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Direct immobilization of chiral auxiliaries on mineral supports and heterogeneous enantioselective alkylation of benzaldehyde with diethylzinc

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Abstract

New solid chiral auxiliaries are used in the enantioselective alkylation of benzaldehyde with diethylzinc. These auxiliaries are obtained by direct immobilization of their homogeneous counterparts, (−)-ephedrine and (−)-*O*-methyl-ephedrine, on the surface of mesoporous micelle templated silicates and aluminosilicates. Hybrid materials are characterized, and the interactions between the heteroatoms of the organic compounds and the surface are studied by FTIR spectroscopy. Efficiency of such hybrid solids is discussed. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

In the recent years, a growing interest has been focused on heterogeneous enantioselective catalysis [1–4] which would be preferable to homogeneous catalysis owing to a variety of practical advantages. An interesting method is concerned with the heterogenization of chiral homogeneous transition metal complexes on supports. These supports play a primary role either in the accessibility to the catalytic sites or in their inertness towards side reactions.

Our interest is focused on enantioselective carbon–carbon bond formation which has attracted much less attention than asymmetric oxidation or hydrogenation reactions. In this domain, a number of organozinc complexes, formed from dialkylzincs and chiral β-aminoalcohols, (2*S*)-(−)- or (2*R*)-(+)-3-*exo*-(dimethylamino)isoborneol, (*R*)-(−)- or (*S*)-(+)-1,1-diphenylprolinol, (1*S*, 2*R*)-(+)- or (1*R*, 2*S*)-(−)-ephedrine, are efficient in the catalytic asymmetric alkylation of prochiral carbonyl compounds. This alkylation leads to the corresponding alcohol, the enantioselectivity of which depends on the chirality of the auxiliary. The mechanism of this reaction is well studied, and recent results of Noyori and co-workers [5] have shown the role of the monomeric alkylzinc aminoalkoxide which acts as the catalytic site. The Zn atom provides a Lewis acidic site which accepts an aldehyde substrate, while the oxygen is a basic center which interacts with dialkylzinc [5]. Moreover, substituents on the carbon bearing the alkoxide moiety are determinant in the enantioselectivity [6].

Numerous works describe the immobilization of such catalysts on supports which feature various compositions. Using polymeric organic supports, ees depend on the auxiliary used, and are always near

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those obtained in homogeneous conditions with similar amounts of chiral auxiliaries [7–13]. Catalytic activities, consistently lower, are certainly related with diffusion limitations of the reactants to reach the catalytic sites. However, high catalytic activity of chiral aminoalcohol ligands anchored to preformed polystyrene resins have been recently reported [14]. On the other hand, attempts to avoid possible diffusion problems have been performed; the most important factor was found to be a favorable interaction of the polymer matrix with the reaction solvent so that the polymer will dissolve or swell to allow the reactants easy access to the catalytic sites [15]. Other drawbacks, such as the stability or the resistance towards stirring may be considered [7].

The first example of immobilization of a β-aminoalcohol on a mineral support was described by Soai and co-workers [16,17]. The (−)-ephedrine was anchored by covalent linkage on silica gel and alumina. ees were moderate and rates low; no attempts were made to improve or to understand the reasons of such results. In our previous works, we studied the efficiency of (−)-ephedrine grafted by covalent linkage on mesoporous micelle templated silicates (MTS) or aluminosilicates (Al-MTS). These materials are characterized by a regular mesoporosity with various pore apertures ranging from 25 to 100 Å. Thus, a double benefit may originate from the use of these mineral supports, firstly, an enhanced accessibility to the chiral sites grafted on the inner surface of the pores, and secondly, the obtention of constrained sites leading to possible substrate's interaction with both the pore walls and the chiral-directing group [1]. Covalent linkage was performed in two steps by reacting these supports with a coupling halogenopropyltrimethoxysilane and by substitution of the halogen moiety by chiral ephedrine. Using (−)- or (+)-ephedrine supported on MTS of 35 Å initial pore diameter in the model reaction of benzaldehyde and diethylzinc [18], lower rates, selectivities and enantioselectivities than in homogeneous catalysis were obtained. Modulation of the characteristics either by changing the support (pore diameter, passivation of the mineral surface with hexamethyldisilazane) or by dilution of the catalytic sites did not lead to improvements of ees [19]. These results were explained by the activity of the naked surface towards the formation of the racemic alcohols. Enantioselectivities are controlled by the ratio of the activity of the chiral sites to the overall activity, which includes the latter activity, the rate of formation of the racemic alcohols and the rate of the uncatalyzed reaction. The overall activity depends on the composition of the support [20] higher when (−)-ephedrine is grafted on the more acidic Al-MTS than MTS support. Recently, Bae et al. [21] have reported the use of a more efficient proline-base ligand grafted on mesoporous silicas in order to improve ees. Higher ees were only obtained after pretreatment of the catalyst with butyllithium. However, they remained lower than in homogeneous conditions.

In comparison, noncovalent linking is easier to carry out than covalent immobilization, and interesting studies have been performed using this method for the catalyst preparation [22–24]. The use of chiral manganese (III) cationic complex embedded into mesoporous silicates [25] or chiral salen MCM-41 [26] was recently reported as efficient olefin epoxidation catalysts. Thus, taking into account that slowing down the density of halogenopropyl moities on the support was accompanied by a higher accessibility of the inorganic surface and the direct immobilization of (−)-ephedrine [19,20], the aim of this work is to characterize catalysts obtained by direct interaction of the auxiliary with the support. The objective is to understand the way by which the auxiliary is interacting with the surface, together with its role played in the enantioselective alkylation of benzaldehyde. For this purpose, chiral catalysts were prepared by direct immobilization of (−)-ephedrine on MTS and Al-MTS supports and used in the model reaction.

2. Experimental

2.1. Supports

MTS support was synthesized using cetyltrimethylammonium bromide as template in ammonia solution [27]. Incorporation of aluminum [28,29] during the synthesis conducted with sodium hydroxide [30,31] led to Al-MTS support with Si/Al = 27. The two supports are characterized by same average pore diameter of 36 Å determined by the $4V/S_{\mathrm{BET}}$ ratio from nitrogen sorption isotherms with $V = 0.52$ and 0.76 ml g^{-1} and $S = 587$ and 833 m^2 g^{-1}, respectively.

Before modification of the surface by loading with auxiliaries **1** and **2**, the template was calcined under a flow of dry air at 550°C for 8 h.

2.2. Direct immobilization of (−)-ephedrine **1** *and (−)-O-methyl-ephedrine* **2** *on MTS and Al-MTS supports*

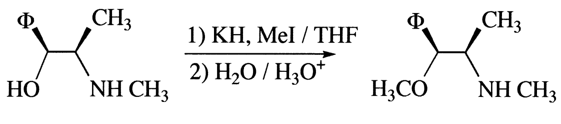
2.2.1. (1R, 2S)-(−)-ephedrine ***1***

The support freshly calcined was activated under vacuum at 140°C for 16 h. Then, 1 g was refluxed with (−)-ephedrine **1** (9.8×10^{-3} mol) (Aldrich-Chemie) in xylene (10 ml) and stirred for 6 h under dry nitrogen. The solid was filtered, washed with diethyl ether and extracted with a solvent of diversified polarity in a soxhlet apparatus for 24 h and dried at 25°C under vacuum. With the MTS support, washing with methanol and dichloromethane/diethyl ether 1/1 led to MTS-E$_1$ **1** and MTS-E$_1$ **2**, respectively. Al-MTS-E$_1$ **1**, Al-MTS-E$_1$ **2**, Al-MTS-E$_1$ **3** and Al-MTS-E$_1$ **4** were obtained from Al-MTS and **1** in the same conditions and consecutive washing with methanol, dichloromethane/diethyl ether 1/1, dichloromethane and toluene, respectively. It should be noticed that **1** is soluble in the solvents used, in homogeneous medium.

2.2.2. (1R, 2S)-(−)-O-methyl-ephedrine ***2***

The synthesis of *O*-methyl-(−)-ephedrine **2** was described elsewhere (Scheme 1) [32,33]. ^{1}H NMR (CDCl$_3$, δ ppm from TMS) $\delta = 1.0$ (d, 3H, CCH$_3$), $\delta = 2.4$ (s, 3H, CH$_3$N), $\delta = 2.7$ (q^2, 1H, CHN), $\delta = 3.3$ (s, 3H, CH$_3$O), $\delta = 4.1$ (d, 1H, HCϕ), $\delta = 7.3$–7.4 (m, 5H, aromatic H). ^{13}C NMR (CDCl$_3$, δ ppm from TMS) $\delta = 14.7$ (CH$_3$), 33.8 (CH$_3$N), 57.1 (CH$_3$O), 59.9 (CHN), 86.1 (CHO), 128.2–127.5–127.2 (tertiary aromatic C), 139.5 (quaternary aromatic C).

Immobilization on Al-MTS was conducted under the same conditions as those described for MTS-E$_1$ **1**, **2** solids. Al-MTS-E$_2$ **1** and Al-MTS-E$_2$ **2** were obtained, respectively, depending on the washing solvent, methanol or dichloromethane/diethyl ether 1/1.



1 **2**

Scheme 1. Synthesis of (−)-*O*-methyl-ephedrine **2**.

2.3. Characterization of the hybrid materials

The loadings in (−)-ephedrine **1**, in *O*-methyl-(−)-ephedrine **2** retained on the surface of the supports (mol $\times\ 10^3$ g^{-1} of dry solid) were determined by elemental analysis (Service Central d'Analyses du CNRS in Solaize) and by differential thermal analysis (Seratam SF 85 balance under air flow).

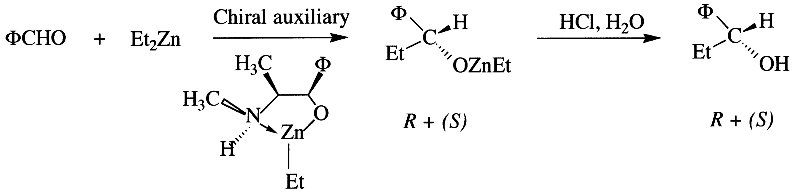
Elemental analysis: MTS-E$_1$ **1**: C% 0.99, N% $<$ 0.05; MTS-E$_1$ **2**: C% 5.09, N% 0.56; Al-MTS-E$_1$ **1**: C% 8.08, N% 0.81; Al-MTS-E$_1$ **2**: C% 11.43, N% 1.32; Al-MTS-E$_1$ **3**: C% 14.93, N% 1.56; Al-MTS-E$_1$ **4**: C% 12.72, N% 1.40; Al-MTS-E$_2$ **1**: C% 6.43, N% 0.47; Al-MTS-E$_2$ **2**: C% 5.79, N% 0.56.

Textural properties have been characterized by nitrogen adsorption at 77 K, on samples outgassed at 150°C, with a Micromeritics ASAP 2000 apparatus [34,35].

Immobilization of (−)-ephedrine **1** or of *O*-methyl-(−)-ephedrine **2** was studied by FTIR spectroscopy performed on a Nicolet 320 spectrometer on self-supported wafers after activation under vacuum at 180°C for 1 h. Adsorption of gaseous dimethylamine (DMA) (Aldrich-Chemie) on Al-MTS support was studied in the same conditions. The spectrum of the activated support was automatically substracted in order to obtain that of the adsorbed species. The intensities of the resulting spectra were normalized using lattice vibrations between 1700 and 2000 cm^{-1}.

2.4. General procedure for the enantioselective addition of diethylzinc to benzaldehyde

The supported chiral auxiliary (0.29 g) was activated at 25°C under vacuum for 1 h. Then, 4 ml of 1.1 M solution of diethylzinc in hexane (4.4 mmol) was added under nitrogen atmosphere. The resulting mixture was stirred at 0°C for 15 min in order to obtain the catalytic sites. Benzaldehyde (1.9 mmol) (Aldrich-Chemie), kept on basic Al$_2$O$_3$ in order to adsorb possible traces of benzoic acid, was added dropwise in 1 ml of toluene. The reaction mixture was stirred at 0°C. The progress of the reaction was monitored by periodically withdrawing samples which were analyzed by gas chromatography on chiral capillary



Scheme 2. Alkylation of benzaldehyde with diethylzinc.

column (LIPODEX E) after acidic treatment (HCl 0.5 M, CH_2Cl_2).

3. Results and discussion

Alkylation of benzaldehyde with diethylzinc leads to 1-phenyl-propan-1-ol (Scheme 2).

The direct immobilization of (−)-ephedrine **1** on the mineral surface may be considered either by acid–base interaction between the acid sites of the surface and the methylamino group of ephedrine (**1a**, Scheme 3), by hydrogen bonding between the hydroxyls of the surface and the hydroxyl moiety of ephedrine (**1b**) or by covalent grafting on the surface through the hydroxyl moiety of ephedrine (**1c**). However, the role of the hydroxyl function of **1** is of prime importance if we take into account that the formation of the catalytic site involves the reaction of this hydroxyl with diethylzinc to obtain ethylzinc aminoalkoxide [5] (Scheme 2). Thus, the understanding of the immobilization mode may be reached not only by the characterization of the chiral materials but also by the catalytic results. In that way, they are compared to those obtained after protection of the hydroxyl moiety in **1** by the methoxy group in **2** (Scheme 1).

Table 1
Loading of (−)-ephedrine **1** and (−)-*O*-methyl-ephedrine **2** (mol × 10^3 g^{-1}) on MTS and Al-MTS surfaces

	MTS		Al-MTS			
Solid **1**	-E_1 **1**	-E_1 **2**	-E_1 **1**	-E_1 **2**	-E_1 **3**	-E_1 **4**
	0.0 (0.9)[a]	0.4	0.6 (0.9)[a]	1.0	1.2	1.0
Solid **2**			-E_2 **1**	-E_2 **2**		
			0.4 (1.7)[a]	0.4		

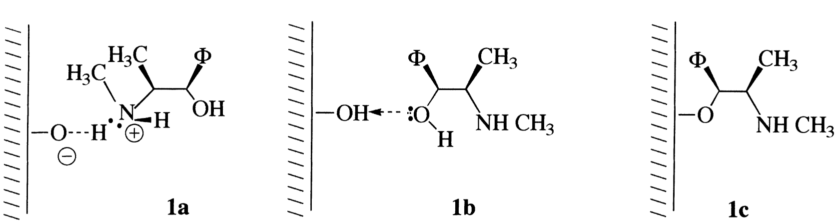
[a] Number of methoxy groups that are added after washing with methanol.

3.1. Characterization of the hybrid materials

3.1.1. Elementary and thermogravimetric analyses

Loadings of chiral auxiliaries obtained by both methods are in good agreement; mean values in moles per gram of dry hybrid material are recorded in Table 1.

The amount of **1**, which remains to interact with the surface, depends mainly on the polarity of the washing solvent whatever the composition of the support. For Al-MTS support washing with a solvent of low polarity (dichloromethane/diethyl ether 1/1, dichloromethane or toluene) leads to an amount which can be averaged to 1.1×10^{-3} mol g^{-1}. A lower loading of 0.4×10^{-3} mol g^{-1} is observed for MTS support



Scheme 3. Interactions of (−)-ephedrine with the surface of the support.

Table 2
Textural characteristics of materials obtained by direct immobilization of (−)-ephedrine **1** and (−)-*O*-methyl-ephedrine **2** on Al-MTS surface

Al-MTS	-E_1 **1**	-E_1 **2**	-E_1 **3**	-E_1 **4**	-E_2 **1**	-E_2 **2**
S ($m^2\,g^{-1}$)	766	757	647	763	860	848
V ($ml\,g^{-1}$)	0.49	0.45	0.41	0.44	0.59	0.60
D (Å)	26	24	25	23	27	28

(MTS-E_1 **2**). After washing with methanol, a decrease to $0.6 \times 10^{-3}\,mol\,g^{-1}$ is noticed for Al-MTS support (Al-MTS-E_1 **1**), while no aminoalcohol remains on the MTS surface (MTS-E_1 **1**). These results are in good agreement with those obtained for functionalization by (−)-ephedrine of Al-MTS hybrid materials with low density of halogen moieties anchored by covalent bonding. The latter reaction proceeds without halogen substitution [20]; aminoalcohol **1** interacts directly with the surface, and amounts are the same in both cases.

Ether **2** remains also to interact with the Al-MTS surface after washing with methanol or an apolar solvent in the same conditions. The loading ($0.4 \times 10^{-3}\,mol\,g^{-1}$) is slightly lower than for **1**. It is worth noting that the same amounts are found for immobilization of **2**, whatever the washing solvent.

Therefore, increasing the polarity of the solvent leads to a decrease for **1** and has no effect for **2**. Taking into account that the loading depends on the presence of an hydroxyl or an ether moiety in **1** or **2**, respectively, the role of the hydroxyl moiety of **1** is shown by the amount which is cancelled out after washing with methanol (O-immobilization, **1b**, **1c**, Scheme 3). We suggest that, if O-immobilization implied weakly hydrogen-bound aminoalcohol molecules **1b**, these links may be broken by methanol under soxhlet washing. If covalent bonds **1c** were previously formed, transesterification may proceed leading to grafting of methoxy moieties. Indeed, methanol washing is accompanied by such a grafting for both **1** and **2** (Table 1) as shown previously for silicas [36].

The role of the amino group (N-immobilization, **1a**) will be discussed thereafter.

The effect of the composition of the support may be explained by the higher surface acidity of the aluminosilicic than of the purely silicic materials [28,29] which leads to a better immobilization of **1** even after washing with methanol. Such Al-MTS material is characterized by a Si/Al ratio equal to 27 which corresponds to an aluminum content of $0.6 \times 10^{-3}\,mol\,g^{-1}$. Thus, Al-MTS loadings of aminoalcohol **1**, after methanol washing, and ether **2** are in good agreement with the number of aluminum sites of the support.

3.1.2. Nitrogen volumetry

Textural characteristics are given in Table 2. Type IV nitrogen sorption isotherms according to the IUPAC classification are maintained after modification of the Al-MTS surface as for hybrid materials synthesized by covalent grafting. The hybrid Al-MTS materials present a decrease in the mesoporous volume together with a decrease of the $4V/S_{BET}$ pore diameter. Even for the more loaded solids, the available volume remains higher than for microporous materials.

Purely silicic materials MTS-E_1 **1** and **2** show a loss of regular mesoporosity; mesopores are created at higher p/p_0 (between 0.37 and 0.66) after treatment with **1**. This is explained by the basicity of ephedrine which may destroy the pore walls partially.

3.1.3. FT IR spectroscopy

Infrared spectra after outgassing at 180°C confirm the immobilization of chiral auxiliaries **1**, **2** on the Al-MTS surface (Figs. 1 and 2).

Interaction of these molecules with the support caused a reduction in the intensity of isolated silanols (ν OH $= 3750\,cm^{-1}$). Some bands such as ν CH aromatic ($3100–3000\,cm^{-1}$), ν CH_3 ($3000–2800\,cm^{-1}$), δ CH aromatic ($1605\,cm^{-1}$) and δ CH_3 ($1400–1500\,cm^{-1}$) are observed in the spectra of **1** and **2** in solution, and are common to all the spectra of the chiral materials excepted MTS-E_1 **1**. Moreover, the IR spectra of the solids washed with methanol (Al-MTS-E_1 **1**, Al-MTS-E_2 **1**) exhibit additional bands (2860 and $2960\,cm^{-1}$) attributed to CH_3O stretching vibrations, which prove the immobilization of MeOH at the surface of these solids [37].

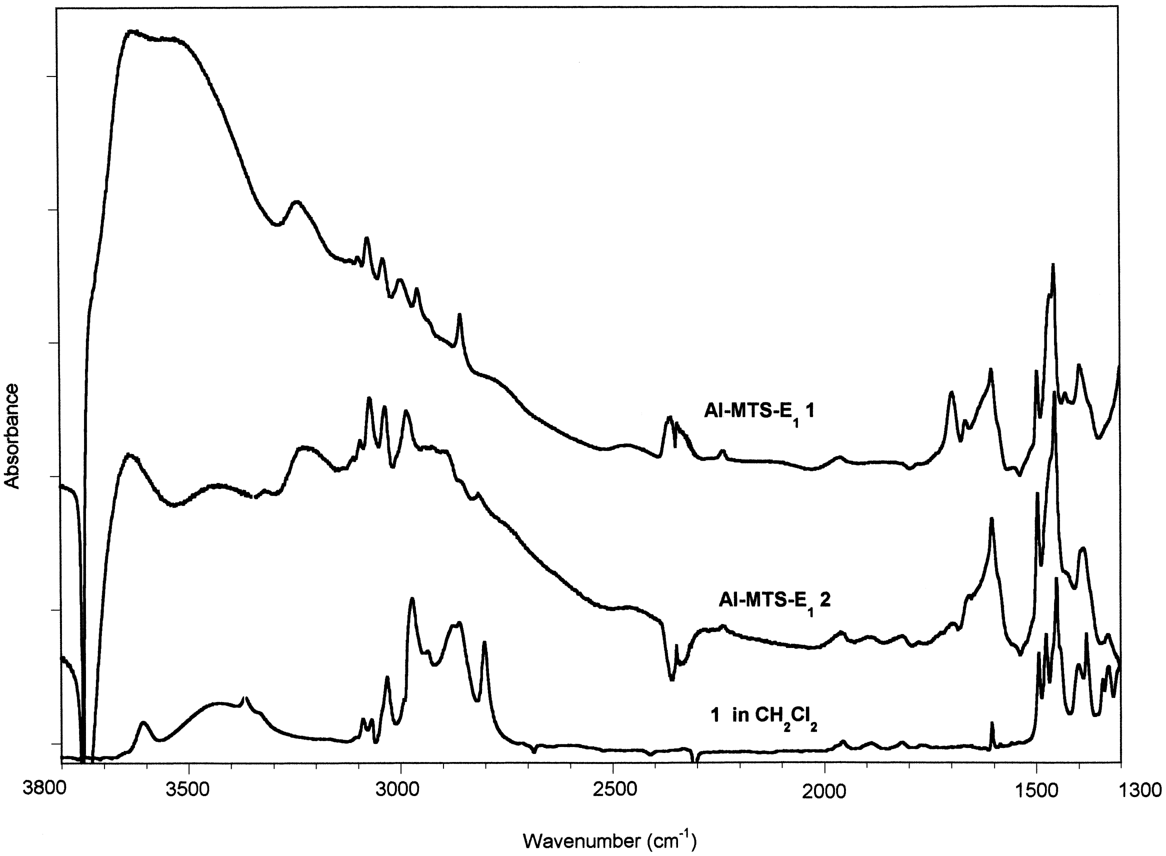


Fig. 1. IR spectra of (−)-ephedrine **1** in interaction with the Al-MTS support after evacuation at 180°C.

In order to distinguish between the possible interactions of the bifunctional compounds **1** or **2** with the acidic surface (Scheme 3) and to clarify the nature of interactions which imply the amino moiety, DMA was chosen as a simple model molecule.

Adsorption of DMA on Al-MTS gives rise to the subsequent observations in the domain of high frequencies: appearance of a broad band at 3240 cm^{-1}, weakening of the ν CH trans to the N lone pair at 2785 cm^{-1} and concomitant formation of broad bands at 2800 and 2460 cm^{-1} (Fig. 3).

Immobilization of **1** on the same surface leads to similar results after washing with methanol (Al-MTS-E$_1$ **1**, Fig. 1). Moreover, the same results are obtained after adsorption of **2** whatever the washing solvent (Al-MTS-E$_2$ **1** and Al-MTS-E$_2$ **2**, Fig. 2). Nevertheless, the IR spectra of Al-MTS-E$_1$ **2**, Al-MTS-E$_1$ **3** and Al-MTS-E$_1$ **4** washed with an apolar solvent show an additional band at 3325 cm^{-1} (Fig. 1) which corresponds to the NH stretching vibration of **1** in CH$_2$Cl$_2$ (3337 cm^{-1}) and thus, to an amino group without interaction with the surface. This band is absent in the spectra of Al-MTS-E$_2$, and neither observed on Al-MTS-E$_1$ **1**.

On Al-MTS surface, two species involving the adsorption by the amine group are discussed. Firstly, the shift of the ν NH band towards lower frequencies, respectively, 120, 90 and 70 cm^{-1} for DMA, **1** and **2** can be explained by forming strong hydrogen bonds between the lone pair of nitrogen atoms acting as a H-bond acceptor and the Brönsted acid sites of the surface acting as a H-bond donor [38]. This phenomenon has been already observed by Rochester et al. for the adsorption of di-*N*-butylamine on silica

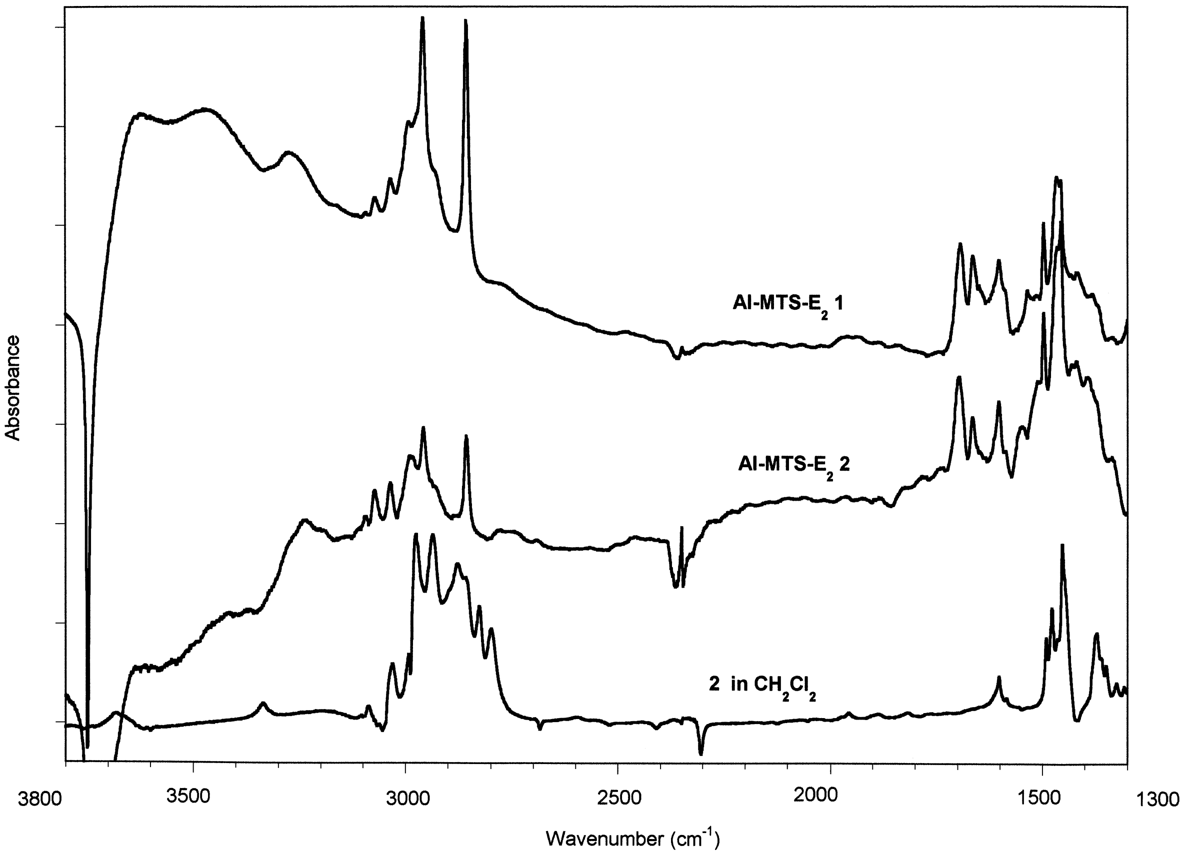


Fig. 2. IR spectra of (−)-*O*-methyl-ephedrine **2** in interaction with the Al-MTS support after evacuation at 180°C.

in CCl_4 [39]. Secondly, the lack of any band near 2785 cm^{-1}, which clearly indicates the direct interaction of the amino group with the surface, and the concomitant appearance of the broad bands below 3000 cm^{-1} points out the formation of NH_2^+ functions (**1a**, Scheme 3) [40]. Such a result is corroborated by comparison with the spectra of the hydrochloride salts for which ν NH_2^+ bands are located at 2782, 2439 and 2753, 2451 cm^{-1} for DMA and **1**, respectively. The relative low frequency of the CH stretching vibration (2785 cm^{-1}) in DMA, **1** and **2** in solution is explained by the effect of the lone pair of the amino group on the strength of the CH bond in *trans* position [41,42] which disappears in the chlorohydrate salt of these compounds. Therefore, the formation of ammonium species resulting from the interaction of the amine moiety with Brönsted acid sites of the surface is proposed, and bands below 3000 cm^{-1} are attributed to the vibrations of the secondary protonated amino group [40]. In the domain of low frequencies, other additional bands are observed between 1500 and 1700 cm^{-1}. These bands are assigned to the bending vibrations of the H-bonded or protonated NH group [40] by comparison with the spectra of hydrochloride salts where NH_2^+ bending vibrations are found at 1587 cm^{-1} for DMA and 1590 cm^{-1} for **1**. In the same domain of frequencies, it should be noted that the CH bending vibrations between 1400 and 1500 cm^{-1} [41] are modified by the adsorption of DMA, **1** and **2** on Al-MTS.

Interaction of **1** with the surface by the hydroxyl moiety (**1b**, **1c**, Scheme 3) in Al-MTS-E_1 **2**, Al-MTS-E_1 **3**, Al-MTS-E_1 **4** solids is pointed out by the presence of a ν NH band practically unchanged

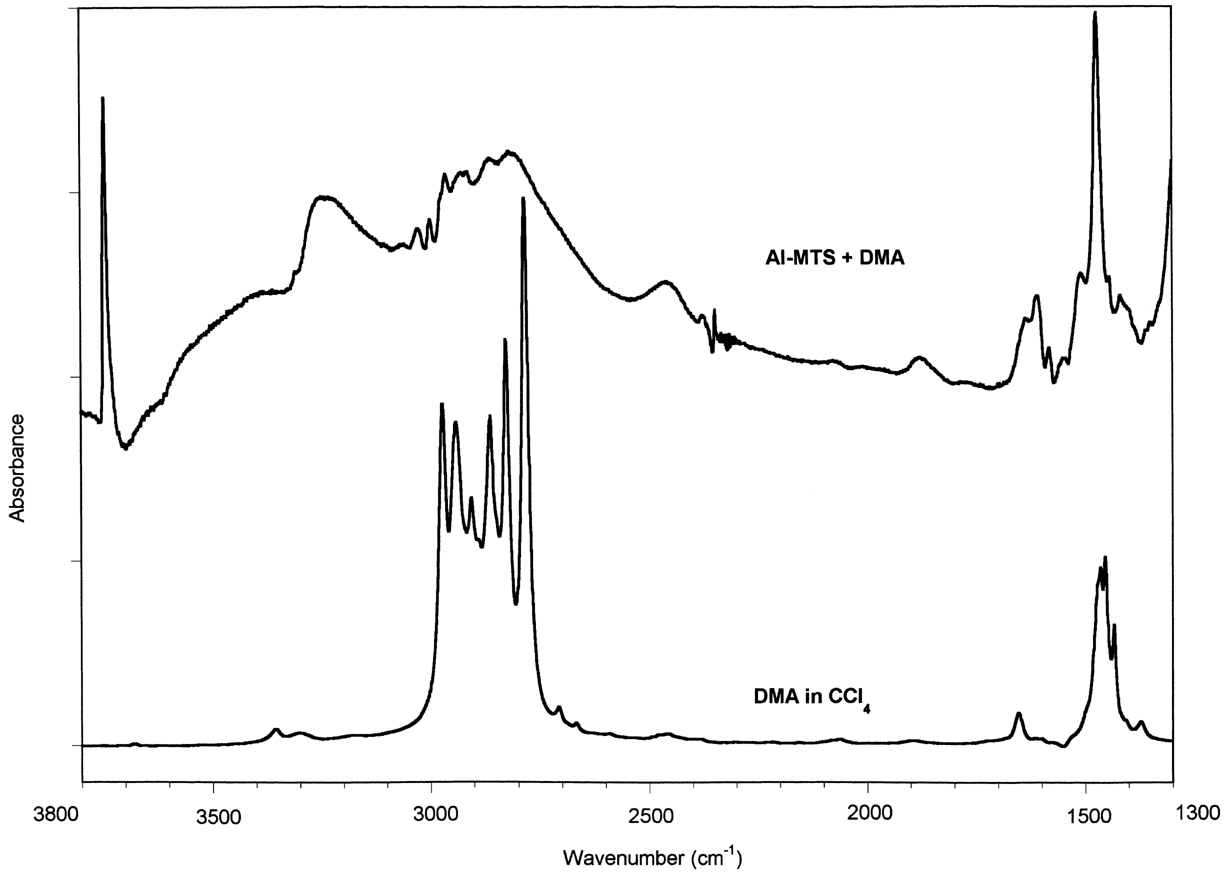


Fig. 3. IR spectra of DMA in interaction with the Al-MTS support after evacuation at 180°C.

compared to the ν NH frequency in solution. Vanishing of this band by washing with methanol shows that the hydroxyl interaction of **1** with the surface (**1b**, **1c**, Scheme 3) is cancelled out, which leads to a lesser amount of supported (−)-ephedrine. Thus, IR results are in good agreement with microanalysis.

Immobilization of **1** on MTS support, after washing with an apolar solvent (MTS-E_1 **2**), is characterized by the presence of the same ν NH band (3335 cm^{-1}) without any additional bands (not shown). As for Al-MTS-E_1 **2**, Al-MTS-E_1 **3**, Al-MTS-E_1 **4**, this band indicates an interaction of **1** with the surface by the hydroxyl moiety (**1b** or **1c**, Scheme 3). The leaching of the aminoalcohol after washing with methanol, as shown by microanalysis, is confirmed by its disappearance.

In conclusion of the FTIR study, two forms of interaction between the lone pair of the nitrogen atom of **1** or **2**, acting as H^+ acceptor, and the Brönsted acid sites of the surface, acting as H^+ donor, are put in light (**1a**, Scheme 3) for the Al-MTS support. They are characterized either by a strong H-bonding or by an ionic bonding. The difference results from a proton transfer from the acid sites to the amine moiety in the latter case. There is no evidence of interaction between amino functions and Lewis acid sites. In fact, this kind of bonding is probably negligible since Al-MTS support before the immobilization of **1** or **2** was activated at a too low temperature (25°C) to allow the formation of Lewis acid sites. Additionally, the presence of a free amine band on Al-MTS-E_1 **2** agrees with the interaction of a part of **1** by the hydroxyl group with

Table 3
Alkylation of benzaldehyde with diethylzinc in hexane at 0°C

Entry	Catalyst	k_{obs}[a] (h^{-1})	Conversion[b] (%)	Selectivity[c] (%)	(−)-Ephedrine (mol%)	ee[d] (%)
1	Without catalyst	1.2×10^{-2}	25	51		0
2	(−)-Ephedrine **1**	0.53	99	97	8.5	62
3	MTS	0.10	81	87	–	0
4	MTS-E_1 **1**	0.10	81	71	0.0	0
5	MTS-E_1 **2**	0.08	85	77	6.1	27
6	Al-MTS	0.17	98	84	–	0
7	Al-MTS-E_1 **1**	0.12	97	85	9.2	35
8	Al-MTS-E_1 **2**	0.15	97	84	15.3	45
9	Al-MTS-E_1 **3**	0.20	98	92	18.3	51
10	Al-MTS-E_1 **4**	0.20	98	92	15.3	50

[a] Fitting of BA (%) vs. time (h) by an exponential regression leads to k_{obs} (h^{-1}).
[b] % Conversion $= 100([BA]_0 - [BA]_t)/[BA]_0$.
[c] % Selectivity $= ([R] + [S])/([BA]_0 - [BA]_t)$.
[d] % ee $= 100([R] - [S])/([R] + [S])$.

the Al-MTS support. For MTS support, strong interaction between the amino group of **1** and the surface is not detected. This result is explained by the lower acidity of the MTS surface compared to the Al-MTS one.

3.2. Enantioselective addition of diethylzinc to benzaldehyde

The chirality of 1-phenyl-propan-1-ol obtained in the model reaction (Scheme 2) is controlled by the auxiliary used, (−)- or (+)-ephedrine giving (*R*)- or (*S*)-1-phenylpropan-1-ol, respectively, with good ees in homogeneous conditions.

3.2.1. Role of the support

Direct immobilization of (−)-ephedrine on the mesoporous supports leads to materials which are effective in the asymmetric ethylation of benzaldehyde. The efficiency of MTS or Al-MTS supported (−)-ephedrine is shown by comparison with the reaction without catalyst or in homogeneous conditions (Table 3). It should be noted that all the catalytic tests were performed using a constant weight of solid.

Whatever the composition of the support, rates are increased but remain lower than in homogeneous medium. They depend on the composition of the support. Moreover, the naked supports catalyze the racemic alkyl transfer (entries 3 and 6), and rates with chiral solids are related with rates determined for the naked support. The higher the support-catalyzed rate is (entries 3 and 6), the higher the rate with the hybrid material is (compare entries 4 and 5 to entries 7–10). Similar results were obtained with covalently-bound aminoalcohol **1** [20]. Consequently, the overall rate appears to be governed by the support activity.

Selectivities, which take into account the formation of benzyl alcohol [18], follow rates in the sense that a lower participation of the uncatalyzed reaction leads to a lower formation of benzyl alcohol. The higher the overall rate is, the higher the selectivity is.

Enantioselectivities are induced by supported (−)-ephedrine. Thus, as shown by elemental and IR analyses, no more **1** remains on the surface of MTS based solids after washing with methanol (Table 3, entry 4); effectively, racemic alcohols were obtained. Moderate enantioselectivity obtained after washing with CH_2Cl_2/Et_2O (entry 5) corroborates the presence of chiral auxiliary on the surface. All the Al-MTS chiral materials are efficient in the enantioselective ethylation of benzaldehyde (Table 3, entries 7–10). It is worth noting that amounts around 15.3–18.3 mol% of **1** resulting from washing with apolar solvents leads to ees (45–51%, entries 8–10) higher than after washing with methanol (35%, entry 7). Thus, ees appear to depend either on the quantity of (−)-ephedrine put

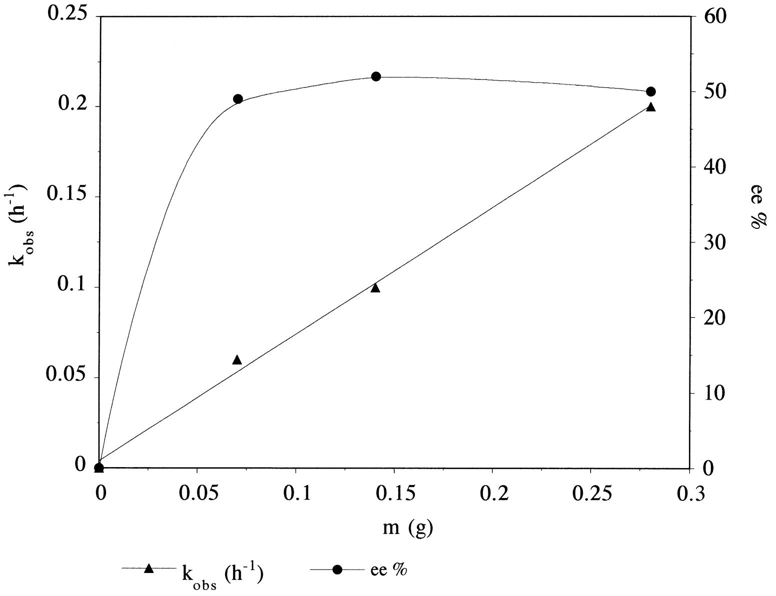


Fig. 4. Effect of the weight of Al-MTS-E_1 **3** on the efficiency of the catalyst in the model reaction.

in the reaction medium or on the solid loading of (−)-ephedrine.

3.2.2. Effect ot the weight of solid chiral auxiliary

Taking into account that reactions are performed with a constant weight of material, the amount of supported (−)-ephedrine depends on the loading of each material (Table 1). In order to control the effect of the amount of **1**, with a constant loading, the weight was varied. Results for Al-MTS-E_1 **3** are shown in Fig. 4.

The initial rate of benzaldehyde disappearance increases linearly with the weight of solid. Selectivity increases with initial rate from 80 to 93%. Enantioselectivity may be considered as constant in the domain 4.4–18.3 mol% (0.07–0.29 g of solid). Similar results were obtained varying the weight for Al-MTS-E_1 **1**. Thus, ee for the same loading, does not vary with the amount of **1**.

Increasing the weight of a chiral solid results in a concomitant increase of the enantioselective catalytic sites, i.e. the supported chiral auxiliary, and of the racemic catalytic sites, i.e. the uncovered mineral surface which catalyzes the formation of racemic alcohols. Such an increase of the total number of sites induces a proportional increase of the rate, indicating that mass transfer phenomena in the liquid phase are negligible even working at 0°C. Invariability of ees is explained in this case by the constancy of the ratio of the enantioselective sites to the racemic sites. Nevertheless, as described before, an increase of the loading of **1** on the Al-MTS support results in an improvement of ees (compare in Table 3, entry 7 to entries 8–10). In this case, the ratio of enantioselective sites to the racemic sites is augmented. The role of the uncovered mineral surface is minored.

3.2.3. Catalytic activity and mode of immobilization of ***1***

The mode of immobilization of **1** either by the amine or by the hydroxyl moiety (Scheme 3) may be questioned in order to understand how can a direct interaction with the support gives an efficient solid. Therefore, **1** hydrochloride and **2** in homogeneous conditions or supported on Al-MTS (Al-MTS-E_2 **1** and Al-MTS-E_2 **2** solids) were tested as catalysts in the model reaction (Table 4).

The (−)-ephedrine hydrochloride is effective in the enantioselective alkylation. Enantioselectivity is not affected by changing **1** (Table 3, entry 2) for **1**, HCl (Table 4, entry 1) but rate is notably lower. In homo-

Table 4
Role of the amino and hydroxyl moieties on the efficiency of the chiral auxiliary

Entry	Catalyst	k_{obs} (h^{-1})	Conversion (%)	Selectivity (%)	Auxiliary (mol%)	ee (%)
1	**1**, HCl	0.07	81	74	8.5	65
2	**2**	0.05	70	78	8.5	−1
3	Al-MTS-E_2 **1**	0.09	89	76	6.1	7
4	Al-MTS-E_2 **2**	0.11	94	81	6.1	5

geneous conditions, protection of the hydroxyl moiety in **1** by the methoxy group in **2** leads to a serious decrease of rate, selectivity and ee (compare Table 3, entry 2 and Table 4, entry 2). Immobilization of the ether **2** on the Al-MTS support leads to results (Table 4, entries 3 and 4) in good agreement with that obtained in homogeneous medium. Thus, the change of supported (−)-ephedrine **1** for **2** is followed by a serious drop of ees. Rates and selectivities are slightly lower than those determined using **1** on Al-MTS surface.

Aminoalcohol salts were precedently reported as efficient catalysts for asymmetric inductions [10,43]. Our catalytic results indicate that an interaction of the amino group of (−)-ephedrine with an acid surface allows to have an active chiral auxiliary in the enantioselective alkylation of benzaldehyde and thus confirm IR attributions for Al-MTS-E_1 auxiliary (**1a**, Scheme 3). The slow down rate may be explained by the possible weakening of the dative link between amine and zinc atoms in the catalyst (Scheme 2).

Catalytic results confirm that the hydroxyl moiety of the chiral auxiliary plays an essential role. Thus, the enantiomeric efficiency of **1** is highly reduced by protection of the hydroxyl moiety. Therefore, covalent immobilization of **1** by hydroxyl group with the MTS or Al-MTS surface (**1c**, Scheme 3) does not allow to perform enantioselective alkylation of benzaldehyde.

Table 5
Catalyst reutilization

Entry	Catalyst	k_{obs} (h^{-1})	Selectivity (%)	ee (%)
1	Al-MTS-E_1 **1**	0.12	85	35
2	Al-MTS-E_1 **1** (reused)	0.05	77	31
3	Al-MTS-E_1 **3**	0.20	92	51
4	Al-MTS-E_1 **3** (reused)	0.06	79	39
5	Al-MTS-Cl-E_1	0.17	93	47
6	Al-MTS-Cl-E_1 (reused)	0.07	87	44

3.2.4. Catalyst reutilization

Recycling of the catalyst (Table 5) was studied for Al-MTS-E_1 **1** and Al-MTS-E_1 **3**, and results compared with those obtained for **1** covalently bound to the surface through halogen substitution (Al-MTS-Cl-E_1) [20].

In every case, the rate decreases after the first run. However, the decrease of ee is low using (−)-ephedrine strongly bound on Al-MTS support (Al-MTS-E_1 **1**, Table 5, entries 1 and 2) and comparable to that obtained for **1** covalently anchored on the same surface (Al-MTS-Cl-E_1, Table 5, entries 5 and 6). Reaction of the silica surface silanols with Et_2Zn [36] may lead to some passivation of the mineral surface, and can explain the decrease of the rate together with the decrease of selectivity. However, no effect on ee is observed. Using the Al-MTS-E_1 **3** auxiliary leads to a drastic decrease of ees, which is explained by the leaching of the weakly bound O-immobilized (−)-ephedrine **1b** (Table 5, entries 3 and 4). Such a result was confirmed, after filtration of the solid, by analysis of the reaction medium by mass spectroscopy which showed the presence of (−)-ephedrine. Thus, participation of the homogeneous reaction cannot be totally turned down for all solids washed with apolar solvents.

4. Conclusion

Heterogeneous chiral auxiliaries efficient in the enantioselective alkylation of benzaldehyde with diethylzinc were obtained by direct immobilization of (−)-ephedrine on MTS and Al-MTS surfaces. Its loading depends on the polarity of the washing solvent and on the acidity of the support. IR results showed that strong ionic bonds between the amine moiety of this aminoalcohol and the Brönsted acid sites of the Al-MTS surface are formed. Good agreement was reached between the structure of the auxiliary and the catalytic activity. Moderate ees were obtained; they are governed by the effect of the uncovered mineral surface which catalyzes the racemic alkyl transfer. Recycling of the catalyst prepared by methanol washing after adsorption led to loss of enantioselectivity equivalent to that obtained for covalently-anchored ephedrine.

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