Supporting Information

Total Synthesis of (±)-Cephalosol

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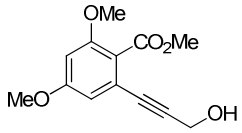
CONTENTS

Part 1. Experimental Procedures and Analytical Data……..…Page S2

Part 2. NMR Spectra of New and Selected Known Compounds……..Page S7

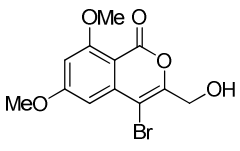
Part 1. Experimental Procedures and Analytical Data

General Methods. Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 (^{1}H at 400 MHz and ^{13}C at 100 MHz) using TMS as the internal standard. Column chromatography was performed on silica gel. Anhydrous dioxane was distilled over sodium benzophenone ketyl under Ar. Anhydrous CH_2Cl_2 was distilled over calcium hydride under Ar. Anhydrous DMF was distilled at reduced pressure over calcium hydride. All other solvents and reagents were used as obtained from commercial sources without further purification.

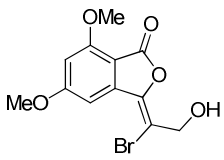


6

Compound 6. To a solution of **5** (5.66 g, 17.6 mmol) in Et_3N (85 mL) were successively added propargyl alcohol (1.95 g, 34.8 mmol), $Pd(PPh_3)_2Cl_2$ (341 mg, 0.486 mmol), and CuI (63 mg, 0.33 mmol). The mixture was exposed to ultrasonic irradiation at 40 ^{o}C for 90 min, cooled to room temperature, filtered, washed with EtOAc, and concentrated. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 2:1) to afford **6** (4.13 g, 94%) as a yellow solid: mp 68–69 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.22 (br s, 1H), 3.74 (s, 3H), 3.75 (s, 3H), 3.85 (s, 3H), 4.40 (d, J = 5.2 Hz, 2H), 6.40 (d, J = 2.4 Hz, 1H), 6.52 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 51.4, 52.5, 55.6, 56.1, 82.7, 91.2, 99.8, 108.4, 118.9, 123.0, 158.1, 161.5, 167.6. ESI-HRMS Calcd for $C_{13}H_{15}O_5$ (M + H) 251.0914, found 251.0907.

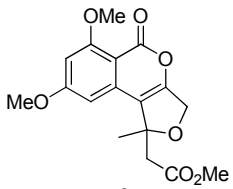


3a



3b

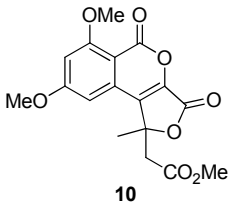
Compounds 3a and 3b. To a solution of **6** (250 mg, 1.00 mmol) in $ClCH_2CH_2Cl$ (10 mL) were added $CuBr_2$ (469 mg, 2.10 mmol) and pyridine (119 mg, 1.50 mmol). The mixture was heated at reflux for 2 h, filtered through a short column of silica gel, and concentrated. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to afford **3a** (224 mg, 71%) and **3b** (40 mg, 13%). Compound **3a**: a white amorphous solid; mp 182–183 ^oC; ^1H NMR (DMSO-d_6, 400 MHz) δ 3.92 (s, 3H), 3.95 (s, 3H), 4.47(d, J = 6.4 Hz, 2H), 5.67 (t, J = 6.4 Hz, 1H), 6.79 (s, 1H),6.81 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 55.9, 56.4, 60.3, 99.0, 99.8, 101.8, 101.9, 139.2, 154.4, 155.9, 163.4, 165.4. ESI-HRMS Calcd for $C_{12}H_{12}BrO_5$ (M + H) 314.9863, found 314.9872. Compound **3b**: a white amorphous solid; mp 159–160 ^oC; ^1H NMR (DMSO-d_6, 400 MHz) δ 3.92 (s, 3H), 3.93(s, 3H), 4.46 (s, 2H), 6.78 (s, 1H), 7.48 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 56.2, 56.2, 61.1, 100.5, 101.2, 104.9, 112.4, 140.4, 141.6, 159.6, 161.6, 166.7. ESI-HRMS Calcd for $C_{12}H_{12}BrO_5$ (M + H) 314.9863, found 314.9861.



2

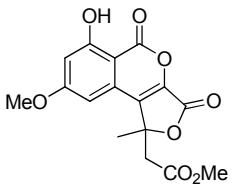
Compound 2. To a solution of triflate **9** (248 mg, 1.00 mmol) in dioxane (6 mL) were successively added bis(pinacolato)diboron (279 mg, 1.10 mmol), $Pd(PPh_3)_2Cl_2$ (35 mg, 50 μmol), PPh_3 (26 mg, 99 μmol), and K_2CO_3 (207 mg, 1.50 mmol). The mixture was heated at 90 ^oC under Ar until complete consumption of **9** as monitored by TLC analysis (in *ca.* 2 h) and cooled to 0 ^oC. Compound **3a** (157 mg, 0.498 mmol), $Pd(PPh_3)_4$ (57 mg, 49 μmol), and H_2O (0.85 mL) were then added. The mixture was heated at 90 ^oC until complete consumption of **3a** as monitored by TLC analysis (in *ca.* 2 h). After a solution of DBU (760 mg, 5.00 mmol) in dioxane (6 mL) was added, the mixture was stirred at rt for 8 h, neutralized with HCl (1 M), and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated

to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to afford **2** (130 mg, 78%) as a yellow thick liquid, which turned into a white solid upon storage at rt: mp 102–103 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.71 (s, 3H), 2.92 (s, 2H), 3.57 (s, 3H), 3.91 (s, 3H), 3.98 (s, 3H), 4.78 (s, 2H), 6.28 (d, J = 2.0 Hz, 1H), 6.47 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.0, 44.7, 51.8, 55.7, 56.4, 68.6, 86.7, 97.5, 97.8, 102.0, 113.7, 137.2, 153.4, 158.8, 165.0, 165.9, 170.2. ESI-HRMS Calcd for $C_{17}H_{19}O_7$ (M + H) 335.1125, found 335.1129.



10

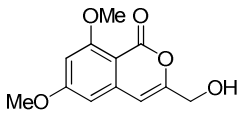
Compound 10. To a suspension of CrO_3 (350 mg, 3.50 mmol) in CH_2Cl_2 (10 mL) was added pyridine (553 mg, 7.00 mmol) at rt. After the mixture was stirred at the same temperature for 20 min and cooled to 0 °C, a solution of **2** (78 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) was added. The mixture was stirred at rt for 4 h, filtered through Celite, and concentrated. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to afford **10** (65 mg, 80%) as a white amorphous solid: mp 198–199 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.85 (s, 3H), 3.02 (d, J = 16.0 Hz, 1H), 3.18 (d, J = 16.0 Hz, 1H), 3.57 (s, 3H), 3.97 (s, 3H), 4.00 (s, 3H), 6.44 (d, J = 2.0 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.7, 42.3, 52.2, 56.1, 56.7, 82.0, 100.1, 100.7, 103.7, 132.9, 133.8, 140.8, 156.4, 162.0, 165.4, 166.1, 168.2. ESI-HRMS Calcd for $C_{17}H_{17}O_8$ (M + H) 349.0918, found 349.0917.



(±)-Cephalosol (**1**)

(±)-Cephalosol (1). To a solution of **10** (75 mg, 0.21 mmol) in CH_2Cl_2 (5 mL) was

added BCl_3 (1 M in CH_2Cl_2, 1.0 mL, 1.0 mmol) at 0 °C. The reaction was completed instantly as monitored by TLC analysis. The mixture was quenched with HCl (1 M, 1 mL) and H_2O (10 mL) followed by extraction with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to afford **1** (67 mg, 93%) as a white amorphous solid: mp 199–200 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.84 (s, 3 H), 3.02 (d, J = 16.0 Hz, 1 H), 3.20 (d, J = 16.0 Hz, 1 H), 3.59 (s, 3 H), 3.93 (s, 3 H), 6.44 (d, J = 2.0 Hz, 1 H), 6.69 (d, J = 2.4 Hz, 1 H), 11.29 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.7, 41.9, 52.2, 56.3, 81.9, 100.2, 102.6, 103.1, 131.1, 134.8, 139.6, 161.6, 164.7, 166.1, 167.2, 168.0 [Note that the ^{13}C NMR chemical shift data of **1** matched those reported in the literature[1] if the solvent peak settings for $CDCl_3$ were adjusted. The ^{13}C NMR chemical shift values for the solvent ($CDCl_3$) peak set by us, Tan,[1a] and Koert[1b] were 77.16, 77.8, and 77.8 ppm, respectively]. ESI-HRMS Calcd for $C_{16}H_{18}NO_8$ (M + NH_4) 352.1027, found 352.1033.

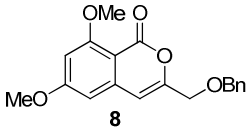


7

Compound 7. To a solution of **3a** (80 mg, 0.25 mmol) in DMF (5 mL) were successively added Et_3N (76 mg, 0.75 mmol), HCO_2H (23 mg, 0.50 mmol), $Pd(OAc)_2$ (2.0 mg, 8.9 μmol), and PPh_3 (4.6 mg, 17 μmol). The mixture was heated at 60 °C for 8 h, cooled to rt, quenched with saturated aqueous NH_4Cl solution, and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc, 2:3) to afford **7** (35 mg, 92% based recycled starting material) and as well as unreacted **3a** (29 mg, 36%). Compound **7**, a white solid: mp 177 – 179 °C; ^{1}H

(1) (a) Zhang, H. W.; Huang, W. Y.; Chen, J. R.; Yan, W. Z.; Xie, D. Q.; Tan, R. X. *Chem. Eur. J.* **2008**, *14*, 10670. (b) Arlt, A.; Koert, U. *Synthesis* **2010**, 917.

NMR ($CDCl_3$, 400 MHz) δ 2.22 (t, J = 6.4 Hz, 1H), 3.90 (s, 3H), 3.97 (s, 3H), 4.44 (d, J = 6.4 Hz, 2H), 6.37 (s, 1H), 6.38 (d, J = 2.0 Hz, 1H), 6.47 (d, J = 2.0 Hz, 1H); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.86 (s, 3H), 3.87 (s, 3H), 4.21 (d, J = 6.0 Hz, 2H), 5.56 (t, J = 6.0 Hz, 1H), 6.50 (s, 1H), 6.58 (d, J = 2.0 Hz, 1H), 6.67 (d, J = 2.4 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 55.8, 56.0, 59.5, 98.5, 100.9, 101.7, 101.9, 141.5, 157.4, 158.1, 162.8, 165.2.



8

Compound 8. To a solution of **7** (8.0 mg, 34 μmol) and benzyl 2,2,2-trichloroacetimidate (10 mg, 40 μmol) in CH_2Cl_2 (1 mL) and cyclohexane (1.5 mL) was added trifluoromethanesulfonic acid (0.76 mg, 5.1 μmol) at rt. The mixture was stirred at rt overnight. After the white precipitate was filtered off, the filtrate was washed successively with saturated aqueous $NaHCO_3$ solution and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 2:1) to afford **8** (7.4 mg, 67%) as a white solid: mp 111–112 ^{o}C; 1H NMR ($CDCl_3$, 400 MHz) δ 3.89 (s, 3H), 3.96 (s, 3H), 4.32 (s, 2H), 4.66 (s, 2H), 6.38 (d, J = 2.4 Hz, 1H), 6.42 (s, 1H), 6.46 (d, J = 2.0 Hz, 1H), 7.26-7.38 (m, 5H).

Part 2. NMR Spectra of New and Selected Known Compounds

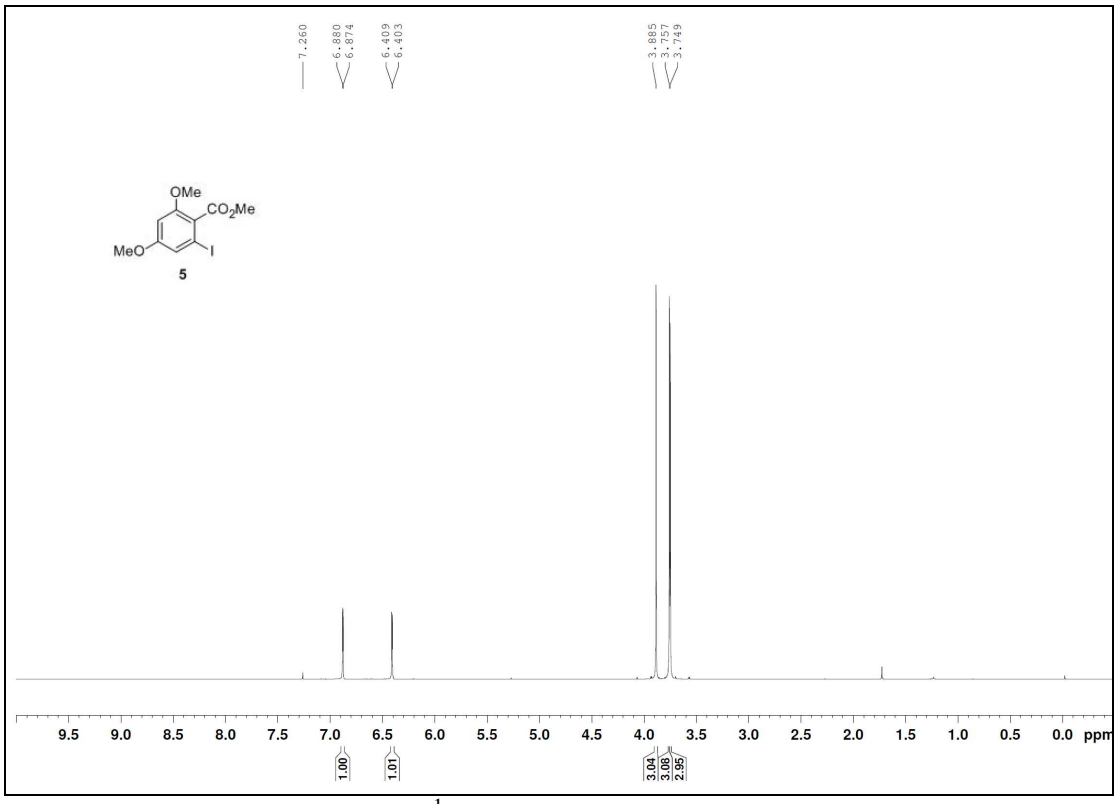


Figure S1. ^{1}H NMR of **5** ($CDCl_3$, 400 Hz)

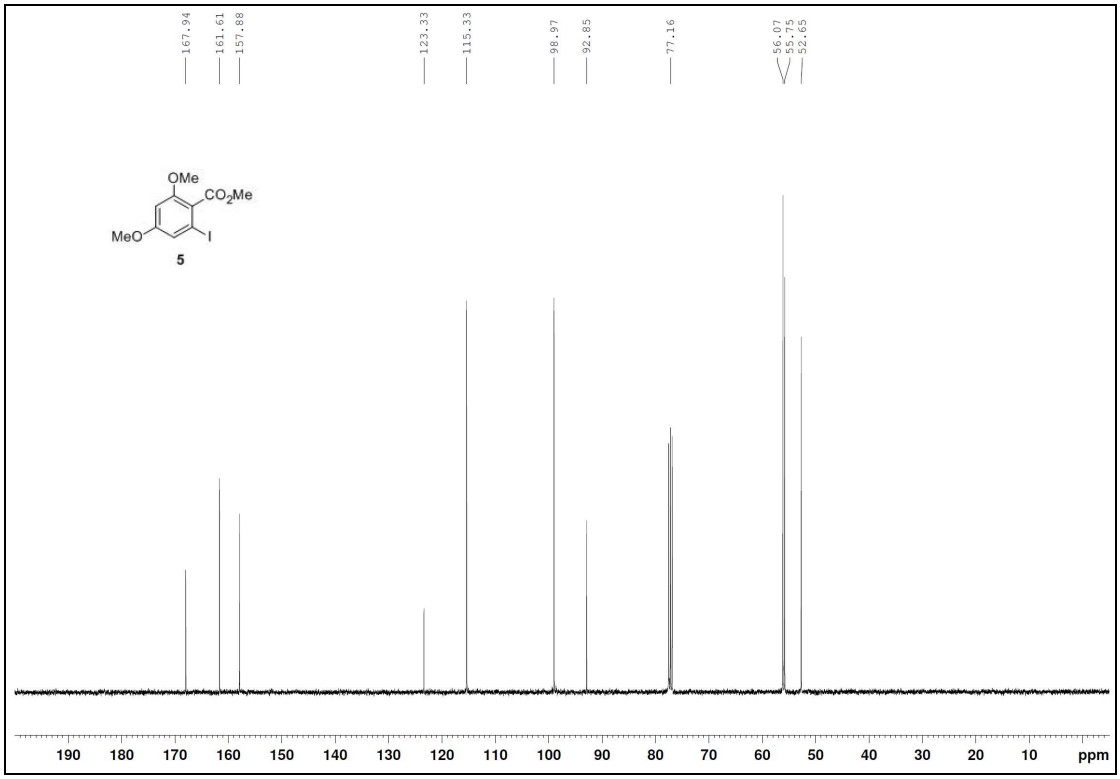


Figure S2. ^{1}H NMR of **5** ($CDCl_3$, 100 Hz)

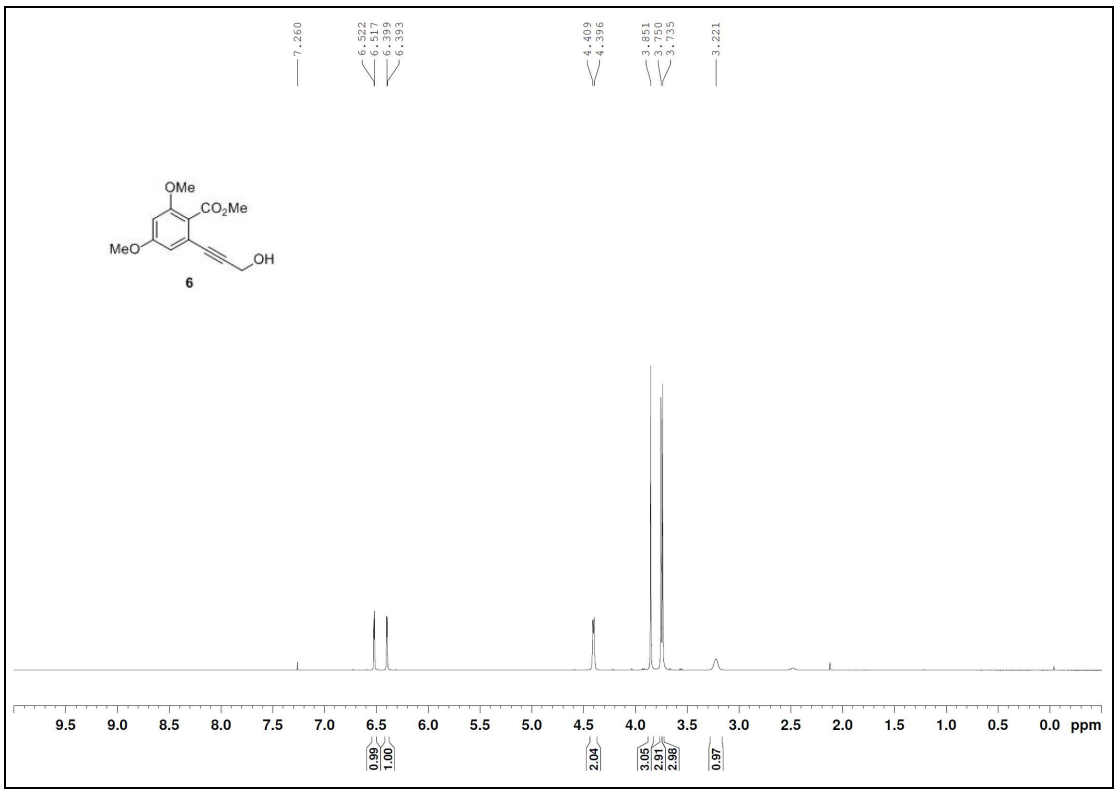


Figure S3. ^{1}H NMR of **6** ($CDCl_3$, 400 Hz)

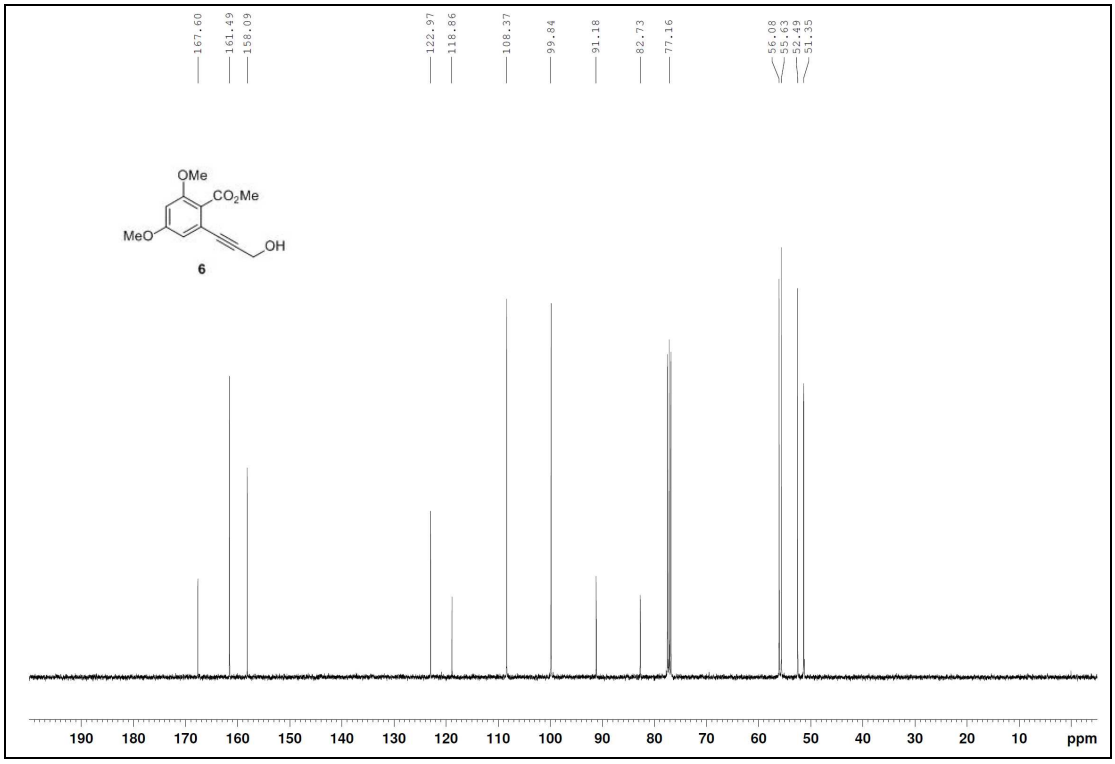


Figure S4. ^{13}C NMR of **6** ($CDCl_3$, 100 Hz)

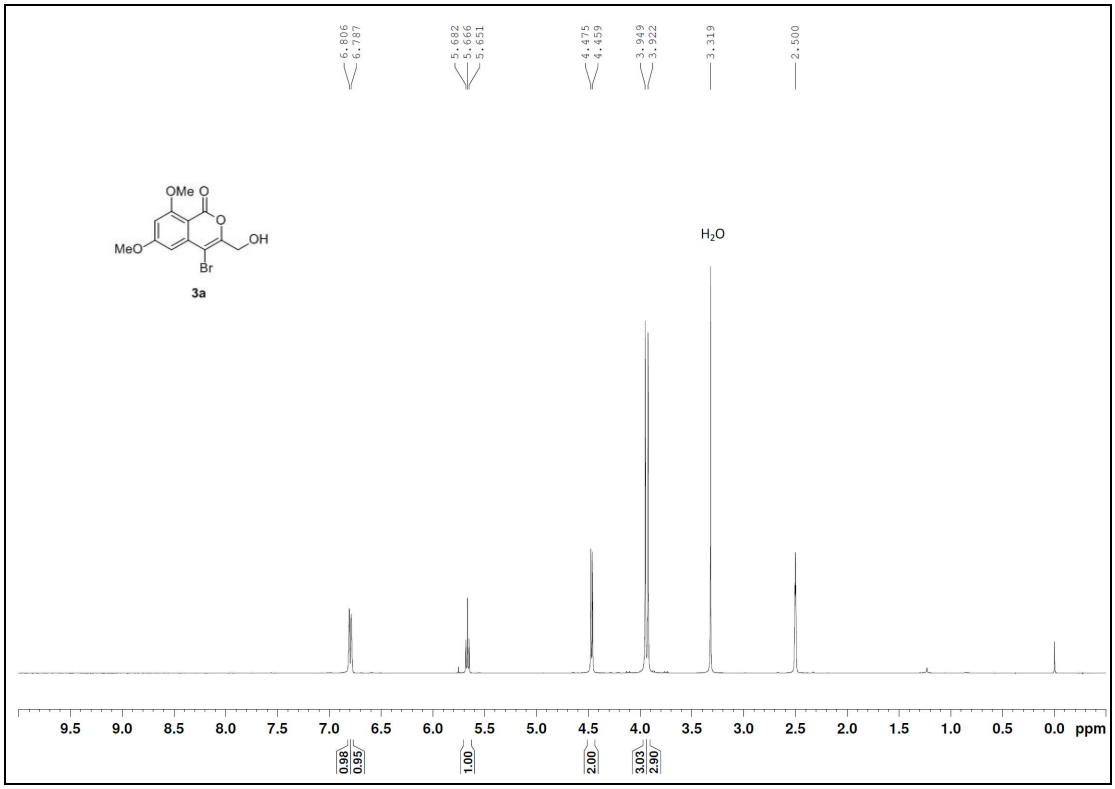


Figure S5. ^{1}H NMR of **3a** (DMSO-d_6, 400 Hz)

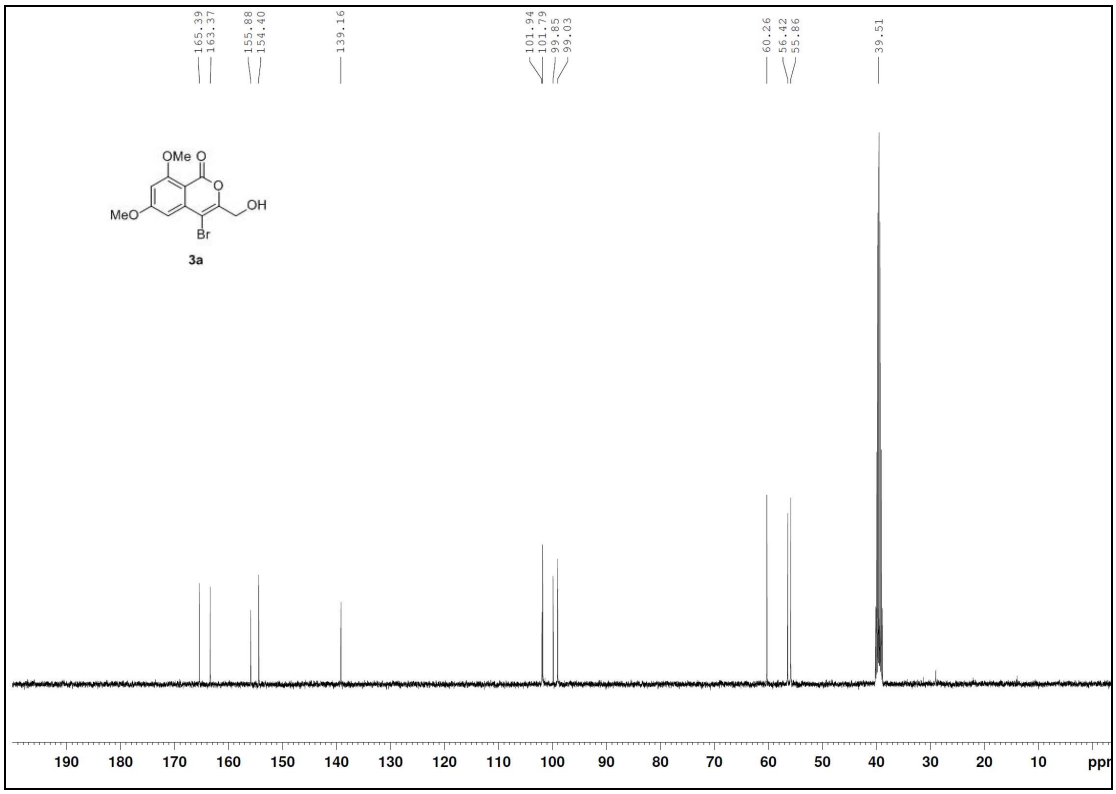


Figure S6. ^{13}C NMR of **3a** (DMSO-d_6, 100 Hz)

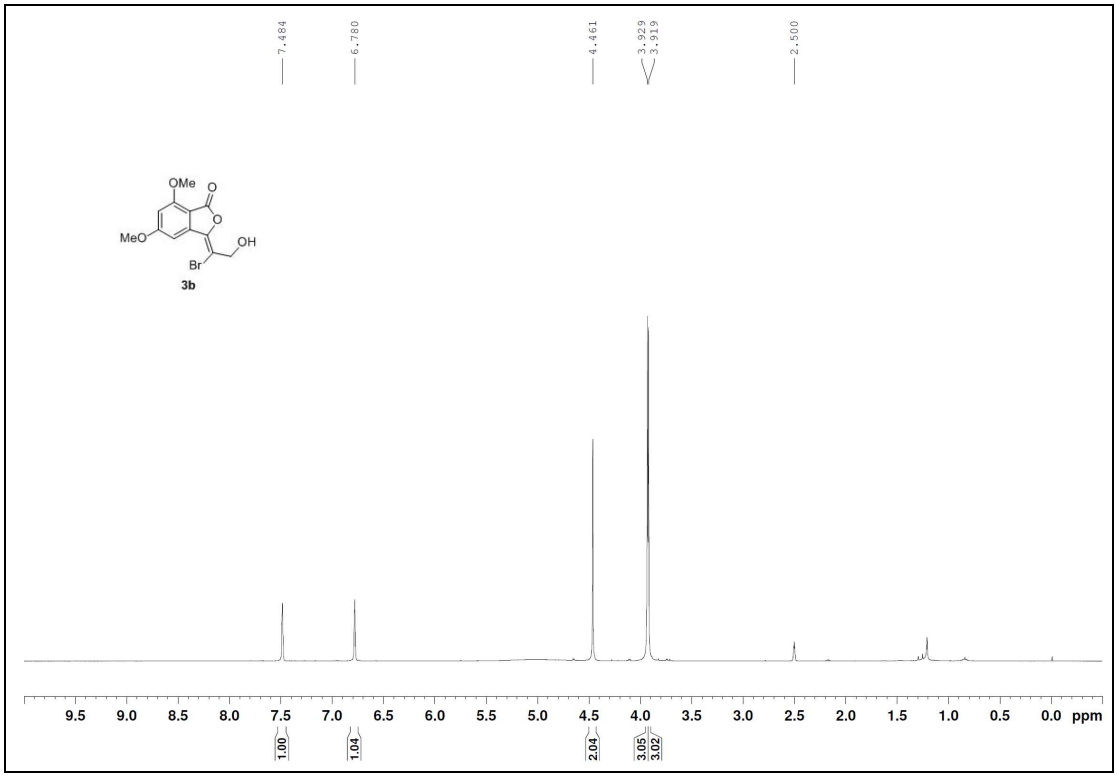


Figure S7. ^{1}H NMR of **3b** (DMSO-d_6, 400 Hz)

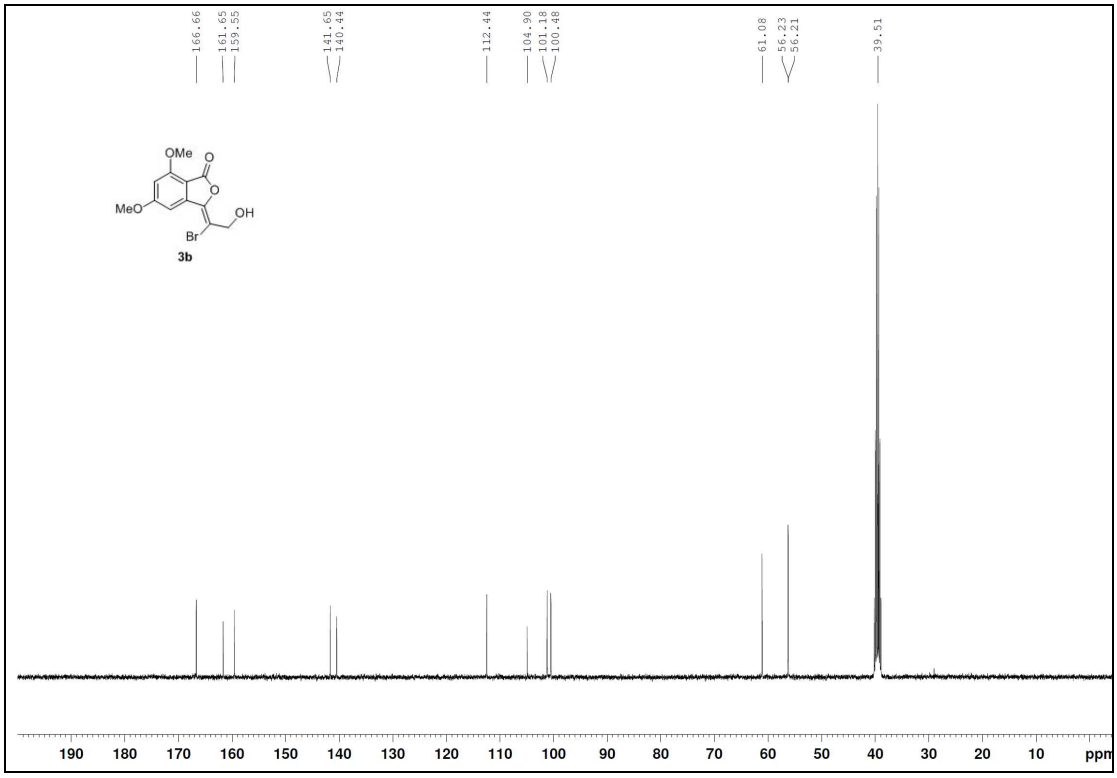


Figure S8. ^{13}C NMR of **3b** (DMSO-d_6, 100 Hz)

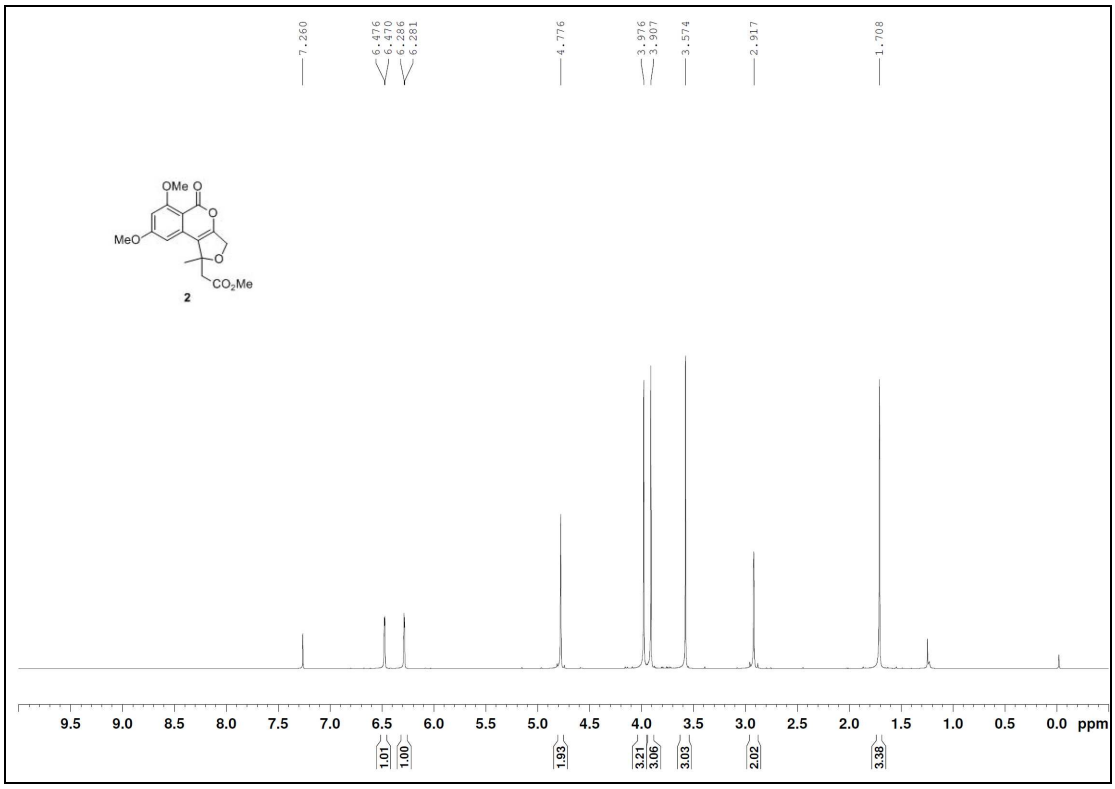


Figure S9. ^{1}H NMR of **2** ($CDCl_3$, 400 Hz)

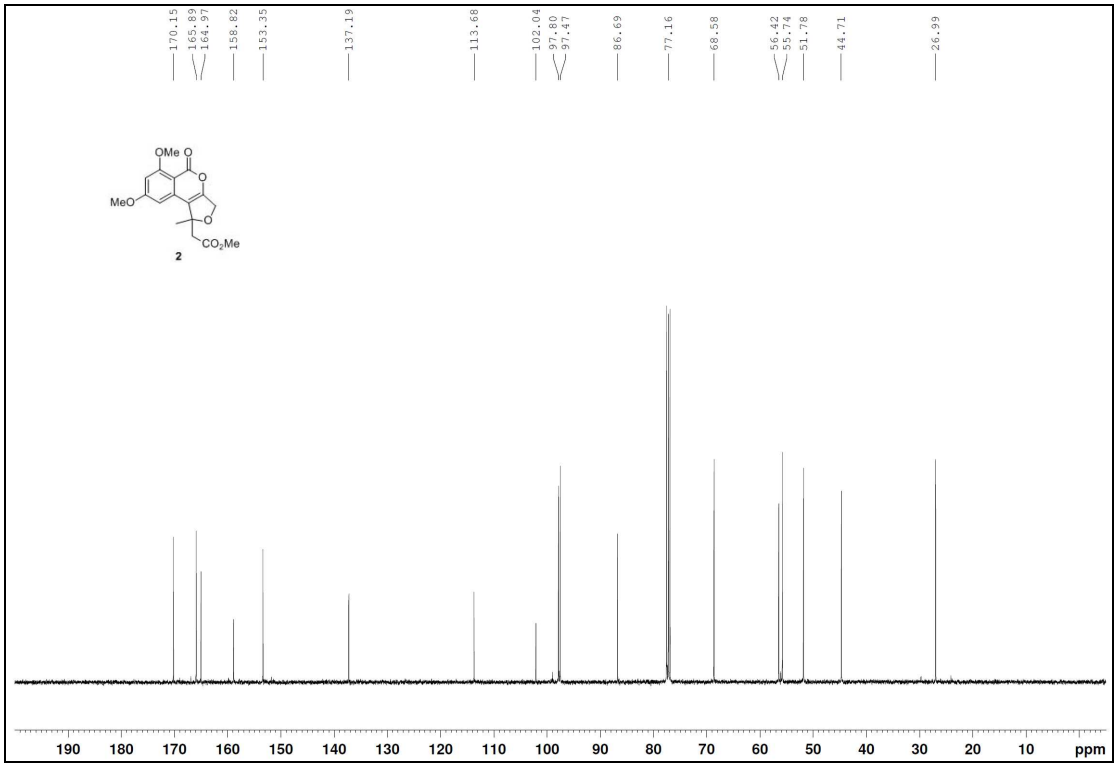


Figure S10. ^{13}C NMR of **2** ($CDCl_3$, 100 Hz)

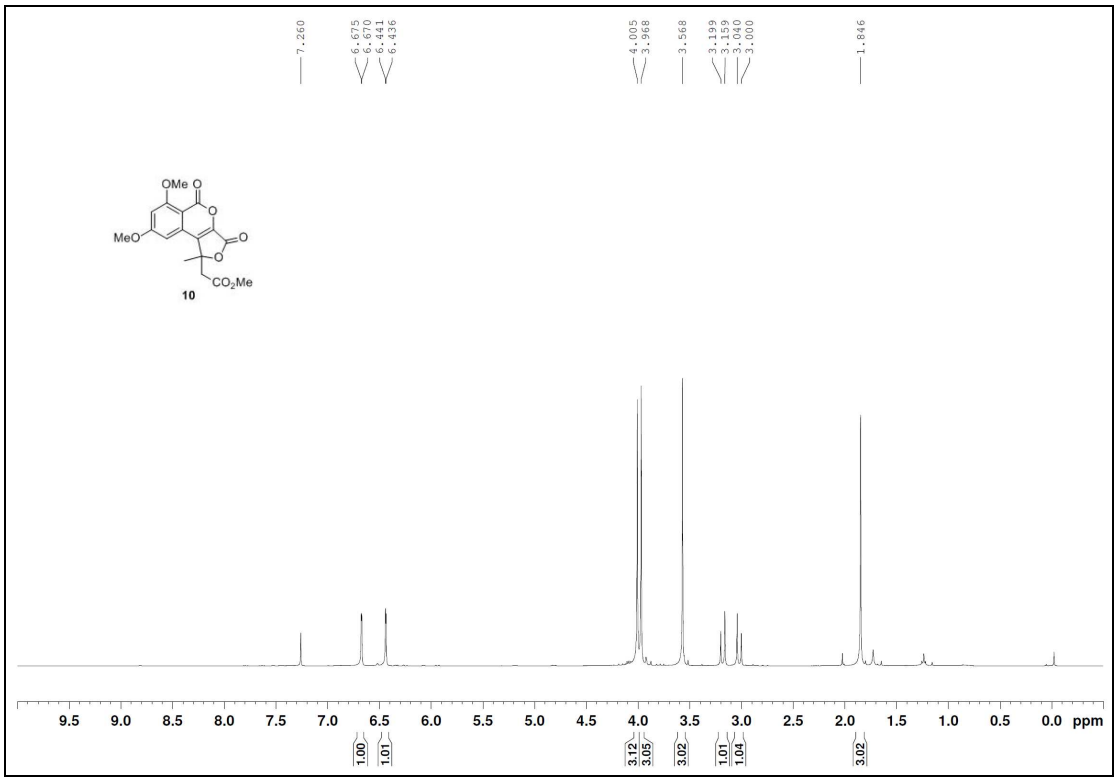


Figure S11. ^{1}H NMR of **10** ($CDCl_3$, 400 Hz)

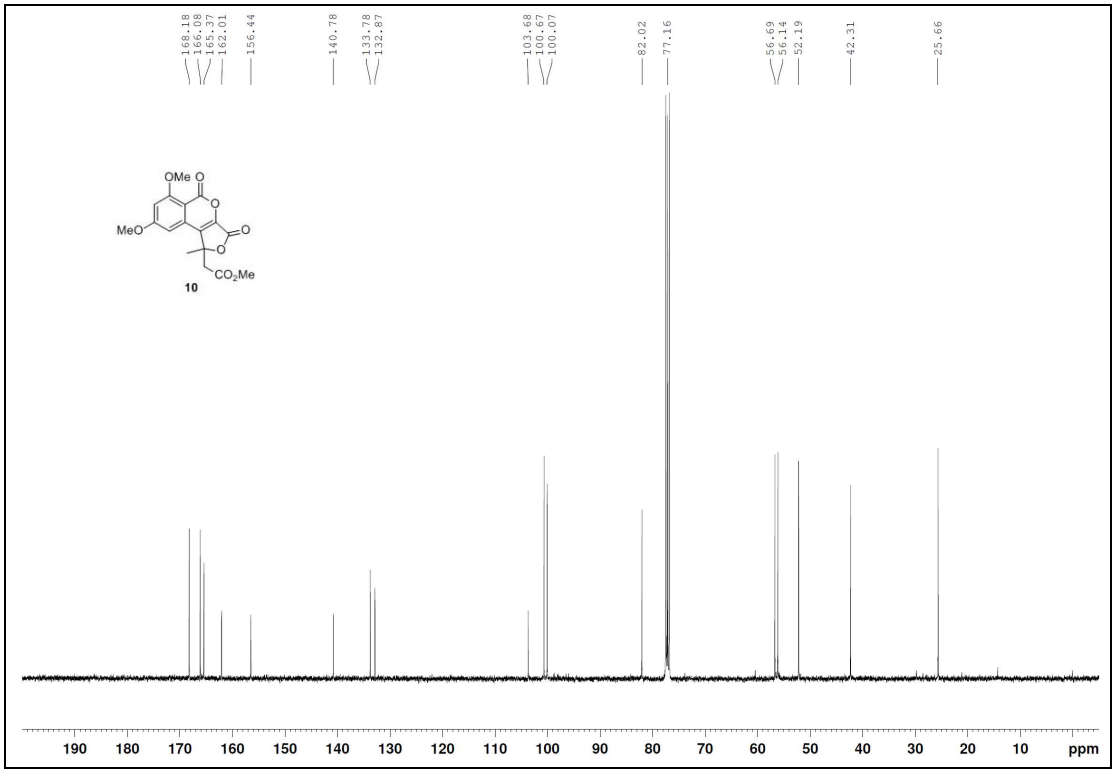


Figure S12. ^{13}C NMR of **10** ($CDCl_3$, 100 Hz)

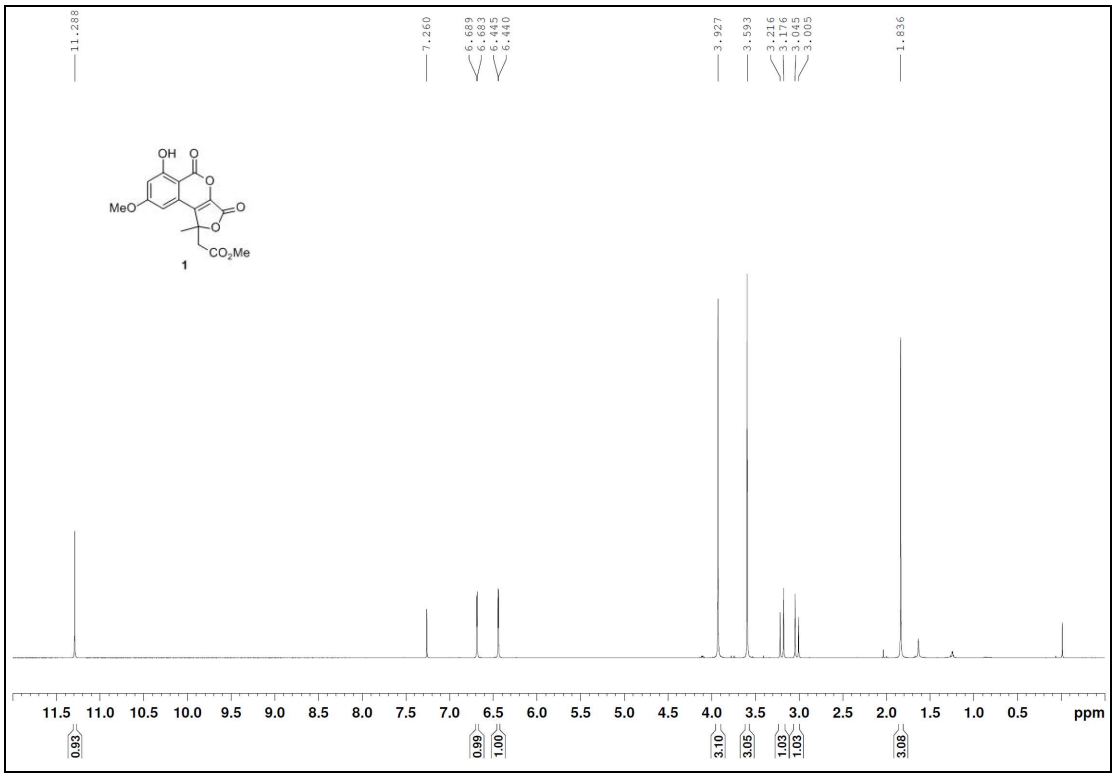


Figure S13. ^{1}H NMR of **1** ($CDCl_3$, 400 Hz)

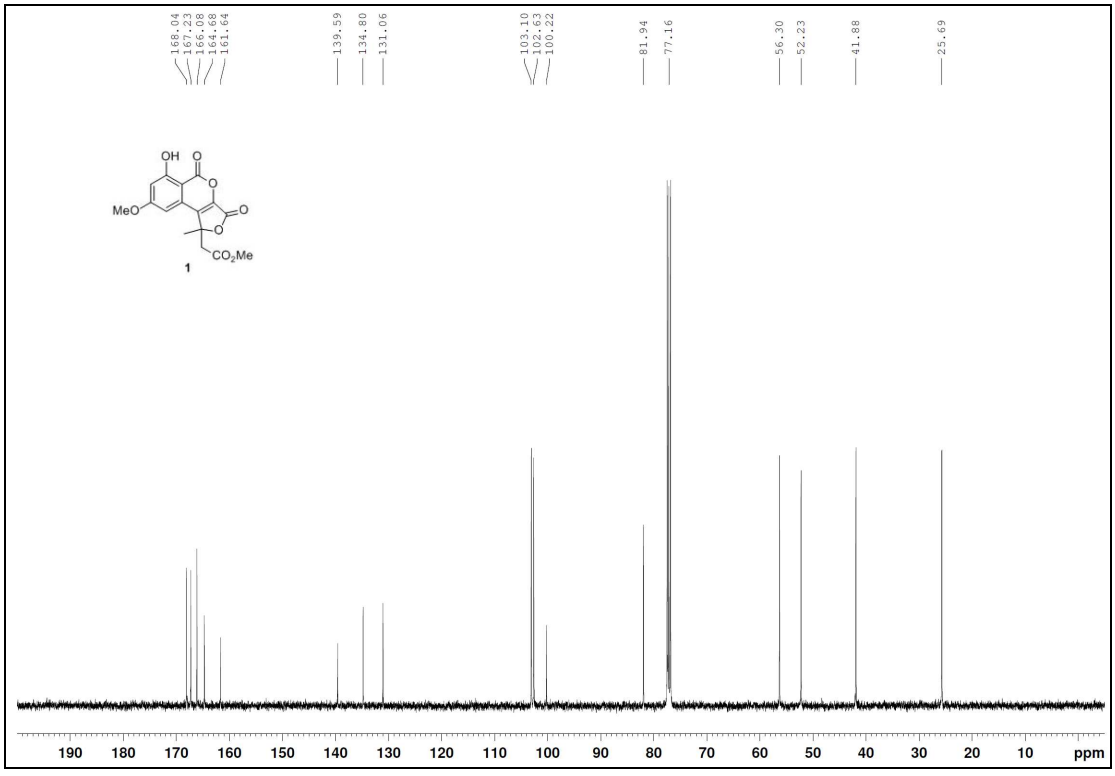


Figure S14. ^{13}C NMR of **1** ($CDCl_3$, 100 Hz)

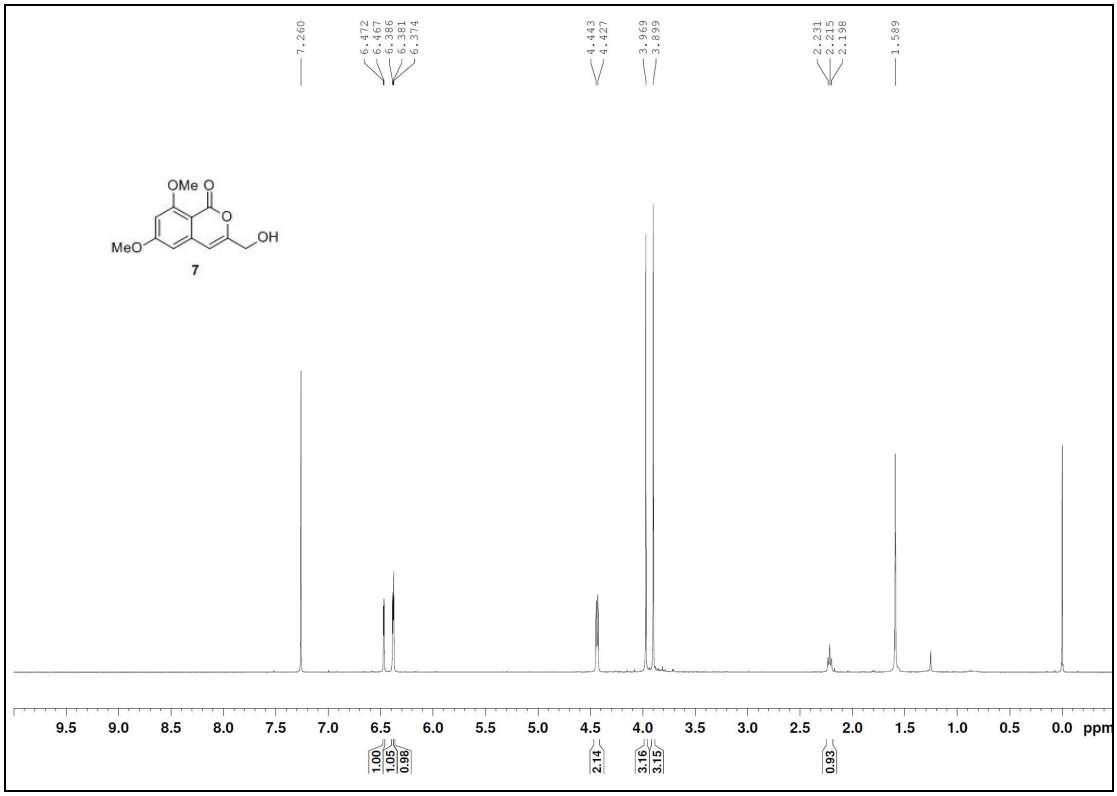


Figure S15. ^{1}H NMR of **7** ($CDCl_3$, 400 Hz)

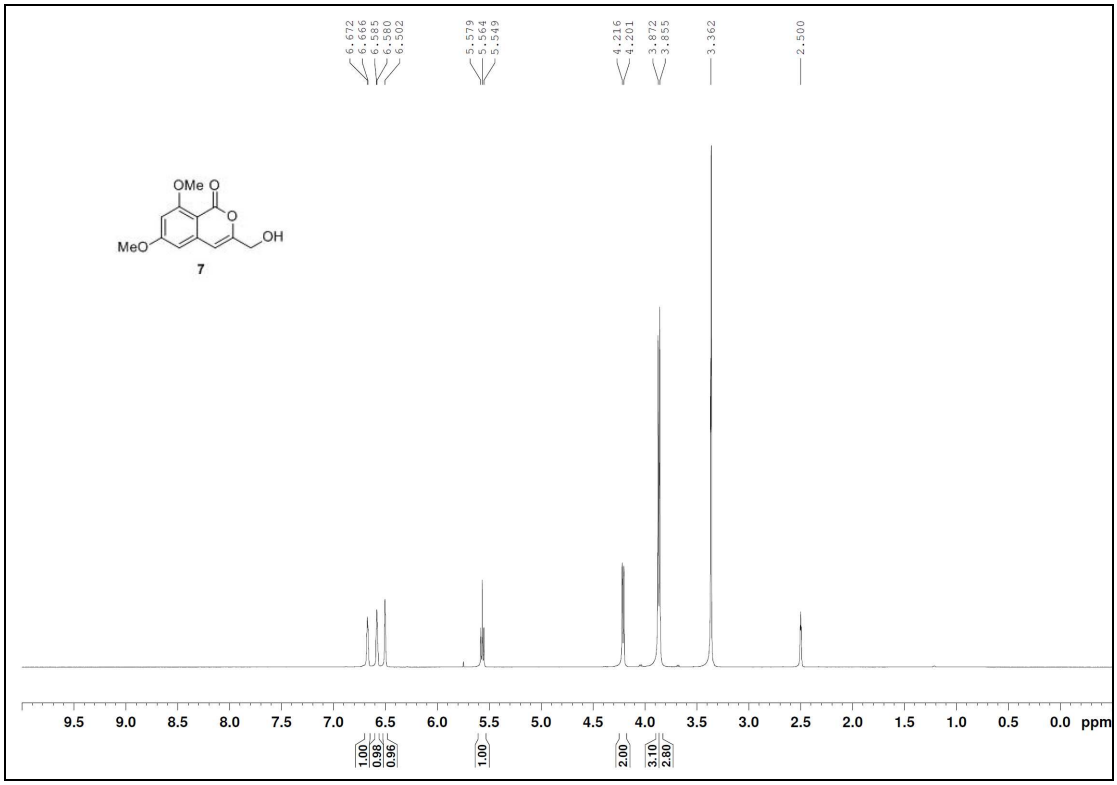


Figure S16. ^{1}H NMR of **7** (DMSO-d_6, 400 Hz)

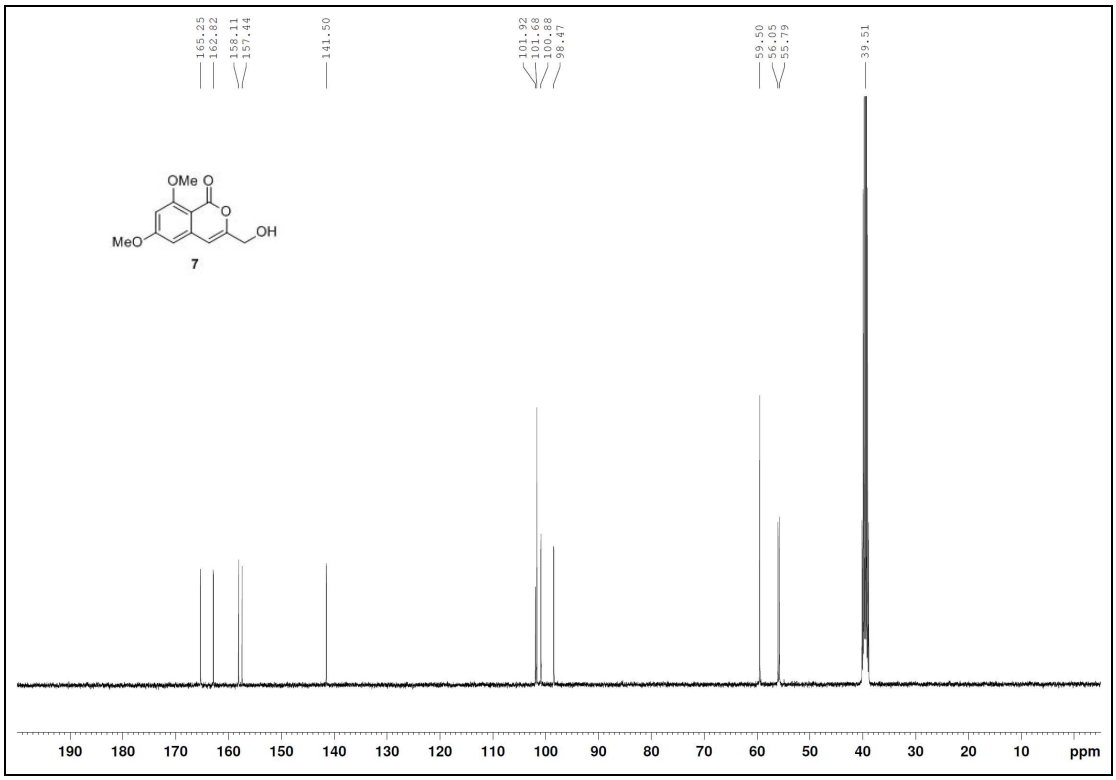


Figure S17. ^{1}H NMR of **7** (DMSO-d_6, 100 Hz)

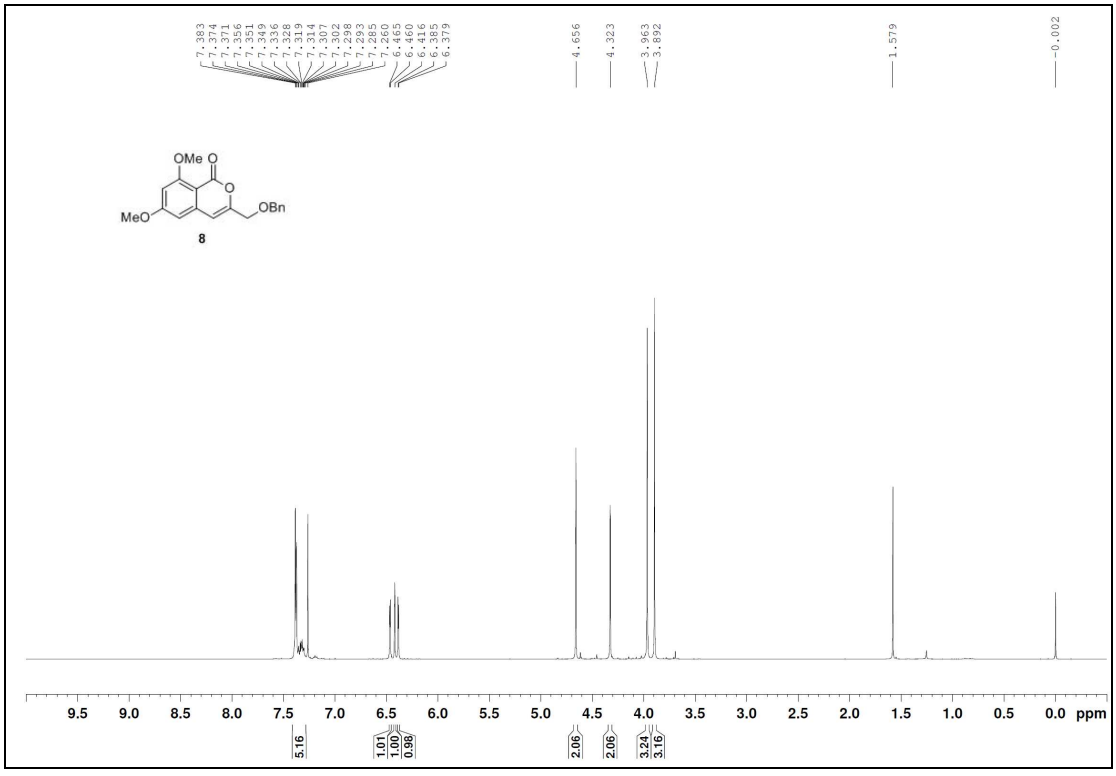


Figure S18. ^{1}H NMR of **8** ($CDCl_3$, 400 Hz)