RSC Advances

This article can be cited before page numbers have been issued, to do this please use: B. M. Bhanage, G. V. More and K. C. Badgujar, *RSC Adv.*, 2014, DOI: 10.1039/C4RA14478C.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Dynamic Article Links ►
View Article Online
DOI: 10.1039/C4RA14478C

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Kinetic resolution of secondary alcohols with *Burkholderia cepacia* lipase immobilized on biodegradable ternary blend polymer matrix; as a highly efficient and heterogeneous recyclable biocatalyst

Ganesh V. More,[a] Kirtikumar C. Badgujar [a] and Bhalchandra M. Bhanage*[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Present work reports highly efficient and biocatalytic heterogeneous protocol for kinetic resolution (KR) of racemic secondary alcohols with vinyl acetate as an acyl donor, using biocatalyst *Burkholderia cepacia* lipase (BCL); immobilized on biodegradable ternary blend support through Polylactic acid (PLA)/ Polyvinyl alcohol (PVA) /Chitosan (CHI); (PLA/PVA/CHI-BCL). The KR reaction with various substituted aromatic, heterocyclic racemic secondary alcohols gave enantiomerically pure alcohol and its enantioriched acetate derivatives with high conversion (45-50%) and excellent enantiomeric excess (up to 99 % ee) at optimized reaction conditions. The reaction works under mild conditions using simple and inexpensive starting materials such as racemic alcohols, vinyl acetate, and immobilized biocatalyst. The given protocol provides excellent recyclability with good yield and enantiomeric excess values up to studied range of five cycles. The resultant products were characterized with the help of different analytical techniques such as ^{1}H and ^{13}C-NMR, Chiral HPLC column, Polarimeter, IR and GC-MS.

Introduction

The development of novel greener methodologies are of the great interest for synthesis of enantiomerically pure compounds; as chiral moieties with single enantiomer is widely found in several applications such as agrochemicals, pharmaceuticals, flavours, fragrances, fine chemicals and materials for electronics biosensor and optics.[1] Enantiomerically pure secondary alcohols is an important class of chiral building blocks and these are utilized for the synthesis of bio-active compounds and chiral auxiliaries for pharmaceutical intermediates.[2] After KR, these enantiopure alcohols can be converted into biologically significant compounds, such as Ezetimibe[3a], Prozac[3b], Emend[3c] & Sotalol[3d] (Figure 1).

From last decades, several strategies were invented for the preparation of enantiopure alcohols such as: (a-i) an asymmetric transfer hydrogenation of ketones using mixture of formic acid-triethylamine, HCO_2Na or IPA as a hydrogen source,(a-ii) an organocatalytic reduction of ketones, (a-iii) reduction of ketone using silane as a hydrogen source with metal,(a-iv) and reduction of ketones by using molecular hydrogen,[4] b) oxidative kinetic resolution (OKR) of alcohol,[5]c) selective hydrolysis of epoxides.[6] These methodologies gave good yield and enantiomeric excess of compounds, but suffers from several drawbacks such as use of molecular hydrogen that requires high pressure autoclave, low enantiomeric excess, longer reaction time, use of expensive metal precursor, phosphine based ligands, additives, multistep synthesized chiral ligands and no catalyst recovery, which limits their practical catalytic applications. Thus, the synthesis of enantiomerically pure alcohol and its acetate derivative is a challenging task, which can be achieved simply via greener biocatalytic pathway. In biocatalysis enzymes are used as catalysts which possessing advantages such as excellent stereo-, regio- and chemo-selectivities, milder reaction condition, no by-products formation and no need of cofactors.[7]

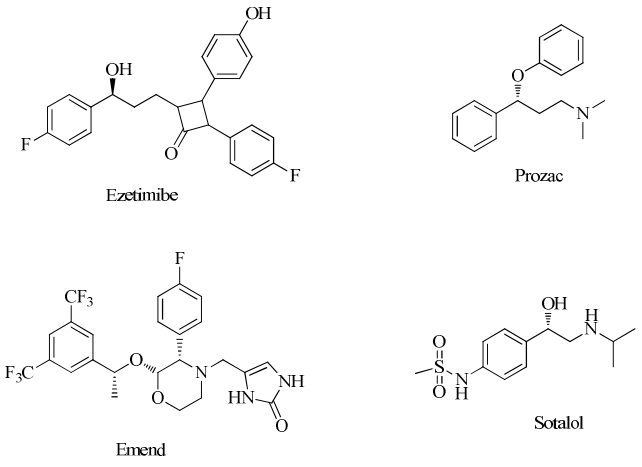


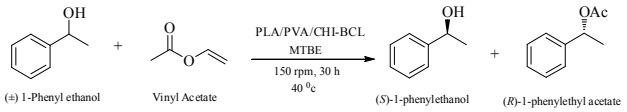
Fig. 1 Enantiopure alcohol motifs in bioactive compounds

In recent years, lipases have been widely used as an eco-friendly biocatalyst for the synthesis of pharmaceutical active intermediates and fine chemicals because of their stability, broad range of substrate scope and easy availability from bacteria and fungi.[8] Kinetic resolution of various racemates using lipases is considered to be a greener method for the separation of

View Article Online
DOI: 10.1039/C4RA14478C

enantiomers as it works at mild reaction conditions without any harm.[9] Kinetic resolution of inexpensive racemic alcohols using lipases is an attractive process for synthesis of expensive optically active alcohol intermediates as compared to hydrogenation of ketones, OKR and hydrolysis of epoxide.[10] However, direct use of free enzymes as a biocatalyst for the synthesis of enantiopure molecules suffers from several drawbacks such as lower activity, low selectivity, low yield, no recyclability, lesser stability in organic solvents and denaturation at higher temperature.[11] Also enzymes are expensive, and discarding them after one use is not economical, which restricts use of free enzymes for further industrial applications. To overcome theses drawbacks, various immobilization protocols are applied which give benefits such as improved stability, activity, reusability and less reaction time to obtain high yield and enantiopure compounds.[12] In literature various reports are present for KR of secondary alcohols but still there is lot of scope to find out new lipases and new immobilization techniques for the synthesis of chiral drug intermediate via KR.[10] In 2007, Sheldon *et al.*[13] proposed that immobilized enzyme on biodegradable polymer can serve great application in membrane and bioreactor coating; considering these aspects, use of the polymer matrix for enzyme immobilization is of great interest.

In continuation of our ongoing research on development of new superficial protocol for the KR of secondary alcohols;[10b] hence we prepared a ternary blend of PLA, PVA and CHI using the Grande *et al.*[14] method and used it for further immobilization of *Burkholderia cepacia* lipase (PLA/PVA/CHI-BCL, as a composition 1:6:1:2) by our procedure reported earlier.[15,16] The prepared immobilized biocatalyst was fully characterized by different techniques such as scanning electron microscopy (SEM) FT-IR and thermo-gravimetric (TGA). In the present study, we report a green and convenient strategy for KR of secondary alcohols catalyzed by PLA/PVA/CHI-BCL as a catalyst and reaction is carried out at 40°C for 30 h, which afforded optically enriched alcohols (up to 99% ee) and its acetate derivatives (up to 99% ee) with high conversion (Scheme 1).



Scheme 1 Kinetic resolution of secondary alcohol

Result and Discussion

Characterization of immobilized PLA/PVA/CHI-BCL

The surface analysis of ternary blend (PLA/PVA/CHI) and immobilized lipase (PLA/PVA/CHI-BCL) was performed by Scanning Electron Microscopy analysis (Figure 2). The ternary blend PLA/PVA/CHI (1:6:1) showed a plane surface (Figure 2A), whereas the immobilized lipase PLA/PVA/CHI-BCL (1:6:1:2) showed well dispersed globules on the surface (Figure 2B). This change in surface morphology indicated that, *Burkholderia cepacia* lipase was successfully immobilized into the ternary blend, which is responsible for the catalytic activity. Similar type of surface morphology was observed in previous report for the HPMC-PVA film immobilized *Rhizopus oryzae* Lipase.[17] The FT-IR spectroscopy is the one of the best technique to study the parent amide functionality present in enzyme due to proteneous nature of enzyme (Figure 3).

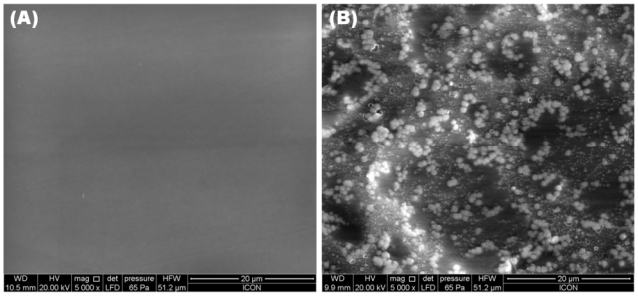


Fig. 2 (A) Ternary blend PLA/PVA/CHI (1:6:1), (B) Immobilized BCL lipase into ternary blend polymer support PLA/PVA/CHI-BCL (1:6:1:2).

In FT-IR analysis the wave number values of ternary blend (PLA/PVA/CHI) are in good agreement with the literature values (Figure 3A).[14] The FT-IR analysis of parent lipase molecules showed three characteristics amide I, II, III bands in between spectral region of 1750-1300 cm^{-1}.[15,18,19] In our FT-IR study of free lipase BCL (Figure 3C), the amide I band was observed at 1600-1750 cm^{-1} which is a characteristic band of the C-O stretching vibrations. The amide II band was observed at 1500-1600 cm^{-1} because of N-H bending and C-N stretching vibrations.[15,18,19] The amide III band is attributed at 1300-1450 cm^{-1} owing to, C-C, C-N stretching and N-H bending vibrations. Similar types of bands were existed in the immobilized lipase PLA/PVA/CHI-BCL also (Figure 3B). Thus, the amide I, II, III bands for the free BCL and ternary blend immobilized PLA/PVA/CHI-BCL (1:6:1:2) lipases were observed in same region, which indicating the existance of the parent amide functionality of enzyme in immobilized biocatalyst (Figure 3B and 3C).

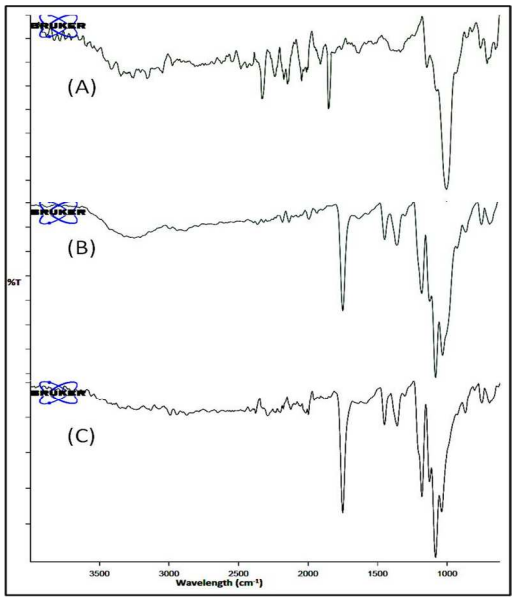


Fig. 3 (A) Ternary blend PLA/PVA/CHI (1:6:1), (b) PLA/PVA/CHI-BCL (1:6:1:2) immobilized lipase on ternary blend (c) free *Burkholderia cepacia* lipase.

Turner and Vulfson[20] proposed that temperature around 90-130 °C is required to eliminate the physically adsorbed water

View Article Online
DOI: 10.1039/C4RA14478C

molecules while temperature between 200-240 °C is required to eliminate tightly bound water which is present in close vicinity of the enzyme (Figure 4). Similar type of results has been observed in the present study. Physically adsorbed water molecules seem to be eliminated around 100-110 °C of temperatures, while closely associated water molecules are eliminated at around 240 °C as evident from the TGA curve. Moreover it can be clearly seen that stability of the immobilized lipase (Figure 4; blue colour line) is considerably improved as compared to free lipase (Figure 4; black colour line). Similar type of improved stability was observed by Dhake *et al.*[17] for the HPMC-PVA film immobilized *Rhizopus oryzae* Lipase.

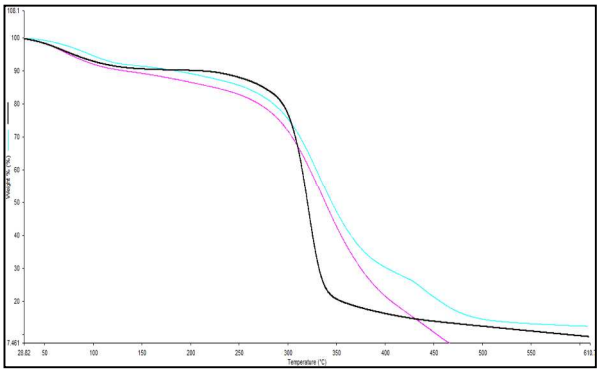


Fig. 4 Pink colour: Ternary blend PLA/PVA/CHI (1:6:1); Blue colour PLA/PVA/CHI-BCL (1:6:1:2) immobilized lipase on ternary blend and Black colour: free *Burkholderia cepacia* lipase.

In the present study, a series of experiments were performed to optimize the various reaction parameters such as catalyst screening, effect of solvent, biocatalyst loading, effect of acyl donors, effect of agitation speed, molar ratio, reaction temperature and time; which are summarized in Table 1 and 2. For screening purpose, we used two enzymes i.e. free BCL and CCL (*Candida cylindracea* lipase), and their ternary blend immobilized form denoted as PLA/PVA/CHI-BCL and PLA/PVA/CHI-CCL (Table 1, entries 1-4). It was observed that among above four biocatalysts; PLA/PVA/CHI-BCL gave 50% conversion with excellent enantioselectivity towards the (*S*)-1-phenylethanol (ee_s) 95% ee and (*R*)-phenylethyl acetate (ee_p) 93% ee, in *n*-hexane as a solvent at 45 °C temperature and hence it was used for further studies (Table 1, entry 1). Subsequently, we studied the effect of the catalyst loading on the conversion and enantioselectivity of the desired products. We screened the catalyst loading ranging from 10 mg to 50 mg (see Table 1, entries 5-9). It was observed that with increase in catalyst concentration from 10 mg to 20 mg increases the enantioselectivity and yield of desired product. (Table 1, entry 6) Further increase in the amount of catalyst concentration did not show significant effect on the yield and enantioselectivity of the desired product (Table 1, entries 7-9). A control experiment in the absence of PLA/PVA/CHI-BCL did not show any conversion, thus elucidating that PLA/PVA/CHI-BCL was solely responsible to catalyze the KR of racemic alcohols (Table 1, entry 10).

Next, by using PLA/PVA/CHI-BCL as a catalyst, the influence of the solvent on the KR of racemic 1-phenylethanol reaction was investigated (Table 2, entries 1-10). Nonpolar solvents like *n*-hexane, *n*-heptane, toluene, methyl tertiary butyl ether (MTBE), dichloromethane (DCM) and polar solvents like tetrahydrofuran (THF), Acetonitrile (ACN), ethyl acetate were screened.

Table 1 Effect of various enzymes and catalyst loading on the kinetic resolution of racemic 1-phenylethanol[a]

Entry	Catalyst	Catalyst loading (mg)	Conversion (%)	% ee_s [b]	% ee_p [c]	E
Biocatalyst Screening						
1	PLA/PVA/CHI-BCL	20	50	95	93	103
2	Free BCL	4	10	10	95	43
3	PLA/PVA/CHI-CCL	20	30	25	57	5
4	Free CCL	4	17	8	40	3
Catalyst Loading						
5	PLA/PVA/CHI-BCL	10	43	68	90	39
6	PLA/PVA/CHI-BCL	20	50	95	93	103
7	PLA/PVA/CHI-BCL	30	50	91	92	76
8	PLA/PVA/CHI-BCL	40	50	93	92	82
9	PLA/PVA/CHI-BCL	50	50	93	94	110
10	PLA/PVA/CHI-BCL	--	NR	--	--	--

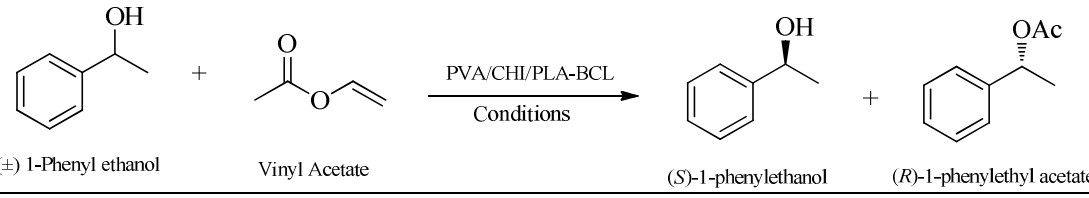
[a] Reaction conditions: 1-phenylethanol-0.5 mmol, vinyl acetate-2 mmol, *n*-hexane-2ml, speed of agitations-150 rpm, temp- 45°C, time-48 h, NR: no reaction, ,[b,c] determined by Chiral HPLC on Chiralcel OD-H column.

It was observed that the nature of solvent marginally affects the conversion and enantioselectivity of the (*R*)-phenylethyl acetate (ee_p) and (*S*)-1-phenylethanol (ee_s) except 1,4 dioxane. All developed immobilized biocatalyst are stable in various screened solvents (except 1, 4 dioxane). Literature survey showed that generally solvent greatly influences the catalytic activity and stability of the lipase enzymes. Present biocatalyst is highly stable and in literature, we rarely find any report which showed such excellent stability and activity of immobilized biocatalyst in various solvents. The activity along with the enantioselectivity was significantly higher in nonpolar solvents such as MTBE gives ee_s 96%ee and ee_p 97%ee with 50% conversion (Table 2, Entry 3) hence; MTBE was used it for further studies. Also one experiment was carried out in under neat condition (solvent free - SF) which provides the 45% conversion with ee_s 78 %ee and ee_p 95 %ee (Table 2, entry 10). It is well known fact that acyl donor plays a crucial role in prediction of the conversion and enantioselectivity in KR reaction; hence we screened various acyl donors such as vinyl acetate, ethyl acetate, acetic anhydride, acetic acid (Table 2, entries 11-13). Among these acyl donors vinyl acetate gives 50 % conversion with ee_s 96%ee and ee_p 97%ee (Table 2, entry 3), while in presence of acetic acid no conversion was observed (NR) (Table 2, entry 13). Thus we used vinyl acetate as an acyl donor for further experiments. However molar ratio study is an important aspect hence we studied effect of the molar ratio on conversion and enantioselectivity, the different molar ratio of alcohol: vinyl acetate was screened ranging from (0.5:1.5) to (0.5:2.5). The molar ratio 0.5:2 (alcohol: vinyl acetate) gave better conversion and enantioselectivity (Table 2, entry 3). The decrease in moles of vinyl acetate from 2 to 1.5 showed decreases in the conversion and enantioselectivity (Table 2, entry 14); whereas increase in moles of vinyl acetate from 2 to 2.5 had no significant effect on the conversion as well as enantioselectivity (Table 2, entry 15).

Influence of temperature is an important aspect which greatly affect on the enantioselectivity in chiral chemistry hence we studied the effect of temperature (30-50 °C) on conversion and enantioselectivity of desired products (Table 2, entries 16-18). It

View Article Online
DOI: 10.1039/C4RA14478C

Table 2 Effect of reaction parameters on the kinetic resolution of racemic 1-phenylethanol[a]



(±) 1-Phenyl ethanol — Vinyl Acetate — (*S*)-1-phenylethanol — (*R*)-1-phenylethyl acetate

Entry	Solvent	Acyl donor	Temp. (°C)	Time (h)	Conversion (%)	% ee_s [b]	% ee_P [c]	E
Effect of Solvent								
1	*n*-hexane	Vinyl acetate	45	48	50	95	93	103
2	Toluene	Vinyl acetate	45	48	42	69	95	81
3	MTBE	Vinyl acetate	45	48	50	96	97	>200
4	DCM	Vinyl acetate	45	48	49	93	96	168
5	THF	Vinyl acetate	45	48	50	97	95	165
6	ACN	Vinyl acetate	45	48	49	94	96	175
7	1,4-Dioxane	Vinyl acetate	45	48	20	22	88	19
8	Ethyl acetate	Vinyl acetate	45	48	50	94	93	98
9	n-heptane	Vinyl acetate	45	48	50	97	93	116
10	SF [d]	Vinyl acetate	45	48	45	78	95	93
Effect of acyl donor								
11	MTBE	Ethyl acetate	45	48	15	6	35	2
12	MTBE	Acetic Anhydride	45	48	34	34	66	7
13	MTBE	Acetic acid	45	48	NR	Racemic	NR	--
14[e]	MTBE	Vinyl acetate	45	48	49	91	95	124
15[f]	MTBE	Vinyl acetate	45	48	49	95	97	>200
Effect of temperature								
16	MTBE	Vinyl acetate	RT	48	35	54	99	>200
17	MTBE	Vinyl acetate	40	48	50	98	99	>200
18	MTBE	Vinyl acetate	50	48	49	96	96	>200
19[g]	MTBE	Vinyl acetate	40	48	49	97	99	>200
20[h]	MTBE	Vinyl acetate	40	48	50	96	99	>200
Effect of time								
21	MTBE	Vinyl acetate	40	1	6	6	99	>200
22	MTBE	Vinyl acetate	40	3	11	12	99	>200
23	MTBE	Vinyl acetate	40	5	15	18	99	>200
24	MTBE	Vinyl acetate	40	10	30	42	99	>200
25	MTBE	Vinyl acetate	40	15	40	66	99	>200
26	MTBE	Vinyl acetate	40	24	48	90	99	>200
27	MTBE	Vinyl acetate	40	30	50	98	99	>200
28	MTBE	Vinyl acetate	40	48	50	98	99	>200

[a] Reaction conditions: 1-phenylethanol- 0.5 mmol, acyl donor- 2 mmol, PLA/PVA/CHI-BCL -20 mg, solvent- 2ml, [b,c] analysis performed by chiral HPLC on Chiralcel OD-H column, [d] SF: solvent free, [e] vinyl acetate 1.5 mmol, [f] vinyl acetate 2.5 mmol, [g] speed of agitation- 165 rpm, [h] speed of agitations-125 rpm, NR: no reaction, RT: room temperature.

was observed that at room temperature, the conversion and enantioselectivity of alcohol (ee_s) was low, whereas increase in the temperature to 40°C increases the conversion up to 50% as well as enantioselectivity of ee_s 98%ee and ee_p 99%ee. Further increase in the temperature up to 50 °C had no profound effect on conversion but slightly decreases the enantioselectivity of product; therefore further experiments were carried at 40°C temperature.

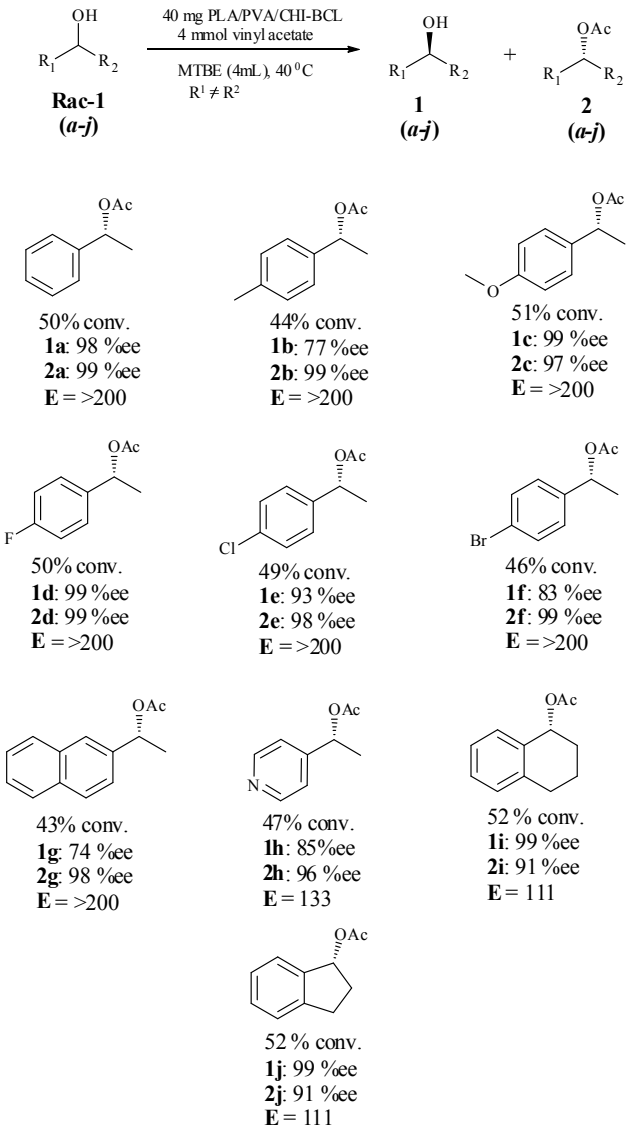
Finally, we examined the effect of the reaction time on the reaction yield and enantioselectivity for a given model reaction (Table 2, entries 21-28). After 30 h, maximum conversion and enantioselectivity of desired product was obtained. Thus, the best optimized reaction parameters to obtain the good yield and enantioselectivity for KR of racemic alcohol are as: 1-phenylethanol (0.5 mmol: 1 eq.), vinyl acetate (2 mmol: 4 eq.), PLA/PVA/CHI-BCL (20 mg), and MTBE (2 mL) at 40°C for 30 h.

Encouraging with these mild and softer optimized reaction conditions, we studied the various racemic secondary alcohols for broaden the scope and general applicability of the developed methodology (Figure 2). It was observed that all substrate gave higher conversion and excellent enantioselectivity. The model reaction of rac 1-phenylethanol with vinyl acetate under the optimized reaction conditions provides 50% conversion and enantiomeric excess as **1a**: 98% ee, **2a**: 99% ee. Among the various electron donating (-Me, -OMe) derivatives furnished good yield of corresponding enantiomerically pure alcohols and its acetate derivatives as **1b**: 77 %ee; **2b**: 99 %ee and **1c**:99 %ee; **2c**: 97% ee. Moreover, derivatives bearing halo-substituents (-F, -Cl, -Br) were also provided good yield of corresponding enantiomerically pure alcohols and its acetate derivatives as for **1d**: 99% ee; **2d**: 99% ee, **1e**:93% ee; **2e**:98% ee, **1f**: 83% ee; **2f**: 99% ee. It was found that bulky Naphthyl-based carbinols providing corresponding enantio-rich alcohol and its acetate derivatives gives **1g**:74% ee, **2g**:98% ee respectively. Next, we also studied heterocyclic derivative which gave enantio-rich

View Article Online
DOI: 10.1039/C4RA14478C

alcohol and its acetate derivatives as **1h**: 85% ee, **2h**: 96% ee respectively. Subsequently, cyclic aromatic derivatives also provided good enantiomeric excess of desired products **1i**: 99% ee; **2i**: 91% ee and **1j**: 99% ee; **2j**: 91% ee.

Fig.2 Kinetic resolution of substituted racemic secondary alcohols[a]



[a] Reaction conditions: racemic alcohol (1 mmol), vinyl acetate (4 mmol), MTBE (4ml) , speed of agitation-150 rpm, temperature- 40°C, analysis performed by Chiral HPLC on Chiralcel OD-H column and Chiralcel OJ-H column.

Biocatalyst recyclability

In order to increase feasibility of our biocatalytic protocol, we determined reusability of PLA/PVA/CHI-BCL for KR reaction. It was found that immobilized biocatalyst was used for five consecutive cycles (Figure 3). There was marginal (1-2% ee) decrease in enantiomeric excess with respect to acetate derivative in all five recycles. Alcohol also showed the good enantiomeric excess in three recycle however; while enantiomeric excess declined up to 75 % ee for the fifth cycle. The decrease in enantiomeric excess was believed to be deactivation of lipase due to continuous exposure to alcoholic substrate.[17,18]

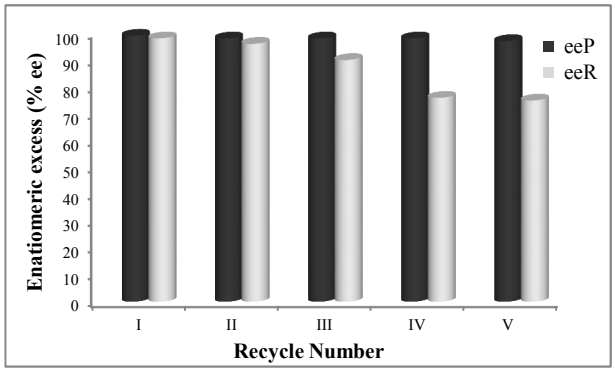


Fig. 3 Recyclability study of immobilized lipase

Conclusions

In this work, we have developed a robust and efficient immobilized PLA/PVA/CHI-BCL catalyst for the synthesis of enantiopure alcohols and its acetate derivative via KR methodology. The protocol showed excellent enantiomeric excess (up to 99%ee) when the reaction was carried out at mild condition such as 40 °C. Obviously, this is a new immobilized biocatalyst which having great competitive advantages such as high thermal stability, low catalyst loading, high enantioselectivity and good conversion of desired products. Catalyst PLA/PVA/CHI-BCL is highly stable in polar and nonpolar solvents with good activity and recyclability (up to 5 cycles). This biodegradable catalyst shows attractive results and has bright future in pharmaceutical science for synthesis of active pharmaceutical ingredients (APIs).

Acknowledgements

G.V.M. is thankful to the Council of Scientific and Industrial Research (CSIR), New Delhi for providing a senior research fellowship. The authors also thank to Department of Science and Technology (DST)-SERB, India (project file NO.SR/S1/OC-09-2012) for financial support.

References

[a] *Institute of Chemical Technology, Department of Chemistry ,Matunga, Mumbai-400019. India. Fax: +91 22 3361 1020; Tel: 022 33612601; E-mail: bm.bhanage@gmail.com*

† Electronic Supplementary Information (ESI) available: general experimental procedure, Copies of the ^{1}H and ^{13}C NMR spectra and the Chiral HPLC chromatograms of the products.
See DOI: 10.1039/b000000x/

1 *(a)* Houben-Weyl: Methods of Organic Chemistry, Vol. E21 (Eds.: G. Helmchen, R.W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, 1995; *(b)* Nogradi, Stereoselective Synthesis, Wiley-VCH, Weinheim, 1995; *(c)* FDA's statement for the development of new stereoisomeric drugs, *Chirality*., 1992, **4**, 338-340*; (d)* V. Farina, J. T. Reeves, C. H. Senanayake, and J. J. Song, *Chem. Rev*., 2006, **106**, 2734-2793; *(e)* D. Muñoz Solano, P. Hoyos, M. J. Hernáiz, A. R. Alcántara, and J. M. Sánchez-Montero, *Bioresour. Technol.,* 2012, **115**, 196-207.

2 *(a)* Collins, A. N.; Sheldrake, G. N.; Crosby, J., Eds. Chirality in Industry: John Wiley & Sons:Chichester, 1992; *(b)* Wang, G.; Liu, X.; Zhao, G. *Tetrahedron: Asymmetry,* 2005., **16**, 1873-1879; *(c)*

View Article Online
DOI: 10.1039/C4RA14478C

G.V. More and B.M. Bhanage *Eur. J. Org. Chem.,* 2013, **30**, 6900-6906; *(d)* Zhu, D.; Mukherjee, C.; Hua, L. *Tetrahedron: Asymmetry,* 2005, **16**, 3275-3278; *(e)* Lennon, I. C.; Ramsden, J. A. *Org. Process Res. Dev.,* 2005., **9**, 110-112; *(f)* M. Fuchs, D. Koszelewski, K. Tauber, J. Sattler, W. Banko, A. K. Holzer, M. Pickl, W. Kroutil, and K. Faber, *Tetrahedron,* 2012, **68**, 7691-7694; *(g)* M. Reilly, D. R. Anthony, and C. Gallagher, *Tetrahedron Lett.*, 2003, **44**, 2927-2930; *(h)* K. Han, C. Kim, J. Park, and M.-J. Kim, *J. Org. Chem.*, 2010, **75**, 3105-3108; *(k)* T. Ohkuma, H. Doucet, T. Pham, K. Mikami, T. Korenaga, M.Terada, and R. Noyori*, J. Am. Chem. Soc.,* 1998, **120**, 1086-1087.

3 *(a)* B. Bertrand, S. Durassier, S. Frein, and A. Burgos, *Tetrahedron Lett.*, 2007, **48**, 2123–2125; *(b)* D. M. Perrine, N. R. Sabanayagam, and K. J. Reynolds, *J. Chem. Educ.*, 1998, **75**, 1266; *(c)* P. J. Vankawala, R.R. C. Elati, N. K.Kolla, S. R. Chamala, S. Gangula, Pub. No. : *US 2011/0094321 A1; (d)* Paul R. Brodfuehrer, Patrick Smith, John L. Dillon, and Purushotham Vemishetti, *Org. Process Res. Dev.,* 1997, **1**, 176-178

4 *(a)* A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, and R. Noyori, *J. Am. Chem. Soc.,* 1996, **118**, 2521-2522; *(b)* M. Watanabe, M. Watanabe, K. Murata, K. Murata, T. Ikariya, and T. Ikariya, *J. Org. Chem.*,2002, **67**, 1712-1715; *(c)* Hae Yoon Rhyoo, Hee-Jung Park and Young Keun Chung, *Chem. Commun.,* 2001,**20**, 2064-2065; *(d)* H. Y. Rhyoo, Y. A. Yoon, H. J. Park, and Y. K. Chung, *Tetrahedron Lett.,* 2001, **42**, 5045-5048; (e) T. Langer and G. Helmchen, *Tetrahedron Lett.*, 1996, **37**, 1381-1384; *(f)* D. Cuervo, M. P. Gamasa, and J. Gimeno, *Chem. Eur. J.,* 2004, **10**, 425-432; *(g)* D. R. Li, A. He, and J. R. Falck, *Org. Lett.*, 2010, **12**, 1756-1759; *(h)* T. Inagaki, A. Ito, J. I. Ito, and H. Nishiyama, *Angew. Chemie. Int. Ed.*, 2010, **49**, 9384-9387; *(i)* M. Tokunaga, J. F. Larrow, F. Kakiuchi, E. N. Jacobsen, *Science*, 1997, **277**, 936-938; *(j)* R. Noyori, T. Ohkuma, *Angew. Chemie. Int. Ed.*, 2001, **40**, 40-73.

5 *(a)* J. T. Bagdanoff, E. M. Ferreira, and B. M. Stoltz, *Org. Lett.*, 2003, **5**, 835-837; *(b)* J. T. Bagdanoff, and B. M. Stoltz, *Angew. Chemie. Int. Ed.*, 2004, **43**, 353-357; *(c)* S. K. Mandal, D. R. Jensen, J. S. Pugsley, and M. S. Sigman, *J. Org. Chem.,* 2003, **68**, 4600-4603.

6 *(a)* D. A. Annis and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1999, **121**, 4147-4154; *(b)* E. N. Jacobsen, *Acc. Chem. Res.*, 2000, **33**, 421-431; *(c)* N S. E. Schaus, B. D. Brandes, J. F. Larrow, M. Tokunaga, K. B. Hansen, A. E. Gould, M. E.Furrow, and E. N. Jacobsen, *J. Am. Chem. Soc.,* 2002, **124**, 1307-1315.

7 F. Hasan, A. A. Shah, and A. Hameed, *Enzyme Microb. Technol.*, 2006, **39**, 235-251.

8 *(a)* S. Benjamin and A. Pandey, *Yeast*, 1998, **14**, 1069-1087; *(b)* K. E. Jaeger and M. T. Reetz, *Trends Biotechnol.*, 1998, **16**, 396-403.

9 *(a)* J. M. Keith, J. F. Larrow, and E. N. Jacobsen, *Adv. Synth. Catal.*, 2001, **343**, 5-26; *(b)* M. Breuer, K. Ditrich, T. Habicher, B. Hauer, M. Keßeler, R. Stürmer, and T. Zelinski, *Angew.Chemie. Int. Ed.,* 2004, **43**, 788-824; *(c)* A. Ghanem and H. Y. Aboul-Enein, *Chirality*, 2005, **17**, 1-15.

10 *(a)*R.V.Muralidhar, R.Marchant, P.Nigam, *J. Chem. Technol. Biotechnol.,* 2001, **76** , 3-8; *(b)* N K. P. Dhake, K. M. Deshmukh, Y. S. Wagh, R. S. Singhal, and B. M. Bhanage, *J. Mol. Catal.B Enzym.,* 2012, **77**, 15-23; *(c)* G.D. Yadav, S. Devendran , *J. Mol. Catal. B Enzym.,* 2012, **81**, 58-65; *(d)* Borén, L., Martín-Matute, B., Xu, Y., Córdova, A. and Bäckvall, J.-E, *Chem. Eur. J.,* 2006, **12**, 225-232; *(e)* B. S. Chen and U. Hanefeld, *J. Mol. Catal. B Enzym.*, 2013, **85-86**, 239-242; *(f)*E. A. Manoel, K. C. Pais, M. C. Flores, L. S. D. M. E Miranda, M. A. Z. Coelho, A. B. C.Simas, D. M. G. Freire, and R. O. M. A. De Souza, *J. Mol. Catal. B Enzym.,* 2013, **87**, 139-143; *(g)* Micro review: J.H. Lee, K. Han, M. Kim, J. Park, *Eur. J. Org. Chem. 2010*, 999-1015; (*h*) L.H. Andradea, L.P. Rebeloa, C. G.C.M. Netto, H.E.Toma, *J. Mol. Catal. B Enzym.,* 2010, **66**, 55-62.

11 *(a)* Reetz MT, *Curr Opin Chem Biol.,* 2002, **6**,145-150; *(b)* C. Mateo, J. M. Palomo, G. Fernandez-Lorente, J. M. Guisan, and R. Fernandez-Lafuente,*Enzyme Microb. Technol.,* 2007, **40**, 1451-1463.

12 *(a)*X. Liu, Y. Guan, R. Shen, and H. Liu, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.,* 2005,**822**, 91-97; *(b)* X. Wenlei and M. Ning, *Energy and Fuels*, 2009, **23**,1347-1353; *(c)* J. C. Santos, P. D. Mijone, G. F. M. Nunes, V. H. Perez, and H. F. de Castro, *Colloids Surfaces B Biointerfaces,* 2008, **61**, 229-236; *(d)* P. Adlercreutz, *Chem. Soc. Rev.*, 2013, **42**, 6406-36.

13 R. A. Sheldon, *Adv. Synth. Catal.*, 2007, **349**, 1289-1307.

14 R. Grande and A. J. F. Carvalho, *Biomacromolecules*, 2011, **12**, 907-914.

15 K. C. Badgujar, K. P. Dhake, and B. M. Bhanage, *Process Biochem.*, 2013, **48**, 1335-1347.

16 K. C. Badgujar, B. M. Bhanage, *Enzyme Microb. Technol.*, 2014, **57**, 16-25.

17 K. P. Dhake, P. J. Tambade, Z.S. Qureshi, R.S. Singhal, B. M. Bhanage, *ACS Catal.,* 2011, **1**, 316-322.

18 K. C. Badgujar, K. P. Dhake, and B. M. Bhanage, *Process Biochem.*, 2013, **49**, 1304-1313.

19 K. Ramani, R. Boopathy, C. Vidya, L. John Kennedy, M. Velan, G. Sekaran, *Process Biochem*, 45, 986-992

20 N. A. Turner, E. N. Vulfson, Enzym Microb Technol, 27, 108-113

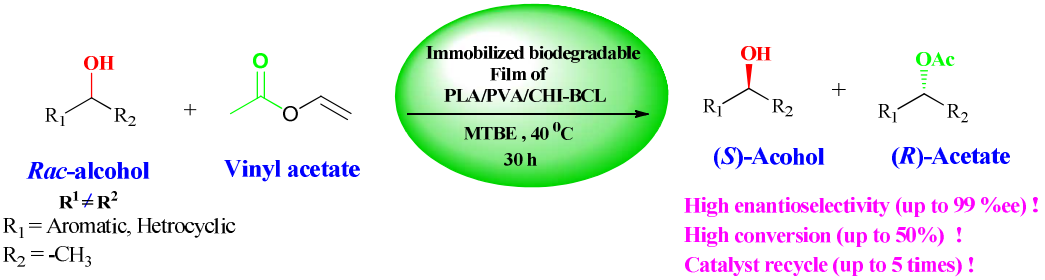
View Article Online
DOI: 10.1039/C4RA14478C

Kinetic resolution of secondary alcohols with *Burkholderia cepacia* lipase immobilized on biodegradable ternary blend polymer matrix; as a highly efficient and heterogeneous recyclable biocatalyst

Ganesh V. More,[a] Kirtikumar C. Badgujar,[a] and Bhalchandra M. Bhanage*[a]

Department of Chemistry, Institute of Chemical Technology
Matunga, Mumbai-400019. India.
Fax: +91 22 3361 1020

E-mail: bm.bhanage@gmail.com, bm.bhanage@ictmumbai.edu.in



A greener and superficial protocol for the synthesis of enantiomerically pure alcohols and its enantioriched acetate derivatives using biodegradable heterogeneous recyclable catalyst with high conversion has been developed.