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The synthesis of silica-supported chiral BINOL: Application in Ti-catalyzed asymmetric addition of diethylzinc to aldehydes

Kavita Pathak, Irshad Ahmad, Sayed H.R. Abdi *, Rukhsana I. Kureshy, Noor-ul H. Khan, Raksh V. Jasra

Discipline of Inorganic Materials and Catalysis, Central Salt and Marine Chemicals Research Institute (CSMCRI), Bhavnagar 364002, Gujarat, India

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Abstract

Chiral BINOL was covalently anchored on two different pore sized mesoporous silica (SBA-15 (7.5 nm) and MCF (14 nm)). These heterogenized ligands were used in Ti-catalyzed asymmetric addition of diethylzinc to aldehydes. High catalytic activity with excellent enantioselectivity (up to 94% ee) for secondary alcohols was achieved using MCF supported chiral BINOL under heterogeneous reaction conditions. Good to excellent enantioselectivity (ee, 68–91%) was also achieved with various small to bulkier aldehydes. The MCF supported catalyst was reused in multiple catalytic runs without loss of enantioselectivity.

Keywords: Silica supported BINOL; Asymmetric addition; Diethylzinc; Mesoporous silica; Aldehydes

1. Introduction

Development of new chiral ligands is one of the core research activities in asymmetric catalysis to achieve high level of efficiency and selectivity in a variety of enantioselective organic transformations [1,2]. Chiral ligands embodying the binaphthyl framework such as BINAP and BINOL have earned a prominent place due to their versatility in catalytic asymmetric reactions [3,4]. Chiral BINOL based metal complexes are extensively studied catalysts for the various asymmetric transformations under homogeneous reaction conditions [5]. In recent years, recoverable catalysts have attracted considerable attention because it greatly simplifies the separation of the catalysts from the reaction mixture and allows the efficient recovery and reusability of the catalysts [6,7]. The asymmetric addition of dialkylzinc to aldehydes is one of the most important and vigorously pursued areas in the asymmetric C–C bond formations that afford chiral secondary alcohols as synthetically and pharmaceutically useful compounds [8–10]. Some of the significant reports on recoverable catalysts demonstrated the use of β-amino alcohols [11–19] and TADDOL [20–23] supported on inorganic and organic polymer/dendrimers in asymmetric addition of dialkylzinc to aldehydes. Chiral BINOL was also immobilized on a number of supports such as polymers [24–30], dendrimers [31–34], siliceous supports [35], monolayer protected Au cluster [36], ionic liquid [37] and fluorous biphasic system [38–41] to catalyze asymmetric addition of dialkylzinc to various aldehydes.

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 [42,43]. 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 [44–53]. In recent years, covalent immobilization of chiral ligands and metal complexes on siliceous supports received great attention as they offer to design a catalyst that is homogeneously and molecularly dispersed in the pores of mesoporous silica by introducing functional groups such as amine or thiols onto the surface [54], such

* Corresponding author. Tel.: +91 278 2567760; fax: +91 278 2566970.
E-mail address: shrabdi@csmcri.org (S.H.R. Abdi).

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a functionalized surface provides anchoring sites for the target catalyst.

We have earlier reported the immobilization chiral BINOL on to the siliceous supports (Silica gel, MCM-41 and SBA-15) and their use in asymmetric C–C bond forming reactions [35,55]. In the present contribution, we report the synthesis of silica-supported chiral BINOL on two different relatively large pore sized mesoporous silicas-SBA-15 (7.5 nm) and MCF (14 nm) by covalent grafting method using *N*-methyl-3-aminopropyltriethoxysilane (MAPTES) as reactive surface modifier. It has been known that the silanol groups of silica surface might affect the activity of immobilized catalyst [15,35,53]. Therefore, we have also examined the performance of supported catalysts by changing surface environment of siliceous supports with TMS groups. These heterogeneous solid chiral auxiliaries were used in Ti-promoted asymmetric addition of diethylzinc to aldehydes. High yields (97%) with excellent enantioselectivity (up to 94% ee) for secondary alcohols were achieved under heterogeneous reaction conditions. The MCF supported catalyst was reused in multiple catalytic runs without loss of enantioselectivity. To the best of our knowledge, these are the excellent results so far reported for the heterogenization of asymmetric addition of diethylzinc to aldehydes on siliceous supports except for the report where Ti-TADDOL was grafted covalently onto controlled porous glass [21].

2. Experimental

2.1. Materials and analytical methods

All experiments were carried out under an atmosphere of dry nitrogen. The solvents were dried using standard methods and stored over activated 4 Å molecular sieves. Poly-(ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide)block copolymer (Pluronic 123, MW: 5800), tetraethoxysilane (TEOS), 1,3,5-trimethylbenzene (TMB), benzyldehyde, *o*-methylbenzyldehyde, *m*-methoxylbenzyldehyde, *p*-methylbenzyldehyde, *p*-fluorobenzyldehyde, 1-naphthaldehyde, *trans*-cinnamaldehyde, *N*-methyl-3-aminopropyltriethoxysilane (MAPTES), diethylzinc 1 M in hexanes, $Ti(O^iPr)_4$ and hexamethyldisiloxane (HMDS) were purchase from Aldrich Chemicals and used without further purification. (*S*)-BINOL was purchased from Fluka. ^1H (200 MHz) and ^{13}C (50 MHz) NMR spectra were recorded in $CDCl_3$ using a Bruker, F113V. The IR spectra were recorded in KBr on PerkinElmer Spectrum GX spectrophotometer. Microanalysis was done on CHNS analyzer, PerkinElmer model 2400. Specific rotation was measured by polarimeter model Digipol 781 Rudolph instruments, USA. The pore sizes and surface area were determined with Micromeritics ASAP-2010 at 77 K. TEM analysis was accomplished by Transmission electron microscope Philips Tecnai 20. The conversion and ee of secondary alcohols was determined by HPLC (Shimadzu SCL-10AVP) using Chiralcel OD column. Flash chromatography was performed using silica gel (60–200 mesh) purchased from s.d. Fine-Chemicals Limited, Mumbai (India).

2.2. Synthesis of ligands

2.2.1. (S)-2,2′-Dimethoxy-1,1′-binaphthyl 2

The compound **2** was synthesized from (*S*)-2,2′-dihydroxy 1,1′-binaphthyl (BINOL) **1** according to the reported procedure [56].

2.2.2. (S)-6-Chloroacetyl-2,2′-dimethoxy-1,1′-binaphthyl 3

The compound **3** was synthesized according to the modified reported procedure [56]. A mixture of **2** (3 gm, 9.5 mmol), anhydrous $AlCl_3$ (1.26 g, 9.8 mmol) and CH_2Cl_2 (60 mL) was stirred at 0 °C for 15 min in an argon atmosphere. Chloro acetyl chloride (1.1 mL, 9.8 mmol) was added dropwise in the reaction mixture and the resulting brown reaction mixture was warmed to room temperature and stirred magnetically for 18–20 h. The reaction mixture was quenched with aqueous 1N HCl (150 mL) and extracted with CH_2Cl_2 (75 mL). The organic extract was dried over anhydrous Na_2SO_4. After the removal of the solvent the residue was purified by column chromatography over silica gel using *n*-Hexane/EtOAc (98:2) to get **3** as light yellow solid. (Yield; 1.82 gm, 60%); $[\alpha]_D^{25} = +26.7$ (*c* 0.5, $CHCl_3$); IR (KBr): $\nu = 2921, 2847, 1689, 1591, 1462, 1262, 1173, 1062, 806, 748, 678\ cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 3.75$ (s, 6H), 4.72 (s, 2H), 7.19 (d, $J = 8.8$ Hz, 1H), 7.28 (d, $J = 9$ Hz, 1H), 7.17–7.35 (m, 3H), 7.42 (d, $J = 3.8$ Hz, 1H), 7.48 (d, $J = 3.5$ Hz, 1H), 7.84 (d, $J = 8.5$ Hz, 1H), 7.88 (d, $J = 9$ Hz, 1H), 7.95 (d, $J = 9$ Hz, 1H), 8.02 (d, $J = 2$ Hz, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 46.6, 56.8, 114.7, 115.0, 115.4, 117.7, 124.1, 124.9, 125.7, 126.5, 127.1, 127.6, 128.7, 129.5, 129.8, 130.2, 130.6, 130.8, 131.3, 132.3, 157.8, 174.1, 196.5$ ppm; LC–MS *m/z* 392 ($M^+ + H$); Anal. Calcd. for $C_{24}H_{19}O_3Cl$ (wt%): C, 73.75; H, 4.87. Found (wt%): C, 73.71; H, 4.84.

2.3. Synthesis of MCF (B)

Siliceous mesocellular form (MCF) was synthesized using a modified procedure reported by Stucky et al. [57]. Triblock copolymer P123 (8 g) was dispersed in 60 g of double-distilled water stirred for 3 h at room temperature. After a solution of 1,3,5-trimethylbenzene (TMB) (11.42 g) was added slowly to a stirred solution and stirred for 30 min at room temperature. Then 300 g of 2 M aqueous HCl was added under stirring at ambient temperature (25–30 °C) for 1 h. Finally, silica source TEOS (18.8 g) was added to the homogeneous solution under stirring to form a gel at 100 °C for 24 h, and then allowed to stand for crystallization under static hydrothermal conditions at 110 °C for 48 h in a Teflon Parr reactor. The crystallized product was filtered off, washed with warm distilled water, air-dried at 35 °C. Calcination at 550 °C for 6 h.

2.4. Synthesis of N-methylaminopropyl functionalized SBA-15 (A-4) and MCF (B-4)

The predried calcined silica (3.5 g) and *N*-methyl-3-aminopropyltriethoxysilane (MAPTES) (1.8 mL, 7.2 mmol) was refluxed in dry toluene (30 mL) under a nitrogen atmosphere for 5–6 h. The solids were filtered, washed successively

with toluene and acetone finally dried at 100 °C under vacuum for 4–5 h. **A-4**: IR: $\nu = 3450, 2925, 1088, 795, 461\ cm^{-1}$; Elemental analysis: found (wt%): C 8.26, H 1.2, N 0.35. **B-4**: IR: $\nu = 3454, 2929, 1085, 798, 460\ cm^{-1}$; Elemental analysis: found (wt%): C 9.52, H 2.10, N 0.43.

2.5. Immobilization of *3* onto N-methylaminopropyl functionalized SBA-15 and MCF

The *N*-methylaminopropyl functionalized silicas **A-4/B-4** (2.0 g) and modified chiral BINOL ligand **3** (3 mmol) were allowed to stir at reflux temperature under a nitrogen atmosphere for 24 h. After cooling, the powder was collected by filtration, washed successively with dry toluene, and then dried under vacuum. Dried material was subjected to soxhlet-extraction with dichloromethane for 24 h. Finally the samples **A-5/B-5** were dried under vacuum at 45–50 °C for 4–5 h. Removal of the protecting group using 1 M BBr_3 [35] to get desired supported chiral ligand **A-BINOL-6** and **B-BINOL-6**.

A-BINOL-6: IR: $\nu = 3435, 2952, 2856, 1637, 1472, 1088, 807, 693, 459\ cm^{-1}$. Elemental analysis: found (wt%): C 8.71, H 0.75, N 0.39.
B-BINOL-6: IR: $\nu = 3429, 2962, 2858, 1620, 1470, 1089, 808, 691, 461\ cm^{-1}$; Elemental analysis: found (wt%): C 9.22, H 0.79, N 0.42.

2.6. TMS modification of BINOL-immobilized SBA-15 and MCF (*A-BINOL-7* and *B-BINOL-7*)

TMS modification was carried out using earlier reported procedure [35].

A-BINOL-7: IR: $\nu = 2972, 2850, 1641, 1476, 1080, 845, 804, 691, 460\ cm^{-1}$. Elemental analysis: found (wt%): C 10.20, H 1.30, N 0.38.
B-BINOL-7: IR: $\nu = 2961, 2858, 1647, 1473, 1074, 846, 800, 695, 460\ cm^{-1}$. Elemental analysis: found (wt%): C 11.57, H 1.42, N 0.40. ^{13}C CP MAS: $\delta = 0.6\ (Me_3SiO–), 8, 17, 28, 39, 60, 122, 132, 144, 153, 170\ (CH_2–N=)$ ppm.

2.7. General procedure for asymmetric addition of diethylzinc to aldehydes

Supported ligand (0.05 mmol) was dried under vacuum for 6 h at 110 °C then taken in 2 mL dry CH_2Cl_2 and was stirred with $Ti(O^iPr)_4$ (1.5 mmol) for 2 h at room temperature under a nitrogen atmosphere. To the above suspension a solution of Et_2Zn (1 M solution in hexane, 3.0 mmol) was added, cooled to 0 °C, aldehyde (1.0 mmol) was added dropwise in the resulting mixture was allowed to stir at 0 °C for 15 h. The progress of the catalytic reaction was monitored on HPLC. After completion of the reaction, the supported catalyst was filtered off from the reaction mixture, washed with CH_2Cl_2, dried under vacuum and kept for reuse experiments. The filtrate and combined washings was quenched with saturated NH_4Cl solution (10 mL), washed with water and dried over anhydrous Na_2SO_4. It was filtered and crud product was analyzed on HPLC chiralcel OD column to determine the optical purity. The isolated yields of products were carried out using flash column chromatography (silica gel, *n*-hexane/EtOAc: 4:1). The absolute configuration of the product was determined by comparison of retention time with literature data [25].

2.7.1. (S)-1-Phenyl-1-propanol (Table 2, entry 5)

Colorless oil, $[\alpha]_D^{25} = -41.3$ ($c = 0.5$, $CHCl_3$) ^1H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, $J = 7.4$ Hz, 3H), 1.70–1.87 (m, 3H), 4.59 (t, $J = 6.4$ Hz, 1H), 7.25–7.36 (m, 5H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 10.1, 31.8, 75.8, 126.0, 127.3, 128.3, 144.7 ppm; HPLC (Chiralcel OD column): *n*-hexane/iPrOH = 90:10, flow rate = 0.5 mL/min, 254 nm, $t_1 = 14.9$ min, t_2 17.1 min.

2.7.2. (S)-1-(1′-Naphthyl)-1-propanol (Table 3, entry 10)

Yellow oil, $[\alpha]_D^{25} = -53.3$ ($c = 0.5$, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 1.03 (t, $J = 7.1$ Hz, 3H), 1.85 (s, 1H), 1.88–2.09 (m, 2H), 5.43 (dd, $J = 5.1$, 7.4 Hz, 1H), 7.47–8.10 (m, 7H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 10.5, 31.1, 72.5, 123.0, 123.3, 125.4, 125.5, 125.9, 127.8, 128.9, 130.6, 133.9, 140.3 ppm; HPLC (Chiralcel OD-H column): *n*-hexane/iPrOH = 90:10, flow rate = 0.5 mL/min, 254 nm, $t_1 = 16.5$ min, t_2 27.5 min.

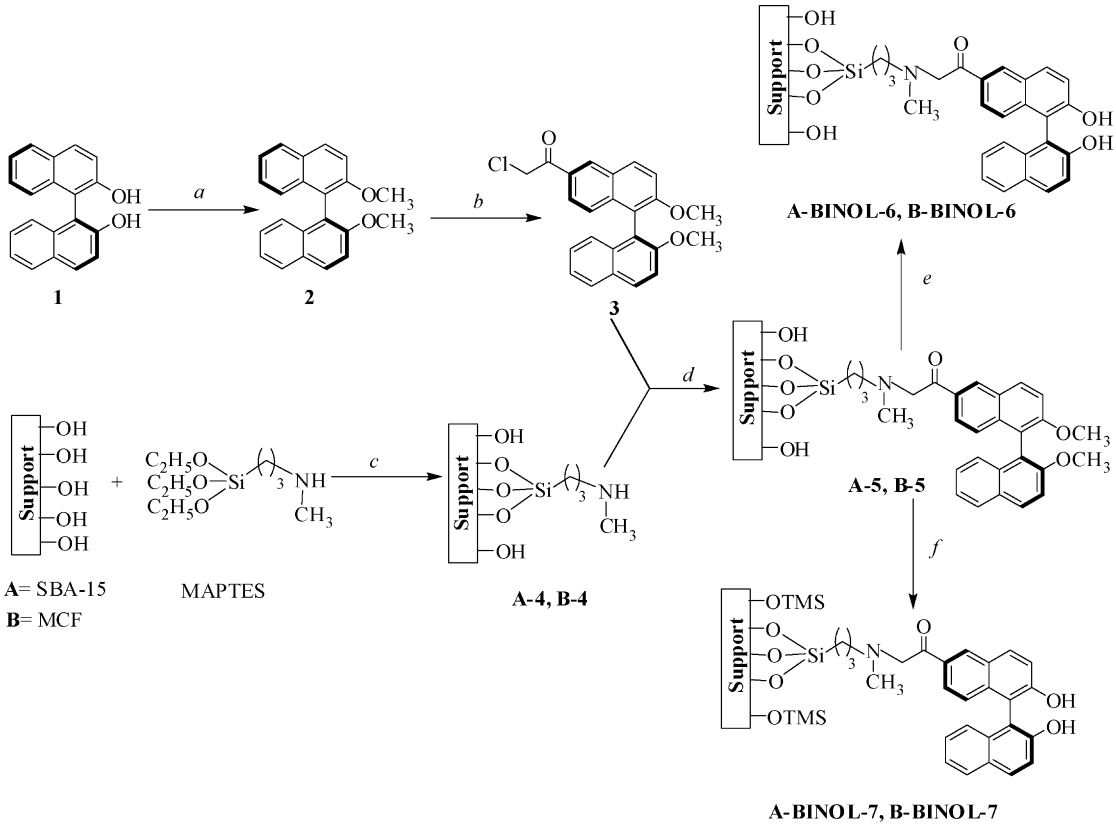
2.8. General procedure for recycling of silica-supported ligand

After fourth catalytic run, silica-immobilized ligand **B-BINOL-7** was washed sequentially with 10% HCl in MeOH (20 mL), H_2O (15 mL), and acetone (15 mL) and dried under vacuum at 110 °C for 16 h. The catalyst was used for the next catalytic cycle with reloaded with Ti metal.

3. Results and discussion

3.1. Synthesis and characterization of silica-supported chiral BINOL

To immobilize (*S*)-2,2′-dihydroxy-1,1′-binaphthyl **1** on the inorganic supports, chloro acetyl group was selectively introduced at 6th position of the naphthyl ring of the O-methylated BINOL **2**. The chloroacetylated compound **3** was then allowed to react with amino groups present on the surface modified mesoporous silicas (Scheme 1). Accordingly, the hydroxyl groups of BINOL **1** were protected with CH_3I under basic condition to get compound **2**. The O-methylated BINOL **2** was reacted with chloroacetyl chloride in the presence of powdered anhydrous $AlCl_3$ in dry CH_2Cl_2 at 0 °C to afford (*S*)-6-chloroacetyl 2,2′-dimethoxy-1,1′-binaphthyl **3** in 60% yield after purification on a silica gel column. In this study, we have synthesized two different pore sized mesoporous silica *viz*. SBA-15 and MCF, to study the effect of pore size of silica on enantioselectivity of catalyst. The siliceous SBA-15 **A** (7.5 nm) was synthesized by using amphiphillic triblock copolymer P123 as a structure directing agent as per the reported procedure [50], while MCF **B** was



Scheme 1. The immobilization of chiral BINOL onto silica surface; reagents and conditions: (a) CH_3I, K_2CO_3, acetone, reflux, 18 h, 87%; (b) Cl–CH_2COCl, anhydrous $AlCl_3$, CH_2Cl_2, 0 °C, 4 h, 60%; (c and d) toluene, reflux, 24 h; (e) BBr_3, CH_2Cl_2, −78 °C; (f) (i) HMDS, reflux, 12 h; (ii) BBr_3, CH_2Cl_2, −78 °C.

synthesized using amphiphillic triblock copolymer P123 as a structure directing agent and mesitylene was used as a swelling agent. MCF has a high surface area of 500–800 m^2/g, and a 3-D pore structure with ultra large, cell-like pores (23–42 nm) that are connected by windows of 9–22 nm. Such a pore structure would minimize any steric effects associated with the immobilization of bulky compounds, and facilitate the diffusion of large substrates [57]. The surface modification of silicas was achieved by MAPTES as a reactive surface modifier to give **A-4** and **B-4** (Scheme 1). After successful surface modification, compounds **A-4** and **B-4** were refluxed with modified ligand **3** in dry toluene for 24 h to get **A-5** and **B-5**, respectively, which on demethylation with 1 M BBr_3 in CH_2Cl_2 afforded immobilized ligands **A-BINOL-6** and **B-BINOL-6**, respectively. Further, free hydroxyl groups present on the surface of silica matrix were passivated in order to eliminate the possibility of creating non-chiral catalytic sites by their co-ordination with the metal ion used in catalysis and thereby minimizing the drop in enantioselectivity [15,35]. Therefore, we modified the accessible free silanol sites of **A-5** and **B-5** by treating it with hexamethyldisiloxane (HMDS) a reflux temperature for 12 h which on demethylation afforded immobilized ligands **A-BINOL-7** and **B-BINOL-7**, respectively. The characterizations of the mesoporous silica supported ligands were accomplished by various physico-chemical techniques. The elemental analysis of supported chiral ligands based on the wt.% of N demonstrated that the loading of the chiral ligands was 22–24 mg/gm, respectively. Fig. 1 shows representative ^{13}C CP MAS spectra of functionalized SBA-15 **A-4**

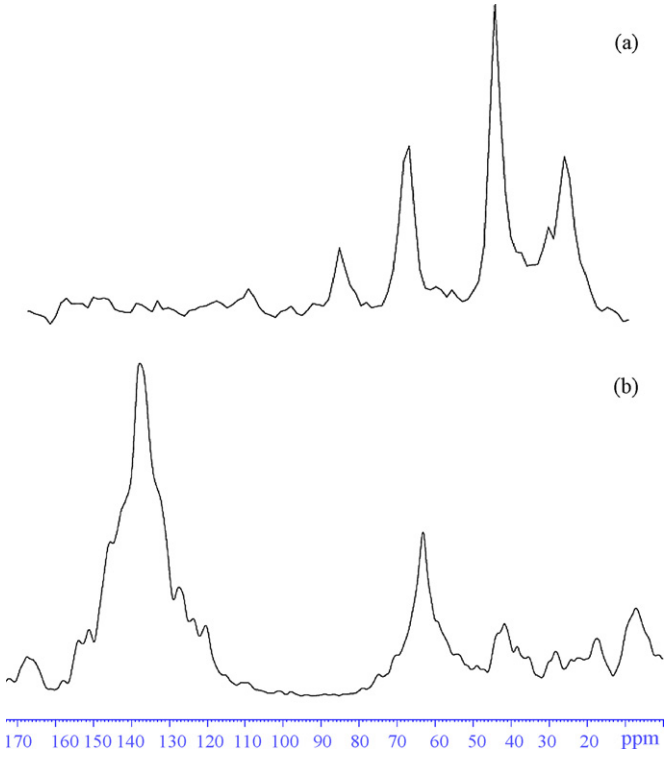


Fig. 1. ^{13}C CP MAS NMR spectra of **A-4** (a), **A-BINOL-6** (b).

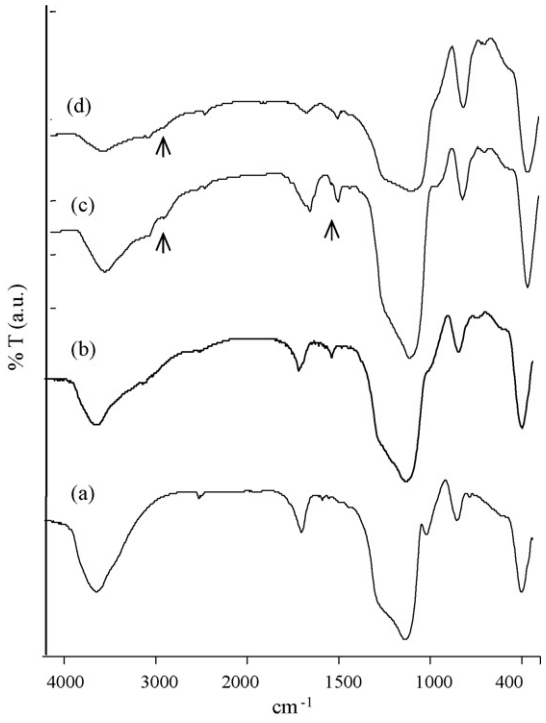


Fig. 2. FT-IR spectra of pristine **A** (a), **A-4** (b), **A-BINOL-6** (c), **A-BINOL-7** (d).

and supported ligand **A-BINOL-6**, which showed peaks 63, 41, 28, 9 ppm due to the surface modification by MAPTES [58], 120–155 ppm for aromatic carbons due to naphthyl groups of BINOL [35] and 170 ppm (CH_2–NH group) further confirmed the successful attachment of BINOL on silica.

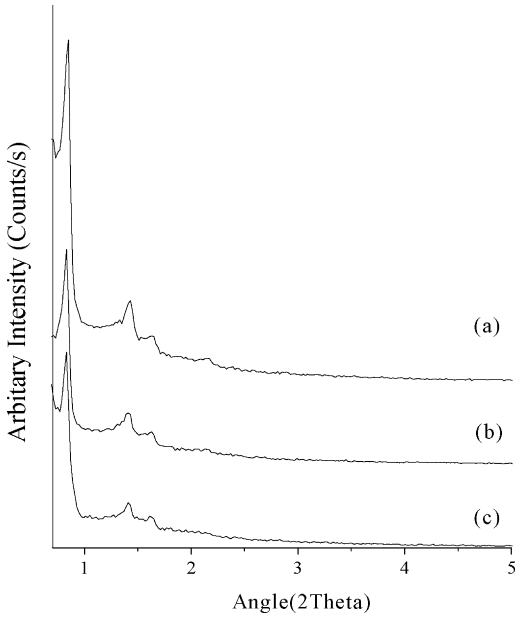


Fig. 3. Powder XRD patterns of pristine **A** (a), **A-4** (b) and **A-BINOL-7** (c).

FT-IR spectra of heterogenized ligands were in good agreement with the expected chemical structure of the organic moieties (Fig. 2). New peaks at 2952, 2856 (C–H stretching vibrations), 1637 (C–N vibration), 1472 (C=C stretching vibration) cm^{-1} in comparison with the inorganic supports before grafting, indicate the formation of the organic-inorganic hybrid ligands. Moreover, FT-IR spectra illustrated significant decrease in free Si–OH stretching at ~3400 cm^{-1} after silanol capping with trimethylsilyl group (TMS) on siliceous supports.

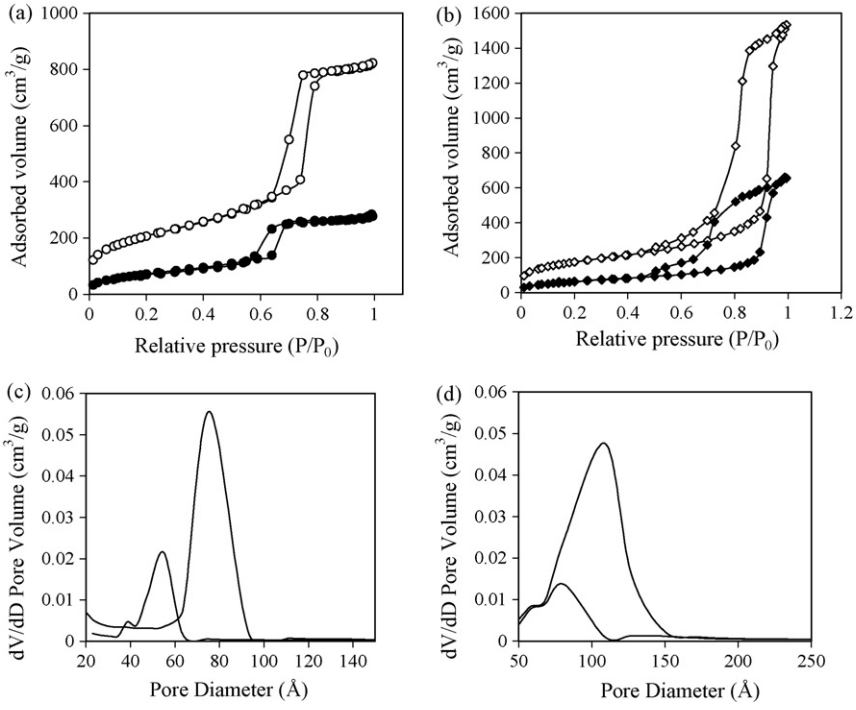


Fig. 4. Nitrogen isotherms at 77 K of pristine SBA-15 **A** and immobilized ligand **A-BINOL-7** (a), pristine MCF **B** and **B-BINOL-7** (b) and their pore size distribution curves (c) and (d), respectively (adsorption branch).

Table 1
Textural parameters of samples taken from nitrogen adsorption data

Sample	S_{BET} ($m^2\ g^{-1}$)	ΔS_{BET} (%)[a]	V_p ($cm^3\ g^{-1}$)	ΔV_p (%)[b]	d_{BJH} (nm)
A	745	–	1.25	–	7.5
A-4	600	−20	0.98	−22	7.2
A-BINOL-6	435	−28	0.65	−34	6.9
A-BINOL-7	237	−46	0.32	−51	6.7
B	635	–	2.20	–	14.0
B-4	545	−15	1.84	−17	13.2
B-BINOL-6	410	−25	1.10	−41	11.0
B-BINOL-7	217	−48	0.52	−53	9.5

[a] Variation of surface area in relation to parent mesoporous material.
[b] Variation of total pore volume in relation to parent mesoporous material.

The powder XRD patterns of pristine SBA-15 show a very intense peak assigned to reflection at (1 0 0) and two additional peaks with low intensities at (1 1 0) and (2 0 0) reflections, which can be indexed for a hexagonal unit cell (Fig. 3). It is observed that on functionalization with MAPTES, the intensities of all of the peaks of decrease marginally with a little shift toward lower 2θ values. These peaks do not change significantly after the attachment of modified chiral BINOL unit **3** to functionalized silicas suggesting that the structure of silica do not collapse after chiral BINOL is supported on surface of silica.

Fig. 4 shows N_2 sorption isotherms and pore size distribution curves of pristine silica and supported ligands. Unmodified SBA-15 and MCF exhibit a reversible type IV adsorption–desorption isotherm, characteristic of a mesoporous solids. Pristine MCF shows steep hystereses of type H1 at high relative pressures (Fig. 4b), which exhibit capillary condensation and evaporation and have large pore sizes with narrow size distributions. The isotherms of the functionalized SBA-15 and MCF samples show a lower N_2 uptake, pointing to a decrease in the specific surface area and pore volume (Table 1). This effect is more pronounced for the trimethylsilylated samples **A-BINOL-7** and **B-BINOL-7**, for which S_{BET} decreased more than 49% and V_p decreased more than 45%. The height of the capillary condensation step and the p/p_0 coordinate of the inflection point slightly decrease, indicating changes in pore size distribution due to grafting of the internal silica surface with the organic species. This is confirmed by comparing the pore size distributions (PSD) of the pristine and modified silica materials (Fig. 4c and d). Fig. 5 shows TEM micrographs of pristine MCF and immobilized **B-BINOL-7** revealed that a disordered array of silica struts, which is the characteristic structural feature of the MCF. TEM analyses indicate that the phase transition from the undulated SBA-15-type, ordered structure with *p6mm* symmetry to the strut like MCF structure. So it is revealed that MCF has ink-bottle-type pores, in which large spherical cells (bodies of the ink bottles) are interconnected by narrower windows (bottlenecks) [57]. Thus structure of mesoporous support was unaffected by immobilization of chiral modified BINOL.

3.2. Asymmetric addition of diethylzinc to aldehydes

Asymmetric addition of diethylzinc to benzaldehyde was carried out using Ti complex of (*S*)-BINOL **1** as catalyst under homogeneous reaction condition. Excellent conversion to 1-phenyl-1-propanol with high ee (92%) was achieved in 7 h (Table 2, entry 1) using CH_2Cl_2 as solvent. When the immobilized chiral ligands **A-BINOL-6** and **B-BINOL-6** were screened for its activity towards the addition of diethylzinc to benzaldehyde under similar reaction conditions, (92–95%) conversion with enantioselectivity (ee; 70–72%) were achieved (Table 2, entries 2 and 3). Passivation of the free SiOH moieties on the silica surface with TMS (**A-BINOL-7** and **B-BINOL-7**) significantly improved conversion (99%) with excellent enantioselectivity (ee, 89–94%) of 1-phenyl-1-propanol (Table 2, entries 4 and 5). Several common factors which are known to affect the enantioselectivity of the catalyst system such as choice of solvent and reaction temperature have been studied using *in situ* generated Ti-complex of immobilized ligands **A-BINOL-7** and **B-BINOL-7** as catalysts and benzaldehyde as a substrate. Consequently, the use of toluene and diethyl ether as solvent gave good conversion (90–98%) with enantioselectivity (80–87%) (Table 2, entries 6–9) nevertheless, results obtained with the use of CH_2Cl_2 are better for the present catalytic system. When reaction was conducted at lower temperature (−20 °C) in

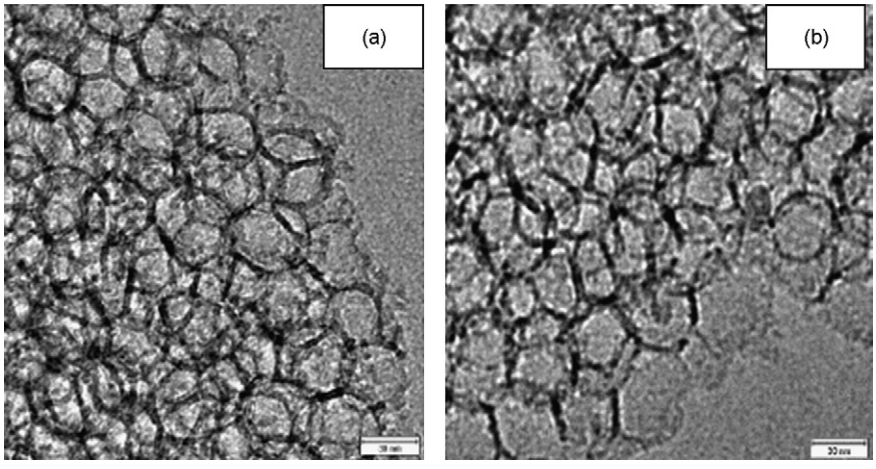
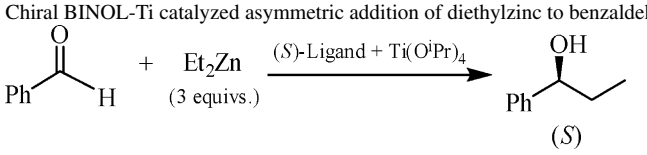


Fig. 5. TEM images of pristine **B** (a), **B-BINOL-7** (b).

Table 2
Chiral BINOL-Ti catalyzed asymmetric addition of diethylzinc to benzaldehyde under various reaction conditions[a]



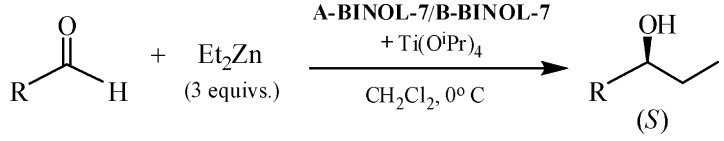
Entry	Ligand	Solvent	Temperature (°C)	Conversion (%)[b]	Selectivity (%)[c]	ee (%)[d]
1	**1**	CH_2Cl_2	0	99	>99	92
2	**A-BINOL-6**	CH_2Cl_2	0	92	92	70
3	**B-BINOL-6**	CH_2Cl_2	0	95	96	72
4	**A-BINOL-7**	CH_2Cl_2	0	97	98	89
5	**B-BINOL-7**	CH_2Cl_2	0	99 (97)[e]	>99	94
6	**A-BINOL-7**	Toluene	0	96	98	84
7	**B-BINOL-7**	Toluene	0	98	99	87
8	**A-BINOL-7**	Diethyl ether	0	90	93	80
9	**B-BINOL-7**	Diethyl ether	0	93	95	83
10	**A-BINOL-7**	CH_2Cl_2	−20	71	73	89
11	**B-BINOL-7**	CH_2Cl_2	−20	74	75	91
12	**A-BINOL-7**	CH_2Cl_2	rt	98	62	79
13	**B-BINOL-7**	CH_2Cl_2	rt	99	65	83
14	**TMS capped A**	CH_2Cl_2	0	15	–	–

[a] Reactions were carried out with 0.05 mmol ligand **1** (homogeneous reaction condition) for 7 h and 0.05 mmol of supported chiral ligand (heterogeneous reaction condition) using 1.5 mmol $Ti(O^iPr)_4$, 3.0 mmol Et_2Zn and 1.0 mmol substrate in 2 mL solvent for 15 h.
[b] Determined by ^1H NMR spectroscopy of crude products.
[c] %Selectivity: 100 ([*R*] + [*S*])/([*R*] + [*S*] + [$PhCH_2OH$]).
[d] Determined by HPLC using Daicel Chiralcel OD column.
[e] Isolated yield.

CH_2Cl_2, the enantioselectivity increased only marginally but conversion slowed down significantly. Moreover, the selectivity was found to be lower when the reaction was carried out at room temperature (Table 2, entries 12 and 13). The catalytic activity of the TMS capped MCF without a chiral ligand was checked under the same reaction conditions gave 15% conversion and the product obtained was found to be racemic. This shows that silica surface itself is benign for imparting enantioselectivity [15].

Silica-supported chiral BINOL (**A-BINOL-7** and **B-BINOL-7**) were further used in asymmetric addition of

Table 3
Supported chiral BINOL-Ti catalyzed asymmetric addition of diethylzinc for smaller to bulkier aldehydes[a]



Entry	RCHO	Supported ligand	Conversion (%)[b]	Selectivity (%)[c]	ee (%)[d]
1	*p*-MeC_6H_4CHO	**A-BINOL-7**	92	94	82
2		**B-BINOL-7**	98	99	87
3	*p*-FC_6H_4CHO	**A-BINOL-7**	94	95	85
4		**B-BINOL-7**	98	99	90
5	*m*-$MeOC_6H_4CHO$	**A-BINOL-7**	95	97	80
6		**B-BINOL-7**	99	96	85
7	*o*-MeC_6H_4CHO	**A-BINOL-7**	87	85	68
8		**B-BINOL-7**	94	95	70
9	1-NaphthylCHO	**A-BINOL-7**	90	93	85
10		**B-BINOL-7**	98 (95)[e]	96	91
11	*t*-$C_6H_5CH{=}CHCHO$	**A-BINOL-7**	80	88	79
12		**B-BINOL-7**	88	93	86

[a] Reactions were carried out with 0.05 mmol supported chiral ligand using 1.5 mmol $Ti(O^iPr)_4$, 3.0 mmol Et_2Zn and 1.0 mmol substrate in 2 mL CH_2Cl_2 for 15 h.
[b] Determined by ^1H NMR spectroscopy of crude products.
[c] %Selectivity: 100 ([*R*] + [*S*])/([*R*] + [*S*] + [$PhCH_2OH$]).
[d] Determined by HPLC using Daicel Chiralcel OD column.
[e] Isolated yield.

Table 4
Recycling data for asymmetric addition of diethylzinc to benzaldehyde using **B-BINOL-7** with $Ti(O^iPr)_4$ as catalyst[a]

Catalytic run	Conversion (%)	ee (%)
1	99	94
2	98	93
3	98	92
4	73	85
5[b]	94	93
6	95	94
7	95	94

[a] 0.05 mmol **B-BINOL-7** for 15 h at 0 °C.
[b] After washed with 10% HCl in MeOH, H_2O and acetone and reloaded with Ti metal.

diethylzinc to various other aldehydes in CH_2Cl_2 under heterogeneous reaction condition (Table 3). The active catalyst was generated *in situ* by the interaction of supported BINOL with $Ti(O^iPr)_4$ in CH_2Cl_2. Smaller to bulkier aldehydes like *o*-methyl benzaldehyde, *m*-methoxy benzaldehyde, *p*-methyl benzaldehyde, *p*-fluoro benzaldehyde, 1-naphthaldehyde and *trans*-cinnmaldehyde gave respective chiral secondary alcohols in good to excellent conversion and ee. However, the substituents on benzaldehyde derivative had some influence on the reactivity and enantioselectivity, *p*-substituted aldehydes showed better reactivity (Table 3, entries 1–4) with respect to conversion and ee than *o*-substituted aldehyde (entries 7, 8) with supported catalysts. This is probably due to the strong steric effect of the *o*-substitutent which may deteriorate the coordination of the substrate to the chiral catalyst thus lowering the reactivity, although activity and selectivity was found to be very good to excellent for different substrates in terms of their steric and electronic features with both catalysts. Excellent enantioselectivity (ee, 91%) with high yields (95%) was achieved with 1-naphthaldehyde using catalyst **B-BINOL-7** (Table 3, entry 10).

3.3. Recovery and recycling of supported chiral catalyst

The supported chiral catalyst **B-BINOL-7** was taken as representative candidate for recycling experiments (Table 4). The supported catalyst was readily recovered before quenching the reaction mixture by NH_4Cl solution. The recovered catalyst was washed with CH_2Cl_2 and dried under vacuum at 110 °C for 5–6 h and kept in desiccators for further use. The supported catalyst was reused in multiple catalytic runs. However, in the fourth reuse experiment there was notable decrease in the conversion and enantioselectivity probably due to the blockage of catalytic sites with the reactants. Therefore, the catalyst recovered after fourth run was washed sequentially with 10% HCl in MeOH, H_2O and finally with acetone under centrifugation [35]. The regenerated ligand thus obtained was used for the next catalytic run with the fresh supply of Ti. We observed that the above treatment restored the activity and enantioselectivity of the catalyst for another three successive reuse cycles.

4. Conclusion

In summary, we have synthesized silica supported chiral BINOL on robust large pore sized siliceous SBA-15 and MCF as supports. The new assembled heterogeneous organic–inorganic hybrid materials were used in Ti-catalyzed asymmetric addition of diethylzinc to aldehydes. The supported catalysts were studied under a variety of reaction conditions with varying substrates. Excellent conversion (99%) with high chiral induction was achieved (up to 94% ee) in the case of benzaldehyde. Good to excellent enantioselectivity (ee, 68–91%) was also achieved with various small to bulkier aldehydes. The MCF supported BINOL catalyst was reused in several catalytic runs without significant drop of enantioselectivity. The pore size of silica supports and capping of free silanol groups with TMS groups on the silica surface were found to be important towards achieving high enantioselectivities.

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