Diastereoselective Chelation-Controlled Additions to β-Silyloxy Aldehydes

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I. General Methods

All reactions were performed under N_2 atmosphere using flame-dried glassware and standard Schlenk and vacuum line techniques. The progress of reactions were monitored by thin-layer chromatography (TLC) using Whatman precoated silica gel 60 F-254 plates and visualized by staining with ceric ammonium molybdate or 4-dinitrophenylhydrazine stains or ultra-violet light. Toluene and dichloromethane were passed through alumina columns and degassed before use. Alkyl zinc halides and dicyclohexyl borane were prepared using literature procedures.[1,2] The aldehydes[3,4] were prepared within one day of use or stored at –16 °C under nitrogen atmosphere. The ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were obtained using a Bruker AM-500 Fourier transform NMR spectrometer at 500 and 125 MHz, respectively. ^{1}H NMR were referenced to tetramethylsilane in $CDCl_3$, and ^{13}C{^{1}H} NMR spectra were referenced to residual solvent. Coupling constants are reported in hertz. The infrared spectra were obtained using a Perkin-Elmer 1600 series spectrometer. The optical rotations were recorded using a JASCO DIP-370. Silica gel (230-400 mesh, Silicycle) was used for flash chromatography. Reagents were obtained from TCI America, Acros, Sigma-Aldrich, or GFS Chemicals and used without further purification. Analysis of diastereomeric ratios was performed by gas chromatography using a

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[1] Fabicon, R. N.; Richey, H. G. *Organometallics* **2001**, *19*, 4018-4023.

[2] Oppolzer, W.; Schroeder, F.; Kahl, S. *Helv. Chim. Acta*. **1997**, *80*, 2047-2056.

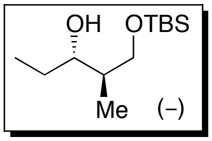
[3] Roush, W. R.; Palkowitz, A. D.; Ando, K. J. *J. Am. Chem. Soc.* **1990**, *112*, 63.

[4] Smith, A. B., III.; Brandt, B. M. *Org. Lett.* **2001**, *3*, 1685-1688.

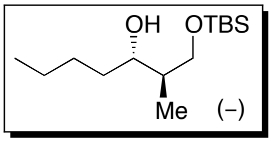
Hewlett-Packard 6890 GC with a Beta-Dex Column or by ^{1}H NMR of the crude or purified reaction products. High resolution mass spectra were measured using a Waters LCTOF- Xe Premier ESI mass spectrometer. Relative stereochemistry was confirmed by modified Mosher ester analysis.[5,6,7]

II. Diastereoselective Dialkylzinc Addition to β-Silyloxy Aldehydes

General Procedure A: A 10 mL Schlenk equipped with magnetic stirrer and septum was flame-dried under vacuum and back-filled with N_2. To the flask was added R_2Zn (0.670 mmol, neat) and CH_2Cl_2 (0.3 mL). The flask was cooled to –78 °C in a dry ice/acetone bath. Triflic acid (33 µL, 0.371 mmol) was added dropwise, and the reaction was allowed to stir at –78 °C for 5 min. The reaction was then stirred at rt for 45 min to 1 h and then cooled to 0 °C. A solution of aldehyde (0.247 mmol) in dichloromethane (0.19 mL) was added dropwise and the reaction was allowed to slowly warm to rt. After 16 h, the reaction was quenched with a saturated solution of NH_4Cl (15 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The crude products were concentrated *in vacuo* and added to a silica gel column.



(2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylpentan-3-ol (2).[8] Procedure A was applied to Et_2Zn (0.67 mL, 1.34 mmol, 2M in CH_2Cl_2), triflic acid(66 µL, 0.75 mmol), and (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (98.0 mg, 0.484 mmol, in 0.3 mL CH_2Cl_2). The crude products were concentrated *in vacuo* and added to a silica gel column. The crude product was purified by flash chromatography (EtOAc:hexanes, 1:49 to 1:24) to afford the title compound as a clear oil (87.5 mg, 78% yield, dr 15.4:1). The major diastereomer was separated and characterized. $[\alpha]_D^{20}$ = –20.6 (c = 1.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.08 (s, 3H), 0.85 (d, J = 7.0 Hz, 3H), 0.90 (s, 9H), 0.97 (t, J = 7.5 Hz, 3H), 1.44 (m, 1H), 1.58, (m, 1H), 1.71 (m, 1H), 3.45 (m, 1H), 3.58 (dd, J = 7.5 Hz, 10.0 Hz, 1H), 3.68 (bs, 1H), 3.79 (dd, J = 4.1 Hz, 10.0 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz): δ –5.46, –5.53, 9.8, 13.8, 18.3, 26.0, 28.0, 39.4, 68.6, 78.0. IR (neat): 3445, 2958, 2930, 2858, 1471, 1463, 1256, 1084, 850 cm^{-1}. HRMS calcd for $C_{12}H_{29}O_2Si$ $(MH)^+$: 233.1937, found 233.1943. GC condition for TMS-protected **2**: Supelco Beta Dex 120 fused silica capillary column 60 m x 0.25 m x 0.25 µm film thickness, t = 30.3 min, t = 33.7 min (oven: 98 °C, 1.4 mL/min).



(2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylheptan-3-ol (3). A 10 mL Schlenk equipped with magnetic stirrer and septum was flame-dried under vacuum and back-filled with N_2. To the flask was added *n*-Bu_2Zn (1.11 mL, 1.11 mmol, 1M in heptane). The septum was replaced with a glass stopper, and the flask was evacuated for 3 min and back-filled with N_2 3 times. The glass stopper was replaced with a septum, and CH_2Cl_2 (0.25 mL) was added. The rest of the

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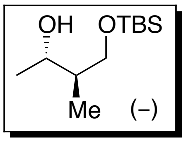
[5] Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *11*, 4092-4096.

[6] Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1968**, *14*, 3732-3738.

[7] Hoye, T. R.; Jeffrey, C. S.; Shao, F. *Nat. Protoc.* **2007**, *2*, 2451-2458.

[8] Riatto, V. B. Pilli, R. A. *J. Braz. Chem. Soc.* **1999**, *10*, 363-368.

procedure is the same as General Procedure A employing triflic acid (33 µL, 0.371 mmol) and (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol, in 0.25 mL CH_2Cl_2). The crude products were concentrated *in vacuo* and added to a silica gel column. The crude product was purified by flash chromatography (EtOAc:hexanes, 1:49 to 1:24) to afford the title compound as a clear oil (46.7 mg, 73% yield, dr 16:1). The major diastereomer was separated and characterized. $[\alpha]_D^{20}$ = –24.2 (c = 1.03, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.08 (s, 6H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.90 (m, 12H), 1.42 (m, 6H), 1.7 (m, 1H), 3.52 (m, 1H), 3.57 (dd, *J* = 7.7 Hz, 10.0 Hz, 1H), 3.80 (dd, *J* = 4.0 Hz, 10.0 Hz, 1H), 3.84 (d, *J* = 3.2 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz): δ −5.5, −5.4, 13.8, 14.3, 18.3, 23.1, 26.0, 27.7, 35.1, 40.0, 68.8. IR (neat): 3446, 2931, 2859, 1471, 1464, 1255. 1090, 837, 777 cm^{-1}. HRMS calcd for $C_{14}H_{33}O_2Si$ $(MH)^+$: 261.2250, found 261.2244.



(2*S*,3*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-methylbutan-2-ol (4).[9] General Procedure A was applied to Me_2Zn (88 µL, 0.670 mmol, neat), triflic acid (33 µL, 0.371 mmol), and (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol, in 0.19 mL CH_2Cl_2). The crude products were concentrated *in vacuo* and added to a silica gel column. The crude product was purified by flash chromatography (EtOAc:hexanes, 1:49) to afford the title compound as a clear oil (33.3 mg, 62% yield, dr 5:1). The product was characterized as a 5:1 mixture of diastereomers. ^1H NMR ($CDCl_3$, 500 MHz) major: δ 0.08 (s, 6H), 0.81 (d, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 1.18 (d, *J* = 6.30 Hz, 3H), 1.65 (m, 1H), 3.55 (dd, *J* = 8.5 Hz, 10.0 Hz, 1H), 3.69 (m, 1H), 3.78 (dd, *J* = 4.1 Hz, 10.2 Hz, 1H), 3.98 (d, *J* = 2.3 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: δ −5.5, −5.4, 13.5, 18.3, 21.5, 26.0, 41.6, 69.2, 73.4. IR (neat): 3435, 2958, 2930, 2859, 1472, 1463, 1256, 1079, 836, 776 cm^{-1}. HRMS calcd for $C_7H_{17}O_2Si$ $(M–C_4H_9)^+$: 161.0998, found 161.0997.

III. Diastereoselective Addition of (*E*)-Di- and Tri-substituted Vinyl Zinc Additions to β-Silyloxy Aldehydes

Genaral Procedure B (Preparation of EtZnOTf and EtZnONf): To a flame-dried 25 mL Schlenk flask equipped with magnetic stirrer and septum was added Et_2Zn (0.2 mL, 0.4 mmol, 2 M in CH_2Cl_2). The solution was cooled to –78 °C in a dry ice/acetone bath, and triflic acid or nonafluorobutane-1-sulfonic acid (0.371 mmol) was added dropwise. The reaction was allowed to stir and –78 °C for 5 min and was then warmed to rt and stirred for 1 h. The septum was replaced with a glass stopper, and the solvent was removed under reduced pressure.

General Procedure C: A 10 mL Schlenk flask equipped with magnetic stirrer and septum was flame-dried under vacuum and back-filled with N_2. To the flask was added $HBCy_2$ (43 mg, 0.24 mmol) and CH_2Cl_2. The flask was cooled to 0 °C, and the alkyne (0.24 mmol) was added dropwise. The reaction mixture was allowed to stir at 0 °C for 5 min and then stirred at rt for 15 min. The flask was cooled to –78 °C, Et_2Zn (.12 mL, 2M in toluene) was added dropwise, and the reaction mixture was allowed to stir at –78 °C for 30 min. EtZnONf (118 mg, 0.3 mmol) was added at –78 °C, and the flask was transferred to a cooling bath at –15 °C. The aldehyde (0.2

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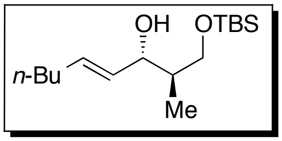
[9] Tanner, D.; Somfai, P. *Tetrahedron* **1987**, *43*, 4395-4406.

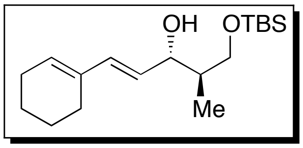
mmol) was added dropwise as a solution in toluene, and the reaction was allowed to stir at –15 °C for 14–18 h. The reaction was quenched with a saturated solution of NH_4Cl (15 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The crude products were concentrated *in vacuo* and purified by flash-chromatography on silica gel.

General Procedure D: The procedure follows General Procedure C, except EtZnOTf (73 mg, 0.3 mmol) is employed.



2*R*,3*S*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylnon-4-en-3-ol (5).[10] General Procedure C was applied to $HBCy_2$ (2.7 mg, 0.296 mmol), CH_2Cl_2 (0.41 mL), 1-hexyne (34 µL, 0.296 mmol), Et_2Zn (0.15 mL, 0.30 mmol), EtZnONf (146 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.26 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (43.2 mg, 64% yield, dr 10:1). The product was characterized as a 10:1 mixture of diastereomers. ^{1}H NMR ($CDCl_3$, 500 MHz) major: δ 0.08 (s, 6H), 0.81 (d, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 1.34 (m, 4H), 1.74 (m, 1H), 2.05 (m, 2H), 3.57 (dd, *J* = 7.7 Hz, 9.9 Hz, 1 H), 3.74 (d, *J* = 3.0 Hz, 1H), 3.78 (dd, *J* = 4.3 Hz, 10.1 Hz, 1H), 3.95 (m, 1H), 5.44 (dd, *J* = 7.2 Hz, 15.3 Hz, 1H), 5.66 (m, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: –5.4, 13.7, 14.1, 18.3, 22.5, 26.0, 31.6, 32.1, 40.3, 68.4, 78.4, 131.7, 133.1. δ IR (neat): 3432, 2957, 2929, 2858, 1670, 1471, 1255, 1095, 1006, 970, 836, 776 cm^{-1}. HRMS calcd for $C_{16}H_{33}OSi$ $(M–OH)^+$: 269.2301, found 269.2290.

General Procedure D was applied to $HBCy_2$ (2.7 mg, 0.296 mmol), CH_2Cl_2 (0.41 mL), 1-hexyne (34 µL, 0.296 mmol), Et_2Zn (0.15 mL, 0.30 mmol), EtZnOTf (90 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.26 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (56.0 mg, 79% yield, dr 4:1).



(3*S*,4*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-1-(cyclohex-1-en-1-yl)-4-methylpent-1-en-3-ol (6). General Procedure C was applied to $HBCy_2$ (93.4 mg, 0.524 mmol), CH_2Cl_2 (0.71 mL), 1-ethynylcyclohexene (62 µL, 0.524 mmol), Et_2Zn (0.26 mL, 0.52 mmol), EtZnONf (258 mg, 0.656 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (88.5 mg, 0.437 mmol), and toluene (0.47 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (90 mg, 66% yield, dr 5.8:1). The product was characterized as a 5.8:1 mixture of diastereomers. ^{1}H NMR ($CDCl_3$, 500 MHz) major: δ 0.08 (s, 1H), 0.83 (d, *J* = 7.0 Hz, 3H), 0.91 (s, 9H), 1.64 (m, 4H), 1.78 (m, 1H), 2.13 (bs, 4H), 3.58 (dd, *J* = 7.4 Hz, 10.0 Hz, 1H), 3.73 (d, *J* = 3.1 Hz, 1H), 3.79 (dd, *J* = 4.2 Hz, 10.1 Hz, 1H), 4.04 (m, 1H), 5.53 (dd, *J* = 7.6 Hz, 16.0 Hz, 1H), 5.74 (bs,

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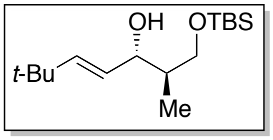
[10] Wipf, P.; Xu, W. *J. Org. Chem.* **1993**, *58*, 825-826.

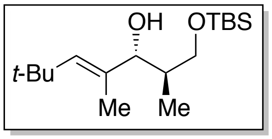
1H), 6.21 (d, J = 15.5 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: δ –5.36, –5.44, 11.6, 13.8, 18.3, 22.7, 22.8, 24.8, 26.0, 40.6, 68.3, 78.4, 127.2, 129.7, 135.1, 135.4. IR (neat): 3429, 2929, 2857, 1651, 1625, 1471, 1463, 1255, 1092, 1006, 965, 814, 776, 667 cm^{-1}. HRMS calcd for $C_{18}H_{35}O_2Si$ $(MH)^+$: 311.2406, found 311.2412.

General Procedure D was applied to $HBCy_2$ (93.4 mg, 0.524 mmol), CH_2Cl_2 (0.71 mL), 1-ethynylcyclohexene (62 µL, 0.524 mmol), Et_2Zn (0.26 mL, 0.52 mmol), EtZnOTf (160 mg, 0.656 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (88.5 mg, 0.437 mmol), and toluene (0.47 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (68.3 mg, 50% yield, dr 2.3:1).



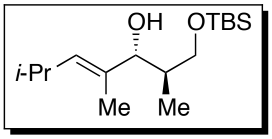
(2*R*,3*S*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,6,6-trimethylhept-4-en-3-ol (7). General Procedure C was applied to $HBCy_2$ (97.1 mg, 0.545 mmol), CH_2Cl_2 (0.76 mL), 3,3-dimethyl butyne (67 µL, 0.545 mmol), Et_2Zn (0.27 mL, 0.545 mmol), EtZnONf (268 mg, 0.681 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (91.9 mg, 0.454 mmol), and toluene (0.49 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (86.0 mg, 70% yield, dr 10:1). The product was characterized as a 10:1 mixture of diastereomers. ^1H NMR ($CDCl_3$, 500 MHz) major: δ 0.08 (s, 6H), 0.79 (d, J = 7.0 Hz, 3H), 0.91 (s, 9H), 1.02 (s, 9H), 1.75 (m, 1H), 3.56 (dd, J = 7.9 Hz, 9.7 Hz, 1H), 3.79 (dd, J = 4.0 Hz, 9.9 Hz, 1H), 3.82 (d, J = 2.7 Hz, 1 H), 3.95 (m, 1H), 5.34 (dd, J = 7.4 Hz, 15.8 Hz, 1H), 5.68 (d, J = 15.6 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: δ –5.5, –5.4, 13.7, 18.3, 26.0, 29.8, 33.0, 40.3, 68.5, 78.7, 126.4, 143.9. IR (neat): 3438, 2859, 1662, 1472, 1463, 1362, 1256, 1095, 1024, 1006, 974, 836, 776 cm^{-1}. HRMS calcd for $C_{16}H_{33}OSi$ $(M–OH)^+$: 269.2301, found 269.2312.

General Procedure D was applied to $HBCy_2$ (97.1 mg, 0.545 mmol), CH_2Cl_2 (0.76 mL), 3,3-dimethyl butyne (67 µL, 0.545 mmol), Et_2Zn (0.27 mL, 0.545 mmol), EtZnOTf (166 mg, 0.681 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (91.9 mg, 0.454 mmol), and toluene (0.49 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (86.0 mg, 70% yield, dr 3.6:1).



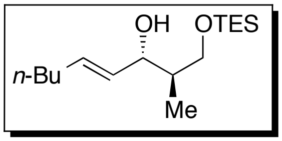
(2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (8). General Procedure A was applied to $HBCy_2$ (52.7 mg, 0.296 mmol), CH_2Cl_2 (0.41 mL), 4,4-dimethyl-2-pentyne (40 µL, 0.30 mmol), Et_2Zn (0.15 mL, 0.30 mmol), EtZnOTf (90.2 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.26 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (59 mg, 80% yield, dr > 20:1). $[\alpha]_D^{20}$ = –29.7 (c = 1.03, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.09 (s, 6H), 0.69 (d, J=6.9 Hz, 3H), 0.91 (s, 9H), 1.12 (s, 9H), 1.71 (s, 3H), 1.84 (m, 1H), 3.58 (t, J=8.4 Hz, 1H), 3.74 (d, J=8.7 Hz, 1H), 3.79 (dd, J=4.0 Hz, 9.9 Hz, 1H), 4.02 (bs, 1H), 5.39 (s, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz): δ -5.5, -5.4, 12.1, 13.8, 18.3, 26.0, 31.0, 32.4, 37.5, 69.2, 85.8, 134.4, 138.5. IR (neat): 3445, 2931, 2859, 1660, 1471, 1464, 1254, 1091, 1006, 836, 777 cm^{-1}. HRMS calcd for $C_{17}H_{36}O_2NaSi$ (M + Na)$^+$: 323.2382, found 323.2379.

General Procedure D was applied to $HBCy_2$ (52.7 mg, 0.296 mmol), CH_2Cl_2 (0.41 mL), 4,4-dimethyl-2-pentyne (40 µL, 0.30 mmol), Et_2Zn (0.15 mL, 0.30 mmol), EtZnOTf (90.2 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.26 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (56.9 mg, 79% yield, dr 11:1).



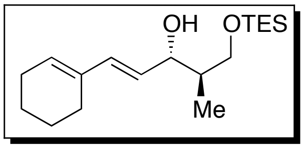
(2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6-trimethylhept-4-en-3-ol (9). General Procedure C was applied to $HBCy_2$ (88 mg, 0.494 mmol), CH_2Cl_2 (0.41 mL), 4-methyl-2-pentyne (57 µL, 0.494 mmol), Et_2Zn (0.25 mL, 0.50 mmol), EtZnONf (146 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.16 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (55 mg, 78% yield, dr 17:1). The major diastereomer was separated and characterized. $[\alpha]_D^{20}$ = –23.0 (c = 0.847, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.09 (s, 6H), 0.70 (d, *J* = 7.0 Hz, 3H), 0.91 (s, 9H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 1.61 (d, *J* = 1.2 Hz, 3H), 1.85 (m, 1H), 2.55 (m, 1H), 3.58 (dd, *J* = 8.1 Hz, 9.8 Hz, 1H), 3.79 (m, 2H), 3.98 (d, *J* = 2.2 Hz, 1H), 5.20 (d, *J* = 9.3 Hz, 1H). ^{13}C{^{1}H} ($CDCl_3$, 125 MHz): δ –5.5, –5.4, 11.2, 13.8, 18.3, 23.1, 23.1, 26.0, 27.0, 37.5, 69.0, 84.2, 133.4, 136.0. IR (neat): 3452, 2930, 2859, 1669, 1464, 1254, 1089, 1006, 836, 777 cm^{-1}. HRMS calcd for $C_{16}H_{33}OSi$ (M – OH)$^+$: 269.2301, found 269.2300.

General Procedure D was applied to $HBCy_2$ (88 mg, 0.494 mmol), CH_2Cl_2 (0.41 mL), 4-methyl-2-pentyne (57 µL, 0.494 mmol), Et_2Zn (0.25 mL, 0.50 mmol), EtZnOTf (90.3 mg, 0.371 mmol), (*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methylpropanal (50.0 mg, 0.247 mmol), and toluene (0.16 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (54.6 mg, 77% yield, dr 7.7:1).



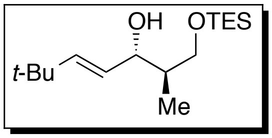
(2*R*,3*S*,*E*)-1-((Triethylsilyl)oxy)-2-methylnon-4-en-3-ol (10). General Procedure A was applied to $HBCy_2$ (71.2 mg, 0.400 mmol), CH_2Cl_2 (0.55 mL), 1-hexyne (46 µL, 0.400 mmol), Et_2Zn (0.20 mL, 0.40 mmol), EtZnONf (197 mg, 0.500 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (67.1 mg, 0.332 mmol), and toluene (0.35 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (62 mg, 66% yield, dr 11:1). The product was characterized as a 6.2:1 mixture of diastereomers. ^{1}H NMR ($CDCl_3$, 500 MHz) major: δ 0.62 (q, 6H), 0.81 (d, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 1.34 (m, 4H), 1.77 (m, 1H), 2.05 (m, 2H), 3.58 (dd, *J* = 7.9 Hz, *J* = 10.0 Hz, 1H), 3.78 (dd, *J* = 4.2 Hz, *J* = 10.0 Hz, 1H), 3.88 (d, *J* = 2.8 Hz, 1H), 3.94 (m, 1H), 5.44 (dd, *J* = 7.5 Hz, *J* = 15.4 Hz, 1H), 5.66 (m, 1H). ^{13}C{^{1}H} ($CDCl_3$, 125 MHz) major: δ 4.4, 6.9, 13.7, 14.1, 22.4, 31.6, 32.1, 40.3, 68.2, 78.6, 131.7, 133.1. IR (neat): 3435, 2915, 2876, 1670, 1458, 1415, 1239, 1093, 1008, 970, 804, 745 cm^{-1}. HRMS calcd for $C_{16}H_{34}O_2NaSi$ (M + Na)$^+$: 309.2226, found 309.2238.

Procedure A was applied to $HBCy_2$ (71.2 mg, 0.400 mmol), CH_2Cl_2 (0.55 mL), 1-hexyne (46 μL, 0.400 mmol), Et_2Zn (0.20 mL, 0.40 mmol), EtZnOTf (122 mg, 0.500 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (67.1 mg, 0.332 mmol), and toluene (0.35 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (57.3 mg, 60% yield, dr 6.2:1).



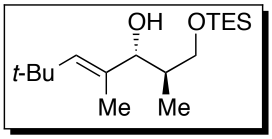
(3*S*,4*R*,*E*)-5-((Triethylsilyl)oxy)-1-(cyclohex-1-en-1-yl)-4-methylpent-1-en-3-ol (11). General Procedure C was applied to $HBCy_2$ (102 mg, 0.572 mmol), CH_2Cl_2 (0.80 mL), 1-ethynylcyclohexene (65 μL, 0.572 mmol), Et_2Zn (0.29 mL, 0.58 mmol), EtZnONf (282 mg, 0.716 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (96.5 mg, 0.477 mmol), and toluene (0.51 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (116 mg, 78% yield, dr 9:1). The product was characterized as a 9:1 mixture of diastereomers. ^1H NMR ($CDCl_3$, 500 MHz) major: δ 0.62 (q, 6H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.97 (t, *J* = 8.1 Hz, 9H), 1.63 (m, 4H), 1.78 (m, 1H), 2.12 (m, 4H), 3.59 (dd, *J* = 7.9 Hz, *J* = 10.0 Hz, 1H), 3.79 (dd, *J* = 4.2 Hz, *J* = 9.9 Hz, 1H), 3.88 (d, *J* = 2.9 Hz, 1H), 4.04 (m, 1H), 5.53 (dd, *J* = 7.4 Hz, *J* = 15.8 Hz, 1H), 5.74 (bs, 1H), 6.21 (d, *J* = 15.7 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: δ 4.4, 6.9, 13.8, 22.7, 22.7, 24.8, 26.1, 40.6, 68.2, 78.6, 127.2, 129.7, 135.1, 135.4. IR (neat): 3428, 2876, 1650, 1625, 1458, 1414, 1240, 1092, 1011, 965, 803, 744 cm^{-1}. HRMS calcd for $C_{18}H_{34}N_6NaSi$ $(M + Na)^+$: 333.2226, found 333.2215.

General Procedure D was applied to $HBCy_2$ (102 mg, 0.572 mmol), CH_2Cl_2 (0.80 mL), 1-ethynylcyclohexene (65 μL, 0.572 mmol), Et_2Zn (0.29 mL, 0.58 mmol), EtZnOTf (174 mg, 0.716 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (96.5 mg, 0.477 mmol), and toluene (0.51 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (99.8 mg, 67% yield, dr 4.6:1).



(2*R*,3*S*,*E*)-1-((Triethylsilyl)oxy)-2,6,6-trimethylhept-4-en-3-ol (12). General Procedure C was applied to $HBCy_2$ (99.8 mg, 0.560 mmol), CH_2Cl_2 (0.78 mL), 3,3-dimethyl butyne (70 μL, 0.70 mmol), Et_2Zn (0.28 mL, 0.56 mmol), EtZnONf (275 mg, 0.700 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (99.5 mg, 0.467 mmol), and toluene (0.50 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (95 mg, 71% yield, dr 18:1). The major diastereomer was characterized as a 18:1 mixture of diastereomers. ^1H NMR ($CDCl_3$, 500 MHz) major: δ 0.62 (q, 6H), 0.79 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 8.1 Hz, 9H) 1.02 (s, 9H), 1.75 (m, 1H), 3.58 (dd, *J* = 8.1 Hz, *J* =10.0 Hz, 1H), 3.79 (dd, *J* = 4.2 Hz, *J* = 10.0 Hz, 1H), 3.94 (dd, *J* = 2.7 Hz, 7.5 Hz, 1H), 3.96 (d, *J* = 2.5 Hz, 1H), 5.35 (dd, *J* = 7.2 Hz, *J* = 15.6 Hz, 1H), 5.68 (dd, *J* = 0.74 Hz, *J* = 15.6 Hz, 1H). $^{13}C\{^1H\}$ ($CDCl_3$, 125 MHz) major: δ 4.4, 6.9, 13.7, 29.8, 33.0, 40.3, 68.3, 78.9, 126.5, 143.9. IR (neat): 3436, 2910, 2877, 1661, 1460, 1415, 1363, 1239, 1094, 1010, 974, 805, 744 cm^{-1}. HRMS calcd for $C_{16}H_{34}O_2NaSi$ $(M + Na)^+$: 309.2226, found 309.2236.

Procedure D was applied to $HBCy_2$ (99.8 mg, 0.560 mmol), CH_2Cl_2 (0.78 mL), 3,3-dimethyl butyne (70 μL, 0.70 mmol), Et_2Zn (0.28 mL, 0.56 mmol), EtZnOTf (171 mg, 0.700 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (99.5 mg, 0.467 mmol), and toluene (0.50 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (60.8 mg, 45% yield, dr 10:1).

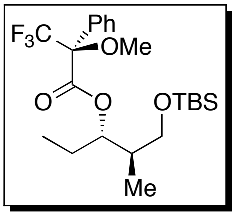


(2*R*,3*R*,*E*)-1-((Triethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (13). General Procedure C was applied to HBCy$_2$ (64.8 mg, 0.364 mmol), CH$_2$Cl$_2$ (0.51 mL), 4,4-dimethyl-2-pentyne (49 µL, 0.364 mmol), Et$_2$Zn (0.18 mL, 0.364 mmol), EtZnONf (179 mg, 0.455 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (61.3 mg, 0.303 mmol), and toluene (0.33 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (68.8 mg, 76% yield, dr > 20:1). $[\alpha]_D^{20}$ = –21.2 (c = 0.920 CHCl$_3$). ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.63 (q, 6H), 0.68 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 1.12 (s, 9H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.85 (m, 1H), 3.58 (dd, *J* = 8.6 Hz, *J* = 9.8 Hz, 1H), 3.74 (dd, *J* = 1.4 Hz, *J* = 8.5 Hz, 1H), 3.78 (dd, *J* = 4.16 Hz, *J* = 10.0 Hz, 1H), 4.16 (d, *J* = 1.7 Hz, 1H), 5.39 (s, 1H). ^{13}C{^{1}H} (CDCl$_3$, 125 MHz): δ 4.4, 6.9, 12.0, 13.8, 31.1, 32.4, 37.6, 69.1, 86.1, 134.4, 138.6. IR (neat): 3486, 2911, 2877, 1659, 1460, 1364, 1237, 1091, 1006, 838, 797, 745 cm^{-1}. HRMS calcd for $C_{17}H_{36}O_2NaSi$ (M + Na)$^+$: 323.2382, found 323.2394.

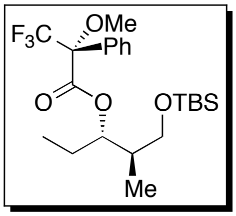
General Procedure D was applied to HBCy$_2$ (64.8 mg, 0.364 mmol), CH$_2$Cl$_2$ (0.51 mL), 4,4-dimethyl-2-pentyne (49 µL, 0.364 mmol), Et$_2$Zn (0.18 mL, 0.364 mmol), EtZnOTf (111 mg, 0.455 mmol), (*R*)-3-((triethylsilyl)oxy)-2-methylpropanal (61.3 mg, 0.303 mmol), and toluene (0.33 mL). The crude product was purified by flash chromatography (EtOAc:hexanes, 1:50 to 1:25) to afford the title compound as a clear oil (68.8 mg, 76% yield, dr 17.5:1).

IV. Determination of the Absolute Configuration of 1,3-Diol products. Mosher's Method for the Determination of Absolute Stereochemistry.

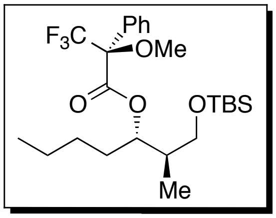
General Procedure E: Synthesis of *O*-Mosher Ester. To a solution of the 1,3-diol, pyridine (10 drops), and CH$_2$Cl$_2$ (0.7 mL) was added (*R*)-(–)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ((*R*)-MTPA-Cl) at 0 °C. The reaction was warmed to rt and allowed to stir for a period of time as outlined below. Water (1 mL) was added, and the product was extracted with diethyl ether (3 mL x 3). The combined organic phases were dried over MgSO$_4$ and filtered. The solvent was removed *in vacuo*, and the crude product was purified by flask chromatography on silica gel. The same procedure was used with (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ((*S*)-MTPA-Cl).



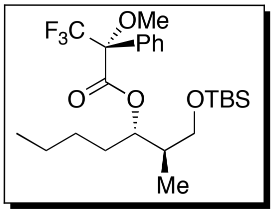
Preparation of the (*S*)-*O*-Mosher Ester of (2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylpentan-3-ol (14). General Procedure E was applied to (2*R*,3*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2-methylpentan-3-ol (10.7 mg, 0.046 mmol) and (*R*)-MTPA-Cl (15 µL, 0.082 mmol). The reaction stirred for 3 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes to 5% EtOAc in hexanes) to give the desired product as a clear oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.02 (s, 3H), 0.02 (s, 3H), 0.81 (t, *J*=7.4 Hz, 3H), 0.89 (s, 9H), 0.91 (d, *J*=7.1 Hz, 3H), 1.60 (m, 1H), 1.68 (m, 1H), 2.03 (m, 1H), 3.46 (dd, *J*=6.4 Hz, 10.3 Hz, 1H), 3.54 (s, 3H), 3.55 (dd, *J*=5.5 Hz, 10.3 Hz, 1H), 5.12 (m, 1H), 7.50 (m, 3H), 7.55 (m, 2H). HRMS calcd for $C_{22}H_{36}O_4F_3Si$ (MH)$^+$: 449.2335, found 449.2348.



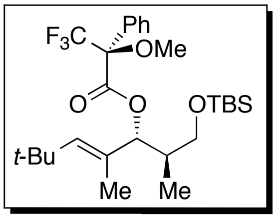
Preparation of the (*R*)-*O*-Mosher Ester of (2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylpentan-3-ol (15). General Procedure E was applied to (2*R*,3*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2-methylpentan-3-ol (10.4 mg, 0.045 mmol) and (*S*)-MTPA-Cl (15 µL, 0.082 mmol). The reaction stirred for 3 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes to 5% EtOAc in hexanes) to give the desired product as a clear oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.00 (s, 3H), 0.00 (s, 3H), 0.83 (d, *J*=6.9 Hz, 3H), 0.88 (s, 9H), 0.92 (t, *J*=7.4 Hz, 3 H), 1.66 (m, 1H), 1.74 (m, 1H), 2.01 (m, 1H), 3.38 (dd, *J*=6.5 Hz, 10.0 Hz, 1H), 3.51 (dd, *J*=5.7 Hz, 10.1 Hz, 1H), 3.56 (d, *J*=1.1 Hz, 1H), 5.11 (m, 1H), 7.40 (m, 3H), 7.56 (m, 2H). HRMS calcd for $C_{22}H_{35}O_4NaSiF_3$ (M + Na)$^+$: 471.2154, found 471.2149.



Preparation of the (*S*)-*O*-Mosher Ester of (2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylheptan-3-ol (16). General Procedure E was applied to (2*R*,3*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2-methylheptan-3-ol (10.5 mg, 0.040 mmol) and (*R*)-MTPA-Cl (14 µL, 0.077 mmol). The reaction stirred for 18 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes) to give the desired product as a clear oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.03 (s, 3H) 0.03 (s, 3H), 0.83 (t, *J*=7.2 Hz, 3H), 0.90 (s, 9H), 0.91 (d, *J*=7.0 Hz, 3H), 1.20 (m, 4H), 1.58 (m, 2H), 2.04 (m, 1H), 3.47 (dd, *J*=6.2 Hz, 10.0 Hz, 1H), 3.56 (m, 4H), 5.20 (m, 1H), 7.41 (m, 3H), 7.56 (m, 2H). HRMS calcd for $C_{24}H_{39}O_4F_3NaSi$ (M + Na)$^+$: 499.2467, found 499.2483.

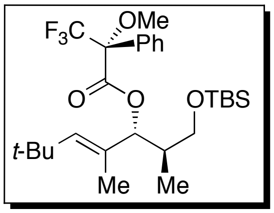


Preparation of the (*R*)-*O*-Mosher Ester of (2*R*,3*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-methylheptan-3-ol (17). General Procedure E was applied to (2*R*,3*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2-methylheptan-3-ol (9.3 mg, 0.035 mmol) and (*S*)-MTPA-Cl (14 µL, 0.077 mmol). The reaction stirred for 18 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes) to give the desired product as a clear oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.01 (s, 3H), 0.01 (s, 3H), 0.83 (t, *J*=6.9 Hz, 3H), 0.89 (m, 12H), 1.29 (m, 4H), 1.65 (m, 2H), 2.01 (m, 1H), 3.39 (dd, *J*=6.5 Hz, 10.1 Hz, 1H), 3.51 (dd, *J*=6.0 Hz, 10.1 Hz, 1H), 3.56 (s, 3H), 5.19 (m, 1H), 7.41 (m, 3H), 7.56 (m, 2H). HRMS calcd for $C_{24}H_{39}O_4NaF_3Si$ (M + Na)$^+$: 499.2467, found 499.2461.



Preparation of the (*S*)-*O*-Mosher Ester of (2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (18). General Procedure B was applied to (2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (10.7 mg, 0.036 mmol) and (*R*)-MTPA-Cl (13 µL, 0.068 mmol). The reaction stirred for 18 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes) to give the desired product as a clear oil.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.03 (s, 6H), 0.84 (d, *J*=7.0 Hz, 3H), 0.90 (s, 9H), 1.12 (s, 9H), 1.48 (s, *J*=1.2 Hz, 3H), 1.97 (m, 1H) 3.56 (m, 4H), 3.58 (dd, *J*=3.1 Hz, 8.4 Hz, 1H), 5.13 (d, *J*=10.2 Hz, 1H), 5.60 (*J*=1.4 Hz, 1H), 7.39 (m, 3H), 7.49 (m, 2H). HRMS calcd for $C_{27}H_{43}O_4F_3NaSi$ (M + Na)$^+$: 539.2780, found 539.2796.



Preparation of the (*R*)-*O*-Mosher Ester of (2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (19). General Procedure E was applied to (2*R*,3*R*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4,6,6-tetramethylhept-4-en-3-ol (10.3 mg, 0.034 mmol) and (*S*)-MTPA-Cl (13 µL, 0.068 mmol). The reaction stirred for 18 h. The crude product was purified by column chromatography on silica gel (2% EtOAc in hexanes) to give the desired product as a clear oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 0.00 (s, 6H), 0.89 (d, *J*=6.9 Hz, 3H), 0.89 (s, 9H), 1.14 (s, 9H), 1.69 (d, *J*=1.1 Hz, 3H), 1.97 (m, 1H), 3.38 (dd, (*J*=6.2 Hz, 9.7 Hz, 1H), 3.50 (dd, *J*=3.1 Hz, 9.7 Hz, 1H), 3.53 (s, 3H), 5.20 (d, *J*=10.2 Hz, 1H), 5.65 (s, 1H), 7.38 (m, 3H), 7.48 (m, 2H). HRMS calcd for $C_{27}H_{43}O_4F_3NaSi$ (M + Na)$^+$: 539.2780, found 539.2802.

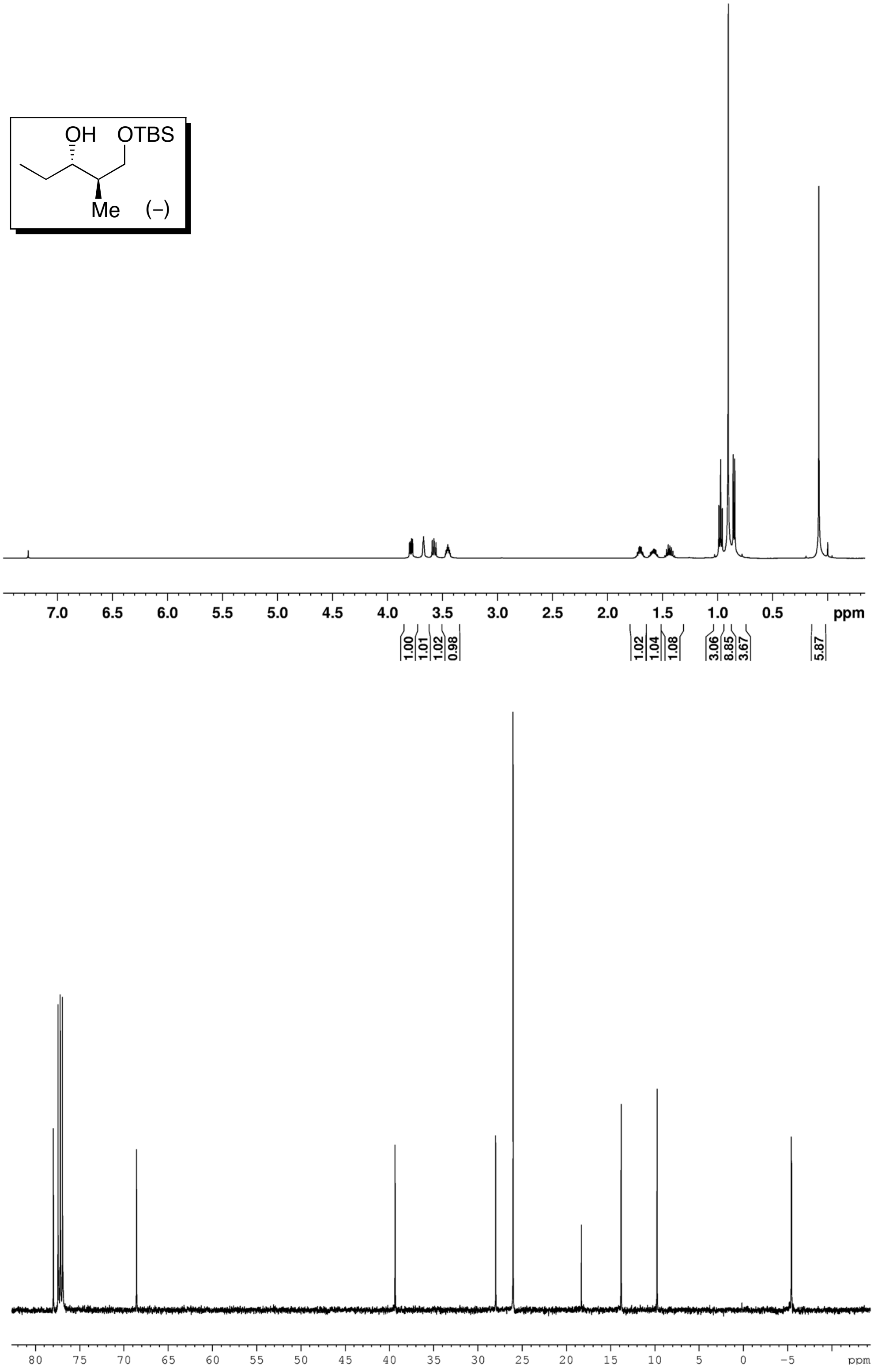


Figure SI-1. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **2**

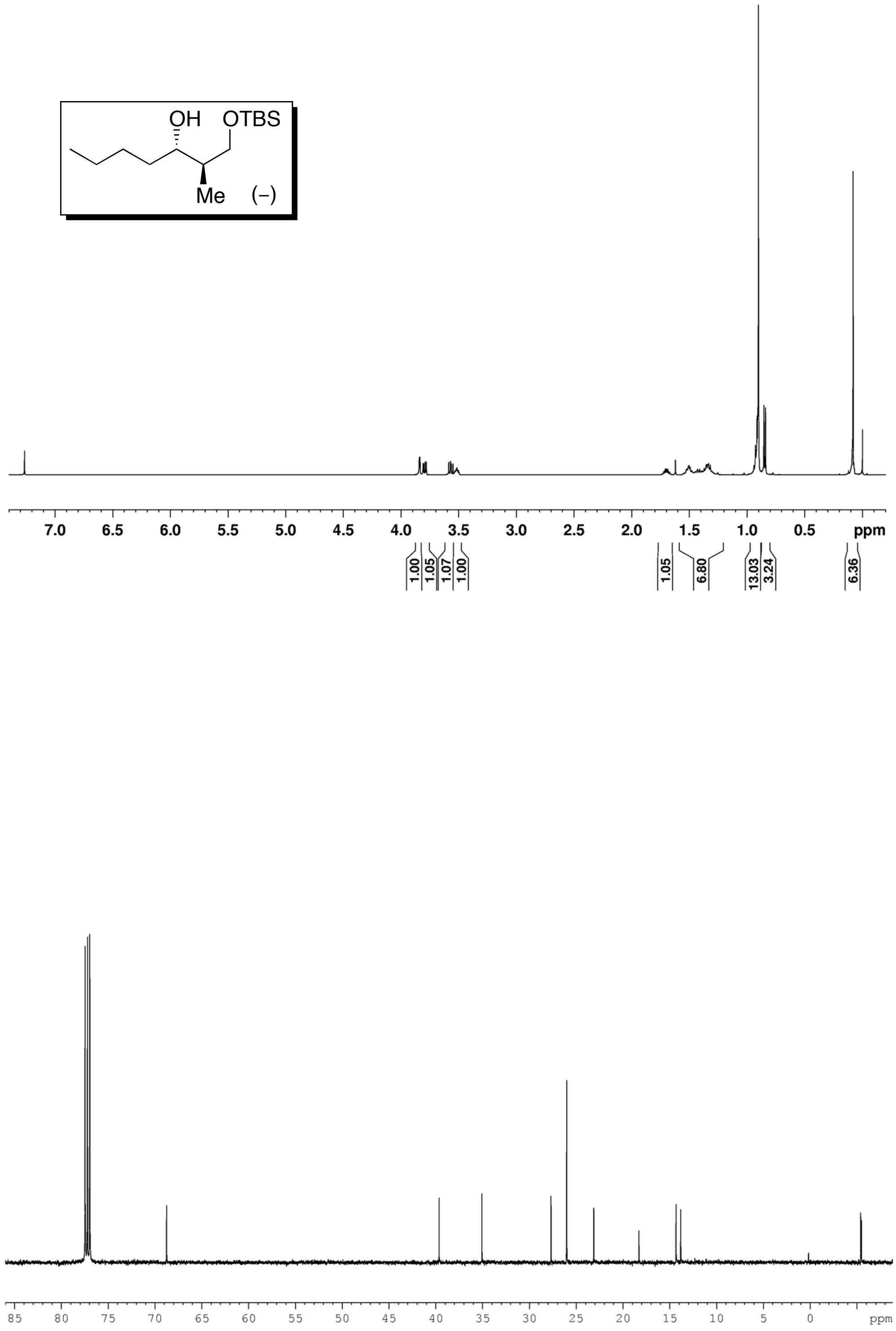


Figure SI-2. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **3**

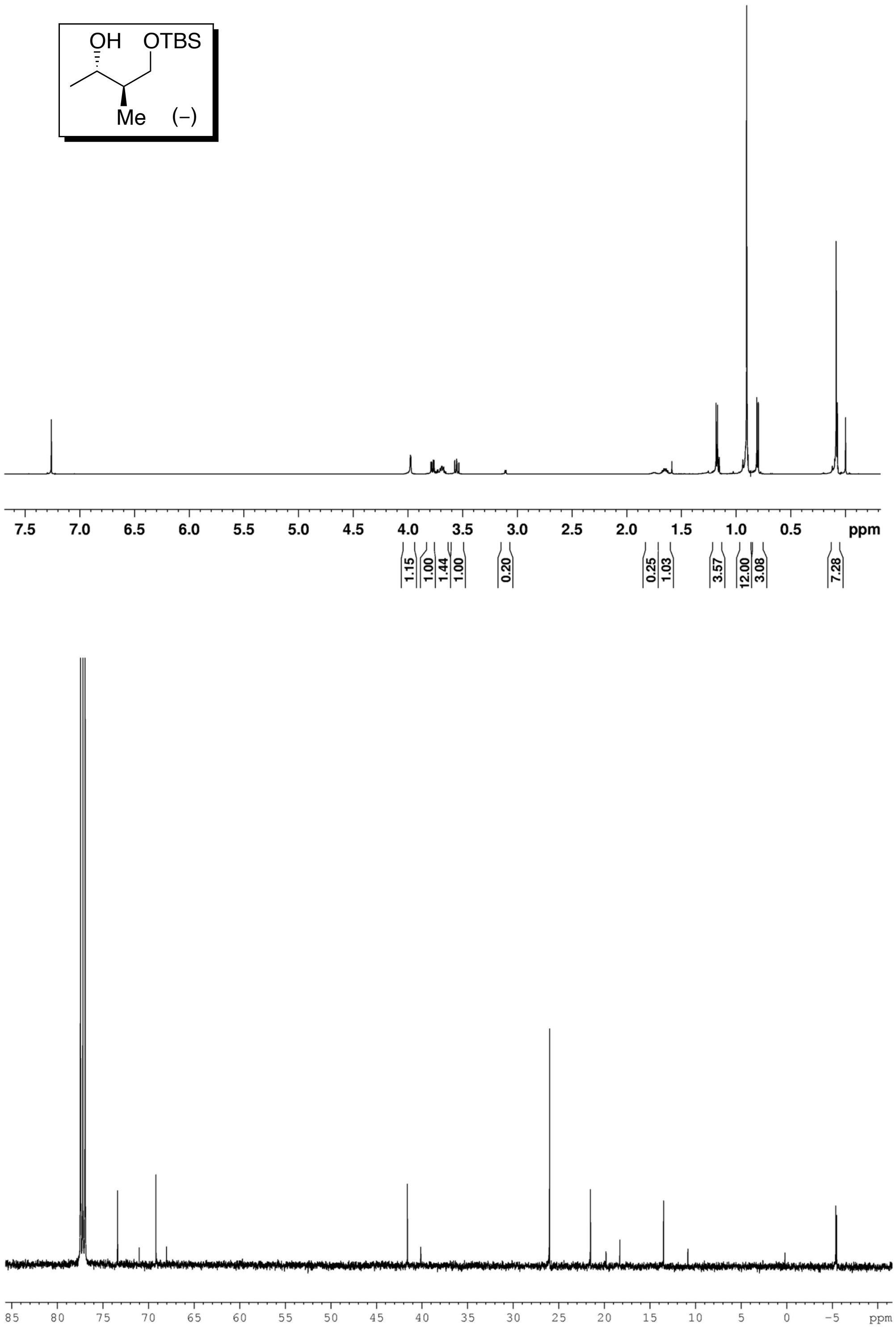


Figure SI-3. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in $CDCl_3$ of **4**

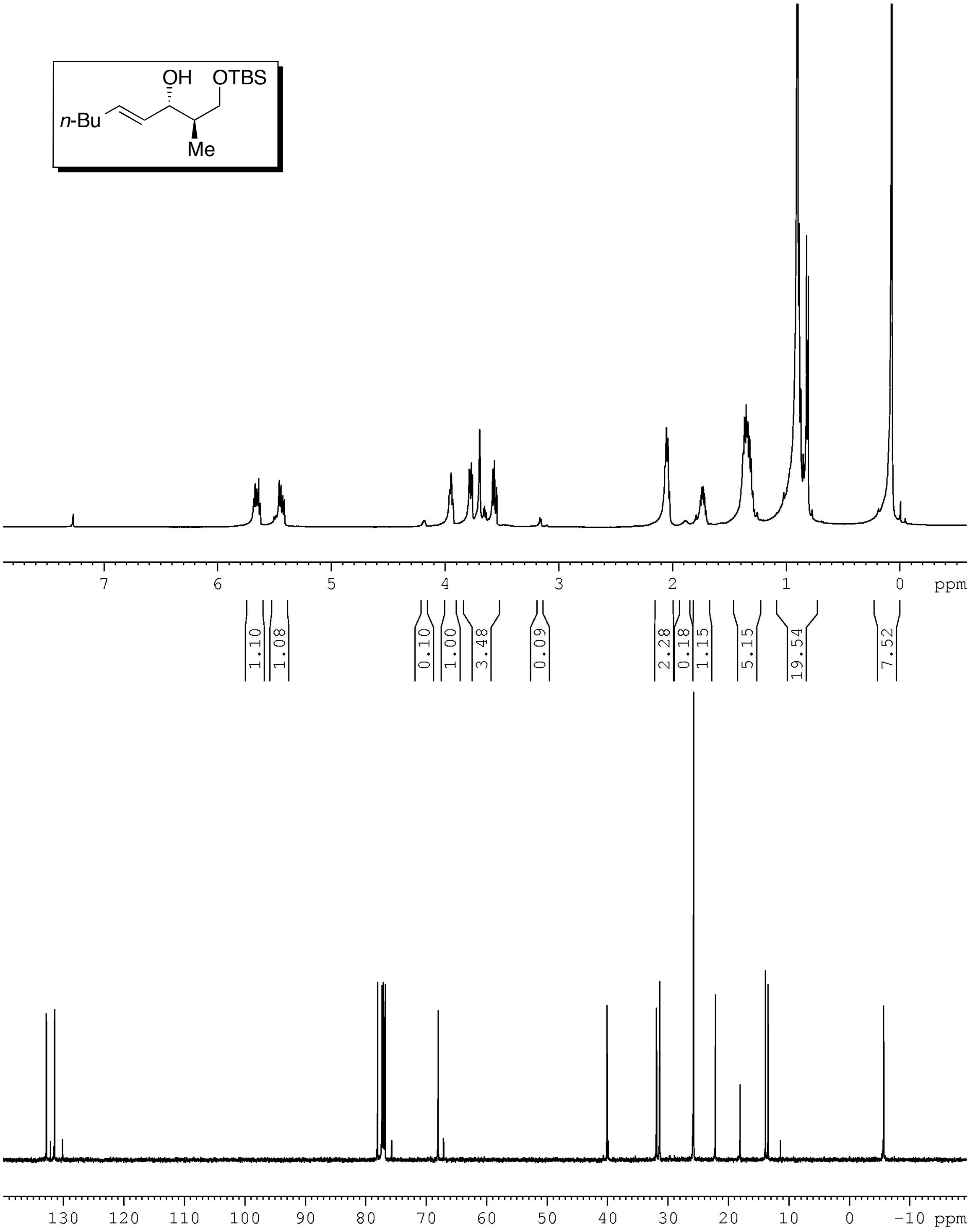


Figure SI-4. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **5**

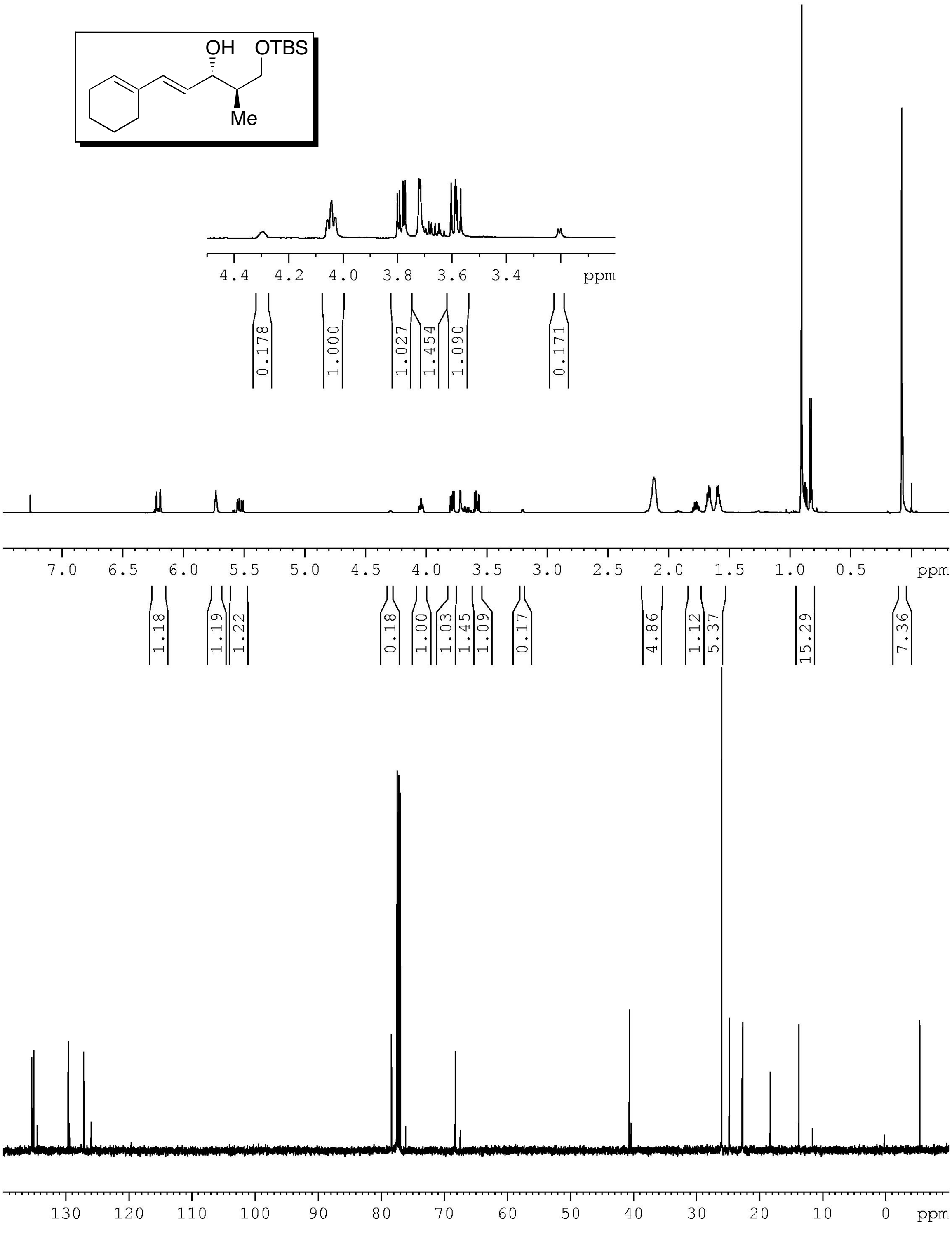


Figure SI-5. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in $CDCl_3$ of **6**

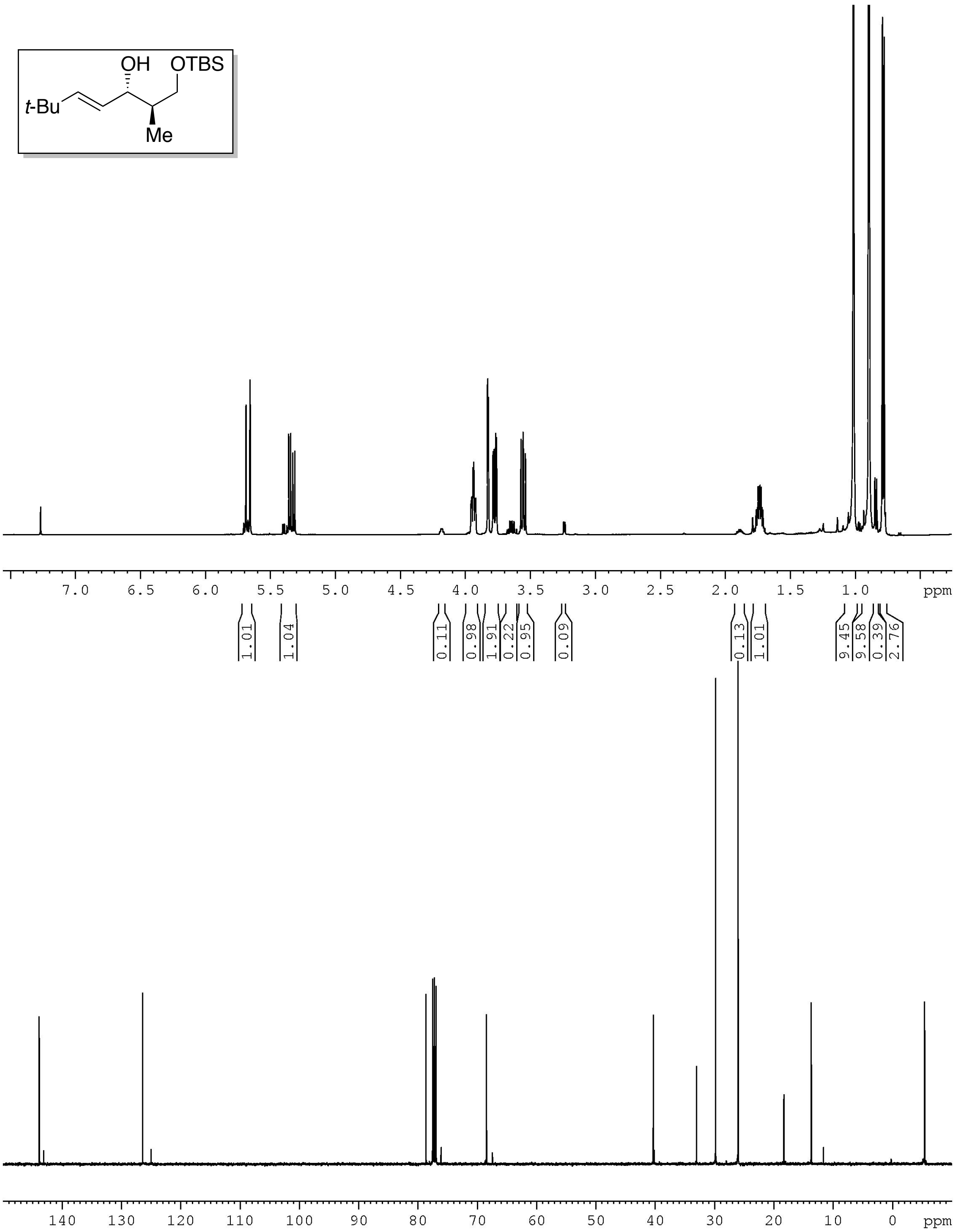


Figure SI-6. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in $CDCl_3$ of **7**

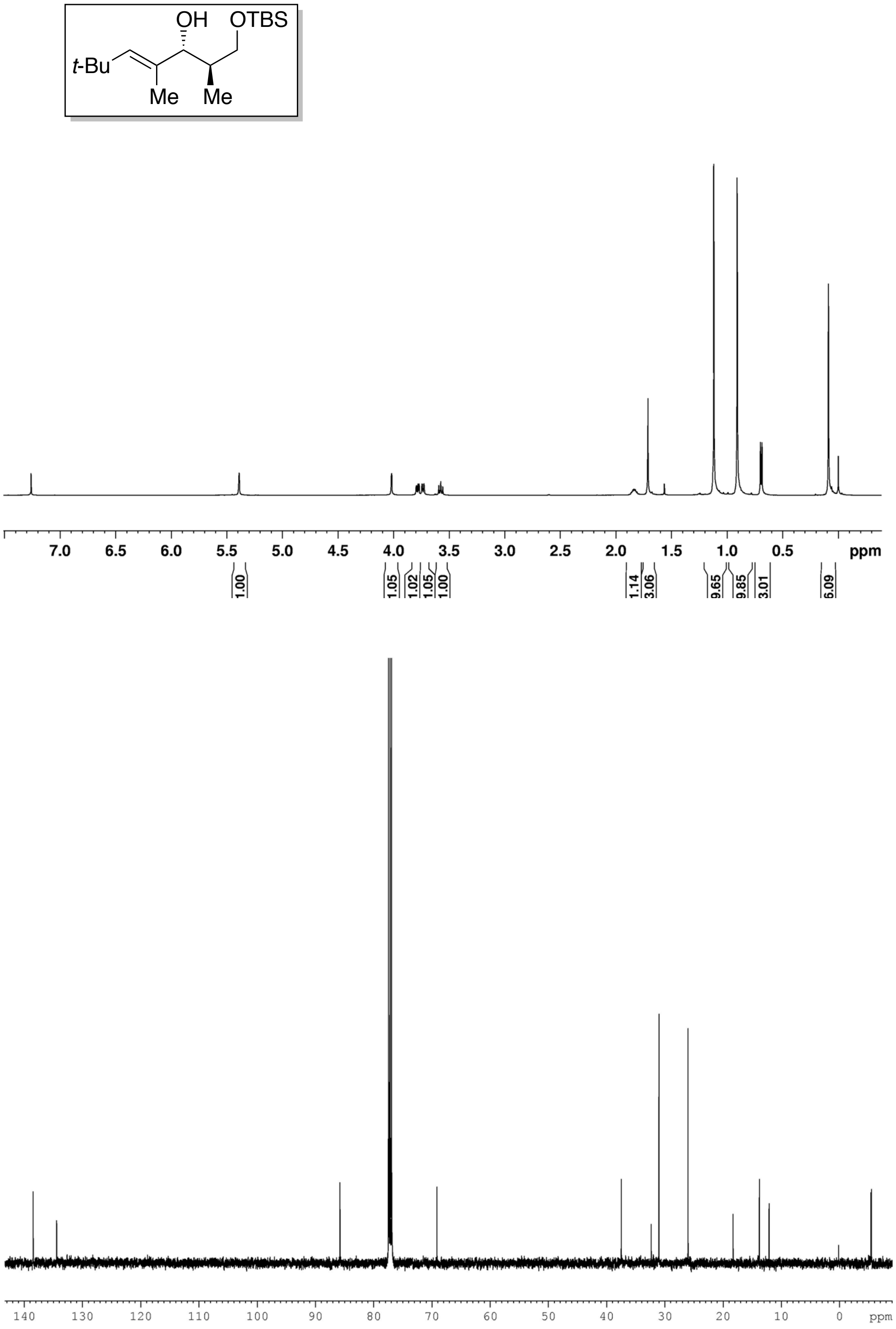


Figure SI-7. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **8**

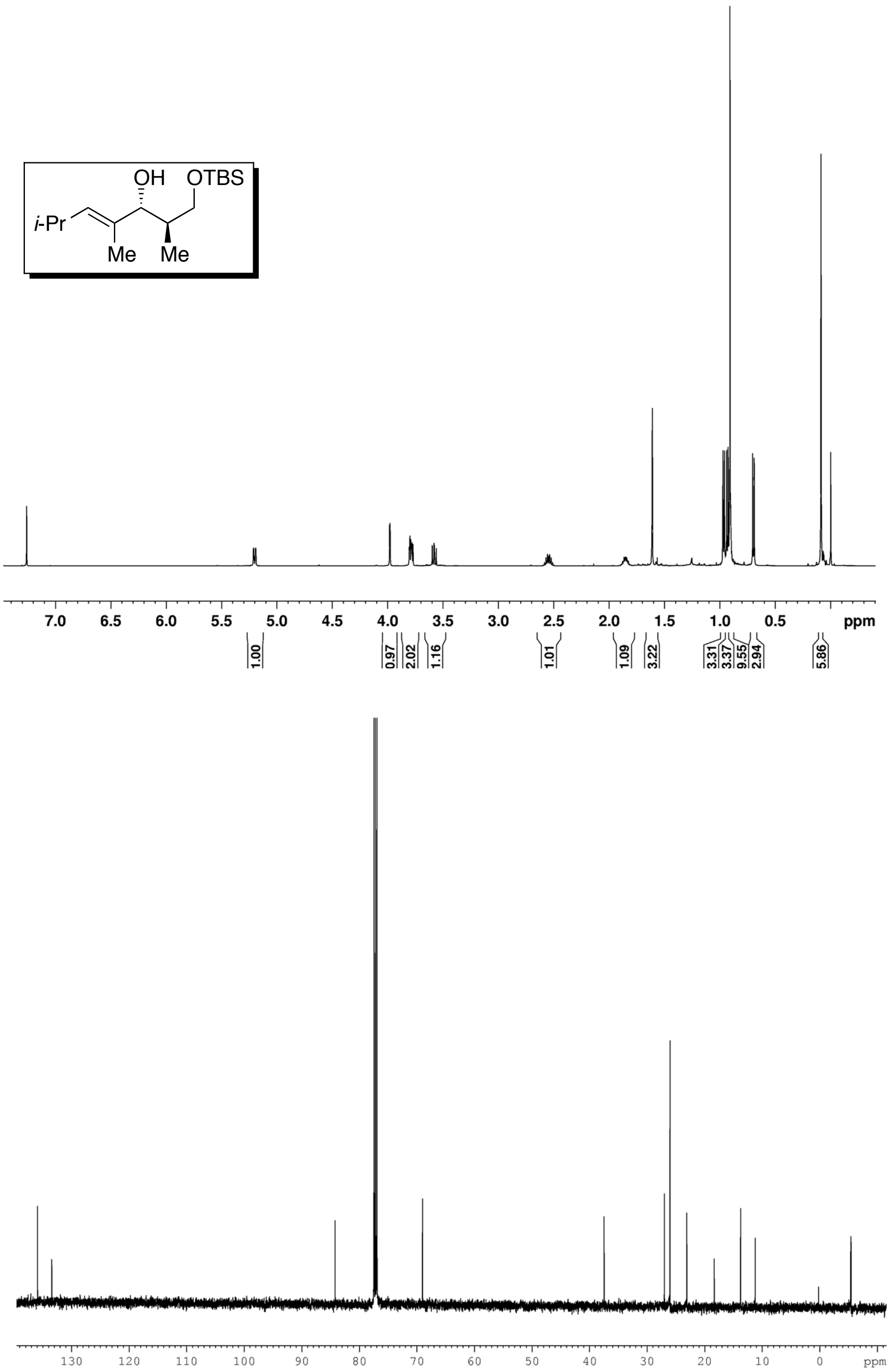


Figure SI-8. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **9**

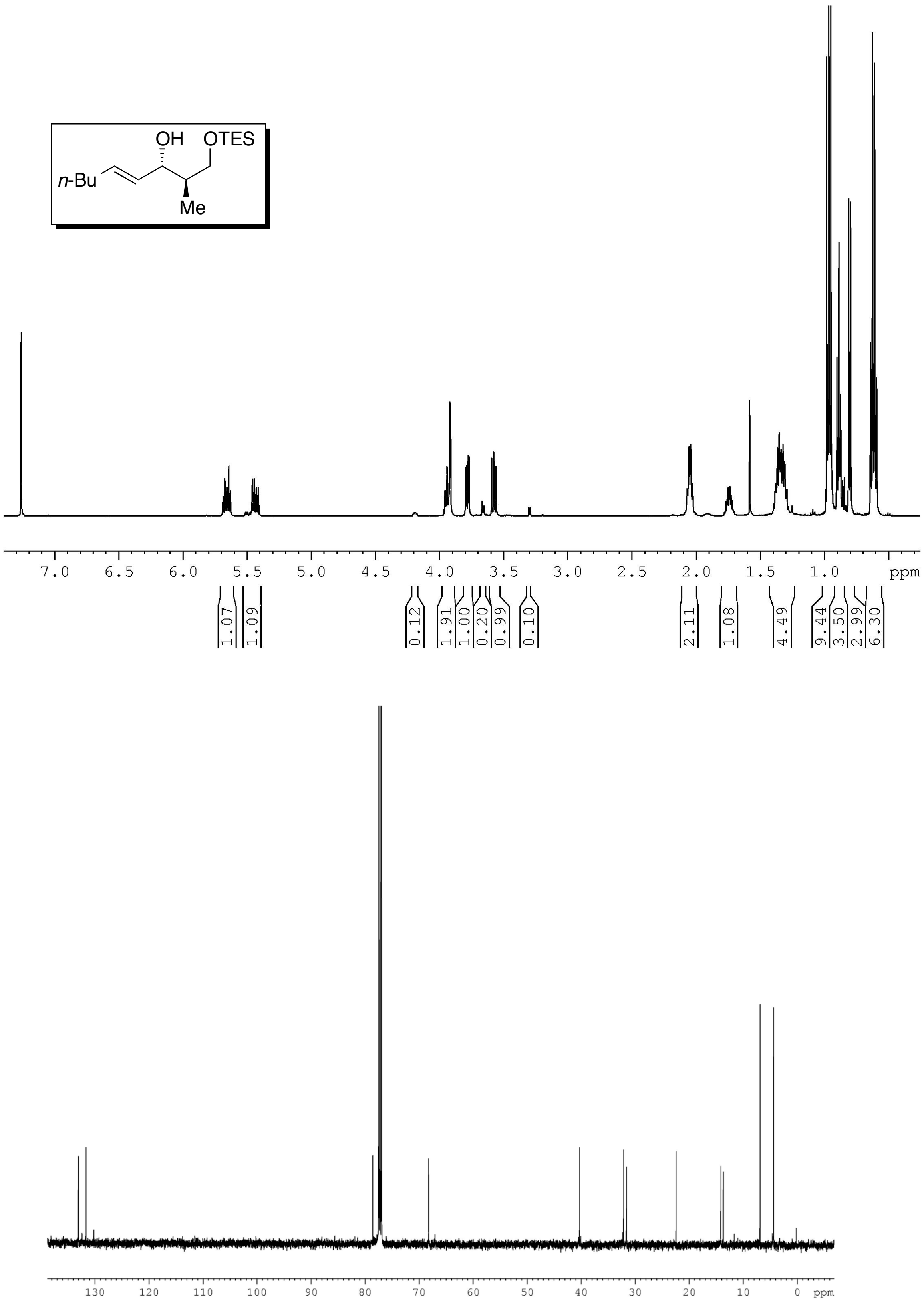


Figure SI-9. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **10**

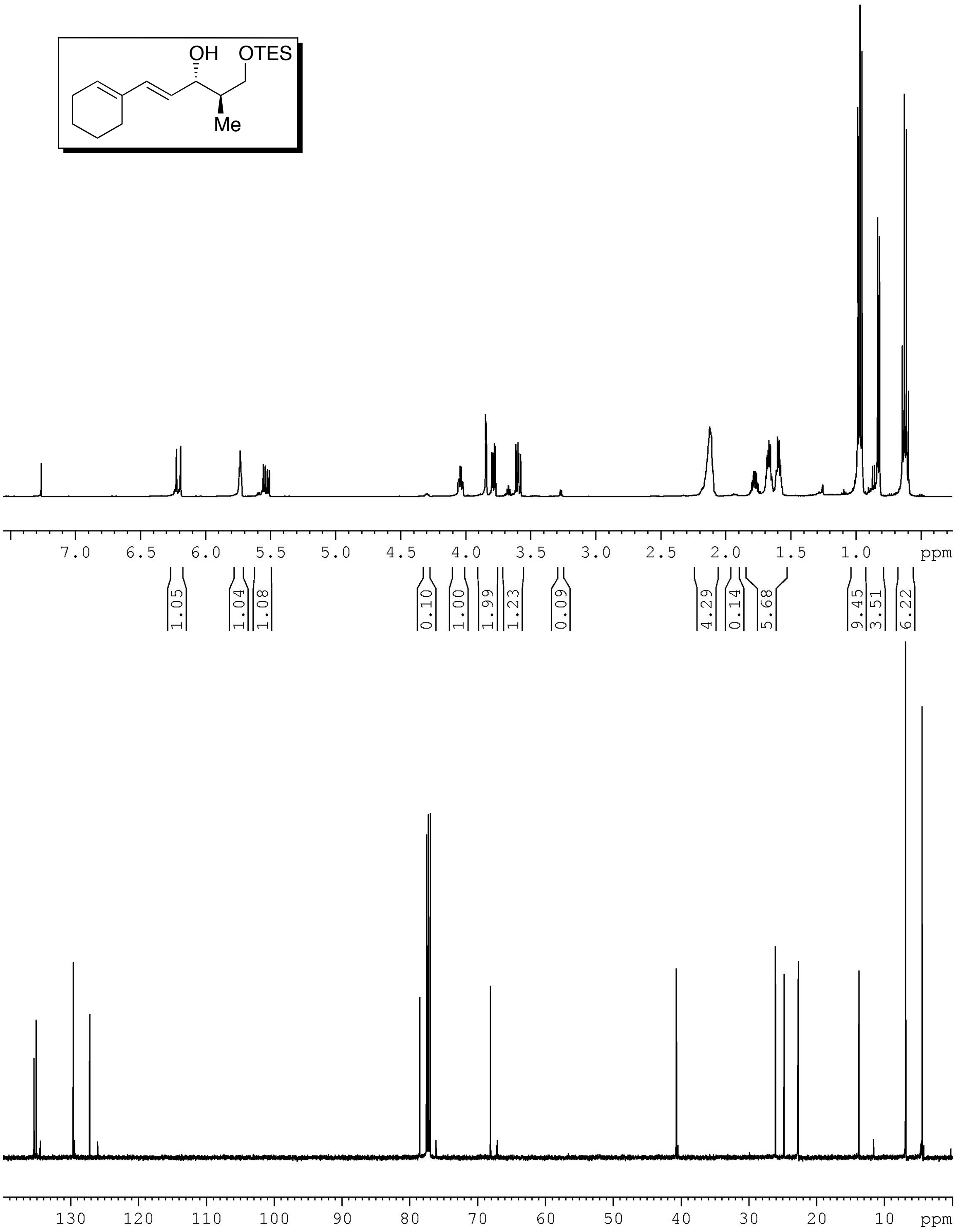
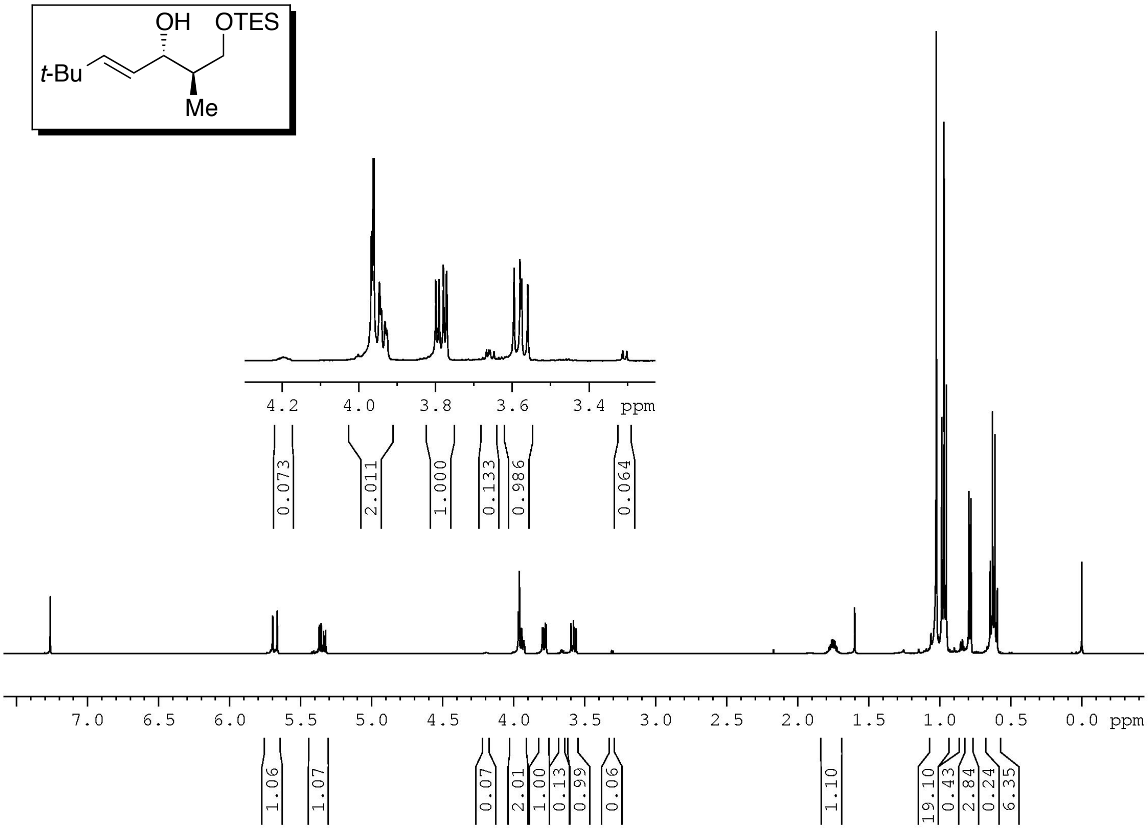


Figure SI-10. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in $CDCl_3$ of **11**



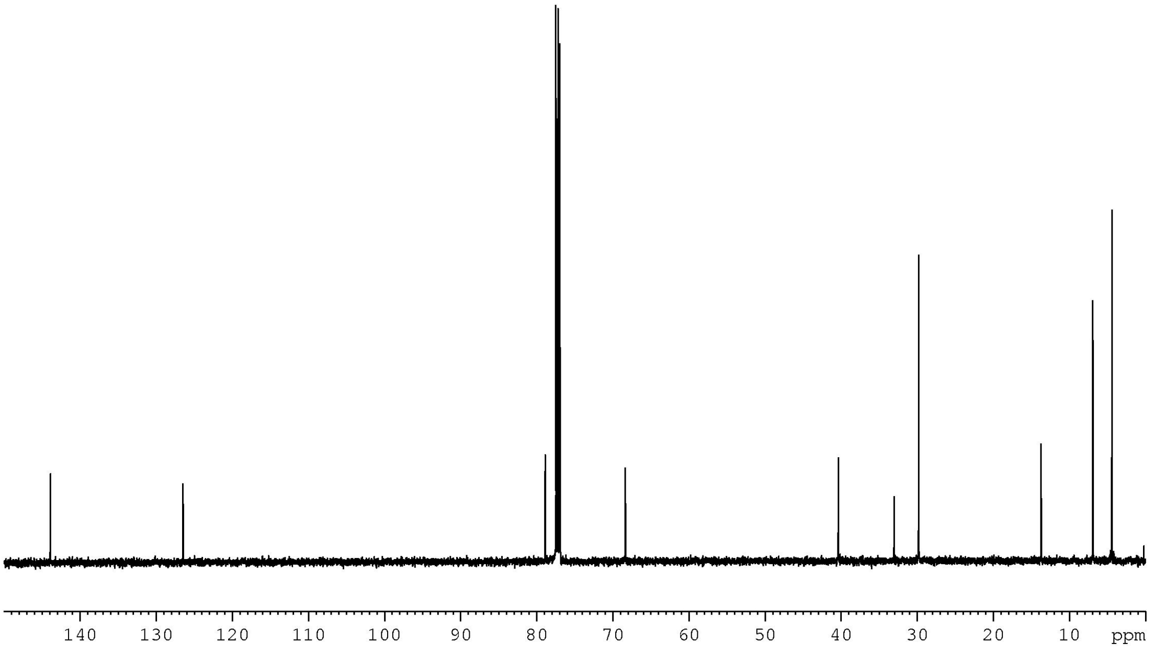


Figure SI-11. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **12**

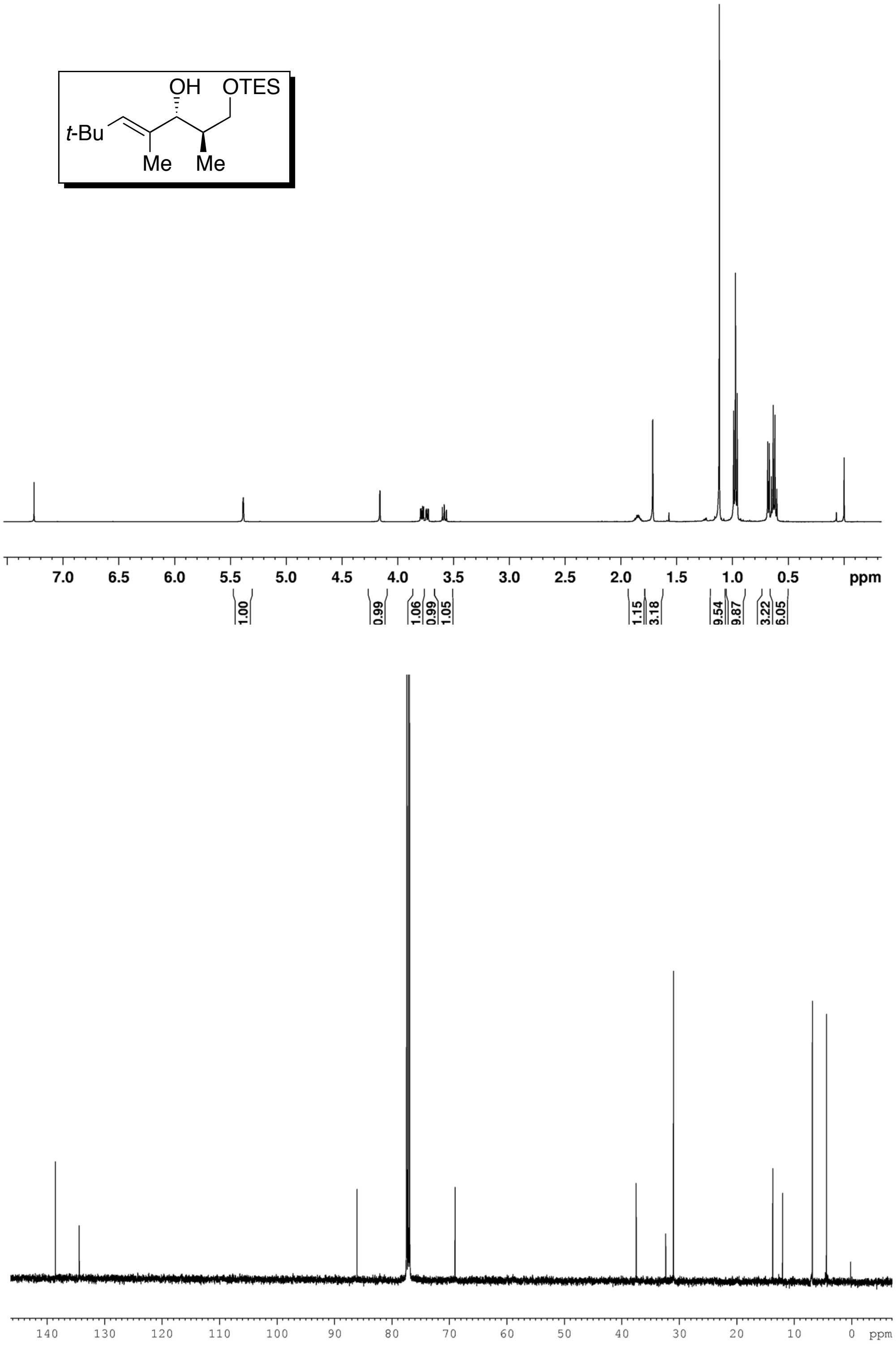


Figure SI-12. 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR in CDCl$_3$ of **13**

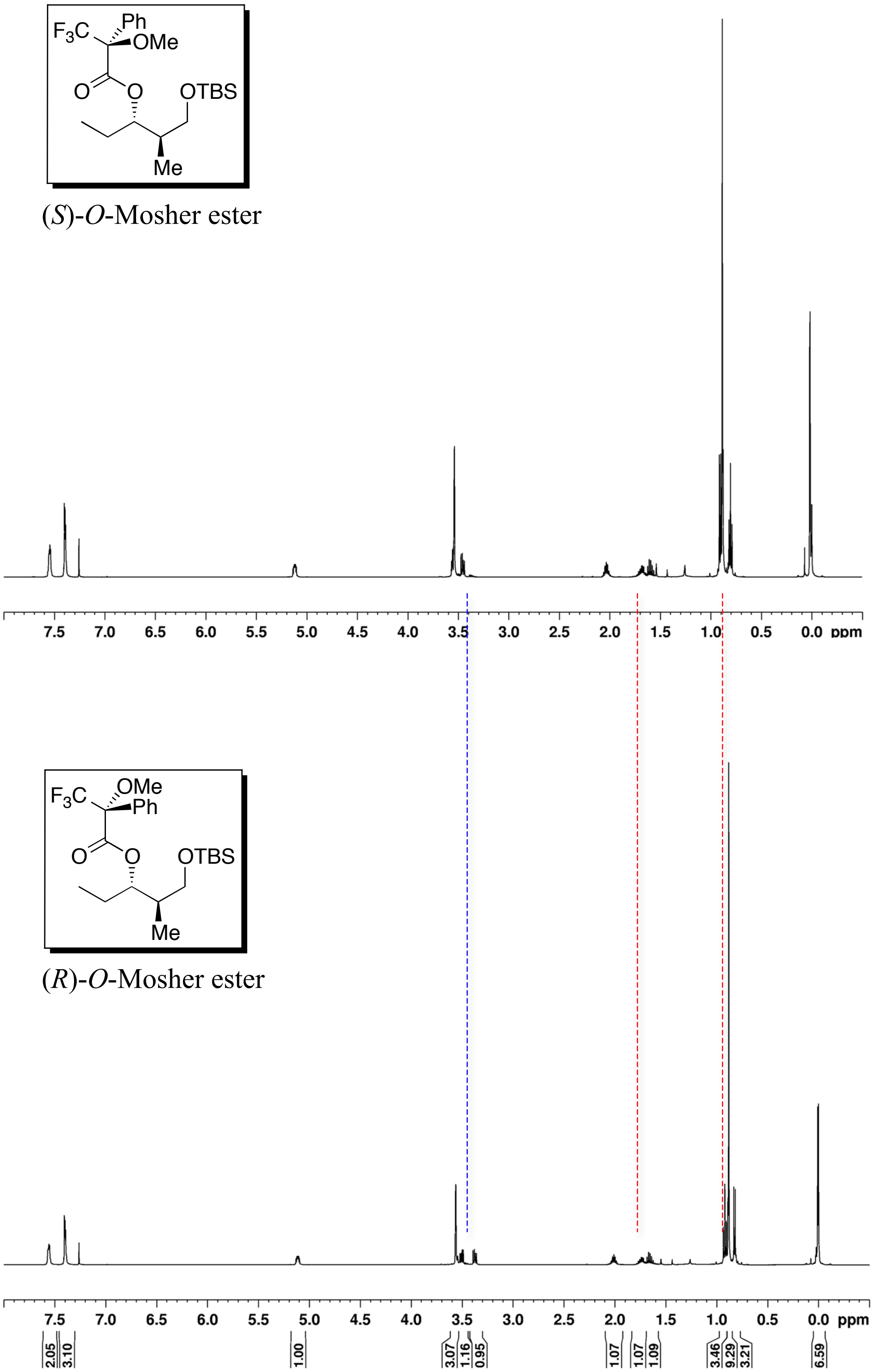


Figure SI-13. 500 MHz ^{1}H NMR of (*S*)-*O*-Mosher ester **14** and (*R*)-*O*-Mosher ester **15** in $CDCl_3$

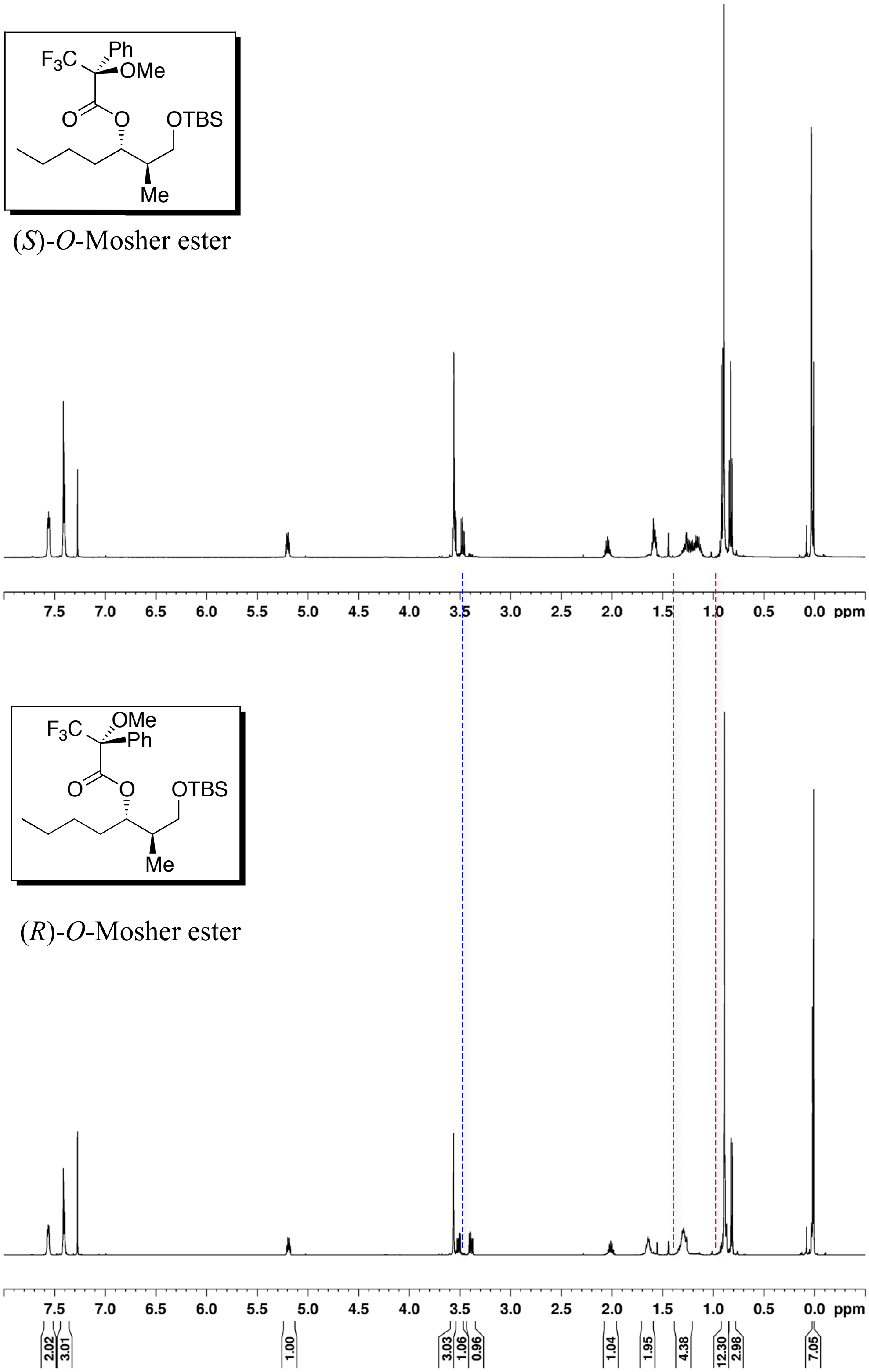
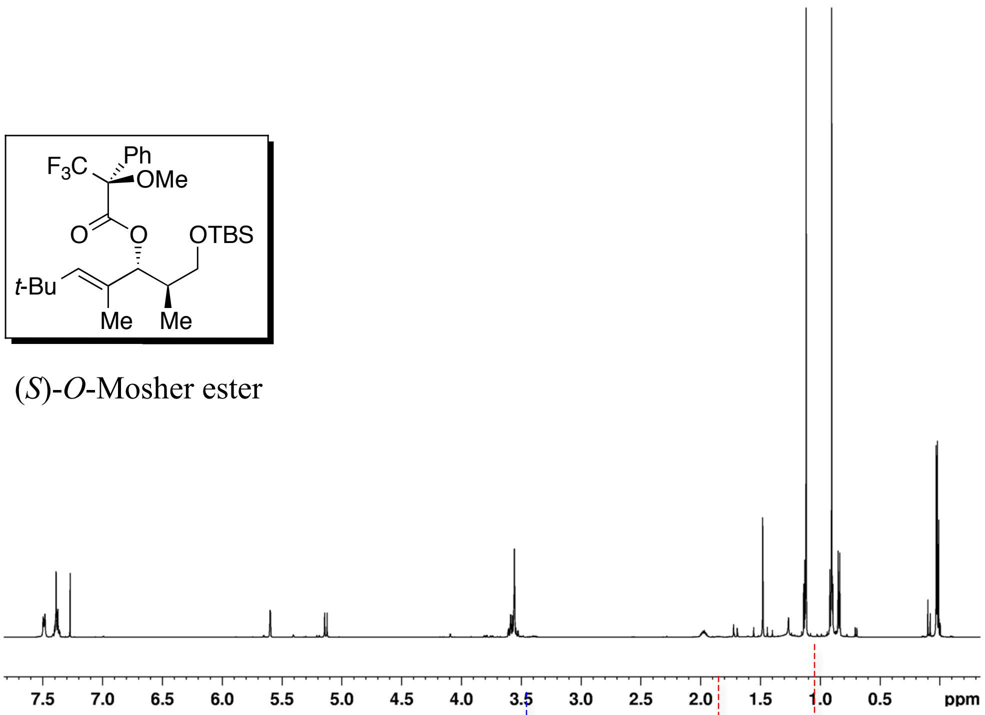


Figure SI-14. 500 MHz ^{1}H NMR of (*S*)-*O*-Mosher ester **16** and (*R*)-*O*-Mosher ester **17** in $CDCl_3$


(*S*)-*O*-Mosher ester

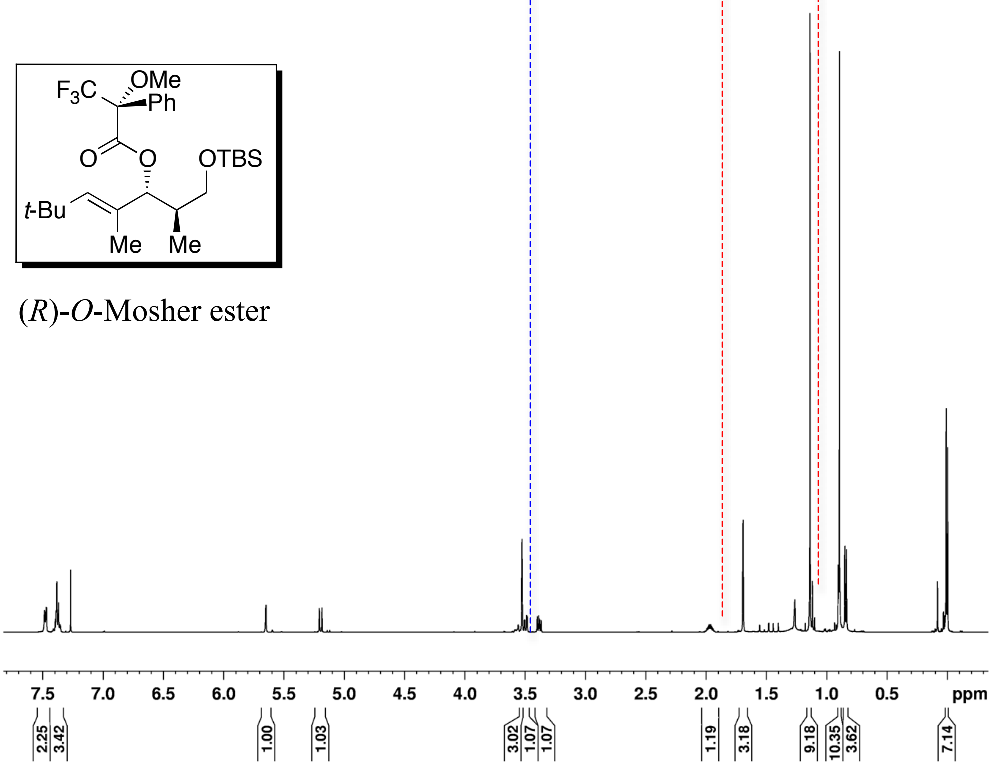

(*R*)-*O*-Mosher ester

Figure SI-15. 500 MHz ^{1}H NMR of (*S*)-*O*-Mosher ester **18** and (*R*)-*O*-Mosher ester **19** in $CDCl_3$