

## Supporting Information

### Asymmetric Total Synthesis of Pleurospiroketals A and B

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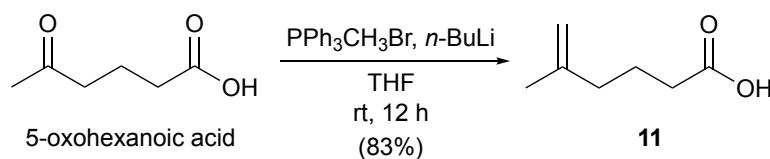
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## General

All reactions involving air- and moisture-sensitive reagents were carried out using standard syringe-septum cap techniques. Unless otherwise noted, all solvents and reagents were obtained from commercial suppliers and used without further purification. Routine monitoring of reactions were carried out Merck silica gel 60 F254 TLC plates. Column chromatography was performed on Kanto Chemical Silica gel 60N (spherical, neutral 60-230  $\mu\text{m}$ ) with the solvents indicated.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured with a Jeol ECZ-400s (400 MHz) or a Burker AV-600 (600 MHz) spectrometer. Chemical shifts were expressed in ppm using  $\text{CHCl}_3$  (7.26 ppm for  $^1\text{H}$  NMR, 77.0 ppm for  $^{13}\text{C}$  NMR) in  $\text{CDCl}_3$  as internal standard. Infrared spectral measurements were carried out with a JASCO FT/IR-4700 FT-IR and only noteworthy absorptions were listed. HRMS spectra measured on a Micromass LCT spectrometer.

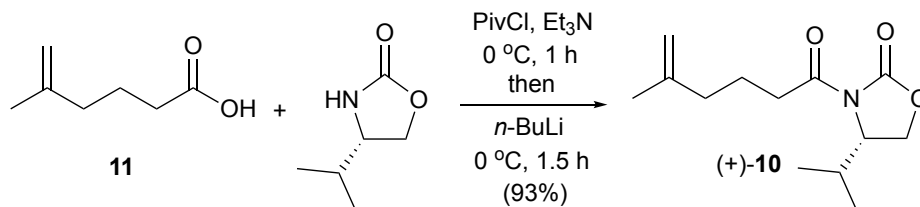
### 5-Methylhex-5-enoic acid (**11**).



To a stirred solution of methyltriphenylphosphonium bromide (25.7 g, 72.0 mmol) in THF (320 mL) was added a solution of  $n$ -butyllithium (45.0 mL, 72.0 mmol, 1.6 M in hexane) at 0  $^\circ\text{C}$ , and the mixture was stirred for 1 h at same temperature under Ar. To a mixture was added 5-oxohexanoic acid (2.84 mL, 3.12 g, 24.0 mmol) at 0  $^\circ\text{C}$ , and the mixture was stirred for 24 h at room temperature. The reaction was quenched with 1 M HCl aqueous solution, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over  $\text{MgSO}_4$ , and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford **11** (2.28 g, 83%) as colorless oil. The spectral data of **11** was identified with those of the previous report.<sup>1</sup>

1. E. E. Lee, T. Rovis, *Org. Lett.*, **2008**, *10*, 1231-1234.

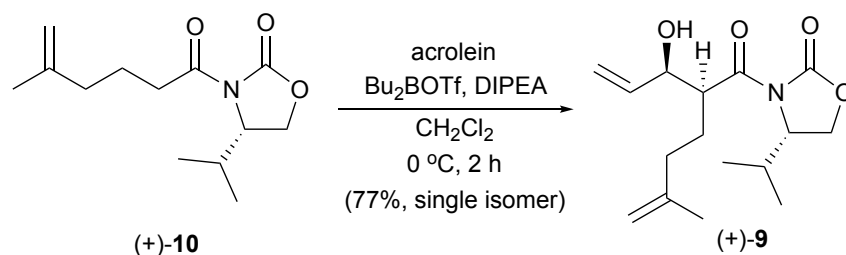
(*S*)-4-Isopropyl-3-(5-methylhex-5-enoyl)oxazolidin-2-one (+)-**10**.



To a stirred solution of (*S*)-4-isopropylloxazolidinone (1.45 g, 11.3 mmol) in THF (35 mL) was added a solution of *n*-butyllithium (7.03 mL, 11.3 mmol, 1.6 M in hexane) at  $-78$  °C, and the reaction mixture was stirred for 20 min at same temperature under Ar. In a second flask, to a stirred solution of **11** (1.44 g, 11.3 mmol) in THF (110 mL) was added triethylamine (1.56 mL, 1.14 g, 11.3 mmol) and pivaloyl chloride (1.37 mL, 1.36 g, 11.3 mmol) at 0 °C, and the mixture was stirred for 1 h at same temperature under Ar. After cooling to  $-78$  °C, the suspension of (*S*)-4-isopropylloxazolidinone /BuLi which prepared above was added and the reaction mixture was stirred for 1 h at same temperature. After the reaction mixture was stirred for 1.5 h at 0 °C, the reaction was quenched with saturated Na<sub>2</sub>CO<sub>3</sub> solution, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 5:1) to afford (+)-**10** (2.51 g, 93%) as colorless oil.

$[\alpha]_D^{25} +71.2$  (c 1.00, CHCl<sub>3</sub>); IR (neat) 3074, 2965, 1782, 1702, 1387, 1302, 1247, 1205 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.85 (3H, d,  $J = 6.9$  Hz), 0.89 (3H, d,  $J = 6.9$  Hz), 1.70 (3H, s), 1.73-1.86 (2H, m), 2.06 (2H, t,  $J = 7.8$  Hz), 2.35 (1H, dq,  $J = 4.1, 6.9, 6.9$  Hz), 2.80-2.88 (1H, m), 2.91-2.99 (1H, m), 4.18 (1H, dd,  $J = 3.2, 9.2$  Hz), 4.25 (1H, t,  $J = 8.7$  Hz), 4.39-4.43 (1H, m), 4.67 (1H, s), 4.71 (1H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.7, 18.0, 22.3(2C), 28.4, 35.0, 37.1, 58.4, 63.4, 110.7, 145.0, 154.1, 173.2; HRESIMS calcd for C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>Na [M + Na]<sup>+</sup> 262.1419, found 262.1413.

(*S*)-3-((*S*)-2-((*R*)-1-Hydroxyallyl)-5-methylhex-5-enoyl)-4-isopropylloxazolidin-2-one (+)-**9**).

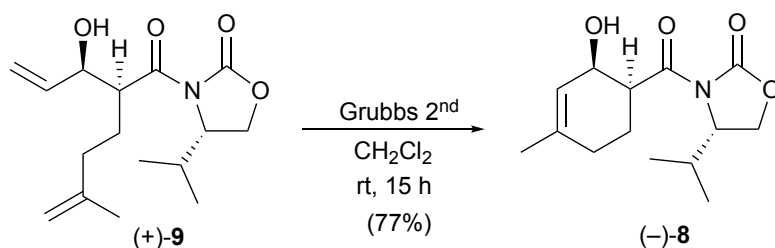


To a stirred solution of (+)-**10** (2.51 g, 10.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (35 mL) was added a solution of dibutylboryl trifluoromethanesulfonate (26.2 mL, 26.2 mmol, 1.0 M in  $\text{CH}_2\text{Cl}_2$ ) at  $-78\text{ }^\circ\text{C}$  under Ar. After a mixture was stirred for 5 min at  $-78\text{ }^\circ\text{C}$ , *N,N*-diisopropylethylamine (5.47 mL, 4.06 g, 31.4 mmol) was added to the reaction mixture at same temperature. The reaction mixture was stirred at  $-78\text{ }^\circ\text{C}$  for 1 h and at  $0\text{ }^\circ\text{C}$  for further 15 min. Then a solution of acrolein (1.75 mL, 1.47 g, 26.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added, and the reaction mixture was stirred for 2 h. A mixture of pH 7 buffer and aqueous  $\text{H}_2\text{O}_2$  (30%, 2:1) was added at  $0\text{ }^\circ\text{C}$ , the mixture was stirred for 1 h, and then the layers were separated. The organic layer was washed with a saturated solution of  $\text{NaHCO}_3$  and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried over  $\text{MgSO}_4$ , and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford (+)-**9** (2.37 g, single isomer, 77%) as colorless oil.

$[\alpha]_D^{25} +56.8$  (c 1.03,  $\text{CHCl}_3$ ); IR (neat) 3491, 3076, 2966, 1779, 1697, 1387, 1301, 1203  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (3H, d,  $J = 6.9$  Hz), 0.92 (3H, d,  $J = 7.3$  Hz), 1.68 (3H, s), 1.72-1.83 (1H, m), 1.89-2.05 (3H, m), 2.30-2.65 (2H, m), 4.13-4.28 (3H, m), 4.35-4.38 (1H, m), 4.48 (1H, dt,  $J = 3.6, 8.3$  Hz), 4.67 (2H, d,  $J = 14.6$  Hz), 5.17-5.20 (1H, m), 5.26-5.32 (1H, m), 5.87 (1H, ddd,  $J = 6.0, 10.5, 17.4$  Hz);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.7, 18.1, 22.3, 25.7, 28.4, 35.5, 47.5, 58.8, 63.2, 73.7, 110.7, 116.7, 137.5, 145.1, 154.3, 174.8; HRESIMS calcd for  $\text{C}_{16}\text{H}_{25}\text{NO}_4\text{Na}$   $[\text{M} + \text{Na}]^+$  318.1681, found 318.1673.



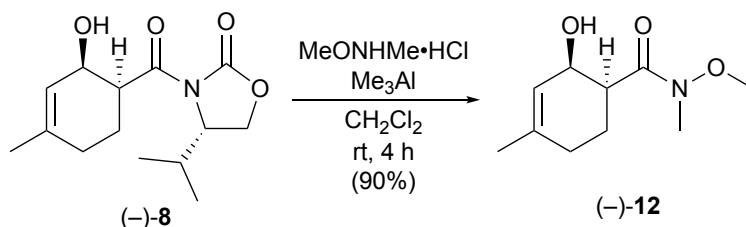
(*S*)-3-((1*S*,2*R*)-2-Hydroxy-4-methylcyclohex-3-ene-1-carbonyl)-4-isopropylloxazolidin-2-one  
(-)-(8).



To a stirred solution of (+)-9 (4.78 g, 16.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (245 mL) was added Grubbs catalyst second generation (69.3 mg, 0.082 mmol) at room temperature under Ar. After the reaction mixture was stirred for 15 h at room temperature, the mixture was concentrated in vacuo to give the crude products, which were purified by column chromatography (hexane-AcOEt, 1:1) to afford (-)-8 (3.32 g, 77%) as a colorless crystal.

M.p. 120-122 °C;  $[\alpha]_{\text{D}}^{26} = -16.2$  (c 0.93,  $\text{CHCl}_3$ ); IR (neat) 3485, 2964, 1778, 1701, 1387, 1308, 1242, 1206  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.88 (3H, d,  $J = 6.9$  Hz), 0.92 (3H, d,  $J = 7.3$  Hz), 1.72 (3H, s), 1.83-1.89 (1H, m), 2.01-2.21 (3H, m), 2.37 (1H, dq,  $J = 4.1, 6.9, 6.9$ ), 3.65 (1H, dt,  $J = 2.8, 11.8$  Hz), 4.22 (1H, dd,  $J = 3.2, 9.1$  Hz), 4.30 (1H, t,  $J = 9.2$  Hz), 4.39-4.41 (1H, m), 4.48 (1H, dt,  $J = 3.2, 8.7$  Hz), 5.61-5.62 (1H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.8, 18.0, 20.6, 23.5, 28.5, 30.3, 44.1, 58.5, 63.5, 64.1, 122.1, 139.8, 153.7, 176.1; HRESIMS calcd for  $\text{C}_{14}\text{H}_{21}\text{NO}_4\text{Na}$   $[\text{M} + \text{Na}]^+ 290.1368$ , found 290.1358.

(1*S*,2*R*)-2-Hydroxy-*N*-methoxy-*N*,4-dimethylcyclohex-3-ene-1-carboxamide (-)-(12).

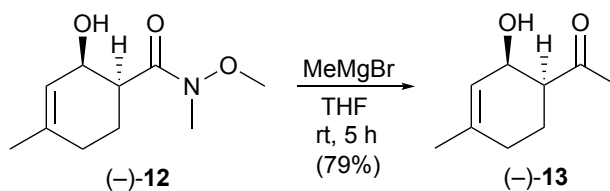


To a stirred solution of *N*,*O*-dimethylhydroxylamine hydrochloride (287 mg, 2.94 mmol) in  $\text{CH}_2\text{Cl}_2$  (12 mL) was added dropwise trimethylaluminum (2.10 mL, 2.94 mmol, 1.4 M in hexane) at 0 °C under Ar. To this mixture was added dropwise a solution of (-)-8 (394 mg,

1.47 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at -15 °C, and stirred for 4 h at room temperature. The reaction was quenched with sat. potassium sodium tartrate aqueous solution, and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford (-)-**12** (257 mg, 90%) as colorless oil.

[ $\alpha$ ]<sub>D</sub><sup>26</sup> -46.4 (c 1.01, CHCl<sub>3</sub>); IR (neat) 3426, 2937, 2829, 1633, 1429, 1389, 1176, 1065 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.67-1.76 (1H, m), 1.70 (3H, s), 2.03-2.15 (3H, m), 2.77-2.79 (1H, m), 3.20 (3H, s), 3.70 (3H, s), 4.32-4.34 (1H, m), 5.63-5.65 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  20.1, 23.5, 30.5, 32.1, 40.6, 61.6, 64.1, 122.5, 138.9, 176.9; HRESIMS calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>3</sub>Na [M + Na]<sup>+</sup> 222.1106, found 222.1094.

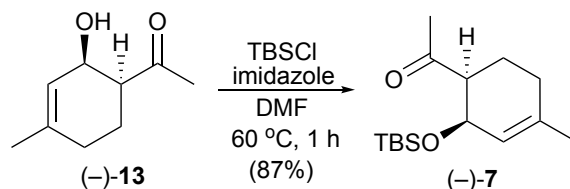
1-((1*S*,2*R*)-2-Hydroxy-4-methylcyclohex-3-en-1-yl)ethan-1-one (-)-(**13**).



To a stirred solution of (-)-**12** (1.15 g, 5.75 mmol) in THF (58 mL) was added methylmagnesiumbromide (42.4 mL, 40.3 mmol, 0.95 M in THF) at 0 °C under Ar, and the mixture was stirred for 5 h at room temperature. The reaction was quenched with sat. NH<sub>4</sub>Cl aqueous solution, and extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford (-)-**13** (702 mg, 79%) as yellow oil.

[ $\alpha$ ]<sub>D</sub><sup>24</sup> -243.0 (c 1.00, CHCl<sub>3</sub>); IR (neat) 3418, 3009, 2911, 1708, 1430, 1354, 1229, 1156 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.70 (3H, s), 1.77-1.92 (2H, m), 1.95-2.09 (2H, m), 2.22 (3H, s), 2.47 (1H, dt, *J* = 3.2, 11.9 Hz), 4.45-4.47 (1H, m), 5.59-5.61 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  19.1, 23.5, 28.6, 30.3, 52.5, 64.5, 122.4, 140.0, 211.7; HRESIMS calcd for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup> 177.0891, found 177.0887.

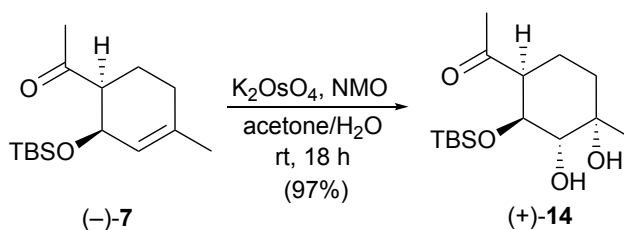
1-((1*S*,2*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohex-3-en-1-yl)ethan-1-one (-)-**7**.



To a stirred solution of (-)-**13** (372 mg, 2.41 mmol) in DMF (9 mL) was added imidazole (887 mg, 13.0 mmol) and TBSCl (945 mg, 6.27 mmol) at 0 °C. After stirred for 1 h at 60 °C, H<sub>2</sub>O was added to this reaction mixture at 0 °C, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 50:1) to afford (-)-**7** (565 mg, 87%) as yellow oil.

$[\alpha]_{\text{D}}^{25}$  -230.5 (c 1.02, CHCl<sub>3</sub>); IR (neat) 2956, 2930, 2886, 2857, 1716, 1254, 1083, 1037 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.00 (3H, s), 0.01 (3H, s), 0.79 (9H, s), 1.66 (3H, s), 1.71-1.94 (3H, m), 1.97-2.07 (1H, m), 2.15 (3H, s), 2.31 (1H, dt, *J* = 3.7, 12.3 Hz), 4.54 (1H, t, *J* = 4.1 Hz), 5.47-5.48 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ -4.7, -3.4, 18.1, 18.4, 23.4, 25.7 (3C), 28.4, 30.0, 53.5, 66.3, 122.9, 139.0, 209.8; HRESIMS calcd for C<sub>15</sub>H<sub>28</sub>O<sub>2</sub>NaSi [M + Na]<sup>+</sup> 291.1756, found 291.1747.

1-((1*S*,2*S*,3*R*,4*S*)-2-((*tert*-Butyldimethylsilyl)oxy)-3,4-dihydroxy-4-methylcyclohexyl)ethan-1-one (+)-**14**.

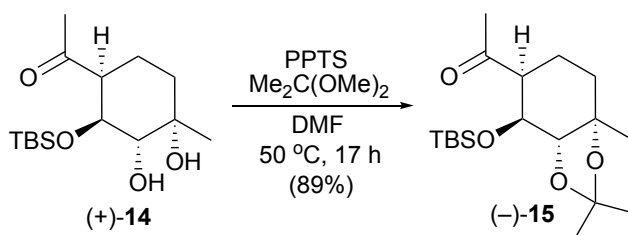


To a stirred solution of (-)-**7** (841 mg, 3.13 mmol) in acetone/H<sub>2</sub>O (4:1, 15 mL) was added 4-methylmorpholine *N*-oxide (808 mg, 6.89 mmol) and potassium osmate (46.2 mg, 0.13 mmol) at 0 °C, and the mixture was stirred for 18 h at room temperature. The reaction was quenched with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> aqueous solution, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The

resulting residue was purified by column chromatography (hexane-AcOEt, 2:1) to afford (+)-**14** (920 mg, 97%) as yellow oil.

$[\alpha]_D^{26} +30.8$  (c 1.02, CHCl<sub>3</sub>); IR (neat) 3437, 2930, 2858, 1706, 1360, 1254, 1109, 1047 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.09 (3H, s), 0.10 (3H, s), 0.87 (9H, s), 1.31 (3H, s), 1.57-1.85 (4H, m), 2.17 (3H, s), 2.97 (1H, q, *J* = 4.6 Hz), 3.74 (1H, d, *J* = 6.8 Hz), 4.11 (1H, dd, *J* = 4.6, 6.9 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ -4.7, -4.2, 18.1, 20.8, 25.8 (3C), 27.1, 31.0, 33.0, 51.8, 72.1, 73.1, 75.6, 209.9; HRESIMS calcd for C<sub>15</sub>H<sub>30</sub>O<sub>4</sub>NaSi [M + Na]<sup>+</sup> 325.1811, found 325.1802.

1-((3*aR*,4*S*,5*S*,7*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2,2,7*a*-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)ethan-1-one (-)-**15**.

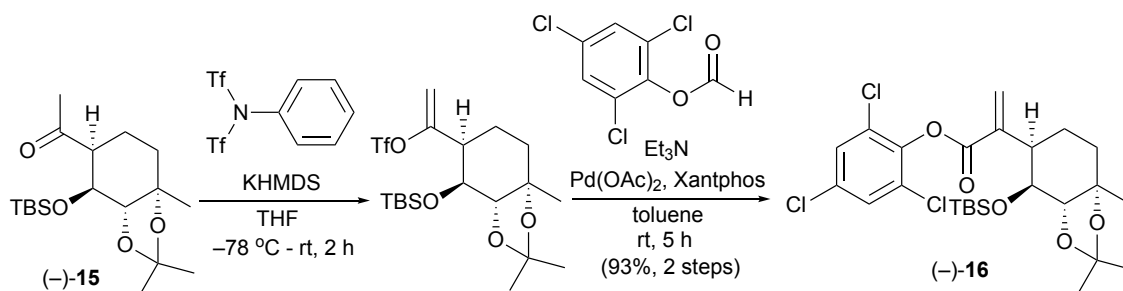


To a stirred solution of (+)-**14** (2.12 g, 7.02 mmol) in DMF (7 mL) was added 2,2-dimethoxypropane (1.72 mL, 1.46 g, 14.0 mmol) and pyridinium *p*-toluenesulfonate (177 mg, 0.70 mmol) at room temperature, and the mixture was stirred for 24 h at 50 °C. The reaction was quenched with sat. NaHCO<sub>3</sub> aqueous solution, and extracted with Et<sub>2</sub>O. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford (-)-**15** (2.14 g, 89%) as yellow oil.

$[\alpha]_D^{27} -36.6$  (c 1.02, CHCl<sub>3</sub>); IR (neat) 2933, 2859, 1716, 1462, 1370, 1241, 1108, 1062 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.03 (3H, s), 0.10 (3H, s), 0.85 (9H, s), 1.35 (6H, s), 1.47 (3H, s), 1.58-1.75 (3H, m), 1.81-1.92 (1H, m), 2.16 (3H, s), 2.66 (1H, td, *J* = 2.7, 11.9 Hz), 3.70 (1H, d, *J* = 2.7 Hz), 4.60-4.62 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: -3.4, -3.8, 18.1, 19.0, 24.8, 25.8 (3C), 27.4, 28.4, 28.7, 35.1, 51.7, 69.5, 79.1, 81.4, 107.7, 209.2; HRESIMS calcd for C<sub>18</sub>H<sub>34</sub>O<sub>4</sub>NaSi [M + Na]<sup>+</sup> 365.2124, found 365.2118.

2,4,6-Trichlorophenyl

2-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2,2,7a-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)acrylate (–)-**(16)**.



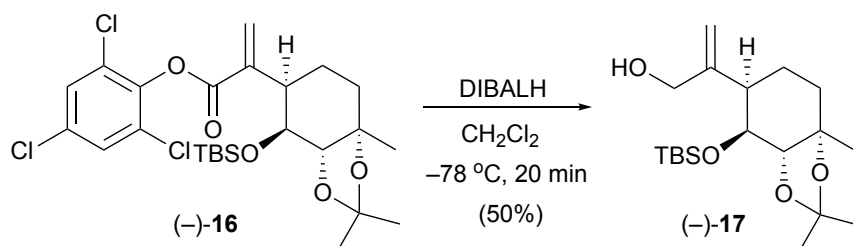
To a stirred solution of (–)-**15** (2.26 g, 6.59 mmol) in THF (45 mL) was added potassium bis(trimethylsilyl)amide (19.8 mL, 9.89 mmol, 0.5 M in toluene) at –78 °C under Ar, and the mixture was stirred for 40 min at same temperature. Then to this solution was added a solution of *N*-phenyltrifluoromethanesulfonamide (3.06 g, 8.57 mmol) in THF (20 mL) at –78 °C, and the mixture was stirred for 2 h at room temperature. The reaction was quenched with H<sub>2</sub>O, and extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 30:1) to afford the corresponding vinyl triflate including some impurity. The mixture was used for next step without further separation.

To a mixture of palladium (II) diacetate (59.2 mg, 0.263 mmol), Xantphos (305 mg, 0.527 mmol) and 2,4,6-trichlorophenyl formate (2.97 g, 13.2 mmol) was added a solution of the vinyl triflate obtained above in toluene (41 mL) at room temperature, then the mixture was stirred for 5 min at same temperature. Then to this solution was added Et<sub>3</sub>N (1.83 mL, 1.33 g, 13.2 mmol) at room temperature, and the mixture was stirred for 5 h at same temperature. The reaction mixture was quenched with H<sub>2</sub>O, and extracted with Et<sub>2</sub>O. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue purified by column chromatography (hexane-AcOEt, 50:1) to afford (–)-**16** (3.35 g, 92% for 2 steps) as a colorless crystal.

M.p. 111–112 °C;  $[\alpha]_D^{28}$  –32.1 (c1.02, CHCl<sub>3</sub>); IR (neat) 3081, 2932, 2858, 1749, 1565, 1449, 1238, 1005 cm<sup>–1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.00 (3H, s), 0.08 (3H, s), 0.90 (9H, s), 1.34 (3H, s), 1.40 (3H, s), 1.49 (3H, s), 1.72–1.97 (4H, m), 3.11–3.14 (1H, m), 3.74 (1H, d, *J* = 2.8 Hz), 4.32–4.34 (1H, m), 5.86 (1H, s), 6.70 (1H, s), 7.37–7.38 (2H, m); <sup>13</sup>C NMR (100 MHz,

CDCl<sub>3</sub>)  $\delta$  -4.4, -4.2, 18.2, 22.3, 25.0, 26.1 (3C), 27.3, 28.5, 36.6, 39.1, 68.8, 77.3, 78.9, 81.6, 107.7, 128.6 (3C), 129.9, 130.5, 131.9, 139.3, 143.3, 163.3; HRESIMS calcd for C<sub>25</sub>H<sub>35</sub>O<sub>5</sub>NaSiCl<sub>3</sub> [M + Na]<sup>+</sup> 571.1217, found 571.1211.

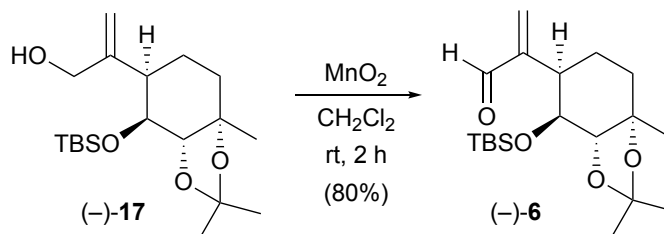
2-((3*aR*,4*S*,5*R*,7*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2,2,7*a*-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-ol (-)-**(17)**.



To a stirred solution of (-)-**16** (334 mg, 0.608 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added diisobutylaluminium hydride (1.52 mL, 1.52 mmol, 1.0 M in hexane) at -78 °C under Ar. After stirred for 20 min at same temperature, saturated potassium sodium tartrate aqueous solution was added to this reaction mixture at 0 °C, and the mixture was stirred for 1 h at room temperature. The mixture was extracted with AcOEt and the combined organic layers were dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 5:1) to afford (-)-**17** (108 mg, 50%) as colorless amorphous.

$[\alpha]_D^{28}$  -20.1 (c 1.89, CHCl<sub>3</sub>); IR (neat) 3466, 2933, 2859, 1462, 1372, 1246, 1104, 1060 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  -0.04 (3H, s), 0.06 (3H, s), 0.87 (9H, s), 0.90-0.94 (1H, m), 1.36 (6H, d, *J* = 9.1 Hz), 1.49 (3H, s), 1.69-1.89 (3H, m), 2.43-2.46 (1H, m), 3.70 (1H, d, *J* = 2.3 Hz), 4.10-4.14 (3H, m), 4.93 (1H, br s), 5.17 (1H, br s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  -4.9, -4.3, 18.2, 21.9, 24.8, 26.0 (3C), 27.4, 28.5, 36.5, 40.5, 65.4, 69.6, 79.2, 81.8, 107.5, 112.1, 148.9; HRESIMS calcd for C<sub>19</sub>H<sub>36</sub>O<sub>4</sub>NaSi [M + Na]<sup>+</sup> 379.2281, found 379.2278.

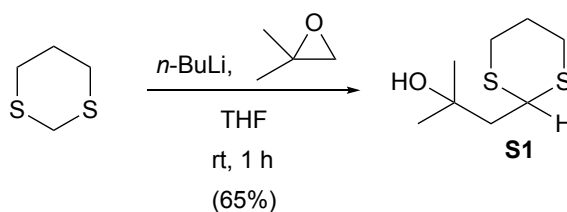
2-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-Butyldimethylsilyloxy)-2,2,7a-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)acrylaldehyde (–)-**6**.



To a stirred solution of (–)-**17** (119 mg, 1.19 mmol) was added manganese dioxide (1.19 g) at room temperature, and the mixture was stirred for 2 h at same temperature. Manganese dioxide was removed by filtration and the filtrate was concentrated in vacuo to give crude products, which were purified by column chromatography (hexane-AcOEt, 20:1) to afford (–)-**6** (94.8 mg, 80%) as colorless oil.

$[\alpha]_D^{28}$  –30.3(c 0.97, CHCl<sub>3</sub>); IR (neat) 2932, 2859, 1696, 1369, 1251, 1211, 1103, 1004 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ –0.19 (3H, s), –0.01 (3H, s), 0.82 (9H, s), 1.21-1.30 (1H, m), 1.34 (6H, d, *J* = 7.8 Hz), 1.48 (3H, s), 1.67-1.88 (3H, m), 2.96-2.99 (1H, m), 3.66 (1H, d, *J* = 2.3 Hz), 4.20 (1H, s), 6.09 (1H, s), 6.23 (1H, s), 9.51 (1H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ –4.8, –4.4, 18.1, 21.3, 24.6, 26.0 (3C), 27.2, 28.5, 36.1, 36.2, 68.3, 78.8, 81.5, 107.6, 136.4, 150.8, 194.4; HRESIMS calcd for C<sub>19</sub>H<sub>34</sub>O<sub>4</sub>NaSi [M + Na]<sup>+</sup> 377.2124, found 377.2119.

1-(1,3-Dithian-2-yl)-2-methylpropan-2-ol (**S1**).

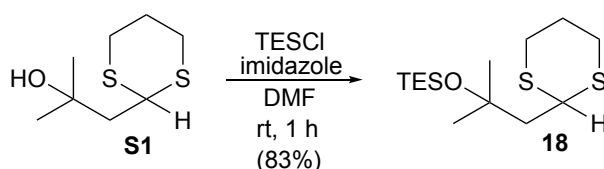


To a stirred solution of 1,3-dithiane (1.0 g, 8.32 mmol) in THF (26 mL) was added a solution of *n*-butyllithium (5.2 mL, 8.32 mmol, 1.6 M in hexane) at –78 °C under Ar, and the mixture was stirred for 1 h at same temperature. Then to this solution was added a solution of isobutylene oxide (0.750 mL, 600.0 mg, 8.32 mmol) in THF (26 mL) at –78 °C, the mixture was stirred for 1 h at same temperature. After the mixture was stirred for further 1h at 0 °C, H<sub>2</sub>O was added to

this reaction mixture at 0 °C, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 6:1) to afford **S1** (1.05 g, 65%) as yellow oil. The spectral data of **S1** was identified with those of the previous report.<sup>2</sup>

2. C. Palomo, M. Oiarbide, J. M. Garcia, P. Banuelos, J. M. Odriozola, J. Razkin and A. Linden, *Org. Lett.*, 2008, **10**, 2637.

((1-(1,3-Dithian-2-yl)-2-methylpropan-2-yl)oxy)triethylsilane (**18**).

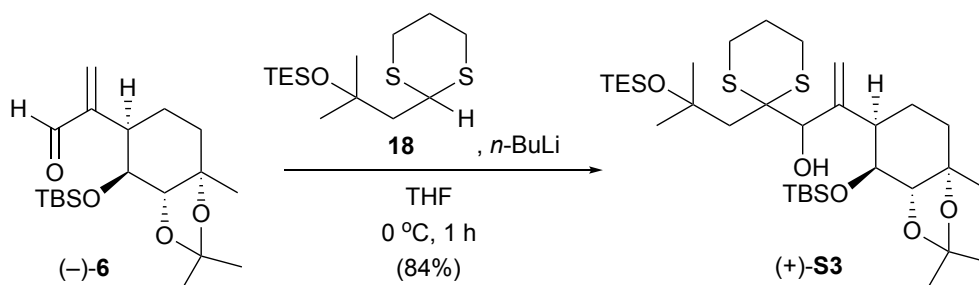


To a stirred solution of **S1** (1.05 g, 5.44 mmol) in DMF (21 mL) was added imidazole (2.00 g, 29.4 mmol) and TESCi (2.46 mL, 2.21 g, 14.7 mmol) at 0 °C. After stirred for 12 h at room temperature, H<sub>2</sub>O was added to this reaction mixture at 0 °C, and the mixture was extracted with Et<sub>2</sub>O. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 80:1) to afford **18** (1.38 g, 83%) as colorless oil.

IR (neat) 2906, 2875, 1458, 1421, 1414 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.59 (6H, q, *J* = 8.8 Hz), 0.96 (9H, t, *J* = 8.1 Hz), 1.29 (6H, s), 1.79 (2H, d, *J* = 4.9 Hz), 2.04-2.10 (1H, m), 2.77 (2H, dt, *J* = 4.0, 15.0 Hz), 2.92 (2H, td, *J* = 3.5, 13.6 Hz), 4.21 (1H, t, *J* = 5.0 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 6.7, 7.1, 25.4, 30.5 (2C), 31.2 (2C), 42.9, 50.8, 73.0; HRESIMS calcd for C<sub>14</sub>H<sub>30</sub>OS<sub>2</sub>Na [M + Na]<sup>+</sup> 329.1405, found 329.1404.



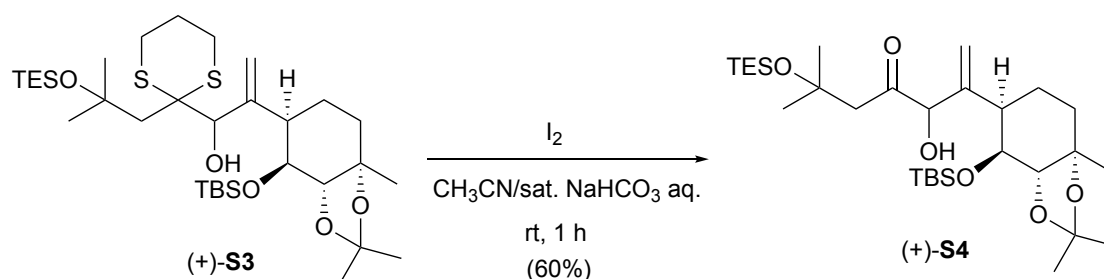
2-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-2,2,7a-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)-1-(2-(2-methyl-2-((triethylsilyl)oxy)propyl)-1,3-dithian-2-yl)prop-2-en-1-ol (+)-**S3**.



To a stirred solution of **18** (321 mg, 1.05 mmol) in THF (3 mL) was added a solution of *n*-butyllithium (0.64 mL, 1.05 mmol, 1.6 M in hexane) at 0 °C under Ar, and the mixture was stirred for 30 min at same temperature. Then to this solution was added a solution of (-)-**6** (82.6 mg, 0.233 mmol) in THF (3 mL) at 0 °C, the mixture was stirred for 1 h at same temperature. The reaction mixture was quenched with saturated NH<sub>4</sub>Cl aqueous solution, and extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue purified by column chromatography (hexane-AcOEt, 10:1) to afford (+)-**S3** (127 mg, 84%) as colorless oil.

$[\alpha]_D^{28} +26.6$  (c 0.67, CHCl<sub>3</sub>); IR (neat) 3436, 2954, 1366, 1242, 1215, 1101, 1059, 1003 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0 (3H, s), 0.06 (3H, s), 0.64 (6H, dd, *J* = 7.8, 15.6 Hz), 0.90 (9H, s), 0.95 (9H, t, *J* = 7.8 Hz), 1.34 (3H, s), 1.38 (6H, d, *J* = 5.9 Hz), 1.50 (3H, s), 1.55 (3H, s), 1.65- 2.00 (6H, m), 2.07-2.11 (1H, m), 2.58-2.62 (1H, m), 2.68-2.76 (1H, m), 2.77-2.88 (3H, m), 3.06-3.09 (1H, m), 3.71 (1H, d, *J* = 2.7 Hz), 4.03 (1H, s), 4.40 (1H, s), 4.63 (1H, s), 5.15 (1H, s), 5.20 (1H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ -4.4, -4.1, 6.7 (3C), 7.2 (3C), 18.2, 23.3, 25.0, 25.1, 26.3 (3C), 26.4, 26.6, 27.3, 28.6, 30.0, 33.2, 37.4, 39.7, 49.4, 59.4, 70.0, 76.1, 79.0, 79.1, 82.2, 107.4, 118.2, 146.0; HRESIMS calcd for C<sub>33</sub>H<sub>64</sub>O<sub>5</sub>NaSi<sub>2</sub>S<sub>2</sub> [M + Na]<sup>+</sup> 683.3631, found 683.3635.

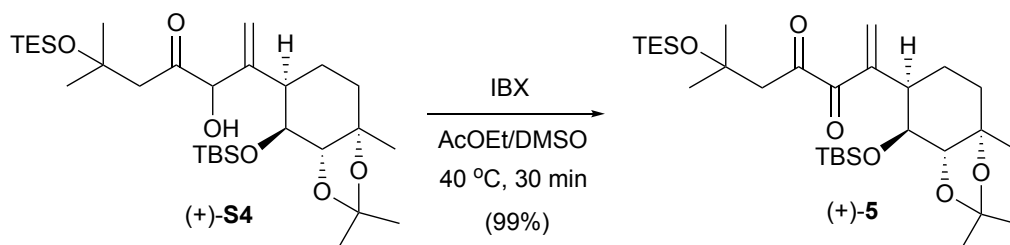
2-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-2,2,7a-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)-3-hydroxy-6-methyl-6-((triethylsilyl)oxy)hept-1-en-4-one (+)-**S4**.



To a stirred solution of (+)-**S3** (45.0 mg, 68.1  $\mu\text{mol}$ ) in  $\text{CN}_3\text{CN}$  (1.5 mL) and saturated  $\text{NaHCO}_3$  aqueous solution (0.5 mL) was added iodine (69.1 mg, 0.272 mmol) at 0 °C under Ar, and the mixture was stirred for 3 h at same temperature. After stirred for further 1 h at room temperature,  $\text{Et}_2\text{O}$  (9 mL), saturated  $\text{Na}_2\text{S}_2\text{O}_3$  aqueous solution (3 mL) and saturated  $\text{NaHCO}_3$  aqueous solution (3 mL) were added to this reaction mixture at room temperature, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 4:1) to afford (+)-**S4** (23.4 mg, 60%) as yellow amorphous.

$[\alpha]_D^{29} +49.5$  (c 0.84,  $\text{CHCl}_3$ ); IR (neat) 3463, 2955, 2877, 1368, 1244, 1102, 1060, 1005  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.03 (3H, s), 0.07 (3H, s), 0.58 (6H, dd,  $J = 7.8, 15.6$  Hz), 0.90 (9H, s), 0.93 (9H, t,  $J = 8.2$  Hz), 1.05-1.12 (1H, m), 1.25 (3H, s), 1.33 (3H, s), 1.34 (3H, s), 1.36 (3H, s), 1.46 (3H, s), 1.60-1.71 (2H, m), 1.79-1.96 (1H, m), 2.04 (1H, dt,  $J = 2.3, 12.3$  Hz), 2.33 (1H, d,  $J = 13.7$ ), 2.98 (1H, d,  $J = 13.8$  Hz), 3.66 (1H, d,  $J = 2.8$  Hz), 4.31 (1H, s), 4.72 (1H, s), 5.20 (1H, s), 5.36 (1H, s);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  -4.5, -4.2, 6.6 (3C), 7.1 (3C), 18.2, 23.8, 24.9, 26.2 (3C), 27.3, 28.5, 29.3, 31.2, 36.7, 38.7, 50.5, 69.9, 73.4, 78.7, 81.8, 84.8, 107.4, 119.6, 145.7, 209.6; HRESIMS calcd for  $\text{C}_{30}\text{H}_{58}\text{O}_6\text{NaSi}_2$   $[\text{M} + \text{Na}]^+$  593.3670, found 593.3676.

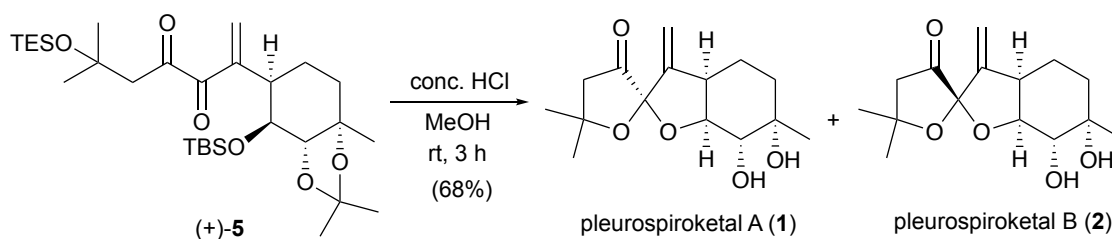
2-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2,2,7a-trimethylhexahydrobenzo[*d*][1,3]dioxol-5-yl)-6-methyl-6-((triethylsilyl)oxy)hept-1-ene-3,4-dione (+)-**5**.



To a stirred solution of (+)-**S4** (12.8 mg, 0.022 mmol) in AcOEt (2 mL) and DMSO (1 mL) was added 2-iodoxybenzoic acid (37.7 mg, 0.135 mmol) at room temperature. After stirred for 30 min at 40 °C, saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> aqueous solution (1 mL) and saturated NaHCO<sub>3</sub> aqueous solution (1 mL) were added to this reaction mixture at room temperature, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford (+)-**5** (12.7 mg, 99%) as colorless oil.

[ $\alpha$ ]<sub>D</sub><sup>24</sup> +4.1 (c 0.66, CHCl<sub>3</sub>); IR (neat) 3398, 2957, 1666, 1368, 1260, 1213, 1103, 1060 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  -0.11 (3H, s), 0.01 (3H, s), 0.54 (6H, dd, *J* = 7.8, 16.0 Hz), 0.86 (9H, s), 0.90 (9H, t, *J* = 7.8 Hz), 1.25 (3H, s), 1.35-1.36 (6H, m), 1.38 (3H, s), 1.52 (3H, s), 1.74-1.91 (4H, m), 2.54 (1H, d, *J* = 13.7 Hz), 3.08 (1H, d, *J* = 11.0 Hz), 3.29 (1H, d, *J* = 13.7 Hz), 3.70 (1H, d, *J* = 2.3 Hz), 4.18 (1H, s), 6.07 (1H, s), 6.33 (1H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  -5.0, -4.3, 6.6 (3C), 7.0 (3C), 18.1, 21.8, 24.8, 26.1 (3C), 27.3, 28.5, 29.7, 30.0, 30.9, 36.5, 37.4, 52.7, 68.6, 73.4, 78.9, 81.6, 107.7, 134.6, 193.8, 202.2; HRESIMS calcd for C<sub>30</sub>H<sub>57</sub>O<sub>6</sub>Si<sub>2</sub> [M + H]<sup>+</sup> 569.3694, found 569.3699.

Pleurospiroketal A (**1**) and Pleurospiroketal B (**2**).



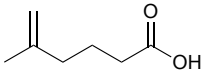
To a stirred solution of (+)-**5** (29.8 mg, 0.052 mmol) in MeOH (0.5 mL) was added conc. HCl (2 drops) at room temperature. After stirred for 3 h at room temperature, saturated NaHCO<sub>3</sub> aqueous solution was added to this reaction mixture at room temperature, and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 1:1) to afford 1 : 1 mixture (ratio was determined by <sup>1</sup>H NMR) of **1** and **2** (10.1 mg, 69%). The mixture could easily be separated by HPLC (YMC-Pack SIL-06, hexane-AcOEt, 1:2) to afforded (+)-**1** (3.9 mg) as a colorless crystal and (+)-**2** (3.6 mg) as colorless oil.

Data for pleurospiroketal A (**1**) :

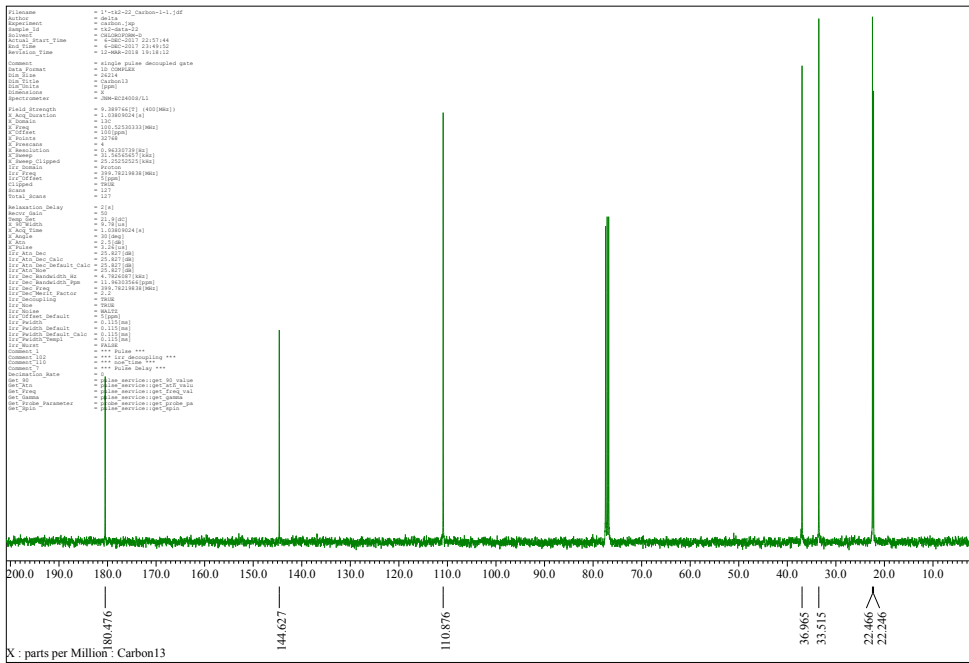
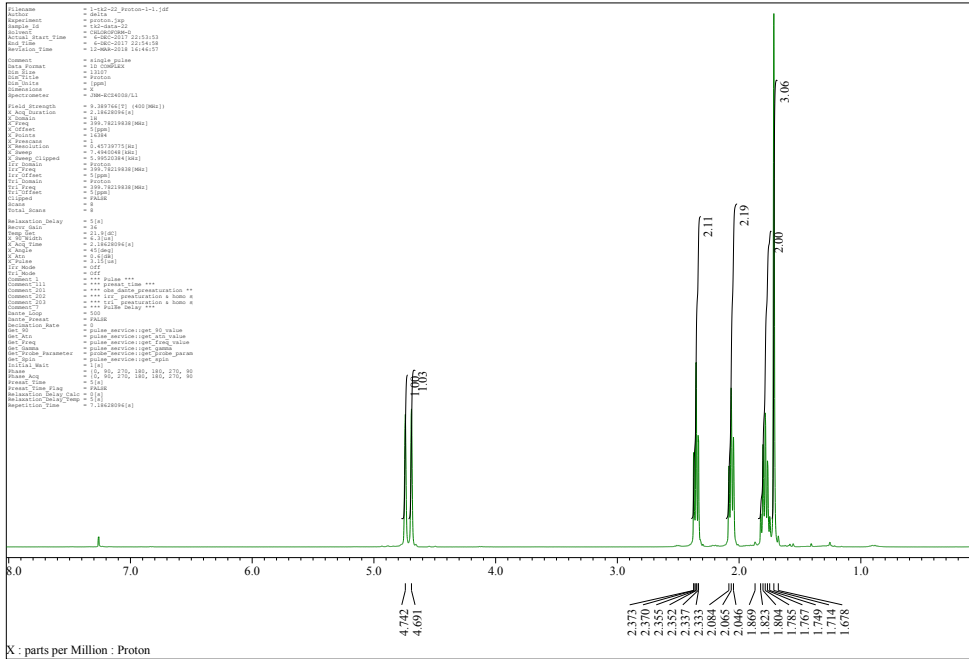
M.p. 179-180 °C; [ $\alpha$ ]<sub>D</sub><sup>29</sup> +94.0 (c 0.97, MeOH); IR (neat) 3584, 2930, 1764, 1373 cm<sup>-1</sup>; <sup>1</sup>H NMR (600 MHz, CD<sub>3</sub>OD)  $\delta$  1.18 (3H, s), 1.44-1.49 (2H, m), 1.45 (3H, s), 1.49 (3H, s), 1.78-1.82 (1H, m), 2.06-2.13 (1H, m), 2.53 (1H, d, *J* = 17.8 Hz), 2.54 (1H, d, *J* = 18.1 Hz), 3.03-3.05 (1H, m), 3.23 (1H, d, *J* = 8.7 Hz), 4.15 (1H, t, *J* = 8.3 Hz), 5.14 (1H, d, *J* = 2.6 Hz), 5.19 (1H, d, *J* = 3.0 Hz); <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD)  $\delta$  19.4, 26.8, 29.5, 29.7, 33.4, 43.6, 48.4, 73.3, 77.8, 79.7, 84.0, 108.5, 109.6, 150.3, 212.3; HRESIMS calcd for C<sub>15</sub>H<sub>22</sub>O<sub>5</sub>Na [M + Na]<sup>+</sup> 305.1365, found 305.1359.

Data for pleurospiroketal B (**2**) :

[ $\alpha$ ]<sub>D</sub><sup>25</sup> +17.1 (c 1.14, MeOH); IR (neat) 3453, 2970, 2931, 1764, 1372, 1120, 1079, 1022 cm<sup>-1</sup>; <sup>1</sup>H NMR (600 MHz, CD<sub>3</sub>OD)  $\delta$  1.22 (3H, s), 1.44, (3H, s) 1.46 (3H, s), 1.42-1.48 (1H, m), 1.57 (1H, td, *J* = 4.9, 14.0 Hz), 1.85 (1H, tdd, *J* = 4.5, 9.1, 14.0 Hz), 1.96-2.02 (1H, m), 2.58 (1H, d, *J* = 18.1 Hz), 2.69 (1H, d, *J* = 18.1 Hz), 3.03-3.04 (1H, m), 3.33-3.34 (1H, m), 4.26 (1H, t, *J* = 7.2 Hz), 5.01 (1H, d, *J* = 3.1 Hz), 5.19 (1H, d, *J* = 2.6 Hz); <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD)  $\delta$  20.5, 26.4, 29.8, 29.9, 33.5, 42.2, 49.5, 73.0, 76.7, 79.5, 84.0, 107.9, 110.1, 151.2, 212.5; HRESIMS calcd for C<sub>15</sub>H<sub>22</sub>O<sub>5</sub>Na [M + Na]<sup>+</sup> 305.1365, found 305.1359.

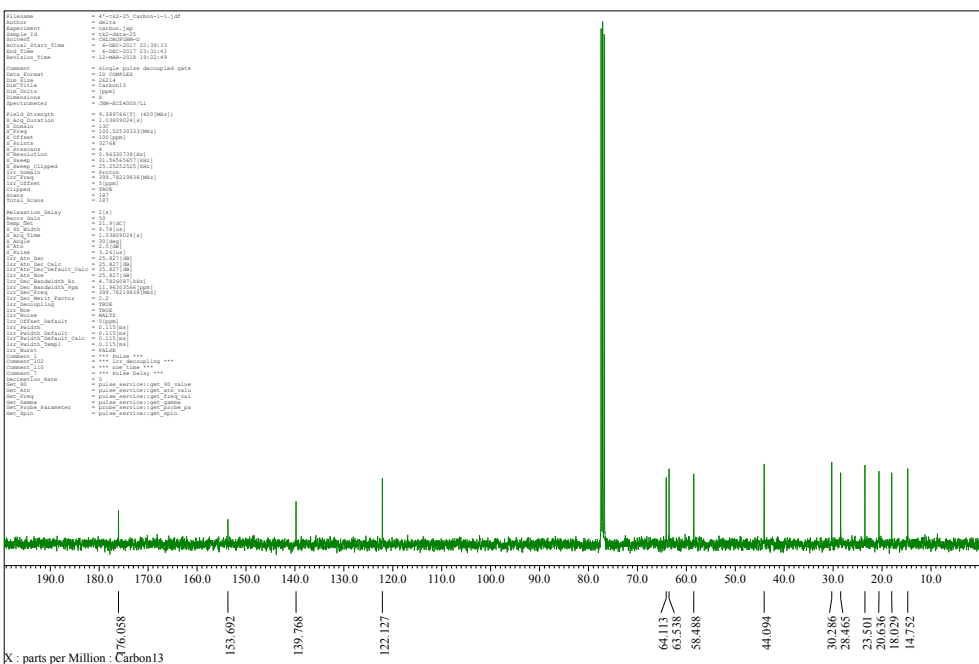
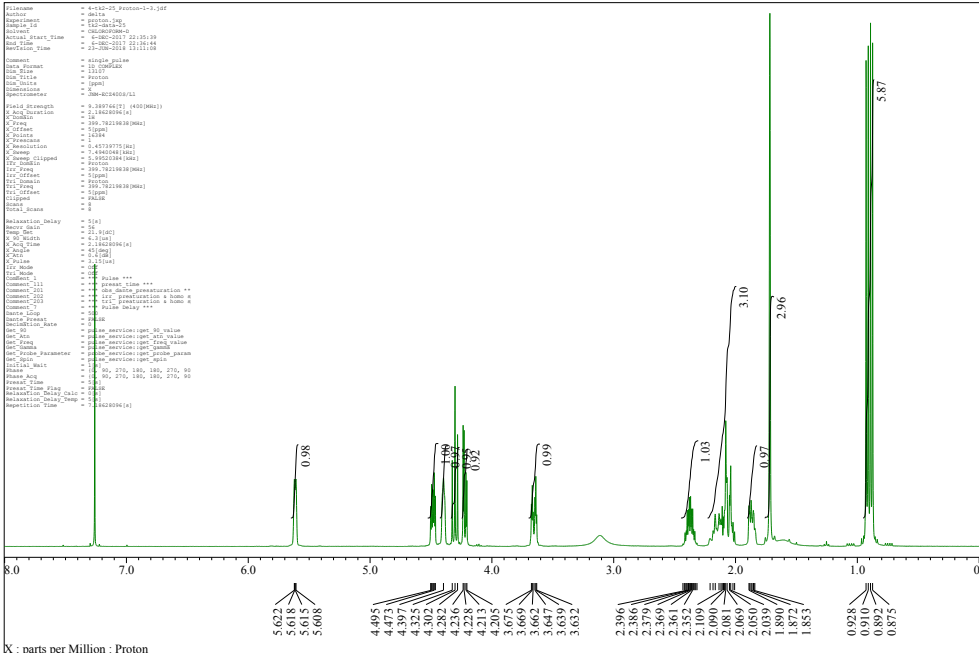
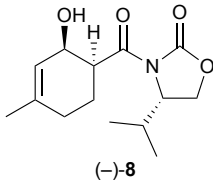


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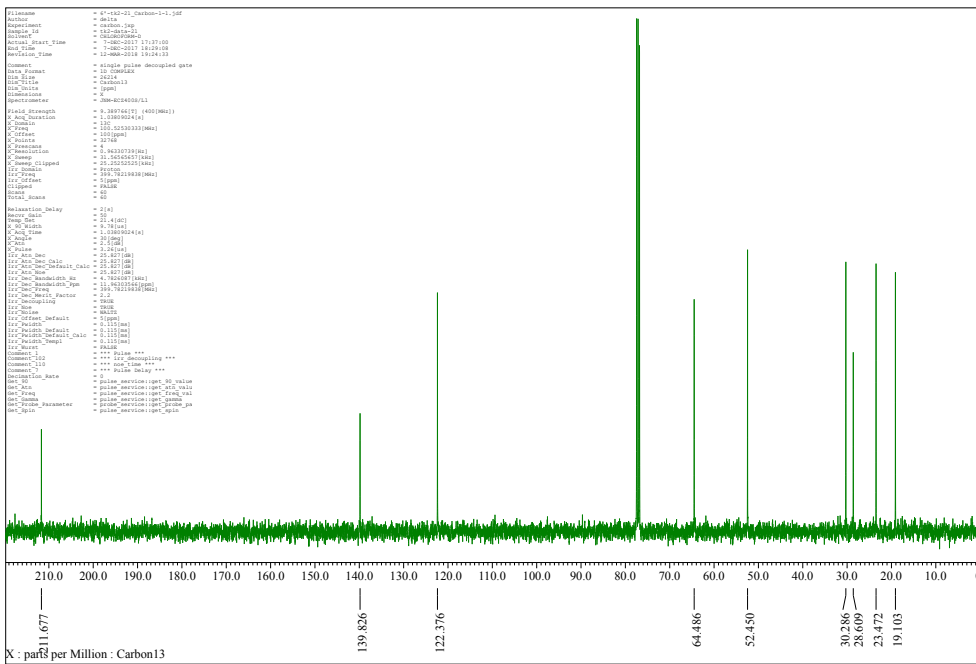
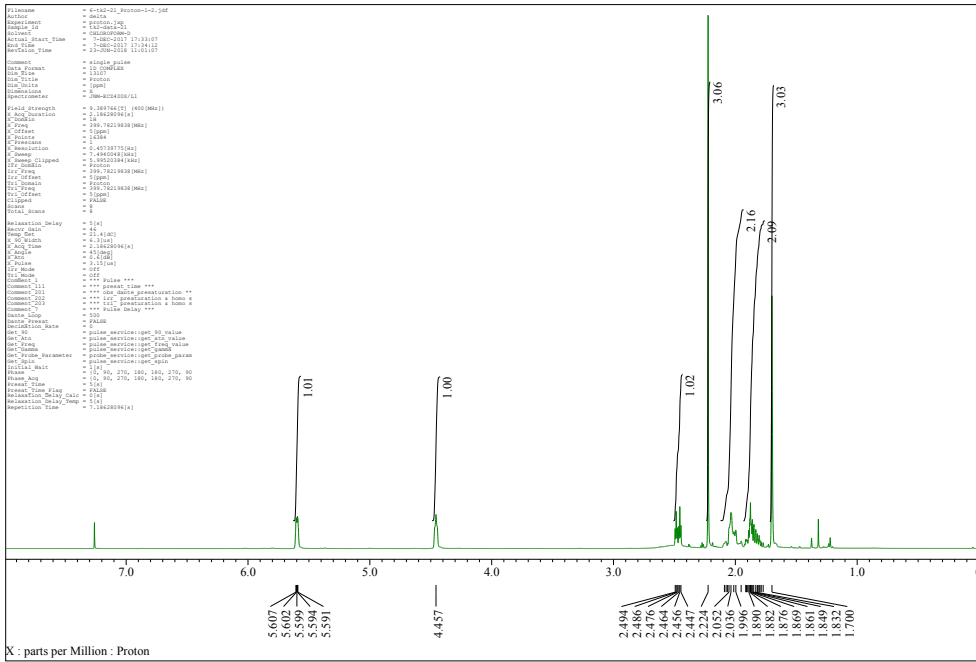
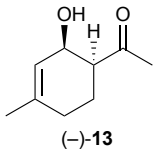


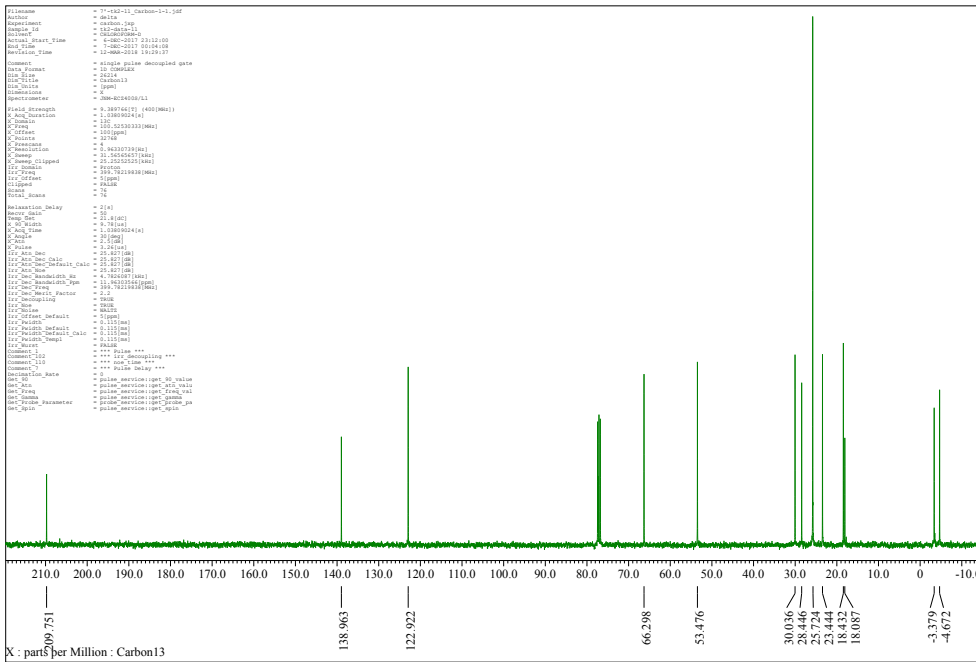
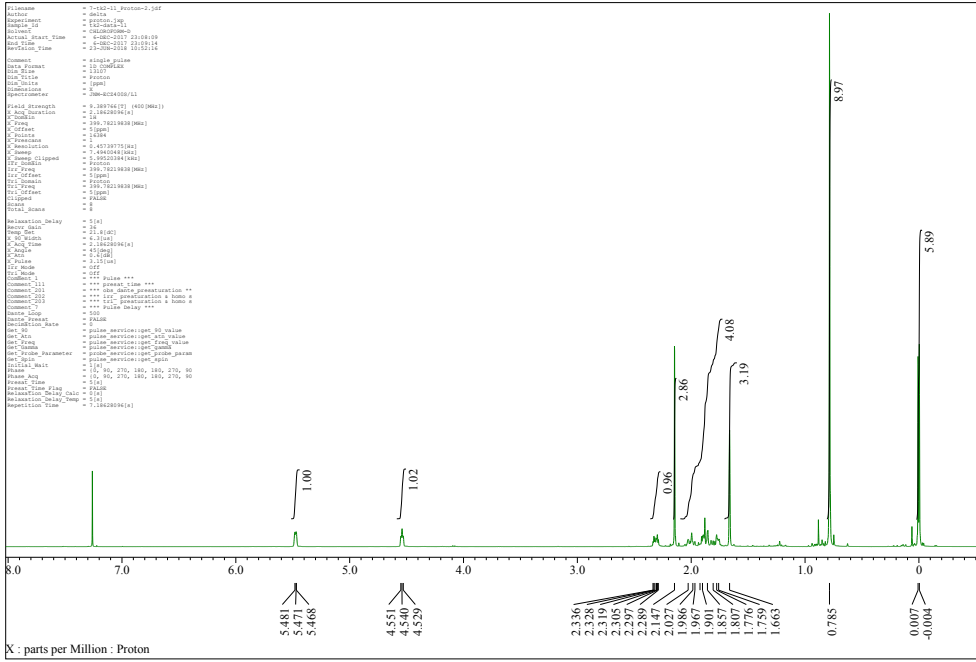
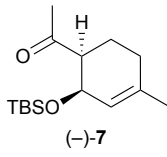






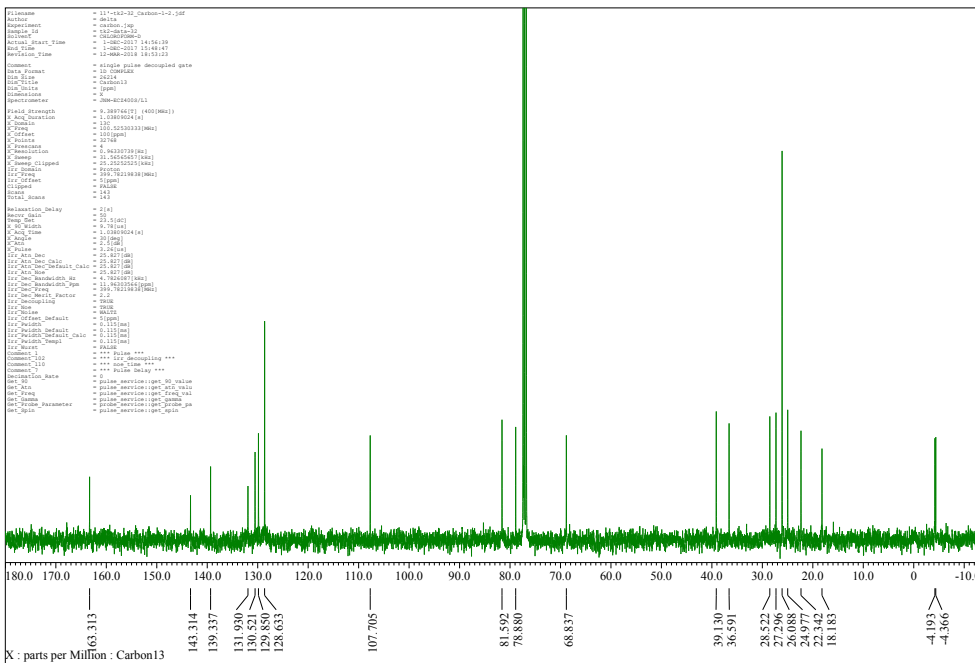
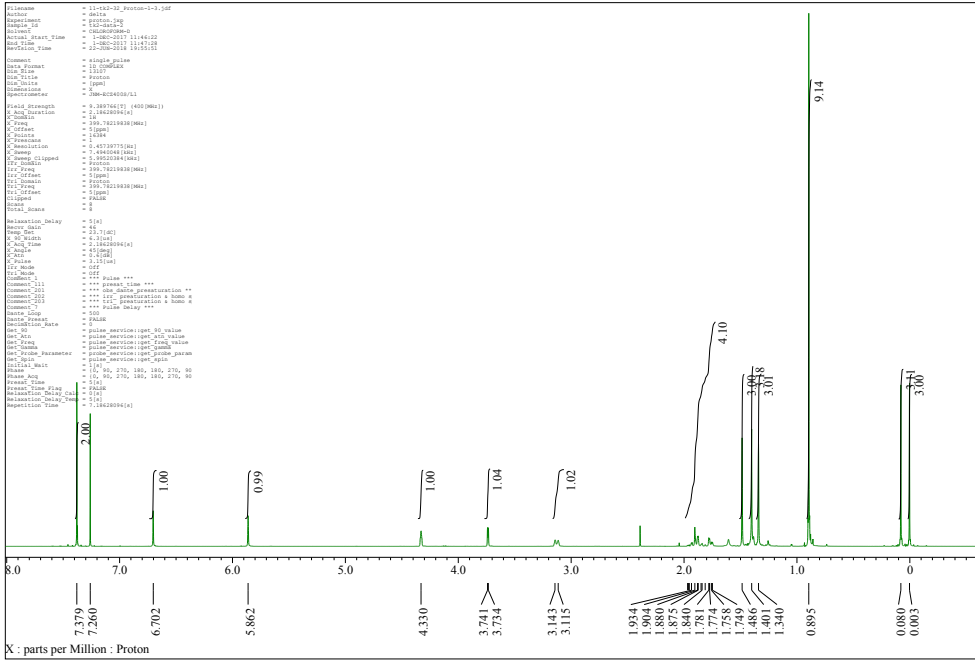
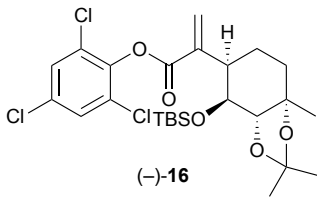








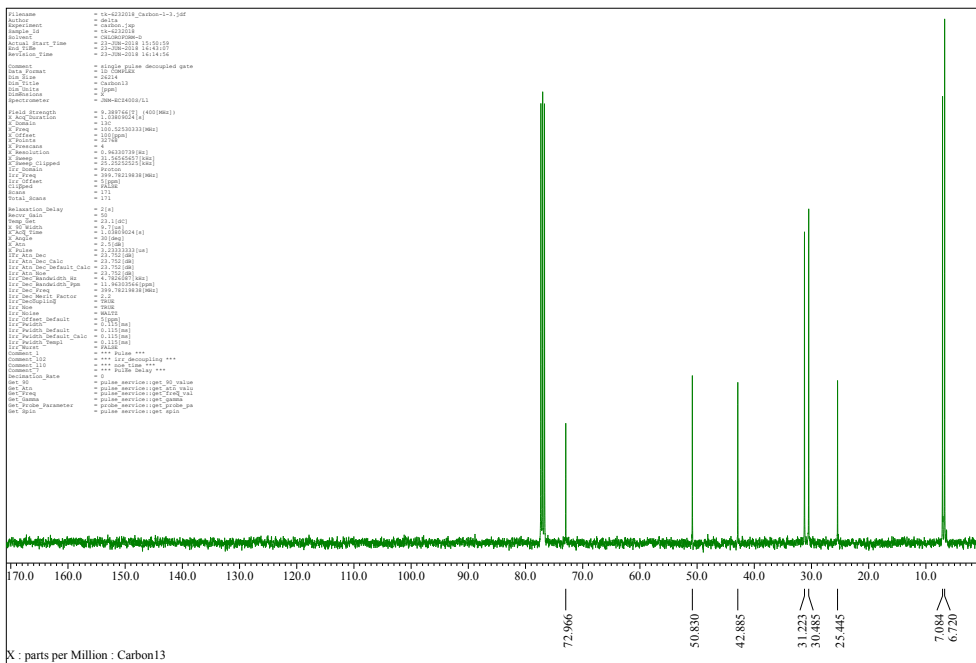
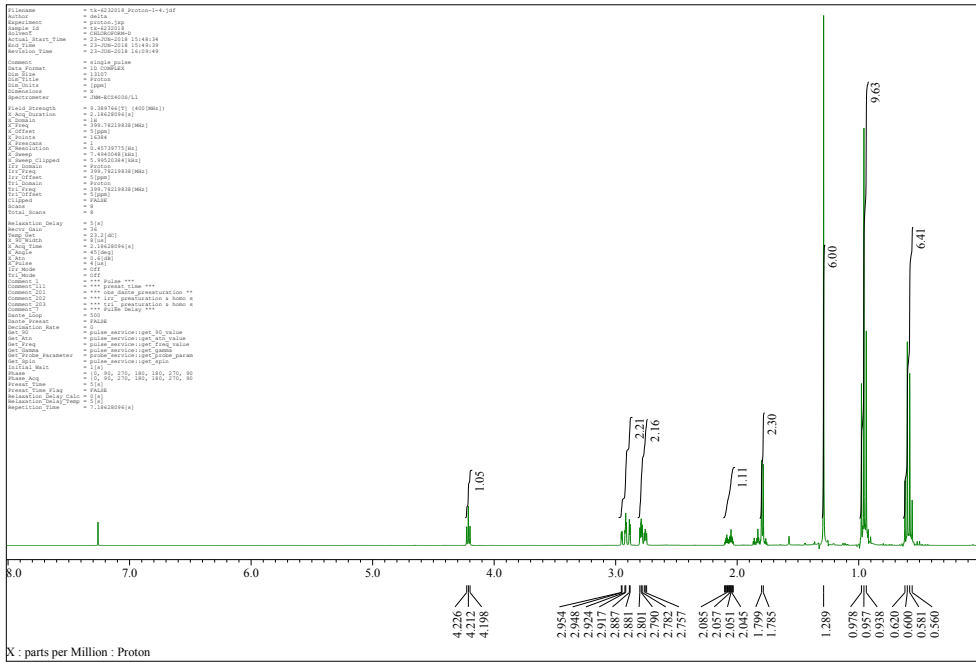
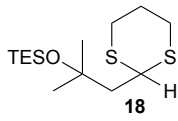


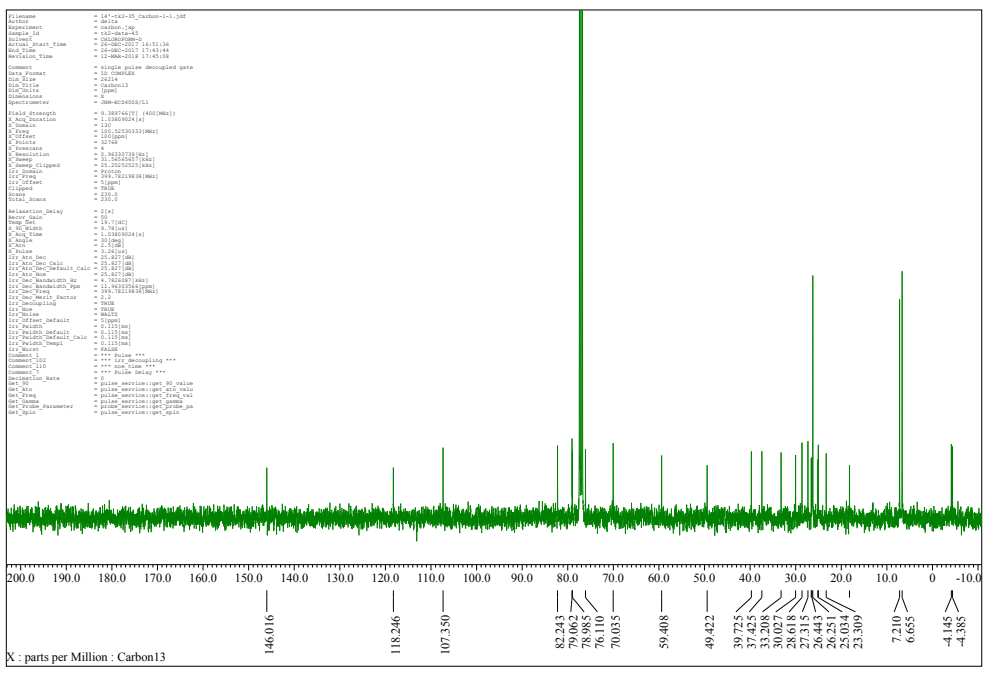
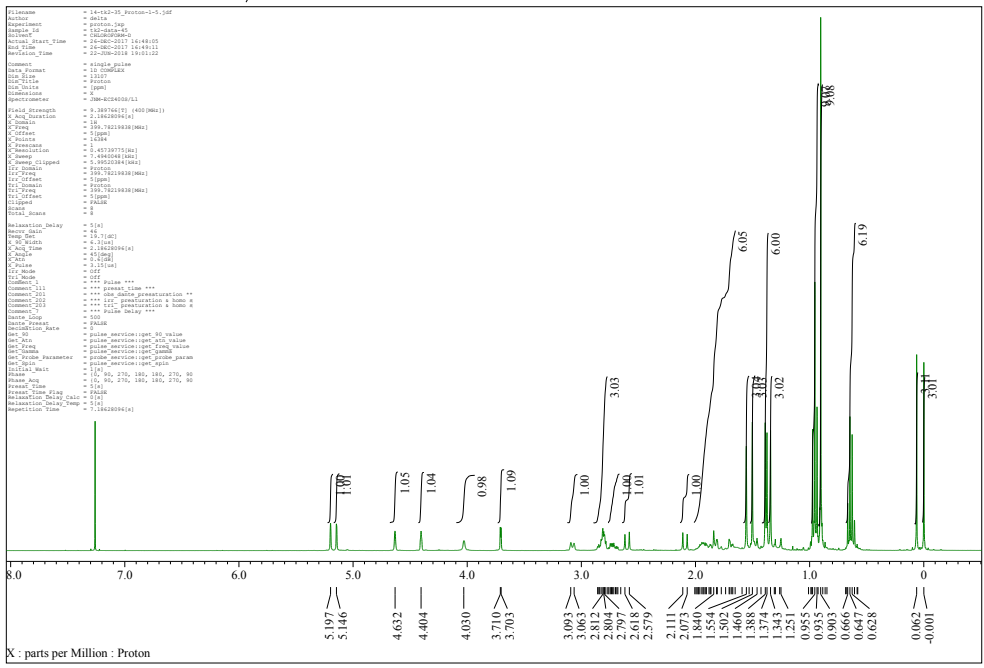
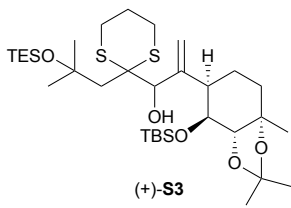


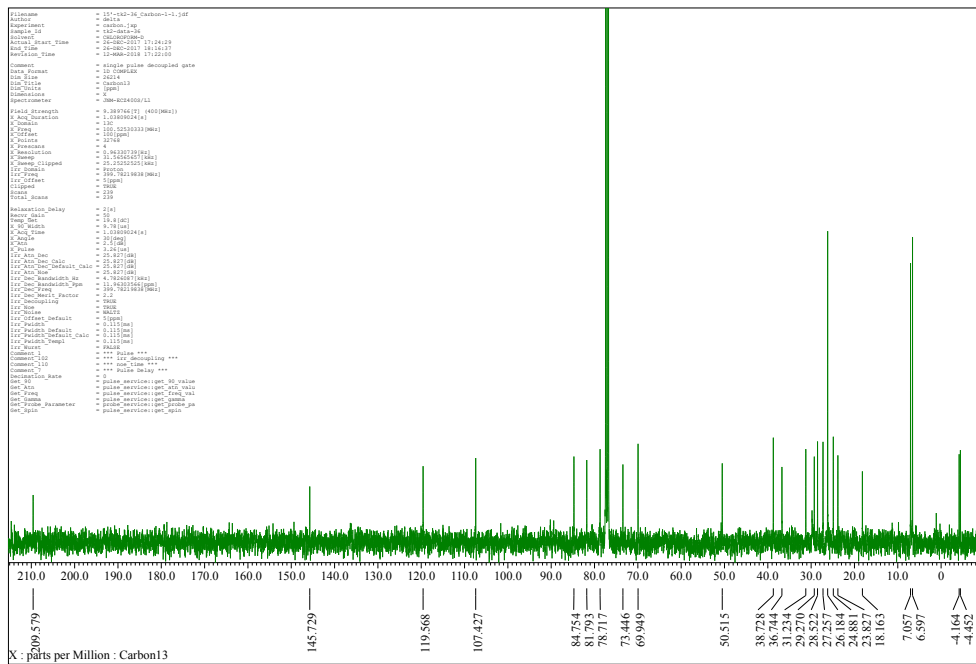
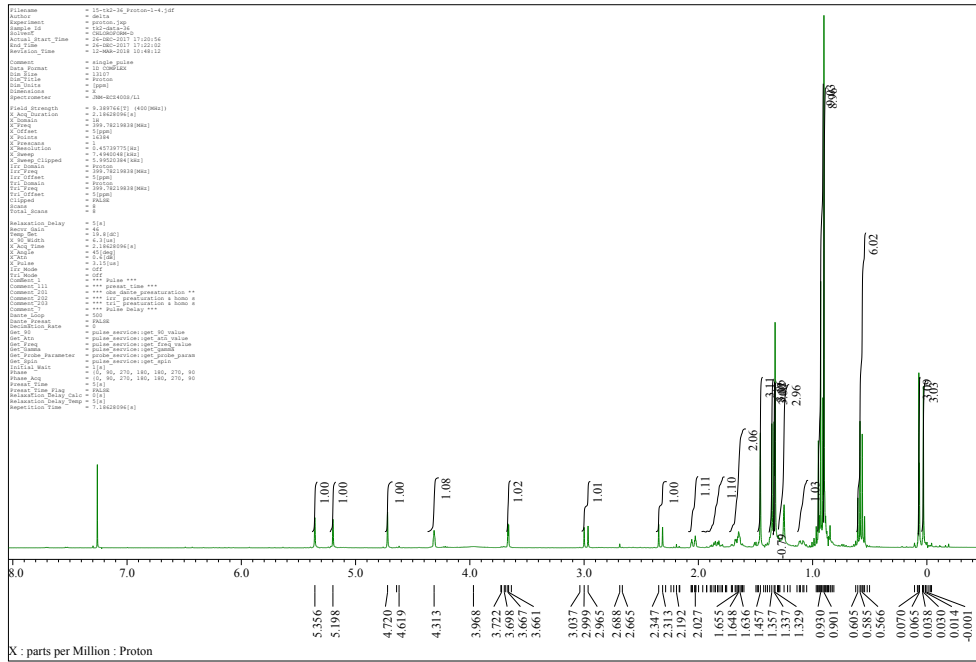
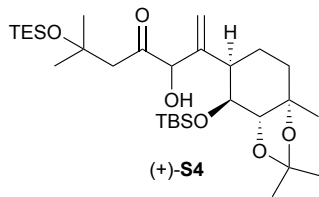


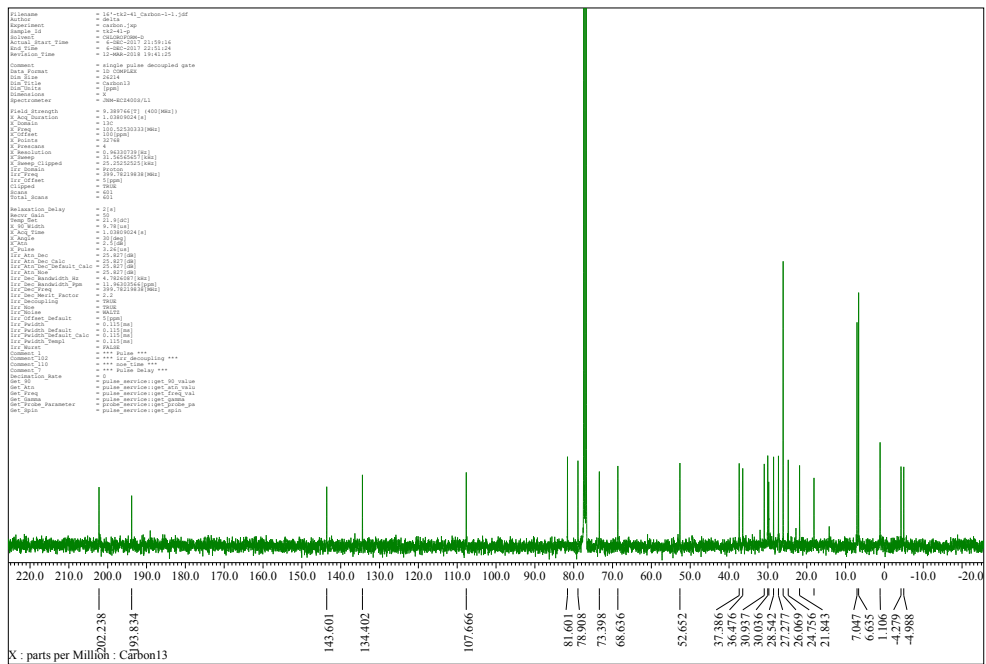
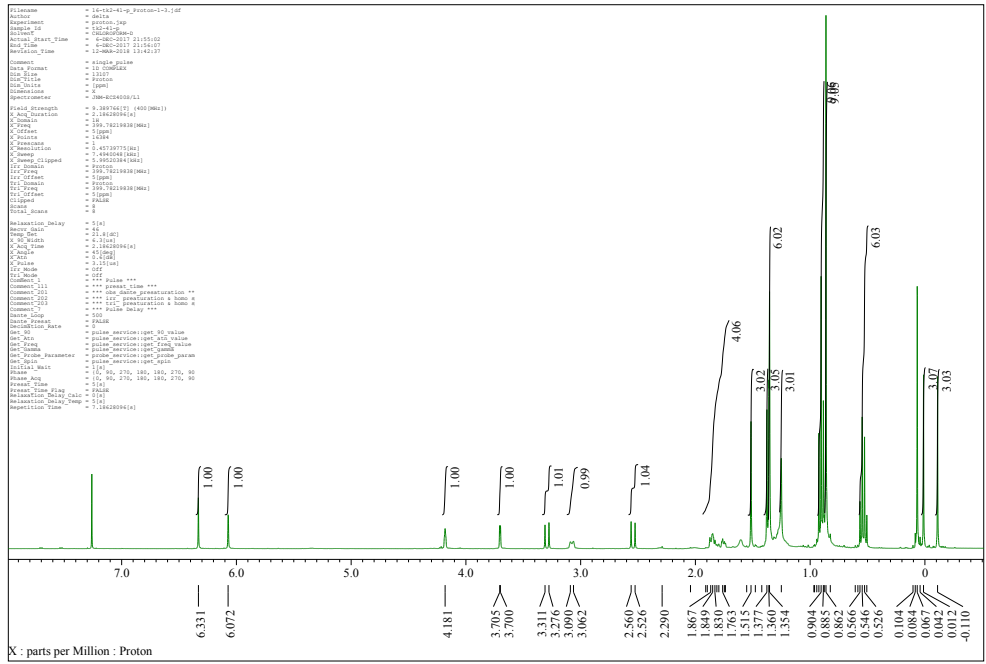
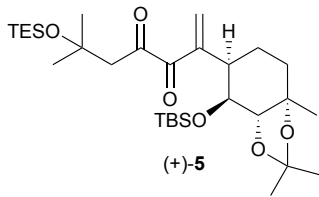


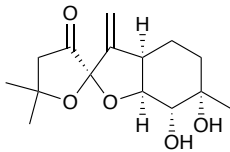




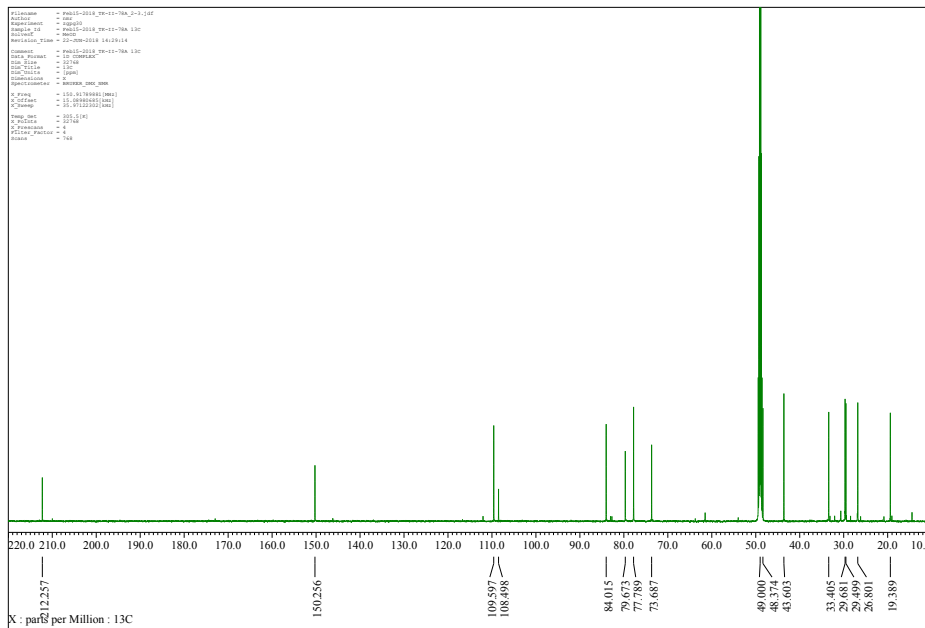
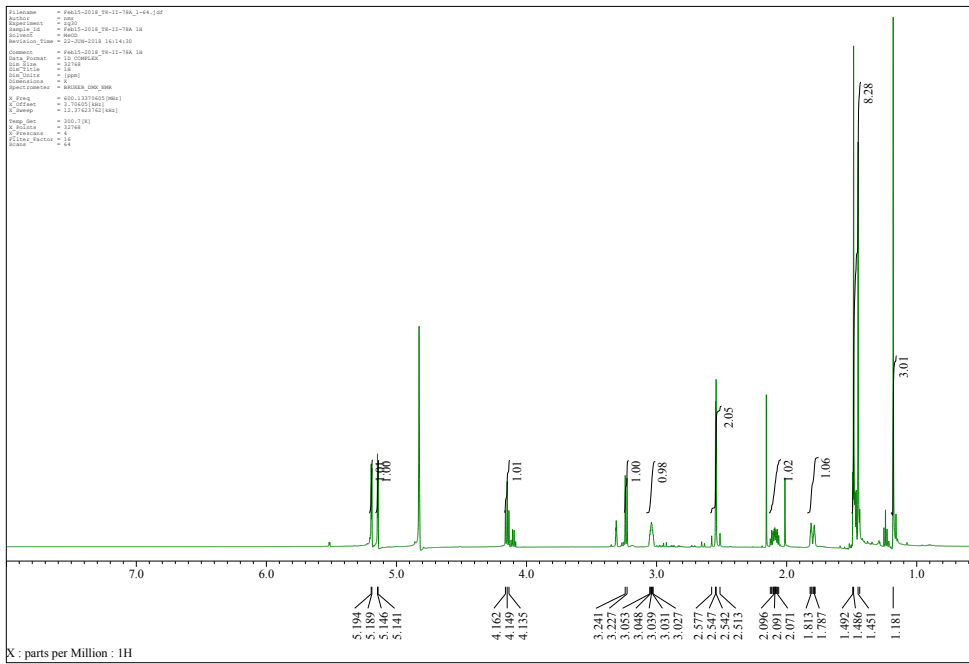


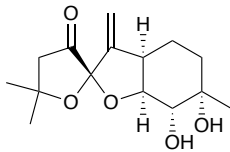






pleurospiroketal A (1)





pleurospiroketal B (2)

