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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 710–716

A structurally simple L-proline derivative promotes the asymmetric allylation of aldehydes with tribromoallyltin

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Received 29 November 2006; accepted 28 February 2007

Abstract—An asymmetric allylation of aldehydes with the allyltin tribromide was achieved using the L-proline derivative as a chiral promoter in dichloromethane in the presence of a Lewis base. Various optically active homoallylic alcohols were obtained in high yields with moderate enatioselectivities of up to 62% ee.

1. Introduction

The catalytic asymmetric allylation of aldehydes is considered as one of the most fundamental and important synthetic operations in asymmetric synthesis,[1,2] with a number of catalytic procedures recently elaborated upon for this purpose.[3–6] However, in previously reported catalytic allylations of aldehydes, allylstannane such as allyltributyltin or tetra-allyltin is usually used. Obviously, there are two drawbacks. The first is a low atomic economy, meaning that the three butyl groups are not completely used for allyltributyltin, and only two allyl groups of the tetra-allyl tin can be employed at best. The second drawback is that the allyltin reagents only act as allyl group donor, the product's enantioselectivity comes mainly from the chiral environment produced by the complex of the additional Lewis acid and chiral ligand.

Over the past few decades, the Barbier-type coupling reaction between allyl halide and carbonyl compounds promoted by low valent metal tin or tin halides has been developed to be an efficient way to prepare homoallylic alcohols, and has received more and more attention due to its suitable activity, low cost and low toxicity of the final inorganic tin derivatives. Such reactions are believed to involve the in situ formation of solvated monoallyltin trihalides or diallyltin dihalides as active allyltin species and subsequent addition of the allyl-Sn bond across the carbonyl function of a range of aldehydes and ketones. Nevertheless, such Barbier-type asymmetric allylation mediated by the metal tin has not been hitherto reported; there are several reports regarding a related Indium-mediated process.[7,8] In respect that the allyltin trihalide is the key intermediate in the Barbier-type coupling reaction mediated by tin dichloride, we herein report the first example of asymmetric allylation of aldehydes promoted by an L-proline derivative in the presence of Lewis base, using the allyltin tribromide, which acts not only as an allyl group donor but also as an intrinsic Lewis acid combining with the chiral ligand. This reaction will hopefully establish groundwork for the Barbier-type asymmetric allylation of aldehydes with organotin reagents.

2. Results and discussion

In our initial study, we investigated the asymmetric allylation of benzaldehyde by using the various L-proline derivatives and some other chiral ligands under the following standardized protocol (Fig. 1 and Table 1).

These compounds **1a**–**1d**, **1e**, **1f**, **1h**, and **1i** were prepared according to the previous literature reports.[9–13] Among the chiral ligands investigated, we found that *N*-alkyl groups of the chiral amino alcohol greatly influenced the enantioselectivity (entries 1–4). In the case of chiral ligand **1e**, the six-coordinated intermediary tin complex was considered to constitute preferential coordination between tin and the nitrogen atom rather than the oxygen atom of

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0957-4166/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tetasy.2007.02.025

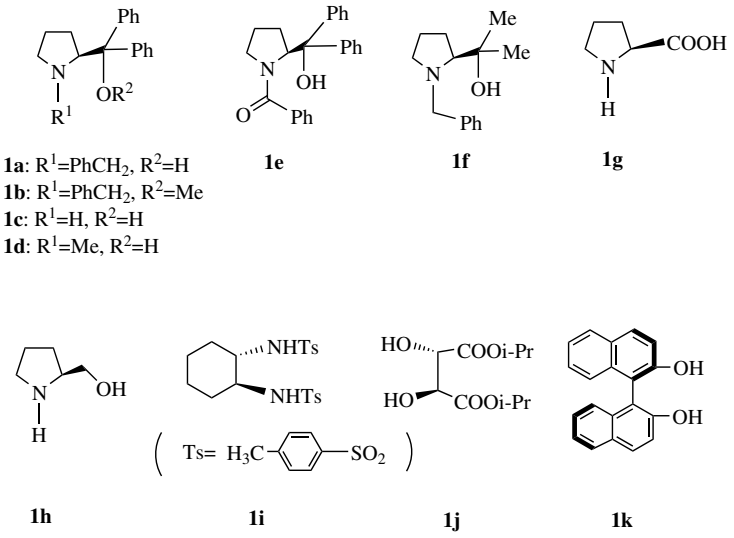
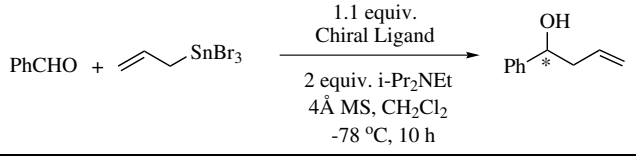


Figure 1. Screening various chiral ligands.

Table 1. Asymmetric allylation of benzaldehyde with tribromoallyltin promoted by various chiral ligands[a]



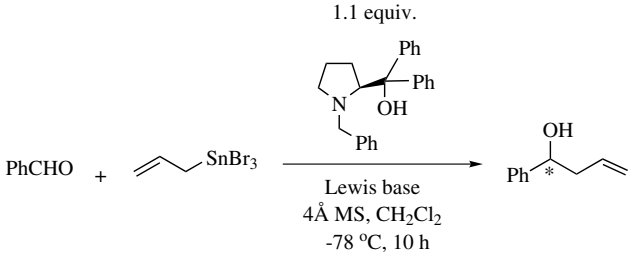
Entry	Ligand*	Yield[b] (%)	ee[c,d] (%)
1	**1a**	75	56 (*R*)
2	**1b**[e]	52	<10 (*R*)
3	**1c**	61	<10 (*R*)
4	**1d**	45	14 (*R*)
5	**1e**[e]	52	0
6	**1f**	65	10 (*S*)
7	**1g**	71	12 (*R*)
8	**1h**	65	16 (*S*)
9	**1i**	69	<10 (*R*)
10	**1j**	28	<10 (*R*)
11	**1k**	56	26 (*R*)

[a] The reactions were run with tribromoallyltin (1 equiv), chiral auxiliary (1.1 equiv), diisopropylethylamine (DIPEA) (2 equiv) in dry dichloromethane at room temperature for 2 h, and followed by adding the benzaldehyde (1 equiv) into the above reaction mixture at −78 °C for 10 h.
[b] Isolated yield of analytically pure product.
[c] Determined by chiral GC analysis.
[d] Absolute configuration determined by comparison of the optical rotation with the literature value.[8]
[e] The reaction was performed within 24 h.

the amide group to form the five-membered chelate ring based on the unchanged IR absorption peak ν (cm^{-1}) value of the carbonyl function of the amide group. When L-prolinol or ((*S*)-1-benzylpyrrolidin-2-yl)dimethylmethanol were used, the homoallylic alcohol was obtained in the contrary configuration, although with low enantiomeric excess (entries 6 and 8). Promoted by the chiral diamine (entry 9) and chiral dialcohol (entries 10 and 11), the reaction was able to proceed smoothly, however, the enantioselectivity decreased. By all appearance, ((*S*)-1-benzylpyrrolidin-2-yl)diphenylmethanol **1a** was the most effective chiral promoter in the allylation of benzaldehyde with tribromoallyltin (Table 1, entry 1).

The effect of the Lewis base on the chemical yield and enantioselectivity was then studied. Some results using ((*S*)-1-benzyl-pyrrolidin-2-yl)diphenylmethanol **1a** as chiral promoter were shown in Table 2. Among the Lewis bases tested, diisopropylethylamine (DIPEA) was optimal and the suitable amount of DIPEA was two equivalents with respect to the aldehyde.

Table 2. Asymmetric allylation of benzaldehyde with tribromoallyltin in the presence of various Lewis bases[a]



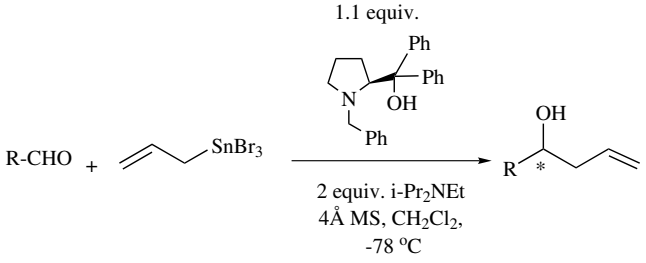
Entry	Lewis base	Amount of LB (equiv)	Yield[b] (%)	ee[c,d] (%)
1	—	—	44	6 (*R*)
2	DIPEA	1	22	2 (*R*)
3	DIPEA	2	75	56 (*R*)
4	Et_3N	2	29	39 (*R*)
5	DBU	2	20	30 (*R*)
6	2,6-Lutidine	2	51	8 (*R*)
7	Pyridine	2	52	2 (*R*)

[a] The reactions were run with tribromoallyltin (1 equiv), chiral auxiliary (1.1 equiv), Lewis base in dry dichloromethane at room temperature for 2 h, and followed by adding the benzaldehyde (1 equiv) into the above reaction mixture at −78 °C for 10 h.
[b] Isolated yield of analytically pure product.
[c] Determined by chiral GC analysis.
[d] Absolute configuration was determined by comparison of the specific rotation with the literature value.[8]

To evaluate the generality of this reaction, using an optimized chiral ligand and Lewis base, we performed the allylation of various aldehydes (Table 3). As can be seen from the summarized results, except for benzaldehyde, other aromatic aldehydes could also be smoothly allylated to give the corresponding optically active homoallylic alcohols with moderate enantioselectivity. Not only aromatic aldehydes but also α,β-unsaturated and aliphatic aldehydes showed moderate reactivity although the enantioselectivity of these aldehydes was relatively low. Upon closer inspection of the data in Table 3, we noticed that aldehydes with a strong electron-donating group at the *para*-position (Table 3, entries 5 and 6) gave a lower enantiomeric excess than those with an electron-withdrawing group in the *para*-position (Table 3, entries 3 and 4, and entries 7 and 8) except for *p*-fluorobenzaldehyde (Table 3, entry 2). With regards to the aromatic aldehydes with substituent at the *ortho*-position, they gave lower yields but higher enantioselectivities than those with the corresponding substituent at the *para*-position (Table 3, entries 11–14 to entries 2–4, 8). This may be due to the larger steric hinderance of *ortho*-position than that of *para*-position. However, *o*-chlorobenzaldehyde was an exception, its ee value was relatively low. Currently, we do not know the reason. As for entries 9 and 16 in Table 3, a strong electron-withdrawing group at the *meta*-position influenced the enantioselectivity especially for entry 16. When using the aromatic aldehyde with a 3,5-substituted electron-donating group, we obtained the homoallylic alcohol in much more lower yield (Table 3, entry 10) but in moderate enantioselectivity. The homoallylic alcohol with considerable yield and moderate enantioselectivity was obtained in the allylation of 2,4-dichlorobenzaldehyde with allyltin tribromide (Table 3, entry 20). Unfortunately, this reaction could not run in the case of the aromatic aldehydes with active hydrogen atoms such as an amino- and hydroxy-group in the *para*-position (Table 3, entries 18 and 19).

With the aim of understanding how the chiral ligand affected the stereochemical outcome of the reaction, we traced the reaction by ^{119}Sn NMR. Due to tin's reactivity, allyltin tribromide may exist not only in monomer but also in polymer. Also owing to its insolubility in $CDCl_3$, we could not directly obtain a satisfactory ^{119}Sn NMR spectra. Therefore, we envisioned another way to study the mechanism by adding a few drop of anhydrous CH_3OH into the nuclear magnetic tube with tribromoallyltin and $CDCl_3$. As a result, there were two peaks in the ^{119}Sn NMR; the

Table 3. Asymmetric allylation of various aldehydes with tribromoallyltin[a]



Entry	*R*	Temp (°C)	Time (h)	Yield[b] (%)	ee[c] (%)	Config.[d]
1	Ph	−78	10	75	56	(*R*)
2	*p*-FC_6H_4	−78	10	59	33	(*R*)
3	*p*-ClC_6H_4	−78	10	78	42	(*R*)
4	*p*-BrC_6H_4	−78	10	72	44	(*R*)
5	*p*-MeC_6H_4	−78	10	57	43	(*R*)
6	*p*-$MeOC_6H_4$	−78	10	40	32	(*R*)
7	*p*-$CF_3C_6H_4$	−78	10	60	47	(*R*)
8	*p*-$NO_2C_6H_4$	−78	10	80	40	(*R*)
9	*m*-ClC_6H_4	−78	10	77	50	(*R*)
10	3-Methoxy-5-hydroxy-C_6H_3	−78	10	30	50	(*R*)
11	*o*-FC_6H_4	−78	10	54	62	(*R*)
12	*o*-ClC_6H_4	−78	10	50	17	(*R*)
13	*o*-BrC_6H_4	−78	10	43	51	(*R*)
14	*o*-$NO_2C_6H_4$	−78	10	65	48[e]	—
15	Ph–CH=CH–	−78	10	62	34	(*R*)
16	*m*-$CF_3C_6H_4$	−78	10	60	13	(*R*)
17	Citral	−78	10	36	51	(*R*)
18	*p*-$NH_2C_6H_4$	−78, rt	10, 12	—	—	—
19	*p*-HOC_6H_4	−78, rt	10, 12	—	—	—
20	2,4-DichloroC_6H_3	−78	10	66	41	(*R*)

[a] The reactions were run with tribromoallyltin (1 equiv), chiral auxiliary (1.1 equiv), diisopropylethylamine (DIPEA) (2 equiv) in dry dichloromethane at room temperature for 2 h, and followed by adding the aldehyde (1 equiv) into the above reaction mixture at −78 °C for 10 h.
[b] Isolated yield of analytically pure product.
[c] Determined by chiral GC analysis.
[d] Absolute configuration was determined by comparison of the specific rotation with the literature value,[8] all others were assigned by analogy.
[e] Absolute configuration was unknown.

chemical shift values were −42.822 ppm, −330.334 ppm, respectively. According to the previous report (allyltin trichloride ^{119}Sn NMR: δ −29.0 ppm),[14] we presumed that chemical shift value of tribromoallyltin was −42.822 ppm and it existed in four coordinate bond form. Another peak is the association of tribromoallyltin and the methanol. Subsequently, tracing our reaction system including chiral ligand, Lewis base, and tribromoallyltin in $CDCl_3$ by ^{119}Sn NMR, the result showed that only one peak was found, and its value was −173.670 ppm. Thus, the reaction was considered to proceed via an active intermediate (Fig. 2, A), which provides a chiral environment for the next step. Continuing to trace our reaction system with the addition of benzaldehyde under the standardized conditions in $CDCl_3$, we found that there was one major peak in ^{119}Sn NMR (−647.500 ppm). Here, the tin was coordinated by the aldehyde and the chiral ligand via a six-membered cyclic transition (Fig. 2, B). In this model, the bulky proline residue effectively blocks one side of the adduct and accommodates the aldehyde better than the sterically more demanding allyl residue as its *trans*-substituent. The proposed model of stereoselection is in agreement with (i) the observed formation of (*R*)-homoallylic alcohols, (ii) the large influence exerted on the stereoselectivity by the presence of the benzyl substituent on the nitrogen atom of the prolinol derivative (as above mentioned in Table 1). As a whole, the mechanism of chiral ligand [(*S*)-1-benzylpyrrolidin-2-yl]diphenylmethanol **1a** promoted allylation of an aldehyde with tribromoallyltin has not been fully elucidated at this stage.

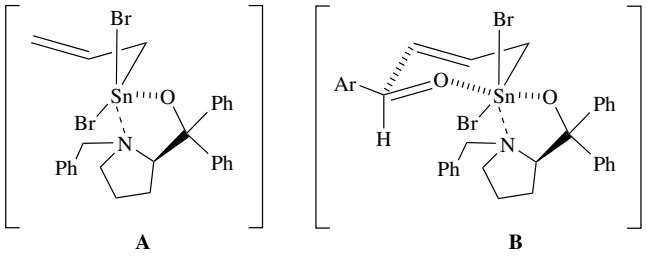


Figure 2. Proposed reaction transition states.

3. Conclusion

In conclusion, different protocols for the enatioselective addition of tribromoallyltin to aromatic aldehydes in the presence of amino alcohols derived from L-proline have been studied. This may establish the groundwork for the Barbier-type asymmetric allylation of aldehydes with organotin reagents. Work is in process in our research group.

4. Experimental

4.1. General procedure

All reactions were performed under a dry nitrogen atmosphere using standard Schlenk techniques. Dichloromethane was distilled from CaH_2; commercially available $SnBr_4$ was stored under a nitrogen atmosphere; $CDCl_3$ was stored over molecular sieves 4 Å. Analytical thin layer chromatography (TLC) was performed using Merck 60 F_{254} precoated silica gel plate. Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with acidic solution of ceric molybdate, followed by heating on a hot plate. Column chromatography was conducted with 200–300 mesh silica gel. ^{1}H NMR spectra were recorded on 400 MHz spectrometers. Chemical shifts of ^{1}H NMR spectra were reported relative to tetramethylsilane (δ 0) or chloroform (δ 7.26). Splitting patterns are indicated as s, singlet; d, double; t, triplet; q, quartet; m, multiplet; br, broad. Analytical gas chromatography was done using a Supelco beta-cyclodextrin 120 chiral GC column (30 m × 0.25 mm). Optical rotations were measured on a polarimeter. Tribromoallyltin was prepared by a redistribution reaction, which was carried out between diallyltin dibromide and tin tetrabromide in neat.

4.2. Synthesis

4.2.1. Preparation of dibromodiallyltin ($(CH_2{=}CHCH_2)_2SnBr_2$). To an oven dried 250 ml four-necked flask equipped with a magnetic stirring bar, a reflux condenser and a thermometer were added 150 ml toluene, tin powder (17.8 g, 0.15 mol) and $HgCl_2$ (0.5 g, 0.002 mol). The mixture was refluxed for 30 min, then cooled to room temperature, adding triethylamine (0.275 ml) into the resulting suspension, again heating until refluxing, and dropping 1-bromopropene (18.2 g, 0.15 mol) within 30 min. After dropping, the mixture was continued to reflux for 3 h. At last, the reaction mixture was cooled to room temperature, filtered, and concentrated in vacuo. The residual crude product was distilled under reductive pressure and resulted in 19.5 g of a slight yellow colored oil: bp 70–72 °C/0.5 mm Hg, Yield 72%. The oil was analyzed by ^{1}H NMR.

4.2.2. Preparation of allyltin tribromide ($CH_2{=}CHCH_2SnBr_3$). To the above prepared diallyltin dibromide(10.83 g, 30 mmol) in an oven dried Schlenk flask, $SnBr_4$ (13.15 g, 30 mmol) was added, the reaction mixture carried out in neat at room temperature for 4 h. A two-fold amount product (allyltin tribromide) was obtained (yield 100%). ^{1}H NMR ($CDCl_3$): δ 3.25–3.27 (d, 2H, J_{HSn} = 108 Hz, CH_2–Sn), 5.31–5.55 (m, 2H, CH_2), 5.91–6.0 (m, 1H, CH). Since allyltin tribromide was not soluble in the $CDCl_3$, the concentration of allyltin tribromide was too low to obtain satisfactory ^{13}C and ^{119}Sn NMR spectra.

4.2.3. Preparation of ((*S*)-1-benzylpyrrolidin-2-yl)diphenylmethanol 1a. ((*S*)-1-Benzylpyrrolidin-2-yl)diphenylmethanol **1a** was prepared according to the previous literature.[9] Yield 70%, mp 115–116 °C, $[\alpha]_D^{20} = +95$ (*c* 1, $CHCl_3$) (literature: mp 113–115 °C, yield 75%, $[\alpha]_D^{24} = +76.2$ (*c* 1.6, CH_2Cl_2)); ^{1}H NMR ($CDCl_3$): δ 1.56–1.78 (m, 3H), 1.92–2.02 (m, 1H), 2.32–2.38 (m, 1H), 2.89–2.94 (m, 1H), 3.01–3.04 (d, J = 12 Hz, 1H, PhCH_2), 3.21–3.24 (d, J = 12 Hz, 1H, PhCH_2), 3.96–3.99 (m, 1H), 4.93 (s, 1H, *OH*), 7.03–7.73 (m, 15H).

4.3. General procedure for asymmetric allylation of aldehydes with allyltin tribromide promoted by ((*S*)-1-benzylpyrrolidin-2-yl)diphenymethanol 1a

A mixture of L-proline derivative **1a** (189 mg, 0.55 mmol), tribromoallyltin (200 mg, 0.5 mmol), diisopropylethylamine (DIPEA) (129 mg, 1 mmol) and 4 Å MS was dissolved in dry DCM (3 ml) under a nitrogen atmosphere and stirred at room temperature for 2 h. To the resulting solution was added the aldehyde (0.5 mmol) at −78 °C. The mixture was stirred for another 10 h at this temperature. A saturated $NaHCO_3$ aqueous solution was added to quench the reaction at ambient temperature. The aqueous layer was extracted with DCM (3 × 10 ml) and the combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated in vacuo after filtration. The residual crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum as the eluant) to afford the desired optically active homoallylic alcohol.

4.3.1. (*R*)-(+)-1-Phenyl-3-buten-1-ol (entry 1 in Table 3). $[\alpha]_D^{20} = +22.3$ (*c* 2, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.02 (s, 1H, O*H*), 2.52 (t, $J = 8$ Hz, 2H), 4.74 (t, $J = 7.6$ Hz, 1H), 5.14–5.20 (m, 2H), 5.77–5.87 (m, 1H), 7.27–7.37 (m, 5H); enantiomeric excess was determined to be 56% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 40.43 min, and t_R for the (*S*)-alcohol = 40.88 min. The absolute stereochemistry was determined by comparison of the sign of the specific rotation with reported literature values.[8]

4.3.2. (*R*)-(+)-1-(*p*-Fluorophenyl)-3-buten-1-ol (entry 2 in Table 3). $[\alpha]_D^{20} = +21.5$ (*c* 2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 1H, O*H*), 2.46–2.52 (m, 2H), 4.71 (t, $J = 5.6$ Hz, 1H), 5.13–5.19 (m, 2H), 5.72–5.88 (m, 1H), 7.03–7.09 (m, 2H), 7.29–7.37 (m, 2H); enantiomeric excess was determined to be 33% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 41.67 min, and t_R for the (*S*)-alcohol = 42.49 min. The absolute stereochemistry was determined by comparison of the sign of optical rotation with reported literature values.[8]

4.3.3. (*R*)-(+)-1-(*p*-Chlorophenyl)-3-buten-1-ol (entry 3 in Table 3). $[\alpha]_D^{20} = +15.5$ (*c* 2.4, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 1H, O*H*), 2.43–2.45 (m, 2H), 4.68 (t, $J = 4.4$ Hz, 1H), 5.08–5.14 (m, 2H), 5.71–5.79 (m, 1H), 7.20–7.32 (m, 4H); enantiomeric excess was determined to be 42% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 62.04 min, and t_R for the (*S*)-alcohol = 62.89 min. The absolute stereochemistry was determined by comparison of the sign of the specific rotation with reported literature values.[8]

4.3.4. (*R*)-(+)-1-(*p*-Bromophenyl)-3-buten-1-ol (entry 4 in Table 3). $[\alpha]_D^{20} = +12.6$ (*c* 3.5, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 1H, O*H*), 2.41–2.46 (m, 2H), 4.66 (m, 1H), 5.12–5.16 (m, 2H), 5.71–5.81 (m, 1H), 7.18–7.28 (m, 4H); enantiomeric excess was determined to be 44% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 69.41 min, and t_R for the (*S*)-alcohol = 70.23 min. The absolute stereochemistry was determined by comparison of the sign of the specific rotation with reported literature values.[8]

4.3.5. (*R*)-(+)-1-(*p*-Methylphenyl)-3-buten-1-ol (entry 5 in Table 3). $[\alpha]_D^{20} = +15.5$ (*c* 2, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (d, $J = 3.2$ Hz, 1H, O*H*), 2.34 (s, 3H), 2.48–2.52 (m, 2H), 4.70 (t, $J = 8$ Hz, 1H), 5.12–5.18 (m, 2H) 5.76–5.86 (m, 1H), 7.16 (d, $J = 8$ Hz, 2H), 7.25 (d, $J = 8$ Hz, 2H); enantiomeric excess was determined to be 43% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 47.42 min, and t_R for the (*S*)-alcohol = 48.18 min. The absolute stereochemistry was determined by comparison of the sign of optical rotation with reported literature values.[8]

4.3.6. (*R*)-(+)-1-(*p*-Methoxyphenyl)-3-buten-1-ol (entry 6 in Table 3). $[\alpha]_D^{20} = +15.4$ (*c* 1.6, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 1H, O*H*), 2.47–2.50 (m, 2H), 3.80 (d, $J = 3.2$ Hz, 3H), 4.67 (t, $J = 6$ Hz, 1H), 5.10–5.16 (m, 2H), 5.76–5.82 (m, 1H), 6.86–6.89 (dd, $J = 3.2$ Hz and 3.2 Hz, 2H), 7.25–7.28 (dd, $J = 2.8$ Hz and 3.2 Hz, 2H); enantiomeric excess was determined to be 32% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 63.11 min, and t_R for the (*S*)-alcohol = 63.69 min. The absolute stereo-chemistry was determined by comparison of the sign of the specific rotation with reported literature values.[8]

4.3.7. (*R*)-(+)-1-(*p*-Trifluorophenyl)-3-buten-1-ol (entry 7 in Table 3). $[\alpha]_D^{20} = +14.2$ (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 1H, O*H*), 2.42–2.58 (m, 2H), 4.81 (t, $J = 3.6$ Hz, 1H), 5.17–5.21 (m, 2H), 5.74–5.85 (m, 1H), 7.48 (d, $J = 8$ Hz, 2H), 7.61 (d, $J = 8$ Hz, 2H); enantiomeric excess was determined to be 47% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 39.54 min, and t_R for the (*S*)-alcohol = 40.87 min. The absolute stereochemistry was determined by comparison of the sign of specific rotation with reported literature values.[8]

4.3.8. (*R*)-(+)-1-(*p*-Nitrophenyl)-3-buten-1-ol (entry 8 in Table 3). $[\alpha]_D^{20} = +12.9$ (*c* 3.5, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41–2.53 (m, 2H), 2.63 (s, 1H, O*H*), 4.83 (t, $J = 3.2$ Hz, 1H), 5.11–5.15 (m, 2H), 5.69–5.80 (m, 1H), 7.48–7.50 (d, $J = 8$ Hz, 2H), 8.13–8.15 (d, $J = 8$ Hz, 2H); enantiomeric excess was determined to be 40% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol =

93.37 min, and t_R for the (*S*)-alcohol = 93.97 min. The absolute stereochemistry was determined by comparison of the sign of the specific rotation with reported values.[8]

4.3.9. (*R*)-(+)-1-(*m*-Chlorophenyl)-3-buten-1-ol (entry 9 in Table 3). $[\alpha]_D^{20} = +18.3$ (*c* 2, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 1H, O*H*), 2.44–2.50 (m, 2H), 4.70 (t, $J = 3.2$ Hz, 1H), 5.14–5.19 (m, 2H), 5.74–5.83 (m, 1H), 7.21–7.35 (m, 4H); enantiomeric excess was determined to be 50% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 58.50 min, and t_R for the (*S*)-alcohol = 59.15 min. To our knowledge, this compound has no standard specific rotation value.

4.3.10. (*R*)-(+)-1-(3-Methoxy-5-hydroxyphenyl)-3-buten-1-ol (entry 10 in Table 3). $[\alpha]_D^{20} = +1.2$ (*c* 1.2, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.0 (s, 1H, O*H*), 2.48–2.51 (m, 2H), 3.90 (s, 3H), 4.65–4.69 (m, 1H), 5.13–5.19 (m, 2H), 5.59 (s, 1H, OH), 5.77–5.84 (m, 1H), 6.83–6.94 (m, 3H), 7.29–7.37 (m, 2H); enantiomeric excess was determined to be 50% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 56.56 min, and t_R for the (*S*)-alcohol = 56.98 min. To our knowledge, this compound has no standard optical rotation value.

4.3.11. (*R*)-(+)-1-(*o*-Fluorophenyl)-3-buten-1-ol (entry 11 in Table 3). $[\alpha]_D^{20} = +37.8$ (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (d, $J = 4$ Hz, 1H, O*H*), 2.45–2.53 (m, 1H), 2.56–2.63 (m, 1H), 5.05–5.09 (m, 1H), 5.15–5.20 (m, 2H), 5.78–5.88 (m, 1H), 7.02–7.28 (m, 3H), 7.46–7.50 (ddd, $J = 1.6$ Hz, 2 Hz, and 2 Hz, 1H); enantiomeric excess was determined to be 62% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 39.06 min, and t_R for the (*S*)-alcohol = 39.25 min. The absolute stereochemistry was determined by comparison of the sign of optical rotation with reported literature values.[8]

4.3.12. (*R*)-(+)-1-(*o*-Chlorophenyl)-3-buten-1-ol (entry 12 in Table 3). $[\alpha]_D^{20} = +21.2$ (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 1H, O*H*), 2.34–2.42 (m, 1H), 2.61–2.67 (m, 1H), 5.15–5.23 (m, 3H), 5.82–5.93 (m, 1H), 7.19–7.36 (m, 3H), 7.56–7.58 (d, $J = 7.6$ Hz, 1H); enantiomeric excess was determined to be 17% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 54.27 min, and t_R for the (*S*)-alcohol = 54.79 min. To the best of our knowledge, this compound has no standard optical rotation value.

4.3.13. (*R*)-(+)-1-(*o*-Bromophenyl)-3-buten-1-ol (entry 13 in Table 3). $[\alpha]_D^{20} = +50.5$ (*c* 2.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 1H, O*H*), 2.31–2.38 (m, 1H), 2.62–2.65 (m, 1H), 5.10 (t, $J = 3.2$ Hz, 1H), 5.17–5.22 (m, 2H), 5.82–5.93 (m, 1H), 7.11–7.14 (m, 1H), 7.31–7.35 (m, 1H), 7.50–7.56 (m, 2H); enantiomeric excess was determined to be 51% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 63.92 min, and t_R for the (*S*)-alcohol = 64.80 min. To our knowledge, this compound has no standard optical rotation value.

4.3.14. (*S*)-(−)-1-(*o*-Nitrophenyl)-3-buten-1-ol (entry 14 in Table 3). $[\alpha]_D^{20} = -37.1$ (*c* 2.9, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35–2.46 (m, 2H), 2.70–2.74 (m, 1H, O*H*), 5.19–5.24 (m, 2H), 5.31–5.34 (m, 1H), 5.85–5.96 (m, 1H), 7.41–7.45 (t, $J = 8$ Hz, 1H), 7.64–7.68 (t, $J = 8$ Hz, 1H), 7.83–7.85 (d, $J = 8$ Hz, 1H), 7.93–7.95 (d, $J = 8$ Hz, 1H); enantiomeric excess was determined to be 48% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, $t_R = 93.37$ min, 93.97 min respectively. To our knowledge, this compound has no standard specific rotation value.

4.3.15. (*R*,*E*)-1-Phenylhexa-1,5-dien-3-ol (entry 15 in Table 3). $[\alpha]_D^{20} = +12.9$ (*c* 3.5, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 1H, O*H*), 2.40–2.48 (m, 2H), 4.38 (t, $J = 6$ Hz, 1H), 5.18–5.23 (m, 2H), 5.83–5.93 (m, 1H), 6.23–6.29 (dd, $J = 6.4$ Hz and 6.4 Hz, 1H), 6.60–6.64 (d, $J = 15.6$ Hz, 1H), 7.32–7.41 (m, 5H), 8.13–8.15 (d, $J = 8$ Hz, 2H); enantiomeric excess was determined to be 34% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 93.37 min, and t_R for the (*S*)-alcohol = 93.97 min. The absolute stereochemistry was determined by comparison of the sign of the specific rotation with reported literature values.[3]

4.3.16. (*S*)-(−)-1-(*m*-Trifluorophenyl)-3-buten-1-ol (entry 16 in Table 3). $[\alpha]_D^{20} = +7.8$ (*c* 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 1H, *OH*), 2.42–2.55 (m, 2H), 4.78 (m, 1H), 5.16–5.19 (m, 2H), 5.74–5.84 (m, 1H), 7.44–7.63 (m, 4H); enantiomeric excess was determined to be 13% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 36.25 min, and t_R for the (*S*)-alcohol = 36.95 min. To our knowledge, this compound has no standard specific rotation value.

4.3.17. (*R*,*E*)-7,11-Dimethyldodeca-1,6,10-trien-4-ol (entry 17 in Table 3). $[\alpha]_D^{20} = +12.9$ (*c* 3.5, benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60–1.73 (m, 9H), 2.03–2.27 (m, 6H), 4.09–4.14 (q, $J = 6.8$ Hz, 7.2 Hz, and 7.2 Hz, 1H), 4.35–4.44 (m, 1H), 5.09–5.20 (m, 3H), 5.75–5.86 (m, 1H), 7.48–7.50 (d, $J = 8$ Hz, 2H), 8.13–8.15 (d, $J = 8$ Hz, 2H); enantiomeric excess was determined to be 51% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 93.37 min, and t_R for the (*S*)-alcohol = 93.97 min. To our knowledge, this compound has no standard optical rotation value.

4.3.18. (*R*)-(+)-1-(2,4-Dichlorophenyl)-3-buten-1-ol (entry 20 in Table 3). $[\alpha]_D^{20} = +42.5$ (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28–2.35 (m, 2H), 2.57 (s, 1H,

O*H*), 5.06–5.08 (m, 1H), 5.15–5.19 (m, 2H), 5.79–5.84 (m, 1H), 7.24–7.49 (m, 3H); enantiomeric excess was determined to be 41% by chiral GC analysis (Supelco β-DEX 120 column). GC conditions: oven 100 °C for 5 min, then 1 deg/min to 200 °C, 10 min at that temperature, t_R for the (*R*)-alcohol = 69.67 min, and t_R for the (*S*)-alcohol = 71.15 min. To our knowledge, this compound has no standard specific rotation value.

Acknowledgments

This work was supported by the NSFC (20372033) and the Nankai University.

References

1. Reviews: (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1993, p 1; (b) Maruoka, K.; Yamamoto, H. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; p 413; (c) Mikami K. In *Advance in Catalytic Process*; Doyle, M. P., Ed.; JAI: Greenwich, 1995, p 1; (d) Hoveyda, A. H.; Morken, J. P. *Angew. Chem., Int. Ed.* **1996**, *35*, 1262–1284; (e) Yanagisawa, A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; p 965; (f) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; p 299; (g) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; p 403.
2. (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293; (b) Hoppe, D.; Roush, W. R.; Thomas, E. J. In Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thomas in Stereoselective Synthesis; Thieme: Stuttgart, 1996; Vol. 3, p 1357.
3. CAB complex: (a) Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561–562; (b) Marshall, J. A.; Tang, Y. *Synlett* **1992**, 653–654; (c) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490–11495.
4. BINOL/Ti(IV) complex: (a) Aoki, S.; Mikami, K.; Terada, M.; Nakai, T. *Tetrahedron* **1993**, *49*, 1783–1790; (b) Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001–7002; (c) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467–8468; (d) Keck, G. E.; Geraci, L. S. *Tetrahedron Lett.* **1993**, *34*, 7827–7828; (e) Keck, G. E.; Krishnamurthy, D.; Grier, M. C. *J. Org. Chem.* **1993**, *58*, 6543–6544; (f) Keck, G. E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett.* **1994**, *35*, 8323–8326; (g) Faller, J. W.; Sams, D. W.; Liu, X. *J. Am. Chem. Soc.* **1996**, *118*, 1217–1218; (h) Gauthier, D. R., Jr.; Carreira, E. M. *Angew. Chem., Int. Ed.* **1996**, *35*, 2363–2365; (i) Weigand, S.; Brückner, R. *Chem. Eur. J.* **1996**, *2*, 1077–1084; (j) Yu, C.-M.; Choi, H.-S.; Jung, W.-H.; Lee, S.-S. *Tetrahedron Lett.* **1996**, *37*, 7095–7098; (k) Yu, C.-M.; Choi, H.-S.; Jung, W.-H.; Kim, H.-J.; Shin, J. *Chem. Commun.* **1997**, 761–762; (l) Yu, C.-M.; Choi, H.-S.; Yoon, S.-K.; Jung, W.-H. *Synlett* **1997**, 889–890; (m) Marshall, J. A. *Chemtracts* **1997**, *10*, 649; (n) Keck, G. E.; Yu, T. *Org. Lett.* **1999**, *1*, 289–292; (o) Brenna, E.; Scaramelli, L.; Serra, S. *Synlett* **2000**, 357–358.
5. BINAP/AgOTf complex: Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 4723–4724.
6. Bis(oxazoline)/Zn(II) or Rh(II) complex: (a) Cozzi, P. G.; Orioli, P.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron Lett.* **1997**, *38*, 145–148; (b) Motoyama, Y.; Narusawa, H.; Nishiyama, H. *Chem. Commun.* **1999**, 131–132.
7. (a) Loh, T.-P.; Zhou, J.-R.; Yin, Z. *Org. Lett.* **1999**, *1*, 1855–1857; (b) Loh, T.-P.; Zhou, J.-R.; Li, X.-R. *Tetrahedron Lett.* **1999**, *40*, 9333–9336; For an asymmetric Reformatsky reaction using indium and cinchonidine see: (c) Johar, P. S.; Araki, S.; Batsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1992**, 711–713.
8. Lacie, C.; Hirayama, S. G.; Daniel, K.; Derek, S.; Kelly, D.; Bakthan, S. *Tetrahedron Lett.* **2005**, *46*, 2315–2318.
9. Bucher, V. C. B.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1995**, *78*, 935–947.
10. Kanth, J. V. B.; Periasamy, M. *Tetrahedron* **1993**, *49*, 5127–5132.
11. Xu, Q. Y.; Zhu, G. M.; Pan, X. F.; Albert, S. C. C. *Chirality* **2002**, *14*, 716–723.
12. Mckennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568–3571.
13. Guo, C.; Qiu, J.; Zhang, X. M.; Verdugo, D.; Larter, M. L.; Christie, R.; Kenney, P.; Waish, P. J. *Tetrahedron* **1997**, *53*, 4145–4158.
14. Thoonen, S.; Deelman, B. J.; Koten, G. V. *Tetrahedron* **2003**, *59*, 10261–10268.