Asymmetric Allylboration of Ketones Catalyzed by Chiral Diols

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Supporting Information

Table of Contents

General information.....	S2
Preparation of allyldiisopropoxyborane.....	S2
Preparation of crotyldiisopropoxyborane.....	S3
General procedure for asymmetric allylboration of ketones.....	S4
Analytical data for allylboration products 11a-o , 13a-b	S5
Positive non-linear effect.....	S11
Kinetic study.....	S12
NMR Experiments.....	S13
HPLC traces for 11a-o , 13a-b	S18

General Information. All ^1H NMR, and ^{13}C NMR spectra were recorded using Varian Unity Plus 400 (93.94 kG, ^1H 400 MHz) or Varian Gemini 300 (70.5 kG, ^{13}C 75 MHz) spectrometers at ambient temperature in CDCl_3 . Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, and integration. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR ESP spectrophotometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm, and were reported as $[\alpha]_D$ (concentration in grams/100 mL solvent). Analytical thin layer chromatography was performed using EMD 0.25 mm silica gel 60-F plates. Flash column chromatography was performed on Sorbent Technologies 60 Å silica gel. Chiral HPLC analysis was performed using an Agilent 1100 series HPLC or Waters Breeze HPLC System with a diode array detector. Chiral columns include Chiralcel[®]OD (Chiral Technologies Inc., 24cm×4.6mm I.D.), Chiralcel[®]OD-H (Chiral Technologies Inc., 15cm × 4.6 mm I.D.), Chiralpak[®]AD-H (Chiral Technologies Inc., 15cm × 4.6 mm I.D.), and Chiralpak[®]AD-H (Chiral Technologies Inc., 25cm × 4.6 mm I.D.). Chiral GC analysis was performed using an Agilent 6850 series GC system and Chiraldex B-DM as chiral column (Chiral Technologies Inc., 30 m × 0.25 mm I.D.). All reactions were performed under argon, in oven dried glassware with magnetic stirring. Chiral diols, including (–)-TADDOL **1**, (+)-hydrobenzoin **2**, (+)-diethyltartrate **3**, (S)-BIPHEN **4**, (S)-BINOL **5a** and 6,6'-Br-BINOL **7**, were purchased from Sigma-Aldrich, STREM, and Alpha Aesar and used without further purification. Diols **5b**, **5c**, **6a**, **6b** were prepared according to literature procedure.¹ Monomethyl ether **8** was prepared by alkylating one alcohol using NaH and CH_3I as previously described in the literature.^{1c} Kinetic parameters for the asymmetric allylboration reaction were determined by *in situ* monitoring of the disappearing of acetophenone (**9a**) at 1690.27 cm^{-1} using a ReactIR 4000 system (Mettler Toledo-AutoChem). The ReactIR 4000 system, running software version 3.1, was fitted with a FiberConduit and a 6 mm DiComp Probe. IR spectra, comprised of 64 scans per spectrum, were collected every one minute at a resolution of 8 cm^{-1} .

Preparation of allyldiisopropoxyborane 10a

A 250 mL pressure-equilized addition funnels charged separately, one with a 1.0 M solution of triisopropyl borate (154.2 mL, 154.2 mmol) in diethyl ether and the other with a 1.0 M solution of allylmagnesium bromide (150.4 mL, 150.4 mmol) in diethyl ether, were attached to a dry 1L three neck flask under Ar. The flask was cooled to $-78\text{ }^\circ\text{C}$ and both reagents were added dropwise simultaneously over 1 hour with vigorous stirring. After addition was completed, the reaction mixture was slowly warmed up to $0\text{ }^\circ\text{C}$ and stirred for 3 hour. The mixture was cooled to $-78\text{ }^\circ\text{C}$ and 2.0 N HCl (150.4mL, 150.4mmol) in ether solution was slowly added over 30 minutes. The solution was warmed to $0\text{ }^\circ\text{C}$ and stirred for 1hour. Precipitate was removed by filtration and the filtrate was concentrated to 100mL. The bottom oily layer was removed and the remaining solvent was concentrated under reduced pressure. The impure oil was pipetted from the residue and run through a small plug of Na_2SO_4 . Oil was cooled to $-78\text{ }^\circ\text{C}$ and filtered

(1) (a) Wipf, P.; Jung, J-K. *J. Org. Chem.* **2000**, *20*, 6319. (b) McDougal, N. T.; Trevellini, W. L.; Rodgen, S. A.; Kliman, L. T.; Schaus, S. E. *Adv. Synth. Catal.* **2004**, *346*, 1231. (c) Liu, H.; Liu, Y.; Zhu, C.; Liu, M.; Wang, C.; Chen, C.; Xi, F. *Synthetic Metals* **2002**, *131*, 135.

through a small plug of Na₂SO₄. The colorless oil was then dissolved in toluene to make 1.0 M solution. The spectral data was in agreement with reported values.²

Preparation of Crotyldiisopropoxyborane³ (*E*)-But-2-enyldiisopropoxyborane 12a

A 250 mL three-neck round bottom flask was charged with a magnetic stir bar and a thermometer. 100 mL THF and KO*t*-Bu (4.65 g, 41.5 mmol) were added. The mixture was flushed with Ar and cooled to -78°C . Trans-2-butene (2.5 g, 44 mmol), condensed into a rubber-stoppered test tube kept at -78°C , was added via cannula. *n*-BuLi (1.6 M in hexane, 26 mL, 41.5 mmol) was added dropwise over 1 hour with an addition funnel so that the internal temperature did not rise at all. After completion of the addition, the reaction mixture was allowed to warm until the internal temperature reached -52°C . The solution was maintained at -52°C for 15 minutes, and then cooled back to -78°C . Triisopropylborate (10.5 mL, 45.6 mmol) was then added dropwise over 30 minutes through an addition funnel. The reaction mixture was maintained at -78°C for 2 hours and then rapidly poured into a 500 mL separation funnel containing 80 mL of 1N HCl saturated with NaCl. The aqueous layer is adjusted to pH 1 by using 1 N HCl. The organic phases were separated, and the aqueous layer was extracted with additional Et₂O (3 $\times$ 50 mL). The combined extracts were dried with Na₂SO₄ and filtered. The filtrate was concentrated to about 100 mL and was treated with isopropyl alcohol (6.34 mL, 83 mmol) and 3 Å molecular sieves (8.0 g). The mixture was stirred under Ar for 24 hours at room temperature. Stirring was discontinued and the clear supernatant ether layer was transferred in to another flask, the molecular sieves were washed once again with ether (100 mL). The ethereal extracts were combined and ether was removed under reduced pressure. The flask having clear liquid left was put on high vacuum pump to pump off any volatile solvent. Some white solid was formed during the course and the liquid was quickly filtered through a cotton plug and stored as 1.0 M toluene solution at 0°C . This solution was used in the crotylboration reaction without any further purification. The analytical sample was obtained by distillation under reduce pressure (90°C , 0.1 Torr) and the pure sample was sensitive to moisture. ¹H NMR (400 MHz, CDCl₃): δ 5.43(m, 1H), 5.30 (m, 1H), 4.42-4.27 (m, 2H), 1.61 (br d, J = 6.0 Hz, 2H), 1.56 (br d, J = 6.0 Hz, 3H), 1.10 (d, J = 6.0 Hz, 12H); ¹³C NMR (75.0 MHz, CDCl₃): δ 129.0, 128.2, 69.1, 24.6, 24.5, 21.5, 18.1.

(*Z*)-But-2-enyldiisopropoxyborane 12b

A 250 mL three-neck round bottom flask was charged with a magnetic stir bar and a thermometer. 100 mL THF and KO*t*-Bu (4.65 g, 41.5 mmol) were added in. The mixture was flushed with Ar and cooled to -78°C . Cis-2-butene (2.50g, 44 mmol), condensed into a rubber-

(2) Brown, H. C.; Rachela, U. S.; Pellechia, P. J. *J. Org. Chem.* **1990**, 55, 1868.

(3) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, 112, 6339.

stoppered test tube kept at $-78\text{ }^{\circ}\text{C}$, was added via cannula. *n*-BuLi (1.6 M in hexane, 26 mL, 41.5 mmol) was added dropwise over 0.5 hour with an addition funnel. After completion of the addition, the reaction mixture was allowed to warm until the internal temperature reached $-25\text{ }^{\circ}\text{C}$. The solution was maintained at $-25\text{ }^{\circ}\text{C}$ for 30 minutes, and then cooled back to $-78\text{ }^{\circ}\text{C}$. Triisopropylborate (10.5 mL, 45.6 mmol) was then added dropwise over 30 minutes through an addition funnel. The reaction mixture was maintained at $-78\text{ }^{\circ}\text{C}$ for 2 hours and then rapidly poured into a 500 mL separation funnel containing 80 mL of 1N HCl saturated with NaCl. The aqueous layer is adjusted to pH 1 by using 1N HCl. The organic phases are separated, and the aqueous layer is extracted with additional Et_2O ($3 \times 50\text{ mL}$). The combined extracts are dried with Na_2SO_4 and filtered. The filtrate was concentrated to about 100 mL and was treated with isopropyl alcohol (6.34 mL, 83 mmol) and 3 Å molecular sieves (8.0 g). The mixture was stirred under Ar for 24 hours at room temperature. Stirring was discontinued and the clear supernatant ether layer was transferred in to another flask, the molecular sieves were washed once again with ether (100 mL), and the ethereal extracts were combined and ether was removed under reduced pressure. The flask having clear liquid left was put on high vacuum pump to pump off any volatile solvent. Some white solid was formed during the course and the liquid was quickly filtered through a cotton plug and stored as 1.0 M Toluene solution at $0\text{ }^{\circ}\text{C}$. This solution was used in the crotylboration reaction without any further purification. The analytical sample was obtained by distillation under reduced pressure ($90\text{ }^{\circ}\text{C}$, 0.1 Torr) and the pure sample was sensitive to moisture. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.52 (m, 2H), 4.47 (m, 1H), 4.36 (m, 1H), 1.64 (br d, $J = 7.2\text{ Hz}$, 2H), 1.58 (br d, $J = 6.0\text{ Hz}$, 3H), 1.18 (d, $J = 6.0\text{ Hz}$, 12H); $^{13}\text{C NMR}$ (75.0 MHz, CDCl_3): δ 126.9, 124.8, 68.1, 24.8, 24.7, 20.3, 12.7.

General Procedure for Asymmetric Allylboration of Ketones.

A 10 mL one neck round bottom flask was charged with stir bar and flushed with Ar. To this flask was added 3,3'-dibromo-1,1'-bi-2-naphthol (33 mg, 0.075 mmol), α, α, α -trifluorotoluene (3.75 mL), toluene (0.75 mL) and acetophenone (87.5 μL , 0.75 mmol). The mixture was stirred under Ar at room temperature for 5 minutes and cooled at $-35\text{ }^{\circ}\text{C}$. The allyldiisopropoxyborane toluene solution (500 μL , 0.5 mmol, 1.0 M solution) was syringed in dropwise. The reaction mixture was stirred at $-35\text{ }^{\circ}\text{C}$ for 15 h. and quenched with saturated NH_4Cl aqueous solution (5 mL) at $-35\text{ }^{\circ}\text{C}$. The biphasic mixture was stirred at room temperature for 10 minutes. The organic layer was separated and dried over Na_2SO_4 . After filtration, the filtrate was purified by flash chromatography over silica gel directly (elution with 2%-5% ethyl acetate in hexanes) to afford homoallylic alcohol as a clear oil. 3,3'-Dibromo-1,1'-bi-2-naphthol can be easily separated and recovered by eluting silica gel column with 10% diethyl ether in benzene.

General Procedure for preparation of racemic products.

A 15 × 100 mm oven dried glass vessel was charged with stir bar and flushed with Ar. To this flask was added toluene (1.0 mL) and acetophenone (44 μ L, 0.375 mmol). The mixture was stirred under Ar at room temperature for 5 minutes. The allyldiisopropoxyborane toluene solution (250 μ L, 0.25 mmol, 1 M solution) was added in dropwise. The reaction mixture was stirred at room temperature for 15 h. and quenched with saturated NH_4Cl aqueous solution (1.0 mL). The biphasic mixture was stirred at room temperature for 30 minutes. The organic layer was separated and dried over Na_2SO_4 . After filtration, the filtrate was directly purified by flash chromatography over silica gel (elution with 2%-5% ethyl acetate in hexanes) to afford the desired homoallylic alcohol as a clear oil.

(S)-(-)-2-Phenylpent-4-en-2-ol (11a)

The crude mixture was purified by flash column chromatography with elution by 2% ethyl acetate in hexanes. **Yield:** 67 mg, 83%; **ee:** 94%; $[\alpha]_{\text{D}}^{23} = -56^\circ$ ($c = 0.5$, CHCl_3); Lit⁴: $[\alpha]_{\text{D}} = -48.8^\circ$ ($c = 0.84$, CHCl_3 , 82%ee); **HPLC Analysis**, t_{r} minor: 8.77min., t_{r} major: 9.23min., [Chiralpak[®] AD-H column, 15cm × 4.6 mm I.D., Hexanes:IPA = 99:1, 1.0 mL/min]; Other sepectral data was in agreement with reported data.⁴

(S)-(-)-2-(3-Bromophenyl)-pent-4-en-2-ol (11b)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 24mg, 81% **ee:** 91% $[\alpha]_{\text{D}}^{23} = -31.7^\circ$ ($c = 0.92$, CHCl_3); **HPLC Analysis**, t_{r} minor: 9.6 min., t_{r} major: 10.7 min., [Chiralpak[®] AD-H column, 15cm × 4.6 mm I.D., Hexanes:IPA = 99:1 1.0mL/min]; Other spectral data was in agreement with reported data.⁵

(S)-(-)- 2-(4-Bromophenyl)-pent-4-en-2-ol (11c)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 26mg, 86% **ee:** 99%

(4) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, 126, 8910.

(5) Cunningham, A.; Mokai-Parekh, V.; Wilson, C.; Woodward, S. *Org. Biomol. Chem.* **2004**, 2, 741.

$[\alpha]_D^{23} = -51.1^\circ$ ($c = 0.23$, CHCl_3); Lit⁶ : $[\alpha]_D^{26} = -44^\circ$ ($c = 1.6$, CHCl_3 , 98% ee); **HPLC Analysis**, t_r minor: 10.9 min., t_r major: 11.9 min., [Chiralpak[®] AD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 99:1, 1.0mL/min]; Other spectral data was in agreement with reported data.⁶

(S)-(-)-2-(3-Trifluoromethylphenyl)-pent-4-en-2-ol (11d)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 26mg, 89% **ee:** 91% $[\alpha]_D^{23} = -36.2^\circ$ ($c = .32$, CHCl_3); Lit⁷ : $[\alpha]_D^{31} = +34.3^\circ$ ($c = 0.26$, CHCl_3 , 90%ee (+)-isomer); **Chiral GC Analysis**, t_r minor: 19.4 min., t_r major: 18.8 min., [Chiraldex β -DM column, 20m $\times$ 0.25 mm I.D., 60-170 $^\circ\text{C}$, 30min]; Other spectral data was in agreement with reported data.⁷ Absolute stereochemistry was assigned by analogy of optical rotation with **11a**.

(S)-(-)-2-(4-Methoxyphenyl)-4-penten-2-ol (11e)

Reaction was run at 0.125 mmol scale and .2M concentration. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 20mg, 83% ; **ee:** >99% $[\alpha]_D^{23} = -64.0^\circ$ ($c =$, CHCl_3); Lit⁶ : $[\alpha]_D^{31} = +43.1^\circ$ ($c = 0.57$, CHCl_3 , 79%ee, (+)-isomer); **HPLC Analysis**, t_r minor: 9.2 min., t_r major: 10.1 min., [Chiralpak[®] OD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 99:1, 1.0mL/min]; Other spectral data was in agreement with reported data.⁷

(S)-(-)-2-(Naphthalen-2-yl)pent-4-en-2-ol (11f)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 21mg, 81% **ee:** 93% $[\alpha]_D^{23} = -60.7^\circ$ ($c = 0.53$, CHCl_3); Lit⁸ : $[\alpha]_D = +39.8^\circ$ ($c = 0.92$, CH_2Cl_2 , 84% ee, (+) isomer); **HPLC Analysis**, t_r minor: 15.1 min., t_r major: 16.4 min., [Chiralpak[®] AD-H column, 15cm $\times$

(6) Canales, E.; Prasad, K. G.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, 127, 11572.

(7) Kim, J. G.; Waltz, K. M.; Garcia, I. F.; Kwiatkowski, G. D.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, 126, 12580.

(8) Teo, Y. -C.; Goh, J. -D.; Loh, T. -P. *Org. Lett.* **2005**, 7, 2743.

4.6 mm I.D., Hexanes:IPA = 99:1 1.0mL/min]; Other spectral data was in agreement with reported data.⁹

(S)-(-)-2-Thiophen-2-yl-pent-4-en-2-ol (11g)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 18mg, 87% **ee:** 94% $[\alpha]_D^{23} = -38.3^\circ$ ($c = 0.22$, CHCl_3); **HPLC Analysis**, t_r minor: 42.2 min., t_r major: 45.0 min., [Chiralpak[®] AD-H column, 25cm $\times$ 4.6 mm I.D., Hexanes:IPA = 999:1 1.0mL/min]; Other spectral data was in agreement with reported data.⁹ Absolute stereochemistry was assigned by analogy of optical rotation with **11a**.

(S)-(-)-2-Thiophen-3-yl-pent-4-en-2-ol (11h)

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 18mg, 88% **ee:** 94% $[\alpha]_D^{23} = -46.2^\circ$ ($c = 0.44$, CHCl_3); Lit³ : $[\alpha]_D^{26} = -47.1^\circ$ ($c = 1.17$, CHCl_3 , 94% ee); **HPLC Analysis**, t_r minor: 52.5 min., t_r major: 61.0 min., [Chiralpak[®] AD-H column, 25cm $\times$ 4.6 mm I.D., Hexanes:IPA = 999:1 1.0mL/min]; Other spectral data was in agreement with reported data.⁵ Absolute stereochemistry was assigned by analogy of optical rotation with **11a**.

(S)-(-)-3-Phenylhex-5-en-3-ol (11i)

The reaction was run in 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2% ethyl acetate in hexanes. **Yield:** 18.5 mg, 83%; **ee:** 95%; $[\alpha]_D^{23} = -24^\circ$ ($c = 1.1$, CHCl_3); Lit¹⁰ : $[\alpha]_D = -22.4^\circ$ ($c = 0.71$, CHCl_3 , 94% ee); **HPLC Analysis**, t_r minor: 6.23 min., t_r major: 6.74 min., [Chiralpak[®] AD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 99:1, 1.0 mL/min]; Other spectral data was in agreement with reported data.⁴

(S)-(-)-1-Chloro-2-phenyl-pent-4-en-2-ol (11j)

(9) Gomes, P., Gosmini, C., Perichon, J. *Synthesis* **2003**, 12, 1909.

(10) Canales, E.; Prasad, K. G.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, 127, 11572.

Reaction was run at 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 19mg, 76% **ee:** 96% $[\alpha]_D^{23} = -18.1^\circ$ ($c = 0.44$, CHCl_3); **HPLC Analysis**, t_r minor: 8.2 min., 9.7 t_r major: min., [Chiralpak[®] AD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 99:1 1.0mL/min]; Other spectral data was in agreement with reported data.¹¹ Absolute stereochemistry was assigned by analogy of optical rotation with **11i**.

(S)-(-)-1-Allyl-2,3-dihydro-1H-inden-1-ol (11k)

The reaction was run in 0.5 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 76.5 mg, 88%; **ee:** 92%; $[\alpha]_D^{23} = -8.8^\circ$ ($c = 0.24$, CHCl_3); Lit¹²: $[\alpha]_D^{31} = +6.2^\circ$ ($c = 0.25$, CHCl_3 , 91%ee, (+)-isomer); **HPLC Analysis**, t_r major: 6.85 min., t_r minor: 8.57 min., [Chiralcel[®] OD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 98:2, 1.0 mL/min]; Other spectral data was in agreement with reported data.⁵ Absolute stereochemistry was assigned by analogy of optical rotation with **11l**.

(S)-(-)-1-Allyl-1,2,3,4-tetrahydronaphthalen-1-ol (11l)

The reaction was run in 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 20.7 mg, 87%; **ee:** 96%; $[\alpha]_D^{23} = -41.4^\circ$ ($c = 0.5$, CHCl_3); Lit¹⁰: $[\alpha]_D^{31} = -28.5^\circ$ ($c = 1.17$, CHCl_3 , 84%ee); **HPLC Analysis**, t_r minor: 6.56 min., t_r major: 7.40 min., [Chiralcel[®] OD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 98:2, 1.0 mL/min]; Other spectral data was in agreement with reported data.¹³

(S)-(-)-4-Allyl-3,4-dihydro-2H-chromen-4-ol (11m)

The reaction was run in 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 19.7 mg, 83%; **ee:** 92%; $[\alpha]_D^{23} = -10^\circ$ ($c = 1.05$, CHCl_3); Lit¹⁰: $[\alpha]_D^{28} = -15.8^\circ$ ($c = 0.71$, CHCl_3 , 92%ee); **HPLC Analysis**, t_r minor: 8.52 min., t_r major: 10.48 min., [Chiralcel[®] OD-H column, 15cm $\times$ 4.6 mm

(11) Barluenga, J.; Florez, J.; Yus, M. *J. Chem. Soc. Perkin Trans. I* **1983**, 12, 3019.

(12) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, 127, 14556.

(13) Casolari, S.; D'Addario, D.; Tagliavine, E. *Org. Lett.* **1999**, 1, 1061.

I.D., Hexanes:IPA = 98:1, 1.0 mL/min]; Other spectral data was in agreement with reported data.⁵ Absolute stereochemistry was assigned by analogy of optical rotation with **11l**.

(S)-(-)-2-Cyclohexenylpent-4-en-2-ol (11n)

The reaction was run in 0.125 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 20 mg, 91%; **ee:** 93%; $[\alpha]_D^{23} = -30.5^\circ$ ($c = 0.75$, CHCl_3); Lit² : $[\alpha]_D^{28} = -35.6^\circ$ ($c = 1.40$, CHCl_3 , 90%ee); **Chiral GC Analysis**, t_r minor: 18.9 min., t_r major: 19.4 min., [Chiraldex β -DM column, 20m $\times$ 0.25 mm I.D., 60-170 $^\circ\text{C}$, 30min]; Other spectral data was in agreement with reported data.¹⁰ Absolute stereochemistry was assigned by analogy of optical rotation with **11a**.

(S)-(-)-1,3-Diphenylhex-5-en-1-yn-3-ol (11o)

The reaction was run in 0.5 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 115 mg, 93%; **ee:** 90%; $[\alpha]_D^{23} = -5^\circ$ ($c = 0.42$, CHCl_3); **HPLC Analysis**, t_r minor: 5.63 min., t_r major: 6.33 min., [Chiralcel[®] OD-H column, 15cm $\times$ 4.6 mm I.D., Hexanes:IPA = 95:5, 1.0 mL/min]; Other spectral data was in agreement with reported data.¹⁴ Absolute stereochemistry was assigned by analogy of optical rotation with **11a**.

(2S, 3S)-3-Methyl-2-phenylpent-4-en-2-ol (13a)

The reaction was run in 0.25 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 30 mg, 72%; **ee:** 98%; $[\alpha]_D^{23} = -67.8^\circ$ ($c = 0.2$, CHCl_3); Lit⁴ : $[\alpha]_D = -72.8^\circ$ ($c = 1.05$, CHCl_3 , 85%ee); **HPLC Analysis**, t_r minor: 25.6 min., t_r major: 29.80 min., [Chiralpak[®] AD-H column, 25cm $\times$ 4.6 mm I.D., Hexanes:IPA = 999:1, 1.0 mL/min]; Other spectral data was in agreement with reported data.⁴ The relative stereochemistry was determined by comparison of Chemical Shift in ^1H -NMR with literature values.¹⁵

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(15) Seebach, D.; Widler, L. *Helv. Chim. Acta* **1982**, 65, 1972.

(2*S*,3*R*)-3-Methyl-2-phenylpent-4-en-2-ol (13b)

The reaction was run in 0.25 mmol scale. The crude mixture was purified by flash column chromatography with elution by 2-5% ethyl acetate in hexanes. **Yield:** 32 mg, 75%; **ee:** 98%; $[\alpha]_D^{23} = +5.7^\circ$ ($c = 0.25$, CHCl_3); Lit⁴ : $[\alpha]_D^{22} = +4.4^\circ$ ($c = 1.09$, CHCl_3 , 83%ee); **HPLC Analysis**, t_r major: 26.1 min., t_r minor: 29.0 min., [Chiralpak[®] AD-H column, 25cm $\times$ 4.6 mm I.D., Hexanes:IPA = 999:1, 1.0 mL/min]; Other sepectral data was in agreement with reported data.⁴

Nonlinear Effect Studies

Eight 0.15 M solution of acetophenone and 3,3'-Br₂-BINOL **5b** (0.015 M) of varying ee were prepared by mixing CF₃Ph : CH₃Ph (3 : 1) solution (**S**)-**5b** and (**R**)-**5b** in appropriate proportions. The ee of these catalysts solution were determined by calculation. 1 mL acetophenone and catalyst mixture solution was added in 15 × 100 mm oven dried glass vessels equipped with stir bar under Ar. The solution was placed in -35 °C bath and allyldiisopropylborane (100 μL, 1M toluene solution) was added. The reaction mixture was stirred at -35 °C for 15 hours and quenched with ammonium chloride aqueous solution (1 mL). The biphasic mixture was stirred at room temperature for 15 min. The organic layer was separated and run through a anhydrous Na₂SO₄ plug. The solution was purified by flash column chromatography on SiO₂ directly without concentration. The isolated products were analyzed by chiral HPLC (Chiralpak® AD-H 25cm × 4.6 mm, 1 mL / min, 999:1 hexanes:*i*-PrOH) to determine the ee. Similar (+)-NLE and yield trend were reported for BINOL-Ti catalyst.¹⁶

Table S1. Nonlinear effect of the asymmetric allylboration reaction.

Catalyst 5b ee (%)	Yield of 11a (%)	Product 11a ee (%) ^a
0	6	1
10	14	35
25	22	64
35	35	69
50	47	83
60	56	90
75	64	91
100	83	90

^a Determined by HPLC analysis

Figure S1. Positive non-linear effect in allylboration of acetophenone

Kinetic Experiments

General experimental to determine catalyst order. A 5 mL vial equipped with a stir bar was charged with (*S*)-3,3'-Br₂-BINOL (11 mg, 0.025 mmol, 10 mol% catalyst loading) and toluene (1 mL). The vial was sealed with a septum and equipped with the DiComp ReactIR 4000 Probe. The solution was cooled at 0 °C for 10 min and background was taken at this moment. To this catalyst solution was added acetophenone (30 µL, 0.25 mmol) and stirred for 5 min. Allyldiisopropoxyborane (90 µL, 0.50 mmol) was added. The solution was stirred at 0 °C for 120 min and the carbonyl stretch of acetophenone **10a** was monitored at 1690.27 cm⁻¹ by ReactIR at real time.

Table S2. Effect of initial (*S*)-3,3'-Br₂-BINOL concentration on the rate of allylboration reaction.

$[(S)\text{-}5b]_{\text{initial}}$ (M)	k_{obs} (mM/min)
0.00625	0.37
0.0125	1.06
0.025	2.12
0.0375	3.50

Figure S2. First order of catalyst in allylboration of acetophenone

NMR Experiments:**¹H-NMR of authentic samples**

To an a dry NMR tube purged with Ar, a pure sample and CD₃C₆D₅ (1.0 mL) were added. The ¹H-NMR was taken at room temperature. Three single peaks (7.10 ppm, 7.02 ppm, 6.98 ppm) were used as reference peaks in CD₃C₆D₅. The impurity in allyldiisopropoxyborane was allylboronic acid due to the slight hydrolysis.¹⁷ In ¹H-NMR of monomethyl protected 3,3'-Br₂-BINOL **8**, the peak at 7.95 ppm was assigned to H_a based on the chemical shift caused by methyl protection.¹⁸

(17) 4 Å molecular sieves as additive was proved to diminish the enantioselectivity in the addition of allyldiisopropoxyborane to acetophenone.

(18) Orasawara, K.; Takahashi, M. *Tetrahedron: Asymmetry* **1997**, 8, 3125.

Exchange of one isopropoxy ligand of boronate 10 with 3,3'-Br₂-BINOL

To a dry NMR tube, allyldiisopropoxyborane (40 μL , 0.10 mmol) and $\text{CD}_3\text{C}_6\text{D}_5$ (1.0 mL) were added under Ar. 3,3'-Br₂-BINOL (6.8 mg, 0.015 mmol) was added. The solution was left under Ar at room temperature for 20 hours and an ^1H -NMR was taken. Dissymmetrical chemical shifts of 3,3'-Br₂-BINOL aromatic proton were observed. We attribute this differentiation to the exchange of one boronate isopropoxy ligand with 3,3'-Br₂-BINOL as indicated in the following structure. Peak at 7.97 ppm was assigned to H_a according to the reported chemical shift of BINOL boronate¹⁹ and comparison of the ^1H -NMR of 3,3'-Br₂-BINOL mono-methyl ether **8**. The further downfield chemical shift of H_a than H_b is presumably due to the bonding of BINOL oxygen to boron. Peak at 7.94 ppm was assigned to H_b and the downfield chemical shift is probably caused by H-bonding to the boronate isopropoxy ligand.

Acceleration effect of external alcohol in the formation of 3,3'-Br₂-BINOL boronate complex and the allylboration of ketones.

To a dry NMR tube, allyldiisopropoxyborane (40 μ L, 0.10 mmol) and CD₃C₆D₅ (1.0 mL) were added under Ar. 3, 3'-Br₂-BINOL (6.8 mg, 0.015 mmol) and *t*-BuOH (2 μ L, 0.015 mmol) were subsequently added. The solution was left under Ar at room temperature for 30 min and an ¹H-NMR was taken. 60% of 3,3'-Br₂-BINOL had been converted to desired BINOL boronate complex according to the integrations of H_a, H_b, and H_c. Without *t*-BuOH, only 10% of BINOL boronate complex formation was observed after 30 min. This experiment indicates the external alcohol accelerates the BINOL boronate complex formation.

To a dry NMR tube, allyldiisopropoxyborane (40 μ L, 0.10 mmol) and CD₃C₆D₅ (1.0 mL) were added under Ar. 3, 3'-Br₂-BINOL (6.8 mg, 0.015 mmol), *t*-BuOH (2 μ L, 0.015 mmol) and acetophenone (33 μ L, 0.015 mmol) were subsequently added. The solution was left under Ar at room temperature and a ¹H-NMR was taken. 60% conversion to the product was observed after 30 min according to the integrations of H_d and H_e. Without *t*-BuOH, only 25% conversion to the product was observed. This experiment indicates the external alcohol help the turn over of the catalyst.

Monitoring allylboration of acetophenone by ^1H -NMR

To a dry NMR tube, acetophenone (33 μL , 0.015 mmol) and $\text{CD}_3\text{C}_6\text{D}_5$ (1.0 mL) were added under Ar. 3, 3'- Br_2 -BINOL (6.8 mg, 0.015 mmol) was added and the solution was shaken for 2 min until it became clear. Allyldiisopropoxyborane (40 μL , 0.10 mmol) was subsequently added. The reaction mixture was monitored by ^1H -NMR at room temperature. ^1H -NMR was taken at 30 min, 60 min, 120 min and 20 hours. The 4,4'-proton, H_a and H_b , differentiation of **5b** was observed immediately after addition of allyldiisopropoxyborane. We attribute this differentiation to the exchange of one boronate isopropoxy ligand with one BINOL **5b** alcohol. 80% of **5b** boronate complex was formed after 2 hours and maintained during the course of the reaction.

Table 2, entry 1: 11a Chiralpak® AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	8.782	4918989	50.14
2	9.308	4892440	49.86

	Retention Time	Area	% Area
1	8.771	607070	2.83
2	9.231	20852446	97.17

Table 2, entry 2: 11b Chiralpak[®] AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	9.960	49096258	49.69
2	10.886	49714575	50.31

	Retention Time	Area	% Area
1	9.645	1418275	4.51
2	10.674	30029064	95.49

Table 2, entry 3: 11c Chiralpak[®] AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	10.922	42537363	49.57
2	12.315	43282435	50.43

	Retention Time	Area	% Area
1	10.868	34495	0.54
2	11.933	6360294	99.46

Table 2, entry 4: 11d ChiralGC, Chiraldex B-DM column, 30m × 0.25 mm I.D., 60-170 °C, 30min, FID

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	width [min]	Area [pA*s]	Height [pA]	Area %
1	18.745	BB	0.0692	505.51361	98.04071	49.85277
2	19.353	BB	0.0714	508.49957	95.08043	50.14723
Totals :				1014.01318	193.12114

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	width [min]	Area [pA*s]	Height [pA]	Area %
1	18.791	MM	0.0813	191.96854	39.37783	95.38730
2	19.423	MM	0.0706	9.28314	2.19145	4.61270
Totals :				201.25167	41.56928	

Table 2, entry 5: 11e Chiralcel[®] OD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	9.441	22497132	50.18
2	10.026	22332979	49.82

	Retention Time	Area	% Area
1	9.177	31281	0.10
2	10.138	31455156	99.90

Table 2, entry 6: 11f Chiralpak[®] AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	16.772	118659504	48.31
2	18.272	126978155	51.69

	Retention Time	Area	% Area
1	15.070	177464	3.54
2	16.387	4838350	96.46

Table 2, entry 7: 11g Chiralpak® AD-H Column, Hexane:IPA = 999:1, 1.0 mL/min, 230 nm

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.909	BB	0.9267	5337.92676	85.93272	50.4324
2	45.210	BB	1.0852	5246.40283	71.40190	49.5676
Totals :				1.05843e4	157.33463

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	42.163	MM	1.3822	188.47493	2.27263	2.9992
2	44.953	MM	1.6039	6095.65918	63.34020	97.0008
Totals :				6284.13411	65.61283

Table 2, entry 8: 11h Chiralpak® AD-H Column, Hexane:IPA = 999:1, 1.0 mL/min, 230 nm

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.956	BB	1.1679	9658.67383	127.19793	50.0266
2	61.719	BB	1.4300	9648.42090	93.95693	49.9734
Totals :				1.93071e4	221.15486

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.531	MM	1.0237	581.80164	9.47239	2.7689
2	60.999	MM	2.0661	2.04306e4	164.81070	97.2311
Totals :				2.10124e4	174.28309

Table 2, entry 9: 11i Chiralpak® AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	6.066	7275498	49.85
2	6.610	7320204	50.15

	Retention Time	Area	% Area
1	6.235	619379	2.46
2	6.749	24537200	97.54

Table 2, entry 10: 11j Chiralpak® AD-H Column, Hexane:IPA = 99:1, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	8.751	25265681	49.41
2	9.258	25870163	50.59

	Retention Time	Area	% Area
1	8.206	159526	1.83
2	9.691	8564743	98.17

Table 2, entry 11: 11k Chiralcel[®]OD-H Column, Hexane:IPA = 98:2, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	6.404	14341456	49.79
2	8.021	14461913	50.21

	Retention Time	Area	% Area
1	6.848	27703502	96.40
2	8.567	1035546	3.60

Table 2, entry 12: 11l Chiralcel® OD-H Column, Hexane:IPA = 98:2, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	6.955	12484847	50.32
2	7.534	12326624	49.68

	Retention Time	Area	% Area
1	6.565	257219	2.37
2	7.404	10608317	97.63

Table 2, entry 13: 11m Chiralcel[®] OD-H Column, Hexane:IPA = 98:2, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	8.797	9527777	50.08
2	10.672	9495838	49.92

	Retention Time	Area	% Area
1	8.524	207217	3.77
2	10.475	5295730	96.23

Table 2, entry 14: 11n ChiralGC, Chiraldex B-DM column, 30m × 0.25 mm I.D., 60-170 °C, 30min, FID

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	width [min]	Area [pA*s]	Height [pA]	Area %
1	18.927	MM	0.1431	2278.65649	265.39578	50.76946
2	19.261	MM	0.1592	2209.58643	231.25914	49.23054
Totals :				4488.24292	496.65492

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	width [min]	Area [pA*s]	Height [pA]	Area %
1	18.910	BB	0.1291	3165.27930	310.14694	96.64559
2	19.412	BB	0.0850	109.86178	17.80644	3.35441
Totals :				3275.14108	327.95339

Table 2, entry 15: 11o Chiralcel® OD-H Column, Hexane:IPA = 95:5, 1.0 mL/min, 214 nm

	Retention Time	Area	% Area
1	5.594	18036153	49.25
2	6.299	18584565	50.75

	Retention Time	Area	% Area
1	5.629	610630	4.94
2	6.327	11745517	95.06

Scheme 1: Chiralpak® AD-H Column, Hexane:IPA = 999:1, 1.0 mL/min, 214 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.306	PV	0.5853	5752.53076	152.77165	13.8381
2	25.335	VV	0.7861	1.49244e4	276.34940	35.9017
3	27.522	VV	0.8384	1.42130e4	248.06790	34.1902
4	29.229	VB	1.0788	6680.35156	84.45525	16.0700
Totals :				4.15703e4	761.64420

syn : anti = 70 : 30
racemic

anti-13a: Chiralpak[®] AD-H Column, Hexane:IPA = 999:1, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.606	PB	0.6128	6144.15332	151.59756	49.6663
2	28.401	VB	1.0625	6226.72803	81.21508	50.3337
Totals :				1.23709e4	232.81264

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.587	MM	0.5183	199.24777	4.62903	1.2983
2	29.807	BB	1.3890	1.51478e4	144.97780	98.7017
Totals :				1.53470e4	149.60683

syn-13a: Chiralpak[®] AD-H Column, Hexane:IPA = 999:1, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.717	BV	0.4735	798.91400	26.36596	2.1299
2	23.500	VV	0.7358	1.76076e4	353.07904	46.9415
3	25.392	VV	0.8265	1.80332e4	318.51807	48.0760
4	27.739	VP	0.8588	1070.03833	15.66738	2.8527
Totals :				3.75098e4	713.63045

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.102	PB	0.8646	1.06722e4	180.81383	98.5075
2	29.017	MM	0.7377	161.69867	3.65321	1.4925
Totals :				1.08339e4	184.46704