Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Total Synthesis of Bi-magnolignan

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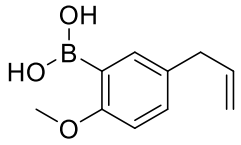
Experimental Procedures

Unless otherwise stated, all reactions were conducted in glassware that had been flame-dried and all reactions were carried out under N_2 atmosphere, all reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200–300 meshes) using petrol etherand ethyl acetate as eluent. ^{1}H and ^{13}C NMR spectra were recorded on 500 MHz Brucker spectrometer. High resolution mass spectra were taken on Waters mass spectrometer.

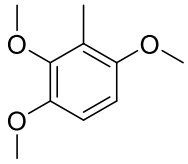
(5-allyl-2-methoxyphenyl)boronic acid (13)



13

To a solution of 4-allylanisole **15** (5.00 g, 33.74 mmol) in THF (120 mL) at -78 °C was added TMEDA (5.06 mL, 33.74 mmol) and *s*-BuLi (39.00 mL, 50.61 mmol of a 1.3 M solution in hexanes) dropwise over 15 min and the solution was stirred for 1 h. The reaction mixture was then warmed to room temperature and stirred for 1 h before $B(OMe)_3$ (3.77 mL, 33.74 mmol) was added and the reaction was stirred for a further 24 h. The reaction was acidified (1 M HCl to pH 3) and stirred for an additional 1 h. The reaction was diluted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography gave **13** (4.08 g, 63%) as a colorless solid. ^{1}H NMR (500 MHz, Chloroform-d) δ: 7.67 (d, J = 2.5 Hz, 1H), 7.27 (dd, J = 2.5 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.28 (d, J = 20.5 Hz, 2H), 5.96 (m, 1H), 5.09 – 5.03 (m, 2H), 3.9 (s, 3H), 3.36 (d, J = 6.7 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ: 163.0, 137.7, 136.9, 132.8, 132.6, 115.6, 110.0, 55.6, 39.3.

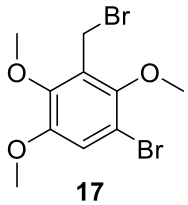
1,2,4-trimethoxy-3-methylbenzene (16)



16

n-BuLi (36.00 mL of 2.5 M solution in hexane, 89.18 mmol) was added dropwise to a solution of 1,2,4-trimethoxybenzene (10 g, 59.45 mmol) in THF (150 mL) over 5 min at -78 °C. After stirring for 15 min at this temperature, the reaction was allowed to warm to room temperature and keep stirring for 1 h. Then the reaction was cooled to -78 °C again and MeI (5.60 mL, 59.45 mmol) was added. The mixture was allowed to warm to room temperature and keep stirring for 1 h. The reaction was quenched with a saturated aqueous NH_4Cl solution and extracted with EtOAc. The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography gave **16** (10.72 g, 99%) as a colorless solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 6.70 (d, J = 8.9 Hz, 1H), 6.54 (d, J = 8.8 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 152.2, 147.9, 146.9, 120.8, 109.0, 104.9, 60.0, 55.9, 55.5, 8.7.

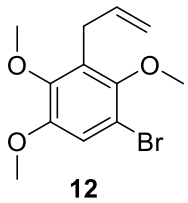
1-bromo-3-(bromomethyl)-2,4,5-trimethoxybenzene (17)



17

A solution of **16** (0.95 g, 5.22 mmol) in carbon tetrachloride (20 mL) was mixed with NBS (2.14 g, 11.48 mmol) and AIBN (0.09 g, 0.52 mmol) and the mixture was refluxed at 80 °C for 8 h. The reaction was quenched by adding water and extracted with DCM, the combined organic phase was dried over Na_2SO_4 and concentrated to afford **17** (1.62 g, 91%) as a white solid without further purification. m.p. 106～110 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.05 (s, 1H), 4.63 (s, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 149.8, 149.3, 147.5, 127.5, 116.9, 110.6, 61.5, 61.0, 56.2, 22.6. HRMS calcd for $C_{10}H_{12}O_3NaBr_2$ $[M+Na]^+$: 360.9047, found 360.9051.

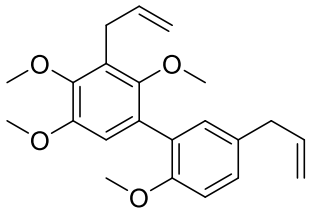
3-allyl-1-bromo-2,4,5-trimethoxybenzene (12)



12

To a solution of CuI (0.26 mg, 1.67 mmol), Bipy (0.32 mg, 1.67 mmol) and **17** (5.67 g, 16.66 mmol) in dry THF (40 mL) the solution of vinylmagnesium bromide (7.5 mL of a 1.0 M solution in THF) was slowly added at -20 °C. The mixture was stirred at the room temperature for 8 h. Then the reaction was quenched with saturated aqueous NH_4Cl solution, and extracted with MTBE. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After removing solvent, the residue was purified by column chromatography to give **12** (3.95 g, 83%) as a colorless oil; ^{1}H NMR (500 MHz, Chloroform-d) δ: 6.97 (s, 1H), 5.98 (m, 1H), 5.07 – 4.95 (m, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.45 (dt, J = 6.1, 1.7 Hz, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ: 149.8, 149.3, 147.2, 136.8, 129.1, 115.3, 114.4, 110.8, 61.3, 60.8, 56.1, 29.4. HRMS calcd for $C_{12}H_{15}O_3NaBr$ $[M + Na]^+$: 309.0102, found 309.0099.

3,5'-diallyl-2,2',4,5-tetramethoxy-1,1'-biphenyl(11)

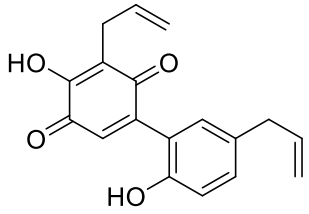


11

A mixture of **13** (3.00 g, 15.60 mmol), **12** (4.07 g, 14.18 mmol) in dioxane (47 mL) and H_2O (16 mL) was mixed with $Pd(PPh_3)_4$ (0.82 g, 0.71 mmol) and K_2CO_3 (42.54 mmol, 5.88 g), and the mixture was refluxed at 100 °C for 10 h. Then the reaction was cooled to room temperature, diluted with water and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After removing

solvent, the residue was purified by column chromatography to give **11** (4.24 g, 84%) as a colorless oil; ^{1}H NMR (500 MHz, Chloroform-*d*) δ: 7.16 (dq, J = 5.1, 2.4 Hz, 2H), 6.95 – 6.92 (m, 1H), 6.74 (s, 1H), 6.11 – 5.93 (m, 2H), 5.11 – 5.01 (m, 4H), 3.87 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 3.50 (dt, J = 6.2, 1.7 Hz, 2H), 3.39 – 3.36 (m, 2H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.1, 150.2, 148.5, 146.8, 137.8, 137.7, 131.8, 131.7, 128.5, 127.6, 127.2, 126.7, 115.4, 114.7, 113.2, 111.1, 61.0, 60.7, 55.9, 55.8, 39.2, 29.0. HRMS calcd for $C_{22}H_{26}O_4Na$ $[M + Na]^+$: 377.1729, found 377.1727.

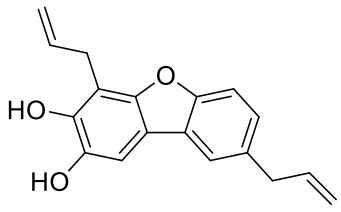
3,5'-diallyl-2',4-dihydroxy-[1,1'-biphenyl]-2,5-dione (18)



18

To a solution of **11** (117 mg, 0.33 mmol) in DCM (3 mL) was added a solution of BBr_3 (1 M in DCM, 1.32 mL, 1.32 mmol) at -78 °C. The solution was warmed to rt slowly and stirred for 3 hours, then poured into ice water. The two layers were separated and the aqueous fraction was extracted with DCM and EtOAc. The organic layer was dried over anhydrous Na_2SO_4 and filtered. After removing solvent, the residue was purified by column chromatography to give **18** (87.00 mg, 89%) as a brown oil; ^{1}H NMR (500 MHz, Chloroform-d) δ: 7.22 (s, 1H), 7.18 (dd, J = 8.3, 2.2 Hz, 1H), 7.11 (s, 1H), 6.97 (d, J = 2.2 Hz, 1H), 6.92 (d, J = 8.2 Hz, 1H), 6.79 (s, 1H), 5.99 – 5.80 (m, 2H), 5.15 (dq, J = 17.1, 1.6 Hz, 1H), 5.11 – 5.02 (m, 3H), 3.33 (dd, J = 6.7, 1.6 Hz, 2H), 3.28 (dq, J = 6.5, 1.5 Hz, 2H). ^{13}C NMR (126 MHz, CH2Cl2) δ: 189.2, 182.7, 152.3, 151.5, 149.5, 137.1, 133.4, 132.9, 132.9, 131.0, 130.5, 122.2, 119.5, 118.9, 116.7, 116.1, 39.1, 27.3. HRMS calcd for $C_{18}H_{16}O_4Na$ $[M + Na]^+$: 319.0946, found 319.0943.

4,8-diallyldibenzo[b,d]furan-2,3-diol l (9)

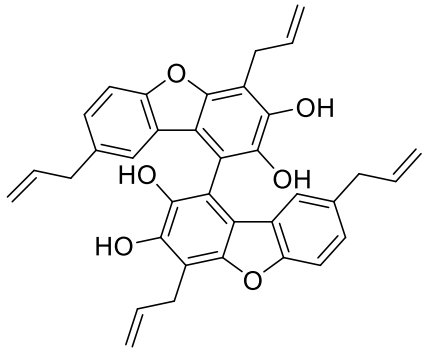


9

18 (1.17 g, 3.93 mmol) was added in small portions to a refluxing solution of Hydroquinone (4.33 g, 39.32 mmol) and sulphuric acid (2 M, 31.5 mL) in acetic acid (15 mL) under air. After refluxing for an additional 20 min the mixture was cooled. The mixture was quenched with saturated aqueous $NaHCO_3$ solution carefully and extracted with DCM. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography gave **9** (605 mg, 55%) as a white solid; ^{1}H NMR (500 MHz, Chloroform-d) δ: 7.59 (s, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.29 (s, 1H), 7.20 – 7.15 (m, 1H), 6.09 (m, 2H), 5.64 (s, 1H), 5.39 (s, 1H), 5.24 (dq, J = 17.2, 1.8 Hz, 1H), 5.19 (dq, J = 10.0, 1.6 Hz, 1H), 5.15 – 5.08 (m, 2H), 3.78 (d, J = 6.1 Hz, 2H), 3.52 (d, J = 6.6 Hz, 2H). ^{13}C NMR (126 MHz,) δ: 154.9, 149.9, 142.4, 140.5, 138.0, 135.3, 134.2, 126.3, 125.0, 119.6, 116.5, 115.94, 115.7,

111.1, 109.7, 103.7, 40.1, 28.6. HRMS calcd for $C_{18}H_{17}O_3$ $[M + H]^+$: 281.1178, found 281.1178.

Bi-magnolignan (1)

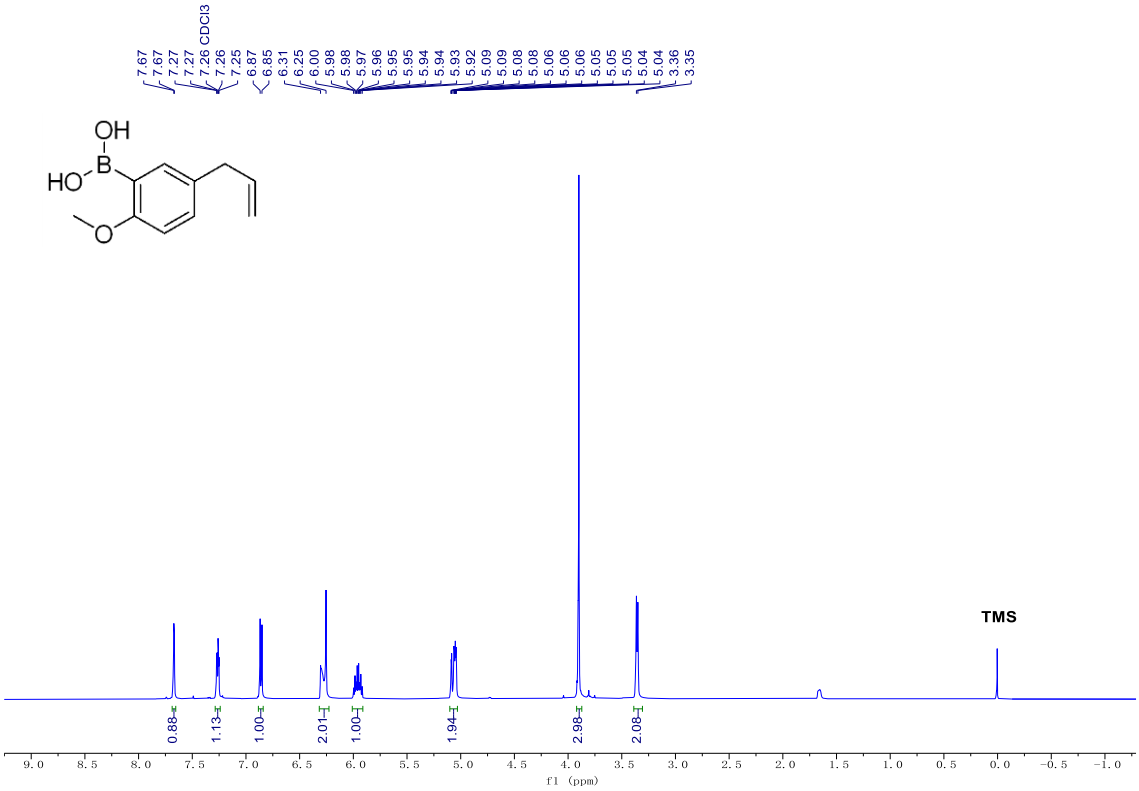


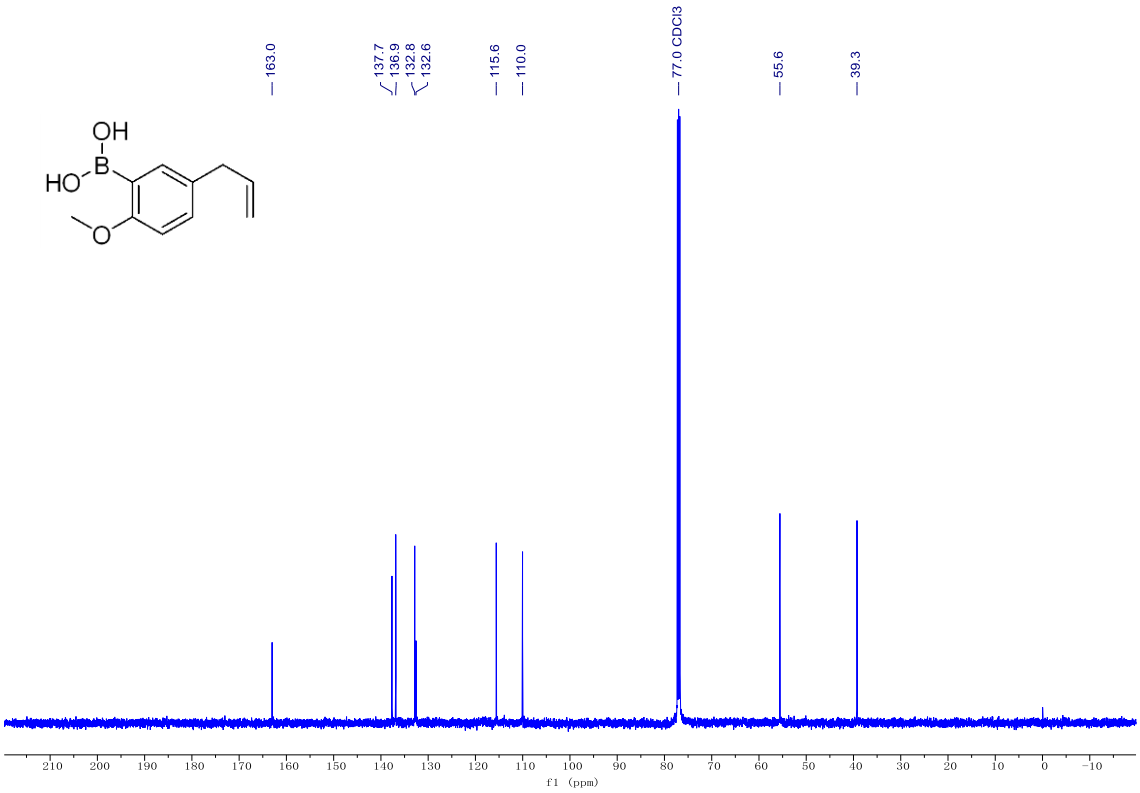
bi-magnolignan (**1**)

To a solution of 2 (497 mg, 1.77 mmol) in dry CH_2Cl_2 (20 mL) were added anhydrous $FeCl_3$ (29 mg, 0.18 mmol) and m-CPBA (306 mg, 1.77 mmol) under nitrogen. The reaction solution was stirred at room temperature for 1 h and then quenched with water. The aqueous phase was extracted with DCM. The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by OSD chromatography (methanol-H_2O) gave bi-magnolignan (277 mg, 56%) as a white solid; ^{1}H NMR (500 MHz, Chloroform-d) δ: 7.39 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.55 (s, 2H), 6.24 (ddt, J = 16.5, 10.2, 6.2 Hz, 2H), 5.99 (s, 2H), 5.55 (ddt, J=16.8, 10.1, 6.6 Hz, 2H), 5.28 (dd, J = 17.1, 2.0 Hz, 2H), 5.19 (dd, J = 10.0, 1.8 Hz, 2H), 4.83 (dd, J = 10.0, 1.9 Hz, 2H), 4.74 (dd, J = 17.0, 1.9 Hz, 2H), 3.89 (d, J =6.2 Hz, 4H), 3.11 (d, J = 6.8 Hz, 4H). ^{13}C NMR (126 MHz, Chloroform-d) δ: 155.0, 150.4, 143.2, 137.5, 137.2, 135.1, 134.0, 126.5, 124.1, 120.5, 116.0, 115.5, 114.2, 111.1, 110.7, 110.3, 39.6, 28.5. HRMS calcd for $C_{36}H_{30}O_6Na$ $[M + Na]^+$: 581.1940, found 581.1934.

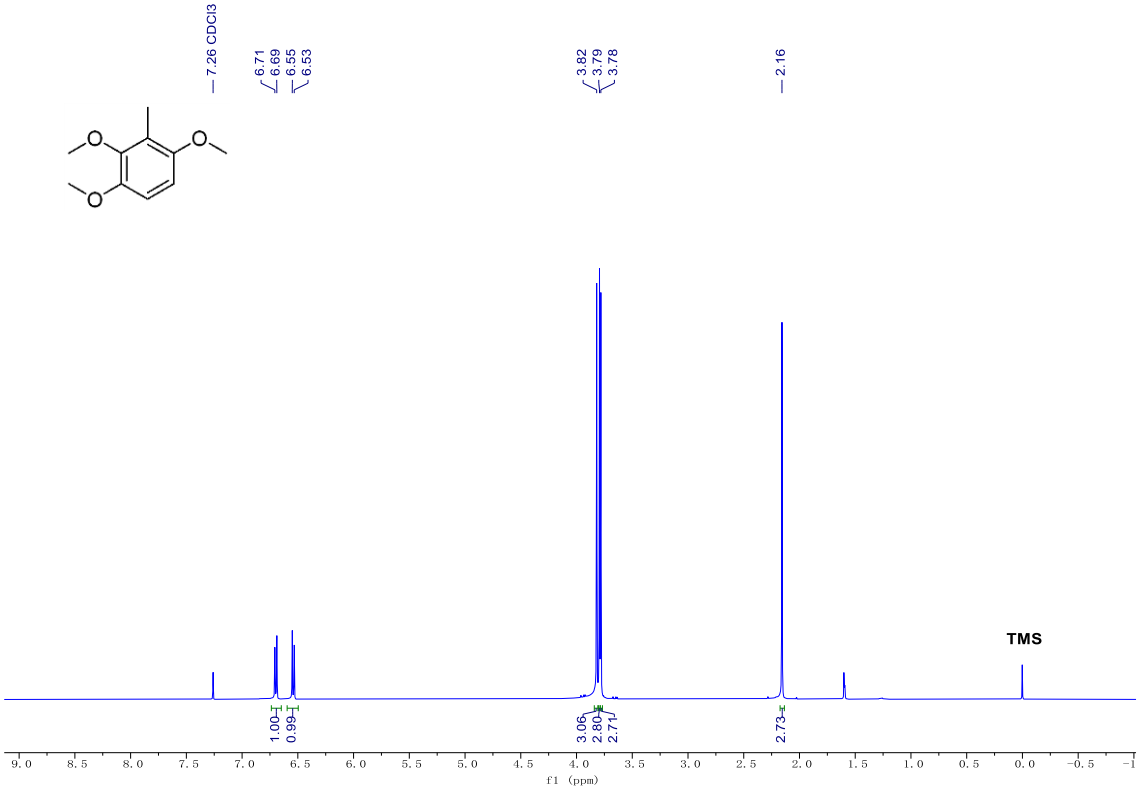
^{1}H and ^{13}C NMR spectra of compounds 1, 9, 11-13, 16-18.

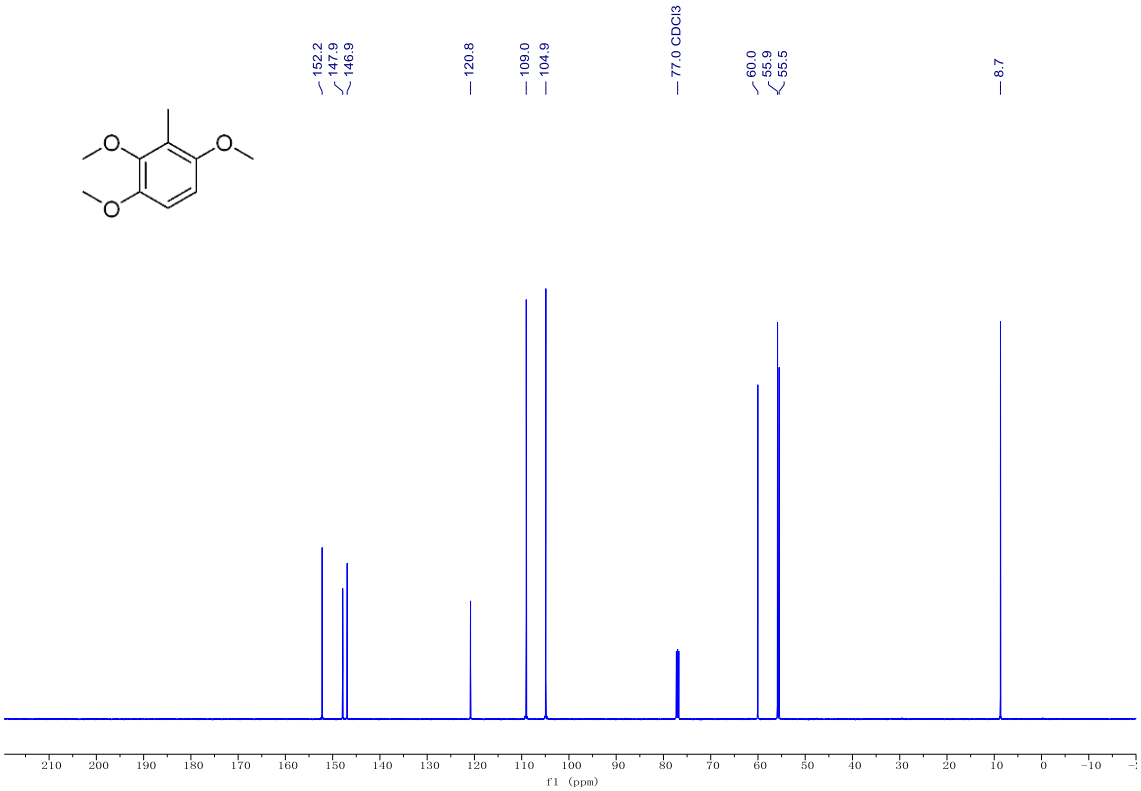
^{1}H and ^{13}C NMR spectra of compound **13**



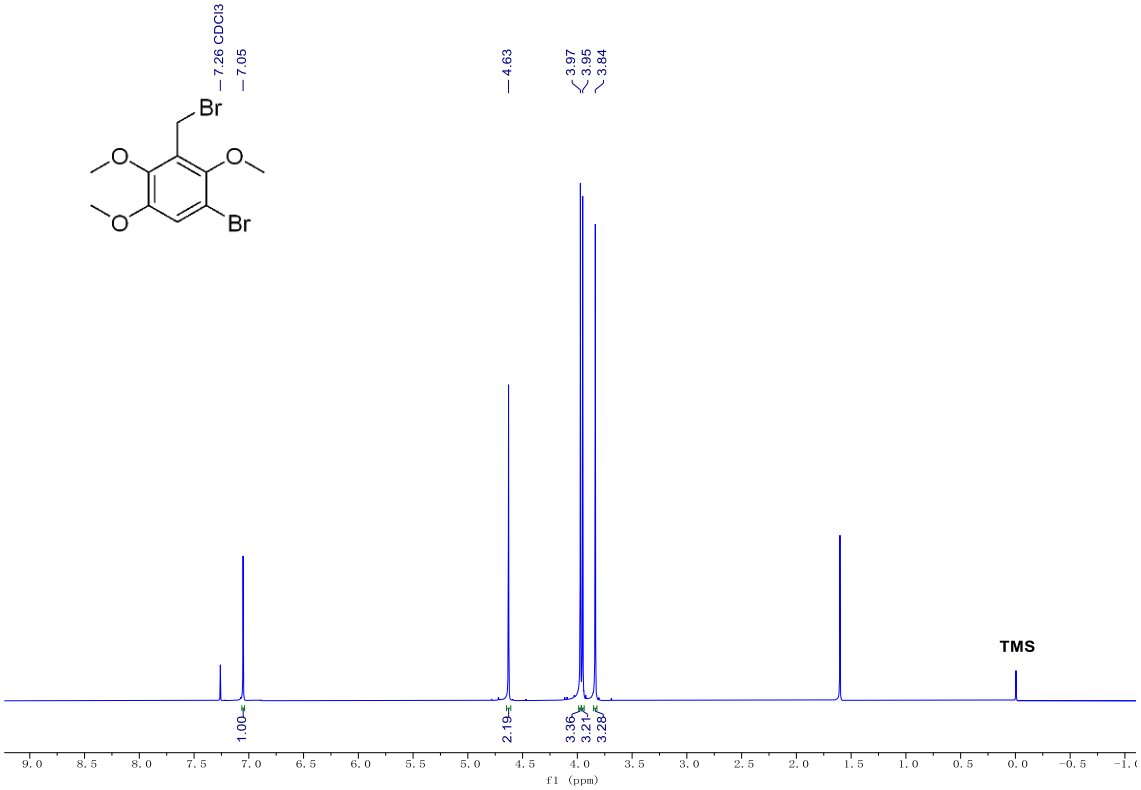


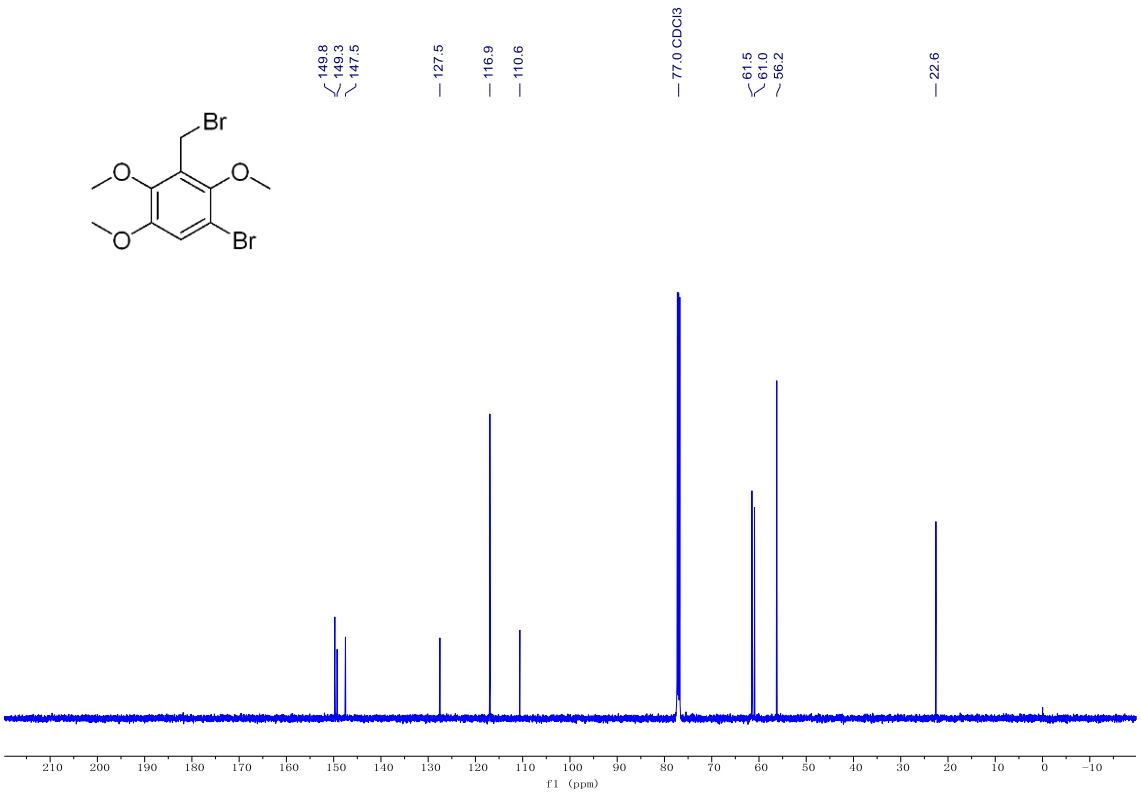
^{1}H and ^{13}C NMR spectra of compound **16**



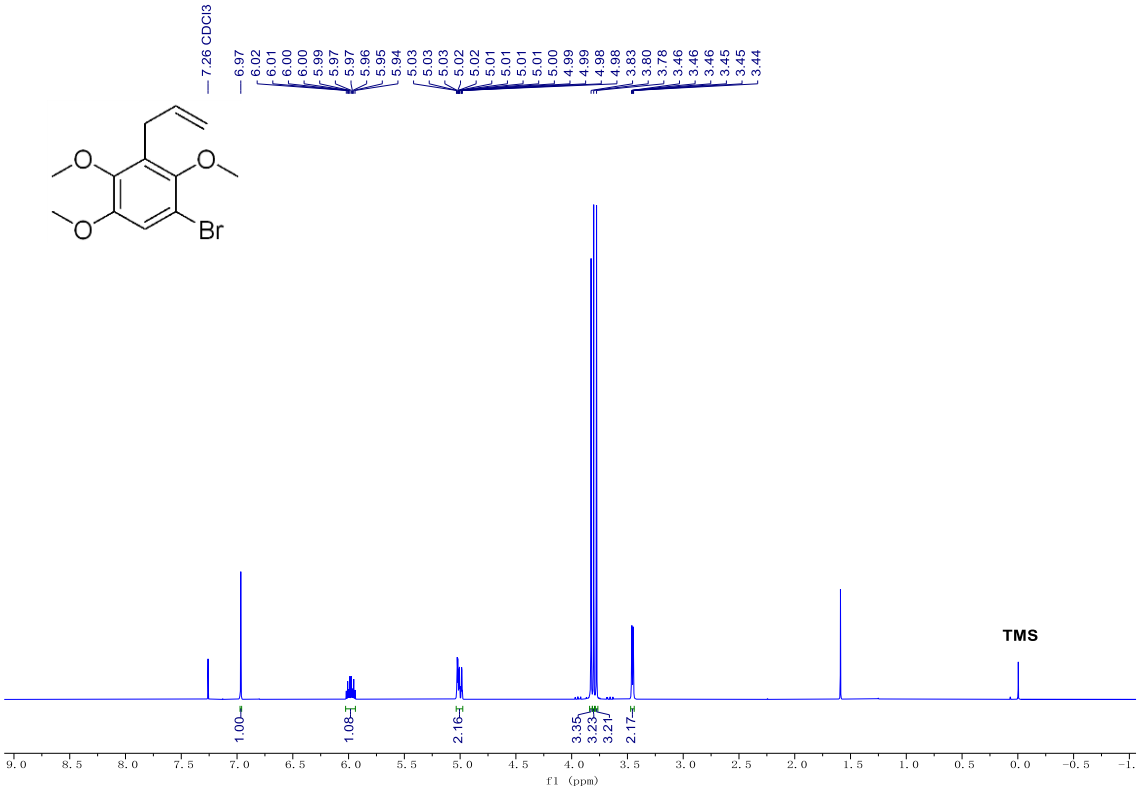


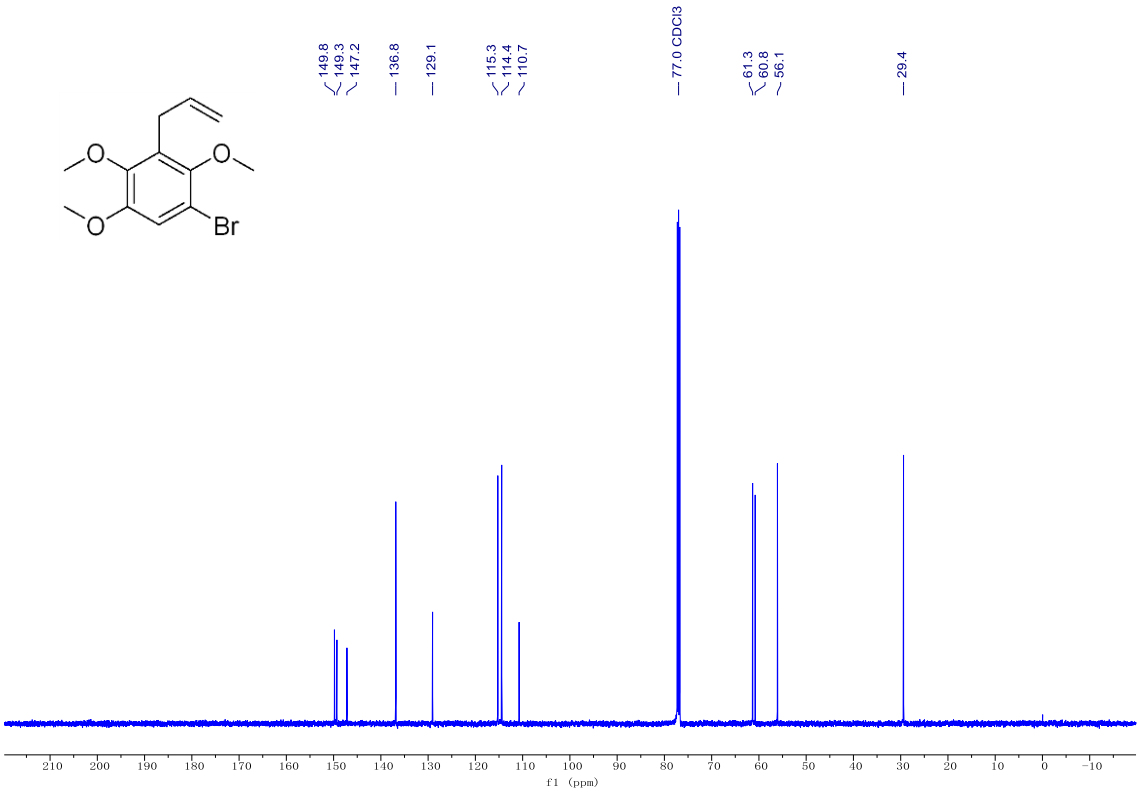
^{1}H and ^{13}C NMR spectra of compound **17**



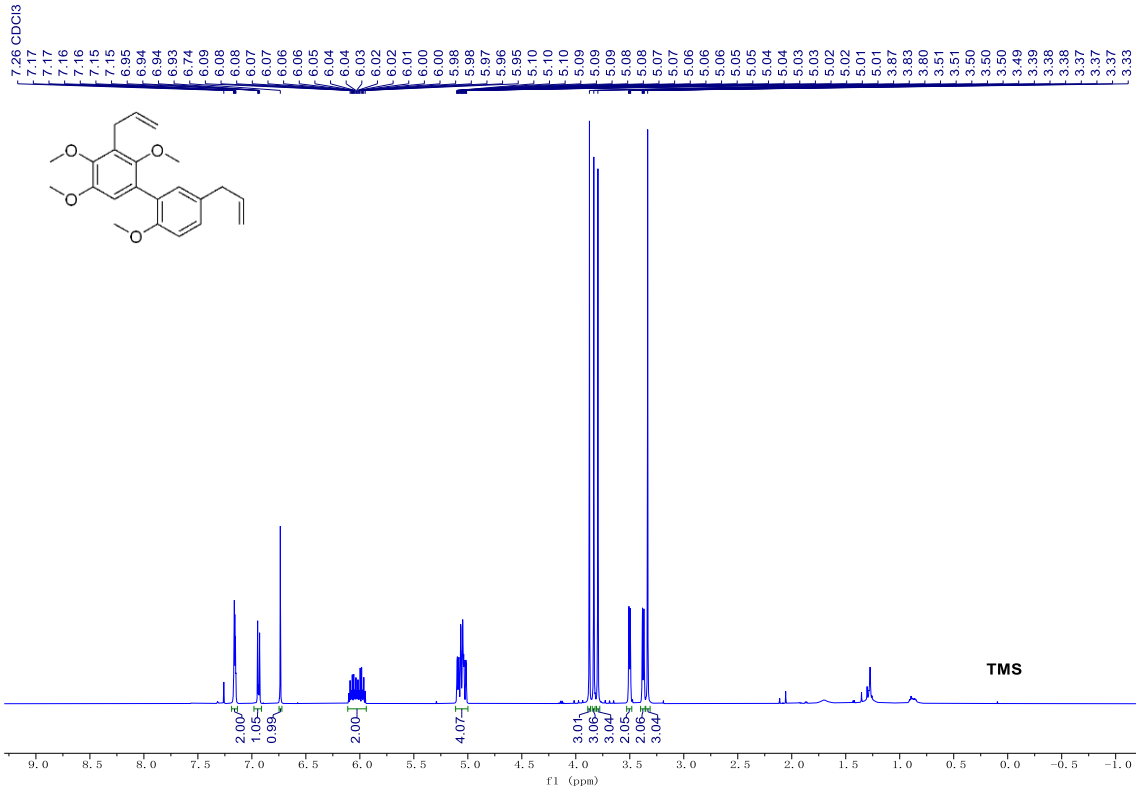


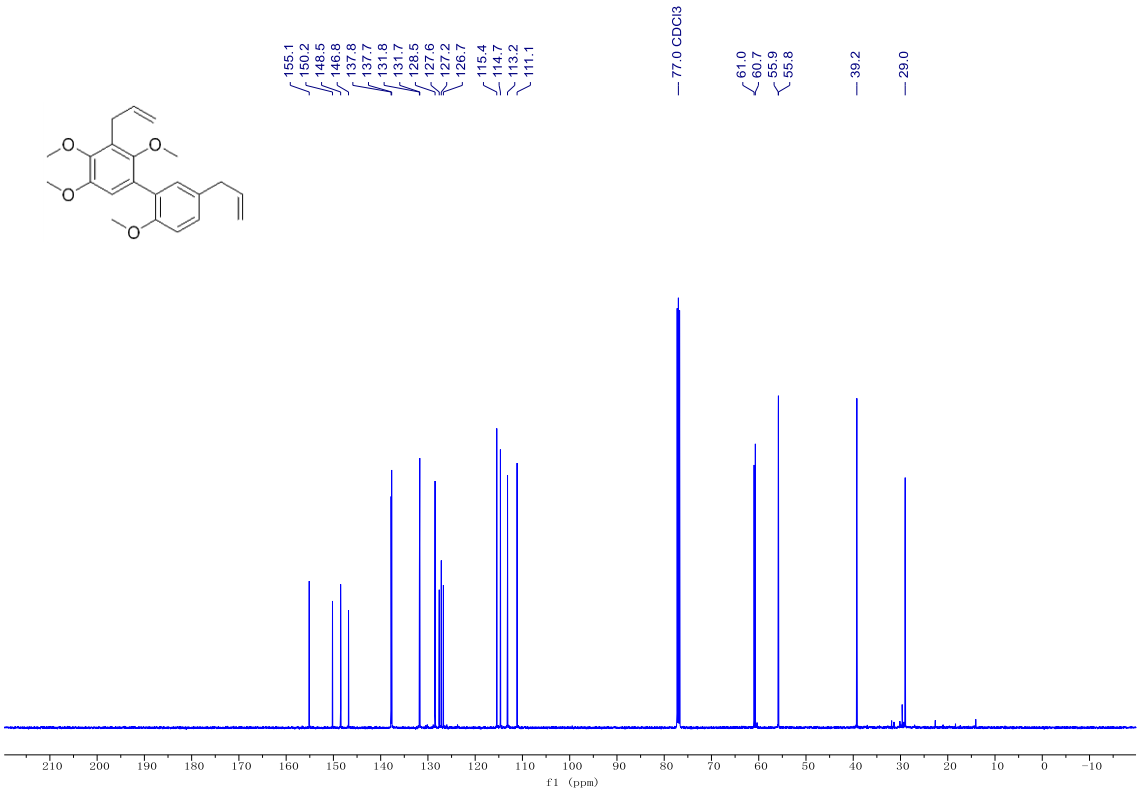
^{1}H and ^{13}C NMR spectra of compound **12**



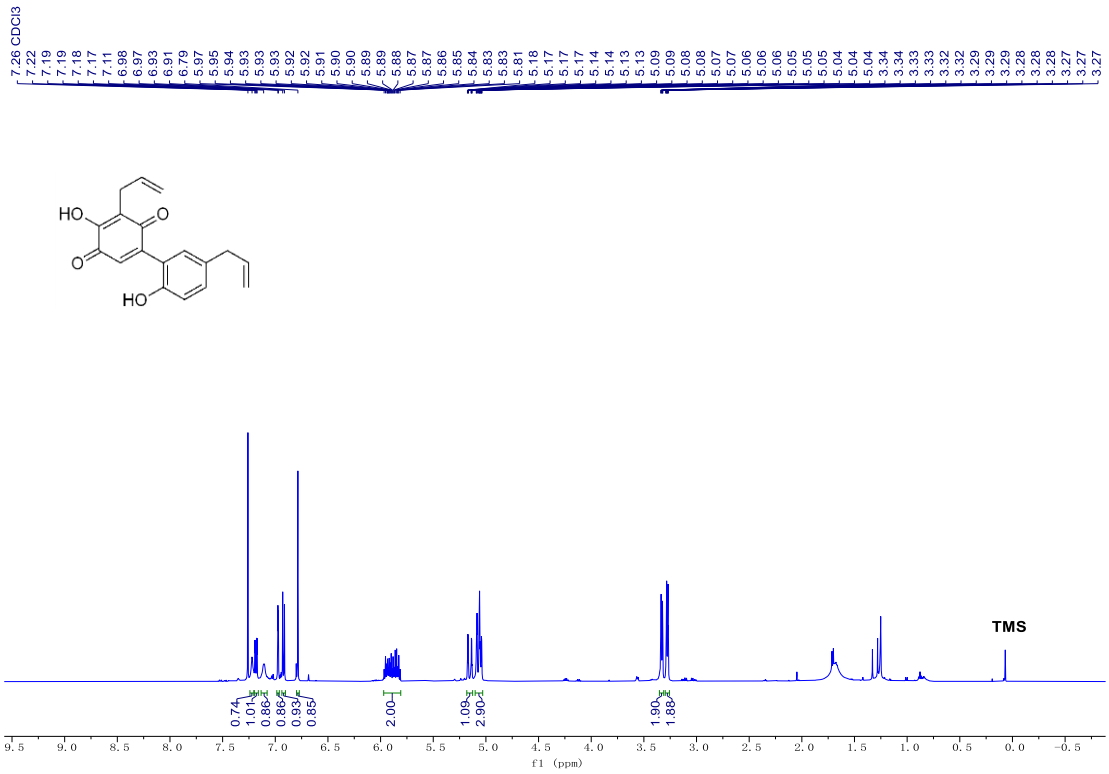


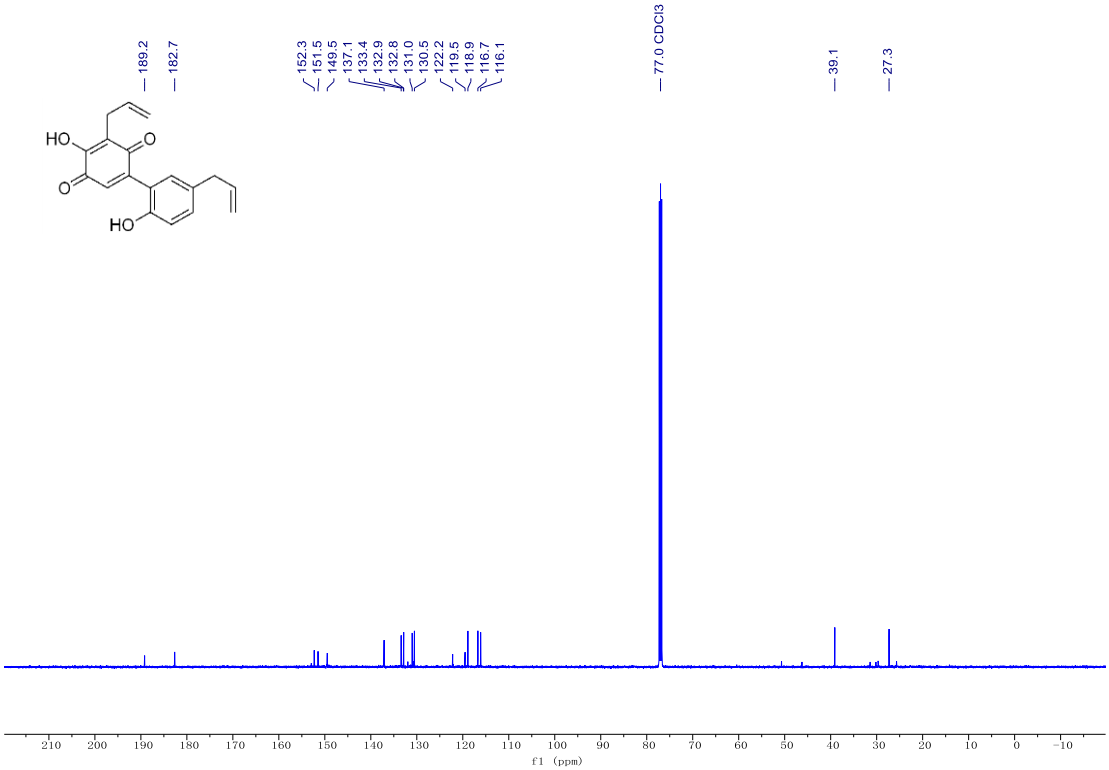
^{1}H and ^{13}C NMR spectra of compound **11**



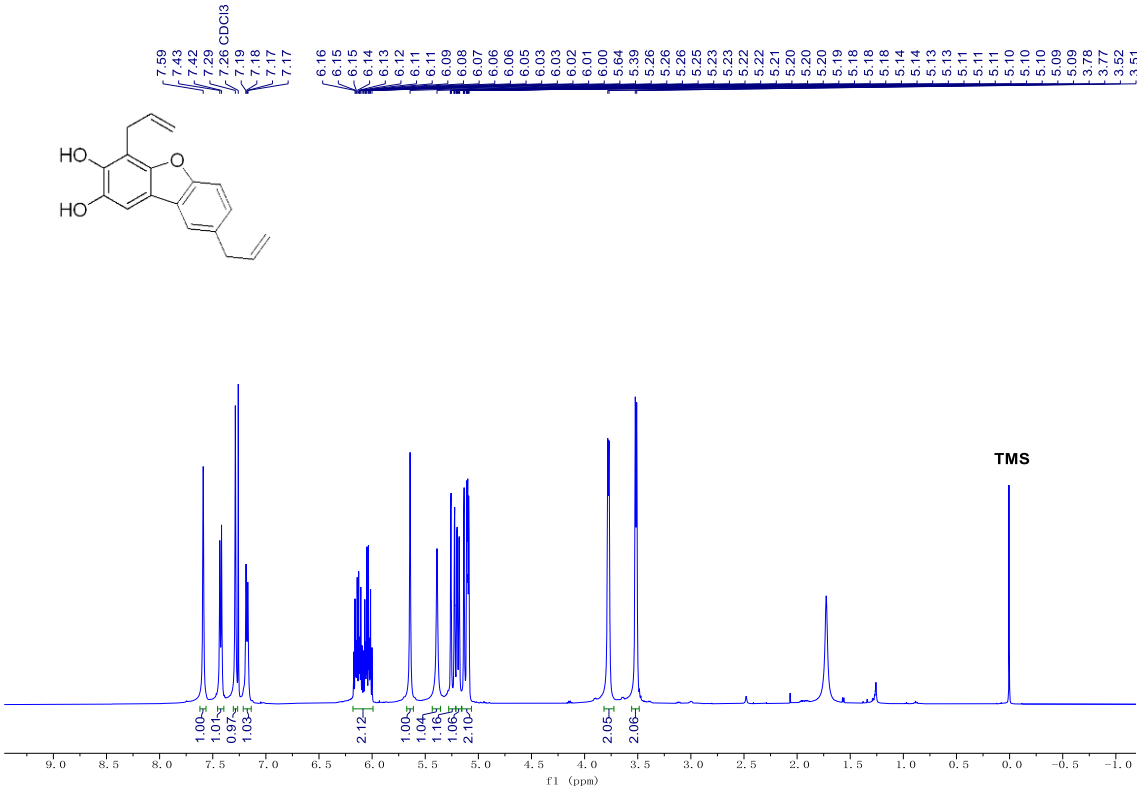


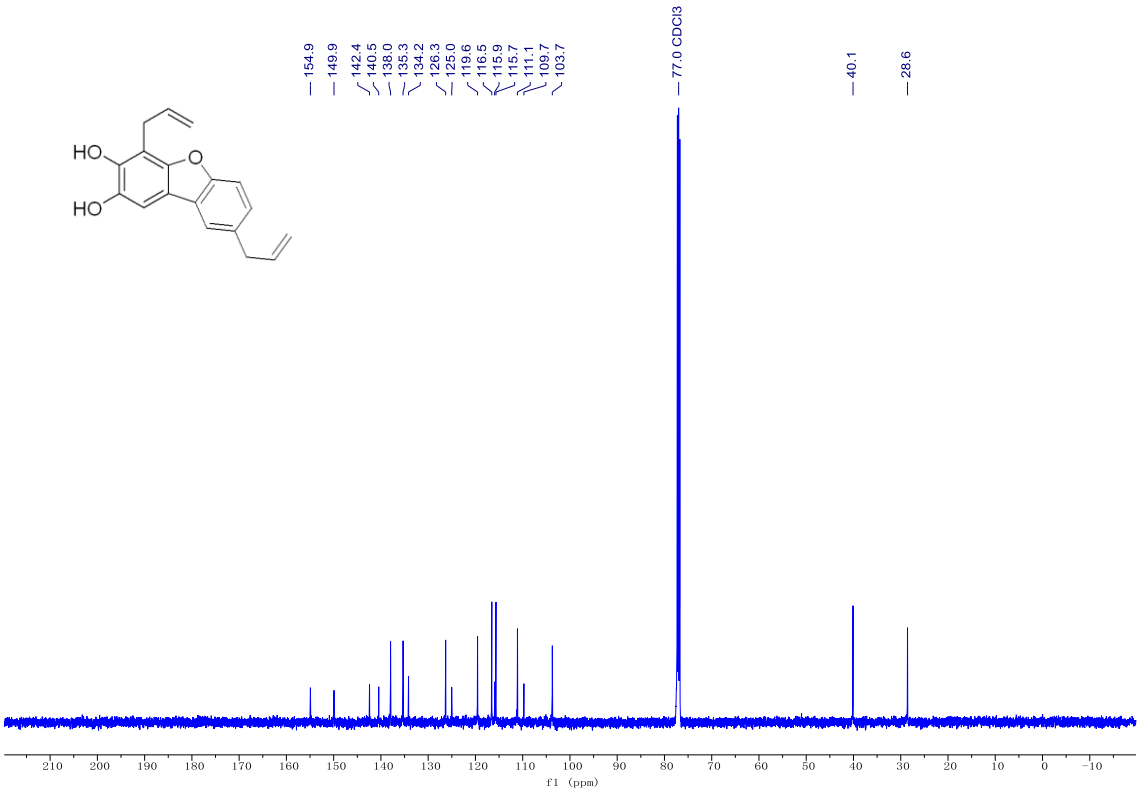
^{1}H and ^{13}C NMR spectra of compound **18**





^{1}H and ^{13}C NMR spectra of compound **9**





^{1}H and ^{13}C NMR spectra of compound **magnolignan(1)**