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Chemoenzymatic synthesis of optically active heterocyclic homoallylic and homopropargylic alcohols

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Abstract—A chemoenzymatic methodology has been developed using indium-mediated allylation of heterocyclic aldehydes under aqueous conditions followed by *Pseudomonas cepacia* lipase-catalyzed enantioselective acylation of racemic homoallylic and homopropargylic alcohols in organic media. It is observed that the lipase immobilized on ceramic particles (PS-C Amano II) catalyzes the resolution in a highly enantioselective manner in less time as compared to the native enzyme (PS Amano). The approach provides new functionalized chiral synthons useful in the synthesis of natural and pseudonatural products. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The discovery and development of new methods for the synthesis of chiral synthons for complex molecules of natural and unnatural origin remains an enduring challenge. The synthesis of enantiomerically pure unsaturated alcohols is of current interest as a result of their utility in the synthesis of natural products.[1] Enantiomerically pure homoallylic and homopropargylic alcohols are useful chiral synthons which find use in the asymmetric synthesis of a wide variety of natural products[2] and enantiopure molecules including *cis*-2,6-dialkyltetrahydropyran,[3] γ-lactones,[4] tetrahydrofurans,[5] *C*-aryl glycosides,[6] α,β-unsaturated lactones,[7] antitumour macrolides,[8] alkaloids,[9] Baylis–Hillman adducts,[10] cyclopropyl carbinols,[11] chiral epoxy alcohols,[12] β-hydroxy carbonyl compounds,[13] and optically pure 1,3-diols.[14] In addition, enantiomerically pure heterocyclic homoallylic and homopropargylic alcohols constitute a special class of chiral synthons that can be transformed to new chiral heterocyclic molecules and heterocyclic pseudonatural products exhibiting useful biological activities.[15]

The addition of various allylmetal reagents to aldehydes is now an established, important and useful synthetic method for the synthesis of enantiomerically pure homoallylic alcohols. Stereoselectivity in such reactions has been achieved using 'substrate controlled' processes,[16] chiral reagents,[17] and most recently via catalytic asymmetric reactions.[18] The last two decades of intensive research in the development and application of homoallylic and homopropargylic alcohols has provided spectacular successes and as a result many useful methods are available for installation of homoallylic and homopropargylic subunits with excellent stereoselectivity particularly diastereoselectivity. Nevertheless, there remain important challenges in the area of enantioselective synthesis.[19] Furthermore, most of these catalysts are moisture and air sensitive, so they tend to decompose or are deactivated under the reaction conditions. As a result, the reactions need to be carried under an inert atmosphere and at low temperatures. Another problem in the synthesis of nitrogen-containing heterocyclic derivatives arises from the possibility of complexation of the nitrogen with the reagent or catalysts.[20]

Due to its wide applicability to a variety of carbonyl compounds and the mild conditions of the method, indium-mediated allylation has emerged as one of the most useful methods for the preparation of synthetically useful homoallylic alcohols.[21,22] The lipase-catalyzed transformation of racemic alcohols or esters is recognized as an indispensable method for the synthesis of optically active compounds.[23] Therefore, seeking an effective, yet mild and environmentally benign approach for the synthesis of enantiomerically pure heterocyclic homoallylic alcohols, we examined the indium-mediated 'green' allylation of aldehydes under aqueous conditions, followed by kinetic resolution of

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the product alcohol with lipase using vinyl acetate as an acyl donor in THF (Scheme 1).

These optically active homoallylic alcohols are key intermediates in the synthesis of piperidine and pyrrolidine alkaloids including (*S*)-anabasine/(*S*)-anatabine,[24] nicotine,[25] (+)-sedamine[26] etc.

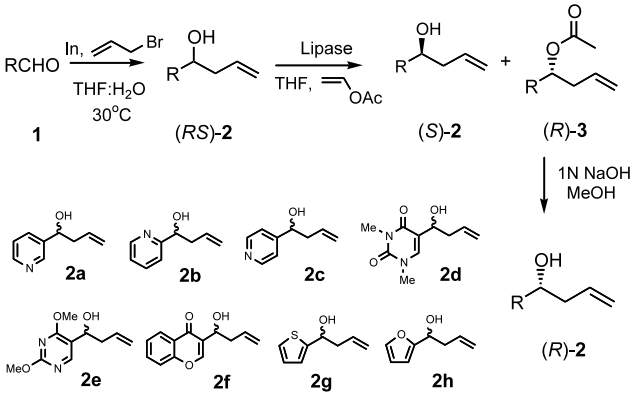
Furthermore, the synthetic utility of homopropargylic alcohols[27,28] encouraged us to extend this methodology to allow the enzymatic resolution of these alcohols. In continuation of our preliminary studies on kinetic resolution of uracil- and chromen-4-one-derived homoallylic alcohols, we present herein the chemoenzymatic synthesis of pyridyl, thienyl and furyl homoallylic and homopropargylic alcohols.

2. Results and discussion

2.1. Synthesis of racemic alcohols

Indium-mediated reactions in aqueous media have attracted increasing interest not only due to environmental and economical concerns,[21] but also because organic reactions in water display unique reactivity and selectivity. Indium has been found to mediate a variety of carbon–carbon bond forming reactions such as allylation of aldehydes and ketones, reductive coupling of aldimines,[30] Reformatsky and Aldol reactions,[31] ring expansion of carbocycles[32] and allenylation of aldehydes[33] in aqueous conditions. Since the objective of the present work was to develop an environment friendly procedure for the synthesis of chiral homoallylic alcohols, so this approach has been employed for procuring the racemic heterocycle substituted homoallylic and homopropargylic alcohols.

Sirring a mixture of the heterocyclic aldehydes, allyl bromide and indium metal in THF–H_2O (1:1) at 30°C under Barbier conditions and subsequent workup with saturated aqueous NH_4Cl solution provides the respective racemic homoallylic alcohols in 62–84% yields (Table 1). The structures were assigned on the basis of the spectroscopic data given in Section 4. It was



Scheme 1. Allylation followed by kinetic resolution.

Table 1. Synthesis of (*RS*)-**2a–h** by In-mediated allylation

Entry	Aldehyde	Homoallylic alcohol	Reaction time (h)	Yield (%)
1	**1a**	**2a**	12	72
2	**1b**	**2b**	10 min	76
3	**1c**	**2c**	10	68
4	**1d**	**1d**	16	76
5	**1e**	**2e**	14	80
6	**1f**	**2f**	12	84
7	**1g**	**2g**	10	62
8	**1h**	**2h**	7	68

observed that 2-pyridinecarboxaldehyde **1b** is allylated in a much shorter time (10 min) as compared to other aldehydes, which require 7–16 h. This could be rationalized by considering the two probable transition states for the reaction. All of the aldehydes (except **1a**) favorably form transition state **A**, where coordination of indium to the carbonyl oxygen provides a suitable means of activation and delivery of allyl residue. In the case of 2-pyridinecarboxaldehyde the faster rate of reaction indicates that a different transition state, **B**, is involved, which takes into account the chelation of the proximal pyridine, as reported by Paquette[34,35] (Fig. 1).

2.2. Synthesis of racemic homopropargylic alcohols

Stirring a mixture of 3-pyridinecarboxaldehyde **1a**, propargyl bromide and indium metal in THF–H_2O (1:1) at 30°C for 16 h (TLC) affords the homopropargylic alcohol **4a** in 70% yield and the allenic alcohol **5a** in 20% yield. Similar propargylation of 2-pyridinecarboxaldehyde **1b** provides exclusively the homopropargylic alcohol **4b**, while no formation of allenic alcohol was observed (Scheme 2).

Thus, the indium-mediated allylation and propargylation of heterocyclic aldehydes in THF–H_2O (1:1) medium is an efficient and environmentally benign method for the synthesis of racemic homoallylic and homopropargylic alcohols.

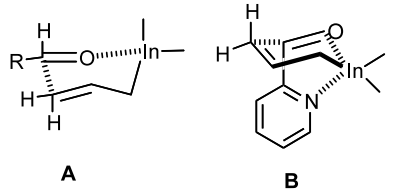
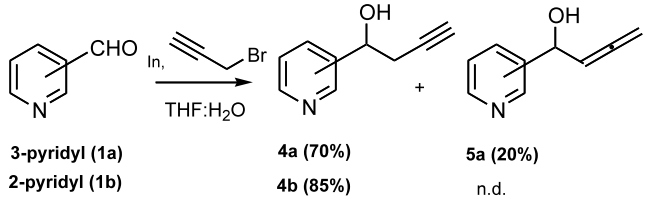


Figure 1.



Scheme 2.

2.3. Kinetic resolution of racemic homoallylic alcohols

In recent years, lipases have been used for the resolution of a variety of functionalized alcohols, but there are few reports[29] on the resolution of homoallylic and homopropargylic alcohols. Functionalized chiral heterocyclic homoallylic and homopropargylic alcohols are important chiral synthons for the synthesis of non-natural/ pseudo-natural products, which are potential bioactive molecules.

Enantiomerically pure 1-(3-pyridyl)-3-buten-1-ol **2a** is a common chiral intermediate used in the synthesis of pyridine ring-containing natural products and their analogues.[24–26] The standard synthetic approach for the preparation of enantiopure (*R*)- and (*S*)-**2a** is asymmetric allylboration of 3-pyridinecarboxaldehyde with (+)- and (−)-*B*-allyldiisopinocampheyl borane, respectively.[24–26] Of the six lipases scanned for transesterification *viz*. *Humicola lanuginosa* lipase (HLL), *Candida antarctica* lipase (CAL-B), *Rhizomucor meihei* lipase (RML), *Candida rugosa* lipase (CRL), *Pseudomonas fluorescens* lipase (PFL) and *Pseudomonas cepacia* lipase (PS Amano) at 24°C, it was found that the latter catalyzes the kinetic resolution of racemic homoallylic alcohols in a highly enantioselective manner. Accordingly, *P. cepacia* lipase (PS Amano) was used in further investigations. The transesterification of racemic **2a** catalyzed by PS Amano using vinyl acetate as acyl donor and THF as solvent affords (*S*)-**2a** in 92% ee and (*R*)-**3a** in 96% ee after 49% conversion in 72 h, the *E* value[37] (enantiomeric ratio) of the reaction being 162 (Table 1, entry 1). To obtain the alcohol (*R*)-**2a**, the acetate (*R*)-**3a** was hydrolyzed quantitatively with 1N methanolic NaOH.

We also compared the effectiveness of the native form of *P. cepacia* lipase (PS 'Amano'-containing diatomaceous earth as a filler), with that of lipase immobilized on ceramic particles chemically modified with a methacryl group (PS-C 'Amano' II). To our delight, significantly higher enantioselectivity was observed with the immobilized lipase and much shorter times were seen. PS-C converted 49% of (±)-**2a** in 30 h to provide (*R*)-**3a** with 98% ee and unreacted alcohol (*S*)-**2a** with 96% ee giving an *E* value of 392 (Table 1, entry 2). So, these results show a considerable advantage of the immobilized form over the free enzyme. Furthermore, the immobilized lipase can be used again without loss of activity. Thus, encouraged by the remarkable enantioselectivity and enhanced rate of reaction of PS-C lipase in all the cases studied so far, we limited all our further studies employing PS-C lipase only. The 2- and 4-pyridyl derivatives, i.e. **2b** and **2c** undergo enzymatic resolution under similar conditions to provide the corresponding *R*-acetates and *S*-alcohols with high enantiomeric purity (92–99%) (Table 2).

The ee of (*S*)-**2a** and (*R*)-**3a** was determined by ^{1}H NMR analysis of the acetates in the presence of the chiral shift reagent (+)-Eu(hfc)$_3$.[38] Analysis of the ^{1}H NMR spectrum of the racemic acetate **3a** in the presence of (+)-Eu(hfc)$_3$ showed splitting of the initial singlet at δ 2.08 ppm (due to the acetyl group) into two singlets (at δ 2.41 and δ 2.45 ppm). The enantiomeric excess was calculated from integration of the two signals in the ^{1}H NMR spectra of (*R*)-**3a** and (*S*)-**3a**. The non-transformed alcohol **2b** was assigned *S*-configuration by comparison of the sign of the specific rotation reported in literature[17g] and all the non-transformed substrates were then assigned the absolute configuration by the same analogy. Furthermore, the assignments of absolute configuration are in complete concordance with the empirical rule[39] proposed by Kazlauskas and Burgess, according to which, the resolution of secondary alcohols with lipases should provide the acetates having *R*-configuration.

The five-membered heteroaryl homoallylic alcohol viz. 1-(2-thienyl)but-3-en-1-ol **2g** is also efficiently resolved by PS-C Amano II lipase to give (*R*)-**3g** in 98% ee and (*S*)-**2g** in 80% ee ($E=244$) after 45% conversion in 20 h. Astonishingly, the 1-(2-furyl)but-3-en-1-ol **2h** is resolved much faster (4 h) than all other heteroaryl derivatives to give the *R*-acetate and *S*-alcohol in 96 and 84% ee, respectively ($E=131$) (Table 2).

Thus, the chemoenzymatic route as discussed above provides a facile procedure to procure optically active homoallylic alcohols and homoallylic acetates. Generally, the latter are prepared by a tedious method involving addition of allylsilane to aldehydes followed by in situ acylation with acetic anhydride.[40] This method produces some side products in addition to the desired homoallylic acetates.

2.4. Kinetic resolution of homopropargylic alcohols

To determine the generality of this methodology, it was further used for the synthesis of enantiomerically pure homopropargylic alcohols and acetates. The lipase PS-C-catalyzed transesterification of (±)-1-(3-pyridyl)but-3-yn-1-ol **4a** after workup and column chromatography provided the (*R*)-**6a** and (*S*)-**4a** in 98 and 82% ee, respectively ($E=254$) (Table 3). The ee was determined using ^{1}H NMR chiral shift analysis of the corresponding acetates and the absolute configuration have been assigned on the basis of empirical rule.

Additionally, PS-C catalyzes the transesterification of (±)-1-(2-pyridyl)but-3-yn-1-ol **4b** to provide (*R*)-**6b** (97% ee) and (*S*)-**4b** (91% ee) after the reaction was stopped at 48% conversion (26 h) (Table 3). PS-C also resolves the allenic alcohol **5a** to give (*R*)-**7a** in 94% ee and (*S*)-**5a** in 72% ee with a enantioselectivity ratio of 70.

Thus, the high enantioselectivity observed in the resolution of homopropargylic and allenic alcohols. This coupled with the extremely convenient methodology gives great synthetic potential and utility to the method presented herein.

Table 2. Enantioselective acylation of alcohols (*RS*)-**2a–h** by transesterification with lipases

Entry.	Substrate	Lipase	Temp. (°C)	Time (h)	Conv. (%)[a]	Yield[b] (*S*)-**2**	ee[c] (*S*)-**2**	Yield[b] (*R*)-**3**	ee[c] (*R*)-**3**	E_s[d]
1	**2a**	PS-Amano	24	72	49	49	92	44	96	162
2	**2a**	PS-C Amano II	24	30	49	50	96	45	98	392
3	**2b**	PS-Amano	24	48	49	50	94	45	99	713
4	**2b**	PS-C Amano II	24	30	49	50	95	45	99	747
5	**2c**	PS-C Amano II	24	22	48	50	92	44	99	659
6	**2d**	PS-C Amano II	40	59	42	55	72	41	98	216[e]
7	**2e**	PS-C Amano II	32	48	29	69	39	26	95	57[e]
8	**2f**	PS-C Amano II	50	56	46	53	83	44	97	172[e]
9	**2g**	PS-C Amano II	24	20	45	52	80	40	98	244
10	**2h**	PS-C Amano II	24	4	47	50	84	42	96	131

[a] The conversion (%*c*) was calculated from the enantiomeric excess of the starting alcohol (ee_s) and the product (ee_p) according to %*c* $ee_s/(ee_s+ee_p)$, Ref. 37.

[b] Yields refer to % age of pure isolated products after column chromatography.

[c] Enantiomeric excess calculated by ^{1}H NMR analysis of the acetate using 0.1 M (+)-Eu(hfc)$_3$ in $CDCl_3$. The (*S*) alcohol was converted into (*S*)-acetate with acetyl chloride. The absolute configurations have been assigned on the basis of empirical rule.

[d] Enantiomeric ratio (*E*) were determined from the ee of starting alcohol (ee_s) and the extent of conversion according to $E=\ln[(1-c)(1-ee_s)]/\ln[(1-c)(1+ee_s)]$, Ref. 37.

[e] For preliminary communication see Ref. 36.

Table 3. Enantioselective acylation of alcohols (*RS*)-**4** and **5** with lipase PS-C at 24 ± 1°C

Substrate	Time (h)	Conv. (%)	(*S*)-Alcohol		(*R*)-Acetate		*E*
			Yield	ee	Yield	ee	
4a	28	46	52	82	44	98	254
4b	26	48	50	91	45	97	210
5a	24	43	55	72	40	94	70

3. Conclusion

In summary, the ready access to racemic homoallylic and homopropargylic alcohols via indium-mediated allylation coupled with efficient and facile enzymatic resolution provides a convenient methodology for obtaining highly enantiomerically enriched heterocyclic homoallylic and homopropargylic alcohols and their acetates.

4. Experimental

4.1. General

NMR spectra were obtained at 200 (Bruker AC 200E) or 300 MHz (Bruker AC-E 300) for ^{1}H and at 50 or 75 MHz for ^{13}C NMR with Me_4Si (in $CDCl_3$) as internal standard. The chemical shifts are reported in δ values relative to TMS and coupling constants (*J*) are expressed in Hz. Spectral patterns are designated as s = singlet; d = doublet; dd = doublet of doublets; q = quartet; t = triplet; br = broad; m = multiplet. When necessary, assignments were aided by DEPT-135 and decoupling experiments. IR spectra were obtained with Nicolet Avatar 320 FTIR and are reported in wavenumbers (cm^{-1}). Mass spectra were recorded on GCMS-QP-2000 mass spectrometer by EI method. Optical rotations at the sodium D-line were determined at 27°C using a JASCO DIP-360 digital polarimeter. Analytical thin-layer chromatography (TLC) was performed on aluminum sheets pre-coated with silica gel $60F_{254}$ (Merck). Column chromatography was performed on Acme's silica gel (100–200 mesh) using an increasing concentration of ethyl acetate in hexane as eluent. 1,3-Dimethyl-5-formyl uracil **1d**[41] and 2,4-dimethoxy-5-formyl pyrimidine **1e**[42] were prepared by reported procedures. A 0.1 M solution of Eu(hfc)$_3$ in $CDCl_3$ was used for the determination of ee by ^{1}H NMR. *Humicola lanuginosa* lipase (HLL), *C. antarctica* lipase (CAL-B), *Rhizomucor meihei* lipase (RML) was obtained from Novo Nordisk while *C. rugosa* lipase (Lipase AY), *P. fluorescens* lipase (Lipase AK) and *P. cepacia* lipase (Lipase PS 'Amano') and lipase PS-C 'Amano' II were obtained from Amano, Japan.

4.2. Determination of enantiomeric excess

The ee was determined by ^{1}H NMR analysis of acetates using the chiral shift reagent Eu(hfc)$_3$. Analysis of ^{1}H NMR spectra of the racemic acetates in the presence of chiral Eu(hfc)$_3$ showed splitting of the initial single peak due to acetyl group into two singlets due to each enantiomer. The corresponding acetates of *S*-alcohols and racemic alcohols were prepared by stirring the alcohol with an excess (5 equiv.) of acetyl chloride and finally washing with 20% Na_2CO_3 solution. It was observed that in the presence of (+)-Eu(hfc)$_3$ the singlet

due to acetyl group was observed downfield for *R*-enantiomer and upfield for *S*-enantiomer in all cases. Absolute configurations were assigned by comparison of the sign of the specific rotation (**2a**–**c**, **2g**–**h**) with those reported in the literature[17g] and on the basis of the empirical rule (**2d**–**f**).

4.3. General method for synthesis of racemic homoallylic and homopropargylic alcohols

To a magnetically stirred solution of corresponding aldehyde (**1a**–**g**) (4 mmol) in 20 ml 50% aq. THF (water alone in case of **1h**) was added indium metal (0.506 mg, 4.4 mmol) and allyl bromide (970 mg, 0.75 ml, 8 mmol). The reaction was allowed to proceed until no aldehyde remained (TLC). After the completion of reaction, a saturated solution of NH_4Cl was added and the resulting mixture was extracted with CH_2Cl_2. The separated aqueous phase was basified with aqueous $NaHCO_3$ solution (20 ml) and extracted with CH_2Cl_2 (3×20 ml). The combined organic solutions were dried and concentrated to give **2a**–**g**, which were purified with column chromatography.

The homopropargylic alcohols **4a**–**b** and allenic alcohol **5a** were prepared similarly by replacing allyl bromide with propargyl bromide.

4.3.1. (*RS*)-1-(3-Pyridyl)but-3-en-1-ol, 2a. Brown liquid (72%); IR (neat): 3340, 2990, 1610 cm^{-1}; MS (*m*/*z*): 149 (M^+), 131 (M−18), 108 (100); ^1H NMR ($CDCl_3$): δ 2.47–2.57 (m, 2H), 2.68 (brs, 1H), 4.78 (t, 1H, $J=4.7$ Hz), 5.13–5.19 (m, 2H), 5.73–5.87 (m, 1H), 7.26–7.30 (m, 1H), 7.72 (d, 1H, $J=5.4$ Hz), 8.46–8.49 (m, 1H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 43.50, 70.79, 118.43, 123.43, 133.73, 134.06, 139.95, 147.20, 147.91.

4.3.2. (*RS*)-1-(2-Pyridyl)but-3-en-1-ol, 2b. Yellow liquid turns black on storage (76%); IR (neat): 3305, 3074, 2980, 1572 cm^{-1}; MS (*m*/*z*): 149 (M^+), 131 (M−18), 108; ^1H NMR ($CDCl_3$): δ 2.44–2.67 (m, 2H), 4.03 (brs, 1H), 4.81 (diffused t, 1H, $J=4.1$ Hz), 5.08–5.14 (m, 2H), 5.77–5.90 (m, 1H), 7.18–7.30 (m, 2H), 7.68 (t, 1H, $J=5.0$ Hz), 8.55 (d, 1H, $J=2.9$ Hz); ^{13}C NMR ($CDCl_3$): δ 42.52, 72.39, 117.60, 120.28, 122.09, 134.03, 136.49, 148.02, 161.70.

4.3.3. (*RS*)-1-(4-Pyridyl)but-3-en-1-ol, 2c. Brown oil (68%); IR (neat): 3320, 2990, 1600 cm^{-1}; MS (*m*/*z*): 149 (M^+), 131 (M−18), 108 (100); ^1H NMR ($CDCl_3$): δ 2.09 (brs, 1H), 2.40–2.57 (m, 2H), 4.74–4.80 (m, 1H), 5.14–5.23 (m, 2H), 5.70–5.94 (m, 1H), 7.30 (d, 2H, $J=6.2$ Hz), 8.56 (d, 2H, $J=6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 43.33, 71.64, 118.43, 121.30, 133.75, 148.77, 154.48.

4.3.4. (*RS*)-3-(1-Hydroxybut-3-en-1-yl)chromen-4-one, 2f. Yellow liquid (84%); IR (neat): 3320, 2990, 1590 cm^{-1}; MS (*m*/*z*): 216 (M^+), 215, 173 (100); ^1H NMR ($CDCl_3$): δ 2.48–2.80 (m, 2H), 3.33 (brs, 1H), 4.76 (diffused t, 1H, $J=5.7$ Hz), 5.12–5.20 (m, 2H), 5.76–5.97 (m, 1H), 7.38–7.49 (m, 2H), 7.65–7.74 (m, 1H), 7.94 (s, 1H), 8.20–8.24 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 40.25, 66.61, 117.65, 123.14, 124.66, 125.03, 125.25, 133.30, 133.87, 152.98, 155.72, 177.01.

4.3.5. (*RS*)-1-(2-Thienyl)but-3-en-1-ol, 2g. Yellow liquid (62%); IR (neat): 3340, 2980, 160 cm^{-1}; MS (*m*/*z*): 154 (M^+), 136 (M−18); ^1H NMR ($CDCl_3$): δ 2.29 (s, 1H), 2.59–2.68 (m, 2H), 5.00 (t, 1H, $J=6.5$ Hz), 5.14–5.26 (m, 2H), 5.74–5.91 (m, 1H), 6.96–7.00 (m, 2H), 7.2–7.34 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 43.70, 69.31, 118.67, 123.67, 124.51, 126.58, 133.85, 147.80.

4.3.6. Synthesis of (*RS*)-1-(2-furyl)but-3-en-1-ol, 2h. To a magnetically stirred solution of 2-furaldehyde (**1h**) (384 mg, 4 mmol) in water (20 ml) was added indium metal (0.506 mg, 4.4 mmol) and allyl bromide (970 mg, 0.75 ml, 8 mmol). The reaction was allowed to proceed until no aldehyde remained (7 h). Finally saturated aqueous NH_4Cl solution was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried and concentrated to give **2h** as a pale green liquid (375 mg, 68%) after column chromatography. IR (neat): 3410, 2990 cm^{-1}; MS (*m*/*z*): 138 (M^+), 120; ^1H NMR ($CDCl_3$): δ 2.07 (brs, 1H), 2.60–2.68 (m, 2H), 4.72–4.82 (m, 1H), 5.13–5.25 (m, 2H), 5.72–5.89 (m, 1H), 6.25–6.26 (m, 1H), 6.33–6.36 (m, 1H), 7.38–7.40 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 39.90, 66.83, 106.03, 110.03, 117.92, 133.87, 141.74, 156.14.

4.3.7. (*RS*)-1-(3-Pyridyl)but-3-yn-1-ol, 4a. Violet liquid (70%); IR (neat): 3440, 3300 cm^{-1}; MS (*m*/*z*): 147 (M^+), 146, 108, 107 (100); ^1H NMR ($CDCl_3$): δ 2.05 (t, 1H, $J=2.6$ Hz), 2.63–2.68 (m, 2H), 4.89 (t, 1H, $J=6.4$ Hz), 7.24–7.30 (m, 1H), 7.75–7.81 (m, 1H), 8.39–8.42 (m, 1H), 8.50 (diffused d, 1H, $J=1.4$ Hz); ^{13}C NMR ($CDCl_3$): δ 29.21, 69.80, 71.34, 79.96, 123.45, 133.95, 138.54, 147.41, 148.62.

4.3.8. (*RS*)-1-(2-Pyridyl)but-3-yn-1-ol, 4b. Dark violet liquid (85%); IR (neat): 3410, 3305 cm^{-1}; MS (*m*/*z*): 147 (M^+), 146, 139 (M−18), 107 (100); ^1H NMR ($CDCl_3$): δ 2.03 (t, 1H, $J=2.6$ Hz), 2.73 (dd, 2H, $J=6.0$ and 2.7 Hz), 4.40 (brs, 1H), 4.93 (t, 1H, $J=3.8$ Hz), 7.23–7.29 (m, 1H), 7.40–7.44 (m, 1H), 7.68–7.76 (m, 1H), 8.58 (d, 1H, $J=4.7$ Hz); ^{13}C NMR ($CDCl_3$): δ 28.25, 70.77, 71.25, 80.54, 120.76, 122.58, 136.70, 148.10, 160.2.

4.3.9. (*RS*)-1-(3-Pyridyl)buta-2,3-dien-1-ol, 5a. Violet liquid (20%); IR (neat): 3340, 1980 cm^{-1}; MS (*m*/*z*): 147 (M^+), 129 (M−H_2O), 108; ^1H NMR ($CDCl_3$): δ 4.89 (dd, 2H, $J=6.2$ and 2.0 Hz), 5.30–5.34 (m, 1H), 5.46 (q, 1H, $J=6.5$ Hz), 7.25–7.31 (m, 1H), 7.74–7.80 (m, 1H), 8.42–8.44 (m, 1H), 8.54 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 69.71, 78.16, 94.66, 123.43, 134.19, 138.77, 147.59, 148.39, 207.45.

4.4. General procedure for resolution

To a solution of the (±)-**2a**–**h** (1 mmol) in anhydrous THF (1 ml) and vinyl acetate (0.9 ml, 10 mmol) in a 25 ml round bottom flask, was added lipase (1 equiv. w/w). The reaction mixture was stirred at constant temperature (24±1, 32±1, 40±1 and 50±1°C) and monitored by TLC and recording ^1H NMR of aliquots taken at regular intervals. On achieving the desired conversion the reaction was stopped by filtering the enzyme on a sintered glass funnel. The filtrate was

concentrated and column chromatographed on silica gel (100–200 mesh) using mixtures of hexane and ethyl acetate as eluents to afford ***R***-acetates and ***S***-alcohol.

4.4.1. (*R*)-1-(3-Pyridyl)but-3-en-1-yl acetate, (*R*)-3a. Light yellow oil; $[\alpha]_D^{27}$ +55.1 (*c* 1.40, CH_2Cl_2) for 98% ee; IR (neat): 2926, 1738, 1574 cm^{-1}; MS (*m*/*z*): 191 (M^+), 148, 132, 108; ^1H NMR ($CDCl_3$): δ 2.08 (s, 3H), 2.56–2.75 (m, 2H), 5.00–5.10 (m, 2H), 5.60–5.75 (m, 1H), 5.80 (t, 1H, $J=6.7$ Hz), 7.25–7.30 (m, 2H), 7.61–7.65 (m, 1H), 8.51–8.59 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.91, 40.27, 72.84, 118.68, 123.25, 132.30, 134.19, 135.45, 148.12, 149.12, 169.90.

4.4.2. (*S*)-1-(3-Pyridyl)but-3-en-1-ol, (*S*)-2a. $[\alpha]_D^{27}$ −39.9 (*c* 1.15, CH_2Cl_2) and −26.32 (*c* 1.15, EtOH) for 96% ee.

4.4.3. (*R*)-1-(2-Pyridyl)but-3-en-1-yl acetate, (*R*)-3b. Light yellow oil; $[\alpha]_D^{27}$ +78.7 (*c* 1.50, CH_2Cl_2) for 99% ee; IR (neat): 2930, 1740 cm^{-1}; MS (*m*/*z*): 191 (M^+), 148, 132, 108 (100); ^1H NMR ($CDCl_3$): δ 2.13 (s, 3H), 2.69–2.76 (m, 2H), 5.01–5.12 (m, 2H), 5.72–5.89 (m, 2H), 7.21–7.32 (m, 2H), 7.63–7.68 (m, 1H), 8.57–8.61 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.96, 38.99, 75.54, 118.00, 121.06, 122.64, 133.01, 136.49, 149.23, 158.70, 170.15.

4.4.4. (*S*)-1-(2-Pyridyl)but-3-en-1-ol, (*S*)-2b. $[\alpha]_D^{27}$ −46.4 (*c* 0.86, CH_2Cl_2) and −55.9 (*c* 0.86, EtOH) for 95% ee.

4.4.5. (*R*)-1-(4-Pyridyl)but-3-en-1-yl acetate, (*R*)-3c. Brown oil; $[\alpha]_D^{27}$ +58.7 (*c* 1.30, CH_2Cl_2) for 99% ee; IR (neat): 1745, 1630 cm^{-1}; MS (*m*/*z*): 191 (M^+), 148, 108 (100); ^1H NMR ($CDCl_3$): δ 2.12 (s, 3H), 2.53–2.62 (m, 2H), 5.02–5.11 (m, 2H), 5.61–5.79 (m, 2H), 7.21–7.26 (m, 2H), 8.56–8.59 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 20.80, 40.06, 73.39, 118.68, 120.96, 132.02, 148.68, 149.67, 169.81.

4.4.6. (*S*)-1-(4-Pyridyl)but-3-en-1-ol, (*S*)-2c. $[\alpha]_D^{27}$ −59.5 (*c* 0.71, CH_2Cl_2) and −24.52 (*c* 0.71, EtOH) for 92% ee.

4.4.7. (*R*)-5-(1-Acetoxybut-3-en-1-yl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione, (*S*)-3d. Pale yellow liquid; $[\alpha]_D^{27}$ +66.5 (*c* 0.52, CH_2Cl_2) for 98% ee.

4.4.8. (*S*)-5-(1-Hydroxybut-3-en-1-yl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione, (*S*)-2d. $[\alpha]_D^{27}$ −38.55 (*c* 0.90, CH_2Cl_2) for 72% ee.

4.4.9. (*R*)-1-(2,4-Dimethoxypyrimidin-5-yl)but-3-en-1-yl acetate, (*R*)-3e. Yellow liquid; $[\alpha]_D^{27}$ +49.4 (*c* 1.05, CH_2Cl_2) for 95% ee.

4.4.10. (*S*)-1-(2,4-Dimethoxypyrimidin-5-yl)but-3-en-1-ol, (*S*)-2e. $[\alpha]_D^{27}$ −24.35 (*c* 1.40, CH_2Cl_2) for 39% ee.

4.4.11. (*R*)-3-(1-Acetoxybut-3-en-1-yl)chromen-4-one, (*R*)-3f. Light brown liquid; $[\alpha]_D^{27}$ +51.21 (*c* 0.82, CH_2Cl_2) for 97% ee; IR (neat): 2980, 1745, 1615 cm^{-1}; MS (*m*/*z*): 258 (M^+), 215, 173 (100); ^1H NMR ($CDCl_3$): δ 2.11 (s, 3H), 2.65–2.78 (m, 2H), 5.05–5.14 (m, 2H), 5.64–5.86 (m, 1H), 5.99–6.05 (m, 1H), 7.38–7.47 (m, 2H), 7.64–7.68 (m, 1H), 7.91 (s, 1H), 8.21–8.25 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.85, 37.56, 68.38, 117.88, 118.25, 122.52, 123.72, 125.05, 125.57, 132.71, 133.58, 153.22, 155.92, 169.60, 175.74.

4.4.12. (*S*)-3-(1-Hydroxybut-3-en-1-yl)chromen-4-one, (*S*)-2f. $[\alpha]_D^{27}$ −40.9 (*c* 0.99, CH_2Cl_2) for 83% ee.

4.4.13. (*R*)-1-(2-Thienyl)but-3-en-1-yl acetate, (*R*)-3g. Pale yellow liquid; $[\alpha]_D^{27}$ +35.2 (*c* 1.40, CH_2Cl_2) for 98% ee; IR (neat): 1730, 1600 cm^{-1}; MS (*m*/*z*): 196 (M^+), 154, 136 (100); ^1H NMR ($CDCl_3$): δ 2.06 (s, 3H), 2.62–2.75 (m, 2H), 5.06–5.17 (m, 2H), 5.67–5.75 (m, 1H), 6.10 (t, 1H, $J=6.8$ Hz), 6.87–7.06 (m, 2H), 7.28–7.34 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 29.54, 38.50, 68.08, 118.26, 128.24, 132.61, 135.07, 136.33, 144.52, 169.83.

4.4.14. (*S*)-1-(2-Thienyl)but-3-en-1-ol, (*S*)-2g. $[\alpha]_D^{27}$ −8.2 (*c* 1.20, CH_2Cl_2) and −5.08 (*c* 1.20, EtOH) for 80% ee.

4.4.15. (*R*)-1-(2-Furyl)but-3-en-1-yl acetate, (*R*)-3h. Yellow liquid; $[\alpha]_D^{27}$ +23.20 (*c* 1.06, CH_2Cl_2) for 96% ee; IR (neat): 1736, 1620 cm^{-1}; MS (*m*/*z*): 138 (M^+), 95, 70; ^1H NMR ($CDCl_3$): δ 2.03 (s, 3H), 2.59–2.62 (m, 2H), 5.10–5.23 (m, 2H), 5.72–5.92 (m, 2H), 6.20–6.29 (m, 1H), 6.41–6.46 (m, 1H), 7.32–7.42 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 32.38, 41.67, 68.76, 107.96, 112.00, 120.36, 135.57, 143.82, 157.89, 167.24.

4.4.16. (*S*)-(+)-1-(2-Furyl)but-3-en-1-ol, (*S*)-2h. $[\alpha]_D^{27}$ −32.6 (*c* 0.50, CH_2Cl_2) for 84% ee.

4.4.17. (*R*)-1-(3-Pyridyl)but-3-yn-1-yl acetate, (*R*)-6a. Violet liquid; $[\alpha]_D^{27}$ +49.25 (*c* 0.54, CH_2Cl_2) for 98% ee; IR (neat): 3320, 1740 cm^{-1}; MS (*m*/*z*): 189 (M^+), 146, 108, 107 (100); ^1H NMR ($CDCl_3$): δ 2.01 (t, 1H, $J=1.6$ Hz), 2.13 (s, 3H), 2.75–2.81 (m, 2H), 5.90 (t, 1H, $J=6.5$ Hz), 7.29–7.34 (m, 1H), 7.71–7.77 (m, 1H), 8.56–8.60 (m, 1H), 8.66 (d, 1H, $J=2.05$); ^{13}C NMR ($CDCl_3$): δ 20.85, 26.08, 71.23, 71.43, 78.40, 123.29, 134.36, 147.99, 149.34, 169.71.

4.4.18. (*S*)-1-(3-Pyridyl)but-3-yn-1-ol, (*S*)-4a. $[\alpha]_D^{27}$ −41.0 (*c* 0.20, CH_2Cl_2) for 82% ee.

4.4.19. (*R*)-1-(2-Pyridyl)but-3-yn-1-yl acetate, (*R*)-6b. Light blue liquid. IR (neat): 3310, 1735 cm^{-1}; MS (*m*/*z*): 189 (M^+), 146, 108 (100); ^1H NMR ($CDCl_3$): δ 1.88 (t, 1H, $J=2.6$ Hz), 2.16 (s, 3H), 2.79–3.03 (m, 2H), 5.91 (t, 1H, $J=6.2$ Hz), 7.19–7.26 (m, 1H), 7.37 (d, 1H, $J=7.8$ Hz), 7.64–7.69 (m, 1H), 8.58–8.61 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.80, 24.29, 70.46, 73.78, 79.23, 121.49, 122.92, 136.33, 148.24, 157.25, 169.69.

4.4.20. (*S*)-1-(2-Pyridyl)but-3-yn-1-ol, (*S*)-4b. $[\alpha]_D^{27}$ = n.d.;[43] e.e. = 91%.

4.4.21. (*R*)-1-(3-Pyridyl)buta-2,3-dien-1-yl acetate, (*R*)-7a. Violet liquid; $[\alpha]_D^{27}$ −63.9 (*c* 0.81, CH_2Cl_2) for 94% ee; IR (neat): 3320, 1970, 1740 cm^{-1}; MS (*m*/*z*): 189 (M^+), 146, 108, 107 (100); ^1H NMR ($CDCl_3$): δ 2.12 (s, 3H), 4.85–4.90 (m, 2H), 5.45 (q, H, $J=6.6$ Hz), 6.29–6.34 (m, 1H), 7.27–7.33 (m, 1H), 7.68–7.72 (m, 1H),

8.55–8.58 (m, 1H), 8.64 (d, 1H, $J=2.0$ Hz); ^{13}C NMR ($CDCl_3$): δ 20.97, 71.23, 78.31, 90.99, 123.21, 134.56, 148.43, 149.37, 169.72, 208.74.

4.4.22. (*S*)-1-(3-Pyridyl)buta-2,3-dien-1-ol, (*S*)-5a. $[\alpha]_D^{27}$ +52.3 (*c* 0.17, CH_2Cl_2) for 72% ee.

4.5. General procedure for chemical hydrolysis of the (*R*)-acetates

To a solution of the acetates viz. (*R*)-**3a**–**h**, (*R*)-**6a**–**b** and (*R*)-**7a** (0.2 mmol) in methanol (4 ml) and water (1 ml), a 1N solution of NaOH (0.2 ml, 0.2 mmol) was added. The mixture was stirred at room temperature until the hydrolysis was complete (TLC). The solution was extracted with chloroform, dried with anhydrous Na_2SO_4 and evaporated to give respective (*R*)-alcohols, which were purified with column chromatography eluting with a hexane:ethyl acetate mixture and the optical rotation of these alcohols was determined.

4.5.1. (*R*)-1-(3-Pyridyl)but-3-en-1-ol, (*R*)-2a. $[\alpha]_D^{27}$ +48.4 (*c* 0.90, CH_2Cl_2) and +28.92 (*c* 0.90, EtOH).

4.5.2. (*R*)-1-(2-Pyridyl)but-3-en-1-ol, (*R*)-2b. $[\alpha]_D^{27}$ +47.1 (*c* 1.20, CH_2Cl_2) and +58.91 (*c* 1.20, EtOH).

4.5.3. (*R*)-1-(4-Pyridyl)but-3-en-1-ol, (*R*)-2d. $[\alpha]_D^{27}$ +70.0 (*c* 0.95, CH_2Cl_2) and +29.31 (*c* 0.95, EtOH).

4.5.4. (*R*)-5-(1-Hydroxybut-3-en-1-yl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione, (*R*)-2d. $[\alpha]_D^{27}$ +55.40 (*c* 0.37, CH_2Cl_2).

4.5.5. (*R*)-1-(2,4-Dimethoxypyrimidin-5-yl)but-3-en-1-ol, (*R*)-2e. $[\alpha]_D^{27}$ +60.5 (*c* 0.92, CH_2Cl_2).

4.5.6. (*R*)-3-(1-Hydroxybut-3-en-1-yl)chromen-4-one, (*R*)-2f. $[\alpha]_D^{27}$ +54.1 (*c* 0.61, CH_2Cl_2).

4.5.7. (*R*)-1-(2-Thienyl)but-3-en-1-ol, (*R*)-2g. $[\alpha]_D^{27}$ +10.1 (*c* 0.80, CH_2Cl_2) and +6.14 (*c* 0.80, EtOH).

4.5.8. (*R*)-(+)-1-(2-Furyl)but-3-en-1-ol, (*R*)-2h. $[\alpha]_D^{27}$ +37.2 (*c* 0.90, CH_2Cl_2).

4.5.9. (*R*)-1-(3-Pyridyl)but-3-yn-1-ol, (*R*)-4a. $[\alpha]_D^{27}$ +48.28 (*c* 0.35, CH_2Cl_2).

4.5.10. (*R*)-1-(2-Pyridyl)but-3-yn-1-ol, (*R*)-4b. $[\alpha]_D^{27}$ = n.d.[43]

4.5.11. (*R*)-1-(3-Pyridyl)buta-2,3-dien-1-ol, (*R*)-5a. $[\alpha]_D^{27}$ −71.42 (*c* 0.64, CH_2Cl_2).

4.6. General procedure for chemical acetylation of (*S*)-alcohols and (±)-alcohols

Acetyl chloride (5 mmol) was added to the corresponding alcohols (1 mmol) kept at 0°C. The solution was stirred for 2 h. Finally the excess of acetyl chloride was evaporated on a steam bath and the resultant reaction mixture was washed with 20% Na_2CO_3 solution and extracted with CH_2Cl_2 (3×10 ml). The combined extracts were dried with anhydrous Na_2SO_4 and evaporated to give the respective crude acetates, which were purified with column chromatography using mixtures of hexane: ethyl acetate as eluent.

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References

1. (a) Nicalaou, K. C.; Roschangar, F.; Vourloumis, D. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2014 and references cited therein; (b) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: Chichester, 1997; Chapter 4; (c) Zhu, B.; Panek, J. S. *Tetrahedron Lett.* **2000**, *41*, 1863; (d) Evans, P. A.; Murthy, V. S.; Roseman, J. D.; Rheingold, A. L. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3175; (e) VanBrunt, M. P.; Standaert, R. F. *Org. Lett.* **2000**, *2*, 705.
2. (a) Held, C.; Frohlich, R.; Metz, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1058; (b) Metz, P.; Stolting, J.; Lage, M.; Krebs, B. *Angew. Chem., Int. Ed.* **1994**, *33*, 2195; (c) Ooi, H.; Urushibara, A.; Esumi, T.; Iwabuchi, Y.; Hatakeyama, S. *Org. Lett.* **2001**, *3*, 953.
3. (a) Jaber, J. J.; Mitsui, K.; Rychnovsky, S. D. *J. Org. Chem.* **2001**, *66*, 4679 and references cited therein; (b) Samoshin, V. V.; Smoliakova, I. P.; Han, M.; Gross, P. H. *Mendeleev Commun.* **1999**, 219.
4. (a) Brown, H. C.; Kulkarni, S. V.; Racherla, U. S. *J. Org. Chem.* **1994**, *59*, 365; (b) Wuts, P. G. M.; Obrzut, M. L.; Thompson, P. A. *Tetrahedron Lett.* **1984**, *25*, 4051; (c) Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc.* **1999**, *121*, 11680.
5. (a) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. *J. Am. Chem. Soc.* **2001**, *123*, 2450; (b) Adam, W.; Saha-Moller, C. R.; Schmid, K. S. *J. Org. Chem.* **2001**, *66*, 7365.
6. Schmidt, B. *Org. Lett.* **2000**, *2*, 791.
7. Keck, G. E.; Li, X.-Y.; Knutson, C. E. *Org. Lett.* **1999**, *1*, 411.
8. Machajewski, T. D.; Wong, C.-H. *Synthesis* **1999**, 1469.
9. Felpin, F. X.; Girard, S.; Vo-Thanh, G.; Robins, R. J.; Villieras, J.; Lebreton, J. *J. Org. Chem.* **2001**, *66*, 6305 and references cited therein.
10. Cha, J. H.; Pae, A. N.; Choi, K. I. I.; Cho, Y. S.; Koh, H. Y.; Lee, E. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2079.
11. Winker, J. D.; Gretler, E. A. *Tetrahedron Lett.* **1991**, *32*, 5733.
12. (a) Dimitrov, V.; Philipova, I.; Simova, S. *Tetrahedron: Asymmetry* **1996**, *7*, 1493; (b) Hoveyda, A. H. *Chem. Rev.* **1993**, *93*, 1307; (c) Jorgensen, K. A. *Chem. Rev.* **1989**, *89*, 431.
13. (a) Yatagai, H.; Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 4548; (b) Hayashi, T.; Konishi, M.;

Kumada, M. *J. Org. Chem.* **1983**, *48*, 281; (c) Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **1999**, *64*, 3798.
14. (a) Dreher, S. D.; Hornberger, K. R.; Sarraf, S. T.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 3197; (b) Dimitrov, V.; Kostova, K.; Hesse, M. *Tetrahedron: Asymmetry* **1994**, *5*, 1891.
15. (a) Chiu, P.; Lautens, M. *Stereoselective Heterocyclic Synthesis*; Metz, P., Ed.; Springer-Verlag: Berlin Heidelberg, 1999; Chapter 1; (b) Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. *Heterocycles in Life and Society*; John Wiley & Sons: Chichester, 1997; (c) Moreno-Manas, M.; Pleixats, R. *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Academic Press: California, 1996; Vol. 66, Chapter 2; (d) Wu, Y.-C.; Chang, F.-R.; Duh, C.-Y.; Wang, S.-K. *Heterocycles* **1992**, *34*, 667; (e) Myint, S. H.; Cortes, A.; Laurens, A.; Hocquemiller, R.; Lebeouf, M.; Cave, A.; Cotte, J.; Quero, A.-M. *Phytochemistry* **1991**, *30*, 3335; (f) Jossang, A.; Dubaele, B.; Cave, A.; Bartoli, M.-H.; Beriel, H. *J. Nat. Prod.* **1991**, *54*, 967; (g) Marshall, J. A.; Xie, S. *J. Org. Chem.* **1995**, *60*, 7230; (h) Marshall, J. A.; Liao, J. *J. Org. Chem.* **1998**, *63*, 5962.
16. For recent reviews for allylmetal additions, see: (a) Denmark, S. E.; Almstead, N. G. *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH; Weinheim, 2000; Chapter 10; (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (c) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G.; Livingston, A. B. *J. Am. Chem. Soc.* **1995**, *117*, 6619; (d) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 265; (e) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927; (f) Keck, G. E.; Abbott, D. E.; Wiley, M. R. *Tetrahedron Lett.* **1987**, *28*, 139; (g) Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889.
17. (a) Brown, H. C.; Vara Prasad, J. V. N.; Zee, S.-H. *J. Org. Chem.* **1986**, *51*, 432; (b) Corey, E. J.; Yu, C.-M.; Kim, S.-S. *J. Am. Chem. Soc.* **1989**, *111*, 5495; (c) Roush, W. R.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 1143; (d) Hafner, A.; Duthaler, R. O.; Marti, R.; Rihs, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321; (e) Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043; (f) Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 401; (g) Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1992**, *57*, 6614.
18. (a) Loh, T.-P.; Zhou, J.-R.; Yin, Z. *Org. Lett.* **1999**, 1855; (b) Keck, G. E.; Geraci, L. S. *Tetrahedron Lett.* **1993**, *34*, 7827; (c) Keck, G. E.; Krishnamurthy, D.; Grier, M. C. *J. Org. Chem.* **1993**, *58*, 6543; (d) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940; (e) Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001; (f) Keck, G. E.; Krishnamurthy, D. *Org. Synth.* **1998**, *62*, 12; (g) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467; (h) Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc.* **2001**, *123*, 6199.
19. Some representative reviews and articles for enantioselective allylation are: (a) Marshall, J. A. *Chemtracts-Organic Chemistry* **1996**, *9*, 280; (b) Cozzi, P. G.; Tagliavini, E.; Umani-Ronchi, A. *Gaz. Chim. Ital.* **1997**, *127*, 247; (c) Gauthier, D. R.; Carreira, E. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2363l; (d) Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561.
20. (a) Hull, K. G.; Visnick, M.; Tautz, W.; Sheffron, A. *Tetrahedron* **1997**, *53*, 12405; (b) Ng, P. L.; Lambert, J. N. *Synlett* **1999**, *11*, 1749; (c) Raatz, D.; Innertsberger, C.; Reiser, O. *Synlett* **1999**, 1907; (d) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952.
21. For a review, see: (a) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023; (b) Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181; (c) Cintas, P. *Synlett* **1995**, 1087; (d) for mechanistic studies, see: Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228; (e) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831; (f) Paquette, L. A.; Lobben, P. C. *J. Am. Chem. Soc.* **1996**, *118*, 1917; (g) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931; (h) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2318; (i) Paquette, L. A.; Mitzel, T. M.; Isaac, M. B.; Crasto, C. F.; Schomer, W. W. *J. Org. Chem.* **1997**, *62*, 4293; (j) Hirashita, T.; Kamei, T.; Horie, T.; Yamamura, H.; Kawai, M.; Araki, S. *J. Org. Chem.* **1999**, *64*, 172; (k) Paquette, L. A.; Rothaar, R. R. *J. Org. Chem.* **1999**, *64*, 217; (l) Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149.
22. Prenner, R. H.; Binder, W. H.; Schmid, W. *Liebigs Ann. Chem.* **1994**, 73.
23. (a) Roberts, S. M. *Biocatalysts for Fine Chemicals Synthesis*; John Wiley & Sons: Chichester, 1999; (b) Jaeger, K.-E.; Reetz, M. T. *Trends Biotechnol.* **1998**, *16*, 396; (c) Silverman, R. B. *The Organic Chemistry of Enzyme-Catalyzed Reactions*; Acedemic Press: USA, 2000; (d) Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1475; (e) Carrea, G.; Riva, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 2226; (f) *Stereoselective Biocatalysis*; Patel, R. N., Ed.; Marcel Dekker: New York, 1999; (g) Kadereit, D.; Waldmann, H. *Chem. Rev.* **2001**, *101*, 3367; (h) *Enzymatic Reactions in Organic Media*, Koskinen, A. M. P.; Klibanov, A. M., Eds.; Blackie Academic & Professional: Glasgow, 1996; (i) *Hydrolases in Organic Synthesis*, Bornscheuer, U. T.; Kazlauskas, R. J., Eds.; Wiley-VCH: Weinheim, 1999.
24. Felpin, F. X.; Vo-Thanh, G.; Robins, R. J.; Villieras, J.; Lebreton, J. *Synlett* **2000**, 1646.
25. Girard, S.; Robins, R. J.; Villieras, J.; Lebreton, J. *Tetrahedron Lett.* **2000**, *41*, 9245.
26. Cossy, J.; Willis, C.; Bellosta, V.; Bouzbouz, S. *Synlett* **2000**, 1461.
27. For synthesis of non-racemic homopropargylic alcohols, see: (a) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214; (b) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1998**, *63*, 3812.
28. (a) Chattopadhyay, A. *J. Org. Chem.* **1996**, *61*, 6104; (b) Keck, G. E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett.* **1994**, *35*, 8323.
29. For enzymatic resolution of racemic homoallylic alcohols, see: (a) Master, H. E.; Newadkar, R. V.; Rane, R. A.; Kumar, A. *Tetrahedron Lett.* **1996**, *37*, 9253; (b) Adam, W.; Saha-Moller, C. R.; Schmid, K. S. *Tetrahedron: Asymmetry* **1999**, *10*, 315; (c) Bierstedt, A.; Stolting, J.; Frohlich, R.; Metz, P. *Tetrahedron: Asymmetry* **2001**, *12*, 3399; (d) Uenishi, J.; Hiraoka, T.; Hata, S.; Nishiwaki, K.; Yonemitsu, O.; Nakamura, K.; Tsukube, H. *J. Org. Chem.* **1998**, *63*, 2481; (e) Morgan, B.; Oehlschlager, A. C.; Stokes, T. M. *J. Org. Chem.* **1992**, *57*, 3231; (f) Pai, Y.-C.; Fang, J.-M.; Wu, S.-H. *J. Org. Chem.* **1994**, *59*, 6018.

30. Kalyanam, N.; Rao, G. V. *Tetrahedron Lett*. **1993**, *34*, 1647.
31. Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem*. **1994**, *72*, 1181.
32. Li, C. J.; Haberman, J. X. *Tetrahedron Lett*. **1997**, *38*, 4735.
33. Chan, T. H.; Isacc, M. B. *J. Chem. Soc., Chem. Commun*. **1995**, 1003.
34. Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem*. **1999**, *64*, 217.
35. Isaac, M. B.; Paquette, L. A. *J. Org. Chem*. **1997**, *62*, 5333.
36. Singh, S.; Kumar, S.; Chimni, S. S. *Synlett* **2002**, 1277.
37. Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J.; Ulick, S. *J. Am. Chem. Soc*. **1982**, *104*, 7294.
38. The acetates of (***S***)-alcohols and racemic alcohols were prepared by stirring with excess (5 equiv.) of acetyl chloride and finally washing with 20% Na_2CO_3 solution.
39. (a) Kazlauskas, R. J.; Weissfloch, A. N. E.; Rapport, A. T.; Cuccia, L. A. *J. Org. Chem*. **1991**, *56*, 2656; (b) Weissfloch, A. N. E.; Kazlauskas, R. J. *J. Org. Chem*. **1995**, *60*, 6959; (c) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc*. **1991**, *113*, 6129; (d) Kim, M.-J.; Cho, H. J. *J. Chem. Soc., Chem. Commun*. **1992**, 1411.
40. Aggarwal, V. K.; Vennall, G. P. *Synthesis* **1998**, 1822 and references cited therein.
41. Hirota, K.; Kitade, Y.; Senda, S. *J. Org. Chem*. **1985**, *50*, 1512.
42. Stogryn, E. L. *J. Heterocycl. Chem*. **1974**, *11*, 251.
43. The $[\alpha]_D$ could not be recorded as there were wide fluctuations in the value given by polarimeter (when a solution of (*R*)-**6b** or (*S*)-**4b** was used) and no stable value could be obtained.