

SUPPORTING MATERIAL

Aldol-type Chirons From Asymmetric Hydrogenation of Trisubstituted Alkenes

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General Experimental Methods

All reactions were carried out under an atmosphere of dry nitrogen. Glassware was oven-dried prior to use. Unless otherwise indicated, common reagents or materials were obtained from commercial source and used without further purification. All the solvents were used after appropriate distillation or purification.

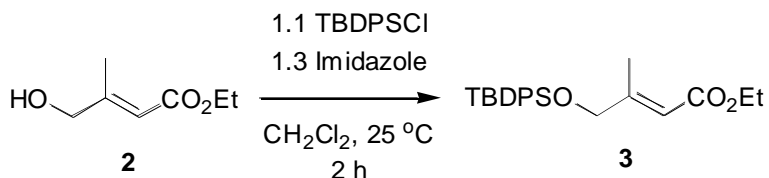
Flash column chromatography was performed using silica gel 60 (230-400 mesh). Analytical thin layer chromatography (TLC) was carried out on Merck silica gel plates with QF-254 indicator and visualized by UV. IR spectra were recorded on a Bruker Tensor 27 spectrometer. Optical rotations were measured on Jasco DIP-360 digital polarimeter. ^1H and ^{13}C spectra were recorded on a Varian 300 (300 MHz ^1H ; 75 MHz ^{13}C) spectrometer at room temperature. Chemical shifts were reported in ppm relative to the residual CDCl_3 (δ 7.26 ppm ^1H ; δ 77.0 ppm ^{13}C). Coupling constants (J) were reported in Hertz.

Iridium catalysts **L-1** and **D-1** were prepared using literature methods.¹ Compound **2** was prepared using literature procedure.²

General Catalytic Hydrogenation Conditions

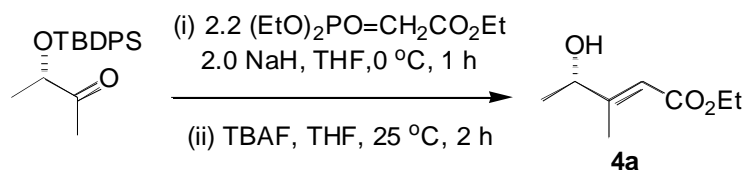
The alkene was dissolved in CH_2Cl_2 (0.2 M) and the iridium catalyst (**L-1** or **D-1**) (0.5 mol%) was then added. The resulting solution was degassed by three cycles of freeze-pump-thaw using nitrogen, then transferred to a Parr Bomb. The bomb was flushed with hydrogen for 1 min without stirring. The mixture was then stirred at 700 rpm under 5 atm of H_2 . After 12 h, the bomb was vented and the solvent was evaporated. The crude product was passed through a silica plug ($\text{EtOAc/hexanes} = 3/7$). The enantiomeric and diastereomeric ratios of the crude materials were measured via chiral capillary GC analysis using β - or γ -CD column.³ GC conditions A: stable at 90 °C for 10 min, then increase temperature to 200 °C at 5 °C/min, stable for 5 min; GC conditions B: stable at 90 °C for 30 min, then increase temperature to 200 °C at 5 °C/min, stable for 5 min.

***E* Ethyl 4-(*tert*-Butyl-diphenyl-silanyloxy)-3-methyl-but-2-enoate (3)⁴**



To a solution of imidazole (6.5 mmol) and ethyl 4-hydroxy-3-methyl-but-2-enoate (5.0 mmol) in 10 mL CH₂Cl₂, *t*-butyldiphenylsilyl chloride (5.5 mmol, 1.85 mL) was added at 0 °C dropwise over 5 min. After stirring at 25 °C for 2 h, the reaction mixture was quenched with saturated NaHCO₃ solution (10 ml) and extracted with CH₂Cl₂ (3 x 20 ml). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (5%) gave the protected ester (89%) as a colorless oil. ¹H NMR (CDCl₃) δ 1.17 (s, 9H), 1.36 (t, *J* = 7.2 Hz, 3H), 2.08 (d, *J* = 0.9, 3H), 4.21-4.29 (m, 4H), 6.31 (d, *J* = 1.5 Hz, 1H), 7.42-7.48 (m, 6H), 7.73-7.77 (m, 4H); ¹³C NMR (CDCl₃) δ 14.3, 15.3, 19.1, 26.7, 59.4, 67.4, 113.4, 127.7, 129.7, 132.7, 135.3, 156.5, 166.9; IR (neat) 3071, 2958, 2932, 2858, 1716 cm⁻¹; HRMS calcd for C₂₃H₃₀O₃Si [M+Li]⁺ 389.2124. Found 389.2123.

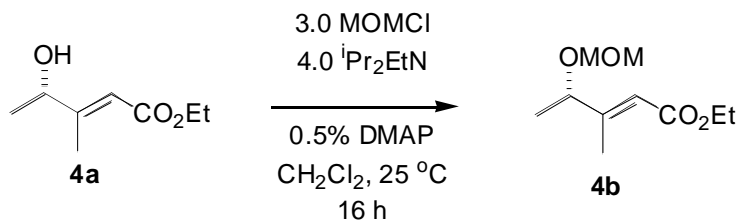
***E*-(*S*)-Ethyl 4-Hydroxy-3-methyl-pent-2-enoate (4a)⁵**



To the solution of NaH (20.0 mmol) in 40 mL THF, ethyl diethylphosphonoacetate (22.0 mmol) was added dropwise at 0 °C. After stirring at 0 °C for 30 min, ketone (10.0 mmol) in 10 mL THF was added slowly.⁶ After 1 h at 0 °C, the reaction mixture was quenched with saturated NH₄Cl solution (20 ml) and extracted with Ether (3 x 20 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (5%) gave the protected ester (75%) as a colorless oil. The obtained compound was dissolved in 20 mL THF, followed by 9 mL of TBAF solution (1.0 M), and was stirred at 25 °C for

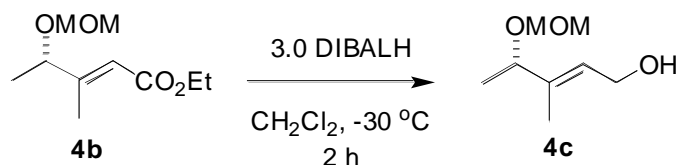
2 h, then quenched with Brine and extracted with Ether (3 x 20 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (50%) gave the alcohol (75%) as a colorless oil. $[\alpha]_D^{21} +4.3$ (*c* 0.024, CHCl₃), (lit.⁵ $[\alpha]_D^{25} +3.6$ (*c* 1.1, CHCl₃)); ¹H NMR (CDCl₃) δ 1.20-1.26 (m, 6H), 2.05 (d, *J* = 1.2 Hz, 3H), 2.76 (br, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 3.3 Hz, 1H), 5.89 (q, *J* = 1.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.1, 14.8, 21.5, 59.7, 72.1, 113.8, 161.5, 167.1; ¹³C NMR (CDCl₃) δ 14.3, 15.3, 19.1, 26.7, 59.4, 67.4, 113.4, 127.7, 129.7, 132.7, 135.3, 156.5, 166.9; IR (neat) 3437 (br), 2981, 2936, 1715, 1652 cm⁻¹; HRMS calcd for C₈H₁₄O₃ [M+H]⁺ 159.1016. Found 159.1025.

***E*-(*S*)-Ethyl 4-Methoxymethoxy-3-methyl-pent-2-enoate (4b)**



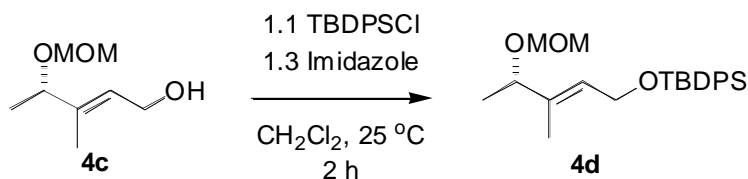
Alcohol **4a** (5.0 mmol) obtained from previous procedure was dissolved in 20 mL CH₂Cl₂, then methoxy chloromethane (15.0 mmol) and ⁱPr₂NEt (20.0 mmol) were added sequentially followed by a catalytic amount of DMAP. The reaction solution was stirred at 25 °C for 16 h, then quenched with Brine and extracted with ether (3 x 20 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (10%) gave the ester (72%) as a colorless oil. $[\alpha]_D^{21} -9.1$ (*c* 0.0125, CHCl₃); ¹H NMR (CDCl₃) δ 1.20-1.25 (m, 6H), 2.05 (d, *J* = 1.5 Hz, 3H), 3.31 (s, 3H), 4.10 (q, *J* = 6.9 Hz, 3H), 4.51 (s, 2H), 5.83 (q, *J* = 0.9 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.2, 19.9, 55.3, 59.6, 76.1, 94.1, 115.8, 158.5, 166.5; IR (neat) 2981, 2936, 2824, 1717, 1654 cm⁻¹; HRMS calcd for C₁₀H₁₈O₄ [M+Li]⁺ 209.1365 Found 209.1391.

***E*-(*S*)-4-Methoxymethoxy-3-methyl-pent-2-en-1-ol (4c)**



DIBALH (6 mL, 1.0 M in hexane) solution (6.0 mmol) was added to a solution of ester **4b** (2.0 mmol) in 20 mL CH_2Cl_2 at -78°C dropwise over 10 min. The reaction solution was then warmed to -30°C . After stirring for 2 h, the reaction solution was warmed to 25°C , and was quenched with methanol (5 mL) and saturated potassium sodium tartrate tetrahydrate (20 mL). After stirring for 1 h, the aqueous phase was extracted with CH_2Cl_2 (2 x 20 mL), and the combined organic layers were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (50%) gave the alcohol (89%) as a colorless oil. $[\alpha]_D^{21} -11.5$ (c 0.021, CHCl_3); ^1H NMR (CDCl_3) δ 1.05 (d, $J = 6.6$ Hz, 3H), 1.41 (d, $J = 0.6$ Hz, 3H), 3.15 (s, 3H), 3.56 (br, 1H), 3.88-3.96 (m, 3H), 4.29 (d, $J = 6.6$ Hz, 1H), 4.39 (d, $J = 6.9$ Hz, 1H), 5.36-5.40 (m, 1H); ^{13}C NMR (CDCl_3) δ 10.6, 19.3, 54.7, 58.0, 76.4, 93.0, 126.5, 137.0; IR (neat) 3417(br), 2978, 2934, 2888, 1669 cm^{-1} ; HRMS calcd for $\text{C}_8\text{H}_{16}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 167.1259. Found 167.1257.

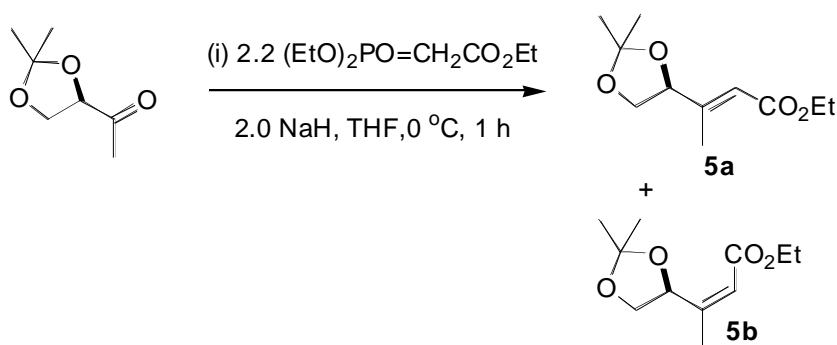
***E*-(*S*)-tert-Butyl-(4-methoxymethoxy-3-methyl-pent-2-enyloxy)-diphenyl-silane (**4d**)**



This compound was prepared using the same procedure as described in compound **3**. $[\alpha]_D^{21} -29.5$ (c 0.044, CHCl_3); ^1H NMR (CDCl_3) δ 1.04 (s, 9H), 1.22 (d, $J = 6.6$ Hz, 3H), 1.39 (d, $J = 1.2$ Hz, 3H), 3.37 (s, 3H), 4.10 (q, $J = 6.6$ Hz, 1H), 4.25-4.28 (m, 2H), 4.48

(d, $J = 6.3$ Hz, 1H), 4.57 (d, $J = 6.6$ Hz, 1H), 5.59-5.64 (m, 1H), 7.35-7.43 (m, 6H), 7.67-7.70 (m, 4H); ^{13}C NMR (CDCl_3) δ 11.1, 19.1, 19.8, 26.8, 55.3, 60.7, 76.5, 93.5, 127.1, 127.6, 129.6, 133.8, 135.5, 136.3; IR (neat) 2931, 2857, 1472, 1428, 1111, 1027 cm^{-1} ; HRMS calcd for $\text{C}_{24}\text{H}_{34}\text{O}_3\text{Si}$ $[\text{M}+\text{Li}]^+$ 405.2427. Found 405.2422.

***E*-(*S*)-Ethyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-but-2-enoate (5a) and *Z*-(*S*)-Ethyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-but-2-enoate (5b)**



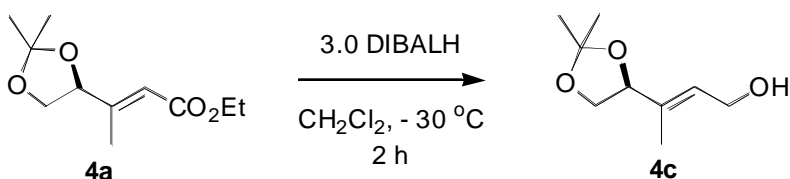
NaH (40.0 mmol) was added into 100 mL CH_2Cl_2 , and ethyl diethylphosphonoacetate (44.0 mmol) was added dropwise at 0 °C. The solution obtained was stirred for 30 min. The ketone solution in CH_2Cl_2 obtained by literature procedure (100 mL, 0.2 M, this ketone is very volatile, removing solvent by rotavap caused substantial loss of material)⁷ was added into the reaction solution over 20 min. After 1 h stirring at 0 °C, the reaction mixture was quenched with saturated NH_4Cl solution (50 ml). The organic layers were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography eluting with EtOAc/hexanes (8%) gave the *E* ester (70%) and *Z* ester (10%) as colorless oil, respectively.

E isomer: $[\alpha]_D^{21} +31.1$ (c 0.018, CHCl_3); ^1H NMR (CDCl_3) δ 1.22 (t, $J = 7.2$ Hz, 3H), 1.35 (s, 3H), 1.41 (s, 3H), 2.04 (d, $J = 1.2$ Hz, 3H), 3.59 (q, $J = 7.2$, 1H), 4.07-4.18 (m,

3H), 4.44-4.50 (m, 1H), 5.95-5.97 (m, 1H); ^{13}C NMR (CDCl_3) δ 14.1, 14.7, 25.4, 26.0, 59.7, 68.5, 76.6, 110.1, 115.3, 154.7, 166.4; IR (neat) 2986, 2938, 1716, 1660 cm^{-1} ; HRMS calcd for $\text{C}_{11}\text{H}_{18}\text{O}_4$ $[\text{M}+\text{H}]^+$ 215.1283. Found 215.1289.

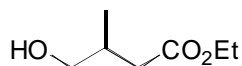
Z isomer: $[\alpha]_D^{21} +18.9$ (c 0.020, CHCl_3); ^1H NMR (CDCl_3) δ 1.16 (t, $J = 6.9$ Hz, 3H), 1.28 (s, 3H), 1.37 (s, 3H), 1.83 (d, $J = 1.5$ Hz, 3H), 3.45 (q, $J = 6.9$ Hz, 1H), 4.02 (q, $J = 6.6$ Hz, 2H), 4.26-4.31 (m, 1H), 5.59-5.65 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.0, 19.7, 24.8, 25.9, 59.7, 68.6, 68.7, 74.4, 109.5, 117.1, 158.4, 165.4; IR (neat) 2985, 2937, 1712, 1646 cm^{-1} ; HRMS calcd for $\text{C}_{11}\text{H}_{18}\text{O}_4$ $[\text{M}+\text{Li}]^+$ 221.1365. Found 221.1370.

(E)-(S)- 3-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-but-2-en-1-ol (5c)



This compound was prepared using the same procedure described in **4c**. $[\alpha]_D^{21} +20.5$ (c 0.024, CHCl_3); ^1H NMR (CDCl_3) δ 1.34 (d, $J = 0.6$ Hz, 3H), 1.40 (d, $J = 0.6$ Hz, 3H), 1.61 (d, $J = 0.6$ Hz, 3H), 2.31 (br, 1H), 3.57-3.62 (m, 1H), 4.00-4.15 (m, 3H), 4.44 (t, $J = 6.9$, 1H), 5.65-5.70 (m, 1H); ^{13}C NMR (CDCl_3) δ 11.6, 25.3, 26.2, 58.7, 67.9, 80.2, 109.3, 126.7, 135.0; IR (neat) 3483 (br), 2986, 2935, 2879, 1674 cm^{-1} ; HRMS calcd for $\text{C}_9\text{H}_{16}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 179.1259. Found 179.1252.

(S)- Ethyl 4-Hydroxy-3-methyl-butrate

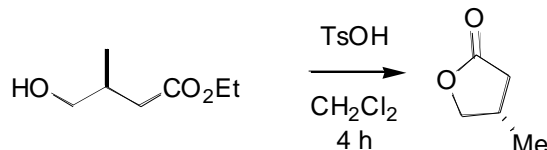


$[\alpha]_D^{19} = -9.3$ (c = 0.015, CHCl_3); ^1H NMR (CDCl_3) δ 0.96 (d, $J = 6.6$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.97 (br, 1H), 2.10-2.24 (m, 2H), 2.39-2.46 (m, 1H), 3.42-3.59 (m, 2H), 4.13 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.2, 16.7, 33.0, 38.6, 60.4, 67.5, 173.5; IR

(neat) 3504 (br), 2964, 3935, 2877, 1733 cm^{-1} ; HRMS calcd for $\text{C}_7\text{H}_{14}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 153.1103. Found 153.1105.

Determination of relative stereochemistry:

The alcohol product from alkene **2** was transformed to a lactone and its optical rotation data was compared with data reported

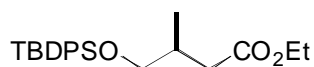


$[\alpha]_{\text{D}}^{19} = -23.6$ ($c = 2.72$, MeOH) ((lit.⁸ $[\alpha]_{\text{D}}^{25} = -17.2$, ($c = 1.3$, MeOH))

The alcohol was subjected to GC using conditions B. Enantiomeric excess = 96%.

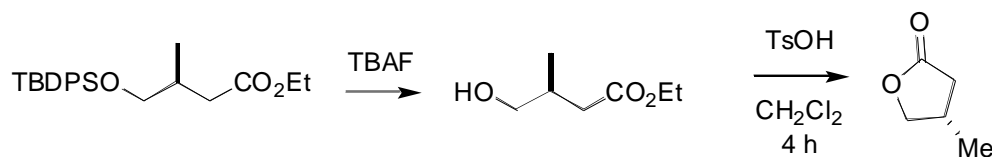
Retention time (min)	46.9	47.1
Area	6.45	302.6

(S)-4-(tert-Butyl-diphenyl-silanyloxy)-3-methyl-butrate



$[\alpha]_{\text{D}}^{21} = -3.7$ ($c = 0.043$, CHCl_3); ^1H NMR (CDCl_3) δ 0.98 (d, $J = 6.6$ Hz, 3H), 1.08 (s, 9H), 1.26 (t, $J = 6.6$ Hz, 3H), 2.12-2.28 (m, 2H), 2.60 (dd, $J = 14.7, 5.1$ Hz, 1H), 3.47-3.60 (m, 2H), 4.13 (q, $J = 7.2$ Hz, 2H), 7.36-7.47 (m, 6H), 7.66-7.69 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.2, 16.6, 19.3, 26.8, 33.0, 38.3, 60.1, 68.0, 127.6, 129.6, 133.7, 135.5, 173.2; IR (neat) 2960, 2895, 2859, 1736 cm^{-1} ; HRMS calcd for $\text{C}_{23}\text{H}_{32}\text{O}_3\text{Si}$ $[\text{M}+\text{Li}]^+$ 391.2281. Found 391.2281.

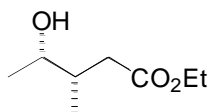
Determination of relative stereochemistry:



The ester product was deprotected and then transformed to the lactone. $[\alpha]_D^{19} = -18.5$ ($c = 0.24$, MeOH) ((lit. $[\alpha]_D^{25} = -17.2$. ($c = 1.3$, MeOH)). The alcohol obtained from TBAF deprotection was subjected to GC conditions B. Enantiomeric excess = 93%.

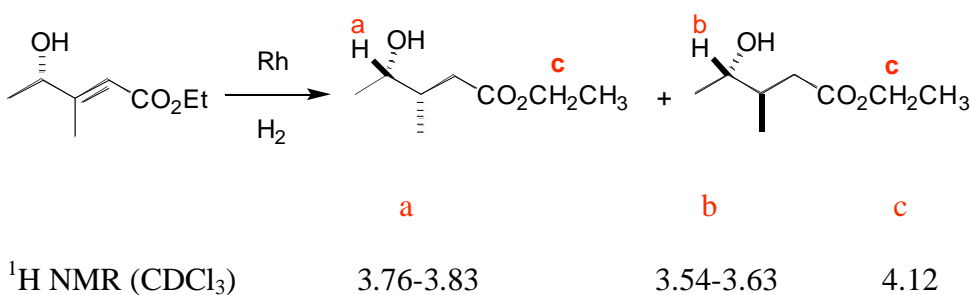
Retention time (min)	46.9	47.1
Area	13.1	383.4

(S)- Ethyl 4-Hydroxy-3-methyl-pentanoate



$[\alpha]_D^{19} = -16.2$ ($c = 0.021$, MeOH), (lit. $[\alpha]_D^{25} = -17.2$. ($c = 1.3$, MeOH)); ^1H NMR (CDCl_3) δ 0.91 (d, $J = 6.9$ Hz, 3H), 1.11 (d, $J = 6.3$ Hz, 3H), 1.23 (t, $J = 6.9$ Hz, 3H), 2.00-2.19 (m, 3H), 2.47 (dd, $J = 14.7, 6.0$ Hz, 1H), 3.74-3.81 (m, 1H), 4.11 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.2, 14.4, 19.4, 36.6, 37.6, 60.4, 70.3, 173.8; IR (neat) 3447 (br), 3055, 2921, 2850, 1732, 1647 cm^{-1} ; HRMS calcd for $\text{C}_8\text{H}_{16}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 167.1259. Found 167.1254.

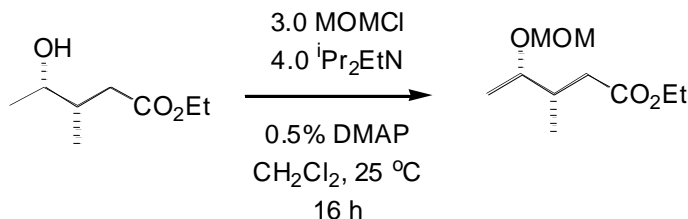
*Determination of relative stereochemistry:*⁹



Literature reported (*syn*):⁷ 3.71 (m, 1H) - 4.06

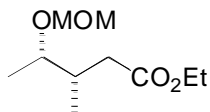
For *syn* compound: $[\alpha]^{19}_D -16.2$ (*c* 0.021, MeOH), (lit.⁷ $[\alpha]^{25}_D -17.2$. (*c* 1.3, MeOH))

Determination of diastereomeric excess is achieved by protecting the alcohol with MOM, and then subjected to GC with conditions A.



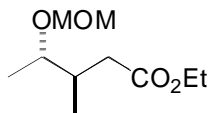
Retention time (min)	18.4	18.7
Area	848.8	8.3

(*S, S*)- Ethyl 4-Methoxymethoxy-3-methyl-pentanoate



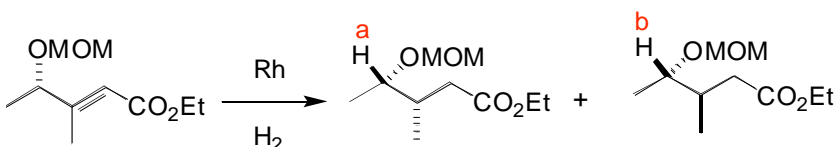
$[\alpha]^{19}_D +4.0$ (*c* 0.010, MeOH); ¹H NMR (CDCl₃) δ 0.93 (d, *J* = 6.6 Hz, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.25 (t, *J* = 6.9 Hz, 3H), 2.09-2.19 (m, 2H), 2.46-2.52 (m, 1H), 3.36 (s, 3H), 3.61-3.69 (m, 1H), 4.13 (q, *J* = 6.9 Hz, 2H), 4.63 (dd, *J* = 15.9, 6.9 Hz, 2H); ¹³C NMR (CDCl₃) δ 14.2, 14.9, 16.4, 35.2, 37.3, 55.4, 60.2, 75.4, 95.0, 173.4; IR (neat) 2978, 2933, 1736, 1038 cm⁻¹; HRMS calcd for C₁₀H₂₀O₄ [M+Li]⁺ 211.1522. Found 211.1514.

(*S, R*)- Ethyl 4-Methoxymethoxy-3-methyl-pentanoate



$[\alpha]_D^{19}$ -1.1 (c 0.019, CHCl_3); ^1H NMR (CDCl_3) δ 0.96 (d, J = 6.3 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.26 (t, J = 6.9 Hz, 3H), 2.07-2.18 (m, 2H), 2.44-2.54 (m, 1H), 3.37 (s, 3H), 3.48-3.56 (m, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.64 (dd, J = 23.4, 6.9 Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.2, 15.7, 35.8, 37.8, 55.4, 55.5, 60.2, 76.4, 95.2, 173.3; ; IR (neat) 2978, 2933, 1735, 1038 cm^{-1} ; HRMS calcd for $\text{C}_{10}\text{H}_{20}\text{O}_4$ $[\text{M}+\text{Li}]^+$ 211.1522. Found 211.1521.

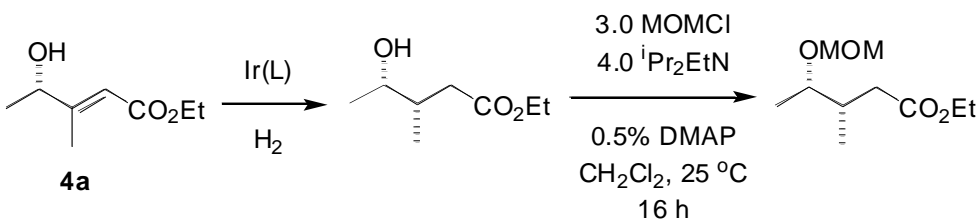
Determination of relative stereochemistry:



Alkene **4b** was hydrogenated using Rh/Al catalyst to afford a mixture of *syn* and *anti* isomers in a 1.8:1.0 ratio. Protons *a* and *b* showed different proton chemical shift. The major isomer corresponds to a set of peak between 3.61-3.69 ppm, which has been confirmed by a comparison with the authentic sample.

	a	b
^1H NMR (CDCl_3)	3.61-3.69 (0.57 H)	3.48-3.56 (0.31 H)
Retention time (Area)	18.4 (154)	18.7 (94)

The authentic sample was prepared by the following method:



Comparison of authentic sample with the product from **L-1** (GC conditions A).

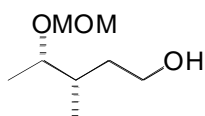
	^1H NMR (CDCl_3)	Retention time(Area)
Authentic sample	3.61-3.69 (1 H)	18.4

This compound	3.61-3.69(1H)	18.4(1288.1), 18.7 (47.5)
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The crude product from **1-D** has been purified by flash chromatograph, and the diastereomeric excess has been determined by GC (Conditions A).

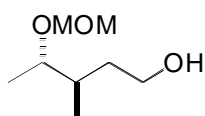
Retention time (min)	18.4	18.7
Area	2.97	92.6

(S, S)- 4-Methoxymethoxy-3-methyl-pentan-1-ol



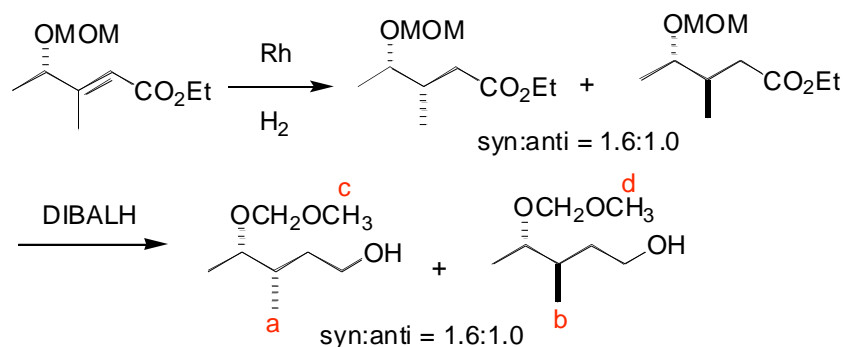
$[\alpha]_D^{19}$ -2.0 (*c* 0.045, CHCl₃); ¹H NMR (CDCl₃) δ 0.90 (d, *J* = 6.9 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.35-1.46 (m, 1H), 1.69-1.86 (m, 2H), 2.36 (br, 1H), 3.36 (s, 3H), 3.56-3.76 (m, 3H), 4.60-4.69 (m, 2H); ¹³C NMR (CDCl₃) δ 15.6, 34.9, 35.4, 55.4, 61.4, 77.4, 95.0; IR (neat) 3422, 2934, 2887, 1101 cm⁻¹; HRMS calcd for C₈H₁₈O₃ [M+Li]⁺ 169.1416. Found 167.1418.

(S, R)- 4-Methoxymethoxy-3-methyl-pentan-1-ol



$[\alpha]_D^{19}$ +38.7 (*c* 0.016, CHCl₃); ¹H NMR (CDCl₃) δ 0.92 (d, *J* = 6.6 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.38-1.49 (m, 1H), 1.63-1.82 (m, 2H), 2.14 (br, 1H), 3.36 (s, 3H), 3.52-3.75 (m, 3H), 4.60-4.70 (m, 2H); ¹³C NMR (CDCl₃) δ 15.8, 16.4, 35.2, 35.6, 55.6, 61.6, 77.6, 95.2; IR (neat) 3418, 2933, 2884, 1104 cm⁻¹; HRMS calcd for C₈H₁₈O₃ [M+Li]⁺ 169.1416. Found 169.1415.

Determination of relative stereochemistry:



Alkene **4b** was hydrogenated by Rh/Al, afforded *syn* and *anti* isomers in a 1.6:1.0 ratio. The mixture was reduced to alcohol by DIBALH, and the major isomer was presumed to be *syn*. Apparently, 0.79 and 3.15 are corresponding to *syn*; 0.85, 3.17 are corresponding to *anti*.

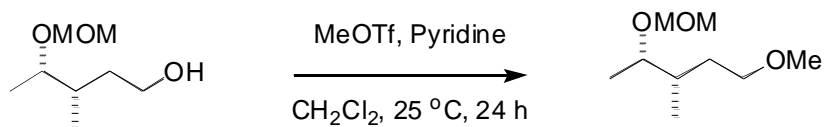
	a	b	c	d
¹ H NMR (C ₆ D ₆)	0.79 (1.6)	0.85 (1.0)	3.17 (1.0)	3.15 (1.6)

This compound

¹ H NMR (C ₆ D ₆)	0.79 (3H)	3.15 (3H)
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Determination of diastereomeric excess:

The obtained alcohol was transformed to methyl ether and then subjected to GC under conditions A.

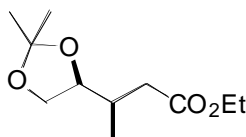


Hydrogenation catalyst	Retention time(Area)	Retention time(Area)
Rh/Al	18.4 (14.3)	18.6 (7.8)
Cat L	18.4 (6.7)	18.6 (0.39)
Cat D	18.5 (0.89)	18.7 (9.2)

(S, S)- tert-Butyl-(4-methoxymethoxy-3-methyl-pentyloxy)-diphenyl-silane

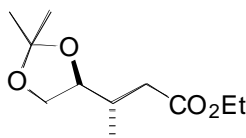
The obtained crude compound from hydrogenation was subjected to 1.2 eq. of TBAF (1.0 M in THF) and stirred for 4 h. Subsequent work up and purification afford (S, S)- 4-methoxymethoxy-3-methyl-pentan-1-ol as the major isomer.

(S, R) Ethyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-butyrate



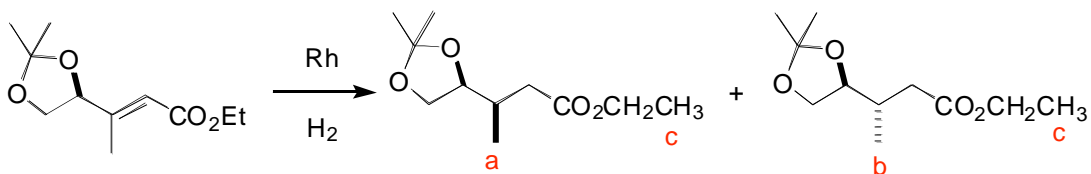
$[\alpha]^{19}_{\text{D}} + 8.2$ (c 0.020, CHCl_3), (lit. $^{10}[\alpha]^{25}_{\text{D}} + 8.43$. (c 1.12, CHCl_3)); ^1H NMR (CDCl_3) δ 0.95 (d, $J = 6.6$ Hz, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 1.29 (s, 3H), 1.35 (s, 3H), 2.04-2.20 (m, 2H), 2.32-2.39 (m, 1H), 3.55-3.63 (m, 1H), 3.91-4.00 (m, 2H), 4.09 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.1, 15.3, 25.1, 16.3, 32.9, 37.4, 60.2, 66.6, 78.7, 108.8, 172.5; IR (neat) 2985, 2936, 1735 cm^{-1} ; HRMS calcd for $\text{C}_{11}\text{H}_{20}\text{O}_4$ $[\text{M}+\text{Li}]^+$ 223.1521. Found 223.1520.

(S, S) Ethyl 3-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-butyrate



$[\alpha]^{19}_{\text{D}} + 4.6$ (c 0.055, CHCl_3); ^1H NMR (CDCl_3) δ 0.89 (d, $J = 6.6$ Hz, 3H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.32 (s, 3H), 1.37 (s, 3H), 2.08-2.16 (m, 2H), 2.56-2.65 (m, 1H), 3.58-3.63 (m, 1H), 3.80-3.87 (m, 1H), 4.00-4.08 (m, 1H), 4.12 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.5, 16.2, 25.7, 26.8, 34.5, 38.4, 60.5, 68.1, 79.7, 109.2, 173.1; IR (neat) 2985, 2937, 2879, 1735 cm^{-1} ; HRMS calcd for $\text{C}_{11}\text{H}_{20}\text{O}_4$ $[\text{M}+\text{Li}]^+$ 223.1521. Found 223.1522.

Determination of stereochemistry:¹⁰



Alkene **5a** was hydrogenated with Rh/Al catalyst, affords two diastereoisomers in a 2.0:1.0 ratio. The major isomer spectra is identical to the reported *syn* compound,⁸ thus the minor isomer should be *anti*.

¹ H NMR (CDCl ₃)	a	b	c
	0.94 (2H)	0.86 (0.9H)	1.20 (3H)
Literature value (<i>syn</i>):	0.94 (3H)		1.20 (3H)

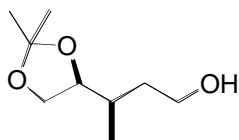
Diastereomeric excess has been determined under conditions A.

Hydrogenation catalyst	Retention time(Area) anti	Retention time(Area) syn
Rh/Al	20.3 (304)	20.7 (683)
L-1	20.3 (1549)	20.7 (65.2)
D-1	20.3 (43.1)	20.7 (1059)

After purified by column.

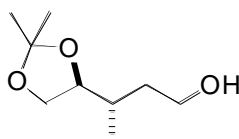
Hydrogenation catalyst	Retention time(Area)	Retention time(Area)
L-1	20.3 (13885)	20.7 (343)
D-1	20.3 (7.3)	20.7 (368)

(*S*, *R*) 3-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-butan-1-ol



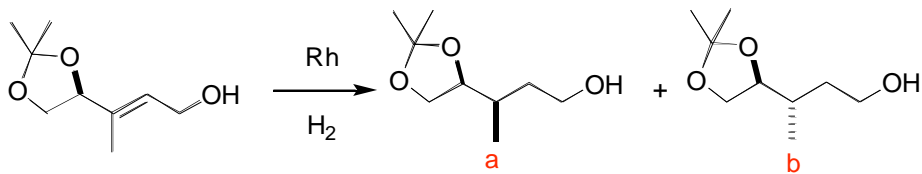
$[\alpha]^{19}_{\text{D}} + 18.0$ (c 0.021, CHCl_3), (lit.¹¹ $[\alpha]^{25}_{\text{D}} + 18.1$. (c 1.12, CHCl_3)); ^1H NMR (CDCl_3) δ 0.95 (d, J = 6.9 Hz, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.57-1.1.85 (m, 2H), 2.50 (br, 1H), 3.57-3.75 (m, 3H), 3.93-4.01 (m, 1H), 3.80-3.96 (m, 1H); ^{13}C NMR (CDCl_3) δ 15.1, 25.3, 26.4, 32.7, 35.5, 60.2, 67.1, 79.6, 108.7; IR (neat) 3446 (br), 2934, 2881, 1059 cm^{-1} ; HRMS calcd for $\text{C}_9\text{H}_{18}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 181.1416. Found 181.1421.

(S, R) 3-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-butan-1-ol



$[\alpha]^{19}_{\text{D}} + 14.2$ (c 0.063, CHCl_3); ^1H NMR (CDCl_3) δ 0.85 (d, J = 6.6 Hz, 3H), 1.34 (s, 3H), 1.38 (s, 3H), 1.42-1.50 (m, 1H), 1.69-1.1.78 (m, 2H), 3.12 (br, 1H), 3.55-3.64 (m, 3H), 3.80-3.87 (m, 1H), 3.99-4.04 (m, 1H); ^{13}C NMR (CDCl_3) δ 15.9, 25.5, 26.4, 34.3, 37.1, 60.5, 68.0, 80.3, 108.7; IR (neat) 3421 (br), 2985, 2935, 2879, 1065 cm^{-1} ; HRMS calcd for $\text{C}_9\text{H}_{18}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 181.1416. Found 181.1420.

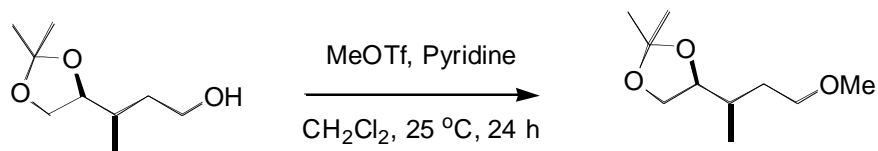
Determination of relative stereochemistry:



^1H NMR (CDCl_3)	a	b
	0.96 (2H)	0.86 (0.9H)
Literature (<i>syn</i>) ¹⁰	0.97 (3H)	

Alkene **5c** was hydrogenated using Rh/Al catalyst, afforded two diastereoisomers in a 2.0:0.9 ratio, thus the major isomer is *syn* and minor is *anti*.

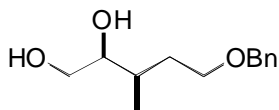
Determination of diastereomeric excess:



The obtained alcohol product from the hydrogenation was transformed to corresponding methyl ether and then subjected to GC using conditions A.

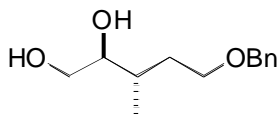
Hydrogenation catalyst	Retention time(Area)	Retention time(Area)
	anti	syn
Rh/Al	13.5(8.4)	13.9 (20.4)
D-1	13.5 (0.51)	13.9 (5.6)
L-1	13.0 (373)	13.5 (7.2)

(*S*, *R*) 5-Benzyloxy-3-methyl-pentane-1,2-diol (6a)



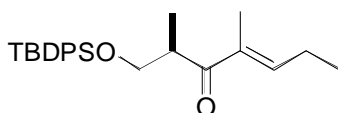
$[\alpha]_D^{19}$ -1.4 (*c* 0.028, CHCl₃); ¹H NMR (CDCl₃) δ 0.87 (d, *J* = 6.6 Hz, 3H), 1.46-1.60 (m, 1H), 1.69-1.89 (m, 2H), 3.40-3.63 (m, 5H), 4.09 (br, 2H), 4.48 (d, *J* = 0.9 Hz, 2H), 7.24-7.36 (m, 5H); ¹³C NMR (CDCl₃) δ 15.9, 32.4, 33.4, 64.4, 68.1, 72.9, 75.9, 127.6, 128.3, 137.8; IR (neat) 3386 (br), 3030, 2926, 2872, 1496 cm⁻¹; HRMS calcd for C₁₃H₂₀O₃ [M+Li]⁺ 231.1572. Found 231.1571.

(*S*, *S*) 5-Benzyloxy-3-methyl-pentane-1,2-diol (6b)¹¹



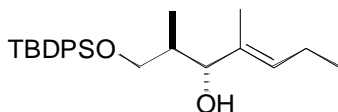
$[\alpha]_D^{19} +11.1$ (c 0.020, CHCl_3); ^1H NMR (CDCl_3) δ 0.91 (d, J = 6.0 Hz, 3H), 1.56-1.81 (m, 5H), 3.47-3.67(m, 2H), 4.52 (s, 2H), 7.30-7.36 (m, 5H); ^{13}C NMR (CDCl_3) δ 14.3, 29.7, 33.4, 64.9, 68.2, 73.2, 74.9, 127.7, 127.8, 128.4, 137.8 ; IR (neat) 3386 (br), 2913, 2926, 2850, 1074 cm^{-1} ; HRMS calcd for $\text{C}_{13}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{Li}]^+$ 231.1572. Found 231.1574.

(R) 1-(tert-Butyl-diphenyl-silanyloxy)-2,4-dimethyl-hept-4-en-3-one (7)



$[\alpha]_D^{19} -21.5$ (c 0.039, CHCl_3); ^1H NMR (CDCl_3) δ 1.05-1.12 (m, 15H), 1.82 (d, J = 0.9 Hz, 3H), 2.22-2.32 (m, 2H), 3.54-3.68 (m, 2H), 3.89-3.95 (m, 1H), 6.61-6.66 (m, 1H), 7.39-7.45 (m, 6H), 7.66-7.70 (m, 4H); ^{13}C NMR (CDCl_3) δ 11.3, 13.0, 14.5, 19.1, 22.3, 26.7, 41.5, 67.0, 127.6, 129.5, 133.4, 133.6, 135.5, 136.8, 144.4, 204.7; IR (neat) 3071, 3049, 2963, 2932, 2858, 1665, 1638 cm^{-1} ; HRMS calcd for $\text{C}_{25}\text{H}_{34}\text{O}_2\text{Si}$ $[\text{M}+\text{Li}]^+$ 401.2488. Found 401.2487.

(R, R) 1-(tert-Butyl-diphenyl-silanyloxy)-2,4-dimethyl-hept-4-en-3-ol (8)

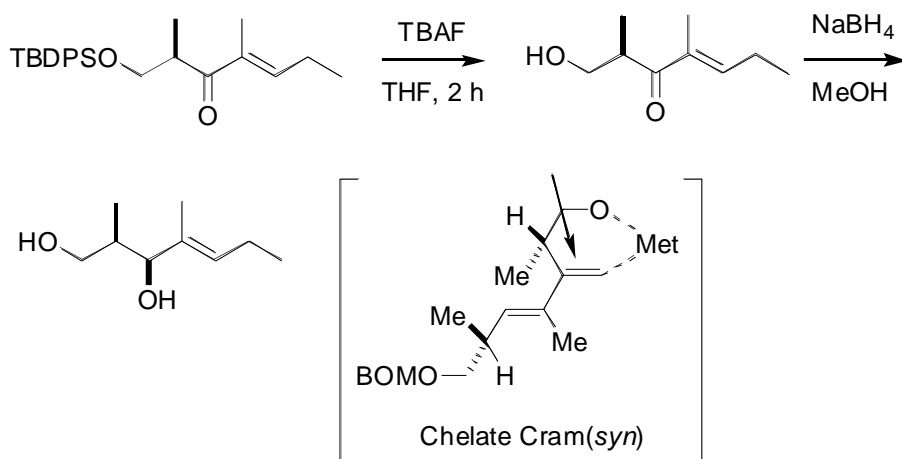


$[\alpha]_D^{19} -21.3$ (c 0.046, CHCl_3); ^1H NMR (CDCl_3) δ 0.79 (d, J = 7.2 Hz, 3H), 0.99 (t, J = 7.5 Hz, 3H), 1.09 (s, 9H), 1.64 (s, 3H), 1.90-2.12 (m, 3H), 3.66 (dd, J = 10.2, 7.8 Hz, 1H), 3.81 (dd, J = 10.2, 4.2 Hz, 1H), 3.93 (d, J = 8.4 Hz, 1H), 5.44 (t, J = 6.9 Hz, 1H), 7.39-7.46 (m, 6H), 7.70-7.73 (m, 4H); ^{13}C NMR (CDCl_3) 10.9, 13.6, 14.0, 19.0, 20.8, 26.8,

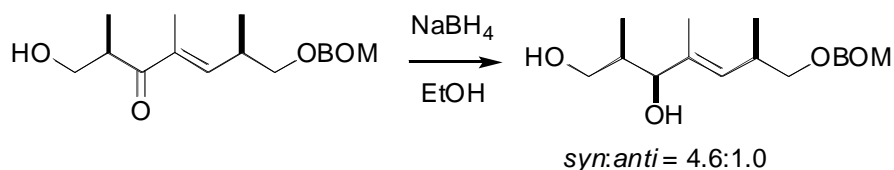
37.4, 69.2, 83.5, 127.7, 129.8, 130.0, 132.0, 132.8, 134.9, 135.5, 135.6; IR (neat) 3492 (br), 3071, 3056, 2961, 2931, 2858, 1471 cm^{-1} ; HRMS calcd for $\text{C}_{25}\text{H}_{36}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$ 403.2645. Found 403.2658.

Determination of relative stereochemistry:

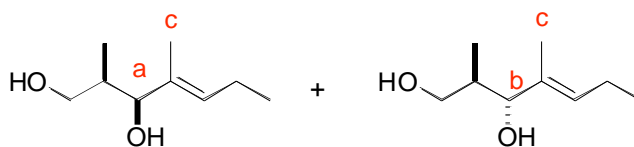
Alkene **7** was treated with TBAF to afford an alcohol. According to the literature reported results, the hydride reduction of this type of alcohol favors *syn* product, presumably due to the chelate-Cram transient state. Indeed, a 4.6:1.0 ratio was observed while this alcohol was reduced by NaBH_4 , and the major isomer was presumed to be *syn*.



Johann Mulzer *et al*, *Synlett* **2005**, 4, 0685

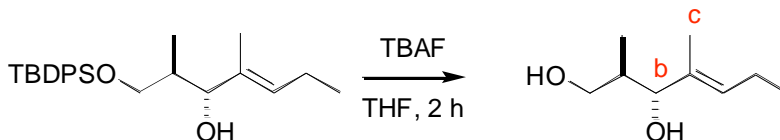


The chemical shift of protons *a* and *b* is different, which can be used to determine the relative stereochemistry. Since the major isomer is at 4.07 ppm, this chemical shift should correspond to the *syn* product.



^1H NMR (CDCl_3)	a	b	c
	4.07 (0.79H)	3.83 (0.17H)	1.58 (3H)

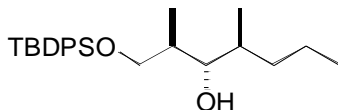
Compound **8** was treated with TBAF, and the diol obtained was isolated. A chemical shift of 3.82 ppm was observed, clearly indicating that the major compound is the *anti* isomer, plus, the NMR spectrum also indicates that the *anti:syn* ratio is >20:1.



Deprotect the product **7**

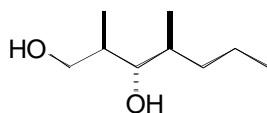
^1H NMR (CDCl_3)	a	b	c
	not present	3.82 (1H)	1.58 (3H)

(*R, R, S*) 1-(tert-Butyl-diphenyl-silanyloxy)-2,4-dimethyl-heptan-3-ol (9)



$[\alpha]_D^{19}$ -30.1 (*c* 0.011, CHCl_3); ^1H NMR (CDCl_3) δ 0.86 (d, J = 6.9 Hz, 3H), 0.91-0.95 (m, 6H); 10.6 (s, 9H), 1.18-1.27 (m, 2H), 1.46-1.63 (m, 3H), 1.85-1.94 (m, 1H), 3.35-3.39 (m, 1H), 3.62-3.82 (m, 2H), 7.38-7.45 (m, 6H), 7.67-7.70 (m, 4H); ^{13}C NMR (CDCl_3) 14.1, 14.4, 16.8, 19.1, 20.4, 26.5, 26.8, 32.1, 35.5, 36.8, 68.9, 81.1, 127.8, 129.8, 135.6, 135.6; IR (neat) 3508, 3071, 2958, 2931, 2859, 1589, 1471 cm^{-1} ; HRMS calcd for $\text{C}_{25}\text{H}_{38}\text{O}_2\text{Si}$ $[\text{M}+\text{Li}]^+$ 405.2801. Found 405.2806.

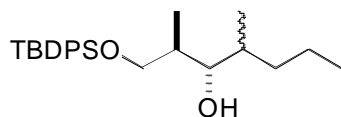
(*R, R, S*) 2,4-Dimethyl-heptane-1,3-diol



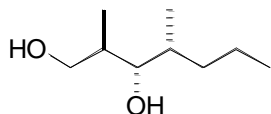
^1H NMR (CDCl_3) δ 0.88-0.96 (m, 9H), 1.11-1.23 (m, 2H), 1.41-1.48 (m, 2H), 1.65-1.68 (m, 1H), 1.85-1.93 (m, 1H), 3.36-3.40 (m, 1H), 3.61-3.78 (m, 2H);

Determination of relative stereochemistry:

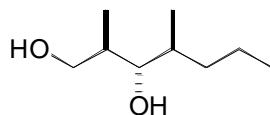
Compound **9** was treated with TBAF and the diol obtained was isolated and compared with the known *anti/syn* compound¹² and the diastereoisomers prepared by Rh/a hydrogenation. Since our compound does not have the same ^1H NMR shifts as the known compound, we concluded that our compound **9** is the *anti/anti* isomer.



^1H NMR 0.81(d) - 0.94 (d)



0.81 (d) 0.87(d) 0.91(t)
literature



0.88 (d) 0.91(t) 0.94(d)
this compound

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