Tetrahedron: *Asymmetry* 19 (2008) 2058–2062

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# Bifunctional chiral phosphine-containing Lewis base catalyzed asymmetric Morita–Baylis–Hillman reaction of aldehydes with activated alkenes

Zhi-Yu Lei [a], Xu-Guang Liu [a], Min Shi [a,b,*], Meixin Zhao [a]

[a] *School of Chemistry and Molecular Engineering, East China University of Science and Technology, Laboratory for Advanced Materials and Institute of Fine Chemicals, 130 Mei Long Road, Shanghai 200237, China*

[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*

ARTICLE INFO

*Article history:*
Received 8 July 2008
Accepted 6 August 2008

ABSTRACT

A series of novel bifunctional chiral phosphine-containing Lewis bases were synthesized and successfully applied to the asymmetric Morita–Baylis–Hillman reaction of aldehydes with methyl vinyl ketone (MVK) and ethyl vinyl ketone (EVK) to give the corresponding adducts in moderate yields and enantioselectivities under mild reaction conditions.

© 2008 Elsevier Ltd. All rights reserved.

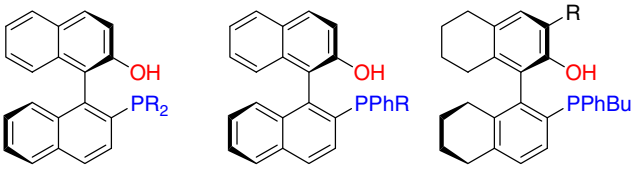
## 1. Introduction

The asymmetric Morita–Baylis–Hillman (MBH) reaction is one of the most useful and attractive C–C bond-forming reactions to give enantiomerically enriched β-hydroxy carbonyl compounds bearing an α-alkylidene group, which are valuable building blocks in the synthesis of medicinally relevant compounds.[1] Due to the great potential of the products and the mild reaction conditions, the catalytic asymmetric version of this reaction has attracted considerable interest and undergone remarkable progress in recent years.[2] However, the asymmetric MBH reaction is often hampered by a low reaction rate and limited substrate generality because the reaction outcome is highly sensitive to the substitutions at both the aldehydes (electrophiles) and Michael acceptors. For example, the MBH reaction of aldehydes with methyl vinyl ketone (MVK) is still in its infancy, and satisfactory reaction outcomes are rare.[3] Therefore, the design and synthesis of efficient organocatalysts for the MBH reaction of aldehydes with MVK still remain a great challenge for organic chemists.

Recently, we have reported that optically active 2′-(alkylphenylphosphinyl)-[1,1′]binaphthalenyl-2-ols are highly effective chiral organocatalysts in the catalytic asymmetric aza-MBH reaction of N-sulfonated imines with MVK to give the corresponding products in excellent yields and with moderate to good ees within 1–5 h.[4] In order to further optimize the catalytic asymmetric MBH reaction catalyzed by chiral phosphine-containing Lewis bases, we now wish to report that these chiral organocatalysts are also fairly effective in the MBH reaction of aldehydes with MVK and ethyl vinyl ketone (EVK), affording the corresponding adducts in moderate yields and enantioselectivities under mild reaction conditions.

## 2. Results and discussion

These newly synthesized chiral phosphine-containing Lewis bases **L1**–**L10** are shown in Figure 1. They can be prepared easily by reduction of the corresponding phosphane oxides[5] in the presence of $Et_3N$ and $HSiCl_3$.[4,6] The chirality at phosphorus atom is lost during reduction of the phosphane oxide. A pair of inseparable diastereoisomers (diastereoisomeric ratio is about 1:1) were acquired and used for the asymmetric MBH reaction.




**L1**: R = Ph
**L2**: R = Bu

**L3**: R = Et
**L4**: R = *i*Pr
**L5**: R = Bu
**L6**: R = Cy
**L7**: R = *i*Bu

**L8**: R = H
**L9**: R = Ph
**L10**: R = Br

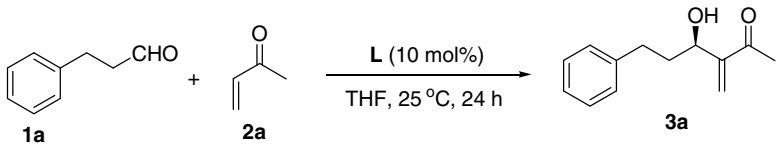
**Figure 1.** Chiral phosphine-containing Lewis base catalysts **L1**–**L10**.

Initial examinations using 3-phenylpropanal **1a** and MVK **2a** as the substrates for the asymmetric MBH reaction in tetrahydrofuran (THF) in the presence of chiral phosphine-containing Lewis bases **L1**–**L10** were aimed at determining the most efficient catalyst in this reaction, and the results of these experiments are summarized in Table 1. Chiral phosphine-containing Lewis base **L1** did not show any catalytic activity in this reaction (Table 1, entry 1). Using **L2** as

* Corresponding author.
*E-mail address:* Mshi@mail.sioc.ac.cn (M. Shi).

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.08.019

**Table 1**
Optimization of the reaction conditions of the catalytic asymmetric MBH reaction of 3-phenylpropanal **1a** with methyl vinyl ketone **2a**




**1a** + **2a** → **3a**

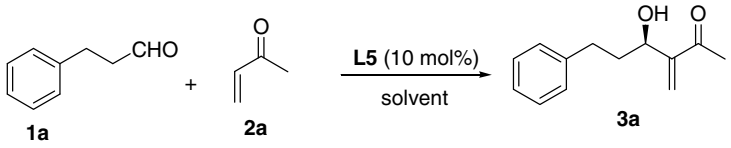
| Entry | L | Time (h) | Yield[a] (%) | ee[b] (%) | Absolute configuration |
|---|---|---|---|---|---|
| 1 | **L1** | 48 | — | | |
| 2 | **L2** | 36 | 58 | 9 | (*R*) |
| 3 | **L3** | 24 | 85 | 53 | (*R*) |
| 4 | **L4** | 24 | 46 | 38 | (*R*) |
| 5 | **L5** | 24 | 86 | 55 | (*R*) |
| 6 | **L6** | 24 | 51 | 34 | (*R*) |
| 7 | **L7** | 24 | 80 | 46 | (*R*) |
| 8 | **L8** | 18 | 93 | 51 | (*R*) |
| 9 | **L9** | 36 | 50 | 17 | (*R*) |
| 10 | **L10** | 24 | 87 | 40 | (*R*) |
| 11 | $PPh_2Me$ | 48 | 17 | | |
| 12[c] | $PPh_2Me$ | 18 | 78 | | |

[a] Isolated yields.
[b] Determined by chiral HPLC.
[c] 10 mol % of 3-nitrophenol was added.

the catalyst, the corresponding adduct **3a** was obtained in 58% yield and 9% ee in THF at 25 °C (Table 1, entry 2). Under similar conditions, chiral phosphine-containing Lewis base **L3** bearing an ethyl and a phenyl group on the phosphorus atom resulted in the corresponding adduct **3a** in 85% yield and 53% ee as an (*R*)-configuration on the basis of the sign of specific rotations when compared with the literature value[3b,d,f,7a,e] (Table 1, entry 3). Hereby, organocatalysts **L4**–**L7**, which are structurally very similar to **L3** were examined under identical conditions. The more sterically encumbered **L4**, **L6** and **L7** did not show any improvement on the enantioselectivity, providing **3a** in 38% ee, 34% ee and 46% ee as an (*R*)-configuration, respectively (Table 1, entries 4, 6 and 7). It was found that chiral phosphine-containing Lewis base **L5** resulted in the corresponding MBH adduct **3a** in 86% yield and 55% ee after 24 h at room temperature (Table 1, entry 5). Moreover, the chiral $H_8$-BINOL derived phosphine-containing Lewis bases **L8** produced the adduct **3a** in 93% yield and 51% ee within 18 h under the standard conditions (Table 1, entry 8). However, the catalytic activity decreased when using **L9** as the catalyst in which a phenyl was introduced into the *ortho*-position of the phenolic hydroxy group (Table 1, entry 9). Using **L10** as the catalyst, the yield and enantioselectivity of **3a** dropped slightly (Table 1, entry 10). These results suggest that the steric bulkiness of these catalysts plays a crucial role for this asymmetric catalytic process. It should be noted that using diphenylmethylphosphine ($PPh_2Me$) as the catalyst afforded the corresponding adduct **3a** in only 17% yield after 48 h without any additive, whereas in the presence of 10 mol % of 3-nitrophenol, compound **3a** was provided in 78% yield within 18 h, suggesting that a phenol group is essential for this reaction (Table 1, entries 11 and 12).

Using **L5** as a catalyst, we next carefully examined the solvent effect on this reaction. The results are outlined in Table 2, and THF was found to be the best solvent in terms of both yield and ee of **3a** (Table 1, entry 5 and Table 2, entries 1–5). Using *N*,*N*-dimethylformamide (DMF) as the solvent, **3a** was obtained in 54% ee, but, the reaction time was prolonged for 36 h, affording **3a** in lower yield (30% yield) (Table 2, entry 5). In dichloromethane, **3a** was not formed (Table 2, entry 1) and in acetonitrile, toluene or ether, **3a** was obtained in 56–88% yields and 4–38% ees as an (*R*)-configuration under identical conditions (Table 2, entries 2–4).

**Table 2**
Optimization of the reaction conditions for the catalytic asymmetric MBH reaction of 3-phenylpropanal **1a** with MVK **2a**

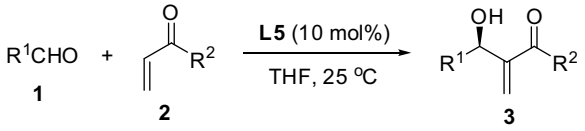


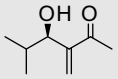
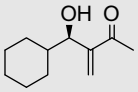
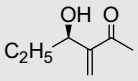
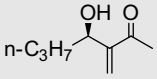
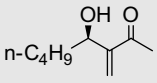
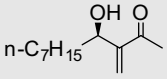
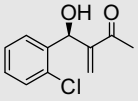
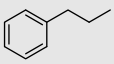
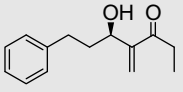

**1a** + **2a** → **3a**

| Entry | Temperature (°C) | Solvent | Time (h) | Yield[a] (%) | ee[b] (%) | Absolute configuration |
|---|---|---|---|---|---|---|
| 1 | 25 | $CH_2Cl_2$ | 48 | — | | |
| 2 | 25 | MeCN | 24 | 76 | 25 | (*R*) |
| 3 | 25 | PhMe | 36 | 56 | 4 | (*R*) |
| 4 | 25 | $Et_2O$ | 36 | 88 | 38 | (*R*) |
| 5 | 25 | DMF | 36 | 30 | 54 | (*R*) |
| 6 | 0 | THF | 36 | 85 | 49 | (*R*) |
| 7 | 50 | THF | 18 | 82 | 53 | (*R*) |
| 8[c] | 25 | THF | 18 | 98 | 45 | (*R*) |
| 9[d] | 25 | THF | 36 | 74 | 56 | (*R*) |

[a] Isolated yields.
[b] Determined by chiral HPLC.
[c] 1.0 equiv of $H_2O$ was added.
[d] 4 Å MS were added.

**Table 3**
Asymmetric MBH reaction of various aldehydes **1** with activated olefins **2** catalyzed by **L5**




| Entry | $R^1$ | $R^2$ | Product | Time (h) | Yield[a] (%) **3** | ee[b] (%) **3** |
|---|---|---|---|---|---|---|
| 1 |  | Me |  **3b** | 24 | 77 | 51 |
| 2 |  | Me |  **3c** | 24 | 78 | 50 |
| 3 | $C_2H_5$– | Me |  **3d** | 24 | 77 | 28 |
| 4 | *n*-$C_3H_7$– | Me |  **3e** | 24 | 70 | 38 |
| 5 | *n*-$C_4H_9$– | Me |  **3f** | 24 | 65 | 40 |
| 6 | *n*-$C_7H_{15}$– | Me |  **3g** | 24 | 68 | 42 |
| 7 |  | Me |  **3h** | 24 | 75 | 29 |
| 8 |  | Et |  **3i** | 30 | 76 | 44 |

[a] Isolated yields.
[b] Determined by chiral HPLC.

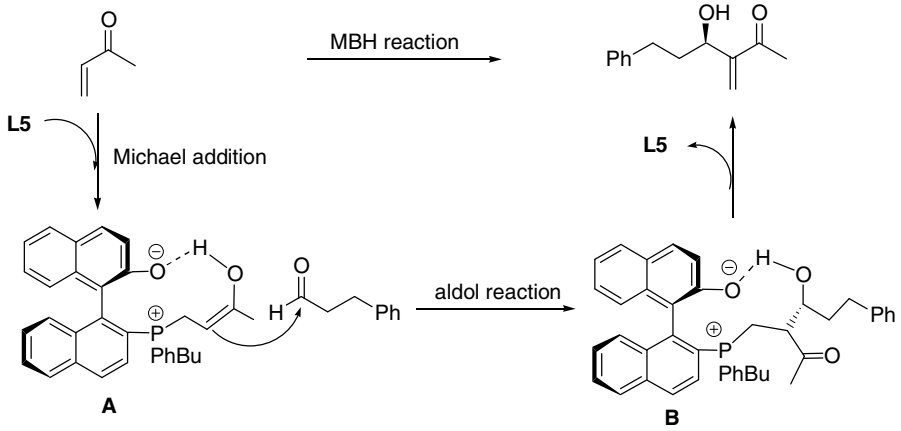
The examination of temperature revealed that no significant improvement upon yield and enantioselectivity of **3a** could be realized at either 50 °C or 0 °C, respectively (Table 2, entries 6 and 7). Adding 1.0 equiv of $H_2O$ into the reaction system afforded **3a** in nearly quantitative yield and 45% ee within 18 h at 25 °C, suggesting that water may take part in intermolecular hydrogen bonding to accelerate the reaction rate (Table 2, entry 8). When 4 Å MS (200 mg) were added into the reaction system to remove the ambient moisture, the yield of **3a** decreased to 74% along with 56% ee after a prolonged reaction time (Table 2, entry 9). Based on the above results, we established the optimal reaction conditions: using 10 mol % of **L5** as the catalyst and THF as the solvent to perform the reaction at 25 °C.

To investigate the scope and limitations of this catalytic asymmetric MBH reaction of aldehydes with MVK and ethyl vinyl ketone (EVK), we examined a variety of aldehydes under the optimized conditions. The results are summarized in Table 3. All reactions proceeded smoothly to give the corresponding products **3** in moderate yields and 28–51% ees as an (*R*)-configuration under the optimal conditions. Using isobutyraldehyde and cyclohexanecarbaldehyde as the substrates afforded the corresponding products **3b** and **3c** in 77% yield and 51% ee as well as 78% yield and 50% ee, respectively (Table 3, entries 1 and 2). Lower enantioselectivities were obtained for linear aliphatic aldehydes, particularly for propanal, affording the corresponding adduct **3d** in 77% yield and 28% ee (Table 3, entry 3). When increasing the length of linear aliphatic aldehydes, an improvement of enantioselectivities could be realized under identical conditions (Table 3, entries 4–6). Using aromatic aldehyde **1h** as the substrate produced the corresponding product **3h** in 75% yield and 29% ee (Table 3, entry 7). As for the reaction of phenylpropanal with EVK, the corresponding adduct **3i** was formed in 76% yield and 44% ee after 30 h (Table 3, entry 8).

A possible transition state of this asymmetric MBH reaction can be explained as a Michael addition and an aldol reaction on the basis of generally accepted reaction mechanism as illustrated in Scheme 1.[2b] Intermediate **A** is first formed from the Michael addition of **L5** with MVK combined with an intramolecular hydrogen bonding, which undergoes aldol reaction with aldehyde from si face to give the product in an (*R*)-configuration.

## 3. Conclusion

In conclusion, we have designed and synthesized a series of novel chiral bifunctional phosphine-containing Lewis base catalysts for the asymmetric MBH reaction of aldehydes with MVK and EVK. We have found that these catalysts performed well under mild conditions and resulted in the formation of corresponding adducts in moderate yields as well as moderate enantioselectivities. These results could lead the way for a highly diastereoselective and/or highly enantioselective reaction of a catalytic asymmetric MBH




**Scheme 1.** Proposed mechanism for the asymmetric MBH reaction of aldehyde with MVK.

reaction with chiral phosphine-containing Lewis bases. Efforts are in progress to elucidate the mechanistic details of this reaction and to study its scope and limitations.

## 4. Experimental

### 4.1. General remarks

$^1$H NMR, $^{31}$P NMR and $^{13}$C NMR spectra were recorded on a Varian Mercury vx-300 spectrometer for solution in DMSO or $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Chiral HPLC was performed on a SHIMADZU SPD-10A series with chiral columns. Elementary analysis (CHN) was taken on a Carlo-Erba 1106 analyzer. Mass spectra were recorded by EI, and HRMS was measured on a HP-5989 instrument. Flash column chromatography was performed using Silica Gel (300–400 mesh). Melting points were uncorrected. All solvents were purified by distillation. Unless otherwise noted, all commercially obtained reagents were used without further purification. All reactions were carried out under an argon atmosphere. Phosphane oxides were synthesized according to literature procedures.[5] Chiral phosphine-containing Lewis bases catalysts **L1**–**L6** were prepared by the methods previously described.[4,6] Products **3a**–**3i** are known compounds.[7] The absolute configuration of MBH adducts **3** was determined by the sign of specific rotations compared with the literature value.[3b,d,f,7a,e]

### 4.2. General procedure for the reduction of the phosphane oxides

At 0 °C, $HSiCl_3$ (8.0 mmol, 0.8 mL) was carefully added to a mixture of phosphane oxide (2.0 mmol) and triethylamine (16 mmol, 2.1 mL) in toluene (50 mL) in a three-necked round-bottomed flask under argon atmosphere. The reaction mixture was heated at reflux for 16–24 h. After being cooled to room temperature, the mixture was diluted with $Et_2O$ and quenched with small amount of saturated $NaHCO_3$. The resulting suspension was filtered through Celite, and the solid was washed with $Et_2O$. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography ($SiO_2$, EtOAc/petroleum ether, 1/10) to give the product as a colourless solid (a pair of diastereoisomers).

### 4.3. (*R*)-1-(2-(Ethyl(phenyl)phosphano)naphthalen-1-yl)naphthalen-2-ol L3

White solid; yield: 520 mg (64%); mp 168–170 °C; $[\alpha]_D^{25} = -16.4$ (*c* 0.93, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3054, 2927, 1708, 1621, 1595, 1514, 1434, 1144, 815 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.79–0.89 (m, 3H, $CH_3$), 1.01 (dt, *J* = 7.2 Hz, 17.4 Hz, 3H, $CH_3$), 1.92 (q, *J* = 7.5 Hz, 2H, $CH_2$), 2.06 (q, *J* = 7.2 Hz, 2H, $CH_2$), 4.50 (br, 1H, OH), 4.84 (br, 1H, OH), 6.54 (d, *J* = 8.4 Hz, 1H, ArH), 6.86–7.05 (m, 7H, ArH), 7.14–7.38 (m, 14H, ArH), 7.46–7.51 (m, 2H, ArH), 7.64–7.78 (m, 3H, ArH), 7.86–8.01 (m, 7H, ArH); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −20.41, −20.83; MS (EI) *m*/*e* 406.1 ($M^+$, 40.59), 405.1 ($M^+$−1, 26.48), 390.2 ($M^+$−16, 25.11), 389.1 ($M^+$−17, 100), 252.1 ($M^+$−154, 13.55); HRMS (EI) calcd for $C_{28}H_{23}OP$ requires 406.1487, found: 406.1487.

### 4.4. (*R*)-1-(2-(Isopropyl(phenyl)phosphanyl)naphthalen-1-yl)naphthalen-2-ol L4

White solid; yield: 486 mg (58%); mp 149–150 °C; $[\alpha]_D^{25} = -13.0$ (*c* 0.58, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3055, 2944, 1714, 1621, 1595, 1515, 1434, 1144, 815 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.83–0.99 (m, 8H, $CH_3$), 1.12–1.19 (m, 4H, $CH_3$), 2.58–2.66 (m, 2H, CH), 4.25 (br, 1H, OH), 4.84 (br, 1H, OH), 6.28 (d, *J* = 9.0 Hz, 1H, ArH), 6.72–6.78 (m, 1H, ArH), 6.93–7.07 (m, 6H, ArH), 7.12–7.51 (m, 16H, ArH), 7.78 (d, *J* = 8.1 Hz, 1H, ArH), 7.88–7.96 (m, 7H, ArH), 8.03 (t, *J* = 8.7 Hz, 2H, ArH); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −10.03, −12.40; MS (EI) *m*/*e* 420.2 ($M^+$, 58.95), 403.2 ($M^+$−17, 100), 377.1 ($M^+$−43, 80.13), 252.1 ($M^+$−168, 25.60); HRMS (EI) calcd for $C_{29}H_{25}OP$ requires 420.1643, found: 420.1643.

### 4.5. (*R*)-1-(2-((Butyl(phenyl)phosphanyl)naphthalen-1-yl)naphthalen-2-ol L5

White solid; yield: 584 mg (67%); mp 68–70 °C; $[\alpha]_D^{25} = -14.3$ (*c* 0.83, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3057, 2969, 1719, 1588, 1509, 1419, 1140, 940 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.68 (t, *J* = 6.9 Hz, 3H, $CH_3$), 0.84 (t, *J* = 6.9 Hz, 3H, $CH_3$), 1.11–1.15 (m, 4H, $CH_2$), 1.34–1.43 (m, 4H, $CH_2$), 1.88 (t, *J* = 7.5 Hz, 2H, $CH_2$), 2.04 (t, *J* = 7.5 Hz, 2H, $CH_2$), 4.54 (br, 1H, OH), 4.83 (br, 1H, OH), 6.54 (d, *J* = 8.7 Hz, 1H, ArH), 6.87–7.06 (m, 7H, ArH), 7.15–7.38 (m, 14H, ArH), 7.47–7.52 (m, 2H, ArH), 7.60–7.64 (m, 1H, ArH), 7.71–7.79 (m, 2H, ArH), 7.87–8.02 (m, 7H, ArH); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −24.68; MS (EI) *m*/*e* 434.2 ($M^+$, 53.07), 417.2 ($M^+$−17, 100), 377.1 ($M^+$−57, 25.42), 268.1 ($M^+$−166, 53.69); HRMS (EI) calcd for $C_{30}H_{27}OP$ requires 434.1800, found: 434.1780.

### 4.6. (*R*)-1-(2-(Cyclohexyl(phenyl)phosphanyl)naphthalen-1-yl)naphthalen-2-ol L6

White solid; yield: 560 mg (61%); mp 74–76 °C; $[\alpha]_D^{25} = -18.8$ (*c* 0.54, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3055, 2926, 1708, 1619, 1596, 1513, 1433, 1144, 814 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.92–1.43 (m, 8H, $CH_2$), 1.51–1.78 (m, 12H, $CH_2$), 2.25–2.44 (m, 2H, CH), 4.24 (br, 1H, OH), 4.81 (br, 1H, OH), 6.31 (d, *J* = 8.7 Hz, 1H, ArH), 6.74–6.79 (m, 1H, ArH), 6.95–6.97 (m, 5H, ArH), 7.03–7.53 (m, 17H, ArH), 7.76–8.05 (m, 10H, ArH); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −15.35, −17.26; MS (EI) *m*/*e* 460.2 ($M^+$, 85.00), 443.2 ($M^+$−17, 100), 377.1 ($M^+$−83, 89.54), 268.1 ($M^+$−192, 55.87); HRMS (EI) calcd for $C_{32}H_{29}OP$ requires 460.1956, found: 460.1956.

### 4.7. (*R*)-1-(2-(Isobutyl(phenyl)phosphanyl)naphthalen-1-yl)naphthalen-2-ol L7

White solid; yield: 62%; mp 80.4–81.8 °C; $[\alpha]_D^{25} = -14.8$ (*c* 0.87, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3054, 2952, 1727, 1616, 1590, 1461, 1434, 1335, 973 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.55–0.60 (m, 6H), 0.92 (d, *J* = 6.6 Hz, 6H), 1.48–1.62 (m, 2H), 1.67–1.74 (m, 1H), 1.86–2.04 (m, 3H), 4.64 (br, 1H), 4.79 (br, 1H), 6.61 (d, *J* = 8.7 Hz, 1H), 6.91–6.97 (m, 2H), 7.01–7.09 (m, 5H), 7.17–7.39 (m, 14H), 7.46–7.54 (m, 3H), 7.65–7.69 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.87–7.98 (m, 7H); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −27.87, −28.45; MS (EI) *m*/*e* 434.2 ($M^+$, 59.58), 417.2 ($M^+$−17, 72.80), 377.1 ($M^+$−57, 48.28), 299.1 ($M^+$−135, 18.99), 268.1 ($M^+$−166, 100); HRMS (EI) calcd for $C_{30}H_{27}OP$ requires 434.1800, found: 434.1802.

### 4.8. (*R*)-1-(2-(Butyl(phenyl)phosphanyl)-5,6,7,8-tetrahydronaphthalen-1-yl)-5,6,7,8-tetrahydronaphthalen-2-ol L8

White solid; yield: 69%; mp 104.5–106.0 °C; $[\alpha]_D^{25} = +5.0$ (*c* 0.62, $CH_2Cl_2$); IR ($CH_2Cl_2$) *ν* 3047, 2929, 2857, 1730, 1591, 1475, 1434, 1276 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, TMS) *δ* 0.79–0.86 (m, 6H), 1.55–1.82 (m, 19H), 1.87–1.96 (m, 6H), 2.01–2.39 (m, 8H), 2.54–2.70 (m, 3H), 2.75–2.88 (m, 8H), 3.65 (br, 1H), 4.38 (br, 1H), 6.56 (d, *J* = 8.1 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.98–7.03 (m, 2H), 7.14–7.26 (m, 12H), 7.32–7.36 (m, 2H); $^{31}$P NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) *δ* −26.03, −26.87; MS (EI) *m*/*e* 442.2 ($M^+$,

52.45), 425.2 ($M^+$−17, 100), 383.2 ($M^+$−59, 23.75), 276.2 ($M^+$−166, 14.24), 268.1 ($M^+$−174, 23.87); HRMS (EI) calcd for $C_{30}H_{35}OP$ requires 442.2426, found: 442.2428.

### 4.9. (*R*)-1-(2-(Butyl(phenyl)phosphanyl)-5,6,7,8-tetrahydronaphthalen-1-yl)-5,6,7,8-tetrahydro-3-phenylnaphthalen-2-ol L9

White solid; yield: 58%; mp 45.6–47.1 °C; $[\alpha]_D^{25} = -43.2$ (*c* 0.84, $CH_2Cl_2$); IR ($CH_2Cl_2$) *v* 2927, 2858, 1731, 1455, 1434, 1275, 975 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 0.87–0.94 (m, 6H), 1.62–1.99 (m, 26H), 2.10–2.47 (m, 8H), 2.68–2.72 (m, 3H), 2.79–2.83 (m, 7H), 3.91 (br, 1H), 4.66 (br, 1H), 7.06–7.35 (m, 18H), 7.40–7.46 (m, 5H), 7.62-7.65 (m, 3H); $^{31}P$ NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) $\delta$ −24.94, −26.36; MS (EI) *m*/*e* 518.3 ($M^+$, 51.04), 501.3 ($M^+$−17, 100), 459.2 ($M^+$−59, 16.89), 279.2 ($M^+$−239, 8.88); HRMS (EI) calcd for $C_{36}H_{39}OP$ requires 518.2739, found: 518.2740.

### 4.10. (*R*)-3-Bromo-1-(2-(butyl(phenyl)phosphanyl)-5,6,7,8-tetrahydronaphthalen-1-yl)-5,6,7,8-tetrahydronaphthalen-2-ol L10

White solid; yield: 66%; mp 119.3–120.9 °C; $[\alpha]_D^{25} = -47.2$ (*c* 0.68, $CH_2Cl_2$); IR ($CH_2Cl_2$) *v* 3529, 2930, 2858, 1726, 1452, 1433, 1266, 1136, 1070 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 0.80–0.87 (m, 6H), 1.13–1.45 (m, 4H), 1.50–1.79 (m, 20H), 1.84–2.42 (m, 11H), 2.61–2.65 (m, 3H), 2.73–2.83 (m, 6H), 4.10 (br, 1H), 5.03 (br, 1H), 7.12–7.28 (m, 15H), 7.34–7.38 (m, 1H); $^{31}P$ NMR ($CDCl_3$, 121 MHz, 85% $H_3PO_4$) $\delta$ −25.61, −25.70; MS (EI) *m*/*e* 522.2 ($M^+$+2, 100), 520.2 ($M^+$, 99.15), 503.2 ($M^+$−17, 94.85), 461.1 ($M^+$−59, 41.44), 275.1 ($M^+$−247, 21.36); HRMS (EI) calcd for $C_{30}H_{34}BrOP$ requires 520.1531, found: 520.1536.

### 4.11. Typical procedure for L5-catalyzed Morita–Baylis–Hillman reaction of aldehyde 1a with MVK

To a solution of 3-phenylpropanal **1a** (26.8 mg, 0.2 mmol), **L5** (8.7 mg, 0.02 mmol) in THF (1.0 mL) was added methyl vinyl ketone (34 μL, 0.4 mmol). Then reaction mixture was stirred at 25 °C. When the reaction was completed as monitored by TLC plate, the solvent was removed and the residue was purified by a flash column chromatography ($SiO_2$, eluent: EA/PE = 1/4) to afford 4-hydroxy-3-methylene-6-phenylhexan-2-one 3a as a colourless oil; yield: 35.2 mg (86%). $^1H$ NMR ($CDCl_3$, TMS, 300 MHz): $\delta$ 1.89–1.97 (m, 2H), 2.35 (s, 3H), 2.63–2.85 (m, 3H), 4.41–4.47 (m, 1H), 6.01 (s, 1H), 6.11 (s, 1H), 7.16–7.31 (m, 5H); $[\alpha]_D^{25} = +18.6$ (*c* 1.34, $CH_2Cl_2$) for 56% ee; Chiralcel AS, hexane/*i*-PrOH = 90/10, 0.7 mL/min, 230 nm, $t_{major}$ = 10.45 min, $t_{minor}$ = 13.25 min.

## Acknowledgements

We thank the Shanghai Municipal Committee of Science and Technology (04JC14083, 06XD14005), and the National Natural Science Foundation of China for financial support (20472096, 203900502, 20672127, 20772030 and 20732008).

## References

1. For reviews of MBH or aza-MBH reaction, see: (a) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001–8062; (b) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653–4670; (c) Ciganek, E. *Org. React.* **1997**, *51*, 201–350; (d) Langer, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3049–3051; (e) Cai, J.-X.; Zhou, Z.-H.; Tang, C.-C. *Huaxue Yanjiu* **2001**, *12*, 54–64; (f) Iwabuchi, Y.; Hatakeyama, S. *J. Synth. Org. Chem. Jpn.* **2002**, *60*, 2–14; (g) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–892; (h) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4614–4628; (i) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev.* **2007**, *36*, 1581–1588; (j) Shi, Y. L.; Shi, M. *Eur. J. Org. Chem.* **2007**, *18*, 2905–2916.
2. For selected asymmetric MBH reactions, see: (a) Miller, S. J. *Acc. Chem. Res.* **2004**, *37*, 601–610; (b) Wang, J.; Li, H.; Yu, X. H.; Zu, L. S.; Wang, W. *Org. Lett.* **2005**, *7*, 4293–4296; (c) Berkessel, A.; Roland, K.; Neudörfl, J. M. *Org. Lett.* **2006**, *8*, 4195–4198; (d) Lattanzi, A. *Synlett* **2007**, 2106–2110; (e) Shi, M.; Liu, X. G. *Org. Lett.* **2008**, *10*, 1043–1046; (f) Iwabuchi, Y.; Nakatani, M.; Yokoyama, N.; Hatakeyama, S. *J. Am. Chem. Soc.* **1999**, *121*, 10219–10220; (g) Yang, K.-S.; Lee, W.-D.; Pan, J.-F.; Chen, K.-M. *J. Org. Chem.* **2003**, *68*, 915–919; (h) McDougal, N. T.; Schaus, S. E. *J. Am. Chem. Soc.* **2003**, *125*, 12094–12095; (i) McDougl, N. T.; Trevellini, W. L.; Rodgen, S. A.; Kliman, L. T.; Schaus, S. E. *Adv. Synth. Catal.* **2004**, *346*, 1231–1240; (j) Maher, D. J.; Connon, S. J. *Tetrahedron Lett.* **2004**, *45*, 1301–1305; (k) Sohtome, Y.; Tanatani, A.; Hashimoto, Y.; Nagasawa, K. *Tetrahedron Lett.* **2004**, *45*, 5589–5592; (l) Roussel, C.; Roman, M.; Andreoli, F.; Delrio, A.; Faure, R.; Vanthuyne, N. *Chirality* **2006**, *18*, 762–771; (m) Matsui, K.; Takizawa, S.; Sasai, H. *Tetrahedron Lett.* **2005**, *46*, 1943–1946; For recent mechanistic investigations of the MBH reaction, see: (n) Price, K. E.; Broadwater, S. J.; Jung, H. M.; McQuade, D. T. *Org. Lett.* **2005**, *7*, 147–150; (o) Aggarwal, V. K.; Fulford, S. Y.; Lloyd-Jones, G. C. *Angew. Chem., Int. Ed.* **2005**, *44*, 1706–1708; (p) Price, K. E.; Broadwater, S. J.; Walker, B. J.; McQuade, D. T. *J. Org. Chem.* **2005**, *70*, 3980–3987.
3. (a) Walsh, L. M.; Winn, C. L.; Goodman, J. M. *Tetrahedron Lett.* **2002**, *43*, 8219–8222; (b) Oishi, T.; Oguri, H.; Hirama, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1241–1244; (c) Barrett, A. G. M.; Cook, A. S.; Kamimura, A. *Chem. Commun.* **1998**, 2533–2534; (d) Shi, M.; Jiang, J.-K. *Tetrahedron: Asymmetry* **2002**, *13*, 1941–1947; (e) List, B. *Tetrahedron* **2002**, *58*, 5573–5590; (f) Imbriglio, J. E.; Vasbinder, M. M.; Miller, S. J. *Org. Lett.* **2003**, *5*, 3741–3743; (g) Shi, M.; Liu, Y. H.; Chen, L. H. *Chirality* **2007**, *19*, 124–128.
4. Lei, Z. Y.; Ma, G. N.; Shi, M. *Eur. J. Org. Chem.* **2008**, 3817–3820.
5. (a) Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277–4280; (b) Olszewski, T. K.; Boduszek, B.; Sobek, S.; Kozłowski, H. *Tetrahedron* **2006**, *62*, 2183–2189; (c) Bigeault, J.; Giordano, L.; Buono, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4753–4757.
6. (a) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945–1948; (b) Ito, K.; Eno, S.; Saito, B.; Katsuki, T. *Tetrahedron Lett.* **2005**, *46*, 3981–3985.
7. (a) Barrett, A. G. M.; Kamimura, A. *J. Chem. Soc., Chem. Commun.* **1995**, 1755–1756; (b) Bailey, M.; Marko, I. E.; Ollis, W. D.; Rasmussen, P. R. *Tetrahedron Lett.* **1990**, *31*, 4509–4512; (c) Iwamura, T.; Fujita, M.; Kawakita, T.; Kinoshita, S.; Watanabe, S.; Kataoka, T. *Tetrahedron* **2001**, *57*, 8455–8462; (d) Basavaiah, D.; Hyma, R. S.; Kumaragurubaran, N. *Tetrahedron* **2000**, *56*, 5905–5908; (e) Koenig, C. M.; Harms, K.; Koert, U. *Org. Lett.* **2007**, *9*, 4777–4779.