Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Asymmetric Synthesis of the Tetracyclic Core of Bufogargarizin C by a Unique Intramolecular [5+2] Cycloaddition

Jian-Hong Fan[†,‡,#], Ya-Jian Hu[†,‡,#], Qiang Guo[‡], Shaoping Li[†], Jing Zhao*[,†], and Chuang-Chuang Li*[,‡]

[†]*Institute of Chinese Medical Sciences, University of Macau, Macau, China*

[‡]*Department of Chemistry and Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen 518055, China*

[#] *These authors contributed equally to this work*

Supplementary Materials

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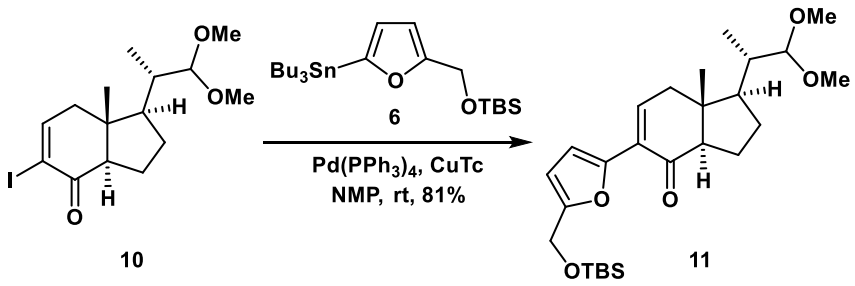
1. General Information

Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere under anhydrous conditions and all reagents were purchased from commercial suppliers without further purification. Solvent purification was conducted according to *Purification of Laboratory Chemicals* (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Yields refer to chromatographically and spectroscopically (^{1}H-NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin layer chromatography on plates (GF254) supplied by Yantai Chemicals (China) using UV light as visualizing agent, an ethanolic solution of phosphomolybdic acid, an acidic solution of *p*-anisaldehyde, or basic aqueous potassium permanganate ($KMnO_4$), and heat as developing agents. If not specially mentioned, flash column chromatography uses silica gel (200-300 mesh) supplied by Tsingtao Haiyang Chemicals (China). Preparative thin layer chromatography (PTLC) separations were carried out 0.50 mm Yantai (China) silica gel plates. NMR spectra were recorded on Bruker AV500, Bruker ARX400, and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, b = broad, m = multiplet.

High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Infrared spectra were recorded on a Shimadzu IR Prestige 21, using thin films of the sample on KBr plates. Optical rotations were measured with a Rudolph autopol I automatic polarimeter using 10 cm glass cells with a sodium 589 nm filter.

2. Experimental Procedures and Characterization Data

Syntheis of enone 11



To a stirred solution of vinyl iodide **10**[1] (15.0 g, 39.7 mmol) in *N*-methyl pyrrolidone (NMP, AR, 100 mL) were sequentially added stannane **6**[2] (23.9 g, 47.6 mmol), $Pd(PPh_3)_4$ (1.38 g, 1.19 mmol), and copper (I) thiophene-2-carboxylate (CuTC, 9.1 g, 47.6 mmol) at room temperature. The resultant mixture was stirred at same temperature for 1 h. The reaction was quenched with saturated NH_4Cl (*aq*.) and diluted with Et_2O (300 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2 x 200 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (40:1 to 20:1, v/v) as eluent to give **11** (14.9 g, 81%) as a brown oil.

$\boldsymbol{R_f}$ = 0.5 (petroleum ether/EtOAc = 6/1);

$\boldsymbol{[\alpha]_D^{25}}$ = +12.0 (*c* 0.25, $CHCl_3$);

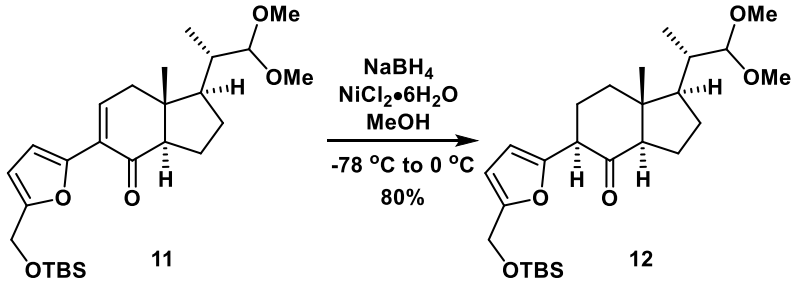
IR (film) $\boldsymbol{\nu_{max}}$ = 2856, 1693, 1463, 1381, 1253, 1076, 837, 779 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 6.1, 2.9 Hz, 1H), 6.84 (d, *J* = 3.3 Hz, 1H), 6.24 (d, *J* = 3.2 Hz, 1H), 4.63 (s, 2H), 4.14 (d, *J* = 2.5 Hz, 1H), 3.46 (s, 3H), 3.40 (s, 3H), 2.78 (dd, *J* = 19.2, 6.2 Hz, 1H), 2.70 (dd, *J* = 11.0, 8.2 Hz, 1H), 2.64 (dd, *J* = 19.3, 2.9 Hz, 1H), 2.01 – 1.93 (m, 1H), 1.89 – 1.78 (m, 3H), 1.73 (ddt, *J* = 10.1, 6.5, 4.1 Hz, 1H), 1.51 – 1.42 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.80 (s, 3H), 0.09 (s, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.7, 153.3, 148.2, 139.9, 129.6, 110.2, 109.4, 108.7, 59.2, 58.3, 57.0, 56.2, 52.6, 47.9, 42.9, 39.2, 27.3, 26.0, 19.8, 18.5, 12.2, 11.7, -5.04;

HRMS (*m/z*): calcd for $C_{26}H_{42}O_5SiNa$ $[M+Na]^+$ 485.2694, found 485.2692.

Synthesis of ketone 12



To a stirred solution of enone **11** (8.48 g, 18.3 mmol) in MeOH (AR, 250 mL) was added $NiCl_2•6H_2O$ (21.7 g, 91.5 mmol) at room temperature. The mixture was cooled to -78 ºC and $NaBH_4$ (6.93 g, 183.0 mmol) was added over 30 min. After stirring for 30 min, the reaction mixture was allowed to warm to 0 ºC for 1 h. Then the reaction mixture was diluted with EtOAc (500 mL) and celite® (30.0 g) was added. After being stirred for another 30 min, the mixture was filtered through celite®-pad and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (20:1 to 10:1, v/v) as eluent to give **12** (6.9 g, 81%) as a yellow oil.

$\boldsymbol{R_f}$ = 0.5 (petroleum ether/EtOAc = 5/1);

$\boldsymbol{[\alpha]_D^{25}}$ = -4.0 (*c* 0.25, $CHCl_3$);

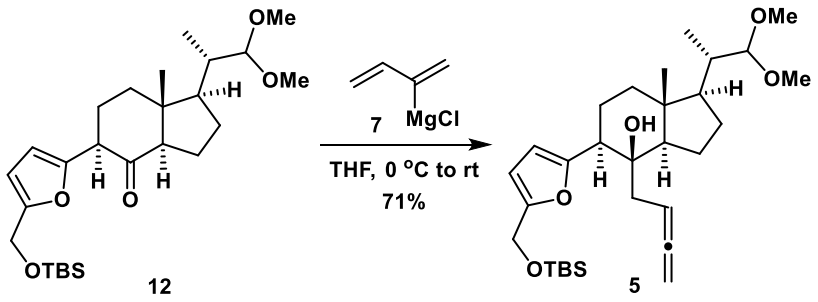
IR (film) $\boldsymbol{\nu_{max}}$ = 2953, 1722, 1714, 1581, 1496, 1384, 1253, 1072, 952 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, *J* = 3.2 Hz, 1H), 6.13 (d, *J* = 3.2 Hz, 1H), 4.60 (s, 2H), 4.12 (d, *J* = 2.4 Hz, 1H), 3.70 – 3.57 (m, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 2.63 – 2.52 (m, 1H), 2.35 – 2.28 (m, 1H), 2.25 – 2.12 (m, 2H), 1.95 –1.87 (m, 1H), 1.86 – 1.80 (m, 1H), 1.80 – 1.73 (m, 2H), 1.72 – 1.66 (m, 1H), 1.61 –1.51 (m, 1H), 1.50 – 1.39 (m, 1H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.70 (s, 3H), 0.06 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1, 153.3, 151.9, 108.9, 108.1, 107.6, 61.6, 58.4, 57.0, 56.1, 52.6, 50.8, 50.4, 39.3, 39.0, 30.4, 27.4, 26.0, 19.4, 18.5, 12.6, 12.0, -5.1, -5.1;

HRMS (*m/z*): calcd for $C_{26}H_{44}O_5SiNa$ $[M+Na]^+$ 487.2850, found 487.2848.

Synthesis of allene 5



A solution of ketone **12** (2.7 g, 5.8 mmol) in THF (20 mL) was cooled to 0 °C and the known Grignard reagent **7**[3] (19.3 mL, 11.6 mmol, 0.6 M in THF) was added dropwise. Then the reaction mixture was allowed to warm to room temperature for 1 h. Upon completion, the reaction mixture was cooled to 0 °C and quenched with saturated NH_4Cl (*aq*.). The layers were separated and the aqueous phase was extracted with diethyl ether (2 x 50 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (30:1 to 20:1, v/v) as eluent to give **5** (2.14 g, 71%) as a colorless oil.

$\boldsymbol{R_f}$ = 0.5 (petroleum ether/EtOAc = 10/1);

$\boldsymbol{[\alpha]_D^{25}}$ = +32.0 (*c* 0.25, $CHCl_3$);

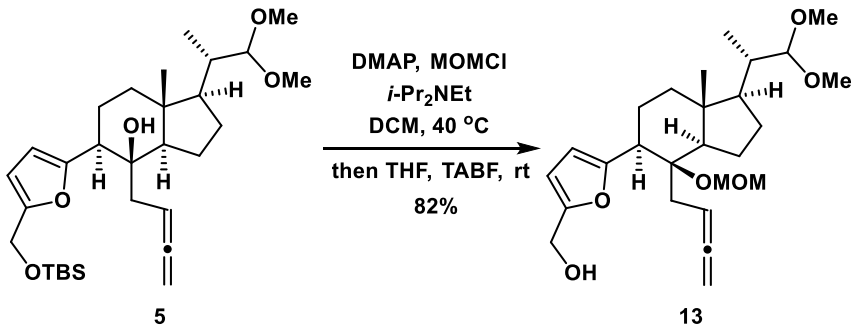
IR (film) $\boldsymbol{\nu_{max}}$ = 2929, 1953, 1462, 1381, 1255, 1143, 1092, 837, 777 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (d, *J* = 3.2 Hz, 1H), 6.06 (d, *J* = 3.1 Hz, 1H), 5.05 (tt, *J* = 8.3, 6.7 Hz, 1H), 4.68 – 4.63 (m, 2H), 4.59 (s, 2H), 4.13 (d, *J* = 2.5 Hz, 1H), 3.45 (s, 3H), 3.39 (s, 3H), 2.81 (dd, *J* = 13.1, 4.1 Hz, 1H), 2.26 – 2.06 (m, 2H), 1.99 (dt, *J* = 12.9, 3.4 Hz, 1H), 1.91 – 1.77 (m, 2H), 1.75 – 1.67 (m, 1H), 1.63 – 1.51 (m, 3H), 1.48 (dd, *J* = 12.0, 8.1 Hz, 1H), 1.44 – 1.36 (m, 2H), 1.34 – 1.28 (m, 1H), 1.03 (s, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.07 (d, *J* = 1.4 Hz, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 210.1, 156.0, 153.2, 109.1, 108.2, 107.8, 85.7, 75.6, 74.2, 58.3, 56.0, 56.1, 53.1, 52.7, 44.1, 42.9, 40.0, 39.3, 39.0, 27.1, 26.0, 25.1, 20.4, 18.5, 13.3, 11.7, -5.0;

HRMS (*m/z*): calcd for $C_{30}H_{50}O_5SiNa$ $[M+Na]^+$ 541.3320, found 541.3321.

Synthesis of 13



5 13

To a solution of **5** (1.5 g, 2.89 mmol) in DCM (15 mL) were sequentially added DMAP (353 mg, 2.89 mmol), *i*-Pr_2NEt (5 mL) and MOMCl (0.44 mL, 5.78 mmol) at room temperature. The reaction mixture was stirred at 40 ºC for 5 h, then *i*-Pr_2NEt (1.9 mL, 17.2 mmol) and MOMCl (0.44 mL, 5.78 mmol) were added again. The reaction mixture was stirred at 40 ºC for another 8 h. The solution was diluted with THF (10 mL) and added tetrabutylammonium fluoride (TBAF, 3.47 mL, 3.47 mmol, 1.0 M in THF) dropwise at room temperature. The reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with saturated NH_4Cl (*aq*.). The layers were separated and the aqueous phase was extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (4:1 to 2:1, v/v) as eluent to give **13** (1.06 g, 82%) as a colorless oil.

$\boldsymbol{R_f}$ = 0.4 (petroleum ether/EtOAc = 2/1);

$\boldsymbol{[\alpha]_D^{25}}$ = +48.0 (*c* 0.25, $CHCl_3$);

IR (film) $\boldsymbol{\nu_{max}}$ = 2945, 1953, 1444, 1143, 1070, 1022, 872, 796 cm^{-1};

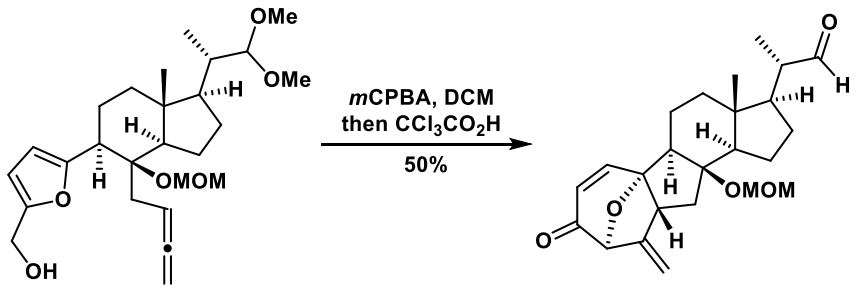
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (d, *J* = 3.1 Hz, 1H), 6.03 (d, *J* = 3.1 Hz, 1H), 5.19 – 5.11 (m, 1H), 4.75 – 4.68 (m, 2H), 4.50 (d, *J* = 2.4 Hz, 2H), 4.33 (d, *J* = 7.3 Hz, 1H),

4.12 – 4.11 (m, 2H), 3.43 (s, 3H), 3.37 (s, 3H), 3.22 (s, 3H), 2.76 (dd, *J* = 13.0, 3.8 Hz, 1H), 2.47 – 2.40 (m, 1H), 2.34 – 2.26 (m, 2H), 2.23 – 2.20 (m, 1H), 1.99 (dt, *J* = 12.9, 3.4 Hz, 1H), 1.85 – 1.79 (m, 1H), 1.72 – 1.67 (m, 1H), 1.61 – 1.58 (m, 1H), 1.57 – 1.48 (m, 2H), 1.43 – 1.33 (m, 2H), 1.31 – 1.25 (m, 1H), 1.01 (s, 3H), 0.94 (d, *J* = 6.7 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 210.4, 156.4, 152.5, 109.0, 108.4, 107.8, 91.1, 86.0, 81.4, 74.3, 57.5, 57.0, 56.0, 55.3, 53.7, 52.7, 42.9, 40.1, 39.0, 32.6, 26.9, 23.8, 20.8, 13.2, 11.6;

HRMS (*m/z*): calcd for $C_{26}H_{40}O_6Na$ $[M+Na]^+$ 471.2717, found 471.2717.

Synthesis of 17



13 **17**

A solution of **13** (1.1 g, 2.46 mmol) in DCM (20 mL) was cooled to 0 ºC, then *m*CPBA (550 mg, 2.71 mmol) and anhydrous $MgSO_4$ (500 mg) were added to the mixture. The reaction mixture was stirred at 0 ºC for 0.5 h. The reaction was diluted with DCM (700 mL) and added CCl_3CO_2H (342 mg, 2.1 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction was quenched with saturated $NaHCO_3$ (*aq.*) (100 mL). The layers were separated after the most of solvent was evaporated *in vacuo*. The aqueous phase was extracted with DCM (2 x 50 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (5:1 to 3:1, v/v) as eluent to give **17** (492 mg, 50%) as a brown oil.

R_f = 0.5 (petroleum ether/EtOAc = 3/1);

$[\alpha]_D^{25}$ = -32.0 (*c* 0.25, $CHCl_3$);

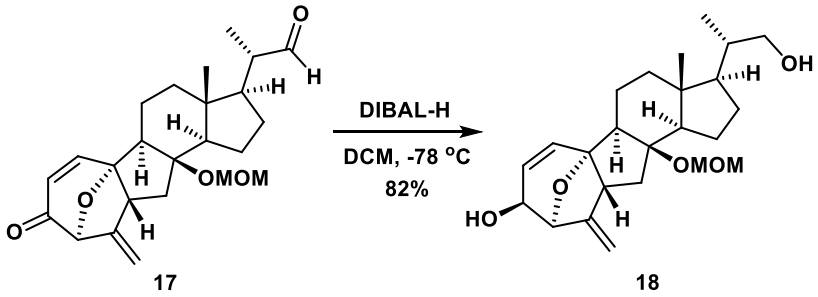
IR (film) ν_{max} = 2937, 1687, 1456, 1153, 1020, 916, 706 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, *J* = 3.1 Hz, 1H), 7.46 (d, *J* = 9.8 Hz, 1H), 5.97 (d, *J* = 9.8 Hz, 1H), 5.39 (d, *J* = 2.4 Hz, 1H), 5.11 (s, 1H), 4.94 (d, *J* = 6.7 Hz, 1H), 4.90 (s, 1H), 4.54 (d, *J* = 6.7 Hz, 1H), 3.46 (dt, *J* = 10.2, 5.4 Hz, 1H), 3.28 (s, 3H), 2.51 (dd, *J* = 12.9, 7.3 Hz, 1H), 2.35 (ddd, *J* = 10.3, 6.8, 3.3 Hz, 1H), 2.08 – 1.99 (m, 2H), 1.88 (dd, *J* = 13.5, 3.4 Hz, 2H), 1.70 – 1.64 (m, 2H), 1.49 – 1.39 (m, 4H), 1.35 (dd, *J* = 16.0, 7.2 Hz, 1H), 1.27 (dd, *J* = 12.6, 3.8 Hz, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.97 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 204.7, 194.8, 155.0, 145.1, 126.3, 111.2, 93.1, 91.4, 91.4, 91.1, 59.5, 56.6, 56.1, 52.3, 50.8, 49.2, 44.2, 40.4, 37.6, 26.8, 23.0, 18.4, 14.2, 13.5;

HRMS (*m/z*): calcd for $C_{24}H_{33}O_5$ $[M+H]^+$ 401.2323, found 401.2326.

Synthesis of diol 18



To a stirred solution of compound **9** (230 mg, 0.574 mmol) in DCM (10 mL) was added diisobutylaluminium hydride (DIBAL-H, 0.96 mL, 1.44 mmol, 1.5 M solution in toluene) dropwise at -78 ºC. Stirring was continued for 30 min at the same temperature. The reaction was quenched with saturated potassium sodium tartrate (*aq*.) (20 mL) at -78 ºC, and allowed to warm to room temperature for 1 h. The layers were

separated and the aqueous phase was extracted with DCM (2 x 20 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (3:1 to 1:1, v/v) as eluent to give **10** (190 mg, 82%) as a white foam.

$\boldsymbol{R_f}$ = 0.3 (petroleum ether/EtOAc = 1/1);

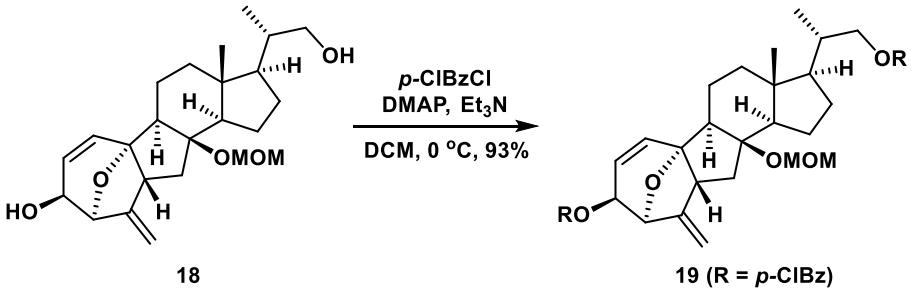
$\boldsymbol{[\alpha]_D^{25}}$ = +28.0 (*c* 0.25, $CHCl_3$);

IR (film) $\boldsymbol{\nu_{max}}$ = 2873, 1752, 1556, 1013, 902, 758, 685 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.21 (dd, *J* = 9.8, 1.5 Hz, 1H), 5.57 (ddd, *J* = 9.8, 2.6, 1.1 Hz, 1H), 5.21 (d, *J* = 2.2, 1.1 Hz, 1H), 5.16 (p, *J* = 0.9 Hz, 1H), 4.92 (d, *J* = 6.6 Hz, 1H), 4.78 (dt, *J* = 6.3, 1.3 Hz, 1H), 4.54 – 4.52 (m, 2H), 3.59 (dd, *J* = 10.5, 3.2 Hz, 1H), 3.43 – 3.38 (m, 1H), 3.32 (dd, *J* = 10.5, 6.8 Hz, 1H), 3.29 (s, 3H), 2.37 (dd, *J* = 12.7, 7.2 Hz, 1H), 2.05 (dt, *J* = 12.9, 3.2 Hz, 1H), 1.90 (qd, *J* = 12.7, 3.4 Hz, 1H), 1.84 – 1.74 (m, 2H), 1.62 – 1.49 (m, 3H), 1.46 – 1.39 (m, 2H), 1.38 – 1.35 (m, 1H), 1.33 – 1.28 (m, 1H), 1.20 – 1.09 (m, 2H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.8, 135.5, 127.4, 111.0, 92.9, 91.0, 90.3, 85.6, 67.7, 66.7, 59.7, 57.2, 57.0, 55.9, 52.3, 43.8, 40.8, 38.4, 37.6, 27.5, 22.7, 18.3, 16.8, 13.9;

HRMS (*m/z*): calcd for $C_{24}H_{36}O_5Na$ $[M+Na]^+$ 427.2455, found 427.2457.

Synthesis of ester 19



18 **19 (R = *p*-ClBz)**

To a stirred solution of **18** (45 mg, 0.11 mmol) in DCM (2 mL) was sequentially

added DMAP (27 mg, 0.22 mmol), Et_3N (93 μL, 0.66 mmol), and 4-chlorobenzoyl chloride (*p*-ClBzCl) (43 μL, 0.33 mmol) at 0 °C. Stirring was continued for 1 h at the same temperature. The reaction was quenched with saturated NH_4Cl (*aq*.) (5 mL). The layers were separated and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (15:1 to 10:1, v/v) as eluent to give **19** (69.7 mg, 93%) as a white powder.

$\boldsymbol{R_f}$ = 0.5 (petroleum ether/EtOAc = 6/1);

$\boldsymbol{[\alpha]_D^{25}}$ = +68.0 (*c* 0.25, $CHCl_3$);

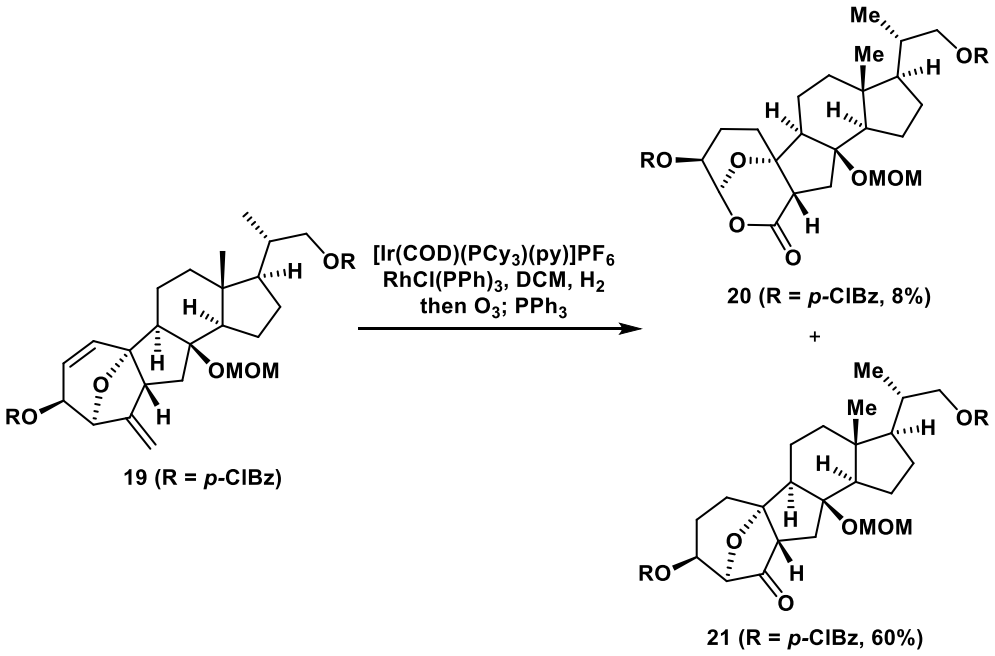
IR (film) $\boldsymbol{\nu_{max}}$ = 2954, 1724, 1593, 1263, 1098, 1006, 756 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.94 (m, 4H), 7.42 – 7.38 (m, 4H), 6.47 (dd, *J* = 9.7, 1.4 Hz, 1H), 5.82 (ddd, *J* = 6.3, 2.9, 1.4 Hz, 1H), 5.66 – 5.63 (m, 1H), 5.12 (d, *J* = 6.2 Hz, 1H), 5.01 (dd, *J* = 4.9, 2.2 Hz, 2H), 4.94 (d, *J* = 6.5 Hz, 1H), 4.57 (d, *J* = 6.5 Hz, 1H), 4.31 (dd, *J* = 10.8, 3.4 Hz, 1H), 4.02 (dd, *J* = 10.8, 7.1 Hz, 1H), 3.56 – 3.52 (m, 1H), 3.35 (s, 3H), 2.43 (dd, *J* = 12.8, 7.3 Hz, 1H), 2.11 (dt, *J* = 12.9, 3.2 Hz, 1H), 1.96 (qd, *J* = 12.8, 3.4 Hz, 1H), 1.90 – 1.81 (m, 3H), 1.64 (ddd, *J* = 15.9, 10.0, 2.9 Hz, 2H), 1.52 – 1.40 (m, 2H), 1.37 – 1.33 (m, 1H), 1.28 – 1.24 (m, 2H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.97 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 165.5, 150.2, 139.6, 139.4, 138.7, 131.1, 131.0, 128.91, 129.0, 128.8, 122.9, 109.46, 92.9, 91.1, 90.4, 83.5, 70.3, 70.1, 59.5, 57.2, 56.5, 56.0, 52.8, 43.9, 40.7, 37.8, 35.7, 27.5, 22.7, 18.3, 17.4, 13.8;

HRMS (*m/z*): calcd for $C_{38}H_{42}Cl_2O_7Na$ $[M+Na]^+$ 703.2200, found 703.2203.

Synthesis of 20 and 21



To a solution of **19** (40 mg, 0.0587 mmol) in DCM (3 mL) was sequentially added $[Ir(COD)(PCy_3)(py)]PF_6$ (4.7 mg, 5.87 μmol) and $RhCl(PPh)_3$ (5.4 mg, 5.87 μmol). The recation mixture was degassed with H_2 for three times and equipped with a H_2 balloon, and stirred at room temperature for 2 h. Then the mixture was cooled to –78 °C and bubbled ozone for 3 min. Then PPh_3 (30.8 mg, 0.117 mmol) was added and stirred for 0.5 h at –78 °C. The reaction mixture was allowed to warm to room temperature for 1 h. Then the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc (10:1 to 5:1, v/v) as eluent to give **21** (24 mg, 60%) as a colorless oil and **20** (3.3 mg, 8%) as a colorless oil.

Characterization data for 20:

$\boldsymbol{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1);

IR (film) $\boldsymbol{\nu_{max}}$ = 3328, 2847, 1764, 1729, 1581, 1332, 1091, 812 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 13.1, 8.2 Hz, 4H), 7.41 (dd, *J* = 8.4, 3.1 Hz, 4H), 5.80 (d, *J* = 3.1 Hz, 1H), 5.16 (dt, *J* = 10.9, 3.8 Hz, 1H), 4.91 (d, *J* = 6.5 Hz, 1H), 4.53 (d, *J* = 6.5 Hz, 1H), 4.31 (dd, *J* = 10.7, 3.3 Hz, 1H), 4.04 (dd, *J* = 10.8, 7.0 Hz, 1H), 3.45 (dd, *J* = 11.2, 7.8 Hz, 1H), 3.32 (s, 3H), 2.76 (dd, *J* = 13.4, 7.9 Hz, 1H),

2.22 (dd, *J* = 10.5, 4.9 Hz, 1H), 2.14 (d, *J* = 12.7 Hz, 1H), 2.04 – 1.95 (m, 3H), 1.87 – 1.84 (m, 1H), 1.76 – 1.66 (m, 4H), 1.60 – 1.58 (m, 1H), 1.50 – 1.42 (m, 2H), 1.36 (dd, *J* = 13.1, 6.5 Hz, 1H), 1.25 -1.20 (m, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.94 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 166.0, 165.0, 140.1, 139.5, 131.4, 131.0, 129.0, 128.9, 128.9, 127.9, 98.3, 93.6, 83.5, 81.3, 70.3, 70.1, 61.1, 57.0, 56.3, 52.7, 46.7, 44.2, 40.2, 36.8, 35.7, 30.0, 27.4, 22.6, 20.8, 17.9, 17.4, 13.5.

HRMS (*m/z*): calcd for $C_{37}H_{43}Cl_2O_9$ $[M+H]^+$ 701.2279, found 701.2283.

Characterization data for 21:

$\boldsymbol{R_f}$ = 0.45 (petroleum ether/EtOAc = 5/1);

$\boldsymbol{[\alpha]_D^{25}}$ = +24.0 (*c* 0.25, $CHCl_3$);

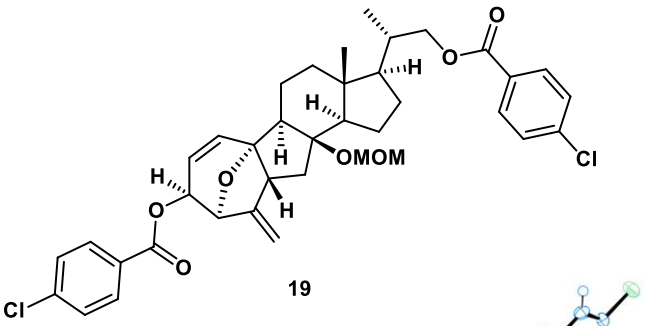
IR (film) $\boldsymbol{\nu_{max}}$ = 3479, 2953, 2875, 1755, 1716, 1593, 1278, 1014, 759 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (t, *J* = 8.5 Hz, 4H), 7.41 (t, *J* = 8.0 Hz, 4H), 5.17 (dt, *J* = 11.2, 5.9 Hz, 1H), 4.92 (d, *J* = 6.6 Hz, 1H), 4.52 (d, *J* = 6.6 Hz, 1H), 4.33 – 4.30 (m, 2H), 4.03 (dd, *J* = 10.8, 7.0 Hz, 1H), 3.33 (s, 3H), 3.23 (dd, *J* = 11.0, 8.0 Hz, 1H), 2.56 (dd, *J* = 13.0, 8.0 Hz, 1H), 2.40 (dt, *J* = 12.7, 5.6 Hz, 1H), 2.14 – 2.04 (m, 2H), 1.94 – 1.78 (m, 6H), 1.65 (d, *J* = 3.5 Hz, 1H), 1.67 – 1.64 (m, 1H), 1.56 (dd, *J* = 13.0, 11.0 Hz, 1H), 1.49 – 1.39 (m, 3H), 1.28 – 1.26 (m, 1H), 1.25 – 1.22 (m, 1H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.95 (s, 3H);

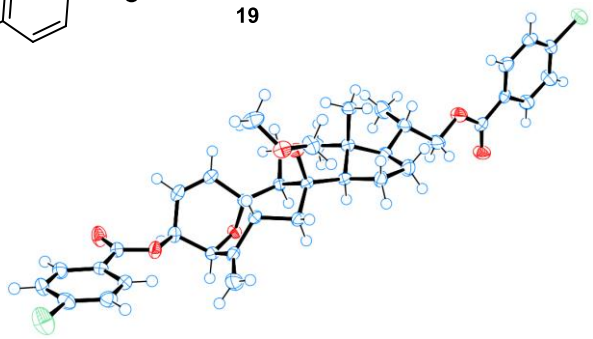
^{13}C NMR (126 MHz, $CDCl_3$) δ 213.6, 166.0, 164.9, 139.9, 139.5, 131.4, 131.0, 129.0, 128.9, 128.9, 128.2, 93.3, 91.7, 89.7, 82.8, 70.1, 68.2, 60.4, 56.8, 55.9, 53.3, 52.8, 44.3, 40.5, 35.7, 33.7, 28.7, 27.5, 24.6, 22.7, 17.8, 17.4, 13.8.

HRMS (*m/z*): calcd for $C_{37}H_{43}Cl_2O_8$ $[M+H]^+$ 685.2335, found 685.2353.

3. X-ray Crystallographic Data



19



Crystal data and structure refinement for **19** (CCDC 1867814):

Identification code	mo_cxy0424_0m
Empirical formula	$C_{38}H_{42}Cl_2O_7$
Formula weight	681.61
Temperature/K	100.0
Crystal system	monoclinic
Space group	C2
a/Å	25.2058(19)
b/Å	7.2704(6)
c/Å	19.2306(15)
α/°	90
β/°	105.306(2)
γ/°	90
Volume/Å^3	3399.1(5)
Z	4
ρ_{calc}g/cm^3	1.332
μ/mm^{-1}	0.241
F(000)	1440.0
Crystal size/mm^3	0.42 × 0.41 × 0.09
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.392 to 55.438
Index ranges	$-32 \le h \le 32$, $-9 \le k \le 9$, $-25 \le l \le 25$
Reflections collected	78192

Independent reflections	7899 [R_{int} = 0.0643, R_{sigma} = 0.0325]
Data/restraints/parameters	7899/1/428
Goodness-of-fit on F^2	1.107
Final R indexes [I>=2σ (I)]	R_1 = 0.0408, wR_2 = 0.0936
Final R indexes [all data]	R_1 = 0.0433, wR_2 = 0.0945
Largest diff. peak/hole / e $Å^{-3}$	0.312/-0.283
Flack parameter	0.04(3)

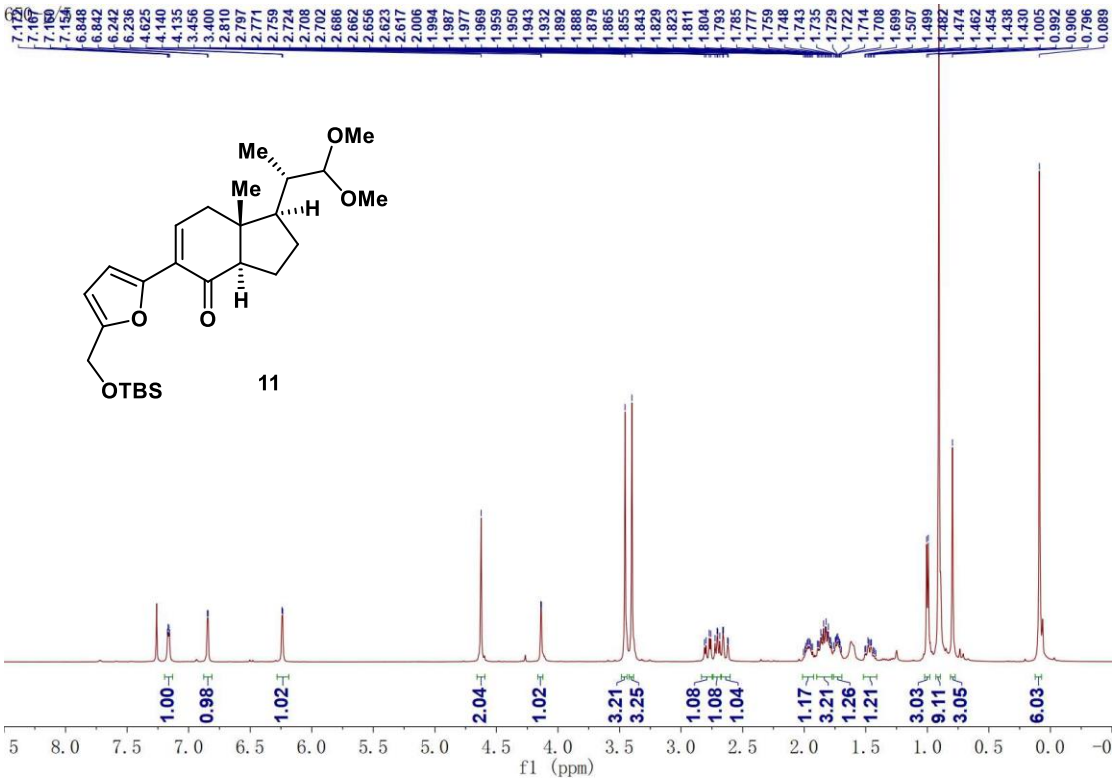
4. References

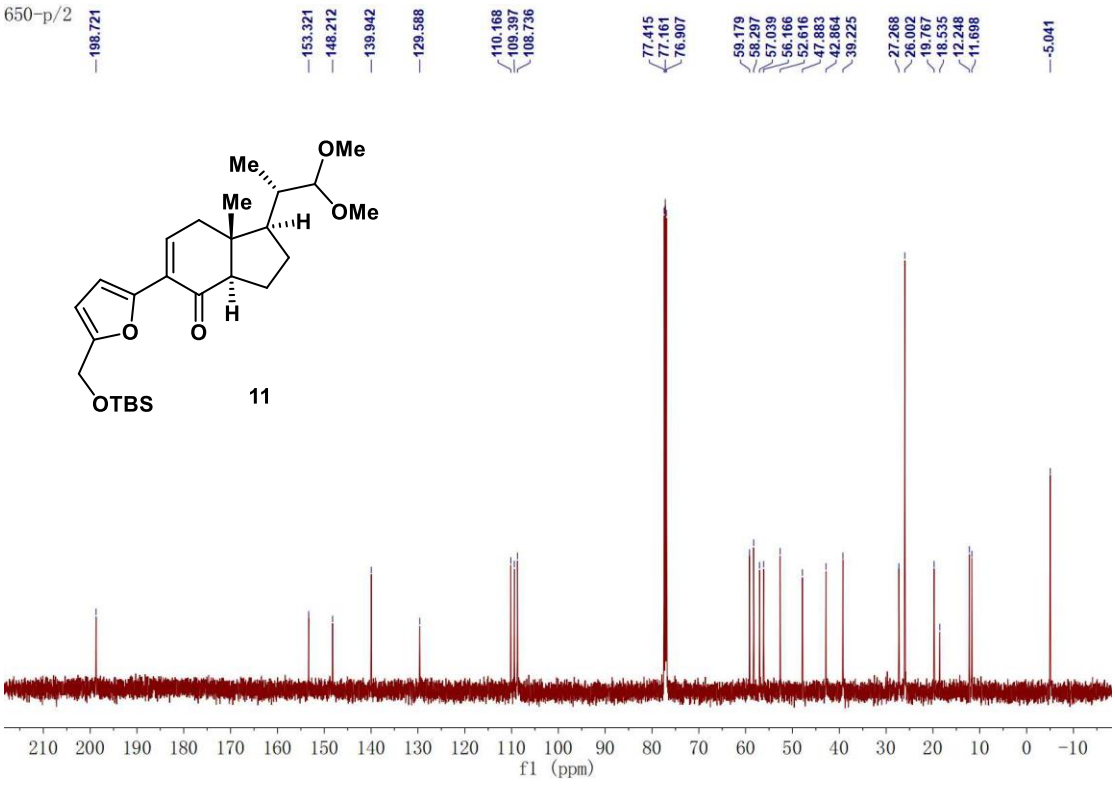
(1) Compound **10** was synthesized according to the reported procedure. See: J. Liu, J. Wu, J. H. Fan, X. Yan, G. Mei and C. C. Li, *J. Am. Chem. Soc.*, 2018, **140**, 5365.

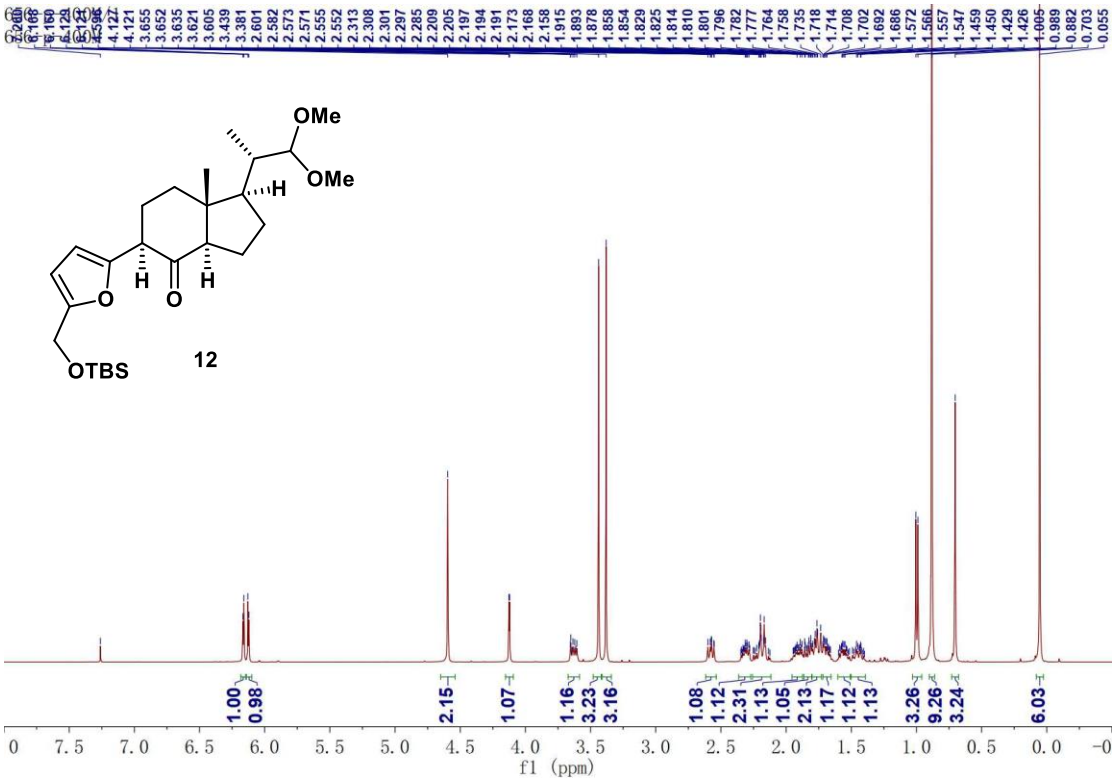
(2) Compound **6** was synthesized according to the reported procedure. See: J. Sandosham and K. Undheim, *Acta Chem. Scand.*, 1994, **48**, 279.

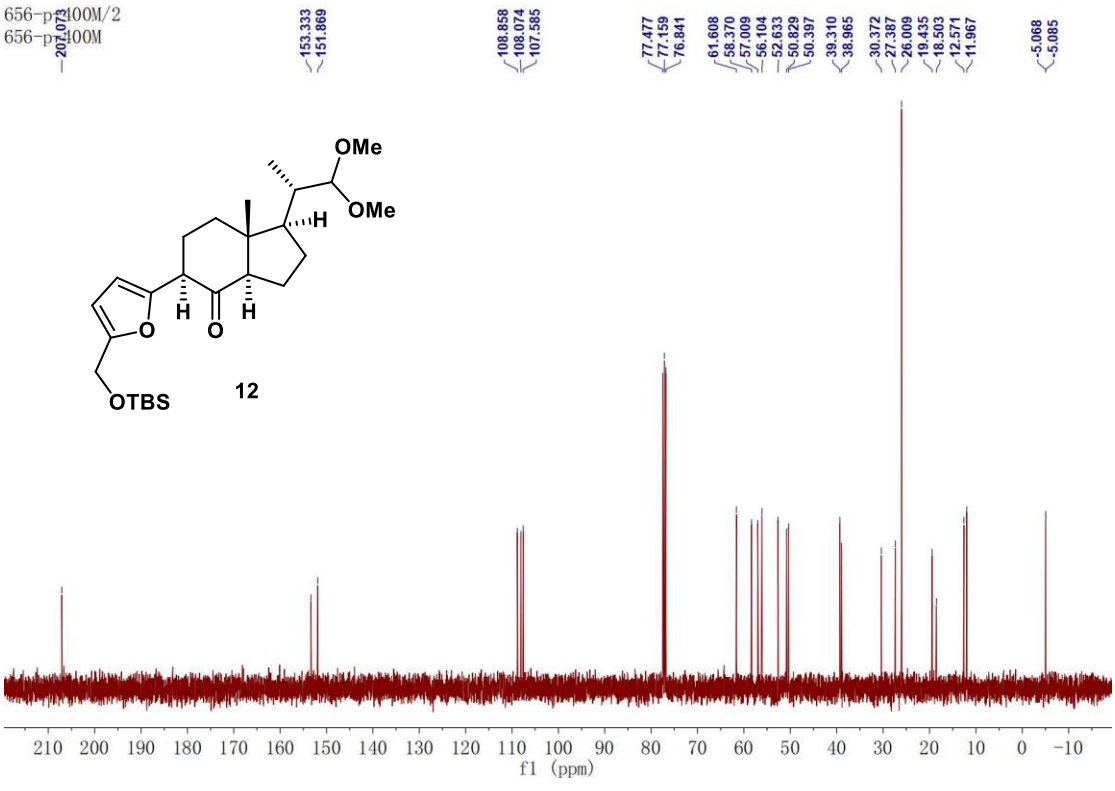
(3) The Grignard reagent **7** was prepared according to the reported procedure. See: (*a*) S. Nunomoto and Y. Yamashita, *J. Org. Chem*., 1979, **44**, 4788; (*b*) T. A. Bradford, A. D. Payne, A. C. Willis, M. N. Paddon-Row and M. S. Sherburn, *Org. Lett*., 2007, **9**, 4861.

5. NMR Spectra






OMe
OMe
H
H
H
O
O
O
OTBS
12
1.00
0.98
2.15
1.07
1.16
3.23
3.16
1.08
1.12
2.31
1.13
1.05
2.13
1.17
1.12
1.13
3.26
9.26
3.24
6.03
f1 (ppm)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656-p-100M
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153.333
151.869
108.858
108.074
107.585
77.477
77.159
76.841
61.608
58.370
57.009
56.104
52.633
50.829
50.397
39.310
38.965
30.372
27.387
26.009
19.435
18.503
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11.967
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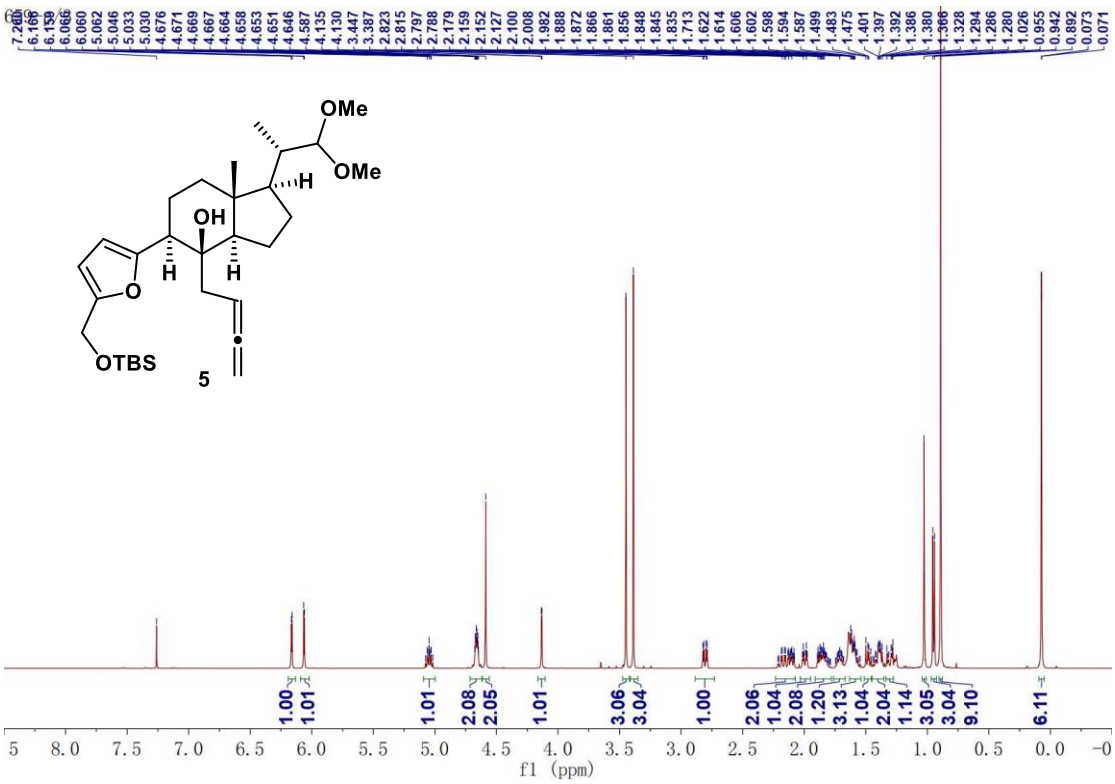
-5.085
OMe
OMe
H
H
H
O
O
O
OTBS
12
f1 (ppm)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OMe
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OH
H
H
O
OTBS
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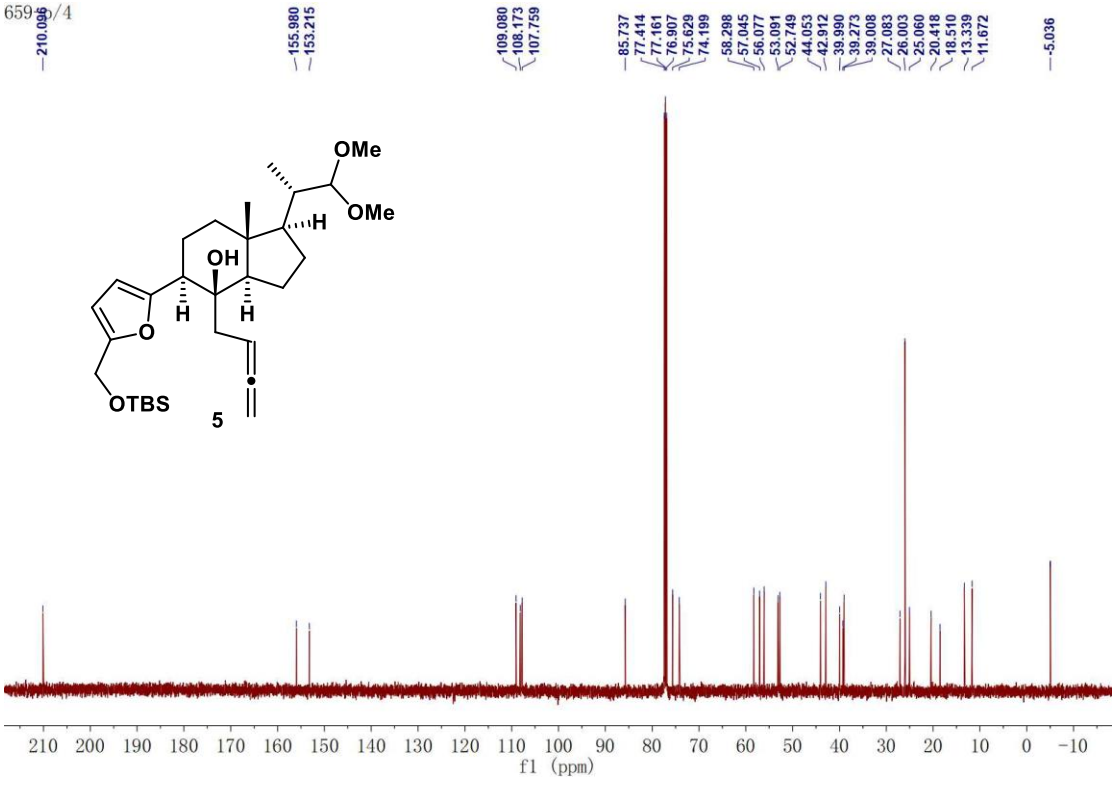
1.01
1.01
2.08
2.05
1.01
3.06
3.04
1.00
2.06
1.04
2.08
1.20
3.13
1.04
2.04
1.14
3.05
3.04
9.10
6.11
f1 (ppm)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OMe
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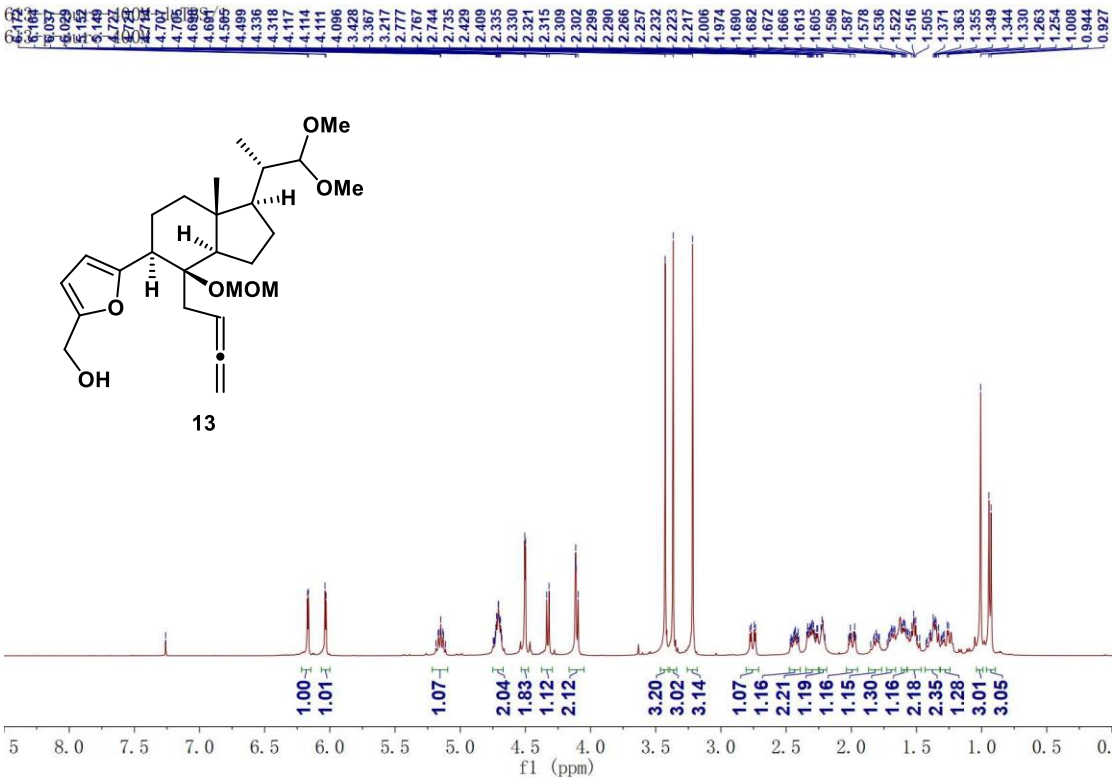
OH
H
H
O
OTBS
5
f1 (ppm)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OMe
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H
H
OMOM
O
OH
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1.01
1.07
2.04
1.83
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2.12
3.20
3.02
3.14
1.07
1.16
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1.19
1.16
1.15
1.30
1.16
2.18
2.35
1.28
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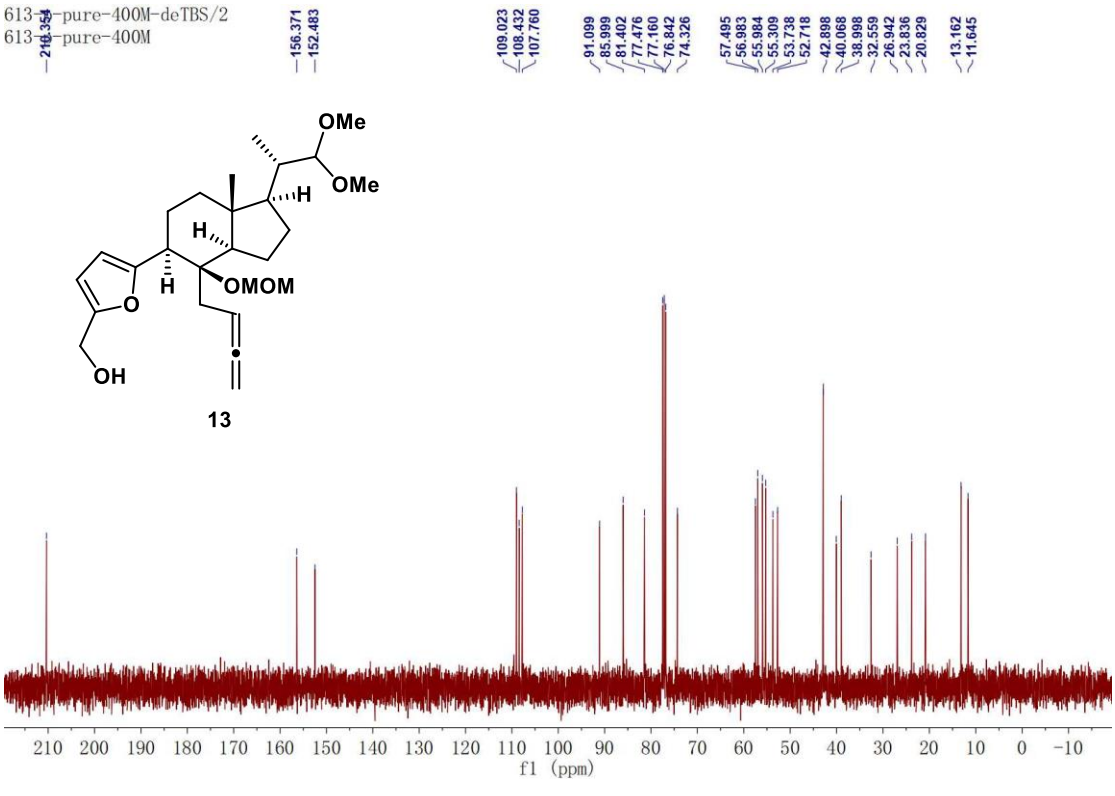
3.05
f1 (ppm)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613--pure-400M
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107.760
91.099
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77.476
77.160
76.842
74.326
57.495
56.983
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55.309
53.738
52.718
42.898
40.068
38.998
32.559
26.942
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13.162
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OMe
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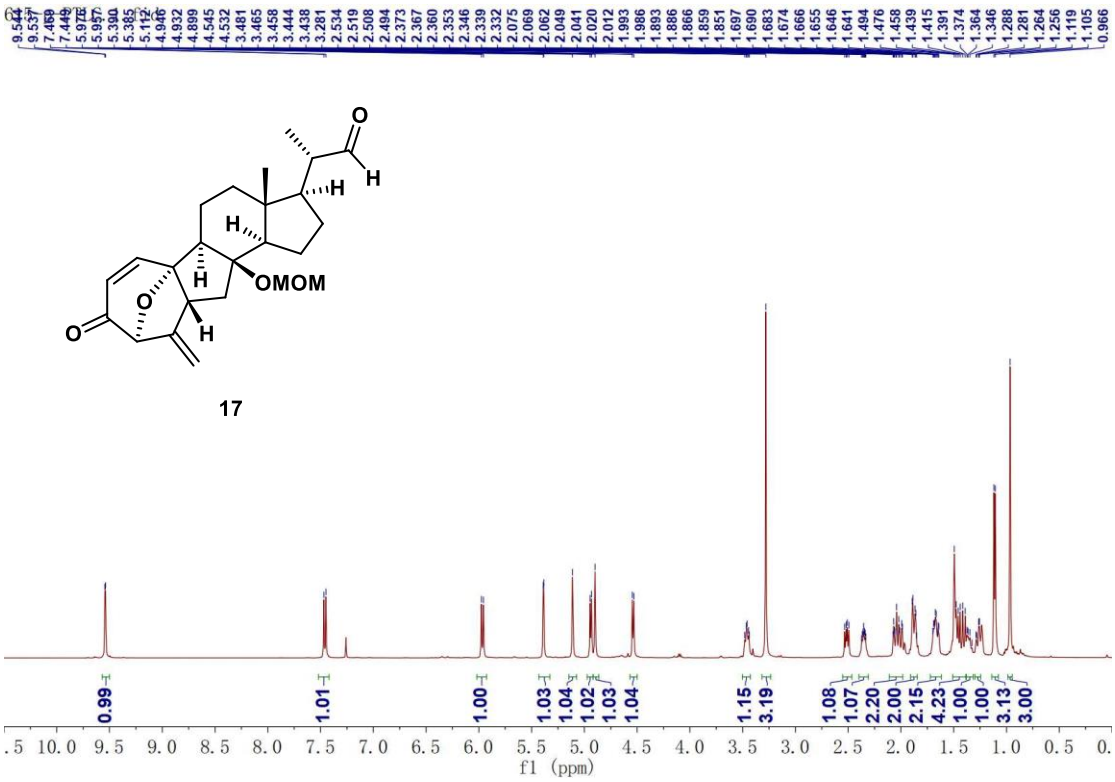
H
H
OMOM
O
OH
13
f1 (ppm)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H
H
H
OMOM
O
O
H
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1.01
1.00
1.03
1.04
1.02
1.03
1.04
1.15
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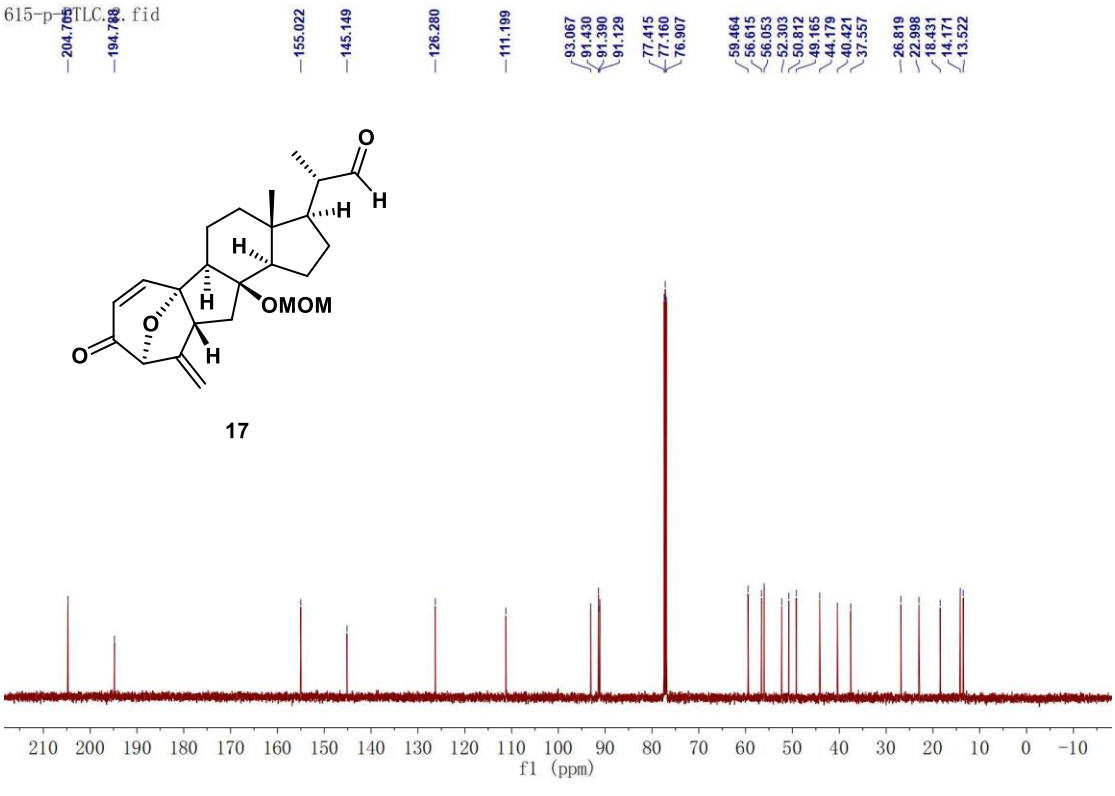
1.00
1.00
3.13
3.00
f1 (ppm)

17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126.280
111.199
93.067
91.430
91.390
91.129
77.415
77.160
76.907
59.464
56.615
56.053
52.303
50.812
49.165
44.179
40.421
37.557
26.819
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14.171
13.522
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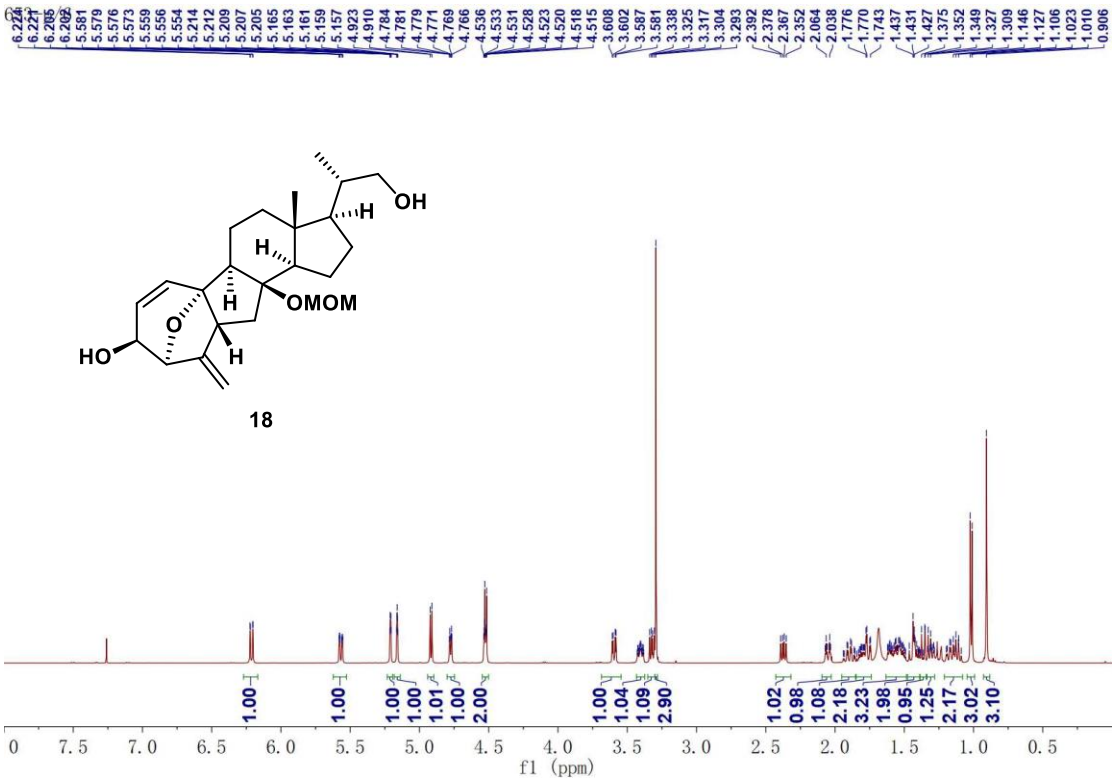
H
H
H
OMOM
O
O
H
f1 (ppm)

17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O
HO
H
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1.04
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2.90
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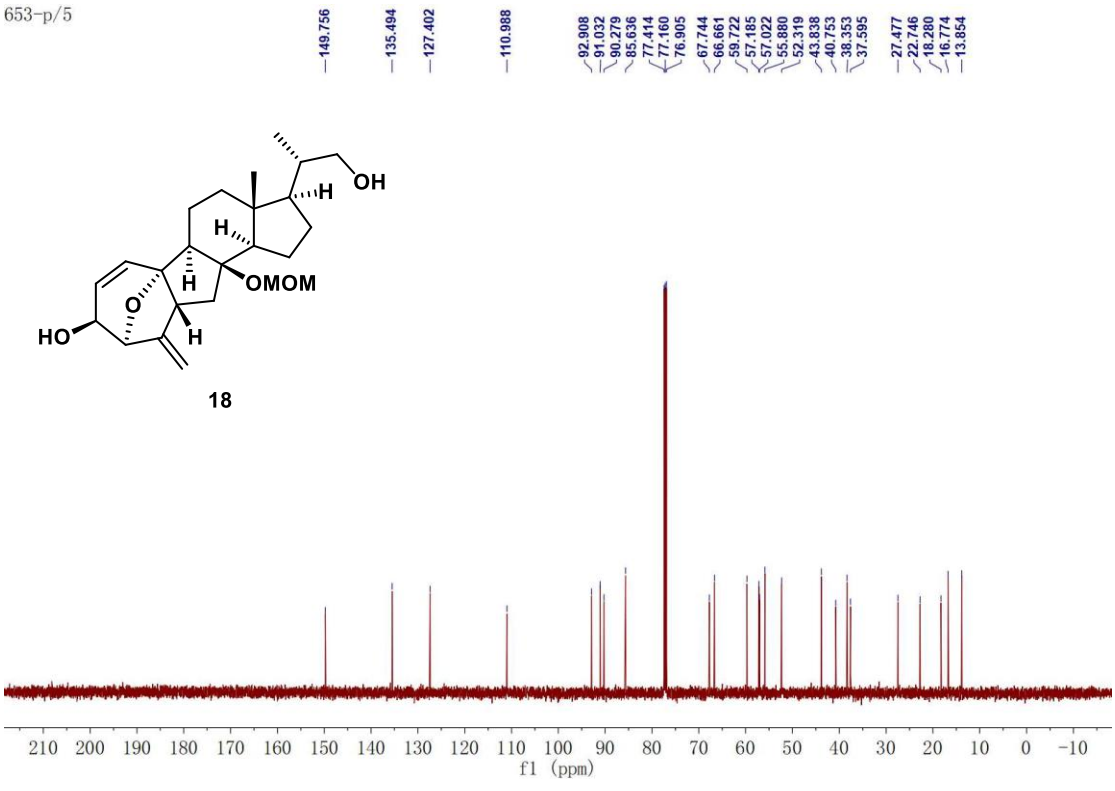
f1 (ppm)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66.661
59.722
57.185
57.022
55.880
52.319
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38.353
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H
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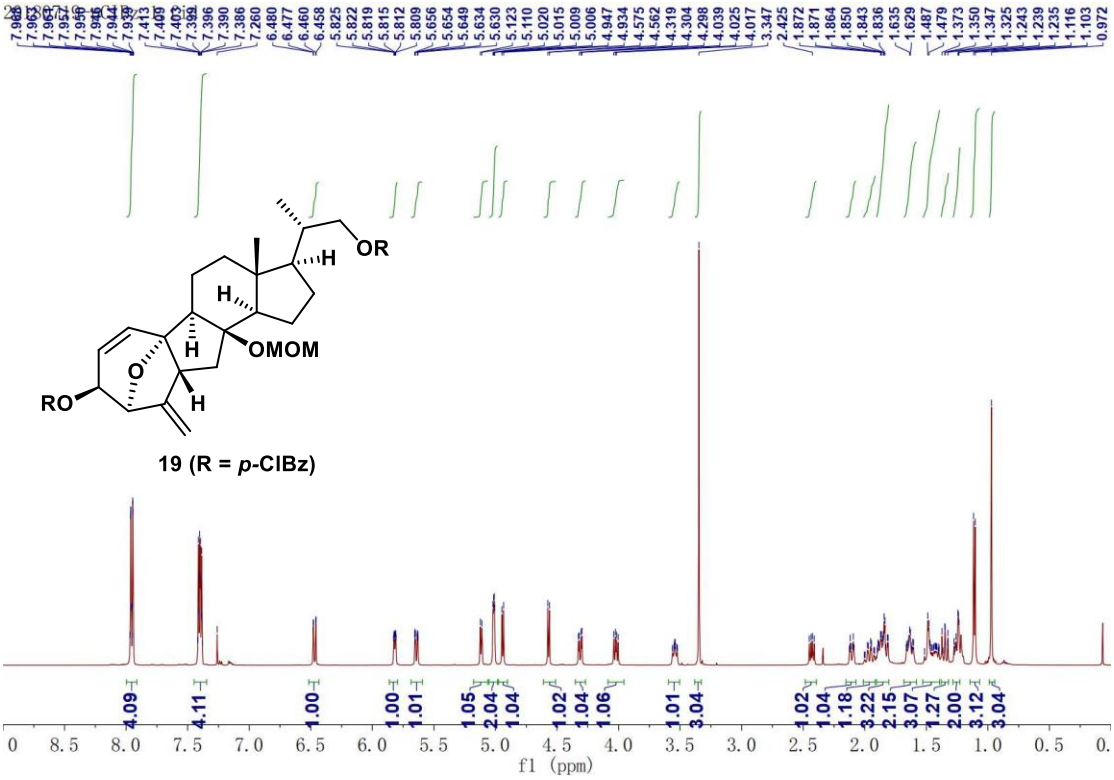
O
HO
H
18
f1 (ppm)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H
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OMOM
O
RO
H
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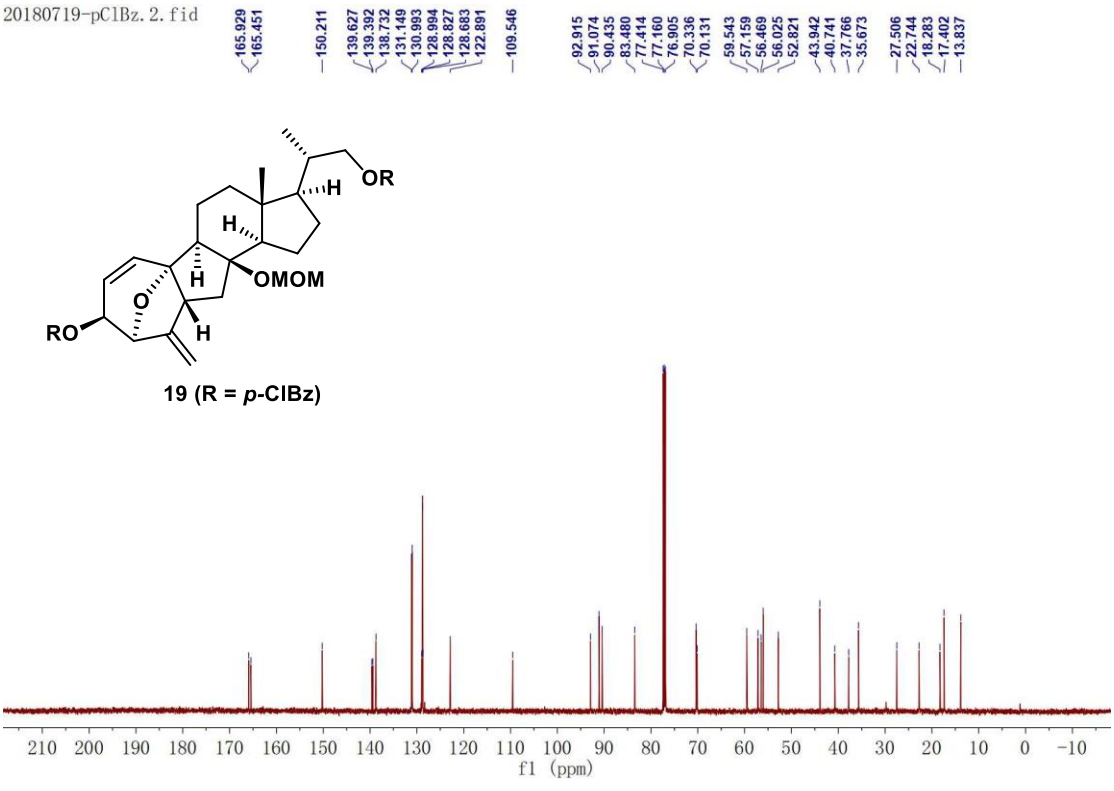
f1 (ppm)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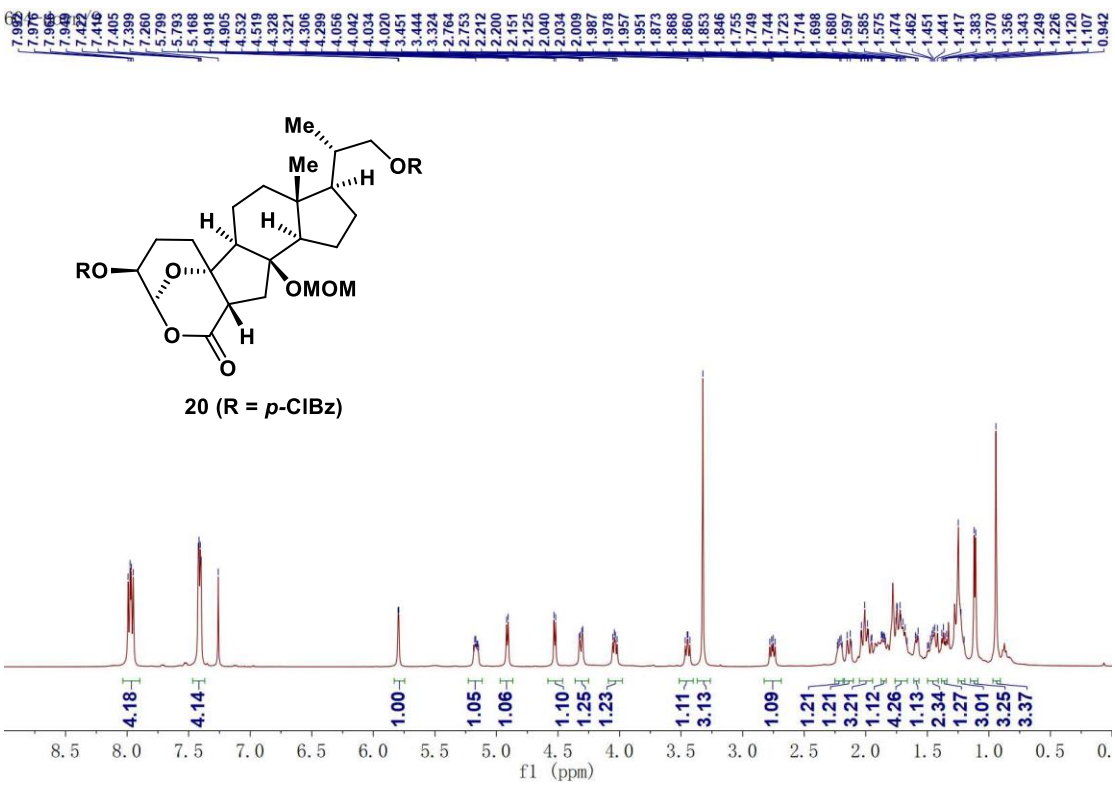
H
H
OMOM
O
RO
H
19 (R = p-ClBz)
f1 (ppm)


Me
Me
OR
H
H
H
RO
O
OMOM
O
H
O
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1.00
1.05
1.06
1.10
1.25
1.23
1.11
3.13
1.09
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1.21
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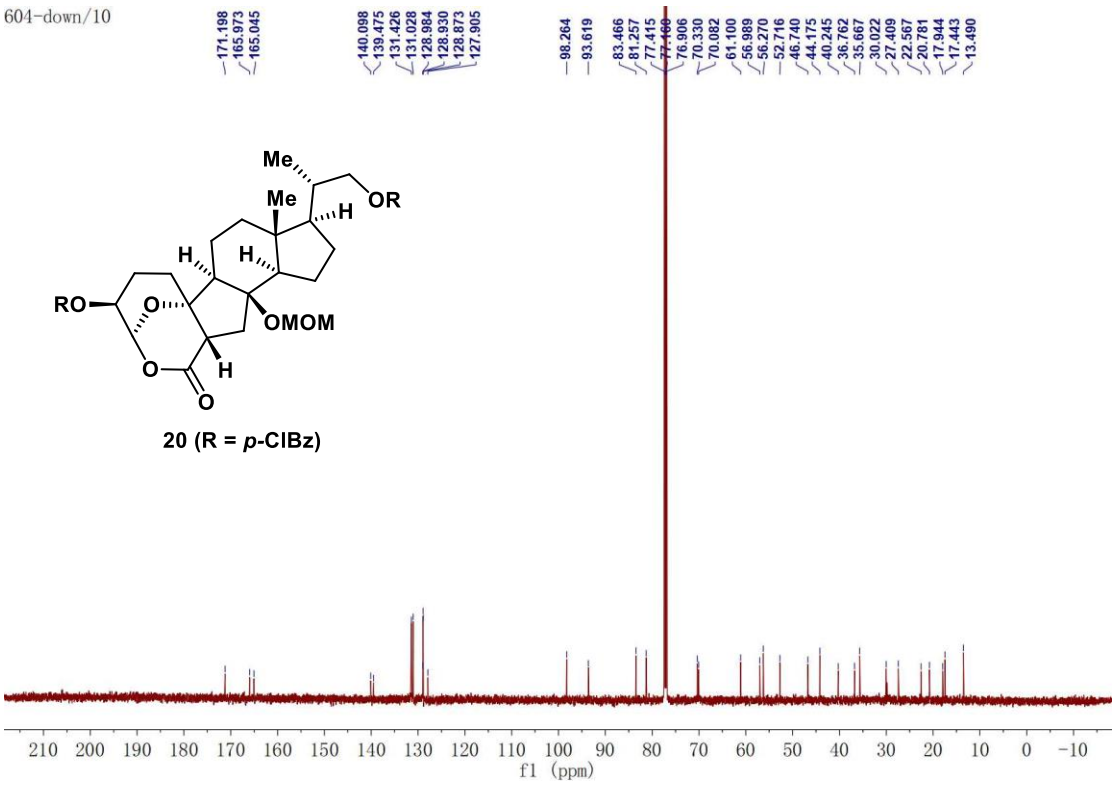
f1 (ppm)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77.160
76.906
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70.082
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52.716
46.740
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35.667
30.022
27.409
22.567
20.781
17.944
17.443
13.490
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H
RO
O
OMOM
O
H
O
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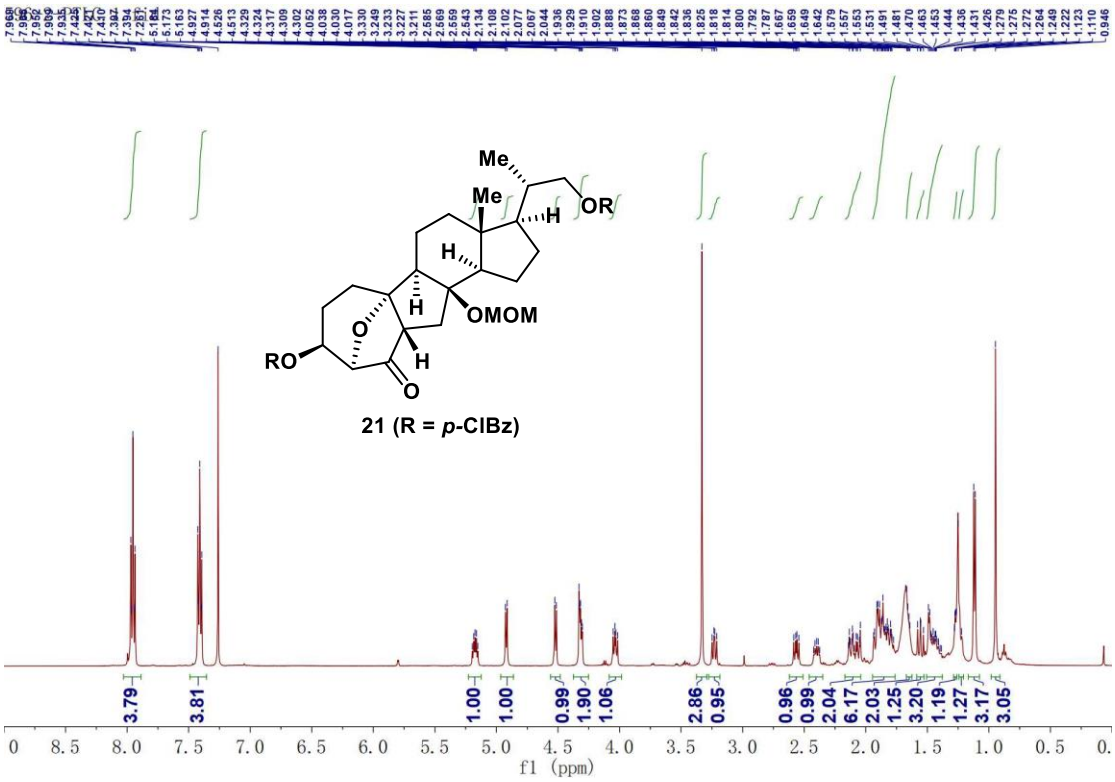
f1 (ppm)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OMOM
O
RO
H
O
21 (R = p-ClBz)
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1.00
0.99
1.90
1.06
2.86
0.95
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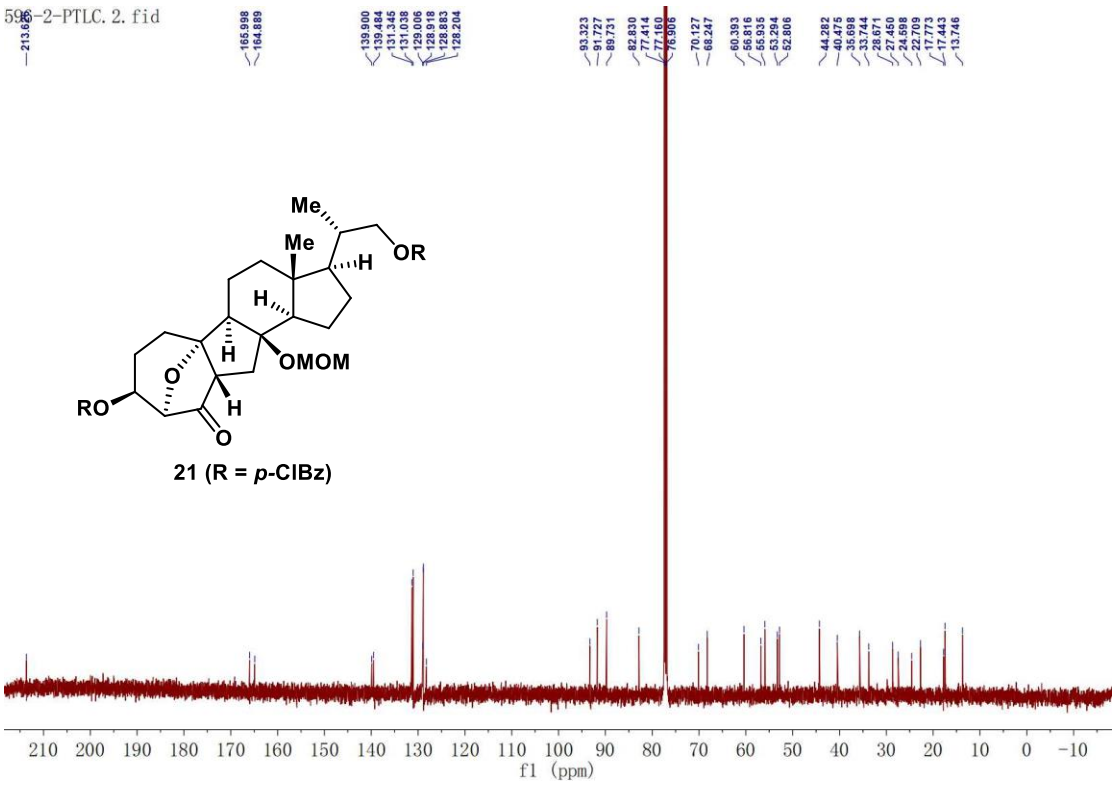
1.19
1.27
3.17
3.05
f1 (ppm)


596-2-PTLC. 2. fid
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Me
H
OR
H
H
OMOM
O
RO
H
O
21 (R = p-ClBz)
f1 (ppm)