Access to the Protoilludane Core by Gold-Catalyzed Allene-Vinylcyclopropane Cycloisomerization

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Supporting information

General Information

Unless otherwise stated, reactions were carried out under argon atmosphere in solvents dried by passing through an activated alumina column on a PureSolv^{TM} solvent purification system (Innovative Technologies, Inc., MA). Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merck GF_{234}) using UV light as visualizing agent, and an acidic solution of vanillin in ethanol or a basic solution of permanganate potassium in water as developing agent. Chromatograpy purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 mm) or automated flash chromatographer CombiFlash Companion. Preparative TLC was performed on 20 cm × 20 cm silica gel plates (2.0 mm thick, catalogue number 02015, Analtech). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

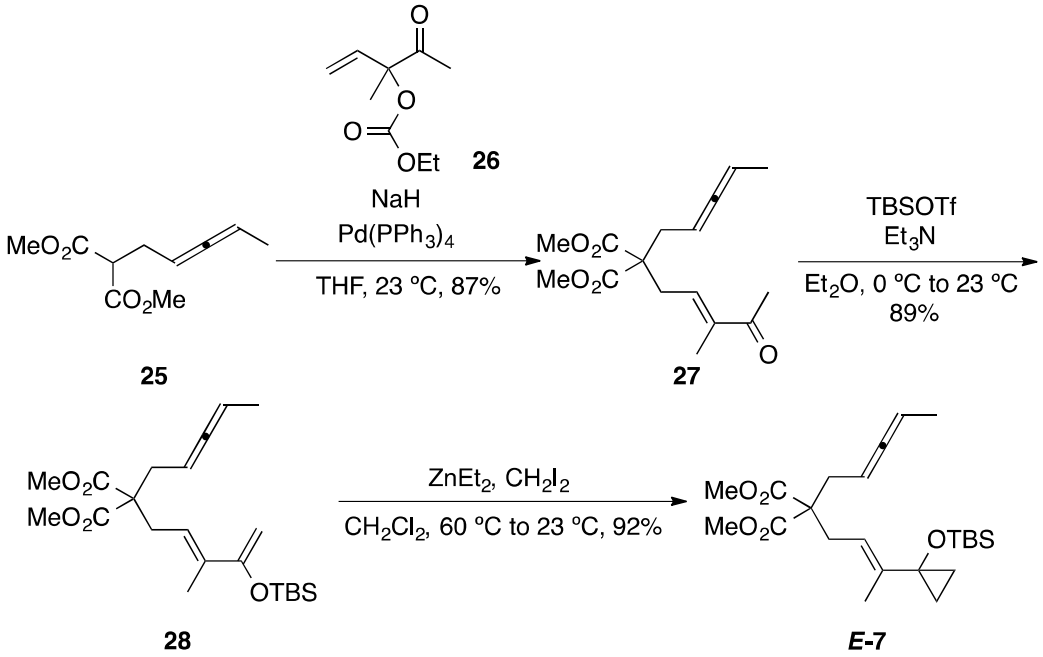
NMR spectra were recorded at 298 K on a Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatus. Mass spectra was recorded on a Waters Micromass LCT Premier (ESI), Waters Micromass GCT (EI, CI) and Bruker Daltonics Autoflex (MALDI) spectrometers. Melting points were determined using a Büchi melting point apparatus.

Crystal structure determinations were carried out using a Bruker-Nonius diffractomer equipped with an APPEX 2 4K CCD area detector, a FR591 rotating anode with MoK_a radiation, Montel mirrors as monochromator and a Kryoflex low temperature device (T = –173 ºC). Full-sphere data collection was used with w and j scans. *Programs used*: Data collection APEX-2, data reduction Bruker Saint V/.60A and absorption correction SADABS. Structure Solution and Refinement: Crystal structure solution was achieved using direct methods as implement in SHELXTL and visualized using the program XP. Missing atoms were subsequently located from

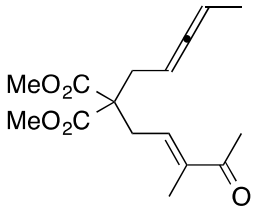
difference Fourier synthesis and added to the atom list. Least-squares refinement on F2 using all measured intensities was carried out using the program SHELXTL. All non-hydrogen atoms were refined including anisotropic displacement parameters.

Synthesis and Characterization of Compounds:

Compound *E*-7:



Compound 27:



A solution of compound **25**[1] (1.17 g, 5.91 mmol) in THF (10 mL) was added to a suspension of NaH (60 wt% in mineral oil, 258 mg, 6.44 mmol) in THF (20 mL), and the resulting mixture was stirred for 30 min at room temperature. Then, the solution was transferred via cannula to a solution of $Pd(PPh_3)_4$ (186 mg, 0.16 mmol, 3 mol%) in THF (10 mL). Finally, solution of **26**[2] (1 g, 5.37 mmol, 1 equiv) in THF (10 mL)

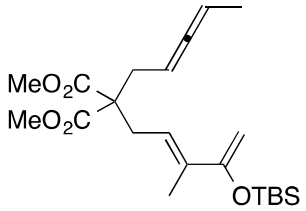
(1) Li, M.; Datta, S.; Barber, D. M.; Dixon, D. D. *Org. Lett.* **2012**, *14*, 6350–6353.

(2) (a) Yamada, W.; Sugawara, Y.; Cheng, H. M.; Ikeno, T.; Yamada, T. *Eur. J. Org. Chem.* **2007**, 2604–2607. (b) Joumier, J. M.; Bruneau, C.; Dixneuf, P. H. *Synlett* **1992**, 453–454.

was added. The reaction mixture was stirred for 3 h at room temperature, and then quenched with saturated $NaHCO_3$ and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Cyclohexane 0:100 to 1:10) to afford compound **27** (1.43 g, 90 %) as a colorless oil.

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.51 (tq, J = 7.4, 1.4 Hz, 1H), 5.12–5.02 (m, 1H), 4.88 (tdd, J = 7.7, 6.3, 3.1 Hz, 1H), 3.73 (2 s, 6H), 2.88 (dt, J = 7.3, 1.1 Hz, 2H), 2.62 (dd, J = 7.7, 2.3 Hz, 2H), 2.28 (s, 3H), 1.77 (d, J = 1.2 Hz, 2H), 1.62 (dd, J = 7.0, 3.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.9, 199.6, 171.1, 171.0, 140.3, 136.7, 86.2, 84.1, 57.6, 52.9, 52.8, 33.5, 32.3, 25.6, 14.3, 11.5; HRMS-ESI: *m/z* calculated for $C_{16}H_{22}O_5Na$ $[M+Na]^+$: 317.1359, found: 317.1364.

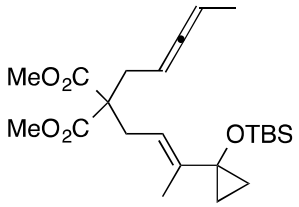
Compound 28:



Anhydrous Et_3N (142 µL, 1.02 mmol) and TBSOTf (117 µL, 0.51 mmol) were added dropwise to a solution of the enone **27** (100 mg, 0.34 mmol) in anhydrous Et_2O (10 mL) at 0 ºC. The resulting mixture was stirred at room temperature overnight. The reaction mixture was quenched with brine and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes/Et_3N 0:100:1 to 10:90:1) to afford silylenol ether **28** (124 mg, 89 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88–5.82 (m, 1H), 5.08–4.98 (m, 1H), 4.88 (m, 1H), 4.42 (dd, J = 1.4, 0.6 Hz, 1H), 4.28–4.20 (m, 1H), 3.70 (s, 6H), 2.85–2.77 (m, 2H), 2.57 (dd, J = 7.8, 2.3 Hz, 2H), 1.77 (d, J = 1.1 Hz, 3H), 1.61 (dd, J = 7.0, 3.2 Hz, 3H), 0.96 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 171.4, 157.1, 134.4, 121.3, 91.8, 85.8, 84.5, 58.0, 52.6, 52.5, 14.4, 13.5, –4.6; HRMS-ESI: *m/z* calculated for $C_{22}H_{37}O_5Si$ $[M+H]^+$: 409.2405, found: 409.2402.

Compound *E*-7:



CH_2I_2 was washed with saturated aqueous Na_2SO_3 (twice), dried over anhydrous $MgSO_4$, filtered and fractionally distilled over CaH_2 ($T°_{eb}$ = 54ºC @ 10 mbar), then stored over 3Å MS under an argon atmosphere.

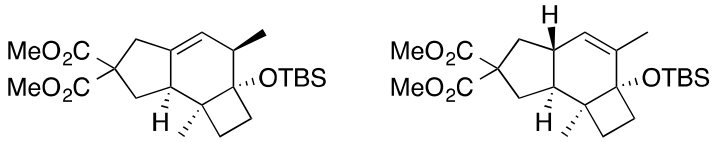
CH_2I_2 (270 µL, 3.35 mmol) was added dropwise to a solution of $ZnEt_2$ (1 M in Hexane, 3.3 mL, 3.30 mmol) in anhydrous CH_2Cl_2 (20 mL) at –60 ºC. The resulting solution was warmed to 0 ºC until a white precipitate appeared, then cooled down to –60 ºC, whereupon a solution of the silylenol ether **28** (1.14 g, 2.79 mmol) in anhydrous CH_2Cl_2 (8 mL) was added dropwise. The resulting mixture was stirred for 3 h at room temperature. The reaction mixture was then quenched with saturated NH_4Cl and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes 0:100 to 10:90) to afford substrate ***E*-7** (1.09 g, 92 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27–5.21 (m, 1H), 5.08–4.99 (m, 1H), 4.90–4.82 (m, 1H), 3.69 (s, 6H), 2.67 (d, J = 7.4 Hz, 2H), 2.54 (dd, J = 7.7, 2.4 Hz, 2H), 1.70 (s, 3H), 1.61 (dd, J = 7.0, 3.2 Hz, 3H), 0.99 (d, J = 7.1 Hz, 3H), 0.83 (s, 9H), 0.79–0.75 (m, 2H), 0.67–0.63 (m, 2H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 171.3, 171.2, 140.4, 117.5, 85.6, 84.3, 60.9, 57.8, 52.4, 52.3, 32.5, 30.5, 25.7, 17.8, 14.3, 14.0, 13.4, –3.8; HRMS-ESI: *m/z* calculated for $C_{23}H_{38}O_5SiNa$ $[M+Na]^+$: 445.2381, found: 445.2371.

Compound 8b:

A dry flask under argon was charged with $[IPrAu(NCPh)]SbF_6$ (6.2 mg, 0.00674 mmol). Then, a solution of compound ***E*-7** (95 mg, 0.225 mmol) in anhydrous CH_2Cl_2 (2.2 mL) was added at 0 ºC. After completion of the reaction (2 h), the solution was quenched with a few drops of Et_3N and filtered through a pad of SiO_2 (elution with EtOAc/hexane 50:50). After removal of the solvent, the crude product was purified by flash column chromatography over silica gel (eluent pentane/EtOAc 98:2) to afford a

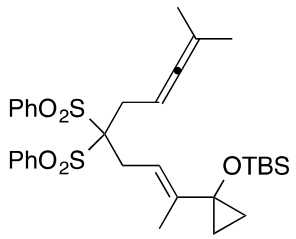
mixture of **8a** and **8b** as a pale yellow oil (89 mg, 94%) in a ratio 6.5:1 (corrected yield for **8a**: 82%). The minor isomer could not be isolated and its structure was tentatively assigned as shown by analogy to that observed in the cyclization of **Z-7** (see compounds **18a 18b**).



8a:8b (6.5:1)

Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35–5.33 (m, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.10–3.03 (m, 1H), 2.84–2.75 (m, 1H), 2.48–2.33 (m, 2H), 2.15–2.10 (m, 1H), 1.91–1.82 (m, 2H), 1.70–1.63 (m, 2H), 1.25–1.21 (m, 1H), 1.11 (s, 3H), 0.99 (d, J = 7.1 Hz, 3H), 0.86 (s, 9H), 0.16 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 172.1, 142.6, 123.3, 81.9, 59.9, 52.8, 52.7, 47.8, 47.7, 39.8, 39.3, 35.3, 27.2, 26.0, 25.9, 22.6, 21.5, 18.4, 14.9, –1.8, –1.9; HRMS-ESI: *m/z* calculated for $C_{23}H_{38}O_5SiNa$ $[M+Na]^+$: 445.2381, found: 445.2366.

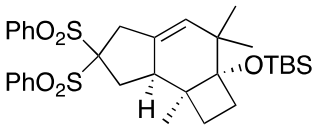
Compound 9:



The compound **9** was prepared according to the same procedure used for compound ***E*-7**.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–8.03 (m, 4H), 7.72–7.68 (m, 2H), 7.59–7.54 (m, 4H), 5.58 (dt, J = 6.1, 1.1 Hz, 1H), 5.11–5.04 (m, 1H), 2.98 (d, J = 6.3 Hz, 2H), 2.95 (d, J = 7.2 Hz, 2H), 1.71 (s, 3H), 1.70 (s, 3H), 1.65 (br s, 3H), 0.84 (s, 9H), 0.81 (d, J = 7.5 Hz, 1H), 0.80 (d, J = 6.6 Hz, 1H), 0.69 (d, J = 6.6 Hz, 1H), 0.67 (d, J = 7.5 Hz, 1H), 0.07 (s, 6H).

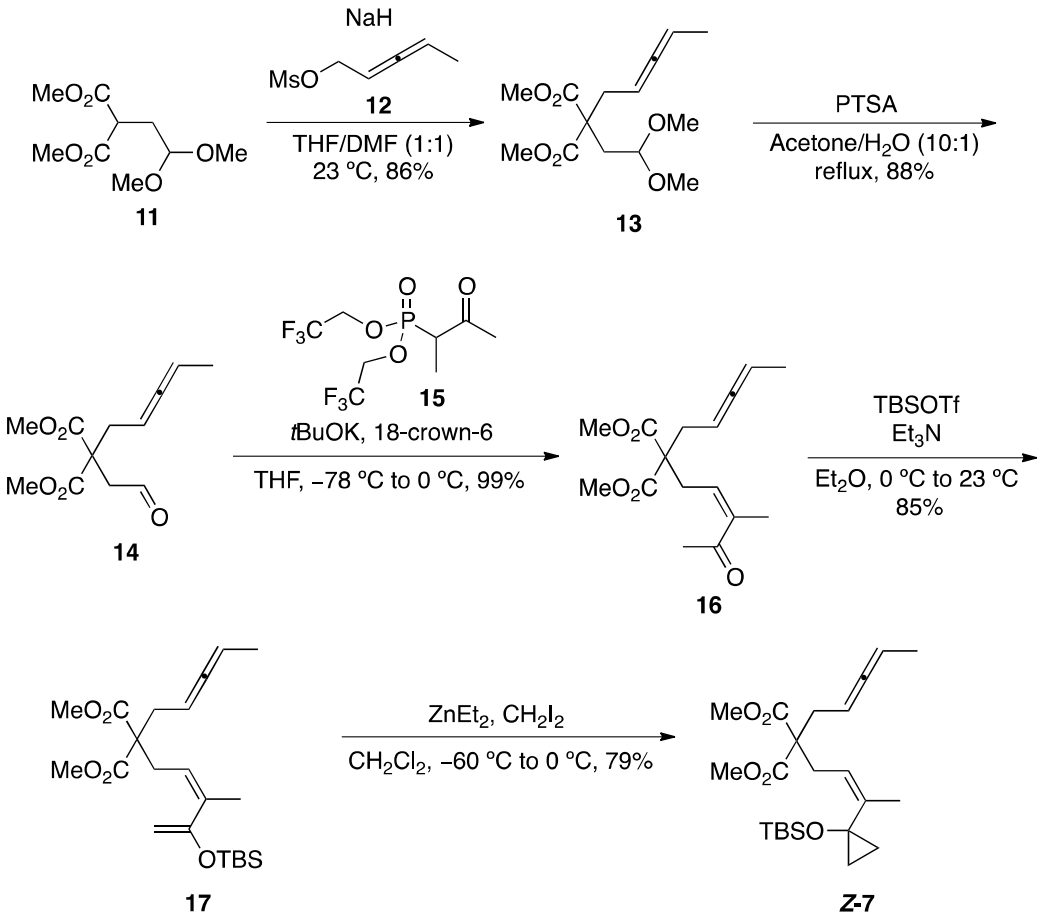
Compound 10:



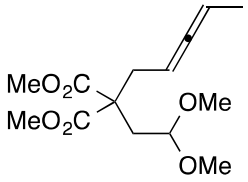
The compound **10** was prepared according to the same procedure used for compound **8**.

Starting from **9** (102 mg, 0.170 mmol), tricyclic product **10** (54.7 mg, 54 %) was obtained as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.06 (m, 2H), 8.00–7.97 (m, 2H), 7.75–7.67 (m, 2H), 7.64–7.54 (m, 4H), 5.45 (q, *J* = 2.2 Hz, 1H), 3.55 (dt, *J* = 19.5, 2.1 Hz, 1H), 3.27 (d, *J* = 19.5 Hz, 1H), 2.53–2.42 (m, 2H), 1.92 (ddd, *J* = 13.5, 11.4, 6.0 Hz, 1H), 1.79 (ddd, *J* = 13.5, 11.1, 7.2 Hz, 1H), 1.46–1.37 (m, 1H), 1.33–1.24 (m, 1H), 0.98 (s, 3H), 0.91 (s, 9H), 0.87 (s, 3H), 0.72 (s, 3H), 0.23 (s, 3H), 0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 137.4, 136.4, 134.6, 134.5, 131.0(1), 130.9(7), 130.3, 128.9, 128.7, 100.0, 93.3, 83.8, 48.2, 47.9, 41.3, 36.8, 33.4, 28.8, 26.9, 26.1, 23.9, 23.4, 23.3, 21.1, 18.8, –1.5, –2.1. HRMS-ESI: *m/z* calculated for $C_{32}H_{44}O_5S_2SiNa$ $[M+Na]^+$: 623.2292, found: 623.2232.

Compound *Z*-7:



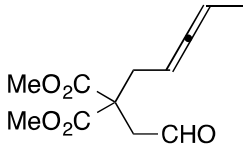
Compound 13:



A solution of acetal **11**[3] (2.23 g, 10.1 mmol) in anhydrous THF (17 mL) was added dropwise to a suspension of NaH (60 wt% in mineral oil, 900 mg, 22.5 mmol) in a mixture of anhydrous THF (34 mL) and anhydrous DMF (34 mL) at 0 ºC. The resulting mixture was stirred until a homogeneous solution was obtained (*ca.* 10-15 min). A solution of the freshly prepared mesylate **12** (1.81 g, 11.1 mmol) in anhydrous THF (17 mL) was added dropwise and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then quenched with saturated NH_4Cl and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes 5:95 to 20:80) to afford compound **13** (2.47 g, 86 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (m, 1H), 4.86 (tdq, *J* = 7.7, 6.3, 3.2 Hz, 1H), 4.45 (t, *J* = 5.6 Hz, 1H), 3.70 (s, 6H), 3.30 (s, 3H), 3.29 (s, 3H), 2.63 (ddd, *J* = 7.9, 2.2, 0.7 Hz, 2H), 2.27 (d, *J* = 5.6 Hz, 2H), 1.62 (dd, *J* = 7.0, 3.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 171.4, 102.1, 85.9, 84.3, 55.6, 53.8, 53.7, 52.6, 52.5, 35.8, 33.4, 14.4.

Compound 14:



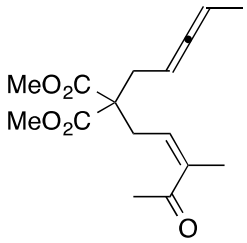
PTSA (276 mg, 1.45 mmol) was added to a solution of the dimethylacetal **13** (4.15 g, 14.5 mmol) in a mixture of acetone (66 mL) and water (6.6 mL). The resulting mixture was refluxed for 5 h, then cooled down to room temperature and diluted with hexanes. The solution was partially concentrated to remove the acetone, then diluted with EtOAc, washed with water, brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed by rotary evaporation. The crude product was purified by

(3) Shitani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54–55.

flash column chromatography (eluent EtOAc/Hexanes 20:80) to afford aldehyde **14** (3.06 g, 88 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (t, *J* = 1.4 Hz, 1H), 5.07 (qt, *J* = 7.1, 2.2 Hz, 1H), 4.89 (tdq, *J* = 7.8, 6.3, 3.2 Hz, 1H), 3.75 (s, 6H), 3.04 (d, *J* = 1.4 Hz, 2H), 2.70 (dd, *J* = 7.8, 2.2 Hz, 2H), 1.62 (dd, *J* = 7.1, 3.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 198.9, 170.5, 86.2, 84.3, 55.2, 53.1, 53.0, 46.2, 34.2, 14.3; HRMS-ESI: *m/z* calculated for $C_{12}H_{16}O_5Na$ $[M+Na]^+$: 263.0890, found: 263.0896.

Compound 16:



In order to perform this reaction and obtain optimal results, several considerations should be followed cautiously. First, the monomethylated phosphonate used in that reaction contains trace quantities of the dimethylated product. The weight purity should be determined by NMR to include it in the stoichiometry. The second recommendation is a direct consequence of the contamination of the monomethylphosphonate: the base (KO*t*Bu) should always be used in slight default compared to phosphonate. Finally, freshly sublimed KO*t*Bu and recrystallized 18-crown-6 should be used.[4]

A freshly prepared solution of KO*t*Bu (1.49 g, 13.3 mmol) in anhydrous THF (13 mL) was added dropwise over 20 min to a suspension of the phosphonate **15**[5,6] (85 wt%, 4.95 g, 13.3 mmol) and 18-crown-6 (4.47 g, 16.9 mmol) in anhydrous THF (160 mL) at −78 ºC. The resulting mixture was stirred for 20 min at −78 ºC, whereupon a solution of the aldehyde **14** (2.91 g, 12.1 mmol) in anhydrous THF (40 mL) was added dropwise over 20 min. The resulting solution was stirred for 1 h at −78ºC, then warmed to 0 ºC over 3 h. The reaction mixture was quenched with saturated NH_4Cl and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation.

(4) Gokel, G. W.; Cram, D. J.; Liotta, C. L.; Harris H. P., Cook F. L. *Org. Synth.* **1977**, *57*, 30.

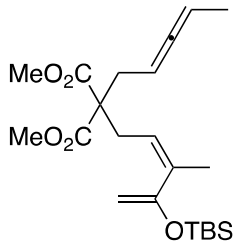
(5) Yu, W.; Su, M.; Jin, Z. *Tetrahedron Lett.* **1999**, *40*, 6725–6728.

(6) See also: Jiao, L.; Yuan, C.; Yu, Z-X. *J. Am. Chem. Soc.* **2008**, *130*, 4421–4430.

The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes 10:90 to 20:80) to afford compound **16** (3.53 g, 99 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (tq, *J* = 7.4, 1.4 Hz, 1H), 5.08–4.99 (m, 1H), 4.93–4.85 (m, 1H), 3.72 (s, 6H), 2.97–2.93 (m, 2H), 2.57 (dd, *J* = 7.7, 2.3 Hz, 2H), 2.24 (s, 3H), 1.93 (q, *J* = 1.4 Hz, 3H), 1.61 (dd, *J* = 7.0, 3.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 202.8, 171.2, 171.1, 138.6, 131.2, 85.9, 84.3, 58.0, 52.7, 52.60, 33.4, 32.5, 30.0, 21.3, 14.4; HRMS-ESI: *m/z* calculated for $C_{16}H_{22}O_5Na$ $[M+Na]^+$: 317.1359, found: 317.1357.

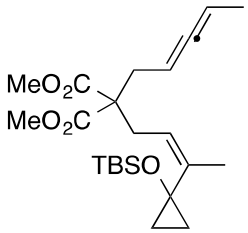
Compound 17:



Anhydrous Et_3N (1.2 mL, 8.45 mmol) and TBSOTf (1.2 mL, 5.07 mmol) were added dropwise to a solution of the enone **16** (994 mg, 3.38 mmol) in anhydrous Et_2O (34 mL) at 0 ºC. The resulting mixture was stirred at room temperature overnight. The reaction mixture was quenched with saturated NH_4Cl and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes/Et_3N 0:100:1 to 10:90:1) to afford silylenol ether **17** (1.17 g, 85 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (dt, *J* = 7.1, 1.4 Hz, 1H), 5.06–4.97 (m, 1H), 4.94–4.86 (m, 1H), 4.34 (d, *J* = 1.0 Hz, 1H), 4.20 (d, *J* = 1.0 Hz, 1H), 3.70 (s, 6H), 2.95–2.88 (m, 2H), 2.56 (dd, *J* = 7.8, 2.3 Hz, 2H), 1.80 (q, *J* = 1.4 Hz, 3H), 1.60 (dd, *J* = 7.0, 3.2 Hz, 3H), 0.93 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 171.6, 171.5, 156.2, 137.2, 122.3, 94.1, 85.5, 84.6, 58.1, 52.5, 52.4, 33.0, 32.4, 25.9, 25.8, 22.8, 18.3, 14.4, –4.5; HRMS-ESI: *m/z* calculated for $C_{22}H_{37}O_5SiNa$ $[M+Na]^+$: 409.2405, found: 409.2406.

Compound *Z*-7:

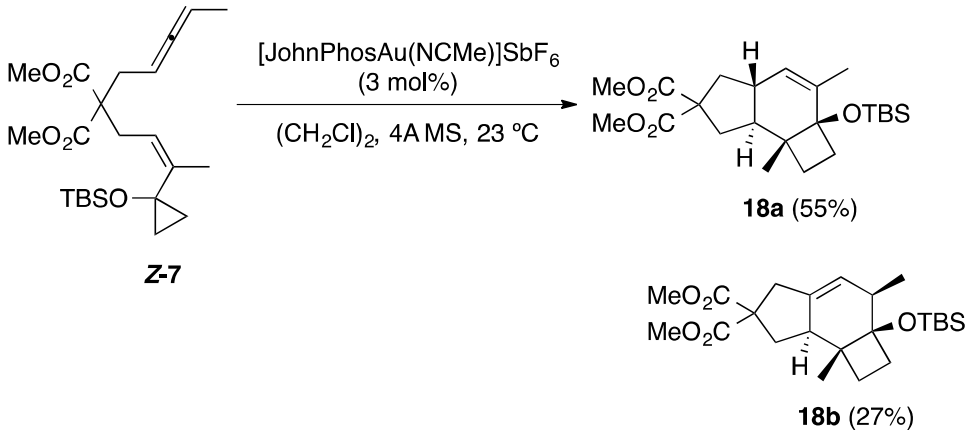


CH_2I_2 was washed with saturated aqueous Na_2SO_3 (twice), dried over anhydrous $MgSO_4$, filtered and fractionally distilled over CaH_2 ($T°_{eb}$ = 54ºC @ 10 mbar), then stored over 3Å MS under an argon atmosphere.

CH_2I_2 (275 μL, 3.41 mmol) was added dropwise to a solution of $ZnEt_2$ (1 M in Hexane, 3.4 mL, 3.41 mmol) in anhydrous CH_2Cl_2 (9.5 mL) at −60 ºC. The resulting solution was warmed to 0 ºC until a white precipitate appeared, then cooled down to −60 ºC, whereupon a solution of the silylenol ether **16** (1.16 g, 2.84 mmol) in anhydrous CH_2Cl_2 (8 mL) was added dropwise. The resulting mixture was stirred for 3 h at room temperature. The reaction mixture was then quenched with saturated NH_4Cl and extracted with Et_2O (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes 0:100 to 10:90) to afford substrate **9** (953 mg, 79 %) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (dt, *J* = 6.9, 1.3 Hz, 1H), 5.05–4.94 (m, 2H), 3.73 (s, 6H), 3.02–2.92 (m, 2H), 2.61 (dd, *J* = 7.7, 2.4 Hz, 2H), 1.76 (d, *J* = 1.3 Hz, 3H), 1.64 (d, *J* = 6.9, 3.2 Hz, 3H), 0.88–0.83 (m, 2H), 0.82 (s, 9H), 0.62–0.60 (m, 2H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 171.7, 171.6, 136.2, 123.6, 85.8, 84.7, 57.9, 55.9, 52.5, 52.4, 33.4, 31.9, 25.8, 22.6, 17.9, 14.5, 14.4, 14.3, −3.66; HRMS-ESI: *m/z* calculated for $C_{23}H_{38}O_5SiNa$ $[M+Na]^+$: 445.2381, found: 445.2381.

Compounds 18a and 18b:



Z-7

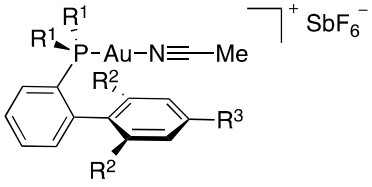
A solution of substrate **9** (942 mg, 2.23 mmol) in anhydrous 1,2-DCE (22 mL) was added to dry flask under argon charged with [JohnPhosAuNCMe]SbF_6 (51.6 mg, 0.0668 mmol) and activated 4Å molecular sieves (balls, 3.37 g) at room temperature. The resulting mixture was stirred for 24 h at room temperature, then quenched with a few drop of Et_3N, and filtered through a short pad of SiO_2 (elution EtOAc/Hexanes 50:50). The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Hexanes 0:100 to 10:90) to afford a mixture of compounds **16** and **17** contaminated by a side-product (936 mg, 99%). The yields of both compounds were determined by ^1H NMR using 1,4-diacetylbenzene as internal standard. Extensive purification did not provide a sample with an appropriate purity for complete characterization. Thus, the mixture was engaged in the next steps to obtain a full characterization of the products.

Screening of catalysts for the formation of **18a** and **18b**:

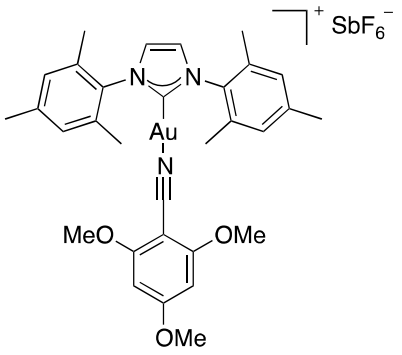
Entry	Catalyst	Solvent	Temperature (ºC)	Time (h)	Yield **18a**:**18b**[a] (%)
1	**A**	CH_2Cl_2	0	24	36 (4:1)
2	**A**	CH_2Cl_2	23	24	69 (3.3:1)
3	**A**	DCE	23	24	73 (2.3:1)
4	**A**	DCE[b]	23	24	82 (2:1)
5	**B**	CH_2Cl_2	0	24	71 (3.5:1)
6	**B**	CH_2Cl_2	23	24	35 (2:1)
7	**C**	CH_2Cl_2	0	24	traces[c]
8	**C**	CH_2Cl_2	23	24	50 (3:1)
9	**D**	CH_2Cl_2	0	24	traces[d]

10	**D**	CH_2Cl_2	23	24	traces[d]
11	**E**	CH_2Cl_2	0	24	30[e] (1:10)
12	**E**	CH_2Cl_2	23	24	31[e] (1:10)

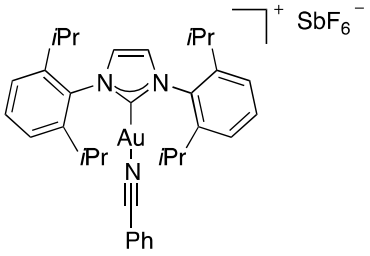
[a] Yields determined by ^{1}H NMR using 1,4-diacetylbenzene as internal standard.
[b] 4 Å molecular sieves added.
[c] Starting material recovered
[d] Starting material + decomposition
[e] Product contaminated by decomposed starting material



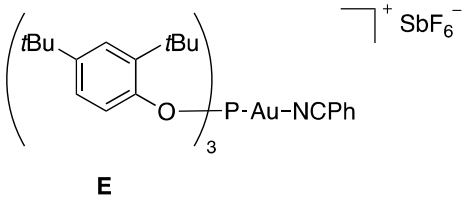
A: R = *t*Bu, R' = R'' = H
C: R = *t*Bu, R' = R'' = *i*Pr



D

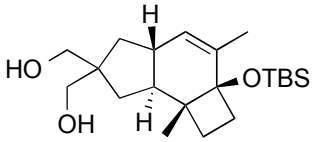


B



E

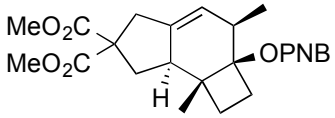
Compound 19:



A solution of compounds **18a** and **18b** (200 mg, 0.473 mmol) in anhydrous Et_2O (2 mL) was added dropwise to a suspension of $LiAlH_4$ (37.7 mg, 0.994 mmol) in anhydrous Et_2O (2 mL) at 0 ºC. The resulting suspension was stirred for 1 h at 0 ºC, then cautiously quenched with aqueous NaOH (1 M). The resulting mixture was vigorously stirred until a white precipitate appeared, then filtered through Celite (eluent EtOAc). The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 25:75) to afford diol 1**9** (90 mg, 52 % over two steps) as white crystals.

White solid: mp = 68–70 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45–5.42 (m, 1H), 3.63–3.55 (m, 4H), 2.61 (bs, 2H), 2.18–2.03 (m, 4H), 1.87–1.72 (m, 4H), 1.57–1.53 (m, 5H), 0.93 (s, 3H), 0.89 (s, 9H), 0.21 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 126.7, 82.0, 71.0, 70.9, 53.3, 46.2, 44.9, 37.3, 36.3, 31.9, 30.8, 28.7, 26.0, 18.7, 17.6, 15.3, –1.8, –2.3; HRMS-ESI: *m/z* calculated for $C_{21}H_{38}O_3SiNa$ $[M+Na]^+$: 389.2482, found: 389.2488.

Compound 20:



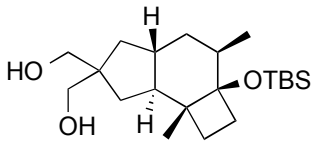
A solution of compounds **18a** and **18b** (50 mg, 0.118 mmol) in anhydrous THF (1 mL) was added to TASF (65 mg, 0.236 mmol), and the resulting mixture was refluxed for 3 h, then cooled down to room temperature and diluted with EtOAc and water. The layers were separated and the organic phase was washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed by rotary evaporation, and the crude product was engaged in the next steps without further purification.

DMAP (43.3 mg, 0.354 mmol) was added to a solution of the intermediate alcohol in anhydrous DCM (2 mL) at room temperature. Et_3N (0.05 mL, 0.354 mmol) and *p*-$NO_2C_6H_4COCl$ (65.7 mg, 0.354 mmol) were successively added and the resulting solution was stirred at room temperature for 24 h, then quenched with water and diluted with DCM. The layers were separated and the organic phase was washed with saturated aqueous $NaHCO_3$, brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 10:90) to give a mixture of esters. Recrystallization by slow diffusion (CH_2Cl_2/pentane) afforded ester **20** as white crystals (10.8 mg, 20%).

White solid: mp = 58–62 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–8.26 (m, 2H), 8.20–8.16 (m, 2H), 5.45–5.42 (m, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.27–3.23 (m, 1H), 3.21–3.15 (m, 1H), 2.94–2.79 (m, 2H), 2.53–2.48 (m, 1H), 2.28–2.20 (m, 1H), 2.11–2.04 (m, 1H), 1.75–1.69 (m, 1H), 1.41–1.35 (m, 1H), 1.22 (s, 3H), 1.01 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 172.0, 163.8, 150.4, 143.3, 136.5, 130.5, 123.5, 122.4, 89.9, 59.8, 52.9, 52.8, 47.8, 47.5, 39.3, 35.1, 33.6, 24.7, 23.1,

20.7, 14.3; HRMS-ESI: *m/z* calculated for $C_{24}H_{27}NO_8Na$ $[M+Na]^+$: 480.1629, found: 480.1624.

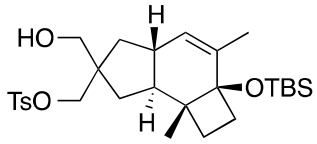
Compound 21:



A mixture of **19** (19 mg, 0.05 mmol) and $Pd(OH)_2/C$ (7 mg, 0.01 mmol, 20 mol%) in MeOH (3 mL) was charged in an autoclave that was pressurized with H_2 and stirred for 2 days at room temperature. The reaction suspension was then filtered though a short pad of silica (elution cyclohexane/EtOAc 1:1) and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 25:75) to afford diol **21** (18 mg, 95%) as a colorless oil.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60–3.52 (m, 4H), 2.14–2.00 (m, 5H), 1.85–1.80 (m, 1H), 1.78–1.74 (m, 1H), 1.61–1.47 (m, 5H), 1.38–1.32 (m, 1H), 1.28–1.24 (m, 1H), 1.04–0.99 (m, 1H), 0.95 (s, 3H), 0.87 (s, 9H), 0.85 (d, J = 7.0 Hz, 3H), 0.16 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 79.2, 71.6, 71.3, 48.1, 47.0, 45.4, 39.6, 35.6, 34.2, 33.9, 31.9, 31.4, 30.6, 26.2, 18.7, 16.8, 14.9, –1.4, –2.1; HRMS-ESI: *m/z* calculated for $C_{21}H_{40}O_3SiNa$ $[M+Na]^+$: 391.2639, found: 391.2638.

Compound 22:

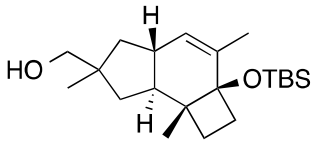


1:1

To a solution of **19** (40 mg, 0.109 mmol) in CH_2Cl_2 (0.5 mL) were added pyridine (0.1 mL) and tosyl chloride (22.9 mg, 0.12 mmol). The reaction mixture was stirred at room temperature overnight. Then, the solution was quenched with saturated NH_4Cl and extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 30:70) to afford tosylate (39 mg, 68 %) as a colorless oil. The product was directly used in the following step.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.79 (m, 2H), 7.36–7.34 (m, 2H), 5.39–5.36 (m, 1H), 3.98–3.94 (m, 1H), 3.90–3.85 (m, 1H), 3.51–3.47 (m, 1H),

3.44–3.39 (m, 1H), 2.45 (s, 3H), 2.15–1.95 (m, 3H), 1.83–1.70 (m, 4H), 1.56–1.44 (m, 5H), 1.16–0.94 (m, 2H), 0.89 (s, 1.5H), 0.88 (s, 4.5H), 0.87 (s, 4.5H), 0.84 (s, 1.5H), 0.20 (s, 3H), 0.14 (s, 1.5H), 0.13 (s, 1.5H).

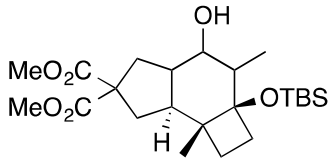


1:1

A solution of tosylate (35 mg, 0.067 mmol) in anhydrous Et_2O (1 mL) was added dropwise to a suspension of $LiAlH_4$ (7.7 mg, 0.202 mmol) in anhydrous Et_2O (1 mL) at 0 ºC. The resulting suspension was stirred for 1 h under reflux. Then, the reaction mixture was cooled down to room temperature, and cautiously quenched with aqueous NaOH (1 M). The resulting mixture was vigorously stirred until a white precipitate appeared, then filtered through Celite (eluent EtOAc). The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 4:96) to afford alcohol **21** (21 mg, 89%) as a colorless oil.

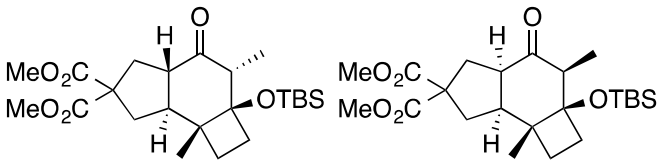
Pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46–5.42 (m, 1H), 3.40–3.34 (m, 2H), 2.21–2.01 (m, 3H), 1.87–1.74 (m, 3H), 1.66–1.58 (m, 1H), 1.57–1.51 (m, 5H), 1.34–1.31 (m, 1H), 1.15–1.11 (m, 1H), 1.07 (s, 1.5H), 1.05 (s, 1.5H), 0.94 (s, 1.5H), 0.92 (s, 1.5H), 0.90 (s, 4.5H), 0.89 (s, 4.5H), 0.21 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.8, 127.3, 127.2, 82.2, 82.1, 72.3, 72.2, 54.7, 53.6, 45.0, 42.1, 41.9, 41.6, 37.7, 36.7, 36.6, 36.2, 30.9, 30.8, 28.8, 28.7, 26.7, 26.5, 26.0, 18.7, 17.6, 15.3, 15.2, –1.8, –2.4; HRMS-ESI: *m/z* calculated for $C_{21}H_{38}O_2SiNa$ $[M+Na]^+$: 373.2534, found: 373.2539.

Compounds 23a and 23b:



BH_3·THF (1 M in THF, 2 mL, 2 mmol) was added to a solution of **18a** and **18b** (196 mg, 0.47 mmol) in THF (5 mL). The mixture was stirred at room temperature overnight and NaOH (10 wt%, 5 mL) followed by H_2O_2 (30 wt%, 5 mL) were added. The resulting mixture was stirred at room temperature for 2 h. EtOAc was added and

phases were separated. The aqueous layer was extracted with EtOAc (3 times). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent EtOAc/Cyclohexane 85:15) to afford the intermediate secondary alcohol as a mixture of diastereoisomers not separable. Thus, the alcohol was engaged in the oxidation step.

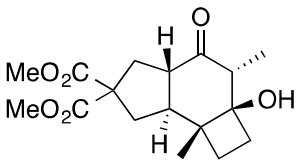


Dess-Martin periodinane (171 mg, 0.40 mmol, 2 equiv) was added in one portion to a solution of the previous alcohol (89 mg, 0.20 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 3 h, and a 1:1 solution of saturated $NaHCO_3$ and saturated Na_2SO_3 was added. The resulting biphasic mixture was stirred until it became clear and phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 times). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent EtOAc/Pentane 1:15) to afford the ketones **23a** (70 mg, 59%) and **23b** (22 mg, 19%).

Ketone **23a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (2 s, 6H), 2.60–2.69 (m, 1H), 2.54–2.41 (m, 3H), 2.35 (qd, J = 7.0, 1.1 Hz, 1H), 2.12–1.74 (m, 5H), 1.53–1.45 (m, 1H), 1.12–1.03 (m, 5H), 0.90 (s, 9H), 0.19 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5, 173.0, 172.8, 87.7, 58.4, 54.0, 53.0, 52.9, 52.3, 50.0, 46.5, 36.2, 32.0, 28.7, 28.4, 26.0, 18.7, 14.9, 9.5, –1.8, –2.1; HRMS-ESI: *m/z* calculated for $C_{23}H_{38}O_6SiNa$ $[M+Na]^+$: 461.2330, found: 461.2320.

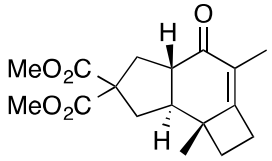
Ketone **23b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.70 (s, 3H), 3.01–3.07 (m, 1H), 2.92 (dd, J = 14.2, 2.2 Hz, 1H), 2.87 (tt, J = 6.7, 1.3 Hz, 1H), 2.47 (ddd, J = 13.7, 7.9, 6.2 Hz, 1H), 2.31 (dd, J = 14.2, 7.4 Hz, 1H), 2.26–2.19 (m, 1H), 2.16–2.08 (m, 1H), 2.02–1.93 (m, 3H), 1.65–1.48 (m, 1H), 1.15 (s, 3H), 0.99 (d, J = 6.7 Hz, 3H), 0.87 (s, 9H), 0.15 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 173.8, 172.0, 84.8, 57.6, 53.0, 52.8, 52.7, 50.4, 50.0, 45.3, 36.8, 33.2, 32.2, 28.1, 26.1, 22.6, 18.6, 8.6, –1.2, –1.9; HRMS-ESI: *m/z* calculated for $C_{23}H_{38}O_6SiNa$ $[M+Na]^+$: 461.2330, found: 461.2325.

Compound 24:



A solution of ketone **23a** (70 mg, 0.16 mmol) in THF (3 mL) was added to TASF (88 mg, 0.32 mmol, 2 equiv) and the mixture was refluxed for 2 h. The reaction mixture was cooled to rt. Water and EtOAc were added and phases were separated. The aqueous layer was extracted with EtOAc (3 times). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent EtOAc/cyclohexane 10:90) to afford alcohol (32 mg, 62%) as a colorless oil. The product was directly engaged in the formation of the enone.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.70 (s, 3H), 3.14–3.01 (m, 1H), 2.78–2.66 (m, 2H), 2.56 (ddd, J = 13.3, 11.0, 7.8 Hz, 1H), 2.40 (dd, J = 12.9, 6.5 Hz, 1H), 2.33–2.08 (m, 2H), 1.98–1.83 (m, 3H), 1.60 (d, J = 1.5 Hz, 3H), 1.32 (d, J = 0.7 Hz, 3H).



Et_3N (0.1 mL, 0.72 mmol), followed by MsCl (0.05 mL, 0.65 mmol) were added to a solution of the previous crude ketoalcohol (32 mg) in CH_2Cl_2 (2 mL) at 0 ºC. The mixture was stirred for 1 h, and DBU (0.2 mL, 1.33 mmol) was then added. The reaction mixture was stirred overnight and quenched with saturated $NaHCO_3$. Phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 times). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent EtOAc/Cyclohexane 1:9) to afford the enone **24** (17 mg, 34% over 2 steps) as a colorless oil.

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.71 (s, 3H), 3.09 (dddd, J = 15.3, 11.3, 7.8, 1.7 Hz, 1H), 2.79–2.67 (m, 2H), 2.57 (ddd, J = 13.3, 11.0, 7.8 Hz, 1H), 2.41 (dd, J = 12.9, 6.5 Hz, 1H), 2.27 (ddd, J = 13.3, 12.2, 6.5 Hz, 1H), 2.17 (dd, J = 14.1, 11.0 Hz, 1H), 2.01–1.81 (m, 3H), 1.61 (d, J = 1.5 Hz, 3H), 1.33 (d, J = 0.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 172.9, 172.8, 169.2, 125.4, 57.8, 54.7,

52.9, 52.8, 49.1, 48.6, 35.3, 33.8, 33.0, 30.4, 16.1, 9.4; HRMS-ESI: *m/z* calculated for $C_{17}H_{22}O_5Na$ $[M+Na]^+$: 329.1359, found: 329.1357.

Crystal data for compound 18

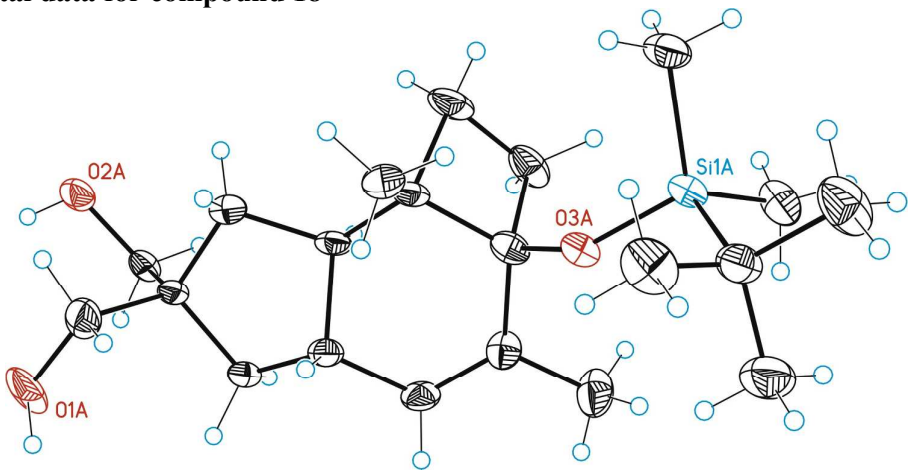


Table 1. Crystal data and structure refinement for mo_dlb357b_0m.

Identification code	mo_dlb357b_0m	
Empirical formula	C21 H38 O3 Si	
Formula weight	366.60	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 13.371(3) Å	a= 90.307(6) °.
	b = 15.006(3) Å	b = 91.421(6) °.
	c = 22.501(4) Å	g = 101.627(6) °.
Volume	4420.5(14) Å^3	
Z	8	
Density (calculated)	1.102 Mg/m^3	
Absorption coefficient	0.122 mm^{-1}	
F(000)	1616	
Crystal size	0.20 x 0.10 x 0.02 mm^3	
Theta range for data collection	0.91 to 26.54 °.	
Index ranges	-16 <=h<=16 ,-18 <=k<=17 ,-28 <=l<=28	
Reflections collected	42414	
Independent reflections	18124 [R(int) = 0.0684]	
Completeness to theta =26.54 °	98.5%	
Absorption correction	Empirical	
Max. and min. transmission	0.9951 and 0.9644	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	18124 / 19 / 979	

Goodness-of-fit on F^2	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0724 , wR2 = 0.1658
R indices (all data)	R1 = 0.1590 , wR2 = 0.2044
Largest diff. peak and hole	1.037 and -0.464 e.Å^{-3}

Crystal data for compound 19

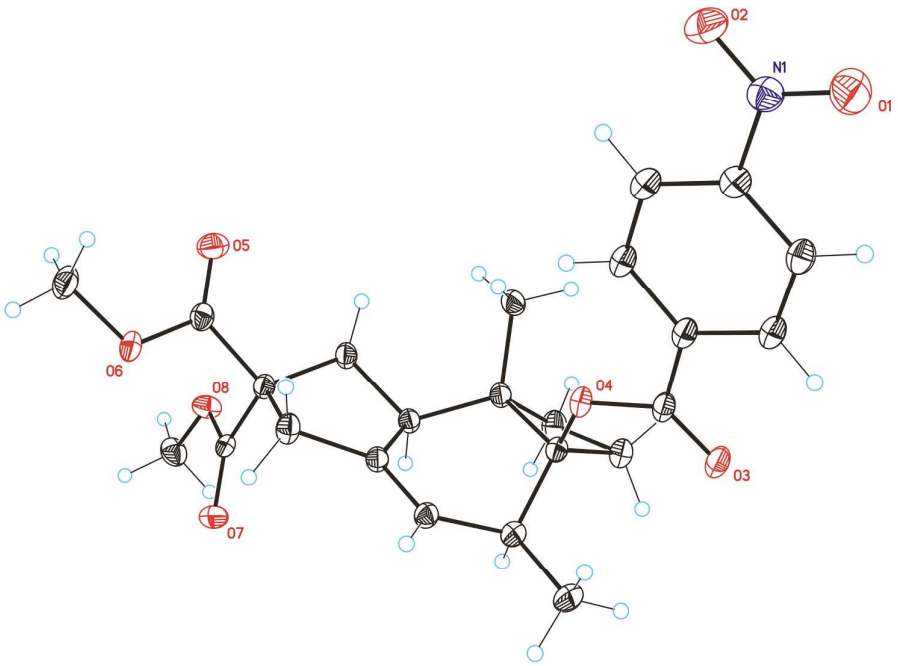
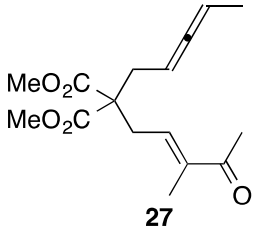


Table 1. Crystal data and structure refinement for JCC150_0m.

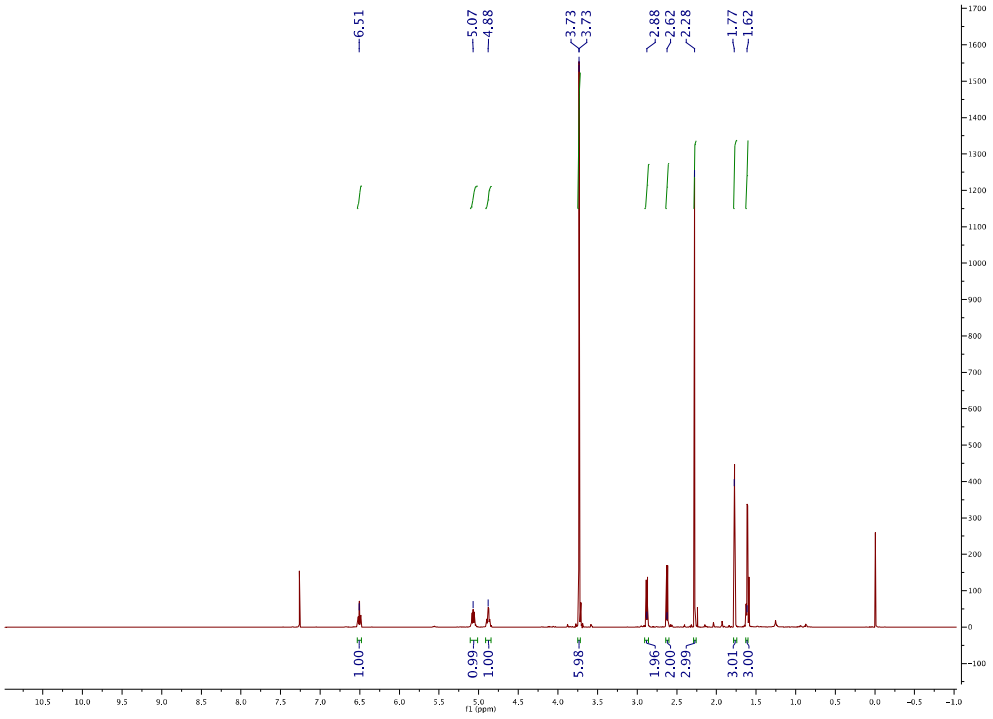
Identification code	JCC150_0m	
Empirical formula	C24 H27 N O8	
Formula weight	457.47	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.5760(4) Å	⟨= 93.034(3) °.
	b = 9.6524(5) Å	® = 90.188(3) °.
	c = 15.2400(8) Å	© = 96.049(2) °.
Volume	1106.65(10) Å^3	
Z	2	
Density (calculated)	1.373 Mg/m^3	

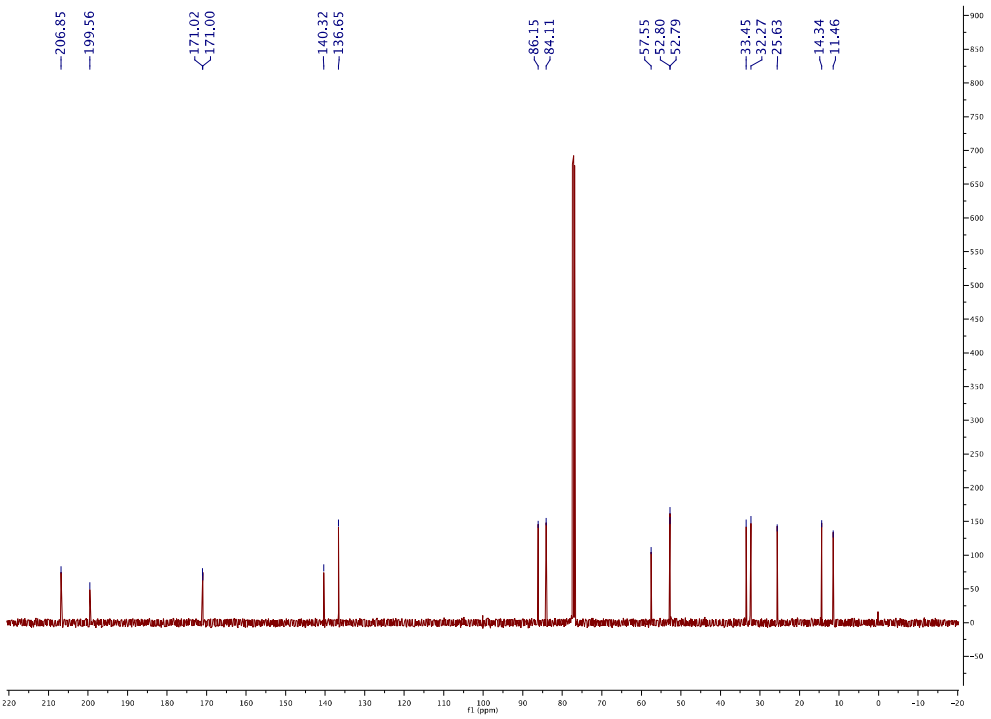
Absorption coefficient	0.103 mm^{-1}
F(000)	484
Crystal size	0.10 x 0.05 x 0.03 mm^3
Theta range for data collection	1.34 to 38.95 °.
Index ranges	-13 <=h<=12 ,-16 <=k<=16 ,-26 <=l<=26
Reflections collected	11136
Independent reflections	11136 [R(int) = 0.0368]
Completeness to theta =38.95 °	0.868 %
Absorption correction	Empirical
Max. and min. transmission	0.9969 and 0.9897
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11136 / 0 / 298
Goodness-of-fit on F^2	1.497
Final R indices [I>2sigma(I)]	R1 = 0.0674 , wR2 = 0.2036
R indices (all data)	R1 = 0.0872 , wR2 = 0.2182
Largest diff. peak and hole	1.264 and -0.408 e.$Å^{-3}$

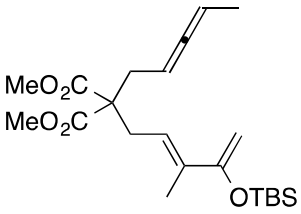
NMR Data


MeO2C
MeO2C
O

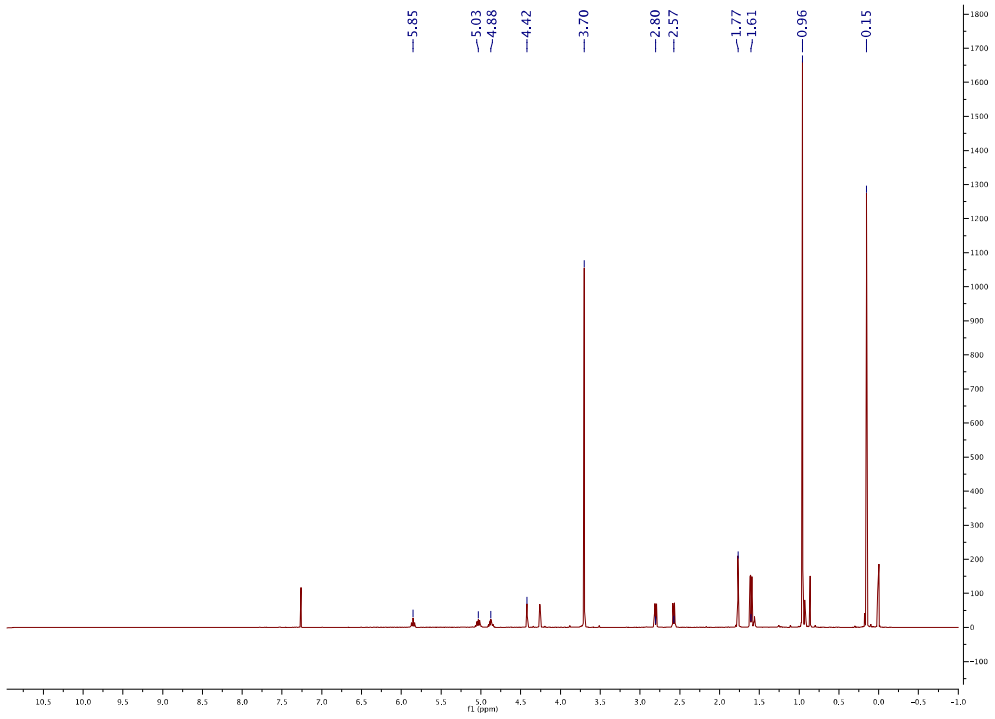
27

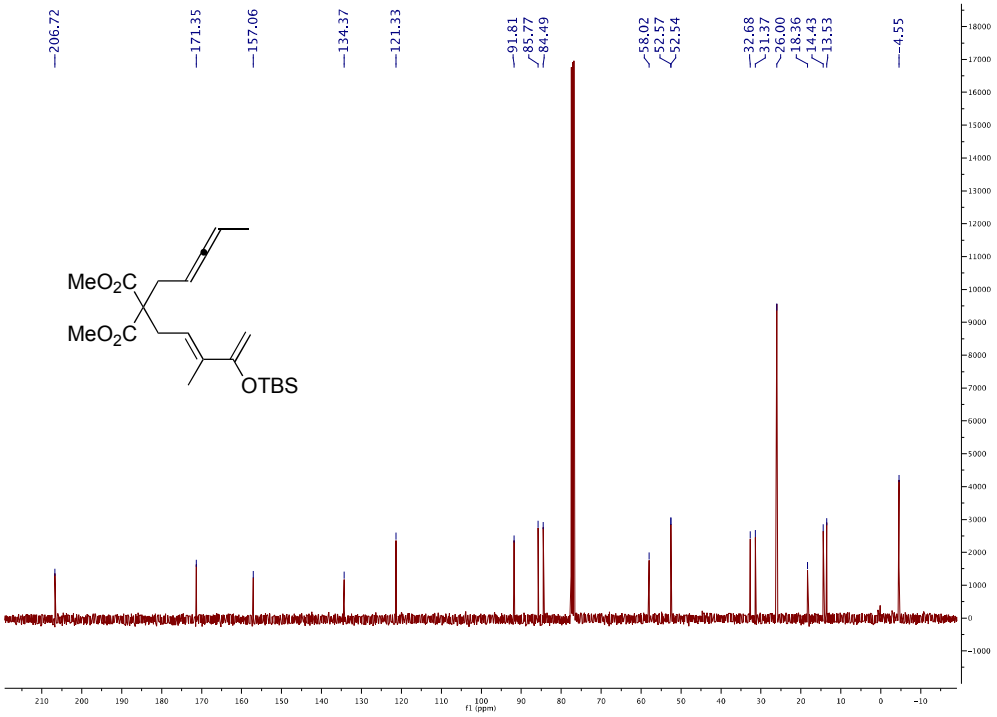

6.51
5.07
4.88
3.73
3.73
2.88
2.62
2.28
1.77
1.62
1.00
0.99
1.00
5.98
1.96
2.00
2.99
3.01
3.00
f1 (ppm)

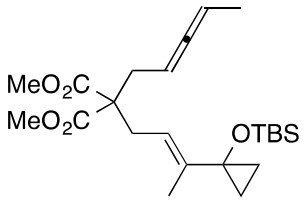

206.85
199.56
171.02
171.00
140.32
136.65
86.15
84.11
57.55
52.80
52.79
33.45
32.27
25.63
14.34
11.46
f1 (ppm)


MeO2C
MeO2C
OTBS

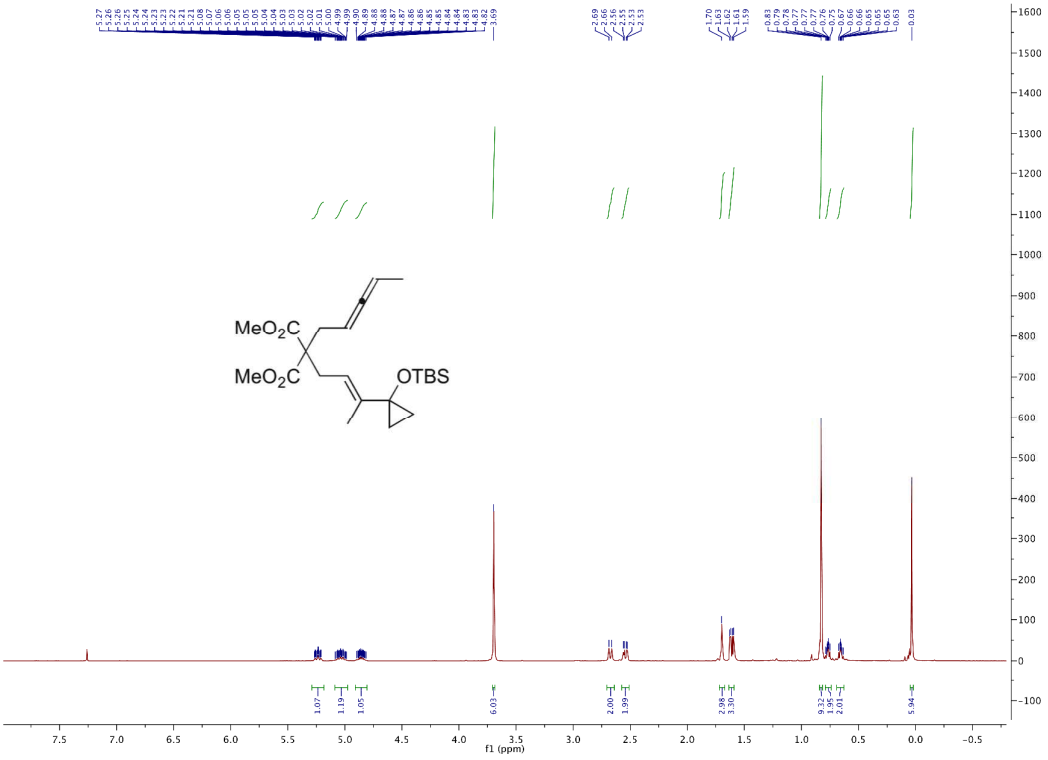
28

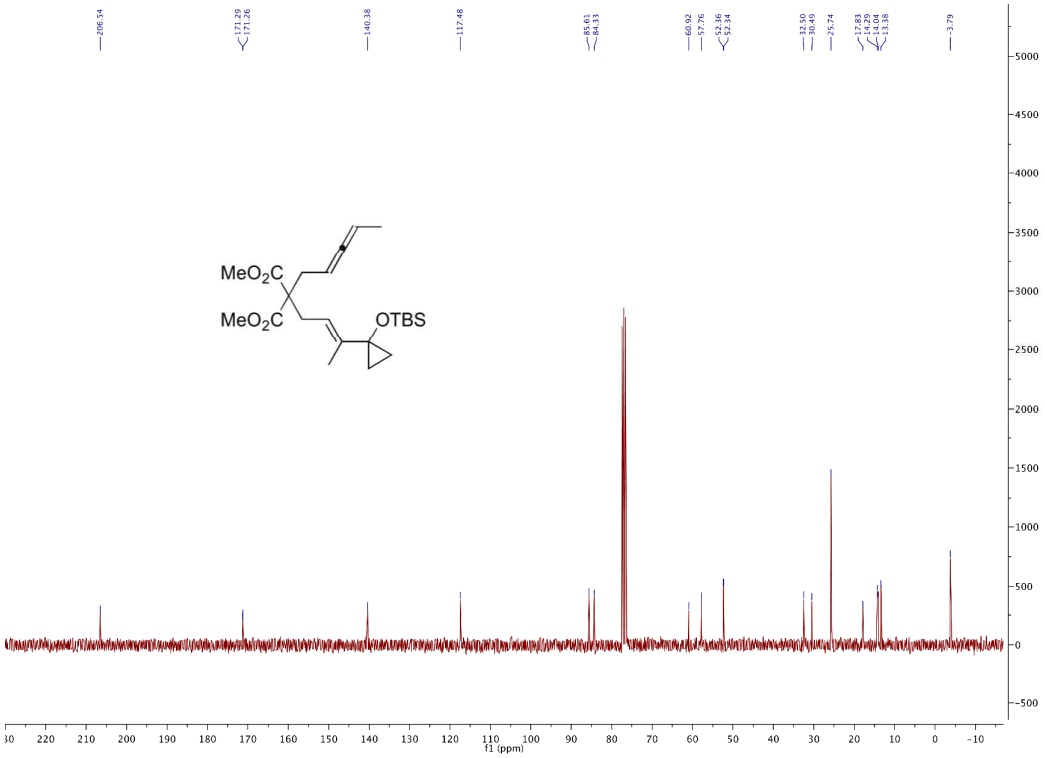

5.85
5.03
4.88
4.42
3.70
2.80
2.57
1.77
1.61
0.96
0.15
f1 (ppm)

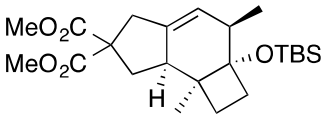

206.72
171.35
157.06
134.37
121.33
91.81
85.77
84.49
58.02
52.57
52.54
32.68
31.37
26.00
18.36
14.43
13.53
4.55
MeO2C
MeO2C
OTBS
f1 (ppm)



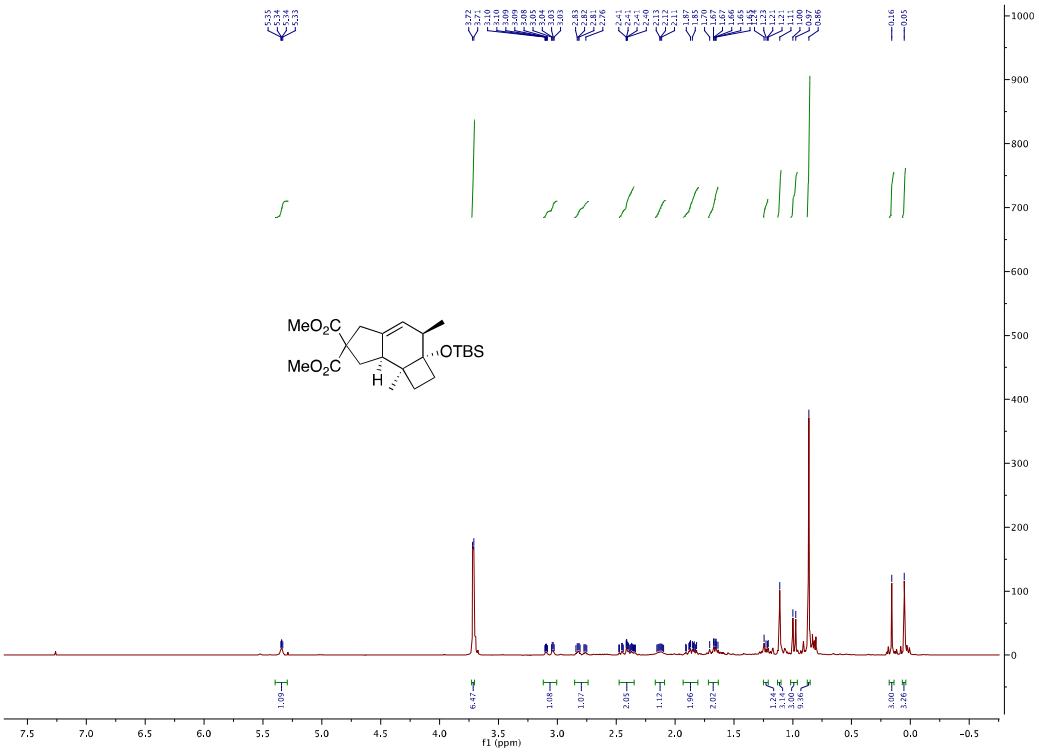
***E*-7**

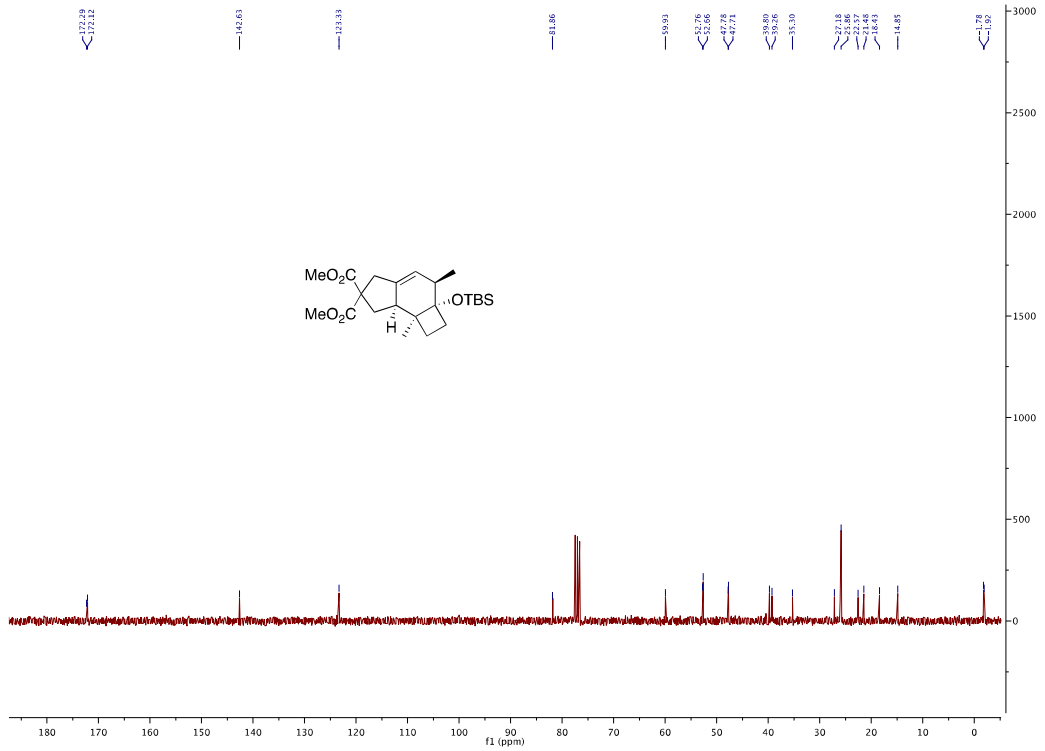


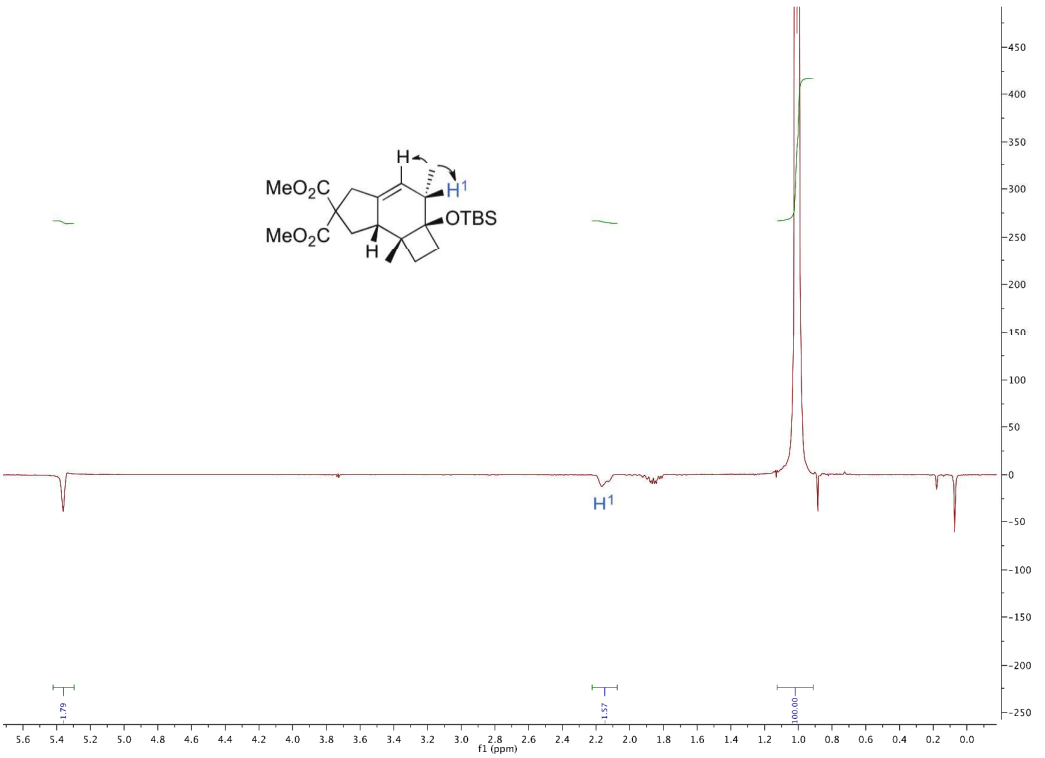

206.54
171.29
171.26
140.38
117.48
85.61
84.33
66.92
57.76
52.46
52.34
32.50
30.49
25.74
17.83
17.25
14.04
13.38
-3.79
MeO2C
MeO2C
OTBS
f1 (ppm)

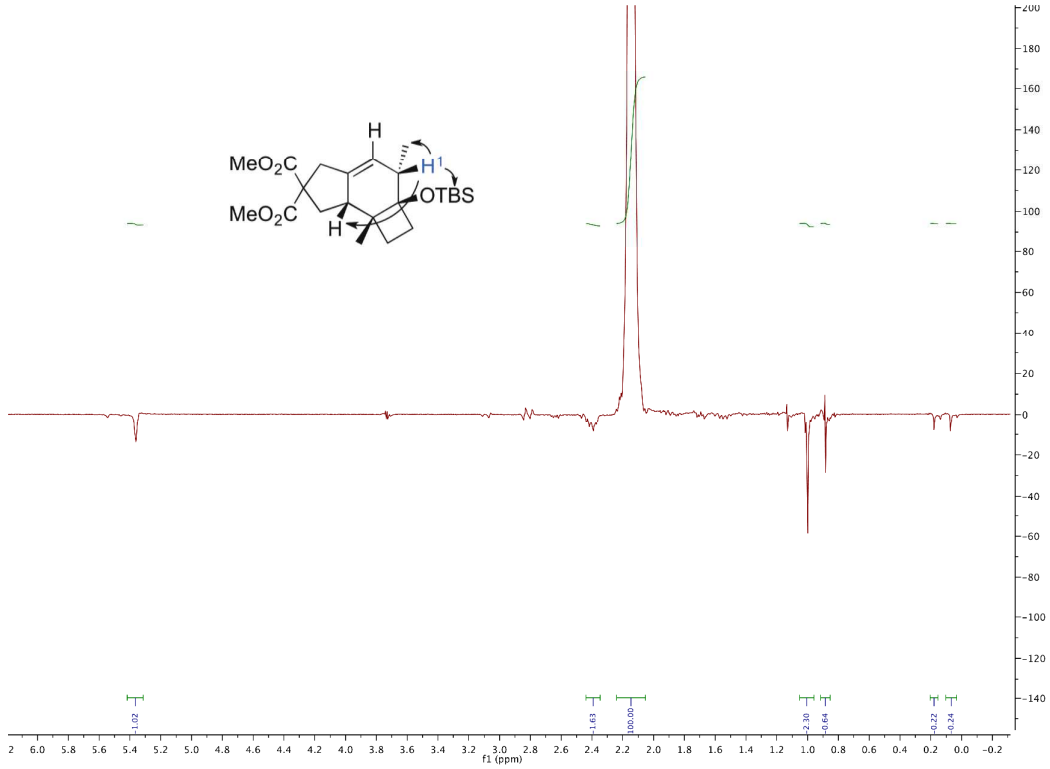


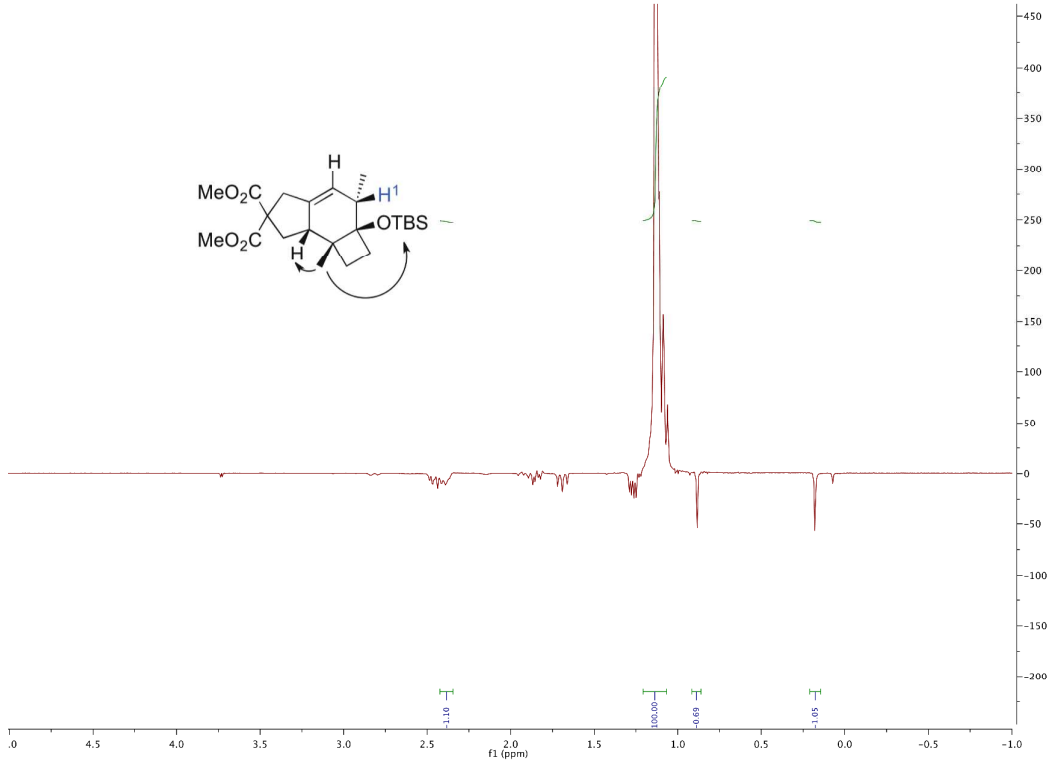
8a

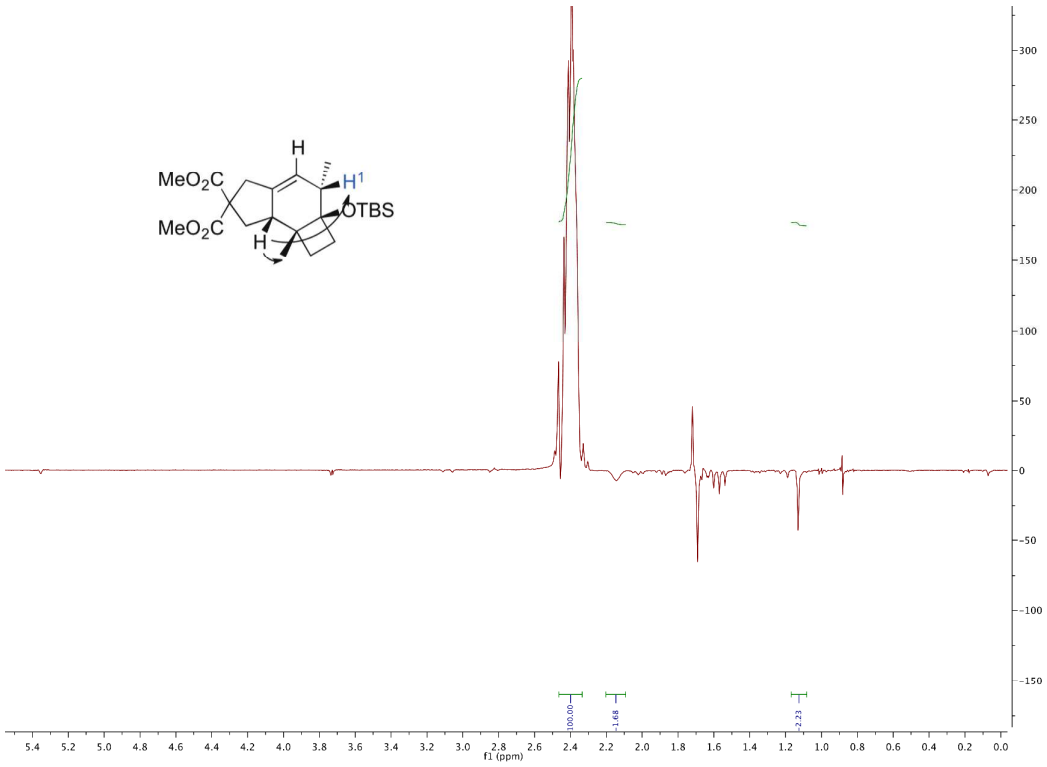


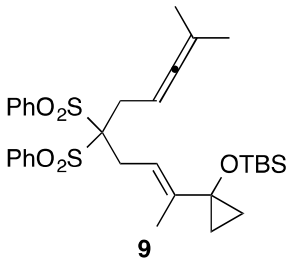

172.29
172.12
142.63
123.33
81.86
59.93
52.76
52.66
47.78
47.71
39.80
39.26
35.30
27.18
25.86
23.77
21.48
18.43
14.85
1.78
1.92
MeO2C
MeO2C
OTBS
H
f1 (ppm)


MeO2C
MeO2C
H
H1
OTBS
H
H1
1.79
1.57
100.00
f1 (ppm)

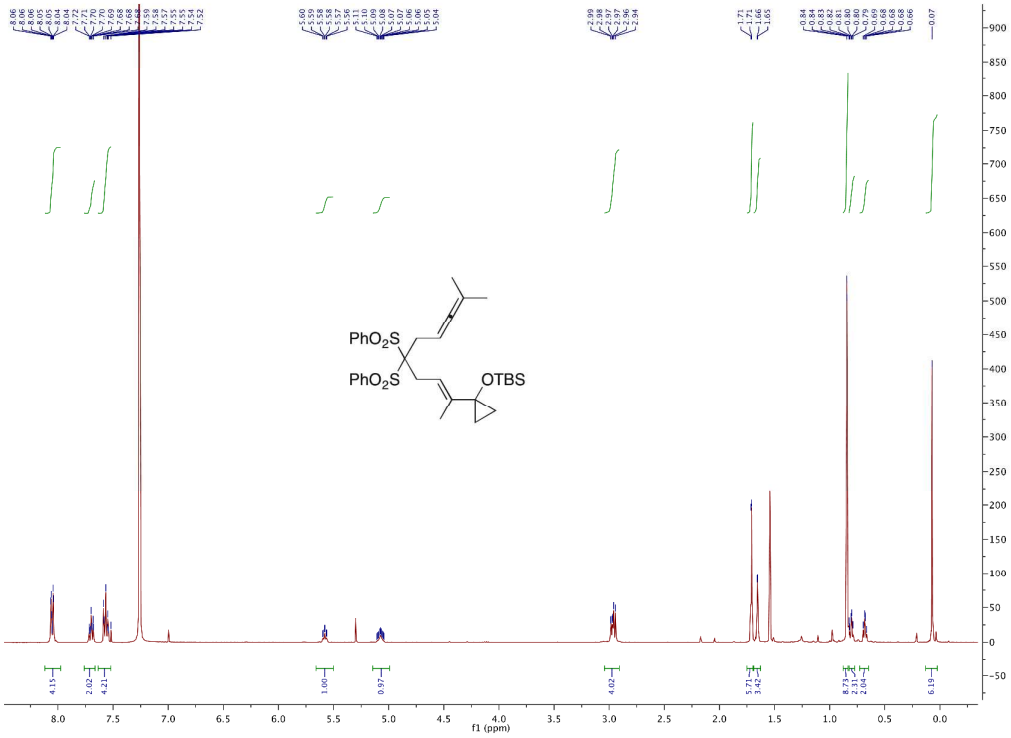

H
MeO2C
MeO2C
H1
OTBS
H
f1 (ppm)

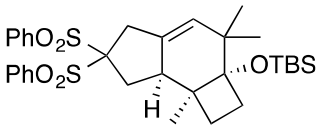

H
MeO2C
MeO2C
H1
OTBS
H
f1 (ppm)


H
MeO2C
H1
OTBS
MeO2C
H
300
250
200
150
100
50
0
−50
−100
−150
100.00
1.68
2.23
5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0
f1 (ppm)

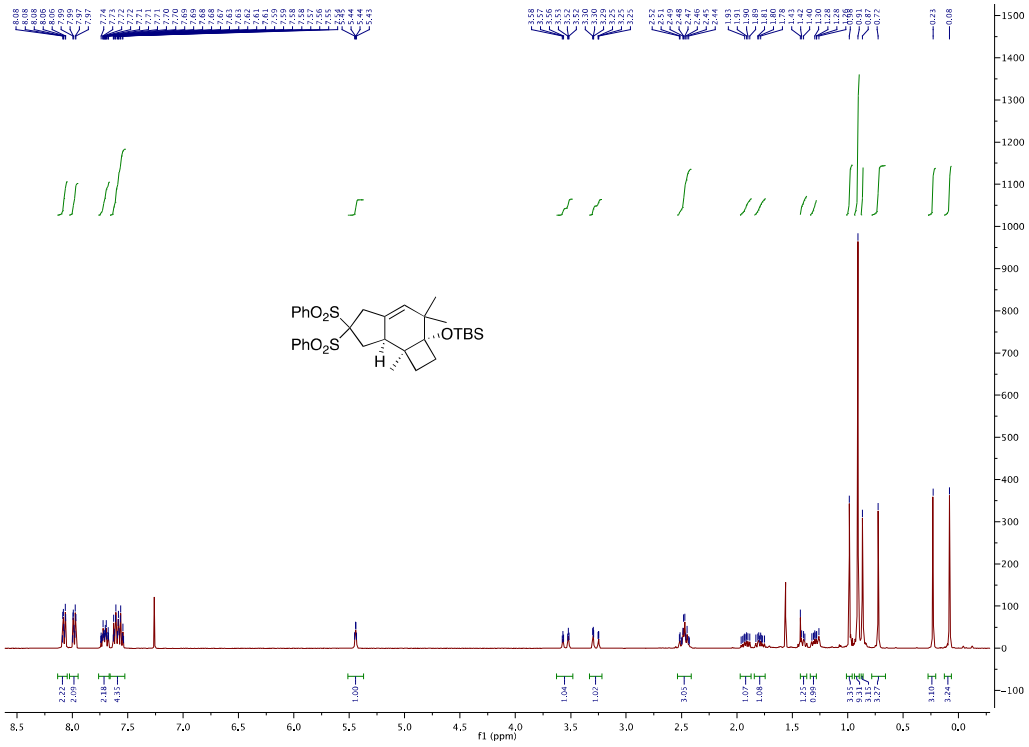


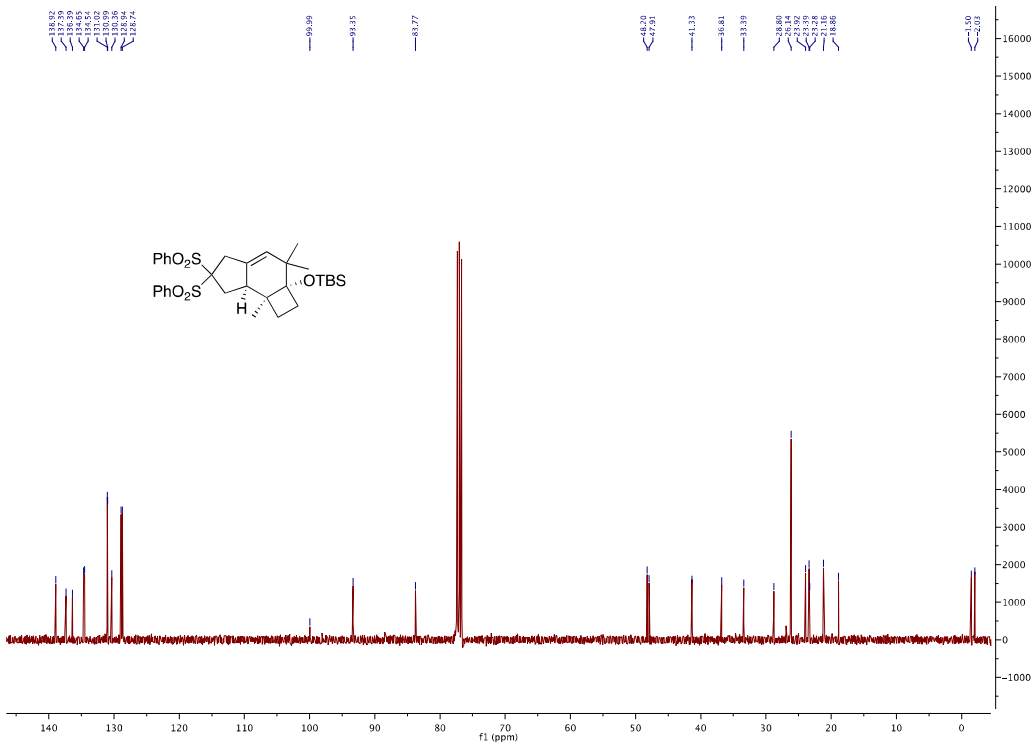
9



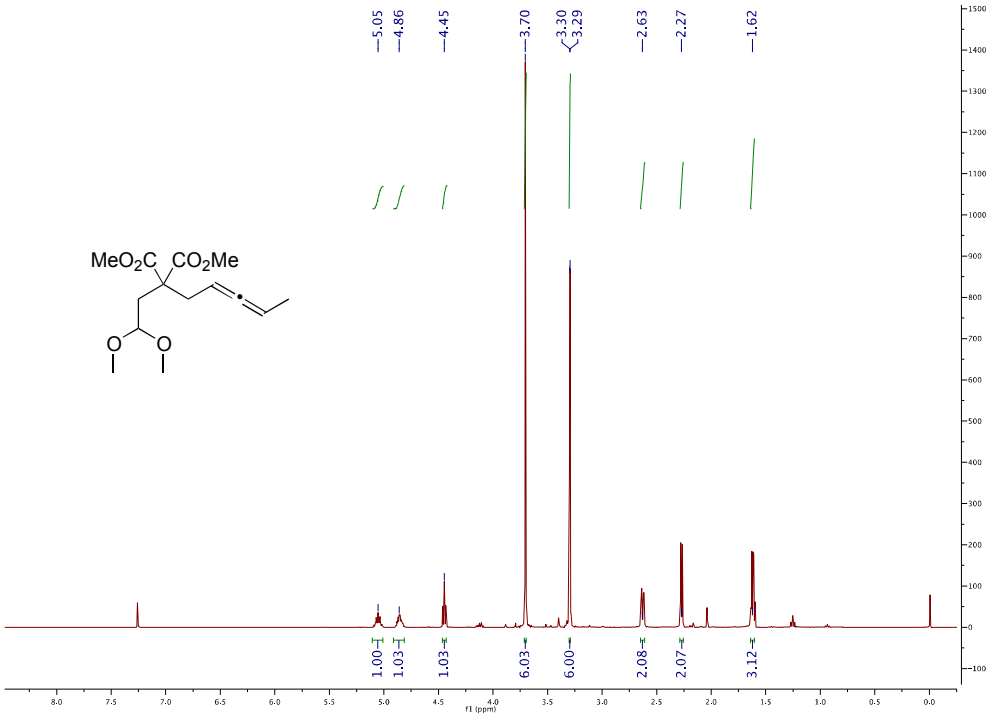


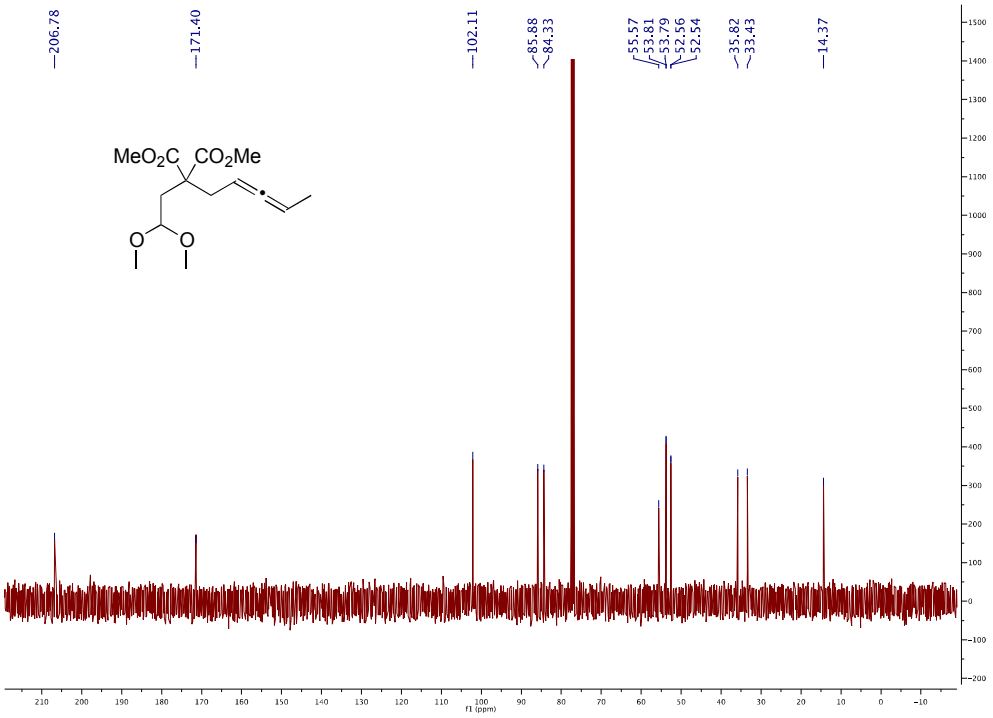
10



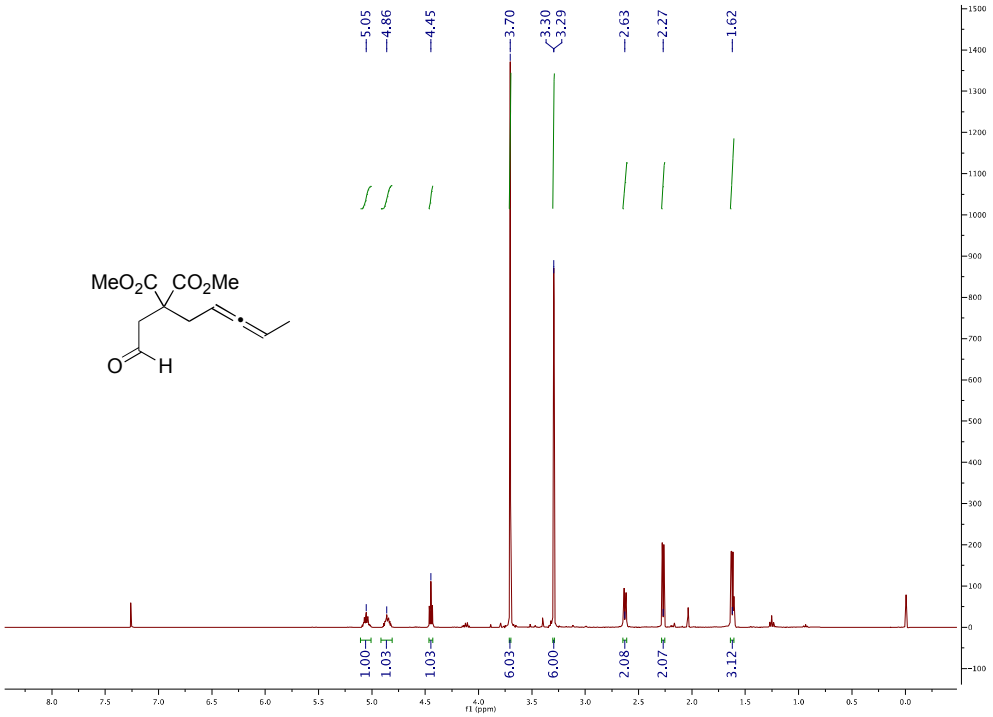

138.52
137.99
136.39
134.65
134.47
131.02
131.00
130.38
128.94
128.74
99.99
93.35
83.77
48.20
47.91
41.33
36.81
33.39
28.80
26.44
23.92
23.79
23.28
21.16
18.86
-1.50
-2.03
PhO2S
PhO2S
OTBS
H
f1 (ppm)

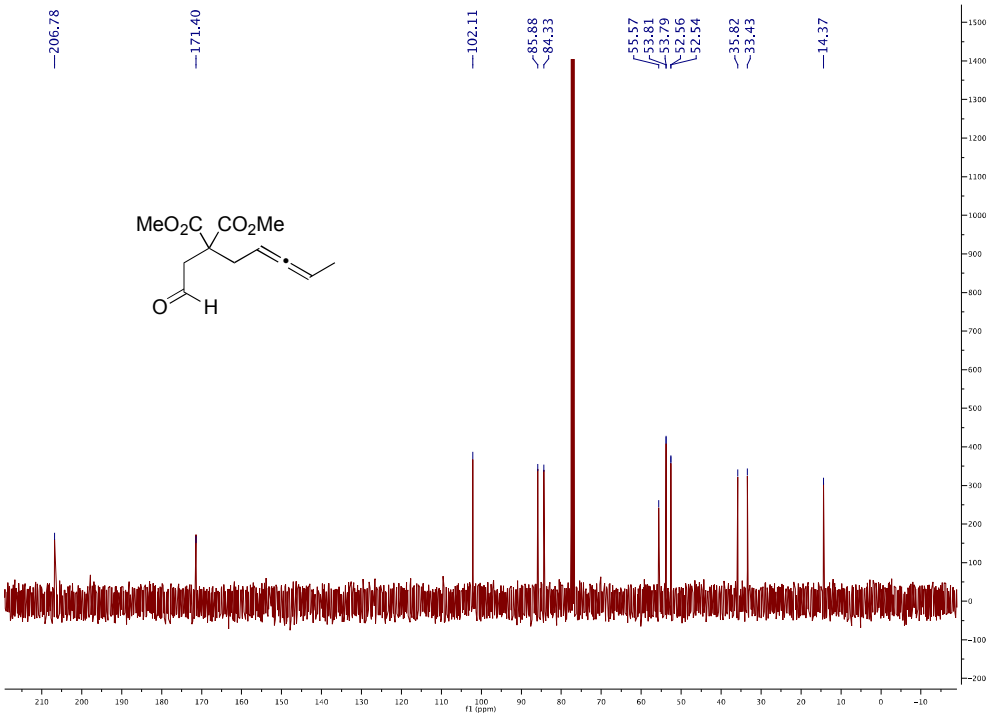
Compound **13**:


5.05
4.86
4.45
3.70
3.30
3.29
2.63
2.27
1.62
MeO2C CO2Me
O
O
1.00
1.03
1.03
6.03
6.00
2.08
2.07
3.12
f1 (ppm)

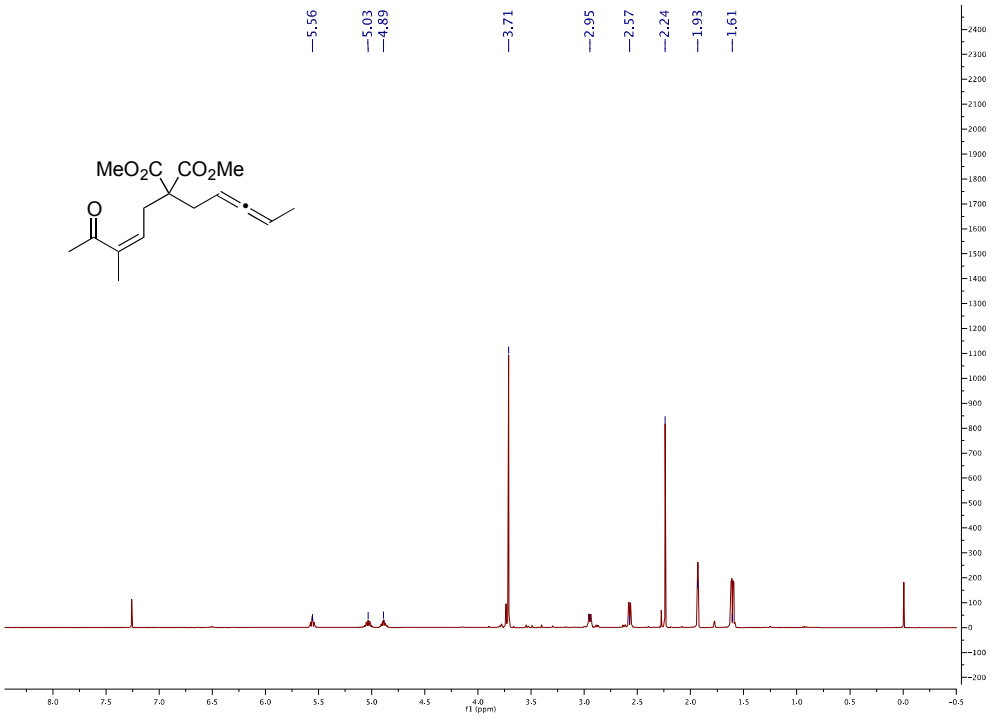

206.78
171.40
102.11
85.88
84.33
55.57
53.81
53.79
52.56
52.54
35.82
33.43
14.37
MeO2C CO2Me
O
O
f1 (ppm)

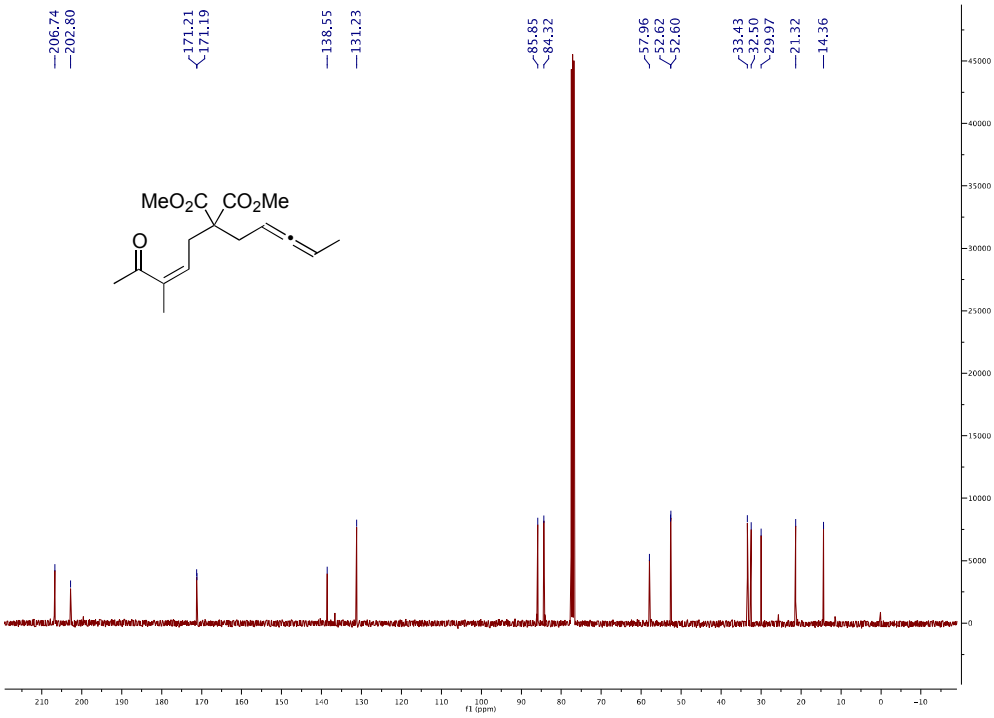
Compound **14**:


5.05
4.86
4.45
3.70
3.30
3.29
2.63
2.27
1.62
MeO2C CO2Me
O H
1.00
1.03
1.03
6.03
6.00
2.08
2.07
3.12
f1 (ppm)

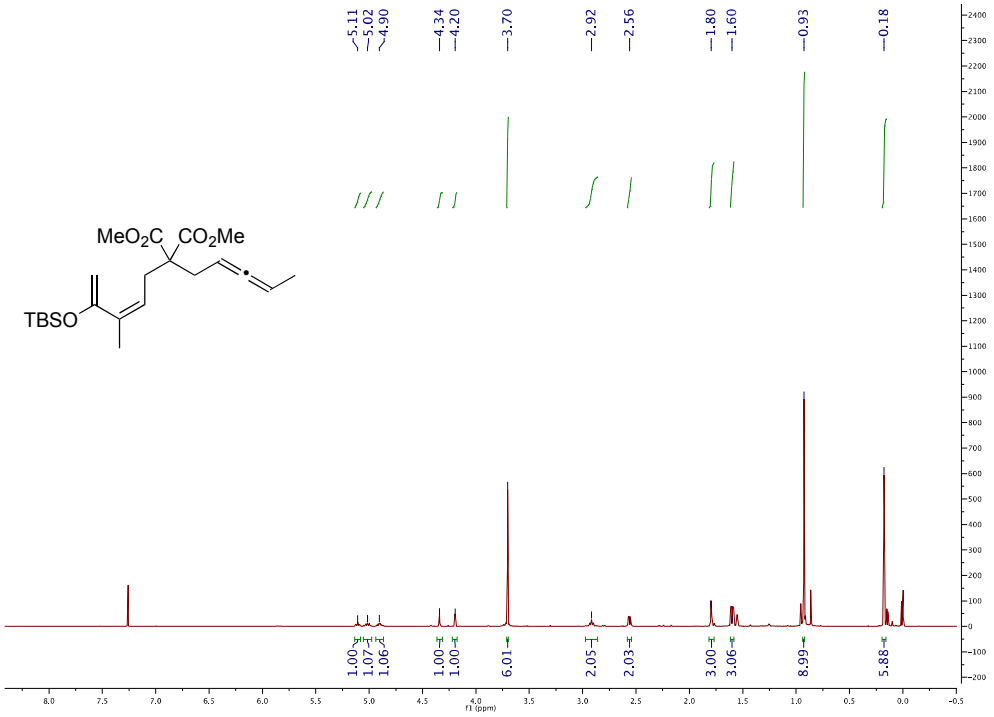

206.78
171.40
102.11
85.88
84.33
55.57
53.81
53.79
52.56
52.54
35.82
33.43
14.37
MeO2C CO2Me
O H
f1 (ppm)

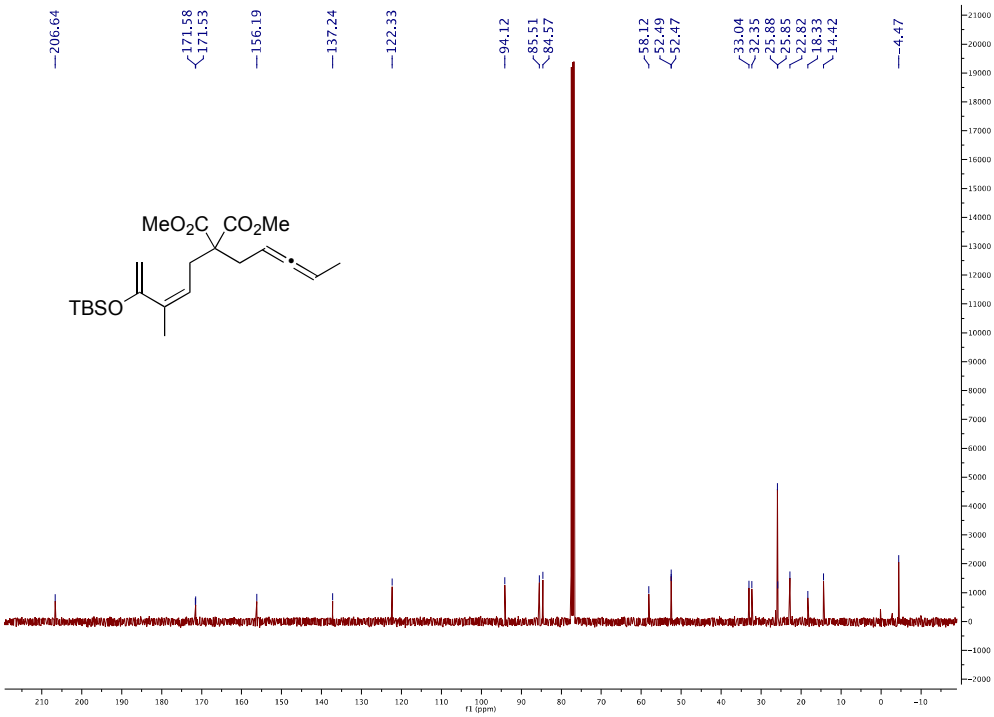
Compound **16**:


5.56
5.03
4.89
3.71
2.95
2.57
2.24
1.93
1.61
MeO2C CO2Me
O
f1 (ppm)

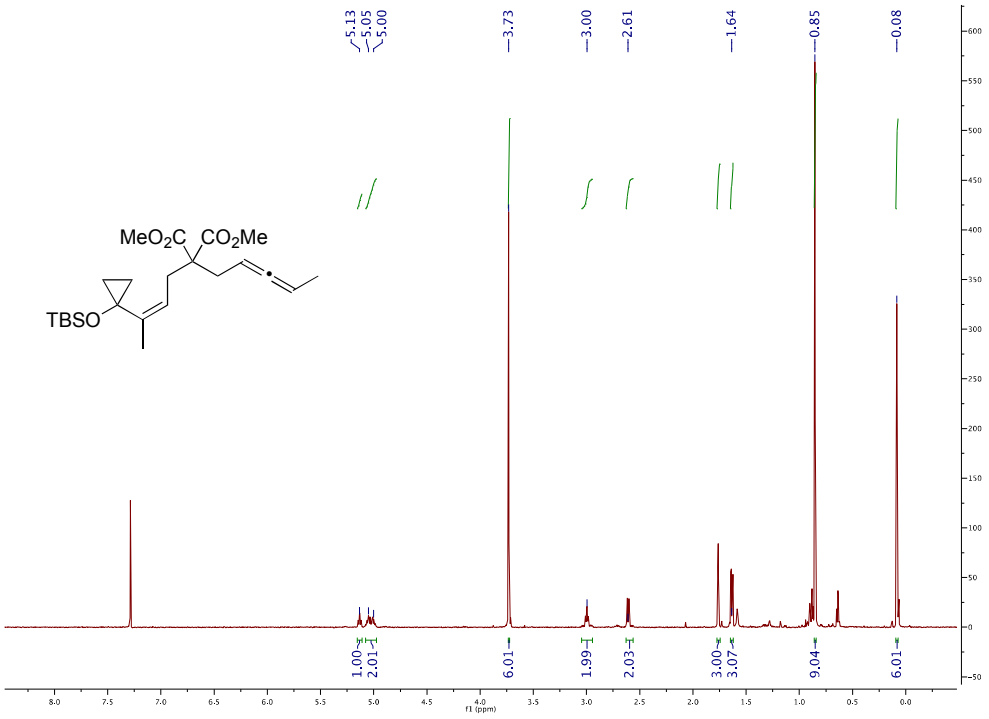

206.74
202.80
171.21
171.19
138.55
131.23
85.85
84.32
57.96
52.62
52.60
33.43
32.50
29.97
21.32
14.36
MeO2C CO2Me
O
f1 (ppm)

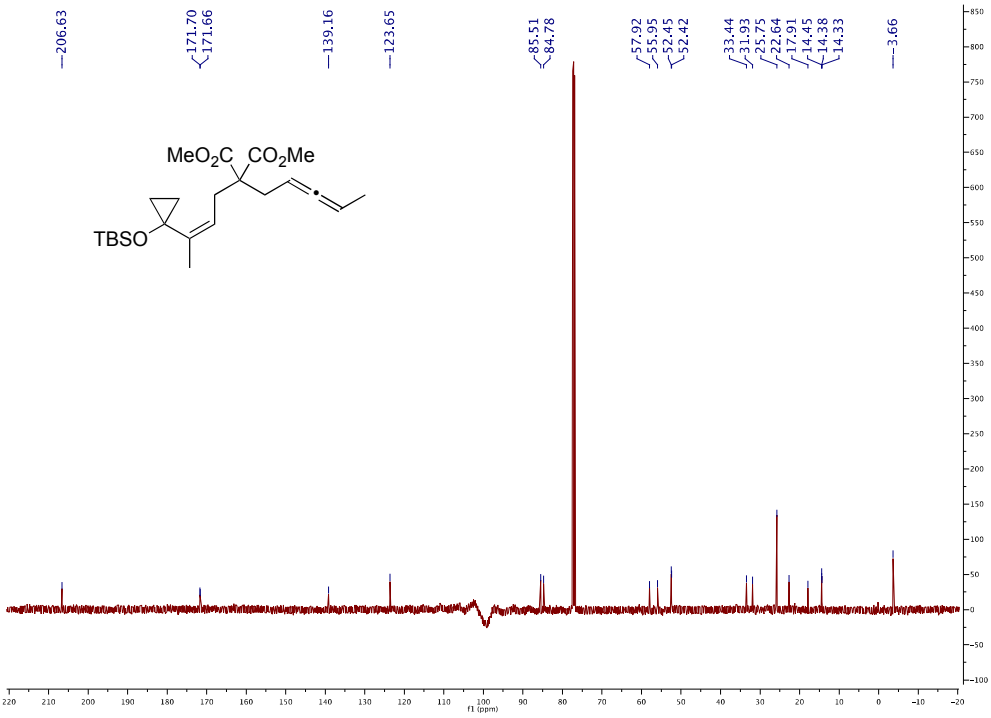
Compound **17**:

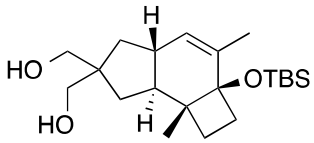

5.11
5.02
4.90
4.34
4.20
3.70
2.92
2.56
1.80
1.60
0.93
0.18
MeO2C CO2Me
TBSO
1.00
1.07
1.06
1.00
1.00
6.01
2.05
2.03
3.00
3.06
8.99
5.88
f1 (ppm)


206.64
171.58
171.53
156.19
137.24
122.33
94.12
85.51
84.57
58.12
52.49
52.47
33.04
32.35
25.88
25.85
22.82
18.33
14.42
-4.47
MeO2C CO2Me
TBSO
f1 (ppm)

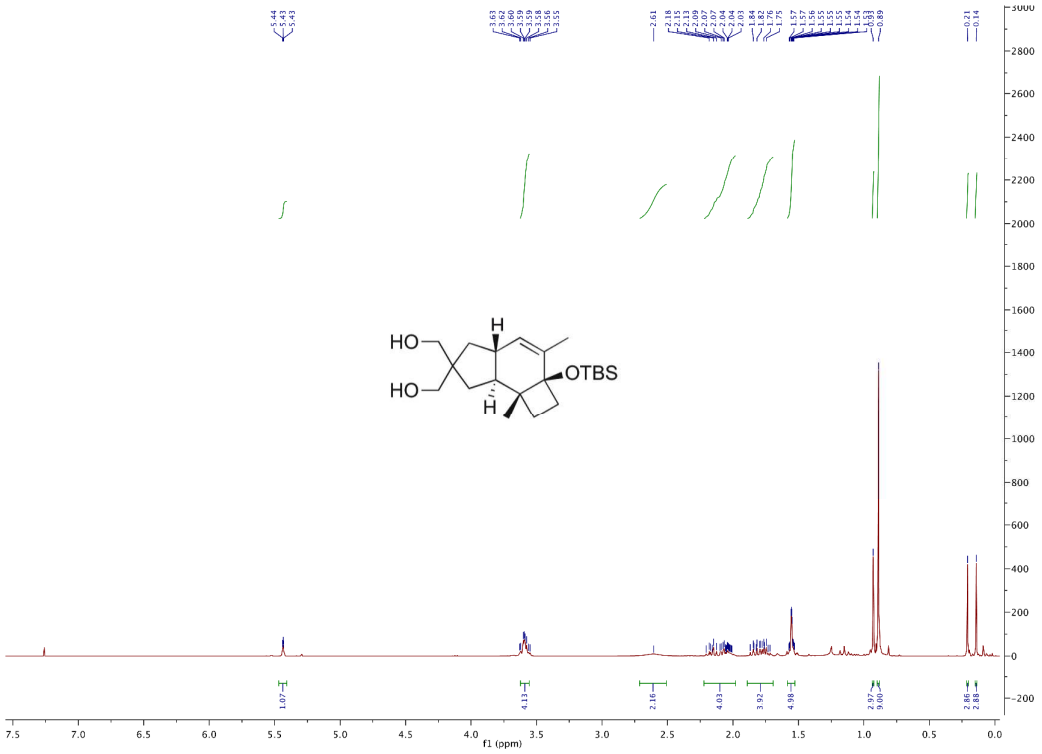
Compound ***Z*-7**:

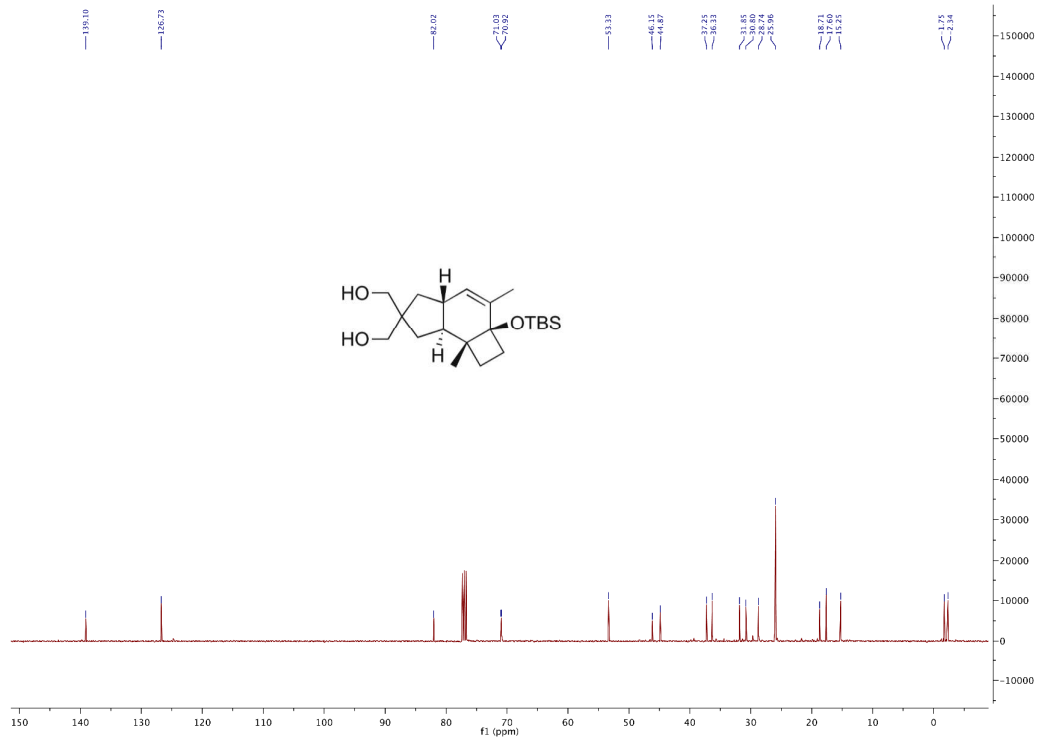

5.13
5.05
5.00
3.73
3.00
2.61
1.64
0.85
0.08
MeO2C CO2Me
TBSO
1.00
2.01
6.01
1.99
2.03
3.00
3.07
9.04
6.01
f1 (ppm)

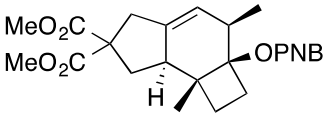

206.63
171.70
171.66
139.16
123.65
85.51
84.78
57.92
55.95
52.45
52.42
33.44
31.93
25.75
22.64
17.91
14.45
14.38
14.33
3.66
MeO2C CO2Me
TBSO
f1 (ppm)



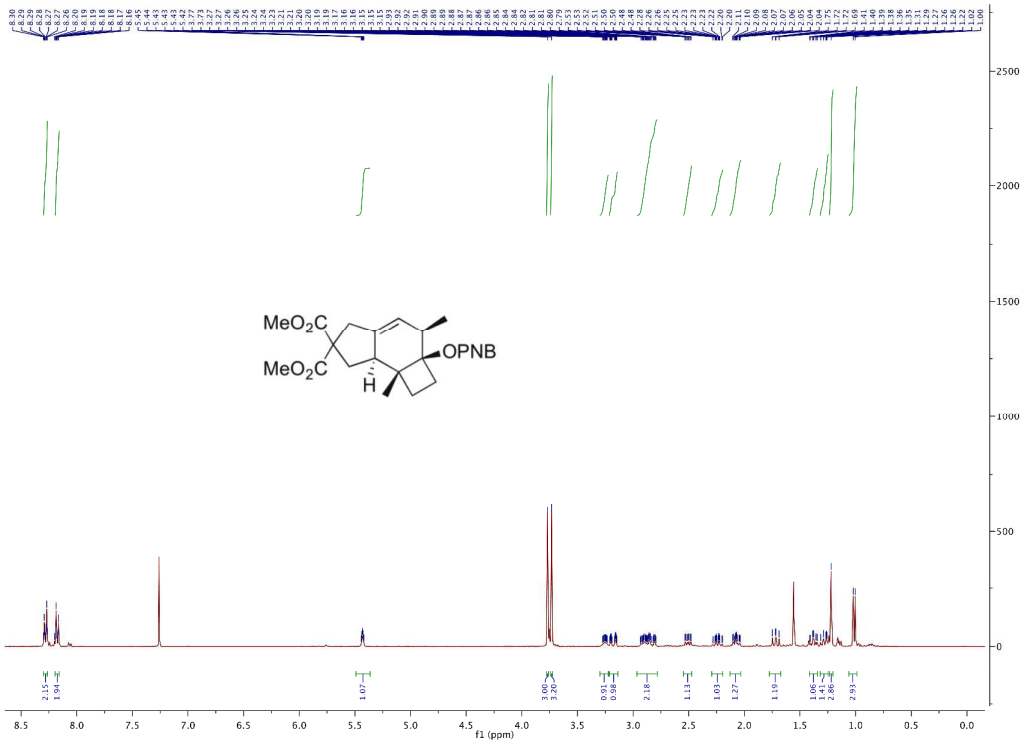
19

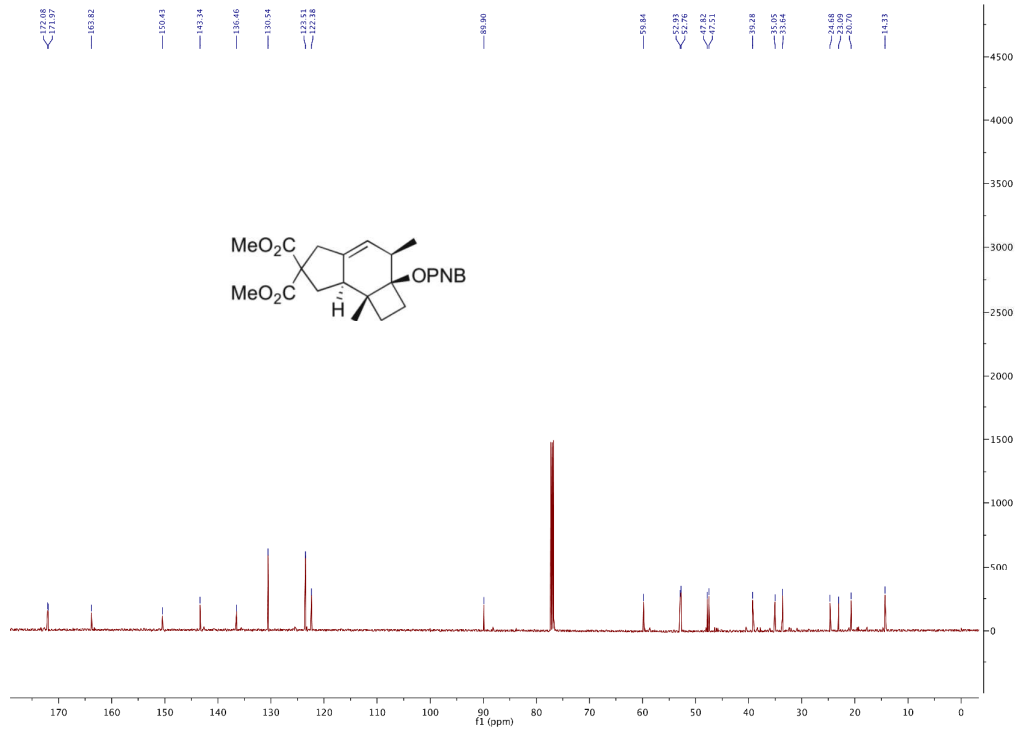


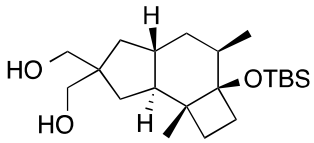



MeO2C
MeO2C
OPNB
H

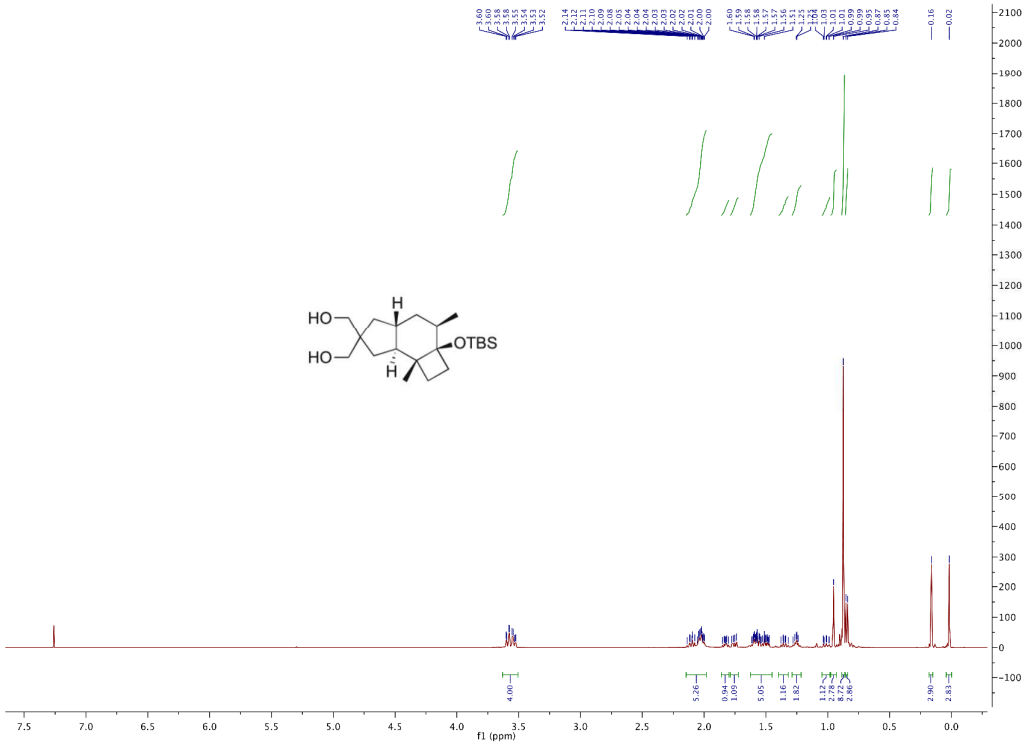
20

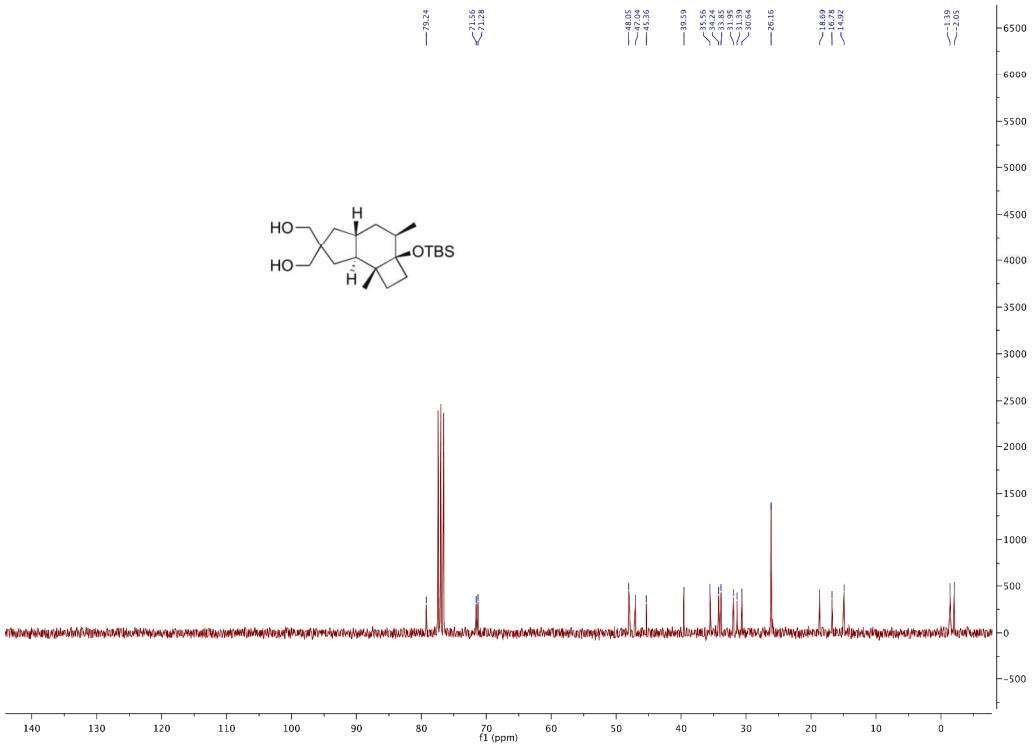

MeO2C
MeO2C
OPNB
H
f1 (ppm)


MeO2C
MeO2C
OPNB
H
f1 (ppm)

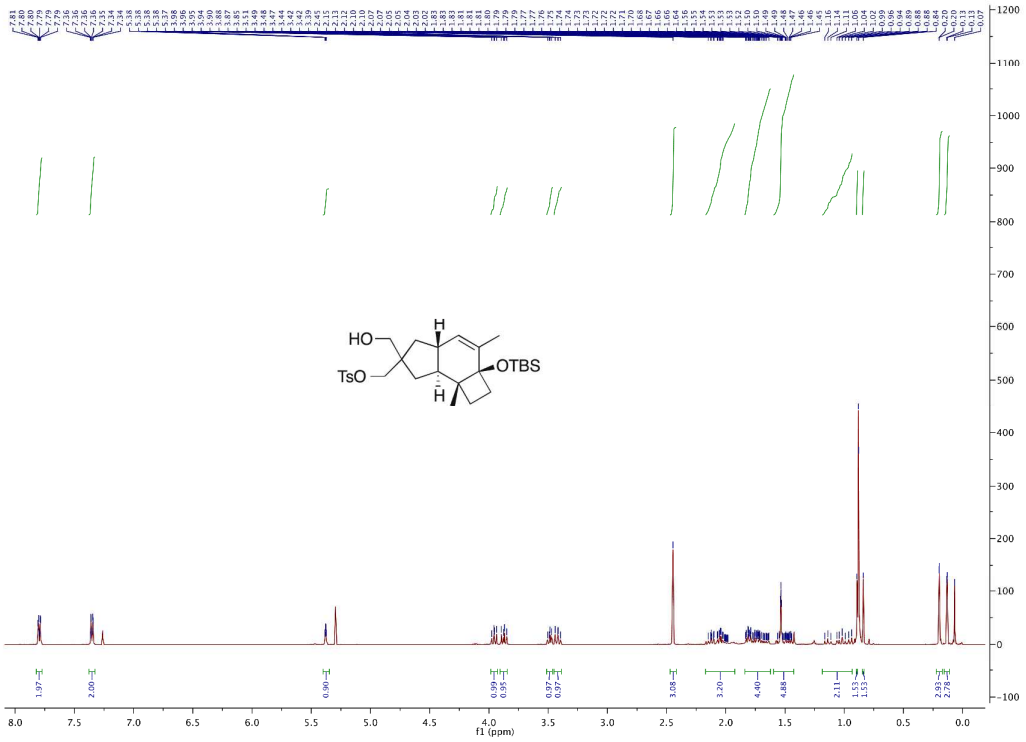


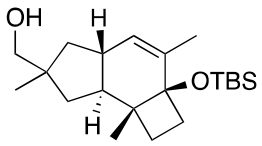
21



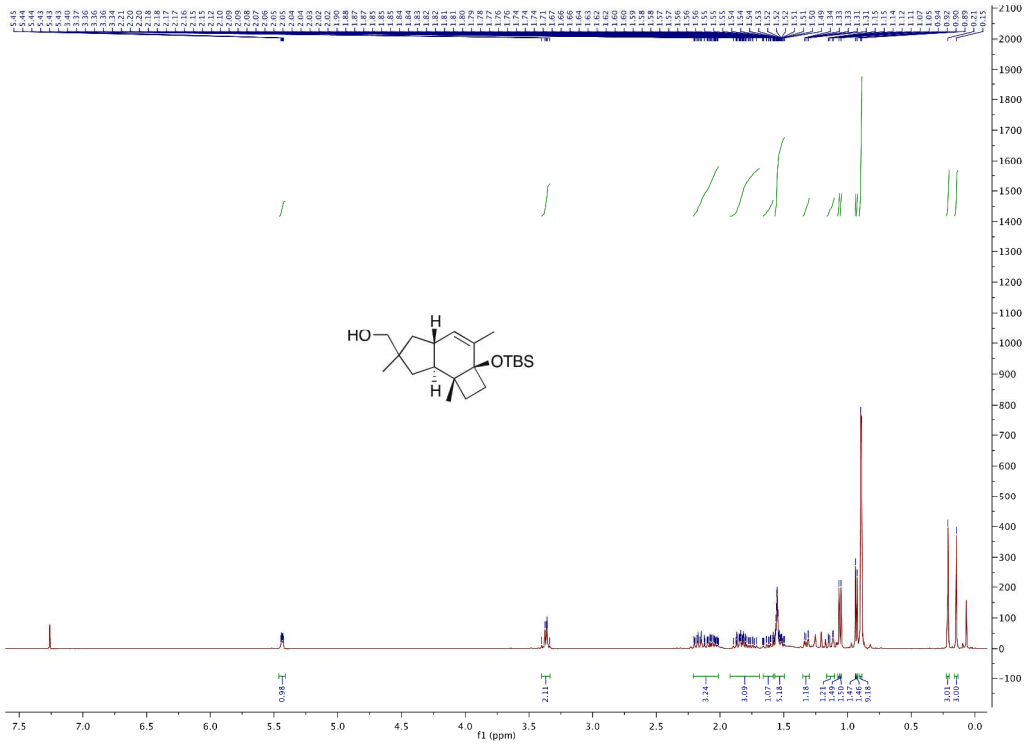


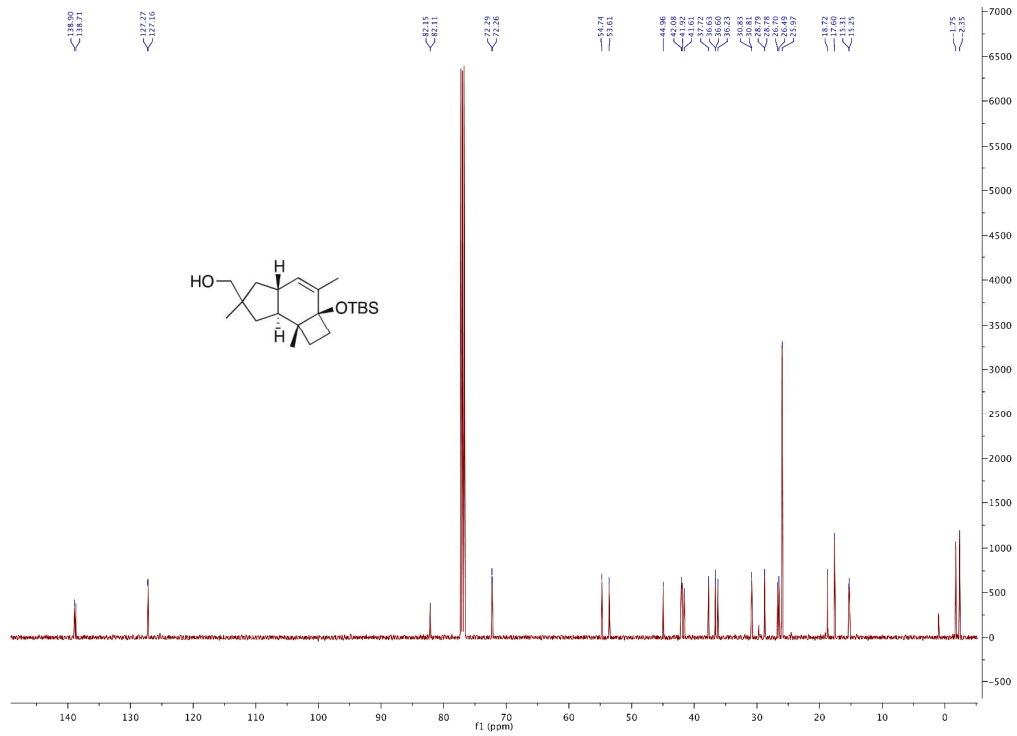
Monotosylate of **21**

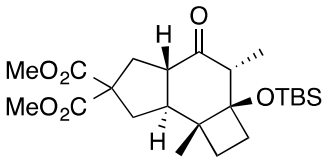




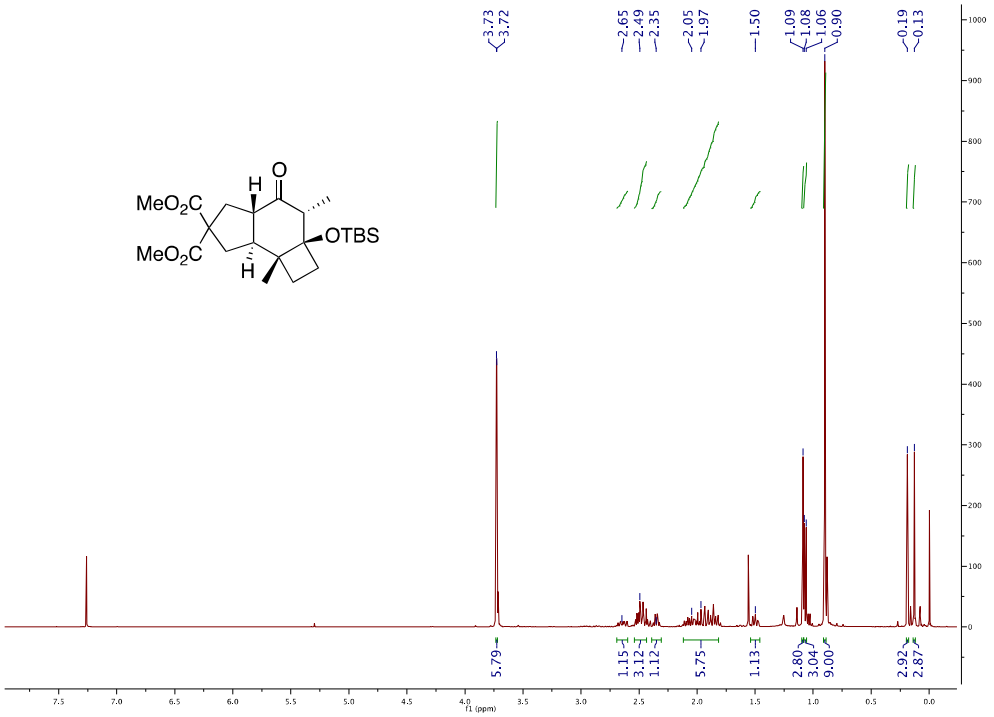
22 (1:1)

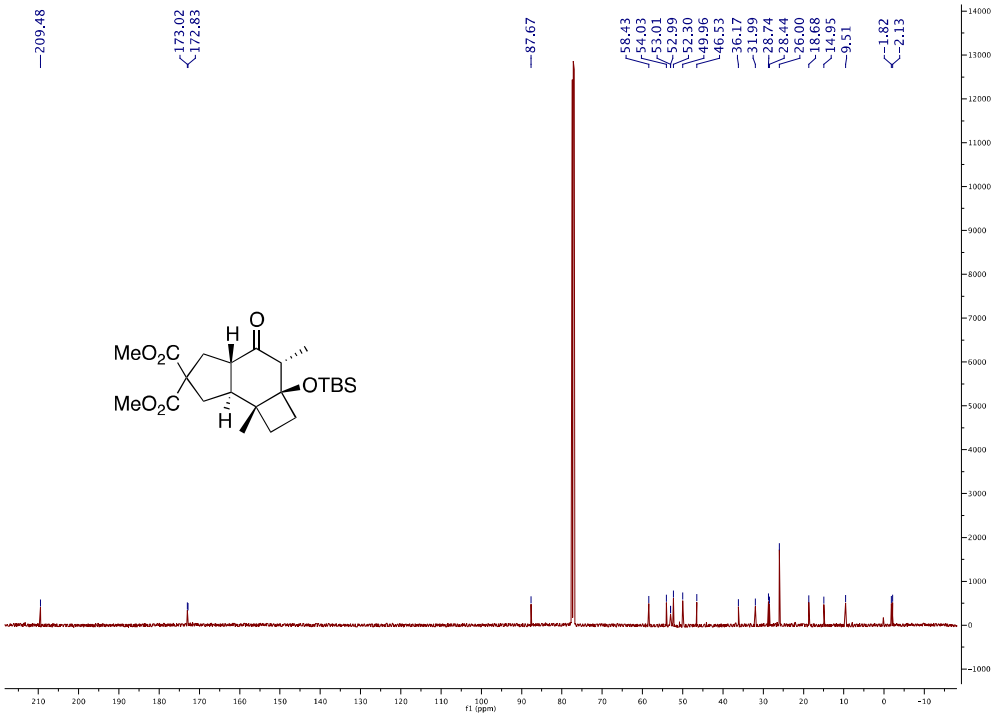


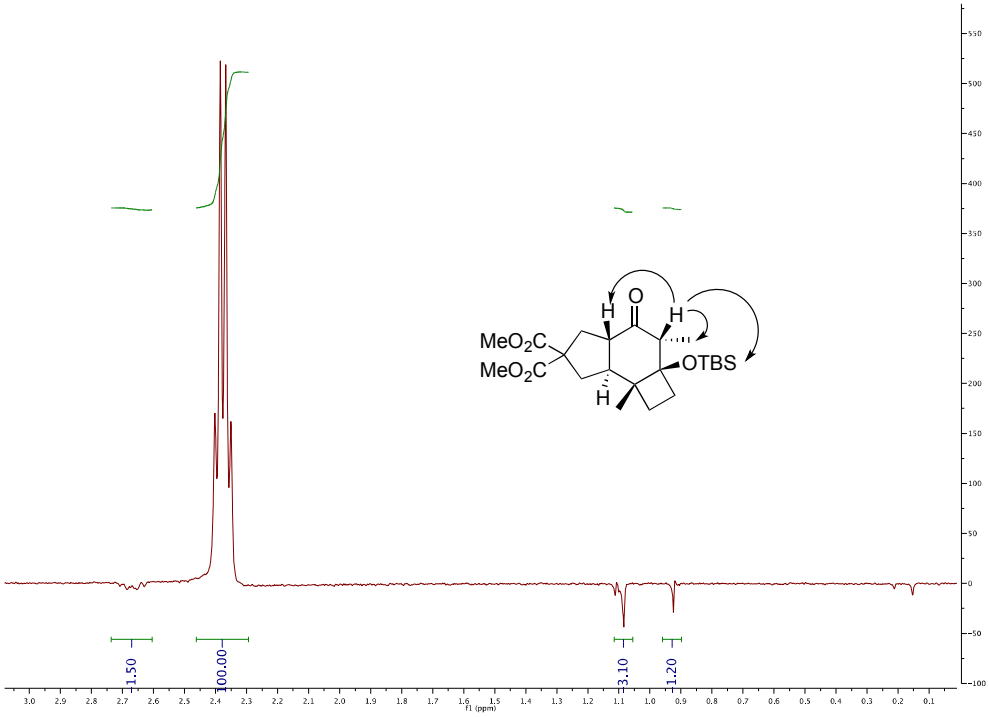


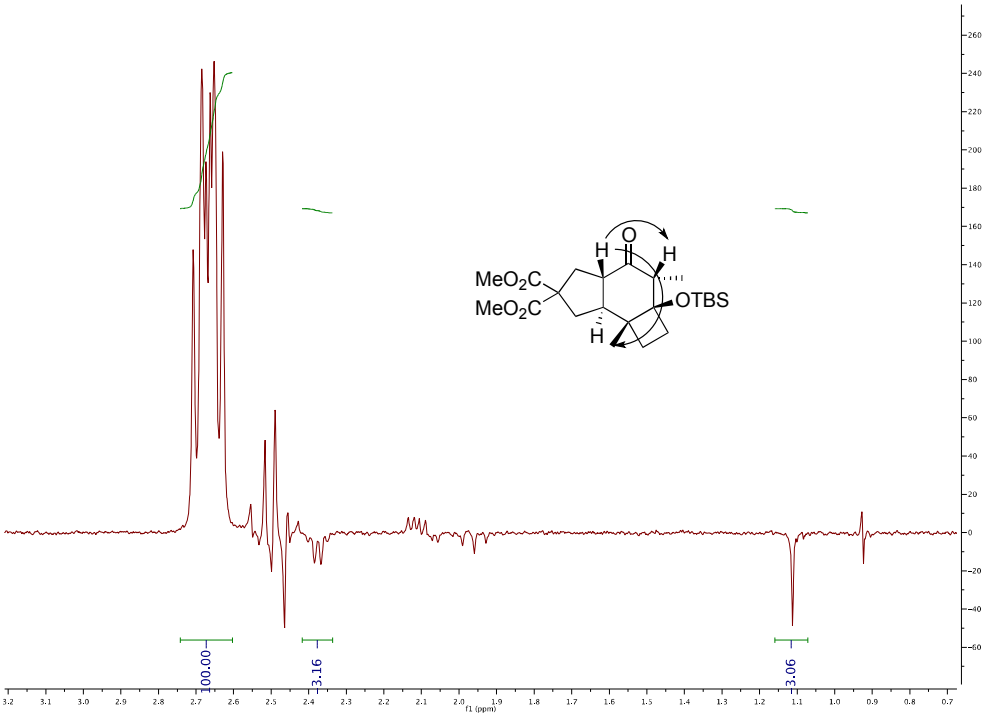

O
H
MeO2C
MeO2C
OTBS
H

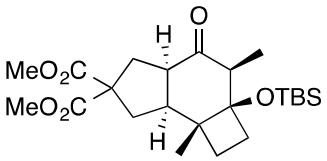
23a


3.73
3.72
2.65
2.49
2.35
2.05
1.97
1.50
1.09
1.08
1.06
0.90
0.19
0.13
5.79
1.15
3.12
1.12
5.75
1.13
2.80
3.04
9.00
2.92
2.87
f1 (ppm)

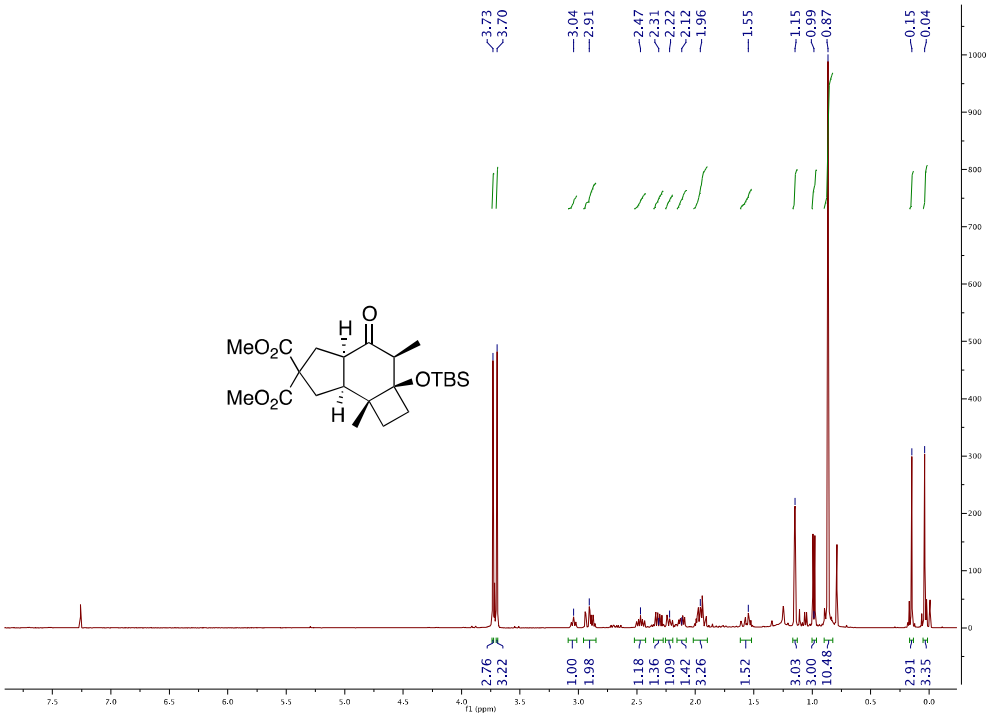

209.48
173.02
172.83
87.67
58.43
54.03
53.01
52.99
52.30
49.96
46.53
36.17
31.99
28.74
28.44
26.00
18.68
14.95
9.51
1.82
2.13
f1 (ppm)

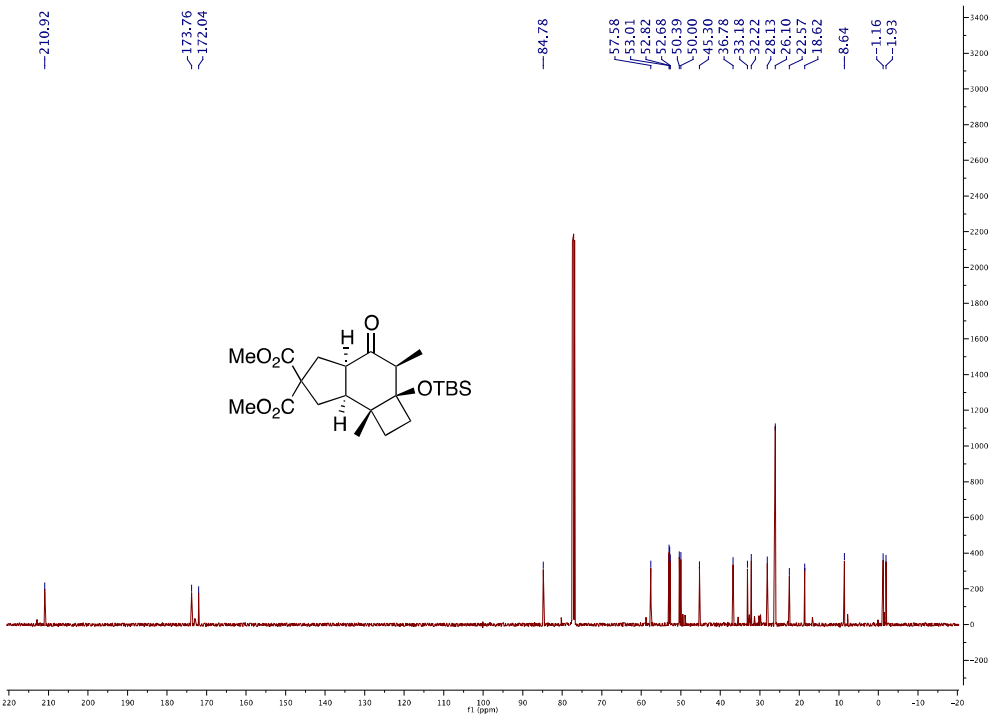

MeO2C
MeO2C
O
H
H
OTBS
H
1.50
100.00
3.10
1.20
f1 (ppm)

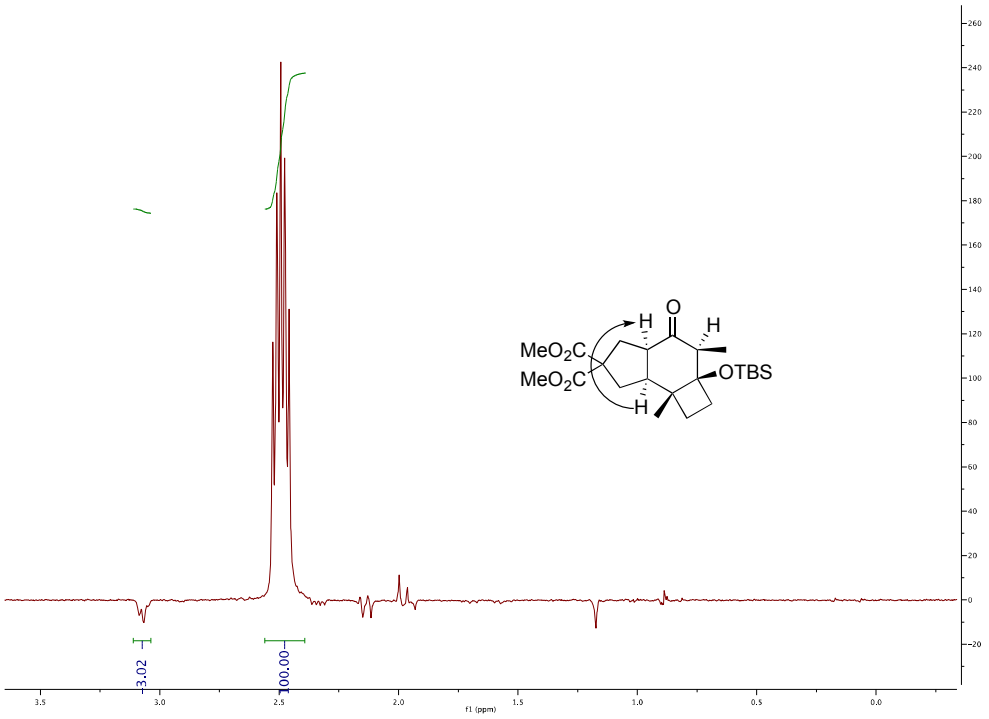

MeO2C
MeO2C
O
H
H
OTBS
H
100.00
3.16
3.06
f1 (ppm)

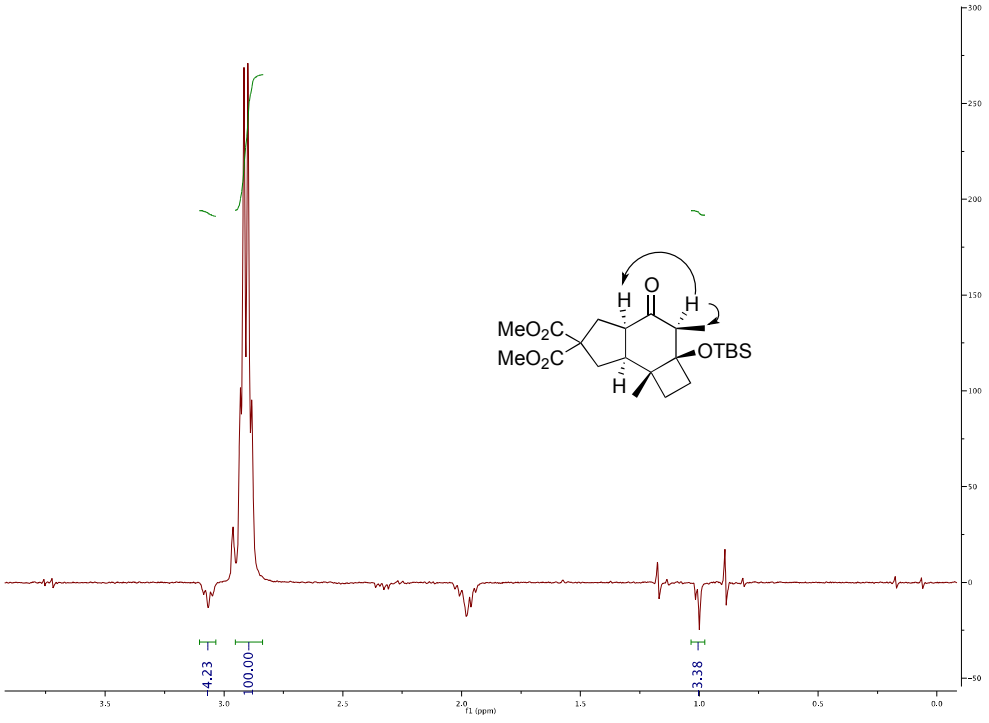

O
H
MeO2C
MeO2C
OTBS
H

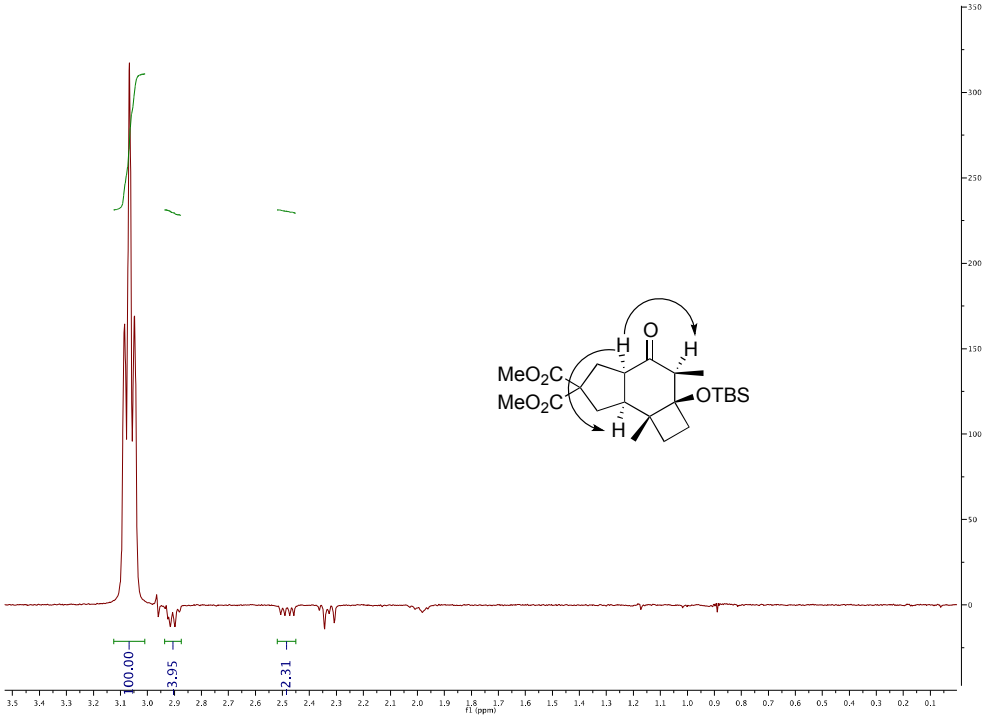
23b


3.73
3.70
3.04
2.91
2.47
2.31
2.22
2.12
1.96
1.55
1.15
0.99
0.87
0.15
0.04
2.76
3.22
1.00
1.98
1.18
1.36
1.09
1.42
3.26
1.52
3.03
3.00
10.48
2.91
3.35
f1 (ppm)

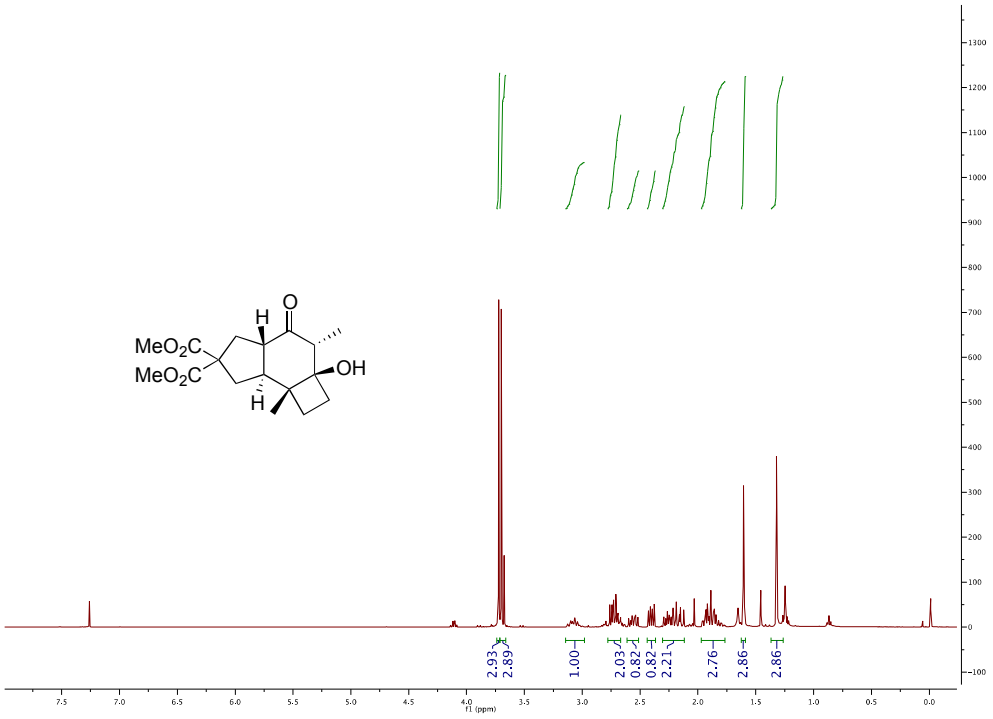

210.92
173.76
172.04
84.78
57.58
53.01
52.82
52.68
50.39
50.00
45.30
36.78
33.18
32.22
28.13
26.10
22.57
18.62
8.64
-1.16
-1.93
f1 (ppm)

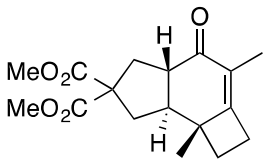

MeO2C
MeO2C
OTBS
H
O
H
H
3.02
100.00
f1 (ppm)


MeO2C
MeO2C
OTBS
H
O
H
H
4.23
100.00
3.38
f1 (ppm)

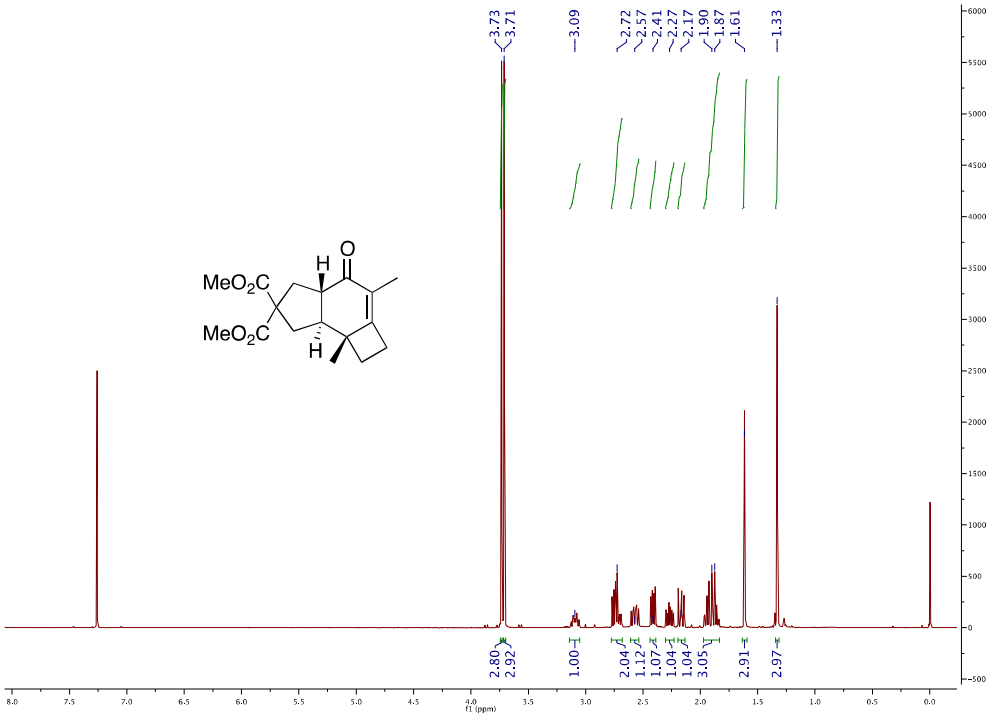

MeO2C
MeO2C
H
O
H
OTBS
H
100.00
3.95
2.31
f1 (ppm)

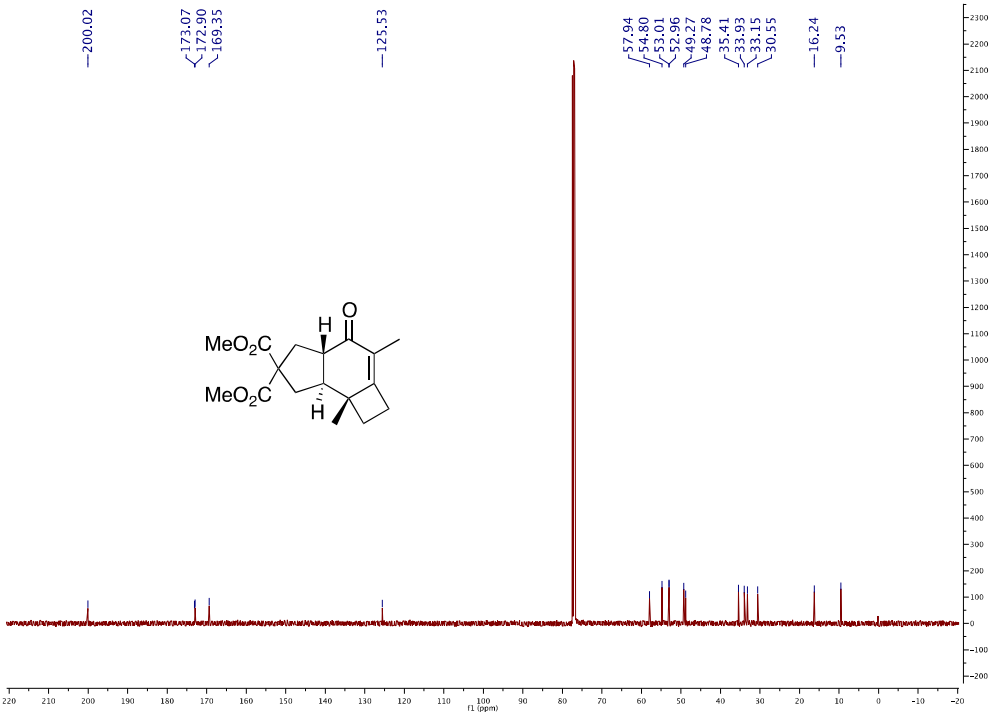
Deprotected alcohol from **23a**




O
H
MeO2C
MeO2C
H

24


3.73
3.71
3.09
2.72
2.57
2.41
2.27
2.17
1.90
1.87
1.61
1.33
2.80
2.92
1.00
2.04
1.12
1.07
1.04
1.04
3.05
2.91
2.97
f1 (ppm)


200.02
173.07
172.90
169.35
125.53
57.94
54.80
53.01
52.96
49.27
48.78
35.41
33.93
33.15
30.55
16.24
9.53
f1 (ppm)