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Synthesis of chiral sulfoxides by enantioselective sulfide oxidation and subsequent oxidative kinetic resolution using immobilized Ti–binol complex

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

[a] Inorganic Chemistry and Catalysis Division, National Chemical Laboratory, Pune 411008, India
[b] Organic Chemistry Technology, National Chemical Laboratory, Pune 411 008, India
[c] Laboratoire de Chemie Organometallique de Surface, CNRS-CPE, Villeurbanne Cedex, France
[d] Catalysis Centre for Molecular Engineering Korea Research Institute of Chemical Technology (KRICT), Jang-dong 100, Yuseong-gu, 305-600 Daejeon, Korea

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ABSTRACT

Chiral Ti–binol complex was immobilized onto ionic liquid modified SBA-15 and characterized by different physicochemical techniques. The catalyst was found to be highly enantioselective in the heterogeneous asymmetric oxidation of prochiral sulfides to sulfoxides and subsequent oxidative kinetic resolution of the sulfoxides using aqueous *tert*-butylhydroperoxide as the oxidant. A positive non-linear effect was observed in the oxidation-kinetic resolution of thioanisole using this supported catalyst. The supported catalyst was reused in multiple catalytic runs without any loss of enantioselectivity.

1. Introduction

Many chiral sulfoxides exhibit interesting biological activities and show promise as therapeutic agents [1–4]. For example, omeprazole and some of its derivatives are used as proton-pump inhibitors to treat acid-related diseases [2]. OPC-29030 is used as a platelet adhesion inhibitor [3]. In addition, optically active sulfoxides are valuable chiral auxiliaries and intermediates in contemporary organic synthesis [4–6]. So, the development of methodologies to synthesize enantiopure sulfoxides has become an important pursuit in chemical research.

One of the major approaches towards enantiomeric pure sulfoxides is the stereospecific substitution of optically active sulfinates with Grignard reagents (Andersen's method) [7]. However, it suffers from important drawbacks such as the tedious procedure and, the limited substrate scope [8]. Other attempts involve stoichiometric chiral oxidants, such as oxaziridines [9], hydroperoxides [10] but this approach is less attractive due to high cost and restricted availability. The only practical synthetic route towards chiral sulfoxides that has already found acceptance by industry during the last two decades is the catalytic enantioselective oxidation of prochiral sulfides [11]. Based on transition metal-promoted sulfoxidation, Brunel et al. and Furia et al. reported independently a modified Sharpless procedure for the asymmetric oxidation of sulfides in the presence of stoichiometric diethyl tartrate (DET) and titanium attaining very high ee values [12–14]. Although the enantioselective oxidation of sulfides catalyzed by chiral complexes of transition metals, such as titanium [15–17], vanadium [18,19], iron [20], manganese [21], Osmium [22] has been extensively studied, Kagan method and its improvements are mainly used in the large scale preparations of sulfoxides.

Kinetic resolution of sulfoxides is the reaction of two enantiomeric sulfoxides at different rates [23]. There are numerous examples of the oxidative kinetic resolution of sulfoxides to sulfones, most of which were discovered during the investigation of asymmetric sulfide oxidation [23–25]. Komatsu and co-workers reported kinetic resolution when carrying out sulfur oxidations using a titanium–binaphthol catalyst with arylmethylsulfoxides of up to 99% ee being obtained in 26% yield [24]. Recently Jia and co-workers optimized this and reported that carrying out the kinetic resolution step at 25 °C gave the best results, obtaining phenylmethylsulfoxide in 29% yield and 95% ee [25]. Synthesis of chiral sulfoxides and their applications has been reviewed several times in the literature [26–30].

Many times the successes in organic transformations by soluble asymmetric catalysts affording high purity optical compounds are not reflected in the industrial front due to severe limitations including lower turn over numbers, difficulties in recovery, recycling

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* Corresponding author. Fax: +82 42 860 7676.
E-mail address: sb_halligudi123@yahoo.co.in (S.B. Halligudi).

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and handling of the soluble catalysts. Therefore, the asymmetric heterogeneous catalysts are preferable because of their ease of handling and separation properties from a technical and commercial point of view, provided the catalyst performance is satisfactory. Mesoporous silica had attracted much attention in many fields of science and engineering such as adsorption, separation, and catalysis due to their unique pore structures [31,32]. In particular, their remarkable textural properties such as high surface area and large pore volume, good hydrothermal stability with varying pore size make them well suitable for application as catalyst supports especially in asymmetric catalysis [33–37]. A number of research papers have been published in the field of heterogeneous sulfide oxidation [38–42]. But a very few reports are there on the immobilization of chiral titanium complex on to mesoporous silica [43,44]. All these heterogeneous catalysts (Ti-MCM-41) provided very low enantiomeric excess (13%) of the sulfoxides.

Recently we have reported the successful immobilization of chiral Mn(III) salen complex by supported ionic liquid phase (SILP) strategy [45]. This involves immobilization of 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 [46–49]. This supported ionic liquid phase (SILP) catalyst allows the application of fixed-bed reactors and makes the separation and catalyst recycling easy. In this paper, we have further utilized this SILP strategy for the immobilization of chiral Ti–binol complex onto the ionic liquid modified mesoporous silica (SBA-15) support. This catalyst system was applied in the sulfide oxidation and subsequent kinetic resolution of sulfoxides and found to be comparable to the homogeneous system in activity and enantioselectivity. Also the non-linear effect was addressed using this catalyst system.

2. Experimental

2.1. General

All the solvents procured from Merck (AR grade), India were distilled and dried prior to their use. Tetraethyl orthosilicate (TEOS), all the sulfides, Ti(OiPr)$_4$, (*S*)-binol, racemic binol, and *tert*-butylhydroperoxide were procured from sigma Aldrich. All the racemic sulfoxides were synthesized from sulfides by oxidation with *tert*-butylhydrogenperoxide using Ti(OiPr)$_4$. The ionic liquid [BMIM]PF$_6$ and the mesoporous silica were synthesized as described in the literature [50,51].

Ti contents in the resulting solids were estimated by ICP-AES. The elemental analysis (C and N) was carried out with a Carlo Erba Instruments EA1108 elemental analyzer. Nitrogen adsorption and desorption isotherms were measured at −196 °C on a Quantachrome Autosorb 1 sorption analyzer. The samples were out gassed for 3 h at 250 °C under vacuum in the degas port of the adsorption analyzer. The specific surface area was calculated using the BET model. The pore size distributions were obtained from the adsorption branch of the nitrogen isotherms by Barrett–Joyner–Halenda method. The XRD patterns of the samples were collected on a Philips X'Pert Pro 3040/60 diffractometer using Cu$K\alpha$ radiation ($\lambda = 1.5418$ Å), iron as filter and X'celerator as detector. The ^{31}P MAS NMR spectrum of the catalyst was recorded using a Bruker DSX-300 spectrometer at 121.5 MHz with high-power decoupling using a Bruker 4-mm probe head. The spinning rate was 10 kHz, and the delay between the two pulses was varied between 1 and 30 s to ensure complete relaxation of the ^{31}P nuclei. The chemical shifts were given relative to external 85% H_3PO_4. NMR spectra were recorded on DRX-300 (200 MHz for ^{1}H and 50.3 MHz for ^{13}C) spectrophotometer using $CDCl_3$ as a solvent and Me_4Si as the internal standard. Shimadzu FT-IR-8201PC unit, in DRS mode, with a measurement range of 450–4000 cm^{-1}, was used to obtain the FT-IR spectra of solid samples.

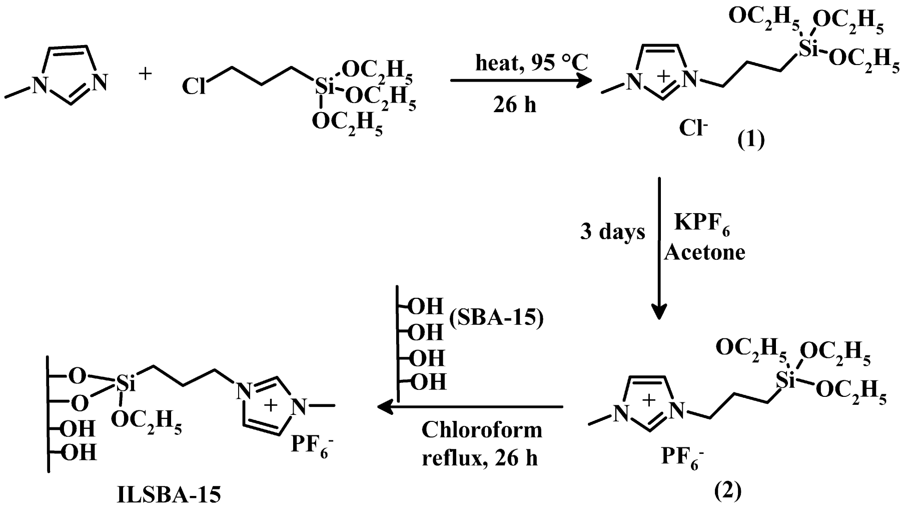
2.2. Catalyst preparation

2.2.1. 1-(3-Trimethoxysilylpropyl)-3-methylimidazoliumchloride (**1**)

A mixture of 1-methylimidazole (3.36 g, 40 mmol) 3-chloropropyltrimethoxysilane (9.63 g, 40 mmol) was heated under argon atmosphere at 95 °C for 24 h (Scheme 1). After cooling viscous oil was obtained. ^{1}H NMR ($CDCl_3$): $\delta = 0.71–0.78$ (m, 2H), 1.25–1.33 (t, 9H), 1.85–1.91 (m, 2H), 3.40–3.52 (m, 6H), 4.11 (s, 3H), 8.26 (d, 1H), 8.34 (d, 1H), 8.53 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 7.0$ ($SiCH_2$), 11.2 (CH_3), 25.1 (CH_2), 36.4 (NCH_3), 51.4 (CH_3O), 52.2 (CH_2N), 122.8, 124.3, 136.1.

2.2.2. 1-(3-Trimethoxysilylpropyl)-3-methylimidazoliumhexafluorophosphate (**2**)

To a solution of the above salt (3.2 g, 10 mmol), in acetone (15 mL), potassium hexafluorophosphate (1.9, 10.5 mmol) was added in one portion. The mixture was stirred at room temperature for 3 days. After this time the mixture was filtered and the solvent evaporated under reduced pressure to give **2** (Scheme 1). The residue was taken up with chloroform.



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

$$\mathrm{Ti(OiPr)_4} + \mathrm{H_2O} + (S)\text{-Binol} + \text{ILSBA-15} \xrightarrow[\text{1h}]{[\text{BMIM}]\mathrm{PF_6},\ \mathrm{CCl_4},\ \text{DCM}} \text{TiILSBA-15}$$

Scheme 2. Immobilizaton of Ti-(S)-binol onto ionic liquid modified SBA-15.

^{1}H NMR ($CDCl_3$), $\delta = 0.61$–0.70 (m, 2H), 1.27–1.35 (t, 9H), 1.88–1.94 (m, 2H), 3.89 (s, 3H), 4.23 (t, 2H), 7.55 (d, 1H), 7.58 (d, 1H), 8.90 (s, 1H), ^{13}C NMR ($CDCl_3$), $\delta = 6.9$ ($SiCH_2$), 10.2 (CH_3), 24.9 (CH_2), 36.0 (NCH_3), 51.3 (CH_2O), 51.5 (CH_2N), 122.4, 124.0, 136.3. ^{31}P NMR ($CDCl_3$), $\delta = 143.6$.

2.2.3. Synthesis of ionic liquid modified SBA-15 (ILSBA-15)

The ionic liquid **2** (2.81 g, 6.5 mmol) was dissolved in chloroform (50 mL) and treated with mesoporous silica (dried under vacuum and heated at 180 °C overnight, 4.00 g). The mixture was heated under reflux (65 °C) for 26 h. After cooling to room temperature, the solid was isolated by filtration and washed with chloroform (50 mL) and diethyl ether (50 mL). The solid was dried under reduced pressure to give a powder.

2.2.4. Synthesis of homogeneous Ti–binol complex

In a round bottom flask (S)-binol (0.2 g, 2 mmol) in 20 mL of CCl_4 was taken. To this ligand solution, $Ti(OiPr)_4$ (0.1 g, 1 mmol) was added drop wise and stirred for 5 min. Then water (0.18 g, 10 mmol) was added and stirred for another 1 h. Then the solvent was evaporated under reduced pressure to provide an orange colored Ti–binol complex (Scheme 2). This complex was characterized by FTIR spectroscopy. FTIR (KBr pellet): 3522, 3056, 1587, 1463, 1338, 1240, 1079, 975, 819, 791 cm^{-1}.

2.2.5. Supported chiral Ti–binol materials (TiILSBA-15)

To a stirred solution of (S)-binol (0.2 g, 2 mmol) in 10 mL of CCl_4, $Ti(OiPr)_4$ (0.1 g, 1 mmol) and water (0.18 g, 10 mmol) were added one after the other drop wise. After that [BMIM] PF_6 (0.5 g) in 10 mL of CH_2Cl_2 was added (Scheme 2). To this solution the ionic liquid modified mesoporous silica (1.5 g) was added. The mixture was stirred for 1 h, and then evaporated under reduced pressure for 3 h to give a powder of TiILSBA-15.

2.3. Catalytic experiments

2.3.1. Typical experimental procedure for heterogeneous asymmetric sulfoxidation and catalyst recycling

Solvent (10 mL) and thioanisole (0.5 mmol) were added to the solid-state catalyst TiILSBA-15 (0.4 g) obtained above. The mixture was stirred for 15 min before TBHP (70% in water, 1 g, 7.5 mmol) was added dropwise at room temperature, and the heterogeneous mixture was stirred at room temperature for 20 h. After the isolation of the solids by filtration, the insoluble catalyst was recharged with CCl_4 (10 mL), substrates (0.5 mmol), and oxidant (0.75 mmol) for the next run. The filtrate was concentrated and the residue was submitted to column chromatography on silica gel using pet ether/ethyl acetate (1:1) as eluent to give (S)-methylphenylsulfoxide as colorless oil in 38% yield; The optical rotation of products was measured by Jasco P-1020 polarimeter. $[\alpha]_D = -134.5$ (c = 1.1, acetone); $[\alpha]_D = +135$ (c = 1, acetone), (R)-enantiomer, 99.2% ee; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.74$ (s, 3 H), 7.52–7.55 (m, 3H), 7.64–7.68 ppm (m, 2H); EIMS: m/z (%): 140 (100) [M]$^+$, 125 (98), 97 (58), 77 (45), 51 (63). The ee value was determined by performing HPLC (CLASS-VP) using a Chiralcel OD-H column: UV detection at $\lambda = 254$ nm; 20 °C; hexane/iPrOH, 9:1; flow rate, 0.5 mL/min (250 psi); $t_{R1} = 24.5$ min (minor isomer), $t_{R2} = 28.3$ min (major isomer).

(S)-p-toluylmethylsulfoxide: $[\alpha]_D = -184.8$ (c = 1.08, acetone), HPLC (Chiralcel OD-H column: UV detection at $\lambda = 225$ nm; 20 °C; hexane/iPrOH, 9:1; flow rate, 0.5 mL/min (230 psi)) $t_{R1} = 22.09$ min (minor isomer), $t_{R2} = 24.6$ min (major isomer), >99.9% ee; ^{1}H NMR (300 MHz, $CDCl_3$): d = 2.42 (s, 3H), 2.71 (s, 3H), 7.32–7.35 (d, 2H, $J = 7.8$ Hz), 7.53–7.56 ppm (d, $J = 7.8$ Hz, 2H); EIMS: m/z (%): 154 (83) [M]$^+$, 139 (100).

(S)-p-bromophenylmethylsulfoxide: $[\alpha]_D = -150.1$ (c = 0.43, acetone), HPLC (Chiralcel OJ-H column: UV detection at $\lambda = 254$ nm; 20 °C; hexane/iPrOH, 9.5:0.5; flow rate, 0.5 mL/min (250 psi)) $t_{R1} = 48.2$ min (major isomer), $t_{R2} = 46.1$ min (minor isomer), >99.9% ee; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.74$ (s, 3H), 7.53–7.55 (d, $J = 8.4$ Hz, 2H), 7.67–7.70 ppm (d, $J = 8.4$ Hz, 2H); EIMS: m/z (%): 220 (66) [M + 1]$^+$, 218 (65) [M − 1]$^+$, 205 (100), 203 (98).

(S)-p-fluorophenylmethylsulfoxide: $[\alpha]_D = -128.6$ (c = 1.5, acetone), 98.6% ee; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.72$ (s, 3H), 7.20–7.26 (m, 2H), 7.63–7.68 ppm (m, 2H); EIMS: m/z (%): 158 (60) [M]$^+$, 143 (100), 115 (1), 95 (36), 75 (39).

(S)-m-bromophenylmethylsulfoxide: $[\alpha]_D = -110.4$ (c = 1.33, acetone), HPLC (Chiralcel OD-H; flow rate 0.8 mL/min; hexane/i-PrOH, 8/2): $t_{R1} = 14.3$ min (minor isomer), $t_{R2} = 11.0$ min (Major isomer) >99.9% ee; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.74$ (s, 3H), 7.40–7.43 (m, 1H), 7.53–7.54 (m, 1H), 7.62 (m, 1H), 7.80–7.81 ppm (m, 1H); EIMS: m/z (%): 220 (81) [M + 1]$^+$, 218 (81) [M − 1]$^+$, 205 (93), 203 (96).

(S)-p-nitrophenylmethylsulfoxide: $[\alpha]_D = -126.5$ (c = 1.2, acetone), 89.1% ee; ^{1}H NMR (300 MHz, $CDCl_3$): d = 2.79 (s, 3H), 7.82–7.85 (m, 2H), 8.38–8.40 ppm (m, 2H); EIMS: m/z (%): 185 (100) [M]$^+$, 170 (29), 140 (11).

(S)-phenylethylsulfoxide: $[\alpha]_D = -97.1$ (c = 1.3, acetone), HPLC (Chiralcel OD-H; flow rate 0.8 mL/min, hexane/i-PrOH, 8/2): $t_{R1} = 17.8$ min (Minor isomer), $t_{R2} = 9.5$ min (major isomer), 75.5% ee; ^{1}H NMR (300 MHz, $CDCl_3$): d = 1.19–1.24 (t, $J = 7.5$ Hz, 3H), 2.75–2.96 (m, 2H), 7.51–7.65 ppm (m, 5H); EIMS: m/z (%): 154 (20) [M]$^+$, 126 (54), 97 (15), 78 (100), 51 (32).

(S)-4-methoxyphenylmethylsulfoxide: $[\alpha]_D = -76$ (c = 1.1, acetone), HPLC (Chiralcel OJ-H; flow rate 0.5 mL/min; hexane/i-PrOH, 9/1): tr (R) = 38.8 min, tr (S) = 41.08 min, ^{1}H NMR (400 MHz): d = 7.61–7.58 (d, $J = 8.9$ Hz, 2H), 7.04–7.02 (d, $J = 8.9$ Hz, 2H), 3.86 (s, 3H), 2.71 (s, 3H);

(S)-4-chlorophenylmethylsulfoxide (6d): $[\alpha]_D = -120$ (c = 1.6, acetone), HPLC (Chiralcel OB; flow rate 0.8 mL/min; hexane/i-PrOH, 8/2): $t_{R1} = 15.2$ min (Minor isomer), $t_{R2} = 10.5$ min (Major isomer) ^{1}H NMR (400 MHz): d = 7.59 (d, $J = 8.6$ Hz, 2H), 7.51 (d, $J = 8.6$ Hz, 2H), 2.73 (s, 3H).

3. Results and discussion

The Ti–binol complex immobilized onto the ionic liquid modified SBA-15 support was characterized by different physicochemical techniques for the confirmation of its presence and the structural integrity of the mesoporous silica support after immobilization. The catalyst was assessed in the asymmetric oxidation of sulfides.

3.1. Catalyst characterization

3.1.1. Low angle XRD

The well-defined XRD patterns were obtained for all the samples which are similar to those recorded for SBA-15 materials as described by Zhao et al. [47]. XRD patterns of calcined SBA-15 and TiILSBA-15 materials (shown in Figs. 1(a) and 1(b) respectively) consists of three well-resolved peaks in the 2θ range of 0.8 to 1.8 correspond to the (100), (110), (200) reflections which are associated with $p6mm$ hexagonal symmetry in the materials. The peak intensities at (100), (110) and (200) reflections of TiILSBA-15 were decreased, indicating the immobilization of Ti–binol complex

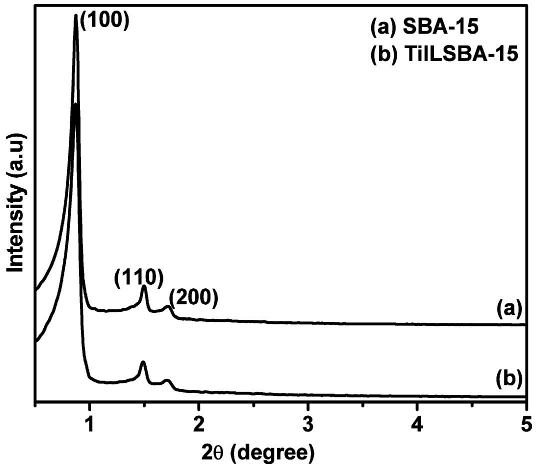


Fig. 1. Low angle XRD patterns of (a) SBA-15 and (b) TiILSBA-15.

inside the mesoporous channels of ionic liquid modified SBA-15. However, the mesoporous structure of the support remained intact under the conditions used for immobilization.

3.1.2. N_2 sorption study

The N_2 adsorption–desorption isotherms of SBA-15, ILSBA-15 and TiILSBA-15 are shown in Fig. 2. Isothermal N_2 adsorption measurements have allowed determining BET surface area, pore size distribution and total pore volume for the prepared materials. All these parameters decrease after the immobilization of ionic liquid and subsequent metal complex incorporation. The surface area observed for ILSBA-15 and TiILSBA-15, are 335 and 116 $m^2 g^{-1}$ respectively compared to 730 $m^2 g^{-1}$ for parent SBA-15. The average pore volume was decreased from 1.10 to 0.69 and 0.26. Also the average pore diameters decreased from 63 to 25 Å after immobilization. The pore size distribution was calculated from the Kelvin equation and is presented as a BJH plot (inset picture, Fig. 2). Although the immobilized samples showed a decrease in surface area, pore diameter and pore volume, isotherms of all the materials were of type IV, as defined by IUPAC and exhibited a H1-type broad hysteresis loop, which was typical of large-pore mesoporous solids. As the relative pressure increases ($p/p_0 > 0.6$), all isotherms exhibited a sharp step characteristic of capillary condensation of nitrogen within uniform mesopores, where the p/p_0 position of the inflection point is correlated to the diameter of the mesopore. This data confirmed the presence of chiral Ti–binol complex in the mesoporous SBA-15 support, and the intactness of the textural property of the support after functionalization.

3.1.3. Microscopic analysis

As can be seen from the SEM images of TiILSBA-15 shown in Fig. 3(a), the micromorphology i.e., rope like structure of mesoporous SBA-15 remained the same even after modification with ionic liquid and Ti–binol complex.

Fig. 3(b) depicts TEM images obtained for the sample TiILSBA-15 catalyst as definitive evidence of the retention of structure ordering of SBA-15 after immobilization. The presence of equidistant parallel fringes demonstrates the nature of separation between layers and the unique well-packed arrangement of such monolayers. The well ordered hexagonal array of mesopores was also observed.

3.1.4. Nuclear magnetic resonance

Regarding the successful immobilization of ionic liquid and the chiral metal complex, the NMR spectra were obtained for the accurate characterization. When looking at the proton spectra (Fig. 4), it showed very sharp lines due to species with a high mobility, probably the $BMIM^+$ species. The peaks at 6.8–7.9 corresponds to the aromatic protons of the binol ligand and the imidazolium moiety of the ionic liquid present and the peaks at 0.27–3.29 correspond to the aliphatic side chain of the imidazolium moiety. The ^{13}C NMR spectra (Fig. 5) shows peaks at 136 and 121, which are due to the aromatic ring carbons and the peaks 13–49 confirm the presence of linker propyl group, ethoxy ($SiOCH_2CH_3$). ^{29}Si MAS NMR spectra of the parent SBA-15 exhibited a broad peak and was dominated by an intense peak at −110 ppm assigned to $Si(OSi)_4$ and one shoulder peak at −102 ppm due to $Si(OSi)_3OH$ (Q3) structural units present in SBA-15. On incorporation of the imidazolium moiety, in addition to the aforementioned three peaks, one peak at 66 ppm appeared (Fig. 6) which is the evidence of presence of T3 moiety only. No peak appeared at −45 and 58 ppm, indicates the absence of free silane moiety physically adsorbed on

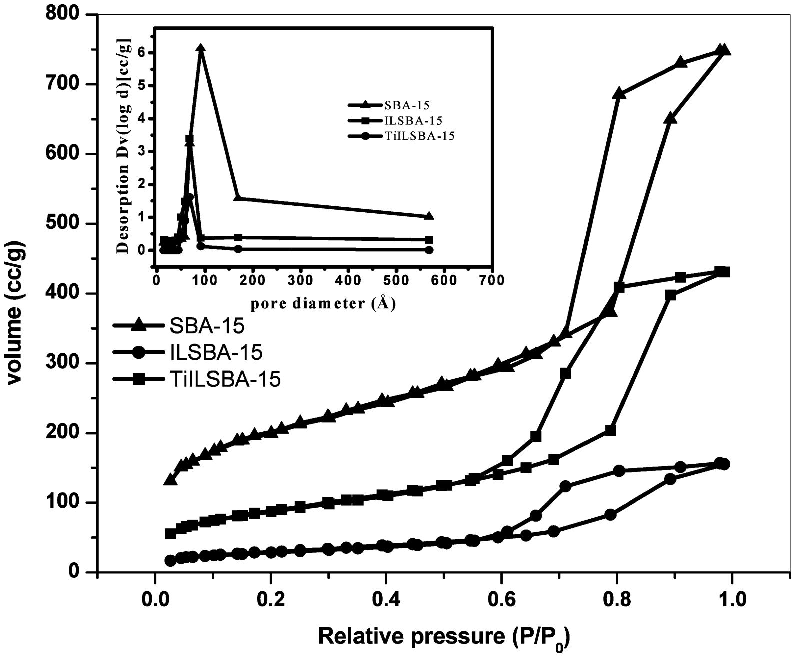


Fig. 2. N_2 adsorption–desorption isotherms of samples: (a) SBA-15, (b) ILSBA-15 and (c) TiILSBA-15. Inset picture: Pore size distribution of these materials.

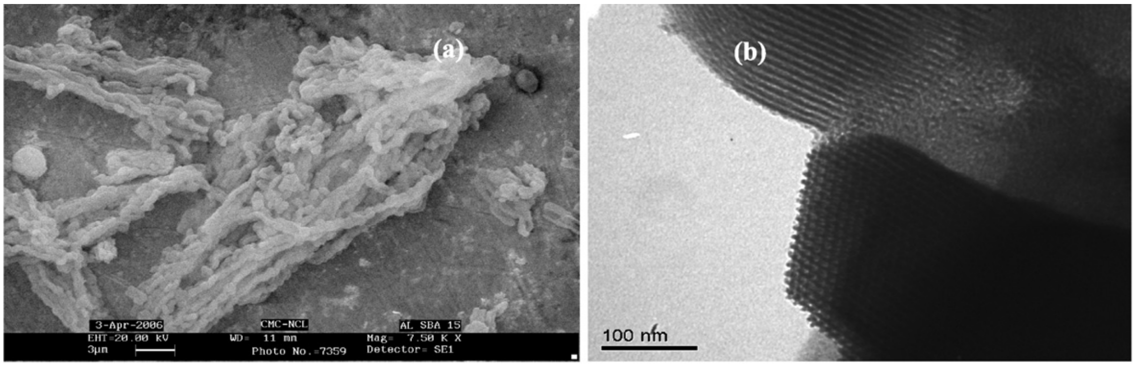


Fig. 3. (a) SEM and (b) TEM photographs of TiILSBA-15.

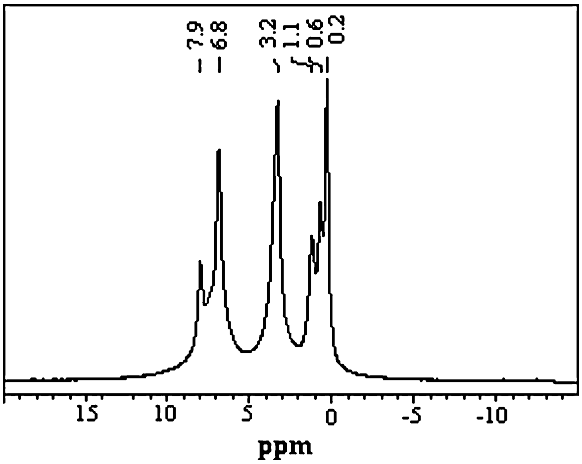


Fig. 4. ^{1}H NMR spectra of TiILSBA-15.

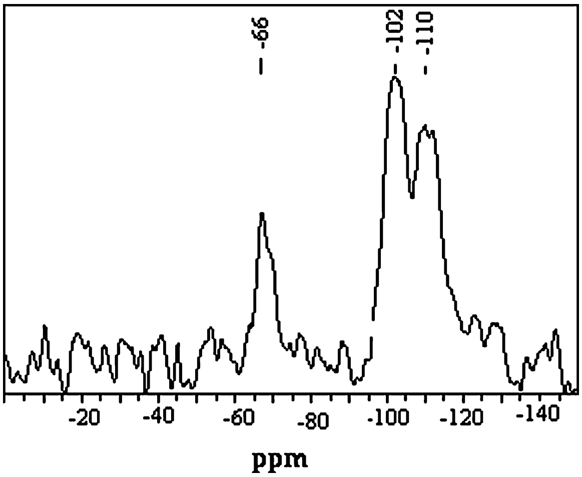


Fig. 6. ^{29}Si CP-MASNMR spectra of TiILSBA-15.

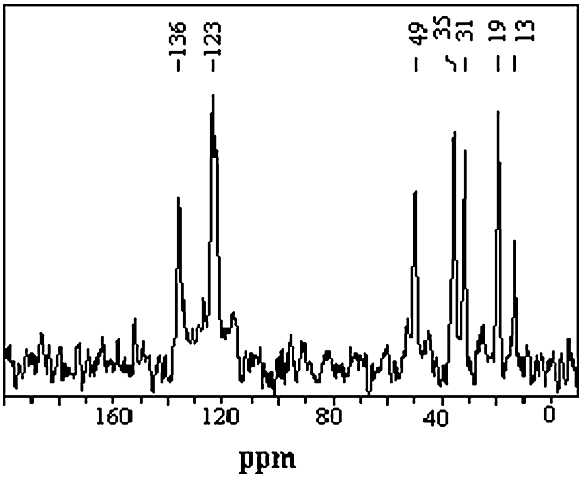


Fig. 5. ^{13}C CP-MAS NMR spectra of TiILSBA-15.

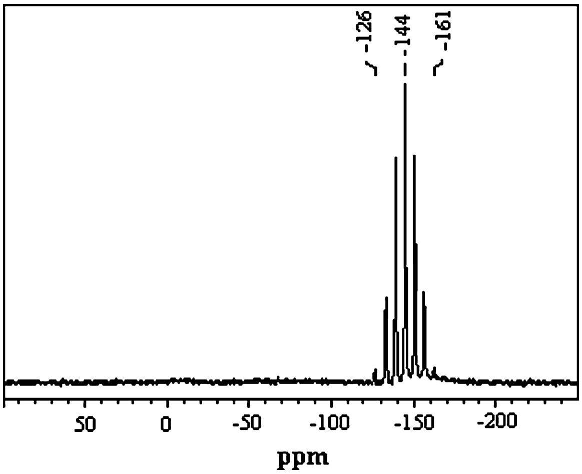


Fig. 7. ^{31}P MAS NMR spectra of TiILSBA-15.

the SBA-15 surface and the T2 moiety respectively. The phosphorus spectrum (Fig. 7) showed only the resonance of PF_6^- of the ionic liquid.

3.1.5. FTIR spectroscopy

Another piece of evidence of the immobilized ionic liquid and the chiral Ti–binol complex was obtained by FTIR spectroscopy. Fig. 8 depicts the representative FTIR spectra in the range 400–4000 cm^{-1} for immobilized Ti–binol catalyst TiILSBA-15. In the spectrum in addition to the specific bands at 1080, 780 and 470 cm^{-1} of the parent mesoporous silica support, the IR bands observed at 3158 and 3110 cm^{-1} are assigned to C–H stretching vibrations of aromatic imidazole ring of the ionic liquid and binol. The bands near 3000 cm^{-1} are due to C–H stretching vibrations of alkyl groups belonging to the silylating agent. The IR bands at 1566 and 1454 cm^{-1} can be attributed to C=C stretching vibrations of imidazole rings and C–H deformation vibrations of alkyl groups, respectively. Besides these, the IR band assigned to C=N stretching vibrations was seen at around 1625 cm^{-1}. Furthermore, new characteristic bands of Ti–binol at 1464, 1334, 978 cm^{-1} were observed which we have observed in case of the IR spectrum of homogeneous complex and in the literature [40]. This indicated

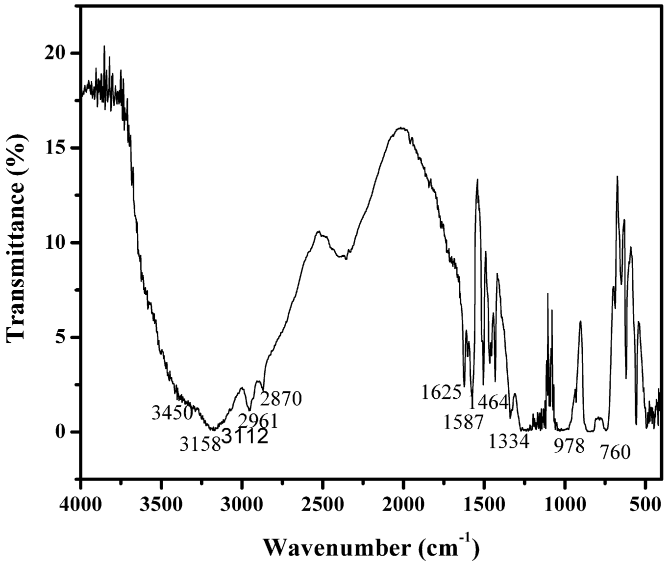
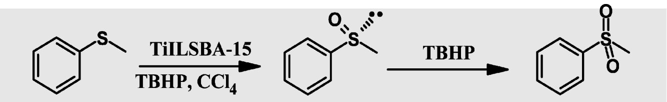


Fig. 8. FTIR spectra of TiILSBA-15.

Table 1
Reaction time study in the TiILSBA-15-catalyzed oxidation of thioanisole.[a]



Entry	Time	Sulfoxide		Sulfone yield [%][b]
		Yield [%][b]	ee [%][c,d]	
1	10	85	75	0
2	12	78	83	10
3	14	75	88	16
4	16	65	93	20
5	18	62	99	25
6	20	59	99	30
7[e]	16	63	99	29

[a] Reaction condition: sulfide/Ti/TBHP (70% aqueous solution of TBHP was used) = 1.0:0.0.5:1.5.

[b] Yields of isolated products.

[c] Determined by HPLC analysis on a Daicel Chiralcel OD column

[d] All in the *S* configuration.

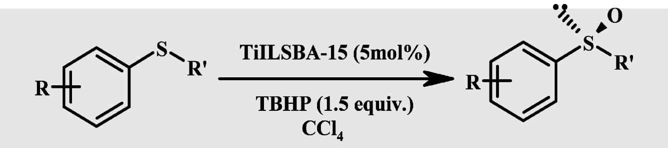
[e] Under homogeneous condition.

that the chiral Ti–binol complex was successfully immobilized on the support.

3.2. Catalytic activity

The TiILSBA-15 catalyst was then tested in the enantioselective oxidation of sulfides taking thioanisole as a test substrate in CCl_4, and aqueous TBHP as the oxidant. First the reaction was carried out with a sulfide/Ti/TBHP ratio of 1:0.05:1. After 10 h of reaction time maximum sulfoxide yield (85%) (Table 1, entry 1) was obtained with a low ee of 75%. Then Uemura's protocol [24] was applied by subjecting it to over oxidation to sulfone after adding another 0.5 equivalent of TBHP. It was observed that after 20 h of reaction time the enantiomeric excess of the sulfoxide was >99% with a sulfone yield of 30% (Table 2, entry 6). It can be well understood from Fig. 9 that with the increase in time, the sulfoxide yield first increases and then decreases, but the enantiomeric excess of the sulfoxide goes on increasing with the increase in time and sulfone yield. This indicates that an oxidative kinetic resolution of the sulfoxide took place as the enantiomeric excess of the sulfoxide increases with the retention in absolute configuration that is the other enantiomer of the sulfoxide get converted to sulfone. In order to check if the overoxidation of sulfoxide to sulfone involved a process of kinetic resolution, racemic methylphenylsulfoxide was reacted under the same conditions. The process was stereoconvergent with the sulfoxidation, in fact, unreacted sulfoxide was isolated as (*S*) prevalent enantiomer. It can be concluded that the high enantiomeric excess of sulfoxide could only be obtained by oxidation of sulfides and subsequent kinetic resolution of the sulfoxides. To confirm this speculation, the kinetic resolution of racemic phenylmethylsulfoxide by using TiILSBA-15 was investigated under the experimental conditions mentioned above with a substrate to oxidant mole ratio of 1:0.75. After 20 h of reaction, the selectivity factor *S*, a measure of the effectiveness of a kinetic resolution process under a particular set of conditions [52], was calculated to be 6.74, with a 43% sulfoxides yield and 72% ee, which were comparable to the values obtained through an analogous homogeneous process reported recently by Chan [25].

Table 2
Enantioselective oxidation of sulfides catalyzed by TiILSBA-15.[a]



Entry	R	R′	Sulfoxides	
			Yield (%)[b]	ee (%)[c,d]
1	H	Me	59	99.9
2	4-Me	Me	62	99.5
3	4-Br	Me	58	99.2
4	4-Cl	Me	61	96.7
5	3-Br	Me	57	99.2
6	4-NO_2	Me	54	88.3
7	H	Et	63	77.2
8	4-OMe	Me	55	99.9
9	4-F	Me	59	98

[a] Reaction condition: sulfide/Ti/TBHP (70% aqueous solution of TBHP was used) = 1.0:0.05:1.5.

[b] Yields of isolated products.

[c] Determined by HPLC analysis on a Chiralcel OD-H column.

[d] All in the *S* configuration.

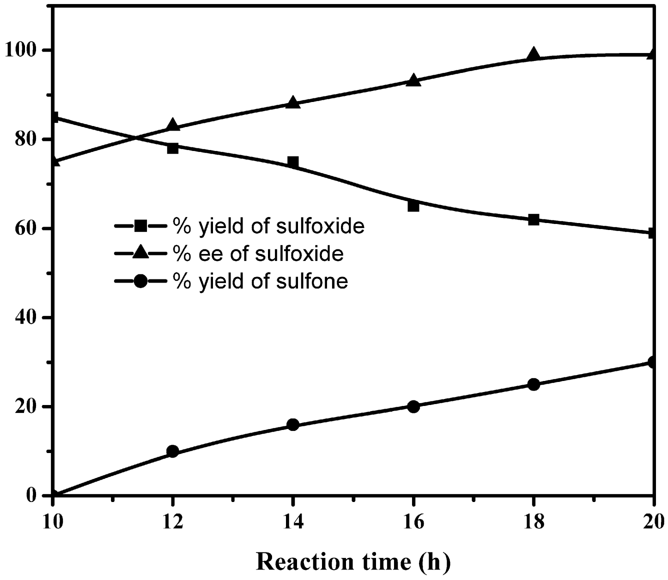


Fig. 9. Time course of the ee (%) of the sulfoxide, yield (%) of sulfoxide and relative concentration (%) of the sulfone.

Different solvents were studied for the asymmetric oxidation of sulfides and subsequent oxidative kinetic resolution of the resulted sulfoxides. Although good yield of sulfoxides was obtained while using toluene, diethyl ether, dichloromethane, the enantiomeric excess was less. Maximum enantiomeric excess (up to 99% ee) was obtained while using CCl_4 as the solvent, which is in accordance to the literature procedure in case of the homogeneous condition [24].

For comparison one experiment was carried out in ionic liquid and CCl_4 mixture under the optimized conditions. Comparable enantiomeric excess and yield (99% ee, 61%) of the methylphenylsulfoxide was obtained as in the case of TiILSBA-15. Without the catalyst, TiILSBA-15, racemic methylphenylsulfoxide was obtained with a very low yield (14%) in 20 h.

Encouraged by our preliminary results described above, we next investigated the heterogeneous catalysis of a variety of arylalkylsulfides with a sulfide/Ti/TBHP ratio of 1:0.05:1.5 in CCl_4 at room temperature. As shown in Table 2, all the sulfides get oxidized to the corresponding sulfoxides with good yield and enantiomeric excess. The oxidation of sulfides having both electron-donating as well as electron withdrawing substituents gave good enantiomeric excess with a sulfoxide yield of about 60% (Table 2, entries 2–5 and 8, 9). As shown in Table 2 both *para*-substituted (entry 3) and *meta*-substituted (entry 5) afforded very high enantioselectivity (99%) in about 55% yield. Notably in the oxidation of the *para*-nitrosubstituted sulfide (Table 2, entry 6), a lower enantiomeric excess of 88% was obtained as compared to the other substrates 7. The increase in steric bulk of the alkyl group in the substrate resulted in a moderate enantioselectivity. The oxidation of ethylphenylsulfide afforded the corresponding sulfoxide with an enantiomeric excess of 77% (Table 2, entry 7). This is in accordance to the literature [40].

3.3. Non-linear effect in asymmetric sulfoxidation

When two enantiomeric catalysts are mixed in various amounts, the prediction of the enantiomeric purity of the products is easy, provided that the mixing does not introduce additional interactions between the enantiomorphic systems. In this ideal behavior, simple additivity rules will give rise to linearity. A deviation from ideal behavior must generate diastereomeric species that are not present in the homochiral systems with, as a possible consequence, a deviation from linearity. In recent years particular attention has been paid to the detection of non-linear effect (NLE) in a variety of asymmetric reactions [53–55], since they can be used to prepare compounds with high ees starting from only enantiomerically enriched ligands or auxiliaries and, furthermore, to obtain mechanistic information. In heterogeneous enantioselective catalysis only the latter "extended" non-linear effect has been studied so far [56–58]. As regards the asymmetric sulfoxidation, Kagan pointed out a negative NLE, (−)-NLE, for the oxidation of methyl-*p*-tolylsulfide in the presence of the modified Sharpless reagent $Ti(O\text{-}i\text{-}Pr)_4/L\text{-DET}/H_2O$, that affected the level of enantioselectivity until the value of 70% ee was reached for DET; then, the linear relationship was observed until enantiomerically pure *L*-DET was used [59]. Recently, Massa et al. has reported a positive non-linear effect in asymmetric sulfoxidation using Ti–(R)-binol as the catalyst [60]. No one has yet reported the non-linear effect in the asymmetric oxidation of sulfides using the immobilized Ti–binol complex. Herein, we studied the non-linear effect by using the immobilized Ti–binol complex onto ionic liquid modified support in the asymmetric oxidation tandem kinetic resolution of thioanisole.

Partially resolved (*S*)-binol was used for this study under identical conditions. All the experiments were carried out for same reaction time (20 h). As shown in Fig. 10, a positive non-linear effect was observed and the curve obtained is of a typical ML_2 type [61] catalyst which shows that heterochiral complex (meso, ML_RL_S) formed is stable and unreactive. The active species involved in this case is a homochiral complex of $M(L_S)_2$ type that is the titanium complex of two *S*-binol ligands. Almost ∼99% ee of the methylphenylsulfoxide was obtained in the case of 60% enantiomerically pure catalyst.

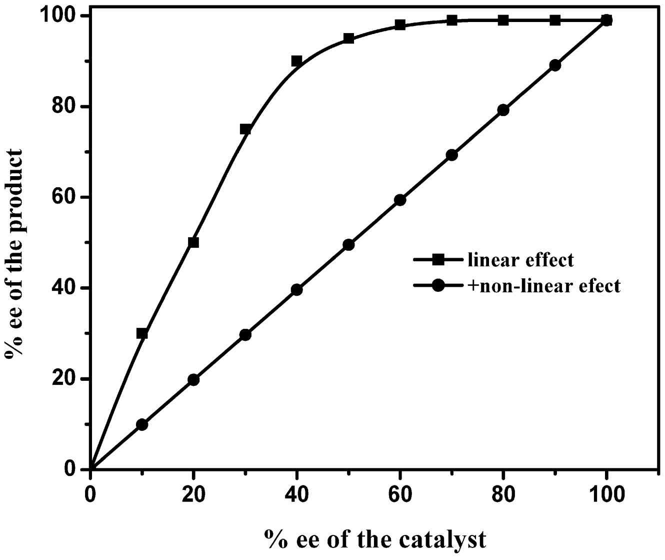


Fig. 10. Positive non-linear effect in the asymmetric oxidation of thioanisole.

Table 3
Recycling and reuse of the heterogeneous catalyst TiILSBA-15 in the enantioselective oxidation of thioanisole.[a]

Run	Time (h)	Yield (%)[b]	ee (%)[c]
1	20	62	99.2
2	20	62	99.0
3	21	60	99.0
4	22	59	98.6
5	22	58	98.6
8	24	56	98.2

[a] All the reactions were performed at room temperature with 1.5 equivalents of TBHP (70% in water) in CCl_4.

[b] Isolated yields.

[c] Determined by performing HPLC using a Chiralcel OD-H column.

3.4. Catalyst stability

The heterogeneous nature of the above catalytic system was confirmed by using the supernatant of the catalyst in CCl_4 for the oxidation of thioanisole under the same conditions. The isolated product was racemic, similar to that obtained from the control experiment in the absence of catalyst under otherwise identical conditions. The inductively coupled plasma (ICP) spectroscopic analyses of the liquid phase after filtration of the insoluble catalysts indicated that no detectable titanium (<0.1 ppm) was leached into the organic solution, which again supported the heterogeneous nature of the present system.

The facile recovery and remarkable stability are the other features exhibited by this type of heterogeneous catalyst. After completion of the reaction, simple filtration in open air enabled the separation of the solid-state catalyst from the product-containing solution. The separated solids were recharged with CCl_4, substrate, and oxidant, for the next run. As shown in Table 3, the catalyst TiILSBA-15 could be used for at least 8 cycles in the sulfoxidation of thioanisole without any loss of enantioselectivity. Moreover, no significant deterioration in activity of the recovered catalyst was observed after eight runs that covered a period of more than one month. Again, the titanium leaching during recycling of the catalysts was determined to be negligible (less than 0.1 ppm by ICP).

4. Conclusions

We have used the SILP strategy for the immobilization of chiral titanium–binol catalyst onto the ionic liquid modified mesoporous silica SBA-15 support. The catalyst was characterized by different physico-chemical techniques for the confirmation of the presence of the chiral complex as well as the retention of structural integrity after the immobilization procedure. The catalyst showed excellent enantioselectivity in the oxidation and subsequent kinetic resolution of sulfides. A positive non-linear effect was observed in this system. 99% ee of methylphenylsulfoxide was obtained using only 60% enantiomerically pure catalyst. Furthermore, the catalyst was highly stable and could be readily recycled and reused for over one month with no apparent loss of activity and enantioselectivity (up to $>99.9\%$). This represents a remarkable example of the heterogeneous catalysis of enantioselective reactions by using titanium catalysts. The features of SILP catalyst, such as facile preparation, robust chiral structure of solid state catalysts, and high density of the catalytically active units in the solids, minimum use of ionic liquid as well as easy recovery and simple recycling are particularly important in developing methods for the synthesis of optically active compounds in industrial processes. The strategy described here indicates a possible new direction in the design of chiral catalysts for asymmetric synthesis.

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Supporting information

Supporting information for this article may be found on ScienceDirect, in the online version.

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References

[1] P. Pitchen, Chem. Ind. (1994) 636.
[2] S. Von Unge, V. Langer, L. Sjlin, Tetrahedron Asymm. 8 (1997) 1967.
[3] M. Matsugi, N. Fukuda, Y. Muguruma, T. Yamaguchi, J. Minamikawa, S. Otsuka, Tetrahedron 57 (2001) 2739.
[4] S. Tashiro, H. Miyagawa, N. Sugita, Y.J. Okada, Pestic. Sci. 18 (1993) 155.
[5] M. Mikolaczyk, J. Drabowicz, Top. Stereochem. 13 (1982) 333.
[6] D.H. Hua, S.N. Bharathi, F. Takusagawa, A. Tsujimoto, J.A.K. Panagan, M.H. Hung, A. Bravo, A.M. Erplelding, J. Org. Chem. 54 (1989) 5659.
[7] K.K. Andersen, W. Gaffield, N.E. Papanikolau, J.W. Foley, R.I. Perkins, J. Am. Chem. Soc. 86 (1964) 5637.
[8] Z. Han, D. Khrishnamurthy, P. Grover, H.S. Wilkinson, Q.K. Fang, X. Su, Z.-H. Lu, D. Magiera, C.H. Senanayake, Angew. Chem. 115 (2003) 2078;
Z. Han, D. Khrishnamurthy, P. Grover, H.S. Wilkinson, Q.K. Fang, X. Su, Z.-H. Lu, D. Magiera, C.H. Senanayake, Angew. Chem. Int. Ed. 42 (2003) 2032.
[9] F.A. Davis, A.C. Sheppard, Tetrahedron 45 (1989) 5703.
[10] A. Lattanzi, S. Piccirillo, A. Scettri, Adv. Synth. Catal. 349 (2007) 357.
[11] P. Pitchen, in: A.N. Collins, G.N. Sheldrake, J. Crosby (Eds.), Chirality in Industry II, Willey, New York, 1997, p. 381.
[12] J.-M. Brunel, P. Diter, M. Duetsch, H.B. Kagan, J. Org. Chem. 60 (1995) 8086.
[13] F. Di Furia, G. Modena, R. Seraglia, Synthesis (1984) 325.
[14] P.P. Pitchen, E. Dunach, M.N. Deshmukh, H.B. Kagan, J. Am. Chem. Soc. 106 (1984) 8188.
[15] N. Komatsu, M. Hashizume, T. Sugita, S. Uemura, J. Org. Chem. 58 (1993) 4529.
[16] M.I. Donnoli, S. Superchi, C. Rosini, J. Org. Chem. 63 (1998) 9392.
[17] G. Pescitelli, L. Di Bari, P. Salvadori, J. Organomet. Chem. 691 (2006) 2311.
[18] C. Bolm, F. Bienewald, Angew. Chem. Int. Ed. 34 (1995) 2640.
[19] H. Vetter, A. Berkessel, Tetrahedron Lett. 39 (1998) 1741.
[20] J. Legros, C. Bolm, Chem. Eur. J. 11 (2005) 1086.
[21] H. Sasaki, R. Irie, Y. Ito, T. Katsuki, Synlett (1994) 356.
[22] M. Lakshmi Kantam, B. Veda Prakash, B. Bharathi, C. Venkat Reddy, J. Mol. Catal. A Chem. 226 (2005) 119.
[23] F.A. Davis, J. Billmers, J. Org. Chem. 48 (1983) 2672–2675.
[24] N. Komatsu, M. Hashizume, T. Sugita, S. Uemura, J. Org. Chem. 58 (1993) 7624.
[25] X. Jia, X. Li, L. Xu, Y. Li, Q. Shi, T.T.L. Au-Yeung, C.W. Yip, X. Yao, A.S.C. Chan, Adv. Synth. Catal. 346 (2004) 723.
[26] H.B. Kagan, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, second ed., Wiley, New York, 2000, p. 327, chap. 6.
[27] C. Bolm, K. Muñiz, J.P. Hildebrand, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, Springer-Verlag, Berlin, 1999, p. 697.
[28] I. Fernandez, N. Khiar, Chem. Rev. 103 (2003) 3651.
[29] K.P. Bryliakov, E.P. Talsi, Curr. Org. Chem. 12 (2008) 386.
[30] J. Legros, J.R. Dehli, C. Bolm, Adv. Synth. Catal. 347 (2005) 19.
[31] M.E. Davis, Nature 417 (2002) 813.
[32] C. Li, Catal. Rev. Sci. Eng. 46 (2004) 419.
[33] B.F.G. Johnson, S.A. Raynor, D.S. Shephard, T. Mashmeyer, J.M. Thomas, G. Sankar, S. Bromley, R. Oldroyd, L. Gladden, M.D. Mantle, Chem. Commun. (1999) 1167.
[34] D. Reechavi, M. Lemaire, Org. Lett. 3 (2001) 2493.
[35] C.G. Arellano, A. Corma, M. Lglesias, F. Sanchez, Adv. Synth. Catal. 346 (2004) 1758.
[36] H. Zhang, Li. Can, Tetrahedron 62 (2006) 6640.
[37] H. Zhang, Y. Zhang, C. Li, J. Catal. 238 (2006) 369.
[38] B.H. Lipshutz, Y.J. Shin, Tetrahedron Lett. 41 (2000) 9515.
[39] V.V. Thakur, A. Sudalai, Tetrahedron Asymm. 14 (2003) 407.
[40] X. Wang, X. Wang, H. Guo, Z. Wang, K. Ding, Chem. Eur. J. 11 (2005) 4078.
[41] B.M. Choudary, S. Shobha Rani, N. Narender, Catal. Lett. 19 (1993) 299.
[42] J. Gao, H. Guo, S. Liu, M. Wang, Tetrahedron Lett. 48 (2007) 8453.
[43] J. Fraile, J. Garcia, B. Lazaro, J. Mayoral, Chem. Commun. (1998) 1807.
[44] M. Iwamato, Y. Tanaka, J. Hirosumi, N. Kita, S. Triwahyono, Microporous Mesoporous Mater. 48 (2001) 271.
[45] S. Sahoo, P. Kumar, F. Lefebvre, S.B. Halligudi, Tetrahedron Lett. 49 (2008) 4865.
[46] A. Riisager, R. Fehrmann, S. Flicker, R. Van Hal, M. Haumann, P. Wasserscheid, Angew. Chem. Int. Ed. 44 (2005) 815.
[47] M. Gruttadauria, S. Riela, C. Aprile, P.L. Meo, F. D'Anna, R. Noto, Adv. Synth. Catal. 348 (2006) 82.
[48] C.P. Mehnert, Chem. Eur. J. 1 (2004) 50.
[49] A. Riisager, R. Fehrmann, M. Haumann, P. Waserscheid, Top. Catal. 40 (2006) 91.
[50] T. Joseph, S. Sahoo, S.B. Halligudi, J. Mol. Catal. A Chem. 234 (2005) 107.
[51] D. Zhao, J. Feng, Q. Huo, N. Melosh, G.H. Fredrickson, B.F. Chmelka, G.D. Stucky, Science 279 (1998) 548.
[52] H.B. Kagan, J.C. Fiaud, Top. Stereochem. 18 (1988) 249.
[53] C. Girard, H.B. Kagan, Angew. Chem. Int. Ed. 37 (1998) 2922.
[54] K. Mikami, M. Terada, T. Korenaga, Y. Matsumoto, M. Ueki, R. Angelaud, Angew. Chem. Int. Ed. 112 (2000) 3532.
[55] H.B. Kagan, Synlett (2001) 888.
[56] W.R. Huck, T. Mallat, A. Baiker, Adv. Synth. Catal. 345 (2003) 255.
[57] A. Tungler, K. Fodor, T. Máthé, R.A. Sheldon, Stud. Surf. Sci. Catal. 108 (1997) 157.
[58] L. Balazs, T. Mallat, A. Baiker, J. Catal. 233 (2005) 327.
[59] C. Puchot, O. Samuel, E. Dunach, S. Zhao, C. Agami, H.B. Kagan, J. Am. Chem. Soc. 108 (1986) 2353.
[60] A. Massa, F.R. Siniscalchi, V. Bugatti, A. Lattanzi, A. Scettri, Tetrahedron Asymm. 13 (2002) 1277.
[61] H.B. Kagan, Adv. Synth. Catal. 343 (2001) 227.