

Supporting Information

Total Synthesis and Structural Determination of the Dimeric Tetrahydroxanthone Ascherxanthone A

Zheming Xiao, Yayue Li, Shuanhu Gao*

Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Department of Chemistry,
East China Normal University, 3663N Zhongshan Road, Shanghai 200062, China.

Email: shgao@chem.ecnu.edu.cn

Fax: (+) 86-21-62604784

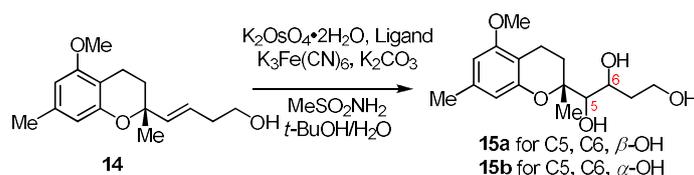
Supporting Information

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General Experimental Procedures:

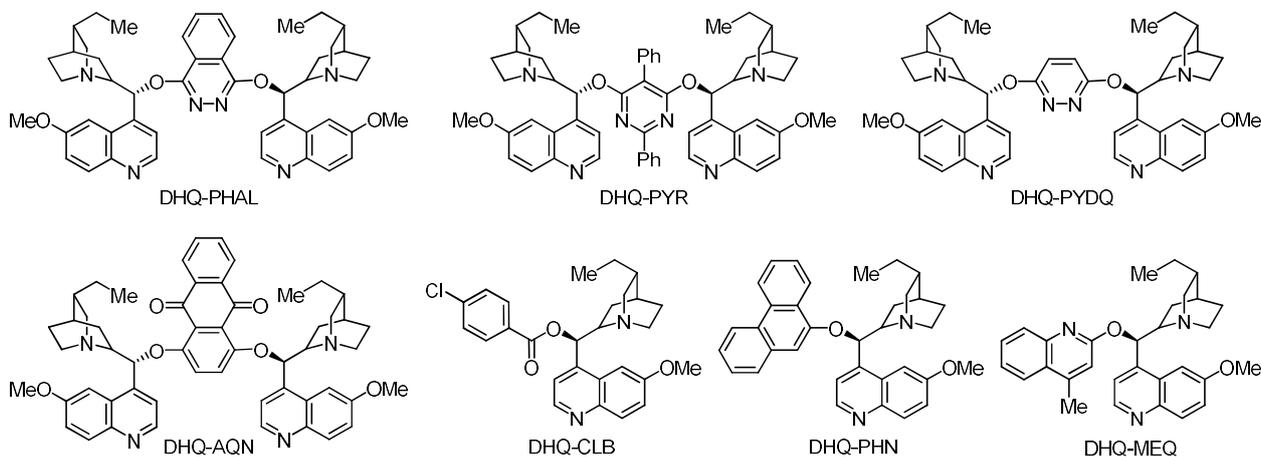
All reactions were carried out under nitrogen unless noted. Anhydrous 1,4-dioxane, dichloromethane, acetonitrile, N,N-dimethylformamide, 1,2-dichloroethane were distilled from calcium hydride. Tetrahydrofuran was distilled from sodium-benzophenone ketyl, anhydrous toluene and *tert*-butyl methyl ether (MTBE) was distilled from sodium. Flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925), employing Qingdao Haiyang silica gel 60 (200–300 mesh). TLC analyses were performed on EMD 250 μ m Silica Gel HSGF₂₅₄ plates and visualized by quenching of UV fluorescence (λ_{max} =254 nm), or by staining ceric ammonium molybdate, ammonium molybdate, phosphomolybdic acid, or potassium permanganate. ¹H and ¹³C NMR spectra were recorded on a Bruker-500, 400, 300 spectrometer. Chemical shifts for ¹H and ¹³C NMR spectra are reported in ppm (δ) relative to residue protium and carbon resonance in the solvent (CDCl₃: δ 7.26, 77.0 ppm) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were acquired on Waters Micromass GCT Premier, Thermo Fisher Scientific LTQ FT Ultra and Mass spectra at Agilent 5975C. HPLC analysis was performed on Dionex U 3000 and Shimadzu LC-20AD. Infrared (IR) spectra were obtained using a Thermo Electron Corporation Nicolet Nexus 670 FT-IR Spectrometer. The $[\alpha]_D$ was recorded using PolAAr 3005 High Accuracy Polarimeter.

Screening ligands of asymmetric dihydroxylation:



entry	ligand	temp	time	yield	dr ^a
1	DHQ-PHAL	0 °C	33 h	80%	4.6:1
2	DHQ-PYR	0 °C	33 h	81%	3.1:1
3	DHQ-PYDQ	0 °C	33 h	81%	4.7:1
4	DHQ-AQN	0 °C	33 h	81%	2.7:1
5	DHQ-CLB	0 °C	33 h	78%	3.0:1
6	DHQ-PHN	0 °C	33 h	77%	5.1:1
7	DHQ-MEQ	0 °C	33 h	85%	6.0:1
8	- ^c	rt	5 d	\	NR
9	- ^d	rt	5 d	73% (81%) ^b	1:5.5

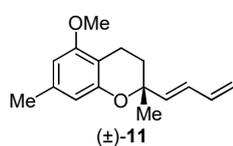
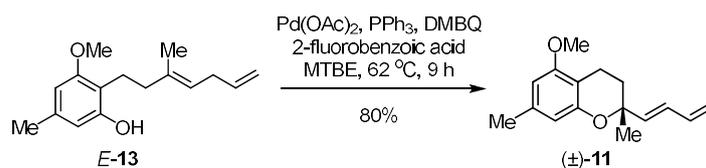
a: all were determined by crude NMR analysis. b: based on starting material.
c: AD-mix- α was used. d: AD-mix- β was used.



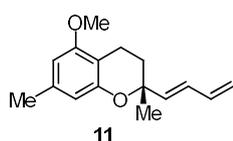
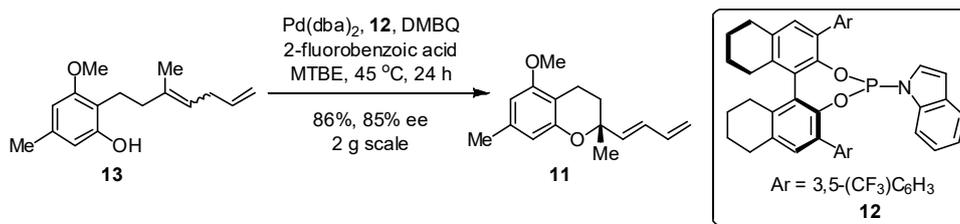
General Procedure: To a solution of *t*-BuOH/H₂O (1 mL, 1:1) was added K₂OsO₄•2H₂O (0.005 mmol, 0.05 equiv), ligand (0.02 mmol, 0.2 equiv), K₃Fe(CN)₆ (0.3 mmol, 3 equiv), K₂CO₃ (0.3 mmol, 3 equiv), MeSO₂NH₂ (0.1 mmol, 1 equiv), then the solution was stirred at room temperature (about 21 °C) for 1 h. **14** (neat, 0.1 mmol, 1 equiv) was added, and the solution was stirred at 0 °C (entries 1-7) or room temperature (entries 8-9). It was quenched by saturated aqueous Na₂SO₃ (5 mL). The mixture was extracted with EtOAc (5 mL×4). The combined organic phase was washed with brine (10 mL×2). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (25% to 50% Ethyl acetate-petroleum ether) to give **15** as a white solid.

Procedure for the preparation of substrates:

We prepared racemic **18**, from racemic **11**, using the same procedures as chiral **18**. Racemic **11** was synthesized following the procedure reported by Gong^[1] using Pd(OAc)₂ as catalyst, PPh₃ as ligand.



Olefin (±)-11. To a dried 500 mL Schlenk bottle was added Pd(OAc)₂ (0.4 g, 1.8 mmol, 0.038 equiv), PPh₃ (1.52 g, 5.8 mmol, 0.12 equiv), 2,6-dimethoxybenzo-1,4-quinone (DMBQ) (7.7 g, 58 mmol, 1.2 equiv) and 2-fluorobenzoic acid (0.5 g, 3.6 mmol, 0.076 equiv) successively, then it was pumped and replaced with N₂ atmosphere for three times, followed by (*E*)-**11** (11.5 g, 46.7 mmol, 1 equiv) and anhydrous *tert*-butyl methyl ether (MTBE) (234 mL) addition. The solution was subjected to three freeze-pump-thaw cycles using liquid nitrogen to degas the solution, and then it was heated to 62 °C and remained for 9 h. After the mixture cooled to rt, it was concentrated, and purified by silica gel column chromatography (10% to 20% CH₂Cl₂-petroleum ether) to give (±)-**11** as a colorless oil (9.13 g, 80%).

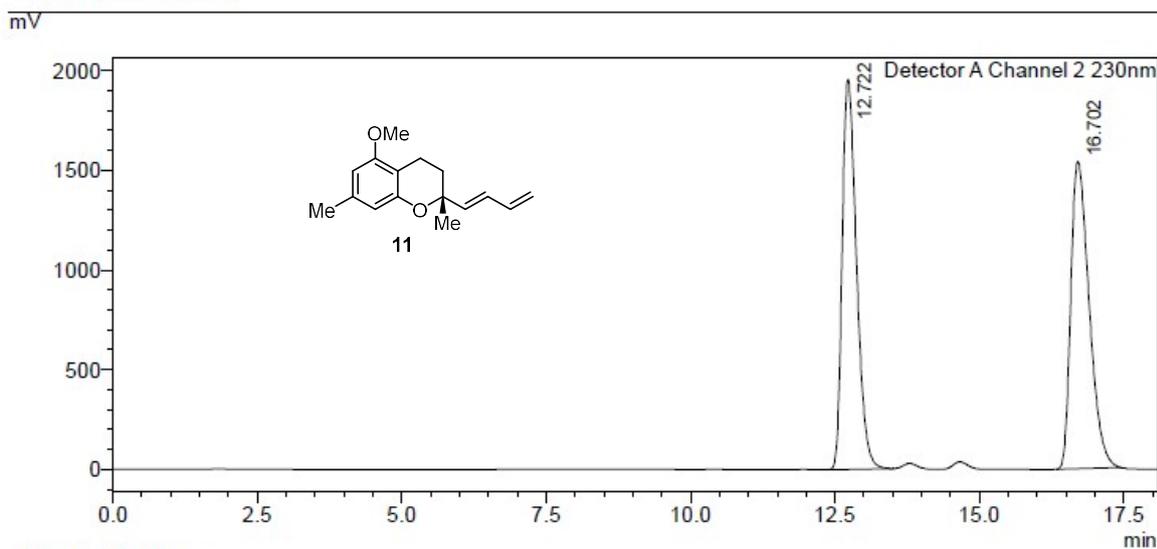


Olefin 11. To a dried 100 mL round bottle flask was added Pd(dba)₂ (102.3 mg, 0.18 mmol, 0.02 equiv), **12** (239.0 mg, 0.28 mmol, 0.03 equiv), 2,6-dimethoxybenzo-1,4-quinone (DMBQ) (1.469 g, 10.8 mmol, 1.2 equiv),

2-fluorobenzoic acid (50.9 mg, 0.36 mmol, 0.04 equiv), then it was pumped and replaced with N₂ atmosphere for three times, followed by anhydrous *tert*-butyl methyl ether (MTBE) (45 mL) addition. The solution was heated to 45 °C and remained for 0.5 h. The mixture was cooled to 23 °C, and **13**^[1] (neat, 2.2168 g, 9 mmol, 1 equiv) was added. After addition, the solution was heated to 45 °C and remained for 24 h. After the mixture cooled to 23 °C, it was concentrated, and purified by silica gel column chromatography (2% to 15% CH₂Cl₂-petroleum ether) to give **11** as a colorless oil (1.883 g, 86%). $R_f = 0.84$ (5% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = +13.0$ ($c = 0.78$, CHCl₃). Enantiomeric excess: 85%, determined by HPLC (CHIRALPAK OD-H, hexane/isopropanol = 99.5/0.5, flow rate 0.5 mL/min, T = 30 °C, 230 nm): $t_R = 12.75$ min (minor), $t_R = 17.10$ min (major). ¹H NMR (400 MHz, CDCl₃) δ 6.35 (s, 1H), 6.32 – 6.13 (m, 3H), 5.73 (d, $J = 15.2$ Hz, 1H), 5.13 (d, $J = 16.0$ Hz, 1.5 Hz, 1H), 5.02 (d, $J = 9.3$ Hz, 1.5 Hz, 1H), 3.77 (s, 3H), 2.62 (dt, $J = 17.0, 5.6$ Hz, 1H), 2.51 – 2.39 (m, 1H), 2.27 (s, 3H), 1.90 (dt, $J = 13.2, 5.7$ Hz, 1H), 1.77 (ddd, $J = 13.7, 9.5, 5.9$ Hz, 1H), 1.41 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 157.5, 154.2, 137.6, 137.0, 136.6, 129.4, 117.0, 110.1, 107.3, 102.7, 75.7, 55.3, 31.7, 26.7, 21.6, 16.8 ppm. IR ν_{max} 2928, 2850, 1616, 1583, 1457, 1419, 1351, 1223, 1159, 1107, 1004, 813 cm⁻¹; HRMS (ED): m/z calcd for C₁₆H₂₀O₂ [M]⁺: 244.1463, found 244.1464. The absolute configuration of **11** was determined by comparing the optical rotation value with Gong' data.^[1]

HPLC of olefin 11.

<Chromatogram>

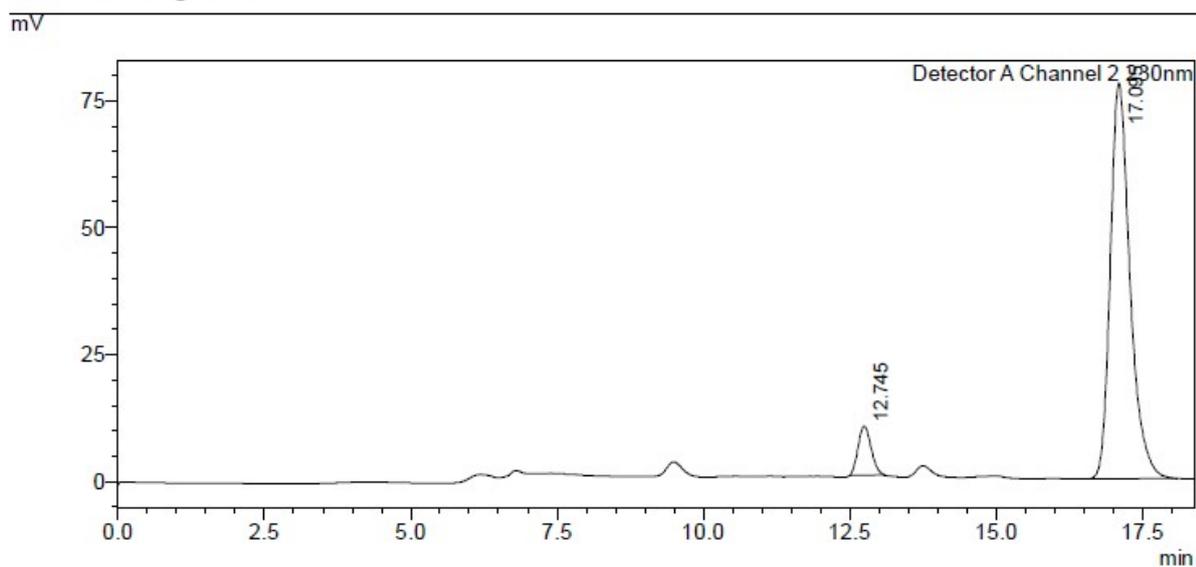


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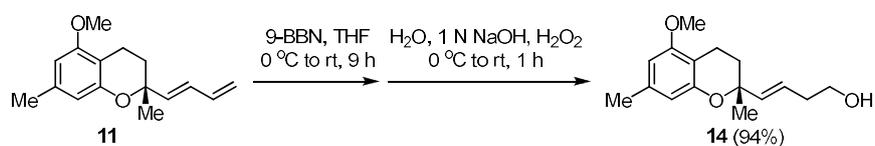
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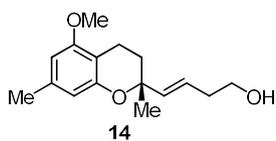


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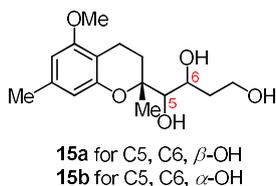
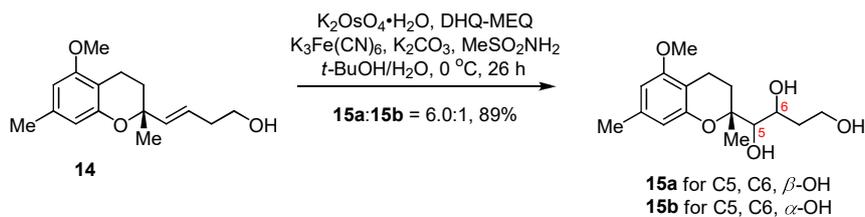
Detector A Channel 2 230nm

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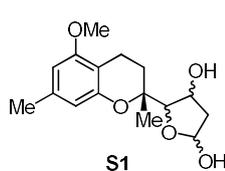
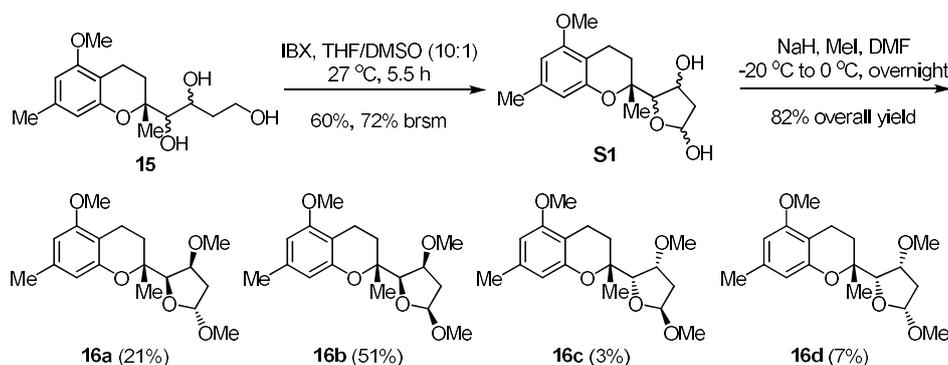


Alcohol 14. To a neat **11** (1.82 g, 7.5 mmol, 1 equiv) in 200 mL dried round bottle flask was added 9-BBN (0.5 M in THF, 30 mL, 15 mmol, 2 equiv) dropwise at 0 °C under N₂ atmosphere. After addition, the solution was stirred at 20 °C overnight, then the solution was cooled to 0 °C. H₂O (1.8 mL) was added dropwise followed by 1 N NaOH (25.8 mL) and H₂O₂ (30% w/w in H₂O, 12.8 mL) addition. After the solution stirred at 20 °C for 1 h, it was cooled to 0 °C and quenched by saturated aqueous Na₂SO₃ (50 mL). The mixture was extracted with EtOAc (100 mL×3). The combined organic phase was washed with brine (200 mL×2). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (10% to 20% Ethyl acetate-petroleum ether) to give **14** (1.8416 g, 94%) as a colorless oil. *R_f* = 0.29 (20% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = +32.2$ (*c* = 1.33, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 6.35 (s, 1H), 6.23 (s, 1H), 5.68 – 5.53 (m, 2H), 3.79 (s, 3H), 3.57 (t, *J* = 6.4 Hz, 2H), 2.64 (dt, *J* = 17.0, 5.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.28 (s, 3H), 2.25 (dd, *J* = 12.3, 6.4 Hz, 2H), 1.88 (dt, *J* = 13.6, 5.8 Hz, 1H), 1.76 (ddd, *J* = 13.6, 9.4, 5.9 Hz, 1H), 1.40 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 157.4, 154.2, 136.9, 136.5, 125.3, 110.0, 107.2, 102.6, 75.7, 61.8, 55.3, 35.6, 31.6, 26.7, 21.6, 16.7 ppm. IR *v*_{max} 3340, 2932, 1617, 1583, 1457, 1350, 1227, 1106, 1046, 968, 813 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₆H₂₂O₃ [M]⁺: 262.1569, found 262.1568.



Triol 15a/15b. To a solution of *t*-BuOH/H₂O (84 mL, 1:1) was added K₂OsO₄·2H₂O (138.1 mg, 0.44 mmol, 0.05 equiv), DHQ-MEQ (855.9 mg, 1.77 mmol, 0.2 equiv), K₃Fe(CN)₆ (8.70 g, 2.64 mmol, 3 equiv), K₂CO₃ (3.72 g, 2.69 mmol, 3 equiv), MeSO₂NH₂ (840.1 mg, 8.83 mmol, 1 equiv), then the solution was stirred at 19 °C for 1 h. After the solution cooled to 0 °C, **14** (neat, 2.23 g, 8.5 mmol, 1 equiv) was added and the mixture was stirred at 0 °C for more 26 h. TLC shows all **14** was consumed, then it was quenched by Na₂SO₃ (40 mL). The mixture was extracted with EtOAc (60

mL×4). The combined organic phase was washed with brine (100 mL×2). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (25% to 50% Ethyl acetate-petroleum ether) to give **15** (2.256 g, 89%) as a white solid. *R_f* = 0.13 (50% Ethyl acetate-petroleum ether). ¹H NMR (400 MHz, CDCl₃) (major) δ 6.25 (s, 2H), 4.35 (dd, *J* = 8.8, 2.7 Hz, 1H), 3.92 – 3.83 (m, 2H), 3.80 (s, 3H), 3.48 – 3.38 (br, OH, 1H), 3.38 – 3.32 (m, 1H), 3.26 – 2.93 (br, OH, 2H) 2.74 (ddd, *J* = 17.2, 6.1, 2.6 Hz, 1H), 2.55 – 2.44 (m, 1H), 2.26 (s, 3H), 2.21 – 2.10 (m, 1H), 2.10 – 1.99 (m, 1H), 1.72 (ddt, *J* = 9.1, 6.4, 3.4 Hz, 2H), 1.28 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) (major) δ 157.6, 152.9, 137.2, 110.1, 107.1, 103.2, 79.6, 77.1, 69.1, 60.5, 55.3, 36.8, 26.7, 21.5, 19.6, 15.8 ppm. IR ν_{max} 3927, 1584, 1459, 1413, 1352, 1232, 1145, 1105, 1019, 814 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₆H₂₄O₅ [M]⁺: 296.1624, found 296.1627.

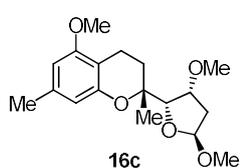


Hemiacetal S1. To a neat **15** (1.4237 g, 4.8 mmol, 1 equiv) in 200 mL round bottle was added 2-iodoxybenzoic acid (IBX) (1.614 g, 5.8 mmol, 1.2 equiv) then it was replaced with N₂ atmosphere for three times. The anhydrous co-sol.

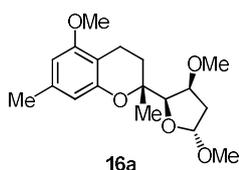
THF/DMSO (10:1, 49.5 mL) was added and the mixture was stirred at 27 °C for 5.5 h. It was quenched by saturated aqueous NaHCO₃ (40 mL) and NaS₂O₃ (10 mL). The mixture was extracted with EtOAc (50 mL×3). The combined organic phase was washed with brine (100 mL×2). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (0.5% to 5% MeOH-CH₂Cl₂) to give **S1** (845.0 mg, 60%, 72% brsm) as a white solid and recovered **15** (245.3 mg).

Acetal 16a/16b/16c/16d. To a mixture of NaH (525.4 mg, 13.14 mmol, 3 equiv) in anhydrous DMF (18 mL) was added **S1** (1.2873 g, 4.37 mmol, 1 equiv) in anhydrous DMF (4 mL) dropwise at -20

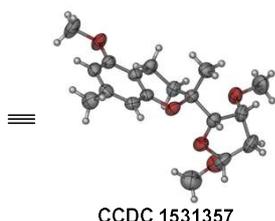
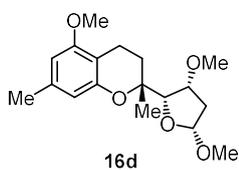
°C. After addition, the reaction mixture was slowly warmed to 0 °C and remained at 0 °C overnight. It was quenched by saturated aqueous NH₄Cl (10 mL). The mixture was extracted with EtOAc (30 mL×3). The combined organic phase was washed with brine (50 mL×3). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (1% to 8% Ethyl acetate-petroleum ether) to give **16a** (295 mg, 21%) as a white solid, **16b** (713 mg, 51%) as a white solid, **16c** (37 mg, 3%) as a white solid, **16d** (95 mg, 7%) as a white solid. **16d** was obtained as a white single crystal from CH₂Cl₂/hexane solution.



Acetal 16c. $R_f = 0.67$ (20% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = -6.8$ ($c = 0.25$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 6.32 (s, 1H), 6.22 (s, 1H), 5.17 (dd, $J = 5.7, 3.1$ Hz, 1H), 4.07 – 3.94 (m, 2H), 3.80 (s, 3H), 3.37 (s, 3H), 3.32 (s, 3H), 2.69 (dt, $J = 17.1, 5.7$ Hz, 1H), 2.53 (ddd, $J = 17.1, 9.8, 7.0$ Hz, 1H), 2.34 – 2.21 (m, 4H), 2.12 – 1.92 (m, 3H), 1.36 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 157.5, 154.1, 136.8, 110.4, 107.3, 103.7, 102.4, 83.4, 81.2, 76.9, 56.9, 55.3 (2 C), 39.0, 27.5, 21.6, 19.8, 15.9 ppm. IR ν_{\max} 2922, 2853, 1585, 1458, 1350, 1228, 1198, 1105, 1040, 965, 818 cm⁻¹; HRMS (EI): m/z calcd for C₁₈H₂₆O₅ [M]⁺: 322.1780, found 322.1776.

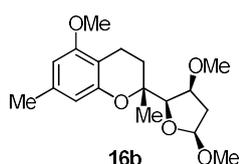


Acetal 16a. $R_f = 0.61$ (20% Ethyl acetate-petroleum ether); $[\alpha]_D^{22} = -33.5$ ($c = 0.26$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 6.37 (s, 1H), 6.22 (s, 1H), 5.22 (dd, $J = 5.8, 2.8$ Hz, 1H), 4.00 (dt, $J = 7.4, 2.8$ Hz, 2H), 3.80 (s, 3H), 3.36 (s, 3H), 3.25 (s, 3H), 2.61 (t, $J = 6.9$ Hz, 2H), 2.31 – 2.15 (m, 4H), 2.04 – 1.79 (m, 3H), 1.42 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 157.2, 153.4, 136.9, 110.6, 106.8, 103.6, 102.4, 82.7, 80.2, 77.0, 56.5, 55.2 (2 C), 38.7, 27.7, 21.6, 20.1, 16.1 ppm. IR ν_{\max} 2929, 1738, 1585, 1460, 1355, 1236, 1106, 1042, 966, 812 cm⁻¹; HRMS (EI): m/z calcd for C₁₈H₂₆O₅ [M]⁺: 322.1780, found 322.1777.

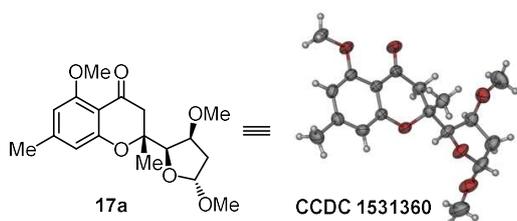


Acetal 16d. $R_f = 0.40$ (20% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = +37.9$ ($c = 0.46$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 6.34 (s, 1H), 6.23 (s, 1H), 5.10 (d, $J = 5.8$ Hz, 1H), 4.09 (d, $J = 4.3$ Hz, 1H), 3.90 (t, $J = 4.7$ Hz,

1H), 3.80 (s, 3H), 3.40 (s, 3H), 3.35 (s, 3H), 2.74 (dd, $J = 17.2, 2.6$ Hz, 1H), 2.58 – 2.44 (m, 1H), 2.34 – 2.00 (m, 7H), 1.30 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 157.3, 153.9, 136.7, 110.5, 107.4, 105.0, 102.4, 87.9, 80.1, 78.1, 57.3, 55.9, 55.2, 37.2, 25.7, 21.6, 18.9, 15.8 ppm. IR ν_{max} 2929, 2888, 1617, 1584, 1455, 1355, 1228, 1199, 1103, 1043, 947, 818 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{26}\text{O}_5$ $[\text{M}]^+$: 322.1780, found 322.1783.

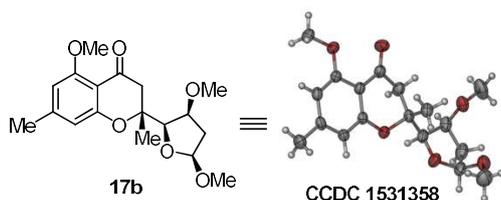


Acetal 16b. $R_f = 0.35$ (20% Ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{22} = +95.6$ ($c = 0.75$, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 6.43 (s, 1H), 6.23 (s, 1H), 5.13 (d, $J = 5.8$ Hz, 1H), 4.04 (d, $J = 4.5$ Hz, 1H), 3.88 (t, $J = 4.8$ Hz, 1H), 3.80 (s, 3H), 3.48 (s, 3H), 3.31 (s, 3H), 2.63 (t, $J = 6.8$ Hz, 2H), 2.26 (s, 3H), 2.22 (d, $J = 14.3$ Hz, 1H), 1.96 (ddd, $J = 14.7, 9.5, 3.5$ Hz, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 157.4, 153.5, 137.1, 110.8, 107.0, 104.9, 102.5, 86.7, 79.4, 78.1, 57.1, 55.9, 55.3, 36.8, 27.4, 21.6, 19.8, 16.2 ppm. IR ν_{max} 2925, 1614, 1582, 1458, 1352, 1222, 1037, 948, 907, 815 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{26}\text{O}_5$ $[\text{M}]^+$: 322.1780, found 322.1784.



Acetal 17a. To a solution of **16a** (48.0 mg, 0.15 mmol, 1 equiv) in acetone (0.8 mL) was added 15% MgSO_4 (w/w in H_2O , 0.2 mL) at 22 $^\circ\text{C}$, then KMnO_4 (141.4 mg, 0.9 mmol, 6 equiv) was added. The solution was stirred at 22 $^\circ\text{C}$ for 5 min. The mixture was heated to 60 $^\circ\text{C}$ and remained for 1 h, then it was cooled to 22 $^\circ\text{C}$. It was quenched by saturated aqueous Na_2SO_3 (1 mL), then the mixture was filtered through Celite, and acetone was removed under vacuum. The remained solution was extracted with EtOAc (5 mL \times 3). The combined organic phase was washed with brine (10 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (10% to 20% Ethyl acetate-petroleum ether, 1% to 3% $\text{MeOH-CH}_2\text{Cl}_2$) to give **16a** (10.4 mg) and **17a** (22.0 mg,

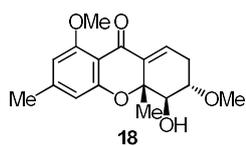
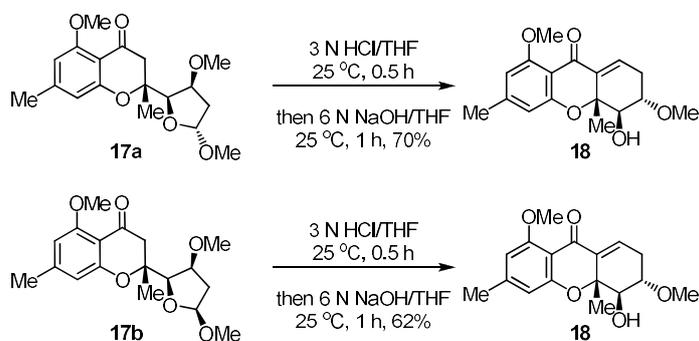
44%, 56% brsm) as a white solid. **17a** was obtained as a white single crystal from EtOAc/hexane solution. $R_f = 0.28$ (50% Ethyl acetate-petroleum ether); $[\alpha]_D^{22} = -70.7$ ($c = 0.29$, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.41 (s, 1H), 6.27 (s, 1H), 5.18 (dd, $J = 5.7, 3.0$ Hz, 1H), 4.14 (d, $J = 4.3$ Hz, 1H), 3.94 (ddd, $J = 6.1, 4.5, 2.0$ Hz, 1H), 3.88 (s, 3H), 3.34 (s, 3H), 3.21 (s, 3H), 2.95 (d, $J = 16.1$ Hz, 1H), 2.73 (d, $J = 16.0$ Hz, 1H), 2.29 (s, 3H), 2.23 (ddd, $J = 14.2, 5.8, 2.0$ Hz, 1H), 1.95 (ddd, $J = 14.3, 5.9, 3.0$ Hz, 1H), 1.52 (s, 3H) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 190.5, 160.8, 159.9, 147.6, 111.0, 108.5, 104.3, 104.0, 81.9, 81.7, 80.2, 56.6, 56.0, 55.3, 45.9, 38.4, 22.4, 20.8 ppm. IR ν_{max} 2923, 1680, 1610, 1566, 1461, 1413, 1355, 1227, 1110, 1038, 961, 817 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_6$ $[\text{M}]^+$: 336.1573, found 336.1567.



Acetal 17b. To a solution of **16b** (745.8 mg, 2.3 mmol, 1 equiv) in acetone (16.2 mL) was added 15% MgSO_4 (w/w in H_2O , 6.9 mL) at 18 °C, then KMnO_4 (2.33 g, 14.7 mmol, 6.4 equiv) was added. The solution was stirred at 18 °C for

5 min. The mixture was heated to 60 °C and remained for 1 h, then it was cooled to 18 °C. It was quenched by saturated aqueous Na_2SO_3 (1 mL), then the mixture was filtered through Celite, and acetone was removed under vacuum. The remained solution was extracted with EtOAc (20 mL \times 3). The combined organic layer was washed with brine (30 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (10% to 20% Ethyl acetate-petroleum ether, 1% to 3% $\text{MeOH-CH}_2\text{Cl}_2$) to give **16b** (134.9 mg) and **17b** as a white solid (323.1 mg, 42%, 51% brsm). **17b** was obtained as a white single crystal from EtOAc/hexane solution. $R_f = 0.20$ (50% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = +94.8$ ($c = 0.43$, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.47 (s, 1H), 6.29 (s, 1H), 5.11 (d, $J = 5.8$ Hz, 1H), 4.23 (d, $J = 4.6$ Hz, 1H), 3.89 (s, 3H), 3.86 (t, $J = 4.9$ Hz, 1H), 3.44 (s, 3H), 3.29 (s, 3H), 2.91 (d, $J = 15.9$ Hz, 1H), 2.81 (d, $J = 15.9$ Hz, 1H), 2.29 (s, 3H), 2.22 (d, $J = 14.4$ Hz, 1H), 1.96 (dt, $J = 14.4, 5.6$ Hz,

1H), 1.58 (s, 3H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 190.6, 160.8, 160.0, 147.7, 111.1, 108.6, 105.2, 104.4, 85.4, 82.8, 79.4, 57.2, 56.0, 55.9, 45.8, 36.8, 22.4, 20.5 ppm. IR ν_{max} 2930, 1678, 1612, 1567, 1463, 1353, 1226, 1109, 1037, 946, 820 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_6$ $[\text{M}]^+$: 336.1573, found 336.1570.



Tetrahydroxanthone 18. To a solution of **17a** (43.7 mg, 0.13 mmol) in THF (0.3 mL) was added 3 N HCl (0.6 mL) at 25 °C, after the solution stirred at 25 °C for 0.5 h, TLC shows all **17a** was consumed, and THF (0.45 mL) was added

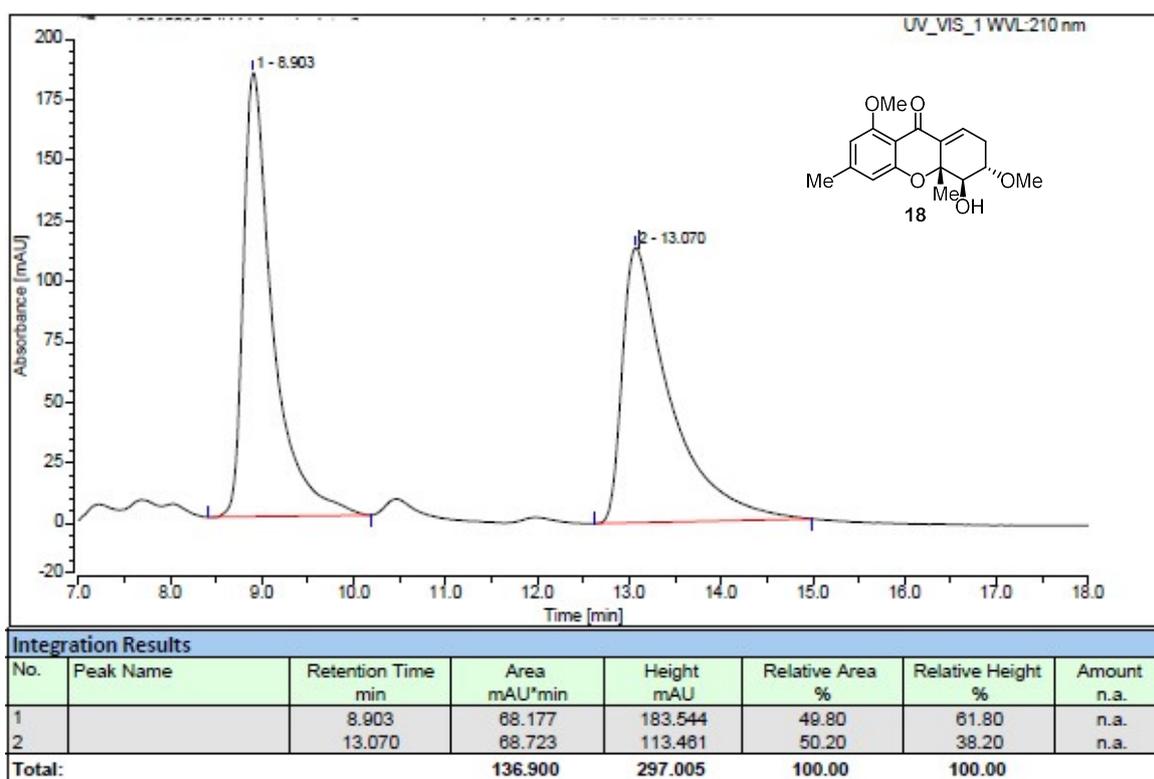
followed by 6 N NaOH (0.45 mL) addition at 25 °C. After the solution stirred at 25 °C for 1 h, it was quenched by saturated aqueous NH_4Cl (5 mL). The mixture was extracted with EtOAc (10 mL \times 3). The combined organic phase was washed with brine (20 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (25% to 50% Ethyl acetate-petroleum ether) to give **18** (27.5 mg, 70%) as a light yellow solid.

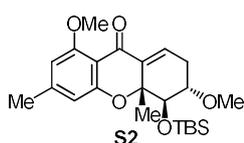
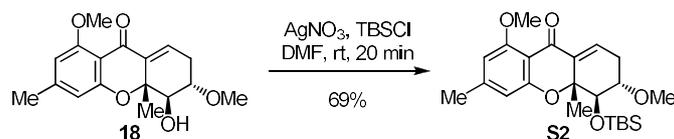
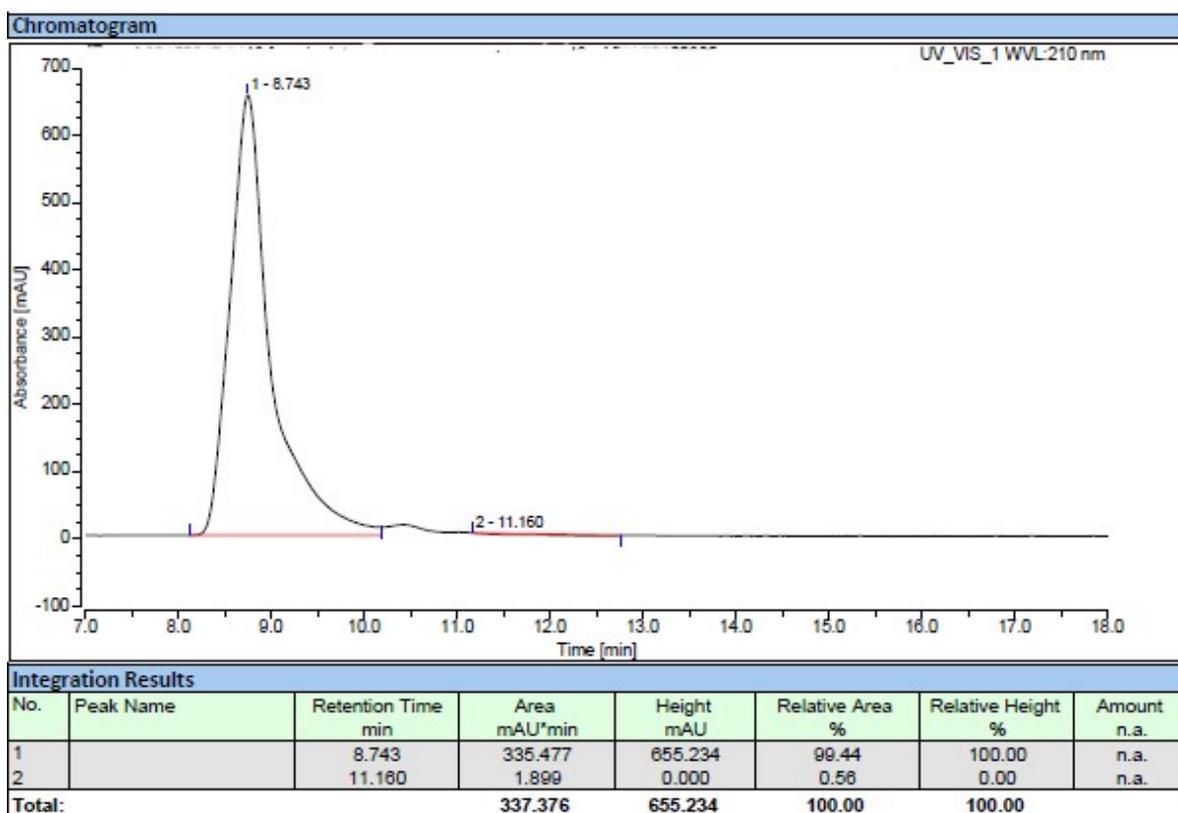
To a solution of **17b** (132.4 mg, 0.39 mmol) in THF (1 mL) was added 3 N HCl (2 mL) at 25 °C. After the solution stirred at 25 °C for 0.5 h, TLC shows all **17b** was consumed, and THF (1.5 mL) was added followed by 6 N NaOH (1.5 mL) addition at 25 °C. After the solution stirred at 25 °C for 1 h, it was quenched by saturated aqueous NH_4Cl (5 mL). The mixture was extracted with EtOAc (15 mL \times 3). The combined organic phase was washed with brine (30 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (25% to 50% Ethyl acetate-petroleum ether) to give **18** (74.1 mg, 62%) as a light yellow solid.

$R_f = 0.36$ (60% Ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{21} = -66.3$ ($c = 0.24$, CHCl_3). Enantiomeric excess: > 99%, determined by HPLC (CHIRALPAK AD-H, hexane/isopropanol = 70/30, flow rate

0.6 mL/min, T = 25 °C, 210 nm): $t_R = 8.90$ min (major), $t_R = 13.07$ min (minor). ^1H NMR (400 MHz, CDCl_3) δ 6.76 (dd, $J = 5.1, 2.9$ Hz, 1H), 6.46 (s, 1H), 6.34 (s, 1H), 4.08 (d, $J = 10.3$ Hz, 1H), 3.91 (s, 3H), 3.48 (s, 3H), 3.45 – 3.37 (m, 1H), 2.94 (s, OH, 1H), 2.89 (ddd, $J = 19.3, 6.0, 5.3$ Hz, 1H), 2.30 (s, 3H), 2.24 (ddd, $J = 19.3, 9.2, 2.9$ Hz, 1H), 1.48 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3) δ 179.4, 161.2, 160.8, 147.9, 136.9, 131.1, 111.4, 108.8, 105.4, 81.8, 76.9, 76.0, 57.1, 56.1, 30.5, 22.4, 19.2 ppm. IR ν_{max} 3561, 2922, 1675, 1611, 1565, 1468, 1260, 1234, 1099, 1003, 909, 814, 736 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{20}\text{O}_5$ $[\text{M}]^+$: 304.1311, found 304.1308.

HPLC of tetrahydroxanthone 18.

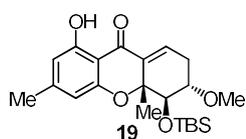
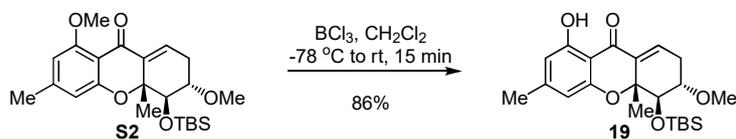




Tetrahydroxanthone S2. To a solution of **18** (46.9 mg, 0.15 mmol, 1 equiv) in anhydrous DMF (1.5 mL) was added AgNO₃ (79.4 mg, 0.47 mmol, 3 equiv) and TBSCl (42.4 mg, 0.28 mmol, 2 equiv) successively at 24 °C. After the

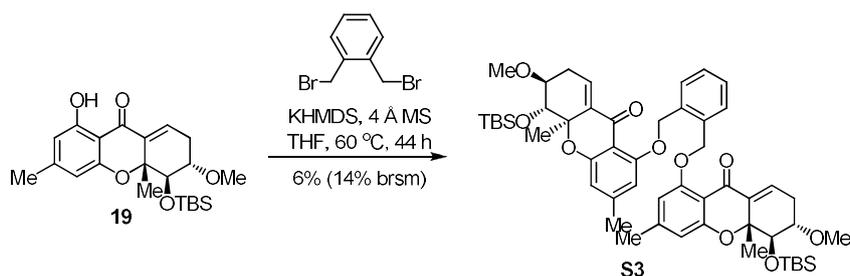
solution stirred at 24 °C for 20 min, TLC shows all **18** was consumed, and it was quenched by saturated aqueous NaHCO₃ (1 mL). The mixture was extracted with EtOAc (5 mL×3). The combined organic phase was washed with brine (10 mL×3). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (15% to 20% Ethyl acetate-petroleum ether) to give **S2** as a light yellow solid (44.4 mg, 69%). *R_f* = 0.62 (50% Ethyl acetate-petroleum ether); $[\alpha]_D^{24} = -26.8$ (*c* = 0.42, CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 6.74 (dd, *J* = 5.0, 3.0 Hz, 1H), 6.31 (s, 2H), 4.02 (d, *J* = 10.1 Hz, 1H), 3.90 (s, 3H), 3.42 (s, 3H), 3.29 (td, *J* = 9.4, 6.4 Hz, 1H), 2.85 (ddd, *J* = 19.7, 6.3, 5.2 Hz, 1H), 2.31 (s, 3H), 2.22 (ddd, *J* = 19.8, 9.1, 3.0 Hz, 1H), 1.43 (s, 3H), 1.00 (s, 9H), 0.22 (s, 3H), 0.17 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ

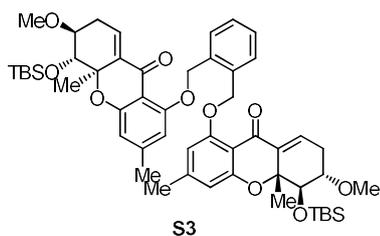
179.8, 161.2 (2 C), 147.6, 137.1, 131.4, 111.0, 108.8, 105.1, 82.6, 77.7, 77.6, 57.9, 56.0, 31.6, 26.0 (3 C), 22.4, 19.7, 18.5, -4.3, -4.6 ppm. IR ν_{\max} 2959, 2925, 2853, 1615, 1461, 1257, 1149, 1087, 1018, 805 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{23}\text{H}_{34}\text{O}_5\text{Si}$ $[\text{M}]^+$: 418.2176, found 418.2174.



Tetrahydroxanthone 19. To a solution of **S2** (72.8 mg, 0.17 mmol, 1 equiv) in anhydrous CH_2Cl_2 (3.5 mL) cooled to $-78\text{ }^\circ\text{C}$ was added BCl_3 (1.0 M in hexane, 0.35 mL, 0.35 mmol, 2 equiv) dropwise. After addition, the cooled

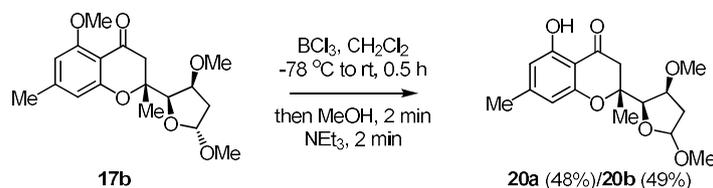
bath was removed; the solution was warmed to $28\text{ }^\circ\text{C}$. After TLC shows all **S2** was consumed, it was quenched by saturated aqueous NaHCO_3 (2 mL) and stirred at $28\text{ }^\circ\text{C}$ for 5 min. The mixture was extracted with EtOAc (10 mL \times 3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (0.5% to 2% Ethyl acetate-petroleum ether) to give **19** (60.3 mg, 86%) as a yellow solid. $R_f = 0.78$ (50% Ethyl acetate-petroleum ether); $[\alpha]_D^{24} = +6.5$ ($c = 0.51$, CHCl_3). ^1H NMR (500 MHz, CDCl_3) δ 12.08 (s, 1H), 6.83 (dd, $J = 5.0, 3.0$ Hz, 1H), 6.31 (s, 1H), 6.17 (s, 1H), 4.04 (d, $J = 10.0$ Hz, 1H), 3.43 (s, 3H), 3.32 (td, $J = 9.4, 6.5$ Hz, 1H), 2.91 (ddd, $J = 20.0, 6.4, 5.2$ Hz, 1H), 2.35 – 2.24 (m, 4H), 1.44 (s, 3H), 1.00 (s, 9H), 0.22 (s, 3H), 0.16 (s, 3H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 185.4, 162.9, 159.2, 150.7, 135.6, 133.7, 109.9, 108.6, 105.2, 83.0, 77.6, 77.2 (CH, dept 135) 58.0, 31.8, 26.0 (3 C), 22.6, 20.2, 18.6, -4.3, -4.6 ppm. IR ν_{\max} 2928, 1638, 1605, 1373, 1207, 1143, 1087, 885, 836, 775 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_{32}\text{O}_5\text{Si}$ $[\text{M}]^+$: 404.2019, found 404.2012.





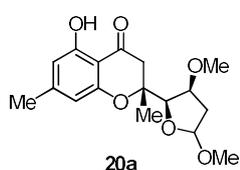
Tetrahydroxanthone S3. To a 10 mL Schlenk tube was added newly activated 4 Å MS (50 mg) under N₂ atmosphere, then **19** (15.8 mg, 0.04 mmol, 1 equiv) in anhydrous THF (1 mL) was added. After the solution stirred at 17 °C for 20 min, KHMDS (1.0 M in

THF, 39 μL, 0.04 mol, 1 equiv) was added dropwise and the solution was stirred at 17 °C for 20 min. 1,3-bis(bromomethyl)benzene (5.16 mg, 0.02 mmol, 0.5 equiv) in anhydrous THF (0.1 mL) was added, then the solution was heated to 60 °C and remained at 60 °C for 44 h. It was cooled to 17 °C then quenched by saturated aqueous NH₄Cl (2 mL). The mixture was extracted with EtOAc (5 mL×3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by PTLC to give **19** (9.0 mg) and **S3** (1.1 mg, 6%, 14% brsm) as a light yellow solid. *R_f* = 0.60 (20% Ethyl acetate-petroleum ether); [α]_D²⁰ = -20.7 (*c* = 0.03, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 7.70 (dd, *J* = 5.4, 3.5 Hz, 2H), 7.37 (dd, *J* = 5.6, 3.4 Hz, 2H), 6.71 (dd, *J* = 4.9, 2.9 Hz, 2H), 6.47 (s, 2H), 6.26 (s, 2H), 5.42 (d, *J* = 12.3 Hz, 2H), 5.35 (d, *J* = 12.3 Hz, 2H), 4.00 (d, *J* = 10.1 Hz, 2H), 3.42 (s, 6H), 3.28 (td, *J* = 9.4, 6.5 Hz, 2H), 2.87 – 2.79 (m, 2H), 2.28 – 2.18 (m, 8H), 1.34 (s, 6H), 0.99 (s, 18H), 0.22 (s, 6H), 0.16 (s, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 179.5 (2 C), 161.0 (2 C), 160.1 (2 C), 147.5 (2 C), 137.2 (2 C), 134.6 (2 C), 131.1 (2 C), 128.6 (2 C), 128.2 (2 C), 111.1 (2 C), 108.9 (2 C), 106.7 (2 C), 82.5 (2 C), 77.7 (2 C), 77.6 (2 C), 69.7 (2 C), 58.0 (2 C), 31.6 (2 C), 26.0 (6 C), 22.5 (2 C), 19.6 (2 C), 18.6 (2 C), -4.3 (2 C), -4.6 (2 C) ppm. IR *v*_{max} 2923, 1615, 1467, 1259, 1096, 1023, 879, 806 cm⁻¹; HRMS (ESI): *m/z* calcd for C₅₂H₇₀O₁₀Si₂Na [M+Na]⁺: 933.4405, found 933.4415.

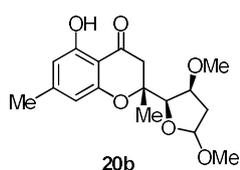


Acetal 20a/20b. To a solution of **17b** (98.8 mg, 0.29 mmol, 1 equiv) in anhydrous CH₂Cl₂ (3 mL) was added BCl₃ (1.0 M in hexane, 0.59 mL, 0.59 mmol, 2 equiv) dropwise at -78 °C. After addition, the cooled bath was removed and the solution was warmed to 26 °C. After TLC shows all **17b** was

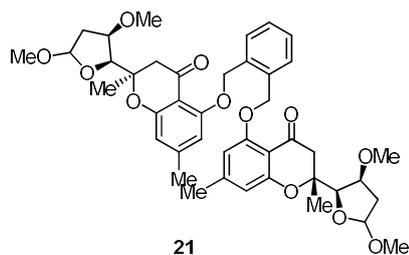
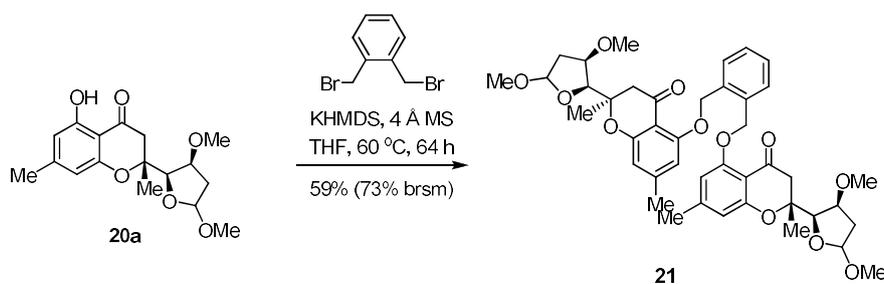
consumed, MeOH (0.5 mL) was added dropwise and stirred at 26 °C for 2 min. Then NEt₃ (1.0 mL) was added. After the solution stirred at 26 °C for more 2 min, it was quenched by saturated aqueous NaHCO₃ (2 mL) and stirred at 26 °C for 5 min. The mixture was extracted with EtOAc (10 mL×3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (10% to 15% Ethyl acetate-petroleum ether) to give **20a** (45.1 mg, 48%) as a white solid and **20b** (46.5 mg, 49%) as a white solid (relative stereochemistry remains uncertain).



Acetal 20a. $R_f = 0.60$ (20% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = -49.6$ ($c = 0.33$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 11.71 (s, 1H), 6.27 (s, 1H), 6.25 (s, 1H), 5.16 (dd, $J = 5.4, 3.1$ Hz, 1H), 4.04 (d, $J = 4.0$ Hz, 1H), 3.92 – 3.82 (m, 1H), 3.35 (s, 3H), 3.20 – 3.04 (m, 4H), 2.71 (d, $J = 17.3$ Hz, 1H), 2.30 – 2.18 (m, 4H), 1.95 (ddd, $J = 14.2, 5.5, 3.2$ Hz, 1H), 1.54 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 196.9, 161.4, 159.1, 150.1, 109.3, 108.5, 105.4, 103.9, 82.5, 81.3, 80.3, 56.1, 55.4, 43.0, 38.5, 23.0, 22.4 ppm. IR ν_{\max} 2930, 1640, 1570, 1448, 1368, 1203, 1037, 752 cm⁻¹; HRMS (EI): m/z calcd for C₁₇H₂₂O₆ [M]⁺: 322.1416, found 322.1418.

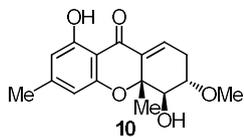
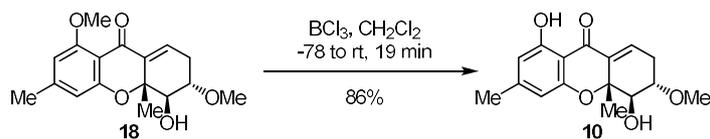


Acetal 20b. $R_f = 0.52$ (30% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = +109.1$ ($c = 0.51$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 11.66 (s, 1H), 6.30 (s, 1H), 6.29 (s, 1H), 5.12 (d, $J = 5.7$ Hz, 1H), 4.18 (d, $J = 4.6$ Hz, 1H), 3.86 (t, $J = 4.8$ Hz, 1H), 3.43 (s, 3H), 3.26 (s, 3H), 3.09 (d, $J = 17.2$ Hz, 1H), 2.80 (d, $J = 17.1$ Hz, 1H), 2.25 (s, 3H), 2.23 (d, $J = 14.4$ Hz, 1H), 2.01 (dt, $J = 14.4, 5.6$ Hz, 1H), 1.57 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 197.1, 161.5, 159.0, 150.5, 109.3, 108.7, 105.6, 105.2, 86.0, 82.6, 79.6, 57.1, 55.9, 43.0, 36.9, 22.5, 21.3 ppm. IR ν_{\max} 2931, 1640, 1570, 1448, 1370, 1307, 1203, 1089, 1036, 935, 831, 750 cm⁻¹; HRMS (EI): m/z calcd for C₁₇H₂₂O₆ [M]⁺: 322.1416, found 322.1415.



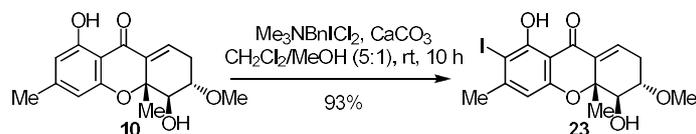
Acetal 21. To a 10 mL Schlenk tube was added newly activated 4 Å MS (100 mg) under N₂ atmosphere, then **20a** (45.1 mg, 0.14 mmol, 1 equiv) in anhydrous THF (2 mL) was added. After the solution stirred at 26 °C for 20 min, KHMDS (1.0 M in THF, 0.14 mL, 0.14 mol, 1 equiv) was added. The solution was stirred at 26

°C for 20 min, and 1,3-bis(bromomethyl)benzene (18.5 mg, 0.07 mmol, 0.5 equiv) in anhydrous THF (0.5 mL) was added, then the solution was heated to 60 °C and remained for 64 h. It was cooled to 26 °C and quenched by saturated aqueous NH₄Cl (2 mL). The mixture was extracted with EtOAc (5 mL×3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (5% to 40% Ethyl acetate-petroleum ether) to give **20a** (8.5 mg) and **21** (30.8 mg, 59%, 73% brsm) as a light yellow solid. $R_f = 0.32$ (40% Ethyl acetate-petroleum ether); $[\alpha]_D^{20} = -123$ ($c = 0.09$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.73 (dd, $J = 5.4, 3.5$ Hz, 2H), 7.38 (dd, $J = 5.6, 3.4$ Hz, 2H), 6.44 (s, 2H), 6.39 (s, 2H), 5.42 (d, $J = 12.4$ Hz, 2H), 5.27 (d, $J = 12.4$ Hz, 2H), 5.19 (dd, $J = 5.6, 3.0$ Hz, 2H), 4.13 (d, $J = 4.3$ Hz, 2H), 3.94 (dd, $J = 7.1, 3.0$ Hz, 2H), 3.35 (s, 6H), 3.21 (s, 6H), 2.93 (d, $J = 15.9$ Hz, 2H), 2.68 (d, $J = 15.8$ Hz, 2H), 2.31 – 2.16 (m, 8H), 1.96 (ddd, $J = 14.2, 5.8, 3.0$ Hz, 2H), 1.48 (s, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 190.1 (2 C), 160.7 (2 C), 158.7 (2 C), 147.4 (2 C), 134.5 (2 C), 128.4 (2 C), 128.1 (2 C), 111.0 (2 C), 108.7 (2 C), 105.9 (2 C), 104.0 (2 C), 82.0 (2 C), 81.7 (2 C), 80.3 (2 C), 69.4 (2 C), 56.6 (2 C), 55.3 (2 C), 45.9 (2 C), 38.5 (2 C), 22.3 (2 C), 20.8 (2 C) ppm. IR ν_{\max} 2921, 1678, 1612, 1565, 1449, 1353, 1230, 1101, 1040, 962, 754 cm⁻¹; HRMS (ESI): m/z calcd for C₄₂H₅₀O₁₂Na [M+Na]⁺: 769.3200, found 769.3196.



Tetrahydroxanthone 10. To a solution of **18** (98.6 mg, 0.32 mmol, 1 equiv) in anhydrous CH_2Cl_2 (6.5 mL) cooled to $-78\text{ }^\circ\text{C}$ was added BCl_3 (1.0 M in hexane, 0.49 mL, 0.49 mmol, 1.5 equiv) dropwise. After addition, the cooled bath was

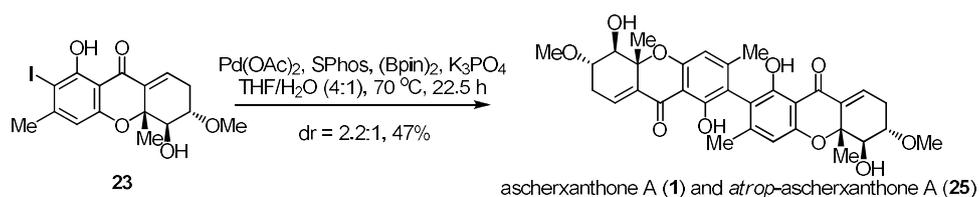
removed and the solution was warmed to $17\text{ }^\circ\text{C}$. After TLC shows all **18** was consumed, it was quenched by saturated aqueous NaHCO_3 (3 mL) and the solution was stirred at $17\text{ }^\circ\text{C}$ for 5 min. Then the mixture was extracted with EtOAc (10 mL \times 3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na_2SO_4 , filtered, concentrated, and purified by silica gel column chromatography (15% to 25% Ethyl acetate-petroleum ether) to give **10** (81.2 mg, 86%) as a yellow solid. $R_f = 0.41$ (40% Ethyl acetate-petroleum ether); $[\alpha]_D^{23} = -17.5$ ($c = 0.32$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 12.06 (s, 1H), 6.86 (dd, $J = 5.0, 2.9$ Hz, 1H), 6.34 (s, 1H), 6.32 (s, 1H), 4.11 (d, $J = 10.3$ Hz, 1H), 3.50 (s, 3H), 3.44 (td, $J = 9.6, 6.4$ Hz, 1H), 3.00 – 2.90 (m, 2H), 2.36 – 2.24 (m, 4H), 1.50 (s, 3H) ppm. $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 185.1, 162.9, 158.8, 150.9, 135.5, 133.2, 110.2, 109.1, 105.2, 82.2, 76.8 (CH, dept 135), 75.8, 57.2, 30.8, 22.6, 19.7 ppm. IR ν_{max} 3554, 2920, 1633, 1604, 1426, 1364, 1200, 1071, 796 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{16}\text{H}_{18}\text{O}_5$ $[\text{M}]^+$: 290.1154, found 290.1158.



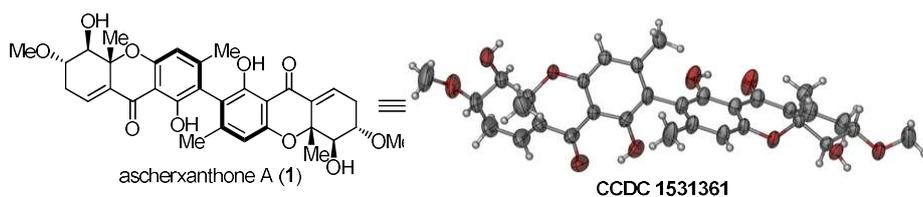
Tetrahydroxanthone 23. To a solution of **10** (81.2 mg, 0.28 mmol, 1 equiv) in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (5:1, 2.8 mL) was added CaCO_3 (205.5 mg, 2 mmol, 7 equiv) and $\text{Me}_3\text{NBnICl}_2$ (97.7 mg, 2.8 mmol, 1 equiv) successively, and the solution

was stirred at $14\text{ }^\circ\text{C}$ for 10 h. It was filtered through Celite, concentrated, and purified by silica gel column chromatography (10% to 25% Ethyl acetate-petroleum ether) to give **23** as a yellow solid (109.1 mg, 93%). $R_f = 0.41$ (40% Ethyl acetate-petroleum ether); $[\alpha]_D^{21} = -62.5$ ($c = 0.19$, CHCl_3). $^1\text{H$

NMR (400 MHz, CDCl₃) δ 13.12 (s, 1H), 6.91 (dd, *J* = 5.0, 2.9 Hz, 1H), 6.55 (s, 1H), 4.12 (d, *J* = 10.3 Hz, 1H), 3.50 (s, 3H), 3.44 (td, *J* = 9.6, 6.3 Hz, 1H), 2.96 (td, *J* = 11.7, 5.8 Hz, 1H), 2.95 (s, OH, 1 H), 2.44 (s, 3H), 2.33 (ddd, *J* = 19.9, 9.1, 2.9 Hz, 1H), 1.50 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ 184.6, 161.5, 158.8, 153.3, 134.7, 134.5, 110.4, 105.1, 82.6, 81.1, 76.7, 75.6, 57.3, 30.8, 29.6, 19.7 ppm. IR ν_{max} 3454, 2923, 1582, 1445, 1373, 1265, 1189, 1072, 844 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₆H₁₇IO₅ [M]⁺: 416.0121, found 416.0117.



To a dried 10 mL Schlenk tube was added **23** (109.1 mg, 0.26 mmol, 1 equiv), Pd(OAc)₂ (11.6 mg, 0.05 mmol, 0.2 equiv), (Bpin)₂ (46.8 mg, 0.18 mmol, 0.7 equiv), K₃PO₄ (170.5 mg, 0.8 mmol, 3 equiv), then it was pumped and replaced with N₂ atmosphere for three times, 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (SPhos) (43.0 mg, 0.1 mmol, 0.4 equiv) was added under N₂ atmosphere. After THF/H₂O (4:1, 3 mL) was added, the solution was subjected to three freeze-pump-thaw cycles using liquid nitrogen to degas the solution, then the mixture was heated to 70 °C and remained for 22.5 h. The solution was cooled to 15 °C, it was quenched by saturated aqueous NH₄Cl (2 mL). The mixture was extracted with EtOAc (10 mL×3). The combined organic phase was washed with brine (15 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated, and purified by silica gel column chromatography (25% to 50% Ethyl acetate-petroleum ether) to give **10** (33.4 mg, 44%) and dimeric products (35.5 mg, 47%) which were further purified by preparative HPLC (SFC, Column: Daicel CHIRALCEL OD-H, 5 μm, 30 mm×250 mm, MeOH + 0.3% FA + CO₂, flow rate: 65 g/min). Ascherxanthone A (**1**) was obtained as a yellow single crystal from the CH₂Cl₂/hexane solution. *Atrop*-ascherxanthone A (**25**) was obtained as a yellow single crystal from the CDCl₃/hexane solution.

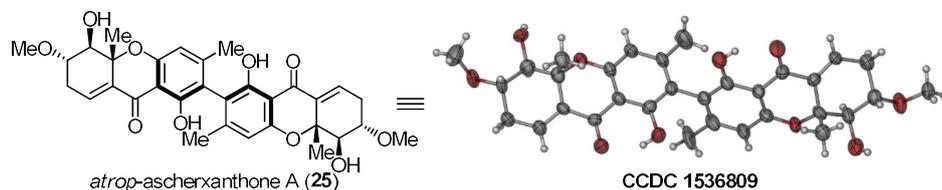


Ascherxanthone A (1).

$R_f = 0.16$ (50% Ethyl acetate -petroleum ether);

$[\alpha]_D^{18} = +137.1$ ($c = 0.645$,

CHCl_3) [Previous report in lit. $[\alpha]_D^{24} = +227$ ($c = 0.2$, CHCl_3), value measured in 2007 by the same group $[\alpha]_D^{27} = +88.3$ ($c = 0.2$, CHCl_3), sample from Prof. Isaka (8:1 mixture of ascherxanthone A and *atrop*-ascherxanthone A) $[\alpha]_D^{18} = +86.1$ ($c = 0.1$, CHCl_3)]. ^1H NMR (500 MHz, CDCl_3) δ 12.35 (s, 2H), 6.87 (dd, $J = 5.0, 2.9$ Hz, 2H), 6.51 (s, 2H), 4.14 (d, $J = 10.2$ Hz, 2H), 3.52 (s, 6H), 3.48 (ddd, $J = 10.2, 9.1, 6.4$ Hz, 2H), 3.01 (br, OH, 2H), 2.96 (ddd, $J = 19.7, 6.4, 5.0$ Hz, 2H), 2.34 (ddd, $J = 19.7, 9.1, 2.9$ Hz, 2H), 2.09 (s, 6H), 1.58 (s, 6H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 185.3 (2 C), 160.5 (2 C), 158.2 (2 C), 150.8 (2 C), 135.6 (2 C), 133.3 (2 C), 115.9 (2 C), 109.5 (2 C), 105.2 (2 C), 82.2 (2 C), 76.8 (CH, dept 135, 2 C), 75.9 (2 C), 57.3 (2 C), 30.8 (2 C), 21.0 (2 C), 20.0 (2 C) ppm. IR ν_{max} 3454, 2920, 1597, 1371, 1263, 1174, 1087, 801 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{32}\text{H}_{34}\text{O}_{10}$ $[\text{M}]^+$: 578.2152, found 578.2154.



***Atrop*-ascherxanthone**

A (25). $R_f = 0.16$ (50% Ethyl acetate

-petroleum ether); $[\alpha]_D^{19}$

$= -251.7$ ($c = 0.265$, CHCl_3) [value measured in 2007 by Prof. Isaka (1.4:1 mixture of ascherxanthone A and *atrop*-ascherxanthone A) $[\alpha]_D^{27} = -56.6$ ($c = 0.2$, CHCl_3)]. ^1H NMR (500 MHz, CDCl_3) δ 12.46 (s, 2H), 6.89 (dd, $J = 5.0, 2.9$ Hz, 2H), 6.52 (s, 2H), 4.15 (d, $J = 10.2$ Hz, 2H), 3.53 (s, 6H), 3.48 (ddd, $J = 10.2, 9.1, 6.4$ Hz, 2H), 2.97 (br, OH, 2H), 3.02 – 2.92 (m, 2H), 2.34 (ddd, $J = 19.7, 9.1, 2.9$ Hz, 2H), 2.02 (s, 6H), 1.59 (s, 6H) ppm. ^{13}C NMR (125 MHz, CDCl_3) δ 185.3 (2 C), 160.4 (2 C), 158.3 (2 C), 150.9 (2 C), 135.6 (2 C), 133.4 (2 C), 115.9 (2 C), 109.7 (2 C), 105.3 (2 C), 82.4 (2 C), 76.8 (CH, dept 135, 2C), 75.9 (2 C), 57.3 (2 C), 30.9 (2 C), 21.0 (2 C), 20.0 (2 C) ppm. IR ν_{max} 3578, 2913, 1617, 1406, 1262, 1175, 1087, 827 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{32}\text{H}_{34}\text{O}_{10}$ $[\text{M}]^+$: 578.2152, found 578.2157.

Reference:

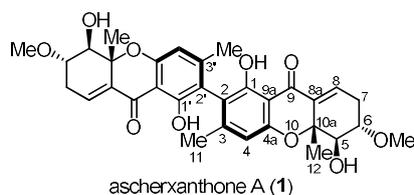
- [1] P. S. Wang, P. Liu, Y. J. Zhai, H. C. Lin, Z. Y. Han, L. Z. Gong, *J. Am. Chem. Soc.* **2015**, *137*, 12732-12735.

Note: During our synthesis, we found the ^1H and ^{13}C NMR spectroscopic data of our synthetic ascherxanthone A have slight differences with the previously reported data by Prof. Isaka. So we contacted with Prof. Isaka. We really appreciate that Prof. Isaka generously response us and also sent us the natural samples. We rechecked their NMR spectrum and optical rotations which matched with our synthetic sample. We also found that the spectral and physical data of the minor coupling isomer, *atrop*-ascherxanthone A (**25**), matched with the minor component of the natural sample. The structure of *atrop*-ascherxanthone A was also confirmed by X-ray diffraction analysis. Based on these results, we concluded that *atrop*-ascherxanthone A also exists in the same natural source as ascherxanthone A.

The following tables itemize the data analysis of the previously reported data, sample from Prof. Isaka and our synthetic ascherxanthone A and *atrop*-ascherxanthone A.

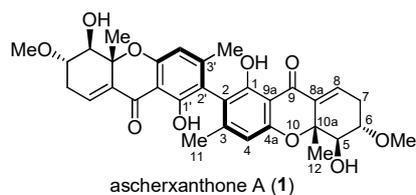
Comparison of NMR spectroscopic data of natural and synthetic ascherxanthone A:

Table 1. Comparison of ¹H NMR spectroscopic data of natural and synthetic ascherxanthone A.



position	previously reported ¹ H NMR δ ¹ H [ppm; mult; <i>J</i> (Hz)] 500 MHz, CDCl ₃	sample from Prof. Isaka δ ¹ H [ppm; mult; <i>J</i> (Hz)] 500 MHz, CDCl ₃	Synthetic sample δ ¹ H [ppm; mult; <i>J</i> (Hz)] 500 MHz, CDCl ₃	deviation (natural–synthetic) $\Delta\delta$ (ppm)
1-OH and 1'-OH	12.36 (2H, s, ^a)	12.35 (s, 2H)	12.35 (s, 2H)	
H-8 and H-8'	6.87 (2H, dd, <i>J</i> = 5.0, 2.8 Hz)	6.87 (dd, <i>J</i> = 5.0, 2.9 Hz, 2H)	6.87 (dd, <i>J</i> = 5.0, 2.9 Hz, 2H)	
H-4 and H-4'	6.51 (2H, s) ^a	6.51 (s, 2H)	6.51 (s, 2H)	
H-5 and H-5'	4.13 (2H, d, <i>J</i> = 10.3 Hz)	4.14 (d, <i>J</i> = 10.3 Hz, 2H)	4.14 (d, <i>J</i> = 10.2 Hz, 2H)	
6-OCH ₃ and 6'-OCH ₃	3.52 (6H, s)	3.52 (s, 6H)	3.52 (s, 6H)	
H-6 and H-6'	3.48 (2H, ddd, <i>J</i> = 10.3, 9.2, 6.2 Hz)	3.47 (ddd, <i>J</i> = 10.3, 9.1, 6.3 Hz, 2H)	3.48 (ddd, <i>J</i> = 10.2, 9.1, 6.4 Hz, 2H)	-0.01
5-OH and 5'-OH		2.97 (br, 2H)	3.01 (br, 2H)	
H-7a and H-7a'	2.97 (2H, ddd, <i>J</i> = 19.4, 6.2, 5.0 Hz)	2.96 (ddd, <i>J</i> = 19.7, 6.3, 5.0 Hz, 2H)	2.96 (ddd, <i>J</i> = 19.7, 6.4, 5.0 Hz, 2H)	
H-7b and H-7b'	2.33 (2H, ddd, <i>J</i> = 19.4, 9.2, 2.8 Hz)	2.34 (ddd, <i>J</i> = 19.7, 9.1, 2.9 Hz, 2H)	2.34 (ddd, <i>J</i> = 19.7, 9.1, 2.9 Hz, 2H)	
H-11 and H-11'	2.10 (6H, s)	2.09 (s, 6H)	2.09 (s, 6H)	
H-12 and H-12'	1.59 (6H, s)	1.58 (s, 6H)	1.58 (s, 6H)	

Table 2. Comparison of ^{13}C NMR spectroscopic data of natural and synthetic ascherxanthone A.

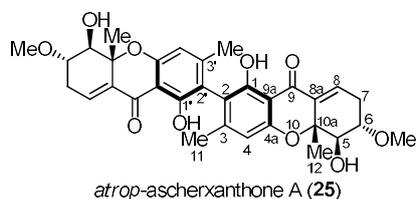


position	previously reported ^{13}C NMR $\delta^{13}\text{C}$ [ppm] 125 MHz, CDCl_3	sample from Prof. Isaka $\delta^{13}\text{C}$ [ppm] 125 MHz, CDCl_3	Synthetic sample $\delta^{13}\text{C}$ [ppm] 125 MHz, CDCl_3	deviation (natural–synthetic) $\Delta\delta$ (ppm)
C-9 and C-9'	185.3	185.3	185.3	
C-1 and C-1'	160.5	160.5	160.5	
C-4a and C-4a'	158.3	158.2	158.2	
C-3 and C-3'	150.8	150.8	150.8	
C-8a and C-8a'	135.6	135.6	135.6	
C-8 and C-8'	133.3	133.24	133.27	-0.03
C-2 and C-2'	115.9	115.9	115.9	
C-4 and C-4'	109.537 ^a	109.537	109.537	
C-9a and C-9a'	105.3	105.2	105.2	
C-10a and C-10a'	82.3	82.2	82.2	
C-6 and C-6'	76.9	76.8 (CH, dept)	76.8 (CH, dept)	
C-5 and C-5'	75.9	75.9	75.9	
6-OCH ₃ and 6'-OCH ₃	57.3	57.3	57.3	
C-7 and C-7'	30.9	30.8	30.8	
C-11 and C-11'	21.0	21.0	21.0	
C-12 and C-12'	20.0	20.0	20.0	

Comparison of NMR spectroscopic data of natural and synthetic *atrop-ascherxanthone A*:

Table 3. Comparison of ¹H NMR spectroscopic data of natural and synthetic *atrop-ascherxanthone*

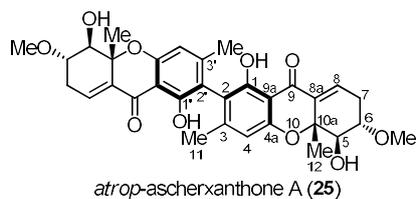
A.



position	sample from Prof. Isaka δ ¹ H [ppm; mult; <i>J</i> (Hz)] 500 MHz, CDCl ₃	Synthetic sample δ ¹ H [ppm; mult; <i>J</i> (Hz)] 500 MHz, CDCl ₃	deviation (natural–synthetic) $\Delta\delta$ (ppm)
1-OH and 1'-OH	12.46 (s, 2H)	12.46 (s, 2H)	
H-8 and H-8'	6.89 (dd, <i>J</i> = 5.0, 2.9 Hz, 2H)	6.89 (dd, <i>J</i> = 5.0, 2.9 Hz, 2H)	
H-4 and H-4'	6.52 (s, 2H)	6.52 (s, 2H)	
H-5 and H-5'	4.15 (d, <i>J</i> = 10.2 Hz, 2H)	4.15 (d, <i>J</i> = 10.2 Hz, 2H)	
6-OCH ₃ and 6'-OCH ₃	3.53 (s, 6H)	3.53 (s, 6H)	
H-6 and H-6'	3.50 – 3.43 (m, 2H)	3.48 (ddd, <i>J</i> = 10.2, 9.1, 6.4 Hz, 2H)	
5-OH and 5'-OH	2.97 (br, 2H)	2.97 (br, 2H)	
H-7a and H-7a'	3.00 – 2.92 (m, 2H)	3.02 – 2.92 (m, 2H)	
H-7b and H-7b'	2.34 (ddd, <i>J</i> = 19.7, 9.1, 2.9 Hz, 2H)	2.34 (ddd, <i>J</i> = 19.7, 9.1, 2.9 Hz, 2H)	
H-11 and H-11'	2.02 (s, 6H)	2.02 (s, 6H)	
H-12 and H-12'	1.59 (s, 6H)	1.59 (s, 6H)	

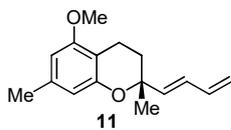
Table 4. Comparison of ^{13}C NMR spectroscopic data of natural and synthetic *atrop*-ascherxanthone

A.

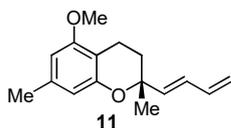
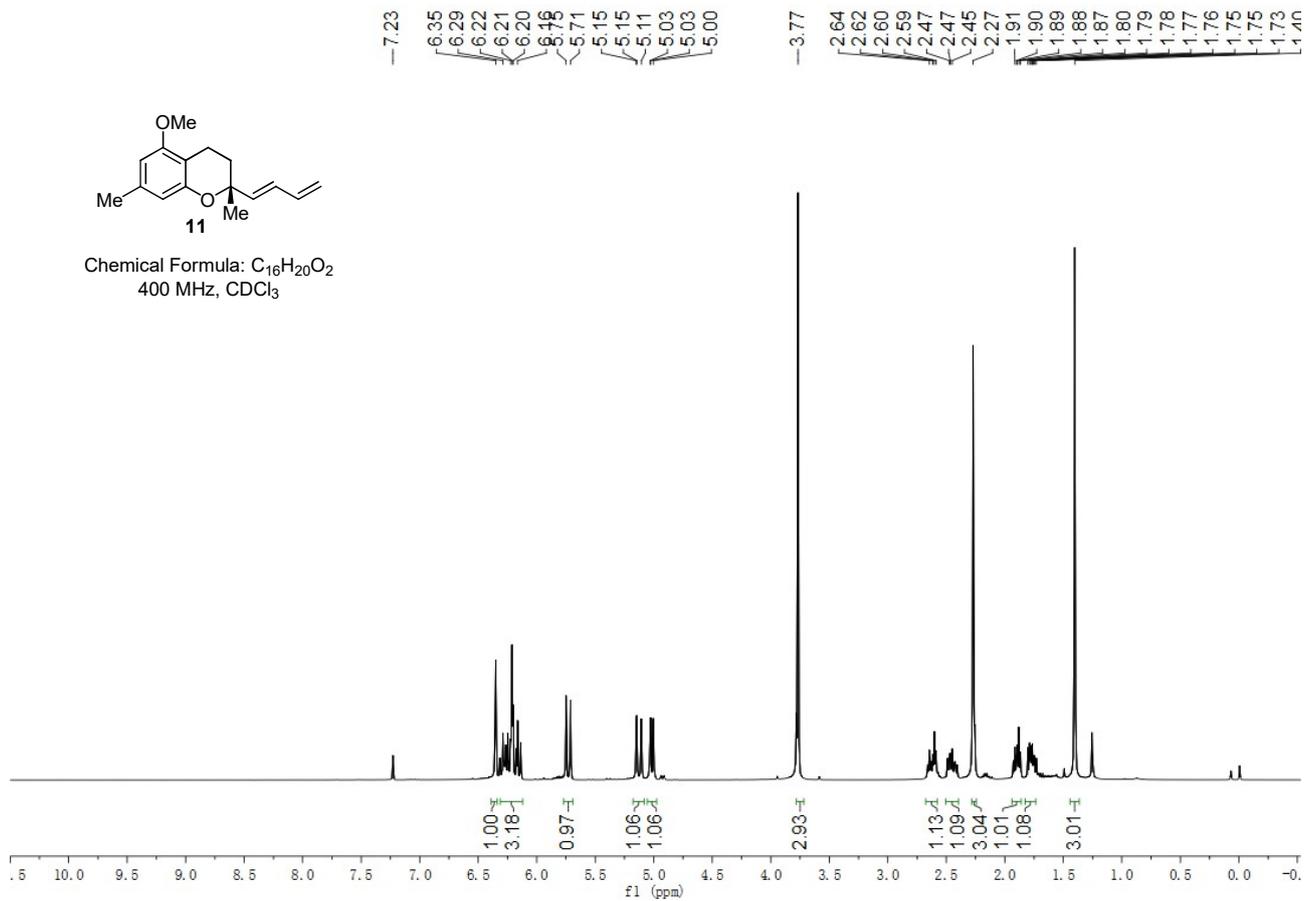


position	sample from Prof. Isaka $\delta^{13}\text{C}$ [ppm] 125 MHz, CDCl_3	Synthetic sample $\delta^{13}\text{C}$ [ppm] 125 MHz, CDCl_3	deviation (natural–synthetic) $\Delta\delta$ (ppm)
C-9 and C-9'	185.3	185.3	
C-1 and C-1'	160.4	160.4	
C-4a and C-4a'	158.3	158.3	
C-3 and C-3'	150.9	150.9	
C-8a and C-8a'	135.6	135.6	
C-8 and C-8'	133.4	133.4	
C-2 and C-2'	115.9	115.9	
C-4 and C-4'	109.7	109.7	
C-9a and C-9a'	105.3	105.3	
C-10a and C-10a'	82.4	82.4	
C-6 and C-6'	76.8 (CH, dept)	76.8 (CH, dept)	
C-5 and C-5'	75.9	75.9	
6-OCH ₃ and 6'-OCH ₃	57.3	57.3	
C-7 and C-7'	30.9	30.9	
C-11 and C-11'	21.0	21.0	
C-12 and C-12'	20.0	20.0	

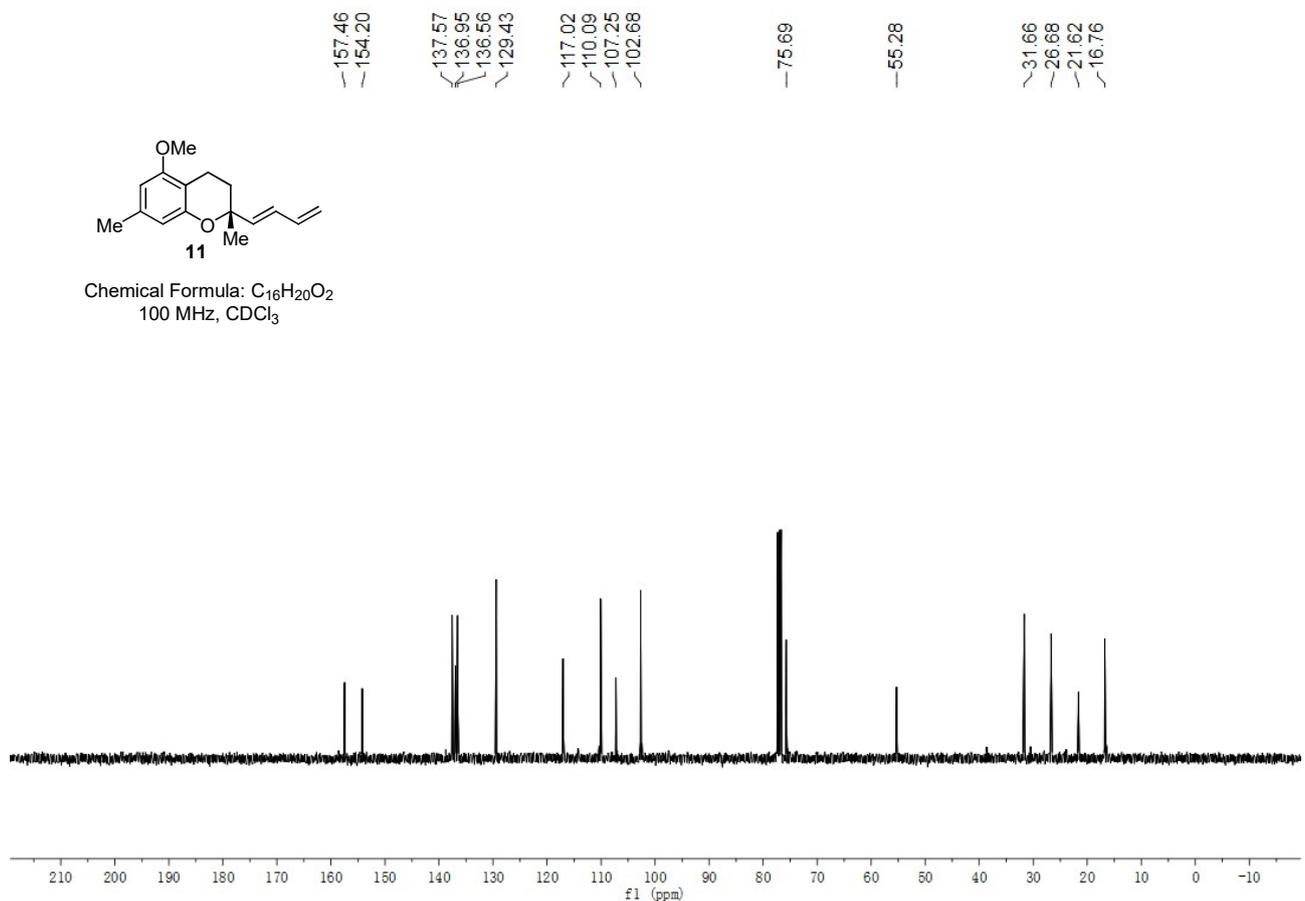
¹H and ¹³C NMR Spectra of the Synthetic Intermediates and Products:

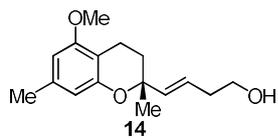


Chemical Formula: C₁₆H₂₀O₂
400 MHz, CDCl₃

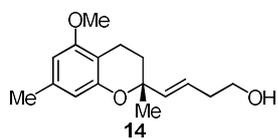
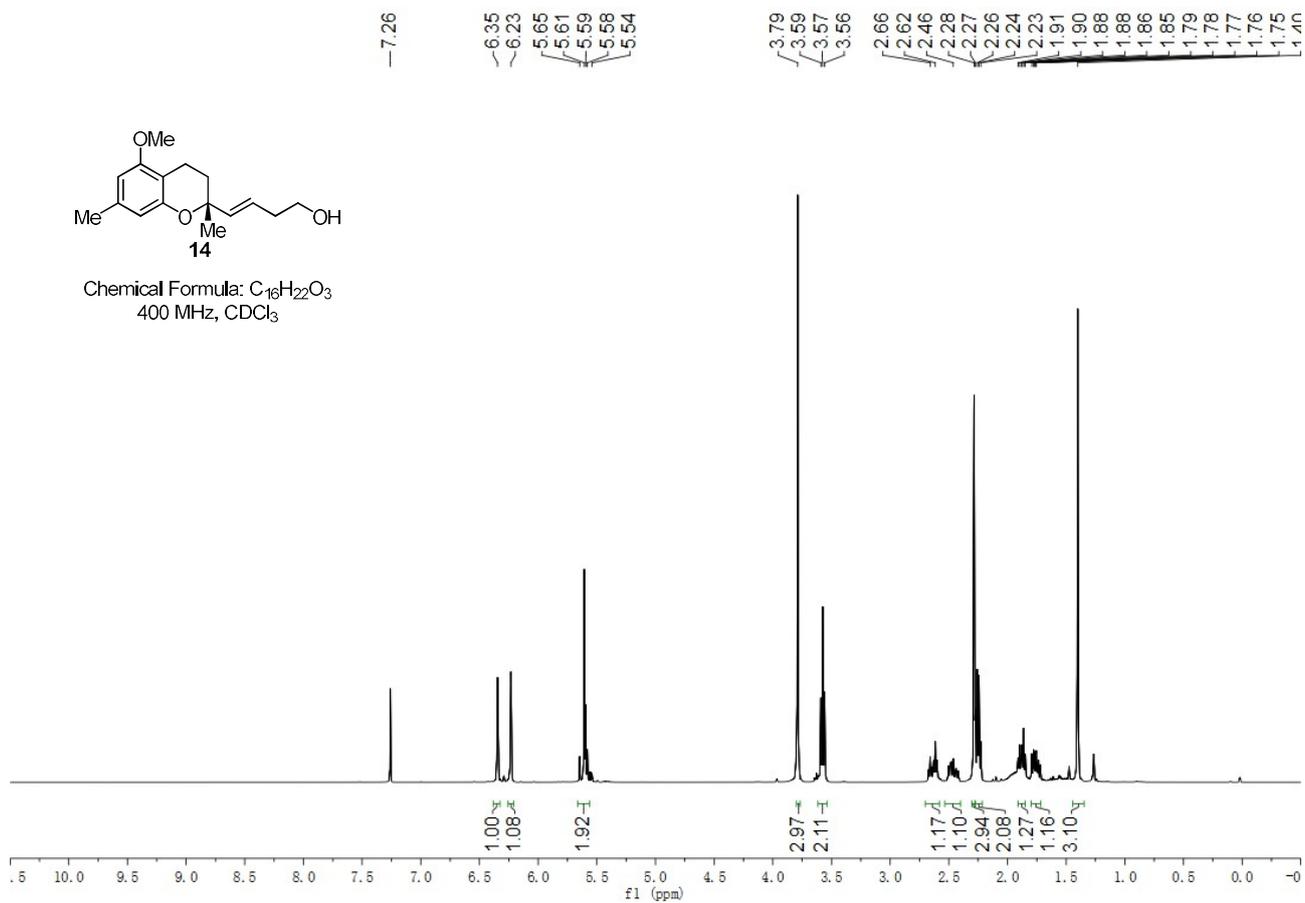


Chemical Formula: C₁₆H₂₀O₂
100 MHz, CDCl₃

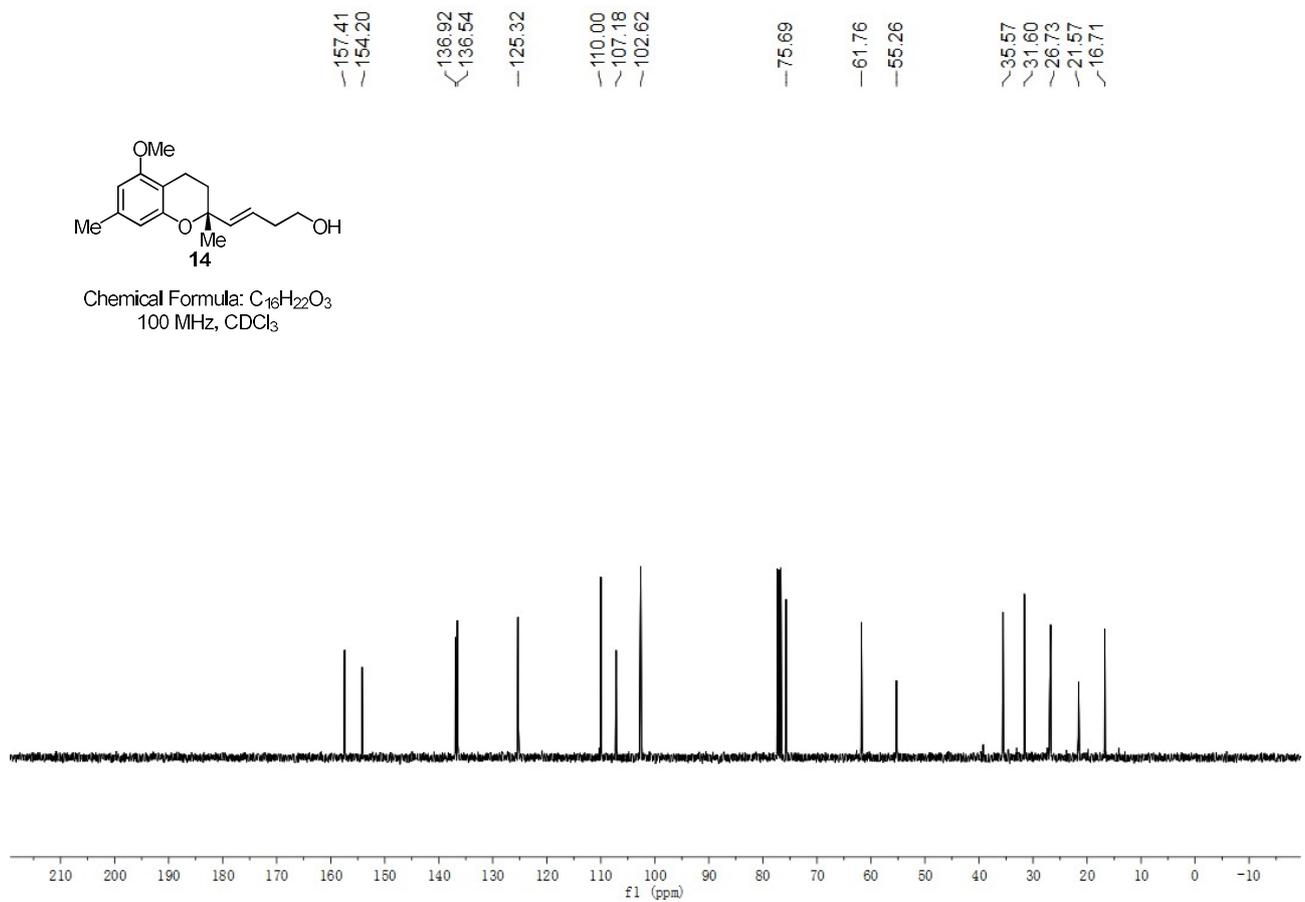




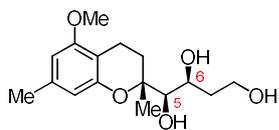
Chemical Formula: C₁₆H₂₂O₃
400 MHz, CDCl₃



Chemical Formula: C₁₆H₂₂O₃
100 MHz, CDCl₃

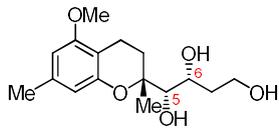


7.26
6.25
4.37
4.36
4.35
3.88
3.87
3.86
3.85
3.84
3.83
3.81
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3.44
3.35
3.17
2.78
2.77
2.76
2.76
2.73
2.73
2.72
2.71
2.54
2.52
2.51
2.49
2.46
2.26
2.19
2.18
2.16
2.14
2.13
2.11
2.06
2.05
2.04
2.04
2.03
2.03
2.02
2.02
2.01
2.01
1.76
1.75
1.74
1.74
1.72
1.72
1.71
1.70
1.69
1.68
1.28



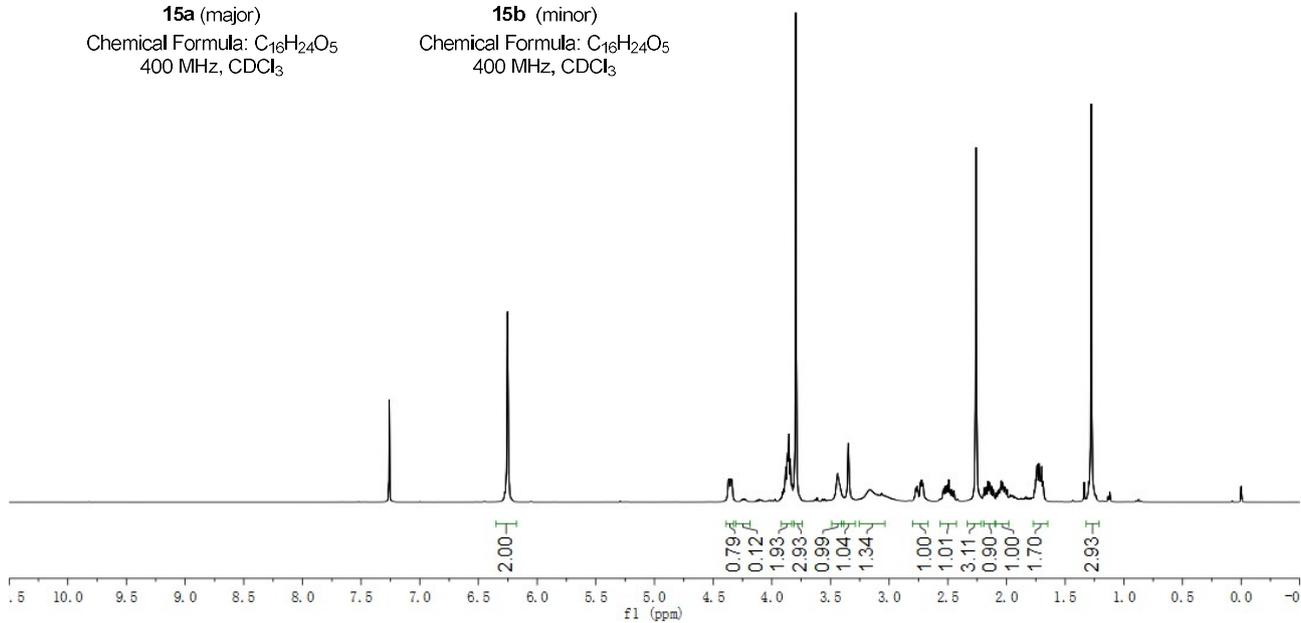
15a (major)

Chemical Formula: C₁₆H₂₄O₅
400 MHz, CDCl₃



15b (minor)

Chemical Formula: C₁₆H₂₄O₅
400 MHz, CDCl₃



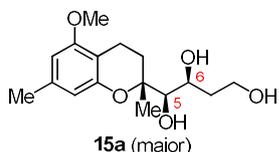
-157.55
-152.91

-137.18

-110.06
-107.13
-103.19

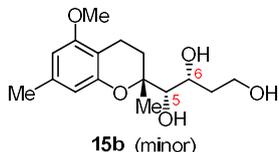
-79.58
-77.10
-69.05
-60.51
-55.32

-36.76
-26.67
-21.52
-19.55
-15.77



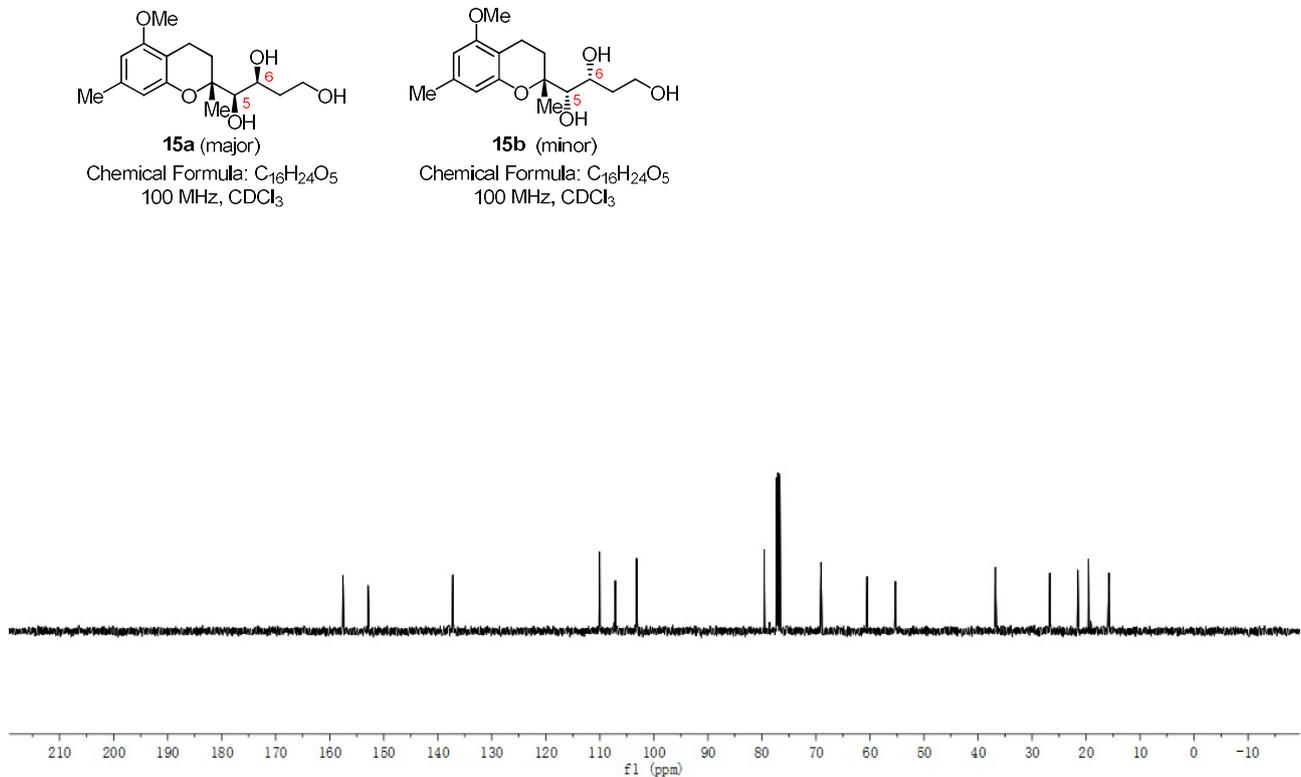
15a (major)

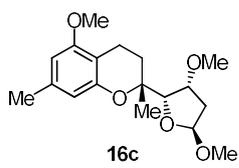
Chemical Formula: C₁₆H₂₄O₅
100 MHz, CDCl₃



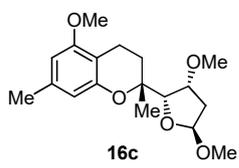
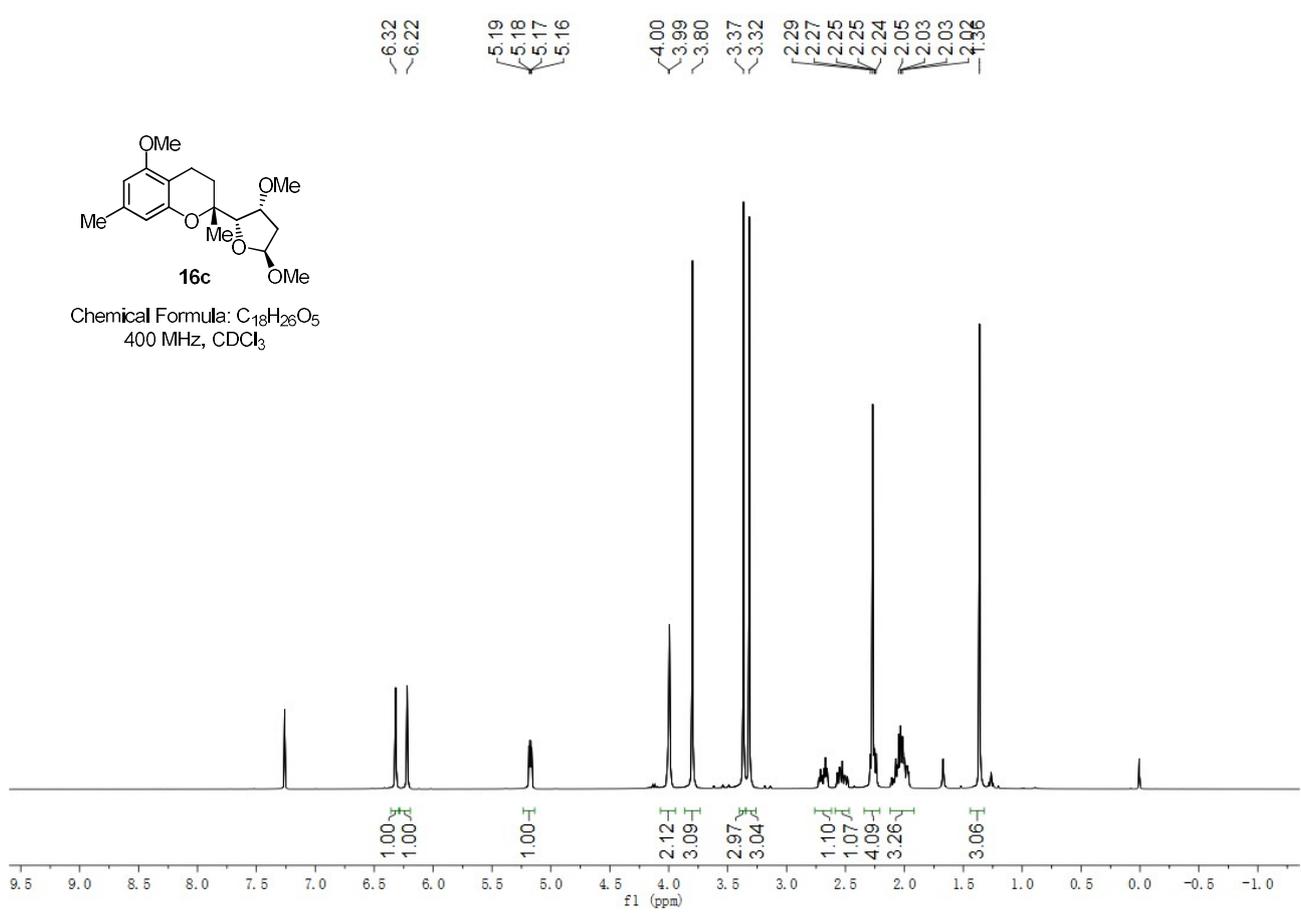
15b (minor)

Chemical Formula: C₁₆H₂₄O₅
100 MHz, CDCl₃

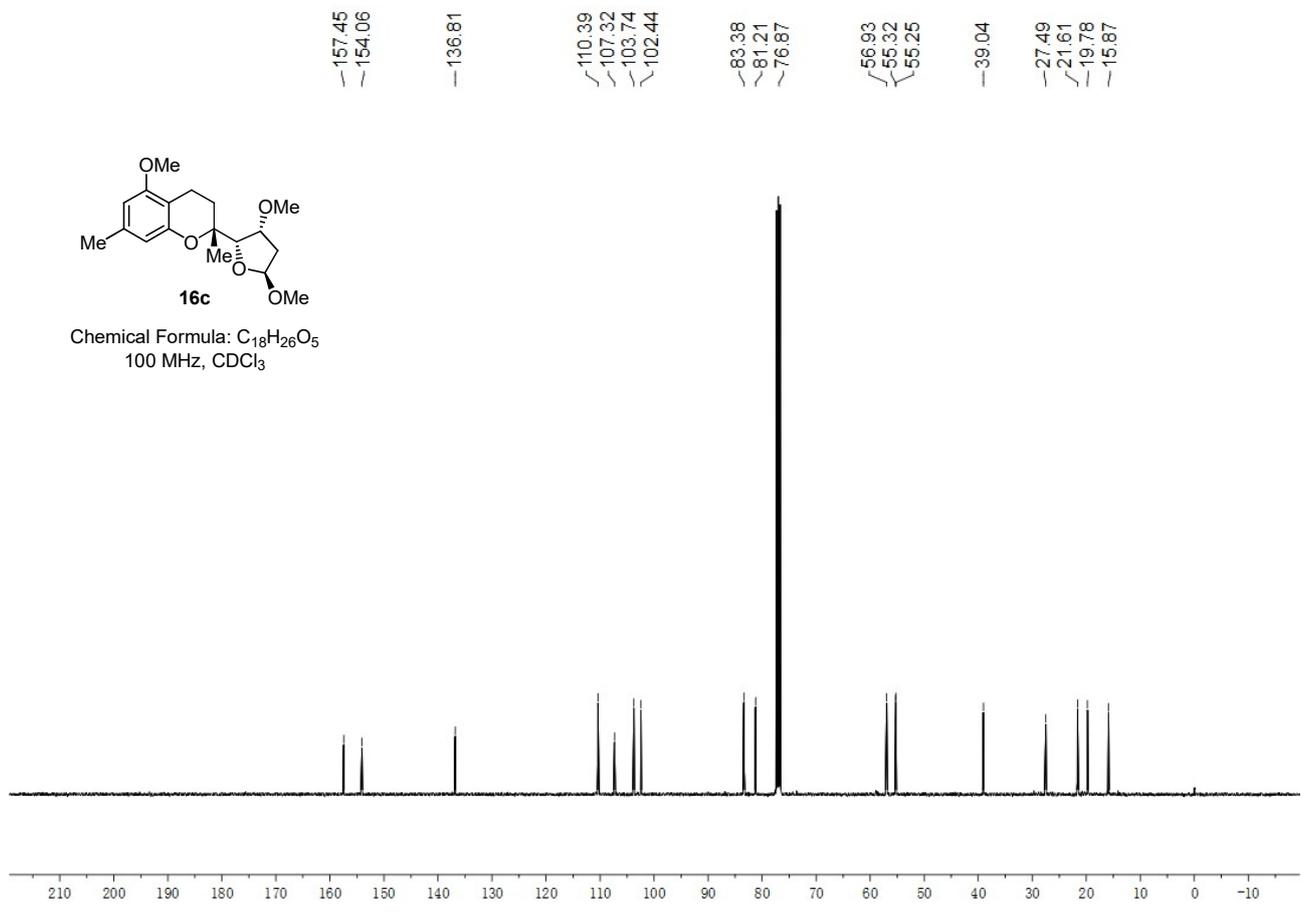


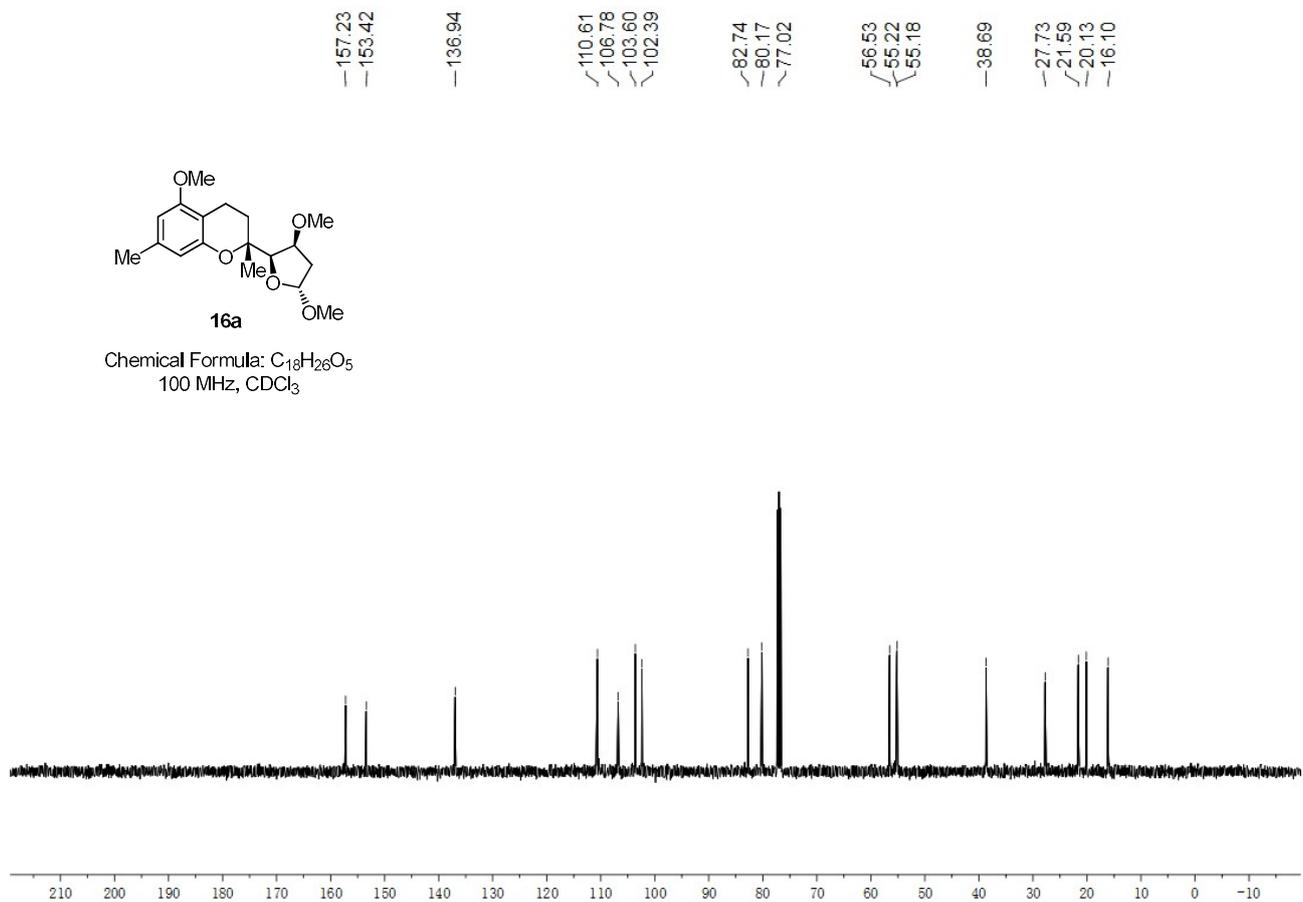
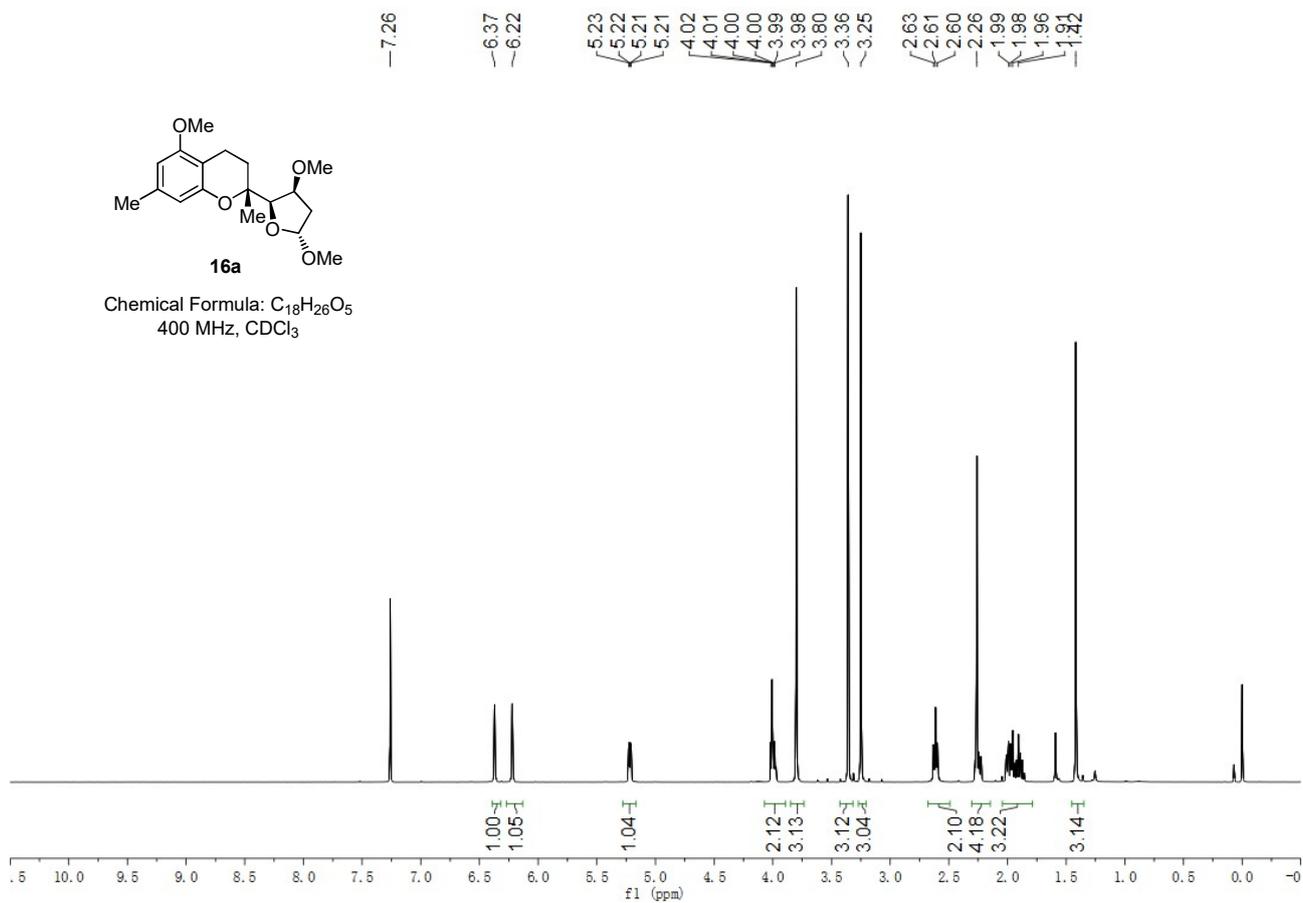


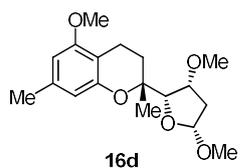
Chemical Formula: C₁₈H₂₆O₅
400 MHz, CDCl₃



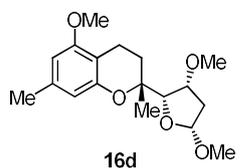
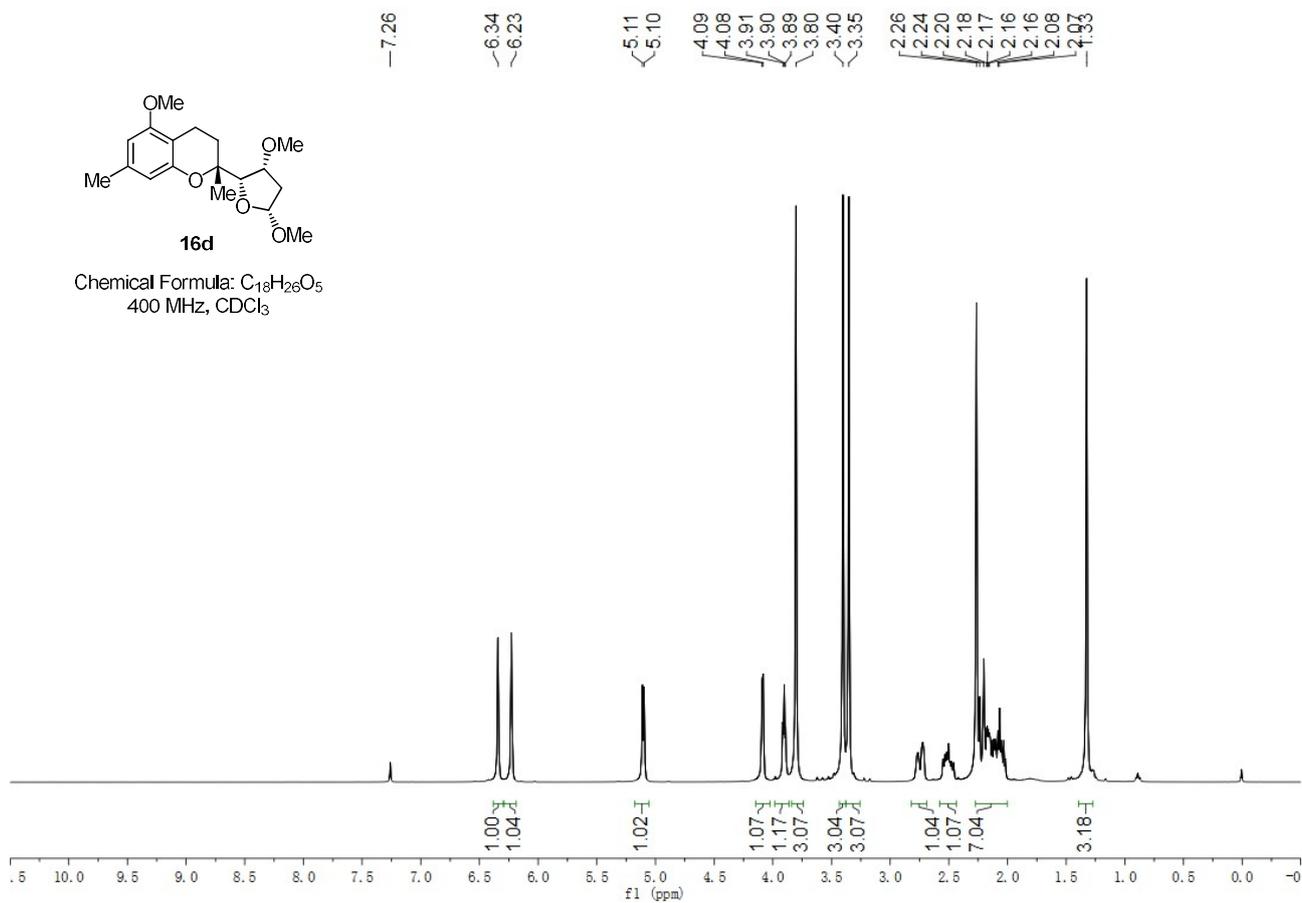
Chemical Formula: C₁₈H₂₆O₅
100 MHz, CDCl₃



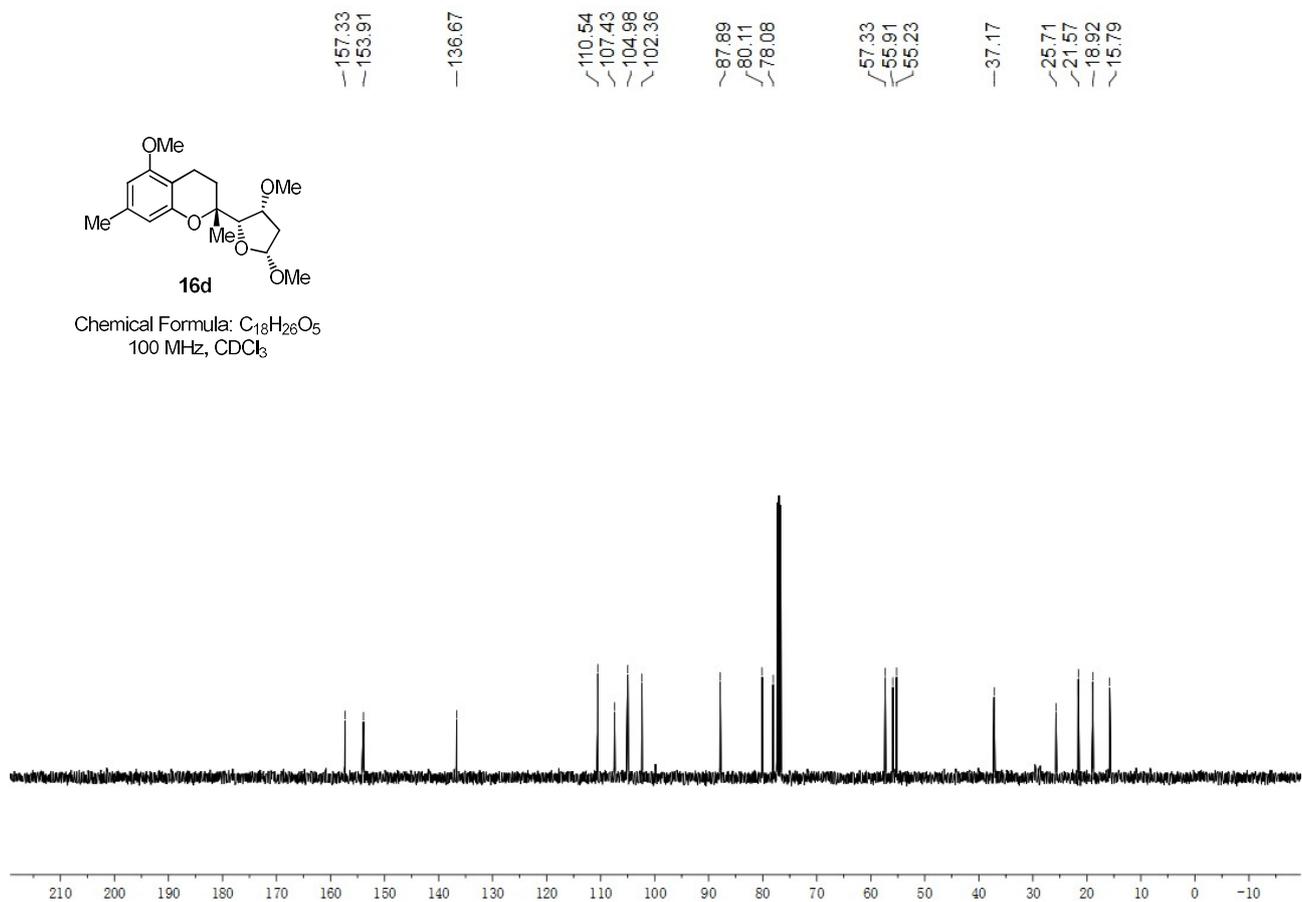


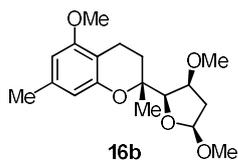


Chemical Formula: C₁₈H₂₆O₅
400 MHz, CDCl₃

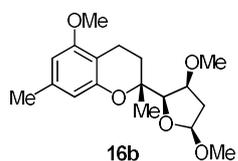
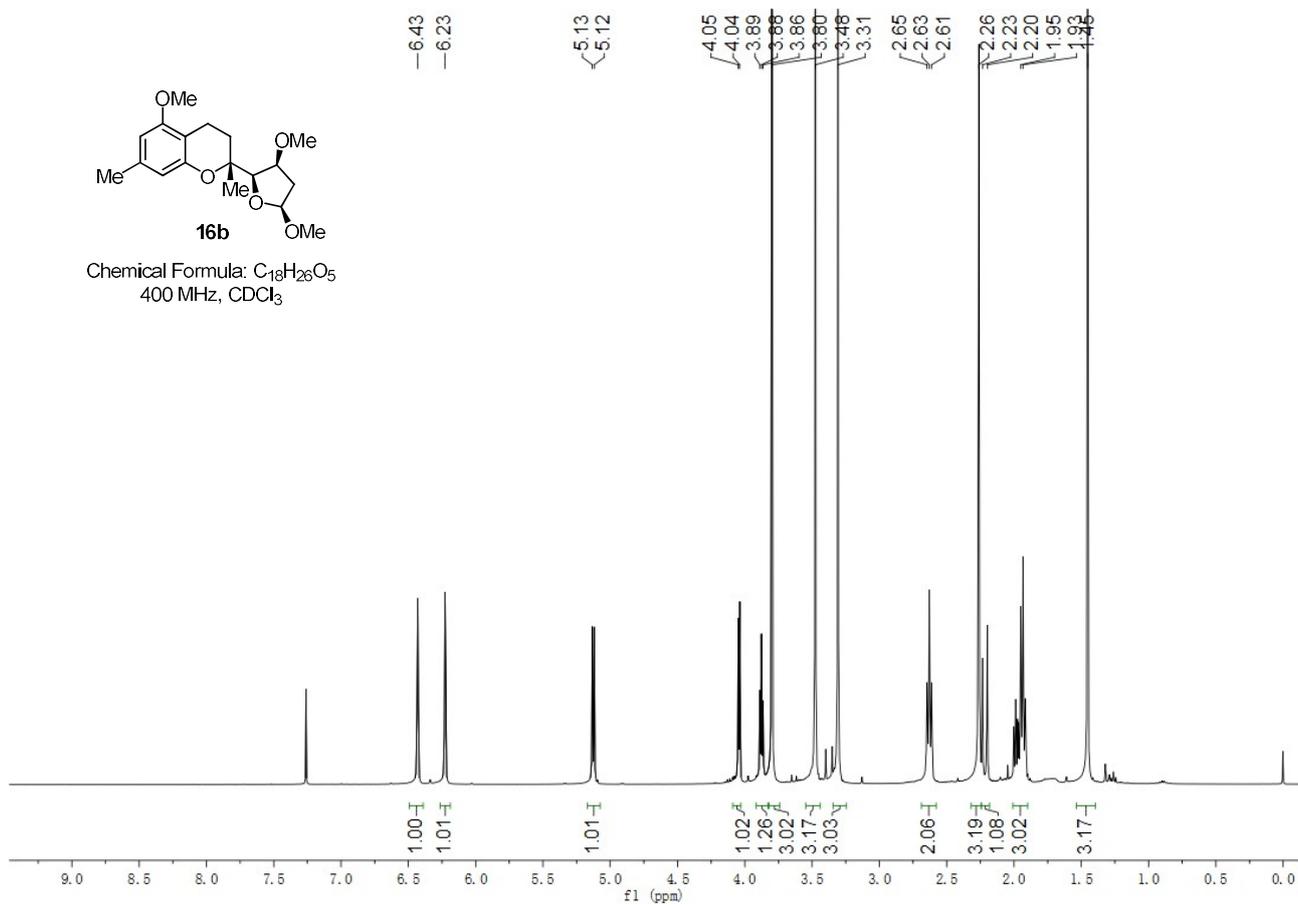


Chemical Formula: C₁₈H₂₆O₅
100 MHz, CDCl₃

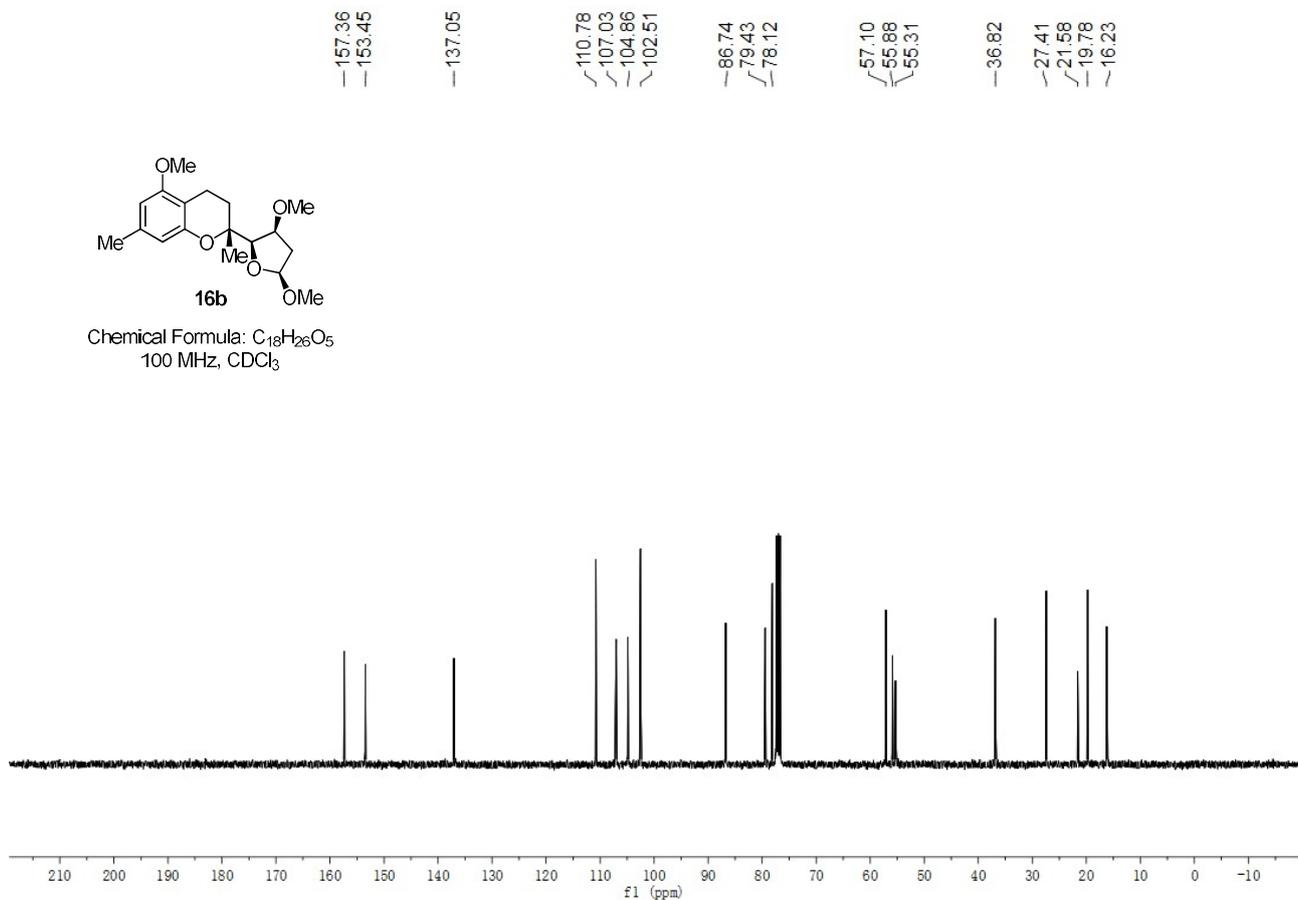


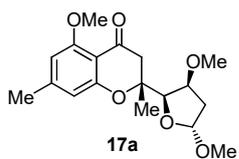


Chemical Formula: C₁₈H₂₆O₅
400 MHz, CDCl₃



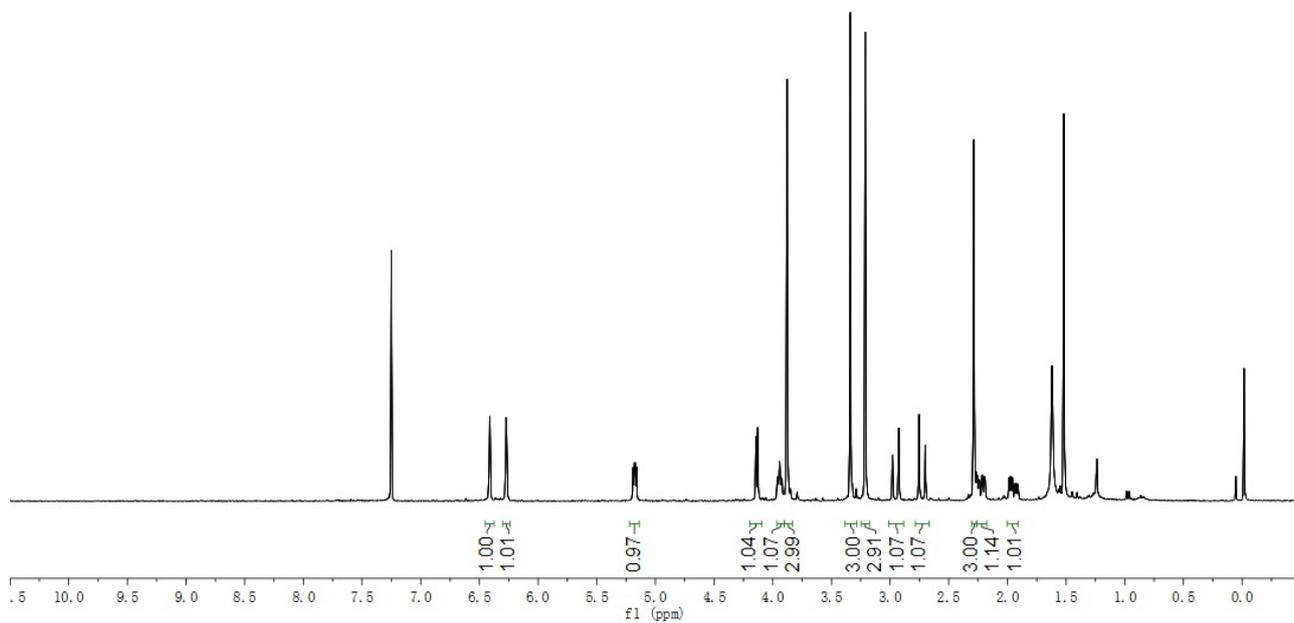
Chemical Formula: C₁₈H₂₆O₅
100 MHz, CDCl₃



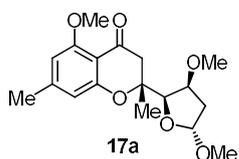


Chemical Formula: C₁₈H₂₄O₆
400 MHz, CDCl₃

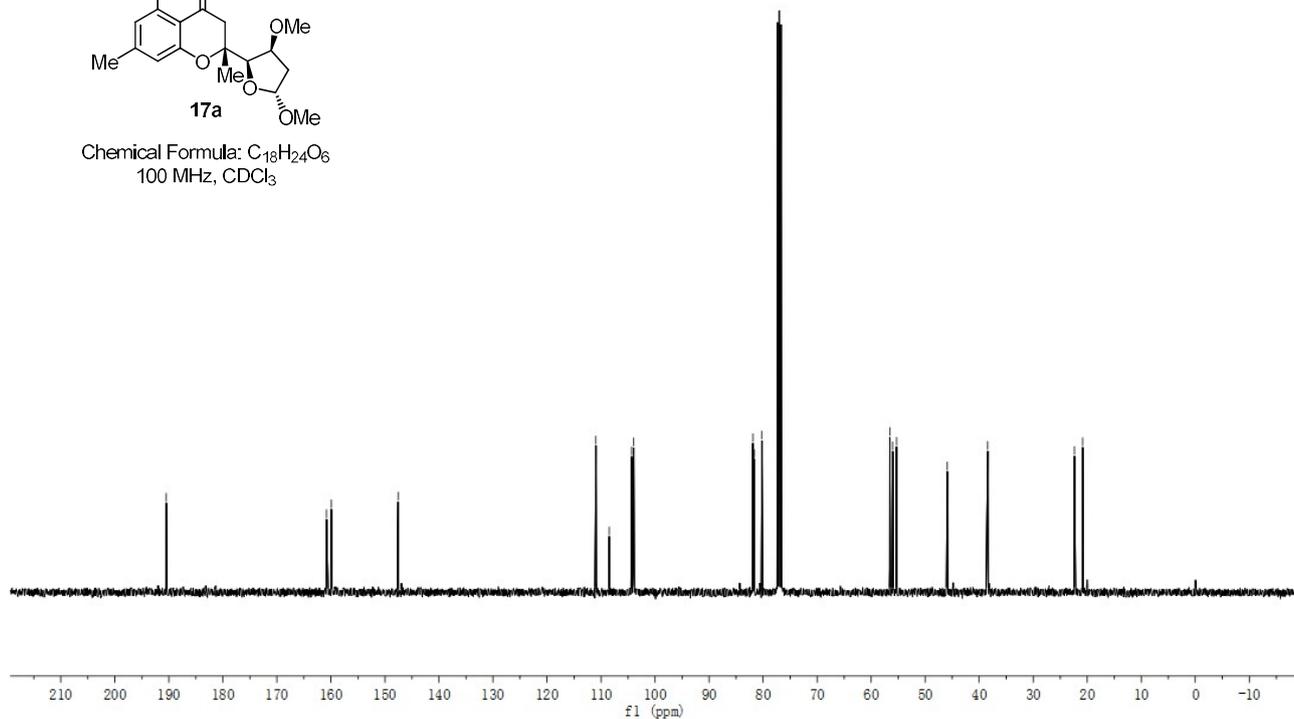
6.41
6.27
5.19
5.18
5.17
5.16
4.14
4.13
3.95
3.94
3.93
3.88
3.34
3.21
2.93
2.75
2.70
2.29
2.27
2.26
1.52

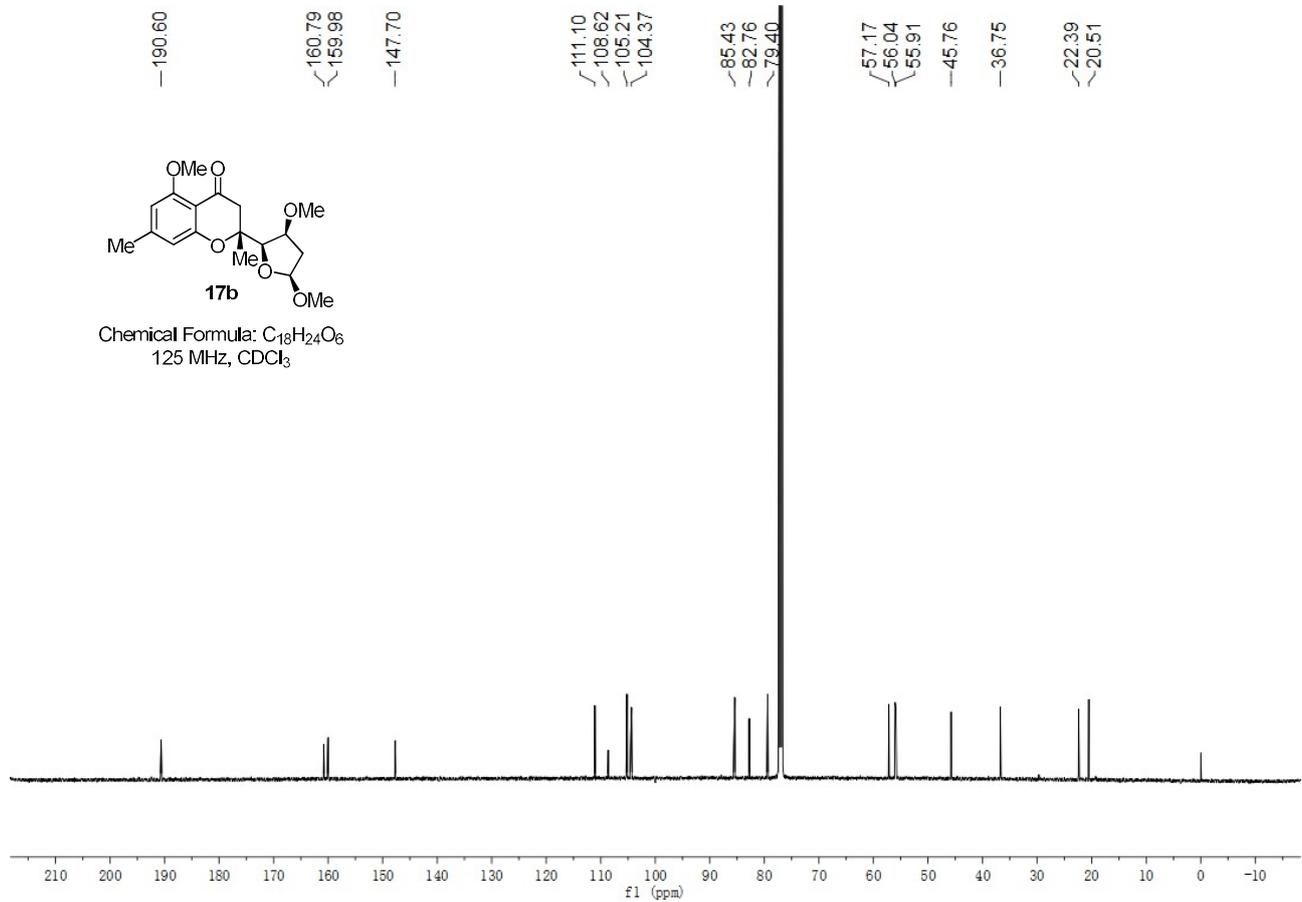
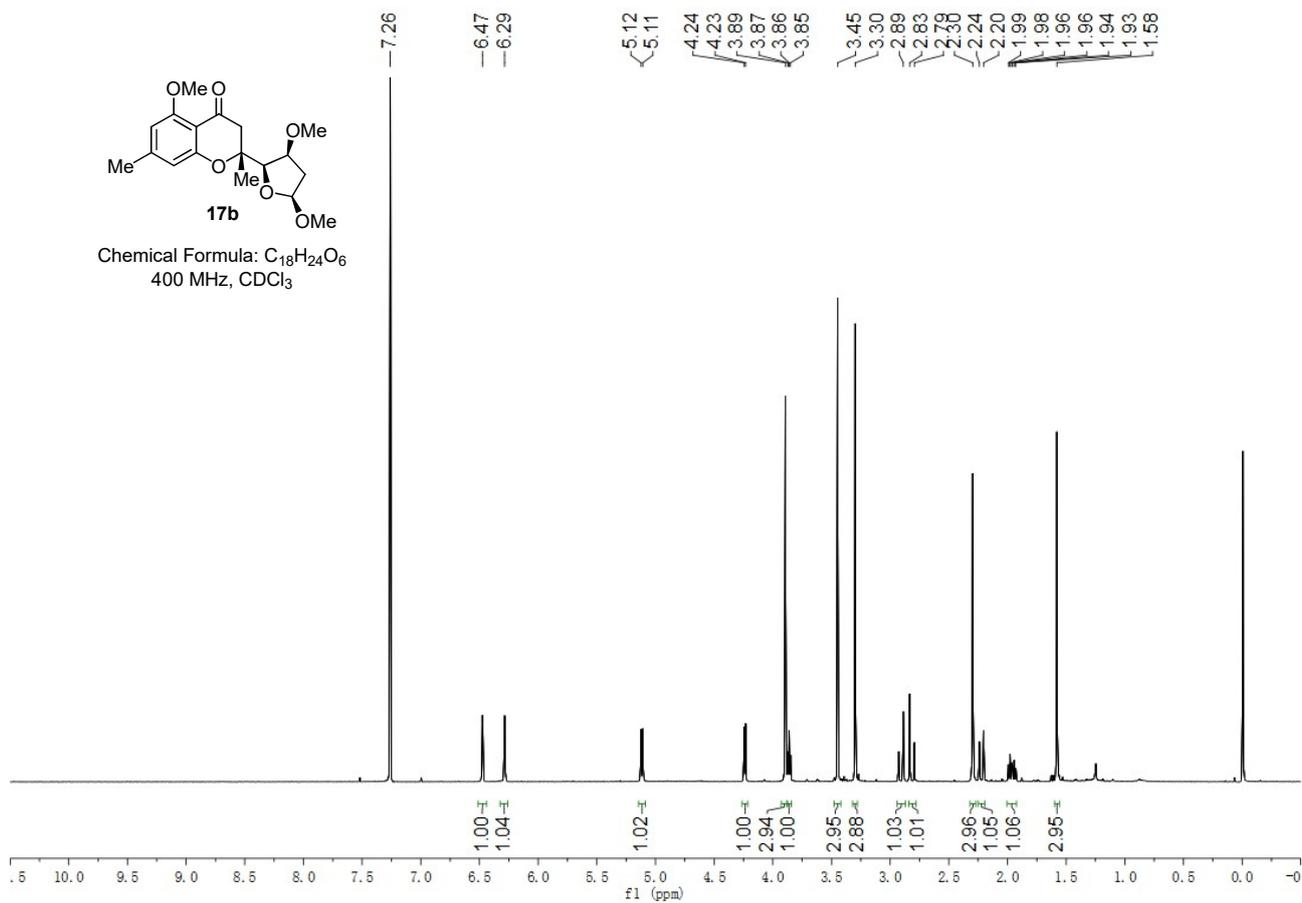


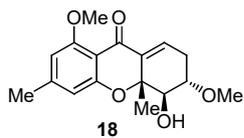
190.48
160.81
159.92
147.55
110.96
108.49
104.33
103.95
81.89
81.65
80.22
56.56
56.01
55.30
45.91
38.43



Chemical Formula: C₁₈H₂₄O₆
100 MHz, CDCl₃

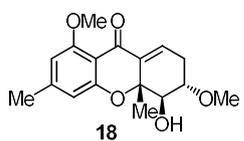
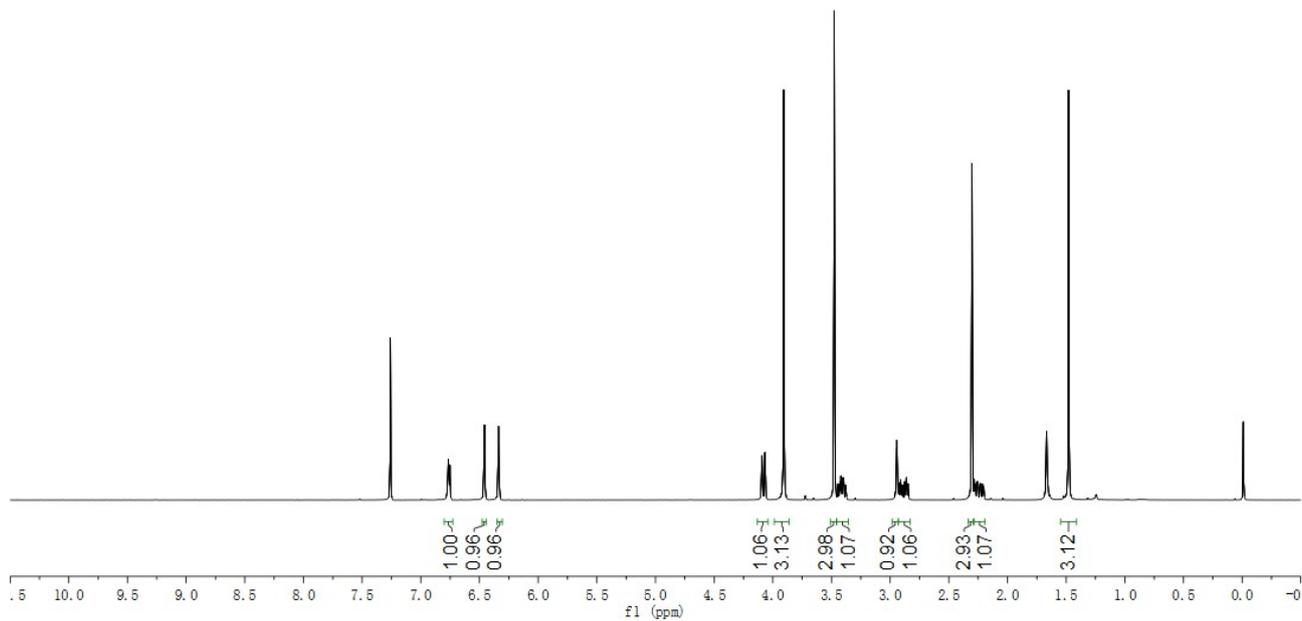






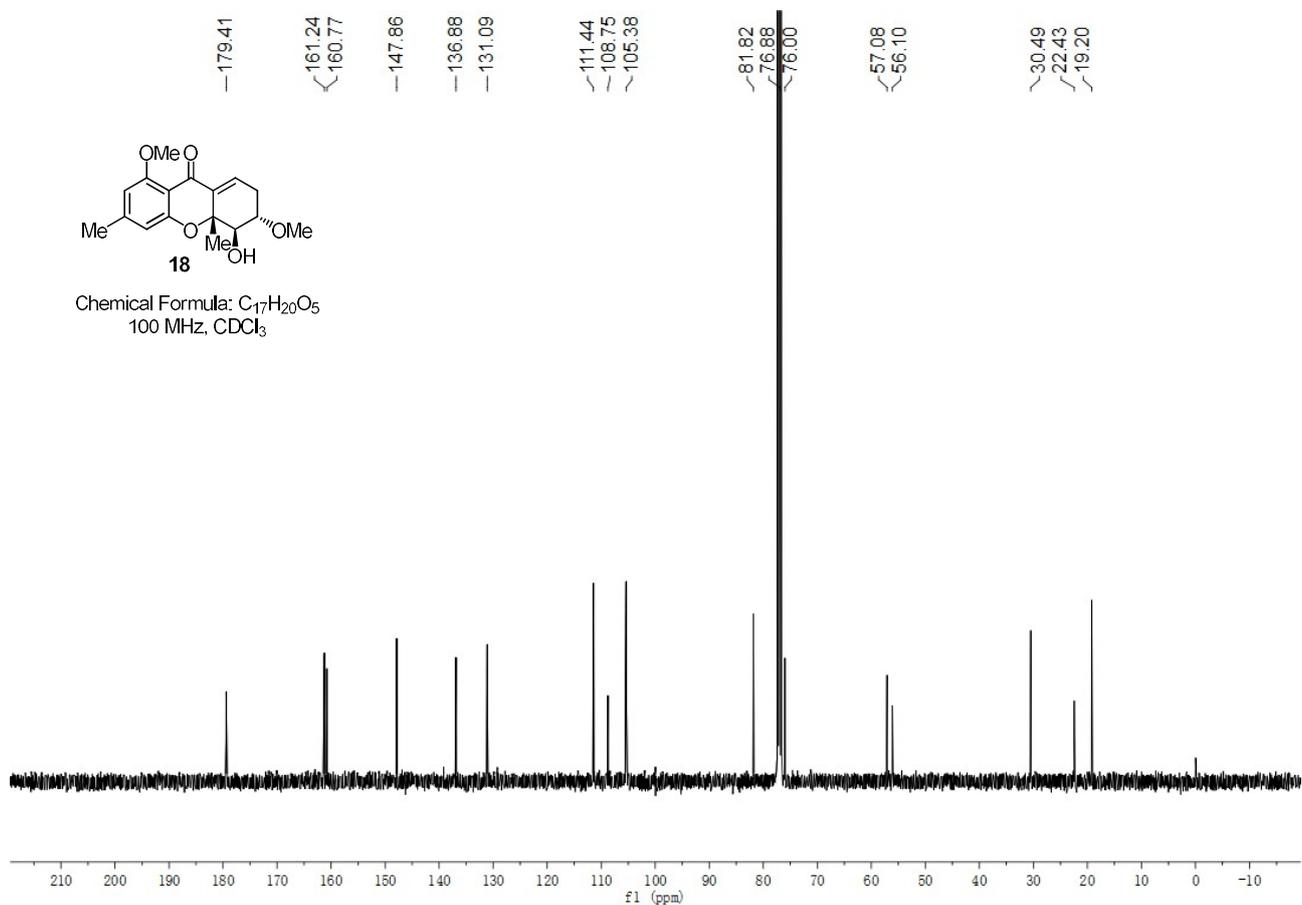
Chemical Formula: C₁₇H₂₀O₅
400 MHz, CDCl₃

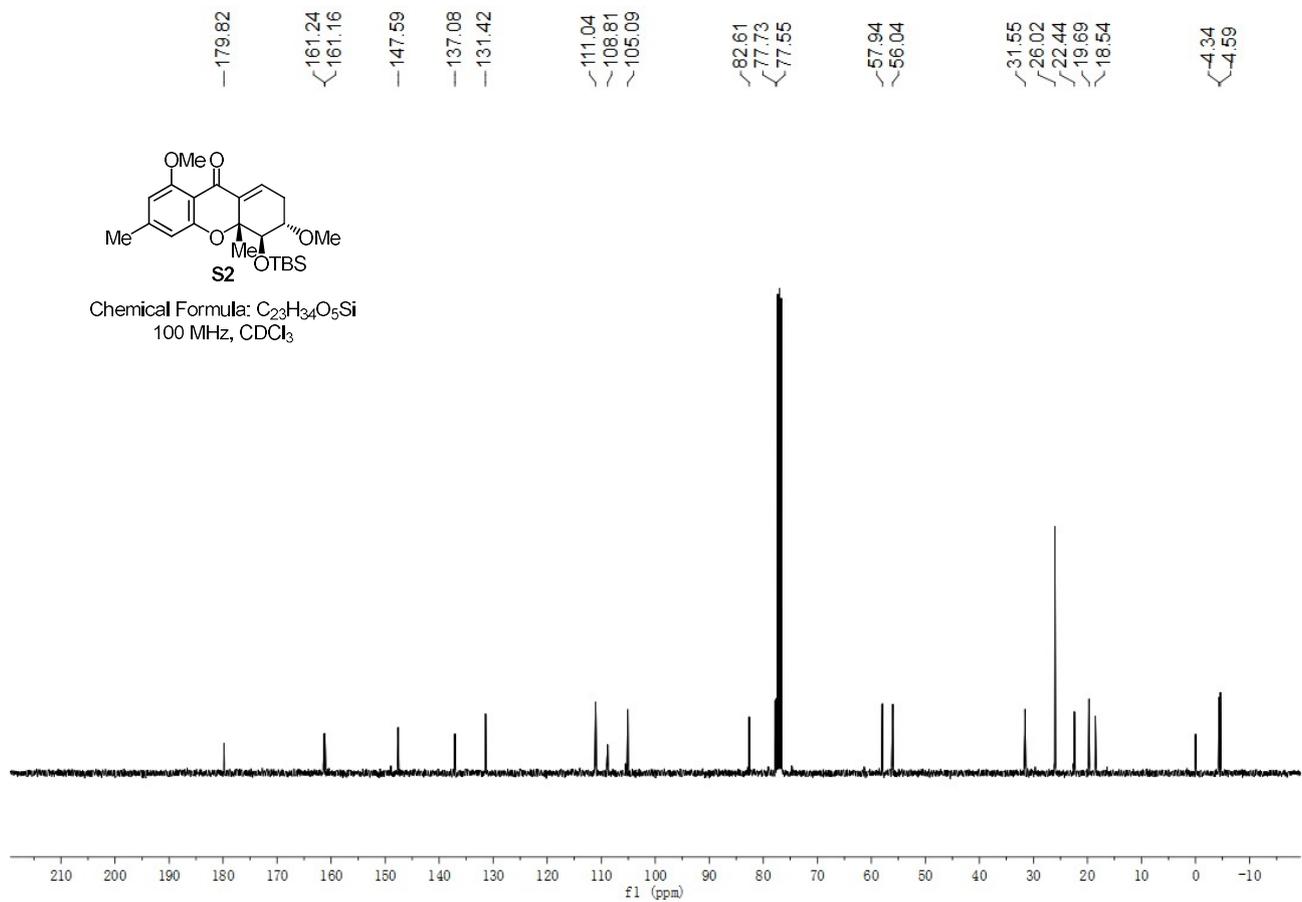
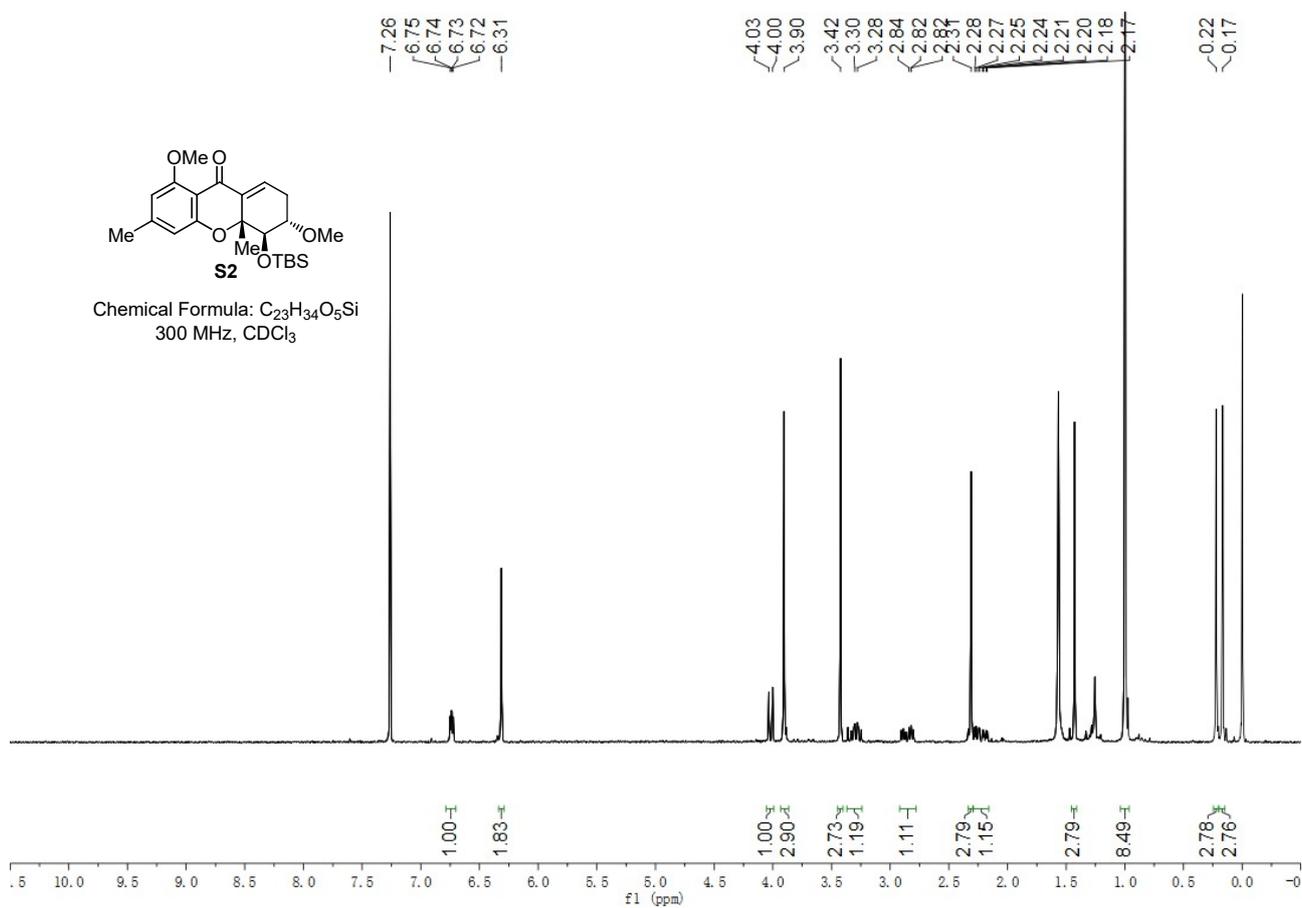
7.26, 6.77, 6.77, 6.76, 6.75, 6.46, 6.46, 6.34, 4.09, 4.07, 3.91, 3.48, 3.42, 2.94, 2.86, 2.86, 2.30, 2.28, 2.28, 2.26, 2.26, 1.48

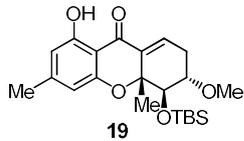


Chemical Formula: C₁₇H₂₀O₅
100 MHz, CDCl₃

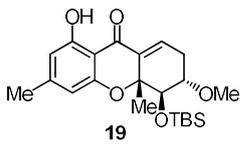
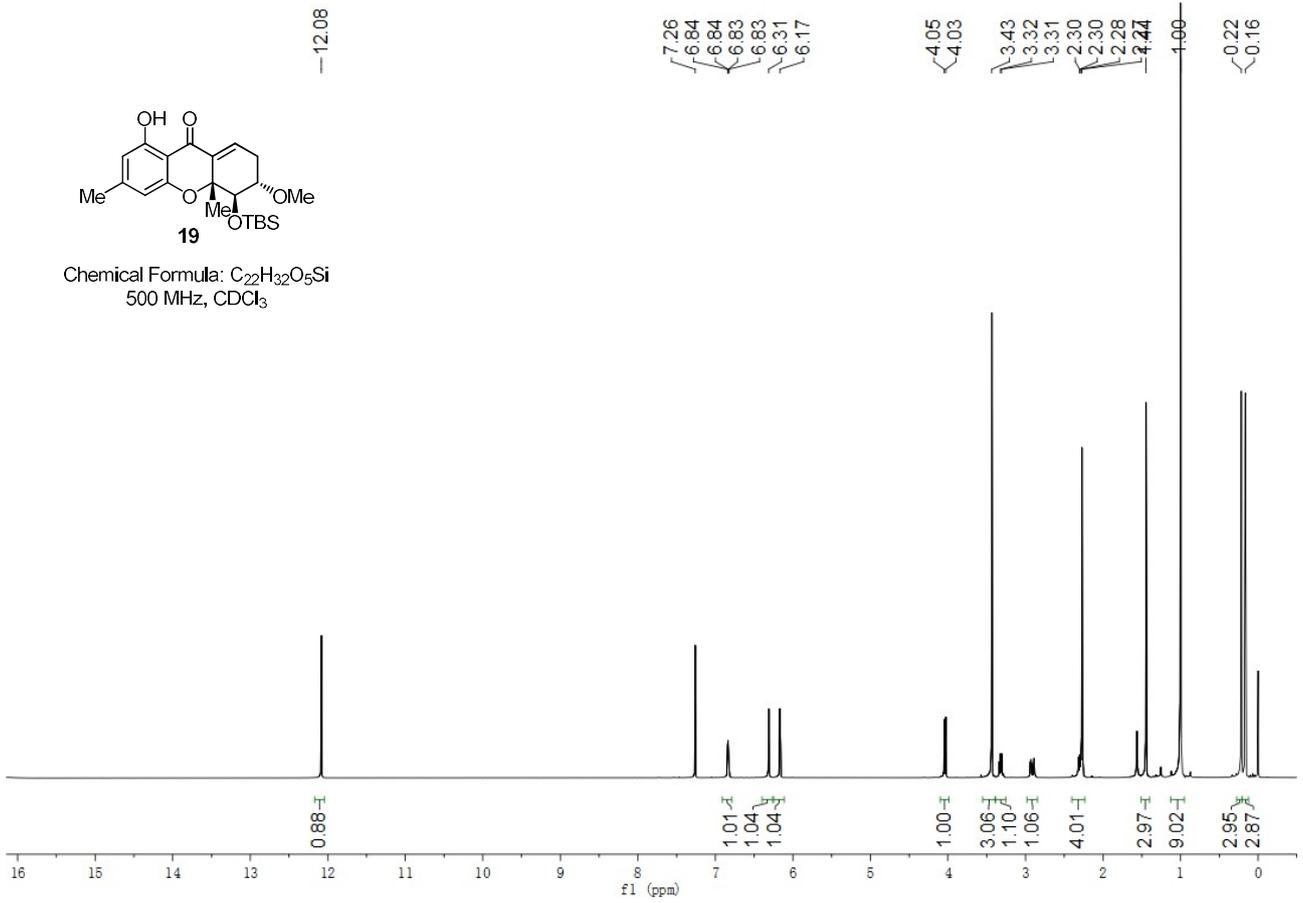
179.41, 161.24, 160.77, 147.86, 136.88, 131.09, 111.44, 108.75, 105.38, 81.82, 76.88, 76.00, 57.08, 56.10, 30.49, 22.43, 19.20



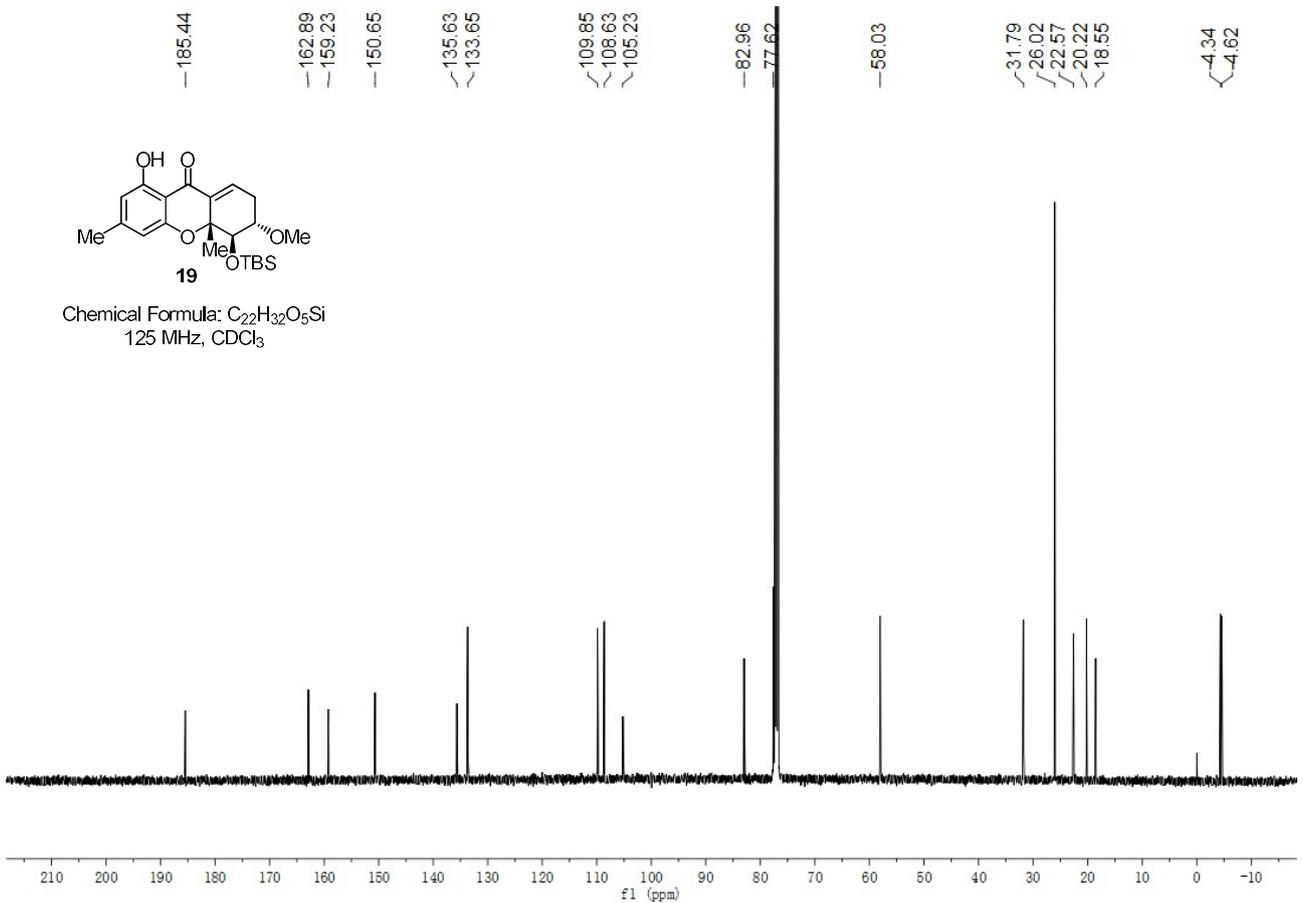


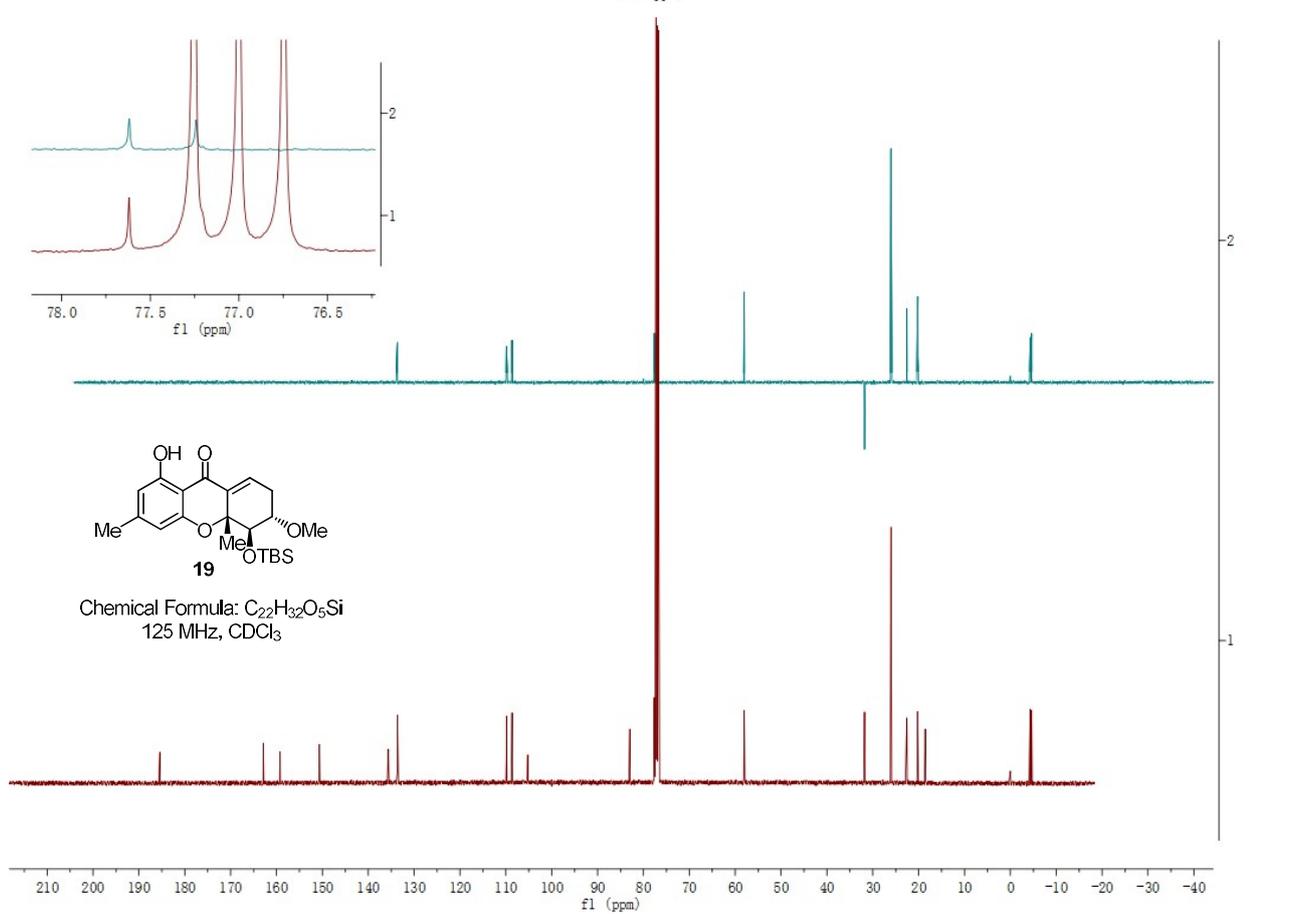
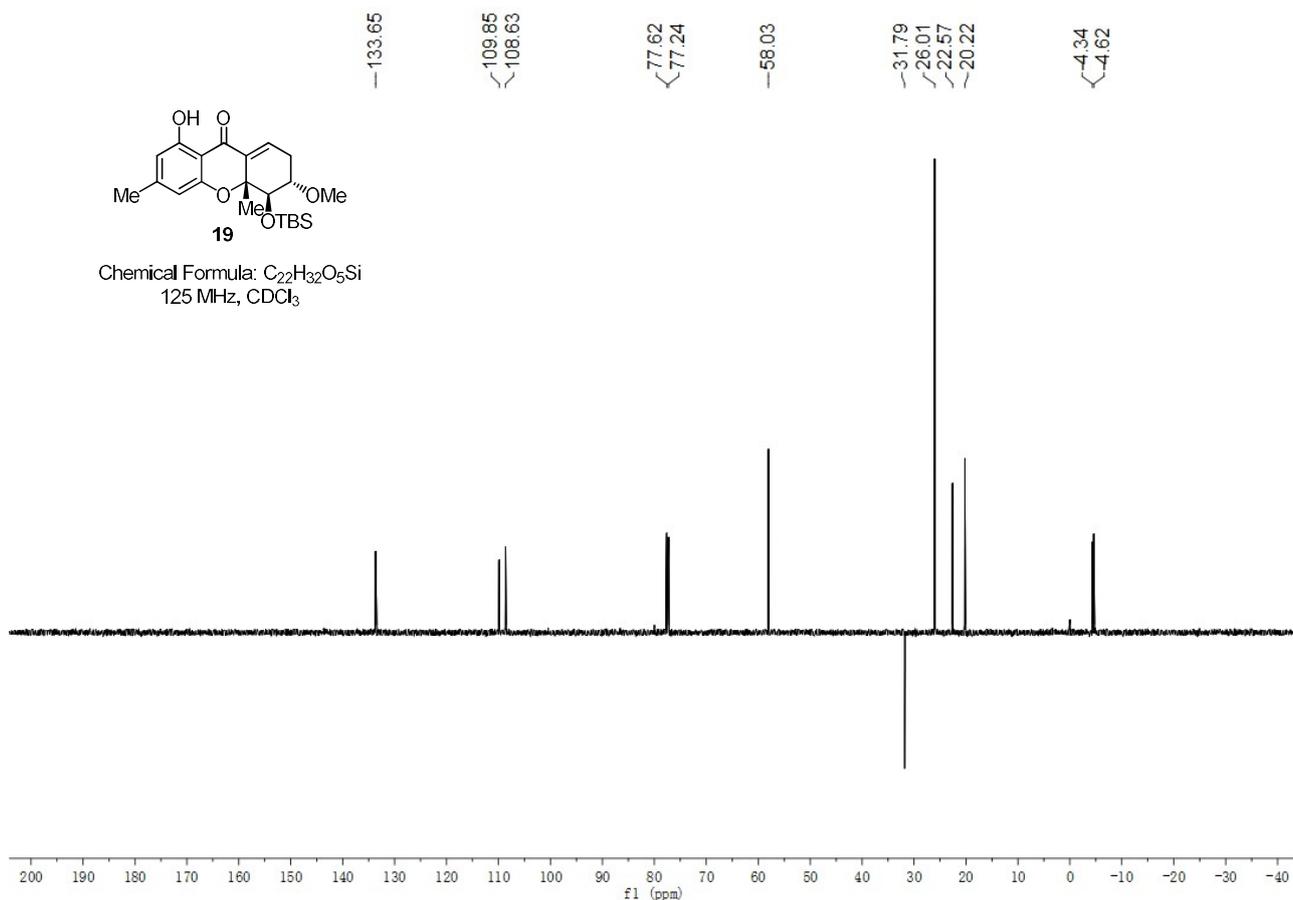


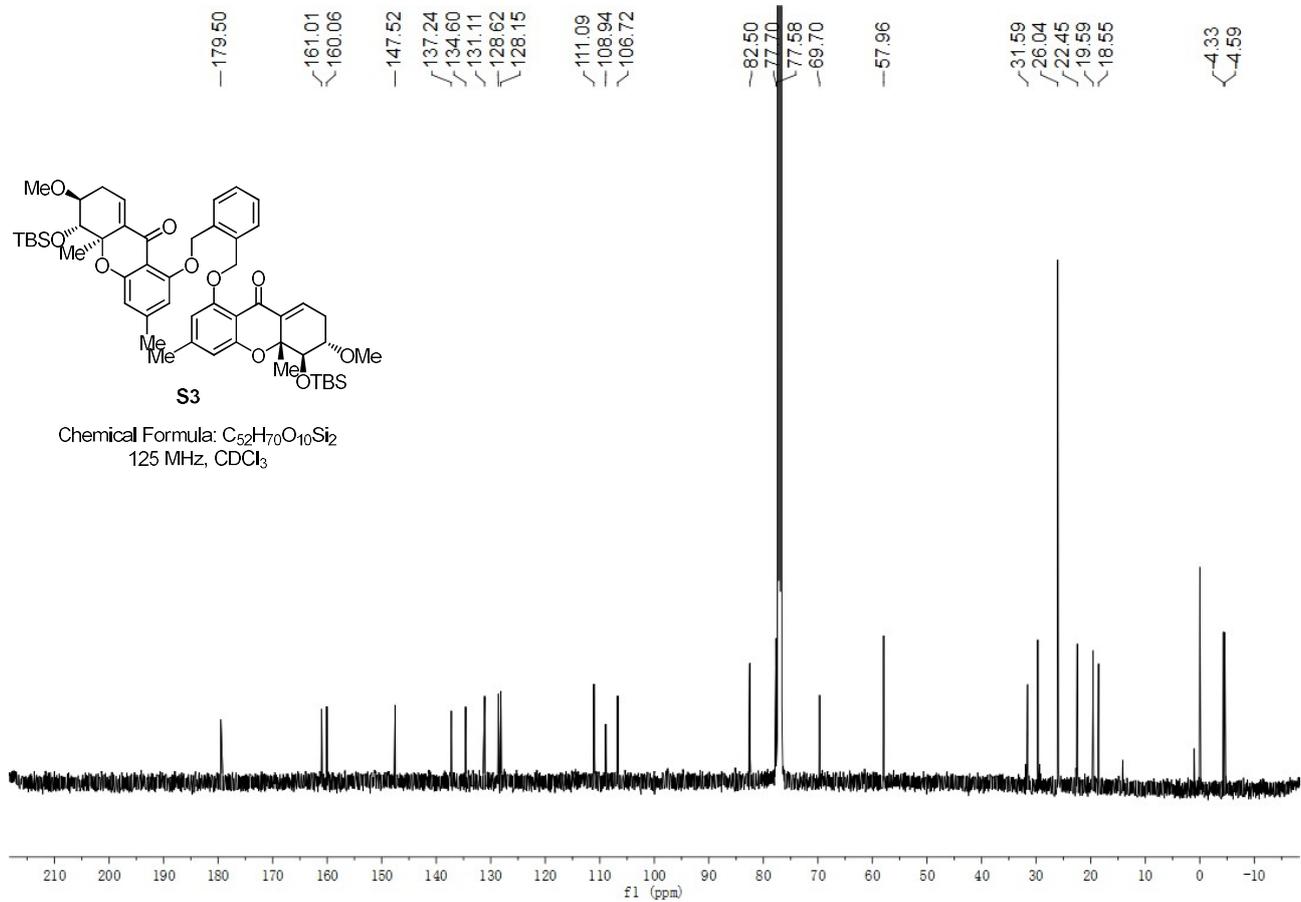
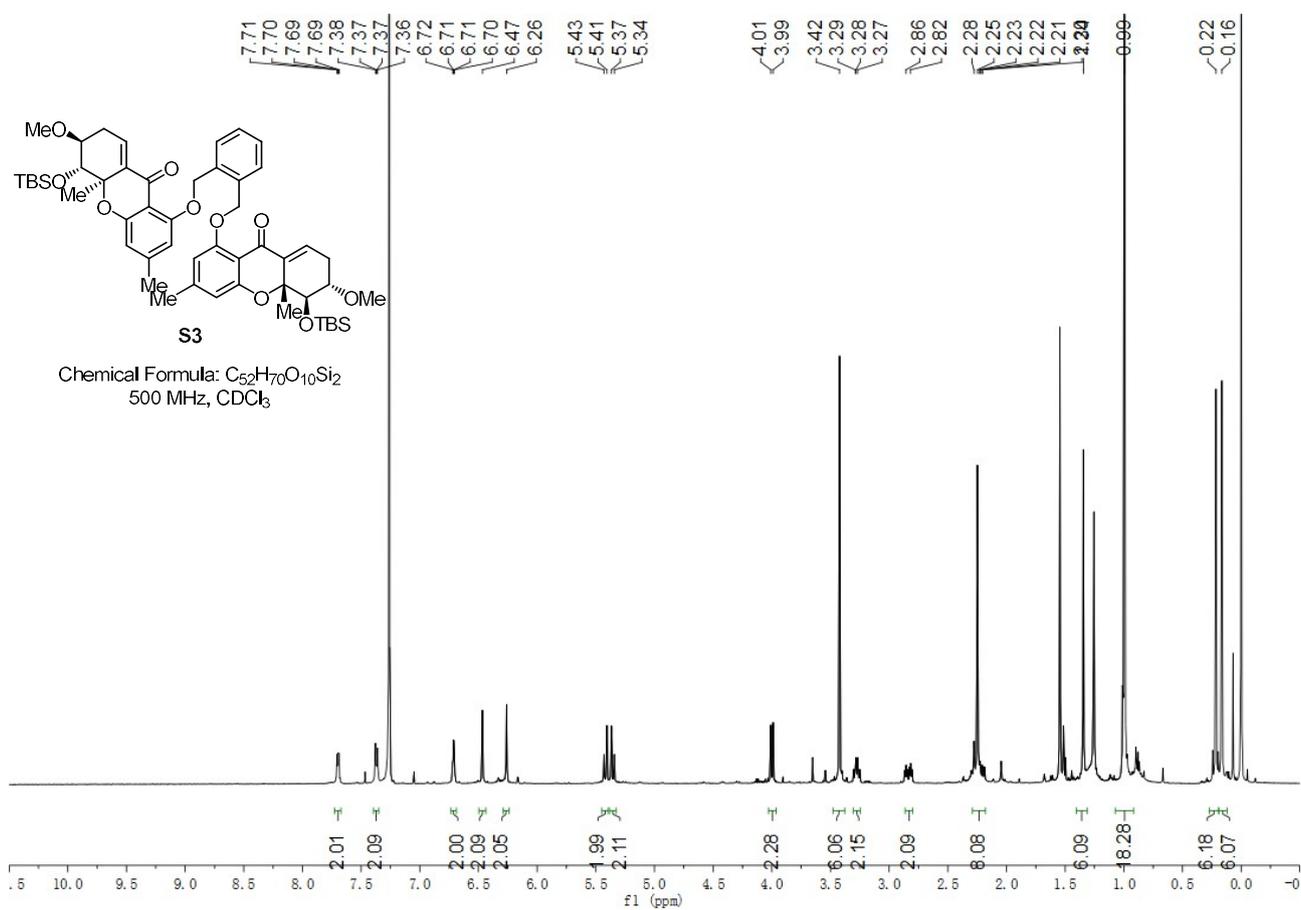
Chemical Formula: C₂₂H₃₂O₅Si
 500 MHz, CDCl₃

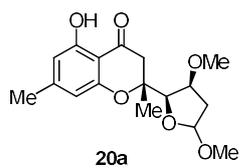


Chemical Formula: C₂₂H₃₂O₅Si
 125 MHz, CDCl₃

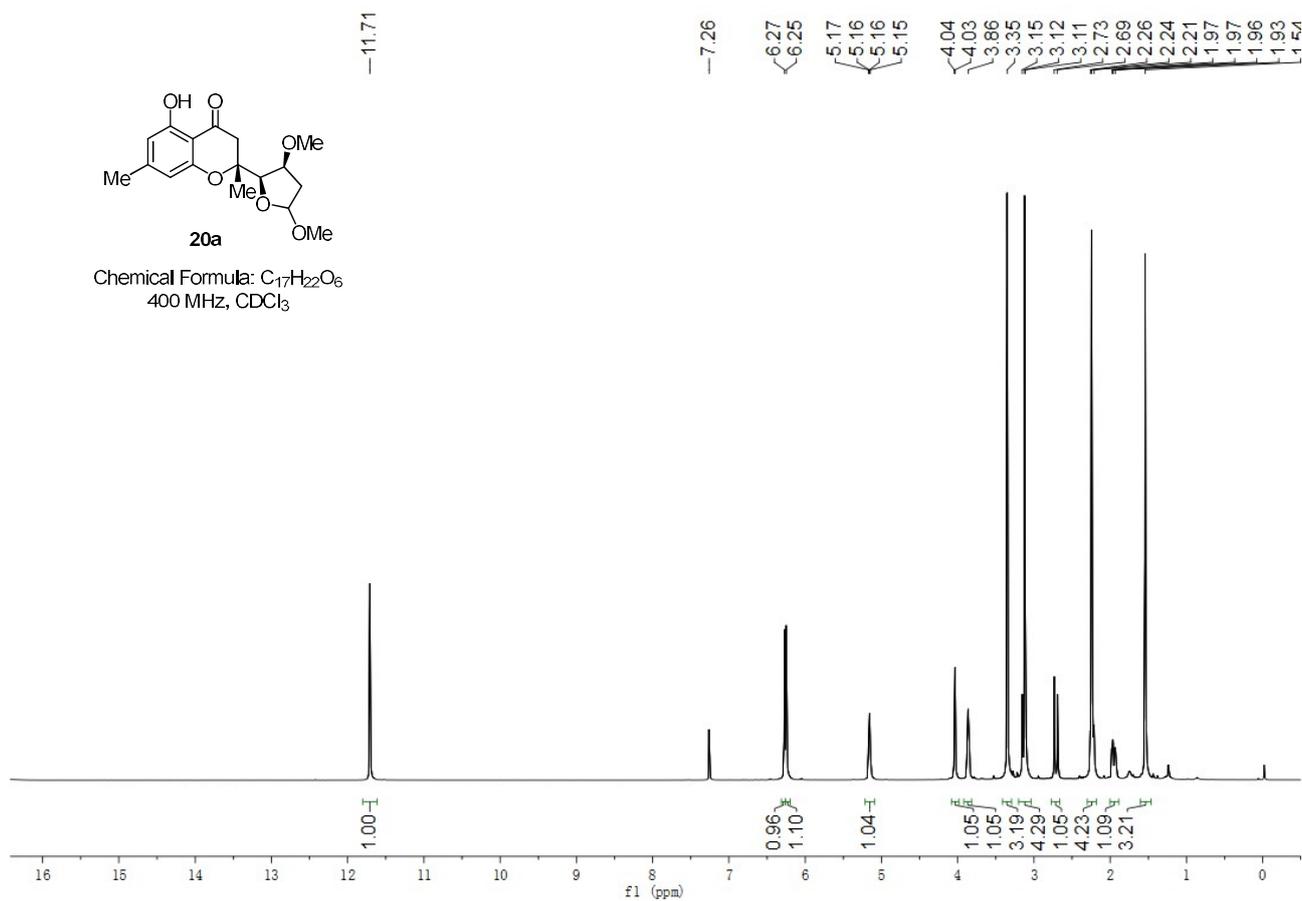








Chemical Formula: C₁₇H₂₂O₆
400 MHz, CDCl₃



196.94, 161.42, 159.06, 150.12

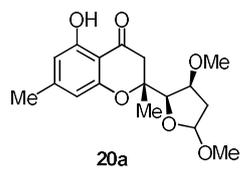
109.30, 108.46, 105.40, 103.90

82.49, 81.30, 80.34

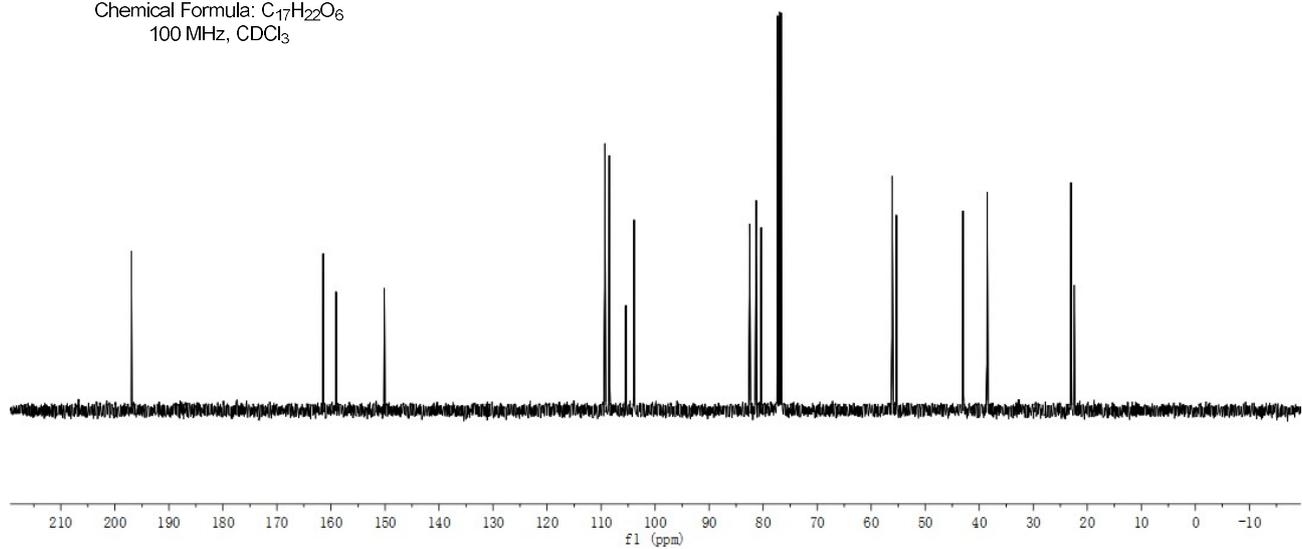
56.12, 55.35

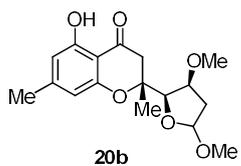
42.99, 38.53

22.99, 22.44

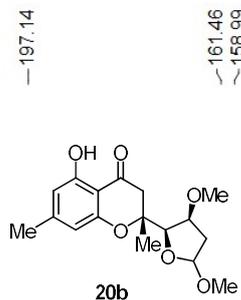
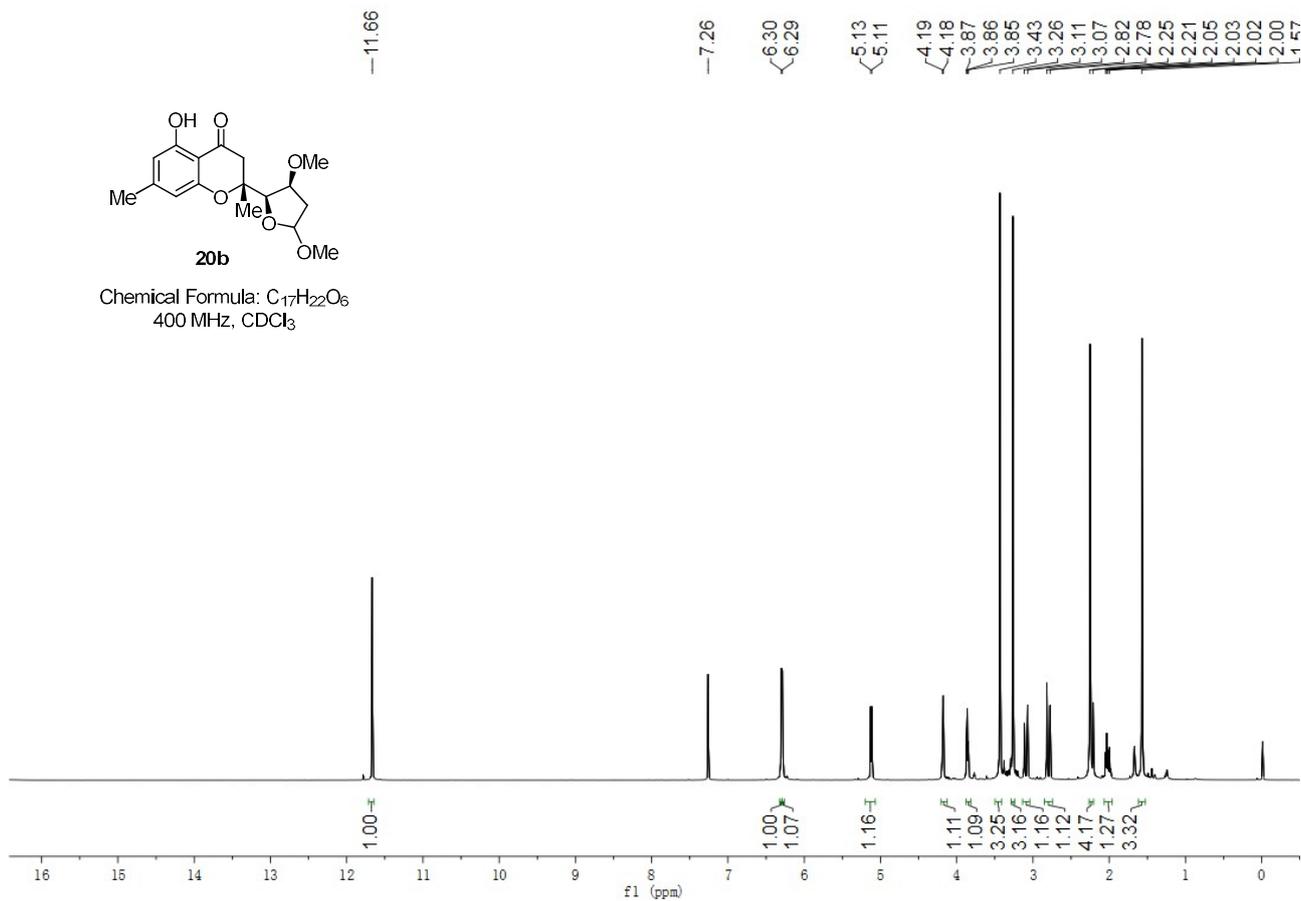


Chemical Formula: C₁₇H₂₂O₆
100 MHz, CDCl₃

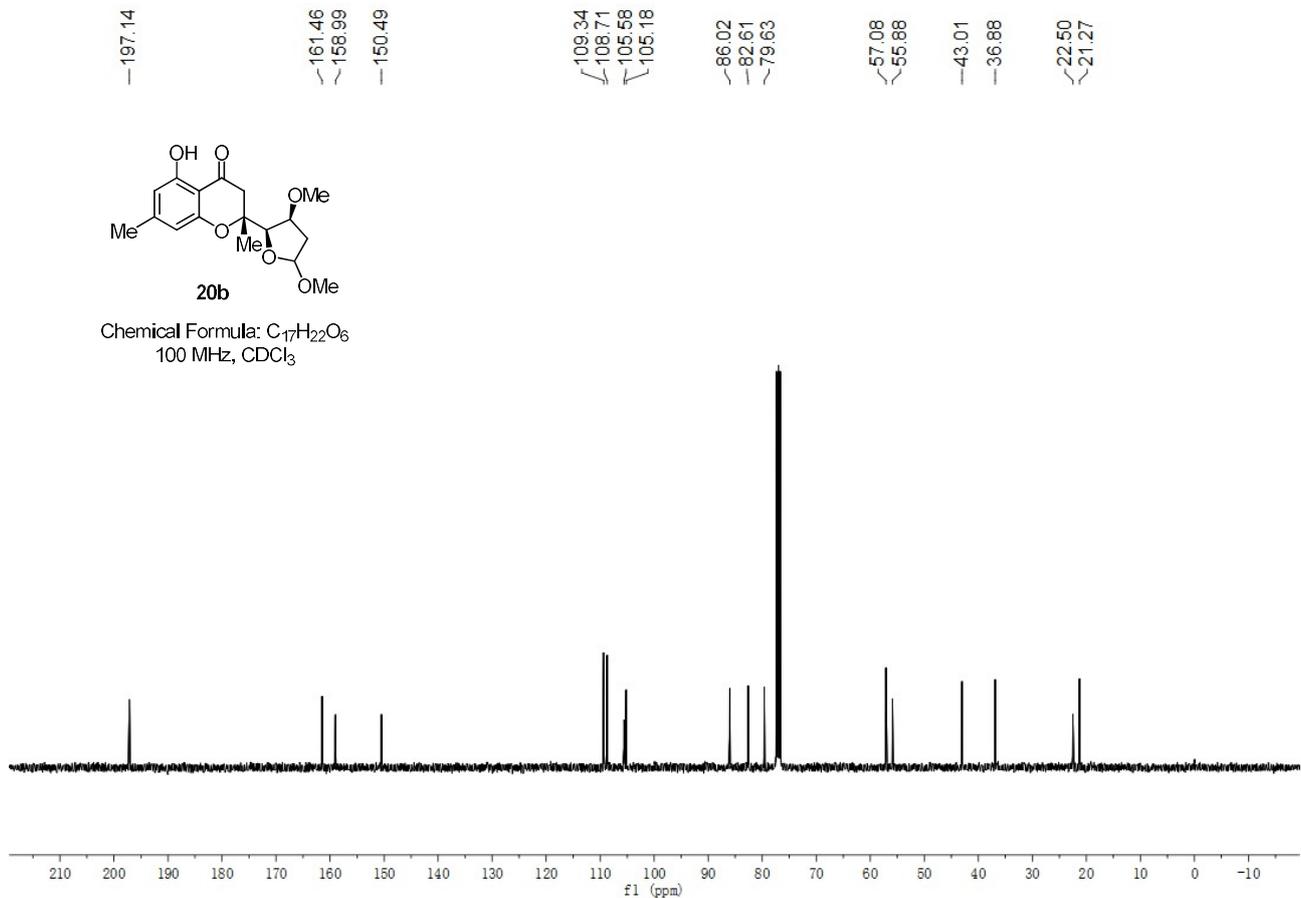


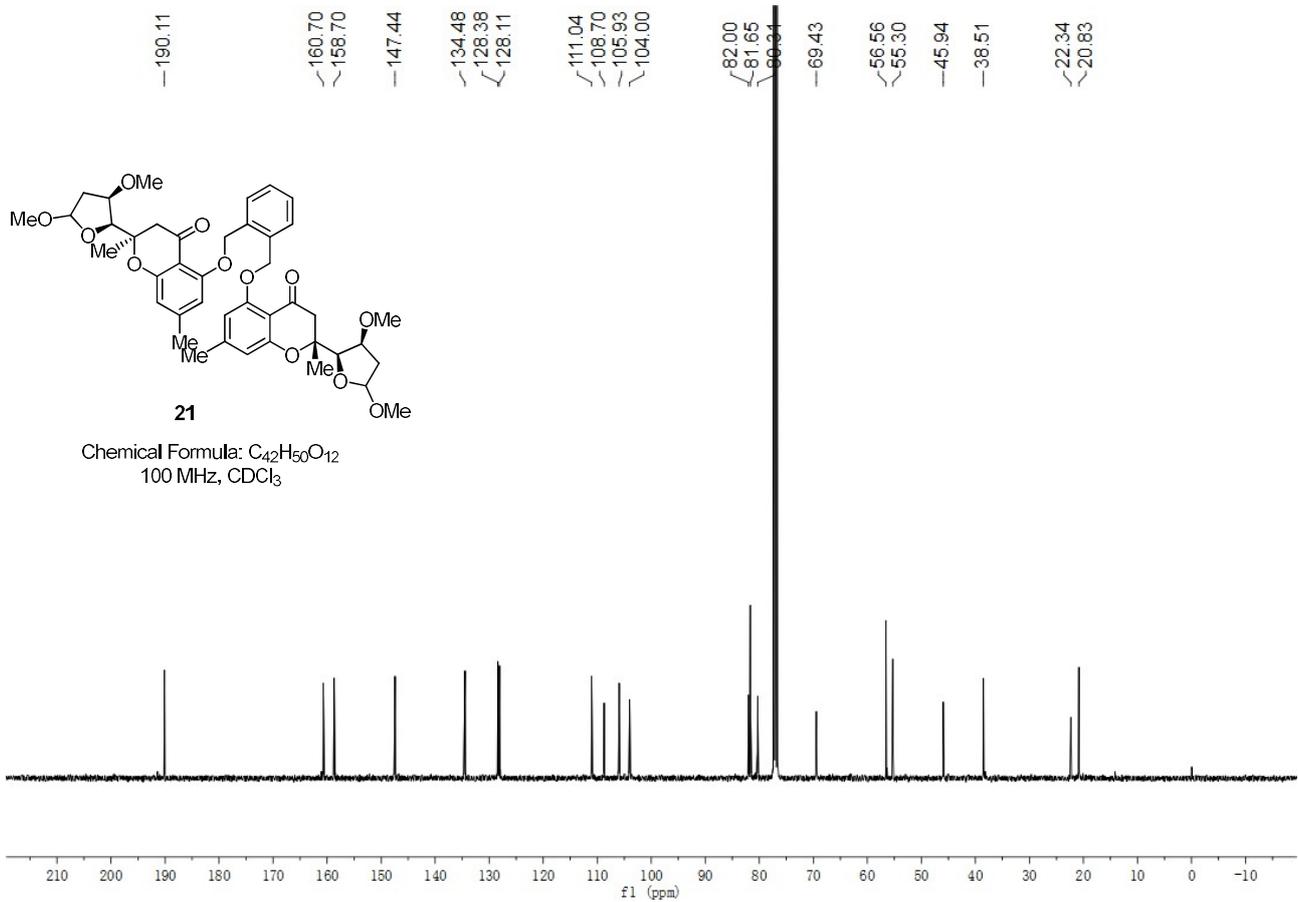
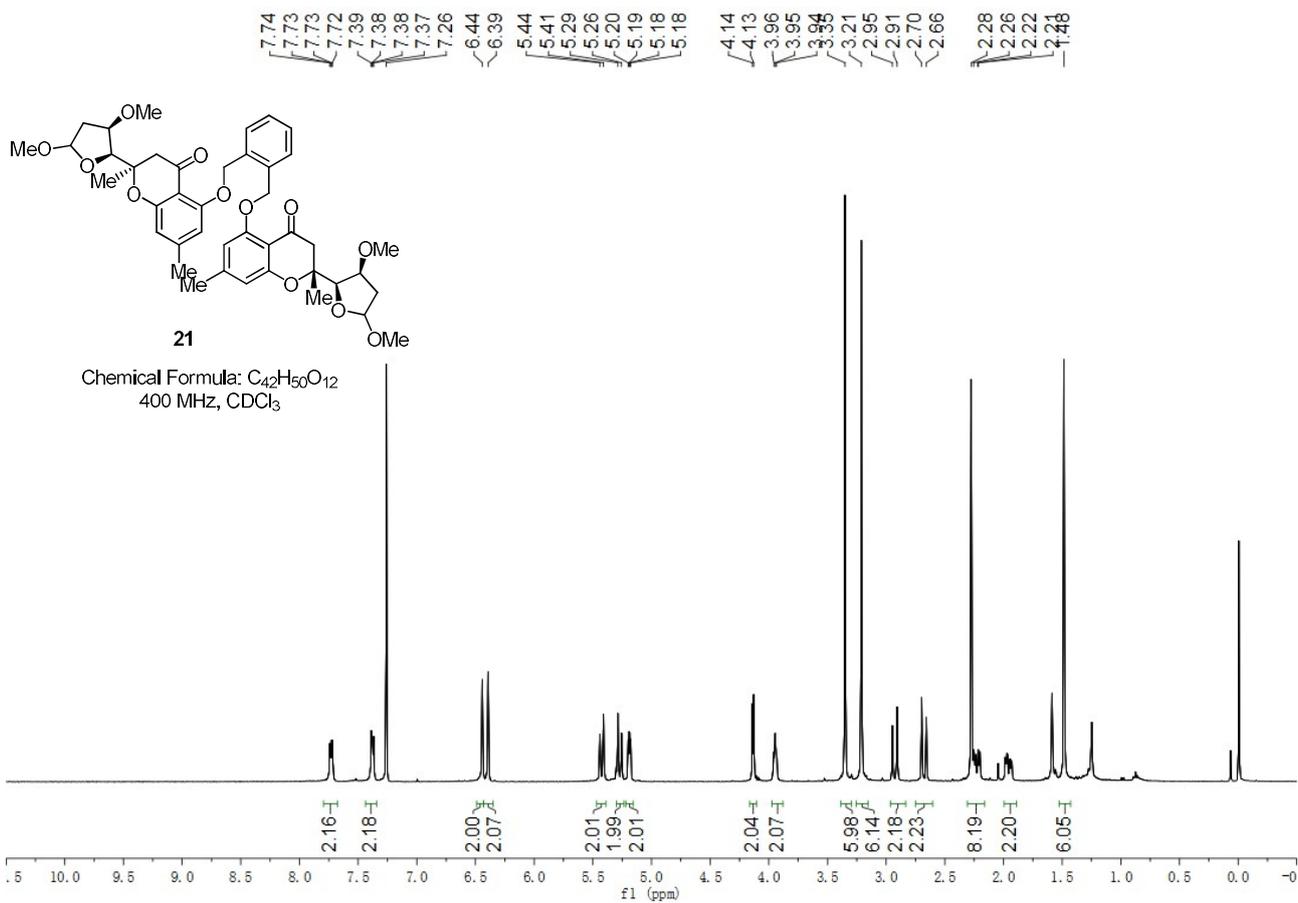


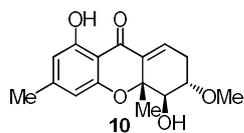
Chemical Formula: C₁₇H₂₂O₆
400 MHz, CDCl₃



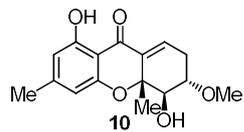
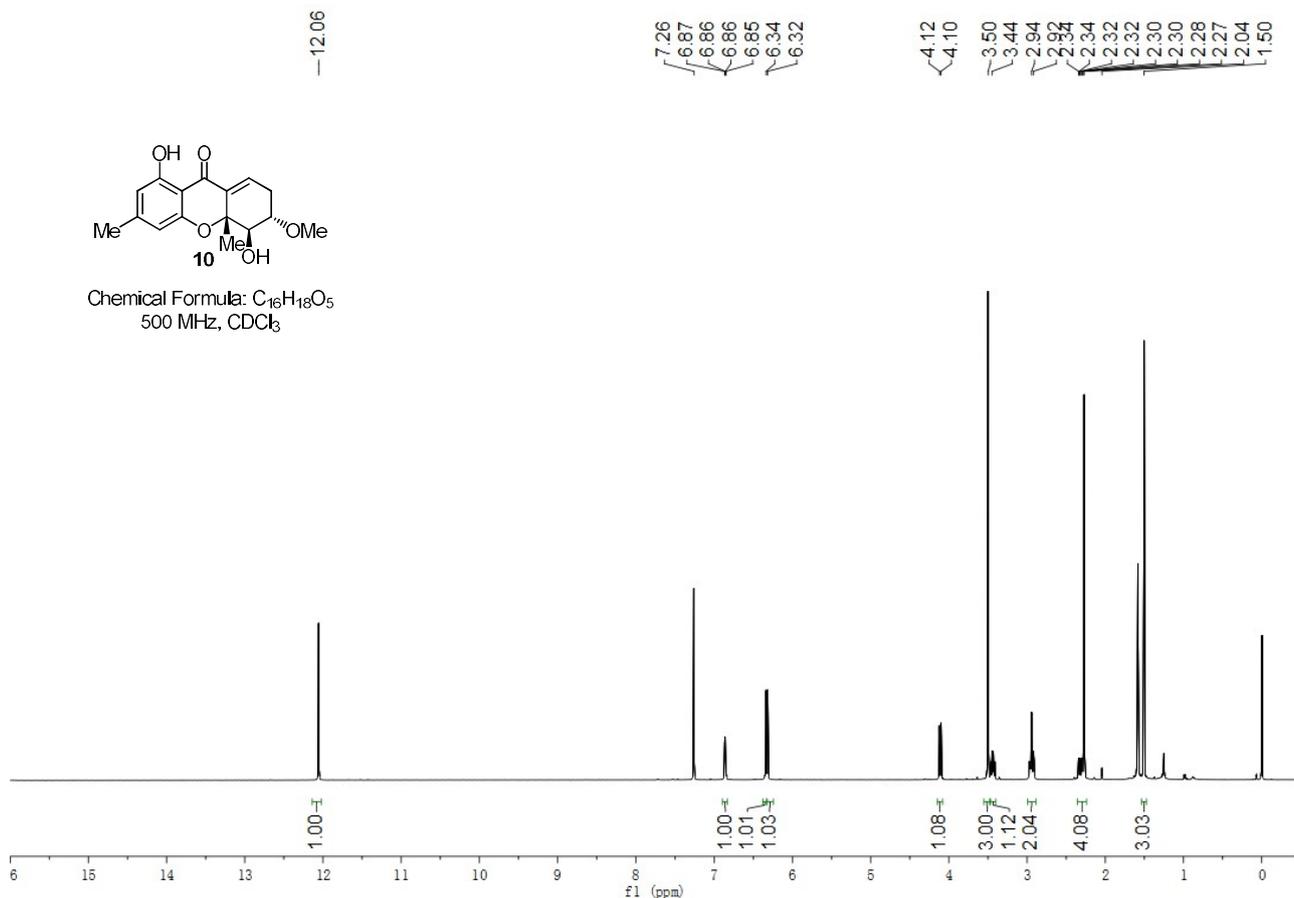
Chemical Formula: C₁₇H₂₂O₆
100 MHz, CDCl₃



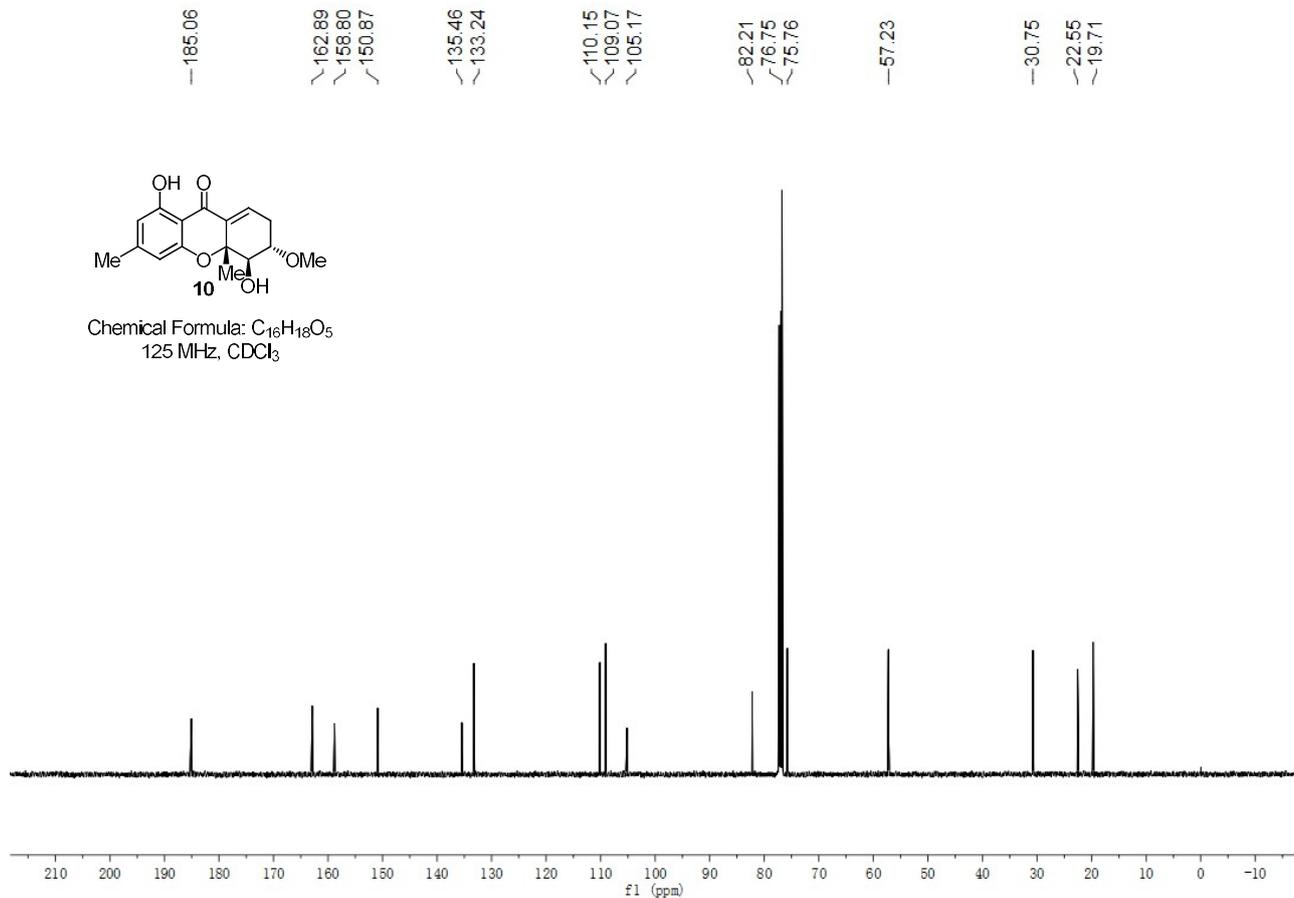


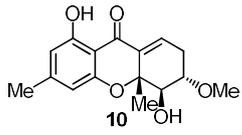


Chemical Formula: C₁₆H₁₈O₅
500 MHz, CDCl₃



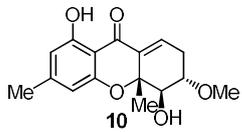
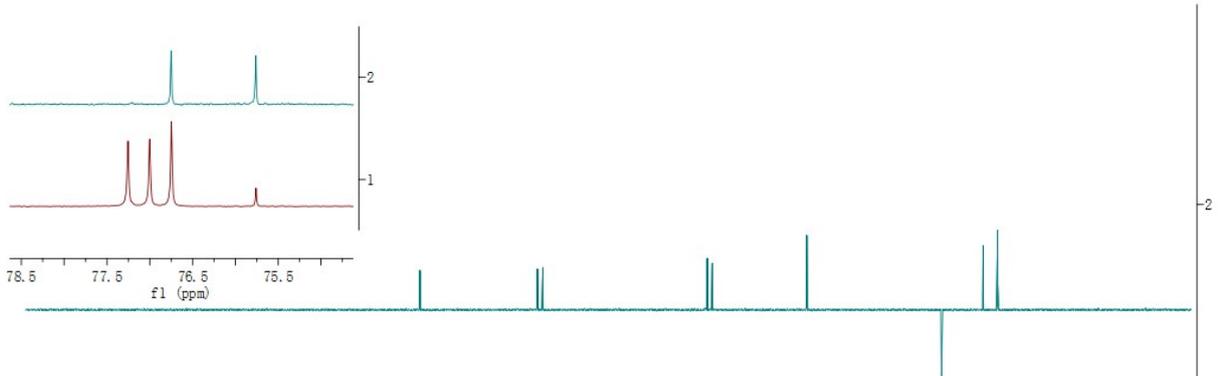
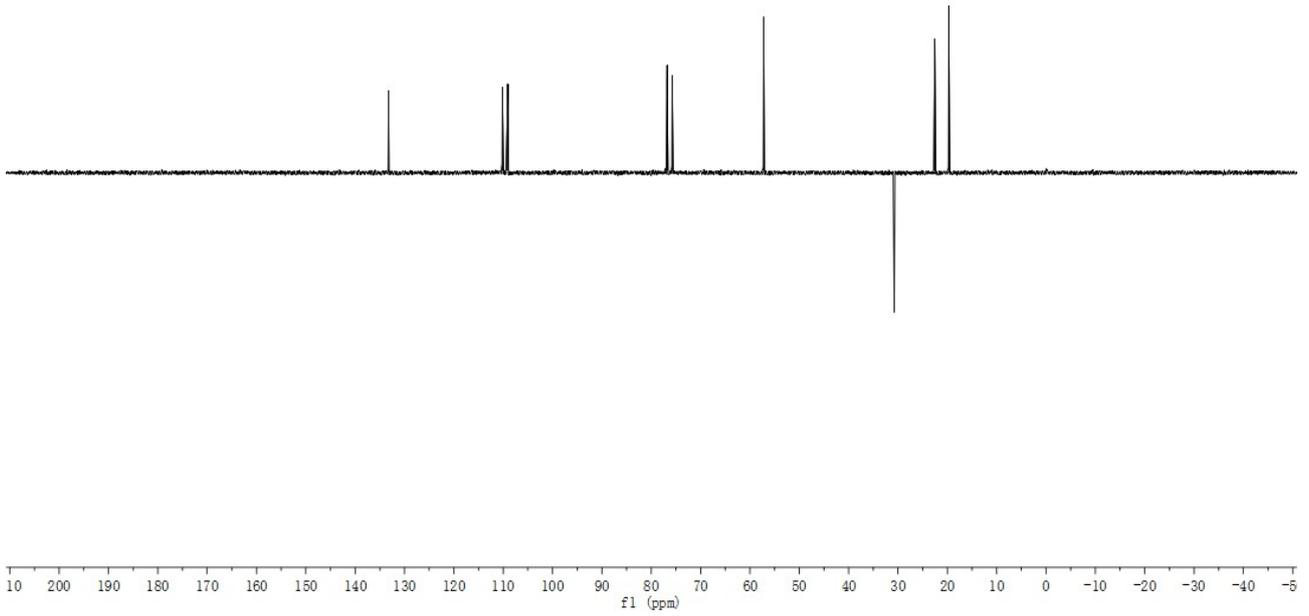
Chemical Formula: C₁₆H₁₈O₅
125 MHz, CDCl₃



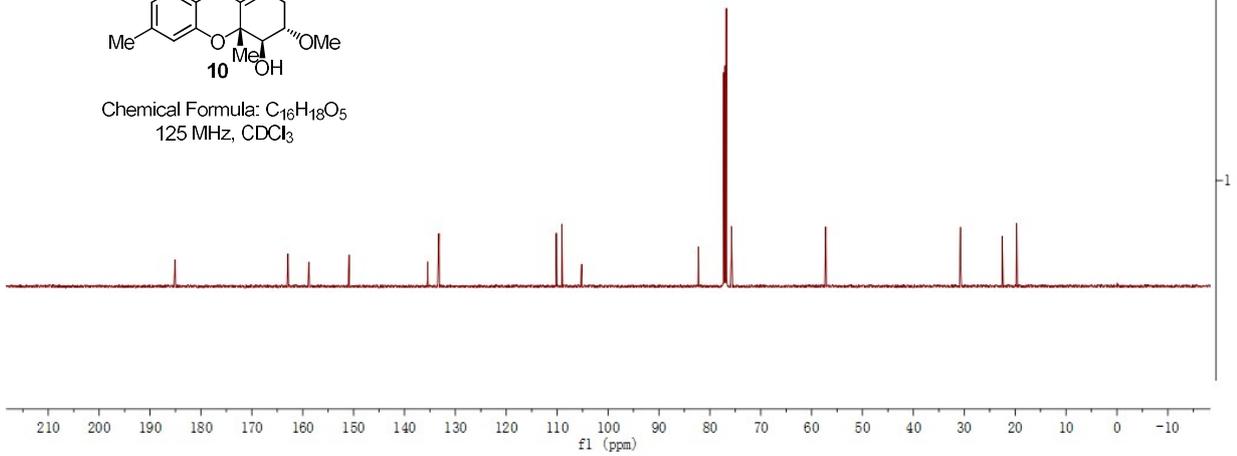


Chemical Formula: C₁₆H₁₈O₅
125 MHz, CDCl₃

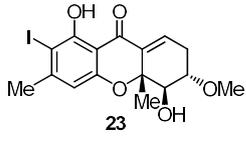
—133.24
 ~110.16
 ~109.07
 ~76.75
 ~75.76
 —57.23
 ~30.75
 ~22.55
 ~19.71



Chemical Formula: C₁₆H₁₈O₅
125 MHz, CDCl₃



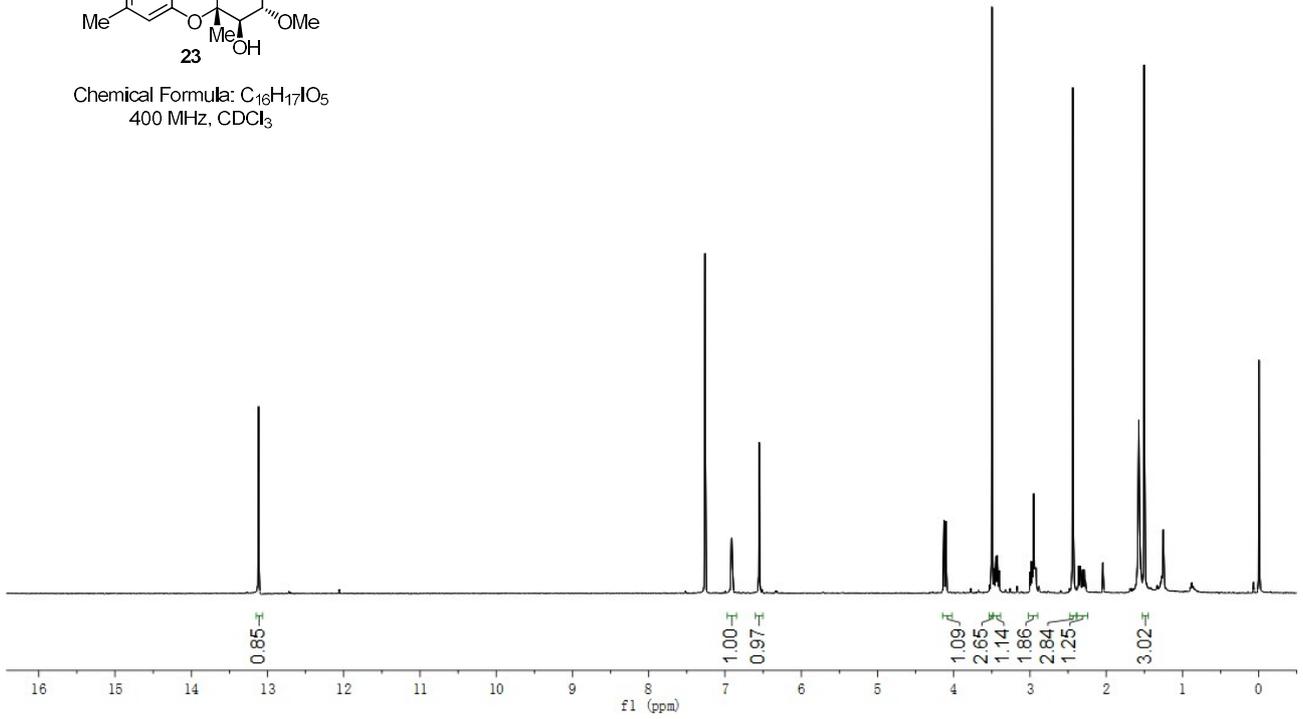
-13.12



Chemical Formula: C₁₆H₁₇O₅
400 MHz, CDCl₃

7.26
6.92
6.92
6.91
6.90
6.55

4.13
4.10
3.50
3.44
3.43
2.98
2.95
2.93
1.56



184.59

161.52

156.80

153.32

134.67

134.48

110.40

105.10

82.56

81.07

76.70

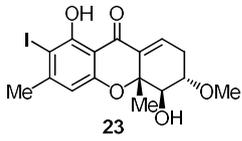
75.60

57.27

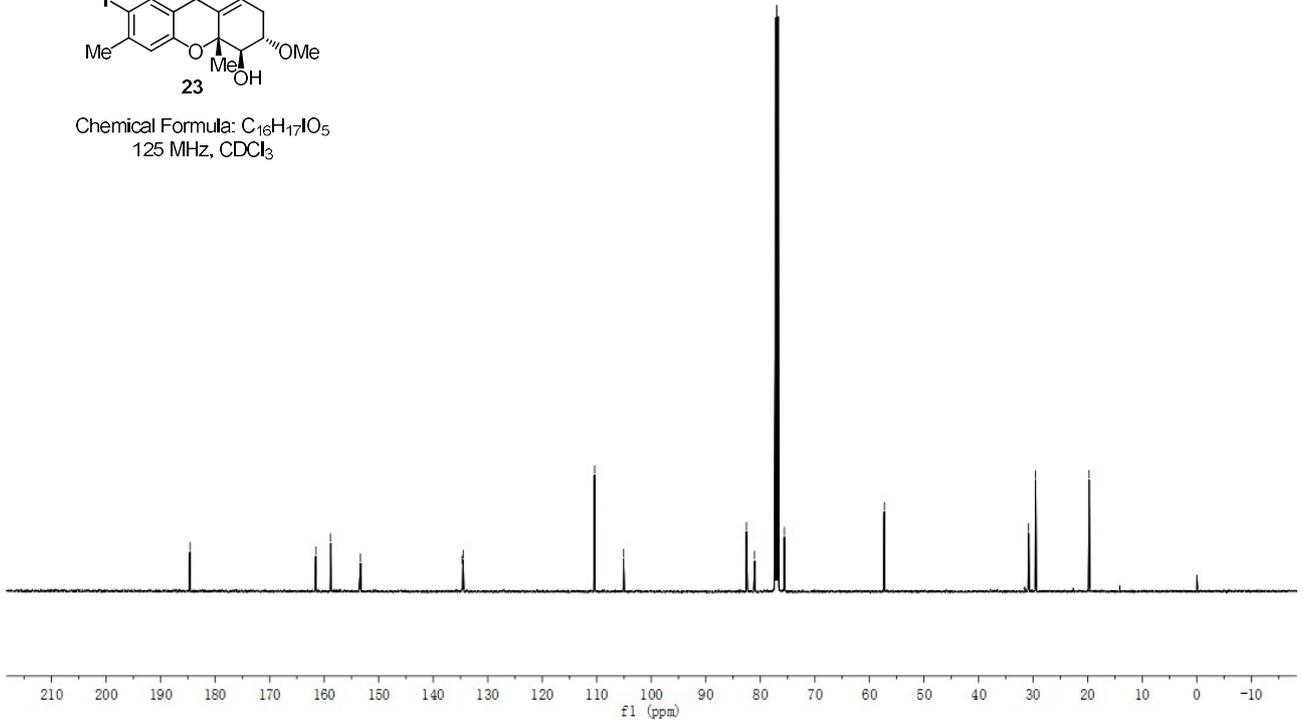
30.83

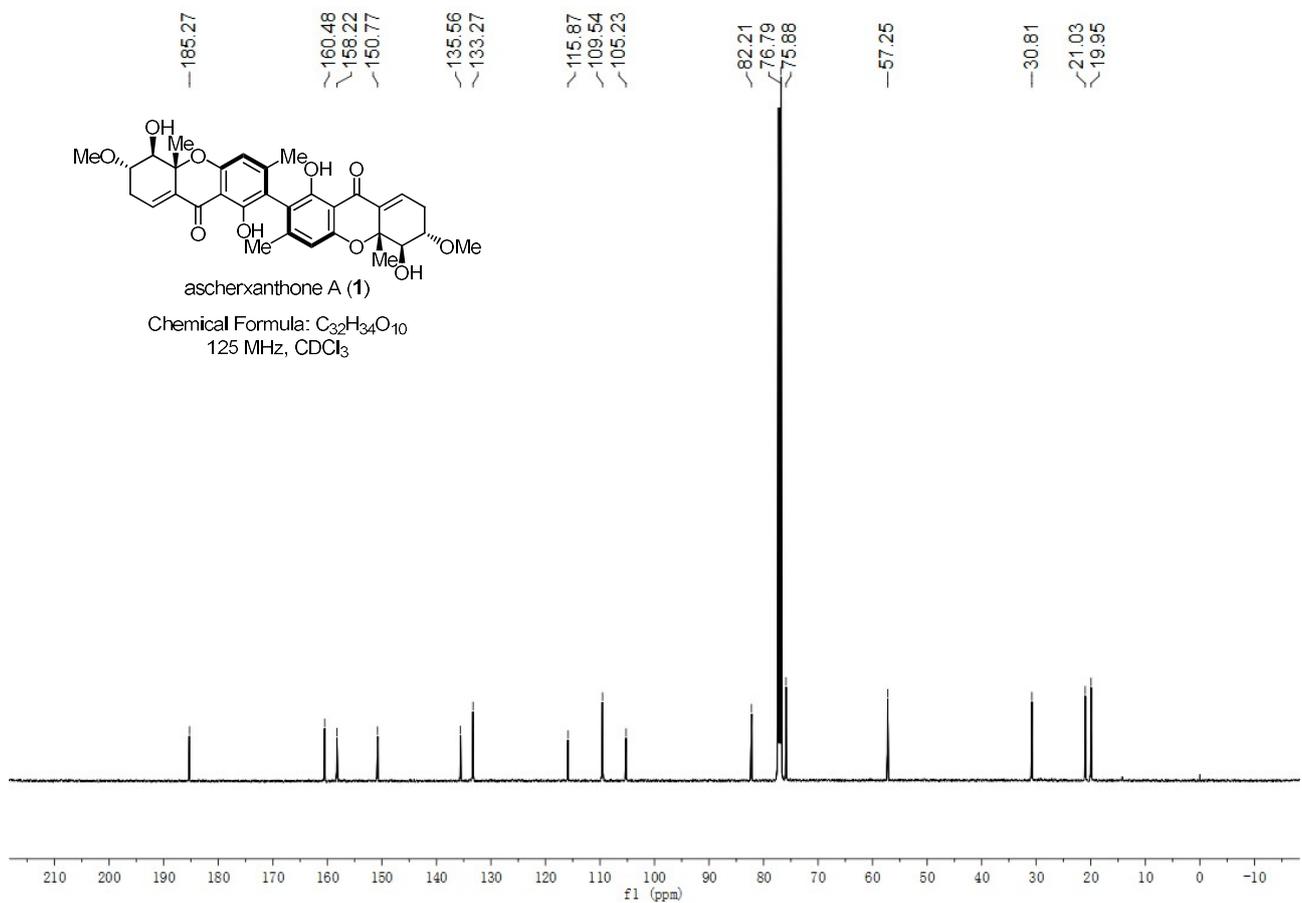
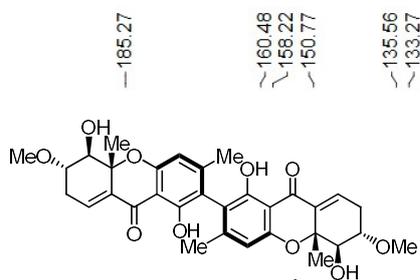
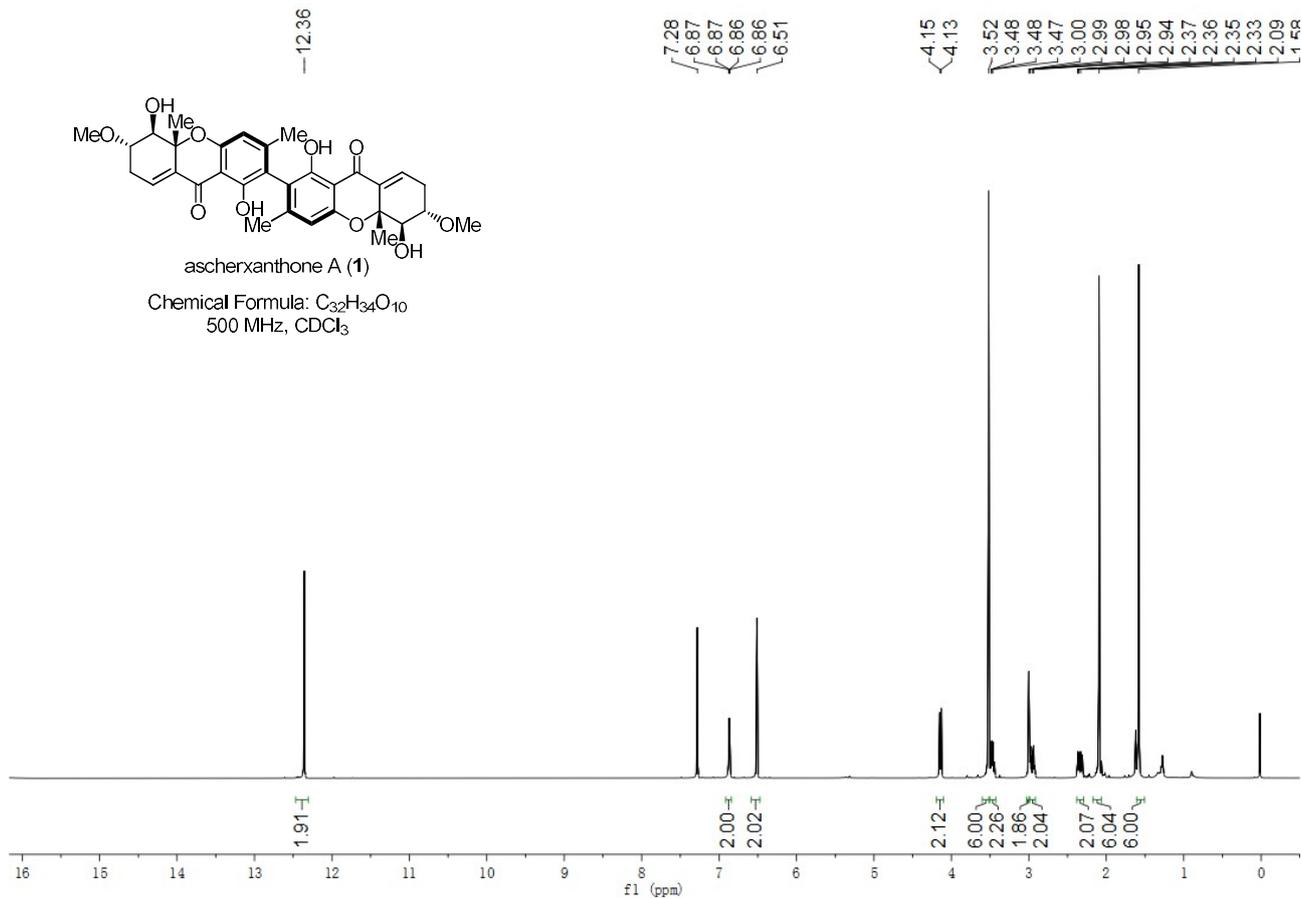
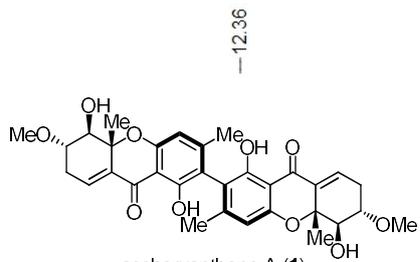
29.56

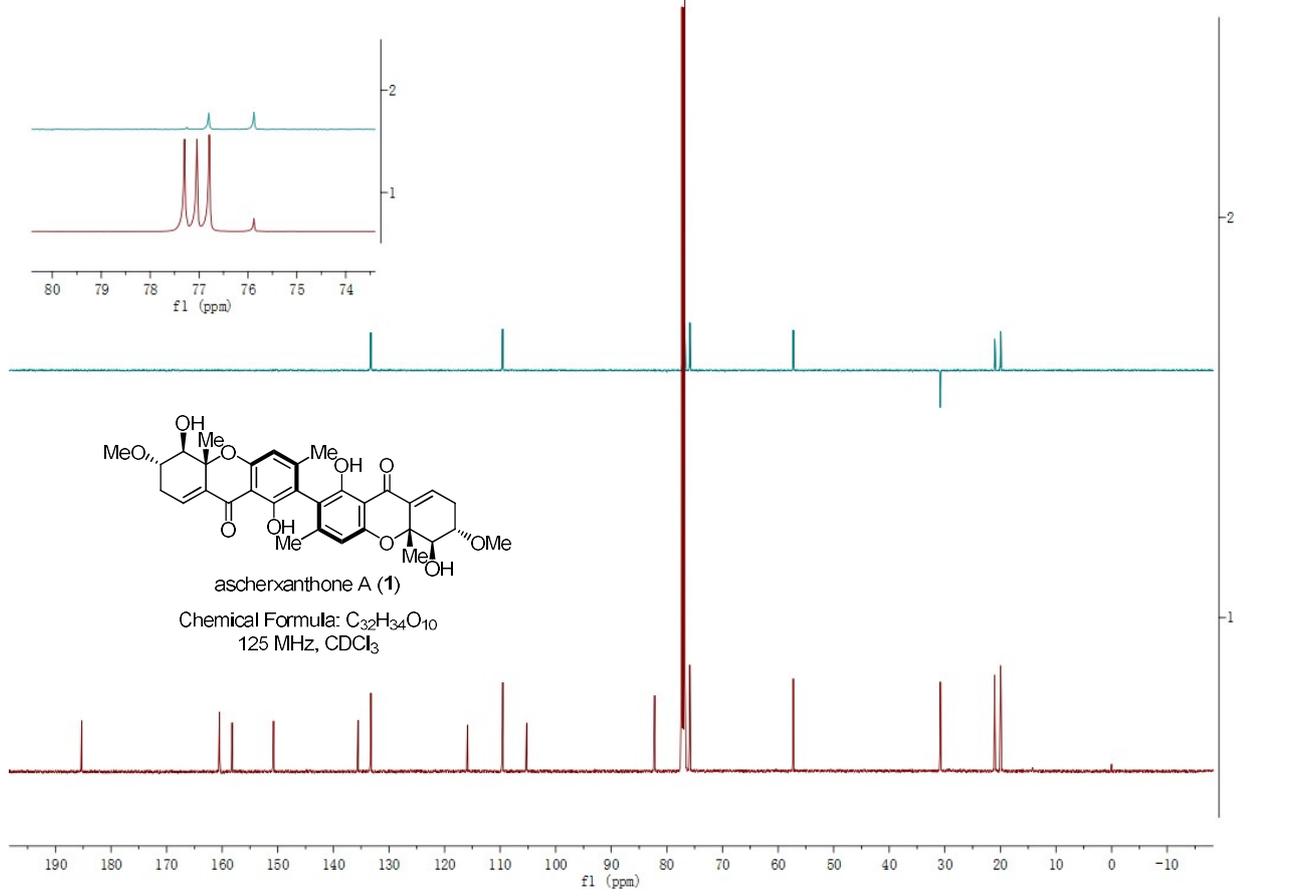
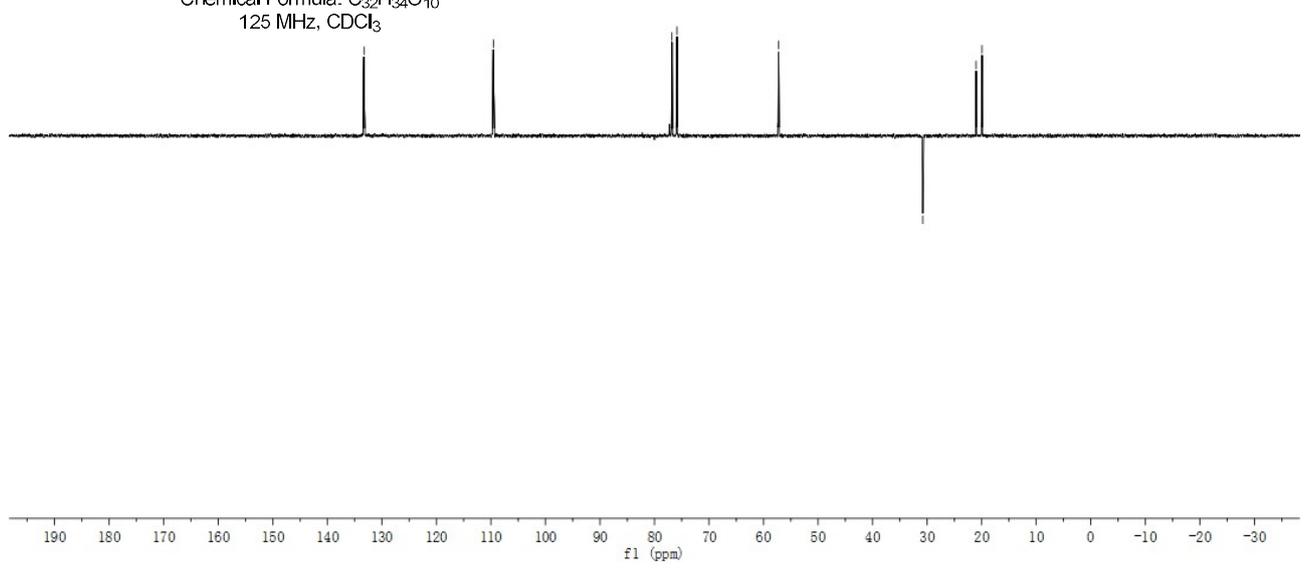
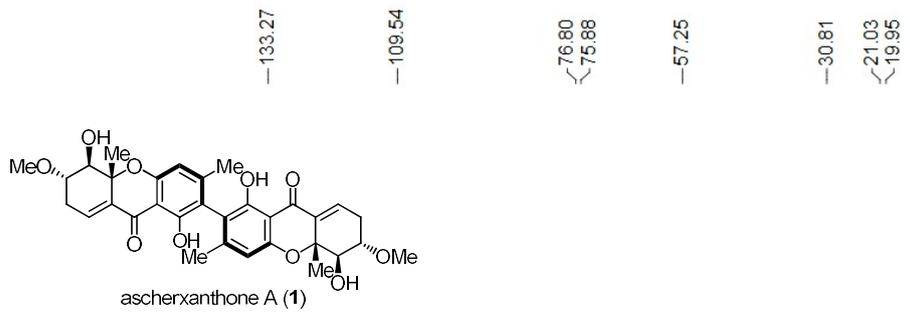
19.73

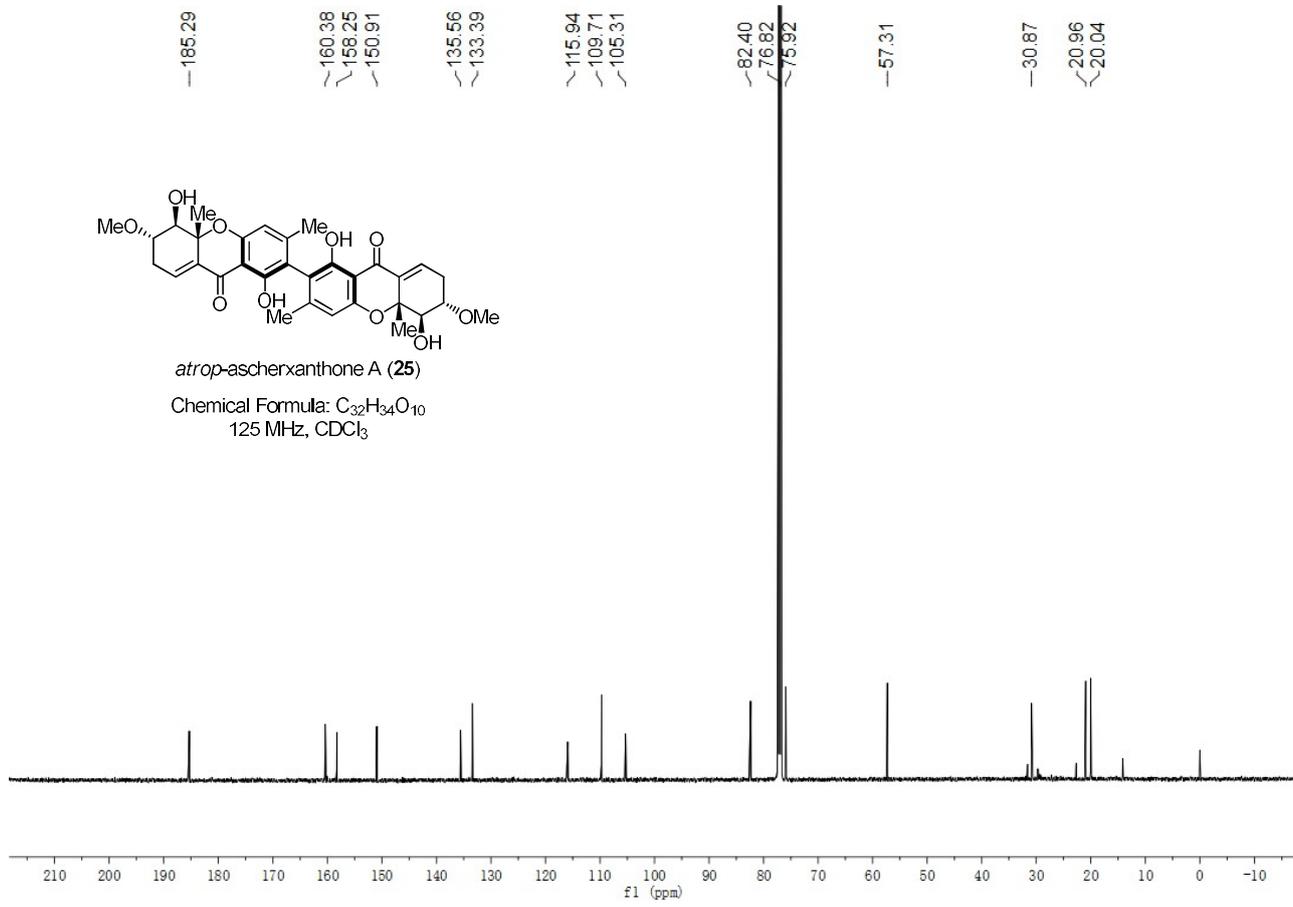
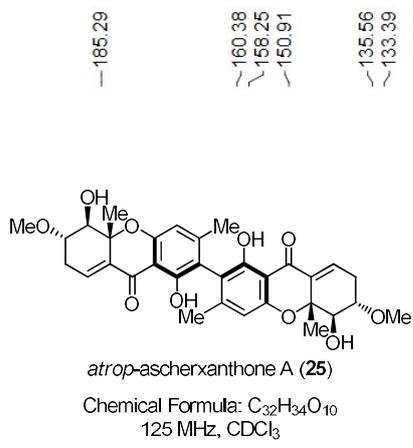
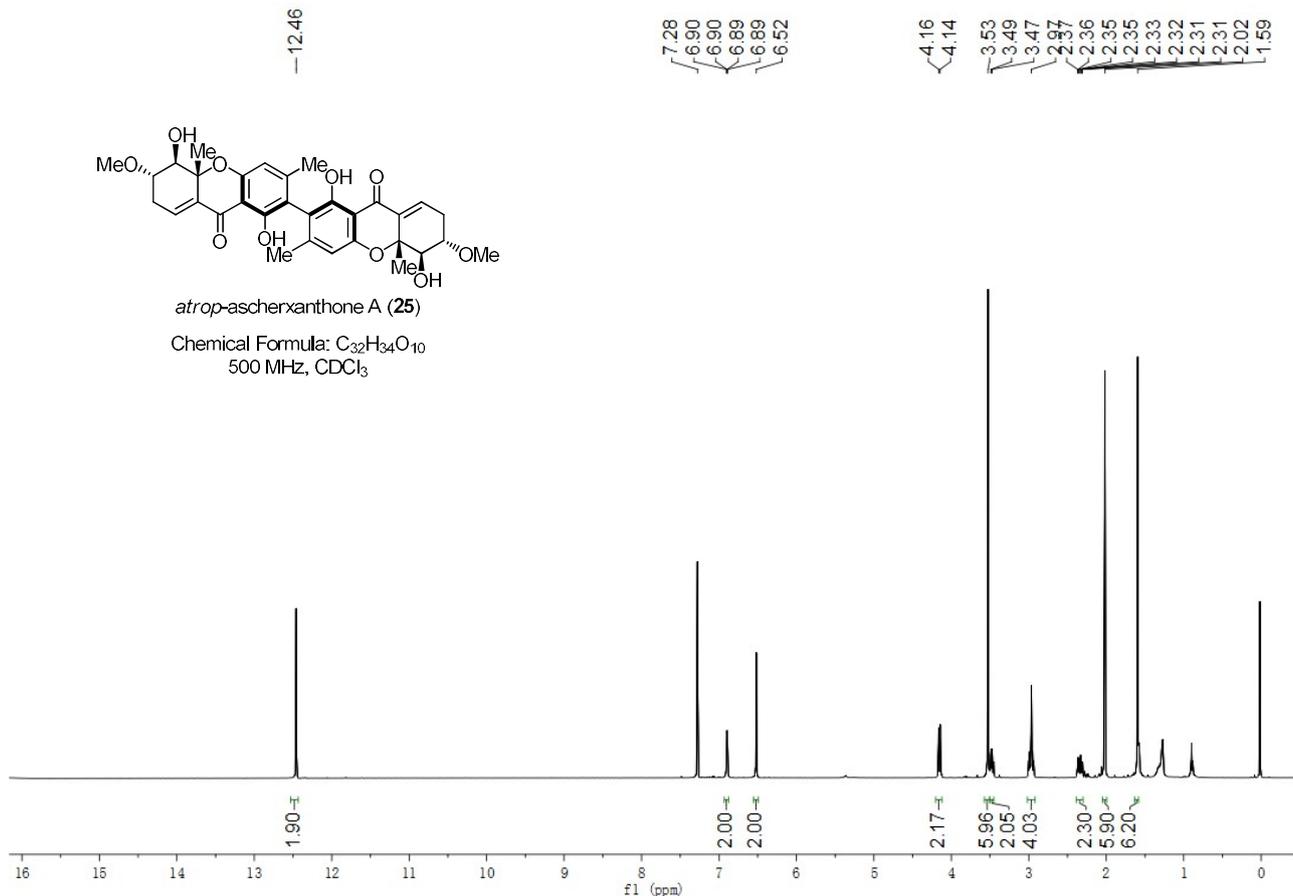
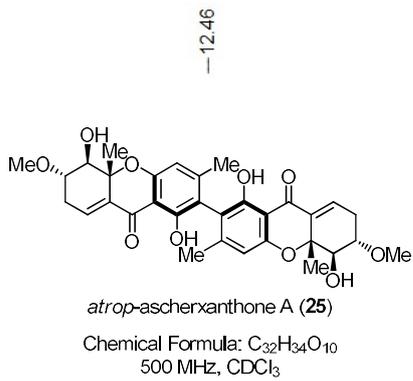


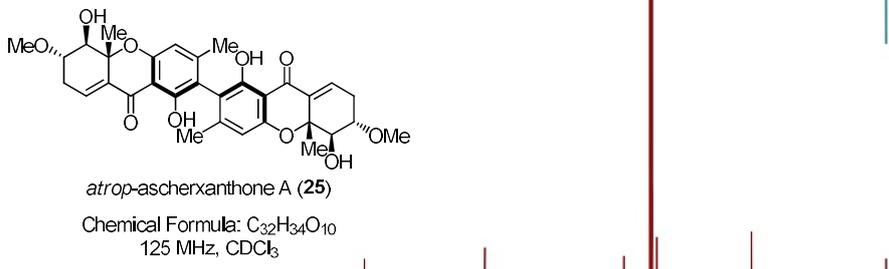
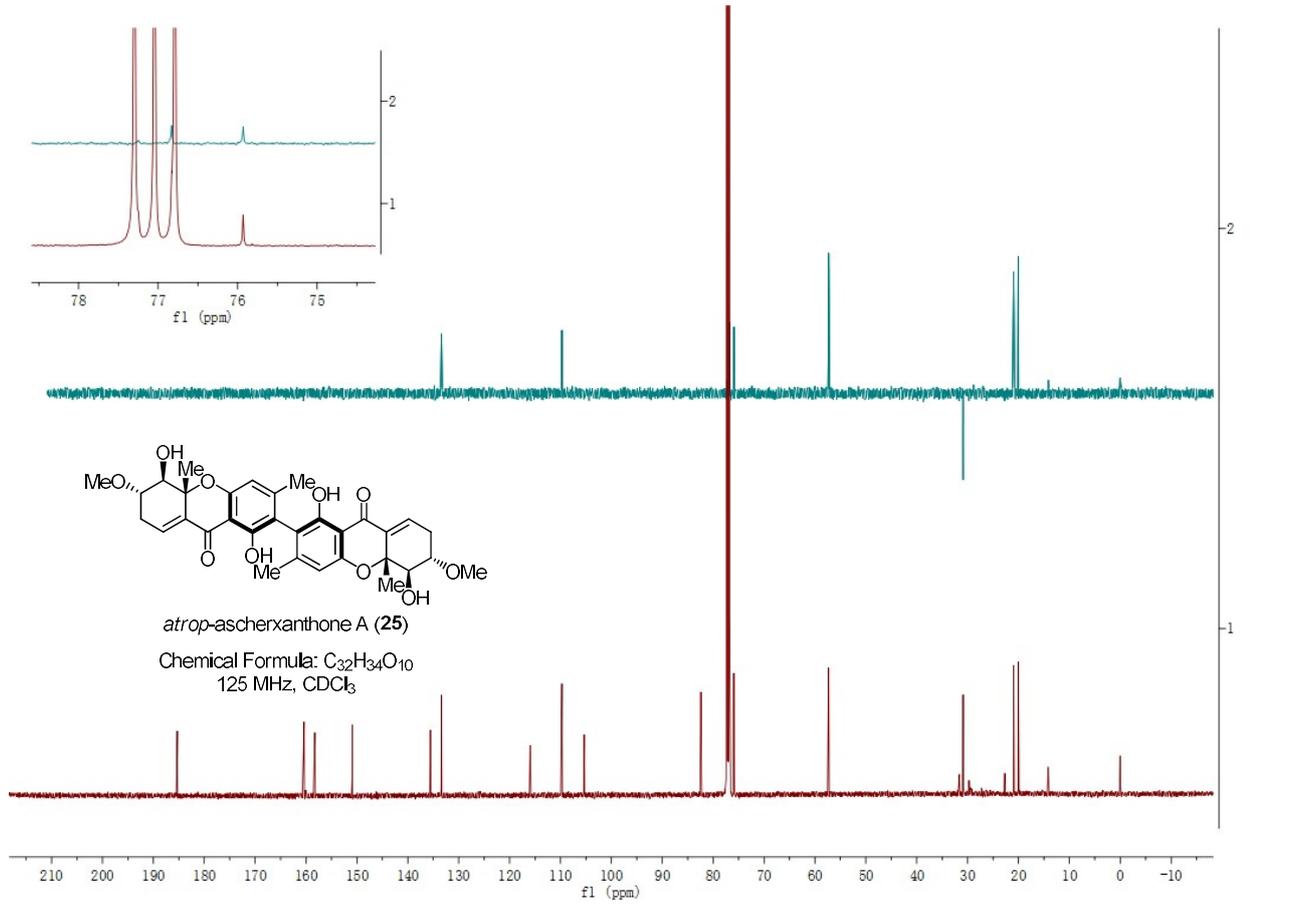
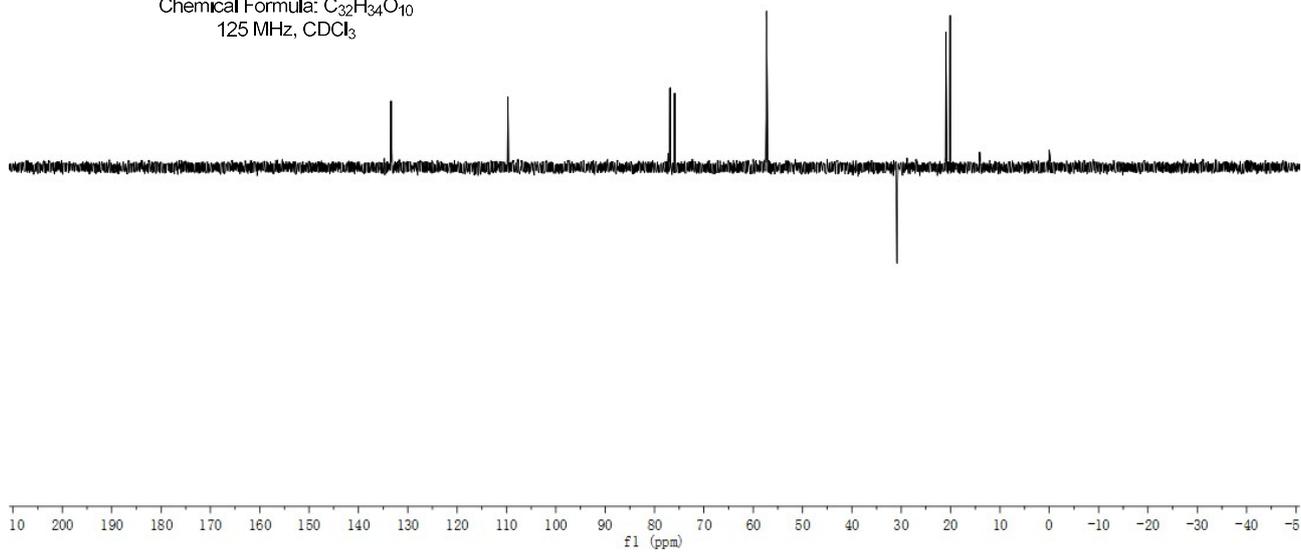
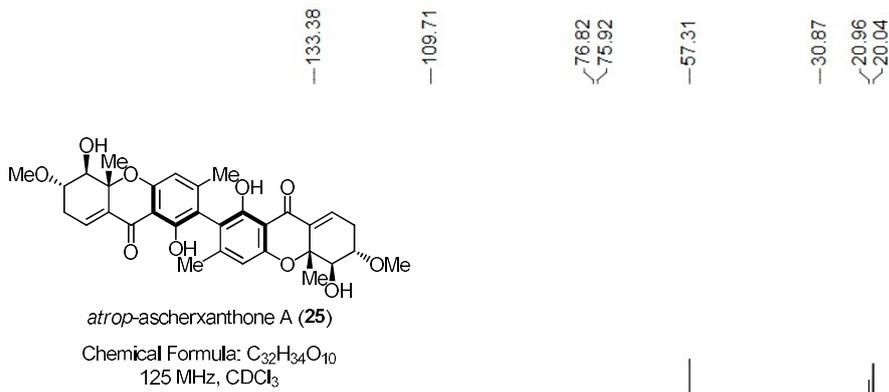
Chemical Formula: C₁₆H₁₇O₅
125 MHz, CDCl₃



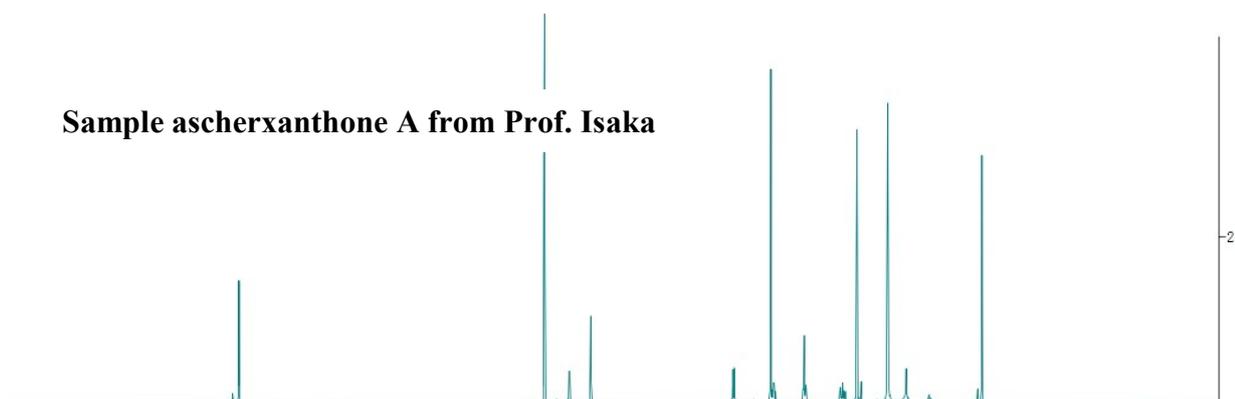




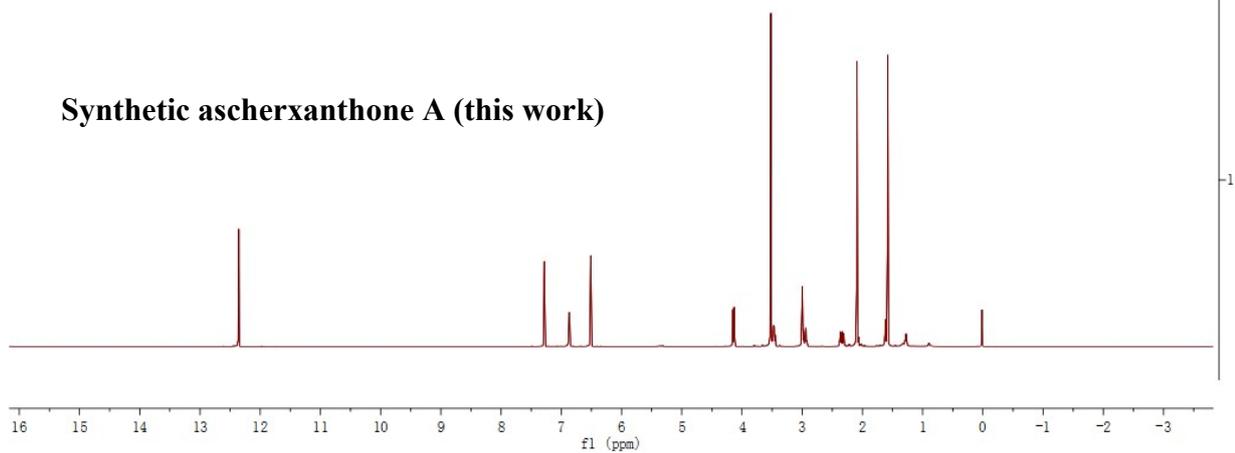




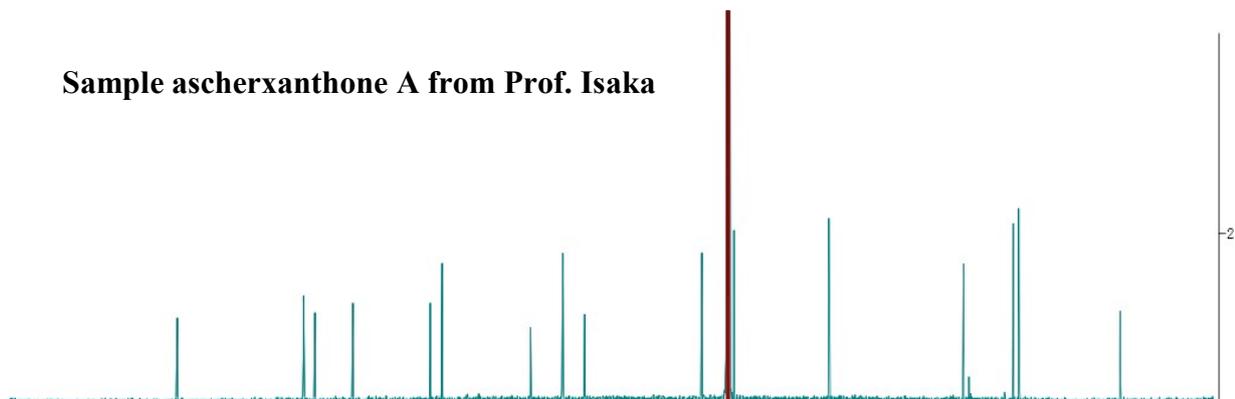
Sample ascherxanthone A from Prof. Isaka



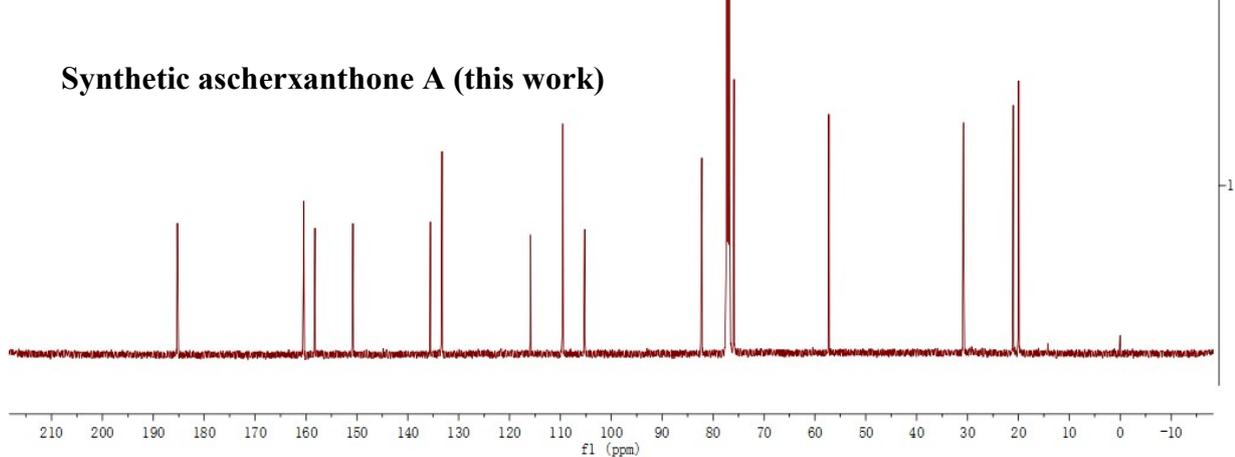
Synthetic ascherxanthone A (this work)



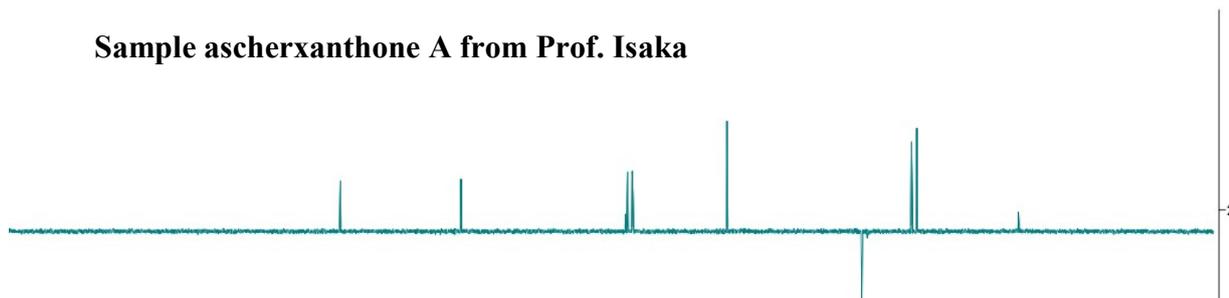
Sample ascherxanthone A from Prof. Isaka



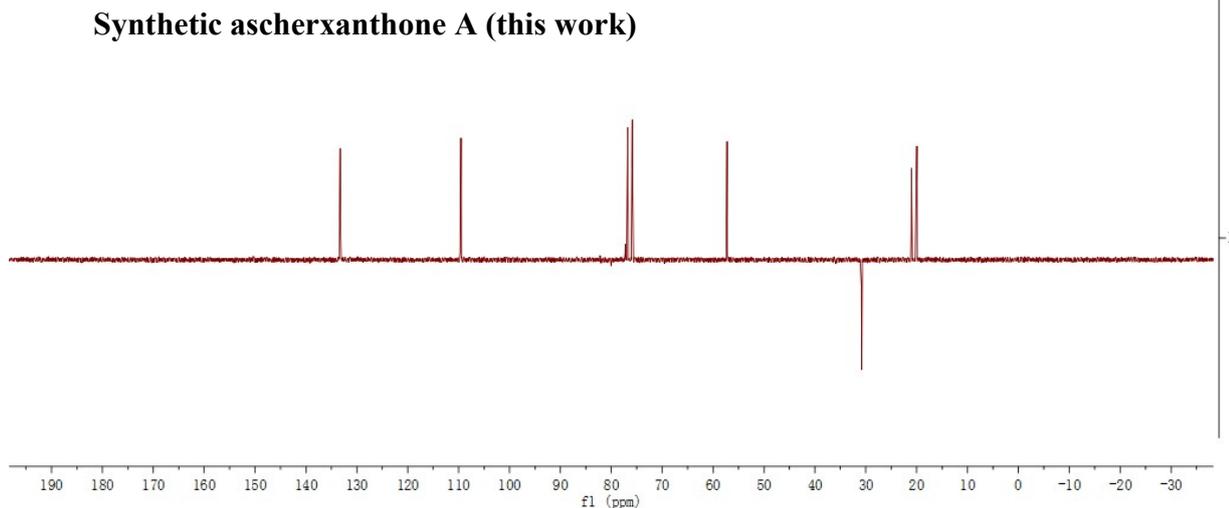
Synthetic ascherxanthone A (this work)



Sample ascherxanthone A from Prof. Isaka

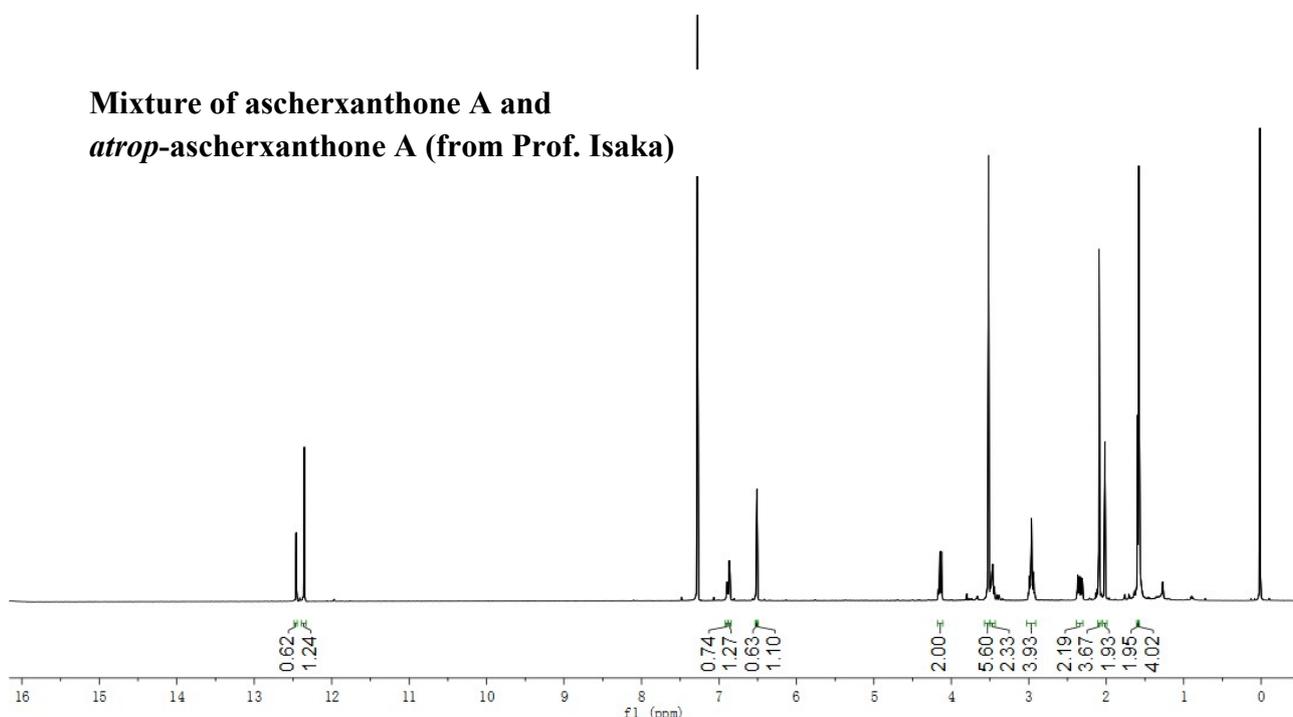


Synthetic ascherxanthone A (this work)

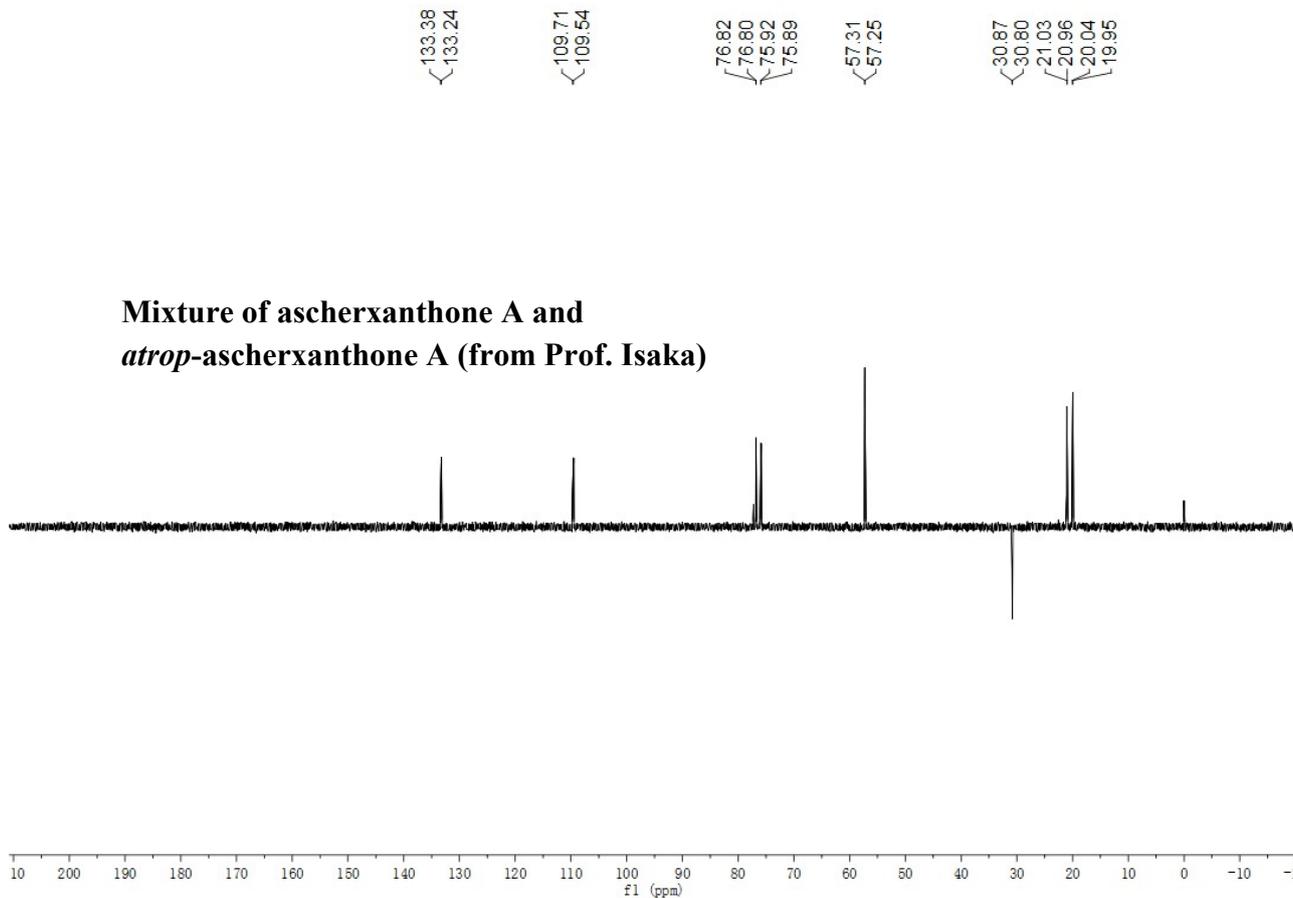
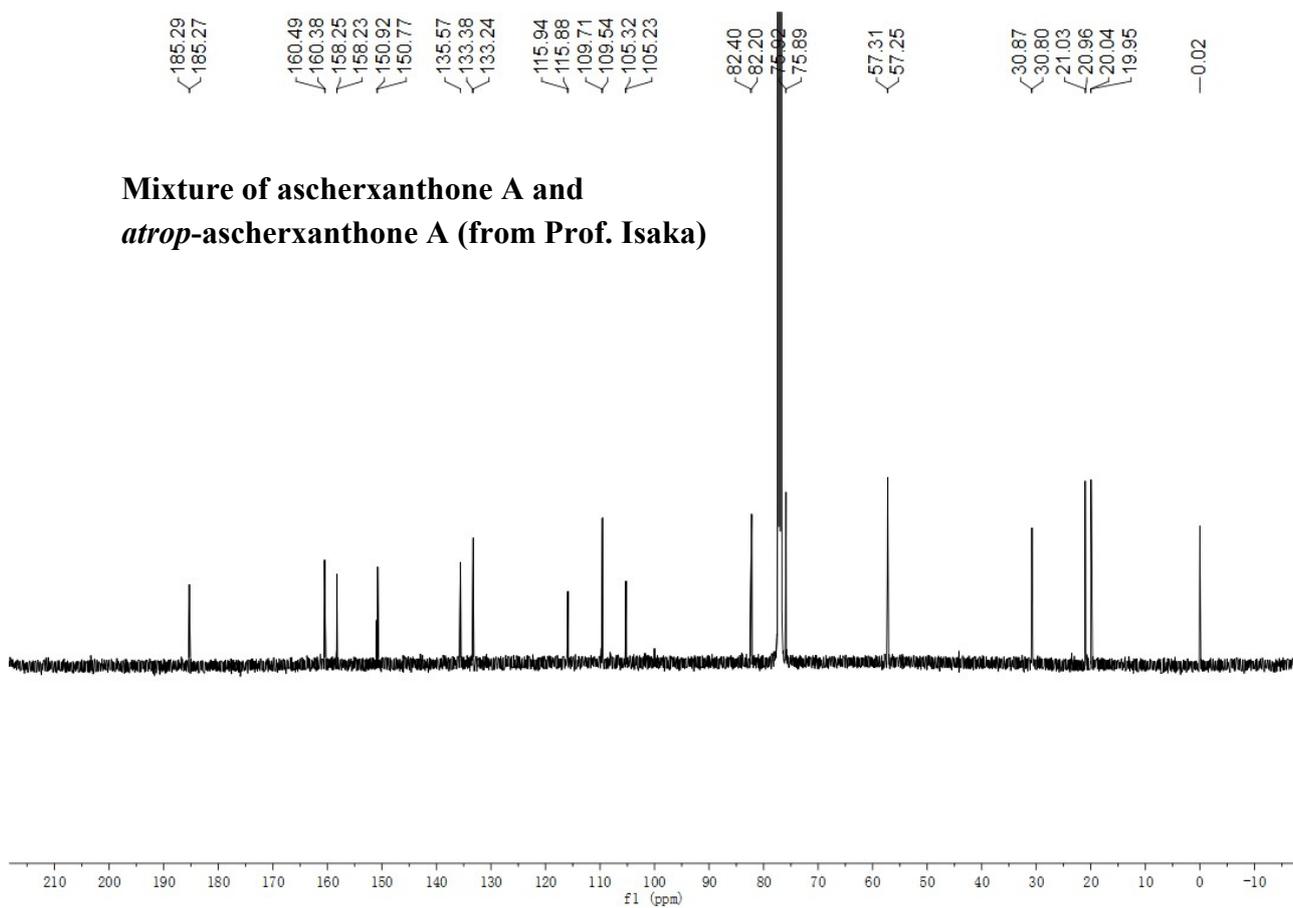


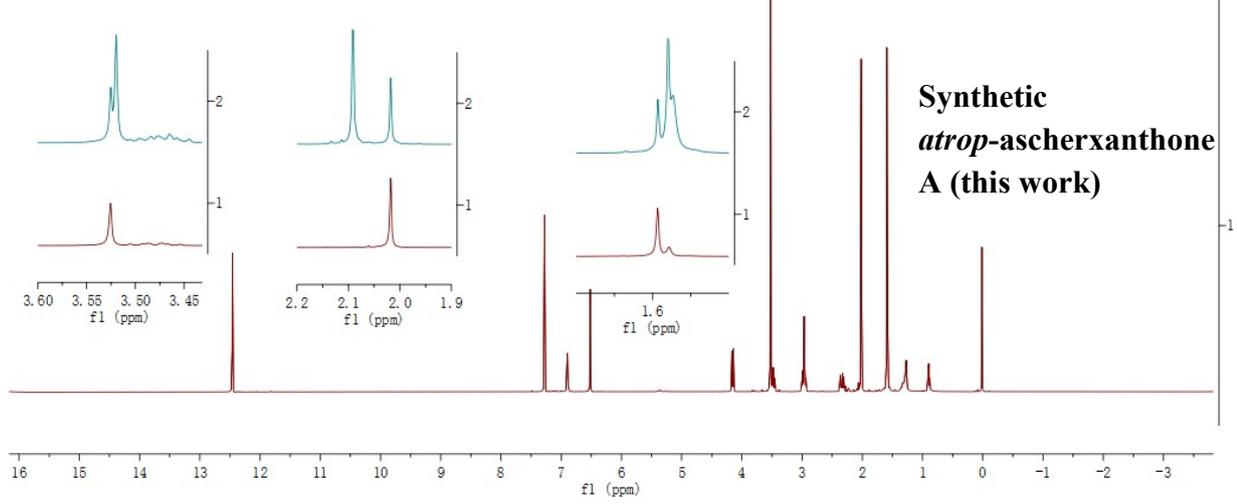
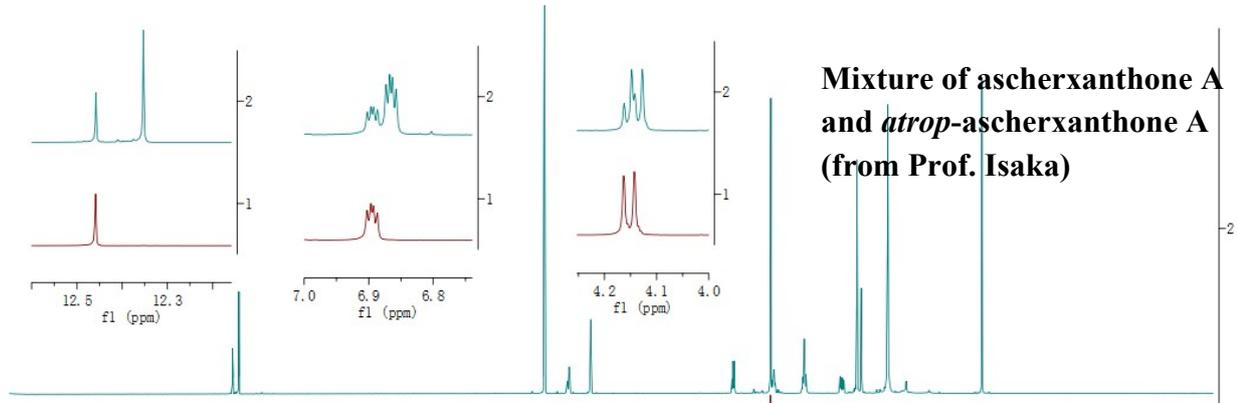
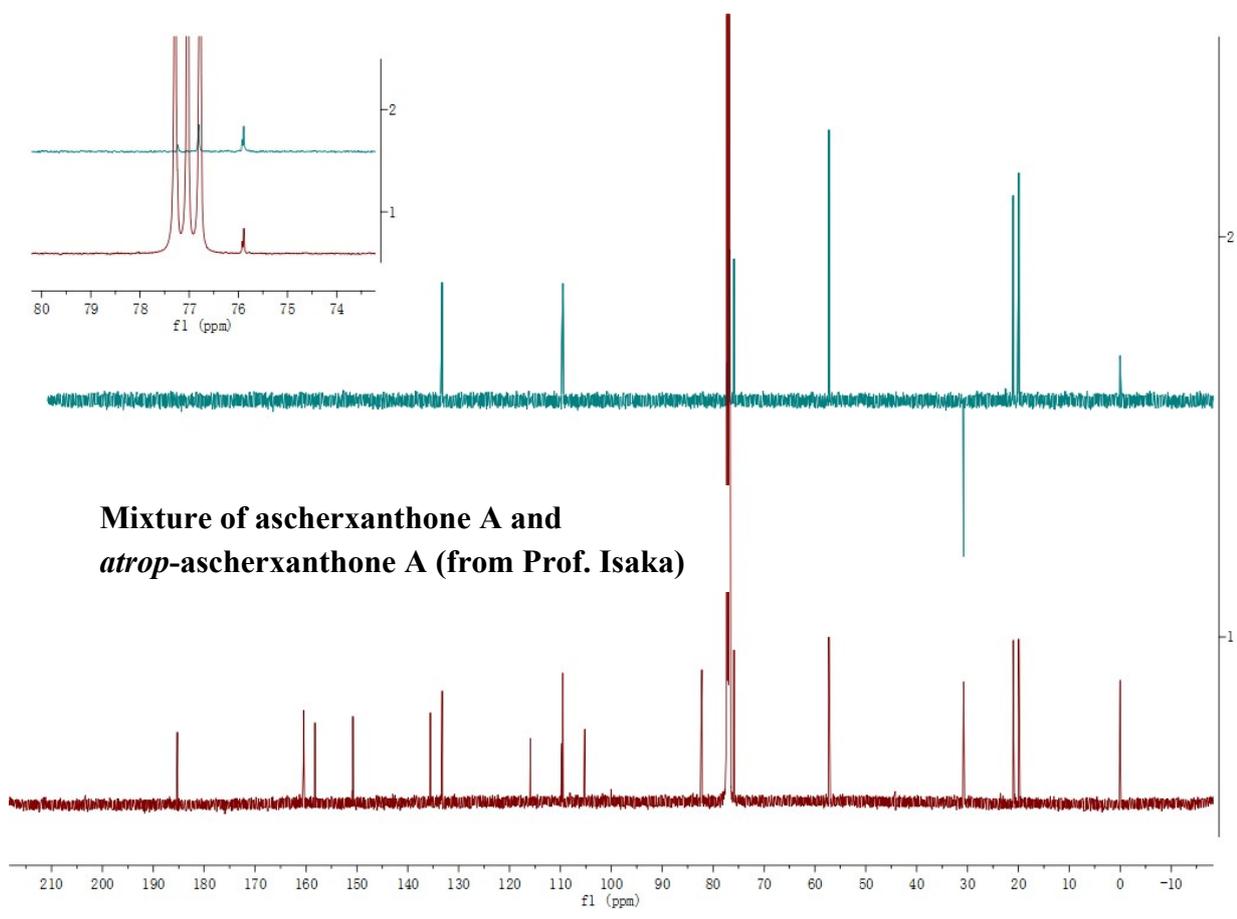
12.46
12.35
7.28
6.90
6.89
6.89
6.87
6.86
6.86
6.52
6.51
4.16
4.15
4.14
4.13
3.53
3.52
3.48
3.48
3.47
2.99
2.98
2.96
2.95
2.94
2.37
2.36
2.35
2.34

**Mixture of ascherxanthone A and
atrop-ascherxanthone A (from Prof. Isaka)**

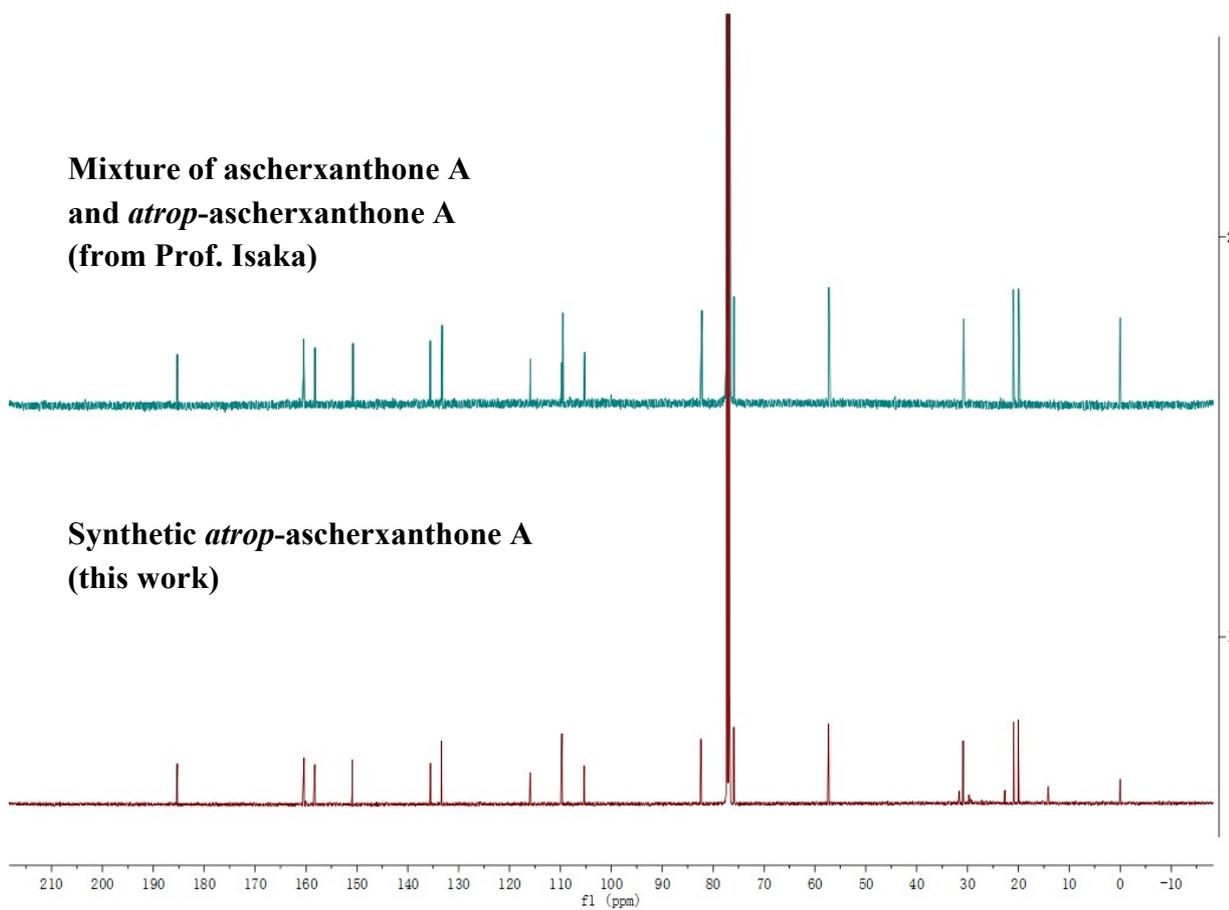


0.62
1.24
0.74
1.27
0.63
1.10
2.00
5.60
2.33
3.93
2.19
3.67
1.93
1.95
4.02





**Mixture of ascherxanthone A
and *atrop*-ascherxanthone A
(from Prof. Isaka)**



**Mixture of ascherxanthone A
and *atrop*-ascherxanthone A
(from Prof. Isaka)**

