Tetrahedron Letters 49 (2008) 4865–4868

Contents lists available at ScienceDirect

Tetrahedron Letters

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

A chiral Mn(III) salen complex immobilized onto ionic liquid modified mesoporous silica for oxidative kinetic resolution of secondary alcohols

Suman Sahoo [a], Pradeep Kumar [b], F. Lefebvre [c], S. B. Halligudi [a,*]

[a] *Inorganic Chemistry and Catalysis Division, National Chemical Laboratory, Pune 411 008, India*
[b] *Organic Chemistry Technology, National Chemical Laboratory, Pune 411 008, India*
[c] *Laboratoire de Chemie Organometallique de Surface, CNRS-CPE, Villeurbanne Cedex, France*

ARTICLE INFO

Article history:
Received 4 March 2008
Revised 30 May 2008
Accepted 3 June 2008
Available online 6 June 2008

Keywords:
Oxidative kinetic resolution
Secondary alcohol
Mn(III) salen
Mesoporous silica SBA-15
Supported ionic liquid

ABSTRACT

A supported ionic liquid strategy has been applied for the immobilization of a chiral Mn(III) salen complex onto ionic liquid modified mesoporous silica SBA-15. The immobilized catalyst demonstrated high enantioselectivity and activity in the oxidative kinetic resolution of secondary alcohols, and could be recycled five times without obvious loss of activity.

Optically active secondary alcohols are extremely useful starting materials and intermediates in the synthetic organic chemistry, agrochemicals and in the pharmaceutical industry.[1] During the last 10 years, significant progress has been made in the development of efficient methods for the chiral metal complex catalyzed transformation of prochiral ketones to chiral alcohols, such as asymmetric hydrogenation,[2a–c] transfer hydrogenation,[2d] hydrosilylation[2e,f] and hydroboration.[2g,h] Kinetic resolution of racemic secondary alcohols is a general efficient synthetic method to obtain optically active alcohols and their variants, and has been used widely for the synthesis of complex natural products and their derivatives.[3] Enzymatic and catalytic kinetic resolution of racemic alcohols through acylation or deacylation has been studied extensively.[4,5] Effective oxidative kinetic resolution of racemic alcohols has been reported by Sigman's and Stoltz's groups, which involved the aerobic oxidative kinetic resolution of secondary alcohols catalyzed by (−)-sparteine/Pd(II) to conveniently access enantiomerically enriched secondary alcohols.[6] Several iridium and ruthenium complexes have also been reported for the oxidative kinetic resolution of secondary alcohols.[1,7] Recently, Sun et al. found that Jacobsen's chiral Mn(III) salen complex was an effective catalyst for the oxidative kinetic resolution of secondary alcohols with excellent enantioselectivity (up to 98% ee) in water in the presence of a phase transfer catalyst with hypervalent iodine as the co-oxidant.[8]

The demand for economical, eco-friendly and recyclable supported catalysts has led some groups to attach chiral complexes onto solid supports.[9,10] However, these systems suffer from various disadvantages such as poor activity, leaching of the active species into the reaction medium, and low accessibility of substrates either due to hydrophobicity or low surface area of the supported catalysts. Ionic liquids have become common in recent years and are important alternative mediums for traditional organic synthesis and catalytic reactions.[11] Moreover, since ionic liquids are expensive, it is desirable to minimize the amount of ionic liquid used in biphasic reaction systems. In addition, the high viscosity of ionic liquids can induce mass transfer limitations if the chemical reaction is fast, in which case, the reaction takes place only within the narrow diffusion layer and not in the bulk of the ionic liquid catalyst solution. These problems can be circumvented by immobilizing a thin film of ionic liquid-containing organometallic complex onto a high surface area support. This allows fixing molecular catalysts in a widely tailorable environment without the drawbacks of complex grafting chemistry.[12] This supported ionic liquid phase (SILP) catalyst allows the application of fixed-bed reactors and makes the separation and catalyst-recycling easy. A few reports on the immobilization of chiral Mn(III) salen complexes for the oxidative kinetic resolution of secondary alcohols have been reported in the literature.[13] Herein, we report for the first time, the kinetic resolution of secondary alcohols using a chiral Mn(III) salen complex immobilized over mesoporous silica by the SILP strategy. This work involves the immobilization of a chiral metal complex

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* Corresponding author. Tel.: +91 20 25902107; fax: +91 20 25902633.
E-mail address: sb.halligudi@ncl.res.in (S. B. Halligudi).

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doi:10.1016/j.tetlet.2008.06.014

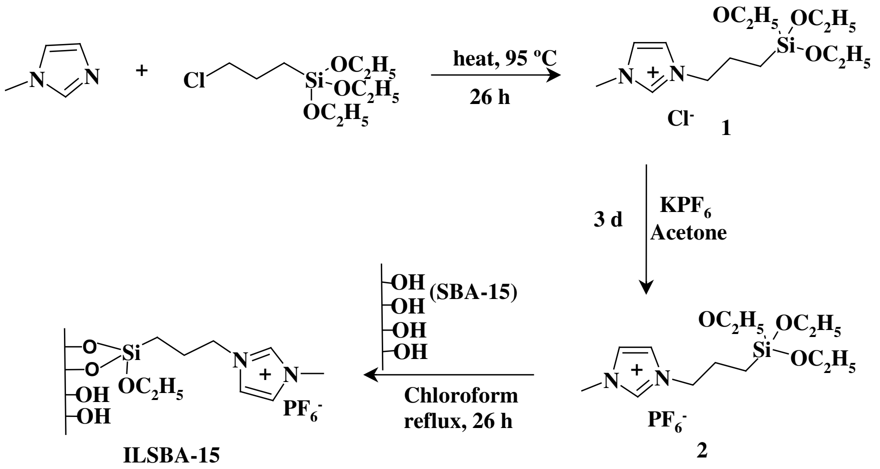
onto an ionic liquid modified mesoporous silica SBA-15 support,[14] which has a long range order, large monodispersed mesopores and thick walls. This immobilized catalyst provided good activities with k_{rel}[15] values compared to that of its homogeneous analogue.

The SBA-15 material was synthesized by the conventional hydrothermal pathway with a gel composition of 4 g polymer: 0.041 TEOS:0.24 HCl:6.67 H_2O.[16] The ionic liquid modified mesoporous silica, SBA-15 catalyst, was synthesized following the literature procedure (Scheme 1).[17] The ionic liquid 1-(3-triethoxysilylpropyl)-3-methylimidazolium hexafluorophosphate (**2**) was synthesized by ion exchange of 1-(3-triethoxysilylpropyl)-3-methylimidazolium chloride (**1**) with potassium hexaflourophosphate. SBA-15 was modified with the ionic liquid (**2**) to provide the covalently anchored ionic liquid (Scheme 1), ILSBA-15. This was added to a solution of [Bmim] PF_6^- and (*S*,*S*)-(+)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride (chiral Mn(III) salen) complex in acetone. After evaporation of the solvent, the catalyst (MnILSBA-15) was obtained as a free-flowing powder (Scheme 2). DRUV–vis, FTIR and NMR spectroscopy (discussed in the Supplementary data) confirmed the successful immobilization of the chiral Mn(III) salen complex onto the mesoporous silica. N_2 sorption, XRD (discussed in the Supplementary data) showed that the long-range mesoporous ordering of the parent SBA-15 support was maintained after the immobilization.

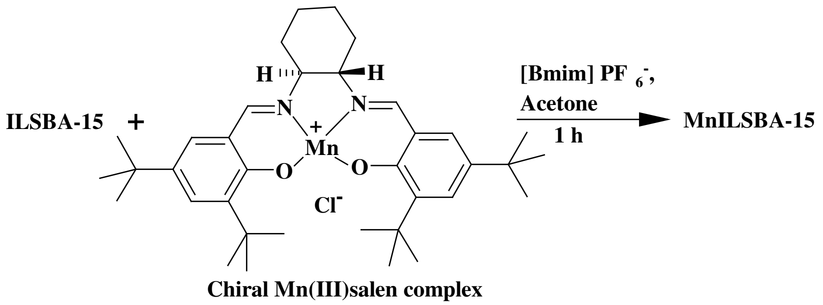
In order to assess the efficiency of the immobilized catalyst in the oxidative kinetic resolution of secondary alcohols, the experimental conditions were first optimized for the oxidative kinetic resolution of α-methyl benzyl alcohol as a model substrate using diacetoxyiodobenzene ($PhI(OAc)_2$) as the oxidant.[18] The reaction was carried out using the different additives listed in Table 1. Among these, $N(CH_3)_4Br$ and KBr gave good results in terms of % ee and k_{rel}, which is in accordance with the literature (Table 1, entries 2 and 6).[8] Additives having bromide as the anion gave excellent enantioselectivities compared to other additives. Low conversion and poor enantioselectivity resulted when the additive was not used. We also tried to use a bromide ion-containing ionic liquid, which could act both as a support and additive (Table 1, entries 9 and 10) and we obtained excellent results. However, the bromide ion-containing ionic liquids are soluble in water and the Mn-salen complex is less soluble in this ionic liquid. So, [Bmim] PF_6^- was chosen as the ionic liquid for the supported ionic liquid catalysis.

The effect of different solvents was studied in the supported ionic liquid phase catalyzed oxidative kinetic resolution of α-methyl benzyl alcohol. In the case of dichloromethane water mixture, a small amount of metal complex leached into the organic phase (from ICP-AES analysis). Hexane and water as well as diethyl ether and water mixtures were found to be the best solvent medium for the kinetic resolution because of less leaching of the metal complex into the organic phase and also in these solvent systems, higher activity and enantioselectivities were obtained.

After determining the optimized conditions, the scope of the method was investigated in different racemic systems. As seen in Table 2, the chosen catalyst system was suitable for a wide range of secondary alcohols. The enantiomeric excess of the secondary

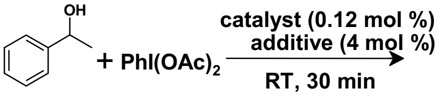


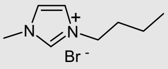
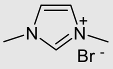
Scheme 1. Synthesis of ionic liquid-modified SBA-15.



Scheme 2. Immobilization of (*S*,*S*)-(+)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride complex onto the ionic liquid-modified SBA-15.

Table 1
Effect of different additives on α-methylbenzyl alcohol conversions[a]



Entry	Additive	Conversion[b] (%)	ee[c] (%)	k_{rel}[d]
1	–	35	18	2.3
2	$N(CH_3)_4Br$	64	99	16.8
3	$N(CH_3)_4Cl$	61	15	1.3
4	$N(C_2H_5)_4Br$	62	97	15.5
5	KCl	59	12	2.2
6	KBr	63	99	18.3
7	NaBr	59	94	18.1
8	CTAB	45	53	7.9
9		64	99	16.8
10		63	98	15.7

[a] Reactions performed at room temperature with MnILSBA-15 (0.03 g, 0.003 mmol), additive (0.1 mmol), substrate (2.5 mmol), $PhI(OAc)_2$ (1.75 mmol), and H_2O/hexane (10 mL/5 mL).

[b] Determined by performing GC analysis.

[c] Determined by performing GC analysis using a CP-Chirasil-Dex CB capillary column.

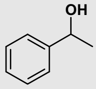
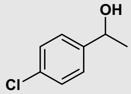
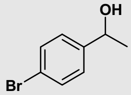
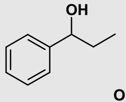
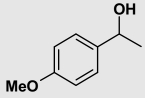
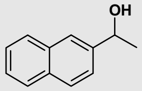
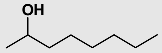
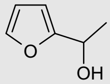
[d] $k_{rel} = \ln[(1 - C)(1 - ee)]/\ln[(1 - C)(1 + ee)]$, where C is the conversion and ee is the enantiomeric excess.

alcohols obtained from these resolution studies was comparable to that of homogeneous analogues. Both aliphatic and aromatic secondary alcohols afforded high conversions, enantioselectivities and k_{rel}. Due to solubility reasons, the oxidative kinetic resolution of 1-naphthylethanol was carried out in a mixture of diethyl ether and water (1:2). Among the substrates studied, α-methyl-*p*-methoxybenzylalcohol and 1-naphthylethanol gave low enantioselectivities (30% and 69%, respectively) and k_{rel} values (4.9, 7.9) (Table 2, entries 5 and 6). 1-Phenyl-1-propanol also gave, in low enantiomeric purity, a k_{rel} value of 5.84 (Table 2, entry 4). α-Methyl-*p*-chlorobenzyl alcohol and α-methyl-*p*-bromobenzyl alcohol were resolved with excellent enantioselectivities of 99% and 99% and with k_{rel} values of 18.3 and 15.6, respectively (Table 2, entries 2 and 3). Oxidative kinetic resolution of 2-decanol resulted in enantioenriched 2-decanol with a k_{rel} value of 16.2 (Table 2, entry 7). Furyl substituted alcohol did not undergo any oxidative kinetic resolution even after 2 h of reaction time (Table 2, entry 8).

The regenerability and recyclability of a catalyst system are most important for any catalytic reaction. After completion of the reaction, the reaction mixture was filtered, washed with hexane, dried and recharged with fresh substrate, additive and oxidant and the reaction was continued for the specified time. Similar catalytic activity and enantioselectivity were observed in all the five recycles with only a slight decrease after the 4th recycle (Table 2, entry 1).

In conclusion, mesoporous silica SBA-15-supported ionic liquid was used for immobilization of a Mn(III) salen complex. The amounts of both ionic liquids as well as the transition metal complex species involved in the preparation of the catalyst were very low and the preparation procedure adopted was simple, thus displaying very good performance from an economic point of view. This supported ionic liquid catalyst performed well in the oxidative kinetic resolution of secondary alcohols. The catalyst could be recovered by simple filtration and reused at least in five consecutive cycles with no significant difference in the conversion and enantioselectivity.

Table 2
Oxidative kinetic resolution of various secondary alcohols using MnILSBA-15[a]

Entry	Substrate	Time (min)	Conversion[b] (%)	ee[c] (%)	k_{rel}[d]
1		30	63	99	18.3
	1st recycle	30	63	99	18.3
	4th recycle	30	61	97	16.8
2		30	65	99	15.6
3		30	63	99	18.3
4		40	44	43	5.84
5		60	40	30	4.9
6		80	55	69	7.2
7		30	59	94	16.2
8.		120	No reaction	–	–

[a] Reactions performed at room temperature with MnILSBA-15 (0.03 g, 0.003 mmol), additive (0.1 mmol), substrate (2.5 mmol), $PhI(OAc)_2$ (1.75 mmol), and H_2O/hexane (10 mL/5 mL).

[b] Determined by performing GC analysis.

[c] Determined by performing GC analysis using a CP-Chirasil-Dex CB capillary column.

[d] $k_{rel} = \ln[(1 - C)(1 - ee)]/\ln[(1 - C)(1 + ee)]$, where C is the conversion and ee is the enantiomeric excess.

Acknowledgement

Suman Sahoo gratefully acknowledges CSIR, New Delhi (India) for the research fellowship.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.06.014.

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16. *Synthesis of SBA-15:*
    In a typical synthesis, 4 g of amphiphilic triblock copolymer, poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol), (average molecular weight = 5800) was dispersed in 30 g of water and 120 g of 2 M HCl solution was added while stirring. It was followed by the addition of 8 g of tetraethyl orthosilicate to the homogeneous solution with stirring. This gel mixture was continuously stirred at 40 °C for 24 h, and finally crystallized in a Teflon-lined autoclave at 100 °C for 2 days. After crystallization the solid product was filtered, washed with distilled water, and dried in air at room temperature. The material was calcined in static air at 550 °C for 24 h to decompose the triblock copolymer and obtain a white powder (SBA-15).
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18. *Typical procedure for the oxidative kinetic resolution:*
    To a solution of racemic secondary alcohol (2.5 mmol) in hexane water mixture (5 and 10 mL respectively), additive (0.1 mmol) and catalyst (0.030 g, 0.003 mmol) were added and the reaction mixture was stirred for 5 min. After this, oxidant diacetoxyiodobenzene (1.75 mmol), was added to the reaction. The reaction was monitored using a gas chromatograph equipped with a chiral column. After completion of the reaction, the catalyst was filtered, washed with 10 mL of hexane dried and recharged with fresh substrate, additive and oxidant for the next catalytic cycle.