

# Stereoselective synthesis of $\alpha$ -methyl ketones from terminal olefins and esters

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**Abstract:** Alkenes bearing a stereocenter in allylic position were found to undergo Kulinkovich hydroxycyclopropanation with good diastereoselectivity. For the isomerization of the resulting cyclopropanols to diastereomerically enriched  $\alpha$ -methyl ketones, a new mild regioselective method has been developed. A sequence of diastereoselective cyclopropanation and cyclopropanol ring opening was successfully employed in the synthesis of steroids for the construction of the C20 stereocenter.

## Table of Contents

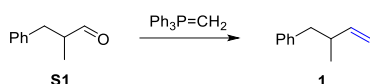
1. General information .....	2
2. Syntheses of starting alkenes .....	2
3. Synthesis of starting esters .....	4
4. Synthesis of cyclopropanols 5 .....	6
6. Synthesis of 6-deoxocathasterone (9) .....	12
7. Reduction of 8g .....	13
8. Arylation, allylation and alkylation of cyclopropanol 5g .....	14
References .....	15

## 1. General information

NMR spectra were obtained on a Bruker AVANCE 500 spectrometer and calibrated using residual solvent as an internal reference [ $^1\text{H}$  NMR:  $\text{CDCl}_3$  (7.26);  $^{13}\text{C}$  NMR:  $\text{CDCl}_3$  (77.16)]. Chemical shifts ( $\delta$ ) are given in ppm and coupling constants ( $J$ ) are given in Hertz (Hz). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), bs (broad singlet), or combinations thereof. IR spectra were measured on a PerkinElmer Spectrum 100 FT-IR spectrometer. High resolution MS were obtained on Agilent technologies 6550 iFunnel Q-TOF LC/MS system using electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) method. The progress of the reaction was checked on thin layer chromatography (TLC) plates (silica gel GF254 plates), and the spots were visualized under 254 nm UV light and/or charring after dipping the TLC plate into a phosphomolybdic acid solution (250 mg phosphomolybdic acid in 50 mL ethanol).

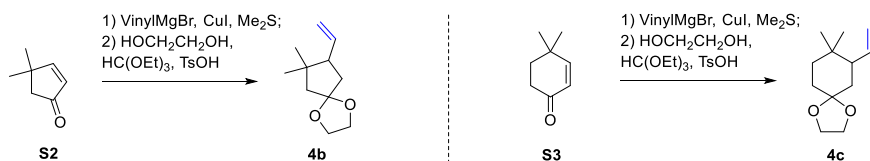
## 2. Syntheses of starting alkenes

### (2-Methylbut-3-en-1-yl)benzene (**1**)



A 1.7M solution of  $n\text{BuLi}$  (1.9 ml, 3.23 mmol) was added at  $0^\circ\text{C}$  to a suspension of  $\text{Ph}_3\text{PCH}_2\text{Br}$  (1.13 g, 3.18 mmol) in THF (10 ml) and the mixture was stirred for 30 min. A solution of aldehyde **S1**<sup>[1]</sup> (235 mg, 1.59 mmol) in THF (1 ml) was added at  $0^\circ\text{C}$  to a solution of ylide, the reaction mixture was stirred for 30 min, diluted with  $\text{Et}_2\text{O}$  (20 ml) and quenched with water (10 ml). The aqueous layer was separated and extracted with  $\text{Et}_2\text{O}$  (3 $\times$ 5 ml). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The residue was purified by column chromatography on  $\text{SiO}_2$  (petroleum ether– $\text{Et}_2\text{O}$  100:0-95:5) to give compound **1** (150 mg, 65%) as a colorless oil. NMR spectra of **1** were identical to those reported in the literature.<sup>[2]</sup>

### 7,7-dimethyl-8-vinyl-1,4-dioxaspiro[4.4]nonane (**4b**) and 8,8-dimethyl-7-vinyl-1,4-dioxaspiro[4.5]decane (**4c**)



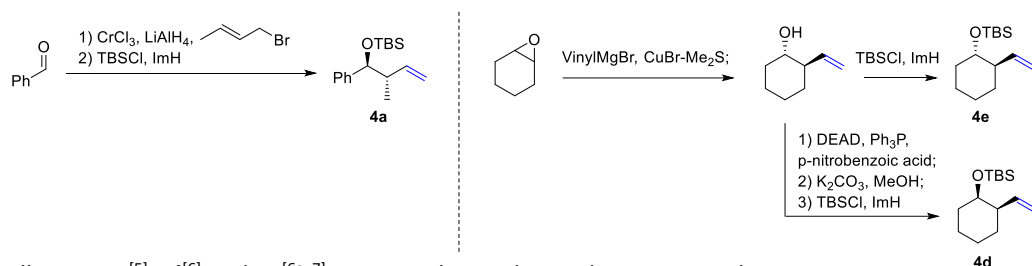
### 7,7-dimethyl-8-vinyl-1,4-dioxaspiro[4.4]nonane (**4b**)

A 1.7 M solution of vinylmagnesium bromide (5 mL, 8.5 mmol) was added to a solution of  $\text{CuI}$  (36 mg, 0.19 mmol) and dimethyl sulfide (1 mL) in THF (13 mL) at  $-78^\circ\text{C}$ . After 15 min, a solution of enone **S2**<sup>[3]</sup> (0.42 g, 3.82 mmol) in THF (1 mL) was added. Then the mixture was stirred for 30 min at the same temperature, quenched with saturated  $\text{NH}_4\text{Cl}$  (20 mL) and extracted with ether (3 $\times$ 5 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The residue was dissolved in  $\text{CH}_2\text{Cl}_2$  (10 mL). Ethylene glycol (0.64 mL, 11.1 mmol), triethyl orthoformate (1.9 mL, 11.4 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg, 0.052 mmol) were added sequentially to the solution. The mixture was stirred at room temperature for 4 h and quenched with saturated  $\text{NaHCO}_3$  (10 mL). The aqueous layer was separated and extracted with  $\text{CH}_2\text{Cl}_2$  (3 $\times$ 10 mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The residue was purified by column chromatography on  $\text{SiO}_2$  (petroleum ether– $\text{Et}_2\text{O}$  40:1-10:1) to give alkene **4b** (290 mg, 42%) as a colorless oil.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.73 (ddd,  $J$  = 17.0, 10.4, 7.8 Hz, 1H),  $\delta$  5.04 – 5.02 (m, 1H), 5.01 – 4.98 (m, 1H), 3.94 – 3.78 (m, 4H), 2.33 (dt,  $J$  = 12.0, 7.8 Hz, 1H), 2.02 (dd,  $J$  = 13.8, 7.5 Hz, 1H), 1.95 (dd,  $J$  = 13.8, 12.0 Hz, 1H), 1.84 (d,  $J$  = 14.0 Hz, 1H), 1.80 (d,  $J$  = 13.9 Hz, 1H), 1.02 (s, 3H), 0.89 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  138.03, 116.28, 115.72, 64.36, 63.88, 52.62, 52.35, 41.80, 40.39, 28.25, 22.66. IR (film) 3077, 2957, 2875, 1466, 1330, 1205, 1120, 914  $\text{cm}^{-1}$ ; HRMS (APCI) calcd for  $\text{C}_{11}\text{H}_{19}\text{O}_2$   $[\text{M}+\text{H}]^+$  183.1380, found 183.1368.

### 8,8-dimethyl-7-vinyl-1,4-dioxaspiro[4.5]decane (**4c**)

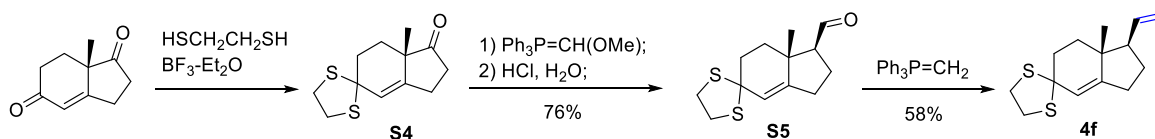
Alkene **4c** (746 mg, 47%) was prepared from enone **S3**<sup>[4]</sup> as a colorless oil using the same procedure as described for **4b**.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.71 (ddd,  $J$  = 17.0, 10.5, 8.3 Hz, 1H), 5.01 – 4.92 (m, 2H), 3.97 – 3.87 (m, 4H), 2.10 (ddd,  $J$  = 12.3, 8.3, 4.2 Hz, 1H), 1.71 – 1.46 (m, 5H), 1.38 (ddd,  $J$  = 13.4, 4.2, 3.1 Hz, 1H), 0.89 (s, 3H), 0.80 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  139.69, 115.24, 109.39, 64.37, 64.31, 48.64, 38.50, 36.65, 32.48, 31.44, 29.92, 19.02; IR (film) 3076, 2950, 2877, 1454, 1189, 1094, 944, 915  $\text{cm}^{-1}$ ; HRMS (APCI) calcd for  $\text{C}_{12}\text{H}_{21}\text{O}_2$   $[\text{M}+\text{H}]^+$  197.1536, found 197.1524.

*tert*-Butyldimethyl(((1*R*,2*RS*)-2-methyl-1-phenylbut-3-en-1-yl)oxy)silane (**4a**), *tert*-butyldimethyl(((1*R*,2*SR*)-2-vinylcyclohexyl)oxy)silane (**4d**) and *tert*-butyldimethyl(((1*R*,2*RS*)-2-vinylcyclohexyl)oxy)silane (**4e**)



Alkenes **4a**,<sup>[5]</sup> **4d**<sup>[6]</sup> and **4e**<sup>[6a,7]</sup> were synthesized using known procedures.

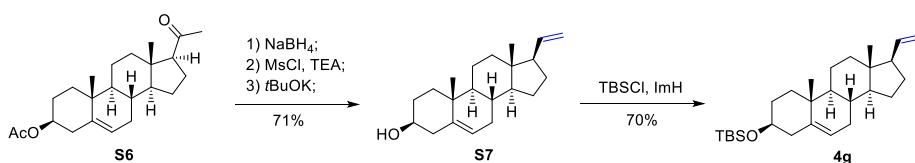
(1*R*,7*aR*)-7*a*-methyl-1-vinyl-1,2,3,6,7,7*a*-hexahydrospiro[indene-5,2'-[1,3]dithiolane] (**4f**)



To a stirred suspension of MeOCH<sub>2</sub>PPh<sub>3</sub>Cl (4.58 g, 13.4 mmol) in THF (45 mL), a solution of KHMDs (0.7M in toluene, 16 mL, 11.2 mmol) was added at -30 °C. The mixture was warmed to 0 °C over 40 min and a solution of ketone **S4**<sup>[8]</sup> (1.07 g, 4.45 mmol) in THF (10 mL) was added. The solution was stirred at room temperature over 24 h, cooled down to 0 °C and a mixture of 4N aqueous solution of HCl (11 mL), MeOH (5.5 mL) and THF (5.5 mL) was added to the reaction mixture. The mixture was stirred for 36 h at room temperature, diluted with water (40 mL) and extracted with ethyl acetate (4×30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether–ethyl acetate 40:1-5:1) to give the aldehyde **S5** (869 mg, 76%) as an oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.81 (s, 1H), 5.47 (s, 1H), 3.46 – 3.34 (m, 3H), 3.25 – 3.18 (m, 1H), 2.55 – 1.52 (m, 9H), 1.00 (s, 3H).

A 1.6M solution of *n*BuLi (2.7 mL, 4.32 mmol) was added dropwise to a suspension of MePPh<sub>3</sub>Br (1.64 g, 4.59 mmol) in THF (30 mL) at -78 °C. The mixture was warmed to 0 °C, stirred at the same temperature for 1 h and cooled to -78 °C. To the resulting solution of ylide, a solution of aldehyde **S5** (860 mg, 3.38 mmol) in THF (25 mL) was added dropwise. The mixture was stirred at 0 °C for 6 h and quenched with saturated NH<sub>4</sub>Cl (50 mL) and extracted with EtOAc (3×60 mL). The organic layers were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether–ethyl acetate 40:1-5:1) to give alkene **4f** (494 mg, 58%) as white crystals. M.p. = 87-90 °C (MeOH); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = 83.0 (c 0.277, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.82 – 5.71 (m, 1H), 5.44 (s, 1H), 5.08 – 5.00 (m, 2H), 3.47 – 3.31 (m, 3H), 3.27 – 3.18 (m, 1H), 2.49 – 2.40 (m, 1H), 2.34 – 2.19 (m, 3H), 2.10 – 2.02 (m, 1H), 1.85 – 1.64 (m, 3H), 1.48 (td, *J* = 13.1, 3.7 Hz, 1H), 0.88 – 0.83 (m, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 150.57, 138.36, 122.05, 115.87, 66.43, 55.40, 43.36, 40.52, 39.74, 38.83, 35.70, 27.87, 26.43, 17.91; IR (KBr) 3077, 2957, 2924, 2846, 1466, 1432, 1273, 1100, 908, 863, 803, 767, 725, 683 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>14</sub>H<sub>21</sub>S<sub>2</sub> [M+H]<sup>+</sup> 253.1079, found 253.1081.

3*B*-*tert*-Butyldimethylsilyloxypregnadien-5,20 (**4g**)



Pregna-5,20-dien-3*B*-ol (**S7**)

Alcohol **S7** was prepared using the reported procedure.<sup>[9]</sup>

To a stirred ice-cooled solution of ketone **S6** (10 g, 27.9 mmol) in methanol (186 mL), NaBH<sub>4</sub> (5.8 g, 153 mmol) was added in small portions. The mixture was stirred over 1.5 h and concentrated under reduced pressure. The residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (200 mL) and the solution was washed with water (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to give crude alcohol (9.9 g, 98%).

The crude alcohol (5.5 g, 15.3 mmol) was dissolved in THF (50 mL) and Et<sub>3</sub>N (5.3 mL, 38.2 mmol) followed by MsCl (2.4 mL, 30.5 mmol) were added to the solution at 0 °C. The mixture was stirred at the same temperature for 15 min and quenched with saturated NaHCO<sub>3</sub> (100 mL). Aqueous layer was separated and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×50 mL). The combined organic

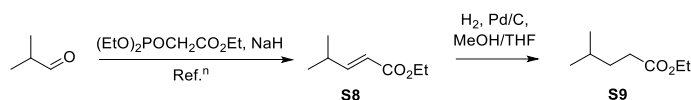
layers were washed with brine (50 mL), then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The resulting crude mesylate was dissolved in toluene (70 mL) and tBuOK (5.14 g, 45.8 mmol) was added to the solution. The mixture was stirred at 90 °C for 90 min, then cooled and quenched with water (70 mL). Aqueous layer was separated and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×50 mL). The combined organic layers were washed with brine (50 mL), then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether–ethyl acetate 40:1-5:1) to give alkene **S7** (3.3 g, 72%) as an oil. Spectra of **S7** were identical to those reported in the literature.<sup>[9]</sup>

### 3*B*-*tert*-Butyldimethylsilyloxypregnadien-5,20 (**4g**)

To an ice cooled solution of **S7** (3.3 g, 11 mmol) and imidazole (1.5 g, 22 mmol) in DMF (30 mL), TBSCl (2.1 g, 14 mmol) was added. The mixture was stirred overnight at room temperature and quenched with water (100 mL) and extracted with petroleum ether (3×30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether–ethyl acetate 40:1-5:1) to give alkene **4g** (3.2 g, 70%) as a white solid. M.p. = 104–107 °C (MeOH);  $[\alpha]_D^{20} = -63.2$  (c 0.538, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 5.81 (ddd, *J* = 16.3, 11.0, 7.8 Hz, 1H), 5.42–5.34 (m, 1H), 5.04–5.03 (m, 1H), 5.01 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 3.59–3.47 (m, 1H), 2.36–2.28 (m, 1H), 2.22 (ddd, *J* = 13.3, 4.9, 2.2 Hz, 1H), 2.11–1.97 (m, 2H), 1.93–0.86 (m, 16H), 1.05 (s, 3H), 0.94 (s, 9H), 0.65 (s, 3H), 0.11 (s, 6H). **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 141.80, 140.00, 121.23, 114.65, 72.77, 56.12, 55.50, 50.67, 43.55, 42.97, 37.60, 37.54, 36.87, 32.23, 32.17 (2C), 27.39, 26.09 (3C), 25.04, 20.83, 19.62, 18.42, 12.89, -4.44 (2C); **IR** (KBr) 3074, 2941, 28999, 2858, 1471, 1381, 1255, 1087, 1002, 870, 838, 771, 670 cm<sup>-1</sup>; **HRMS** (APCI) calcd for C<sub>27</sub>H<sub>47</sub>O<sub>3</sub>Si [M+H]<sup>+</sup> 415.3391, found 415.3403.

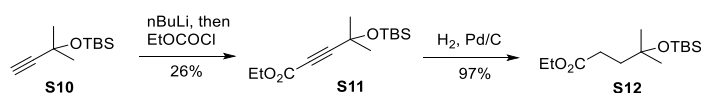
## 3. Synthesis of starting esters

### Ethyl 4-methylpentanoate (**S9**)



To a solution of alkene **S8** (8.27 g, 58.2 mmol) in EtOH (80 mL), 10% Pd/C (0.4 g) was added and the resulting suspension was stirred under hydrogen atmosphere overnight. The mixture was filtered, the catalyst was washed with ethyl acetate (3×5 mL) and the filtrate was concentrated under reduced pressure. The residue was distilled under reduced pressure to give ester **S9** (5.25 g, 63%); bp 60–65 °C (20 mmHg). NMR spectra of **S9** were identical to those reported in the literature.<sup>[10]</sup>

### Ethyl 4-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (**S12**)



### Ethyl 4-((*tert*-butyldimethylsilyl)oxy)-4-methylpent-2-ynoate (**S11**)

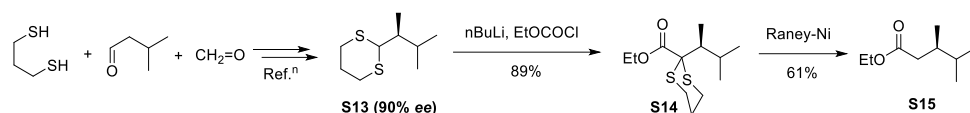
To a stirred solution of **S10**<sup>[11]</sup> (2.6 g, 1.1 mmol) in THF (20 mL), a solution of *n*BuLi (1.6M in hexane, 9 mL, 14.4 mmol) was added at -78 °C. The reaction was stirred for 30 min at the same temperature and a solution of ethyl chloroformate (1.12 mL, 14.4 mmol) in THF (10 mL) was added. The mixture was warmed to room temperature, stirred for 3 h and quenched with saturated aqueous NH<sub>4</sub>Cl (10 mL). The aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether) to give **S11** (920 mg, 26%) as a colorless oil. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 4.23 (q, *J* = 7.1 Hz, 2H), 1.51 (s, 6H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.19 (s, 6H).

### Ethyl 4-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (**S12**)

To a solution of alkyne **S11** (500 mg, 1.85 mmol) in a 2:1 mixture of MeOH and THF (7.5 mL), 10% Pd/C (50 mg) was added and the resulting suspension was stirred under hydrogen atmosphere for 1 h. The mixture was filtered, the catalyst was washed with THF (3×5 mL) and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (petroleum ether – ether) to obtain **S12** (490 mg, 97%) as a colorless oil. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 4.12 (q, *J* = 7.1 Hz, 2H), 2.43–2.37 (m, 2H), 1.78–1.72 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.21 (s, 6H), 0.85 (s, 9H), 0.07 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 174.59, 72.77, 60.39, 39.73, 29.77 (2C), 29.71, 25.97 (3C), 18.23, 14.38, -2.00 (2C); **IR** (film) 2957, 2931, 2896, 2857, 1739, 1472, 1366, 1292, 1254, 1164, 1042, 835, 773, 686 cm<sup>-1</sup>; **GC MS** (EI): *m/z* : 259 [C<sub>13</sub>H<sub>27</sub>O<sub>3</sub>Si<sup>+</sup>] [M-Me]<sup>+</sup>, 229 [C<sub>12</sub>H<sub>25</sub>O<sub>2</sub>Si<sup>+</sup>] [M-OEt]<sup>+</sup>, 217 [C<sub>10</sub>H<sub>21</sub>O<sub>3</sub>Si<sup>+</sup>] [M-<sup>t</sup>Bu]<sup>+</sup>, 115 [C<sub>6</sub>H<sub>15</sub>Si<sup>+</sup>].



### Ethyl (R)-3,4-dimethylpentanoate (**S15**)



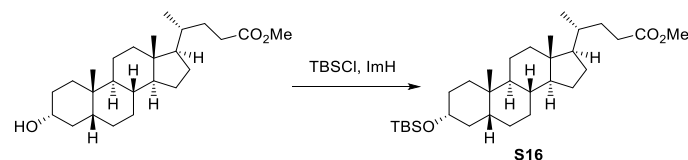
### Ethyl (S)-2-(3-methylbutan-2-yl)-1,3-dithiane-2-carboxylate (**S14**)

1.85 M solution of  $n\text{-BuLi}$  (1.7 ml, 3.16 mmol) was added at room temperature to a solution of dithiane **S13**<sup>[12]</sup> (0.5 g, 2.63 mmol) in THF (9 ml). The mixture was stirred for 15 min and cooled to  $-78^\circ\text{C}$ . A solution of  $\text{EtOCOCI}$  (0.25 mL, 2.63 mmol) was added to the reaction mixture. A solution was warmed to  $0^\circ\text{C}$  and quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (10 ml). The aqueous layer was separated and extracted with  $\text{Et}_2\text{O}$  ( $3 \times 5$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The residue was purified by column chromatography on  $\text{SiO}_2$  (petroleum ether–ethyl acetate 40:1-5:1) to give dithiane **S14** (607 mg, 89%).  $[\alpha]_D^{20} = -5.2$  (c 0.384,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.31 – 4.22 (m, 2H), 3.31 – 3.22 (m, 1H), 3.08 (ddd,  $J = 14.9, 12.7, 2.6$  Hz, 1H), 2.73 – 2.64 (m, 2H), 2.20 (qd,  $J = 7.2, 2.1$  Hz, 1H), 2.13 – 1.98 (m, 2H), 1.88 – 1.77 (m, 1H), 1.33 (t,  $J = 7.1$  Hz, 3H), 1.10 (d,  $J = 7.2$  Hz, 3H), 0.95 (d,  $J = 6.7$  Hz, 3H), 0.94 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.37, 62.35, 62.06, 45.83, 29.49, 28.41, 28.06, 24.93, 24.19, 19.11, 14.33, 9.95. IR (film) 2960, 2929, 2872, 2830, 1721, 1463, 1423, 1389, 1213, 1030  $\text{cm}^{-1}$ ; HRMS (APCI) calcd for  $\text{C}_{12}\text{H}_{23}\text{O}_2\text{S}$   $[\text{M}+\text{H}]^+$  263.1134, found 263.1115

### Ethyl (R)-3,4-dimethylpentanoate (**S15**)

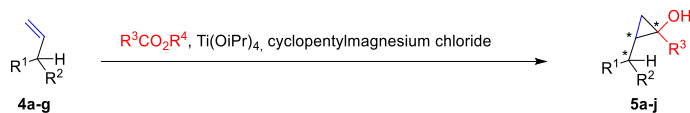
A solution of dithiane **S14** (557 mg, 2.13 mmol) in  $\text{EtOH}$  (5 mL) was added to a stirred suspension of Raney-Ni in  $\text{EtOH}$  (10 mL). The mixture was stirred at  $80^\circ\text{C}$  under Ar atmosphere for 4 hours, cooled to room temperature and then the liquid was decanted. The catalyst was washed with  $\text{Et}_2\text{O}$  ( $3 \times 20$  mL) and the combined organic phases were washed with water ( $3 \times 15$  mL), brine (15 mL), dried over  $\text{Na}_2\text{SO}_4$  and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (pentane– $\text{Et}_2\text{O} = 100:0 - 80:20$ ) to give ester **S15** (206 mg, 61%, 74% ee (determined from  $^1\text{H NMR}$  spectra of amides that were prepared by amidation of (R)- and (S)-1-phenylethylamine with (R)-3,4-dimethylpentanoic acid, which in turn was obtained by saponification of **S15**)) as a colorless oil.  $[\alpha]_D^{20} = 4.5$  (c 0.338,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.12 (q,  $J = 7.1$  Hz, 2H), 2.33 (dd,  $J = 14.6, 5.2$  Hz, 1H), 2.06 (dd,  $J = 14.6, 9.3$  Hz, 1H), 1.92 – 1.82 (m, 1H), 1.58 (dtd,  $J = 13.6, 6.8, 4.8$  Hz, 1H), 1.25 (t,  $J = 7.1$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 0.87 (d,  $J = 6.8$  Hz, 3H), 0.84 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  173.94, 60.25, 39.42, 36.05, 32.24, 19.96, 18.42, 15.94, 14.42; IR (film) 2959, 2932, 2873, 1737, 1465, 1371, 1275, 1178, 1032  $\text{cm}^{-1}$ ; GC MS (EI):  $m/z$  : 113  $[\text{C}_7\text{H}_{13}\text{O}^+]$   $[\text{M}-\text{OEt}]^+$ , 88  $[\text{C}_4\text{H}_8\text{O}_2^{++}]$ , 73  $[\text{C}_3\text{H}_5\text{O}^+]$ , 43  $[\text{C}_3\text{H}_7^+]$ .

### Methyl 3-(tert-butyldimethylsilyl)lithocholate (**S16**)



Ester **S16** was synthesized using known procedures.<sup>[13]</sup>

## 4. Synthesis of cyclopropanols 5



### General procedure A.

To a stirred solution of alkene **4** (1 equiv.), ester (2 equiv. of ethyl acetate (**2**) or 1 equiv. of other esters) and  $Ti(OiPr)_4$  (1 equiv.) in THF (0.05 M) at room temperature under argon atmosphere, a solution of cyclopentylmagnesium chloride in THF (1-1.4 M, 4 equiv.) was added over 1 h. The reaction was stirred for 30 min at the same temperature and quenched with saturated aqueous  $NH_4Cl$  (0.14 mL per 1 mmol of cyclopentylmagnesium chloride) at 0 °C. The suspension was stirred for 5 min, filtered and the precipitate was washed with EtOAc (5×5 mL). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using petroleum ether and ethyl acetate (or ether) as the eluent to obtain cyclopropanol **5**. Diastereomeric purity of the synthesized cyclopropanols before purification is given in the brackets. Complete separation of diastereomers using usual column chromatography is not possible, but fractions with improved dr could be separated.

### General procedure B.

To a stirred solution of alkene **4** (1 equiv.), ester (2 equiv. of ethyl acetate (**2**) or 1 equiv. of other esters) and  $Ti(OiPr)_4$  (1 equiv.) in ether (0.05 M) at 0 °C (or at room temperature) under argon atmosphere, a solution of cyclopentylmagnesium chloride in ether (1.4-1.7 M, 4 equiv.) was added over 1 h. The reaction was stirred for 30 min at the same temperature and quenched with saturated aqueous  $NH_4Cl$  (0.14 mL per 1 mmol of cyclopentylmagnesium chloride) at 0 °C. The suspension was stirred for 5 min, filtered and the precipitate was washed with EtOAc (5×5 mL). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using petroleum ether and ethyl acetate (or ether) as the eluent to obtain cyclopropanol **5**. Diastereomeric purity of the synthesized cyclopropanols before purification is given in the brackets. Complete separation of diastereomers using usual column chromatography is not possible, but fractions with improved dr could be separated.

### Determination of diastereomeric purity of the synthesized cyclopropanols 5.

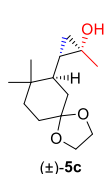
**Method A.** Diastereomeric purity was determined from  $^1H$  NMR spectra of unpurified cyclopropanols ( $\pm$ )-**5b** and ( $\pm$ )-**5c** in  $CDCl_3$  (signals of  $^1H$  in the cyclopropane ring).

**Method B.** Diastereomeric purity was determined from  $^1H$  NMR spectra of unpurified cyclopropanols ( $\pm$ )-**5d-e**, **5f-g** in  $C_6D_6$  (signals of  $^1H$  in the cyclopropane ring).

**Method C.** It was not possible to determine diastereomeric purity of cyclopropanols ( $\pm$ )-**5a**, **5h** and **5j** using NMR spectroscopy and the unpurified cyclopropanols were transformed to  $\alpha$ -methyl ketones ( $\pm$ )-**8a**, **8h** and **8j** followed by the developed procedure (see section 5). Diastereomeric purity of  $\alpha$ -methyl ketones ( $\pm$ )-**8a**, **8h** and **8j** was determined from their  $^1H$  NMR spectra (see section 5).

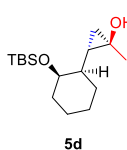
(*1S,2RS*)-2-((*1S,2SR*)-1-((*tert*-butyldimethylsilyloxy)-1-phenylpropan-2-yl)-1-methylcyclopropan-1-ol (( $\pm$ )-**5a**)  
The cyclopropanol ( $\pm$ )-**5a** was obtained following the **general procedure B** from alkene **4a** and ethyl acetate (**2**) at 0 °C in a 76% yield (89 mg, dr 6:1 (determined by **method C**)). Colorless oil.  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.32 – 7.23 (m, 4H), 7.23 – 7.18 (m, 1H), 4.62 (d,  $J$  = 4.5 Hz, 1H), 1.79 (br.s, 1H), 1.40 (s, 3H), 1.22 – 1.14 (m, 1H), 0.94 (d,  $J$  = 6.8 Hz, 3H), 0.89 (s, 9H), 0.83 – 0.73 (m, 2H), 0.02 (s,  $J$  = 3.1 Hz, 3H), -0.01 (dd,  $J$  = 5.4, 4.4 Hz, 1H), -0.17 (s, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  143.27, 127.52 (2C), 127.04 (2C), 126.83, 78.27, 55.29, 43.47, 28.43, 26.01 (3C), 21.03, 20.75, 18.32, 16.54, -4.57, -4.94; IR (film) 3307, 3065, 3029, 2957, 2929, 2896, 2857, 1454, 1372, 1256, 1213, 1065, 836, 775, 701, 672  $cm^{-1}$ ; HRMS (ESI) calcd for  $C_{19}H_{32}NaO_2Si$  [ $M+Na$ ] $^+$ : 343.2064, found 343.2076.

(*1RS,2SR*)-2-((*RS*)-8,8-dimethyl-1,4-dioxaspiro[4.4]nonan-7-yl)-1-methylcyclopropan-1-ol (( $\pm$ )-**5b**)  
The cyclopropanol ( $\pm$ )-**5b** was obtained following the **general procedure A** from alkene **4b** and ethyl acetate (**2**) in a 77% yield (42.5 mg, dr 16:1 (determined by **method A**:  $\delta_{major\ isomer}$  = 0.22 ppm;  $\delta_{minor\ isomer}$  = 0.04 ppm)) as a colorless oil.  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  3.92 – 3.77 (m, 4H), 2.06 (dd,  $J$  = 13.8, 7.6 Hz, 1H), 1.88 (dd,  $J$  = 13.8, 11.7 Hz, 1H), 1.79 (d,  $J$  = 13.7 Hz, 1H), 1.71 (d,  $J$  = 13.9 Hz, 1H), 1.41 (s, 3H), 1.16 – 1.05 (m, 1H), 1.04 (s, 3H), 1.02 (s, 3H), 0.94 – 0.82 (m, 2H), 0.22 (dd,  $J$  = 5.6, 5.2 Hz, 1H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  116.13, 64.27, 63.81, 54.12, 52.44, 49.25, 43.02, 40.57, 29.15, 25.60, 23.07, 20.95, 20.51; IR (film) 3415, 3069, 2958, 2884, 1467, 1444, 1367, 1330, 1201, 1117, 1080, 1031, 830, 710  $cm^{-1}$ ; HRMS (ESI) calcd for  $C_{13}H_{23}O_3$  [ $M+H$ ] $^+$ : 227.1642, found 227.1642.



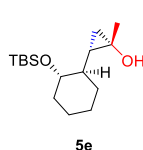
**(1R,2SR)-2-((RS)-8,8-dimethyl-1,4-dioxaspiro[4.5]decan-7-yl)-1-methylcyclopropan-1-ol ((±)-5c)**

To a stirred solution of alkene **4c** (45 mg, 0.23 mmol, 1 equiv.), ethyl acetate (**2**) (45  $\mu$ L, 0.46 mmol, 2 equiv.) and Ti(OiPr)<sub>4</sub> (68  $\mu$ L, 0.23 mmol, 1 equiv.) in THF (4.5 mL) at room temperature under argon atmosphere, a solution of cyclopentylmagnesium chloride (1.08M in THF, 0.85 mL, 0.92 mmol, 4 equiv.) was added over 1 h. Next, ethyl acetate (**2**) (45  $\mu$ L, 0.46 mmol, 2 equiv.) and Ti(OiPr)<sub>4</sub> (68  $\mu$ L, 0.23 mmol, 1 equiv.) were added to the mixture again followed by an addition of a solution of cyclopentylmagnesium chloride (1.08M in THF, 0.85 mL, 0.92 mmol, 4 equiv.) over 1 h. The reaction was stirred for 30 min, cooled down to 0 °C and quenched with saturated aqueous NH<sub>4</sub>Cl (0.135 mL). The suspension was stirred for 5 min, filtered and the precipitate was washed with EtOAc (5 $\times$ 5 mL). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum ether–EtOAc = 100:0 - 80:20) to give starting alkene **4c** (16 mg) cyclopropanol (**±**)-**5c** (23 mg, 42%, 59% based on recovered starting material, dr 7:1 (determined by **method A**:  $\delta_{\text{major isomer}} = 0.24$  ppm ;  $\delta_{\text{minor isomer}} = -0.03$  ppm)) as a colorless oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  3.98 – 3.86 (m, 4H), 1.96 (br.s, 1H), 1.71 – 1.51 (m, 4H), 1.49 – 1.40 (m, 1H), 1.44 (s, 3H), 1.37 – 1.30 (m, 1H), 0.99 – 0.91 (m, 1H), 0.96 (s, 3H), 0.94 (s, 3H), 0.92 – 0.86 (m, 1H), 0.85 – 0.78 (m, 1H), 0.24 (dd,  $J = 6.4, 5.5$  Hz, 1H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  109.36, 64.24, 64.21, 54.18, 45.23, 38.94, 37.80, 33.89, 31.29, 30.34, 27.02, 21.99, 20.65, 19.58; IR (film) 3410, 3068, 2949, 2884, 1453, 1365, 1288, 1219, 1094, 1027, 936, 877, 756 cm<sup>-1</sup>; HRMS (APCI) calcd for C<sub>14</sub>H<sub>25</sub>O<sub>3</sub> [M+H]<sup>+</sup> 241.1798, found 241.1802.



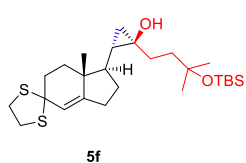
**(1R,2SR)-2-((1R,2RS)-2-((tert-butyldimethylsilyloxy)cyclohexyl)-1-methylcyclopropan-1-ol ((±)-5d)**

The cyclopropanol (**±**)-**5d** was obtained following the **general procedure B** from alkene **4d** and ethyl acetate (**2**) at room temperature in a 86% yield (81 mg, dr 9:1 (determined by **method B**:  $\delta_{\text{major isomer}} = -0.09$  ppm ;  $\delta_{\text{minor isomer}} = -0.15$  ppm)). Colorless oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  3.82 (s, 1H), 1.82 (br.s, 1H), 1.76 – 1.59 (m, 4H), 1.41 (s, 3H), 1.48 – 1.13 (m, 4H), 1.07 (tt,  $J = 10.9, 5.5$  Hz, 1H), 0.91 (s, 9H), 0.75 (dd,  $J = 10.2, 5.1$  Hz, 1H), 0.64 – 0.57 (m, 1H), 0.10 – 0.07 (m, 1H), 0.05 (s, 3H), 0.04 (s, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  68.95, 56.18, 44.67, 34.16, 29.13, 27.32, 26.05, 25.95 (3C), 20.64, 19.89, 19.20, 18.20, -4.47, -4.78; IR (film) 3382, 3067, 2931, 2894, 2857, 1472, 1446, 1253, 1022, 836, 774, 673 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>16</sub>H<sub>33</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 285.2244, found 285.2245.



**(1R,2SR)-2-((1R,2SR)-2-((tert-butyldimethylsilyloxy)cyclohexyl)-1-methylcyclopropan-1-ol ((±)-5e)**

The cyclopropanol (**±**)-**5e** was obtained following the **general procedure B** from alkene **4e** and ethyl acetate (**2**) at 0 °C in a 67% yield (70 mg, *cis*-1,2-dialkyl isomer, single diastereomer (determined by **method A, B**)). Colorless oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  3.42 (td,  $J = 8.3, 4.2$  Hz, 1H), 1.87 – 1.79 (m, 2H), 1.78 (br.s, 1H), 1.74 – 1.64 (m, 1H), 1.63 – 1.53 (m, 1H), 1.43 (s, 3H), 1.32 – 1.11 (m, 4H), 0.92 – 0.86 (m, 1H), 0.88 (s,  $J = 8.6$  Hz, 9H), 0.82 – 0.69 (m, 2H), 0.39 (t,  $J = 5.7$  Hz, 1H), 0.06 (s,  $J = 14.6$  Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  75.67, 54.57, 46.54, 35.58, 31.47, 29.82, 26.08 (3C), 25.05, 24.45, 21.83, 20.93, 18.19, -4.32, -4.46; IR (film) 3318, 3072, 2930, 2857, 1447, 1361, 1258, 1215, 1090, 962, 835, 773, 667 cm<sup>-1</sup>; HRMS (APCI) calcd for C<sub>16</sub>H<sub>33</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 285.2244, found 285.2225.

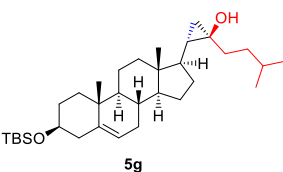


**(1R,2S)-1-(3-((tert-butyldimethylsilyloxy)-3-methylbutyl)-2-((1R,7aR)-7a-methyl-1,2,3,6,7,7a-hexahydro-spiro[indene-5,2'-[1,3]dithiolan]-1-yl)cyclopropan-1-ol (5f)**

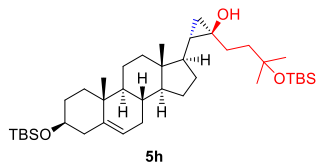
The cyclopropanol **5f** was obtained following the **general procedure A** from alkene **4f** and ester (**S12**) in a 53% yield (55 mg, dr 10:1 (determined by **method B**:  $\delta_{\text{major isomer}} = 0.17$  ppm ;  $\delta_{\text{minor isomer}} = -0.03$  ppm)) as a colorless oil.  $[\alpha]_D^{20} = 14.5$  (c 0.395, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.40 (s, 1H), 3.45 – 3.31 (m, 3H), 3.25 – 3.15 (m, 1H), 2.46 – 2.11 (m, 4H), 1.91 – 1.67 (m, 4H), 1.66 – 1.48 (m, 3H), 1.34 (td,  $J = 13.3, 2.9$  Hz, 1H), 1.27 – 1.18 (m, 7H), 0.99 (s, 3H), 0.95 – 0.86 (m, 1H), 0.84 (s, 9H) 0.22 – 0.17 (m, 1H), 0.07 (m, 7 H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  150.76, 121.73, 73.53, 66.39, 58.21, 51.86, 43.32, 41.45, 40.48, 39.69, 39.03, 36.83, 30.14, 29.98, 28.82, 28.10, 27.86, 26.19, 26.02 (3C), 18.49, 18.27, 18.21, -1.88(2C); IR(film) 3421, 3073, 2956, 2930, 2856, 1462, 1412, 1366, 1254, 1039, 869, 835, 772, 667 cm<sup>-1</sup>; HRMS (APCI) calcd for C<sub>26</sub>H<sub>47</sub>O<sub>2</sub>S<sub>2</sub>Si [M+H]<sup>+</sup> 483.2781, found 483.2784.

**(1R,2S)-1-isopentenyl-2-(36-((tert-butyldimethylsilyloxy)-androst-5-en-17 $\beta$ -yl)-cyclopropan-1-ol (5g)**

The cyclopropanol **5g** was obtained following the **general procedure B** from alkene **4g** and ester **S9** at 0 °C in a 68% yield (620 mg, dr 15:1 (determined by **method B**:  $\delta_{\text{major isomer}} = 0.15$  ppm ;  $\delta_{\text{minor isomer}} = -0.02$  ppm)). Colorless oil.  $[\alpha]_D^{20} = 217$  (c 0.09, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.34 – 5.29 (m, 1H), 3.52 – 3.44 (m, 1H), 2.31 – 2.22 (m, 1H), 2.16 (ddd,  $J = 13.3, 4.8, 2.1$  Hz, 1H), 2.02 – 1.95 (m, 1H), 1.88 – 1.78 (m, 3H), 1.76 (br.s, 1H), 1.74 – 1.35 (m, 13H), 1.16 (ddd,  $J = 24.0, 11.9, 6.4$  Hz, 1H), 1.07 – 0.70 (m, 7H), 1.01 (s, 3H), 0.91 (d,  $J = 6.6$  Hz, 6H), 0.88 (s, 9H), 0.75 (s, 3H), 0.17 – 0.14 (m, 1H), 0.05 (s, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  141.80, 121.22, 72.76, 58.10, 55.93, 51.77, 50.72, 43.24, 42.97, 38.62, 37.59, 36.84, 35.10, 32.23, 32.16 (2C), 32.09, 28.81, 28.45, 26.69, 26.09 (3C), 25.07, 22.93, 22.74, 20.94, 19.61, 18.87, 18.41, 13.24, -4.44 (2C); IR (film) 3415, 3026, 2953, 2934, 2903, 2868, 1470, 1255, 1093, 835, 774, 667 cm<sup>-1</sup>; HRMS (APCI) calcd for C<sub>33</sub>H<sub>59</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 515.4279, found 515.4271.

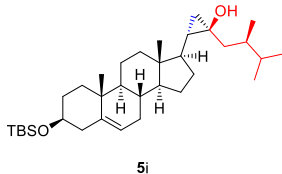


(1*R*,2*S*)-1-(3-((*tert*-butyldimethylsilyl)oxy)-3-methylbutyl)-2-(36-((*tert*-butyldimethylsilyl)oxy)-androst-5-en-17*β*-yl)-cyclopropan-1-ol (**5h**)



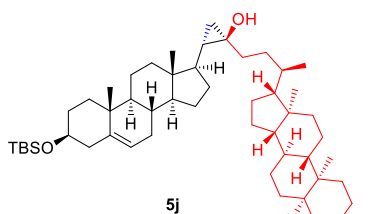
The cyclopropanol **5h** was obtained following the **general procedure B** from alkene **4g** and ester **S12** at 0 °C in a 59% yield (90 mg, dr 15:1 (determined by **method C**)). Colorless oil.  $[\alpha]_D^{20} = -46$  (c 0.446, CHCl<sub>3</sub>). **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 5.32 (d, *J* = 5.1 Hz, 1H), 3.51 – 3.44 (m, 1H), 2.32 – 2.23 (m, 1H), 2.17 (dd, *J* = 13.3, 2.7 Hz, 1H), 2.05 – 1.93 (m, 2H), 1.91 – 1.78 (m, 3H), 1.78 – 1.67 (m, 3H), 1.66 – 1.39 (m, 9H), 1.24 (d, *J* = 5.7 Hz, 6H), 1.23 – 1.10 (m, 2H), 1.01 (s, 3H), 0.89 (s, 9H), 1.10 – 0.71 (m, 6H), 0.85 (s, 9H), 0.75 (s, 3H), 0.18 – 0.15 (m, 1H), 0.08 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 141.85, 121.25, 73.56, 72.79, 58.21, 55.96, 51.72, 50.75, 43.25, 43.00, 41.42, 38.62, 37.60, 36.84, 32.25, 32.19, 32.08, 30.17, 30.02, 28.90 (2C), 26.81, 26.10(3C), 26.07(3C), 25.07, 20.96, 19.62, 18.79, 18.43, 18.30, 13.24, -1.87(2C), -4.43(2C). **IR** (film) 3420, 3028, 2955, 2931, 2901, 2856, 1472, 1254, 1092, 1042, 835, 773, 668 cm<sup>-1</sup>; **HRMS** (APCI) calcd for C<sub>33</sub>H<sub>57</sub>O<sub>2</sub>Si [M-TBSOH+H]<sup>+</sup>: 513.4122, found 513.4114.

(1*R*,2*S*)-2-(36-((*tert*-butyldimethylsilyl)oxy)-androst-5-en-17*β*-yl)-1-((*R*)-2,3-dimethylbutyl)cyclopropan-1-ol (**5i**)



The cyclopropanol **5i** was obtained following the **general procedure B** from alkene **4g** and ester **S15** at room temperature in a 58% yield (83.4 mg). Colorless oil.  $[\alpha]_D^{20} = -56$  (c 0.178, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 5.33 – 5.30 (m, 1H), 3.52 – 3.42 (m, 1H), 2.31 – 2.23 (m, 1H), 2.20 – 2.14 (m, 1H), 2.03 – 1.94 (m, 1H), 1.88 – 1.38 (m, 15H), 1.31 (dd, *J* = 14.5, 7.3 Hz, 1H), 1.24 – 1.12 (m, 1H), 1.01 (s, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 1.08 – 0.69 (m, 7H), 0.77 (d, *J* = 6.8 Hz, 3H), 0.75 (s, 3H), 0.23 (t, *J* = 5.7 Hz, 1H), 0.05 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 141.79, 121.22, 72.75, 56.89, 55.90, 51.97, 50.72, 43.22, 42.97, 38.64, 38.03, 37.58, 36.84, 36.10, 32.22, 32.17, 32.08, 30.48, 28.49, 26.20, 26.08 (3C), 25.03, 20.95 (2C), 19.61, 19.39, 16.80, 15.94, 15.42, 13.24, -4.44 (2C); **IR** (film) 3383, 3070, 2955, 2931, 2855, 1463, 1379, 1253, 1094, 836, 759, 667 cm<sup>-1</sup>; **HRMS** (APCI) calcd for C<sub>34</sub>H<sub>61</sub>O<sub>2</sub>Si [M+H]<sup>+</sup>: 529.4435, found 529.4425.

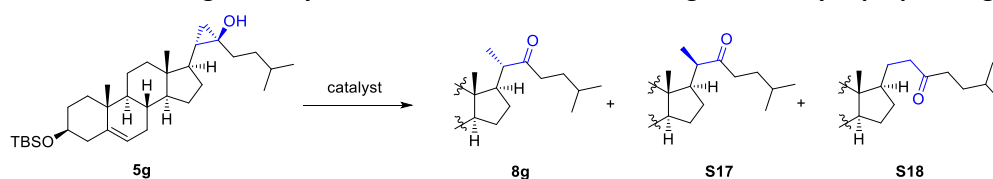
Cyclopropanol **5j**.



The cyclopropanol **5j** was obtained following the **general procedure B** from alkene **4g** and ester **S16** at 0 °C in a 59% yield (78 mg, dr 12:1 (determined by **method C**)). Colorless oil.  $[\alpha]_D^{20} = -32$  (c 0.093, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 5.35 – 5.28 (m, 1H), 3.62 – 3.53 (m, 1H), 3.52 – 3.43 (m, 1H), 2.27 (t, *J* = 12.2 Hz, 1H), 2.16 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.03 – 1.91 (m, 2H), 1.90 – 0.73 (m, 50H), 1.01 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 18H), 0.75 (s, 3H), 0.64 (s, 3H), 0.13 (t, *J* = 5.7 Hz, 1H), 0.05 (s, 12H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 141.79, 121.24, 72.96, 72.77, 58.27, 56.58, 56.32, 55.88, 51.76, 50.70, 43.28, 42.98, 42.87, 42.45, 40.41, 40.34, 38.62, 37.59, 37.08, 36.86, 36.09, 36.03, 35.74, 34.74, 32.24, 32.18, 32.12, 31.98, 31.19, 30.79, 28.85, 28.51, 27.46, 26.92, 26.57, 26.13 (3C), 26.10 (3C), 25.12, 24.42, 23.56, 20.98, 20.96, 19.62, 18.91, 18.80, 18.49, 18.42, 13.26, 12.20, -4.43(4C); **IR** (film) 3394, 3069, 2929, 2856, 1463, 1376, 1252, 1094, 835, 759, 668 cm<sup>-1</sup>; **MALDI MS** 911.9 [M+Na]<sup>+</sup>; **HRMS** (ESI) calcd for C<sub>51</sub>H<sub>85</sub>O<sub>2</sub>Si [M-TBSOH+H]<sup>+</sup>: 757.6313, found 757.6332.

## 5. Synthesis of $\alpha$ -methylketones 8

**Table S1. Screening of catalysts and conditions for the rearrangement of cyclopropanol 5g to  $\alpha$ -methylketone 8g<sup>[a]</sup>**



Catalyst	Solvent	Temperature	<b>8g:S17:S18</b> <sup>[b]</sup>	Yield, %
Al <sub>2</sub> O <sub>3</sub> -ascorbic acid	toluene	100	1:0.14:0.24	75%
ZnO	xylene	120	-	0
CaO	xylene	120	-	0
Na <sub>2</sub> HPO <sub>4</sub>	xylene	140	-	0
Na <sub>2</sub> HPO <sub>4</sub>	tAmOH/H <sub>2</sub> O (4:1)	100	-	0
NaOAc	xylene	140	-	0
NaOAc	tAmOH/H <sub>2</sub> O (4:1)	100	-	0
K <sub>2</sub> CO <sub>3</sub>	xylene	140	-	0
MgSO <sub>4</sub>	xylene	140	-	Complex mixture
MgCO <sub>3</sub> •Mg(OH) <sub>2</sub> •H <sub>2</sub> O	xylene	140	-	Complex mixture
MgO	xylene	120 (30 min)	1:0.14:0.26	-
Mg(OMe) <sub>2</sub>	xylene	100 (10 min)	1:0.16:0.07	-
Mg(OMe) <sub>2</sub>	toluene	40 (25 min)	1:0.06:0.03	66
Mg(OMe) <sub>2</sub>	MeOH	60 (60 min)	1:0.08:0.03	77
Mg(OMe) <sub>2</sub>	THF	60 (60 min)	1:0.05:0.07	75
Mg(OMe) <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	40 (25 min)	1:0.06:0.02	86
Mg(OMe) <sub>2</sub> <sup>[c]</sup>	CH <sub>2</sub> Cl <sub>2</sub>	40 (25 min)	-	Incomplete reaction
<b>Mg(OMe)<sub>2</sub></b>	<b>hexane</b>	<b>40 (45 min)</b>	<b>1:0.04:0.02</b>	<b>86</b>

[a] Reaction conditions: Catalyst (10 fold w/w excess), solvent (5% w/w solution of **5g**); [b] The ratio of the products was determined from <sup>1</sup>H NMR spectra of crude mixture; [c] **5g**:Mg(OMe)<sub>2</sub>=1:1 (w/w)

### Synthesis of Mg(OMe)<sub>2</sub>.

Mg (700 mg, 29.2 mmol) was added to MeOH (35 mL) and the mixture was heated under reflux until magnesium dissolved completely. The solvent was evaporated using rotovap and the residue was dried **under reduced pressure (100 Torr) at 60 °C for 8 min** to obtain free flowing powder of Mg(OMe)<sub>2</sub> (1.58 g, 148%). The catalyst obtained followed by this procedure gives well-reproducible results. However, we observed, *that after prolonged drying in high vacuo, Mg(OMe)<sub>2</sub> catalyzed the reaction with unsatisfactory reproducibility.*

### General procedure for the transformation of cyclopropanols 5 to $\alpha$ -methylketones 8.

To a 5% (w/w) solution of cyclopropanol (diastereomeric purity of the purified cyclopropanols measured from <sup>1</sup>H NMR is given in the brackets) in hexane, a 10 fold excess by mass of Mg(OMe)<sub>2</sub> was added. The suspension was stirred at 40 °C for indicated time and quenched with saturated aqueous NH<sub>4</sub>Cl (3 volumes of solvent). The aqueous layer was separated and extracted with ether. The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using hexane and ether as the eluent to obtain  $\alpha$ -methylketone **8**.

### Determination of diastereomeric purity of $\alpha$ -methylketones 8.

Diastereomeric purity was determined from <sup>1</sup>H NMR spectra in CDCl<sub>3</sub>. To assign signals of minor epimers, the synthesized ketones were epimerized using following procedures.

**Procedure A.** Ketones ( $\pm$ )-**8a**, ( $\pm$ )-**8d-e** (2 mg) were dissolved in CHCl<sub>3</sub>. Neutral Al<sub>2</sub>O<sub>3</sub> (10 mg) was added to the solutions and the solvent was evaporated under reduced pressure. The residue was heated at 100 °C for 1h and Al<sub>2</sub>O<sub>3</sub> was washed with ether. The filtrate was concentrated under reduced pressure and the residue was analyzed by <sup>1</sup>H NMR spectroscopy.

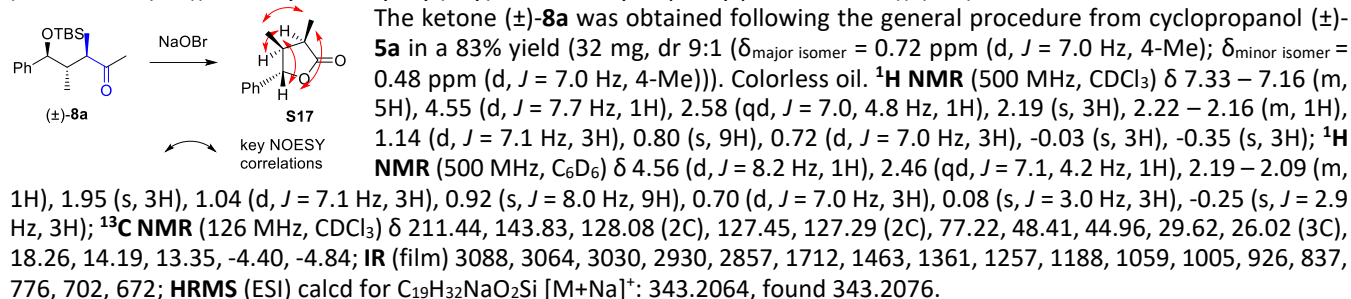
**Procedure B.** Ketones **8f-j** (2 mg) were dissolved in a 5% methanolic solution of tBuOK (20  $\mu$ L). The mixture was stirred at room temperature for 1 h, diluted with water (0.5 mL) and extracted with ether (2 $\times$ 0.5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was analyzed by <sup>1</sup>H NMR spectroscopy.

**Procedure C** Mg(OMe)<sub>2</sub> (20 mg) was added to the solution of ketones ( $\pm$ )-**8b-c** (2 mg) in hexane (50  $\mu$ L). The resulting suspension was stirred at 40 °C for 3h and quenched with saturated aqueous NH<sub>4</sub>Cl (3 volumes of solvent). The aqueous layer was separated and extracted with ether. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was analyzed by <sup>1</sup>H NMR spectroscopy.

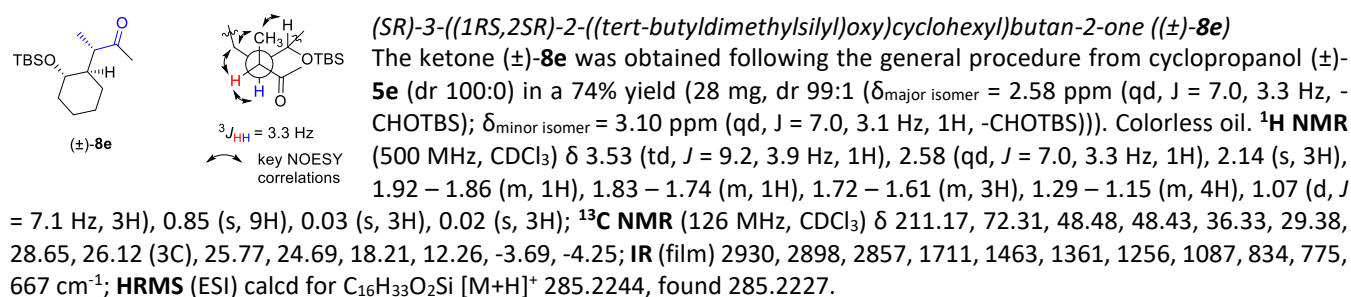
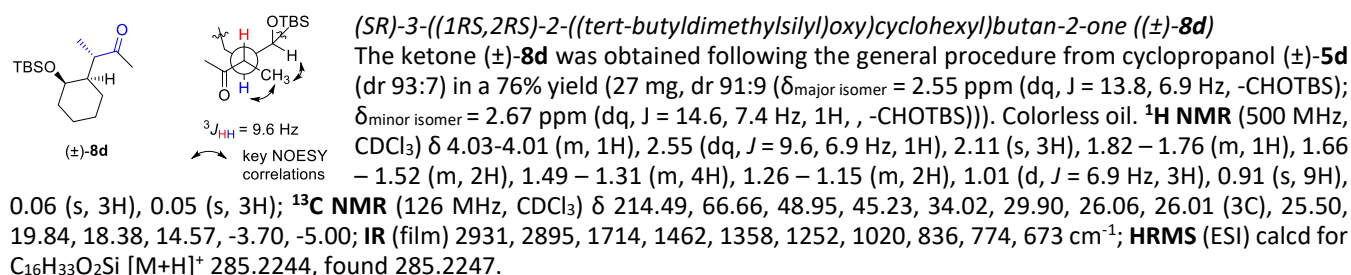
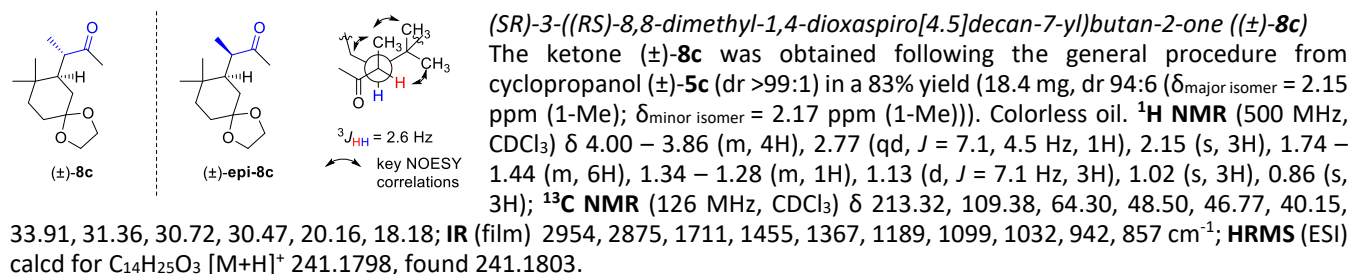
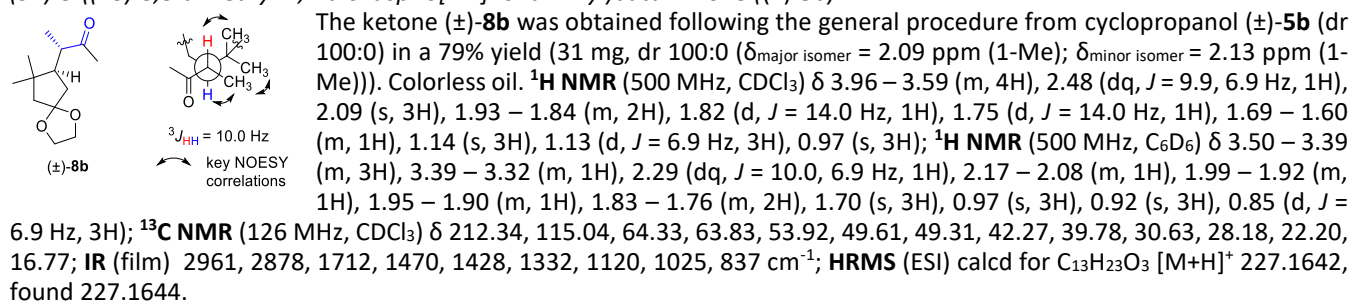
## Determination of relative configuration in $\alpha$ -methylketones 8.

Relative configuration in ( $\pm$ )-**8a** was determined after its transformation to lactone **S17** using 2D  $^1\text{H}$ - $^1\text{H}$  NOESY NMR. Relative configuration of ketones ( $\pm$ )-**8b**, ( $\pm$ )-**8d-e** and **8f** were determined by considering coupling constants and 2D NOESY NMR spectra. Relative configuration in ( $\pm$ )-**8c** was determined not directly but for its epimer ( $\pm$ )-**epi-8c** (unambiguous cross-peaks were observed only in 2D NOESY NMR of the epimer). The key correlations are shown in the figures. Structure of steroids **8g** and **8i** was confirmed by their transformation to known compounds **S20** and **9** and comparison of their  $^{13}\text{C}$  NMR spectra (see section 7, table S2 and table S3).

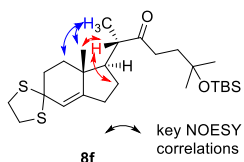
### (3*RS*,4*SR*,5*SR*)-5-((*tert*-butyldimethylsilyl)oxy)-3,4-dimethyl-5-phenylpentan-2-one (( $\pm$ )-**8a**)



### (*SR*)-3-((*RS*)-8,8-dimethyl-1,4-dioxaspiro[4.4]nonan-7-yl)butan-2-one (( $\pm$ )-**8b**)

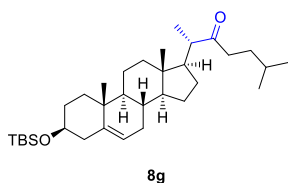






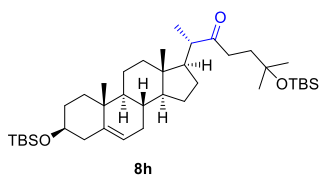
*(S)*-6-((*tert*-butyldimethylsilyloxy)-6-methyl-2-((1*R*,7*aR*)-7*a*-methyl-1,2,3,6,7,7*a*-hexahydrospiro[indene-5,2'-[1,3]dithiolan]-1-yl)heptan-3-one (**8f**)

The ketone **8f** was obtained following the general procedure from cyclopropanol **5f** (dr 91:9) in a 77% yield (18 mg, dr 89:11 ( $\delta_{\text{major isomer}} = 1.12$  ppm (d,  $J = 6.9$  Hz,  $\text{CH}_3\text{CH}$ ));  $\delta_{\text{minor isomer}} = 1.05$  ppm (d,  $J = 6.9$  Hz,  $\text{CH}_3\text{CH}$ ). Colorless oil.  $[\alpha]_D^{20} = 15.6$  (c 0.192,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  3.45 – 3.31 (m, 3H), 3.24 – 3.16 (m, 1H), 2.67 – 2.43 (m, 3H), 2.42 – 2.09 (m, 4H), 1.97 – 1.91 (m, 1H), 1.76 – 1.58 (m, 5H), 1.35 – 1.27 (m, 1H), 1.20 (s, 6H), 1.12 (d,  $J = 6.9$  Hz, 3H), 0.94 (s, 3H), 0.85 (s, 9H), 0.07 (s, 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  214.73, 150.19, 122.45, 72.80, 65.87, 52.48, 49.17, 42.71, 40.50, 39.74, 38.96, 38.23, 38.01, 36.90, 29.94 (2C), 27.80, 26.61, 25.96 (3C), 18.24, 17.36, 16.61, -1.97 (2C); IR (film) 2955, 2928, 2854, 1712, 1462, 1365, 1253, 1039, 834, 773, 689  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{26}\text{H}_{46}\text{NaO}_2\text{S}_2\text{Si}$  [ $\text{M}+\text{Na}$ ] $^+$  505.2601, found 505.2601.



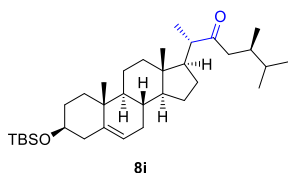
3 $\beta$ -((*tert*-butyldimethylsilyloxy)-cholest-5-en-22-one (**8g**)

The ketone **8g** was obtained following the general procedure from cyclopropanol **5g** (dr 98:2) in a 86% yield (36 mg, dr 96:4 ( $\delta_{\text{major isomer}} = 0.70$  ppm (s, 3H, 18-Me);  $\delta_{\text{minor isomer}} = 0.66$  ppm (s, 3H, 18-Me))). When 612 mg (1.19 mmol) of **5g** was reacted with  $\text{Mg}(\text{OMe})_2$  (6.12 g) in hexane (10 ml), ketone **8g** was obtained in 84% yield (516 mg). White crystals. M.p. = 168–171  $^\circ\text{C}$  (MeOH);  $[\alpha]_D^{20} = -50.0$  (c 0.538,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.32 – 5.29 (m, 1H), 3.51 – 3.44 (m, 1H), 2.52 (dq,  $J = 9.8, 6.7$  Hz, 1H), 2.48 – 2.40 (m, 1H), 2.39 – 2.31 (m, 1H), 2.29 – 2.22 (m, 1H), 2.19 – 2.13 (m, 1H), 1.99 – 1.91 (m, 2H), 1.80 (dt,  $J = 13.2, 3.3$  Hz, 1H), 1.75 – 1.38 (m, 11H), 1.29 (dd,  $J = 12.7, 4.3$  Hz, 1H), 1.09 (d,  $J = 6.9$  Hz, 3H), 1.16 – 0.84 (m, 5H), 1.00 (s, 3H), 0.89 (d,  $J = 6.4$  Hz, 6H), 0.88 (s, 9H), 0.70 (s, 3H), 0.05 (s, 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  215.18, 141.68, 121.19, 72.75, 56.27, 52.21, 50.30, 49.61, 42.95, 42.66, 39.82 (2C), 37.52, 36.72, 32.56, 32.22, 32.02 (2C), 27.86, 27.68, 26.09 (3C), 24.66, 22.57, 22.53, 21.16, 19.58, 18.42, 16.74, 12.23, -4.44 (2C); IR (KBr) 2955, 2928, 2854, 1712, 1462, 1365, 1253, 1039, 834, 773, 689  $\text{cm}^{-1}$ ; HRMS (APCI) calcd for  $\text{C}_{33}\text{H}_{59}\text{O}_2\text{Si}$  [ $\text{M}+\text{H}$ ] $^+$  515.4279, found 515.4275.



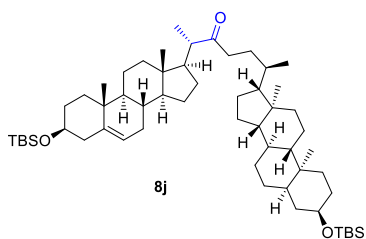
3 $\beta$ ,25-di-((*tert*-butyldimethylsilyloxy)-cholest-5-en-22-one (**8h**)

The ketone **8h** was obtained following the general procedure from cyclopropanol **5h** in a 76% yield (22 mg, dr 97:3 ( $\delta_{\text{major isomer}} = 0.70$  ppm (s, 3H, 18-Me);  $\delta_{\text{minor isomer}} = 0.66$  ppm (s, 3H, 18-Me))). White crystals. M.p. = 117–120  $^\circ\text{C}$  (MeOH);  $[\alpha]_D^{20} = 52.2$  (c 0.115,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.35 – 5.27 (m, 1H), 3.52 – 3.44 (m, 1H), 2.64 – 2.55 (m, 1H), 2.52 (ddd,  $J = 14.0, 10.3, 7.0$  Hz, 1H), 2.50 – 2.42 (m, 1H), 2.30 – 2.23 (m, 1H), 2.16 (ddd,  $J = 13.4, 4.9, 2.1$  Hz, 1H), 2.00 – 1.92 (m, 1H), 1.80 (dt,  $J = 13.1, 3.3$  Hz, 1H), 1.75 – 1.40 (m, 11H), 1.32 – 1.23 (m, 1H), 1.20 (s, 6H), 1.10 (d,  $J = 6.7$  Hz, 3H), 1.17 – 0.91 (m, 6H), 1.00 (s, 3H), 0.89 (s, 9H), 0.85 (s, 9H), 0.70 (s, 3H), 0.07 (s, 6H), 0.05 (s, 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  215.42, 141.69, 121.20, 72.87, 72.76, 56.31, 52.33, 50.32, 49.75, 42.96, 42.68, 39.82, 38.27, 37.53, 36.75, 36.72, 32.23, 32.02 (2C), 30.00, 29.90, 27.68, 26.09 (3C), 25.98 (3C), 24.63, 21.17, 19.58, 18.42, 18.25, 16.80, 12.23, -1.97 (2C), -4.44 (2C); IR (KBr) 2956, 2930, 2857, 1717, 1462, 1366, 1253, 1142, 1091, 1044, 836, 772; HRMS (ESI) calcd for  $\text{C}_{39}\text{H}_{73}\text{O}_3\text{Si}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$ : 667.4912, found 667.4907.



3 $\beta$ -((*tert*-butyldimethylsilyloxy)-campest-5-en-22-one (**8i**)

The ketone **8i** was obtained following the general procedure from cyclopropanol **5i** in a 77% yield (40 mg) as a 4:1 mixture with its regioisomer. Pure ketone **14i** (20 mg) was obtained after crystallization of the mixture from methanol. White crystals. M.p. = 183–185  $^\circ\text{C}$  (MeOH);  $[\alpha]_D^{20} = 245$  (c 0.094,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.34 – 5.28 (m, 1H), 3.48 (tt,  $J = 10.9, 4.7$  Hz, 1H), 2.49 (dq,  $J = 10.4, 6.8$  Hz, 1H), 2.36 (dd,  $J = 17.0, 4.1$  Hz, 1H), 2.30 – 2.22 (m, 1H), 2.24 (dd,  $J = 16.9, 9.3$  Hz, 1H), 2.16 (ddd,  $J = 13.4, 4.9, 2.2$  Hz, 1H), 1.99 – 1.90 (m, 3H), 1.80 (dt,  $J = 13.2, 3.4$  Hz, 1H), 1.74 – 1.67 (m, 2H), 1.66 – 1.39 (m, 8H), 1.31 – 1.23 (m, 1H), 1.08 (d,  $J = 6.9$  Hz, 3H), 1.15 – 0.90 (m, 5H), 1.00 (s, 3H), 0.88 (s, 9H), 0.86 (d,  $J = 6.8$  Hz, 3H), 0.82 (d,  $J = 6.8$  Hz, 3H), 0.79 (d,  $J = 6.8$  Hz, 3H), 0.69 (s, 3H), 0.05 (s, 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  214.50, 141.68, 121.20, 72.75, 56.29, 51.91, 50.31, 49.91, 46.64, 42.96, 42.60, 39.80, 37.52, 36.72, 33.69, 32.25, 32.22, 32.02 (2C), 27.78, 26.09 (3C), 24.69, 21.16, 20.02, 19.58, 18.50, 18.42, 16.48, 16.03, 12.20, -4.44 (2C); IR (KBr) 2960, 2932, 2858, 1709, 1461, 1369, 1257, 1085, 888, 839, 803, 776, 617; HRMS (APCI) calcd for  $\text{C}_{34}\text{H}_{61}\text{O}_2\text{Si}$  [ $\text{M}+\text{H}$ ] $^+$  529.4435, found 529.4425.

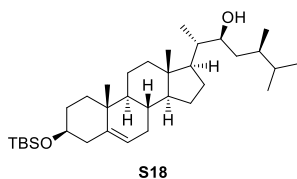


Ketone **8j**

The ketone **8j** was obtained following the general procedure from cyclopropanol **5j** in a 66% yield (32 mg, dr 91:9 ( $\delta_{\text{major isomer}} = 0.70$  ppm (s, 3H, 18-Me);  $\delta_{\text{minor isomer}} = 0.66$  ppm (s, 3H, 18-Me))). White crystals. M.p. 199–200  $^\circ\text{C}$  (*i*PrOH);  $[\alpha]_D^{20} = -14$  (c 0.215,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.34 – 5.26 (m, 1H), 3.64 – 3.53 (m, 1H), 3.53 – 3.43 (m, 1H), 2.51 (dq,  $J = 13.7, 6.7$  Hz, 1H), 2.42 – 2.31 (m, 2H), 2.26 (t,  $J = 11.4$  Hz, 1H), 2.16 (dd,  $J = 12.9, 2.9$  Hz, 1H), 2.00 – 1.89 (m, 3H), 1.88 – 0.80 (m, 47H), 1.09 (d,  $J = 6.9$  Hz, 3H), 1.00 (s, 3H), 0.89 (s, 18H), 0.70 (s, 3H), 0.62 (s, 3H), 0.05 (s, 12H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  215.43, 141.67, 121.20, 72.98, 72.75, 56.55, 56.28, 56.13, 52.17, 50.31, 49.67, 42.95, 42.86, 42.64, 42.44, 40.36, 40.31, 39.80, 38.50, 37.52, 37.07, 36.72, 36.01, 35.73, 35.37, 34.74, 32.22, 32.02, 31.18, 29.70, 28.33, 27.71, 27.45, 26.55, 26.13 (3C), 26.09

(3C), 24.67, 24.37, 23.54, 21.16, 20.96, 19.58, 18.64, 18.49, 18.41, 16.72, 12.24, 12.18, -4.44 (4C); IR (KBr) 2933, 2857, 1712, 1462, 1371, 1252, 1095, 835, 774, 668 cm<sup>-1</sup>; MALDI MS 911.9 [M+Na]<sup>+</sup>; HRMS (ESI) calcd for C<sub>51</sub>H<sub>85</sub>O<sub>2</sub>Si [M-TBSOH+H]<sup>+</sup> 757.6313, found 757.6328.

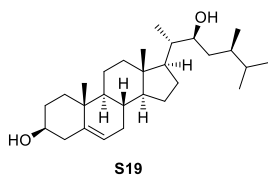
## 6. Synthesis of 6-deoxocathasterone (9)



S18

### (22S)-3β-((tert-butyldimethylsilyl)oxy)-campesterol (S18)

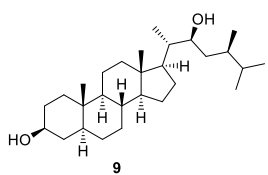
A solution of ketone **8i** (25.1 mg, 0.047 mmol) in Et<sub>2</sub>O (0.8 mL) was added to an ice cooled stirred suspension of LiAlH<sub>4</sub> (1.8 mg, 0.047 mmol) in Et<sub>2</sub>O (0.2 mL). The reaction mixture was stirred at room temperature for 30 min, then quenched with water (7 μL), and filtered. The filter cake was washed thoroughly with CHCl<sub>3</sub> (3×3 mL). The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel (hexane-Et<sub>2</sub>O = 49:1) to give alcohol **S18** (20.8 mg, 83%) as white crystals. M.p. = 192-195 °C (MeOH);  $[\alpha]_D^{20} = -37$  (c 0.192, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.33 – 5.30 (m, 1H), 3.77 (t, *J* = 6.8 Hz, 1H), 3.52 – 3.43 (m, 1H), 2.30 – 2.23 (m, 1H), 2.16 (ddd, *J* = 13.4, 4.8, 2.1 Hz, 1H), 2.02 – 1.89 (m, 3H), 1.80 (dt, *J* = 13.2, 3.3 Hz, 1H), 1.75 – 1.68 (m, 1H), 1.66 – 0.90 (m, 17H), 1.00 (s, 3H), 0.89 (d, *J* = 7.4 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.69 (s, 3H), 0.05 (s, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 141.74, 121.26, 72.79, 71.90, 56.88, 52.72, 50.32, 42.97, 42.43, 39.97, 39.54, 39.50, 37.53, 36.72, 35.50, 32.24, 32.19, 32.11, 32.04, 27.98, 26.09 (3C), 24.37, 21.25, 20.14, 19.59, 18.42, 17.98, 15.94, 11.94, 11.41, -4.44(2C); IR (KBr) 3463, 2957, 2929, 2858, 1463, 1379, 1273, 1122, 1073, 835, 773; HRMS (APCI) calcd for C<sub>34</sub>H<sub>63</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 531.4592, found 531.4469.



S19

### (22S)-3β-((tert-butyldimethylsilyl)oxy)-campesterol (S19)

To a solution of the TBS-protected alcohol **S18** (20.8 mg, 0.039 mmol) in dry THF (0.2 mL) at room temperature, TBAF (164 mg, 0.63 mmol) was added. The reaction mixture was stirred for 2 days, after which time it was quenched with saturated aqueous NH<sub>4</sub>Cl (5 mL) and extracted with CHCl<sub>3</sub> (5 mL). The organic layer was separated, washed with H<sub>2</sub>O (5×3 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane-Et<sub>2</sub>O = 1:1) to give diol **S19** (16.1 mg, 99%) as white crystals. Spectral data of **S19** were identical to those reported in the literature.<sup>[14]</sup>



9

### 6-Deoxocathasterone (9)

A mixture of 10% Pd/C (40 mg), alkene **S19** (16.1 mg, 0.039 mmol) and EtOH (2 mL) was stirred under hydrogen atmosphere for 3 days and then filtered. The filter cake was washed thoroughly with CHCl<sub>3</sub>. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel (hexane-EtOAc = 1:1) to give 6-deoxocathasterone **9** (15.9 mg, 98%) as white crystals.

NMR spectra of **9** were identical to those reported in the literature<sup>[14]</sup> (see Table S2).

**Table S2** Comparison of the NMR chemical shifts of the synthesized in this work deoxocathasterone (**9**) with the data in Ref.<sup>[14]</sup>

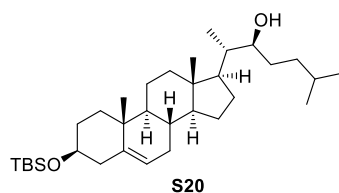
<sup>13</sup> C NMR (126 MHz, CDCl <sub>3</sub> ) δ, ppm <sup>[a]</sup>	<sup>13</sup> C NMR (126 MHz, CDCl <sub>3</sub> ) δ, ppm <sup>[a]</sup> ( Ref. <sup>[14]</sup> )	Δδ, ppm
71.7	71.6	+0.1
71.4	71.3	+0.1
56.4	56.4	0
54.3	54.3	0
52.6	52.6	0
44.8	44.8	0
42.5	42.5	0
40.0	40.0	0
39.3	39.3	0
39.3	39.3	0
38.2	38.1	+0.1
37.0	37.0	0
35.5	35.5	0
35.4	35.4	0
35.3	35.3	0
32.0	32.0	0
31.5	31.5	0
28.7	28.7	0



27.8	27.8	0
24.1	24.1	0
21.3	21.2	+0.1
20.0	20.0	0
17.8	17.8	0
15.8	15.7	+0.1
12.3	12.3	0
12.0	12.0	0
11.2	11.2	0

[a]  $\delta$  (CDCl<sub>3</sub>) = 77.00).

## 7. Reduction of 8g



*(22S)*-36-((*tert*-butyldimethylsilyl)oxy)-cholest-5-en-22-ol (**S20**)

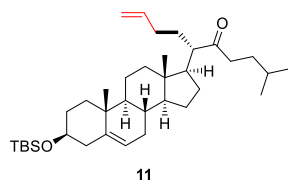
Steroid **S20** was prepared from ketone **8g** using the same procedure as described for **S18**. NMR spectra of **S20** were identical to those reported in the literature<sup>[15]</sup> (see Table S3).

**Table S3** Comparison of the NMR chemical shifts of the synthesized in this work **S20** with the data in Ref.<sup>[15]</sup>

<sup>13</sup> C NMR (126 MHz, CDCl <sub>3</sub> ) $\delta$ , ppm <sup>[a]</sup>	<sup>13</sup> C NMR (126 MHz, CDCl <sub>3</sub> ) $\delta$ , ppm <sup>[a]</sup> ( Ref. <sup>[15]</sup> )	$\Delta\delta$ , ppm
141.6	141.5	+0.1
121.1	121.1	0
73.9	73.9	0
72.6	72.6	0
56.7	56.7	0
52.6	52.6	0
50.2	50.2	0
42.8	42.8	0
42.2	42.2	0
40.2	40.2	0
39.8	39.8	0
37.4	37.4	0
36.6	36.5	+0.1
35.7	35.7	0
33.2	33.2	0
32.1	32.1	0
31.9	32.0	-0.1
31.9	31.9	0
28.2	28.2	0
27.7	27.7	0
25.9	25.9	0
24.2	24.2	0
22.7	22.7	0
22.6	22.5	+0.1
21.1	21.1	0
19.4	19.4	0
18.3	18.2	+0.1
11.8	11.8	0
11.5	11.5	0
-4.6	-4.6	0

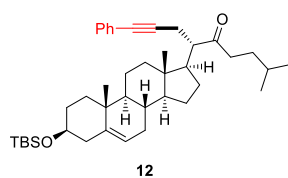
[a]  $\delta$  (CDCl<sub>3</sub>) = 77.00).

## 8. Arylation, allylation and alkylation of cyclopropanol **5g**



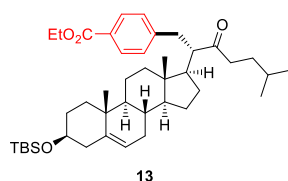
### 21-allyl-36-((tert-butyl dimethylsilyl)oxy)-cholest-5-en-22-one (**11**)

A solution of Et<sub>2</sub>Zn in hexane (0.9 M, 0.13 mL, 0.12 mmol) was added to a stirred solution of cyclopropanol **5g** (60 mg, 0.12 mmol) in THF (0.39 mL) at room temperature under Ar atmosphere. The solution was stirred for 10 min at the same temperature and cooled down to -30 °C. A solution of CuCN•2LiCl in THF (0.7 M, 0.25 mL, 0.175 mmol) was added to the reaction mixture dropwise over 15 min followed by allyl bromide (0.015 mL, 0.175 mmol). The mixture was warmed to room temperature over 1 h, stirred at room temperature for 2 h and quenched with saturated aqueous NH<sub>4</sub>Cl (0.5 mL). The suspension was stirred for 15 min at room temperature, diluted with ethyl acetate (0.5 mL) and stirred for 30 min. The aqueous layer was separated and extracted with EtOAc (3×0.5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (hexane–ether 100:0-50:1) to give ketone **11** (43 mg, 66%). White crystals. M.p. = 50-51 °C (MeOH); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = 128 (c 0.152, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.75 (ddt, *J* = 17.0, 10.2, 6.5 Hz, 1H), 5.34 – 5.24 (m, 1H), 5.04 – 4.96 (m, 1H), 4.96 (d, *J* = 10.4 Hz, 1H), 3.52 – 3.43 (m, 1H), 2.53 (td, *J* = 10.2, 3.0 Hz, 1H), 2.39 (dd, *J* = 8.6, 6.9 Hz, 2H), 2.30 – 2.22 (m, 1H), 2.16 (ddd, *J* = 13.2, 4.7, 1.9 Hz, 1H), 1.99 – 1.89 (m, 3H), 1.88 – 1.75 (m, 3H), 1.75 – 0.89 (m, 19H), 0.99 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 6H), 0.88 (s, 9H), 0.70 (s, 3H), 0.05 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  215.18, 141.68, 138.29, 121.15, 115.08, 72.74, 56.25, 54.94, 51.53, 50.29, 42.94, 42.90, 41.65, 39.89, 37.51, 36.71, 32.20 (2C), 32.08, 31.98, 31.58, 30.45, 27.76, 27.44, 26.09 (3C), 24.49, 22.60, 22.56, 21.21, 19.56, 18.41, 12.31, -4.45 (2C); **IR** (KBr) 3077, 2953, 2932, 2856, 1709, 1464, 1384, 1095, 836, 776 cm<sup>-1</sup>; **HRMS** (APCI) calcd for C<sub>36</sub>H<sub>63</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 555.4592, found 555.4592.



### 21-(2-phenylethyn-1-yl)-36-((tert-butyl dimethylsilyl)oxy)-cholest-5-en-22-one (**12**)

A solution of Et<sub>2</sub>Zn in hexane (0.9 M, 0.097 mL, 0.087 mmol) was added to a stirred solution of cyclopropanol **5g** (45 mg, 0.087 mmol) in THF (0.28 mL) at room temperature under Ar atmosphere. After the mixture had been stirred for 10 min, a solution of CuCN•2LiCl in THF (0.8 M, 0.164 mL, 0.131 mmol) was added to the reaction mixture dropwise over 15 min, followed by a solution of (bromoethynyl)benzene (47.5 mg, 0.262 mmol) in THF (0.28 mL). The mixture was stirred at room temperature over for 30 min and quenched with saturated aqueous NH<sub>4</sub>Cl (1 mL). The suspension was stirred for 15 min at room temperature, diluted with ethyl acetate (1 mL) and stirred for 30 min. The aqueous layer was separated and extracted with EtOAc (3×1 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by column chromatography on SiO<sub>2</sub> (hexane–ether 100:0-50:1) to give ketone **12** (23.6 mg, 44%) as white crystals. M.p. = 110-113 °C (MeOH); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = 200 (c 0.123, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.35 – 7.30 (m, 3H), 7.29 – 7.22 (m, 2H), 5.34 – 5.28 (m, 1H), 3.52 – 3.43 (m, 1H), 2.84 – 2.76 (m, 1H), 2.66 – 2.45 (m, 3H), 2.30-2.22 (m, 1H), 2.17 (ddd, *J* = 13.7, 4.9, 1.9 Hz, 1H), 2.02 – 1.86 (m, 2H), 1.85 – 0.92 (m, 20H), 1.00 (s, 3H), 0.89 (s, 9H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.75 (s, 3H), 0.06 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  213.57, 141.69, 131.68, 131.62, 131.53, 128.34, 128.28, 127.95, 121.09, 87.61, 82.58, 72.71, 56.11, 53.89, 51.42, 50.23, 42.94, 42.77, 41.45, 39.67, 37.50, 36.71, 32.20, 32.07, 31.95, 27.85, 27.77, 27.35, 26.08, 24.49, 22.61, 22.51, 21.67, 21.19, 19.58, 18.41, 12.43, -4.44; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  213.57, 141.69, 131.62 (2C), 128.34 (2C), 127.95, 123.58, 121.09, 87.61, 82.58, 72.71, 56.11, 53.89, 51.42, 50.23, 42.94, 42.77, 39.67, 37.50, 36.71, 32.20, 32.07 (2C), 31.95, 27.77, 27.35, 26.08 (3C), 24.49, 22.61, 22.51 (2C), 21.67, 21.19, 19.58, 18.41, 12.43, -4.44 (2C); **IR** (KBr) 3080, 3054, 3032, 2954, 2931, 2903, 2856, 2223, 1714, 1469, 1368, 1252, 1092, 835, 755, 691 cm<sup>-1</sup>; **HRMS** (ESI) calcd for C<sub>41</sub>H<sub>63</sub>O<sub>2</sub>Si [M+H]<sup>+</sup> 615.4592, found 615.4595.

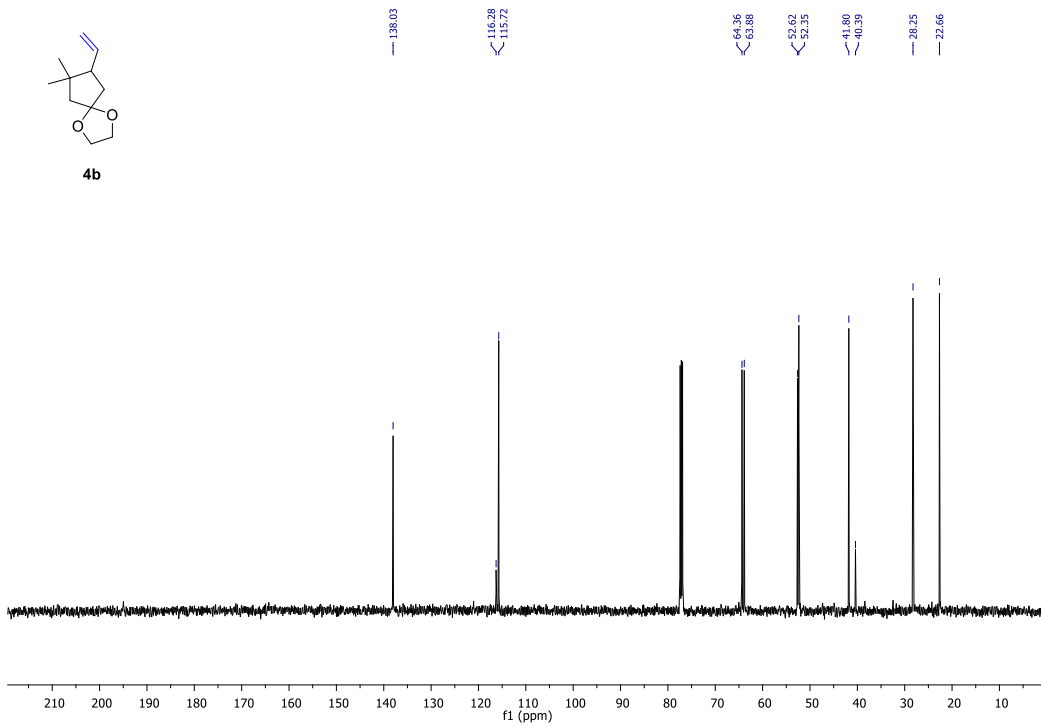
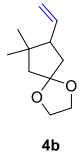
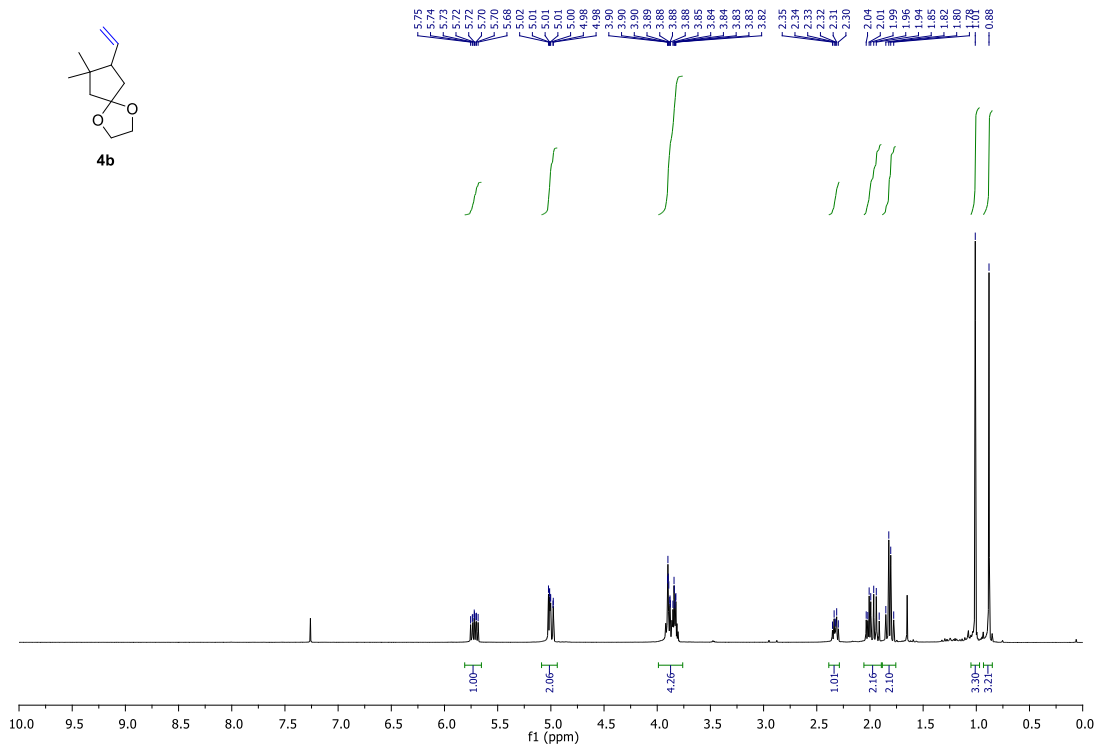
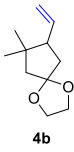


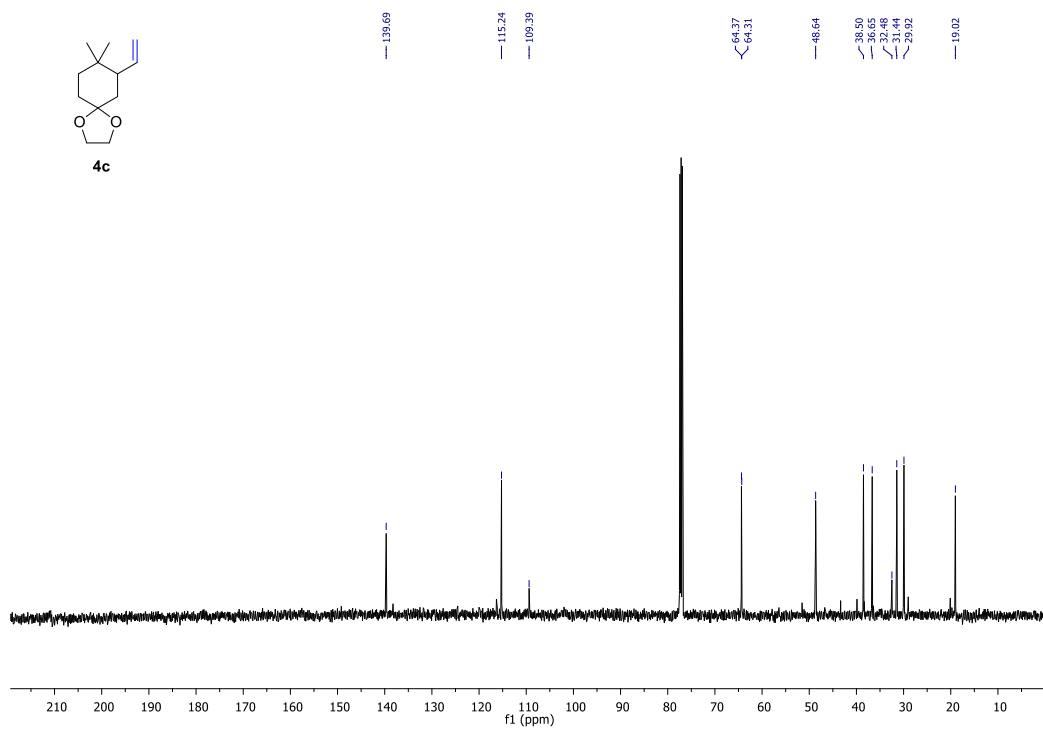
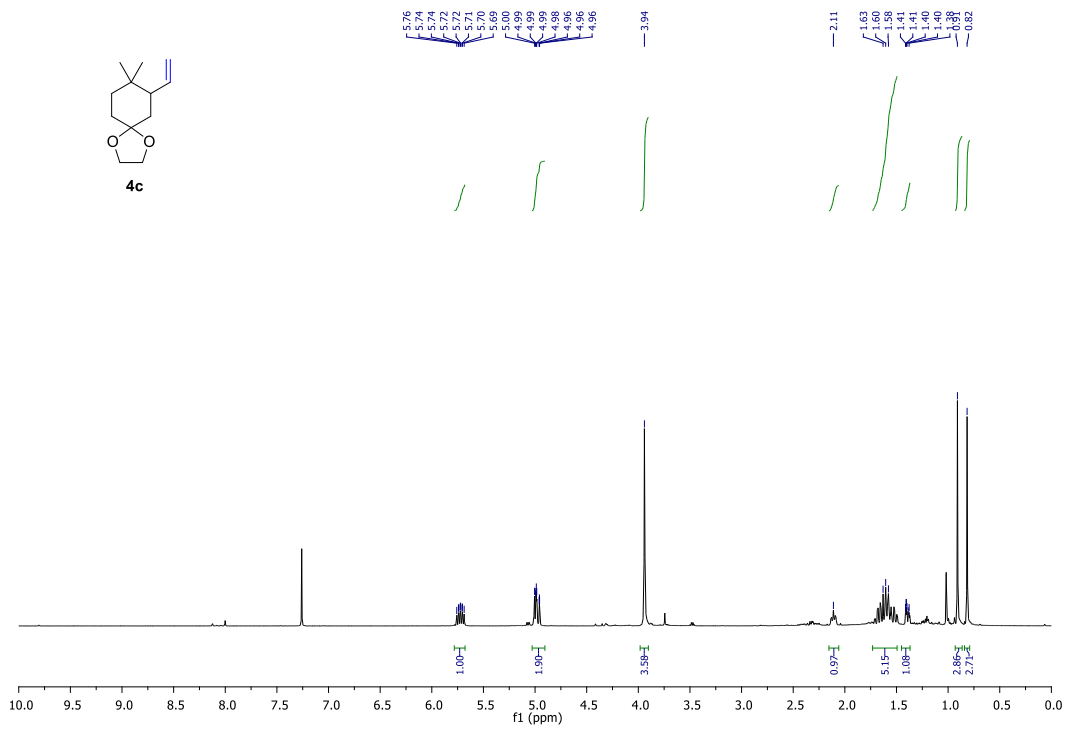
### 21-(4-(ethoxycarbonyl)phenyl-1-yl)-36-((tert-butyl dimethylsilyl)oxy)-cholest-5-en-22-one (**13**)

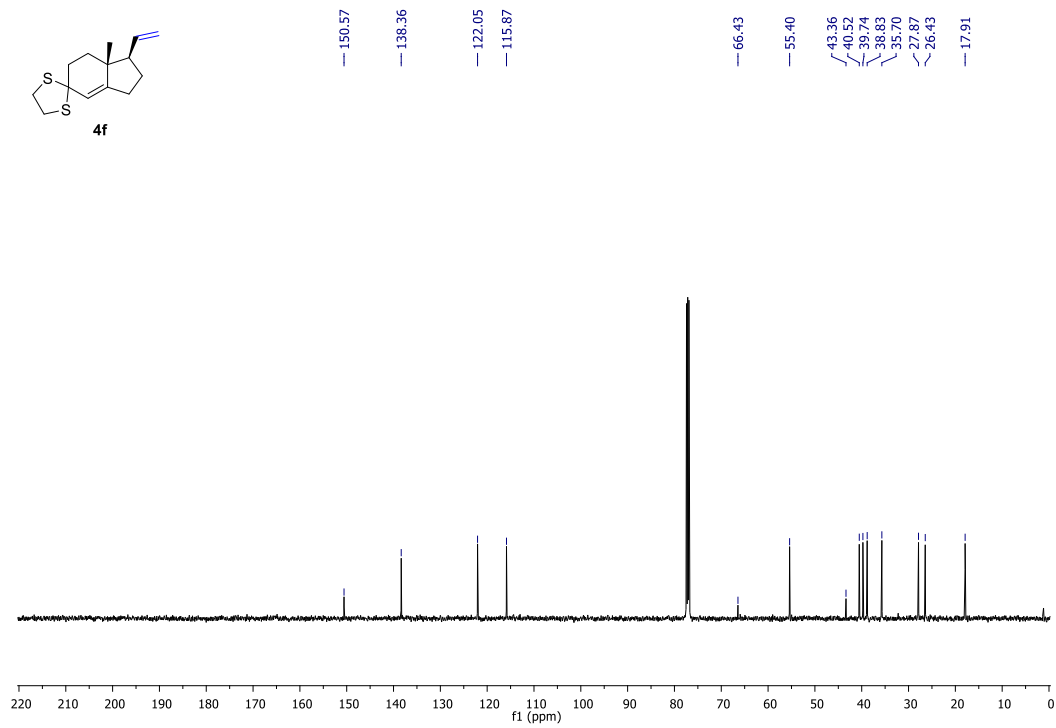
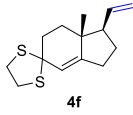
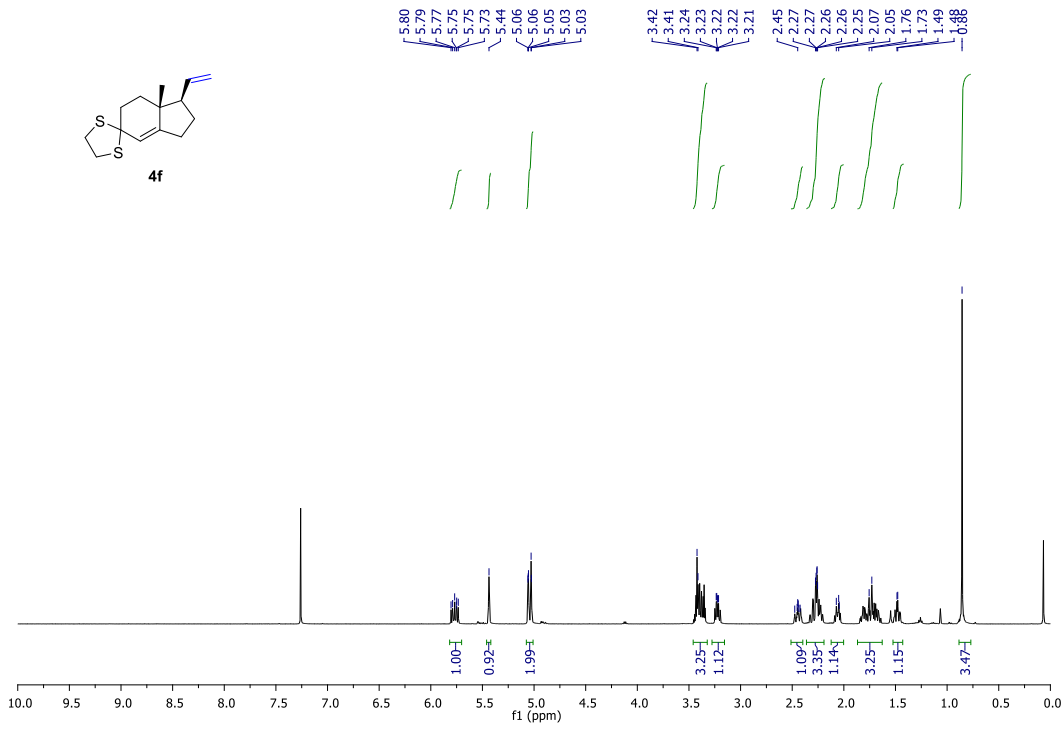
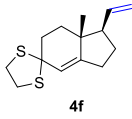
A vial was charged with cyclopropanol **5g** (47.3 mg, 0.092 mmol), Pd(OAc)<sub>2</sub> (2 mg, 0.0092 mmol), dppb (3.9 mg, 0.0092 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (60 mg, 0.18 mmol). After flushing with Ar, toluene (0.92 mL) was added to the vial and the suspension was stirred at room temperature for 5 min. Ethyl 4-bromobenzoate (0.022 mL, 0.14 mmol) was added to the mixture and the suspension was stirred at 80 °C for 1 h, diluted with EtOAc (0.5 mL) and filtered through a pad of silica gel. The filtrate was concentrated under reduced pressure and the residue was chromatographed on SiO<sub>2</sub> (hexane–ether 100:0-50:1) to give ketone **13** (32 mg, 53%) as white crystals. M.p. = 178-181 °C (MeOH); [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -24.4 (c 0.123, CHCl<sub>3</sub>); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.92 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 5.36 – 5.29 (m, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 3.53 – 3.43 (m, 1H), 3.16 (dd, *J* = 12.7, 3.1 Hz, 1H), 2.89 – 2.81 (m, 1H), 2.71 (t, *J* = 12.3 Hz, 1H), 2.31 – 2.23 (m, 1H), 2.17 (dd, *J* = 12.9, 3.2 Hz, 1H), 2.14 – 2.02 (m, 2H), 2.01 – 1.93 (m, 1H), 1.85 – 1.78 (m, 1H), 1.77 – 1.67 (m, 2H), 1.67 – 1.43 (m, 9H), 1.29 – 1.19 (m, 2H), 1.17 – 0.93 (m, 9H), 1.02 (s, 3H), 0.89 (s, 9H), 0.85 (s, 3H), 0.66 (d, *J* = 6.4 Hz, 3H), 0.65 (d, *J* = 6.4 Hz, 3H), 0.06 (s, 6H); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  214.49, 166.64, 145.31, 141.69, 129.89 (2C), 129.02 (2C), 128.69, 121.10, 72.72, 60.99, 57.00, 56.13, 52.26, 50.26, 44.10, 42.95 (2C), 40.00, 38.29, 37.51, 36.72, 32.20, 32.09, 31.95, 31.43, 27.37, 27.29, 26.08 (3C), 24.49, 22.38, 22.27, 21.23, 19.58, 18.41, 14.47, 12.48, -4.45 (2C); **IR** (KBr) 2957, 2932, 2904, 2886, 2867, 2857, 1720, 1634, 1611, 1470, 1385, 1367, 1276, 1253, 1100, 873, 863, 776 cm<sup>-1</sup>; **HRMS** (APCI) calcd for C<sub>42</sub>H<sub>67</sub>O<sub>4</sub>Si [M+H]<sup>+</sup> 663.4803, found 663.4792.

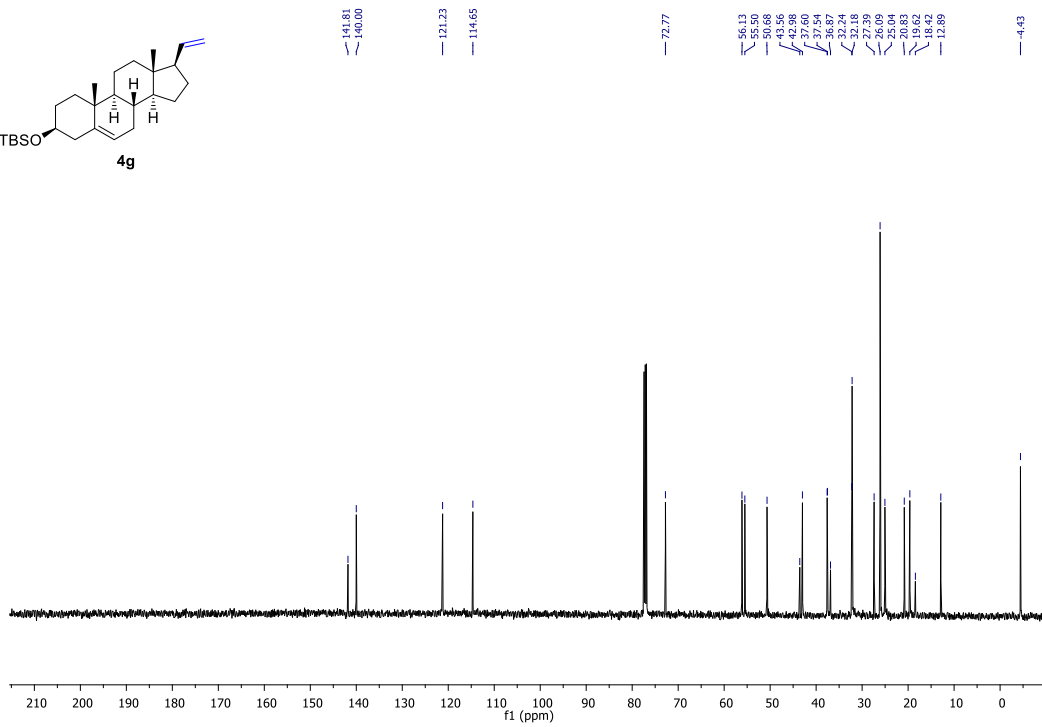
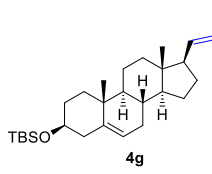
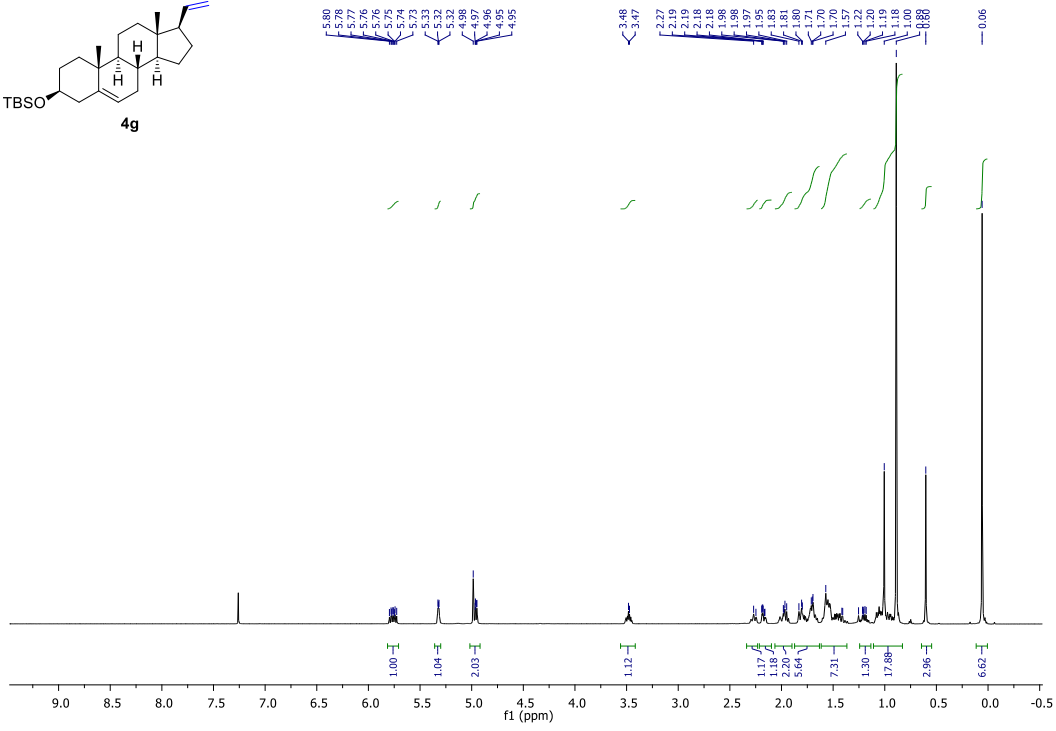
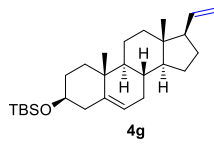
## References

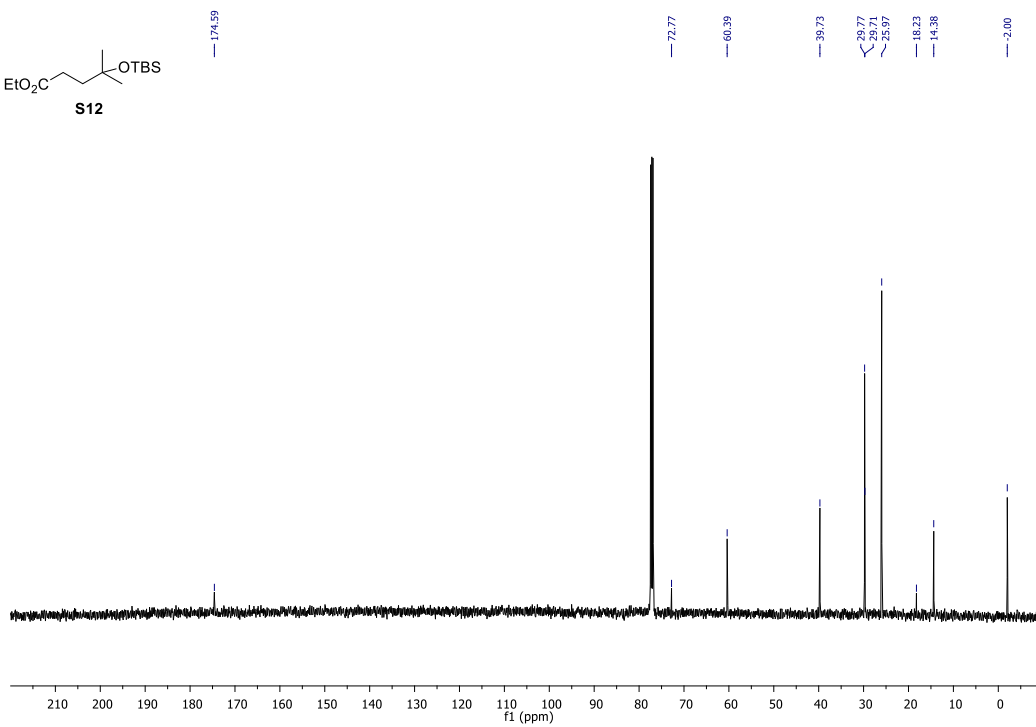
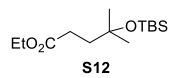
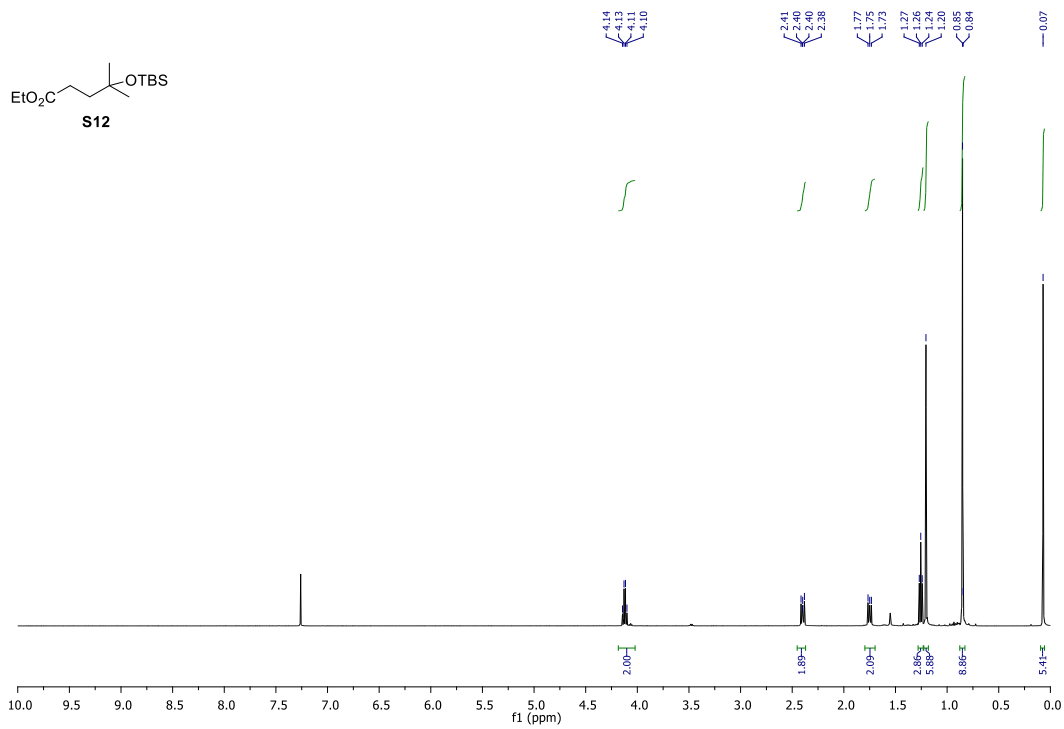
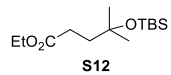
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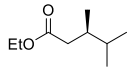




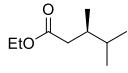
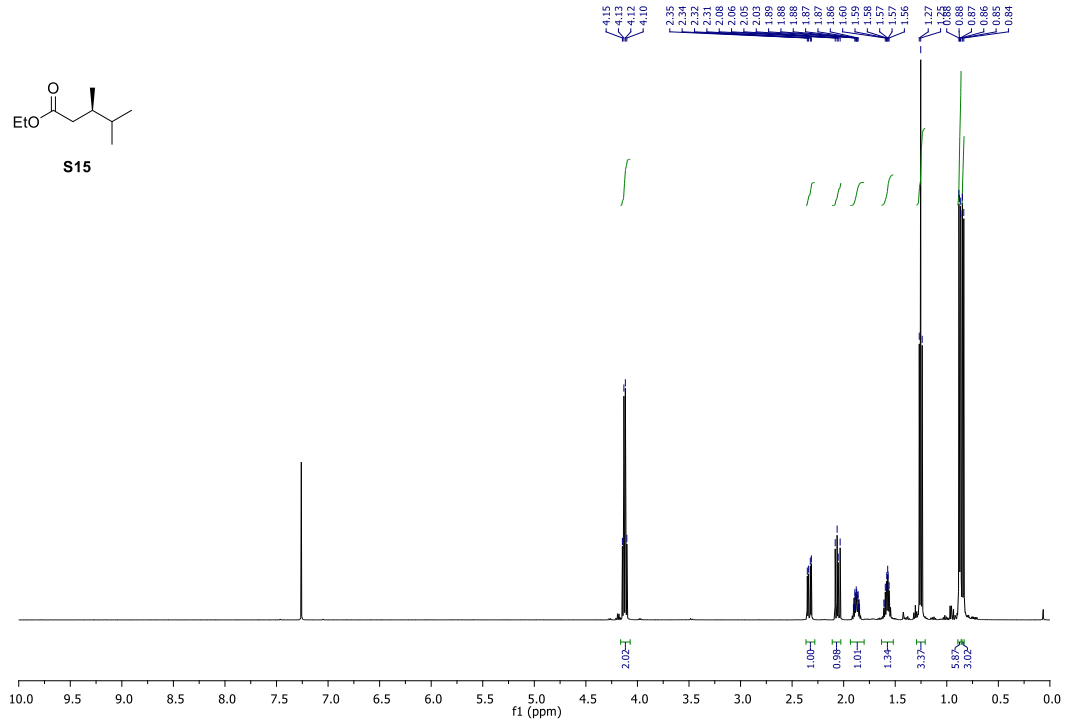




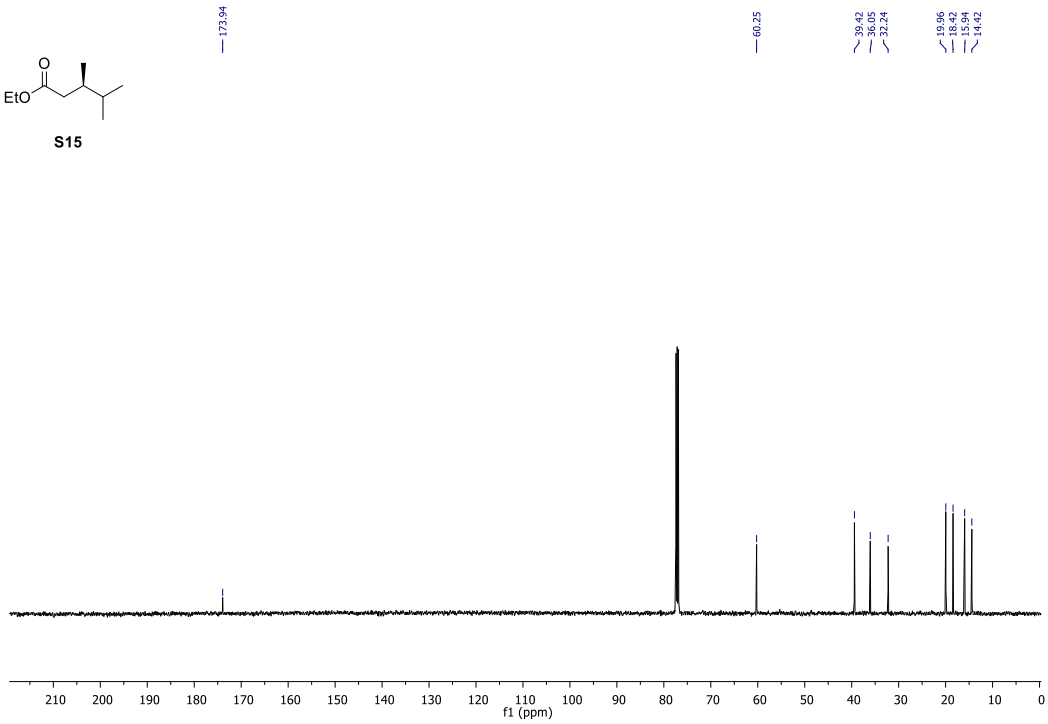


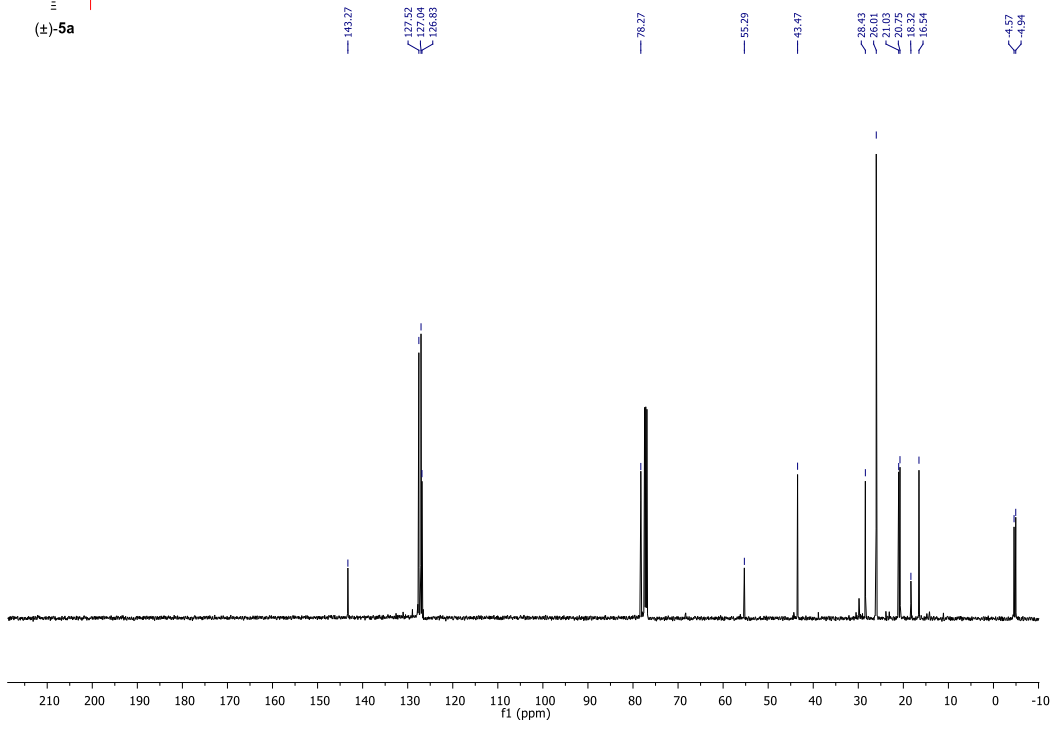
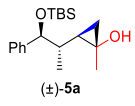
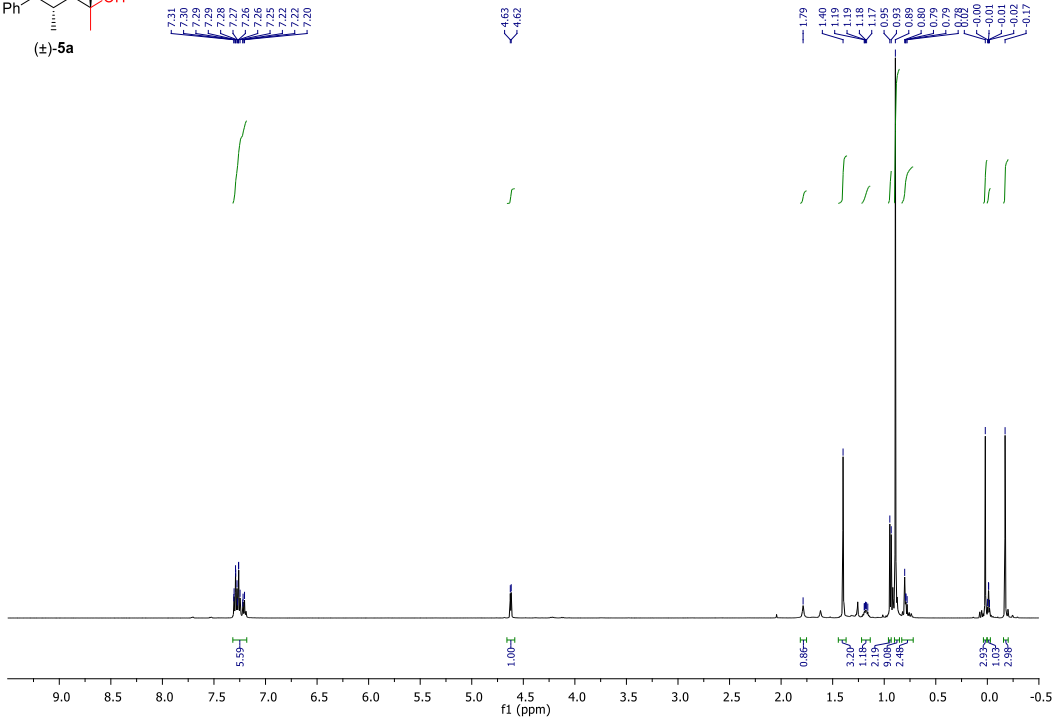
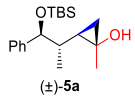


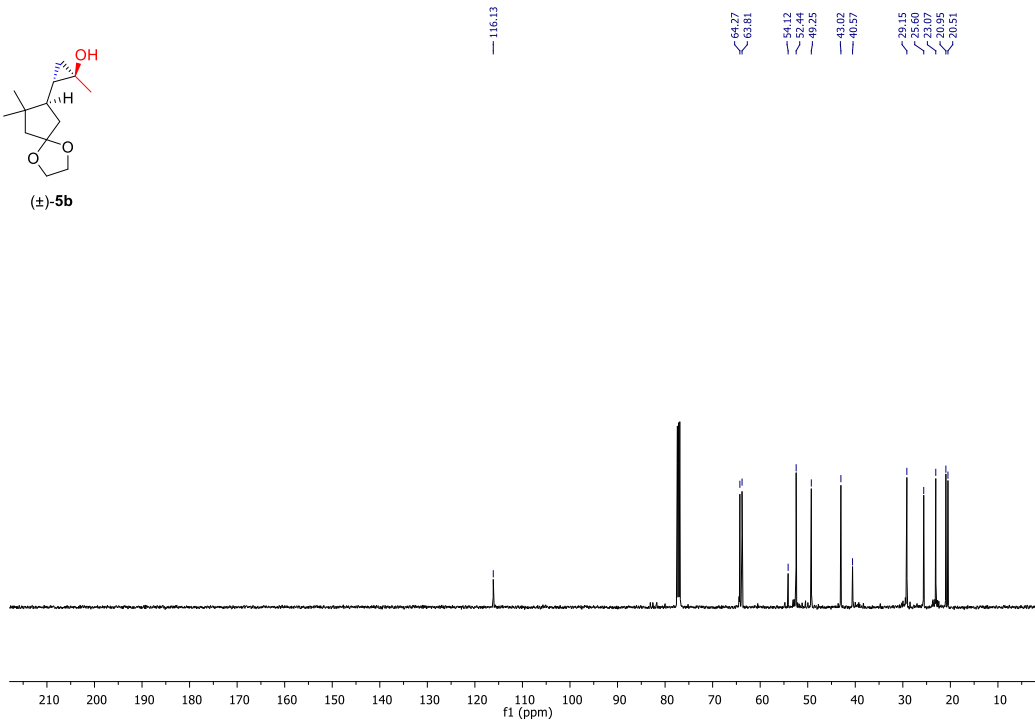
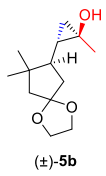
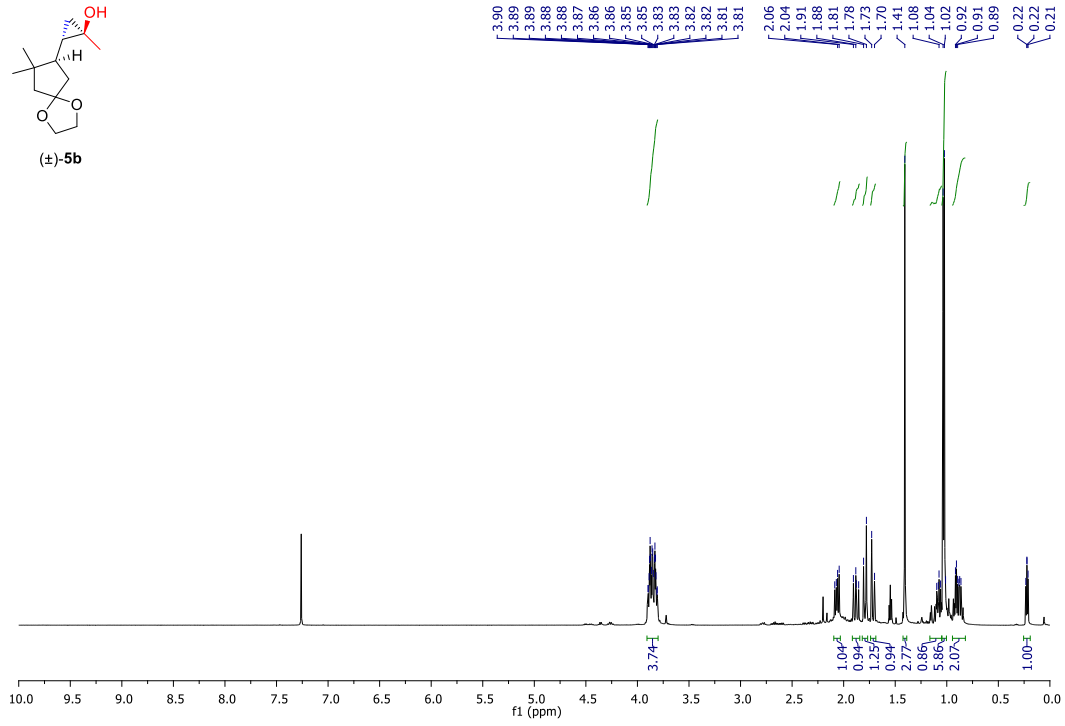
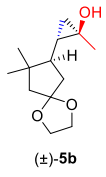
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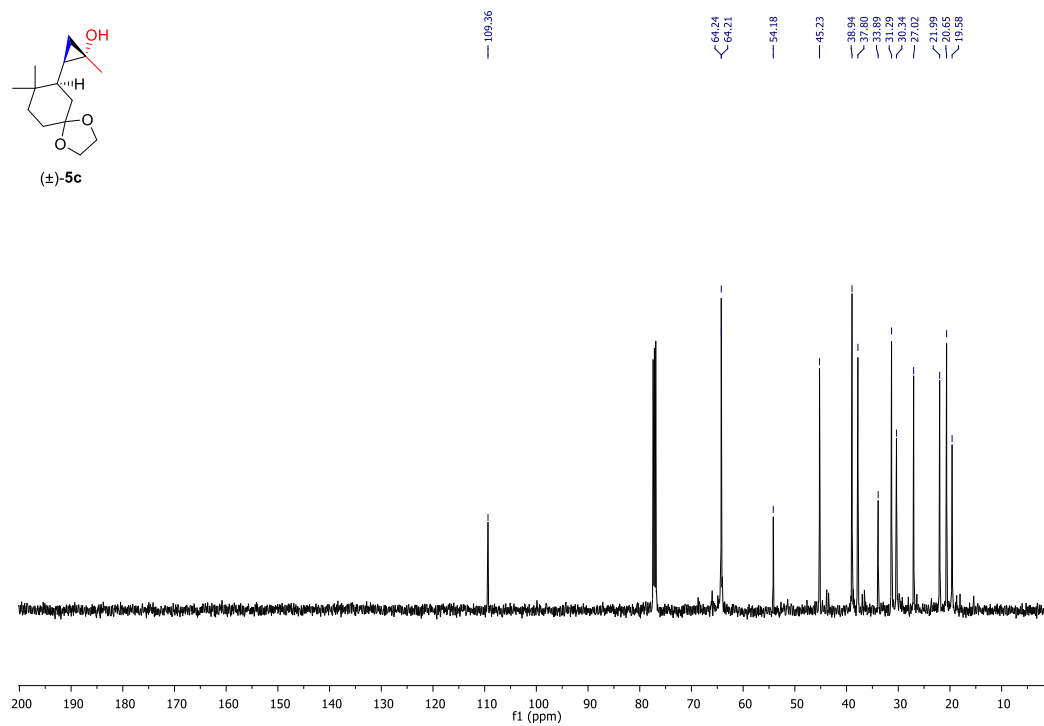
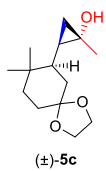
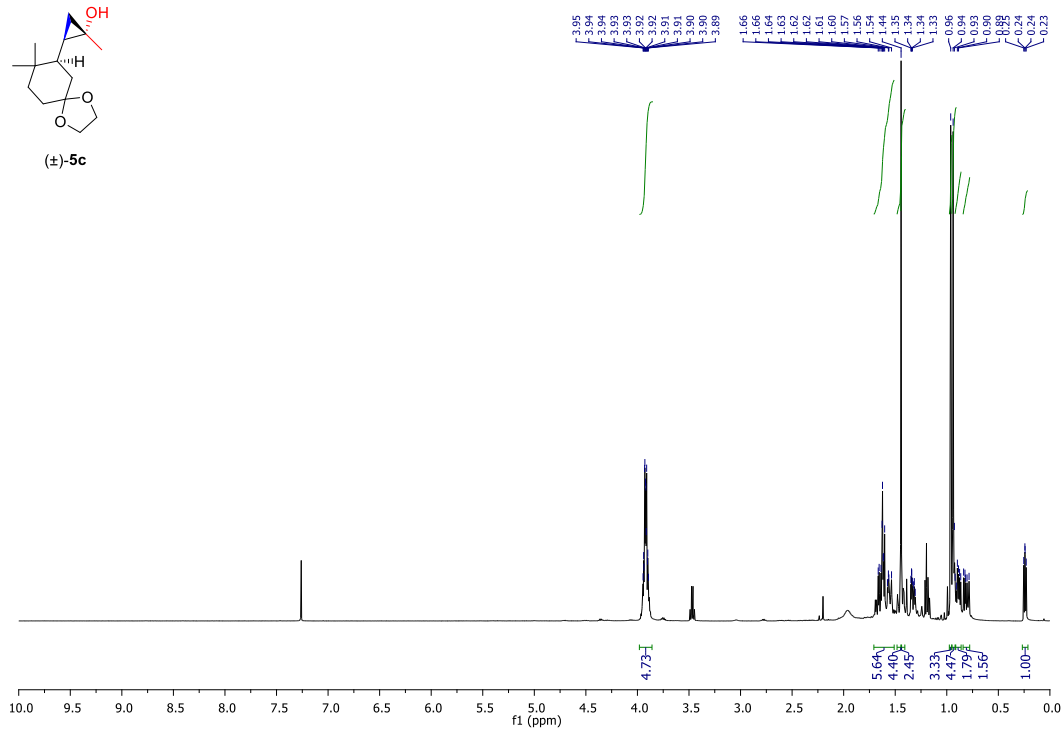
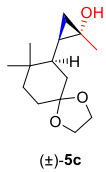


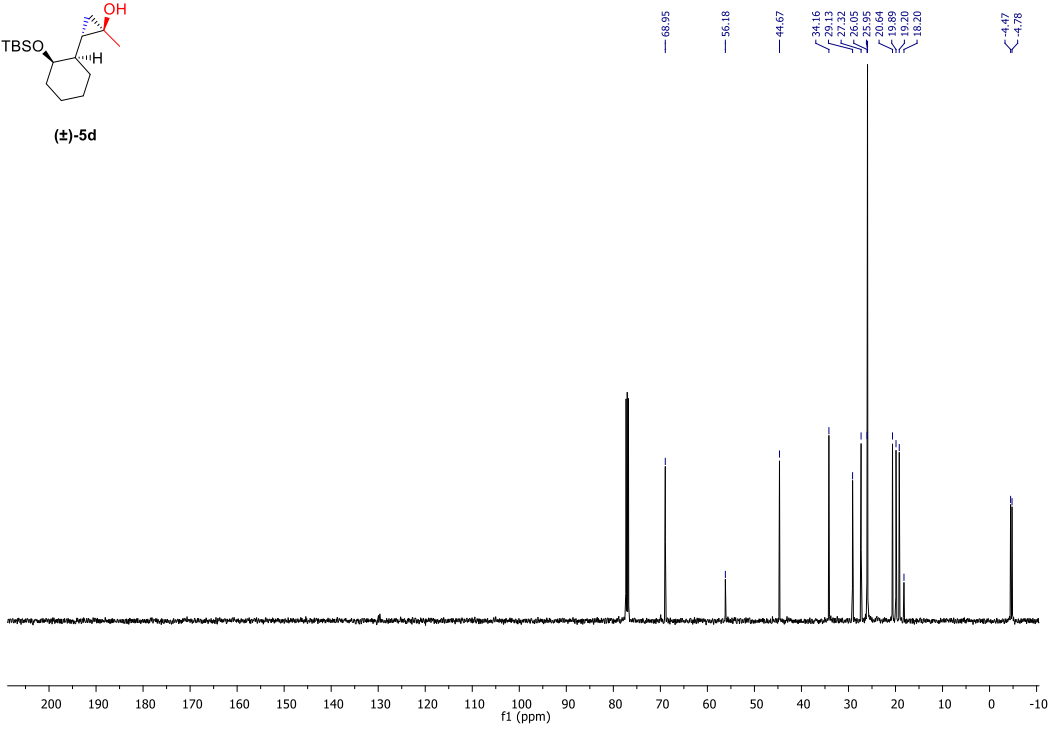
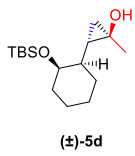
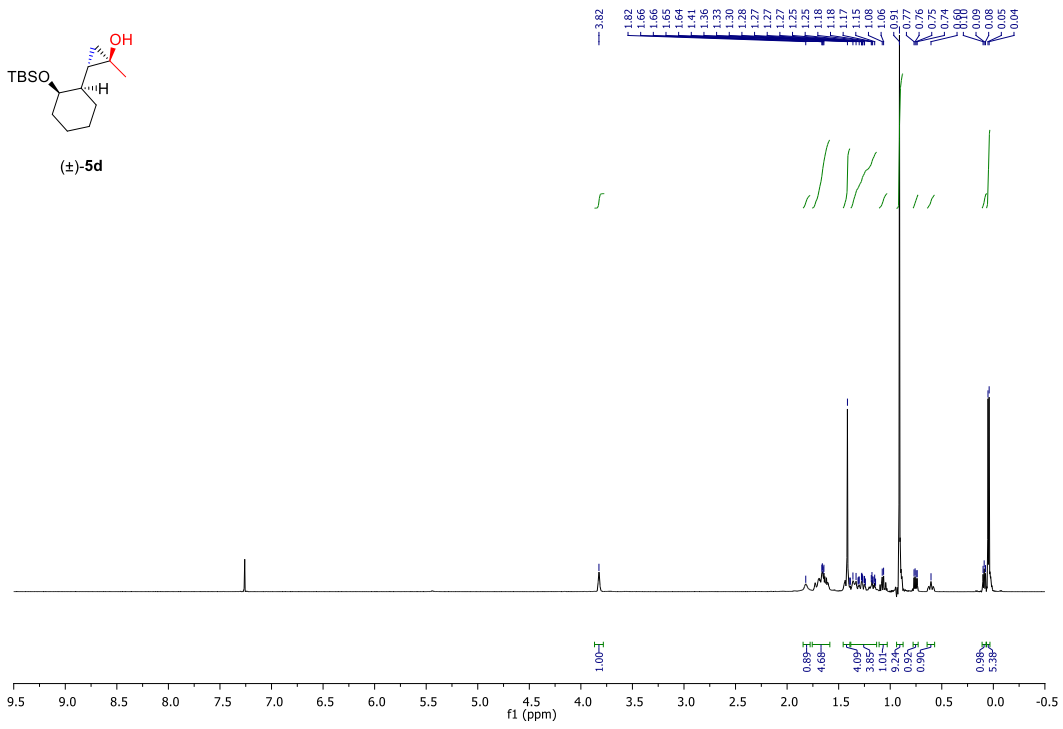
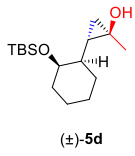
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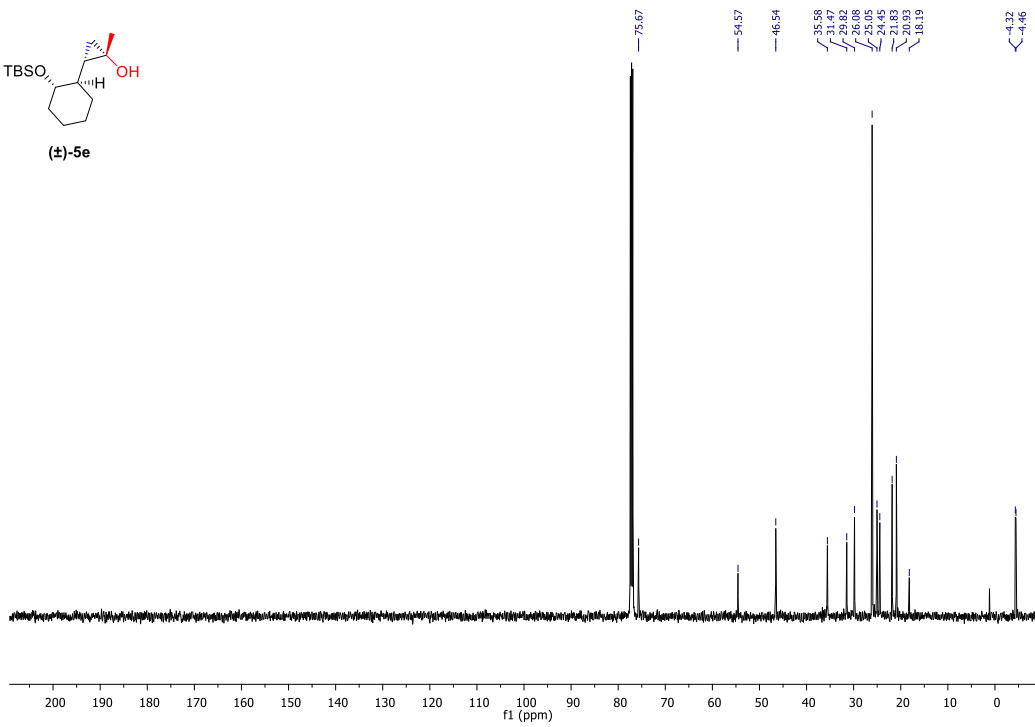
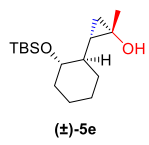
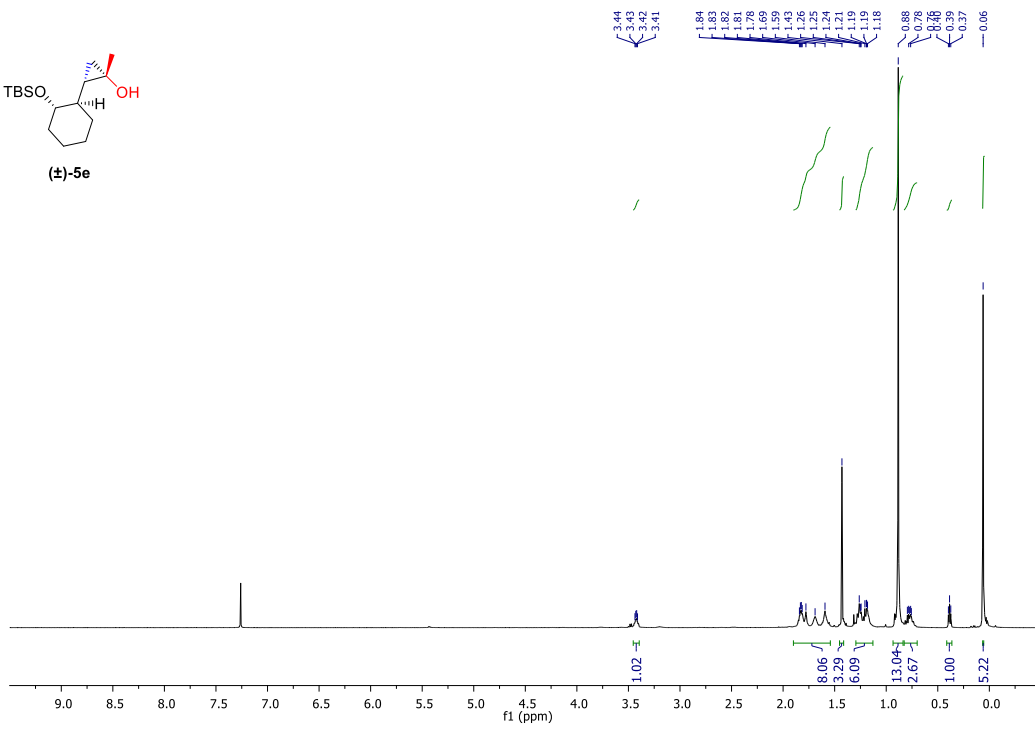
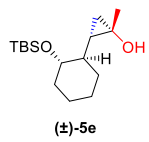


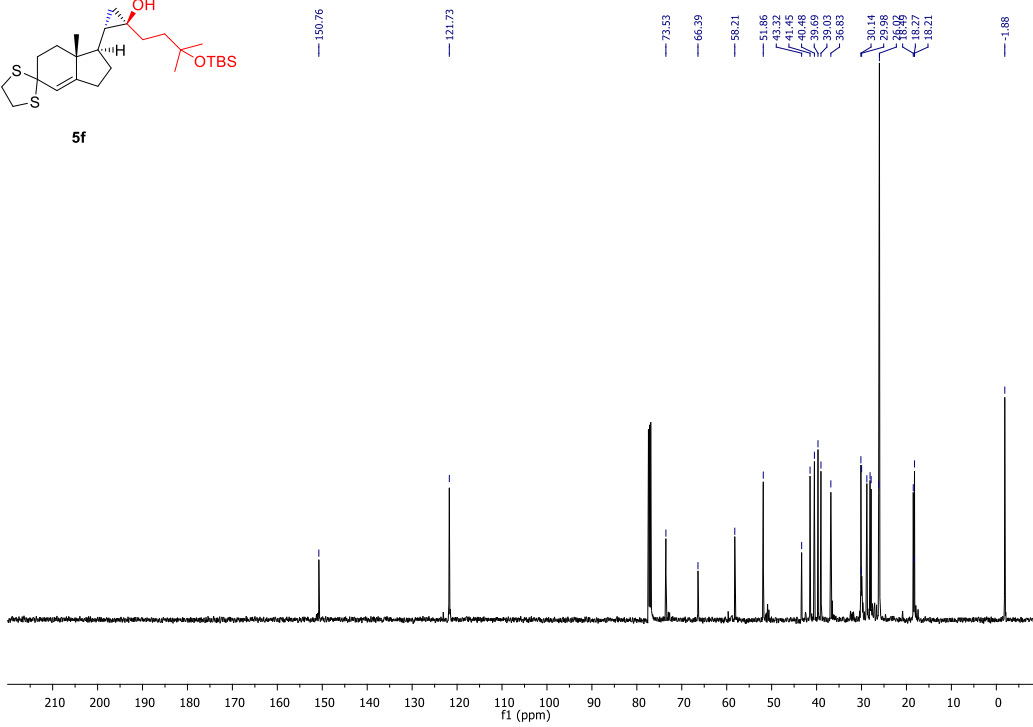
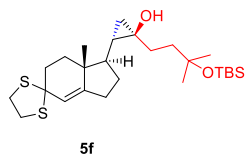
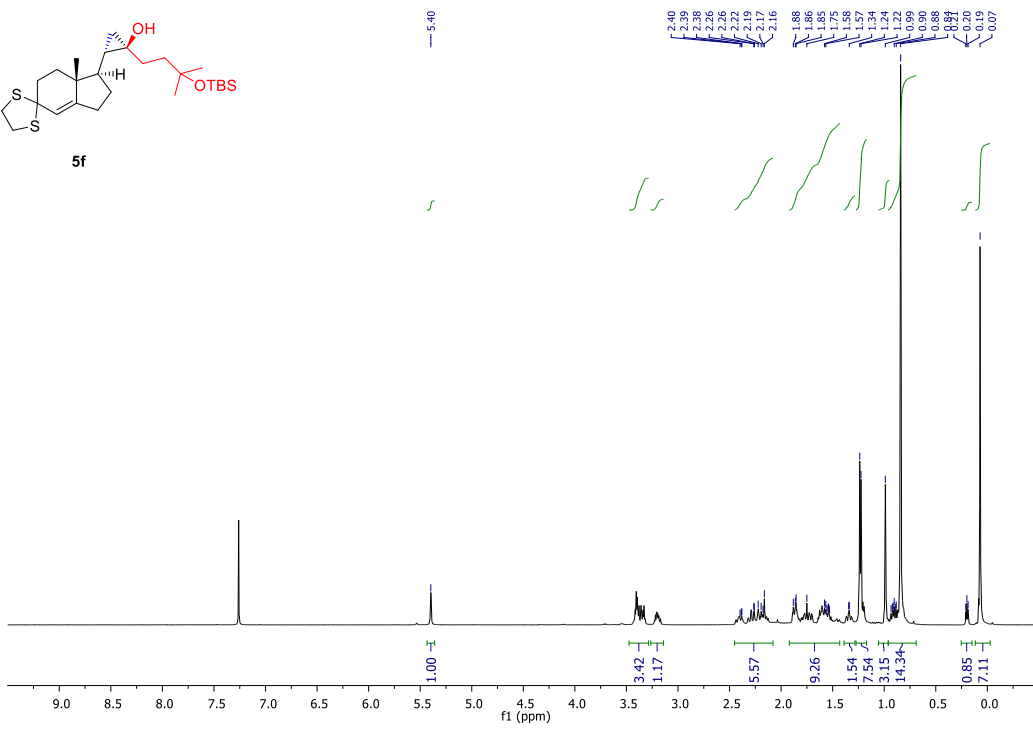
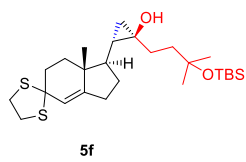


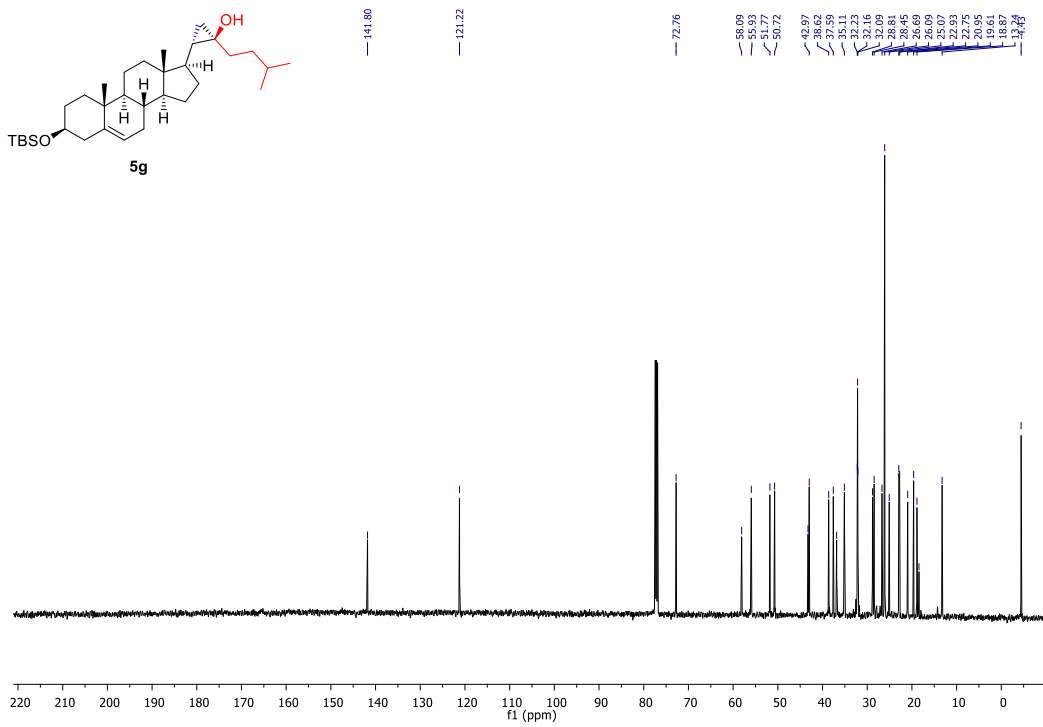
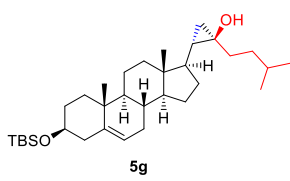
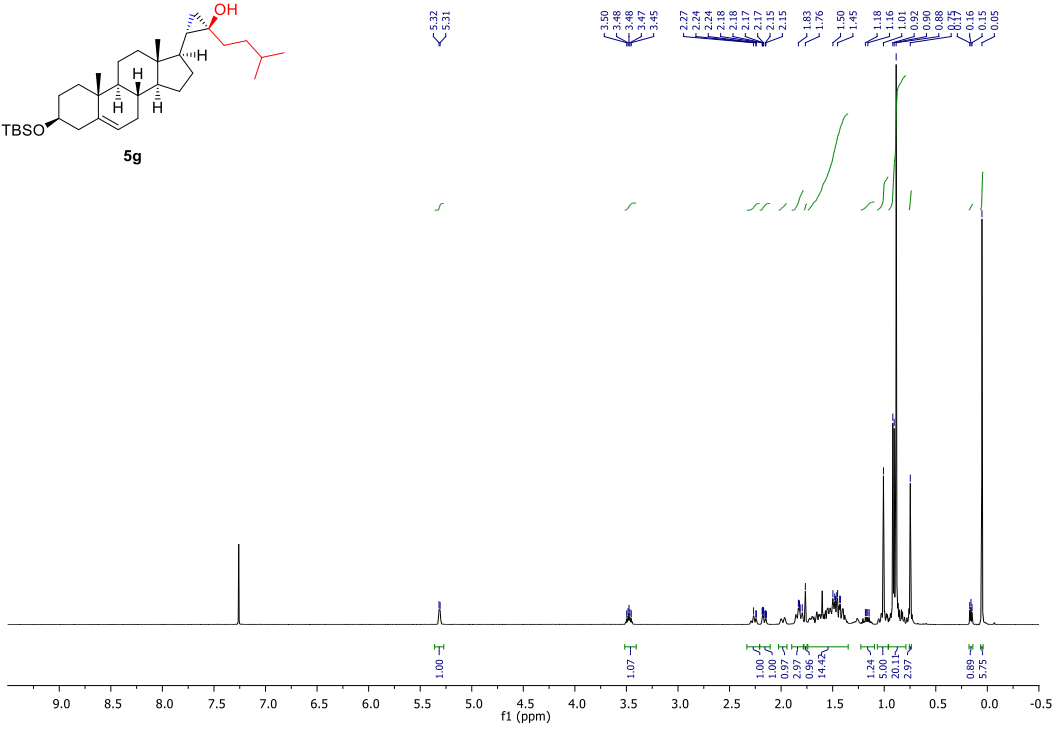
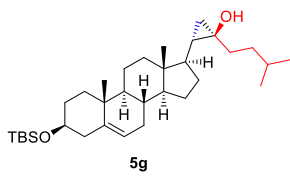




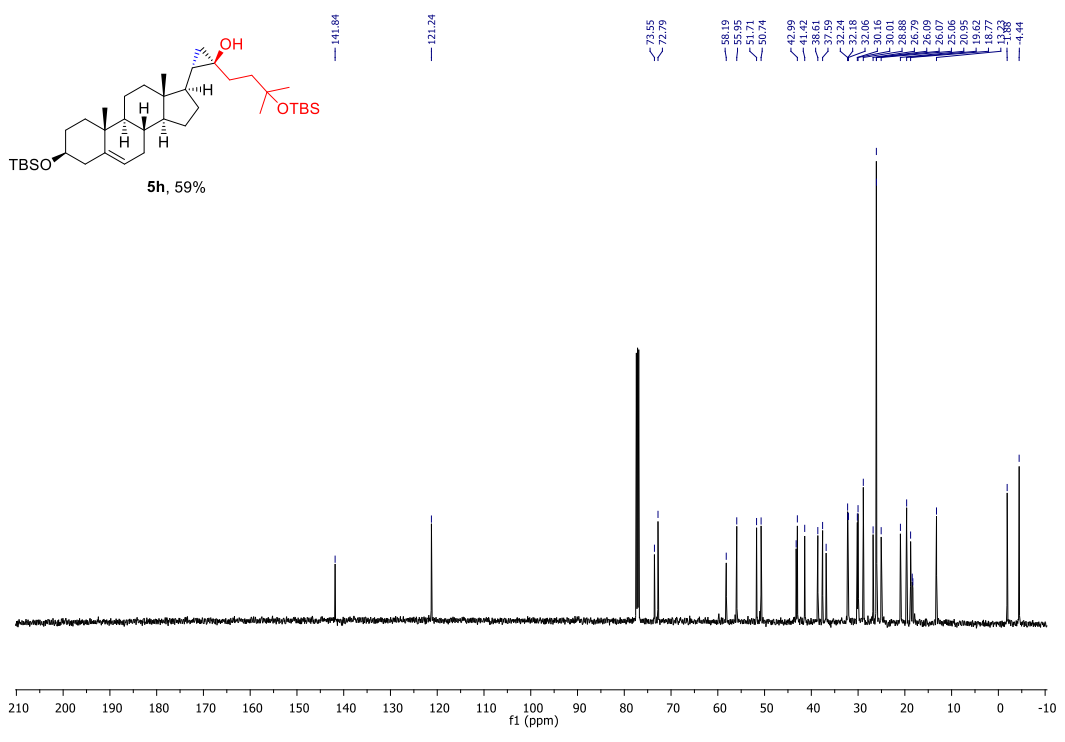
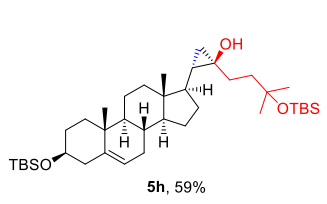
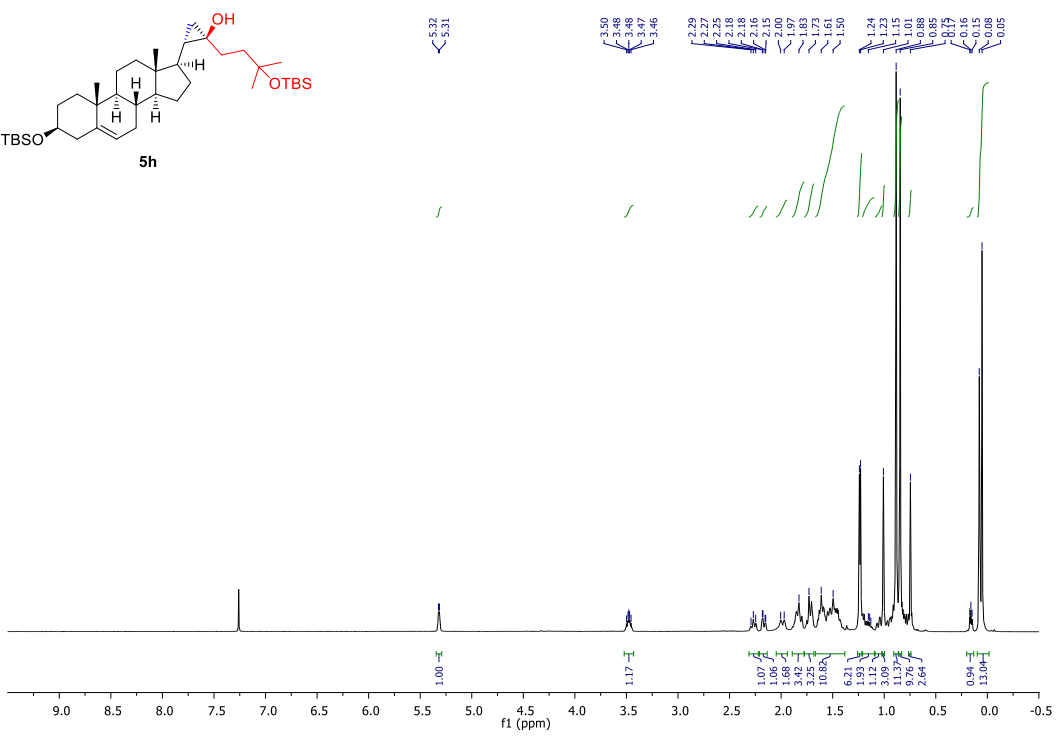
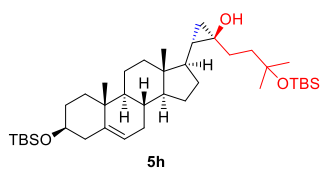


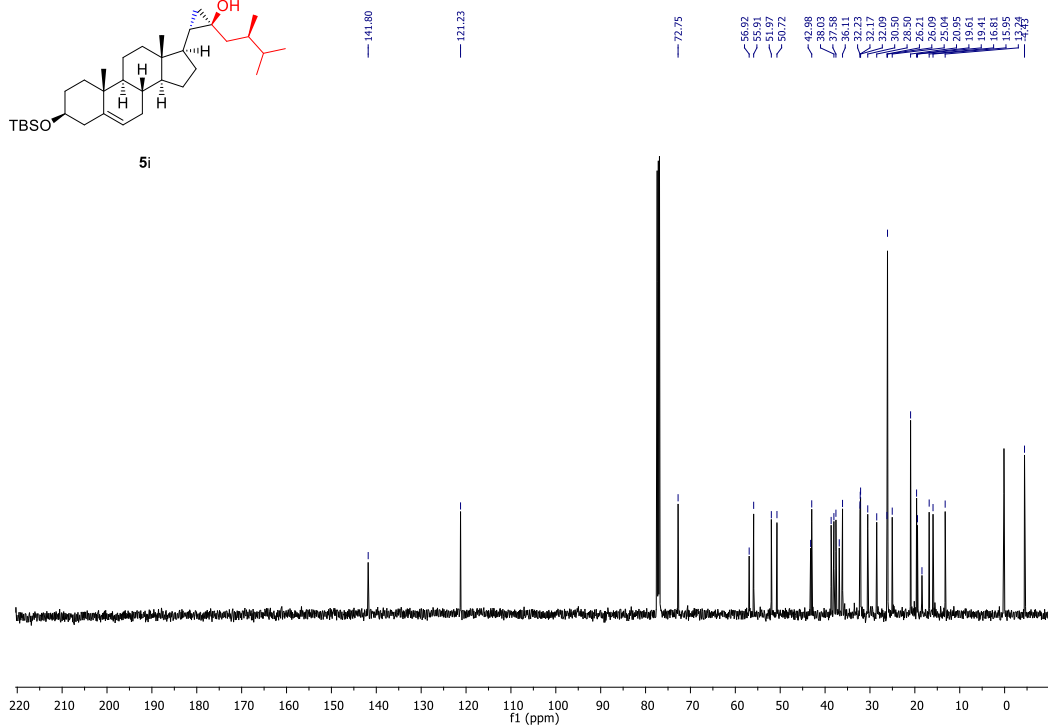
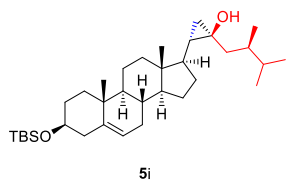
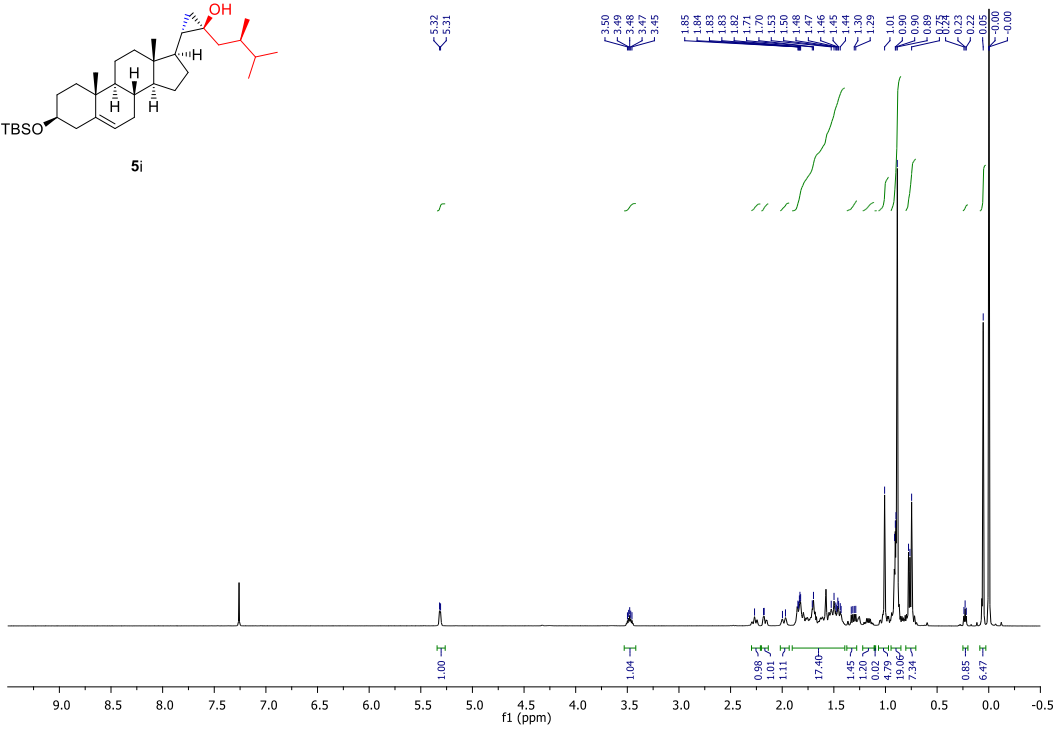
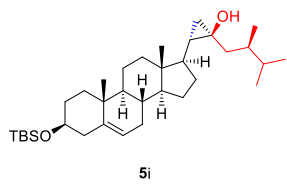


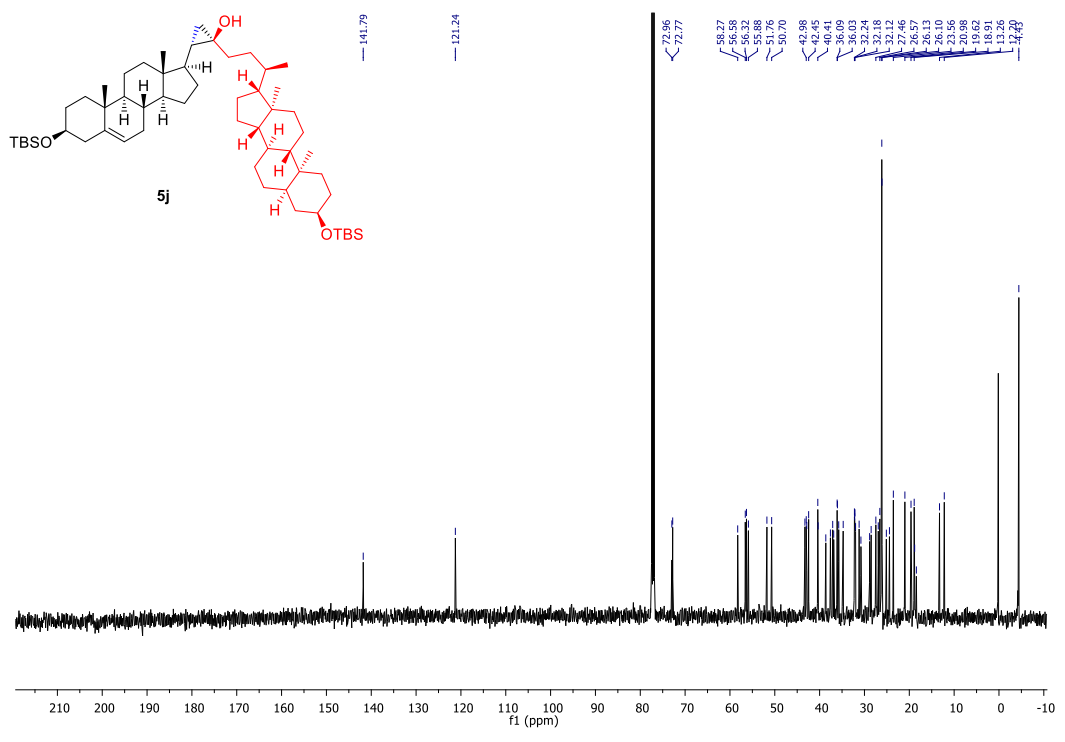
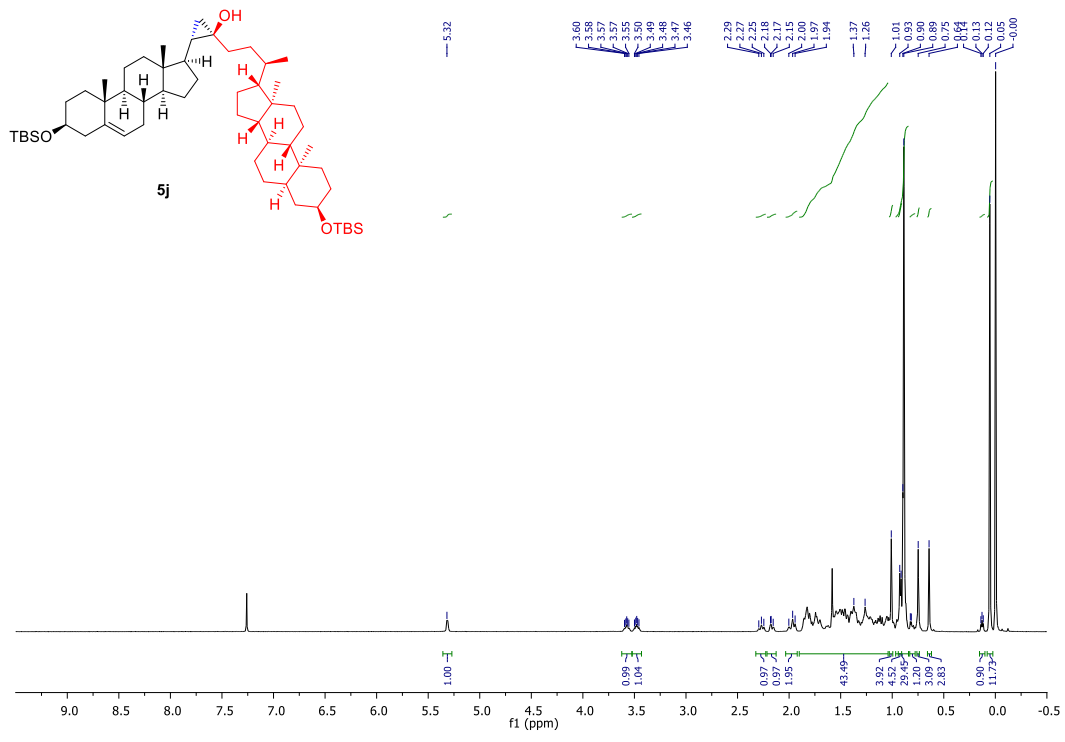




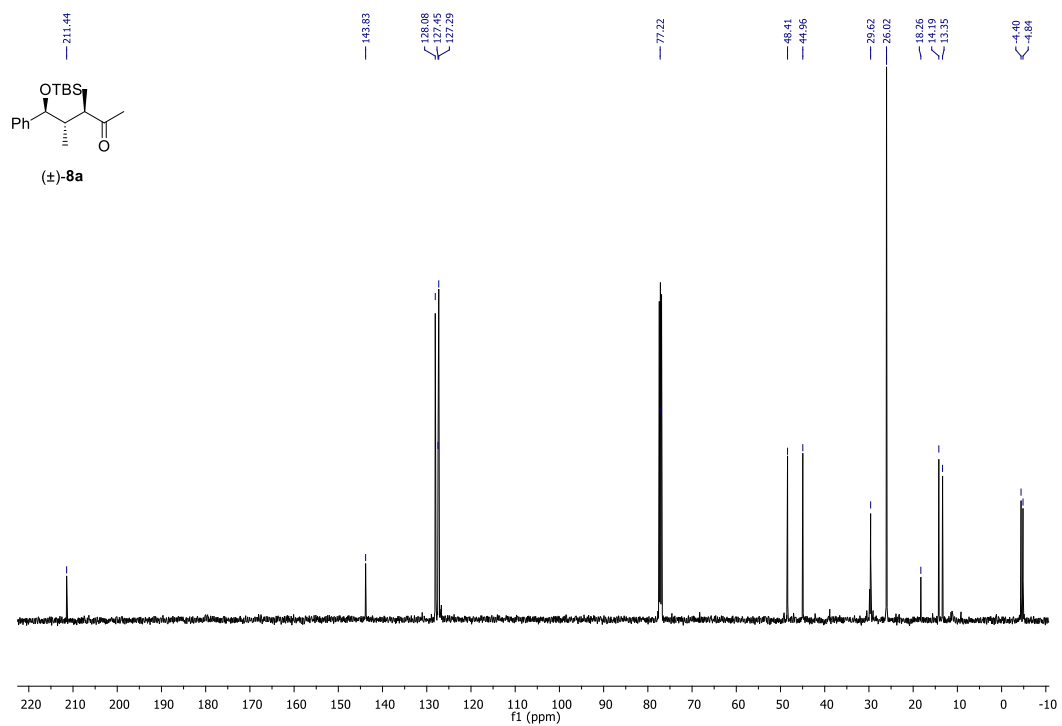
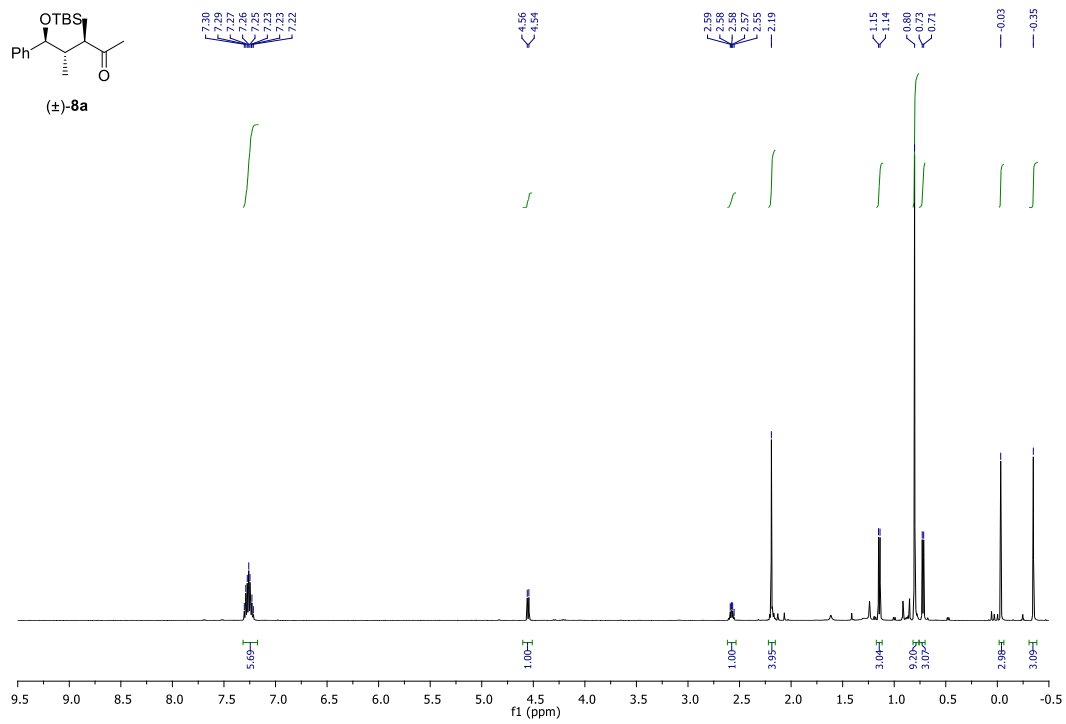


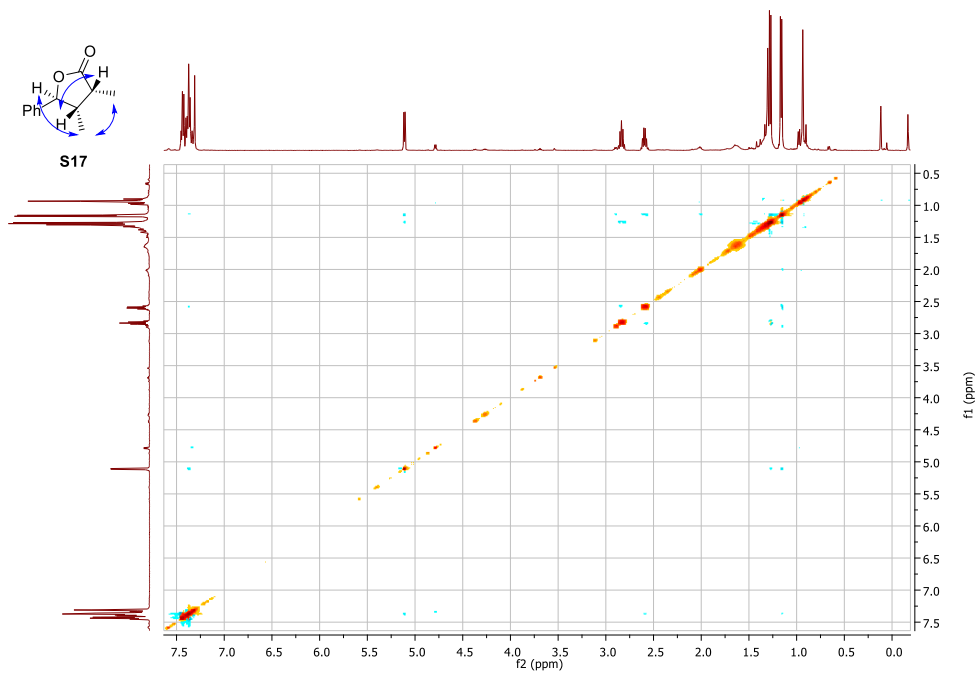
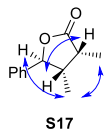
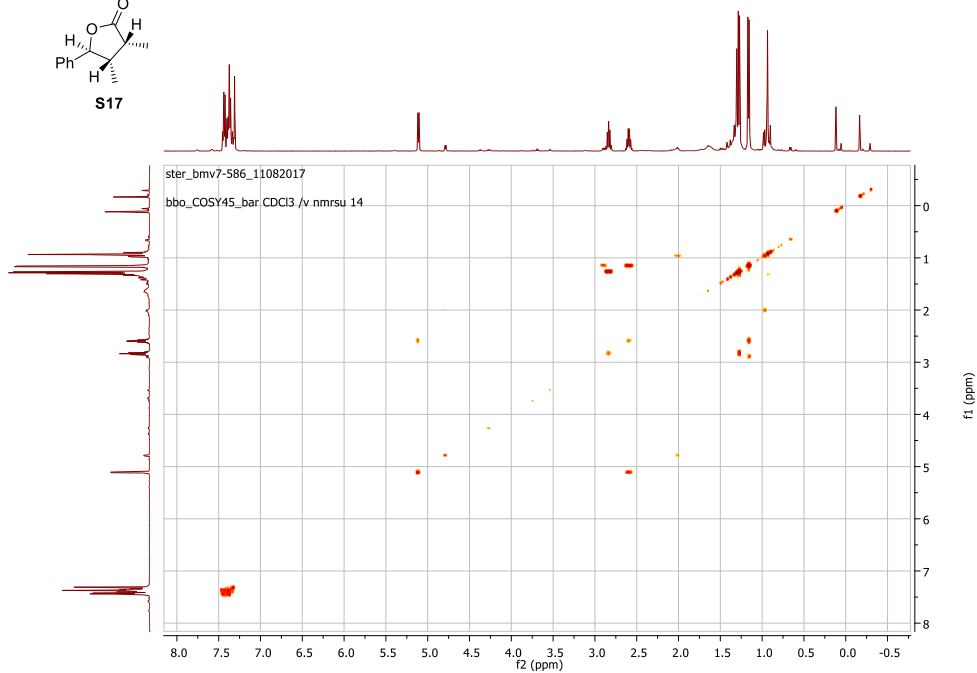
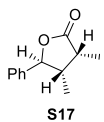


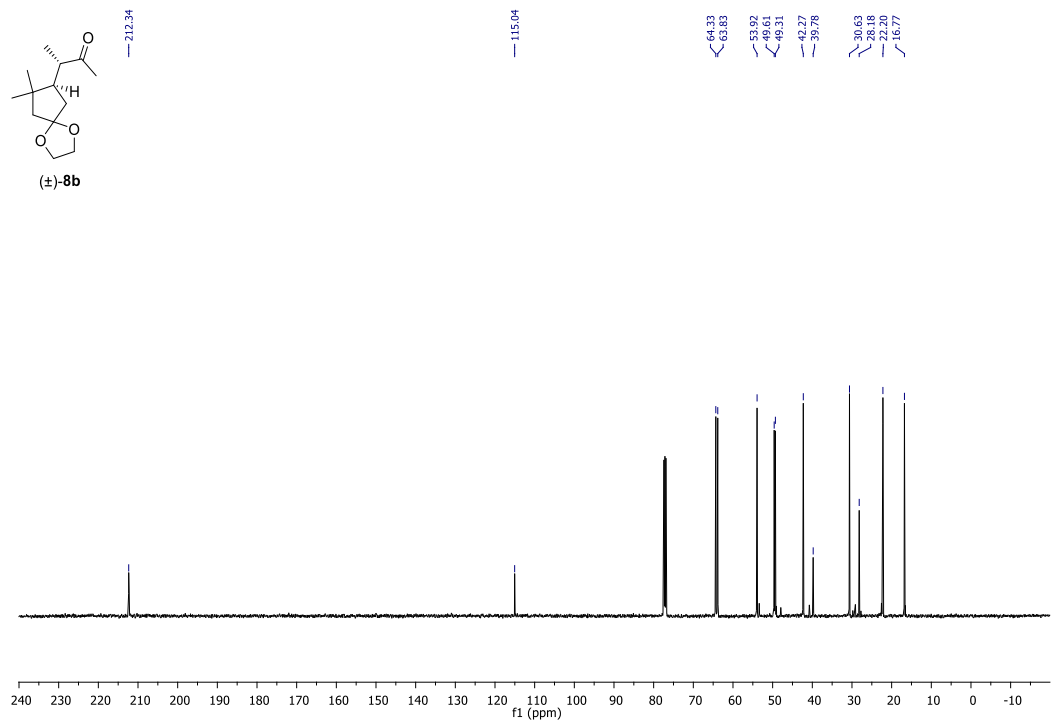
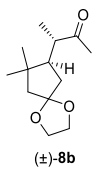
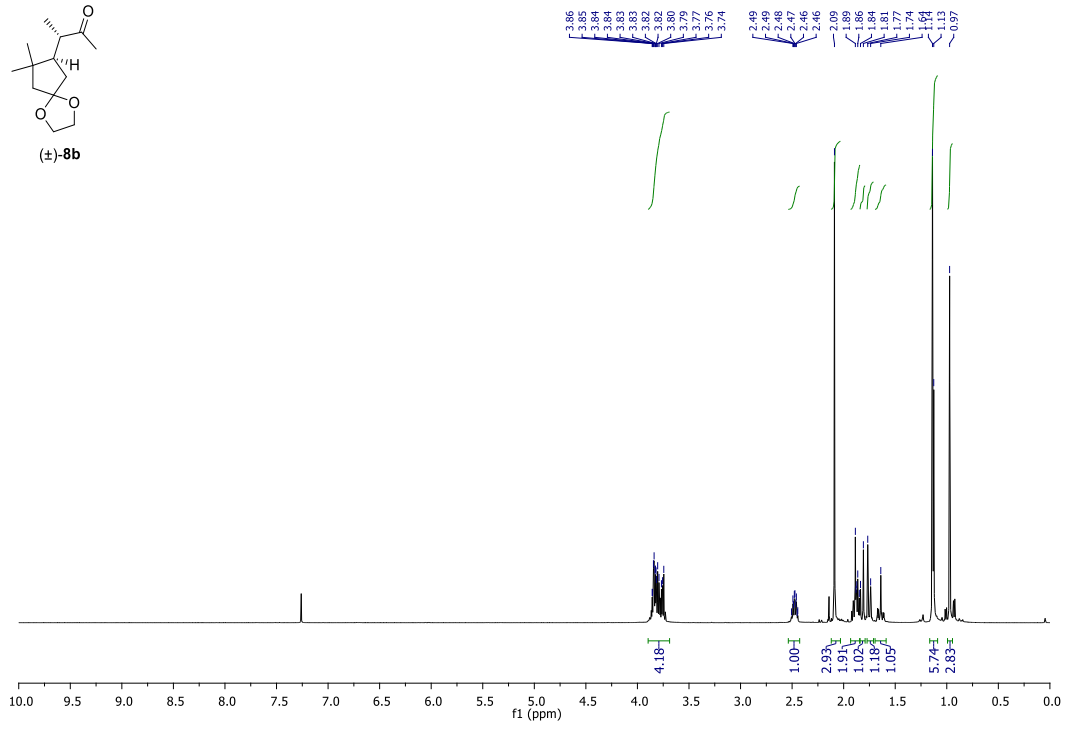
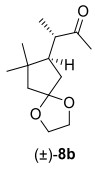


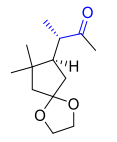




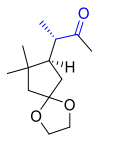
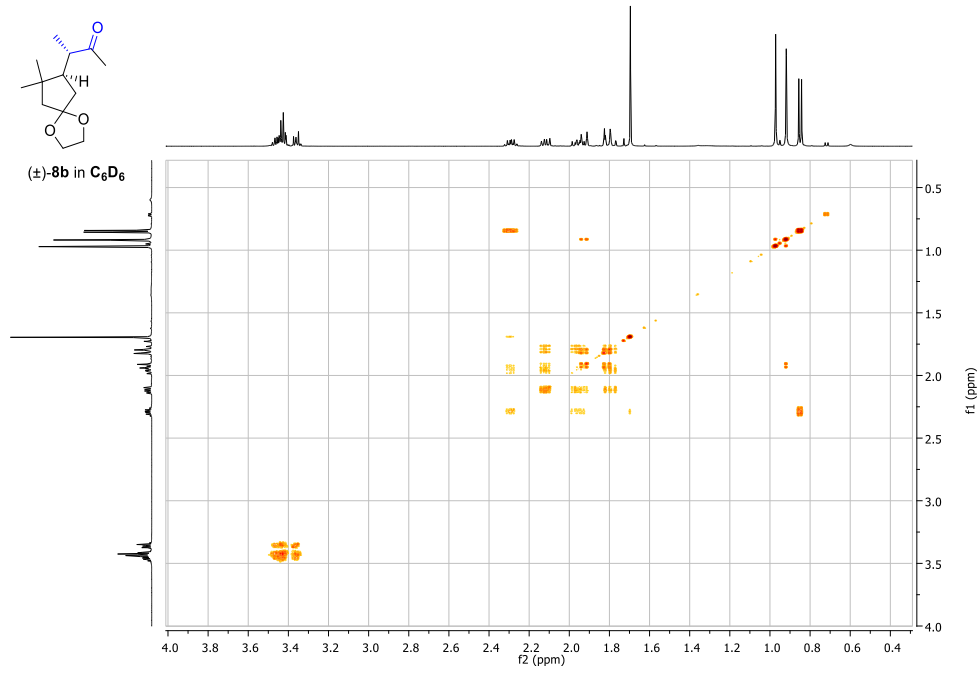




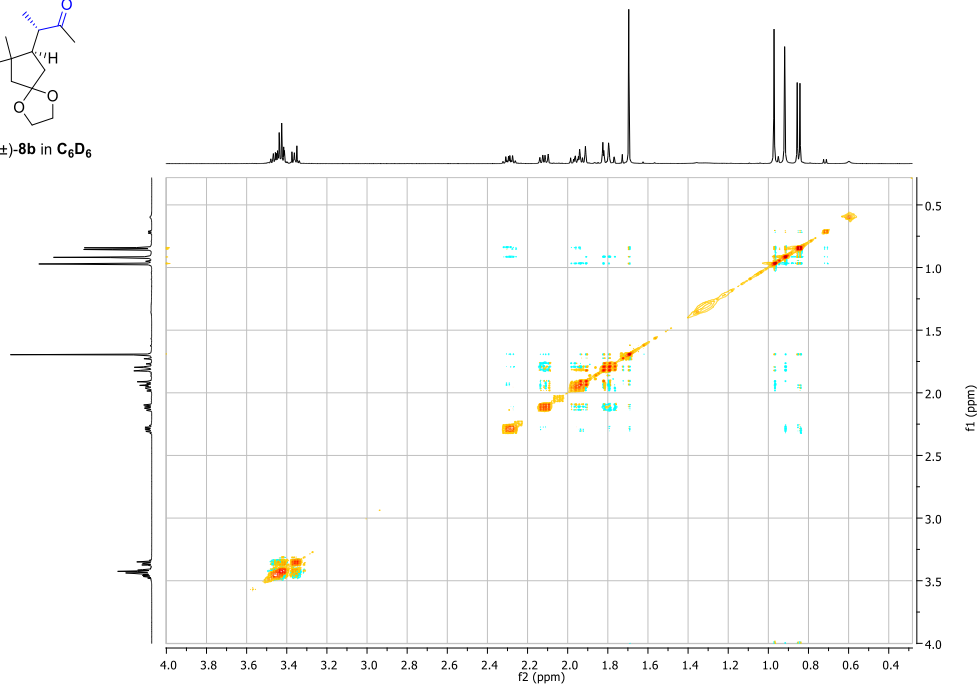




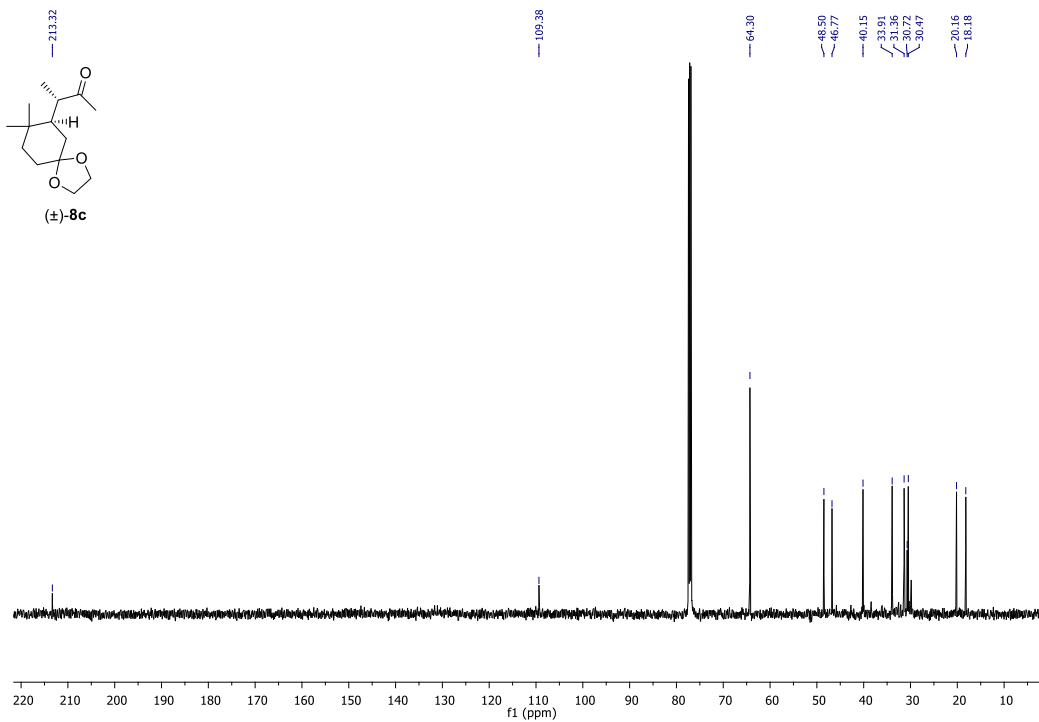
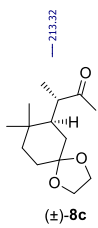
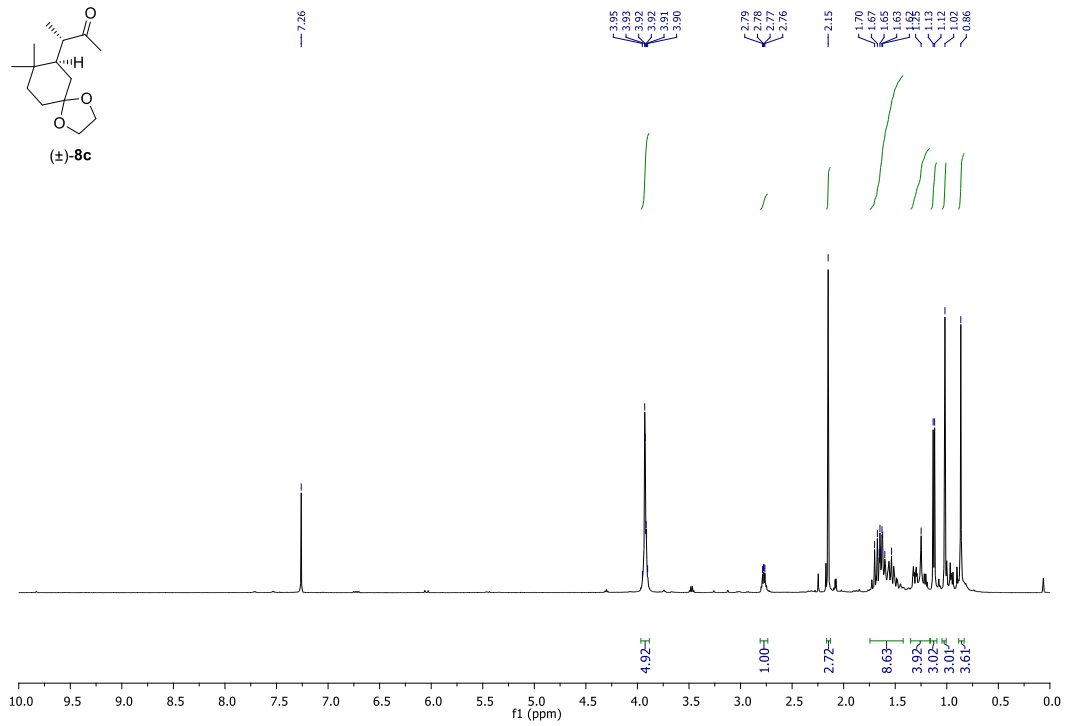
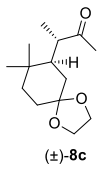
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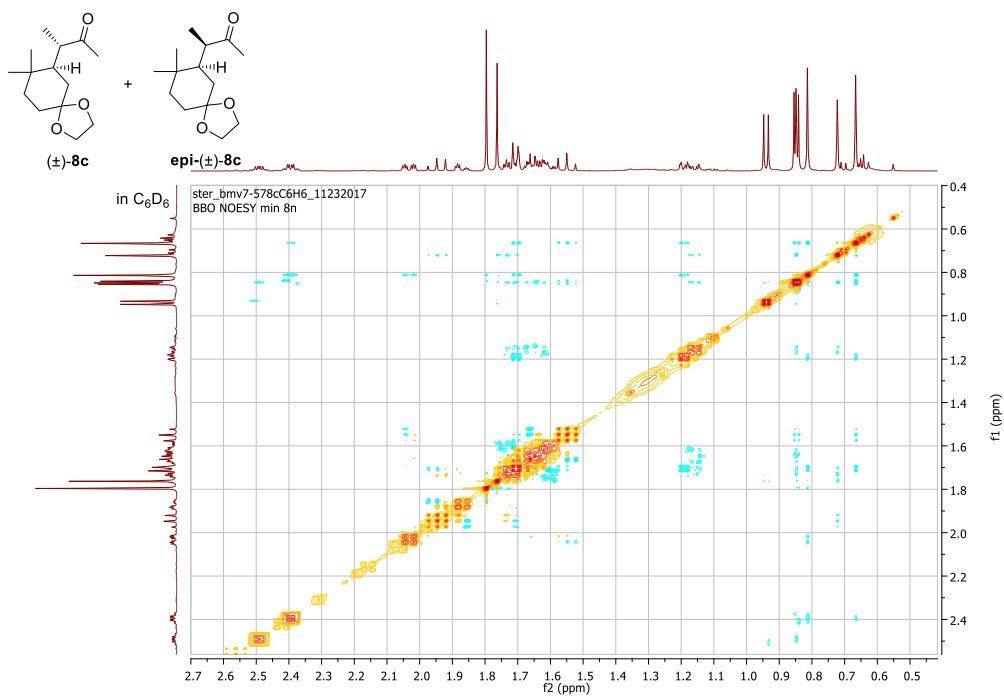
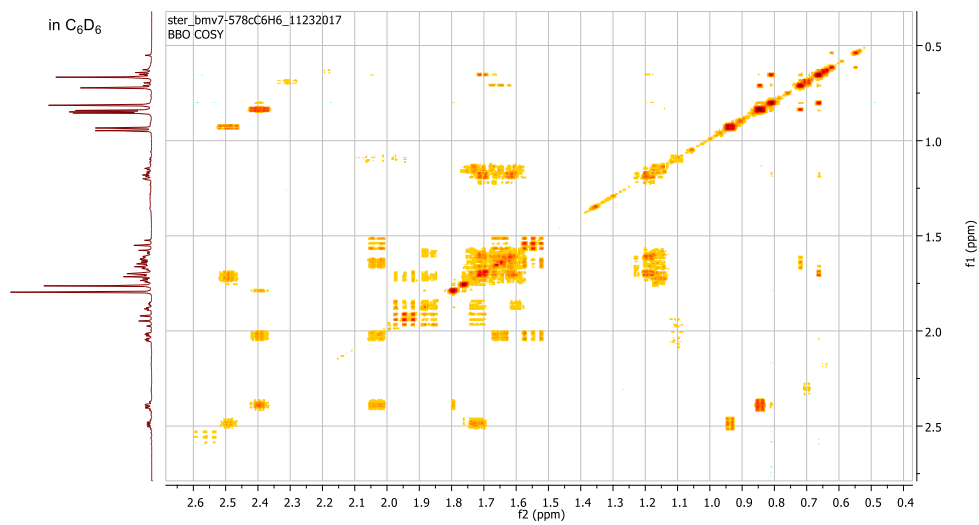
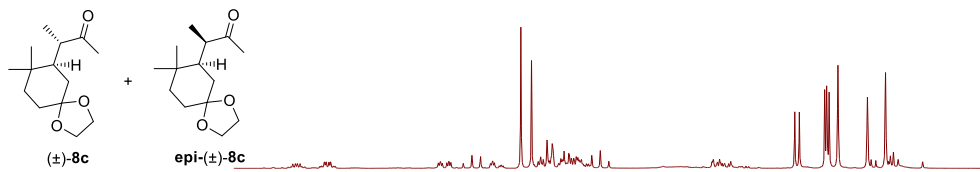


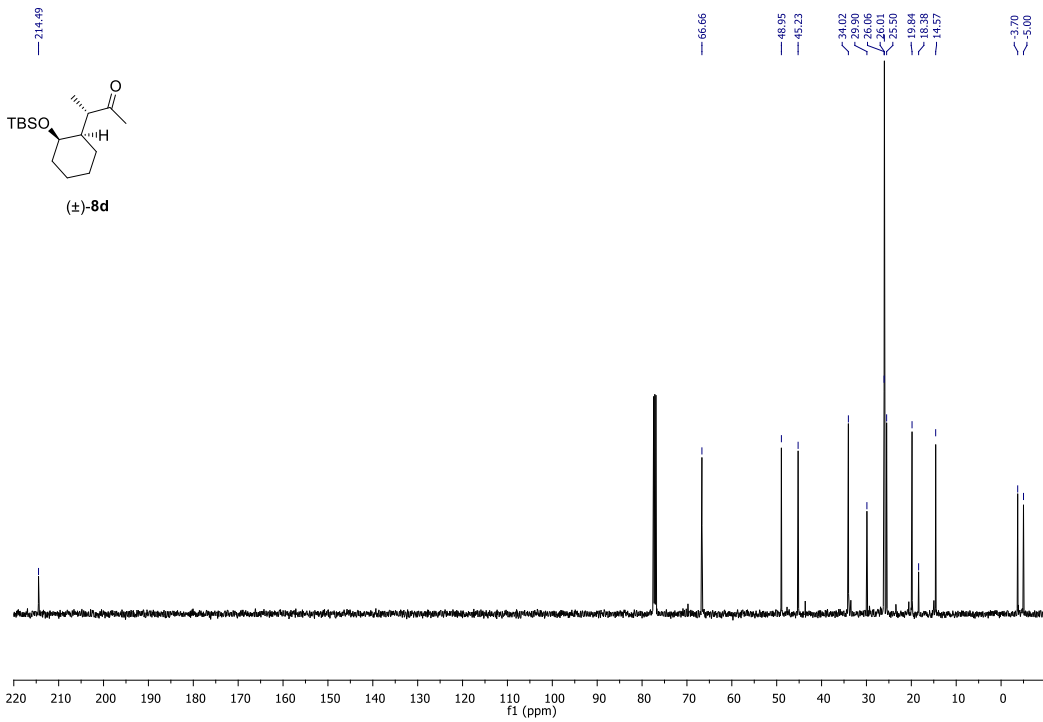
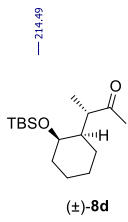
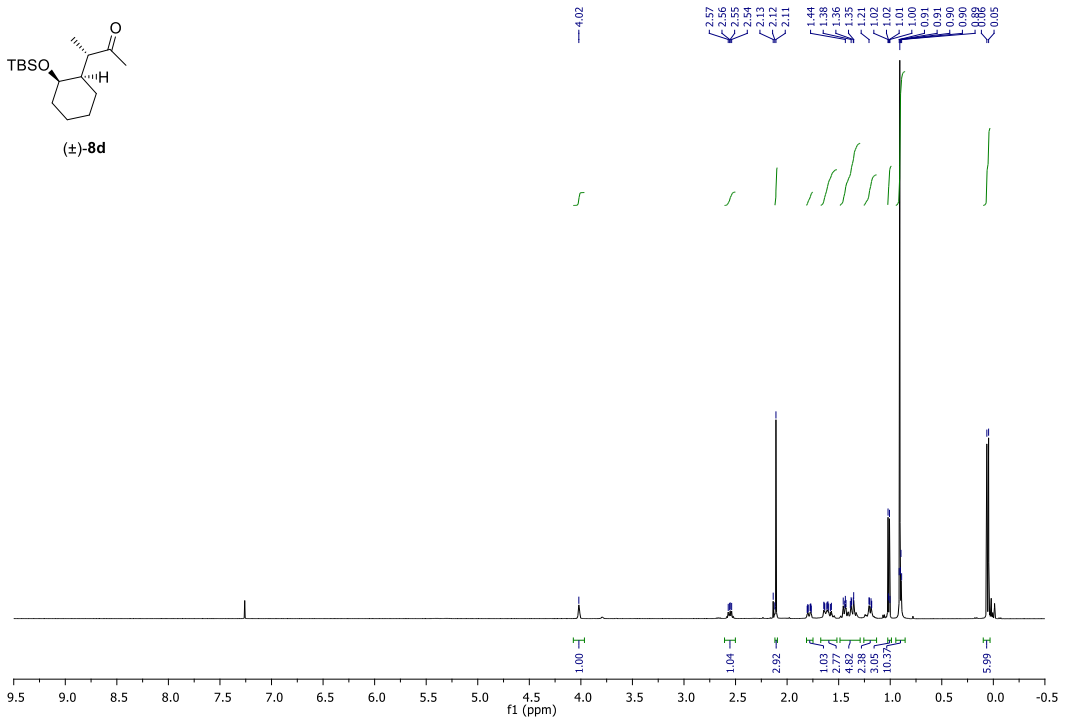
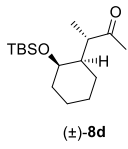
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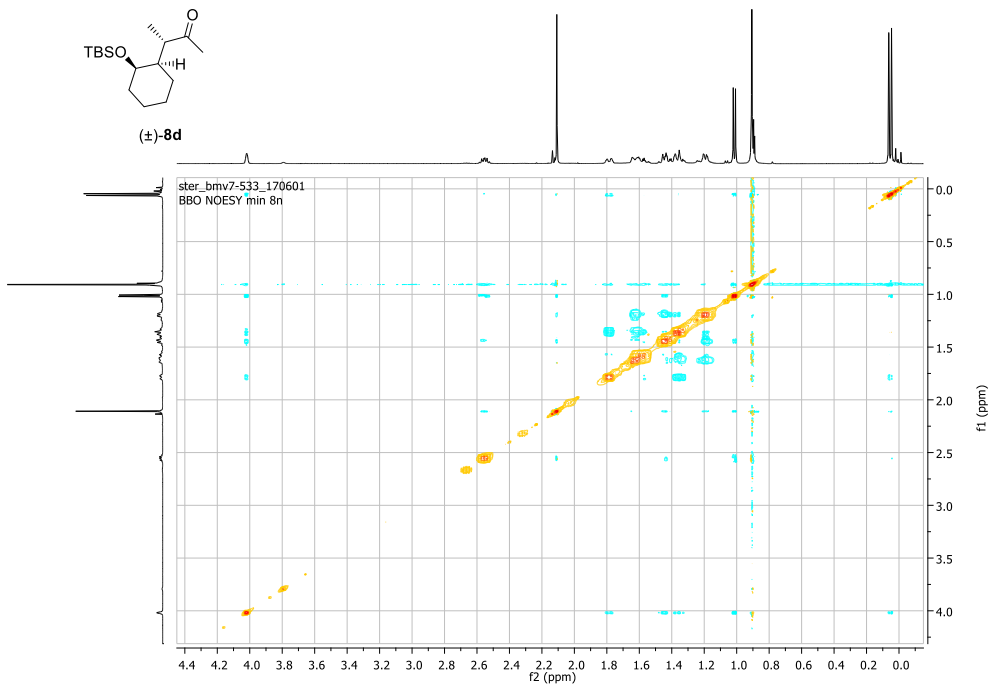
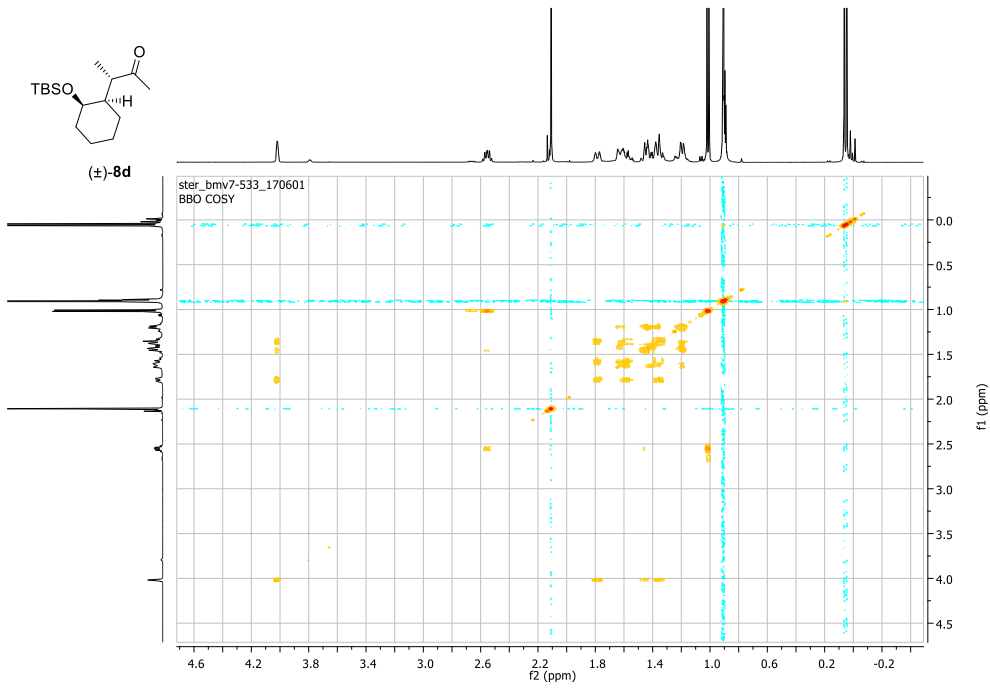


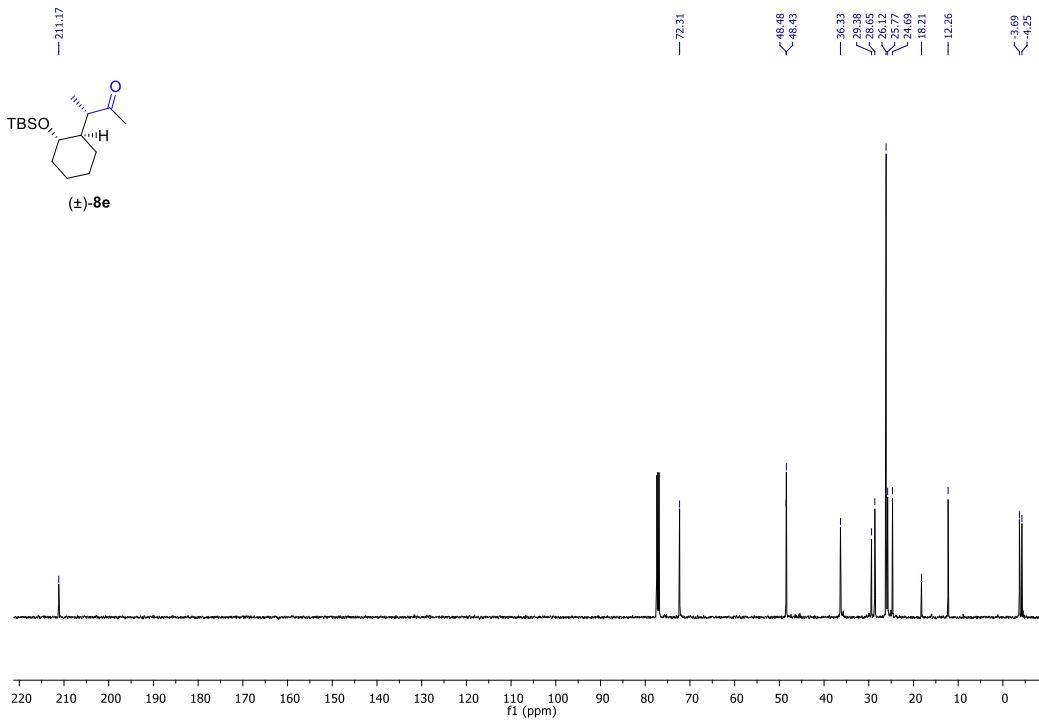
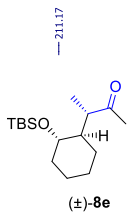
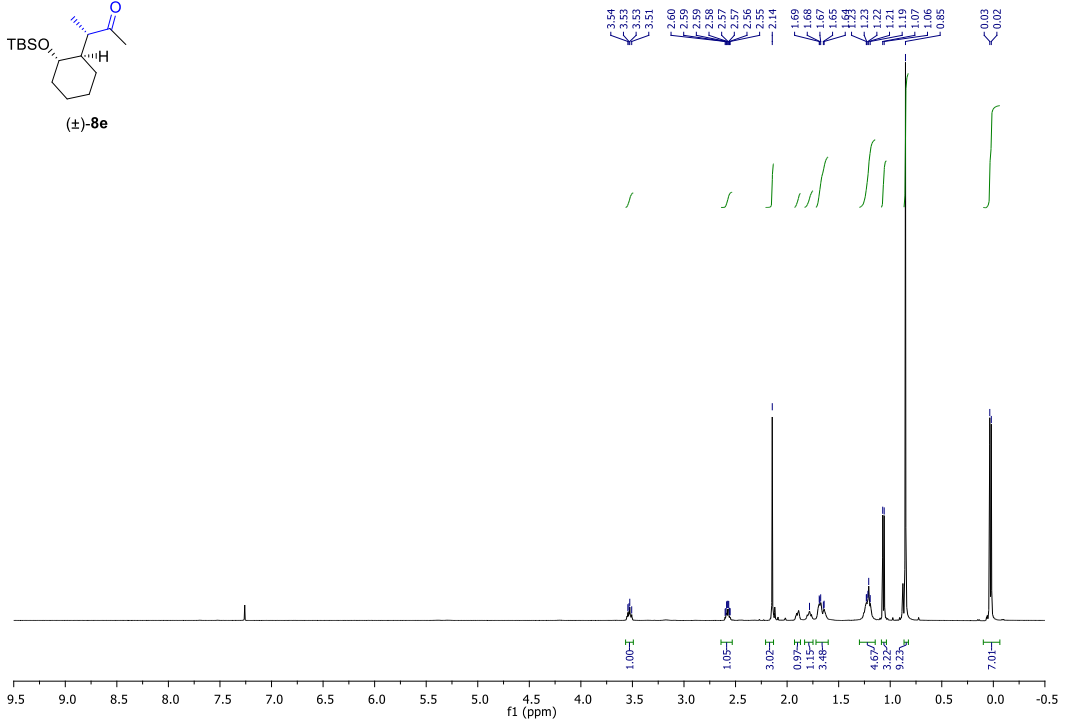
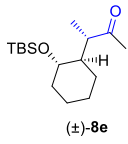


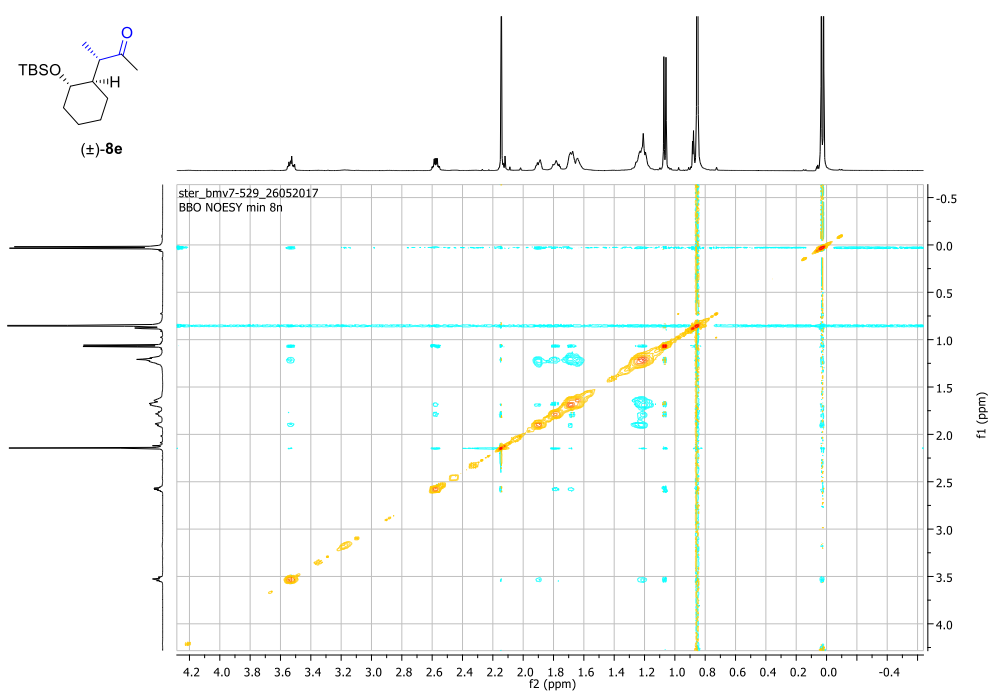
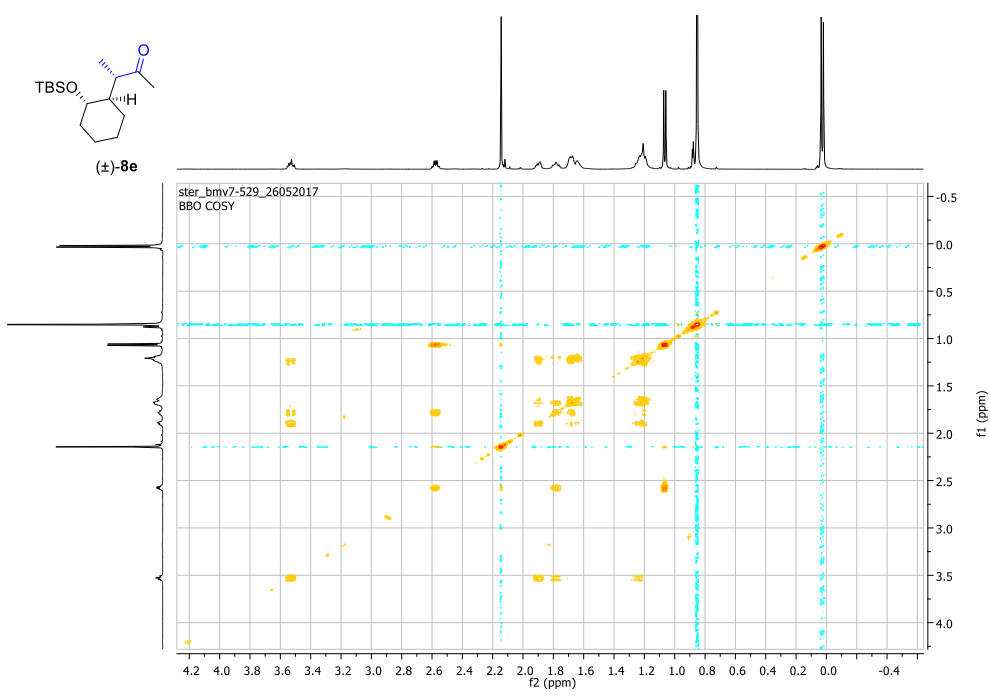


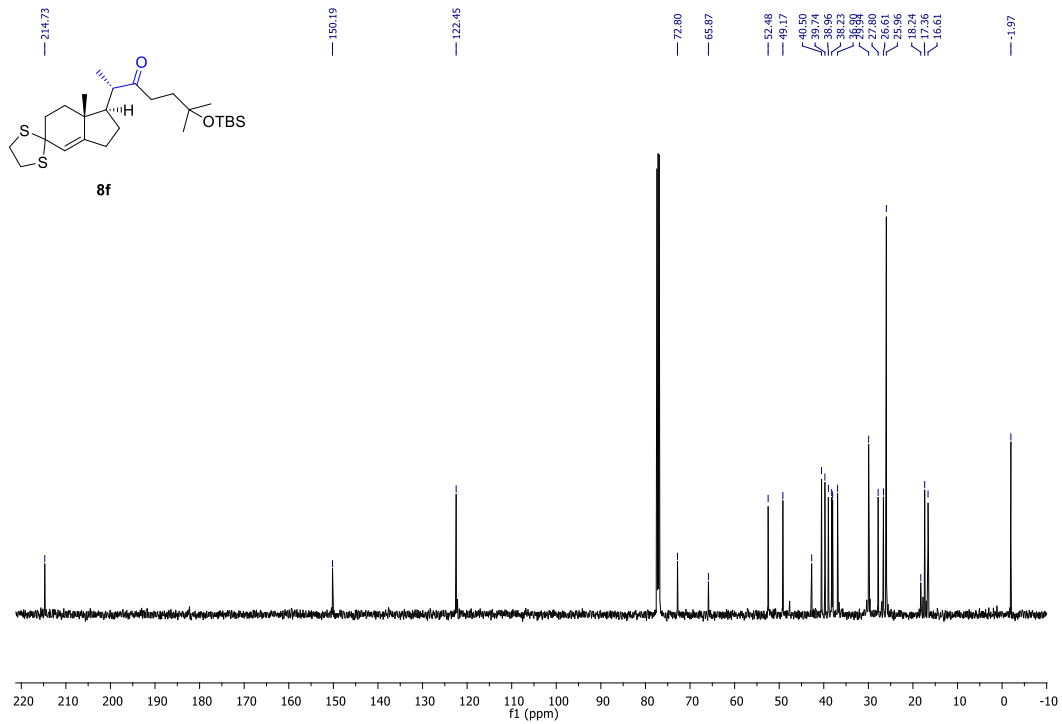
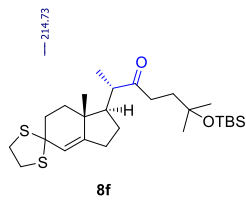
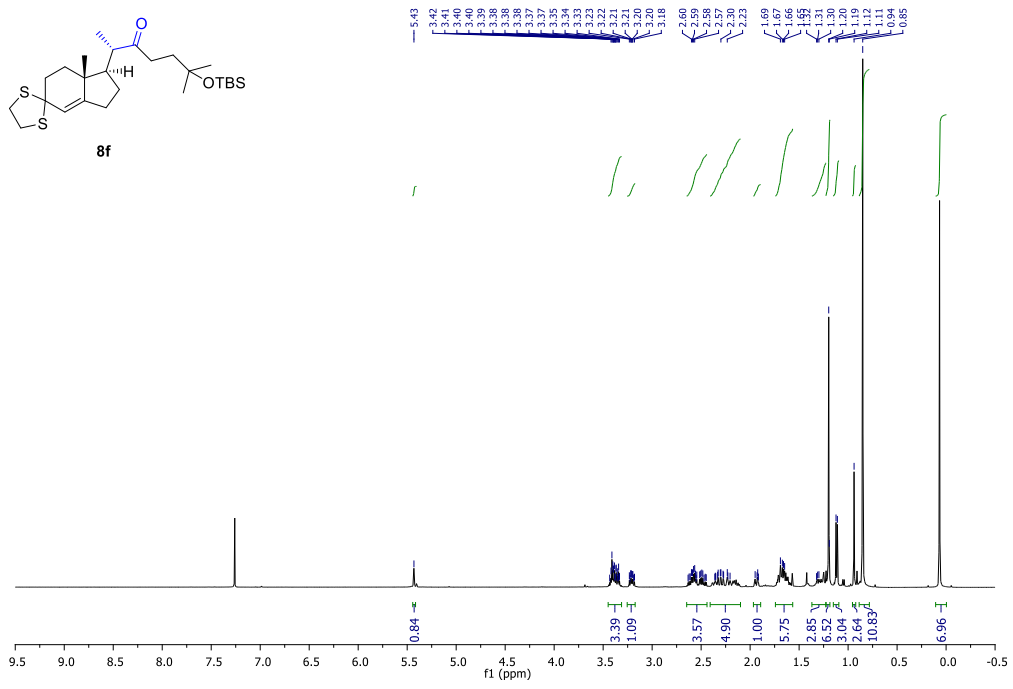
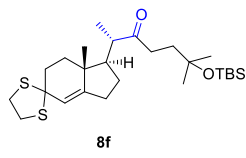


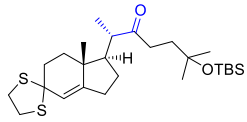




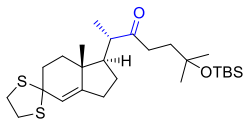
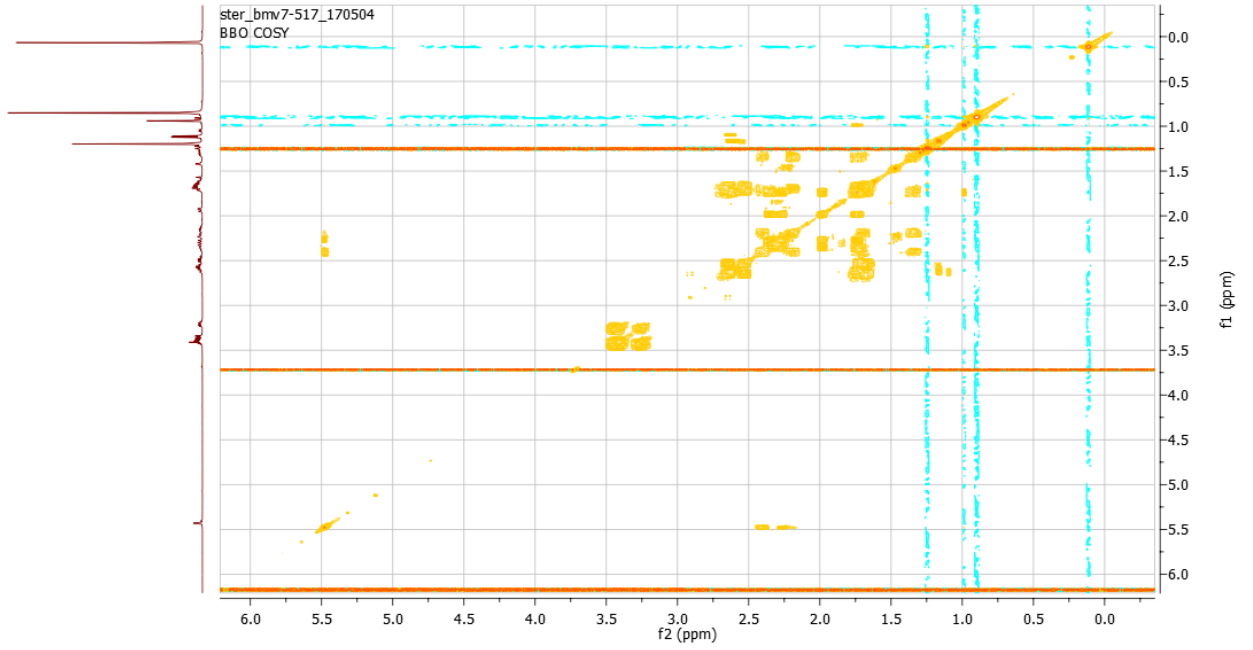




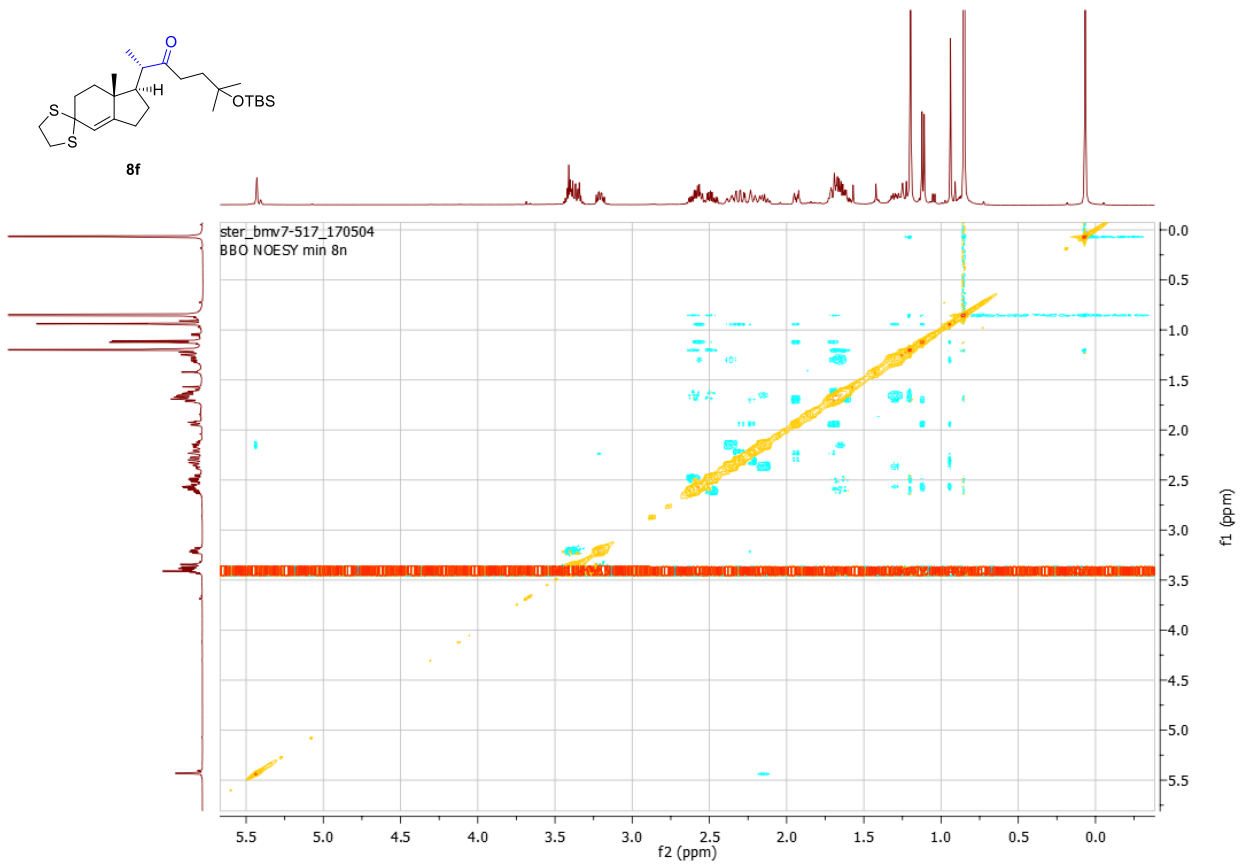




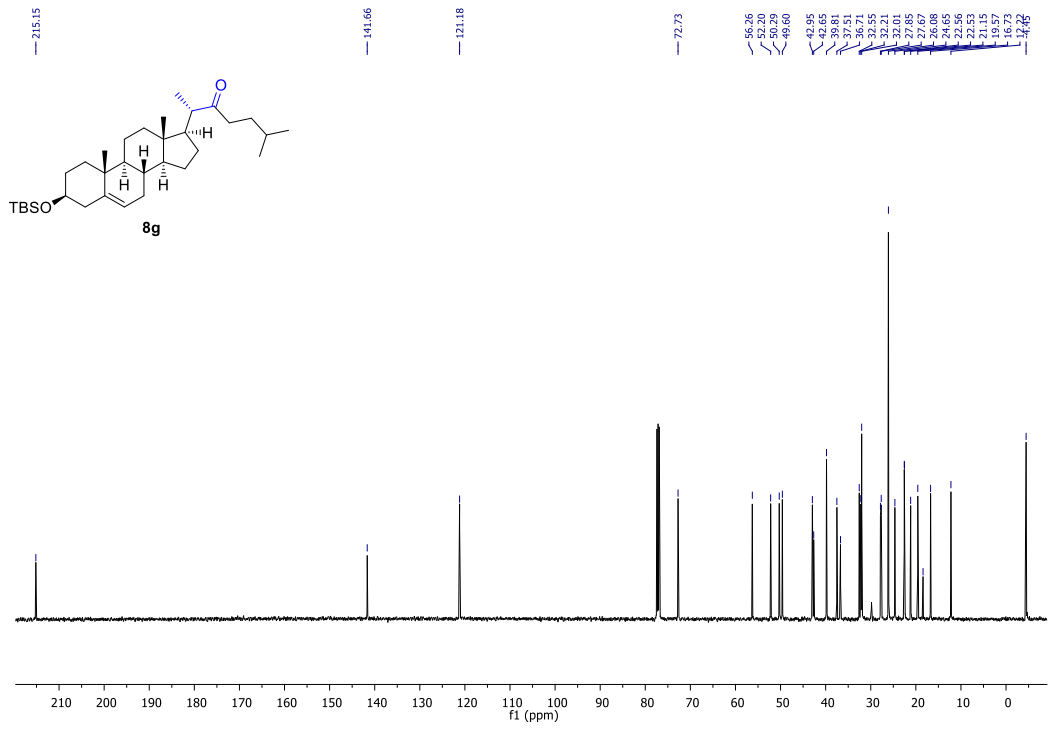
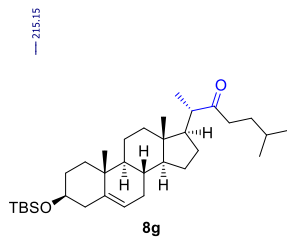
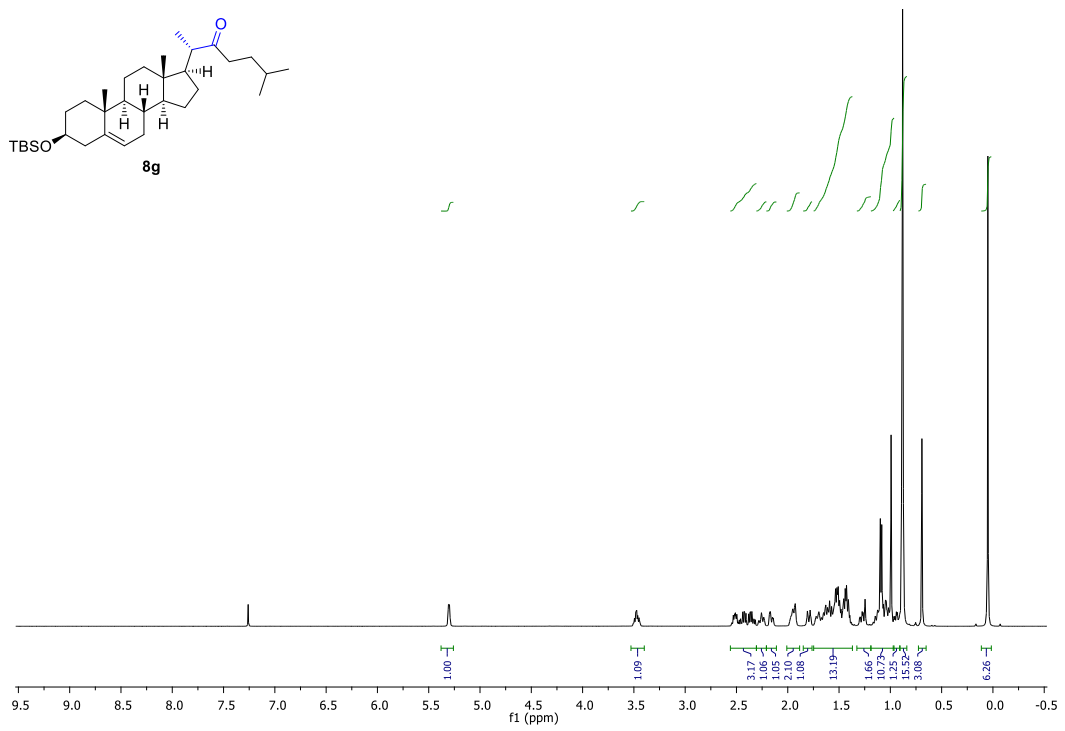
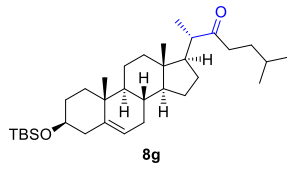
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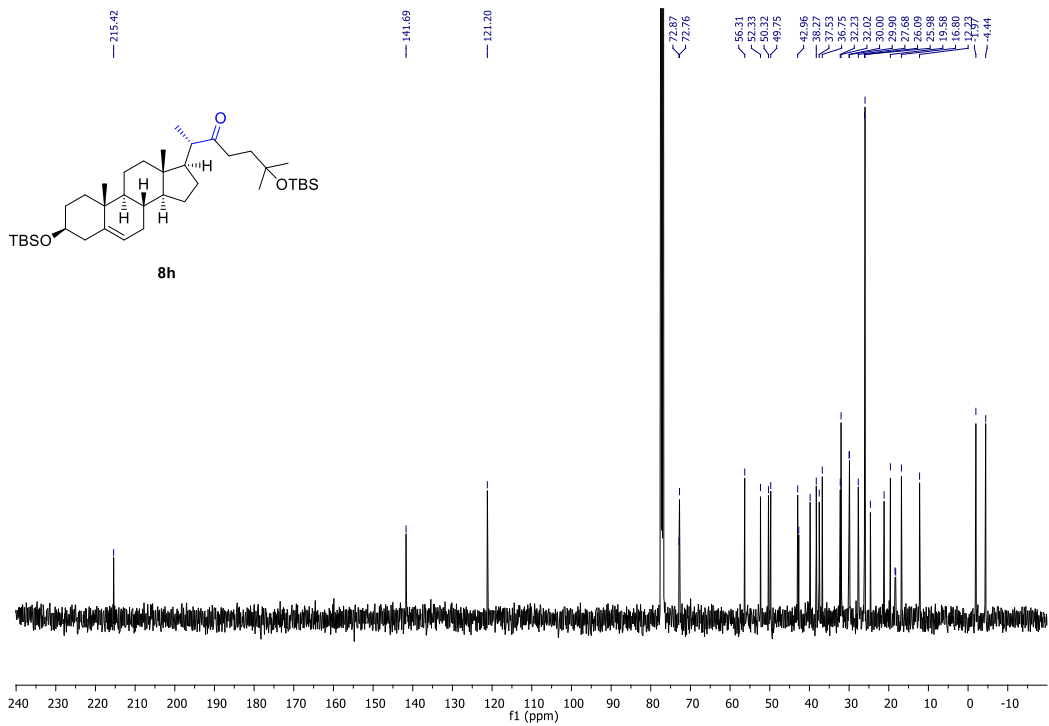
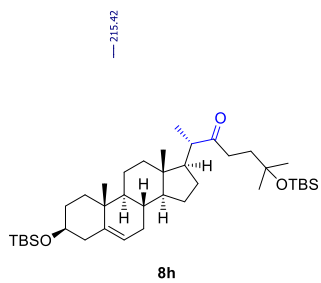
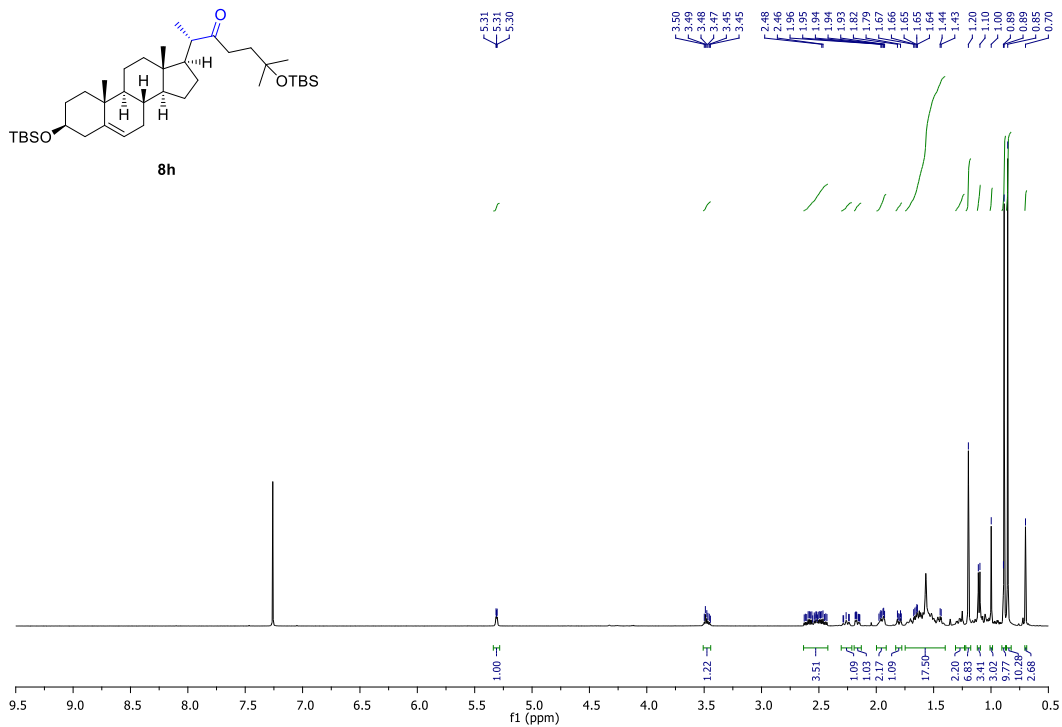
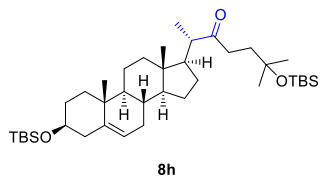


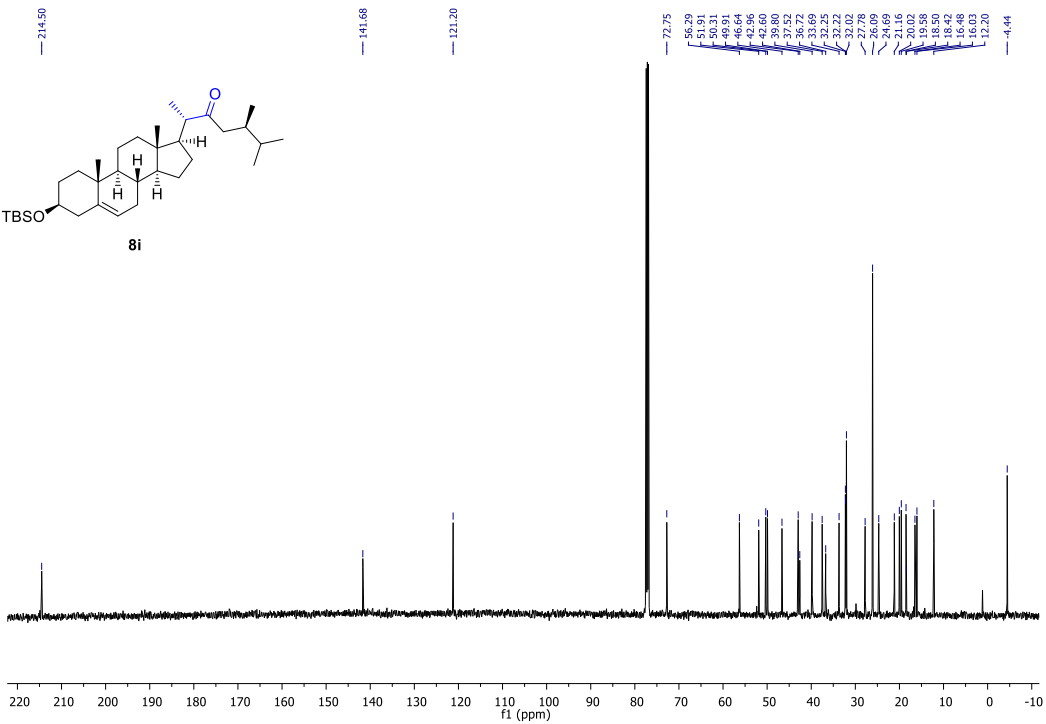
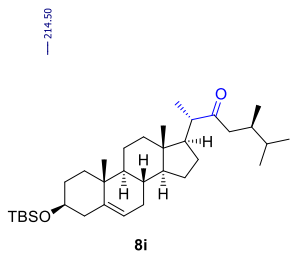
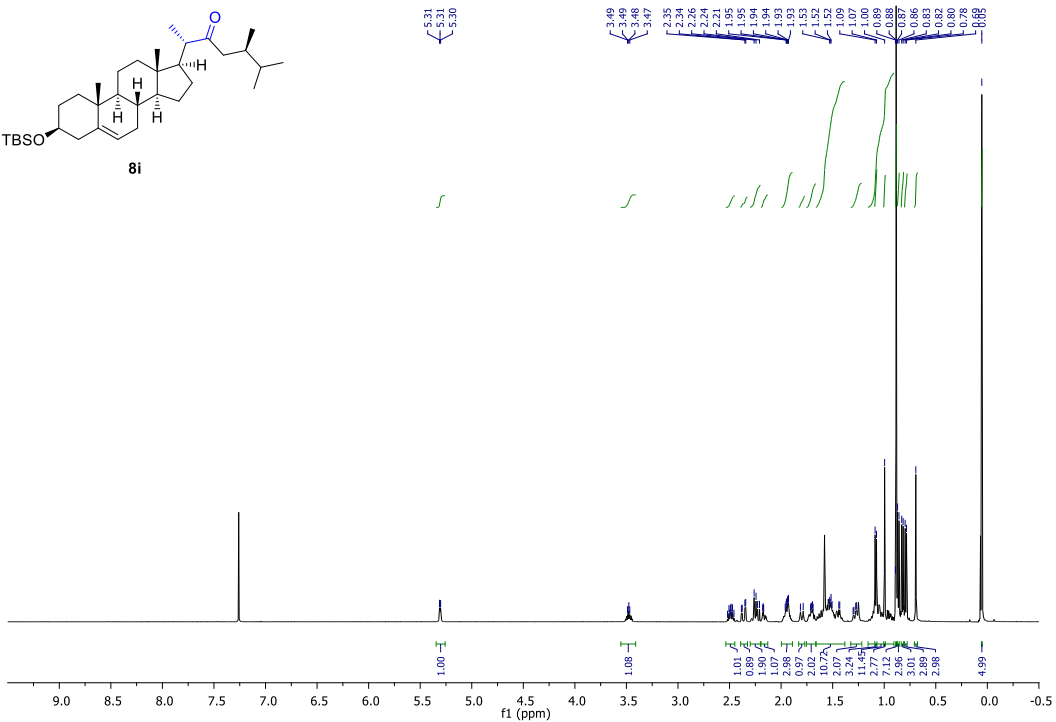
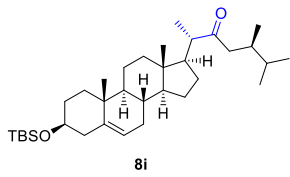
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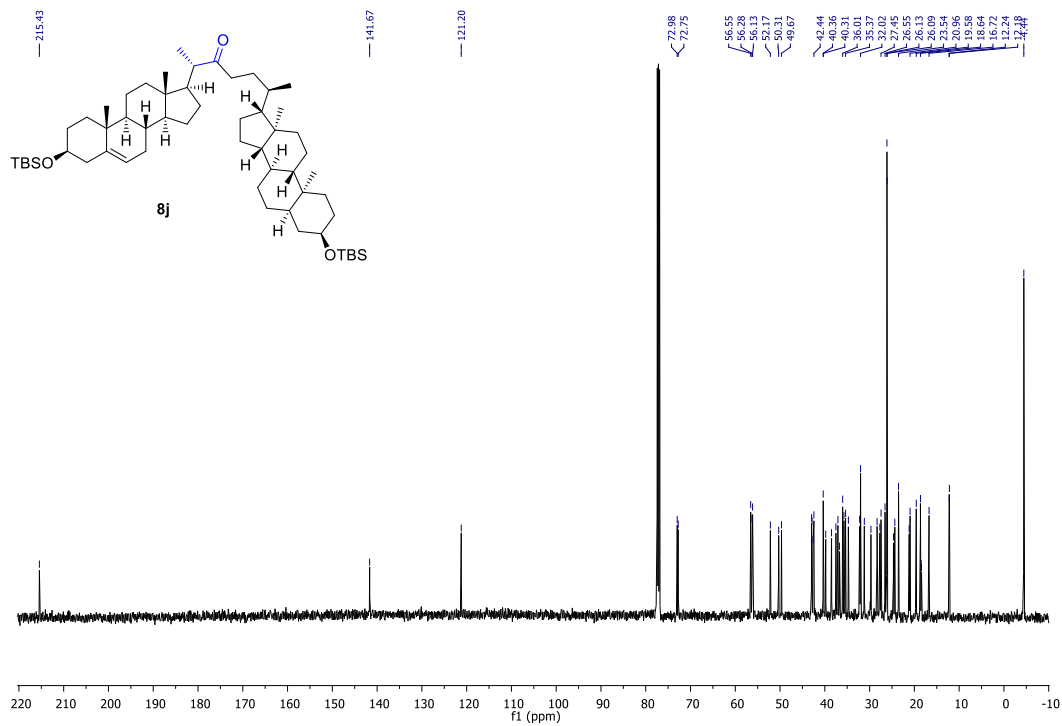
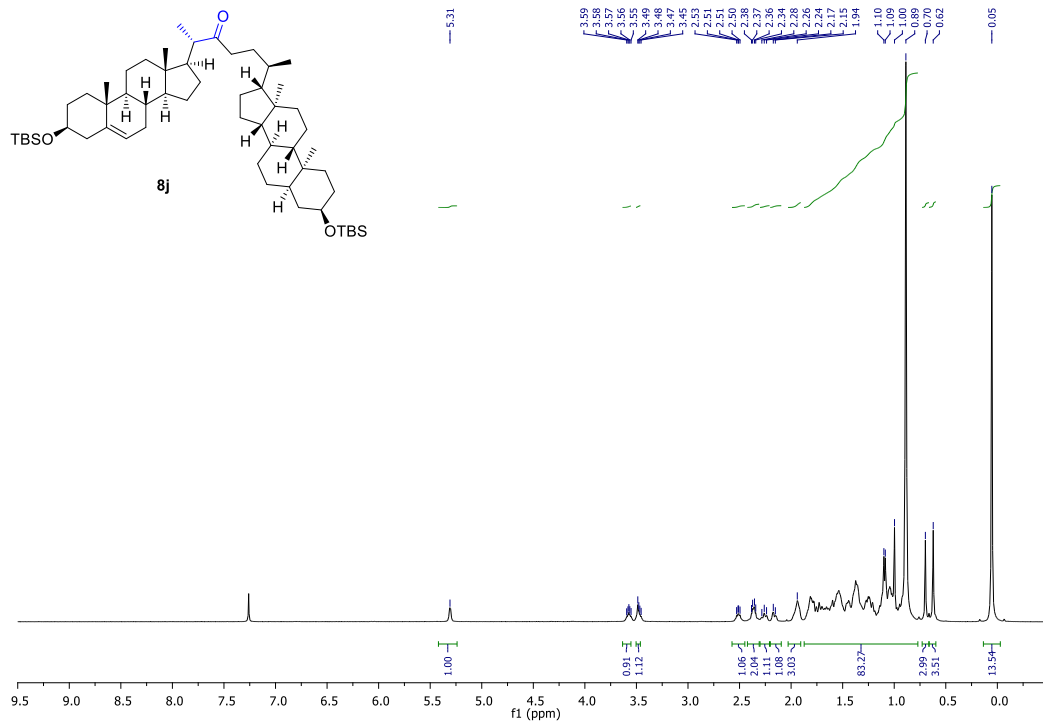


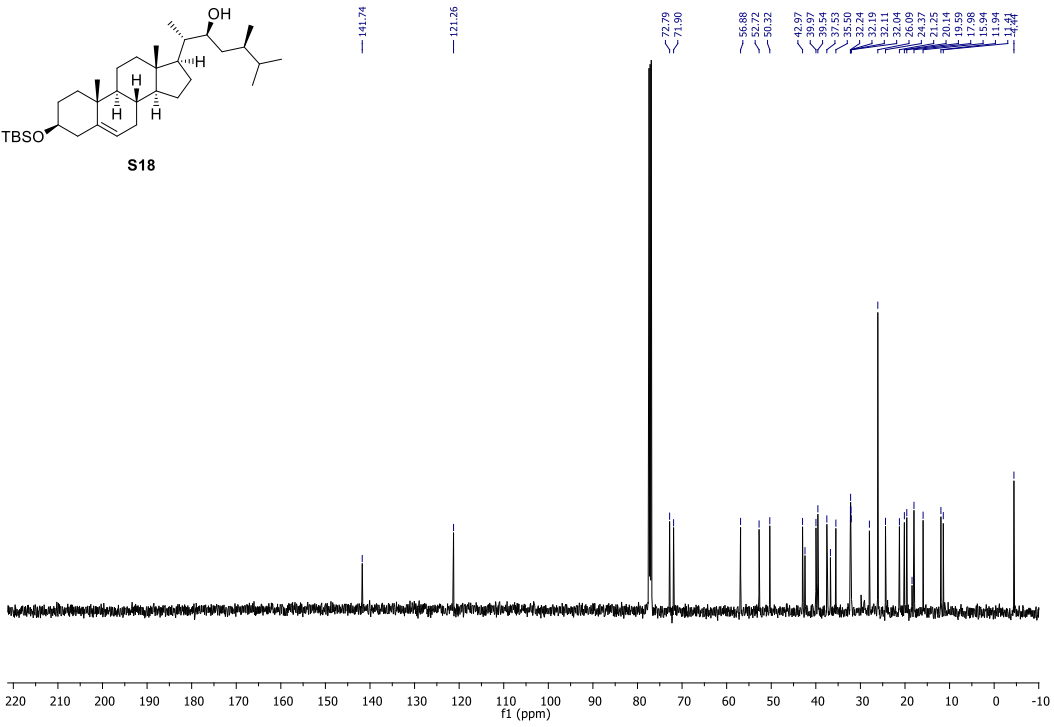
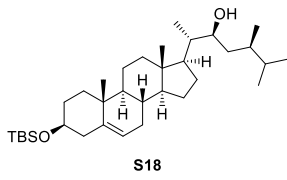
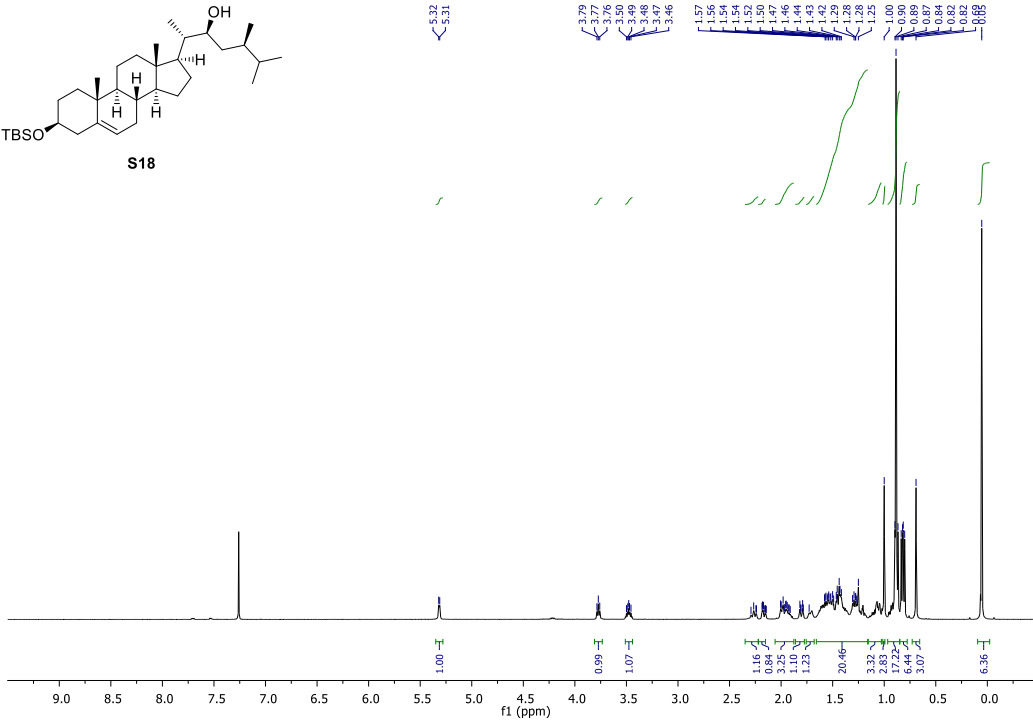
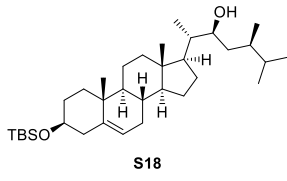


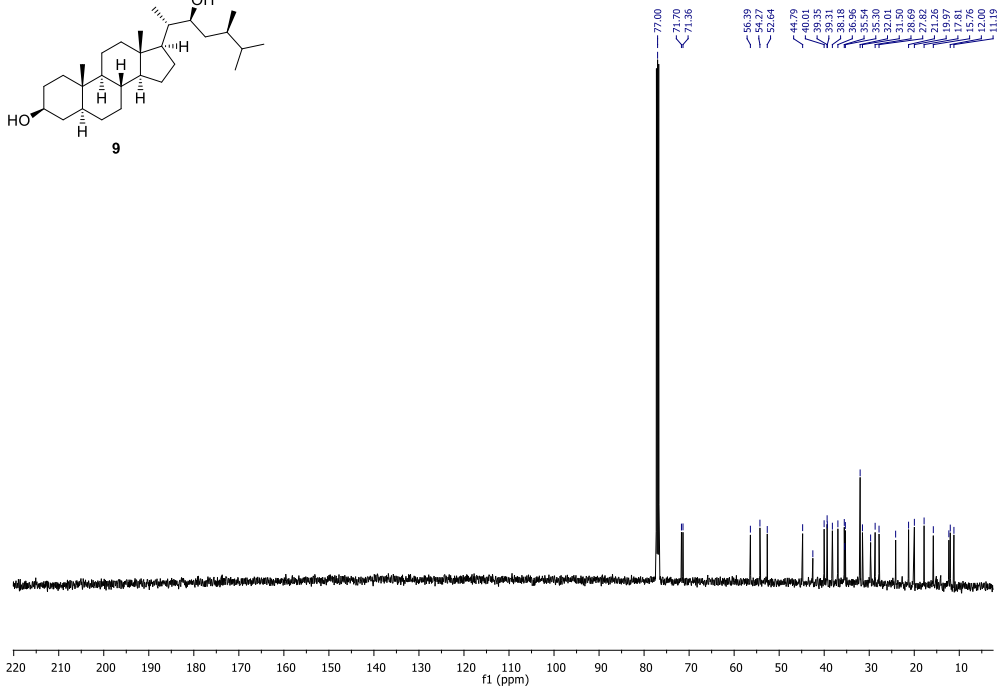
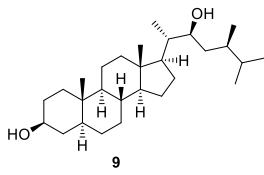
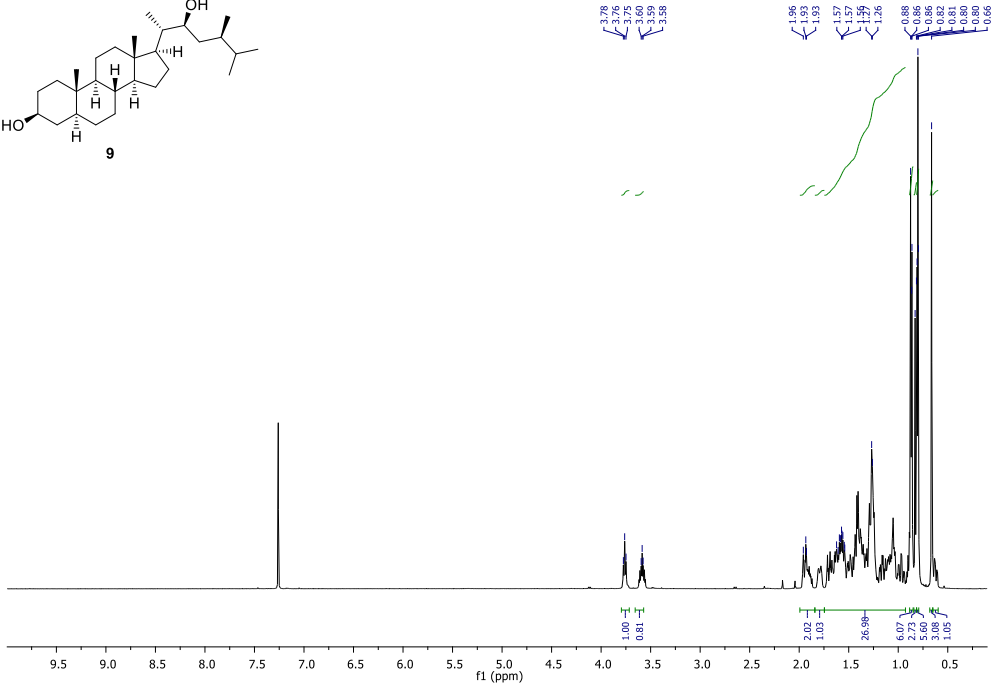
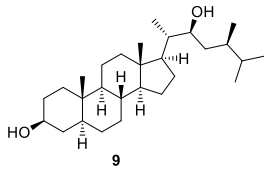


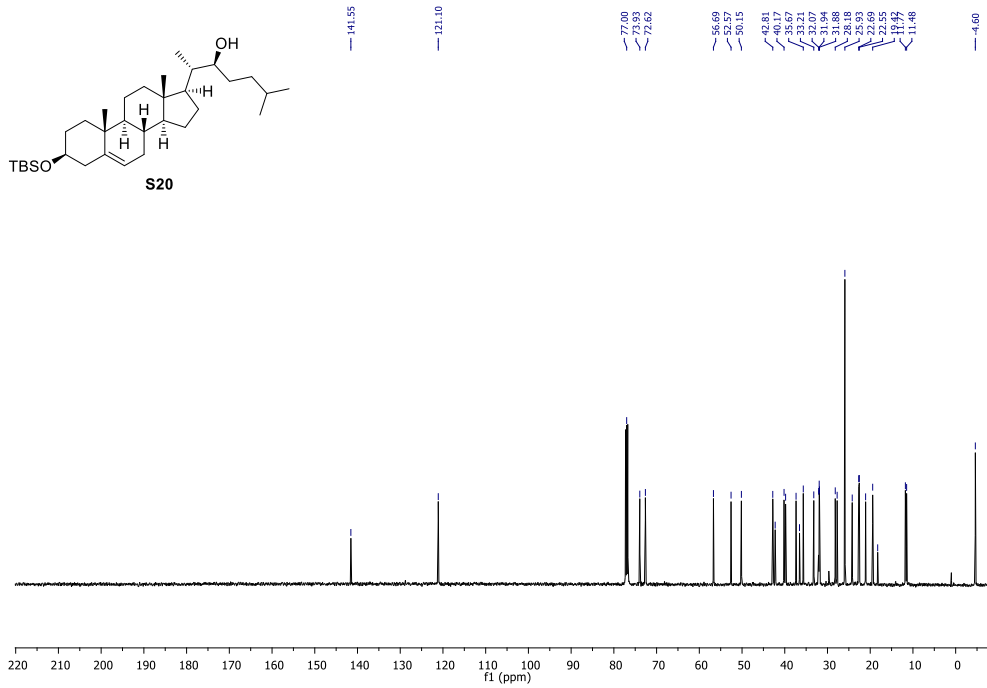
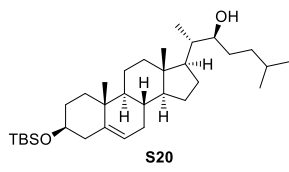
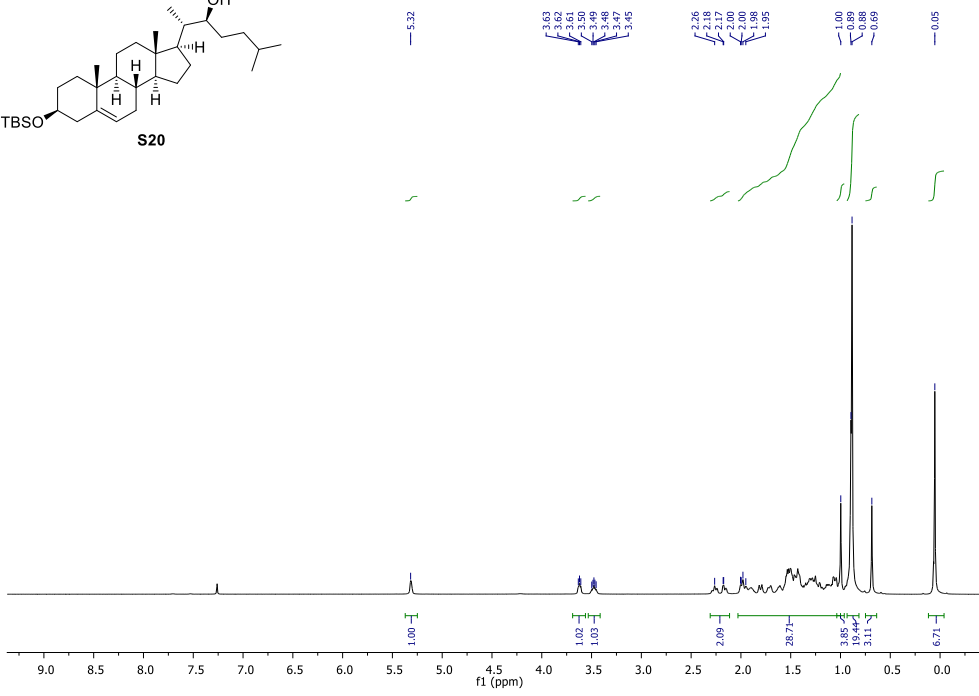
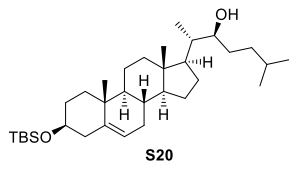


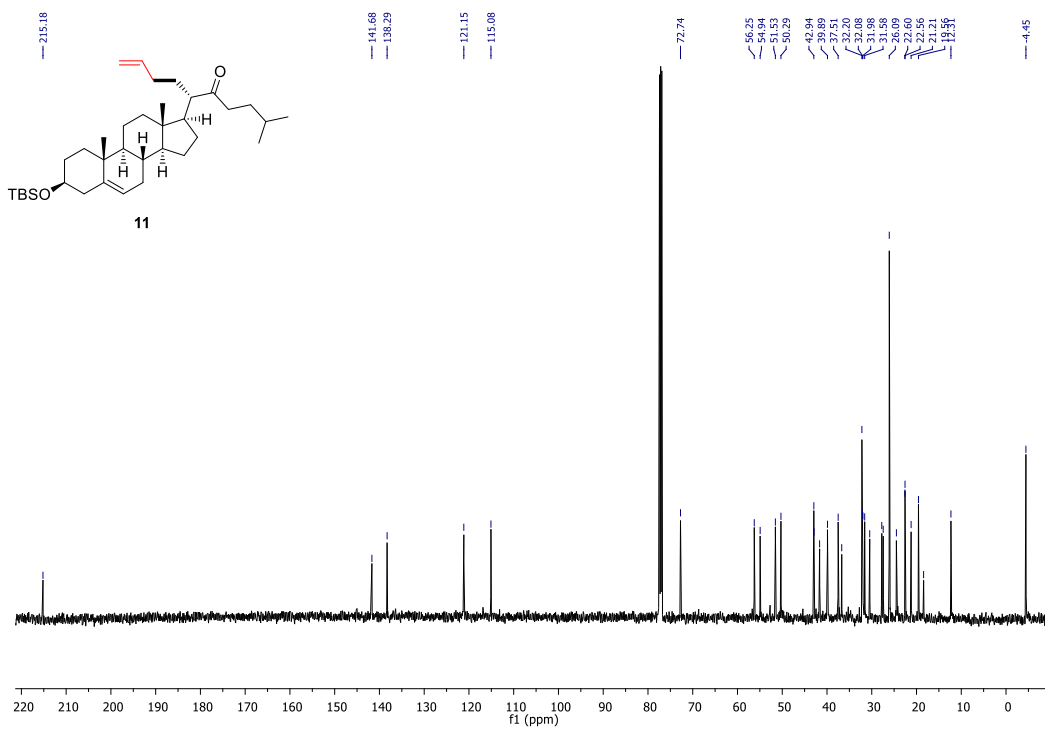
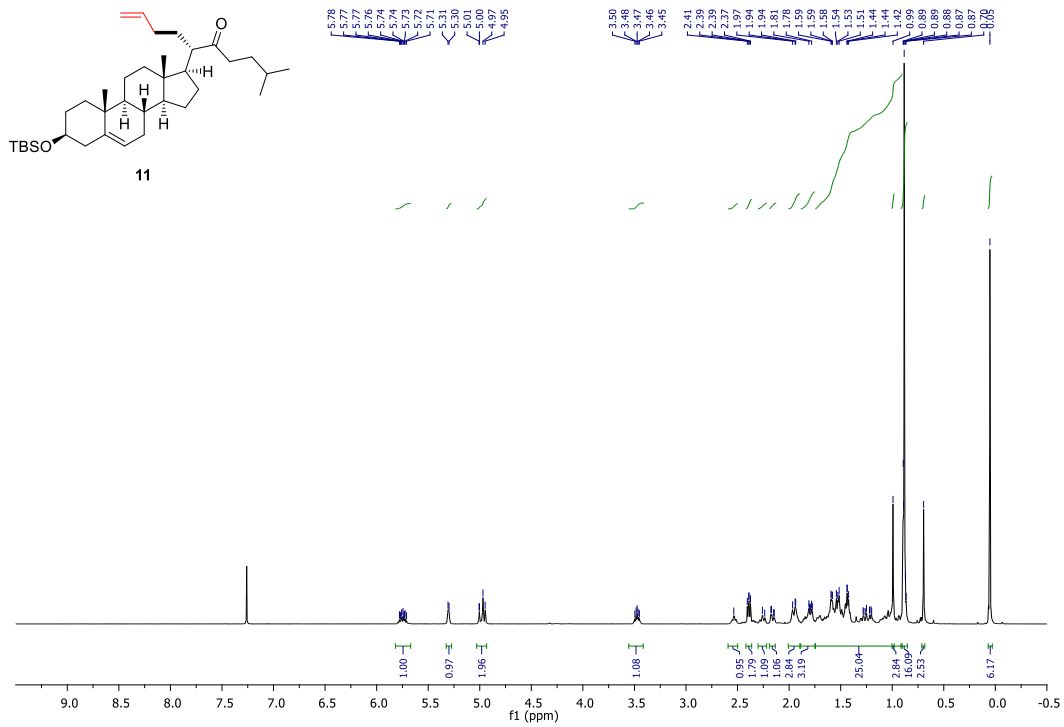




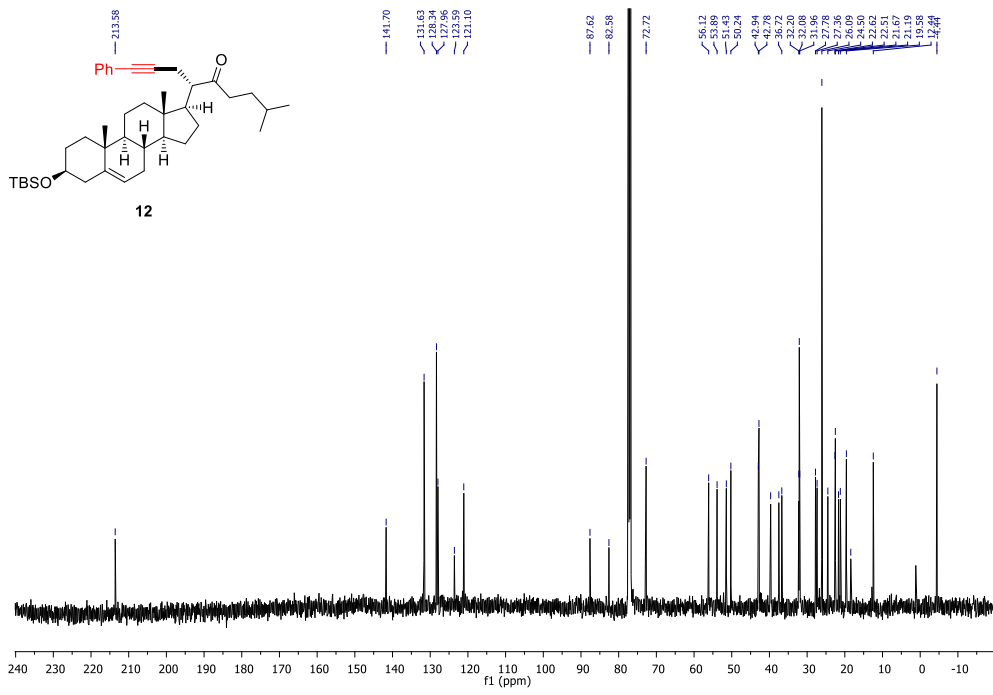
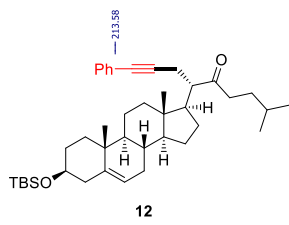
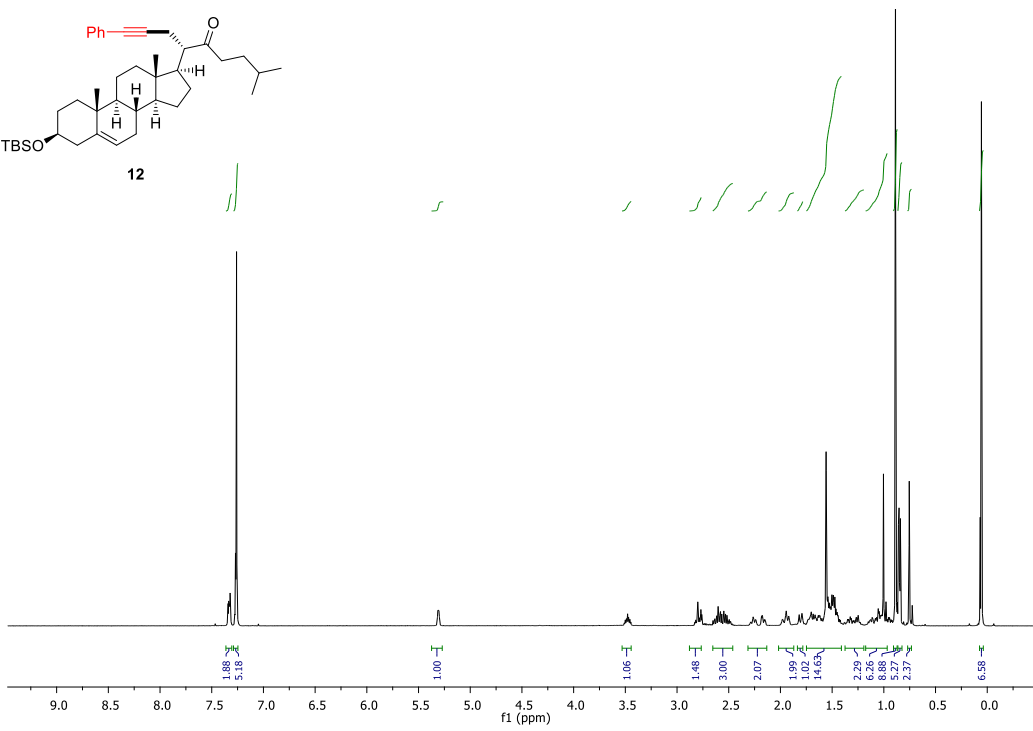
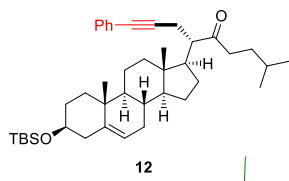


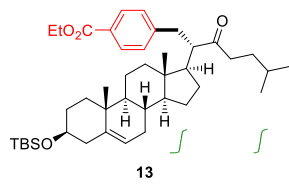












13

