Synthesis of the C14–C21 Acid Fragments of Cytochalasin Z_8 via *anti*-Selective Aldol Condensation and *B*-Alkyl Suzuki–Miyaura Cross-Coupling

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Supporting Information

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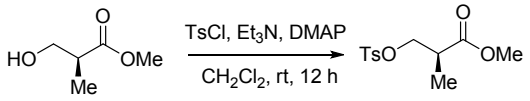
General Methods

All reactions involving air- and moisture-sensitive reagents were carried out using oven dried glassware and standard syringe-septum cap techniques. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer in $CDCl_3$ or acetone-d_6 (400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively) with residual $CHCl_3$ or acetone as the internal reference. IR spectra were taken on a FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were measured by the +ESI method. Optical rotation data were recorded using quartz cells of 3.5 mm ID × 100 mm and 3.5 mm ID × 10 mm, respectively. Silica gel plates pre-coated on glass were used for thin-layer chromatography using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. Silica gel was used for flash column chromatography with mixed ethyl acetate (EtOAc) and petroleum ether (PE; bp 60–90 ºC) as the eluting solvents. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials. Anhydrous THF, Et_2O and PhMe were freshly distilled from sodium benzophenone ketyl under N_2. Anhydrous triethylamine Et_3N, CH_2Cl_2, and N,N-Dimethylformamide (DMF) were freshly distilled over CaH_2. Anhydrous cyclohexane was freshly distilled over $LiAlH_4$. Other reagents were obtained commercially and used as received. Ambient temperature ranges from 10–30 ºC unless otherwise stated.

Experimental Details and Compound Characterization

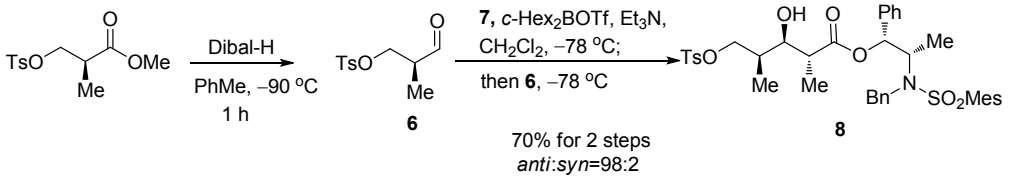
Methyl (*S*)-2-Methyl-3-[(4'-toluenesulfonyl)oxy]propionate[1]



(*S*)-Roche ester 95%

To a solution of methyl (*S*)-(+)-3-hydroxy-2-methylpropionate (Roche ester, 2.50 g, 21.1 mmol) in anhydrous CH_2Cl_2 (30 mL) cooled in an ice–water bath (ca. 0 °C) was sequentially added Et_3N (3.8 mL, 27.5 mmol), DMAP (0.38 g, 3.2 mmol), and *p*-TsCl (4.84 g, 25.4 mmol) followed by stirring for overnight at room temperature. The reaction was quenched with water and the reaction mixture was extracted with EtOAc (2 × 60 mL). The combined organic layer was washed with brine (40 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduce pressure. The residue was purified by flash column chromatography (silica gel, 25% EtOAc in PE) to afford the tosylate (5.45 g, 95%) as a colorless oil. $[\alpha]_D^{14}$ +4.27 (*c* 3.36, $CHCl_3$); lit.[1a] $[\alpha]_D^{17.5}$ +3.8 (*c* 2.0, $CHCl_3$); *Rf* = 0.30 (PE/EtOAc = 4/1); Spectroscopic data matched that previously reported. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 4.18 (dd, *J* = 6.8, 2.8 Hz, 1 H), 4.05 (dd, *J* = 6.8, 2.8 Hz, 1 H), 3.63 (s, 3 H), 2.83–2.77 (m, 1 H), 2.44 (s, 3 H), 1.16 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.0, 144.9, 132.7, 129.8 (×2), 127.9 (×2), 70.7, 52.0, 39.1, 21.6, 13.6.

(2*R*,3*R*,4*S*)-(1*R*,2*S*)-2-(*N*-benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 3-hydroxy-2,4-dimethyl-5-(tosyloxy)pentanoate (8)

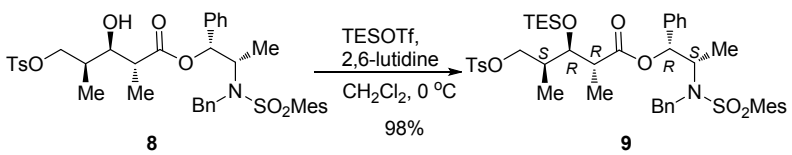


To a solution of above tosylate (1.18 g, 4.3 mmol) in anhydrous toluene (20 mL) cooled in a EtOH–liquid nitrogen bath (ca. –90 °C) was slowly added via syringe a solution of Dibal-H (1.0 M in hexane, 4.8 mL, 4.8 mmol) followed by stirring for 1 h at the same temperature. The reaction was quenched by adding EtOAc (10 mL) and the resultant mixture was allowed to warm up to room temperature. To the mixture was added an aqueous solution of citric acid (1.0 M, 15 mL) with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layer was washed with brine (20 mL), dried over Na_2SO_4, filtrated, and condensed under reduced pressure to afford the

unstable crude aldehyde **6**[1, 2] (ca. 1 g) as a colorless oil which was immediately used for the next step.

To a stirred solution of ester **7** (1.0 g, 2.1 mmol) in dry CH_2Cl_2 (20 mL) cooled at –78 °C was added Et_3N (1.46 mL, 10.5 mmol) under a nitrogen atmosphere. After stirring at –78 °C for 5 min, Cy_2BOTf (1.0 M in hexane, 6.3 mL, 6.3 mmol) was added dropwise over 20 min. The resultant solution was stirred at –78 °C for 2 h. Then the above crude aldehyde **6** was added dropwise followed by stirring at –78 °C for 1 h. The reaction was allowed towarm to –78 °C over 1 h and the reaction was quenched by addition of pH = 7 buffer and MeOH (1/1, v/v, 20 mL). The reaction mixture was diluted with MeOH (20mL) to make a homogeneous solution. After careful addition of 30% H_2O_2 (20 mL), the mixture was stirred at room temperature for 14 h and then concentrated under reduced pressure. The residue was partitioned between water (50 mL) and CH_2Cl_2 (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL) for three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was puried by column chromatography (silica gel; EtOAc/PE = 1/10) to afford the *anti*-aldol product **8** (1.06 g, 70% yield for two steps) as a white solid. mp 123.4~125.3 ºC (EtOAc–hexane); $[\alpha]_D^{24}$ +1.7 (*c* = 1.000, $CHCl_3$); R_f = 0.16 (PE/EtOAc = 4/1); IR (film) 3511, 2979, 1737, 1318, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.76 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.26–7.15 (m, 8 H), 6.92 (s, 1 H), 6.90 (d, *J* = 2.0 Hz, 1 H), 6.87 (s, 2 H), 5.88 (d, *J* = 8.0 Hz, 1H), 4.68, 4.55 (ABq, *J* = 16.8 Hz, 2 H), 4.15–4.06 (m, 1 H), 4.02 (t, *J* = 8.8 Hz, 1 H), 3.91 (dd, *J* = 9.6, 6.0 Hz, 1 H), 3.77–3.72 (m, 1 H), 2.65 (d, *J* = 4.8 Hz, 1H), 2.50 (s, 6 H), 2.43 (s, 3 H), 2.45–2.39 (m, 1 H), 2.27 (s, 3 H), 2.01–1.94 (m, 1H),1.15 (d, *J* = 8.8 Hz, 3H), 1.01 (d, *J* = 7.6 Hz, 3H), 0.82 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) 174.5, 144.8, 142.6, 140.1 (×2), 138.3, 138.0, 133.3, 132.8, 132.1 (×2), 129.8 (×2), 128.4 (×2), 128.3 (×2), 128.0, 127.8 (×2), 127.4 (×2), 127.1, 125.7 (×2)**,** 78.5, 72.4, 70.8, 56.8, 48.2, 43.0, 34.3, 22.9 (×2), 21.6, 20.8, 13.4, 13.0, 8.5; HRMS (ESI+) calcd for $C_{39}H_{47}NO_8S_2Si^+$ $[M+Na]^+$ 744.2635, found 744.2640.

(2*R*,3*R*,4*S*)-(1*R*,2*S*)-2-(*N*-benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 2,4-dimethyl-5-(tosyloxy)-3-((triethylsilyl)oxy) pentanoate (9)

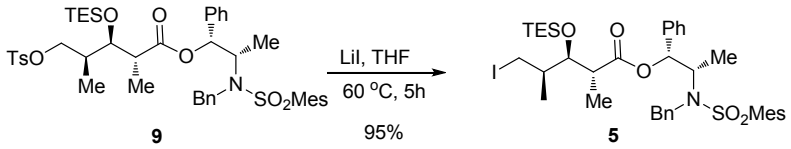


8 **9**

To a solution of **8** (356 mg, 0.49 mmol) in dry CH_2Cl_2 (5 mL) cooled at 0 ºC was

sequentially added 2,6-lutidine (0.19 mL, 0.98 mmol) and TESOTf (0.17 mL, 0.74 mmol) under a nitrogen atmosphere. After stirring at 0 ºC for 1 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ at 0 ºC. The resultant reaction mixture was extracted with EtOAc and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, fltered, and concentrated under reduced pressure. The residue was puried by column chromatography (silica gel; EtOAc/Petroleum Ethers = 1/20) to give the product **9** (400 mg, 98%) as a white solid. $[\alpha]_D^{25}$ +10.26 (*c* = 1.000, $CHCl_3$); R_f = 0.46 (4:1 PE/EtOAc); IR (film) 2956, 1740, 1150, 1012 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.73 (d, *J* = 8.4 Hz, 2H), 7.34–7.16 (m, 7 H), 7.18 (t, *J* = 7.6 Hz, 1 H), 7.08 (t, *J* = 8.4 Hz, 2 H), 6.83 (s, 2 H), 6.78 (d, *J* = 7.6 Hz, 2H), 5.64 (d, *J* = 6.8 Hz, 1H), 4.77, 4.38 (ABq, *J* = 16.4 Hz, 2 H), 4.14–4.07 (m, 1 H), 3.87–3.83 (m, 3 H), 2.52–2.44 (m, 1 H), 2.43 (s, 3 H), 2.63 (s, 6 H), 2.29 (s, 3 H), 1.89–1.83 (m, 1 H), 1.19 (d, *J* = 7.6 Hz, 3H), 0.89–0.84 (m, 12H), 0.80 (d, *J* = 7.6 Hz, 3H), 0.56–0.41 (m, 6 H); ^{13}C NMR (400 MHz, $CDCl_3$) 172.7, 144.7, 142.3, 140.4 (×2), 138.2, 137.8, 132.9, 132.8, 132.1 (×2), 129.7 (×2), 128.4 (×2), 128.3 (×2), 128.2 (×2), 127.9 (×3), 127.4, 126.7 (×2), 77.8, 72.7, 72.6, 56.4, 48.0, 44.6, 35.7, 22.8 (×2), 21.6, 20.9, 15.1, 13.6, 10.4, 7.0(×3), 5.2 (×3); HRMS (ESI+) calcd for $C_{45}H_{61}NO_8S_2Si^+$ $[M+Na]^+$: 858.3500, found 858.3506.

(2*R*,3*S*,4*R*)-(1*R*,2*S*)-2-(*N*-benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 5-iodo-2,4-dimethyl-3-((triethylsilyl)oxy) pentanoate (5)

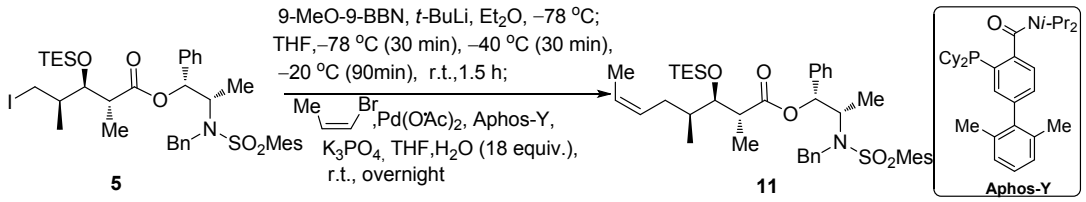


9 **5**

To a solution of **9** (1.47 g, 1.76 mmol) in THF (18 mL) was added LiI (353 mg, 2.64 mmol) followed by heating at 60 ºC for 5 h. The reaction was quenched by water and the reaction mixture was extracted with Et_2O (20 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was puried by column chromatography (silica gel; EtOAc/PE = 1/20) to give the product **5** (1.32g, 95%) as a white solid. $[\alpha]_D^{24}$ +19.8 (*c* = 1.000, CH_2Cl_2); R_f = 0.5 (8:1 PE/EtOAc); IR (film) 2953, 1737, 1455, 1320, 1151, 1006 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.2 Hz, 2H), 7.30–7.17 (m, 4H), 7.11 (t, *J* = 7.6 Hz, 2 H), 6.84 (s, 3 H), 6.81 (s, 1 H), 5.70 (d, *J* = 6.0 Hz, 1 H), 4.80, 4.44 (ABq, *J* = 16.4 Hz, 2 H), 4.15–4.08 (m, 1 H), 3.84 (t, *J* = 4.8 Hz, 1 H), 3.09–2.98 (m, 2H), 2.58–2.51 (m, 1 H), 2.39 (s, 6 H), 2.29 (s, 3 H), 1.69–1.65 (m, 1 H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.10–0.92 (m, 15 H), 0.65–0.58 (m, 6 H); ^{13}C NMR (400 MHz, acetone-d_6) δ 173.1, 143.5,

140.9 (×2), 139.9, 139.2, 134.2, 133.0 (×2), 129.1 (×2), 129.0 (×2), 128.9 (×2), 128.7, 128.1, 127.4 (×2), 78.8, 77.3, 57.6, 48.8, 45.1, 40.0, 23.1 (×2), 20.8, 15.7, 15.3,14.2, 13.5, 7.4 (×3), 6.0 (×3); HRMS(ESI+) calcd for $C_{38}H_{54}INO_5SSi^+$ [M+Na]$^+$ 814.2429, found 814.2433.

(2*R*,3*R*,4*S*,*Z*)-(1*R*,2*S*)-2-(*N*-benzyl-2,4,6-trimethylphenylsulfonamido)-1-phenylpropyl 2,4-dimethyl-3-((triethylsilyl)oxy)oct-6-enoate (11)

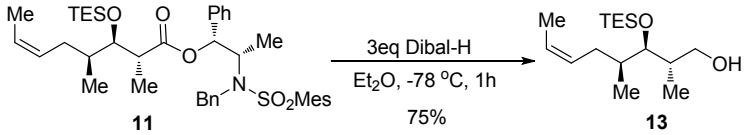


A flame-dried two-neck round bottom flask of 50 mL capacity was charged with the alkyl iodide **5** (245.0 mg, 0.31 mmol) and was then evacuated and backfilled with argon (5 times). A solution of 9-MeO-9-BBN (1 M in hexanes, 1.4 mL, 1.4 mmol) and freshly distilled dry Et_2O (5.0 mL) were added with a syringe at room temperature. The colorless solution was cooled to –78 °C in a dry ice/acetone bath. After stirring for 5 min, a solution of *t*-BuLi (1.6 M in heptane, 0.78 mL, 1.24 mmol) was rapidly added with a syringe in one portion at –78 °C. The resulting milky suspension was stirred for 30 min at the same temperature, and freshly distilled dry THF (5.0 mL) was added. The mixture turned clear and was stirred sequentially at –40 ºC for 30 min, at –20 ºC for 30 min, and then at room temperature for another 1.5 h to form a homogeneous pale yellow solution of the alkyl borinate.

A two-neck round bottom flask of 100 mL capacity was charged with $Pd(OAc)_2$ (6.6 mg, 0.03 mmol), Aphos-Y (25.3 mg, 0.05 mmol),4 and K_3PO_4 (197 mg, 0.93 mmol) and was evacuated and backfilled with argon (5 times). A solution of the (Z)-1-bromoprop-1-ene (132 μL, 1.55 mmol) in degassed THF (5.0 mL) was added with a syringe, followed by the addition of degassed H_2O (100 μL, 5.58 mmol). The mixture was stirred at room temperature for 5 min, and then the above alkyl boriante was transferred with a syringe. After being stirred at room temperature overnight the reaction mixture was filtered off through a plug of Celite and rinsed with EtOAc. The combined organic layer was concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc/PE = 1/20) to give **11** (88.0 mg, 40%) as a colorless oil. $[\alpha]_D^{26}$ +11.2 (*c* = 1.000, CH_2Cl_2); R_f = 0.22 (PE/EtOAc = 20:1); IR (film) 2955, 1742, 1456, 1324, 1152, 1011 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.47 (d, *J* = 6.8 Hz, 2H), 7.34-7.21 (m, 4H), 7.17-7.12 (m, 2 H), 6.98 (s, 2 H), 6.90 (d, *J* = 7.2 Hz, 2H), 5.76 (d, *J* = 6.0 Hz, 1 H), 5.50-5.42 (m, 1 H), 5.36-5.26 (m, 1 H), 4.91, 4.53 (ABq, *J* = 16.4 Hz, 2 H), 4.08-4.01 (m, 1 H), 3.84 (dd, *J* = 6.8, 3.6 Hz, 1 H), 2.71-2.64 (m, 1

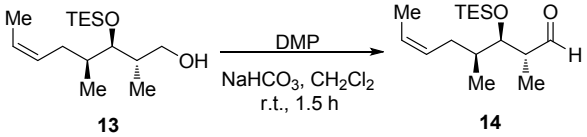
H), 2.41 (s, 6 H), 2.33 (s, 3 H), 1.96 (t, J = 7.2 Hz, 2H), 1.64-1.54 (m, 1 H), 1.55-1.52 (m, 3 H) 1.19 (d, J = 6.8 Hz, 3H), 1.01-0.93 (m, 12 H), 0.85 (d, J = 6.8 Hz, 3H), 0.64 (dd, J = 8.0, 8.0 Hz, 6 H); ^{13}C NMR (400 MHz, acetone-d_6) δ 173.5, 143.5, 140.9, 139.9, 139.3, 134.2, 133.0 (×2), 129.9, 129.1 (×2),129.0 (×5), 128.7, 128.1, 127.3 (×2), 125.4, 78.6, 78.0, 57.6, 48.9, 45.8, 37.1, 32.2, 23.1 (×2), 20.8, 15.4, 13.9, 13.7, 13.1, 7.4 (×3), 6.0 (×3);HRMS (ESI+) calcd for $C_{41}H_{59}NO_5SSi^+$[M+Na]$^+$ 728.3775, found 728.3779.

(2*S*,3*R*,4*S*,*Z*)-2,4-dimethyl-3-((triethylsilyl)oxy)oct-6-en-1-ol (13)



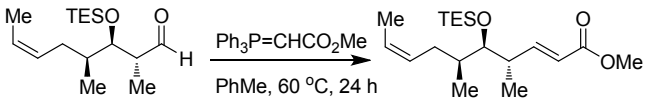
To a solution of the TES ether **11** (35 mg, 0.05 mmol) in dry Et_2O (1 mL) cooled at -78 ºC was added Dibal-H (1.0 M in hexane, 0.18 mL, 0.18 mmol) under a nitrogen atmosphere. The resultant mixture was stirred at the same temperature for 1 h and then allowed to warm to room temperature. The reaction mixture was quenched by carefully adding saturated aqueous Na_2CO_3 (5 mL) and the resultant mixture was diluted with Et_2O (5 mL) with vigorous stirring till the mixture became clear. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×10 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel; EtOAc/PE = 1/20) to give the alcohol **13** as a colorless oil. $[\alpha]_D^{20}$ –3.0 (c = 1.000, CH_2Cl_2); R_f = 0.44 (6:1 PE/EtOAc); IR (film) 2923, 1461, 1378, 1239, 1009 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 5.49–5.39 (m, 2H), 3.69–3.63 (m, 2H), 3.50–3.43 (m, 1H), 3.81 (t, J = 5.2 Hz, 1H), 2.08–2.04 (m, 1H),1.79–1.69 (m, 2H), 1.60 (d, J = 6.0 Hz, 3H), 0.10 (t, J = 8.0 Hz, 9H), 0.94 (d, J = 6.8 Hz, 3H), 0.86 (d, J =6.4 Hz, 3H), 0.67 (q, J = 8.0 Hz, 6H); ^{13}C NMR (400 MHz, acetone-d_6) δ 130.4, 125.0, 78.6, 64.8, 40.6, 37.2, 32.7, 14.7, 13.5, 13.0, 7.3 (×3), 6.0 (×3); HRMS (EI+) calcd for $C_{16}H_{34}O_2Si^+$ [M-C_2H_5]$^+$ 257.1931, found 257.1940.

(2*R*,3*R*,4*S*,*Z*)-2,4-dimethyl-3-((triethylsilyl)oxy)oct-6-enal (14)



To a solution of the alcohol **13** (12 mg, 0.03 mmol) in dry CH_2Cl_2 (5 mL) cooled in an ice–water bath (ca. 0 ºC) was added powdered $NaHCO_3$ (25 mg, 0.3 mmol) and Dess-Martin periodinane (27 mg, 0.06 mmol) followed by stirring at room temperature for 1.5 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ and the resultant mixture was diluted with Et_2O (5 mL) and stirred for 15 min. The organic layer was separated and the aqueous layer was extracted with Et_2O (3×10 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc/PE = 1/50) to give the aldehyde **14** as a colorless oil. $[\alpha]_D^{21}$ –8.36 (*c* = 1.000, CH_2Cl_2); R_f = 0.58 (10:1 PE/EtOAc) IR (film) 2923, 2854, 1728, 1463, 1262, 1099, 1016 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.78 (d, *J* = 2.8 Hz, 1H), 5.55–5.49 (m, 1H), 5.44–5.37 (m, 1H), 6.96 (dd, *J* = 4.0, 2.0 Hz, 1H), 2.64–2.60 (m, 1H), 2.15–2.01 (m, 2H), 1.78–1.73 (m, 2H), 1.61 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 2H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.65 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (400 MHz, acetone-d_6) δ 204.6, 129.8, 125.6, 78.6, 50.9, 38.6, 31.5, 14.3, 13.1, 12.0, 7.3 (×2), 5.9 (×2); HRMS (EI+) calcd for $C_{16}H_{32}O_2Si^+$ $[M\text{-}C_2H_5]^+$ 255.1775, found 255.1775.

(2*E*,4*S*,5*R*,6*S*,8*Z*)-methyl 4,6-dimethyl-5-((triethylsilyl)oxy)deca-2,8-dienoate (15)



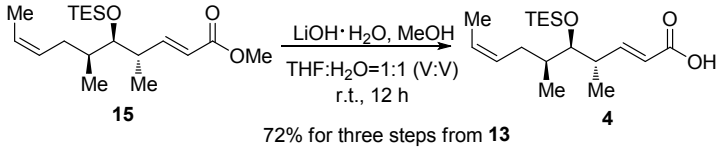
14 **15**

To a solution of the previous aldehyde **14** in dry toluene (2 mL) were added $Ph_3P{=}CHCO_2Me$ (25.4 mg, 0.076 mmol), and the solution was stirred at 60 ºC for 24 h. Then the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purification by flash chromatography (silica gel; EtOAc/PE = 1/50) to afford the *α*, *β*-unsaturated ester **15** as a colorless oil.

$[\alpha]_D^{23}$ –8.88 (*c* = 1.000, CH_2Cl_2); R_f = 0.29 (50:1 PE/EtOAc) IR (film) 2957, 2878, 1726, 1657, 1459, 1240, 1099, 1010 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.04 (dd, *J* = 15.6, 8.4 Hz, 1H), 5.86 (dd, *J* = 16.0, 1.2 Hz, 1H), 5.52–5.46 (m, 1H), 5.41–5.35 (m, 1H), 3.68 (s, 3H), 3.64 (dd, *J* = 5.2, 4.0 Hz, 1H), 2.65–2.58 (m, 1H), 2.09–1.98 (m, 2H), 1.71–1.65 (m, 1H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.66 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (400 MHz, acetone-d_6) δ 167.2, 153.2, 130.1, 125.4, 121.4, 80.5, 51.4, 41.5, 38.5, 31.9, 17.8, 14.3, 13.1, 7.4 (×3), 6.1 (×3); HRMS (EI+) calcd for

$C_{19}H_{36}O_3Si^+$ $[M\text{-}C_2H_5]^+$ 311.2037, found 311.2052.

(2*E*,4*S*,5*R*,6*S*,8*Z*)-4,6-dimethyl-5-((triethylsilyl)oxy)deca-2,8-dienoic acid (4)



72% for three steps from **13**

To a solution of the methyl ester **15** in a mixture of THF/H_2O (3.0 mL, v/v =1:1) was added an aqueous solution of LiOH • H_2O (0.38 mL, 0.38 mmol) and MeOH. The resultant solution was stirred for 12 h at room temperature, and 1 N HCI was added dropwise to reaction mixture till pH=3–4. The reaction mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc/PE = 1/10) to give the acid **4** (7 mg, 72% yield for three steps from **13**) as a colorless oil. $[\alpha]_D^{23}$ –17.5 (*c* = 1.000, CH_2Cl_2); R_f = 0.56 (4:1 PE/EtOAc); IR (film) 2960, 2878, 2334, 1698, 1652, 1417, 1279, 1101, 1015 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.04 (dd, *J* = 15.6, 8.8 Hz, 1H), 5.84 (dd, *J* = 15.6, 0.8 Hz, 1H), 5.53–5.45 (m, 1H), 5.41–5.34 (m, 1H), 3.64 (dd, *J* = 5.2, 4.0 Hz, 1H), 2.65–2.59 (m, 1H), 2.07–2.03 (m, 2H), 1.72–1.67 (m, 1H), 1.59 (d, *J* = 6.4 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.67 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (400 MHz, acetone-d_6) δ 167.3, 153.0, 130.0, 125.2, 121.7, 80.4, 41.3, 38.3, 31.7, 17.7, 14.1, 13.0, 7.2 (×3), 5.9 (×3); HRMS (Maldi-Tof) $C_{18}H_{34}O_3Si^+$ $[M\text{-}C_2H_5\text{+}H^+]$ 298.196, found 298.184.

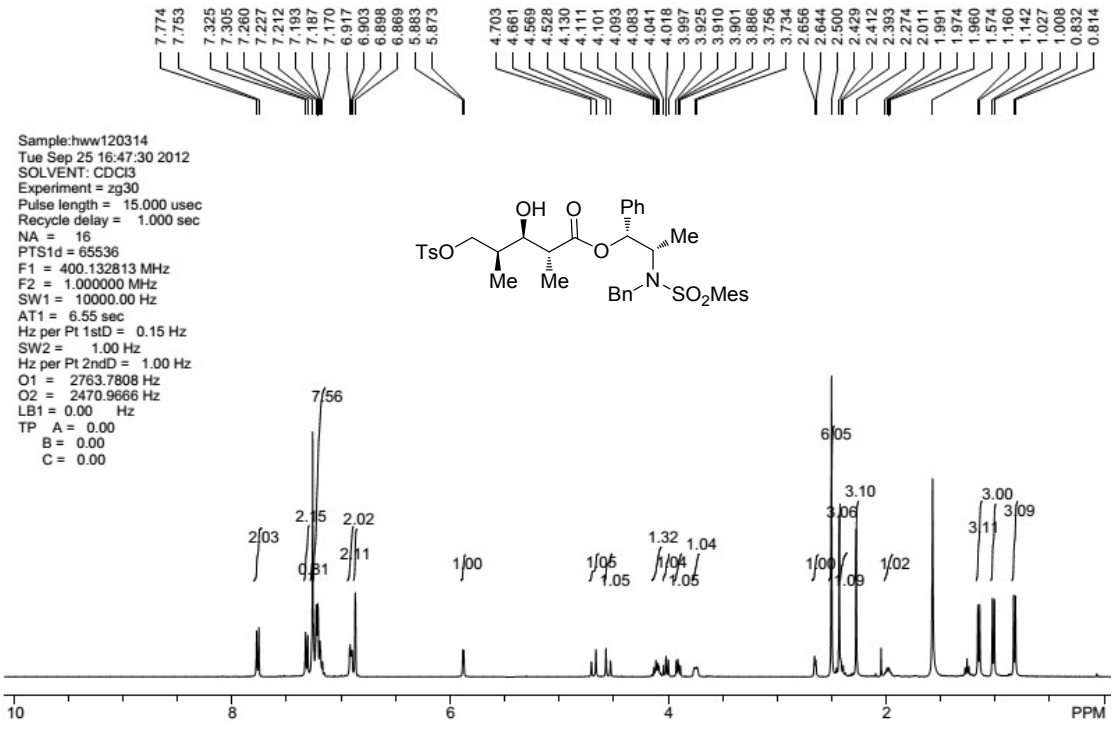
Reference

[1] (a) C. Aissa, R. Riveiros, J. Ragot and A. Fürstner, *J. Am. Chem. Soc.,* 2003, **125**, 15512–15520. (b) D. A. Kummer, J. B. Brenneman, S. F. Martin, *Org. Lett.,* 2005, **7**, 4621–4623.

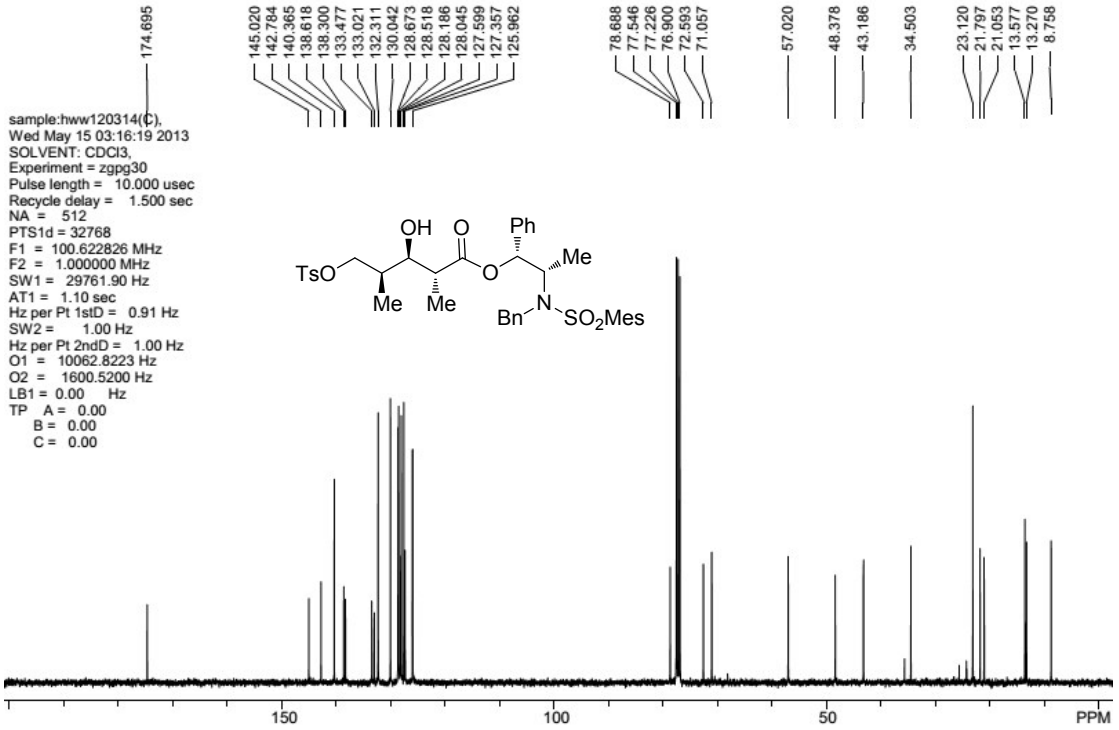
[2] H. Li, J. Wu, J. Luo and W. M. Dai, Chem. Eur. J., 2010, **16**, 11530.

NMR spectra.

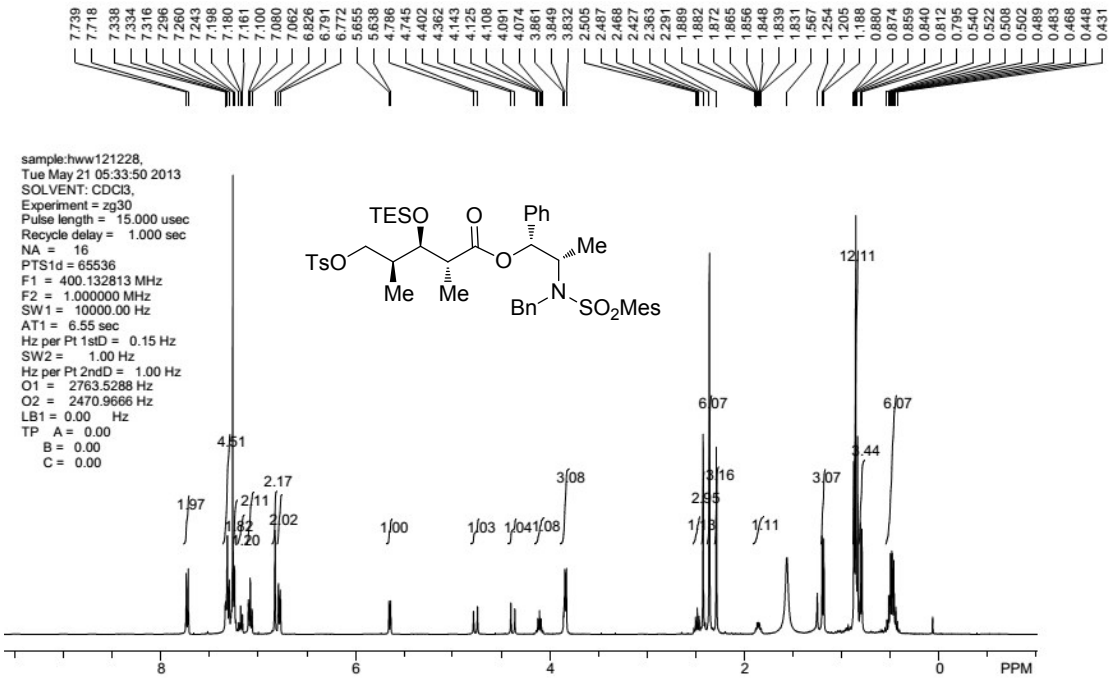
^{1}H NMR of **8**



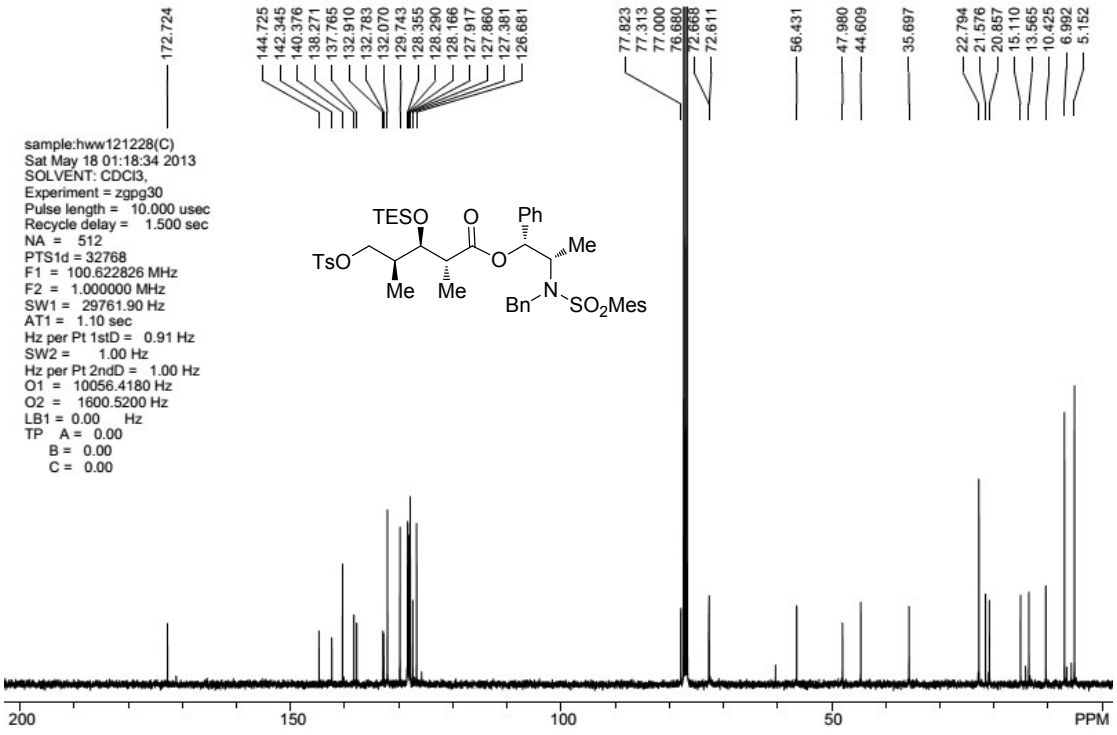
^{13}C NMR of **8**



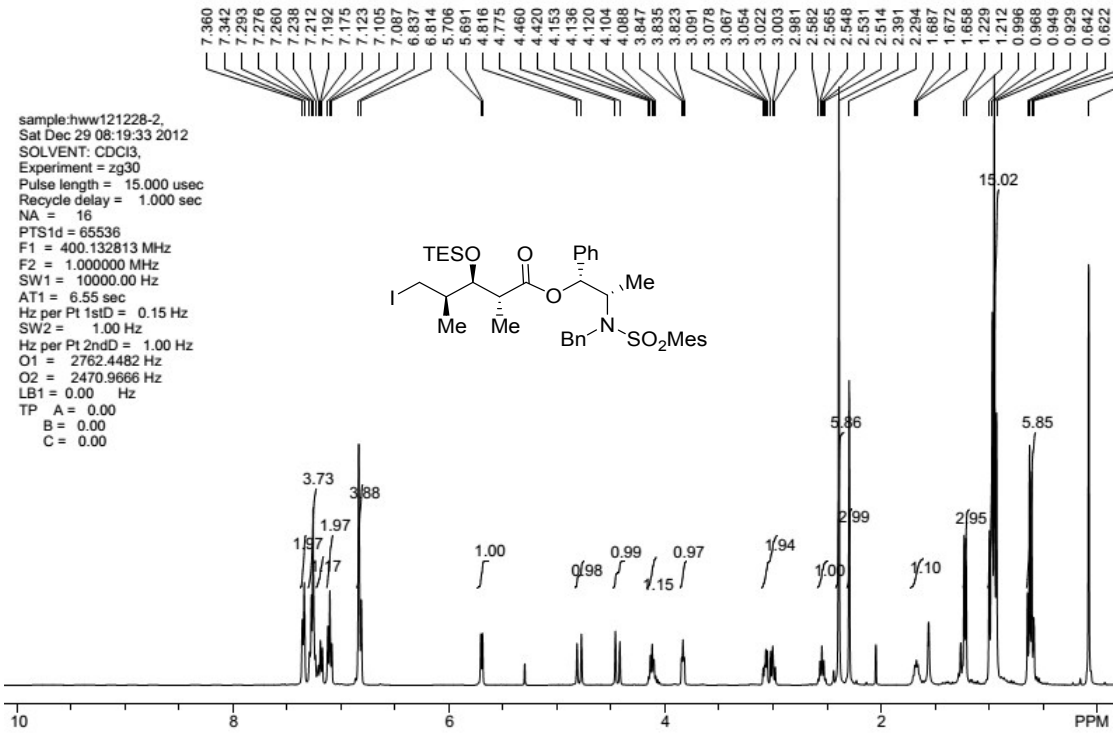
^{1}H NMR of **9**



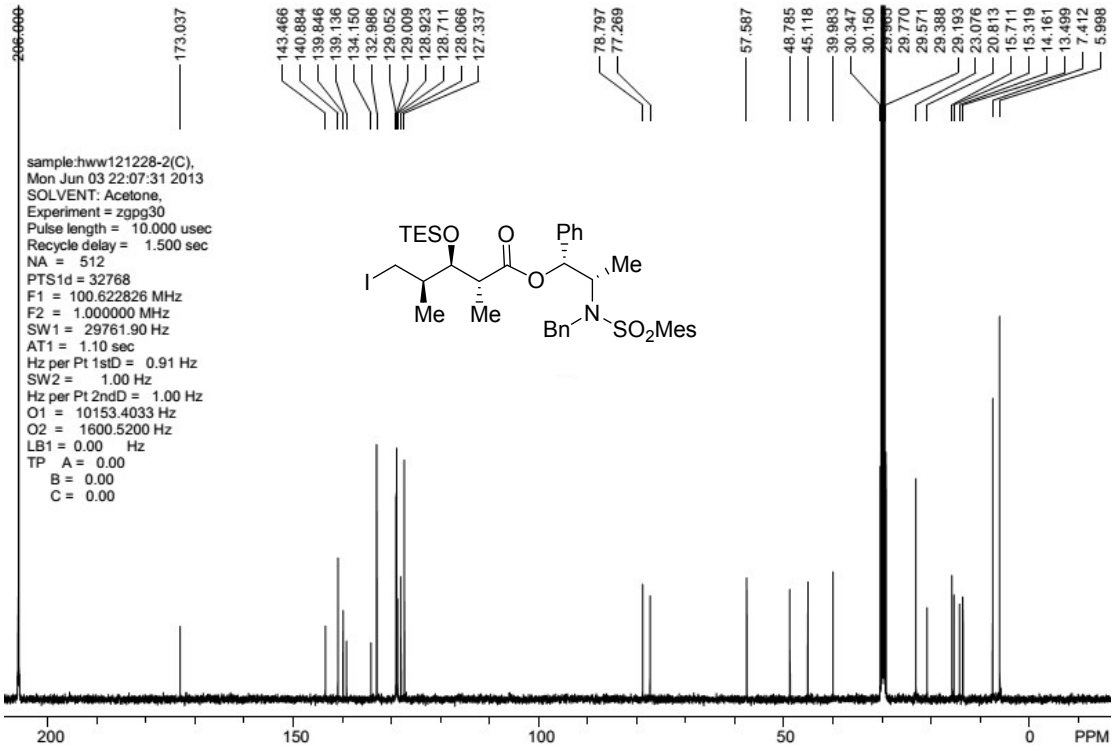
^{13}C NMR of **9**



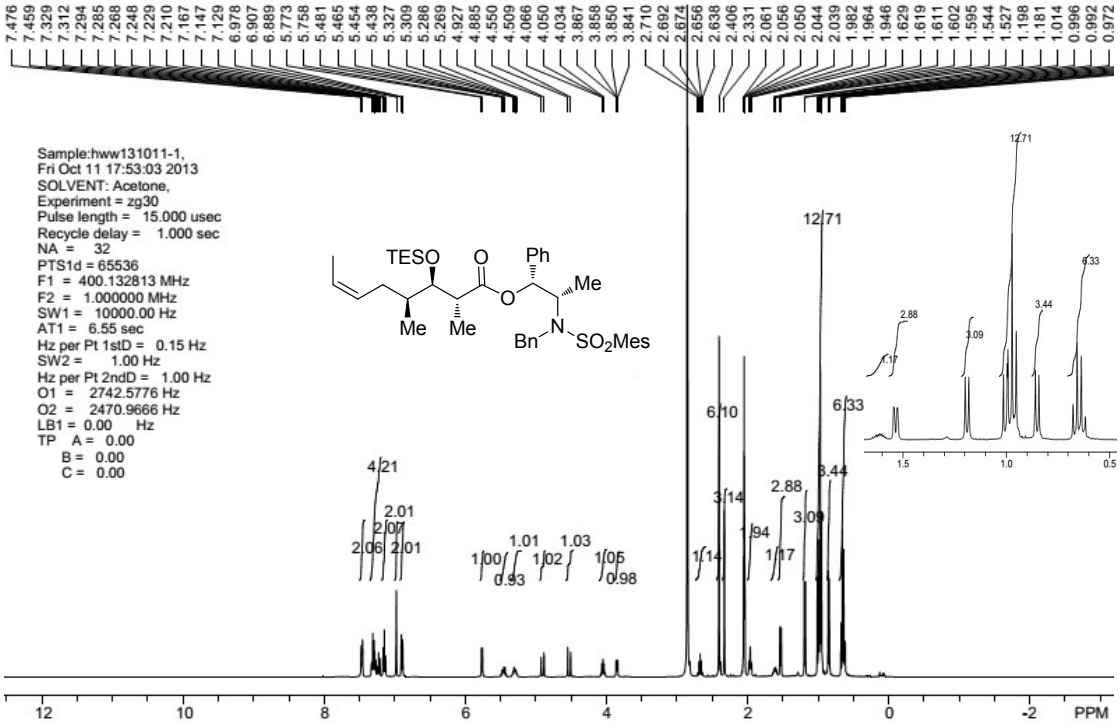
^{1}H NMR of **5**



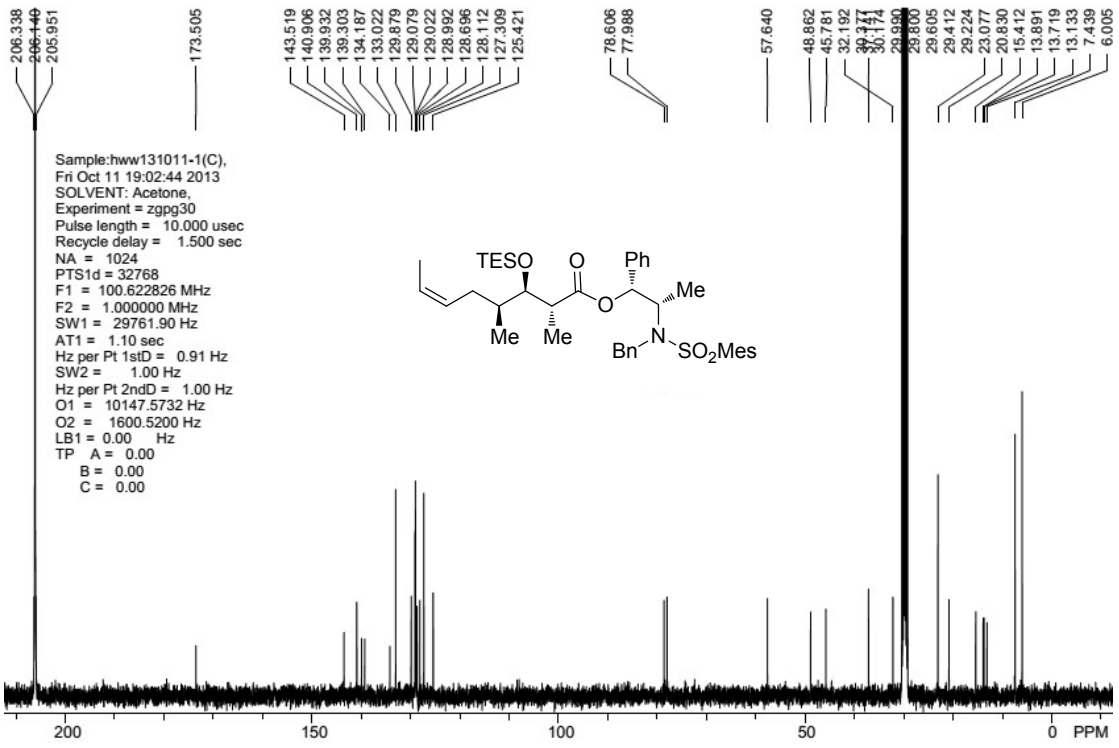
^{13}C NMR of **5**



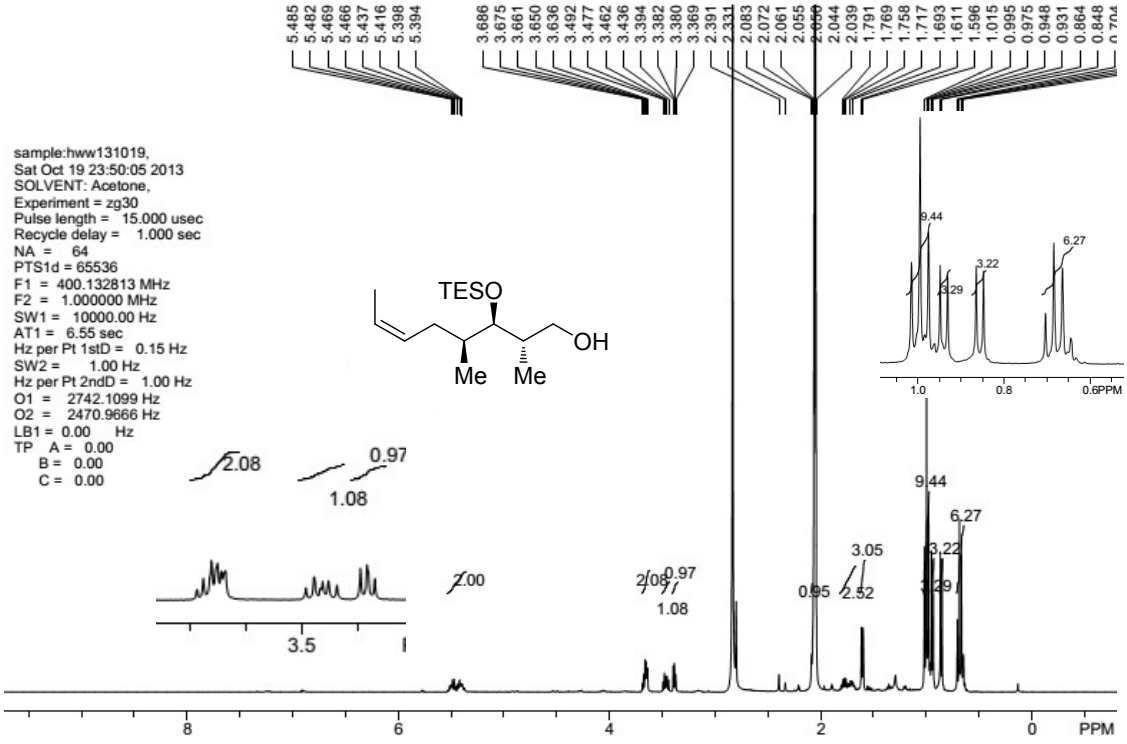
^{1}H NMR of **11**



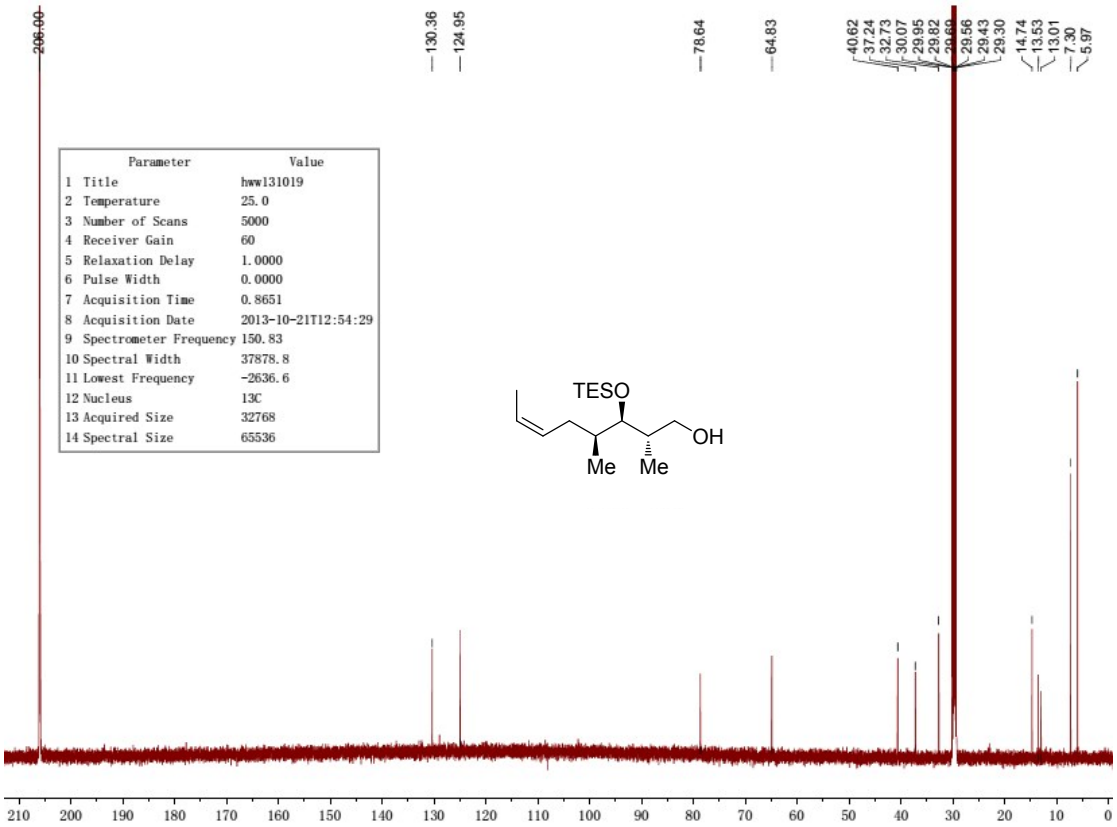
^{13}C NMR of **11**



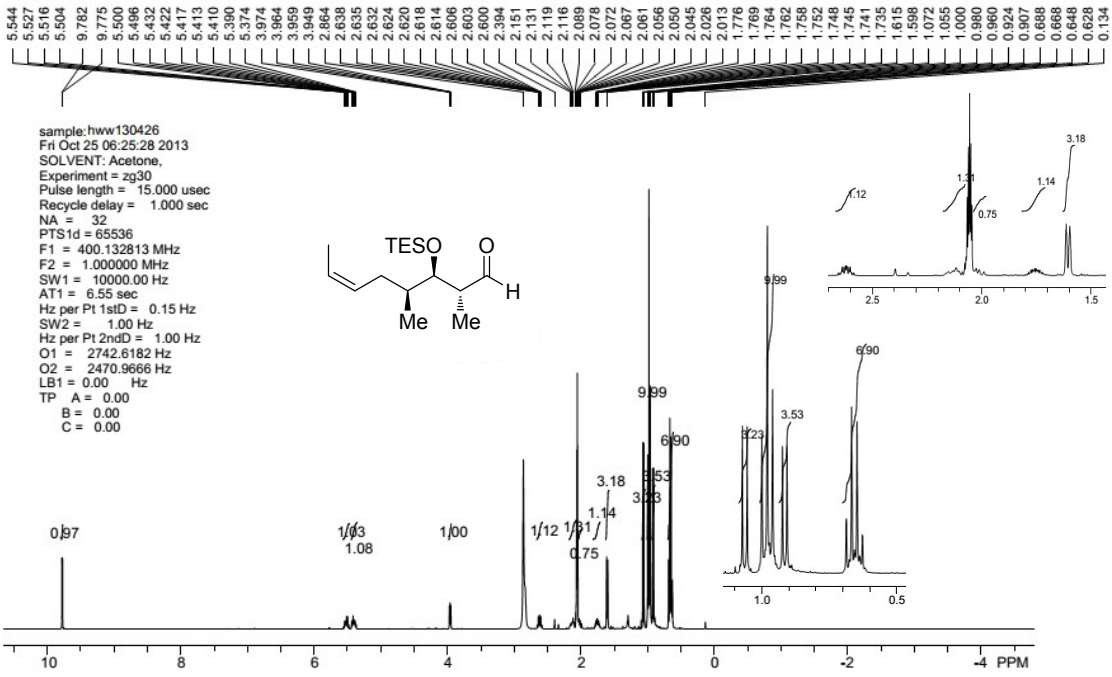
^{1}H NMR of **13**



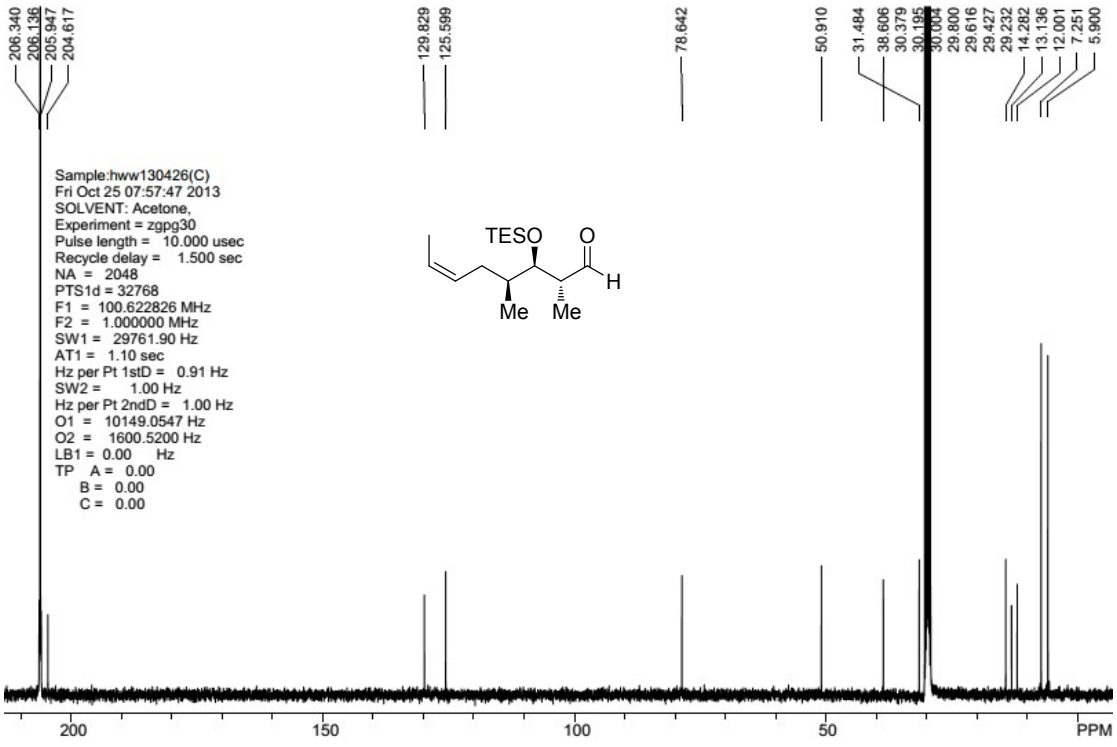
^{13}C NMR of **13**



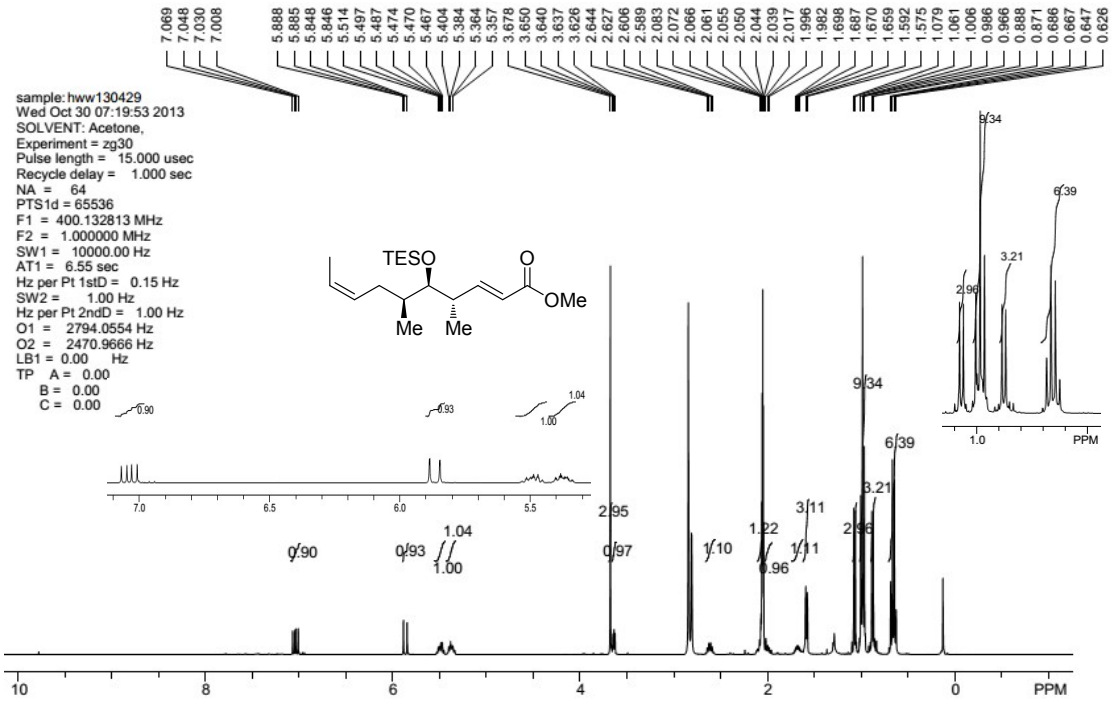
^{1}H NMR of **14**



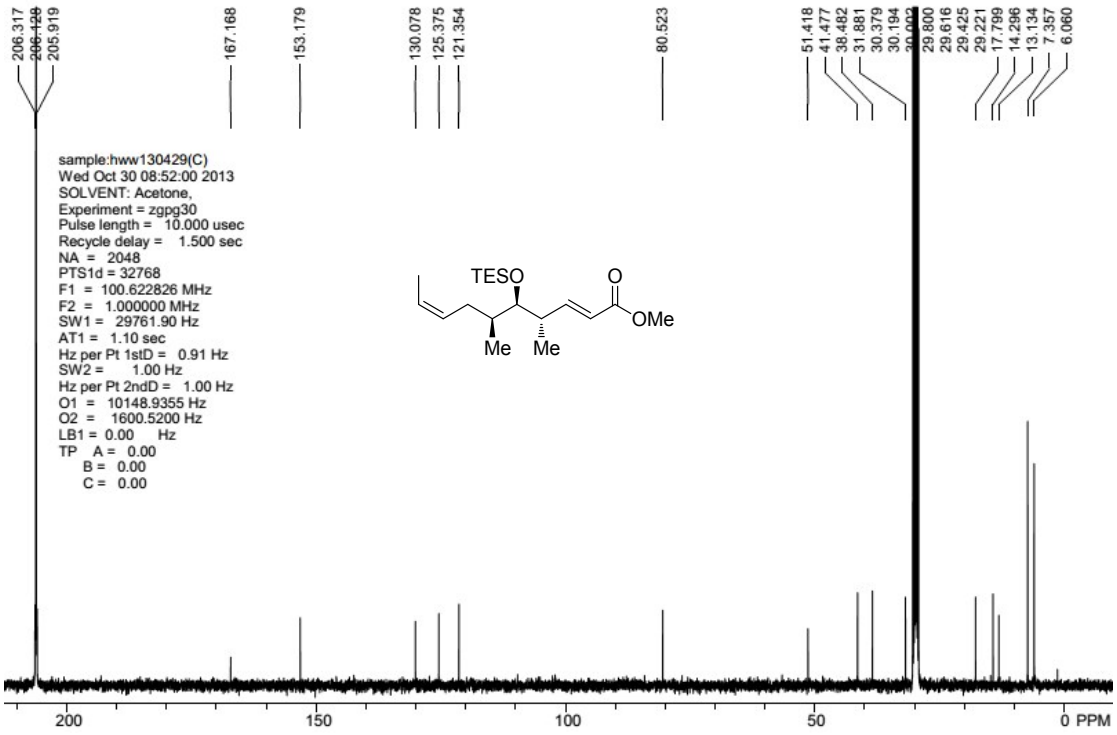
^{13}C NMR of **14**



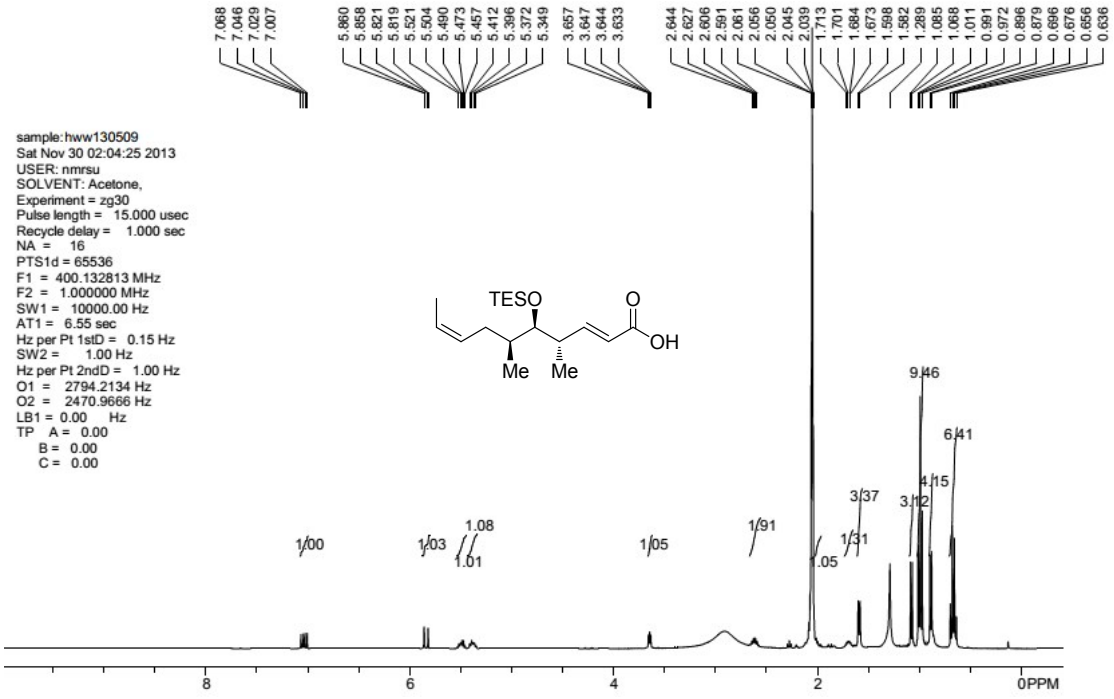
^{1}H NMR of **15**



^{13}C NMR of **15**



^{1}H NMR of **4**



^{13}C NMR of **4**