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Supporting Information

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Asymmetric Synthesis of α-Substituted Allylic Boranes and their Application in the Synthesis of iso-Agatharesinol

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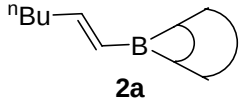
1 General Information

All air and water sensitive reactions were carried out in oven dried glassware under a nitrogen atmosphere. Solvents were dried by standard methods.[1] NMR spectra were recorded on Jeol 270 MHz or Jeol 400 MHz spectrometers using tetramethylsilane as the internal standard (0.00 ppm). $CDCl_3$ was used as the internal standard for ^{13}C NMR spectra (77.4 ppm). CI mass spectra were obtained using a VG Platform mass spectrometer. IR spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Flash chromatography was performed using silica gel (Merck Kieselgel 60). Melting points were determined with a Kofler hot stage apparatus and were not corrected. *p*-Bromomethylphenyl pivaloate,[2] sulfonium salts **1** and **7**,[3] and [*p*-hydroxyphenyl]acetylene[4] were made following literature methods.

2 Synthesis of Vinylborane and Its Derivatives.

Synthesis of *B*-(trans-1-hexenyl)-9-borabicyclo(3,3,1)nonane (2a)[5]



2a

Following the method by Brown,[5] 9-BBN (0.5 M in THF, 40.0 mL, 20.0 mmol) was added dropwise to pre-degassed 1-hexyne (3.60 g, 5.0 mL, 44.0 mmol) at 0 °C. After addition, the reaction mixture was warmed to room temperature and stirred for another two hours. The solvent was removed under reduced pressure. The crude product was purified by distillation under reduced pressure to furnish the desired compound as a pale yellow oil (2.58 g, 60%). B.p. 88-92 ºC/0.15 mbar (lit[5] B.p. 72-74 ºC/0.03 mmHg). ^1H NMR (300 MHz, $CDCl_3$) 0.94 (3H, t, 7.2 Hz), 1.22-1.31 (2H, m), 1.33-1.41 (2H, m),1.43-1.51 (2H, m), 1.67-1.77 (6H, m), 1.84-1.91 (6H,

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[1] A. B. Pangborn, M. A. Giardello,R. M. Grubbs, R. K. Rosen, F. T. Timmers, *Organometallics*, **1996**, *15*, 1518.

[2] Andrus, M. B.; Hicken, E. J.; Stephens, J. C.; Bedke, D. K. *J. Org. Chem*. **2005**, *70*, 9470.

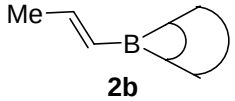
[3] Aggarwal, V. K.; Fang, G. Y.; Andreas, T. S. *J. Am. Chem. Soc*. **2005**, *127*, 1642.

[4] Ting, C.-H.; Chen, J.-T.; Hsu, C.-S. *Macromolecules*, **2002**, *35*, 1180.

[5] Brown, H. C.; Scouten, C. G.; Liotta, R. *J. Am. Chem. Soc*. **1979**, *101*, 96.

m), 2.28 (2H, dt, *J* 7.0, 6.4 Hz), 6.24 (1H, dt, *J* 17.2, 1.5 Hz), 6.85 (1H, dt, *J* 17.2, 6.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 14.1, 22.5, 23.6, 30.7, 33.8, 35.9, 156.3. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

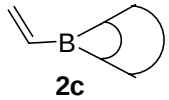
Synthesis of *B*-(trans-1-propenyl)-9-borabicyclo(3,3,1)nonane (2b)[6]



2b

Following the method by Soderquist,[6] propyne (6-10 mL) was condensed in a Schlenk flask, to which was added 9-BBN (0.5 M in THF, 60.0 mL, 30.0 mmol). After addition the mixture was stirred at 0 ºC until the white solid disappeared. Two hours later, the excess propyne and solvent were removed under reduced pressure, and the residue was subjected to high vacuum (0.1 mbar) through a dry ice–acetone condenser. The low boiling point component (the literature reported boiling point of **2b** was 66 ^{o}C/0.9 Torr[6]) was collected as a colourless oil (2.60 g, 54%) . ^{1}H NMR (300 MHz, $CDCl_3$) 1.19-1.30 (2H, m), 1.63-1.75 (6H, m), 1.82-1.91 (6H, m), 1.96 (3H, dd, *J* 6.4, 1.5 Hz), 6.25 (1H. dq, *J* 17.2, 1.5 Hz), 6.86 (1H, dq, *J* 17.2, 6.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 22.1, 23.6, 33.8, 151.2. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

Synthesis of *B*-vinyl-9- borabicyclo(3,3,1)nonane (2c)[7]



2c

Compound **2c** was made following the literature procedure from *B*-bromo-9-borabicyclo(3,3,1)nonane and tributyl(vinyl)tin.[7] *B*-Bromo-9-borabicyclo(3,3,1)nonane (5.10 g, 25.4 mmol), which was made from 9-BBN and bromine as described,[8] was dissolved in anhydrous dichloromethane (20 mL). To this solution was added tributyl(vinyl)tin (8.10 g, 25.4 mmol in 10 mL DCM) at room temperature. The reaction was monitored by ^{11}B NMR (chemical shift for ^{11}B in *B*-bromo-9-BBN in DCM is 84 ppm while in *B*-vinyl-9-BBN it is 78 ppm), and found that the reaction was finished whthin 5 hours. The solvent was removed under reduced pressure, and the residue was distilled through a 15 cm Vigreaux

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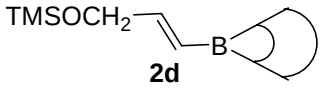
[6] Medina, J. R.; Cruz, G.; Cabrera, C. R.; Soderquist, J. A. *J. Org. Chem*. **2003**, *68*, 4631.

[7] Singleton, D. A.; Martinez, J. P.; Watson, J. V.; Ndip, G. M. *Tetrahedron*, **1992**, *48*, 5831.

[8] Brown, H. C.; Kulkarni, S. U. *J. Organomet. Chem*. **1979**, *168*, 281.

column to afford the product as colourless oil (2.90 g, 78%). B.p. 24-28 ^{o}C/0.18 mbar (lit.[7] 28-30 ^{o}C/0.5-0.30 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$) 1.20-1.30 (2H, m), 1.66-1.78 (4H, m), 1.82-1.95 (8H, m), 6.13 (1H, dd, *J* 12.6, 4.2 Hz), 6.28 (1H, dd, *J* 19.4, 4.2 Hz), 6.67 (1H, dd, *J* 19.4, 12.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 23.5, 33.8, 136.7. ^{11}B NMR (96 MHz, $CDCl_3$) 78.

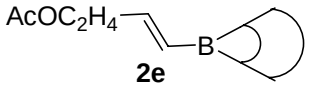
Synthesis of *B*-[*trans*-1-(3-trimethylsilyoxy)-propenyl]-9- borabicyclo(3,3,1)nonane (2d)



2d

9-BBN (0.5 M in THF, 60.0 mL, 30.0 mmol) was added dropwise to pre-degassed 3-trimethylsilanyloxy-propyne (8.40 g, 65.0 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred for two hours. The solvent was removed under reduced pressure, and the crude product obtained was purified by distillation under reduced pressure to furnish the desired compound as a colorless oil (6.30 g, 84%). B.p. 80-85 ºC/0.12 mbar. ^{1}H NMR (300 MHz, $CDCl_3$) 0.05 (9H, s), 1.07-1.18 (2H, m), 1.54-1.81 (12H, m), 4.23 (2H, dd, *J* 4.0, 1.7 Hz), 6.36 (1H, dt, *J* 17.6, 1.7 Hz), 6.70 (1H, dt, *J* 17.6, 4.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) –0.3, 23.5, 33.8, 64.8, 152.6. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

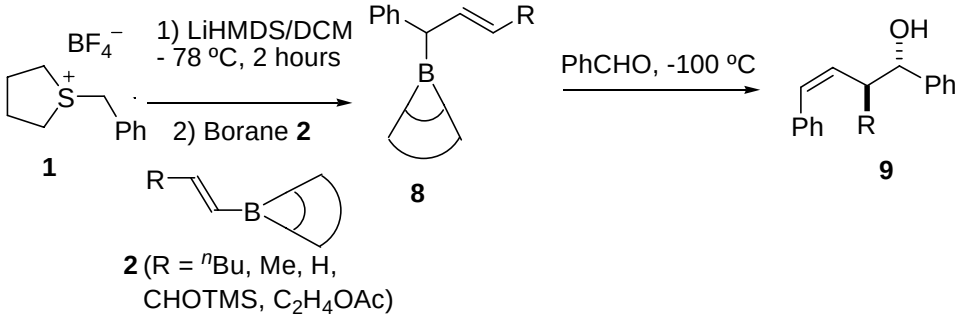
Synthesis of acetic acid 4-(9-bora-bicyclo[3,3,1]non-9-yl)-*trans*-but-3-enyl ester (2e)



2e

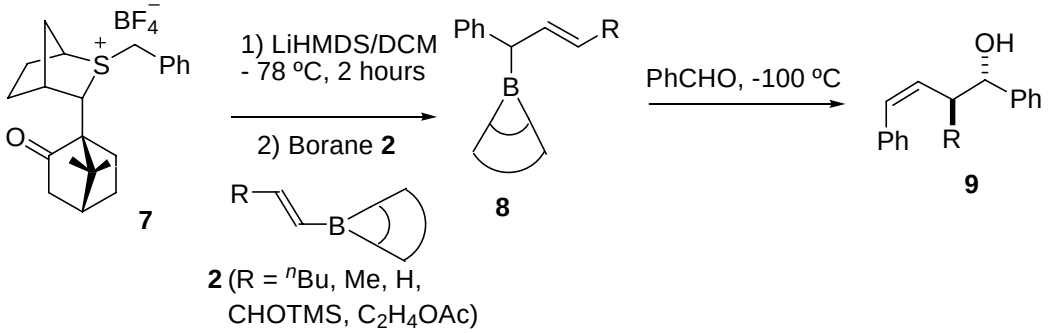
9-BBN (0.5 M in THF, 34.0 mL, 17.0 mmol) was added dropwise to pre-degassed acetic acid *trans*-but-3-ynyl ester (3.80 g, 34.0 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred for two hours. The solvent was removed under reduced pressure, and the crude product obtained was purified by distillation under reduced pressure to furnish the desired compound as a pale yellow oil (1.90 g, 50%). B.p. 85-100 ºC/0.11 mbar. ^{1}H NMR (300 MHz, $CDCl_3$) 1.19-1.29 (14H, m), 2.06 (3H, s), 2.59 (2H, dt, *J* 6.8, 6.4 Hz), 4.22 (2H, t, *J* 6.8 Hz), 6.31 (1H, d, *J* 17.4 Hz), 6.74 (1H, dt, *J* 17.4, 6.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 21.1, 23.5, 33.8, 35.1, 63.1, 149.8, 171.2. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

3 General Procedure for Borane-Ylide Reactions (Procedure A Using Achiral Sulfonium Salt)



To a mixture of the achiral sulfonium salt **1** (0.50 mmol) in DCM (1 mL) was added LiHMDS (1 M in THF, 0.55 mL) at – 78 ºC. The mixture was stirred at – 78 ºC until the salt was dissolved. It was then cooled to – 100 ºC (diethyl ether-liquid nitrogen bath), and a solution of the borane (1 M in THF, 0.55 mL) was added slowly. Twenty minutes after addition, benzaldehyde (1 M in THF, 1.0 mL) was added dropwise, and the mixture was stirred for another 30 mins at – 100 ºC followed by 2 hours at – 78 ºC. The reaction was quenched by adding a mixture of aqueous NaOH solution (2 M, 1 mL) and H_2O_2 solution (30%, 0.5 mL) slowly at – 78 ºC and the mixture was stirred for another 4 hours at room temperature. The reaction mixture was then diluted with NaOH (2 M, 4 mL) and water (10 mL) and extracted with diethyl ether (2 × 30 mL). The ethereal solutions were combined, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Finally, the residue obtained was purified by chromatography.

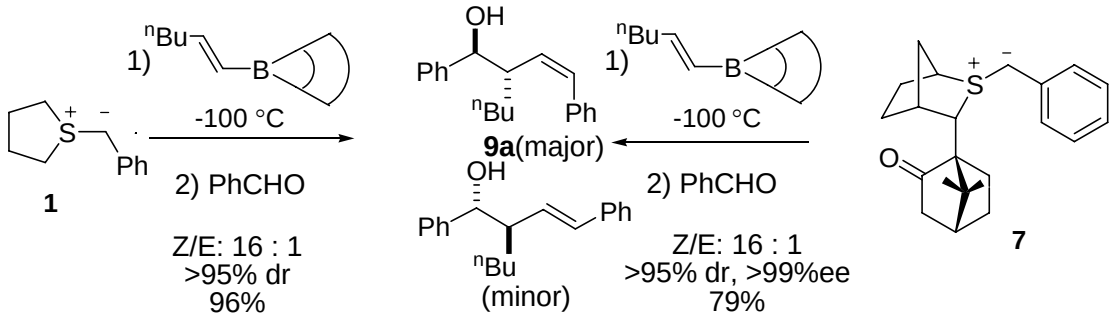
General Procedure for Borane-Ylide Reactions (Procedure A Using Chiral Sulfonium Salt)



To a mixture of the chiral sulfonium salt **7** (0.50 mmol) in DCM (2 mL) was added LiHMDS (1 M in THF, 0.55 mL) at – 78 ºC. The mixture was stirred at –78 ºC until the salt was dissolved. Additional

THF (0.55 mL) was then added to the solution, and it was then cooled to –100 ºC (diethyl ether-liquid nitrogen bath), and a solution of the borane (1 M in THF, 0.55 mL) was added slowly. After twenty mins, benzaldehyde (1 M in THF, 1.0 mL) was added dropwise, and the mixture was stirred for another 30 minutes at -100 ºC followed by 2 hours at -78 ºC. The reaction was quenched by adding a mixture of aqueous NaOH solution (2 M, 1 mL) and H_2O_2 solution (30%, 0.5 mL) slowly at – 78 ºC and the mixture, and was stirred for another 4 hours at room temperature. The reaction mixture was then diluted with NaOH (2 M, 4 mL) and water (10 mL) and extracted with diethyl ether (2 × 30 mL). The ethereal solutions were combined, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Finally, the residue was purified by chromatography.

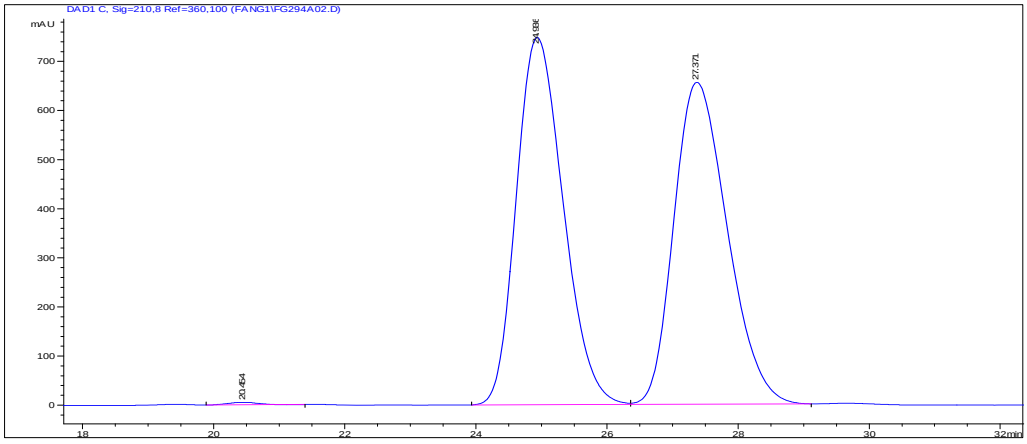
***Anti*-(Z/E)-2-butyl-1,4-diphenyl-but-3-en-1-ol (9a)**

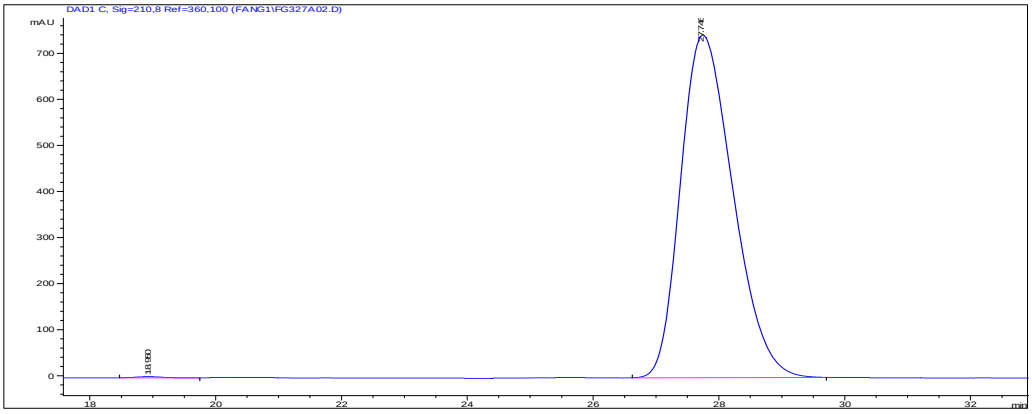


A 16 : 1 mixture of *anti*-(Z)/(E)-2-butyl-1,4-diphenyl-but-3-en-1-ol was obtained as a colorless oil in 96% yield (79% yield when the chiral sulfonium salt **7** was used). $[\alpha]_D^{20}$ +5.6 (*c* = 0.54, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3435, 1493, 1453, 1028. ^1H NMR (400 MHz, $CDCl_3$) 0.73 (3H, t, *J* 7.0 Hz), 0.97-1.27 (6H, m), 2.14 (1H, d, *J* 2.2 Hz), 2.18_{minor} (1H, d, *J* 2.2 Hz) 2.95-3.03 (1H, m), 4.50 (1H, dd, *J* 7.3, 2.2 Hz), 5.53 (1H, dd, *J* 11.7, 11.4 Hz), 6.06_{minor} (1H, dd, *J* 16.0, 9.5 Hz), 6.50_{minor} (1H, d, *J* 16.0 Hz), 6.74 (1H, d, *J* 11.7 Hz), 7.20-7.35 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 22.7, 29.3, 31.4, 45.9, 77.8, 126.7, 127.0, 127.7, 128.1, 128.2, 128.5, 133.1, 133.2, 137.3, 142.7. *m/z* (CI) 263 (MH^+-H_2O, 100), 174 (50), 91 (27). HRMS (ESI) calcd. for $C_{20}H_{24}NaO$, 303.1719. Found: 303.1731.

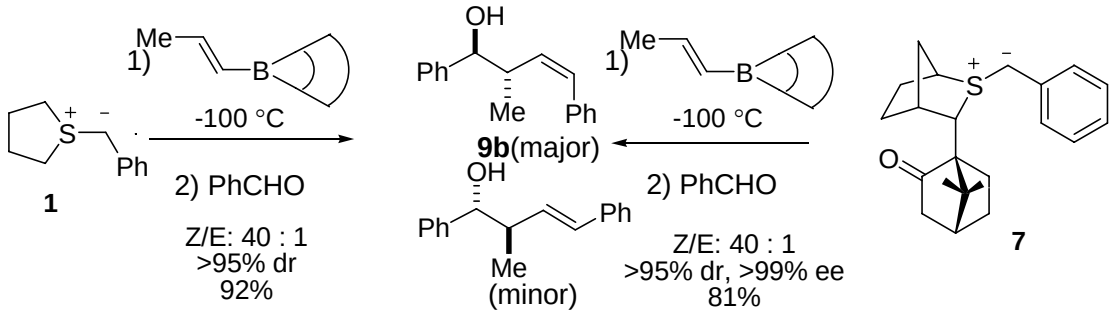
HPLC trace of *Anti*-(Z)-2-butyl-1,4-diphenyl-but-3-en-1-ol (9a) (> 99% ee)

Conditions: OD-H chiralcel column, 1% ipa in hexane, 1 mL/min





***Anti*-(Z/E)-2-methyl-1,4-diphenyl-but-3-en-1-ol (9b)**

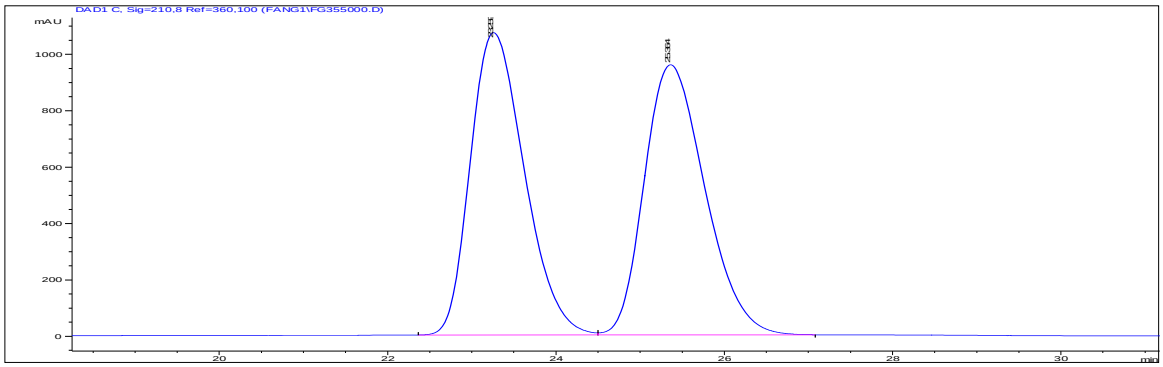


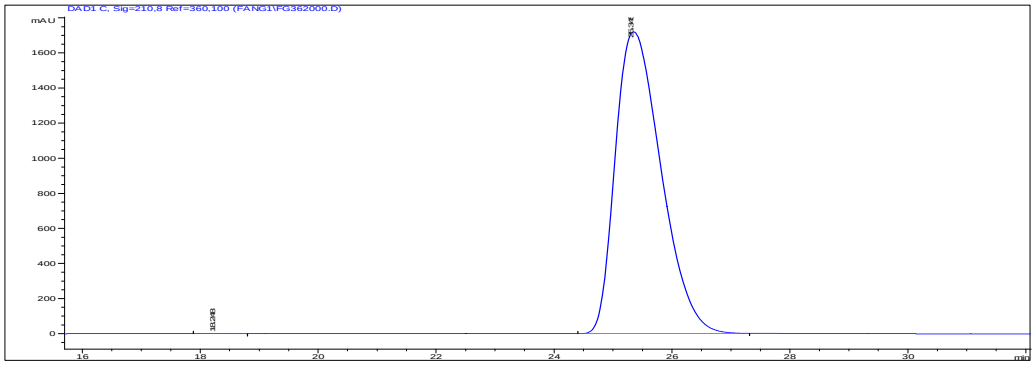
A 40 : 1 mixture of *anti*-(Z)/(E)-2-methyl-1,4-diphenyl-but-3-en-1-ol was obtained as a colorless oil in 92% yield (81% yield when the chiral sulfonium salt **7** was used) . $[\alpha]_D^{20}$ – 20.8 ($CHCl_3$, c = 0.53). ν_{max}/cm^{-1} (neat) 3416, 1452, 1018. ^1H NMR (400 MHz, $CDCl_3$) 0.88 (3H, d, *J* 6.6 Hz), 0.97_{minor} (3H, d, *J* 7.0 Hz), 2.15 (1H, d, *J* 2.0 Hz), 2.20_{minor} (1H, d, *J* 2.4 Hz), $2.61\text{-}2.68_{minor}$ (1H, m), 3.09-3.19 (1H, m),

4.43 (1H, dd, *J* 8.1, 2.0 Hz), 4.46_{minor} (1H, dd, *J* 8.1, 2.4 Hz), 5.61 (1H, t, *J* 11.0 Hz), 6.19_{minor} (1H, dd, *J* 15.7, 8.4 Hz), 6.55_{minor} (1H, d, *J* 15.7 Hz), 6.65 (1H, d, *J* 11.0 Hz), 7.25-7.35 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 17.0, 40.4, 79.0, 126.9, 127.0, 127.8, 128.2, 128.6, 131.3, 134.6, 134.5, 137.1, 142.3. *m/z* (CI) 221 (MH^+-H_2O, 100), 143 (60). HRMS(ESI) calcd. for $C_{17}H_{18}NaO$, 261.1250. Found: 261.1254.

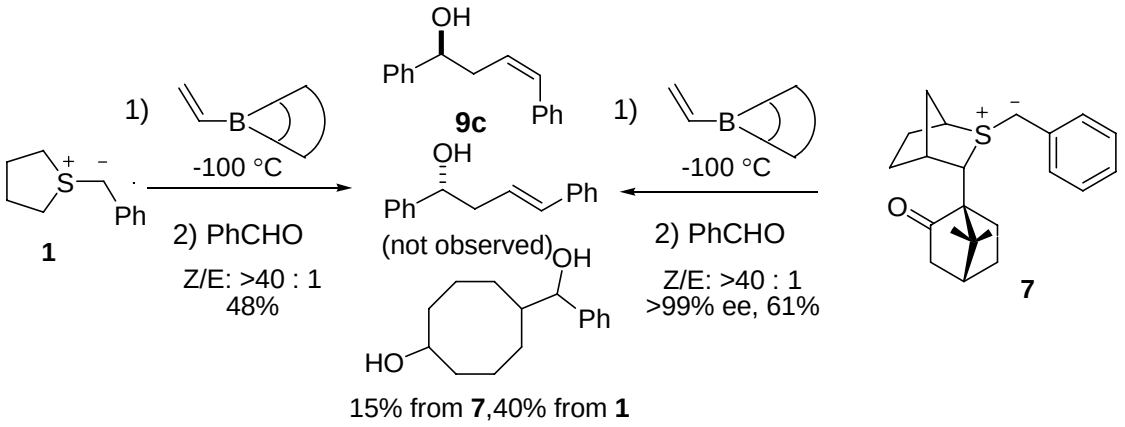
HPLC trace of *Anti*-(Z)-2-methyl-1,4-diphenyl-but-3-en-1-ol (9b) (>99% ee)

Conditions: OD-H chiralcel column, 1.5% ipa in hexane, 1 mL/min





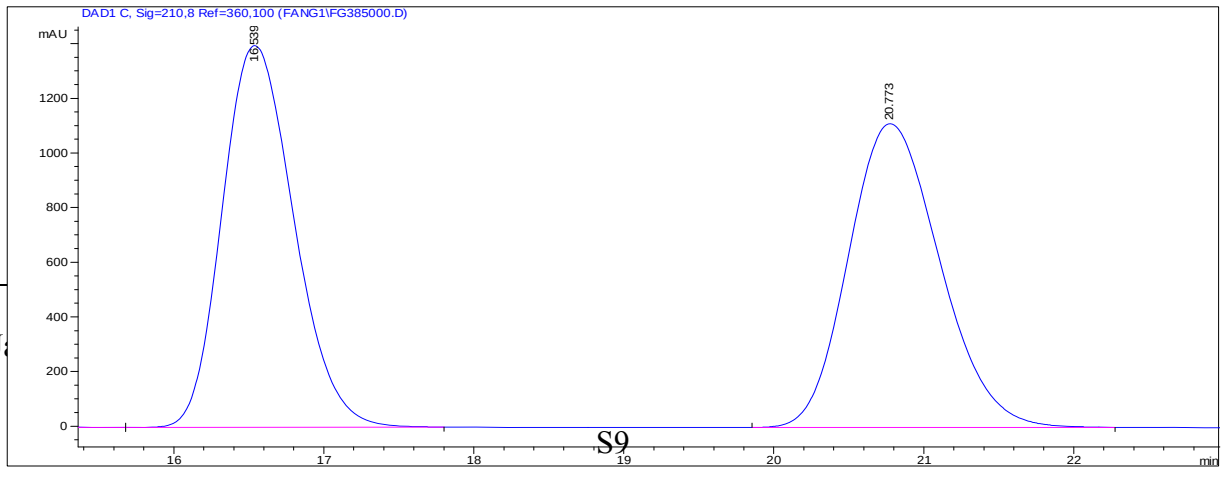
(Z)-1,4-diphenyl-but-3-en-1-ol (9c)[9]



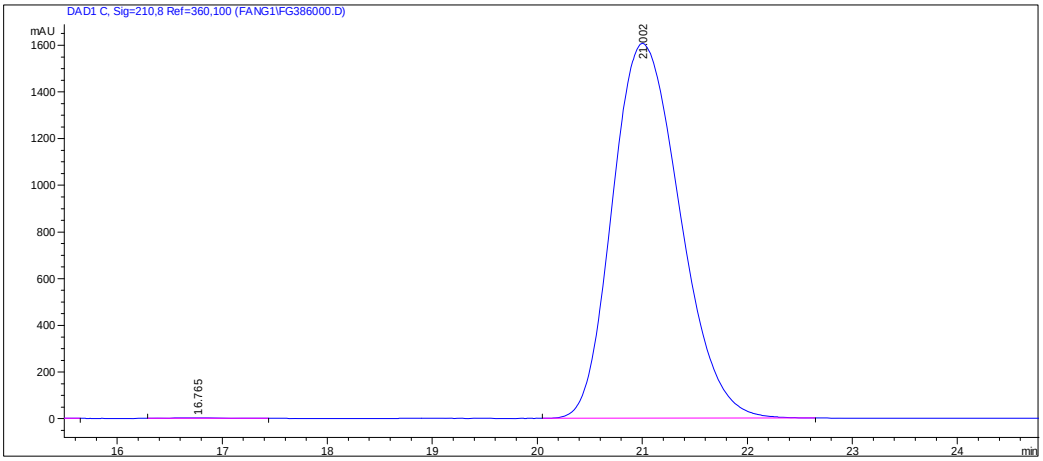
(Z)-1,4-Diphenyl-but-3-1-ol was obtained as a colourless oil in 48% yield (61% yield when the chiral sulfonium salt **7** was used) $[\alpha]_D^{20}$ – 20.3 (*c* = 0.64, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) 2.72 (1H, dddd, *J* 15.0, 7.3, 5.1, 1.8 Hz), 2.84 (1H, dddd, *J* 15.0, 8.1, 7.3, 1.8 Hz), 4.78 (1H, ddd, *J* 8.1, 5.1, 2.9 Hz), 5.71 (1H, dt, *J* 11.7, 7.3 Hz), 6.56 (1H, d, *J* 11.7 Hz), 7.17-7.28 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 38.3, 74.3, 126.0, 126.9, 127.8, 128.0, 128.3, 128.6, 128.8, 131.7, 137.3, 144.0. This data matched the literature.[9] **Analytic data for the eight membered diol**: ν_{max}/cm^{-1} (neat) 3277, 2918, 1451, 1046. ^{1}H NMR (400 MHz, $CDCl_3$) 1.16-1.4 (1H, m), 1.28-1.44 (3H, m), 1.53-1.64 (2H, m), 1.71-1.89 (6H, m), 3.9 (1H, tt, *J* 8.8, 3.3 Hz), 4.39 (1H, d, *J* 7.0 Hz), 7.24-3.76 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 22.9, 23.3, 28.6, 30.5 (2 × C), 36.1, 44.3, 72.1, 79.5, 126.7, 127.5, 128.4, 143.8. *m/z* (CI) 217 (MH^+- H_2O, 100), 199 (52), 107 (60). HRMS(ESI) calcd. for $C_{15}H_{22}O_2Na$, 257.1518. Found: 257.1512.

HPLC trace of (Z)- 1,4-diphenyl-but-3-en-1-ol (9c) (>99% ee)

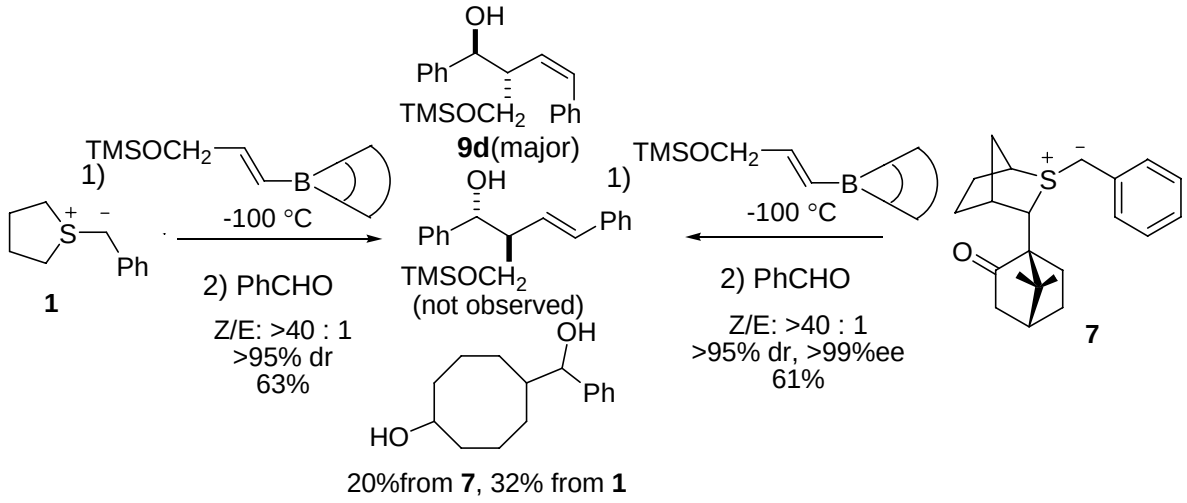
Conditions: OD-H chiralcel column, 3.0% ipa in hexane, 1 mL/min



[9] J



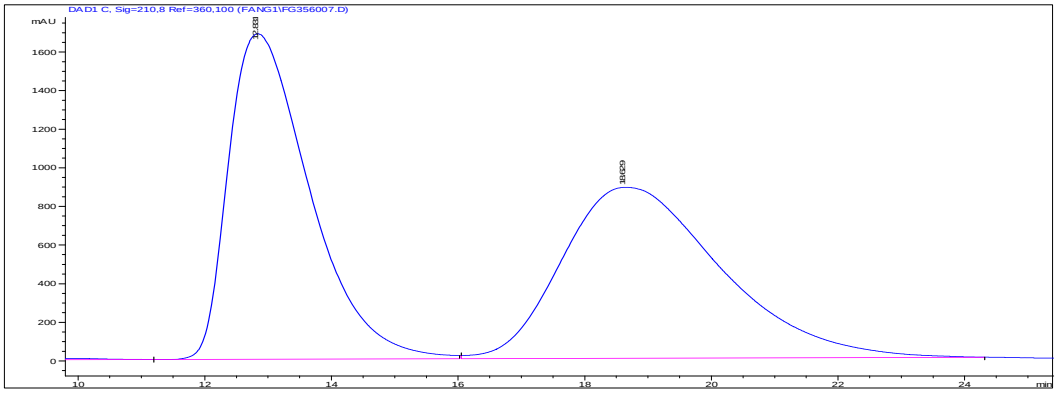
***Anti*-(Z)-2-(trimethylsilyloxymethyl)-1,4-diphenyl-but-3-en-1-ol (9d)**

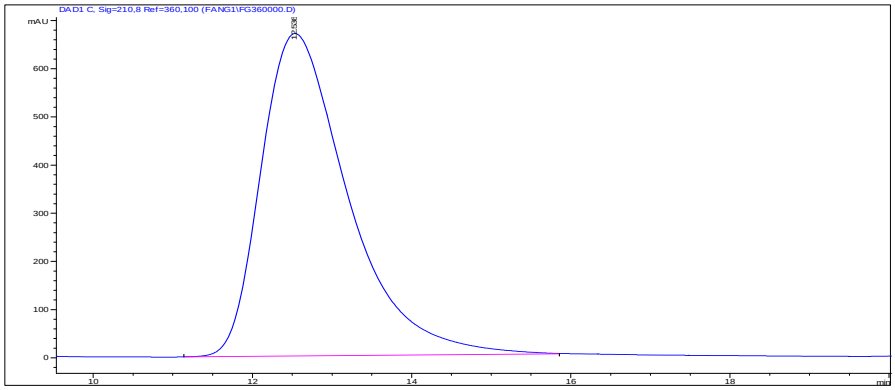


Anti-(Z)-2-(trimethylsilyloxymethyl)-1,4-diphenyl-but-3-en-1-ol was obtained as a colourless oil in 63% yield (61% yield when the chiral sulfonium salt **7** was used). ν_{max}/cm^{-1} (neat) 3441, 1250, 1062. ^{1}H NMR (400 MHz, $CDCl_3$) 0.10 (9H, s), 3.13-3.20 (1H, m), 3.40 (1H, d, *J* 3.9 Hz), 3.64 (2H, d, *J* 5.9 Hz), 4.98 (1H, t, *J* 3.9 Hz), 5.68 (1H, t, *J* 11.7 Hz), 6.63 (1H, d, *J* 11.7 Hz), 7.01 (2H, d, *J* 8.8 Hz), 7.17-7.33 (8H, m). ^{13}C NMR (100 MHz, $CDCl_3$) -0.58, 46.4, 64.9, 75.8, 126.6, 126.8, 127.4, 128.1, 128.2, 128.4 (2 × C), 132.7, 137.2, 142.5. *m/z* (CI) 219 (MH^+-H_2O-$HOSiMe_3$, 100), 130 (55). HRMS (ESI) calcd. for $C_{20}H_{26}NaO_2Si$, 349.1594. Found:349.1600.

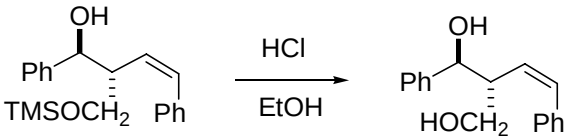
HPLC trace of *Anti*-(Z)-2-(trimethylsilyloxymethyl)-1,4-diphenyl-but-3-en-1-ol (9d) (>99% ee)

Conditions: OJ chiralcel column, 0.7% ipa in hexane, 1 mL/min





***Anti*-(Z)-2-(hydroxymethyl)-1,4-diphenyl-but-3-en-1-ol**

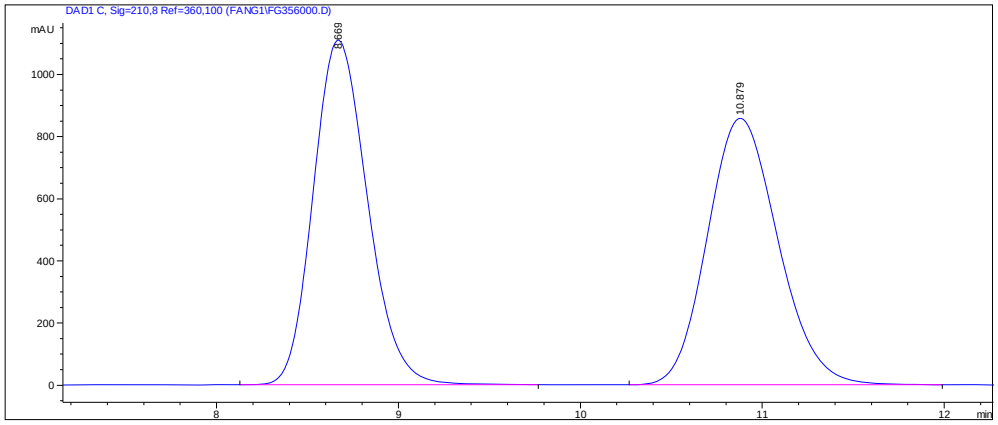


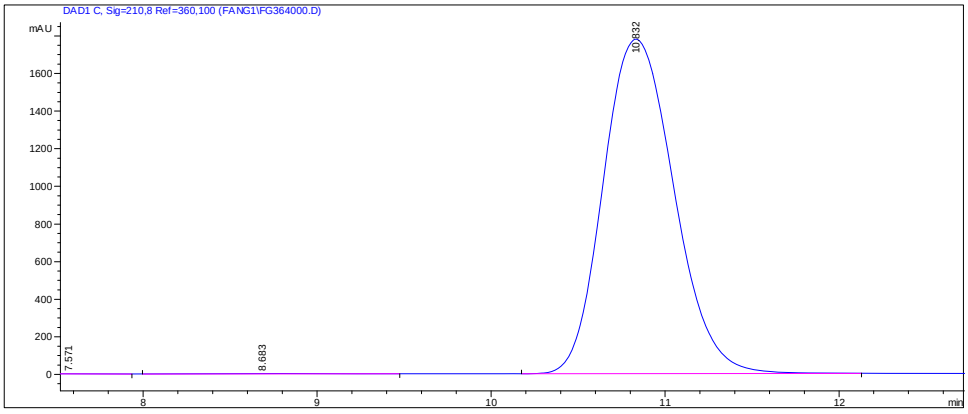
To the solution of *anti*-(Z)-2-(trimethylsilyloxymethyl)-1,4-diphenyl-but-3-en-1-ol (98 mg, 0.30 mmol) in ethanol (5 mL) was added HCl (1.0 M solution in water, 0.30 mL). The mixture was stirred at room temperature overnight, and then it was diluted with DCM (20 mL) and water (2 mL). The aqueous phase was separated, and the organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to furnish the product as white plates (optically active compound) or white rods (racemic diol) in 98% yield. M.p. 109-111 ºC (enantiomerically enriched diol, diethyl ether) and 98-100 ºC (racemic diol, diethyl ether). $[\alpha]_D^{20}$ +12.7 (c = 0.55, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3257, 2937, 2875. ^1H

NMR (400 MHz, $CDCl_3$) 1.82 (1H, dd, *J* 6.2, 5.1 Hz), 2.53 (1H, d, *J* 2.9 Hz), 3.24 (1H, ddt, *J* 11.0, 5.9, 5.5 Hz), 3.63 (1H, ddd, *J* 10.6, 5.5, 5.1 Hz), 3.67 (1H, ddd, *J* 10.6, 6.2, 5.9 Hz), 4.91 (1H, dd, *J* 5.5, 2.9 Hz), 5.68 (1H, dd, *J* 11.7, 11.0 Hz), 6.73 (1H, d, *J* 11.7 Hz), 7.08-7.35 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 47.2, 64.7, 75.9, 126.6, 127.1, 127.9, 128.2, 128.3, 128.4, 128.5, 134.1, 136.9, 142.1. *m/z* (CI) 237 (MH^+-H_2O, 8), 219 (100), 130 (80). HRMS(ESI) calcd. for $C_{17}H_{18}NaO_2$, 277.1199. Found: 277.1210.

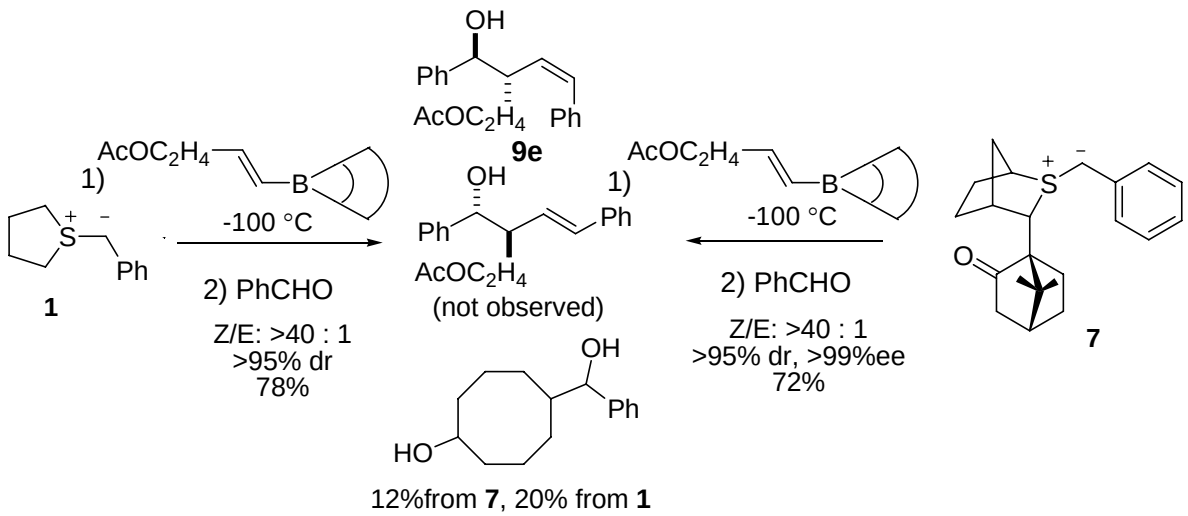
HPLC trace of *Anti*-(Z)-2-hydroxymethyl-1,4-diphenyl-but-3-en-1-ol (9d as the diol) (>99% ee)

Conditions: OD-H chiralcel column, 10.0% ipa in hexane, 1 mL/min





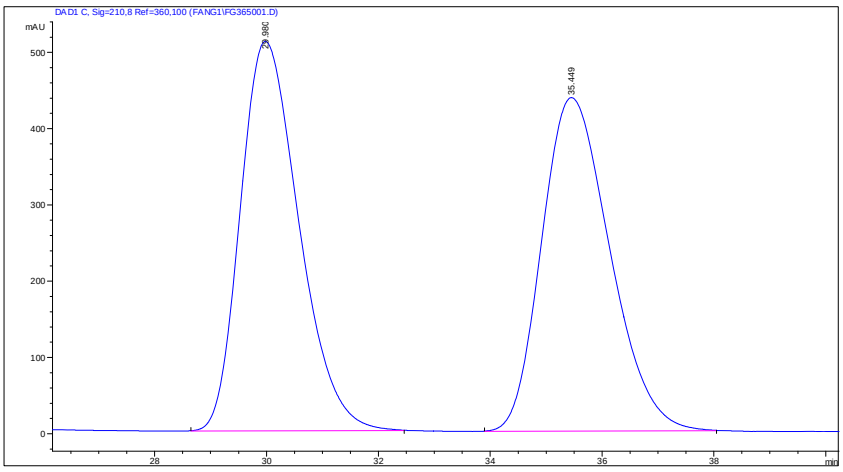
***Anti*-4-hydroxy-4-phenyl-3-[(Z)-2-phenylethenyl]-butan-1-ol acetate (9e)**

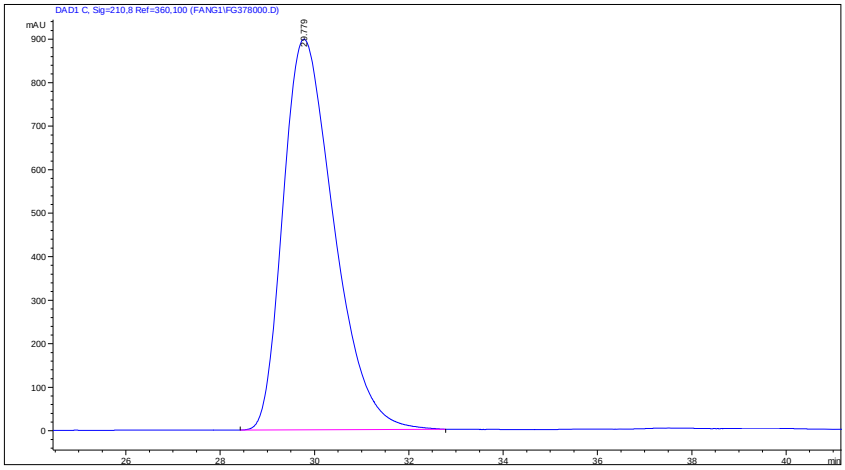


Compound **9e** was obtained as white plates in 78% yield (72% yield when the chiral sulfonium salt was used). M.p. 58-60 ^{o}C (racemic, diethyl ether) and 65-68 ^{o}C (optical active, diethyl ether). $[\alpha]_D^{20}$ +10.8 ($CHCl_3$, c = 0.65). ν_{max}/cm^{-1} (neat) 3434, 1706, 1601. ^{1}H NMR (400 MHz, $CDCl_3$) 1.44-1.53 (1H, m), 1.62-1.70 (1H, m), 1.70 (3H, s), 3.12-3.20 (1H, m), 3.83 (1H, ddd, *J* 10.6, 9.2, 6.2 Hz), 3.95 (1H, ddd, *J* 10.6, 6.6, 4.5 Hz), 4.59 (1H, d, *J* 6.6 Hz), 5.51 (1H, dd, *J* 11.7, 11.0 Hz), 6.73 (1H, d, *J* 11.7 Hz), 7.14 (2H, d, *J* 7.3 Hz), 7.20-7.34 (8H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 20.6, 30.4, 42.3, 62.4, 76.9, 126.9, 127.0, 127.9, 128.2, 128.4, 128.5, 131.3, 133.7, 137.1, 142.5, 171.1. *m/z* (CI) 233 (MH^+-H_2O-HOAc, 100), 205 (38), 155(42). HRMS(ESI) calcd. for $C_{20}H_{22}Na\ O_3$, 333.1461. Found: 333.1466.

HPLC trace of *Anti*-4-hydroxy-4-phenyl-3-[(Z)-2-phenylethenyl]-butan-1-ol acetate (9e) (>99% ee)

Conditions: OD-H chiralcel column, 3.0% ipa in hexane, 1 mL/min

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700
600
500
400
300
200
100
0
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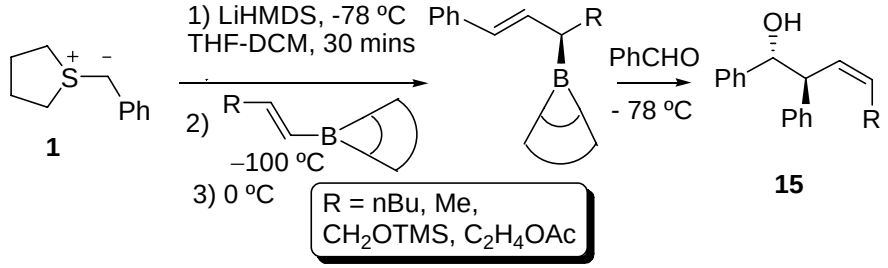
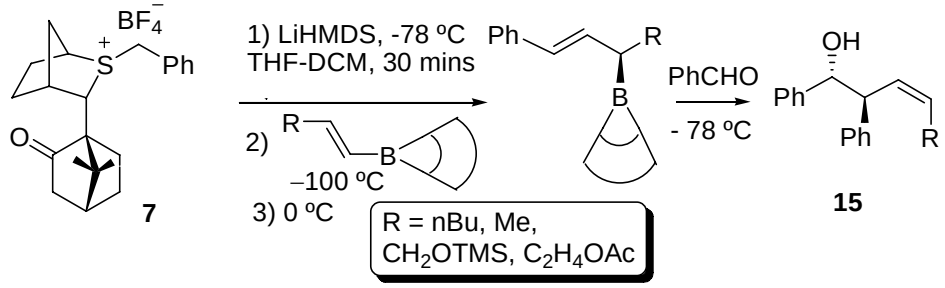
36
38
40
min

4 General Procedure for Borane-Ylide Reactions (Procedure B Using Achiral Sulfonium Salt)



To a mixture of the achiral sulfonium salt **1** (0.50 mmol) in DCM (1 mL) was added LiHMDS (1 M in THF, 0.55 mL) at – 78 ºC. The mixture was stirred at – 78 ºC until the salt dissolved. It was then cooled to – 100 ºC (diethyl ether-liquid nitrogen bath), and a solution of the borane (1 M in THF, 0.55 mL) was added slowly. Twenty minutes after the addition, the cooling bath was removed, and once the temperature rose to 0 ºC the reactants were re-cooled to – 78 ºC followed by addition of benzaldehyde (1 M in THF, 1.0 mL) dropwise. The mixture was stirred for another 30 mins at – 100 ºC followed by 2 hours at – 78 ºC. The reaction was then quenched by adding a mixture of aqueous NaOH solution (2 M, 1 mL) and H_2O_2 solution (30%, 0.5 mL) slowly at – 78 ºC and the mixture was stirred for another 4 hours at room temperature. The reaction mixture was then diluted with NaOH (2 M, 4 mL) and water (10 mL) and extracted with diethyl ether (2 × 30 mL). The ethereal solutions were combined, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure; the residue was purified by chromatography.

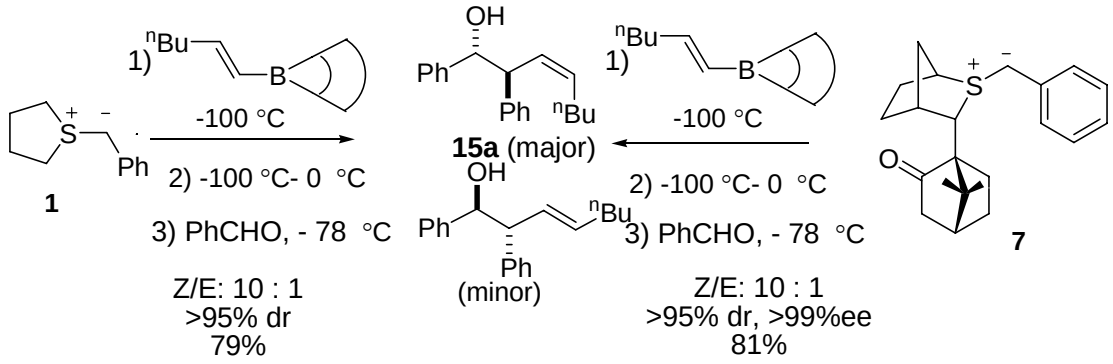
General Procedure for Borane-Ylide Reactions (Procedure B Using Chiral Sulfonium Salt)



To a mixture of the chiral sulfonium salt **7** (0.50 mmol) in DCM (1 mL) was added LiHMDS (1 M in THF, 0.55 mL) at – 78 ºC. The mixture was stirred at – 78 ºC until the salt dissolved. Additional THF (0.55 mL) was then added to the solution, it was then cooled to – 100 ºC (diethyl ether-liquid nitrogen bath), and a solution of the borane (1 M in THF, 0.55 mL) was added slowly. Twenty mins after the

addition, the cooling bath was removed, and once the temperature rose to 0 ºC the reactants were re-cooled to – 78 ºC followed by addition of benzaldehyde (1 M in THF, 1.0 mL) dropwise. The mixture was stirred for another 30 mins at – 100 ºC followed by 2 hours at – 78 ºC. The reaction was then quenched by adding a mixture of aqueous NaOH solution (2 M, 1 mL) and H_2O_2 solution (30%, 0.5 mL) slowly at – 78 ºC and the mixture was stirred for another 4 hours at room temperature. The reaction mixture was then diluted with NaOH (2 M, 4 mL) and water (10 mL) and extracted with diethyl ether (2 × 30 mL). The ethereal solutions were combined, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure; the residue was purified by chromatography.

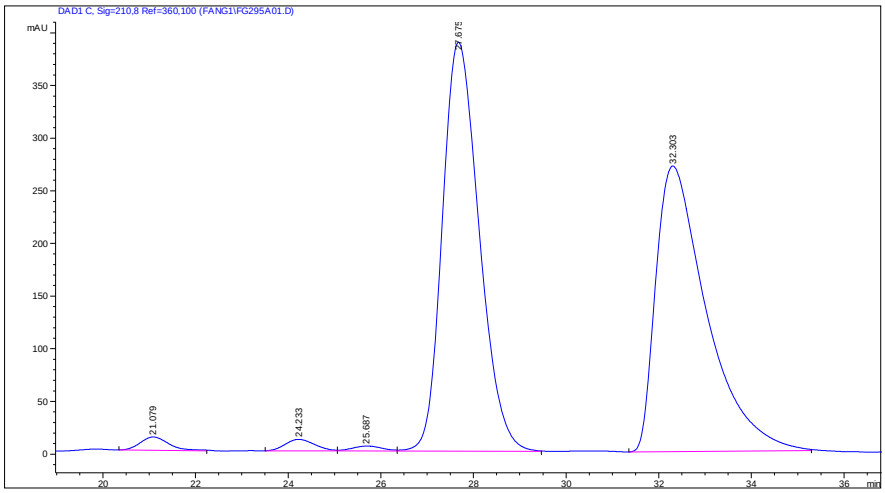
***Anti*-(Z/E)-1,2-diphenyl-oct-3-en-1-ol (16a)**

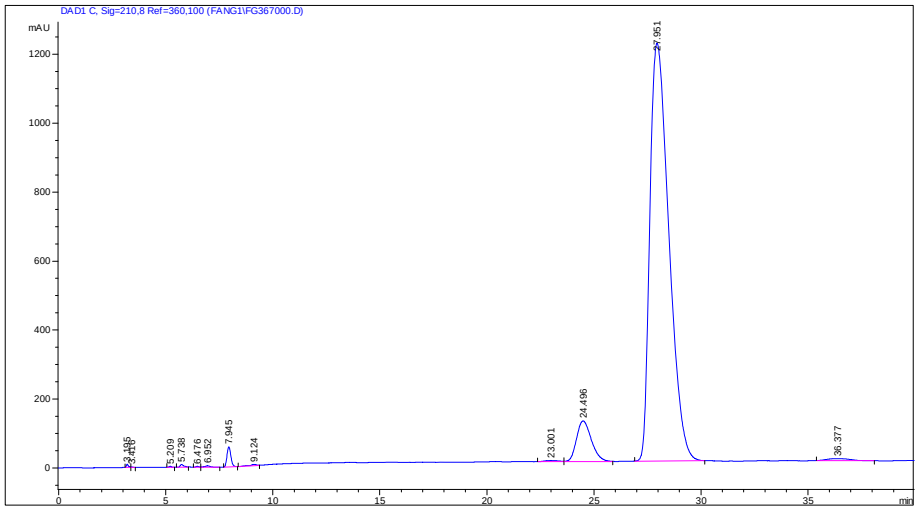


A mixture of *anti*-(Z)/(E)-1,2-diphenyl-oct -3-en-1-ol in a ratio 10 : 1 in favor of (Z) isomer was obtained as a colorless oil in 79% yield (81% yield when the chiral sulfonium salt was used). $[\alpha]_D^{20}$ +16.8 (*c* = 0.95, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3397, 1703, 1493, 1452, 1042. ^1H NMR (400 MHz, $CDCl_3$) 0.83 (3H, t, *J* 7.0 Hz), 1.20-1.24 (4H, m), 1.99-2.05 (2H, m), 2.28 (1H, d, *J* 2.2 Hz), 3.85 (1H, dd, *J* 10.3, 7.3 Hz), 4.80 (1H, dd, *J* 7.3, 2.2 Hz), 5.66 (1H, 1H, dtd, *J* 11.0, 7.3, 1.1 Hz), 5.85 (1H, ddt, *J* 11.0, 10.3, 1.5 Hz), 7.06-7.23 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 22.4, 27.4, 31.6, 52.5, 78.0, 126.5, 126.7, 127.4, 127.9, 128.2, 128.3, 128.4, 134.2, 141.7, 142.1. *m/z* (CI) 263 (MH^+-H_2O, 53), 185 (42), 173 (61), 107 (100). HRMS (ESI) calcd. for $C_{20}H_{24}NaO$, 303.1719. Found: 303.1723.

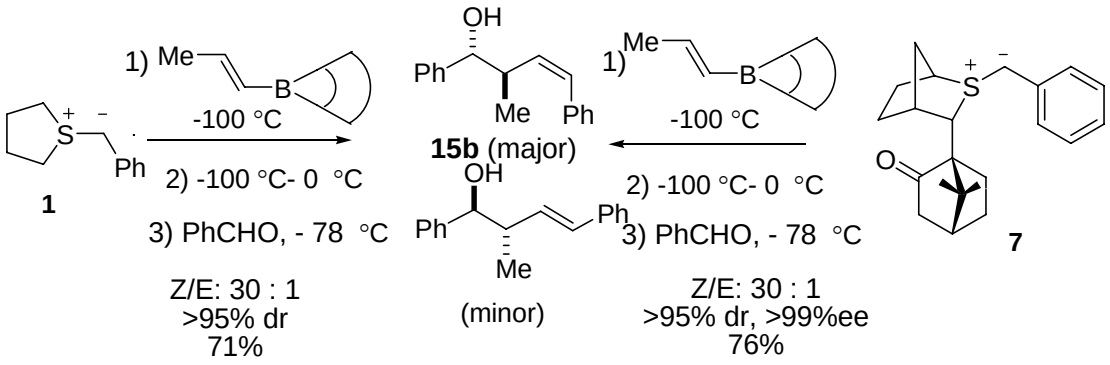
HPLC trace of *Anti*-(Z)-1,2-diphenyl-oct-3-en-1-ol (16a) (>99% ee)

Conditions: OD-H chiralcel column, 1% ipa in hexane, 1 mL/min





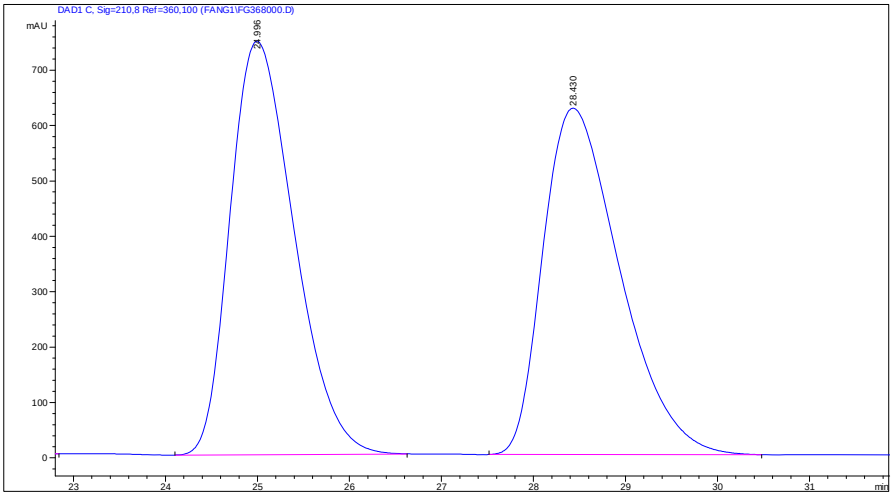
***Anti*-(Z)-1,2-diphenyl-pent-3-en-1-ol and *Anti*-(E)- 1,2-diphenyl-pent-3-en -1-ol (15b)[10]**



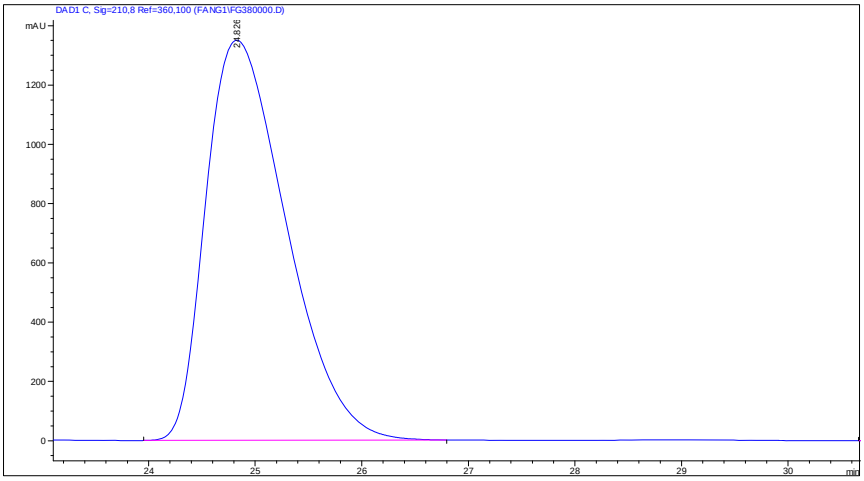
A mixture of *anti*-(Z)/(E)-1,2-diphenyl-pent-3-en-1-ol in ratio 30 : 1 in favor of (Z) isomer was obtained as a colorless oil in 71% yield (76% yield when the chiral sulfonium salt **7** was used). $[\alpha]_D^{20}$ +26.7 (*c* = 0.30, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3429, 1452, 1025. ^1H NMR (400 MHz, $CDCl_3$) 1.59 (3H, dd, *J* 6.8, 2.0 Hz), 1.73_{minor} (3H, dd, *J* 6.8, 1.5 Hz), 2.30 (1H, d, *J* 2.0 Hz), 2.41_{minor} (1H, d, *J* 2.4 Hz), 3.45_{minor} (1H, dd, *J* 10.5, 8.3 Hz), 3.88 (1H, dd, *J* 9.8, 7.3 Hz), 4.74_{minor} (1H, dd, *J* 8.3, 2.4 Hz), 4.80 (1H, dd, *J* 7.3, 2.0 Hz), 5.75 (1H, dqd, *J* 10.7, 6.8, 1.0 Hz), 5.89 (1H, ddq, *J* 10.7, 9.8, 2.0 Hz), 7.06-7.23 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 13.3, 52.2, 78.2, 126.5, 126.7, 127.4, 128.0, 128.1, 128.4 (2 × C), 129.5, 141.5, 142.1. This data matched the literature.[10]

HPLC trace of *Anti*-(Z)-1,2-diphenyl-pent-3-en-1-ol (16b) (>99% ee)

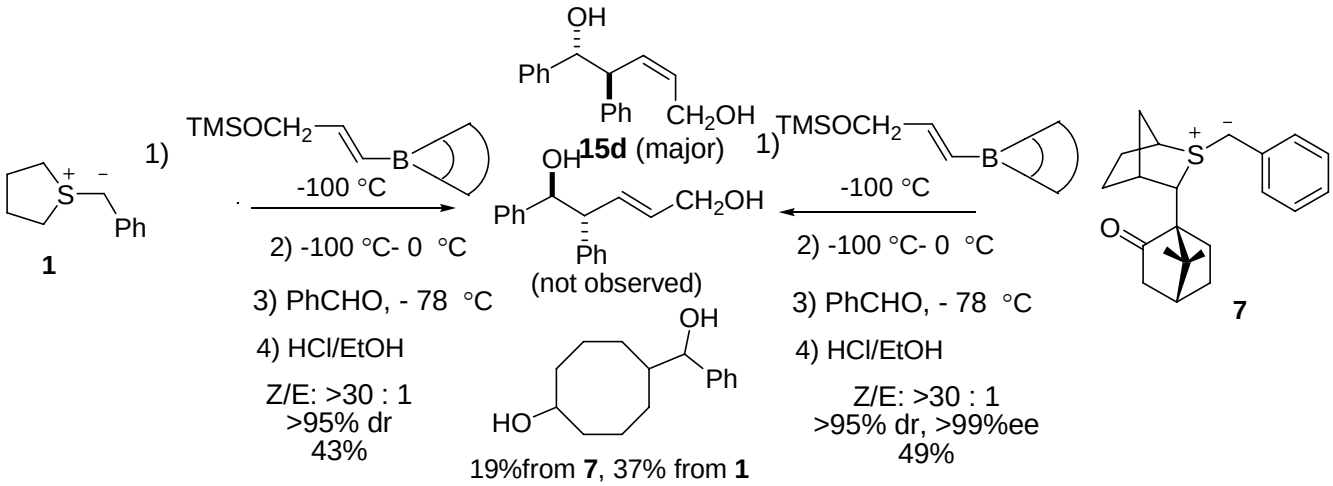
Conditions: OD-H chiralcel column, 1.5% ipa in hexane, 1 mL/min



[10] Hayashi, T.; Matsumoto, Y.; Kiyoi, T.; Ito, Y. *Tetrahedron Lett*. **1988**, *29*, 5667.



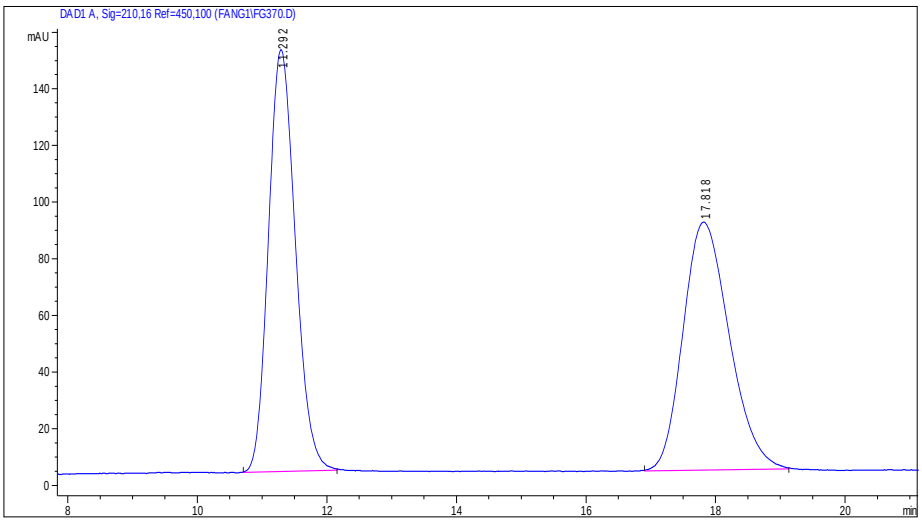
***Anti*-(Z)-1,2-diphenyl-pent-2-en-1,5-diol (15d)**

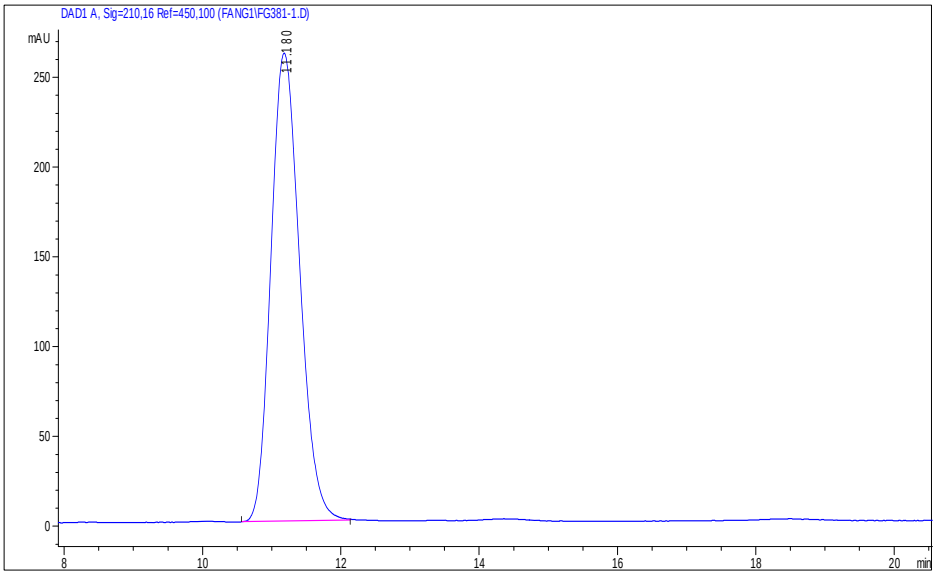


Following the procedure described above (See procedure B), the crude products obtained were dissolved in ethanol (4.0 mL), and HCl (1 M solution in water, 0.2 mL) was added. The mixture was stirred at room temperature overnight, followed by extracting with diethyl ether; the ethereal solution was dried over $MgSO_4$ and concentrated. The crude product obtained was subjected to chromatography to furnish the diol as a white needles in 43% yield (49% yield when the chiral sulfonium salt **7** was used). M.p. (diethyl ether) 72-74 ºC (optical active) and 85-88 ºC (racemic). $[\alpha]_D^{20}$ +29.2 (*c* = 0.65, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3227, 3024, 1044, 1016. ^1H NMR (400 MHz, $CDCl_3$) 3.90 (1H, dd, *J* 10.2, 6.9 Hz), 3.94 (1H, dd, *J* 10.2, 6.9 Hz), 4.19 (1H, ddd, *J* 11.0, 8.0, 1.1 Hz), 4.80 (1H, d, *J* 8.0 Hz), 5.88 (1H, dt, *J* 10.2, 6.9 Hz), 6.04 (1H, dd, *J* 11.0, 10.2 Hz), 7.04-7.22 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 52.4, 58.1, 77.7, 126.6, 126.8, 127.2, 128.1, 128.2, 128.6, 131.0, 132.6, 140.9, 142.2. *m/z* (CI) 237 (MH^+-H_2O, 12), 219 (100), 130 (95). HRMS (ESI) calcd. for $C_{17}H_{18}NaO_2$, 277.1209. Found: 277.1199.

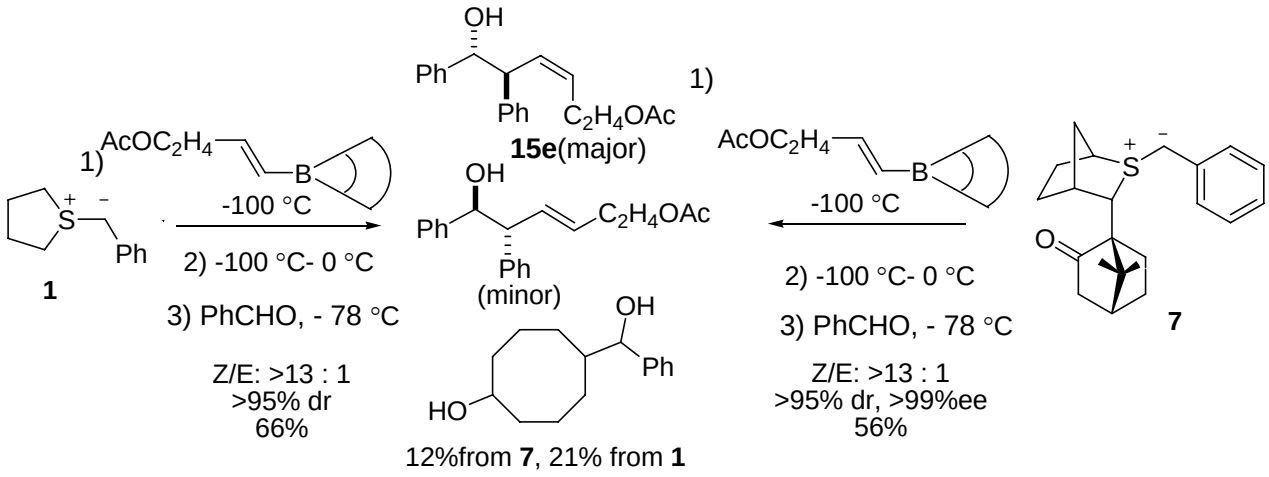
HPLC trace of *Anti*-(Z)-1,2-diphenyl-pent-3-en-1,5-diol (16d) (>99% ee)

Conditions: OD-H chiralcel column, 10.0% ipa in hexane, 1 mL/min



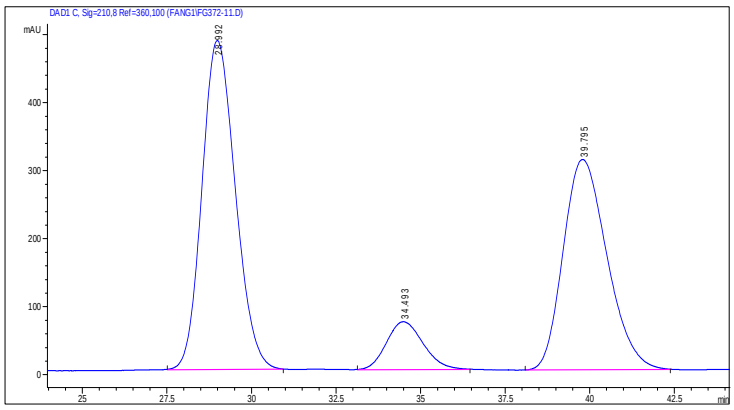


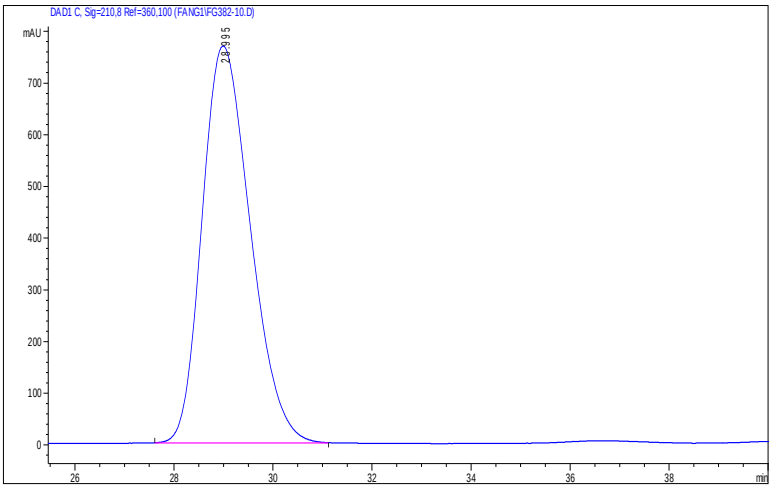
***Anti*-(Z/E)-1,2-diphenyl-1-hydroxy-hex-3-en-1-ol acetate (15e)**



A mixture of *anti*-(Z)-1,2-diphenyl-1-hydroxy-hex-3-en-1-ol acetate and *anti*-(E)- 1,2-diphenyl--1-hydroxy-hex -3-en-1-ol acete in a ratio 13 : 1 in favor of (Z) isomer was obtained as a colorless oil in 66% yield (56% yield when the chiral sulfonium salt **7** was used). Analytical data for the mixture of *anti*-(Z)-1,2-diphenyl-1-hydroxy-hex-3-en-1-ol acetate and *anti*-(E)- 1,2-diphenyl--1-hydroxy-hex -3-en-1-ol acetate: $[\alpha]_D^{20}$ +24 (*c* = 0.25, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3458, 1734, 1236, 1032. ^1H NMR (400 MHz, $CDCl_3$) 1.92 (3H, s), 1.98_{minor} (3H, s), 2.29-2.41 (2H, m), 2.48 (1H, d, *J* 2.4 Hz), 2.53_{minor} (1H, d, *J* 2.4 Hz), 3.49_{minor} (1H, dd, *J* 9.3, 7.8 Hz), 3.66 (1H, dd, *J* 10.3, 6.8 Hz), 3.90-3.98 (2H, m), $4.01\text{-}4.14_{minor}$ (2H, m), 4.79_{minor} (1H, dd, *J* 7.8, 2.4 Hz), 4.84 (1H, dd, *J* 6.8, 2.4 Hz), 5.56_{minor} (1H, dt, *J* 15.1, 7.1 Hz), 5.61 (1H, dt, *J* 10.7, 7.3 Hz), 5.95_{minor} (1H, dd, *J* 15.1, 9.3 Hz), 6.04 (1H, dd, *J* 10.7, 10.3 Hz), 7.03-7.23 (10H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 20.9, 27.3, 52.4, 63.6, 78.0, 126.6 (2 × C), 127.5, 128.0, 128.4 (2 × C), 128.5, 131.5, 141.3, 142.2, 171.2. *m/z* (CI) 293 (MH^+-H_2O, 22), 233 (100), 144 (52). HRMS (ESI) calcd. for $C_{20}H_{22}NaO_3$, 333.1471. Found: 333.1461.

HPLC trace of *Anti*-(Z)-1,2-diphenyl-1-hydroxy-hex-3-en-1-ol acetate (15e) (>99%ee)
Conditions: OD-H chiralcel column, 4.0% ipa in hexane, 1 mL/min

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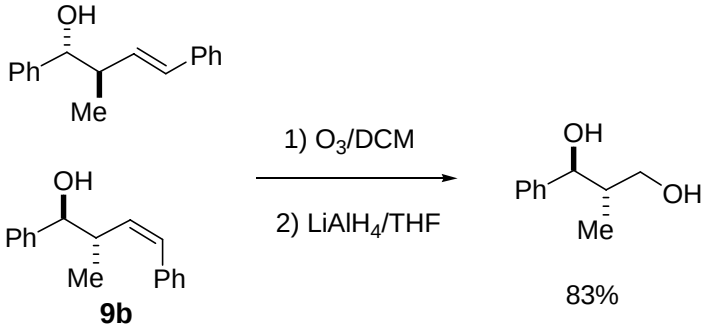
6, Determination of Relative and Absolute Stereochemistry.

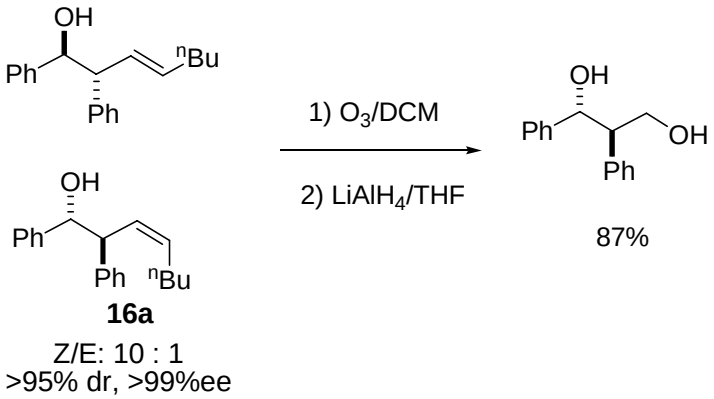
Synthesis of 2-methyl-1-phenylpropane-1,3-diol [11]



To the solution of (Z)-2-methyl-1,4-diphenyl-but-3-en-1-ol (90 mg, 0.38 mmol) in dichloromethane (10.0 mL) at – 78 °C, oxone was bubbled through until a light blue color persisted. Dimethylsulfide (1.2 mL) was added and the mixture was allowed to warm up and stirred at room temperature for 2 hours. The mixture was then concentrated under reduced pressure, and the residue was dissolved in anhydrous THF (10 mL), and $LiAlH_4$ (0.14 g, 3.7 mmol) was added at 0 °C. 1 Hour later, the mixture was diluted with THF (20 mL) and treated successively with water (0.3 mL), 2N NaOH (0.6 mL) and water (0.6 mL). The precipitate was filtered off, washed thoroughly with diethyl ether, and the filtrate was concentrated under reduced pressure to yield the crude product, which was dissolved in diethyl ether, dried over $MgSO_4$, concentrated, and purified by chromatography (silica gel, eluent: 30% ethyl acetate in petrol) to give the diol (52 mg, 83% yield) as a colourless oil. $[\alpha]_D^{20}$ – 43 (*c* = 0.70, $CHCl_3$), [lit.[11] – 51 (c = 0.60, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$) 0.68 (3H, d, *J* 7.0 Hz), 2.02-2.04 (1H, m), 3.67 (1H, dd, *J* 10.8, 7.5 Hz), 3.74 (1H, dd, *J* 10.8, 8.4 Hz), 4.52 (1H, *J* 8.4 Hz), 7.24-7.36 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) 13.8, 41.7, 67.8, 80.6, 126.8, 127.8, 128.4, 143.5.

[11] Pietruszka, J.; Schöne, N. *Eur. J. Org. Chem.* **2004**, 5011.

Synthesis of 1,2-diphenylpropane-1,3-diol[11]

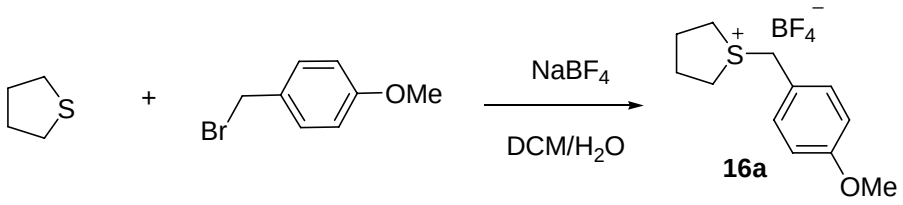


(Z)-1,2-diphenyl-oct-3-en-1-ol (0.11 g, 0.39 mmol) was dissolved in dichloromethane (10.0 mL). Ozone was bubbled through the solution at – 78 °C until a light blue colour persisted. Dimethylsulfide (1.2 mL) was added, and the mixture was then warmed up and stirred at room temperature for 2 hours. The reactants were concentrated under reduced pressure, and the residue was dissolved in anhydrous THF (10 mL). To the THF solution was added $LiAlH_4$ (0.14 g, 3.7 mmol) at 0 °C. After 1 hour, the mixture was diluted with THF (20 mL) and treated successively with water (0.3 mL), 2N NaOH (0.6 mL) and water (0.6 mL). The precipitate was filtered off, washed thoroughly with diethyl ether.The filtrate was concentrated under reduced pressure, and the residue was dissolved in diethyl ether, dried over $MgSO_4$ and purified by chromatography (silica gel, eluent: 30% ethyl acetate in petrol) to obtained the diol (77 mg, 87% yield) as white needles M.p. 108-110 °C [from MeOH-Hexane, lit.[12] 112 °C (MeOH-cyclohexane)]. $[\alpha]_D^{20}$ – 52 (c = 0.40, acetone) [lit.[12] – 64 (*c* = 0.90, acetone)]. ^{1}H NMR (400 MHz, $CDCl_3$) 3.16 (1H, ddd, *J* 8.7, 7.7, 4.4 Hz), 3.96 (1H, dd, *J* 11.1, 4.4 Hz), 4.2 (1H, dd, *J* 11.1, 7.7 Hz), 5.02 (1H, d, *J* 8.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) 54.8, 66.3, 79.6, 126.4, 126.9, 127.6, 128.1, 128.4, 128.5, 139.2, 142.7.

[12] Pelter, A.; Vaughan-Williams, G. F.; Rosser, R. M. *Tetrahedron*, **1993**, *49*, 3007

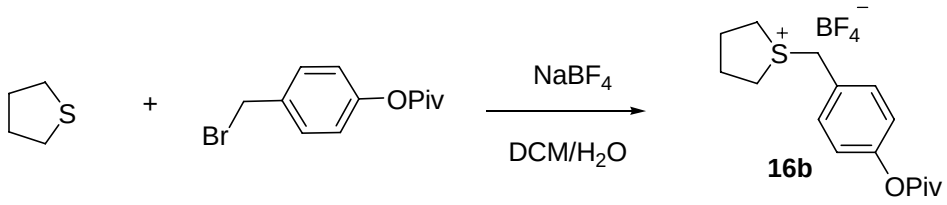
7 Structure Assignment and Total Synthesis of Iso-agatharesinol

Synthesis of 1-(4-methoxybenzyl)-tetrahydrothiophenium tetrafluoroborate (16a)



A modification to the literature procedure,[3] to a 25 mL flask were charged tetrahydrathiophene (1.1 g, 12.0 mmol), *para*-methoxy benzyl bromide (0.80g ,4.0 mmol), dichloromethane (4.0 mL) and a saturated aqueous sodium tetrafluoroborate solution (containing 12 mmol sodium tetrafluoroborate). After stirring for 2 days the biphasic mixture was extracted with dichloromethane (30 mL); the organic solution was dried over Na_2SO_4, and concentrated under reduced pressure to furnish a sticky oil, which was dissolved in water (20 mL) and washed with diethyl ether (2 × 30 mL) to remove excess tetrahydrothiophene and unreacted benzyl bromide. Sodium tetrafluoroborate (4.0 g) was added to the aqueous solution to minimize the solubility of the sulfonium salt in water. The aqueous solution was then extracted with dichloromethane (2 × 30 mL), and the organic solutions were combined and dried over $MgSO_4$. Removing the solvent furnished the sulfonium salt as a white powder (1.0 g, 91% yield). M.p. 99-101 ºC (from dichloromethane) ν_{max}/cm^{-1} (neat) 1609, 1515, 1255, 1025. ^{1}H NMR (400 MHz, $CDCl_3$) 2.22-2.25 (4H, m), 3.35-3.38 (2H, m), 3.45-3.49 (2H, m), 3.77 (3H, s), 4.47 (2H, s), 6.86 (2H, d, *J* 8.5 Hz), 7.36 (2H, d, *J* 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) 28.4, 41.9, 45.8, 55.4, 115.2, 119.6, 132.0, 161.0.

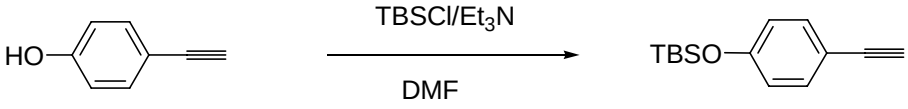
Synthesis of 1-[4-(2,2dimethylpropionyloxy)benzyl]-tetrahydrothiophenium tetrafluoroborate (16b)



A modification to the literature procedure,[3] to a 25 mL flask were charged tetrahydrothiophene (0.79 g, 9.0 mmol), *p*-bromomethylphenyl pivaloate (0.81g, 3.0 mmol), dichloromethane (4.0 mL) and a saturated aqueous sodium tetrafluoroborate solution (containing 6.0 mmol sodium tetrafluoroborate). After stirring for 2 days the biphasic mixture was extracted with dichloromethane (30 mL), and the

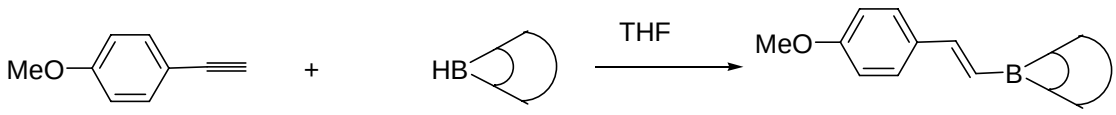
organic solution was dried over Na_2SO_4, and concentrated in reduced pressure to give a sticky oil, which was dissolved in water (20 mL) and washed with diethyl ether (2 × 30 mL) to remove excess tetrahydrothiophene and the unreacted benzyl bromide. Sodium tetrafluoroborate (4.0 g) was added to minimize the solubility of the sulfonium salt in water; and the aqueous solution was extracted with dichloromethane (2 × 30 mL). The organic solutions were combined, dried over $MgSO_4$ and concentrated under reduced pressure to furnish the sulfonium salt as a white amorphous hydroscopic solid (0.95 g, 82 %). ν_{max}/cm^{-1} (neat) 2974, 1744, 1109, 1024. ^{1}H NMR (400 MHz, CD_3OD) 1.34 (9H, s), 2.25-2.39 (4H, m), 3.40-3.51 (4H, m), 4.50 (2H, s), 7.18 (2H, d, *J* 7.8 Hz), 7.56 (2H, d, *J* 7.8 Hz). ^{13}C NMR (100 MHz, CD_3OD) 26.1, 28.2, 38.8, 42.2, 45.1, 122.8, 126.4, 131.6, 152.6, 178.4. *m/z* (ESI) 645 ($[2M\text{-}BF_4^-]^+$, 100), 279 (60). HRMS (ESI) calcd. for $C_{16}H_{23}O_2S$, 279.1427. Found: 279.1413.

Synthesis of [*p*-(tert-butyldimethylsilyoxy)phenyl]acetylene



(*p*-Hydroxyphenyl)acetylene (4.90 g, 42.0 mmol), made from *p*-iodophenol and 2-methyl-3-butyn-2-ol following the literature method,[4] was mixed with imidazole (2.86 g, 42.0 mmol) in DMF (50 mL). To the mixture was added TBSCl (6.25 g, 42.0 mmol in 10 mL DMF). The reactants were stirred at room temperature overnight and it was then quenched by addition of water (150 mL) to form a slurry mixture, which was extracted with petrol ether (2 × 40 mL). The organic solutions were combined, dried over anhydrous $MgSO_4$ and concentrated to yield the crude product in quantitative yield which was used in the synthesis of the vinyl borane **16b** without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) 0.20 (6H, s), 0.98 (9H, s), 2.99 (1H, s), 6.77 (2H, d, *J* 8.8 Hz), 7.37 (2H, d, *J* 8.8 Hz).

Synthesis of *B*-[*trans*-2-(4-methoxyphenyl)vinyl]-9- borabicyclo(3,3,1)nonane (17a)

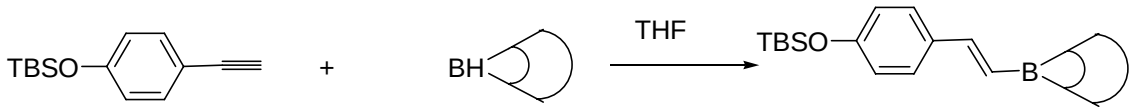


17a

9-BBN (1.83 g, 15.0 mmol in 40 mL THF) was added dropwise to pre-degassed 4-ethynylanisole (2.97 g, 22.5 mmol) at 0 °C. After addition, the reaction mixture was warmed to room temperature and stirred for two hours. Removing the solvent under reduced pressure furnish the crude product, which was further purified by distillation under reduced pressure to give the desired compound as a colorless

oil (1.62 g, 41%). B.p. 125-128 ºC/0.42 mbar. ^{1}H NMR (300 MHz, $CDCl_3$) 1.21-1.36 (2H, m), 1.73-1.98 (12H, m), 3.83 (3H, s), 6.85 (1H, d, *J* 17.8 Hz), 6.91 (2H, d, *J* 8.8 Hz), 7.51 (1H, d, *J* 17.8 Hz), 7.57 (2H, d, *J* 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 23.7, 34.0, 55.4, 114.1, 129.6, 130.6, 149.7, 160.8. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

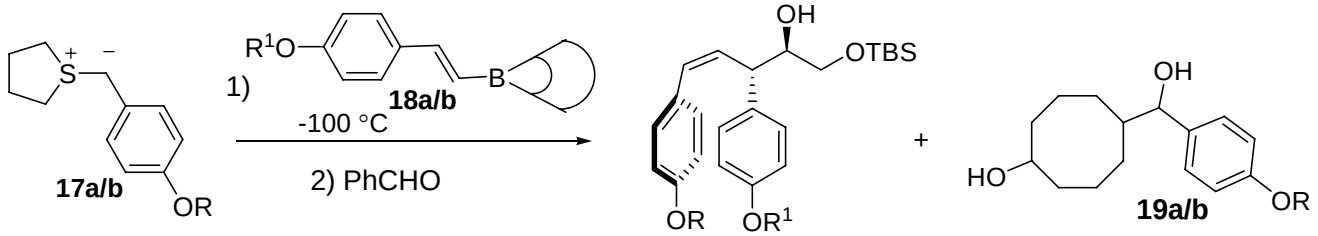
Synthesis of *B*-[*trans*-2-(4-*tert*-butyldimethylsilyoxyphenyl)-vinyl]-9-borabicyclo(3,3,1)nonane (17b)



17b

9-BBN (0.5 M in THF, 20.0 mL, 10.0 mmol) was added dropwise to pre-degassed [*p*-(tert-butyldimethylsilyoxy)phenyl]acetylene (4.64 g, 20.0 mmol) at 0 °C. After addition, the reaction mixture was warmed to room temperature and stirred for two hours. Removing the solvent under reduced pressure afford the crude product as a colorless oil, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) 0.21 (6H, s), 0.99 (9H, s), 1.22-1.34 (2H, m), 1.72-1.97 (12H, m), 6.84 (2H, d, *J* 8.8, Hz), 6.85 (1H, d, *J* 17.8 Hz). 7.50 (1H, d, *J* 17.8 Hz), 7.51 (2H, d, *J* 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) –4.3, 18.4, 23.7, 25.8, 34.0, 120.4, 129.5, 131.1, 149.8, 157.2. ^{11}B NMR (96 MHz, $CDCl_3$) 77.

General Procedure for the Synthesis of Compounds 18aa, 18bb, 19a/b, from 16a/b

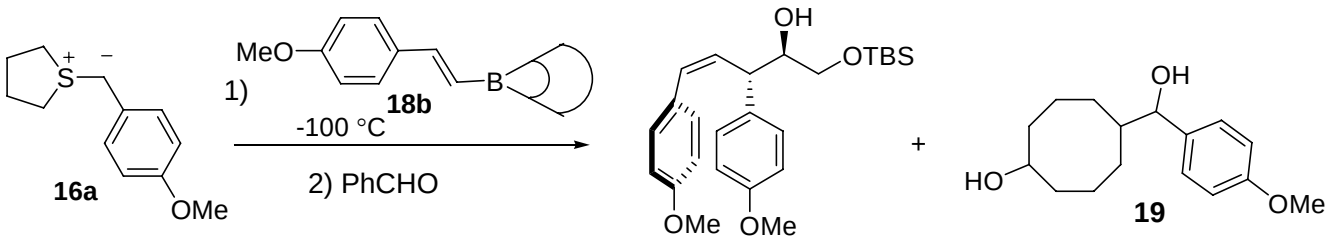


18aa/bb

To the mixture of the achiral sulfonium salt (0.50 mmol) in DCM (2 mL, 4 mL was applied when chiral salt **22** was used) was added LiHMDS (1 M in THF, 0.55 mL) at –78 °C. The mixture was stirred at –78 °C for half an hour followed by addition of THF (0.55 mL, 1.5 mL in the case of chiral salt **22**). It was then cooled at –100 °C (diethyl ether-liquid nitrogen bath), and the borane (1 M in THF, 0.55 mL) was slowly added. After forty minutes, trimethylsilyloxyacetaldehyde (1 M in THF, 1.5 mL) was added

dropwise, and the mixture was stirred for one hour at –100 °C followed by 3 hours at –78 °C. The reaction was quenched by adding the mixture of aqueous NaOH solution (2 M, 1 mL) and H_2O_2 solution (30%, 0.5 mL) slowly at –78 °C, and stirred for a further 4 hours at room temperature. The reaction mixture was then diluted with NaOH (2 M, 4 mL) and water (10 mL) and extracted with diethyl ether (2 × 30 mL). The ethereal solutions were combined, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure; the residue obtained was further purified by chromatography.

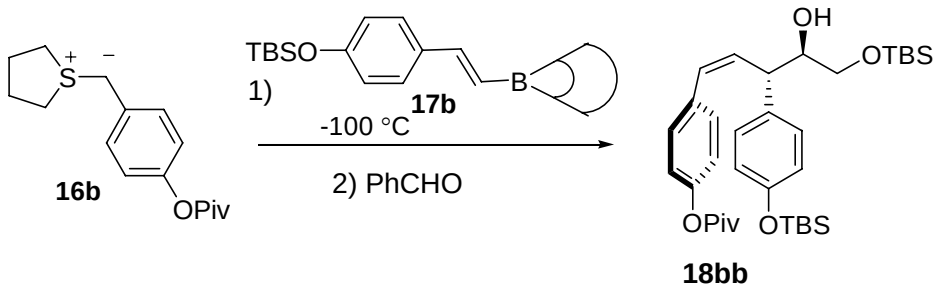
(Z)-*anti*-1-(*tert*-Butyldimethylsilyloxy)-3,5-bis-(4-methoxyphenyl)-pent-4-en-2-ol (18aa) and 1-(*cis*-5-hydroxylcyclooctanyl)-1-(4-methoxylphenyl)methanol (19)



18aa

19aa was isolated as a white plate as one diastereomer in 42% yield; **19** was isolated as a colourless gum in 49% yield. **Analytical data for compound 18aa:** R_f: 0.32 (eluent: 10% ethyl acetate in petrol). M.p. 70-72 °C (from hexane). ν_{max}/cm^{-1} (neat) 3564, 2954, 1606, 1509, 1246, 1229, 1112, 1084. ^{1}H NMR (400 MHz, $CDCl_3$) -0.03 (3H, s), -0.02 (3H, s), 0.83 (9H, s), 2.38 (1H, d, *J* 4.0 Hz), 3.37 (1H, dd, *J* 9.9, 6.7 Hz), 3.47 (1H, dd, *J* 9.9, 3.7 Hz), 3.79 (6H, s), 3.80-3.85 (1H, m), 3.95 (1H, dd, *J* 10.3, 6.7 Hz), 6.01 (1H, dd, *J* 11.4, 10.3 Hz), 6.59 (1H, d, *J* 11.4 Hz), 6.82 (2H, d, *J* 8.8 Hz), 6.86 (2H, d, *J* 8.8 Hz), 7.18 (2H, d, *J* 8.8 Hz), 7.20 (2H, d, *J* 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) -5.5, 18.1, 25.8, 45.5, 55.2(2×C), 64.7, 75.7, 113.5, 114.2, 128.9, 129.8, 129.9, 130.2, 130.3, 134.2, 158.2, 158.4. . *m/z* (CI) 233 (MH^+-H_2O, 4), 279 (31), 253 (70), 147 (41), 121 (100). HRMS(ESI) calcd. for $C_{25}H_{36}NaO_4Si$, 451.2275. Found: 451.2280. **Analytical data for compound 19:** ν_{max}/cm^{-1} (neat) 3414, 3317, 2919, 1610, 1510, 1239, 1034. ^{1}H NMR (400 MHz, $CDCl_3$) 1.04-1.12 (1H, m), 1.18-1.37 (4H, m), 1.45-1.56 (2H, m), 1.60-1.84 (6H, m), 3.74 (3H, s), 3.80-3.85 (1H, m), 4.23 (1H, d, *J* 7.0 Hz), 6.80 (2H, d, *J* 8.4 Hz), 7.15 (2H, d, *J* 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) 22.8, 23.1, 28.8, 30.1, 35.9, 44.1, 55.1, 71.8, 78.7, 113.4, 127.6, 135.9, 159.6. *m/z* (CI) 247 (MH^+-H_2O, 97), 227 (55), 137 (53), 121 (100). HRMS(ESI) calcd. for $C_{16}H_{24}NaO_3$, 287.1618. Found: 287.1628.

2,2- Dimethylpropionic acid, 4-{(Z)-*anti*- 5-(*tert*-butyldimethylsilyloxy)-3-[4-(*tert*-butyldimethylsilanyloxy)phenyl]-4-hydroxy-pent-1-enyl}-phenyl ester (18bb)

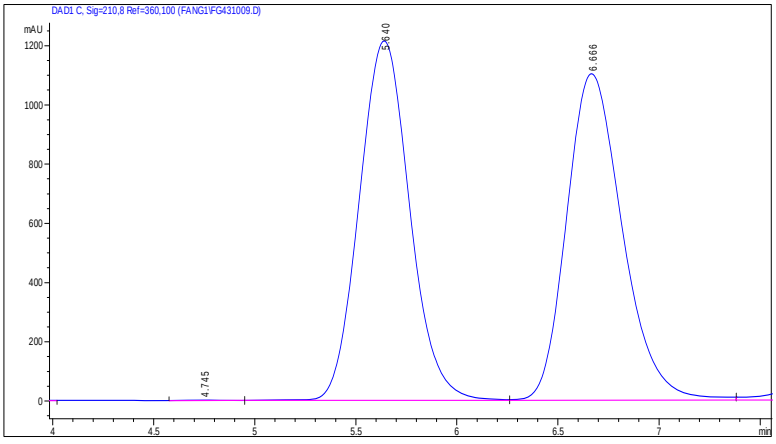


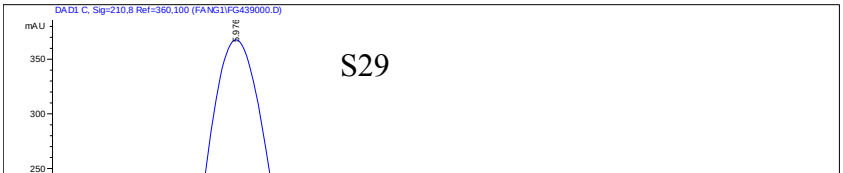
18bb

A 10 : 1 mixture of Z/E isomers of the ester was obtained as a colorless gum in 78% yield (72% yield was obtained in the asymmetric synthesis). R_f: 0.14 (eluent: 5% ethyl acetate in petrol). ν_{max}/cm^{-1} (neat) 1753, 1605, 1506, 1252, 1113. ^1H NMR (400 MHz, $CDCl_3$) 0.12 (3H, s), 0.14 (3H, s), 0.36 (6H, s), 0.99 (9H, s), 1.13 (9H, s), 1.50 (9H, s), 2.59 (1H, d, *J* 3.7 Hz), 3.49 (1H, dd, *J* 10.0, 6.4 Hz), 3.59 (1H, dd, *J* 10.0, 3.4 Hz), 3.95-4.03 (2H, m), 6.26 (1H, dd, *J* 11.5, 10.0 Hz), 6.78 (1H, d, *J* 11.5 Hz), 6.94 (2H, d, *J* 8.5 Hz), 7.14 (2H, d, *J* 8.5 Hz), 7.24 (2H, d, *J* 8.5 Hz), 7.42 (2H, d, *J*, 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) -5.1, -4.1, 18.5, 18.6, 26.1, 26.2, 27.5, 39.4, 46.2, 65.4, 76.1, 120.7, 121.4, 129.2, 130.1, 132.4, 135.0, 135.1, 150.3, 154.7, 177.3. *m/z* (CI) 599 (MH^+, 1.5), 449 (42), 424 (52), 323 (56), 221 (86), 57 (100). HRMS(CI) calcd. for $C_{34}H_{55}O_5Si_2$, 699.3588. Found: 599.3571.

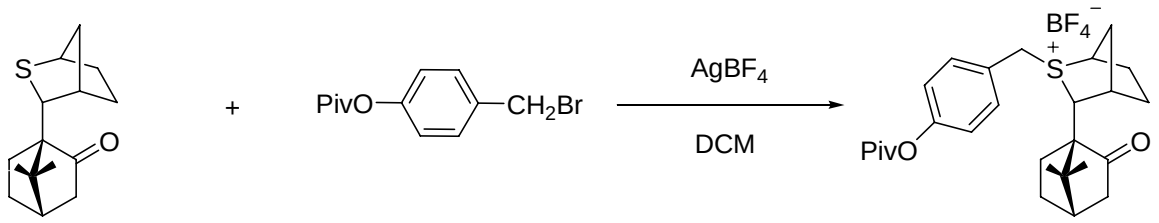
HPLC trace for the enantiomeric excess of 18bb (>99% ee)

Conditions: OD-H chiralcel column, 0.7% ipa in hexane, 1 mL/min





Synthesis of (1R,3R,4S)-2-[4-(2,2dimethylpropionyloxy)benzyl]-3-[(1R,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]-2-thioniabicyclo[2.2.1]heptane tetrafluoroborate (22)



23

Following the literature procedure reported,[3] to a rapidly stirred solution of the corresponding enantiomerically pure sulfide[13] (0.50 g, 2.0 mmol) and *p*-bromomethylphenyl pivaloate (12.0 mmol) in anhydrous dichloromethane (4.0 mL) was added silver tetrafluoroborate (0.60 g, 3.0 mmol) under an argon atmosphere at 0 °C. After addition, the reaction was allowed to warm to room temperature and stirred for 48 h in the dark. The resulting silver bromide precipitate was filtered, and washed with dichloromethane. The filtrate was concentrated under reduced pressure togive a pale yellow oil, which was purified by chromatography (eluent: 5% methanol in CH_2Cl_2) to give a white amorphous solid (0.66 g, 83%). M.p. 95-98 ºC (from MeOH-DCM). ν_{max}/cm^{-1} (neat) 2973, 1737, 1107, 1049, 1028. ^1H NMR (400 MHz, $CDCl_3$) 0.85-0.91 (1H, m), 0.91 (3H, s), 0.95 (3H, s), 1.06-1.03 (1H, m), 1.17 (9H, s), 1.33-1.40 (2H, m), 1.45-1.49 (1H, m), 1.70 (1H, d, *J*, 17.6 Hz), 1.70-1.77 (1H, m), 1.91 (1H, dd, *J* 4.4, 3.9 Hz), 1.94-1.99 (2H, m), 2.05 (1H, d, *J* 12.7 Hz), 2.35 (1H, d, *J* 17.6 Hz), 2.50 (1H, d, *J* 12.7 Hz), 3.00 (1H, s), 3.95 (1H, d, *J* 2.0 Hz), 4.17 (1H, d, *J* 13.7 Hz), 4.21 (1H, d, *J* 3.4 Hz), 4.51 (1H, d, *J* 13.7 Hz), 7.00 (2H, d, *J* 8.3 Hz), 7.41 (2H, d, *J* 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) 18.6, 21.4, 23.9, 26.1,

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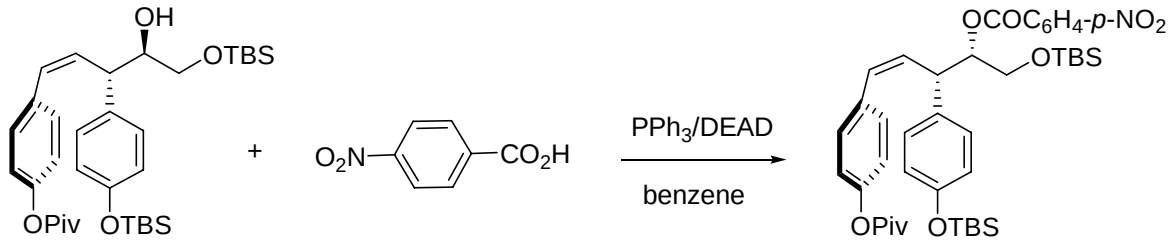
[13] Aggarwal, V. K.; Fang, G. Y.; Kokotos, C. G.; Richardson, J.; Unthank, M. G. *Tetrahedron*, **2006**, ASAP

26.3, 26.6, 33.0, 38.6, 40.7, 43.2, 43.5, 44.8, 47.0, 49.3, 58.5, 59.6, 68.6, 122.4, 125.8, 131.5, 152.0, 176.1, 214.6. *m/z* (ESI)) 441 ([M-BF_4^-]$^+$, 100). HRMS (ESI) calcd. for $C_{27}H_{37}O_3S$, 441.2475. Found: 441.2458.

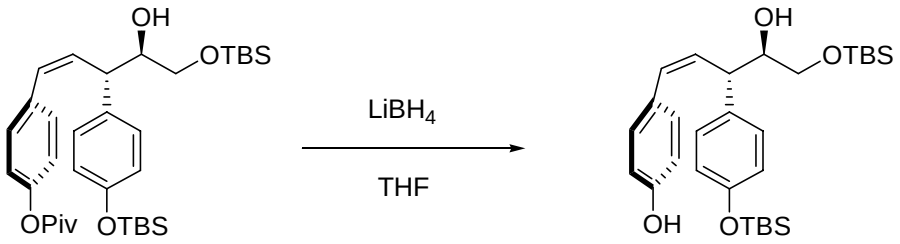
4-Nitro-benzoic acid, (Z)-*syn*- 1-(*tert*-butyldimethylsilyloxymethyl)-2-[4-(*tert*-butyldimethylsilyloxy)phenyl]-4-[4-(2,2-dimethylpropioryloxy)phenyl]-but-3-enyl ester (23)



18bb(10:1 Z/E) **23**(Z only)

To a solution of compound **18bb** (0.30 g, 0.5 mmol), triphenylphosphine (0.79 g, 3.0 mmol) and 4-nitrobenzoic acid (0.50 g, 3.0 mmol) in benzene (10 mL) was added DEAD (0.52 g, 3.0 mmol) dropwise. The reaction mixture was stirred at room temperature for 4 hours, and it was then quenched with saturated aqueous $NaHCO_3$ solution (5 mL). The biphasic mixture was extracted with diethyl ether (2 × 20 mL); the ethereal solutions were combined, dried over $MgSO_4$ and concentrated to yield the crude product, which was purified by chromatography (R_f: 0.21, eluent: 5% ethyl acetate in petrol) to furnish the desired compound as a white powder (0.2 g, 54% yield). M.p. 125-127 °C (form hexane). ν_{max}/cm^{-1} (neat) 1755, 1713, 1603, 1529, 1508, 1276, 1101. ^{1}H NMR (400 MHz, $CDCl_3$) -0.18 (3H, s), -0.13 (3H, s), 0.01 (6H, s), 0.69 (9H, s), 0.84 (9H, s), 1.28 (9H, s), 3.65 (1H, dd, *J* 11.2, 5.9 Hz), 3.74 (1H, dd, *J* 11.2, 3.7 Hz), 4.20 (1H, dd, *J* 10.5, 8.3 Hz), 5.33 (1H, ddd, *J* 8.3, 5.9, 3.7 Hz), 5.93 (1H, dd, *J* 11.5, 10.5 Hz), 6.52 (1H, d, *J* 11.5 Hz), 6.66 (2H, d, *J* 8.5 Hz), 6.93 (2H, d, *J* 8.5 Hz) 7.06 (2H, d, *J* 8.3 Hz), 7.16 (2H, d, *J* 8.3 Hz), 7.92 (2H, d, *J* 8.8 Hz), 8.13 (2H, d, *J* 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) -5.0, -5.1, -4.1, 18.4, 18.5, 26.0, 27.5, 39.5, 44.2, 62.9, 77.2, 79.2, 120.6, 121.6, 123.7, 129.6, 130.0, 130.7, 130.8, 130.9, 133.5, 133.6, 134.6, 136.2, 150.6, 150.9, 154.9, 164.2, 177.2. *m/z* (ESI) 770 (M + Na$^+$, 100), HRMS(ESI) calcd. for $C_{41}H_{57}O_8NSi_2Na$, 770.3502. Found: 770.3515.

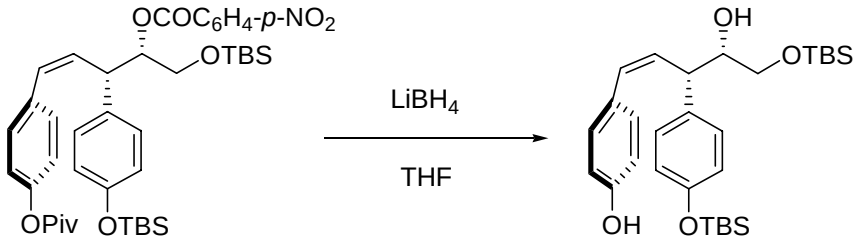
4-{(Z)-(3*S*, 4*S*)-5-(*tert*-butyldimethylsilyloxy)-3-[4-(*tert*-butyldimethylsilyloxy)phenyl]-4-hydroxpent-1-enyl}phenol (24)



18bb (10:1 Z/E) **24**(Z only)

To the solution of compound **18bb** (0.12 g, 0.2 mmol) in THF (6 mL) was added $LiBH_4$ (2 M solution in THF, 0.3 mL, 0.6 mmol). The mixture was stirred at room temperature overnight before the reaction was quenched with saturated ammonium chloride aqueous solution (10 mL). The mixture was extracted with diethyl ether (2 × 25 mL), and the ethereal solutions was combined, dried over $MgSO_4$ and concentrated to give the crude product, which was further purified by chromatography (R_f: 0.15, eluent: 10% ethyl acetate in petrol) to furnish the desired compound as a colorless gum (87 mg, 85% yield). $[\alpha]_D^{20}$ +56.8 ºC (*c* = 0.95, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3352, 2929, 1608, 1508, 1252. ^1H NMR (300 MHz, $CDCl_3$) -0.03 (3H, s), -0.02 (3H, s), 0.20 (6H, s), 0.84 (9H, s), 0.99 (9H, s), 3.37 (1H, dd, *J* 10.3, 6.2 Hz), 3.47 (1H, dd, *J* 10.3, 3.5 Hz), 3.85 (1H, ddd, *J* 7.5, 6.2, 3.5 Hz), 3.95 (1H, dd, *J* 10.5, 7.5 Hz), 5.99 (1H, dd, *J* 11.6, 10.5 Hz), 6.58 (1H, d, *J* 11.6 Hz), 6.73 (2H, d, *J* 8.6 Hz), 6.81 (2H, d, *J* 8.6 Hz), 7.12 (2H, d, *J* 8.6 Hz), 7.14 (2H, d, *J* 8.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) -5.5, -4.4, 18.1, 18.2, 25.7, 25.8, 45.6, 64.6, 76.0, 115.0, 120.3, 128.8, 129.5, 130.1 (2×C), 130.5, 134.5, 154.2, 154.7. *m/z* (ESI) 537 ($M + Na^+$, 100). HRMS(ESI) calcd. for $C_{29}H_{46}O_4Si_2Na$, 537.2831. Found: 537.2827.

4-{(Z)-s*yn*-5-(*tert*-butyldimethylsilyloxy)-3-[4-(*tert*-butyldimethylsilyloxy)phenyl]4-hydrox-pent-1-enyl}phenol (25)

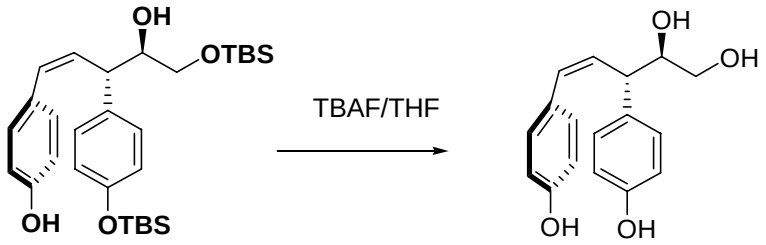


23 **25**

To the solution of the 4-nitro-benzoic acid, but-3-enyl ester **(23)** (0.11 g, 0.15 mmol) in THF (4 mL) was added $LiBH_4$ (2 M solution in THF, 0.3 mL, 0.6 mmol). The mixture was stirred at room temperature overnight before the reaction was quenched with saturated ammonium chloride aqueous solution (10 mL). The mixture was extracted with diethyl ether (2 × 25 mL), and the ethereal solutions was combined, dried over $MgSO_4$ and concentrated under reduced pressure to furnish the crude

product which was purified by chromatography (R_f: 0.15, eluent: 10% ethyl acetate in petrol) to furnish the desired compound as a colorless gum (76 mg, 95% yield). ν_{max}/cm^{-1} (neat) 3358, 1608, 1508, 1253. ^1H NMR (300 MHz, $CDCl_3$) -0.03 (3H, s), -0.01 (3H, s), 0.18 (6H, s), 0.83 (9H, s), 0.97 (9H, s), 3.43 (1H, dd, *J* 10.0, 6.6 Hz), 3.64 (1H, dd, *J* 10.0, 3.7 Hz), 3.79-3.84 (1H, m), 3.92 (1H, dd, *J* 10.5, 7.6 Hz), 5.87 (1H, dd, *J* 11.2, 10.5 Hz), 6.47 (1H, d, *J* 11.2 Hz), 6.74 (2H, d, *J* 8.3 Hz), 6.80 (2H, d, *J* 8.3 Hz), 7.11 (2H, d, *J* 8.5 Hz), 7.15 (2H, d, *J* 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) -5.5, -5.4, -4.4, 18.1, 18.2, 25.7, 25.8, 45.7, 64.9, 75.3, 115.0, 120.1, 129.2, 129.6, 129.7, 130.0, 130.1, 134.1, 154.2, 154.5. *m/z* (CI) 497 (MH^+-H_2O, 1.5), 339 (85), 221 (92), 107 (100). HRMS(ESI) calcd. for $C_{29}H_{46}O_4Si_2Na$, 537.2831. Found: 537.2827.

(Z)-(2*S*, 3*S*)-3,5-Bis(4-hydroxyphenyl)-pent-4-ene-1,2-diol (compound 21, Iso-agatharesinol)



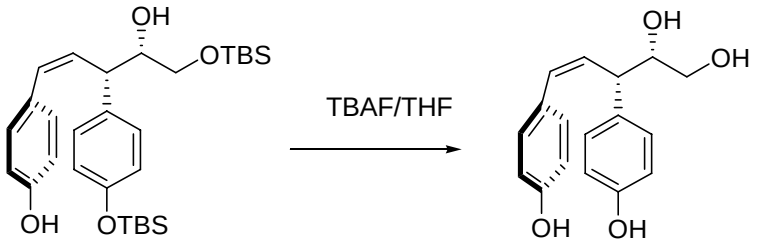
24 **20**

Compound **24** (20 mg, 39 μmol) was dissolved in THF (3 mL). To the solution was added TBAF (1 M solution in THF, 0.2 mL, 0.2 mmol) at 0 ºC. The reaction was monitored by TLC. 3 Hours after addition, it was found that all starting material had disappeared. The mixture was diluted with saturated NH_4Cl aqueous solution (5 mL) and extracted with ethyl acetate (2 × 20 mL). The organic solutions were combined, dried over $MgSO_4$ and concentrated under reduced pressure; the crude product obtained was purified by chromatography (R_f = 0.1, eluent: 10% methanol in chloroform) to furnish iso-agatharesinol as a colourless gum (10 mg, 94% yield). $[\alpha]_D^{20}$ +50.7 ºC (*c* = 0.75, acetone) [lit.[14] $[\alpha]_D^{20}$ +49.7 (*c* = 5.40, acetone)]. ν_{max}/cm^{-1} (neat) 3283, 1607, 1512, 1238. ^1H NMR (400 MHz, acetone-d6) 3.29 (1H, dd, *J* 10.5, 6.8 Hz), 3.36 (1H, dd, *J* 10.5, 4.4 Hz), 3.76-3.80 (1H, m), 3.91 (1H, dd, *J* 10.3, 6.4 Hz), 5.97 (1H, dd, *J* 11.2, 10.7 Hz), 6.43 (1H, d, *J* 11.7 Hz), 6.72 (2H, d, *J* 8.3 Hz), 6.73

[14] Yang, C.-X.; Huang, S.-S.; Yang, X.-P.; Jia, Z.-J. *Planta Med.* **2004**, *70*, 446.

(2H, d, *J* 8.3 Hz), 7.11 (2H, d, *J* 8.3 Hz), 7.13 (2H, d, *J* 8.3 Hz). ^{13}C NMR (100 MHz, acetone-d6) 46.9, 65.4, 77.1, 115.8, 116.1, 129.9, 130.0, 130.4, 130.9, 131.3, 134.8, 156.7, 157.2. *m/z* (CI) 287 (MH^+, 2), 269 (5), 225 (43), 107 (100). HRMS(CI) calcd. for $C_{17}H_{19}O_4$, 287.1283. Found: 287.1279.

(Z)-*syn*-3,5-Bis(4-hydroxyphenyl)-pent-4-ene-1,2-diol (21)



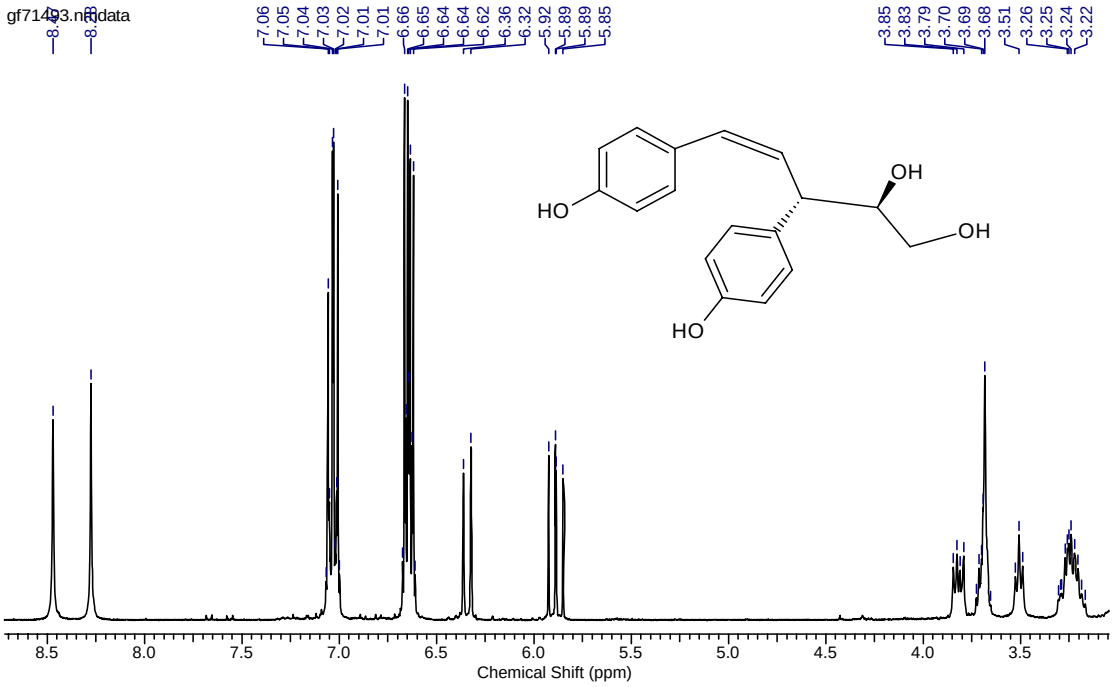
25 **21**

Compound **25** (66 mg, 0.13 μmol) was dissolved in THF (5 mL). To the solution was added TBAF (1M solution in THF, 0.77 mL, 0.77 mmol) at 0 ºC. The reaction was monitored by TLC. 3 Hours later, it was found that all starting material had disappeared. The mixture was diluted with saturated NH_4Cl (5 mL) aqueous solution and extracted with ethyl acetate (2 × 20 mL). The organic solutions were combined, dried over $MgSO_4$ and concentrated under reduced pressure; the crude product obtained was further purified by chromatography (R_f = 0.1, eluent: 10% methanol in chloroform) to furnish compound **21** as a colorless gum (34 mg, 92% yield). ν_{max}/cm^{-1} (neat) 3285, 1609, 1510, 1233. ^{1}H NMR (400 MHz, acetone-d6) 3.36 (1H, dd, *J* 11.0, 7.1 Hz), 3.57 (1H, dd, *J* 11.0, 3.9 Hz), 3.81-3.85 (1H, m), 3.95 (1H, dd, *J* 10.5, 6.8 Hz), 5.98 (1H, dd, *J* 11.7, 10.5 Hz), 6.40 (1H, d, *J* 11.7 Hz), 6.77 (2H, d, *J* 8.5 Hz), 6.79 (2H, d, *J* 8.5 Hz), 7.17 (2H, d, *J* 8.5 Hz), 7.18 (2H, d, *J* 8.5 Hz). ^{13}C NMR (100 MHz, acetone-d6) 47.1, 65.4, 76.5, 115.9, 116.0, 129.4, 129.8, 130.6, 130.9, 131.8, 133.8, 156.7, 157.2. *m/z* (CI) 287 (MH^+, 1), 269 (4), 225 (47), 107 (100). HRMS(CI) calcd. for $C_{17}H_{19}O_4$, 287.1283. Found: 287.1278.

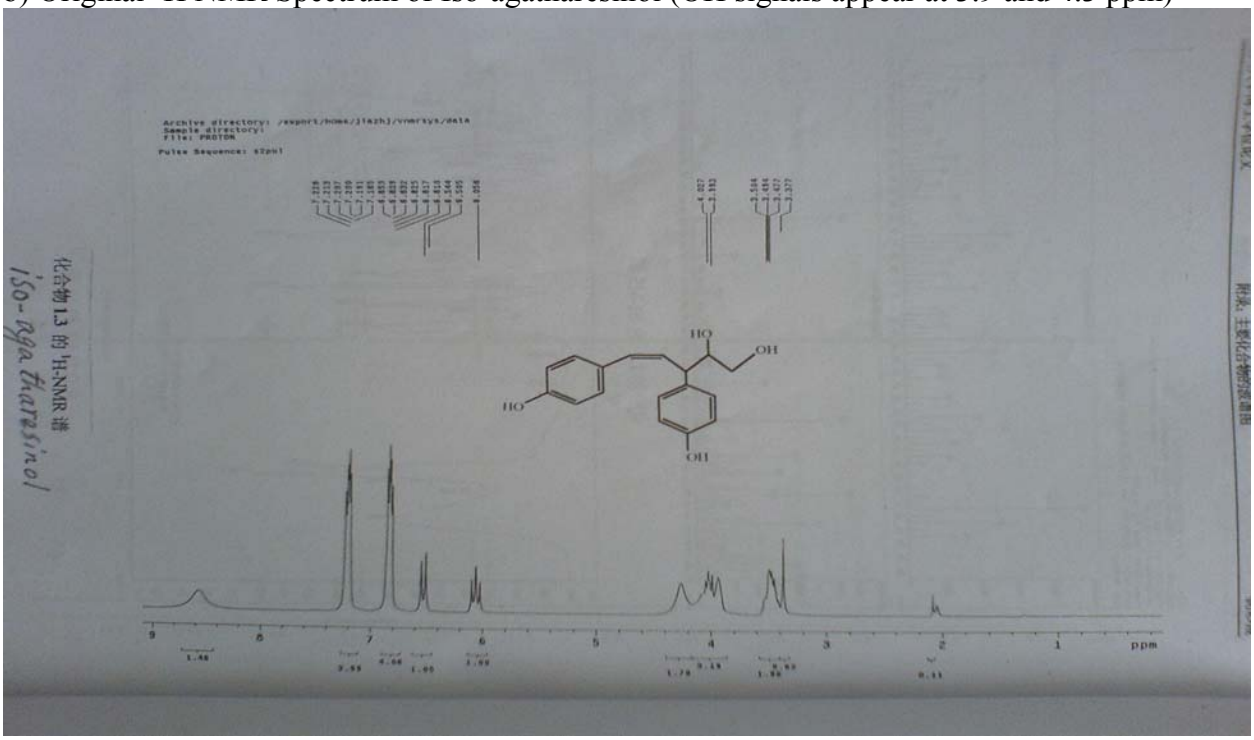
8 ^{1}H NMR Spectra of Compounds 20, 21 and Comparison with Original ^{1}H NMR of Isoagatharesinol Provided by Prof. Jia Z.-J.

1) Comparison of a) 300 MHz ^{1}H NMR Spectrum of Compound 20 and b) Original ^{1}H NMR Spectrum of Isoagatharesinol

a) 300 MHz ^{1}H NMR Spectrum of Compound **20** (OH signals appear at 3.5 and 3.7 ppm)

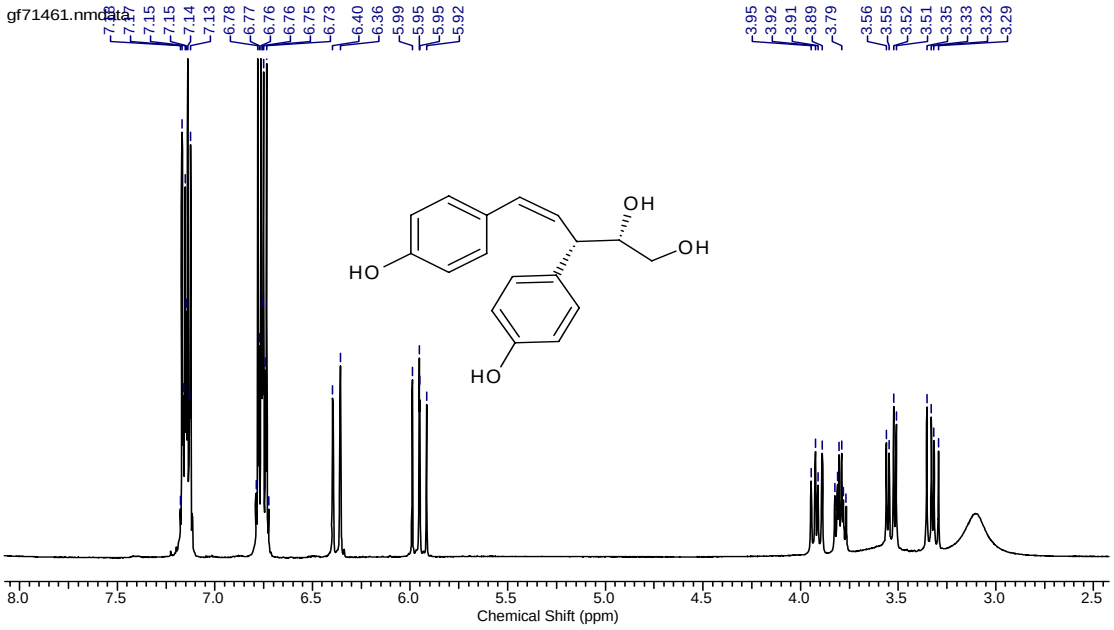


b) Original ^{1}H NMR Spectrum of Iso-agatharesinol (OH signals appear at 3.9 and 4.3 ppm)

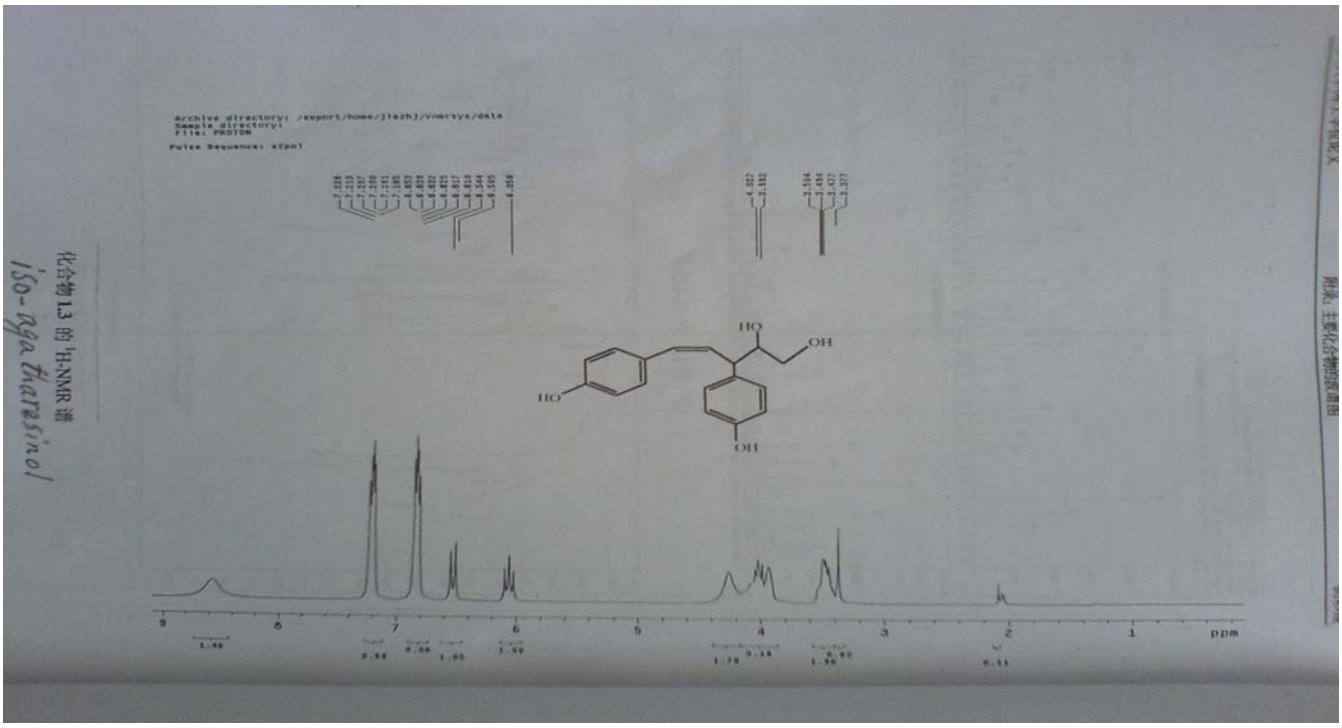


2) Comparison of a) 300 MHz ^{1}H NMR Spectra of Compound 21 and b) Original ^{1}H NMR Spectrum of Isoagatharesinol

a) 300 MHz ^{1}H NMR Spectrum of Compound **21**



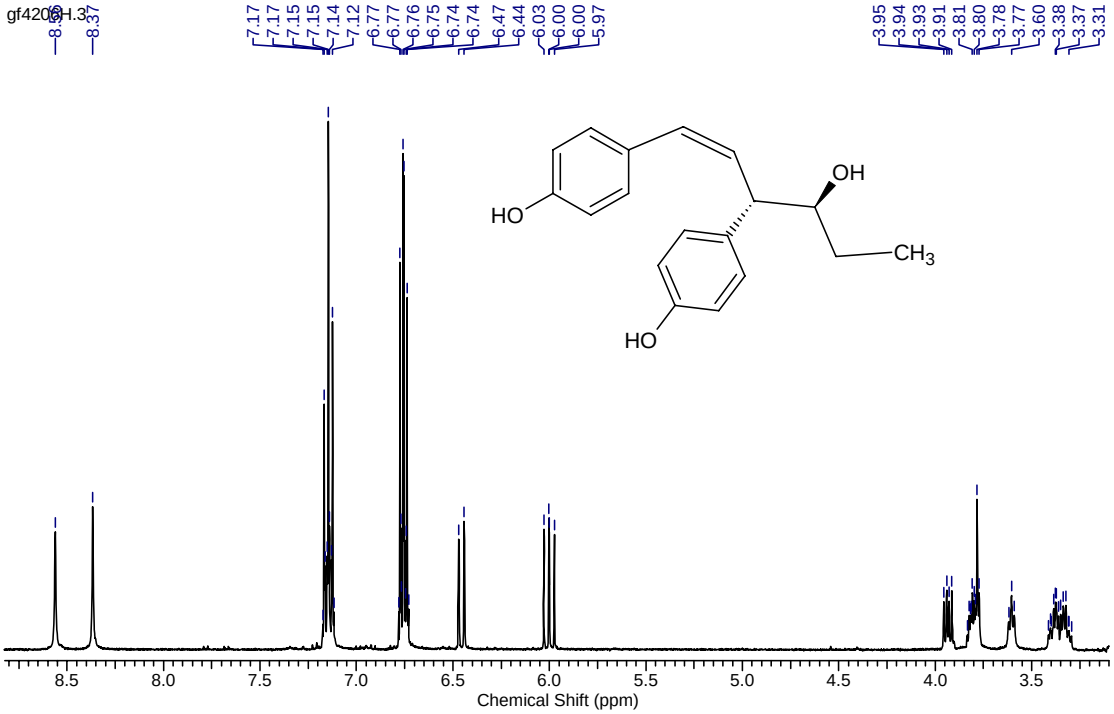
b) Original ^{1}H NMR Spectrum of Iso-agatharesinol



The ^{1}H NMR spectrum of compound **20** mostly matches the original ^{1}H NMR of isoagatharesinol. In particular, the diastereotopic methylene protenes appear close together as a multiplet around 3.37 ppm in iso-agatharesinol, as they do in compound **20**, whereas in **21** they appear as a classic ABX system at 3.30 and 3.55 ppm.

3) Comparison of a) 400 MHz ^{1}H NMR Spectra of Compound 20 and 21

a) 400 MHz ^{1}H NMR Spectrum of Compound **20**



b) 400 MHz ^{1}H NMR Spectrum of Compound **21**