CHIRALITY 22:403–410 (2010)

Effect of the Substrate and Catalyst Chirality on the Diastereoselective Epoxidation of Limonene Using Jacobsen-Type Catalysts

JAIRO CUBILLOS,* MARÍA VARGAS, JULIANA REYES, AÍDA VILLA, AND CONSUELO MONTES DE CORREA

Chemical Engineering Department, Universidad de Antioquia, Medellín, Colombia

ABSTRACT Chiral and achiral Jacobsen's catalysts in their homogeneous form or immobilized on Al-MCM-41 exhibit similar catalytic activity during diastereoselective epoxidation of limonene when in situ generated dimethyldioxirane is used as oxidizing agent. Experimental observations suggest that not only the catalyst chiral center but also the substrate chiral center participates in the preferential formation of most diastereomers. Remarkable turnover numbers (TON), up to 288, was achieved over the heterogeneous catalysts in comparison to their homogeneous counterparts (TON up to 46). Catalyst leaching rather than catalyst oxidative degradation was identified as the main source of catalyst deactivation during reutilization tests. *Chirality 22:403–410, 2010.* © 2009 Wiley-Liss, Inc.

KEY WORDS: chirality; manganese salen complexes; achiral catalyst; heterogeneous catalysis; catalyst degradation

INTRODUCTION

Enantiomerically pure epoxides are synthetically useful for synthesizing many chiral nonracemic compounds.[1] *R*-(+)-1, 2-Limonene oxide is commercially available and relatively inexpensive but, usually marketed as a 1:1 mixture of the *cis*- and *trans*-epoxides (Aldrich, 97% pure). In general, oxidation of *R*-(+)- and *S*-(−)- limonene yield a variety of products. Epoxides are formed if oxidation occurs at olefinic positions due to the reactivity of the more substituted double bonds.[2] These substrates have two olefinic bonds (1, 2 and 8, 9 in Fig. 1) and the oxidation can take place at either or both of these bonds. Furthermore, two types of diastereomers (cis and trans) are expected for each of the epoxide products (see Fig. 2).[3] Typically in these reactions, a 1:1 ratio of the cis/trans diastereomers are formed as the chiral center in the molecule does not seem to affect the orientation of the incoming oxygen atom.[2,3]

Chiral and achiral salen transition metal complexes have become a matter of current interest because of their wide range of applications as catalysts for asymmetric epoxidation reactions.[4] Figure 3 illustrates the general structure of metal salen complexes. When substituents R1 and R3 are equal to R2 and R4, respectively, the complex corresponds to an achiral catalyst. However, in the chiral catalyst either R1 is different from R2 and R3 different from R4.

It is known that any asymmetric reaction requires the presence of a chiral component in the reaction medium.[5] In this way, two types of asymmetric catalytic transformations can be distinguished. Enantioselective reaction, which can take place when the substrate is an achiral or prochiral compound and the catalyst is a chiral compound, or diastereoselective reaction which can occur when the substrate is an enantiomerically pure compound and the catalyst is either chiral or achiral.

Epoxidation of unfunctionalized olefins catalyzed by chiral manganese (III) salen complexes, initially developed by Jacobsen and Katsuki, have emerged as practical methods for the synthesis of optically active epoxides.[6] Among them, the most important catalyst for enantioselective epoxidation of unfunctionalized olefins is the Jacobsen's catalyst (with both optical configuration R,R and S,S), a chiral manganese salen complex which displays high activity and enantioselectivity for asymmetric epoxidation of conjugated *cis*-disubstituted and trisubstituted prochiral olefins in homogeneous phase. However, the separation and recycling of this catalyst are still problematic issues.[7] In addition, salen transition metal complexes are very expensive materials, mainly in their chiral forms.[8] The conventional way to solve these problems is to immobilize chiral manganese (III) salen complexes onto solid supports. Therefore, many efforts have been devoted to heterogenize these catalysts using a solid matrix as support.[9] Various approaches for immobilization of chiral manganese (III) salen complexes have been described in an excellent review, which includes grafting the catalyst on a solid inorganic support such as silica or MCM-41, encapsulation into the pores of zeolites, physical entrapment in a

---

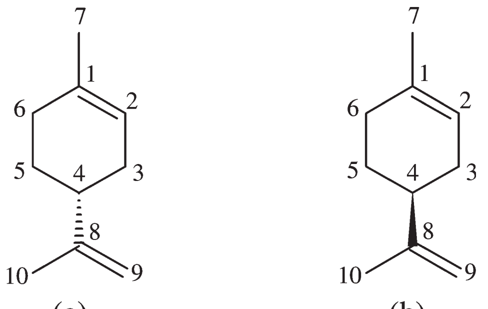
Contract grant sponsor: CENIVAM-Colciencias; Contract grant number: 432-2004

Contract grant sponsor: Universidad de Antioquia

*Correspondence to: Jairo Antonio Cubillos Lobo, Calle 67 No. 53-108, Medellín, Colombia. E-mail: jacubil@gmail.com

Received for publication 16 March 2008; Accepted 22 May 2009

DOI: 10.1002/chir.20755



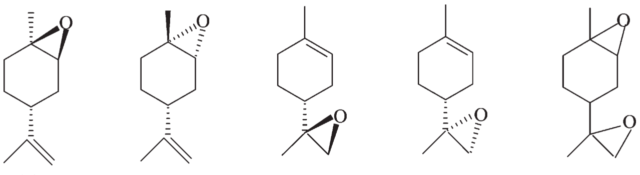
(a) (b)

Fig. 1. Chemical structure of limonene enantiomers: (**a**) *R*-(+)-Limonene, (**b**) *S*-(−)-Limonene.

polydimethylsiloxane membrane (polymer support), clays, and activated carbon.[9] However, heterogenization of homogeneous catalysts generally leads to lower catalytic activity than that reached by their homogeneous counterparts.[9] In addition, the instability of the catalyst itself under reaction conditions avoids its useful reutilization.[9] Therefore, to carry out successful heterogeneous asymmetric epoxidation, not only the design of supported catalysts but also the selection of appropriate oxidation conditions is very important.[10] In this sense, Cubillos et al. reported that the use of in situ generated dimethyldioxirane (DMD) as oxidizing agent improved the stability of the Jacobsen's catalyst during the enantioselective epoxidation of three proquiral olefins in comparison to other common oxygen sources such as sodium hypochlorite and *m*-chloroperbenzoic acid (*m*-CPBA).[11]

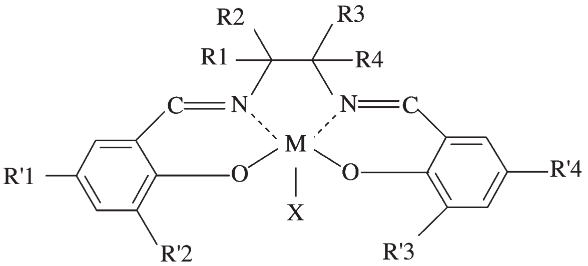
Recently, two research groups independently reported the heterogeneous diastereoselective epoxidation of *R*-(+)-limonene using chiral salen manganese complexes as catalysts in the system oxygen/sacrificial aldehyde, according to Mukaiyama's conditions.[12,13] However, the catalytic behavior of the corresponding achiral catalyst was not explored in these works. Recently, Ratnasamy and coworkers[14] used a heterogeneous achiral Jacobsen's catalyst (without the terbutyl groups) on limonene epoxidation but low catalytic activities were obtained. It is widely known that terbutyl groups favor the approaching of incoming olefin to the catalytically active center.[15]

In this article, we report on the diastereoselective epoxidation of limonene (optical configuration R and S) using the Jacobsen's catalyst in its homogeneous chiral (optical configuration R,R and S,S) and achiral forms, as well as, immobilized on Al-MCM-41 by ionic bond using in situ generated DMD as the oxygen source. The presence of framework aluminum in Al-MCM-41 generates a negative charge which offers the possibility of immobilizing manganese salen complexes of cationic nature.[16] Results suggest that the chiral center of the substrate also plays an important role in the formation of the predominant diastereomer. Additionally, reaction conditions used in this work markedly improved catalyst stability during oxidative degradation, so the utilization of a stable heterogeneous catalyst could be accomplished.



(a) (b) (c) (d) (e)

Fig. 2. Chemical structure of the possible limonene oxides originating from *R*-(+)-limonene epoxidation: (**a**) *cis*-(+)-1,2-limonene oxide, (**b**) *trans*-(+)-1,2-limonene oxide, (**c**) *cis*-(+)-8,9-limonene oxide, (**d**) *trans*-(+)-8,9-limonene oxide, (**e**) diepoxide.



M = Mn, Cr, Co, Cu, V, Ru, Fe, Al, Ti

R1, R2, R3, R4 = H, alkyl or phenyl group

R'1, R'2, R'3, R'4 = H, nitro, alkyl, aryl or alcoxy group

Fig. 3. Chemical structures of metal salen complexes.

MATERIALS AND METHODS

Characterization

FTIR spectra of the solid samples in the 4000–400 cm^{-1} range were obtained with a Nicolet Avatar 330 FTIR spectrometer, using KBr as reference. Atomic absorption analyses of manganese were performed in UNICAM-929 equipment. Thermal gravimetric analysis (TGA) was performed in a TGA 2950 apparatus at a heating rate of 2 K/min. Surface area measurements were performed by N_2 adsorption at −196°C in a Micromeritics ASAP 2010 apparatus. Powder X-ray diffraction (XRD) patterns were recorded on a RIGAKU D-Max/IIIB diffractometer using Cu Kα radiation. UV–vis spectra was recorded in the range 200–800 nm with a Lamba 4 Perkin Elmer spectrometer equipped with a diffuse reflectance attachment, using $BaSO_4$ as reference. Reaction samples were analyzed by GC-FID with a Varian Star 3400 gas chromatograph using helium as carrier gas and two capillary columns, DB-1 (50 m long, 0.32 mm id and 1.20 μm film thickness) and Lipodex-G (50 m long and 0.25 mm id).

Synthesis of Homogeneous Catalysts

The Jacobsen's catalyst in its two optically active forms denoted as *R*,*R*-Jacobsen and *S*,*S*-Jacobsen and a simple achiral version of the Jacobsen's catalyst denoted as achiral Jacobsen (see Fig. 4) were used in this work. These catalysts were prepared according to reported procedures[17] by reacting 8.50 mmol of 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde with the corresponding diamine

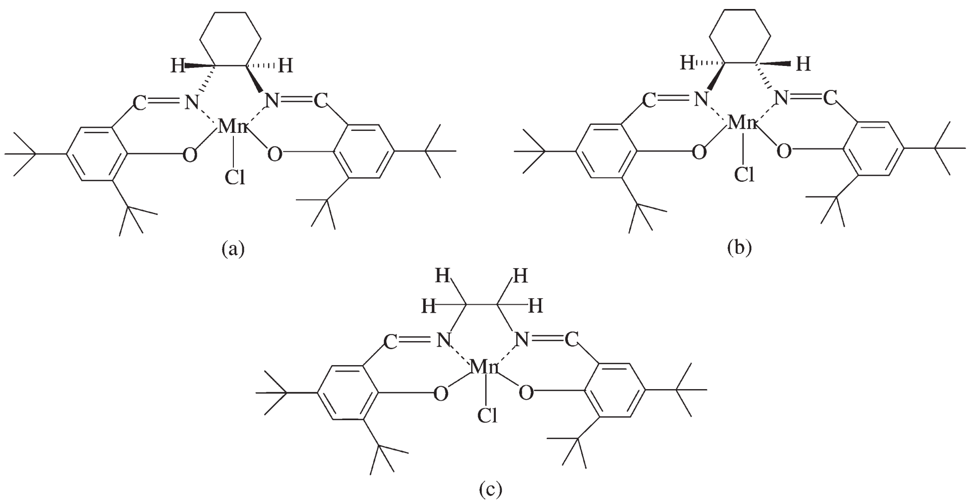


Fig. 4. Manganese (III) salen complexes: (**a**) *R,R*-Jacobsen, (**b**) *S,S*-Jacobsen, (**c**) achiral catalyst.

(4.20 mmol) and subsequent Mn(III) incorporation by metalation of the salen ligand. As diamine component, we used (1*R*, 2*R*)-(+)-1,2-diaminocyclohexane L-tartrate for the *R,R*-Jacobsen, (1*S*, 2*S*)-(+)-1,2-diaminocyclohexane L-tartrate for the *S,S*-Jacobsen, and 1,2-diamino ethane for the achiral Jacobsen. In all cases, 8.50 mmol manganese (II) acetate ($Mn(C_2H_3O_2)_2{\cdot}4H_2O$) was used as the Mn source. Also, the optically pure salen ligands ((*R,R*)-(−)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)cyclohexane-1,2-diamine), ((*S,S*)-(−)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)cyclohexane-1,2-diamine), and achiral salen ligand (bis(3,5-di-*tert*-butylsalicylidene)ethano-1,2-diamine) were prepared. The purity and identity of these soluble materials were confirmed by FTIR, TGA, and UV–vis.

Heterogenization of the Jacobsen's Catalyst

Synthesis of Al-MCM-41. Mesoporous Al-MCM-41 was prepared following the procedure reported by van Hooff[18] with slight modifications. In a typical synthesis, 48 g tetraethylammonium hydroxide (TEAOH, 35 wt %, aqueous), 0.84 g sodium aluminate ($NaAlO_2$), and 116.4 g H_2O were mixed together and stirred at room temperature for 1 h. Then, 40 g of tetradecyltrimethylammonium bromide (TDTMABr) was added and the resulting mixture stirred during 4 h. Finally, Ludox-HS 40 (60.92 g) was added drop wise over a period of 1 h and stirring continued at ambient temperature for additional 4 h. The gel composition was:

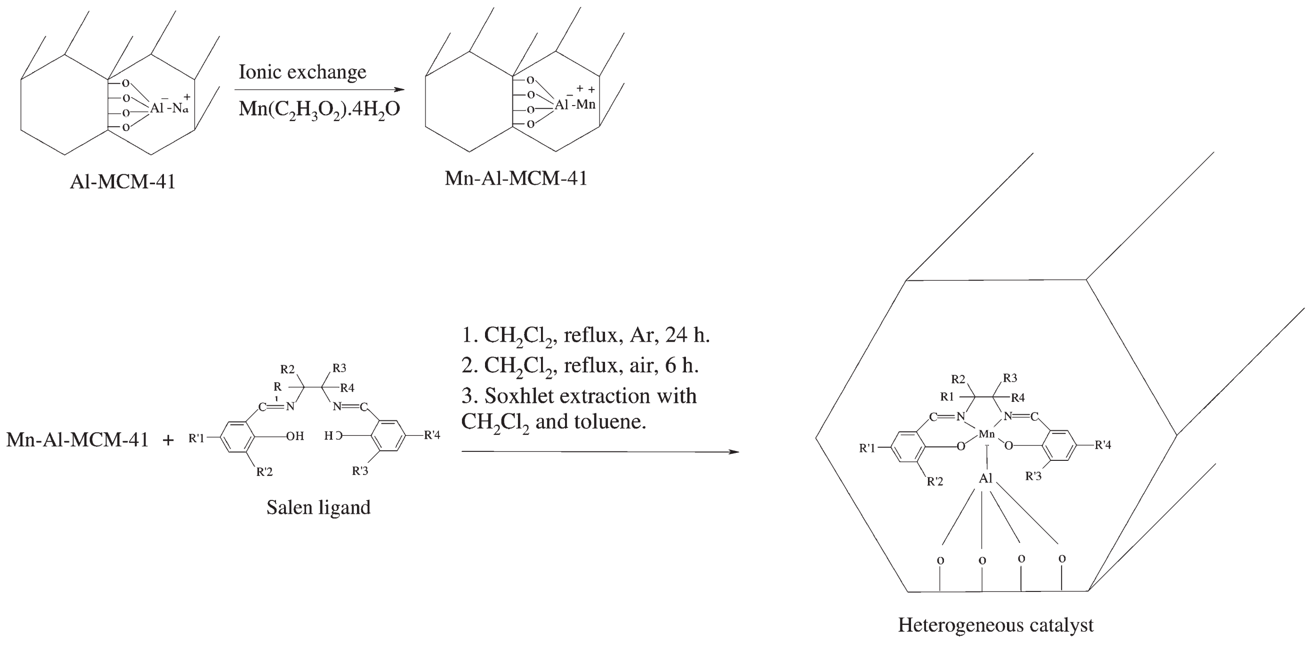


Fig. 5. Immobilization of the homogeneous catalyst by ionic bond in Al-MCM-41.

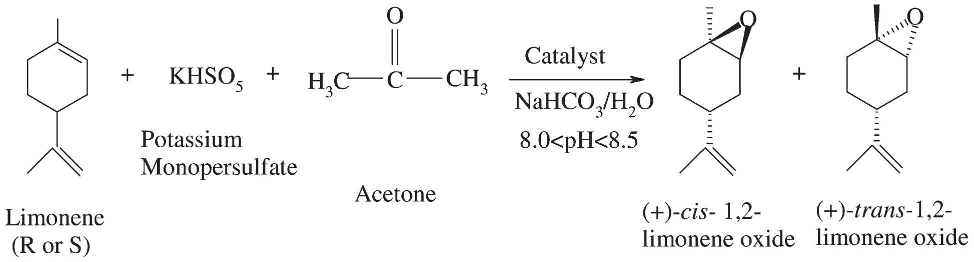


Fig. 6. Diastereoselective epoxidation of *R*-(+)-limonene in the presence of chiral and achiral manganese salen complexes and in situ generated DMD as oxidizing agent.

$$1.0\ \mathrm{NaAlO_2}:\ 40\ \mathrm{SiO_2}:\ 11.6\ \mathrm{TDTMABr}:\ 28\ \mathrm{TEAOH}:\ 800\ \mathrm{H_2O}$$

The gel was heated under static conditions at 110°C for 7 days. After the second, fourth, and sixth day, pH was adjusted to 10.5 using CH_3COOH (10 wt %, aqueous). After crystallization, the solid phase was recovered by filtration and washed with abundant deionized water. The white material was dried at 60°C overnight, followed by calcination in flowing air at 540°C for 6 h (heating rate 1°C/min).

Synthesis of Mn-Al-MCM-41. Calcined Al-MCM-41 (3 g) was added to a manganese (II) acetate solution in water (100 ml, 0.2 M) and stirred for 24 h. The material was then filtered, washed, dried, and stirred again in a fresh manganese (II) acetate solution for additional 24 h. This procedure was repeated twice. Finally, the obtained solid was calcined in flowing air at 550°C for 8 h before use.

Immobilization by Ion Exchange in Mn-Al-MCM-41

A method similar to that reported by Hutchings and coworkers[19] was used to immobilize all homogeneous catalysts. In a typical procedure, dry Mn-Al-MCM-41 (3 g) was treated, under reflux in argon atmosphere for 24 h, with 0.82 g of either optically pure salen ligand or 0.74 g achiral salen ligand in 20 ml CH_2Cl_2. In all cases, an excess of the amount of salen ligand with respect to Mn was used (Mn/salen = 0.5 mmol/mmol) to guarantee the full complexation of the Mn atoms. After that, the inert atmosphere was replaced by flowing air and stirring continued for 6 h. The mixture was cooled to room temperature and the solvent removed by reduced pressure at room temperature. The resulting solid was Soxhlet extracted with CH_2Cl_2 at 60°C and toluene at 140°C until the washing solvent remained colorless. The immobilized catalysts on Al-MCM-41 were coded *R,R*-Al-MCM-41, *S,S*-Al-MCM-41 and achiral-Al-MCM-41. Figure 5 depicts the immobilization method used in this work. The heterogeneous process was confirmed by XRD, N_2-sorption, Mn atomic absorption TGA, and FTIR.

Catalytic Measurements

Catalysts were tested on the diastereoselective epoxidation of *R*-(+)- and *S*-(−)-limonene at room temperature (see Fig. 6). In a typical reaction, 0.702 g of *R*-(+)- or *S*-(−)-limonene, 1 g of sodium bicarbonate, and 0.03 g of homogeneous catalyst (0.047 mmol of optically pure catalysts, 0.052 mmol of achiral catalyst) or 0.1 g of heterogeneous catalyst (0.008 mmol enantiomerically pure

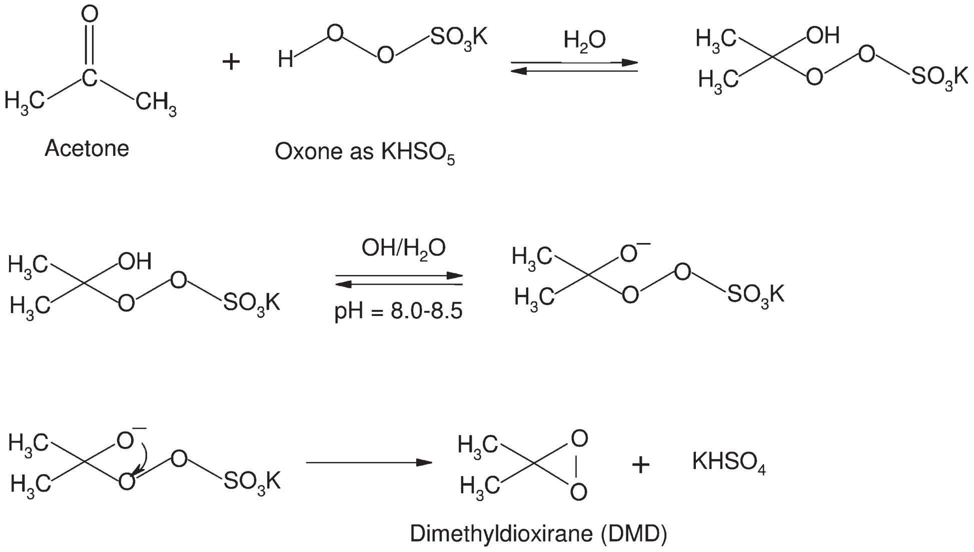


Fig. 7. Formation of DMD from Oxone® ($KHSO_5$ as active agent) and acetone.

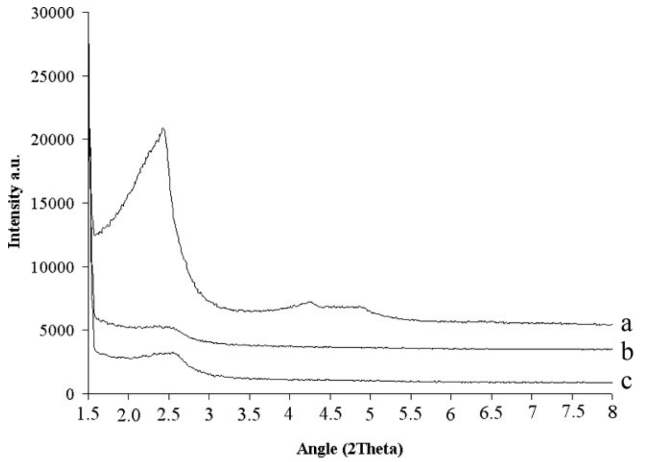


Fig. 8. XRD patterns: (**a**) Al-MCM-41, (**b**) Mn-Al-MCM-41, (**c**) *R,R*-Al-MCM-41.

catalysts, 0.009 mmol achiral catalyst) were dissolved in 30 ml of acetone. The pH of the resulting mixture, denoted A, was adjusted between 8.0 and 8.5 using $NaHCO_3$ (5 wt % aqueous). On the other hand, a solution, denoted B, was prepared by dissolving 1.23 g of Oxone® ($2KHSO_5•KHSO_4•K_2SO_4$) in 25 ml of H_2O. Solution B was slowly added to mixture A while stirring and maintaining the pH in the range 8.0–8.5 with 5 wt % aqueous $NaHCO_3$. The procedure to separate the homogeneous catalyst was as follows: inorganic salts were isolated by centrifugation, the resulting liquid mixture extracted with 30 ml of dichloromethane, the aqueous phase discarded, and the organic layer treated by vacuum distillation (160°C and 0.08 MPa). On the other hand, for heterogeneous reactions, the catalyst was easily separated by filtration and both solid and liquid mixtures were retained for further use. Solid samples were thoroughly washed with water to remove inorganic salts originated from the oxygen source and buffer solution. In both cases, homogeneous and heterogeneous reactions, the catalyst free liquid mixture was concentrated under vacuum and aliquots analyzed by GC-FID using a DB-1 column to determine conversion of *R*-(+)-limonene and selectivity to 1,2-(+)-limonene oxide and a Lipodex-G column to determine percent diasteromeric excess (% de) between *cis*-(+)-1,2-limonene oxide and *trans*-(+)-1,2-limonene oxide.

DMD was obtained in situ from reaction between $KHSO_5$ (active component of Oxone®) and acetone in a slightly basic reaction medium (pH = 8.0–8.5). Figure 7 depicts the formation of DMD.[20]

RESULTS AND DISCUSSION

Catalyst Characterization

Structural and textural properties. The XRD patterns of Al-MCM-41 exhibit a very intense peak at 2θ = 2.5 and two additional peaks with low intensities at 2θ = 4.3 and 2θ = 4.9 (Fig. 8a), which can be indexed to a hexagonal lattice.[21] It is observed that after ionic exchange and catalyst immobilization (Figs. 8b and 8c); peak intensities did remarkably decrease, suggesting that the incorporation of the manganese salen complex destroyed the mesopores of Al-MCM-41.

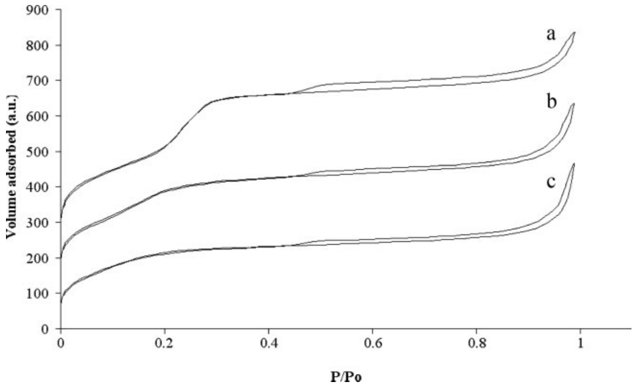


Fig. 9. Nitrogen adsorption-desorption isotherms: (**a**) Al-MCM-41, (**b**) Mn-Al-MCM-41, (**c**) *R,R*-Al-MCM-41.

N_2 adsorption isotherms and textural properties of Al-MCM-41, Mn-Al-MCM-41, and *R,R*-Al-MCM-41 are presented in Figure 9 and Table 1. These isotherms are characteristic of mesoporous materials. During the immobilization process, BET surface area and total pore volume decreased from 1113 m^2/g for Al-MCM-41 to 999 m^2/g for Mn-Al-MCM-41. Mesopore volume decreased from 0.915 for Al-MCM-41 to 0.336 cm^3/g for Mn-Al-MCM-41. BET surface area and mesopore volume of Mn-Al-MCM-41 decreased when transformed to *R,R*-Al-MCM-41. Therefore, it appears that the complex was deposited inside the pore system of the support.[22]

Elemental analysis and TGA. Table 2 shows Mn(III) catalyst loading of *R,R*-Al-MCM-41 determined by atomic absorption and TGA. Neither the Mn atom nor the salen ligand in Al-MCM-41 was detected. After ion exchange, Mn-Al-MCM-41 contained 0.548 wt % Mn. After treatment with the salen ligand, Mn loading decreased to 0.446 wt % in chiral-Al-MCM-41. From TGA a salen ligand loading of 9.105 wt % in chiral-Al-MCM-41 was determined. The *R,R*-Al-MCM-41 was obtained with an excess of ligand (Mn/salen = 0.488 mmol/mmol) which corresponds to that used in the preparation method (Mn/salen = 0.5 mmol/mmol). The fact that salen ligand is in excess after Soxhlet extraction suggests that uncomplexed salen ligand is mainly located in inaccessible sites of the support. As the metal loading is the limiting reagent, the catalyst loading in chiral-Al-MCM-41 corresponds to 5 wt %.

TABLE 1. Surface area and pore volume of synthesized catalysts

Material	BET surface area (m^2/g)	Pore volume BJH (cm^3/g)
Al-MCM-41	1113	0.915
Mn-Al-MCM-41	999	0.336
R,R-Al-MCM-41	712	0.163

TABLE 2. Catalyst loading

Material	Mn loading (wt %)[a]	Salen ligand loading (wt %)[b]	Mn/salen (mmol/mmol)	Catalyst loading (wt %)
Al-MCM-41	0	0	–	0
Mn-Al-MCM-41	0.548	0	–	0
R,*R*-Al-MCM-41	0.446	9.105	0.488	5[c]

[a] Determined by Mn atomic absorption.
[b] Determined by TGA.
[c] Determined from Mn loading.

TABLE 3. Control reactions[a]

Material	Conversion (%)	Selectivity to 1,2-limonene epoxide (%)	Diasteromeric excess (de %)[b]
None	53	34	23
Al-MCM-41	55	61	24
Mn-Al-MCM-41	74	70	29

[a] Reaction conditions: 5 mmol *R*-(+)-limonene or *S*-(−)-limonene; 4 mmol $KHSO_5$; 0.03 g homogeneous catalyst; 0.1 g (5 wt %) heterogeneous catalyst; 1 g $NaHCO_3$; 30 ml acetone; 35 min reaction time; 25°C.
[b] Referred to *cis*-1,2-limonene oxide (predominant epoxide).

Spectral properties. The FTIR spectra of chiral-Al-MCM-41, Figure 10d, show characteristic bands of the organic structure of manganese (III) salen complexes (Fig. 10a).[23] Although these bands are weak and not sufficient enough to elucidate a structure, the typical band at 1540 cm^{-1} is distinguished. This signal is ascribed to the N-Mn and O-Mn stretching vibrations and was absent in the FTIR spectra of Al-MCM-41 (Fig. 10b) and Mn-Al-MCM-41 (Fig. 10c), thus confirming the presence of the Mn salen complex inside the mesoporous support. Additionally, the OH stretching band centered at 3500 cm^{-1} is characteristic of terminal silanol groups from the support.[24]

Catalytic tests

Oxidation of limonene. Oxidation of *R*-(+)- and *S*-(−)-limonene can yield a variety of products, such as (*cis/trans*) 1,2-limonene oxide, (*cis/trans*) 8,9-limonene oxides, (*cis/trans*) 1,2 and 8,9 limonene oxides (epoxides), carveol, and carvone. However, under the reaction conditions used in this study, 1,2-limonene oxide was the main product with minor amounts of diepoxide. It is known that the endocyclic double bond (Fig. 1, bond 1,2) is more reactive than the exocyclic one (Fig. 1, bond 8,9).[2]

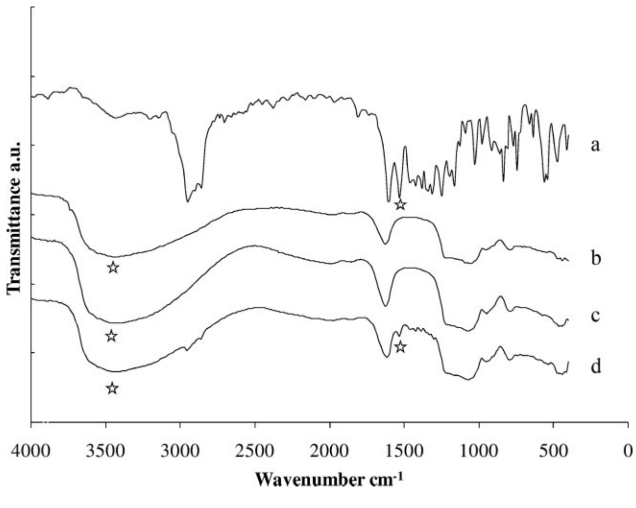


Fig. 10. FTIR spectra: (**a**) chiral catalyst, (**b**) Al-MCM-41, (**c**) Mn-Al-MCM-41, (**d**) *R*,*R*-Al-MCM-41.

In general, low asymmetric inductions were reached (de up to 56%) compared to those reported for *cis*-disubstituted olefins (ee up to 99%),[4] showing a favorable steric interaction between one of the alkene substituents and the active manganese(III) salen complex plane, which can be explained from the side-on approach model.[25] A commercial sample of (*cis/trans*)-1,2-limonene oxide (Aldrich, 97%) was used to identify *cis* and *trans* diastereomers. 10% de of *trans*-(+)-1,2-limonene oxide was quantified in this sample by using a Lipodex-G chromatographic column.

The results of three control experiments are listed in Table 3. In the absence of catalyst, moderate *R*-(+)-limonene conversion (53%), low selectivity to (*cis/trans*) 1,2-limonene oxide (34%), and low de (23%) was obtained. Similar results were obtained with *S*-(−)-limonene. A remarkable selectivity increase was observed over Al-MCM-41 (61%) and Mn-Al-MCM-41 (70%). These results indicate that the support and Mn atoms have a positive effect on the stability of (*cis/trans*) 1,2-limonene oxide. The fact that the initial pH increased from 7.0 to 8.0 in the presence of these materials (Al-MCM-41 and Mn-Al-MCM-41) allows us to infer that the epoxide ring opening reaction rate could be reduced compared with the oxygen transfer reaction.[26] Only a slight increase in conversion was obtained in the presence of Mn-Al-MCM-41. On the other hand, neither Al-MCM-41 nor Mn-Al-MCM-41 produced remarkable effect on de.

Tables 4 and 5 show activity results using the homogeneous catalysts, their corresponding fresh heterogeneous catalysts, as well as, reused heterogeneous catalysts for oxidation of *R*-(+)-limonene and *S*-(−)-limonene, respectively. In general, selectivity improved in the presence of the homogeneous catalysts compared with the uncatalyzed reaction. Additionally, it is worth to note that the product stereochemistry is strongly dependent on the absolute configuration of both the catalyst and the limonene. Thus, the combination of *R*-(+)-limonene with *R*,*R*-Jacobsen or (*S*)-(−)-limonene with *S*,*S*-Jacobsen forms a matched pair (see row 1 in Tables 4 and 5), giving rise to higher de, 56% and 45%, respectively. Whereas *R*-(+)-limonene with *S*,*S*-Jacobsen or *S*-(−)-limonene with *R*,*R*-Jacobsen generates a mismatched pair (see row 2 in Tables 4 and 5) and the corresponding de are reduced to 5–6%. This phenomenon has been described as double asymmetric induction process,[27] and can be rationalized assuming the qualitative transition-state model proposed for trisubsti-

TABLE 4. Results of catalytic activity using *R*-(+)-limonene as substrate[a]

Catalyst	Conversion (%)	Selectivity to 1,2-limonene epoxide (%)	Diastereomeric excess (de %)[b]	TON[c] (mmol *cis*-(+)-1,2-limonene oxide/mmol catalyst)
R,*R*-Jacobsen	55	100	56	46
S,*S*-Jacobsen	60	92	5	7
Achiral Jacobsen	53	100	50	38
R,*R*-Al-MCM-41	100	68	35	288
S,*S*-Al-MCM-41	78	80	23	58
Achiral-Al-MCM-41	81	81	36	260
R,*R*-Al-MCM-41[d]	60	49	25	117
Achiral-Al-MCM-41[d]	70	62	24	157
R,*R*-Al-MCM-41[e]	60	58	22	134
Achiral-Al-MCM-41[e]	71	64	22	160

[a] Reaction conditions: 5 mmol *R*-(+)-limonene; 4 mmol $KHSO_5$; 0.03 g homogeneous catalyst; 0.1 g (5 wt %) heterogeneous catalyst; 1 g $NaHCO_3$; 30 ml acetone; 35 min reaction time; 25°C.

[b] Referred to *cis*-1,2-limonene oxide (predominant epoxide).

[c] Turnover number (TON) = mmol *cis*(+)-1,2-limonene epoxide/mmol catalyst.

[d] First reuse.

[e] Second reuse.

tuted olefins in which the limonene interacts via a skewed side-on approach with the metal-oxo intermediate complex. Additionally, for each substrate, similar de and turnover numbers (TON) were obtained with the best optically pure catalyst and the achiral catalyst (compare rows 1 and 3 either in Table 4 or 5). In particular, the similarity between de values can be due to both substrate and catalyst chiral center. In other words, not only the catalyst chiral center but also the substrate chiral center participates in the preferential formation of *cis*-(+)-1,2-limonene oxide.

With the exception of *S*,*S*-Al-MCM-41 for the oxidation of *S*-(+)-limonene (compare rows 1 and 4, Table 5), higher conversions and TON were reached over the heterogeneous catalysts because lower amount of the manganese salen complex was used in the heterogeneously catalyzed reaction. The TON increase can also be associated with catalyst isolation on the support surface, preventing in this way, deactivation routes by oligomerization.[8] Catalytic activity experiments using commercial limonene oxide instead of *R*-(+)-limonene or *S*-(−)-limonene proved that our heterogeneous catalysts did not promote the kinetic separation among cis/trans isomers. In contrast, it was confirmed that limonene oxide undergoes further epoxidation leading to diepoxide (conversion ca. 50%). This may be the reason why the selectivity to (*cis/trans*) 1,2-limonene oxide over the heterogeneous catalyst was not complete.

Finally, the reutilization issue was addressed. Heterogeneous catalysts underwent a progressive loss of their initial catalytic activity through two reuses. To identify the origin of the catalytic activity loss, the chemical structure of the fresh homogeneous catalyst and reused twice were investigated by FTIR. Figure 11 shows that the catalyst did not suffer oxidative degradation, because the main signal assigned to the catalyst (1540 cm^{-1}) is retained after two consecutive runs. Therefore, the decrease in catalytic

TABLE 5. Results of catalytic activity using *S*-(−)-limonene as substrate[a]

Catalyst	Conversion (%)	Selectivity to 1,2-limonene epoxide (%)	Diastereomeric excess (de %)[b]	TON[c] (mmol *cis*-(+)-1,2-limonene oxide/mmol catalyst)
S,*S*-Jacobsen	80	75	45	11
R,*R*-Jacobsen	60	77	6	6
Achiral Jacobsen	63	87	46	10
S,*S*-Al-MCM-41	68	67	23	43
R,*R*-Al-MCM-41	72	73	20	48
Achiral-Al-MCM-41	76	73	20	50
S,*S*-Al-MCM-41[d]	65	74	18	43
Achiral-Al-MCM-41[d]	70	75	22	49
S,*S*-Al-MCM-41[e]	66	70	20	46
Achiral-Al-MCM-41[e]	68	72	23	46

[a] Reaction conditions: 5 mmol *S*-(−)-limonene; 4 mmol $KHSO_5$; 0.03 g homogeneous catalyst; 0.1 g (5 wt %) heterogeneous catalyst; 1 g $NaHCO_3$; 30 ml acetone; 35 min reaction time; 25°C.

[b] Referred to *cis*-1,2-limonene oxide (predominant epoxide).

[c] Turnover number (TON) = mmol *cis*(+)-1,2-limonene epoxide/mmol catalyst.

[d] First reuse.

[e] Second reuse.

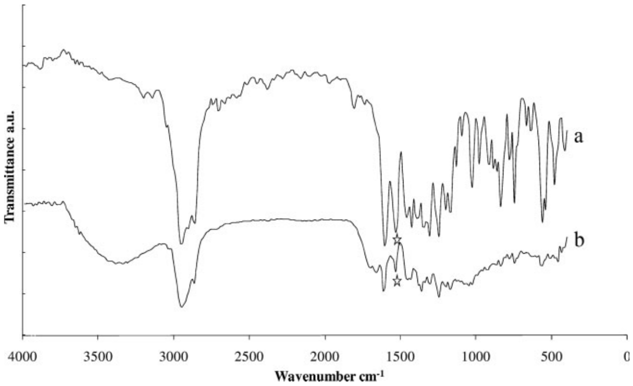


Fig. 11. FTIR spectra of *R,R*-Jacobsen: (**a**) fresh, (**b**) reused twice.

activity of the heterogeneous catalyst is caused by leaching of the catalyst rather than its oxidative degradation.

CONCLUSIONS

Optically active and achiral Jacobsen's catalysts either homogeneous or immobilized on Al-MCM-41 exhibited similar catalytic activity during diastereoselective epoxidation of R-(+)-limonene using in situ generated DMD as oxidizing agent. In particular, the similarity among de values obtained using both the homogeneous and the heterogeneous catalysts, suggests that the *R*-(+)-limonene chiral center, takes part in the preferential formation of *cis*-(+)-1,2-limonene oxide. This result suggests that the chirality of the susbstrate plays an important role in the stereochemical formation of new chiral centers and the process occurs through classical double asymmetric induction.

Catalyst immobilization of the oxo-manganese active species on the support surface favored the stability toward oligomerization leading to improved catalytic productivity. Catalyst reutilization was not successfully accomplished likely due to catalyst leaching rather than oxidative degradation.

LITERATURE CITED

1. Surburg H, Panten J. Common fragrance and flavor materials. Weinheim: Wiley-VCH; 2006. p 3.
2. Royals EA, Leffingwe JC. Reaction of the limonene 1,2-oxides. I. The stereospecific reaction of the (+)-*cis*- and (+)-*trans*-limonene 1,2-oxides. J Org Chem 1966;31:1937–1944.
3. Hutter R, Mallat T, Baiker A. Titania-silica mixed oxides. III. Epoxidation of α-isophorone with hydroperoxides. J Catal 1995;153:177–189.
4. Larrow JF, Jacobsen EN. Asymmetric processes catalyzed by chiral (salen)metal complexes. Topics Organomet Chem 2004;6:123–152.
5. Sheldon RA. Chirotechnology. New York: Marcel Dekker, Inc.; 1993. p 19.
6. Wang D, Wang M, Zhang R, Wang X, Gao A, Ma J, Sun L. Asymmetric epoxidation of styrene and chromenes catalysed by dimeric chiral (pyrrolidine salen)Mn(III) complexes. Appl Catal A: Gen 2006;315: 120–127.
7. McMorn P, Hutching G. Heterogeneous enantioselective catalysts: strategies for the immobilisation of homogeneous catalysts. Chem Soc Rev 2004;33:108–122.
8. Xia Q-H, Ge H-Q, Ye C-P, Liu Z-M, Su K-X. Advances in homogeneous and heterogeneous catalytic asymmetric epoxidation. Chem Rev 2005;105:1603–1662.
9. Baleizão C, García H. Advances in homogeneous and heterogeneous catalytic asymmetric epoxidation. Chem Rev 2006;106:3987–4043.
10. Song CE, Roh EJ, Yu BM, Chi DY, Kim SC, Lee K-J. Heterogeneous asymmetric epoxidation of alkenes catalysed by a polymer-bound (pyrrolidine salen)manganese(III) complex. Chem Commun 2000;615–616.
11. Cubillos J, Hoelderich WF. Jacobsen's catalyst anchored on Al-MCM-41 and NH_2 group modified Si-MCM-41 as heterogeneous enantioselective epoxidation catalyst using in situ generated dimethyldioxirane as oxidant. Rev Fac Ing Univ Antioquia 2007;41:31–47.
12. Schuster C, Möllman E, Tompos A, Hölderich W. Highly stereoselective epoxidation of (−)-α-pinene over chiral transition metal (salen) complexes occluded in zeolitic hosts. Catal Lett 2001;74:69–75.
13. Bhattacharjee S, Anderson JA. Synthesis and characterization of novel chiral sulfonato-salen-manganese(III) complex in a zinc-aluminium LDH host. Chem Commun 2004;554–555.
14. Saikia L, Srinivas D, Ratnasamy P. Chemo-, regio- and stereo-selective aerial oxidation of limonene to the endo-1,2-epoxide over Mn(Salen)-sulfonated SBA-15. Appl Catal A 2006;309:144–154.
15. Gaquere A, Liang S, Hsu F-L, Bu XR. The readily available tert-pentyl group as a most effective simple directing group for asymmetric synthesis: a case study on Salen-Mn(III)-catalyzed epoxidation. Tetrahedron: Asymmetry 2002;13:2089–2093.
16. Piaggio P, McMorn P, Langham C, Bethell D, Bulman-Page PC, Hancock FE. Asymmetric epoxidation of stilbene by manganese(III) chiral salen complex immobilized in Al-MCM-41. N J Chem 1998;22:1167–1169.
17. Larrow JF, Jacobsen EN. A practical method for the large-scale preparation of [*N,N'*-bis(3,5-di-tertbutylsalicylidene)-1,2-cyclohexanediaminato(2-)]manganese(III) chloride, a highly enantioselective epoxidation catalyst. J Org Chem 1994;59:1939–1942.
18. Busio M, Jaenchen J, van Hooff JHC. Aluminum incorporation in MCM-41 mesoporous molecular sieves. Microporous Mater 1995;5: 211–218.
19. Piaggio P, Morn P, Murphy D, Bethell D, Page PCB, Hancock FE, Sly C, Kerton OJ, Hutchings GJ. Enantioselective epoxidation of (Z)-stilbene using a chiral Mn(III)-salen complex: effect of immobilisation on MCM-41 on product selectivity. Chem Soc Perkin Trans 2000;2:2008–2015.
20. Webb KS, Ruszkay SJ. Oxidation of aldehydes with Oxone® in aqueous acetone. Tetrahedron 1998;54:401–410.
21. De Clercq B, Lefebvre F, Verpoort F. Immobilization of multifunctional Schiff base containing ruthenium complexes on MCM-41. Appl Catal A: Gen 2003;247:345–364.
22. Chaube VD, Shylesh S, Singh AP. Synthesis, characterization and catalytic activity of Mn(III)- and Co(II)-salen complexes immobilized mesoporous alumina. J Mol Catal A: Chem 2005;241:79–87.
23. Deshpande S, Srinivas D, Ratnasamy P. EPR and catalytic investigation of Cu(Salen) complexes encapsulated in zeolites. J Catal 1999;188:261–269.
24. Kureshy RI, Ahmad I, Khan NH, Abdi SHR, Phatak K, Jasra RV. Chiral Mn(III) salen complexes covalently bonded on modified MCM-41 and SBA-15 as efficient catalysts for enantioselective epoxidation of nonfunctionalized alkenes. J Catal 2006;238:134–141.
25. Dalton CT, Ryan KM, Wall VM, Bousquet C, Gilheany DG. Recent progress towards the understanding of metal-salen catalysed asymmetric alkene epoxidation. Top Catal 1998;5:75–91.
26. Ready JM, Jacobsen EN. A practical oligomeric [(salen)Co] catalyst for asymmetric epoxide ring-opening reactions. Angew Chem Int Ed 2002;41:1374–1377.
27. Masamune S, Shoy W, Petersen JS, Sita LR. Double asymmetric synthesis and a new strategy for stereochemical control in organic synthesis. Angew Chem Int Ed Engl 1985;24:1–30.