<Supporting Information>

Total Synthesis of Eryvarin H and its Derivatives and their Biological Activity as ERRγ Inverse Agonist

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I. Supporting Figure

Amino acids in 2 Å range from Eryvarin H

CYS269	ALA272	ASP273	GLU275	TRP305	LEU309	TYR326
LEU342	LEU345	HIS434	PHE435	LEU440	GLU441	

Amino acids in 2 Å range from GSK5182

CYS269	ALA272		GLU275		LEU309	TYR326
LEU342	LEU345	HIS434	PHE435	LEU440	GLU441	

Amino acids in 4 Å range from Eryvarin H

LEU265	LEU268	CYS269	ASP270	LEU271	ALA272	ASP273
ARG274	GLU275	LEU276	TRP305	MET306	LEU309	ILE310
VAL313	ARG316	TYR326	MET332	LEU342	LEU345	ASN346
ILE349	ALA431	HIS434	PHE435	ILE438	LEU440	GLU441
MET446	LEU449					

Amino acids in 4 Å range from GSK5182

LEU265	LEU268	CYS269		LEU271	ALA272	ASP273
	GLU275	LEU276	TRP305	MET306	LEU309	ILE310
VAL313	ARG316	TYR326	MET332	LEU342	LEU345	ASN346
ILE349	ALA431	HIS434	PHE435	ILE438	LEU440	GLU441
MET446	LEU449					

Fig. S1. List of interacting amino acids with Eryvarin H and GSK5182, in the range of 2 Å and 4 Å. These diagrams were obtained from Discovery Studio Version 1.5 based on docked ligands to ERRγ.

II. Procedures for biological studies

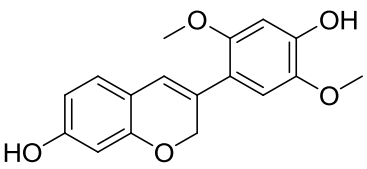
Cell-based Reporter Gene Assay. The HEK-293T cells were seeded into 24-well plates at a density of 2.0-8.0 x 10^4cells/well 24 h prior to the transfection. The cells were transiently transfected with pFR(5xGal4 binding site)-Luc, pCMX-Gal4-ERRγ, ERα, mCAR, HNFα, SF-1 and pCMV-β-gal for the ERR γ reporter gene assay. Transient transfection was performed using SuperFect (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The cells were treated with 100nM E2(estradiol), 10μM GSK5182, 10μM prepared compounds (**1**, **8**–**19**) for the final 24 h. The cells then were harvested 48h after transfection, and luciferase activity was measured. Luciferase activity was normalized to β-galactosidase activity. The data is representative of at least three to five independent experiments.

III. Synthetic Procedures of Compound **1**–**19.**

General information

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-300 [Bruker Biospin, Germany], Varian DD2MR400 and Varian Inova-500 [Varian Assoc., USA]. NMR chemical shifts were measured in ppm downfield from internal tetramethylsilane (TMS) standard or specific solvent signal. Structure diversity of natural product collection was supported from the Korea Bioactive Natural Material Bank (KBNMB). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), td (triplet of doublet), etc. Coupling constants were reported in Hz. Low resolution mass spectrometry (LRMS) analyses were performed with Finnigan MSQ Plus Surveyer HPLC/MS system [Thermo Electron Corp., USA] using electron spray ionization (ESI). The HRMS analyses were conducted at the national center for inter-university research facilities (NCRF) in Seoul National University by direct injection on JEOL JMS AX505WA spectrometer using fast atom bombardment (FAB) method. All reagents in this synthetic procedure were purchased from Sigma-Aldrich [MO, USA], TCI [Japan] and Alfa Aesar [USA]. The progress of reaction was monitored using thin-layer chromatography (TLC) (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm) or by treating the TLC plates with anisaldehyde or phosphomolybdic acid followed by heating. Silica gel 60 (0.040–0.063 mm) used in flash column chromatography was purchased from Merck [Germany]. All reactions were conducted in oven-dried glassware under dry argon atmosphere, unless otherwise specified. All solvents and organic reagents were purchased from commercial venders and used without further purification unless otherwise mentioned.

Compound **1**, **Eryvarin H**, 3-(4-hydroxy-2,5-dimethoxyphenyl)-2H-chromen-7-ol

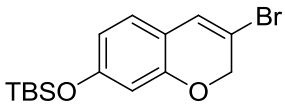


Compound **2a** (0.100 mmol), one of boronic acids/boronic esters (2 equiv.), $Pd(PPh_3)_4$ (5 mol %), Na_2CO_3 (3 equiv.) were suspended in a solvent mixture of Toluene/EtOH/H_2O (2:1:1, total volume of 4 mL). The reaction mixture was stirred at 80 ^{o}C for 4 h and the completion of the reaction was monitored by TLC. When the starting material **2a** was all consumed, the resulting mixture was diluted with ethyl acetate and washed with brine. The combined organic layer was dried over anhydrous $MgSO_4$, then filtered, and concentrated under reduced pressure. After a short silica-gel filtration, the resulting product was used directly for the next reaction without further purification. The solution of previous prepared compound in HF/pyridine/THF (1:1:18, volumetric ratio, total volume of 3 mL) was stirred for 5 h at room temperature in a plastic vessel. After the reaction completion, Additional fluoride source was quenched with excess TMSOEt (6 mL). The mixture was evaporated under reduced pressure, the resultant was purified directly with silica gel flash column chromatography (EtOAc:hexane = 1:4 to EtOAc:hexane = 1:3) to provide the desired product,

compound **1**.

Yield: 73% (2-step yield), R_f = 0.04 (1:6 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (d, 1H, *J* = 8.0 Hz), 6.83 (s, 1H), 6.56 (s, 1H), 6.49 (s, 1H), 6.39–6.41 (m, 2H), 4.98 (d, 2H, *J* = 1.0 Hz), 3.88 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.2, 154.1, 151.6, 147.5, 141.6, 127.8, 127.5, 120.4, 117.1, 115.3, 113.0, 108.7, 102.4, 101.0, 67.7, 56.5, 55.9; HRMS (FAB$^+$) m/z calcd for $C_{17}H_{16}O_5$ $[M]^+$ 300.0998, found 300.0996.

Compound **2a**, *(3-bromo-2H-chromen-7-yloxy)(tert-butyl)dimethylsilane*

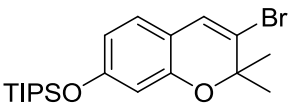


The mixture of **5** (3 mmol, 1 equiv.) and imidazole (1.5 equiv.) was stirred in anhydrous DCM (20 mL) for 15 min at room temperature. To the solution was added TBSCl (1.1 equiv.) and the reaction mixture was stirred for 1 h at room temperature. Then the solution was extracted with excess ethyl acetate and washed with saturated NH_4Cl aqueous solution and brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered. Then, the filtrate was condensed under reduced pressure. The resulting product was used directly for the next reaction without further purification. To a solution of resulting compound (1 equiv.) in EtOH (20 mL), sodium borohydride ($NaBH_4$, 1.2 equiv.) was added at room temperature and the reaction mixture was stirred for 1 h at room temperature. After the completion of reaction monitored by TLC, the resulting mixture was diluted with deionized water and quenched by aqueous NH_4Cl solution, and extracted three times with ethyl acetate. The combined organic layer was washed with brine once, then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting compound is α-bromoalcohol structure 3-bromo-7-(*tert*-butyldimethylsilyloxy)chroman-4-ol as a diastereomeric mixture. To a solution of previous α-bromoalcohol structure (1 equiv.) in anhydrous toluene, p-toluenesulfonic acid monohydrate (p-TSA, 0.1 equiv.) was added and the reaction mixture was heated in capped microwave vessel under microwave irradiation (80 ^{o}C, 120 W) for 20 min. After the reaction completion monitored by TLC, the resulting mixture was diluted with ethyl acetate and washed with brine. The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The desired product **2a** was obtained by the purification using silica-gel flash column chromatography (only hexane to EtOAc:hexane = 1:50).

Yield: 61% (3-step yield), R_f = 0.43 (Only hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, 1H, *J* = 8.0 Hz), 6.68 (s, 1H), 6.37 (dd, 1H, *J* = 2.3, 8.3 Hz), 6.31 (dd, 1H, *J* = 0.5, 2.5 Hz), 4.83 (d, 2H, *J* = 1.5 Hz), 0.96 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 158.0, 154.3, 128.1, 126.8, 117.4, 114.6, 112.7, 108.7, 70.8, 26.2, 19.0, -4.1; HRMS (FAB$^+$) m/z calcd for $C_{15}H_{21}BrO_2Si$ $[M]^+$ 340.0494, found 340.0489.

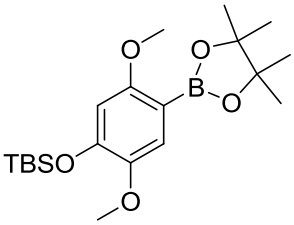
Also, **2a** was obtained from α-bromoalcohol structure by thermal dehydration (80 ^{o}C for 2 h) with the 3-step yield of 24%. Stability of 2a was not quite good, thus it should be kept in -20 ^{o}C and more stable as a solution in ethyl acetate or hexane.

Compound **2b**, (3-bromo-2,2-dimethyl-2H-chromen-7-yloxy)triisopropylsilane



Compound **2b** was previously reported in *Chem. Commun.*, 2006, 2962–2964. (Compound **17a** in the reference)

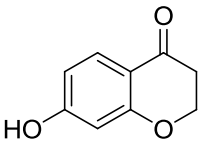
Compound **3**, *tert*-butyl(2,5-dimethoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)dimethylsilane



To the solution of starting material **7** (0.300 mmol, 1 equiv.), $Pd(OAc)_2$ (5 mol %), DPEphos (10 mol %) in 1,4-dioxane (2 mL) was added triethylamine (4 equiv.) and pinacolborane (3 equiv.). The reaction mixture was stirred at 80 ^oC for 12 h. After the completion of the reaction monitored by TLC, the resulting mixture was diluted with aqueous NH_4Cl saturated solution, and extracted three times with ethyl acetate. The combined organic layer was washed with brine once, then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The desired product **3** was obtained by the purification using silica-gel flash column chromatography (EtOAc:hexane = 1:20 to EtOAc:hexane = 1:4).

Yield: 63%, R_f = 0.47 (1:6 = EtOAc:hexane, v/v); ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (s, 1H), 6.43 (s, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 1.34 (s, 12H), 0.99 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 159.9, 149.1, 144.9, 120.5, 105.9, 83.4, 56.8, 56.4, 25.9, 25.0, 18.6, -4.5; HRMS (FAB^+) m/z calcd for $C_{20}H_{35}O_5SiB$ $[M]^+$ 394.2351, found 394.2353.

Compound **4**, 7-hydroxychroman-4-one

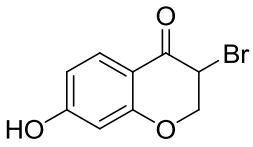


To a mixture of resorcinol (10.0 mmol, 1 equiv.) and 3-chloropropionic acid (1.01 equiv.) was slowly added trifluoromethanesulfonic acid (5 mL). The solution was stirred at 80 ^oC for 1.5 h, and poured into DCM (100 mL). The solution was poured into deionized water and the aqueous layer was extracted with DCM (100 mL) twice. The combined organic layer was dried over anhydrous $MgSO_4$, then filtered, and concentrated under reduced pressure. The resulting product was used directly for the next reaction without further purification, with addition of 2N NaOH (400 mL) aqueous solution was stirred at 0 ^oC for 4 h. After the reaction was completed, the pH was adjusted to 2 with concentrated HCl by checked with pH paper. The mixture was extracted trice with EtOAc, washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The desired product **4** was obtained by recrystallization with EtOAc/hexane (1:5).

Yield: 62% (2-step yield), R_f = 0.41 (1:1 = EtOAc:hexane, v/v); ^1H NMR (500 MHz, acetone-d_6) δ 7.70 (d, 1H, J = 9.0 Hz), 6.54 (dd, 1H, J = 2.3, 8.8 Hz), 6.37 (d, 1H, J = 2.5 Hz), 4.51 (t, 2H, J = 6.3 Hz), 2.67 (t, 2H, J = 6.5 Hz); ^{13}C NMR (125 MHz, acetone-d_6) δ 190.2, 164.9, 164.7, 129.6, 115.6, 111.0, 103.4, 68.1, 38.0; HRMS

(FAB$^+$) m/z calcd for $C_9H_9O_3$ $[M]^+$ 165.0552, found 165.0553.

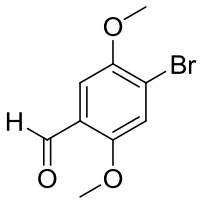
Compound **5**, 3-bromo-7-hydroxychroman-4-one



The compound 4 (1.00 mmol, 1.0 equiv.) was dissolved in a mixed solution of ethyl acetate/chloroform/methanol (5:5:1). Copper (II) bromide ($CuBr_2$, 2.1 equiv.) was added in this solution and the reaction mixture was heated to reflux (70 ^oC) for 4 h. After the completion of the reaction monitored by TLC, the reaction mixture was filter and concentrated *in vacuo*. The resulting residue was dissolved in ethyl acetate and washed 3 times with brine. The combined organic layer was dried over anhydrous $MgSO_4$, then filtered, and concentrated under reduced pressure. The desired product **5** was obtained by recrystallization with EtOAc/hexane (1:5).

Yield: 67%, R_f = 0.48 (1:1 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.76 (d, 2H, J = 8.6 Hz), 6.65 (dd, 1H, J = 2.3, 8.8 Hz), 6.46 (d, 2H, J = 2.0 Hz), 4.75–4.81 (m, 2H), 4.62 (dd, 1H, J = 3.5, 13.0 Hz); ^{13}C NMR (125 MHz, acetone-d_6) δ 184.2, 165.8, 163.6, 130.8, 112.2, 103.4, 72.5, 46.9, 46.9; HRMS (FAB$^+$) m/z calcd for $C_9H_7BrO_3$ $[M]^+$ 241.9579, found 241.9576.

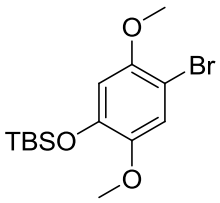
Compound **6**, 4-bromo-2,5-dimethoxybenzaldehyde



To a solution of 2,5-dimethoxybenzaldehyde (6.00 mmol) in glacial acetic acid (10 mL) was added bromine (1.1 equiv.). The reaction mixture was stirred at room temperature for 12 h. Dilution with ice water was poured into reaction mixture, and then the yellow precipitate was collected by filtration. The mono-brominated desired product **6** was obtained by recrystallization with ethanol.

Yield: 62%, R_f = 0.56 (1:6 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.34 (s, 1H), 7.25 (s, 1H), 3.90 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 156.4, 150.7, 124.4, 120.5, 117.9, 109.9, 56.9, 56.6; HRMS (FAB$^+$) m/z calcd for $C_9H_{10}BrO_3$ $[M]^+$ 244.9813, found 244.9819.

Compound **7**, (4-bromo-2,5-dimethoxyphenoxy)(tert-butyl)dimethylsilane



To a solution of compound 6 (1.530 mmol, 1 equiv.) and *meta*-chloroperbenzoic acid (1.5 equiv.) in DCM (5 mL) was stirred at room temperature for 3 h. The reaction mixture was diluted with ethyl acetate and saturated $NaHCO_3$ aqueous solution, and extracted three times with ethyl acetate. The combined organic layer was washed with brine once, then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The evaporated residue was dissolved in methanol (5 mL), and then addition of NaOH (1 equiv.) for ester hydrolysis. The reaction mixture was stirred for 3 h. After the completion of the reaction monitored by TLC, the resulting mixture was diluted with ethyl acetate, and washed with saturated NH_4Cl aqueous solution

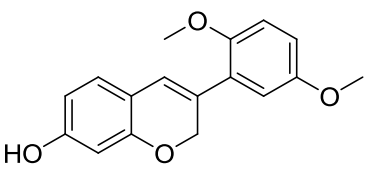
and brine. The combined organic layer was dried over anhydrous $MgSO_4$, then filtered, and concentrated under reduced pressure. The resulting product was used directly for the next reaction without further purification. The remained evaporated residue and imidazole (1.5 equiv.) was stirred in anhydrous DCM (20 mL) for 15 min at room temperature. To the solution was added TBSCl (1.1 equiv.) and the reaction mixture was stirred for 1 h at room temperature. Then the solution was extracted with excess ethyl acetate and washed with saturated NH_4Cl aqueous solution and brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered. Then, the filtrate was condensed under reduced pressure. The desired product **7** was obtained by the purification using silica-gel flash column chromatography (EtOAc:hexane = 1:50).

Yield: 95% (3-step yield), R_f = 0.71 (1:6 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.50 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 0.99 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 145.7, 145.3, 117.4, 106.9, 102.0, 56.9, 56.5, 25.8, 18.6, -4.5; HRMS (FAB$^+$) m/z calcd for $C_{14}H_{23}BrO_3Si$ $[M]^+$ 346.0600, found 346.0598.

General procedure for synthesis of compounds **8**–**19** via Suzuki Coupling Reaction

Compound **2a** or **2b** (0.100 mmol, 1 equiv.), one of boronic acids/boronic esters (2 equiv.), $Pd(PPh_3)_4$ (5 mol %), Na_2CO_3 (3 equiv.) were suspended in a solvent mixture of Toluene/EtOH/H_2O (2:1:1, total volume of 4 mL). The reaction mixture was stirred at 80 ^{o}C for 2 h ~ 8 h and the completion of the reaction was monitored by TLC. When the starting material **2a** or **2b** was all consumed, the resulting mixture was diluted with ethyl acetate and washed with brine. The combined organic layer was dried over anhydrous $MgSO_4$, then filtered, and concentrated under reduced pressure. After a short silica-gel filtration, the resulting product was used directly for the next reaction without further purification. The solution of previous prepared compound in HF/Pyridine/THF (1:1:18, volumetric ratio, total volume of 3 mL) was stirred for 5 h at room temperature in a plastic vessel. After the reaction completion, Additional fluoride source was quenched with excess TMSOEt (6 mL). The mixture was evaporated under reduced pressure, the resultant was purified with silica gel flash column chromatography (with EtOAc:hexane) to provide the desired products, compounds **8**–**19**.

Compound **8**, 3-(2,5-dimethoxyphenyl)-2H-chromen-7-ol

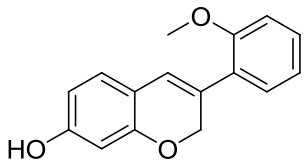


Compound **8** was prepared by the general procedure with **2a** and 2,5-dimethoxyphenylboronic acid as the starting materials.

Yield: 69% (2-step yield), R_f = 0.49 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, 1H, J = 8.0 Hz), 6.88 (s, 1H), 6.82 (d, 1H, J

= 2.0 Hz), 6.59 (s, 1H), 6.38–6.41 (m, 2H), 5.01 (d, 2H, *J* = 1.5 Hz), 3.80 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 155.2, 153.9, 151.7, 129.5, 128.8, 128.0, 122.6, 117.1, 114.7, 113.7, 112.2, 108.7, 103.2, 68.3, 56.2, 56.0; HRMS (FAB$^+$) m/z calcd for $C_{17}H_{16}O_4$ $[M]^+$ 284.1049, found 284.1052.

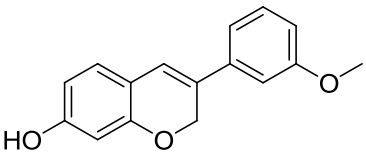
Compound **9**, 3-(2-methoxyphenyl)-2H-chromen-7-ol



Compound **9** was prepared by the general procedure with **2a** and 2-methoxyphenylboronic acid as the starting materials.

Yield: 70% (2-step yield), R_f = 0.25 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.32 (m, 2H), 6.87–6.99 (m, 3H), 6.57 (s, 1H), 6.39–6.42 (m, 2H), 5.01 (d, 2H, *J* = 1.2 Hz), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 156.7, 155.0, 129.6, 129.1, 128.9, 128.0, 127.9, 122.4, 121.1, 117.1, 111.0, 108.7, 103.2, 68.4, 55.5; HRMS (FAB$^+$) m/z calcd for $C_{16}H_{14}O_3$ $[M]^+$ 254.0943, found 254.0947.

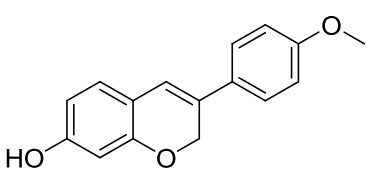
Compound **10**, 3-(3-methoxyphenyl)-2H-chromen-7-ol



Compound **10** was prepared by the general procedure with **2a** and 3-methoxyphenylboronic acid as the starting materials.

Yield: 55% (2-step yield), R_f = 0.24 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.32 (m, 1H), 6.92–7.01 (m, 3H), 6.85 (dd, 1H, *J*=8.2, 2.6 Hz), 6.76 (s, 1H), 6.37–6.42 (m, 2H), 5.12 (d, 2H, *J* = 1.2 Hz), 5.00 (br. s, 1H) 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 156.7, 154.8, 138.5, 129.8, 128.7, 128.2, 120.3, 117.3, 116.5, 113.0, 110.6, 108.8, 103.2, 67.4, 55.5; HRMS (FAB$^+$) m/z calcd for $C_{16}H_{14}O_3$ $[M]^+$ 254.0943, found 254.0945.

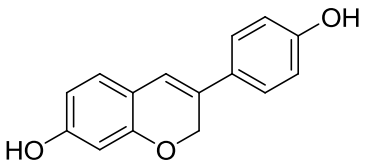
Compound **11**, 3-(4-methoxyphenyl)-2H-chromen-7-ol



Compound **11** was prepared by the general procedure with **2a** and 4-methoxyphenylboronic acid as the starting materials.

Yield: 62% (2-step yield), R_f = 0.24 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, acetone-d_6) δ 7.46 (dd, 2H, *J* = 3.8, 8.3 Hz), 6.94–6.99 (m, 3H), 6.81 (s, 1H), 6.42 (dd, 2H, *J* = 2.5, 8.0 Hz), 6.33 (d, 1H, *J* = 2.5 Hz), 5.08 (d, 2H, *J* = 4.5 Hz), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 155.4, 130.3, 128.7, 126.6, 118.9, 116.5, 115.0, 109.5, 103.5, 67.7, 55.7; HRMS (FAB$^+$) m/z calcd for $C_{16}H_{14}O_3$ $[M]^+$ 254.0943, found 254.0948.

Compound **12**, 3-(4-hydroxyphenyl)-2H-chromen-7-ol

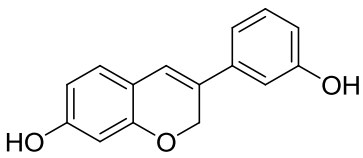


Synthetic procedure of used boronic ester for compound **12** was as follows: To a solution of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol (1.00 mmol, 1 equiv.) and imidazole (1.5 equiv.) in DMF (3 mL) was added TBSCl (1.1 equiv.) and the reaction mixture was stirred for 5 h at room temperature. Then the solution was extracted with excess ethyl acetate and washed with saturated NH_4Cl aqueous solution and brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered. Then, the filtrate was condensed under reduced pressure. The desired boronic ester *tert*-butyldimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)silane was obtained by the purification using silica-gel flash column chromatography (EtOAc:hexane = 1:50). Yield: 84%, R_f = 0.48 (1:30 = EtOAc:hexane, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J* = 8.4 Hz), 6.83 (d, 2H, *J* = 8.4 Hz), 1.33 (s, 12H), 0.98 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 136.6, 119.8, 83.7, 60.5, 25.8, 25.0, 18.4, -4.3.

Compound **12** was prepared by the general procedure with **2a** and prepared *tert*-butyldimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)silane as the starting materials.

Yield: 57% (2-step yield), R_f = 0.42 (1:1 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, CD_3OD) δ 7.29 (d, 2H, *J* = 8.5 Hz), 6.90 (d, 1H, *J* = 8.0 Hz), 6.77–6.81 (m, 2H), 6.66 (s, 1H), 6.26–6.35 (m, 1H), 6.26 (d, 1H, *J* = 2.0 Hz), 5.02 (s, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 159.2, 158.2, 155.7, 129.4, 128.6, 127.5, 127.5, 126.8, 118.5, 117.0, 116.5, 109.6, 103.5, 68.2; HRMS (FAB$^+$) m/z calcd for $C_{15}H_{12}O_3$ $[M]^+$ 240.0786, found 240.0789.

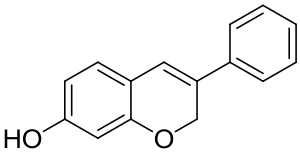
Compound **13**, 3-(3-hydroxyphenyl)-2H-chromen-7-ol



Compound **13** was prepared by the general procedure with **2a** and 3-hydroxyphenylboronic acid as the starting materials.

Yield: 58% (2-step yield), R_f = 0.46 (1:1 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.17 (t, 1H, *J* = 8.0 Hz), 6.98 (d, 1H, *J* = 6.4 Hz), 6.92 (d, 1H, *J* = 6.4 Hz), 6.84–6.86 (m, 2H), 6.34 (dd, 1H, *J* = 1.6, 6.8 Hz), 6.25 (s, 1H), 5.03 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.8, 157.7, 154.2, 137.7, 129.6, 128.1, 127.1, 119.5, 115.1, 114.6, 114.4, 111.0, 108.8, 102.4, 66.3; HRMS (FAB$^+$) m/z calcd for $C_{15}H_{12}O_3$ $[M]^+$ 240.0786, found 240.0788.

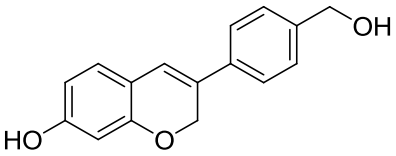
Compound **14**, 3-phenyl-2H-chromen-7-ol



Compound **14** was prepared by the general procedure with **2a** and phenylboronic acid as the starting materials.

Yield: 51% (2-step yield), R_f = 0.71 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.27–7.44 (m, 5H), 6.98 (d, 1H, *J* = 8.5 Hz), 6.80 (s, 1H), 6.41 (dd, 1H, *J* = 2.5, 8.0 Hz), 6.36 (d, 1H, *J* = 1.5 Hz), 5.14 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 157.2, 137.2, 129.1, 128.4, 128.0, 124.8, 120.0, 126.7, 108.9, 103.2, 67.6; HRMS (FAB$^-$) m/z calcd for $C_{15}H_{12}O_3$ $[M]^-$ 223.0759, found 223.0766.

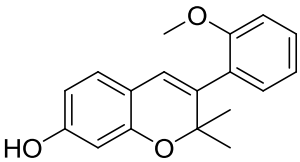
Compound **15**, 3-(4-(hydroxymethyl)phenyl)-2H-chromen-7-ol



Compound **15** was prepared by the general procedure with **2a** and 4-(hydroxymethyl)phenylboronic acid as the starting materials.

Yield: 57% (2-step yield), R_f = 0.41 (1:10 = MeOH:DCM, v/v); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46 (d, 2H, *J* = 8.4 Hz), 7.32 (d, 2H, *J* = 8.4 Hz), 6.98 (d, 1H, *J* = 8.0 Hz), 6.94 (s, 1H), 6.35 (dd, 2H, *J* = 2.0, 8.0 Hz), 6.26 (d, 1H, *J* = 2.0 Hz), 5.08 (d, 1H, *J* = 1.2 Hz), 4.50 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.7, 154.1, 141.9, 134.7, 128.0, 127.0, 126.7, 124.0, 119.1, 114.5, 108.8, 102.4, 66.3, 62.6; HRMS (FAB$^+$) m/z calcd for $C_{16}H_{14}O_3$ $[M]^+$ 254.0943, found 254.0941.

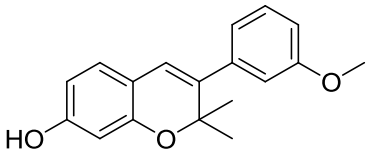
Compound **16**, 3-(2-methoxyphenyl)-2,2-dimethyl-2H-chromen-7-ol



Compound **16** was prepared by the general procedure with **2b** and 2-methoxyphenylboronic acid as the starting materials.

Yield: 71% (2-step yield), R_f = 0.22 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, 1H, *J* = 7.8 Hz), 7.14 (d, 1H, *J* = 6.0 Hz), 6.89–6.96 (m, 3H), 6.39 (br. s, 1H), 6.36 (br. s, 1H), 6.21 (s, 1H), 3.81 (s, 3H), 1.26 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 156.5, 154.2, 137.0, 131.7, 129.1, 129.0, 127.4, 122.7, 120.5, 116.8, 110.7, 108.1, 103.9, 55.3, 26.2; HRMS (FAB$^+$) m/z calcd for $C_{18}H_{18}O_3$ $[M]^+$ 282.1256, found 282.1267.

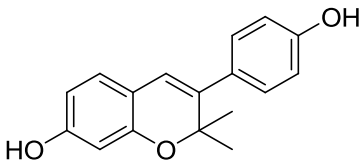
Compound **17**, 3-(3-methoxyphenyl)-2,2-dimethyl-2H-chromen-7-ol



Compound **17** was prepared by the general procedure with **2b** and 3-methoxyphenylboronic acid as the starting materials.

Yield: 75% (2-step yield), R_f = 0.22 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23–7.28 (m, 1H), 6.84–6.93 (m, 4H), 6.38 (br. s, 2H), 6.29 (s, 1H), 3.83 (s, 3H), 1.52 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 156.7, 154.0, 141.2, 139.2, 129.2, 127.5, 122.1, 120.8, 116.5, 114.4, 112.6, 108.3, 103.9, 79.2, 55.4, 27.2; HRMS (FAB$^+$) m/z calcd for $C_{18}H_{18}O_3$ $[M]^+$ 282.1256, found 282.1250.

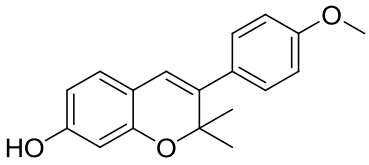
Compound **18**, 3-(4-hydroxyphenyl)-2,2-dimethyl-2H-chromen-7-ol



Compound **18** was prepared by the general procedure with **2b** and prepared *tert*-butyldimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy) silane (Same boronic ester with synthesis of compound **12**) as the starting materials.

Yield: 88% (2-step yield), R_f = 0.54 (1:1 = EtOAc:hexane, v/v); ^{1}H NMR (400 MHz, CD_3OD) δ 7.13 (dd, 2H, *J* = 2.0, 6.8 Hz), 6.86 (d, 1H, *J* = 8.4 Hz), 6.75 (dd, 2H, *J* = 2.2, 6.6 Hz), 6.32 (dd, 1H, *J* = 2.4, 7.6 Hz), 6.25 (d, 1H, *J* = 2.4 Hz), 6.18 (s, 1H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.4, 157.9, 154.9, 140.0, 132.4, 130.4, 128.1, 122.2, 117.0, 115.9, 109.2, 104.3, 79.9, 27.4; HRMS (FAB$^+$) m/z calcd for $C_{17}H_{16}O_3$ $[M]^+$ 268.1099, found 268.1096.

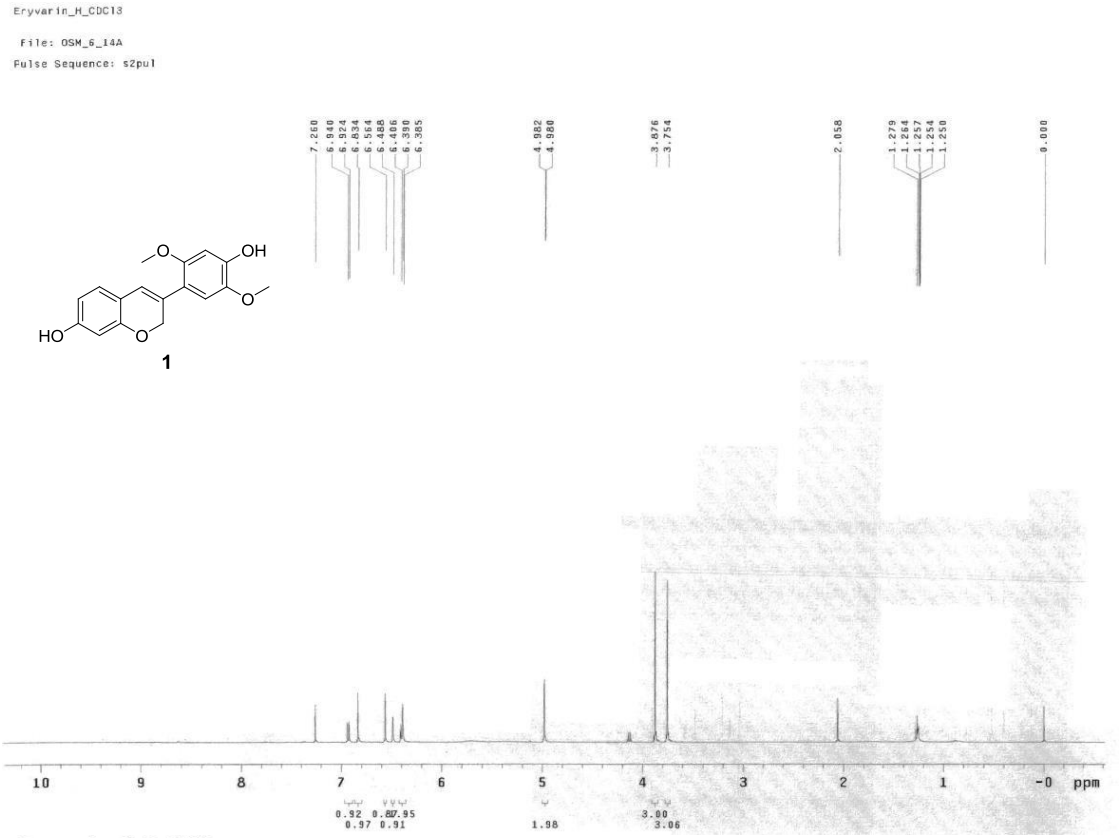
Compound **19**, 3-(4-methoxyphenyl)-2,2-dimethyl-2H-chromen-7-ol

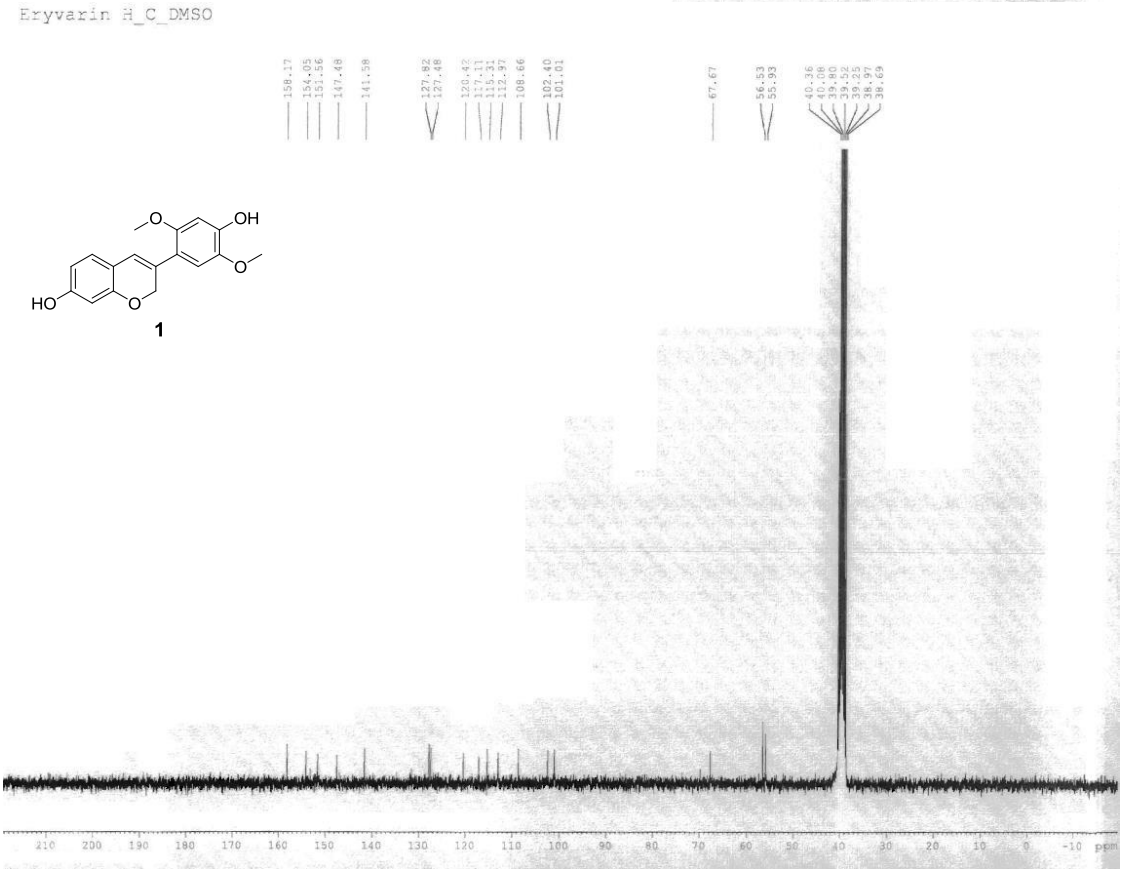


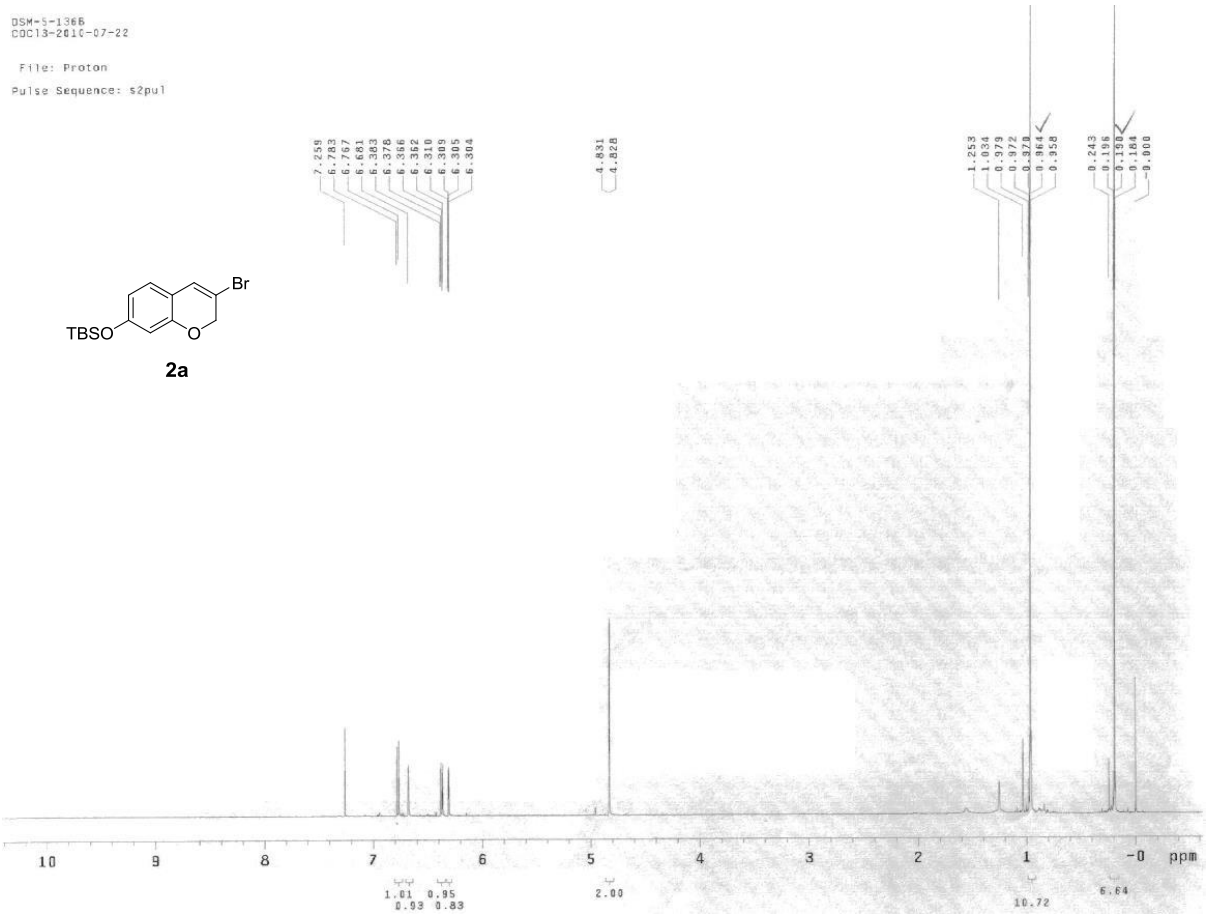
Compound **19** was prepared by the general procedure with **2b** and 4-methoxyphenylboronic acid as the starting materials

Yield: 79% (2-step yield), R_f = 0.22 (1:10 = EtOAc:hexane, v/v); ^{1}H NMR (400 MHz, CD_3OD) δ 7.22 (dd, 2H, *J* = 2.0, 6.8 Hz), 6.87 (dd, 2H, *J* = 1.8, 6.6 Hz), 6.85 (s, 1H), 6.32 (dd, 1H, *J* = 2.4, 8.0 Hz), 6.26 (d, 1H, *J* = 2.0 Hz), 6.20 (s, 1H), 4.89 (br. s, 1H), 3.78 (s, 3H), 1.45 (s, 6H); ^{13}C NMR (100 MHz, CD_3OD) δ 160.4, 159.5, 154.9, 139.6, 133.5, 130.4, 128.2, 122.5, 116.8, 114.5, 109.2, 104.3, 79.8, 55.7, 27.4; HRMS (FAB$^+$) m/z calcd for $C_{18}H_{18}O_3$ $[M]^+$ 282.1256, found 282.1260.

IV. ^{1}H and ^{13}C-NMR spectra for compound **1**–**19**



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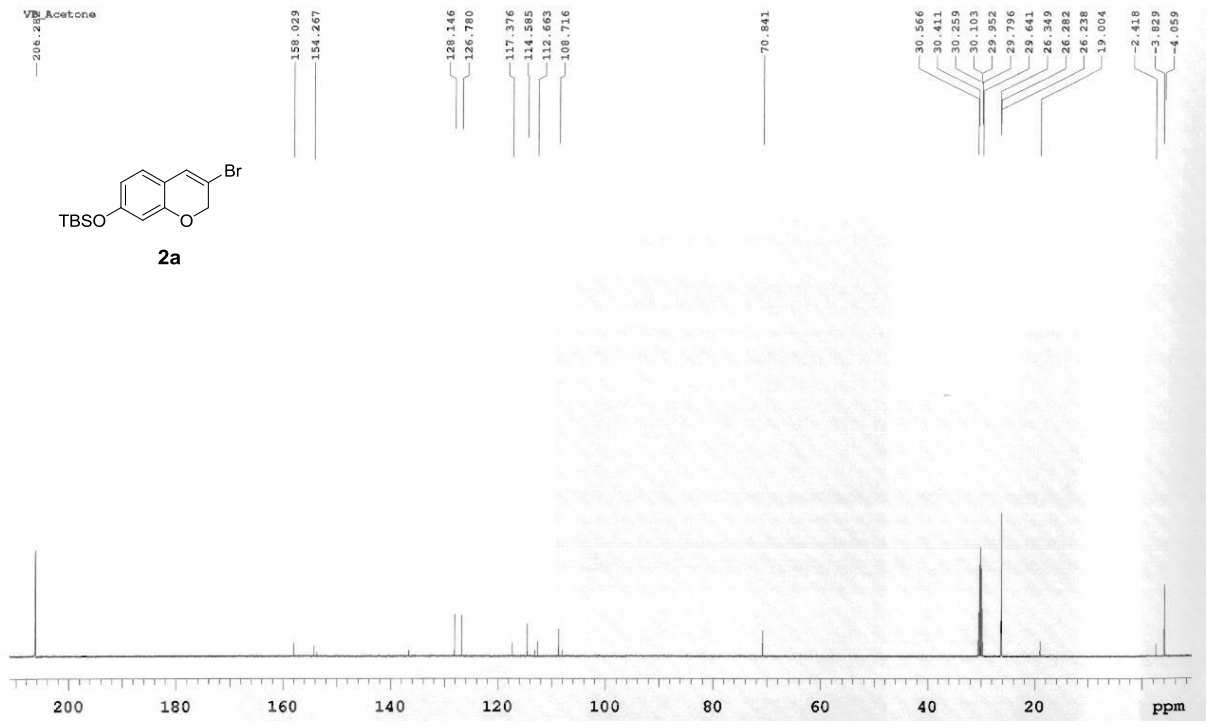
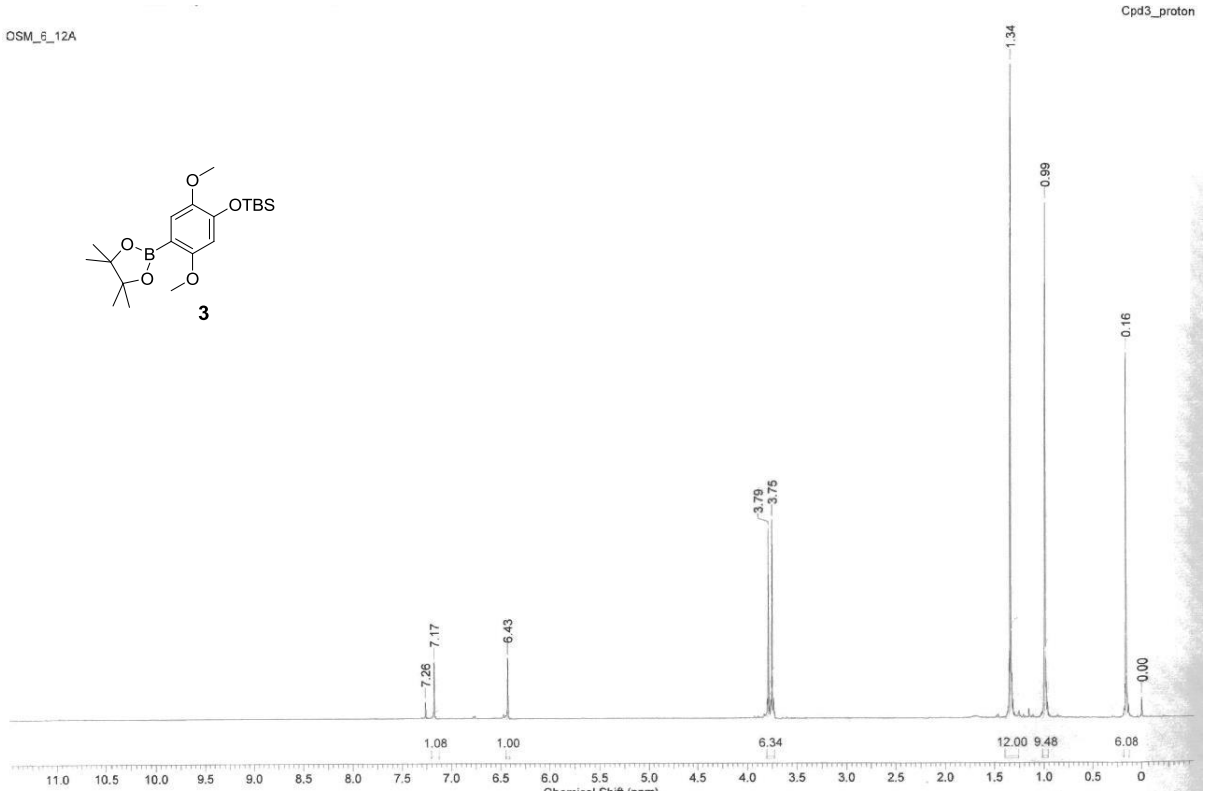
O
2a
ppm


Acetone
Br
TBSO
O
2a
ppm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Cpd3_proton
OTBS
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0.16
3.79
3.75
7.17
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6.43
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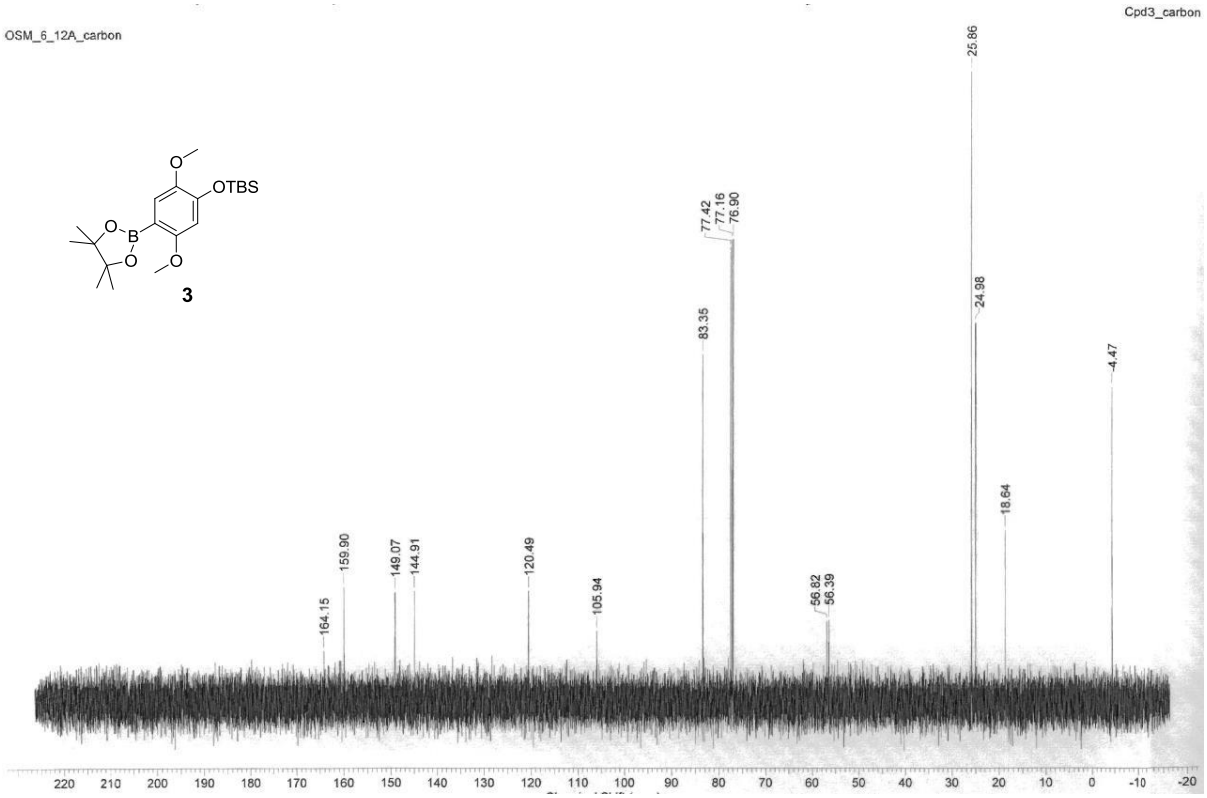
1.08
1.00
6.34
12.00
9.48
6.08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Cpd3_carbon
OTBS
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76.90
24.98
83.35
4.47
18.64
159.90
149.07
144.91
120.49
164.15
105.94
56.82
56.39

KJY-1-72A
Acetone_2010-12-29

File: KJY-1-72A_H_2010-12-29

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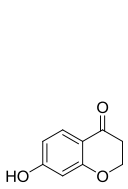

4

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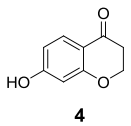
Pulse Sequence: s2pul



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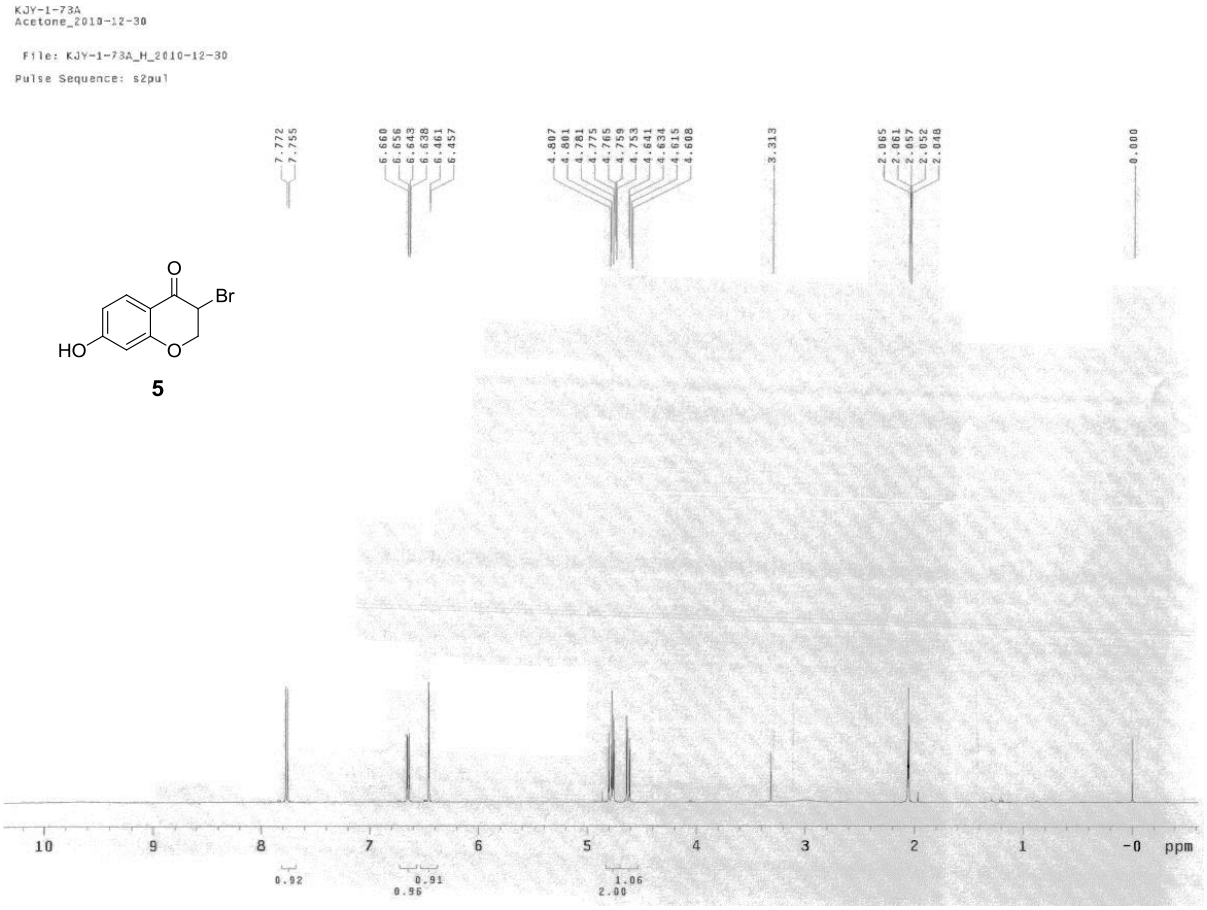

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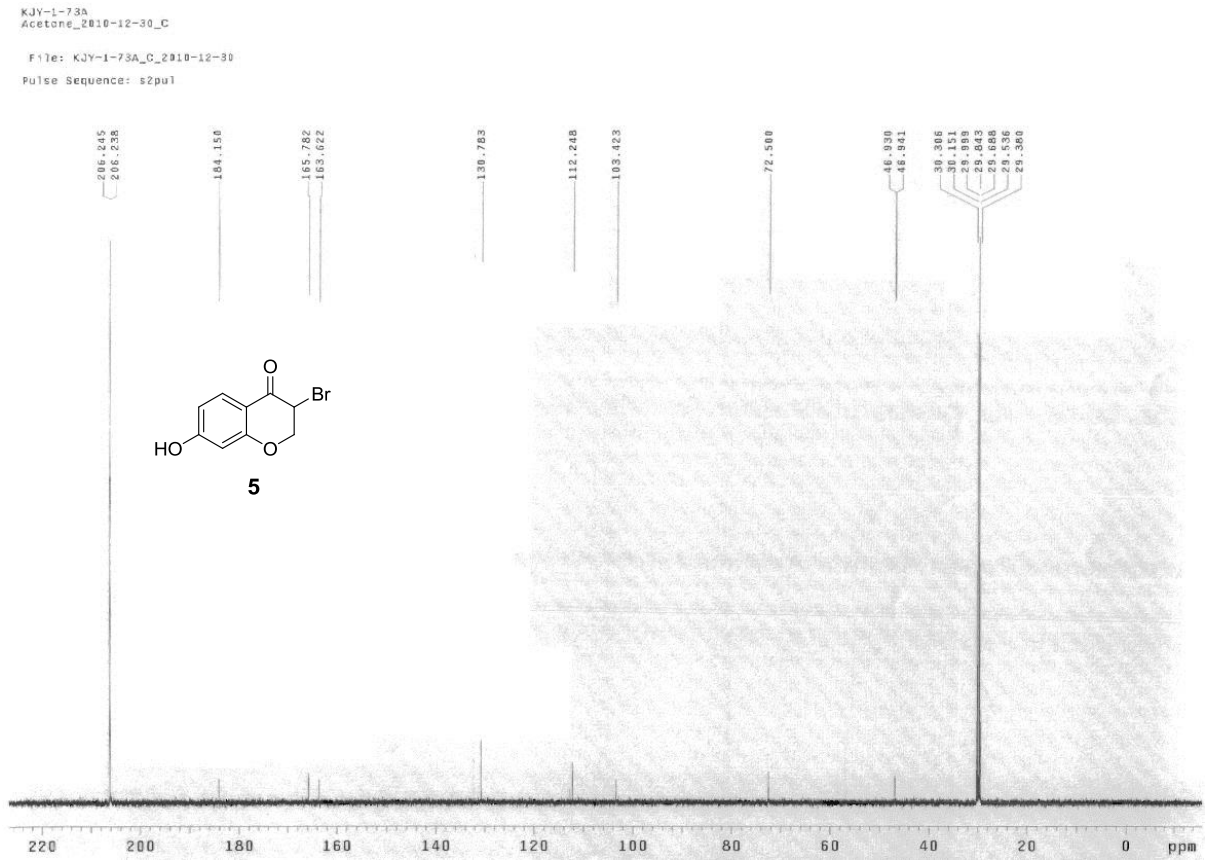

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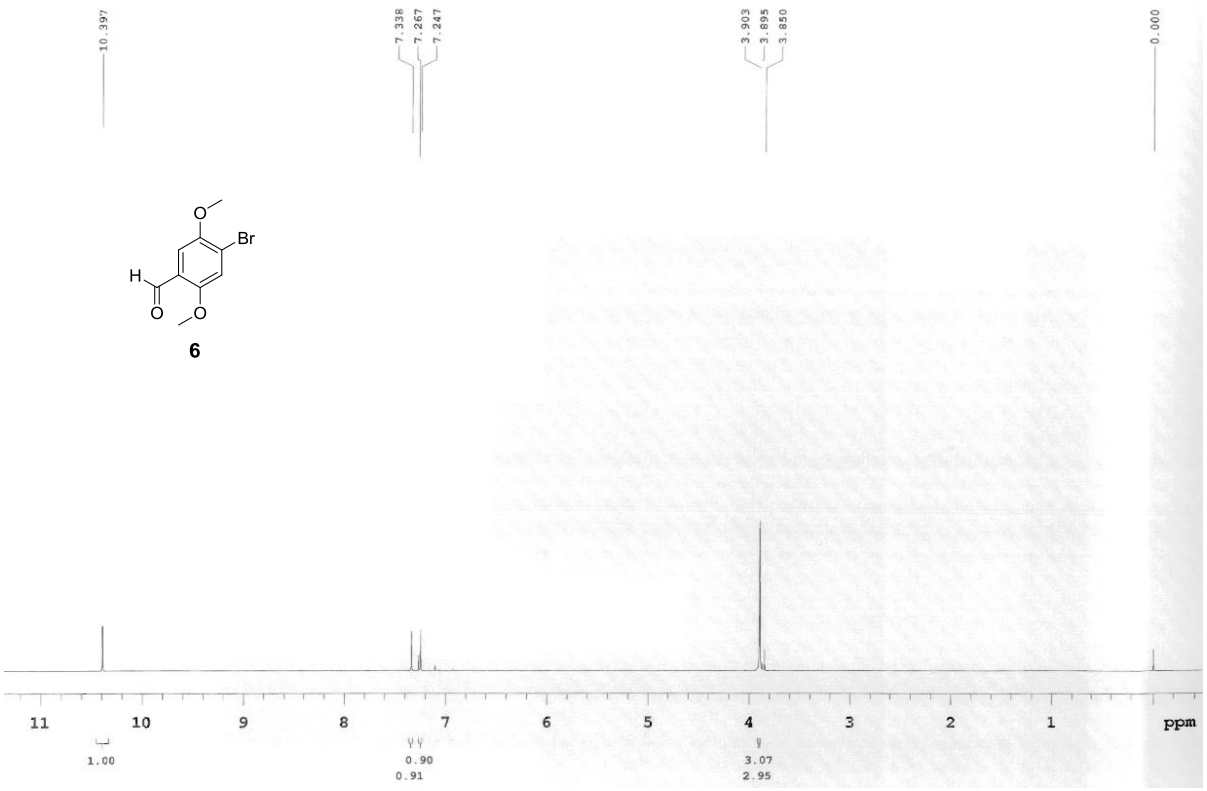

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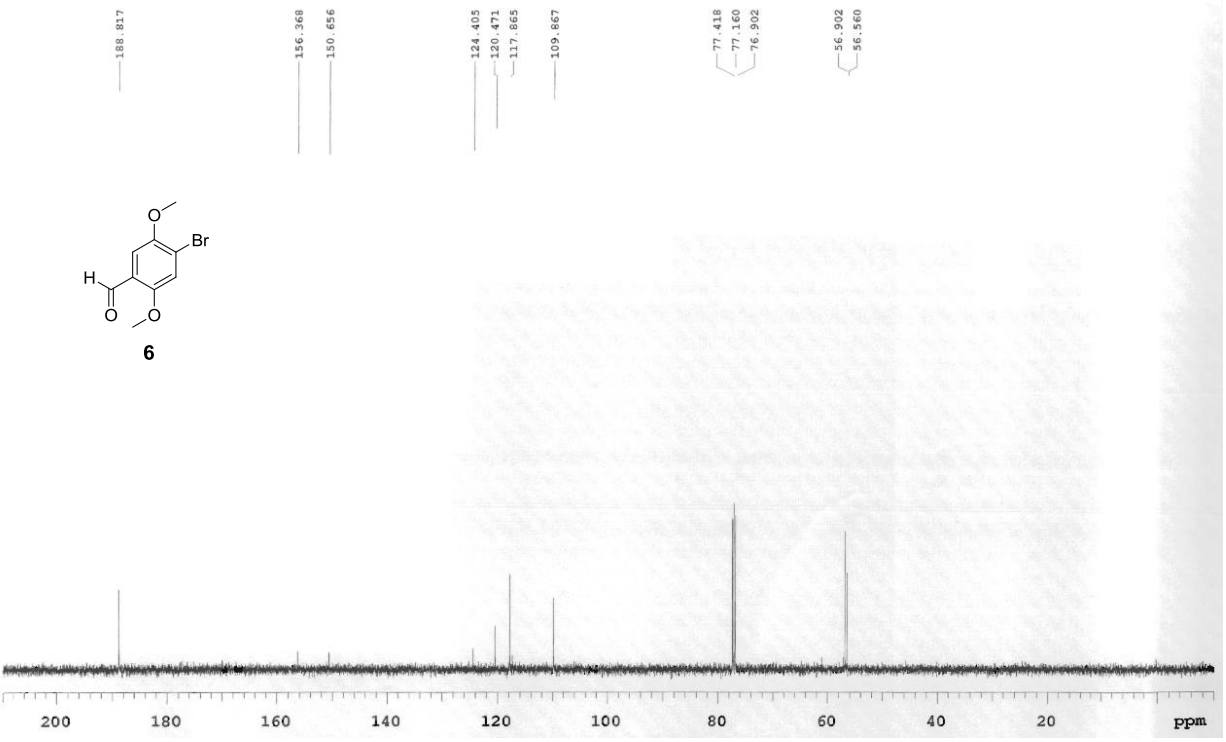

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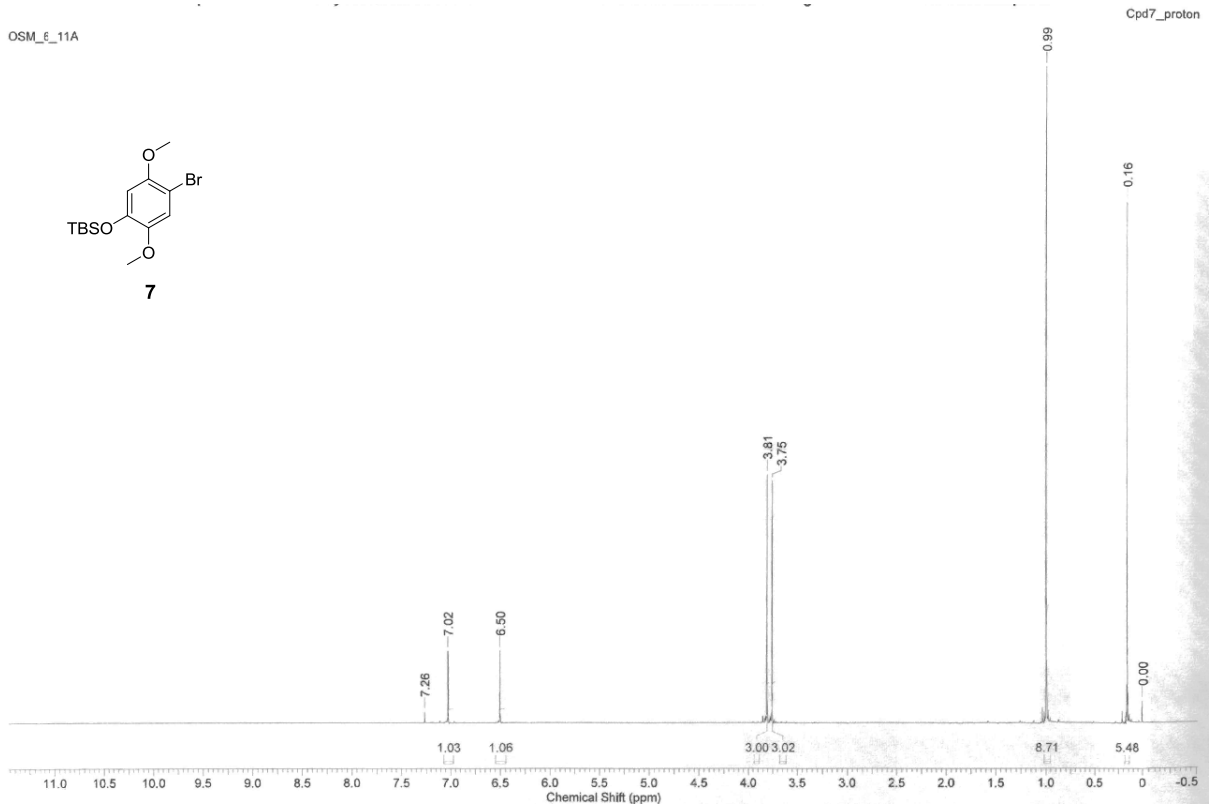
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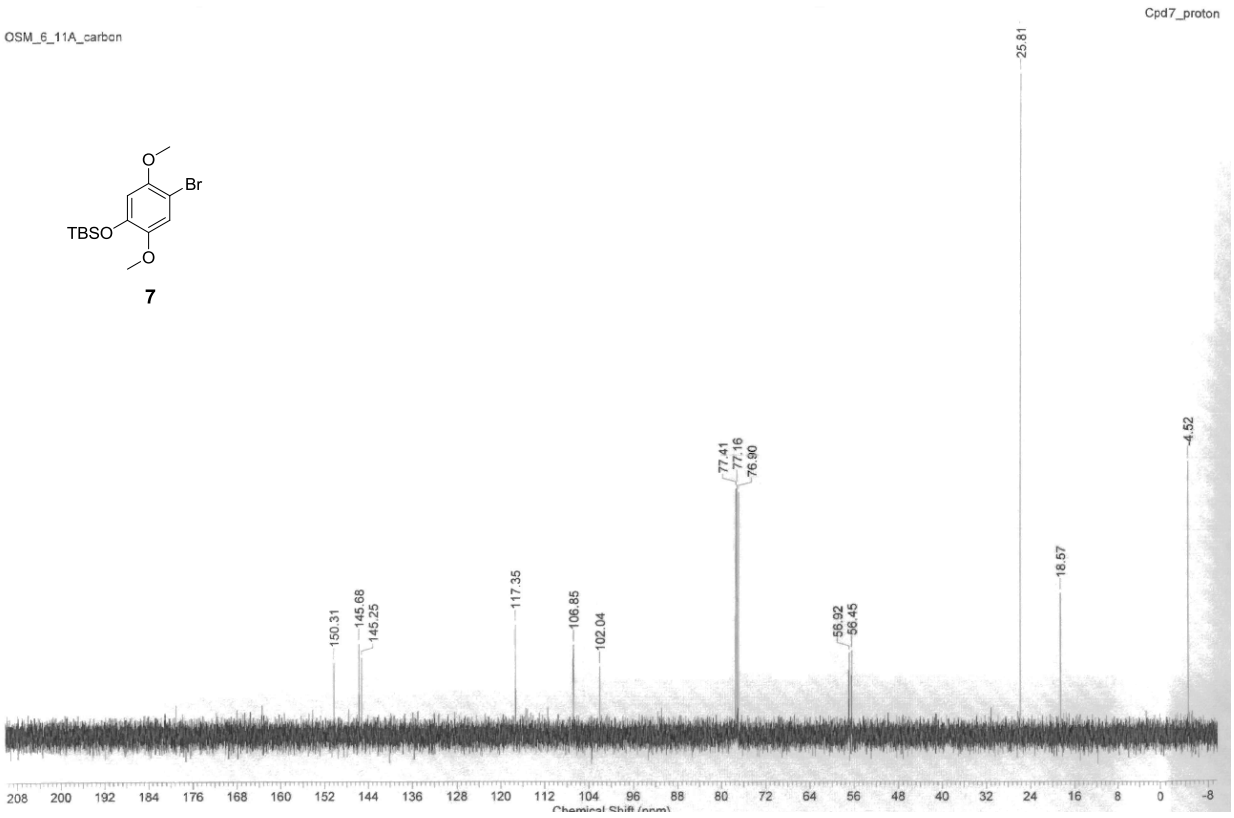
Chemical Shift (ppm)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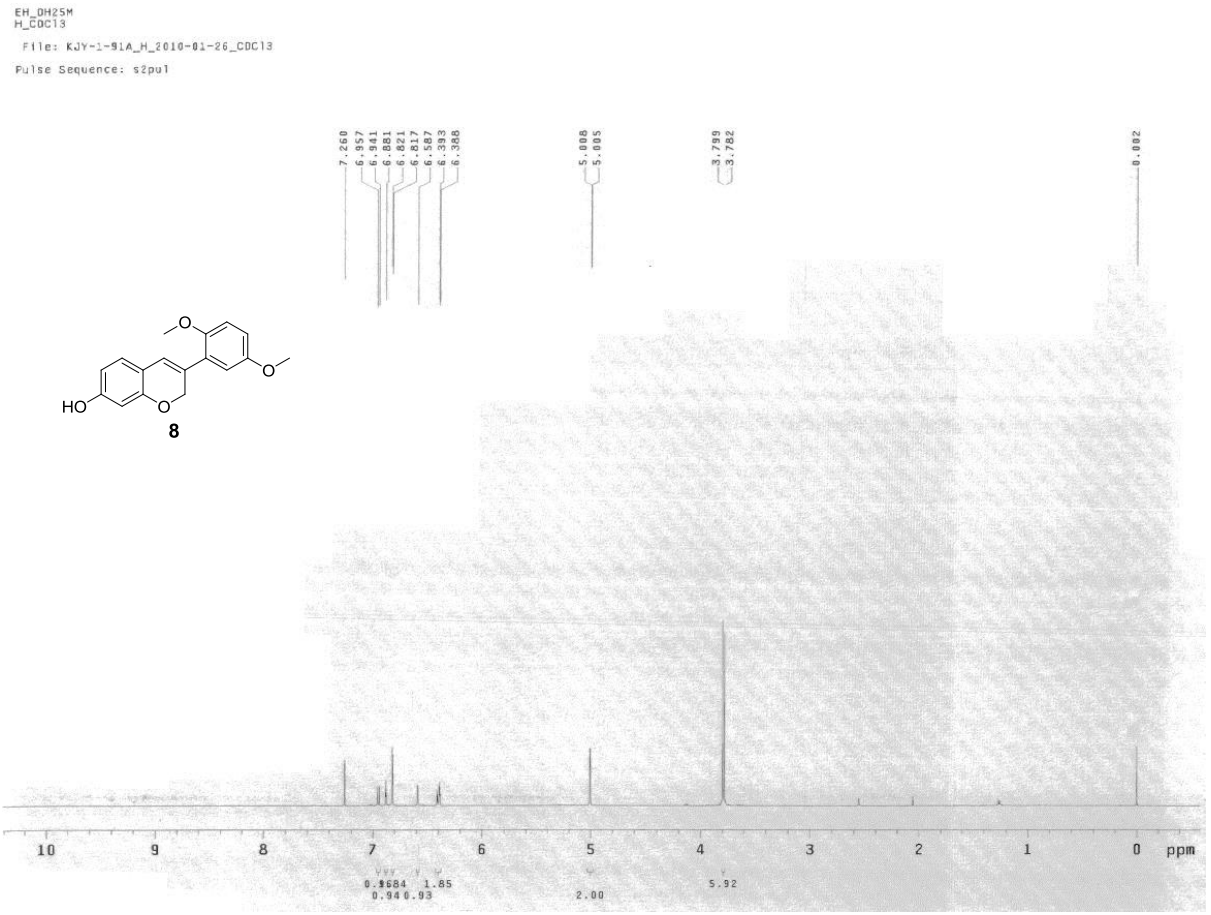
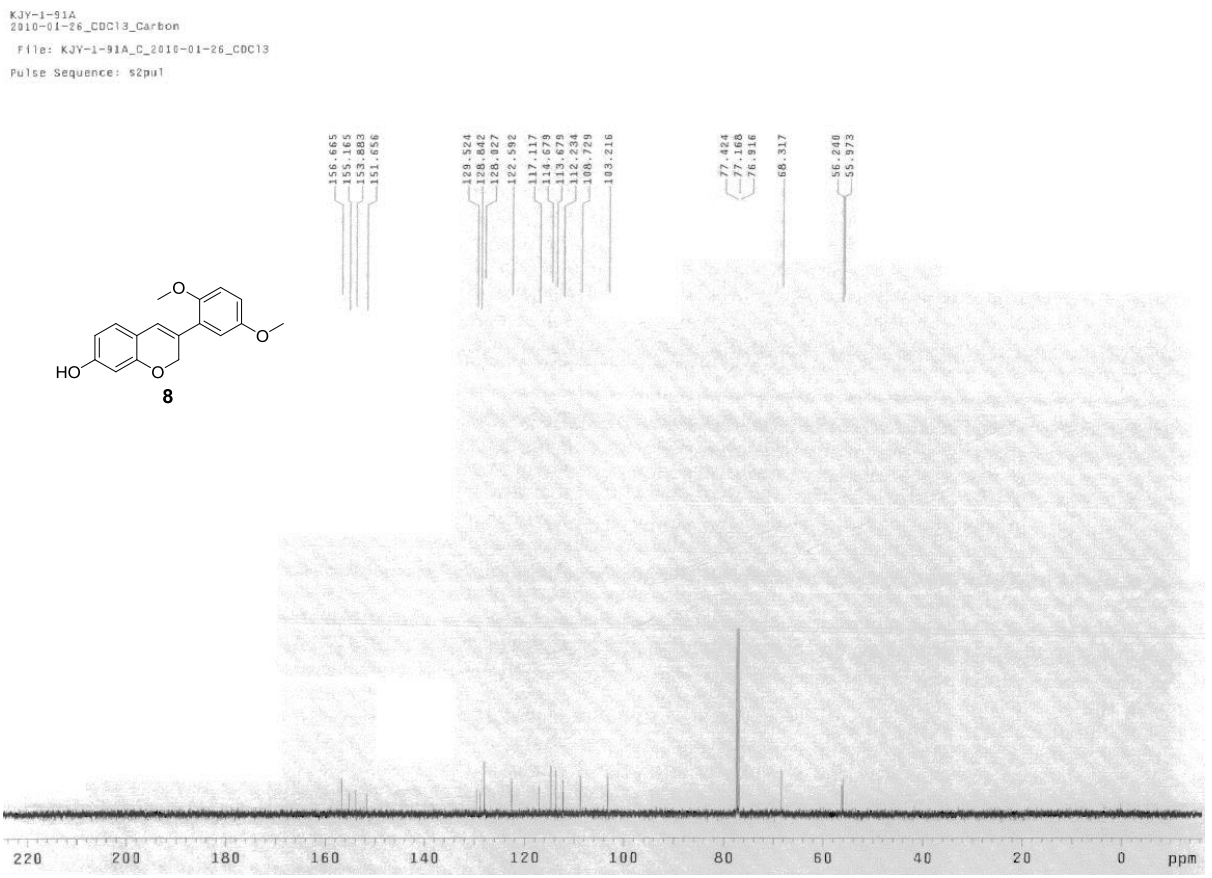
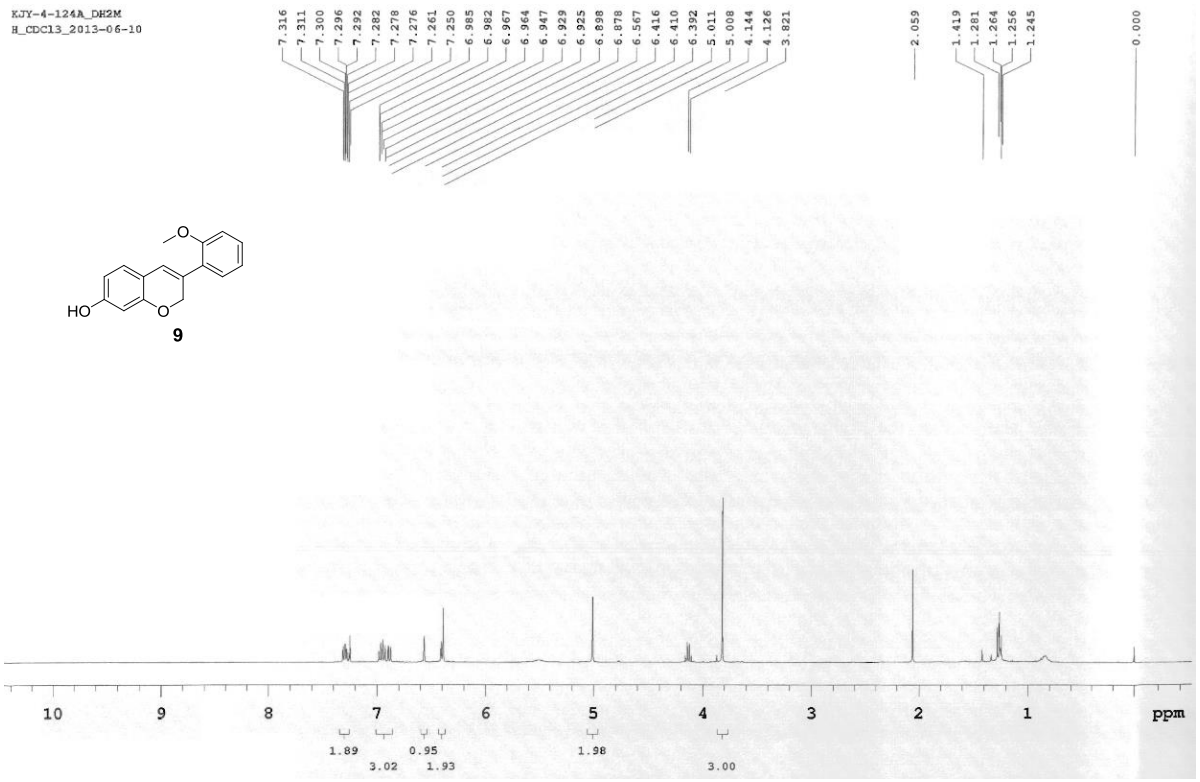
56.45
Chemical Shift (ppm)



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6.898
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6.567
6.416
6.410
6.392
5.011
5.008
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O
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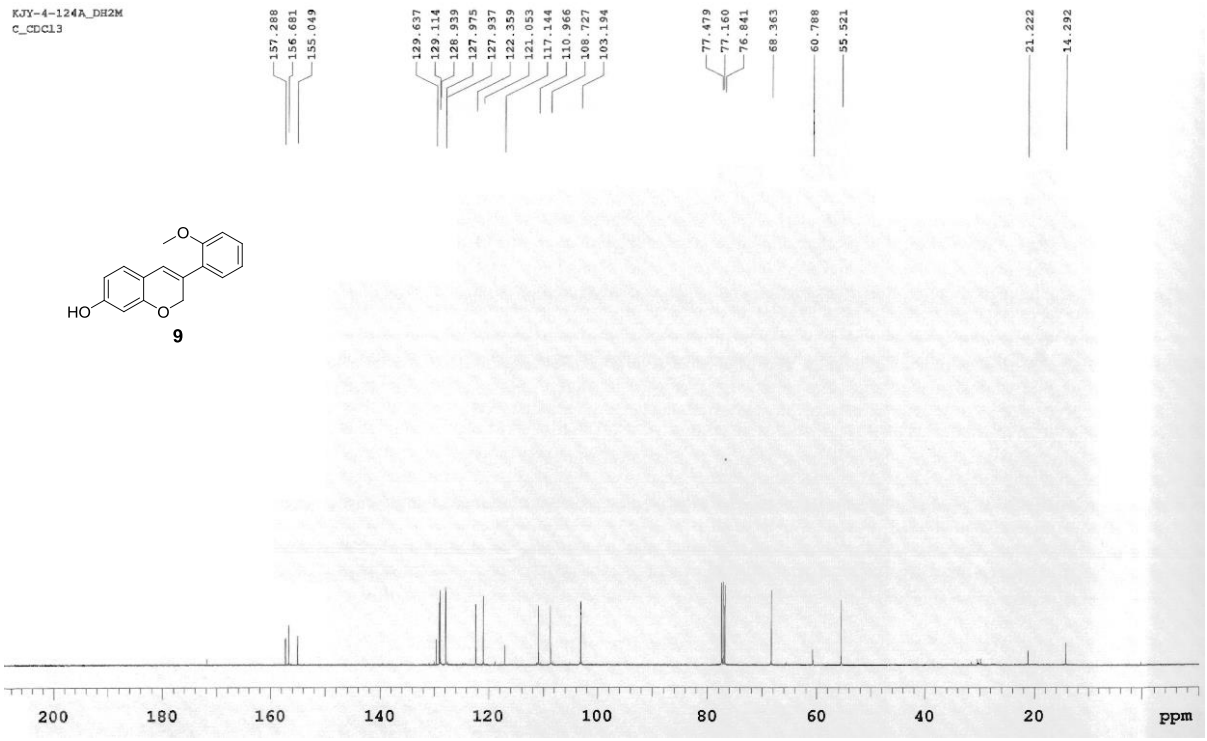
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O
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9
200
180
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140
120
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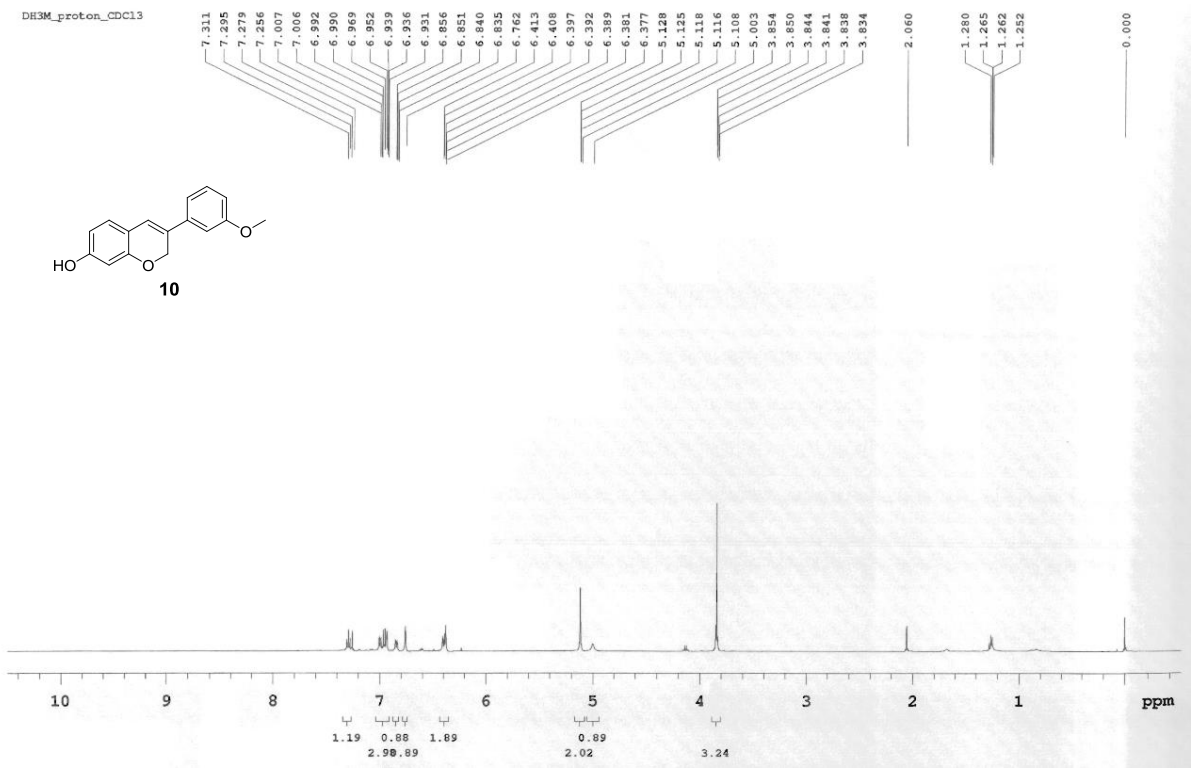
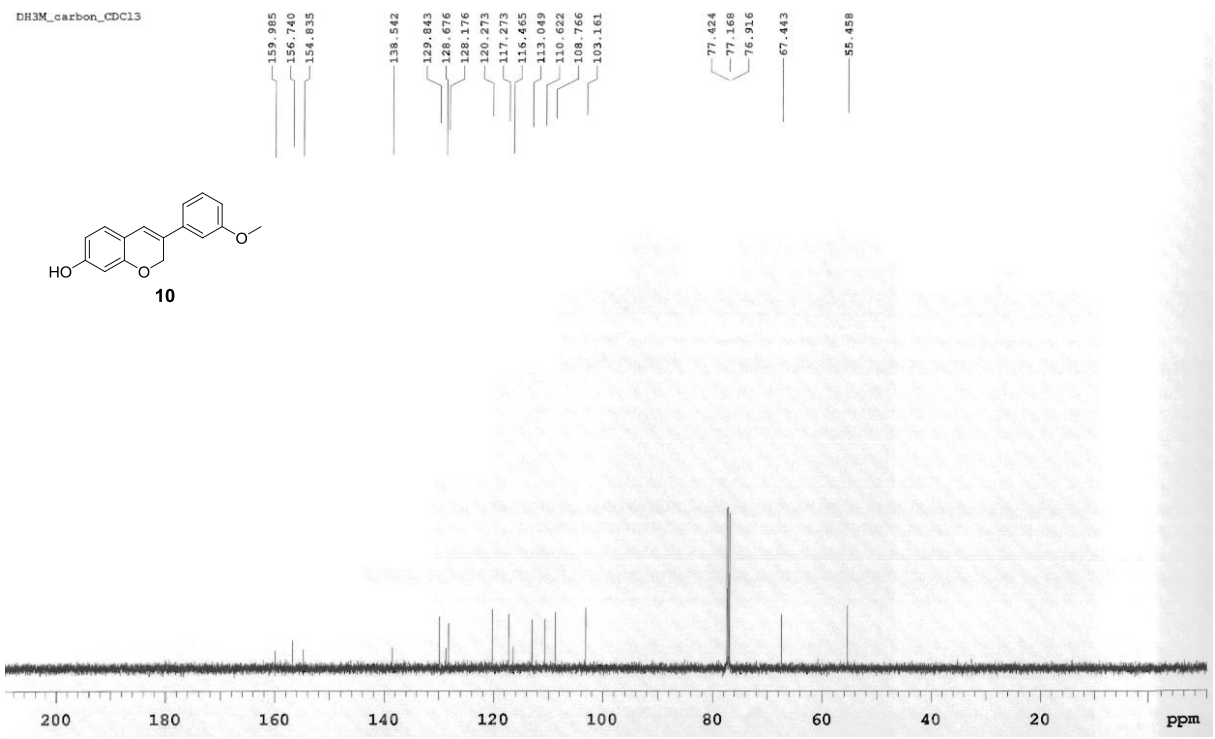
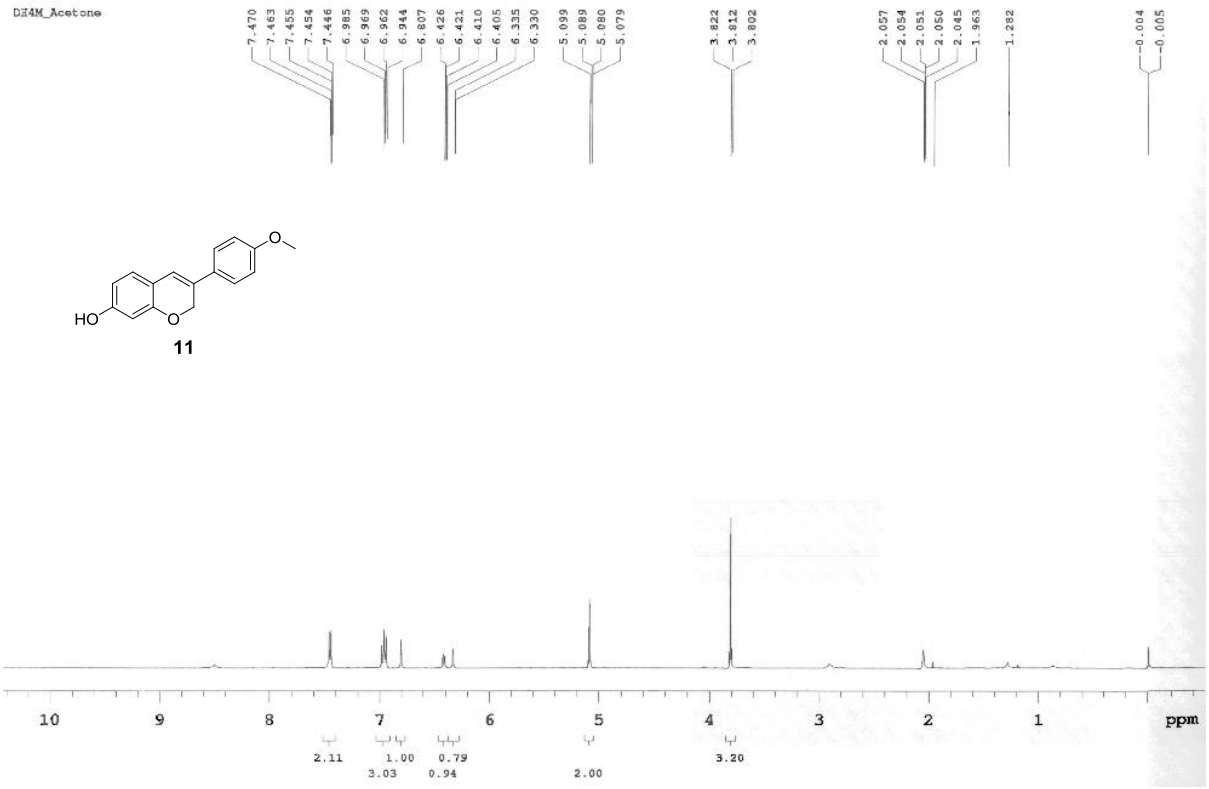
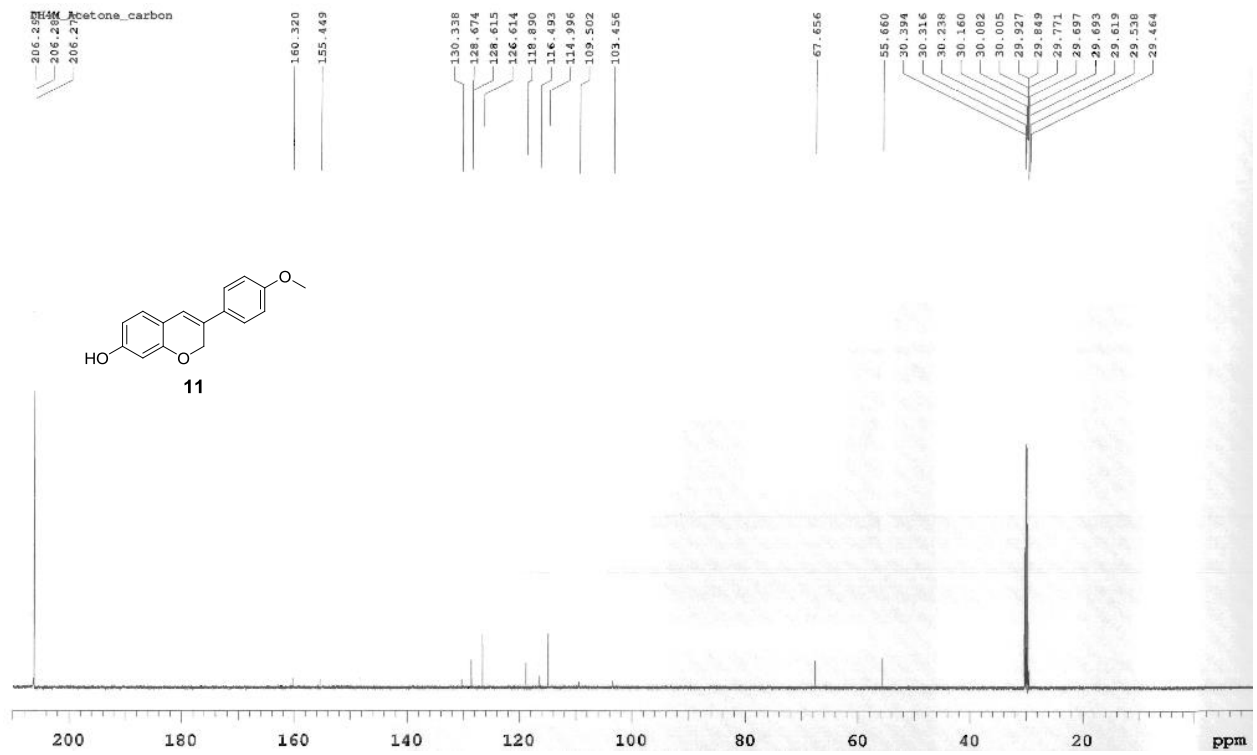
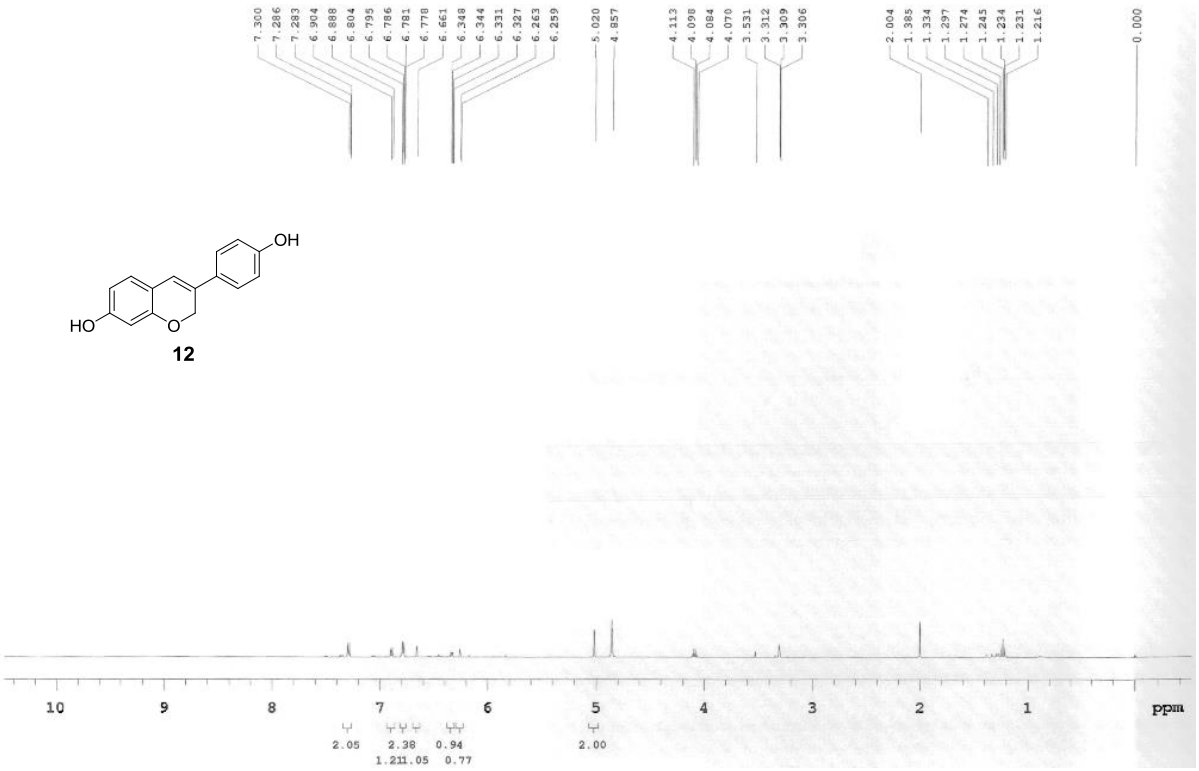
60
40
20
ppm

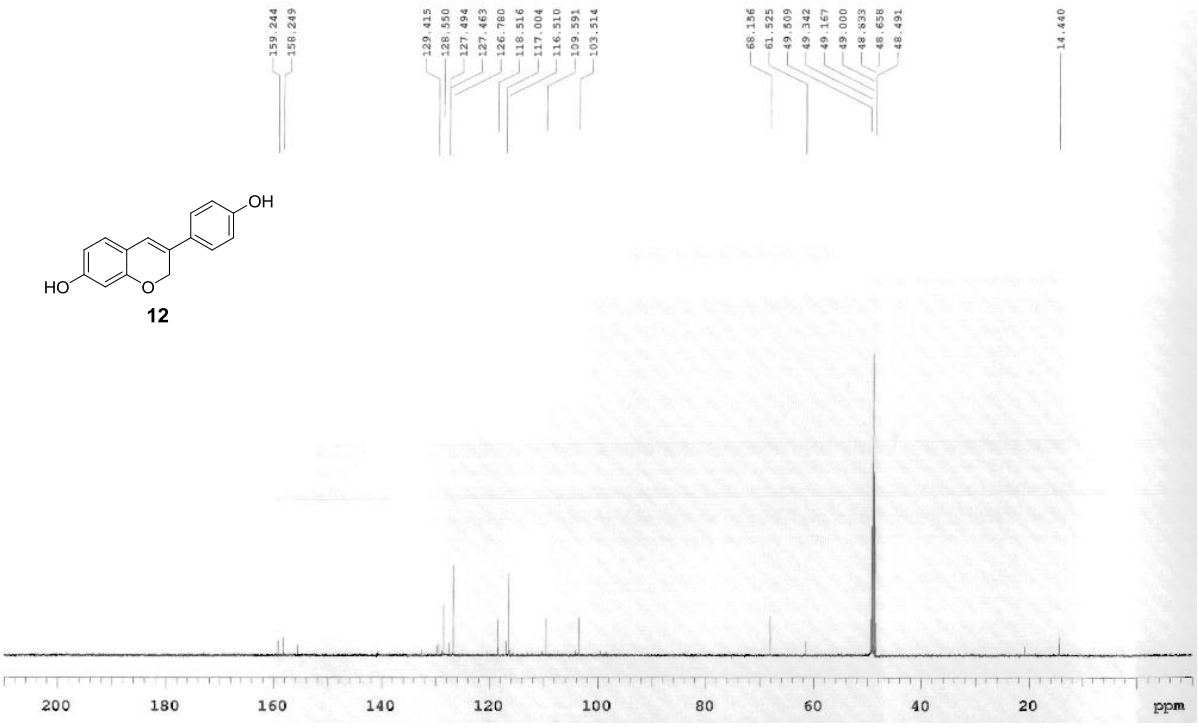


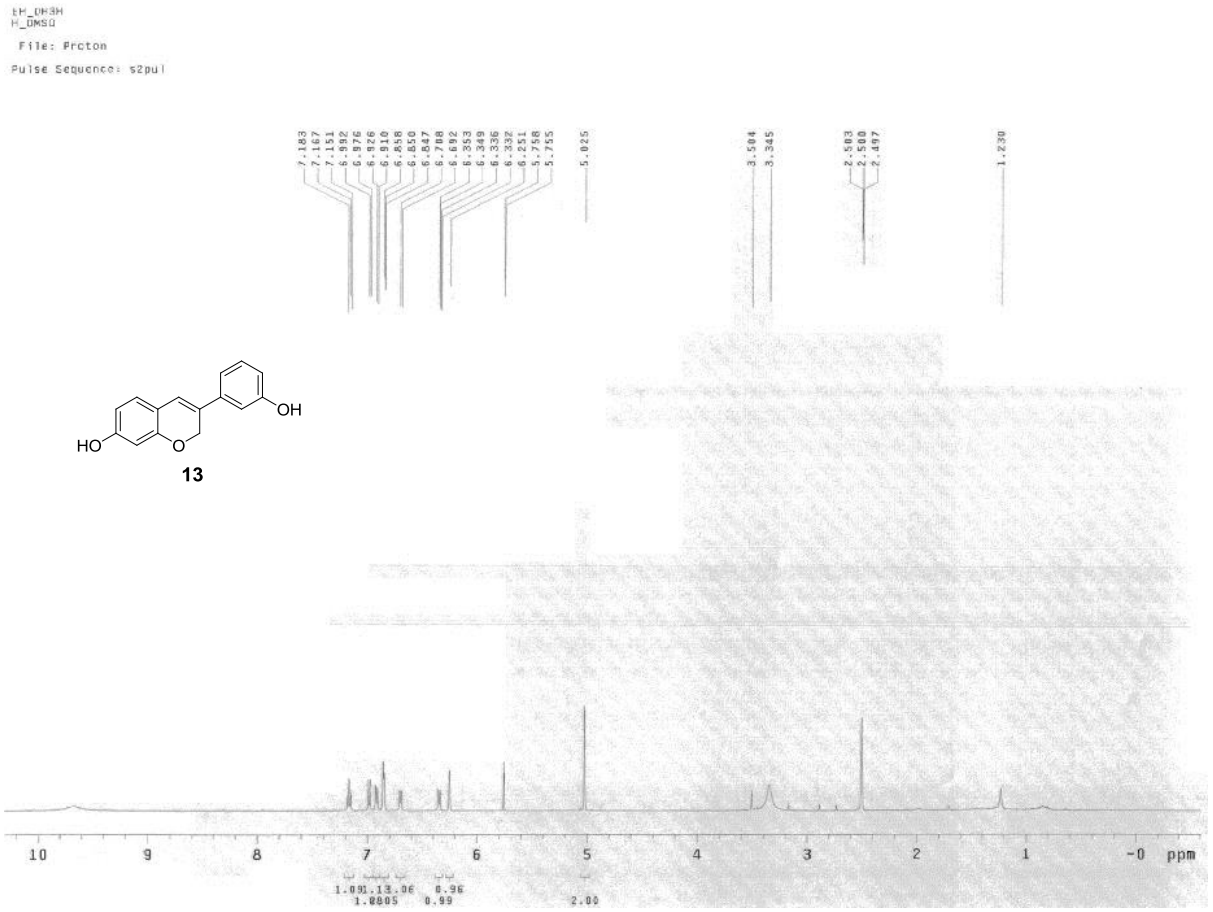


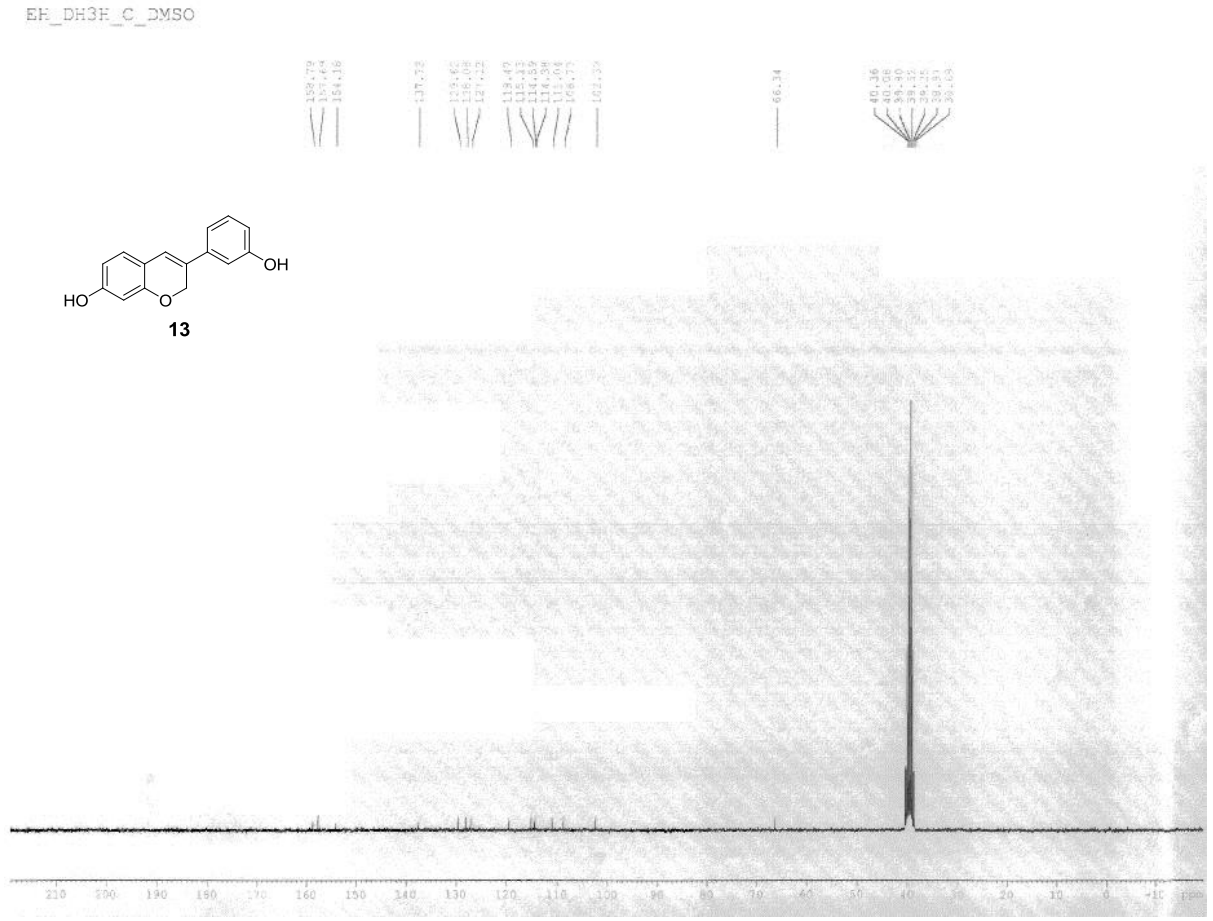

DE4M_Acetone
7.470
7.463
7.455
7.454
7.446
6.985
6.969
6.962
6.944
6.807
6.426
6.421
6.410
6.405
6.335
6.330
5.099
5.089
5.080
5.079
3.822
3.812
3.802
2.057
2.054
2.051
2.050
2.045
1.963
1.282
0.004
-0.005
HO
O
O
11
10
9
8
7
6
5
4
3
2
1
ppm
2.11
1.00
0.79
3.03
0.94
2.00
3.20

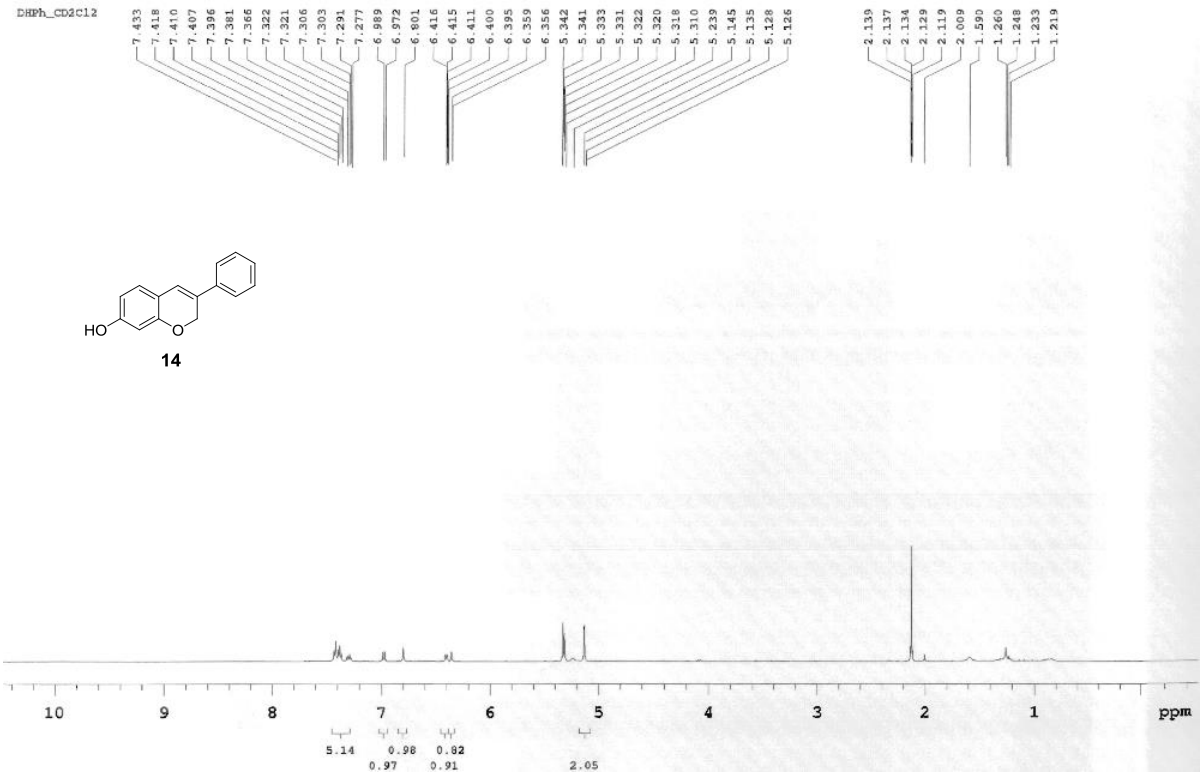

DE4M_Acetone_carbon
206.259
206.288
206.317
160.320
155.449
130.338
128.674
128.615
126.614
118.890
116.493
114.996
109.502
103.456
67.656
55.660
30.394
30.316
30.238
30.160
30.082
30.005
29.927
29.849
29.771
29.697
29.693
29.619
29.538
29.464
HO
O
O
11
200
180
160
140
120
100
80
60
40
20
ppm

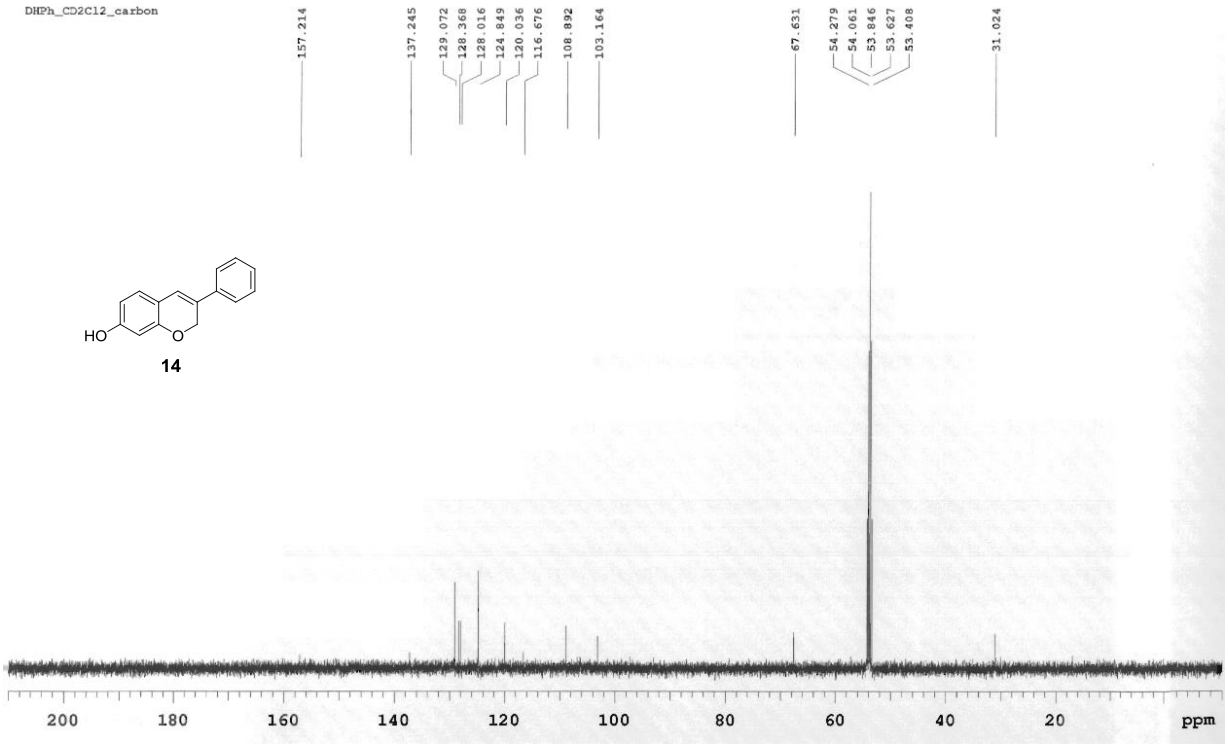


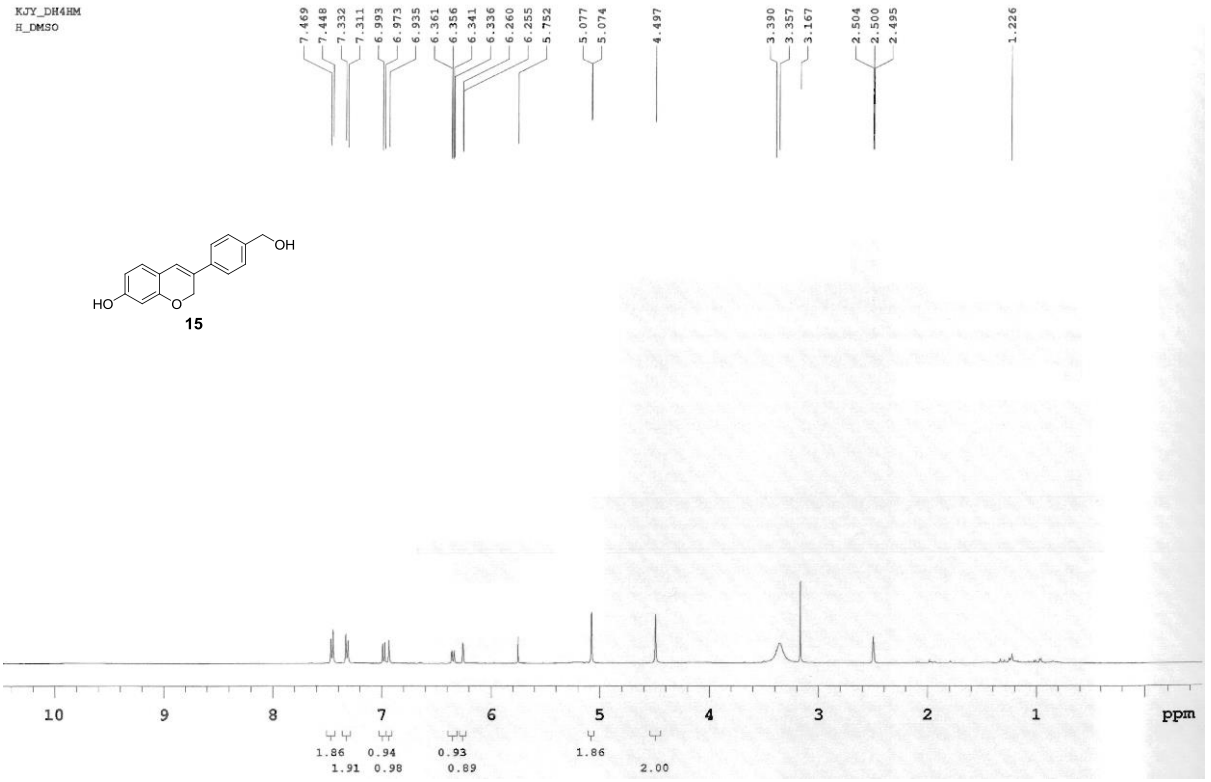


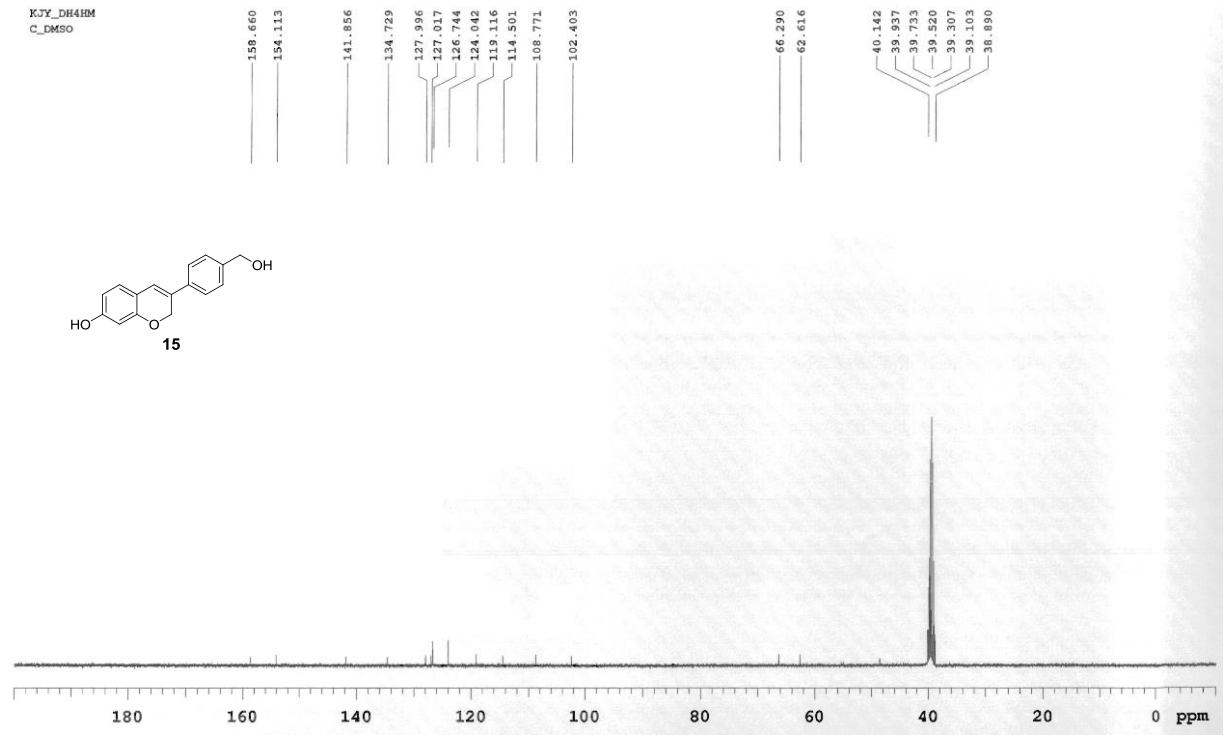


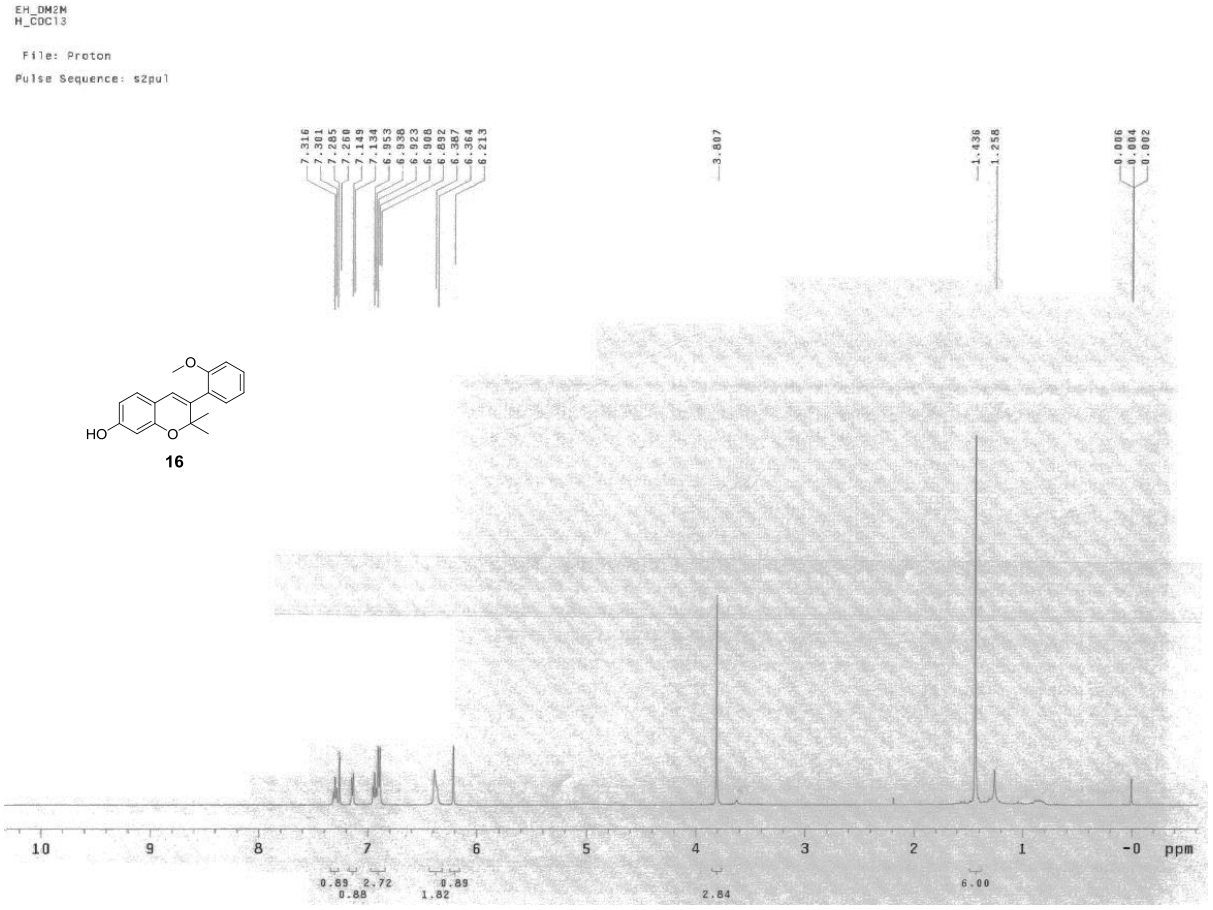


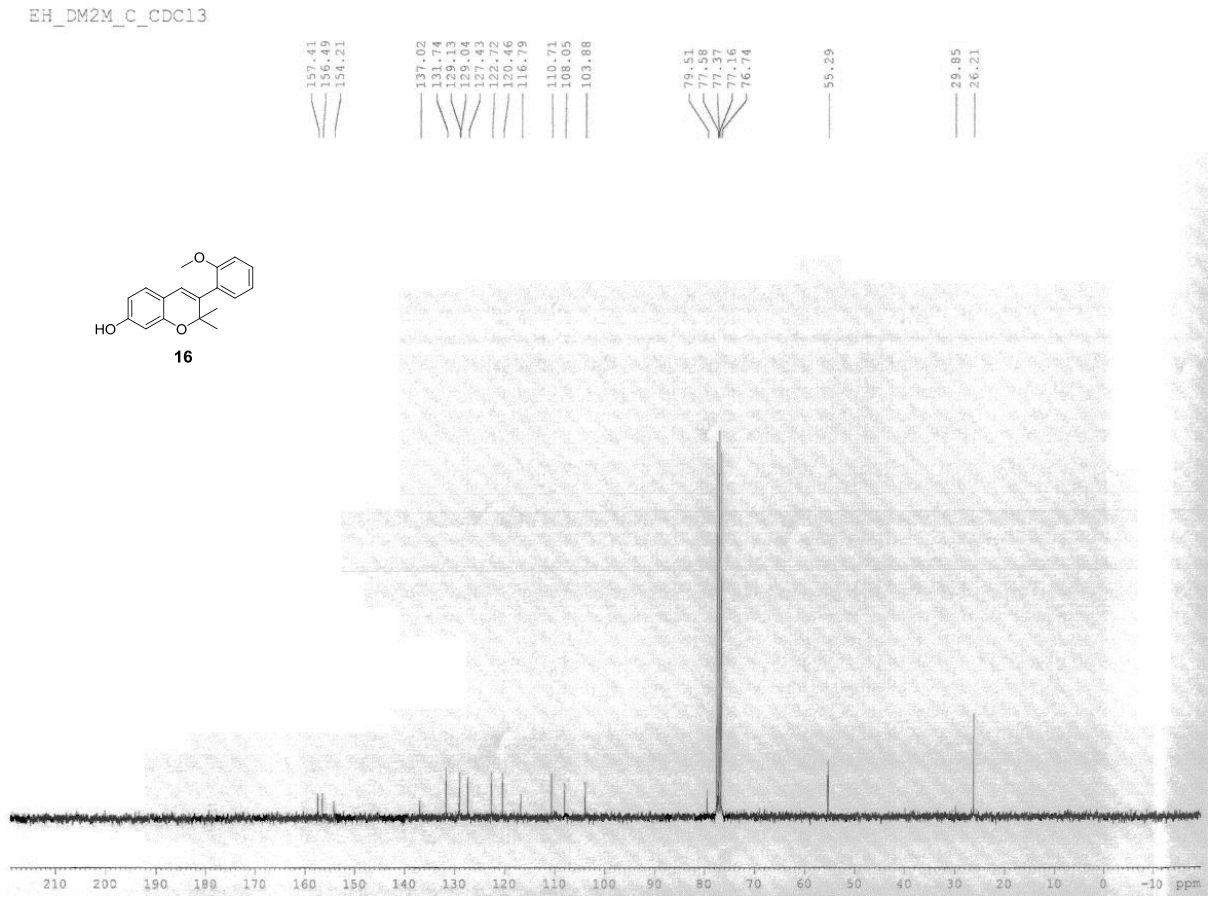

DHPh_CD2Cl2
7.433
7.418
7.410
7.407
7.396
7.381
7.366
7.322
7.321
7.306
7.303
7.291
7.277
6.989
6.972
6.901
6.416
6.415
6.411
6.400
6.395
6.359
6.356
5.342
5.341
5.333
5.331
5.322
5.320
5.318
5.310
5.239
5.145
5.135
5.128
5.126
2.139
2.137
2.134
2.129
2.119
2.009
1.590
1.260
1.248
1.233
1.219
HO
O
14
10
9
8
7
6
5
4
3
2
1
ppm
5.14
0.98
0.82
0.97
0.91
2.05


DHPh_CD2Cl2_carbon
157.214
137.245
129.072
128.368
128.016
124.849
120.036
116.676
108.892
103.164
67.631
54.279
54.061
53.846
53.627
53.408
31.024
HO
O
14
200
180
160
140
120
100
80
60
40
20
ppm


KJY_DH4HM
H_DMSO
7.469
7.448
7.332
7.311
6.993
6.973
6.935
6.361
6.356
6.341
6.336
6.260
6.255
5.752
5.077
5.074
4.497
3.390
3.357
3.167
2.504
2.500
2.495
1.226
OH
HO
O
15
10
9
8
7
6
5
4
3
2
1
ppm
1.86
0.94
0.93
1.86
1.91
0.98
0.89
2.00


KJY_DH4HM
C_DMSO
158.660
154.113
141.856
134.729
127.996
127.017
126.744
124.042
119.116
114.501
108.771
102.403
66.290
62.616
40.142
39.937
39.733
39.520
39.307
39.103
38.890
OH
HO
O
15
180
160
140
120
100
80
60
40
20
0
ppm

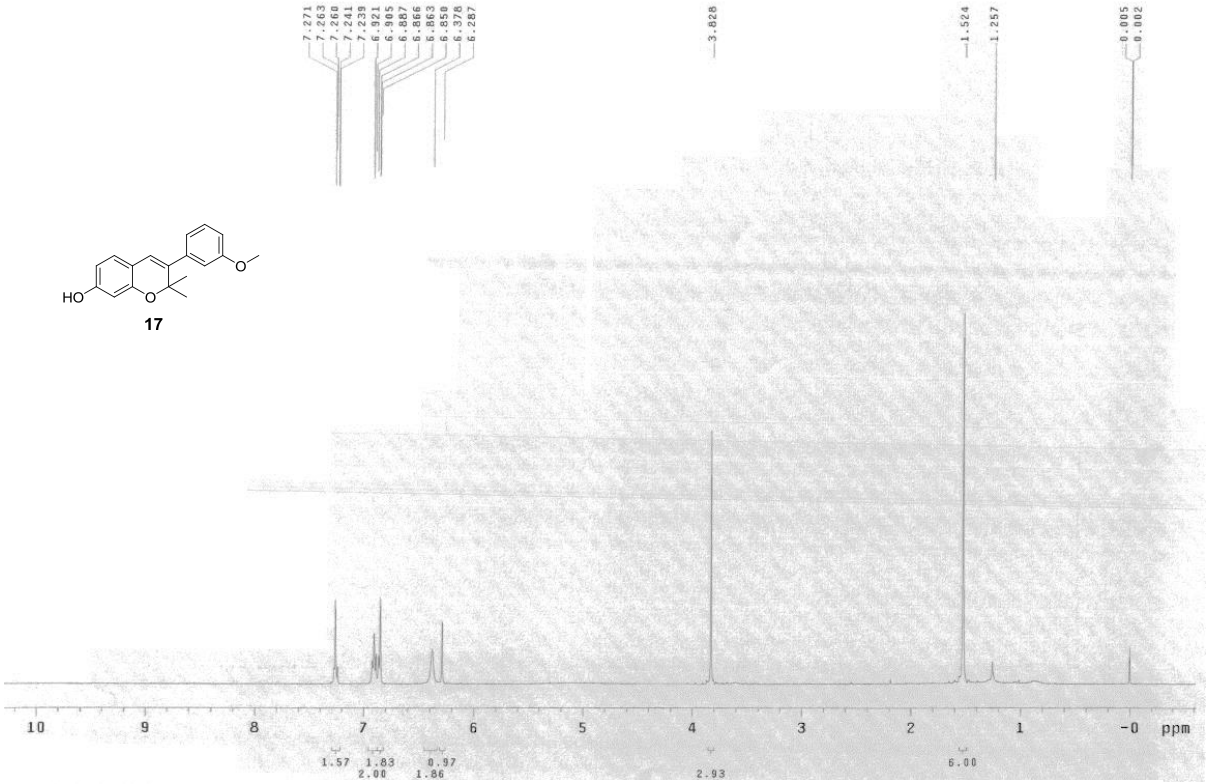




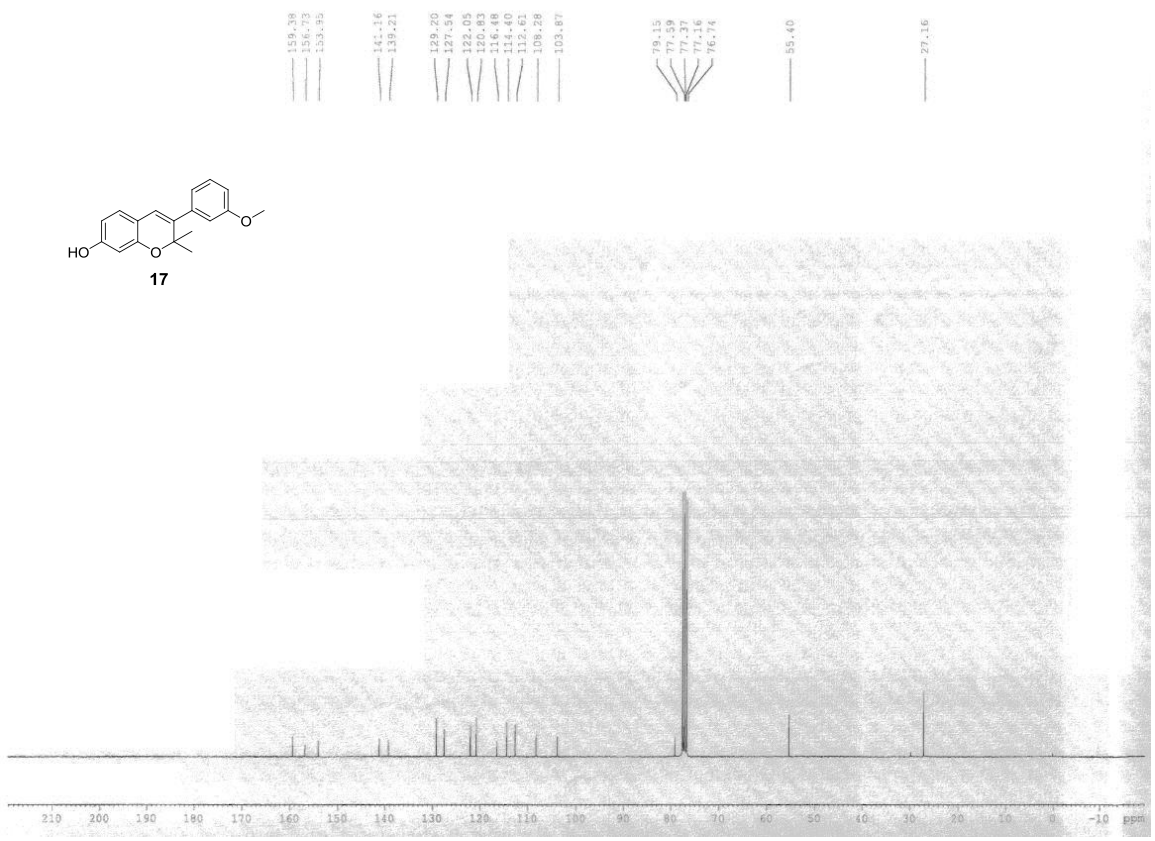
EH_DM3M
H_CDCl3

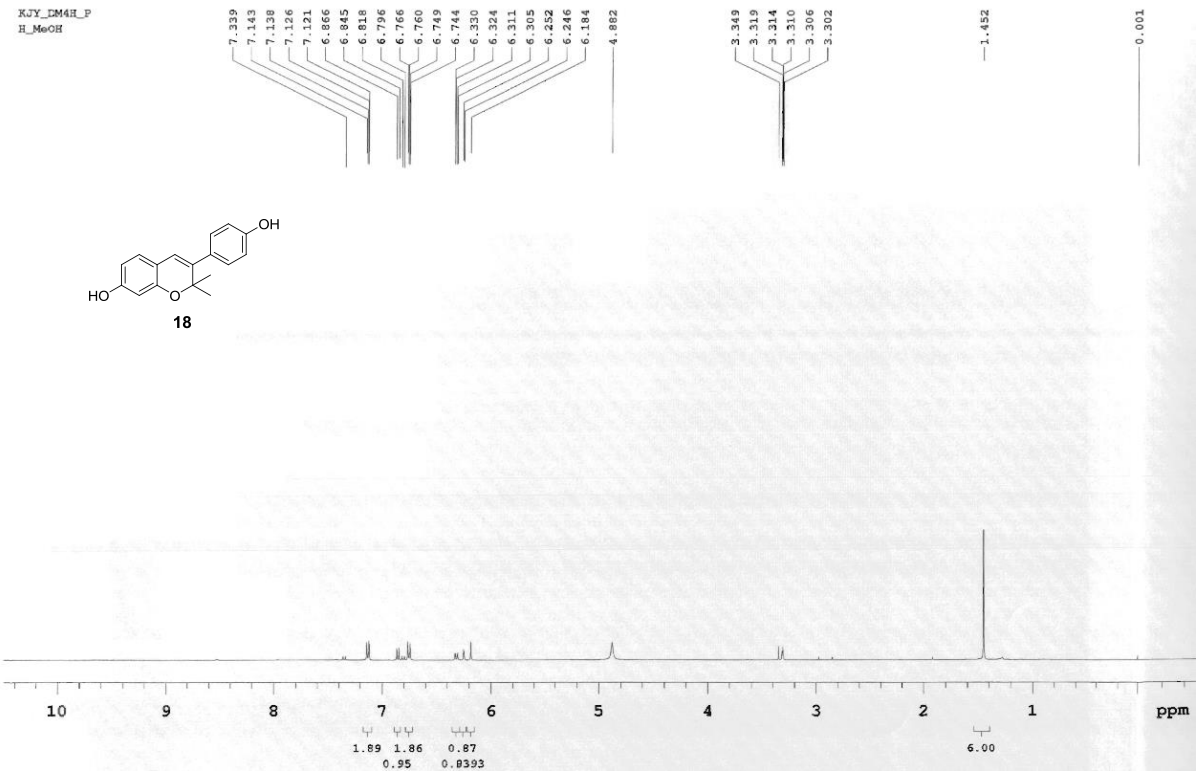
File: Proton

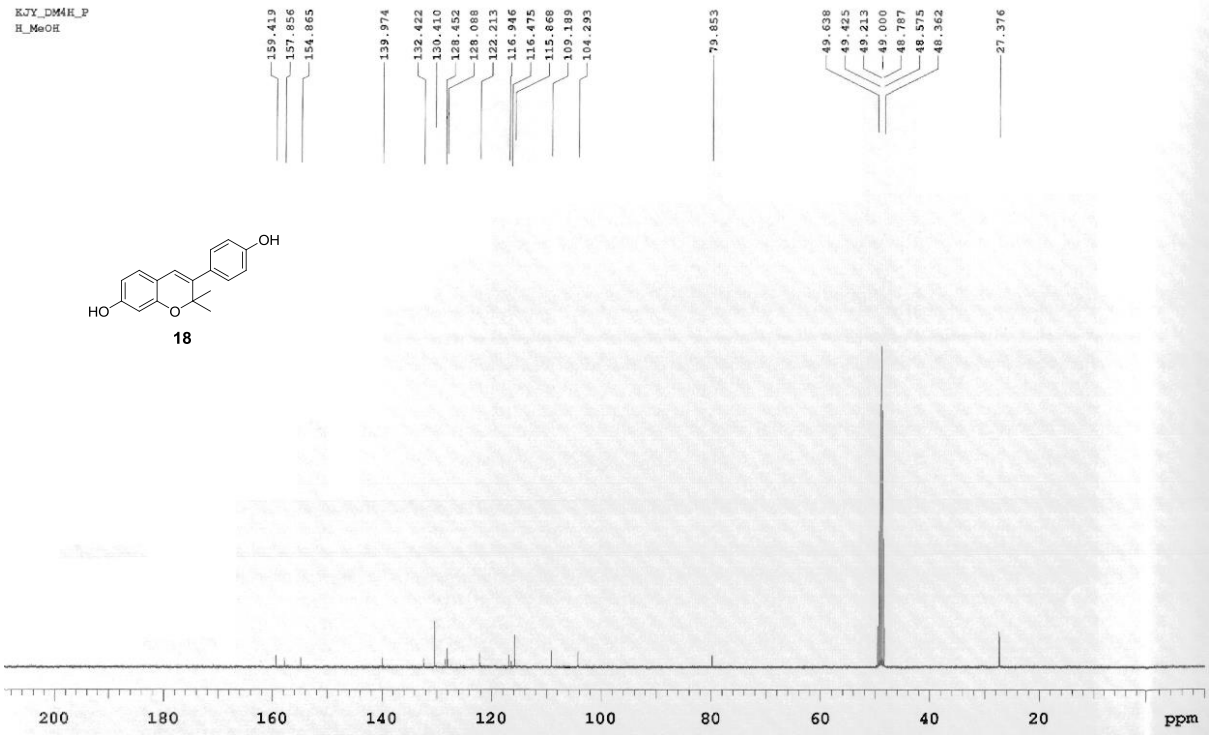
Pulse Sequence: s2pul

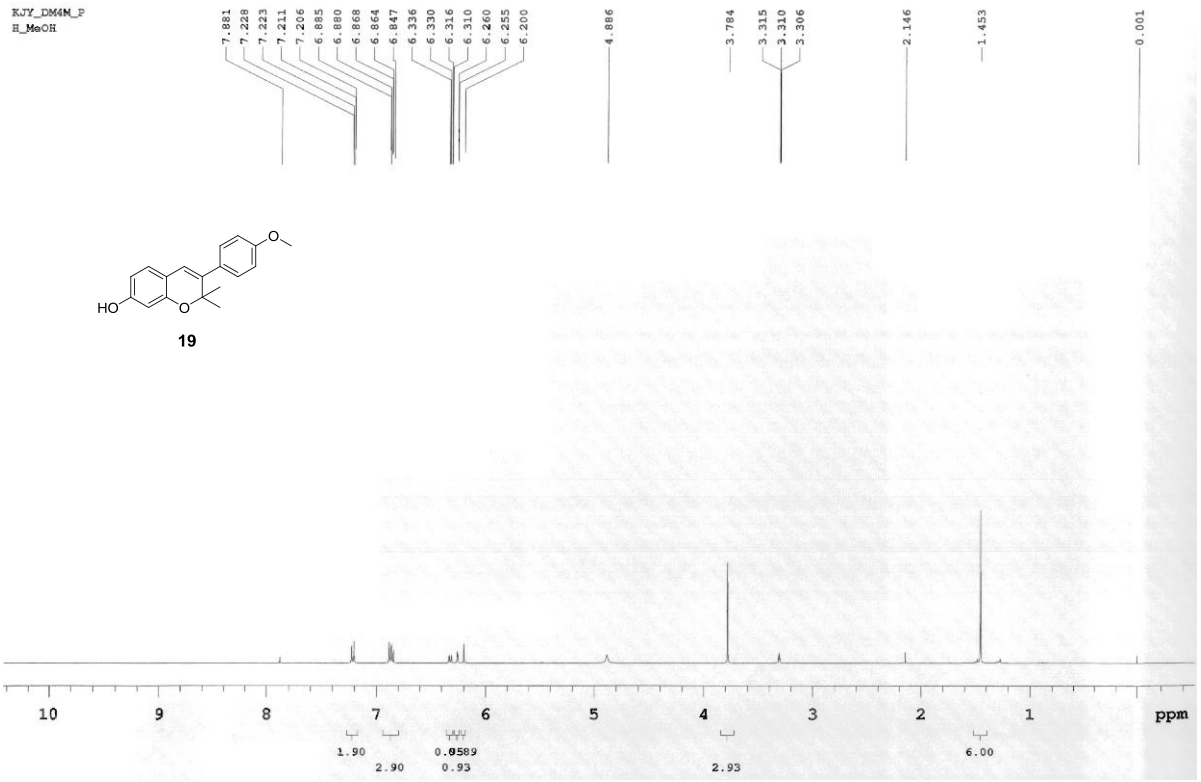


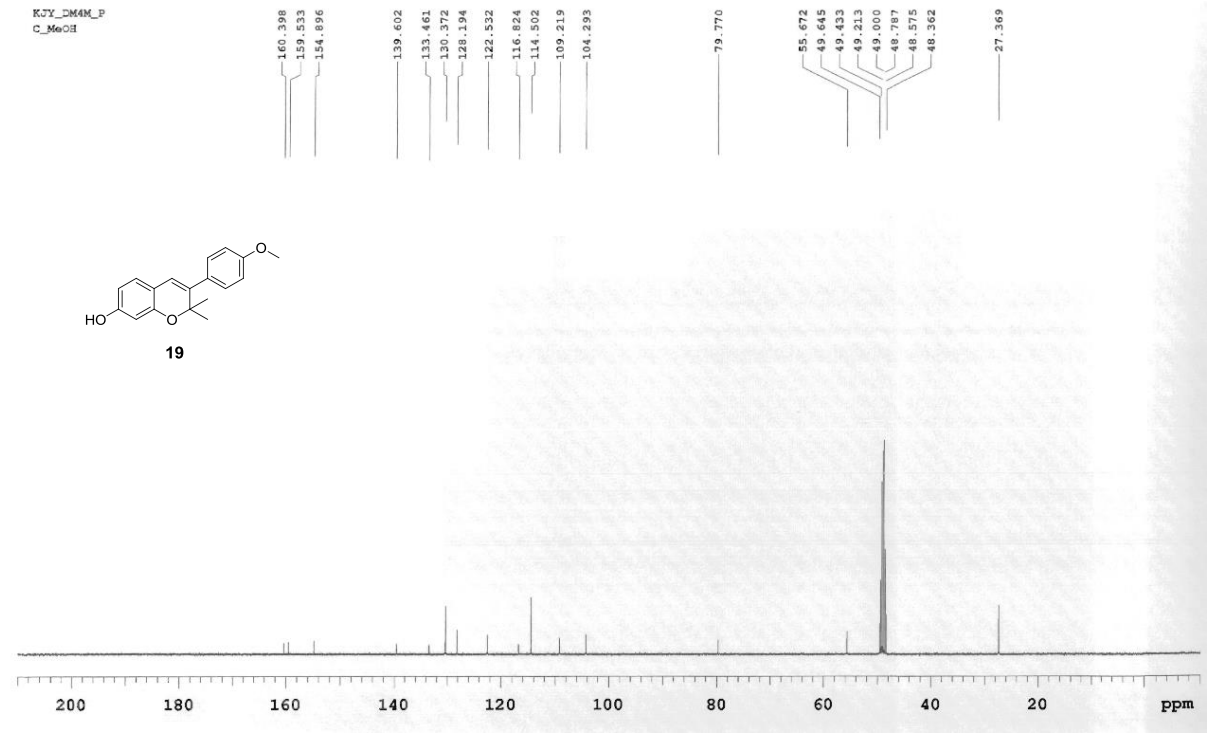
DM3M_C_CDCl3








KJY_DM4M_P
H_MeOH
7.881
7.228
7.223
7.211
7.206
6.885
6.880
6.868
6.864
6.847
6.336
6.330
6.316
6.310
6.260
6.255
6.200
4.886
3.784
3.315
3.310
3.306
2.146
1.453
0.001
HO
O
O
19
10
9
8
7
6
5
4
3
2
1
ppm
1.90
2.90
0.9589
0.93
2.93
6.00


KJY_DM4M_P
C_MeOH
160.398
159.533
154.896
139.602
133.461
130.372
128.194
122.532
116.824
114.502
109.219
104.293
79.770
55.672
49.645
49.433
49.213
49.000
48.787
48.575
48.362
27.369
HO
O
O
19
200
180
160
140
120
100
80
60
40
20
ppm