.2705
2.2190
0.0909
0.0202
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.91 2.93 1.95 2.27 0.99 1.00 6.17 3.10 3.31

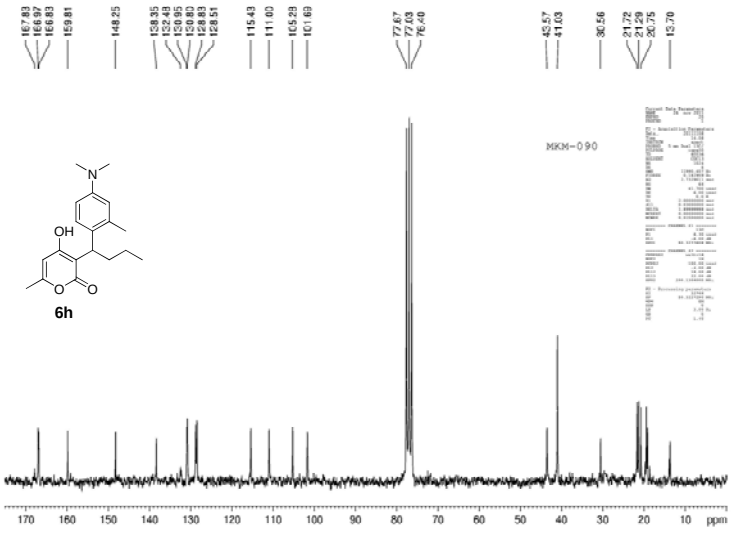

MKM-078
6e
ppm

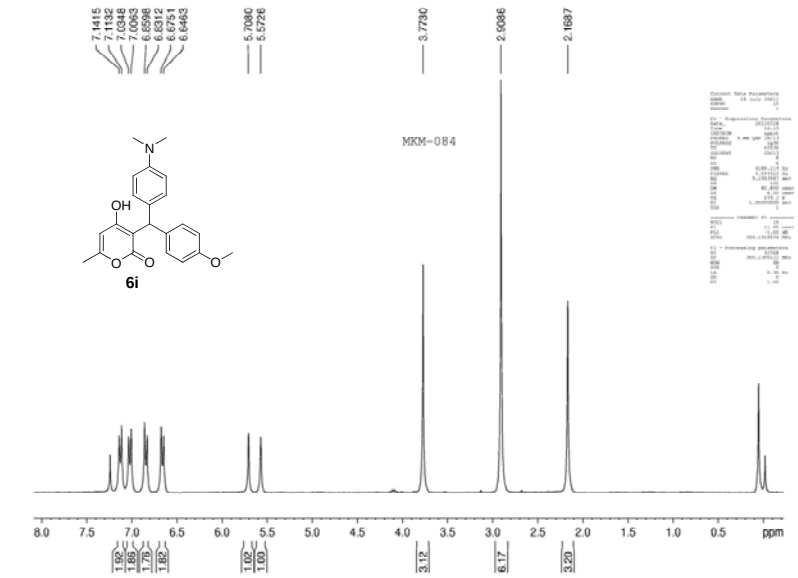

MKM-086
6f
ppm

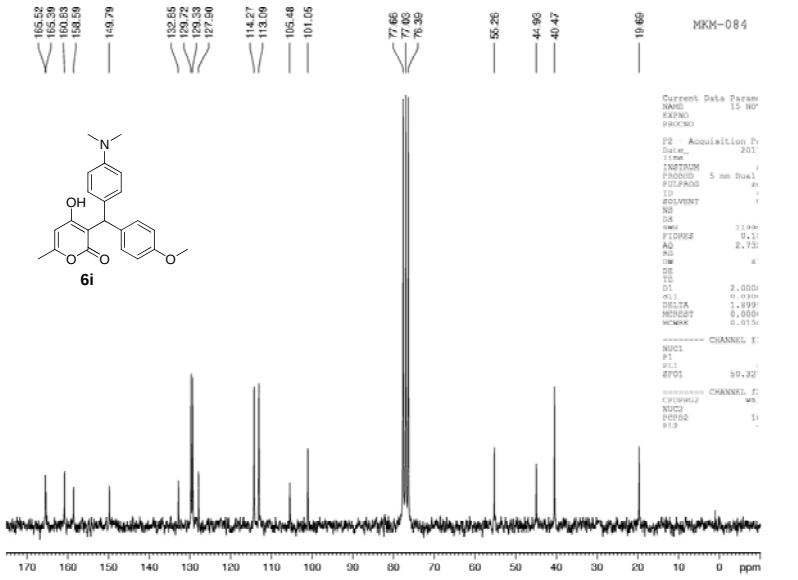

MKM-086
OH
O
O
N
6f

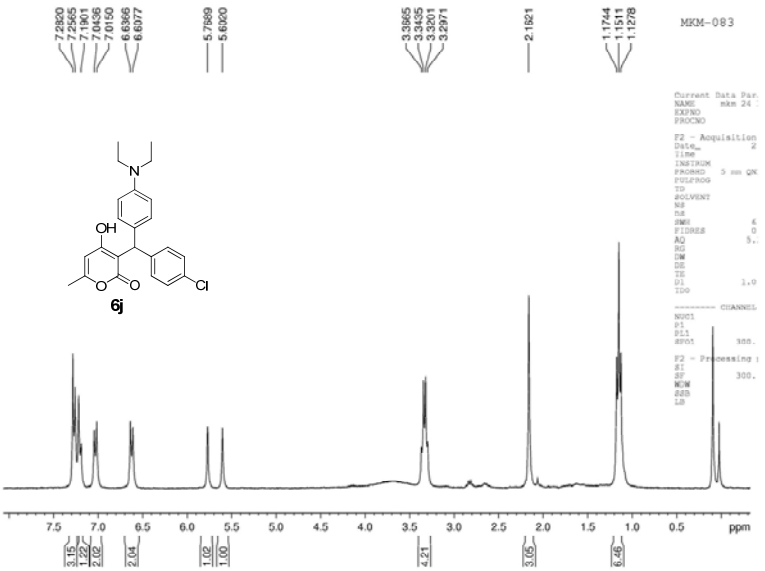

MKM-089
OH
O
O
N
6g

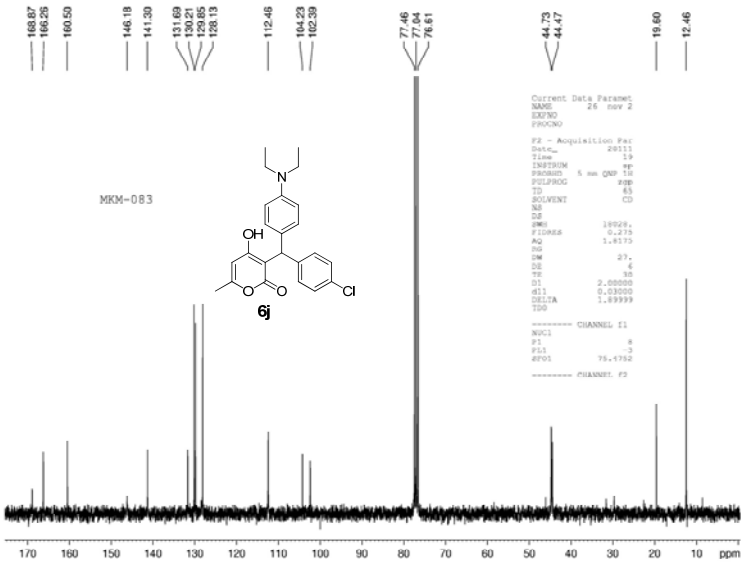

7.5617
7.5336
7.2204
6.6106
5.7897
3.9619
3.9262
2.8847
2.2586
2.0722
0.9691
0.9483
0.8986
0.8731
0.8329
0.8106
0.0294
MKM-090
OH
O
O
N
6h
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.02
2.12
1.00
1.31
6.48
3.37
2.98
3.45
2.98
1.00

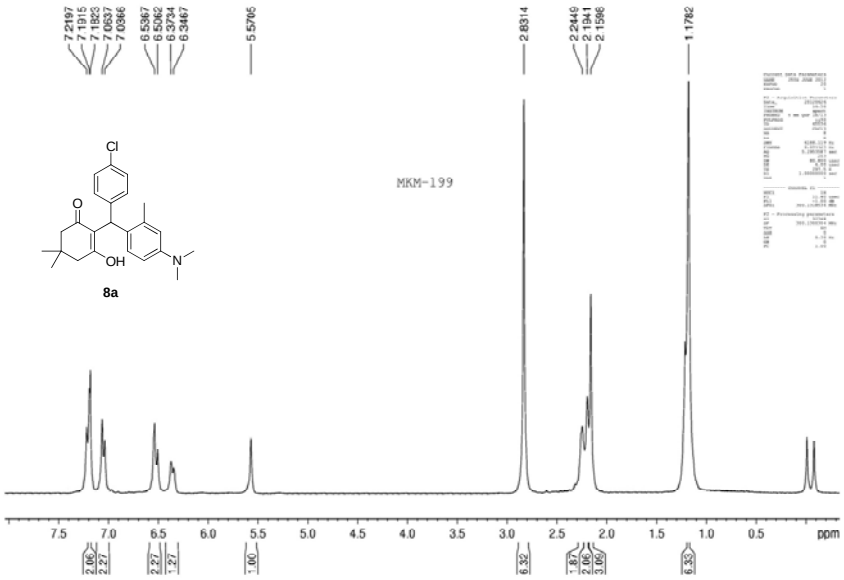

167.83
165.67
165.83
159.81
148.25
138.35
132.48
130.95
130.03
128.83
128.51
115.43
111.00
105.28
101.69
77.67
77.03
76.40
45.57
41.03
36.56
21.72
21.09
20.75
13.70
MKM-090
OH
O
O
N
6h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

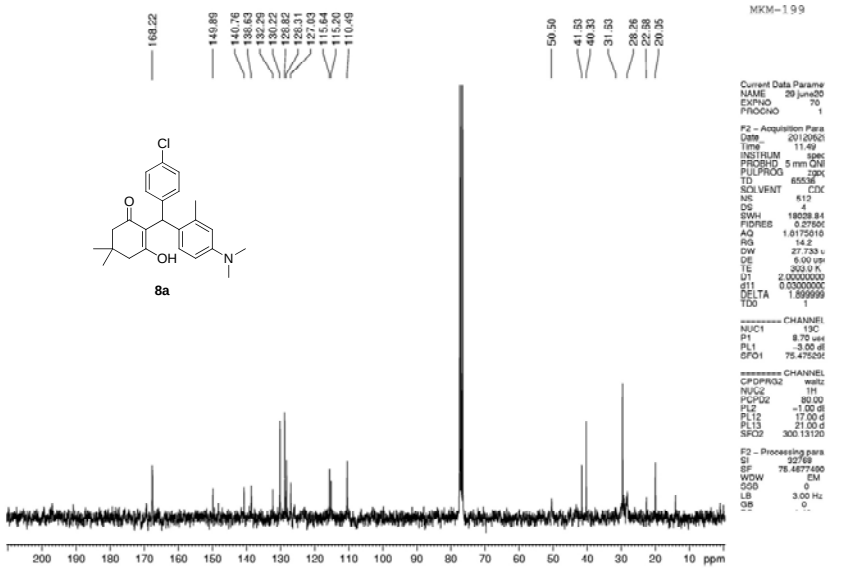

7.1415
7.1132
7.0948
7.0765
6.6598
6.6312
6.6751
6.6463
5.7080
5.5726
3.7730
2.9086
2.1687
MKM-084
OH
O
O
O
6i
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.90
1.86
1.70
1.00
1.82
1.02
1.00
3.12
6.17
3.20

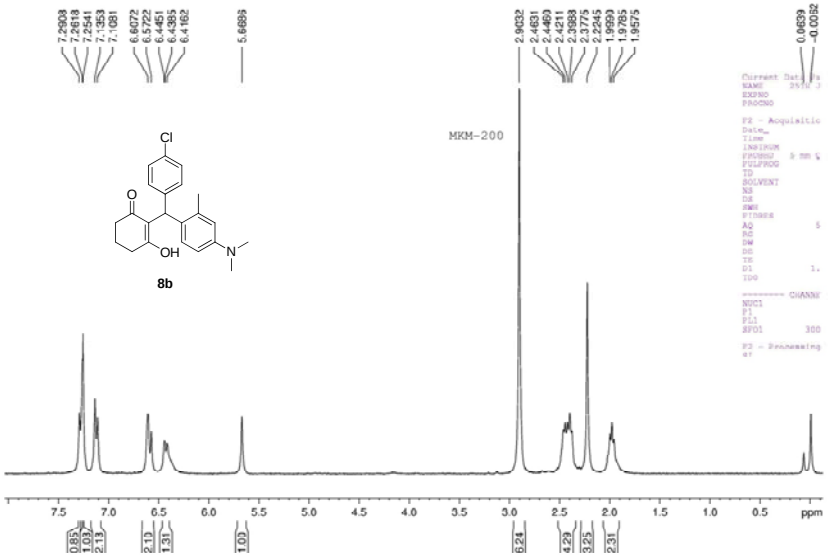

165.52
165.39
160.63
158.59
149.79
132.55
129.72
129.33
127.90
114.27
113.09
105.48
101.05
77.66
77.03
76.39
55.26
44.93
40.47
19.69
MKM-084
OH
O
O
O
6i
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

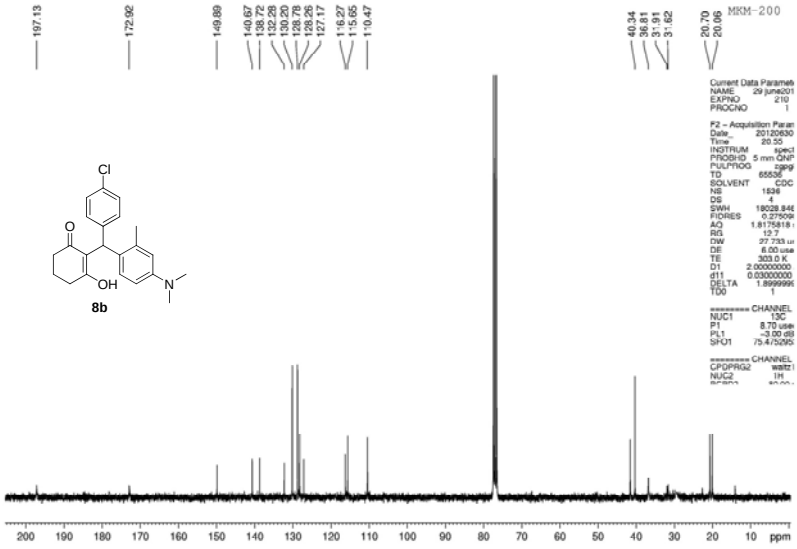

MKM-083
7.2820
7.2565
7.1901
7.0436
7.0150
6.6366
6.6977
5.7869
5.6920
3.3865
3.3435
3.3201
3.2971
2.1821
1.1744
1.1511
1.1278
OH
N
O
O
Cl
6j
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.15
1.22
2.02
2.04
1.02
1.00
4.21
3.05
6.46

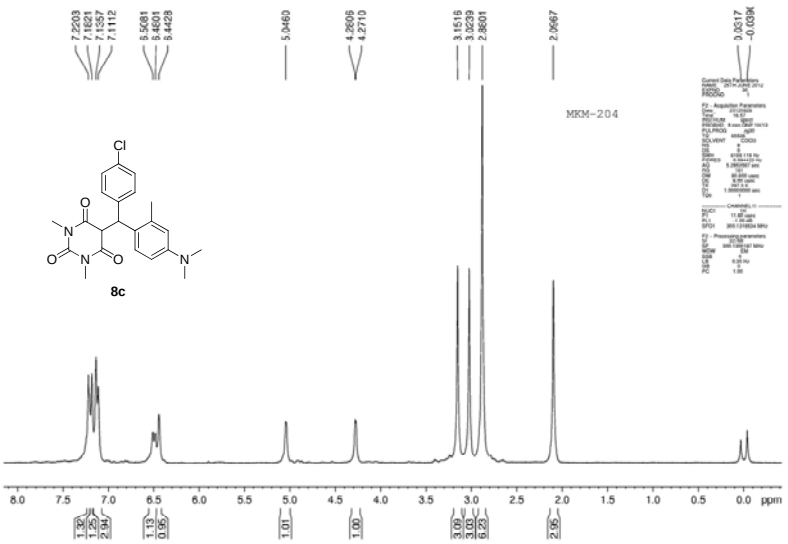

168.87
166.26
160.50
146.18
141.30
131.69
130.21
129.65
128.13
112.46
104.23
102.39
77.46
77.04
76.61
44.73
44.47
19.60
12.46
MKM-083
OH
N
O
O
Cl
6j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

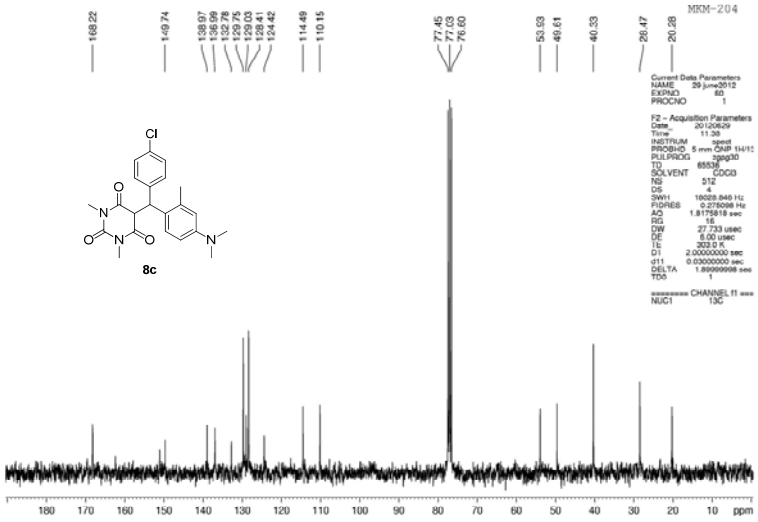

7.2197
7.1915
7.1825
7.0637
7.0366
6.5367
6.5062
6.3734
6.3467
5.5705
2.8314
2.2449
2.1941
2.1596
1.1782
MKM-199
Cl
O
OH
N
8a
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.06
2.27
2.27
1.27
1.00
6.32
1.83
2.00
2.06
6.33

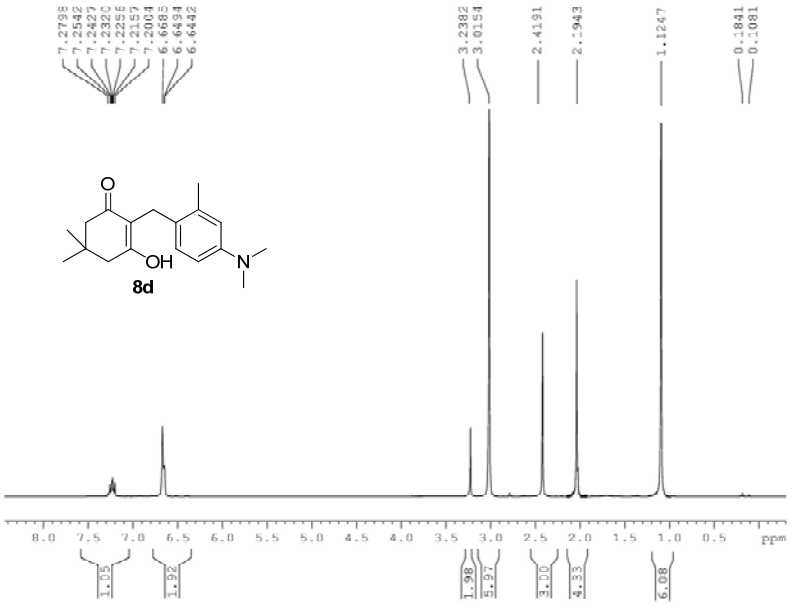

168.22
148.89
140.76
136.63
132.29
130.22
128.82
128.31
127.03
115.64
115.20
110.48
50.50
41.53
40.33
31.53
28.26
22.58
20.35
MKM-199
Cl
O
OH
N
8a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


MKM-200
8b
ppm


MKM-200
8b
ppm


MKM-204
8c


MKM-204
8c


7.2798
7.2542
7.2427
7.2320
7.2256
7.2157
7.2004
6.6685
6.6494
6.6442
3.2382
3.0154
2.4191
2.1943
1.1247
0.1841
0.1081
O
OH
N
8d
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 ppm
1.05
1.92
1.98
5.97
3.00
4.33
6.08