Catalyzed Enantioselective Synthesis of Allyl Alcohols from Aldehydes and Alkenylboronic Acids

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Dedicated to Professor Dr. Marty Semmelhack on the occasion of his 65th birthday

Abstract: Enantiomerically enriched (*E*)-allyl alcohols can be prepared in good yields by asymmetric alkenylation of aldehydes with alkenylboronic acids catalyzed by a chiral ferrocene-based agent.

Key words: C–C bond formation, allyl alcohols, enantioselective catalysis, vinylboronic acid, zinc organyls, vinylation

Since chiral allyl alcohols are important intermediates in the synthesis of numerous biologically active compounds, enantioselective approaches towards their preparation have recently attracted significant attention. Most strategies are either based on asymmetric carbonyl reductions of α,β-unsaturated ketones[1] or enantioselective additions of alkenylzinc reagents to carbonyl compounds.[2–11] The latter transformations are of particular interest due to the generation of a stereogenic center with concomitant formation of a new C–C bond. Early work in this area stems from Oppolzer and Radinov, who employed alkenylzinc reagents prepared in situ by the reaction of either ethenyl Grignard or alkenyllithium reagents with $ZnCl_2$ or $ZnBr_2$.[2] Later, the same authors used the reaction of terminal alkynes with dicyclohexylborane and subsequent boron–zinc exchange for the preparation of the alkenylzinc reagents. With Noyori's 3-*exo*-dimethylaminoborneol (DAIB)[3] as catalyst, asymmetric alkenylations of aldehydes were achieved.[4] Bräse introduced [2.2]paracyclophane-based N,O-ligands for the asymmetric addition of alkenylzinc species to aldehydes.[5] Other amino alcohols were successfully applied by Walsh,[6] Chan,[7] and Soai.[8] Tseng and Yang investigated the use of β-amino thiols in Oppolzer's protocol,[9] and the efficiency of *N*-acylethylenediamines in asymmetric additions of alkenylzinc species to aldehydes was screened by Seto.[10] Wipf developed a protocol for the hydrozirconation of alkynes using Cp_2ZrHCl (Schwartz reagent) for the preparation of alkenylzirconocenes, which were then transmetalated in situ with dimethylzinc to give the corresponding zinc reagents.[11]

In our previous studies, ferrocene **4** (see Table 1) was found to be an excellent catalyst for the asymmetric synthesis of diarylmethanols where either diphenylzinc or triphenylborane was used as the phenyl source.[12] In 2002 we reported a general catalytic asymmetric aryl transfer to aromatic aldehydes with arylzinc species formed in situ from arylboronic acids and diethylzinc.[13] The presence of catalytic amounts of methoxy polyethylene glycols improved the enantioselectivities of these reactions.[14] Propan-2-ol also had a beneficial effect on the enantioselectivity.

These results encouraged us to investigate the applicability of alkenylboronic acids **1** (see Table 1) in the preparation of enantioenriched allyl alcohols. Starting from commercially available reagents **1**, in situ boron-to-zinc exchange was expected to afford alkenylzincs, which we hoped would serve as alkenyl sources in catalyzed asymmetric addition reactions to aldehydes. To test this hypothesis, boronic acids **1** were stirred in toluene in the presence of a threefold excess of $ZnEt_2$ at –2 °C for five minutes. Subsequently, 10 mol% of ferrocene **4** and aldehydes **2** were added at –2 °C. To our delight, allyl alcohols **3** formed in yields ranging from 37–79%. Table 1 and Figure 1 summarize the results of this study.

Initially, commercial samples of boronic acids **1a** and **1c** were used in the catalyzed addition reactions with 4-methylbenzaldehyde (**2b**) and 4-chlorobenzaldehyde (**2c**), respectively (Table 1, entries 5 and 14). Unfortunately, all attempts afforded addition products **3b** and **3i** as racemates. To obtain chemically homogeneous boronic acids and to minimize the presence of boroxines in the commercial samples, boronic acids **1a** and **1c** were refluxed in water for four hours, and the excess water was then removed prior to use (entries 3 and 13). To our delight, those modified conditions led to the formation of allyl alcohols **3b** and **3i** in good yields and in enantioselectivities of 28% and 56%, respectively. Further improvements in both yield and enantioselectivity were achieved when one equivalent of propan-2-ol was used as additive. In the reaction of boronic acid **1a** and 4-methylbenzaldehyde (**2b**) (entries 3 and 2), this effect increased the enantioselectivity from 28% to 34% ee, while the yield remained constant. The reaction between alkenylboronic acid **1c** and aldehyde **2e** was affected similarly (entries 13 and 12), with the yield increasing from 58% to 79% and the ee from 56% to 61%. Interestingly, the use of dimethoxy polyethylene glycol (DiMPEG) was detrimental, and the corresponding product was obtained in only trace amounts (<10%; Table 1, entry 4). The best result was achieved in the formation of **3h** (entry 11), which was

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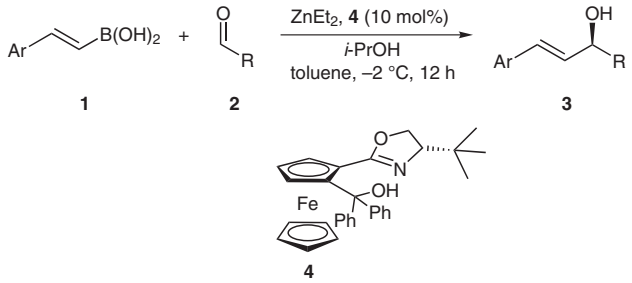
Table 1 Catalyzed Asymmetric Alkenylzinc Addition to Aldehydes[a]



Entry	Ar (**1**)	R (**2**)	Product **3**	Yield[b] (%)	ee[c] (%)
1[d]	Ph (**1a**)	Ph (**2a**)	**3a**	70	43 (*R*)
2[d]	Ph (**1a**)	4-Tol (**2b**)	**3b**	71	34 (*R*)
3[d,e]	Ph (**1a**)	4-Tol (**2b**)	**3b**	72	28 (*R*)
4[d–f]	Ph (**1a**)	4-Tol (**2b**)	**3b**	<10	n.d.[g]
5[h]	Ph (**1a**)	4-Tol (**2b**)	**3b**	41	*rac*
6[d]	Ph (**1a**)	Mes (**2c**)	**3c**	62	29 (*R*)
7[d]	Ph (**1a**)	C_6Me_5 (**2d**)	**3d**	69	12 (*R*)
8[d]	Ph (**1a**)	4-ClC_6H_4 (**2e**)	**3e**	72	55 (*R*)
9[d]	Ph (**1a**)	2-BrC_6H_4 (**2f**)	**3f**	53	51 (*R*)
10[d]	Ph (**1a**)	Cy (**2g**)	**3g**	55	33 (*S*)
11[d]	4-Tol (**1b**)	4-ClC_6H_4 (**2e**)	**3h**	62	75 (*R*)
12[d]	4-ClC_6H_4 (**1c**)	4-ClC_6H_4 (**2e**)	**3i**	79	61 (*R*)
13[d,e]	4-ClC_6H_4 (**1c**)	4-ClC_6H_4 (**2e**)	**3i**	58	56 (*R*)
14[h]	4-ClC_6H_4 (**1c**)	4-ClC_6H_4 (**2e**)	**3i**	37	*rac*
15[d]	4-ClC_6H_4 (**1c**)	C_6Me_5 (**2d**)	**3j**	67	9 (*R*)

[a] Reagents and conditions: **1** (0.6 mmol), **2** (0.25 mmol), **4** (10 mol%), Et_2Zn (1.8 mmol), *i*-PrOH (0.25 mmol), toluene, –2 °C, 12 h.
[b] Yield after column chromatography.
[c] The enantiomer ratios were determined by HPLC on a chiral stationary phase. The absolute configuration of **3a** was established by comparing its rotational values with literature data.[8b,15] Otherwise, the stereochemistry was assigned by assuming identical reaction pathways for the catalyzed product formation.
[d] Boronic acid **1** was stirred in H_2O at 100 °C for 4 h prior to use.
[e] Without *i*-PrOH.
[f] With DiMPEG (1.0 equiv) as additive.
[g] n.d. = not determined.
[h] Boronic acid **1** was not pretreated in H_2O.

obtained in 75% ee in 62% yield from **1b** and 4-chlorobenzaldehyde (**2e**). The reactions between pentamethylbenzaldehyde (**2d**) and boronic acids **1a** and **1c** gave the corresponding products **3d** and **3j** in low enantioselectivities (12 and 9%; entries 7 and 15). 2-Bromobenzaldehyde (**2f**), also an *ortho*-substituted aldehyde, reacted well and gave **3f** in 51% ee and 53% yield (entry 9). The alkenylation of aliphatic aldehyde **2g** with boronic acid **1b** (entry 10) furnished the corresponding allyl alcohol **3g** in 33% ee and a respectable yield of 55%. Noticeable is that the quality of the boronic acid was important in all reactions. Depending on the nature (and purity) of the boronic acid, major differences in yield and enantioselectivity were observed. This effect was particularly pronounced in reactions with boronic acid **1a**.

The reaction between alkenylboronic acid **1a** and aldehyde **2b** at –10 °C led to an interesting observation. The yield of the expected product **3b** decreased to 33%, and the presence of a new compound was detected. The double set of signals in both the ^1H and ^{13}C NMR spectra indicated the formation of a compound structurally very similar to **3b**, and which finally was identified as allyl alcohol **6b**, an isomer of **3b** (Scheme 1). Two-dimensional NMR experiments of the isomer mixture measured in deu-

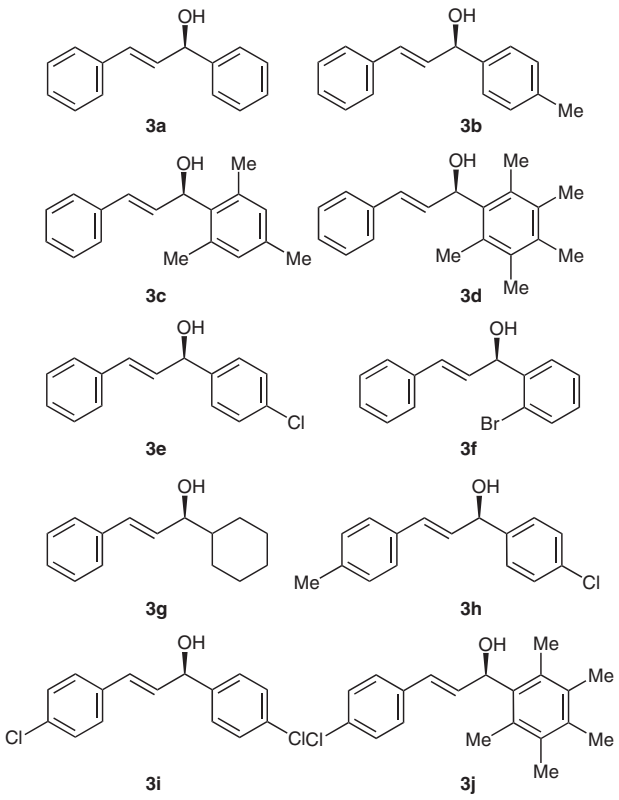
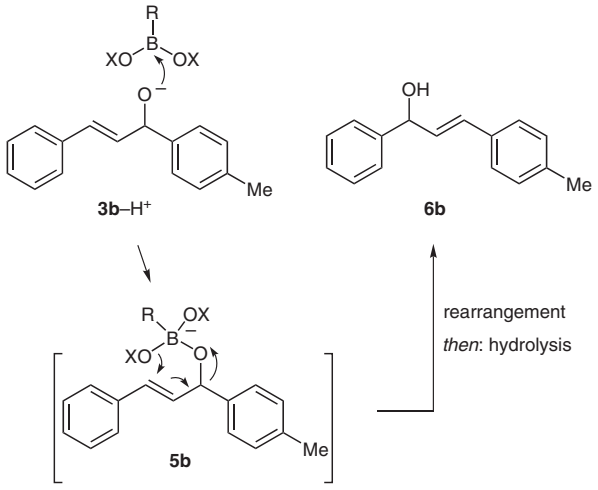


Figure 1 Allyl alcohols **3** obtained by alkenyl transfer onto aldehydes

terated dichloromethane and deutero-pyridine confirmed the assignments of both isomers **3b** and **6b**.[16]

Although the precise mechanism of the formation of **6b** is unknown, we assume that deprotonated **3b** (e.g., alkoxide **3b**-H^+) reacts with the excess of the boron reagent (the boronic acid or its metalated counterpart) to give an intermediate such as **5b** (Scheme 1). The latter then rearranges, leading, after hydrolysis, to isomeric allyl alcohol **6b**. To



Scheme 1 Formation of isomeric products **3b** and **6b** during the alkenyl transfer from **1a** to **2b** at –10 °C (X = H or a metal species)

support this hypothesis and to ensure that the rearrangement was not caused by the presence of aldehyde **2b**, two experiments were carried out. First, (racemic) **3b** was treated with boronic acid **1a** and diethylzinc, and the resulting mixture was kept at –10 °C for 12 hours. Second, the same experiment was performed, but the boronic acid was substituted by the aldehyde. Supporting our suggested scenario, traces of isomerized product **6b** were only formed in the first experiment, whereas no **6b** was found in the second.

In conclusion, we developed a new strategy for the synthesis of enantiomerically enriched allyl alcohols starting from aldehydes and commercially available alkenylboronic acids. The synthetic pathway is very flexible, allowing the introduction of structural diversity in a single reaction step.

All air-sensitive manipulations were carried out under an inert atmosphere of argon and using sealed vials. Toluene was distilled under N_2 from sodium/benzophenone ketyl radical. Et_2O and pentane for column chromatography were distilled before use. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer (300 MHz and 75 MHz, respectively) and on a Varian Inova 400 spectrometer (400 MHz and 100 MHz, respectively). IR spectra of samples prepared as KBr pellets or neat samples (liquid compounds) were measured on a Perkin-Elmer PE 1760 FT instrument; absorptions are given in wave numbers (cm^{-1}). MS spectra were recorded on a Varian MAT 212 or Finnigan MAT 95 spectrometer with EI ionization. Optical rotation measurements were conducted at room temperature with a Perkin-Elmer PE 241 polarimeter at a wavelength of 589 nm. HPLC measurements were performed on a Dionex HPLC system (previously Gynkothek) with autosampler Gina 50, UV detector UVD 170S, degasser DG 503, and gradient pump M480G.

Pretreatment of Alkenylboronic Acids 1a–c; General Procedure

The alkenylboronic acid **1** was suspended in H_2O and the mixture was refluxed for 4 h. Then the aqueous soln was extracted with EtOAc, the organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure; this afforded the boronic acids **1a–c** used in the reactions below.

Allyl Alcohols 3a–j; General Procedure

A 10-mL vial was charged with alkenylboronic acid **1** (0.6 mmol, 2.4 equiv), flushed with argon, and sealed with a septum. Freshly distilled toluene (1.5 mL) was added at –2 °C, followed by 1 M $ZnEt_2$ in heptane (1.8 mL, 1.8 mmol, 7.2 equiv) and *i*-PrOH (20 μL, 0.25 mmol, 1 equiv). The mixture was stirred for 5 min at this temperature. Another vial was charged with ferrocene **4** (12.5 mg, 0.025 mmol, 10 mol%), sealed with a septum, and flushed with argon. Toluene (1 mL) was added and the mixture was cooled to –2 °C. The soln was transferred by syringe to the first one and stirring was continued for 2 min at –2 °C. In a third vial, aldehyde **2** (0.25 mmol) was dissolved in toluene (1 mL), and the soln was cooled to –2 °C and transferred by syringe to the other soln. The mixture was stirred for 12 h at 0 °C. Then the reaction was quenched with H_2O (0.7 mL). The mixture was placed on a pad of Celite, and eluted with CH_2Cl_2. The organic layer was extracted with a sat. $NaHCO_3$ soln (1 × 50 mL) and brine (2 × 50 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. Purification of the product by column chromatography gave allyl alcohol **3**.[17]

(1*R*,2*E*)-1,3-Diphenylprop-2-en-1-ol (3a)[18]
Alcohol **3a** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and benzaldehyde (**2a**; 25.4 μL, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3a** as a pale yellow oil. The absolute configuration of **3a** was established by comparing its rotational values with literature data.[8b,15]

Yield: 36.7 mg (70%); $[\alpha]_D^{20}$ +11.2 (*c* 1.7, CH_2Cl_2).

HPLC (Chiralcel OD, 254 nm, heptane–*i*-PrOH, 90:10, 1.0 mL/min): t_R = 15.3 min (*S*), 20.1 min (*R*).

IR (KBr): 3369, 1491, 1448, 1013, 965, 745, 695 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 2.17 (br s, 1 H, OH), 5.26 (d, *J* = 6.6 Hz, 1 H, CH), 6.28 (dd, *J* = 15.7, 6.6 Hz, 1 H, CH), 6.58 (d, *J* = 15.9 Hz, 1 H, CH), 7.11–7.35 (m, 10 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 75.0 (CH), 126.2 (2 CH), 126.5 (2 CH), 127.6 (CH), 127.7 (CH), 128.5 (2 CH), 128.5 (2 CH), 130.1 (CH), 131.8 (CH), 136.6 (C), 143.0 (C).

MS (EI, 70 eV): *m*/*z* (%) = 210 (54) [M^+], 105 (100), 91 (14), 77 (21).

(1*R*,2*E*)-3-Phenyl-1-(*p*-tolyl)prop-2-en-1-ol (3b)[19]
Alcohol **3b** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and 4-methylbenzaldehyde (**2b**; 29 μL, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3b** as a pale yellow solid. The absolute configuration of **3b** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 31.7 mg (56%); mp 74.0–75.7 °C; $[\alpha]_D^{20}$ +8.0 (*c* 1.4, CH_2Cl_2).

HPLC (Chiralcel OD, 254 nm, heptane–*i*-PrOH, 90:10, 1.0 mL/min): t_R = 13.6 min (*S*), 19.6 min (*R*).

IR (KBr): 3393, 3025, 1509, 1448, 1021, 963, 815, 763, 692 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 2.16 (br s, 1 H, OH), 2.33 (s, 3 H, CH_3), 5.31 (d, *J* = 6.6 Hz, 1 H, CH), 6.36 (dd, *J* = 15.9, 6.5 Hz, 1 H, CH), 6.66 (d, *J* = 15.8 Hz, 1 H, CH), 7.14–7.25 (m, 3 H, H_{Ar}), 7.26–7.34 (m, 4 H, H_{Ar}), 7.35–7.41 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 21.2 (CH_3), 75.1 (CH), 126.4 (2 CH), 126.7 (2 CH), 127.8 (CH), 128.7 (2 CH), 129.4 (2 CH), 130.1 (CH), 132.2 (CH), 136.9 (C), 137.7 (C), 140.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 224 (34) [M^+], 209 (24), 119 (100), 105 (19), 91 (18).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O$: 224.1201; found: 224.1201.

(1*R*,2*E*)-1-Mesityl-3-phenylprop-2-en-1-ol (3c)
Alcohol **3c** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and 2,4,6-trimethylbenzaldehyde (**2c**; 37 μL, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3c** as a pale yellow oil. The absolute configuration of **3c** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 39.2 mg (62%); $[\alpha]_D^{20}$ +11.1 (*c* 1.9, CH_2Cl_2).

HPLC (Chiralcel OD-H, 254 nm, heptane–*i*-PrOH, 90:10, 0.5 mL/min): t_R = 17.9 min (*S*), 27.9 min (*R*).

IR ($CHCl_3$): 2921, 1217, 966, 852, 758, 694 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 1.97 (br s, 1 H, OH), 2.16 (s, 3 H, CH_3), 2.31 (s, 6 H, 2 CH_3), 5.75 (d, *J* = 2.7 Hz, 1 H, CH), 6.43 (d, *J* = 3.0 Hz, 2 H, 2 CH), 6.75 (s, 2 H, H_{Ar}), 7.12 (tt, *J* = 6.3, 1.4 Hz, 1 H, H_{Ar}), 7.17–7.23 (m, 2 H, H_{Ar}), 7.25–7.30 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 20.5 (2 CH_3), 20.6 (CH_3), 71.1 (CH), 126.3 (2 CH), 127.3 (CH), 128.4 (2 CH), 129.1 (CH), 129.9 (2 CH), 130.6 (CH), 135.2 (2 C), 136.4 (2 C), 136.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 252 (19) [M^+], 234 (71), 133 (74), 132 (100), 105 (44).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{20}O$: 252.1514; found 252.1514.

(1*R*,2*E*)-1-(Pentamethylphenyl)-3-phenylprop-2-en-1-ol (3d)
Alcohol **3d** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and pentamethylbenzaldehyde (**2d**; 44.0 mg, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3d** as a pale yellow oil. The absolute configuration of **3d** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 36.7 mg (69%); $[\alpha]_D^{20}$ +4.9 (*c* 2.4, CH_2Cl_2).

HPLC (Chiralcel OD-H, 230 nm, heptane–*i*-PrOH, 90:10, 0.5 mL/min): t_R = 13.4 min (*S*), 22.5 min (*R*).

IR ($CHCl_3$): 3388, 3009, 2925, 1450, 1217, 966, 757, 695 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 1.97 (br s, 1 H, OH), 2.12 (s, 6 H, 2 CH_3), 2.15 (s, 3 H, CH_3), 2.24 (s, 6 H, 2 CH_3), 5.90 (dd, *J* = 4.4, 1.9 Hz, 1 H, CH), 6.37 (dd, *J* = 16.5, 1.9 Hz, 1 H, CH), 6.50 (dd, *J* = 15.9, 4.4 Hz, 1 H, CH), 7.10–7.14 (m, 1 H, H_{Ar}), 7.16–7.22 (m, 2 H, H_{Ar}), 7.24–7.29 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 16.5 (2 CH_3), 16.9 (CH_3), 17.2 (2 CH_3), 71.6 (CH), 126.2 (2 CH), 127.2 (CH), 128.4 (2 CH), 128.9 (CH), 132.0 (CH), 132.1 (2 C), 133.1 (2 C), 134.3 (C), 135.9 (C), 137.1 (C).

MS (EI, 70 eV): *m*/*z* (%) = 280 (12) [M^+], 265 (100), 147 (15), 91 (5).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{24}O$: 280.1827; found 280.1827.

(1*R*,2*E*)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-ol (3e)[20]
Alcohol **3e** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and 4-chlorobenzaldehyde (**2e**; 35.1 mg, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3e** as a pale yellow solid. The absolute configuration of **3e** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 44.6 mg (72%); mp 58.2–59.0 °C; $[\alpha]_D^{20}$ +8.9 (*c* 1.6, CH_2Cl_2).

HPLC (Chiralcel OD, 254 nm, heptane–*i*-PrOH, 90:10, 1.0 mL/min): t_R = 14.9 min (*S*), 22.2 min (*R*).

IR (KBr): 3293, 1089, 1012, 964, 828, 751, 694 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 1.17 (br s, 1 H, OH), 5.23 (d, *J* = 6.6 Hz, 1 H, CH), 6.22 (dd, *J* = 15.7, 6.6 Hz, 1 H, CH), 6.55 (d, *J* = 15.7 Hz, 1 H, CH), 7.11–7.45 (m, 9 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 74.3 (CH), 126.5 (2 CH), 127.7 (2 CH), 127.8 (CH), 128.5 (2 CH), 128.6 (2 CH), 130.6 (CH), 131.3 (CH), 133.1 (C), 136.4 (C), 141.5 (C).

MS (EI, 70 eV): *m*/*z* (%) = 244 (65) [M^+], 209 (17), 141 (32), 139 (100), 105 (31).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}ClO$: 244.0654; found 244.0655.

Anal. Calcd for $C_{15}H_{13}ClO$: C, 73.62; H, 5.35. Found: C, 73.57; H, 5.43.

(1*R*,2*E*)-1-(2-Bromophenyl)-3-phenylprop-2-en-1-ol (3f)
Alcohol **3f** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and 2-bromobenzaldehyde (**2f**; 29 μL, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3f** as a pale yellow oil. The absolute configuration

of **3f** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 38.0 mg (53%); $[\alpha]_D^{20}$ +54.1 (*c* 1.9, CH_2Cl_2).

HPLC (Chiralcel OD-H, 254 nm, heptane–*i*-PrOH, 90:10, 0.5 mL/min): t_R = 33.1 min (*R*), 36.9 min (*S*).

IR ($CHCl_3$): 3358, 1467, 1440, 966, 753, 694 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 1.17 (br s, 1 H, OH), 5.67 (d, *J* = 6.3 Hz, 1 H, CH), 6.27 (dd, *J* = 15.9, 6.3 Hz, 1 H, CH), 6.65 (d, *J* = 15.9, 6.3 Hz, 1 H, CH), 7.05–7.32 (m, 7 H, H_{Ar}), 7.45–7.55 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 73.3 (CH), 122.3 (C), 126.0 (2 CH), 127.7 (CH), 127.8 (CH), 128.0 (CH), 128.5 (2 CH), 129.1 (CH), 129.9 (CH), 130.7 (CH), 132.7 (CH), 136.5 (C), 141.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 288 (35), 209 (100) [M^+], 184 (99), 182 (98), 104 (40), 91 (35).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}BrO$: 288.0149; found: 288.0149.

Anal. Calcd for $C_{15}H_{13}BrO$: C, 62.30; H, 4.53. Found: C, 62.35; H, 4,79.

(1*S*,2*E*)-1-Cyclohexyl-3-phenylprop-2-en-1-ol (3g)[9]

Alcohol **3g** was obtained from *trans*-boronic acid **1a** (88.7 mg, 0.6 mmol, 2.4 equiv) and cyclohexanecarbaldehyde (**2g**; 30 μL, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3g** as a pale yellow solid. The absolute configuration of **3g** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 30.0 mg (55%); mp 60.4–61.7 °C; $[\alpha]_D^{20}$ +2.5 (*c* 1.6, CH_2Cl_2).

HPLC (Chiralcel OD-H, 230 nm, heptane–*i*-PrOH, 90:10, 0.5 mL/min): t_R = 15.0 min (*R*), 21.3 min (*S*).

IR (KBr): 3925, 2851, 1493, 1448, 1011, 969, 752 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 0.89–1.25 (m, 5 H, H_{Cy}), 1.34–1.45 (m, 1 H, H_{Cy}), 1.53–1.72 (m, 5 H, H_{Cy}/OH), 1.77–1.85 (m, 1 H, CH), 3.90 (t, *J* = 7.1 Hz, 1 H, CH), 6.15 (dd, *J* = 15.9, 6.7 Hz, 1 H, CH), 6.45 (d, *J* = 15.9 Hz, 1 H, CH), 7.11–7.17 (m, 1 H, H_{Ar}), 7.19–7.26 (m, 2 H, H_{Ar}), 7.28–7.32 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, C_6D_6): δ = 26.2 (CH_2), 26.3 (CH_2), 26.7 (CH_2), 28.7 (CH_2), 29.0 (CH_2), 44.1 (CH), 77.3 (CH), 126.3 (2 CH), 127.4 (CH), 128.5 (2 CH), 130.5 (CH), 131.6 (CH), 136.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 216 (23) [M^+], 133 (100), 115 (15), 91 (7).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{20}O$: 216.1514; found: 216.1514.

(1*R*,2*E*)-1-(4-Chlorophenyl)-3-(*p*-tolyl)prop-2-en-1-ol (3h)[21]

Alcohol **3h** was obtained from *trans*-boronic acid **1b** (97.0 mg, 0.6 mmol, 2.4 equiv) and 4-chlorobenzaldehyde (**2e**; 35.1 mg, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3h** as a pale yellow solid. The absolute configuration of **3h** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 40.6 mg (62%); mp 56.1–58.5 °C; $[\alpha]_D^{20}$ +11.8 (*c* 2.2, CH_2Cl_2).

HPLC (Chiralcel OD-H, 254 nm, heptane–*i*-PrOH, 90:10, 0.7 mL/min): t_R = 18.0 min (*R*), 21.8 min (*S*).

IR (KBr): 3317, 1488, 1088, 1030, 1012, 968 cm^{-1}.

^1H NMR (400 MHz, C_6D_6): δ = 1.27 (br s, 1 H, OH), 2.09 (s, 3 H, CH_3), 4.91 (d, *J* = 6.4 Hz, 1 H, CH), 6.17 (dd, *J* = 15.9, 6.7 Hz, 1 H, CH), 6.45 (d, *J* = 15.9 Hz, 1 H, CH), 6.94 (d, *J* = 8.0 Hz, 2 H, H_{Ar}), 7.01–7.17 (m, 6 H, H_{Ar}).

^{13}C NMR (100 MHz, C_6D_6): δ = 20.9 (CH_3), 74.0 (CH), 126.5 (2 CH), 127.1 (CH), 127.1 (CH), 128.4 (2 CH), 129.2 (2 CH), 130.4 (CH), 130.5 (CH), 132.9 (C), 133.8 (C), 137.3 (C), 141.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 258 (73) [M^+], 243 (15), 139 (100), 119 (52), 105 (53).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}ClO$: 258.0811; found: 258.0810.

Anal. Calcd for $C_{15}H_{13}BrO$ (258.08): C, 74.24; H, 5.84. Found: C, 74.25; H, 5.97.

(1*R*,2*E*)-1,3-Bis(4-chlorophenyl)prop-2-en-1-ol (3i)[22]

Alcohol **3i** was obtained from *trans*-boronic acid **1c** (109 mg, 0.6 mmol, 2.4 equiv) and 4-chlorobenzaldehyde (**2e**; 35.1 mg, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3i** as a pale yellow solid. The absolute configuration of **3i** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 43.5 mg (79%); mp 82.0–85.7 °C; $[\alpha]_D^{20}$ +15.4 (*c* 2.2, CH_2Cl_2).

HPLC (Chiralcel OD, 254 nm, heptane–*i*-PrOH, 90:10, 1.0 mL/min): t_R = 10.1 min (*R*), 11.7 min (*S*).

IR (capillary): 3383, 1489, 1089, 1013, 968, 822 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 2.20 (br s, 1 H, OH), 5.28 (d, *J* = 6.3 Hz, 1 H, CH), 6.25 (dd, *J* = 15.9, 6.6 Hz, 1 H, CH), 6.57 (d, *J* = 15.9 Hz, 1 H, CH), 7.20–7.33 (m, 8 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 74.2 (CH), 127.7 (2 CH), 127.8 (2 CH), 128.6 (2 CH), 128.6 (2 CH), 129.2 (CH), 132.0 (CH), 132.2 (C), 133.3 (C), 135.0 (C), 141.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 278 (31) [M^+], 243 (12), 139 (100), 125 (21).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{12}Cl_2O$: 278.0265; found: 278.0264.

(1*R*,2*E*)-3-(Chlorophenyl)-1-(pentamethylphenyl)prop-2-en-1-ol (3j)

Alcohol **3j** was obtained from *trans*-boronic acid **1c** (109 mg, 0.6 mmol, 2.4 equiv) and pentamethylbenzaldehyde (**2d**; 44.0 mg, 0.25 mmol, 1 equiv). Column chromatography (silica gel, pentane–Et_2O–Et_3N, 7:2.7:0.3) gave **3j** as a pale yellow oil. The absolute configuration of **3j** was assigned assuming an identical reaction pathway for the catalyzed product formation as for **3a**.

Yield: 44.9 mg (63%); $[\alpha]_D^{20}$ +5.52 (*c* 2.2, CH_2Cl_2).

HPLC (Chiralcel OD-H, 254 nm, heptane–*i*-PrOH, 90:10, 0.5 mL/min): t_R = 12.3 min (*S*), 14.5 min (*R*).

IR (KBr): 3398, 2925, 1489, 1456, 1011, 969 cm^{-1}.

^1H NMR (400 MHz, CD_2Cl_2): δ = 1.11 (s, 6 H, 2 CH_3), 2.13 (s, 1 H, OH), 2.14 (s, 3 H, CH_3), 2.23 (s, 6 H, 2 CH_3), 5.89 (dd, *J* = 4.1, 1.9 Hz, 1 H, CH), 6.34 (dd, *J* = 15.9, 1.9 Hz, 1 H, CH), 6.47 (dd, *J* = 15.9, 4.1 Hz, 1 H, CH), 7.13–7.23 (m, 4 H, CH_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 16.5 (2 CH_3), 16.9 (CH_3), 17.2 (2 CH_3), 71.5 (CH), 127.5 (2 CH), 127.6 (CH), 128.5 (2 CH), 132.1 (2 C), 132.6 (C), 132.8 (CH), 133.2 (2 C), 134.4 (C), 135.8 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 314 (8) [M^+], 175 (100), 147 (12).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{23}ClO$: 314.1437; found: 314.1437.

(2*E*)-1-Phenyl-3-(*p*-tolyl)prop-2-en-1-ol (6b)

^1H NMR (400 MHz, CD_2Cl_2): δ = 2.29 (s, 3 H, CH_3), 2.51 (br s, 1 H, OH), 5.29 (d, *J* = 6.7 Hz, 1 H, CH), 6.29 (dd, *J* = 15.8, 6.7 Hz, 1 H, CH), 6.59 (d, *J* = 15.8 Hz, 1 H, CH) 7.07–7.11 (m, 2 H, H_{Ar}), 7.22–7.41 (m, 7 H, H_{Ar}).

^{13}C NMR (100 MHz, CD_2Cl_2): δ = 21. 3 (CH_3), 75.3 (CH), 126.5 (2 CH), 126.6 (2 CH), 127.7 (CH), 128.7 (2 CH), 129.4 (2 CH), 130.3 (CH), 131.0 (CH), 134.0 (C), 137.9 (C), 143.4 (C).

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References

(1) (a) Bianchini, C.; Farnetti, E.; Glendenning, L.; Graziani, M.; Nardin, G.; Peruzzini, M.; Rocchini, E.; Zanobini, F. *Organometallics* **1994**, *14*, 1489. (b) Jeon, J.-S.; Li, H.; García, C.; LaRochelle, L. K.; Walsh, P. J. *J. Org. Chem.* **2005**, *70*, 448. (c) Xie, J.-H.; Liu, S.; Huo, X.-H.; Cheng, X.; Duan, H.-F.; Fan, B.-M.; Wang, L.-X.; Zhou, Q.-L. *J. Org. Chem.* **2005**, *70*, 2967. (d) Noyori, R.; Ohkuma, T. *Angew. Chem. Int. Ed.* **2001**, *40*, 40; *Angew. Chem.* **2001**, *113*, 40. (e) Khai, B. T.; Arcelli, A. *Tetrahedron Lett.* **1996**, *37*, 6599.

(2) (a) Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1988**, *29*, 5645. (b) Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1991**, *32*, 5777.

(3) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071.

(4) (a) Oppolzer, W.; Radinov, R. N. *Helv. Chim. Acta* **1992**, *75*, 10. (b) Oppolzer, W.; Radinov El-Sayed, E. *J. Org. Chem.* **2001**, *66*, 4766.

(5) Dahmen, S.; Bräse, S. *Org. Lett.* **2001**, *25*, 4119.

(6) (a) Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12225. (b) Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 10677. (c) Garcia, C.; Libra, E. R.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 3210. (d) Lurain, A. E.; Carroll, P. J.; Walsh, P. J. *J. Org. Chem.* **2003**, *68*, 1589.

(7) Ji, J.-X.; Qiu, L.-Q.; Yip, C.-W.; Chan, A. S. C. *J. Org. Chem.* **2003**, *68*, 1589.

(8) (a) Shibata, T.; Nakatsui, K.; Soai, K. *Inorg. Chim. Acta* **1999**, *296*, 33. (b) Soai, K.; Takahashi, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1257.

(9) Tseng, S.-L.; Yang, T.-K. *Tetrahedron: Asymmetry* **2005**, *16*, 773.

(10) (a) Sprout, C. M.; Richmond, M. L.; Seto, C. T. *J. Org. Chem.* **2005**, *70*, 7408. (b) Richmond, M. L.; Sprout, C. M.; Seto, C. T. *J. Org. Chem.* **2005**, *70*, 8835.

(11) (a) Wipf, P.; Xu, W. *Tetrahedron Lett.* **1994**, *35*, 5197. (b) Wipf, P.; Xu, W. *Org. Synth.* **1996**, *74*, 205. (c) Wipf, P.; Ribe, S. *J. Org. Chem.* **1998**, *63*, 6454.

(12) Schmidt, F.; Stemmler, R. T.; Rudolph, J.; Bolm, C. *Chem. Soc. Rev.* **2006**, *35*, 454.

(13) (a) Bolm, C.; Rudolph, J. *J. Am. Chem. Soc.* **2002**, *124*, 14850. (b) Rudolph, J.; Schmidt, F.; Bolm, C. *Synthesis* **2005**, 840.

(14) (a) Rudolph, J.; Hermanns, N.; Bolm, C. *J. Org. Chem.* **2004**, *69*, 3997. (b) Rudolph, J.; Lormann, M.; Bolm, C.; Dahmen, S. *Adv. Synth. Catal.* **2005**, *347*, 1361.

(15) Duan, H.-F.; Xie, J.-H.; Shi, W.-J.; Zhang, Q.; Zhou, Q.-L. *Org. Lett.* **2006**, *8*, 1479.

(16) In these studies, the NMR solvent forms a hydrogen bond to the hydroxy group of the product. The thus formed π-complex (see Figure 2) and the additional ring current effect lead to a shift of the NMR signals to higher ppm values.

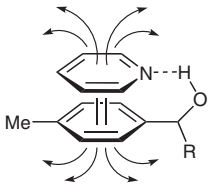

Figure 2

(17) NMR spectra were not recorded in $CDCl_3$ due to decomposition of the product.

(18) Igushi, M.; Doi, H.; Hata, S.; Tomioka, K. *Chem. Pharm. Bull.* **2004**, *52*, 125.

(19) Von Matt, P.; Lloyd-Jones, G. C.; Minidis, A. B. E.; Pfaltz, A.; Macko, L.; Neuburger, M.; Zehnder, M.; Rüegger, H.; Pregosin, P. S. *Helv. Chim. Acta* **1995**, *78*, 265.

(20) Kuroboshi, M.; Tanaka, M.; Kishimoto, S.; Goto, K.; Mochizuki, M.; Tanaka, H. *Tetrahedron Lett.* **2000**, *41*, 81.

(21) Tajbakhsh, M.; Lakouraj, M. M.; Shirini, F.; Habibzadeh, S.; Nikdoost, A. *Tetrahedron Lett.* **2004**, *45*, 3295.

(22) Singh, J.; Kaur, I.; Kaur, J.; Bhalla, A.; Kad, G. L. *Synth. Commun.* **2003**, *33*, 191.