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Chiral vanadyl Schiff base complex anchored on silicas as solid enantioselective catalysts for formation of cyanohydrins: optimization of the asymmetric induction by support modification

Carlos Baleizão,[a,b] Bárbara Gigante,[a,*] Hermenegildo Garcia,[b,*] and Avelino Corma [b,*]

[a] *INETI-Departamento de Tecnologia das Industrias Químicas, Estrada do Paço do Lumiar, 22, 1649-038 Lisboa, Portugal*
[b] *Instituto de Tecnología Química/CSIC-Av. de los Naranjos, s/n, 46022 Valencia, Spain*

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Abstract

A series of vanadyl Schiff base complexes having a terminal carbon–carbon double bond pending alkyl chains of various lengths attached to the *para* position of the salen ligand have been prepared and anchored on three large surface area silicas, namely amorphous silica, ITQ-2, and MCM-41 through mercaptopropysilyl groups. The resulting solids having vanadium content around 0.04 mmol/g were tested as enantioselective catalysts for the reaction of aldehyde with trimethylsilyl cyanide and low ee values compared to solution were found. To optimize the enantioselectivity of the solid catalysts, silylation of the free silanol groups, variation of the linker length, and screening of the solvent were studied. The optimized enantioselective catalyst was found to be that in which the vanadyl salen complex is anchored to amorphous silica with the longest alkyl chain of the series (11 C) and in which the residual silanol groups were masked with trimethylsilyl groups. It was found that under optimal conditions ($CHCl_3$ as solvent and 0 °C) the activity of these solid catalysts is very close to that of the analogous complex in solution. Thus, for the reaction of benzaldehyde (1.64 mmol) with trimethylsilyl cyanide (3 mmol) in the presence of vanadium salen complex anchored on silica (100 mg) using chloroform as solvent at 0 °C the enantiomeric excess was 85% as compared to the 90% measured for the homogeneous catalyst. The solid catalyst can be reused by simple filtration up to three times, retaining a large part of the activity of the fresh catalyst.

Keywords: Asymmetric catalysis; Heterogeneous enantioselective catalysis; Vanadium salen complexes; Chiral cyanohydrins; ITQ-2 as support; MCM-41 as support

1. Introduction

Anchoring a soluble catalyst onto a solid surface is a general methodology to convert a homogeneous into a heterogeneous catalyst [1–4]. The main advantages of heterogeneization are the easy separation of the catalyst from the reaction mixture, allowing the possibility to recover and reuse the catalyst, and the possibility of continuous-flow operation.

The most challenging heterogeneization processes are those related to the transformation of homogeneous enantioselective catalytic reactions. Until quite recently, covalent anchoring of a highly enantioselective catalyst resulted in a significant loss of its activity and asymmetric induction capability with respect to that of the homogeneous phase. However, considerable progress showing that high enantiomeric excesses, sometimes very close to those obtained for the analogous soluble complexes, can be obtained by anchoring pure complexes has been made recently [5,6].

Herein, we describe that covalent anchoring of pure vanadyl salen complexes on the surface of silicas is not enough to achieve high enantiomeric excesses for the cyanohydrin formation from aldehydes as is observed in solution. It is necessary to protect free surface silanol groups, to have a linker of sufficient length, and to choose the appropriate solvent. In this way, the complex behaves like that in homogeneous phase, but still anchored to the solid surface. In this way, the catalysts are truly heterogeneous and retain a significant percentage of their initial activity and enantioselectivity.

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[*] Corresponding authors.
E-mail addresses: barbara.gigante@ineti.pt (B. Gigante), hgarcia@qim.upv.es (H. Garcia), acorma@itq.upv.es (A. Corma).

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2. Experimental

2.1. Compounds and materials

Starting reagents (*trans-R,R*-1,2-cyclohexanediamine, 3-*tert*-butyl-salicylaldehyde, 3,5-di-*tert*-butyl-salicylaldehyde), vanadyl sulfate, azoisobutyrylnitrile, 10-undecen-1-ol, allyl alcohol, 5-hexen-1-ol, trimethylsilyl cyanide (TMSCN), aldehydes, and anhydrous solvents were purchased from Aldrich. The reagent-grade solvents were obtained from Scharlau and used without further purification. Homogeneous vanadyl (IV) complexes **1a** [7] and 5-chloromethyl-3-*tert*-butylsalicyl aldehyde intermediate **4** [8] and the asymmetric ligand **7a–c** [9] and complex **1a–c** [7] were prepared according to the procedures reported in the literature. Silica was purchased from Aldrich; MCM-41 was prepared by hydrothermal crystallization at 100 °C using cetyltrimetyl ammonium bromide as structure directing agent and Aerosil as silica source following the procedure described in detail elsewhere [10,11]. ITQ-2 was synthesized by ultrasound delamination of a MCM-22 precursor previously submitted to swelling by ion exchanging the initial hexamethyleneimine template agent by hexadecyltrimethyl ammonium as reported [12]. The particle size, surface area, and pore volume of these solids were measured by scanning electron microscopy and isothermal nitrogen adsorption, respectively. The values are summarized in Table 1.

2.2. IR spectra

FT-IR spectra of unsupported asymmetric ligand and complex **1a** were recorded in KBr disks at room temperature in a Nicolet 710 FT spectrophotometer. FT-IR spectra of supported complexes were recorded at room temperature under vacuum using a sealed greaseless quartz cell fitted with CaF_2 windows in a Nicolet 710 FT spectrophotometer. Self-supported wafers (∼ 10 mg) were prepared by pressing the silicate powder at 1 Ton cm^{-2} for 3 min. The samples were outgassed at 100 °C under 10^{-2} Pa at 1 h before recording the IR spectra.

Table 1
Structural, textural, and analytical data for the solids used as supports

	SiO_2	ITQ-2	MCM-41
Structure	Amorphous	Layers	Hexagonal channels (38 Å)
Particle size (μm)	–	< 0.5	0.1–0.3
Surface area ($m^2\,g^{-1}$)	350	700	800
Micropore volume ($cm^3\,g^{-1}$)	–	0.009	0.61
Degree of silylation[a]	> 95%	90%	70%
Vanadium content ($mmol\,g^{-1}$)	0.04	0.04	0.04

[a] Estimated by the decrease in the intensity of the OH groups in the IR spectrum of the solids before and after silylation.

2.3. Diffuse reflectance (DR) UV–vis spectra

Transmission UV–vis spectra of transparent solutions were recorded in a Shimadzu UV–vis spectrophotometer. DR spectra of the opaque powders were recorded in a Varian Cary 5G UV–vis NIR spectrophotometer adapted with a praying mantis attachment and using $BaSO_4$ as reference. The reflectance data were converted to the Kubelka–Munk function F(R) that correlates with the absorbance of the complex [13].

2.4. Elemental analysis and atomic absorption

Combustion chemical analyses (C, H, N) of the silicates containing organic material were carried out in a Perkin–Elmer analyzer. Vanadium analyses of the solids were carried out by quantitative atomic absorption spectroscopy after attacking a given amount of the solid with concentrated hydrofluoric acid at 60 °C for 2 days.

2.5. General procedure for the preparation of mercaptopropyl-functionalized solid supports

After dehydration of the solids (1 g at 200 °C under 10^{-2} Torr for 2 h), the required amount of 3-mercaptopropyltrimethoxysilane (3.12 ml, 0.0166 mol) in dry toluene (3.5 ml) was added and the suspension stirred at reflux temperature under nitrogen atmosphere for 48 h. The solid was filtered and Soxhlet-extracted with dichloromethane for 24 h. After drying the solids (at 45 °C under 10^{-1} Torr for 2 h), the density of the 3-mercaptopropyl groups anchored in the solid was estimated from combustion chemical analysis.

2.6. General procedure for the protection of the solid supports

When desired to protect residual silanol groups, solids modified by mercaptopropyl silyl groups were degassed at 50 °C under 10^{-2} Pa for 1 h. Then, an excess of ethoxytrimethylsilane (7.8 ml, 0.033 mol) in dry toluene (5.3 ml) was added and the suspension stirred at reflux temperature under nitrogen atmosphere for 24 h. The solid was filtered, Soxhlet-extracted with dichloromethane for 24 h, and dried (at 45 °C under 10^{-1} Torr for 2 h). The amount of trimethylsilyl groups anchored was estimated from the difference in the C content of the solid before and after silylation. The residual population of unprotected silanol groups was determined by IR spectroscopy.

2.7. Preparation of the metal salen complexes having ω-C=C double bonds

The corresponding ω-unsaturated alcohol (2 mmol) was added to a xylene solution (10 ml) of the mixture of complexes **1a–c** in the statistical proportion indicated in Scheme 2 (600 mg). The solution was stirred at reflux temperature for 24 h. After this time, the solvent was evaporated under vacuum and the crude containing the complex **1d** was used to anchor onto the solid without further purification.

2.8. General procedure for anchoring the vanadyl Schiff base complex on the surface of the modified solids

To the crude of metal salen complexes containing **1d** prepared previously, modified solids (350 mg) and AIBN (100 mg) were added in nitrogen atmosphere. Then, degassed chloroform (10 ml) was added and the suspension stirred magnetically at 80 °C under nitrogen atmosphere for 20 h. The solid was filtered and Soxhlet-extracted with dichloromethane for 24 h. After drying the solids (45 °C under 10^{-1} Torr for 2 h), the quantity of vanadium was determined by quantitative atomic absorption spectroscopy after desegregation of the solid. The data are contained in Table 1.

2.9. General procedure for the asymmetric addition of cyanide to aldehydes

For the control reactions with the homogeneous catalyst **1a**, the experimental procedure described by Belokon et al. [14,15] was followed. Thus, a Schlenk tube was charged with the homogeneous catalyst (0.1 mmol%) and 1.9 ml of dry chloroform. The aldehyde (1.64 mmol) and nitrobenzene (1.64 mmol; internal standard) were also added. The mixture was stirred for 5 min and then TMSCN was added (1.1 eq; 1.8 mmol). The resulting mixture was stirred at room temperature or 0 °C under nitrogen atmosphere and the course of the reaction followed by GC (ChiralDex G-TA chiral column, 30 m, 0.25 mm). For the heterogenized catalysts a similar procedure was followed: 100 mg of heterogeneous catalyst (0.04 mmol/g of V) was suspended in dry chloroform (1.9 ml) followed by the addition of the aldehyde (1.64 mmol) and the nitrobenzene as internal standard (1.64 mmol). The suspension was stirred for 5 min and then TMSCN (4.92 mmol) was added. The heterogeneous reaction mixture was stirred at the corresponding temperature and the course of the reaction followed by analyzing the organic phase by GC (with the same column as before). The physical and analytical data of the trimethylsilyl ethers of corresponding cyanohydrins were consistent with those reported in the literature [16,17]. In all cases, the (*R*,*R*)-isomer of the catalyst gave an excess of the (*S*)-enantiomer of the cyanohydrin derivative by analogy with the literature reports [14,15].

2.10. Leaching tests

The percentage of activity due to the complex or vanadium species leached from the solid and present in the solution was determined by performing the reactions at the corresponding temperature under the reaction conditions described above until the conversion was about 30%. At this conversion, half the volume was filtered and the resulting clear solution let to react. The percentage of leaching was estimated by comparing the time-conversion plot of the twin reactions with and without solid.

3. Results and discussion

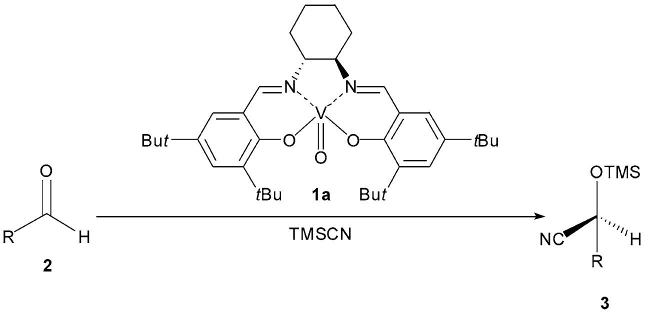
The reaction under study is shown in Eq. (1) and consists of the catalytic addition of trimethylsilyl cyanide to the carbonyl group of an aldehyde, whereby the trimethylsilyl derivative of the corresponding cyanohydrin is formed.

This reaction has been reported to occur with high enantioselectivity in the presence of chiral vanadyl salen complexes having bulky *tert*-butyl groups in the *ortho*–*para* positions of the phenolic moiety (structure **1a**) [14,15]. The substrate to catalyst molar ratio was 1000 and dichloromethane was the solvent of choice for this reaction.

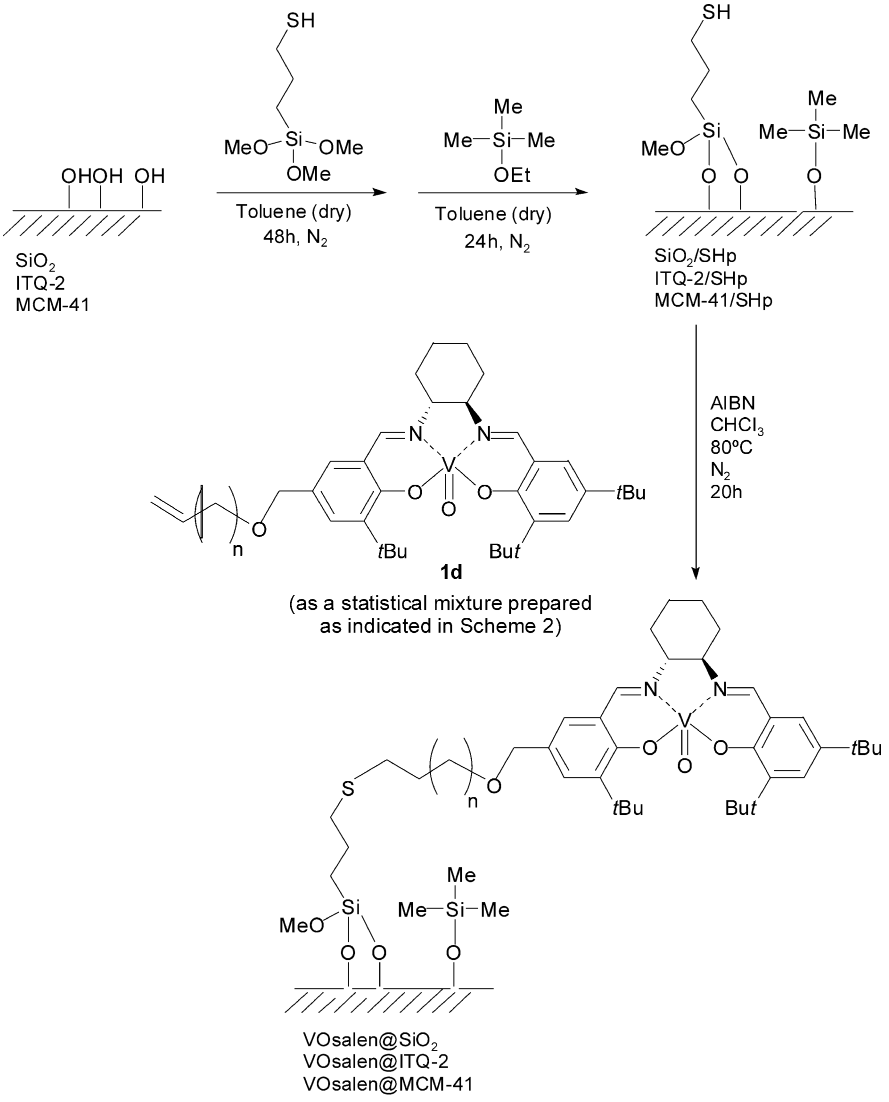
The target of our research is to anchor a chiral vanadyl salen complex having a structure close to that of **1a** on the surface of different silica types. We [18] and others [3] have previously reported the anchoring of metal salen complexes on zeolites and other structured or amorphous silicates, with only limited success with regard to asymmetric induction. In some cases, leaching of the catalyst from the solid to the solution has been observed [16]. In other cases, the e.e. using the immobilized catalyst was much lower than that of the soluble complex due to the presence of undesirable adventitious acid sites on the solid [19] or to the need of a cooperative contribution of two complexes, rendering the process bimolecular from the point of view of the catalyst as for the enantioselective epoxide ring opening with Cr salen complexes [20]. In those cases, immobilization of the catalyst has a considerable negative influence on the obtained e.e. [18].

However, in the reaction under consideration here (Eq. (1)), the catalytic process has been demonstrated [15] to be unimolecular with respect to the catalyst concentration and requires a low catalyst/substrate ratio. Therefore this reaction seems more suitable to being performed with covalently anchored metal salen complexes.

To address the influence of the solid support on the enantioselectivity of the anchored vanadyl complex, three solids



Equation 1.



Scheme 1.

having large surface area were selected in the present study. Table 1 contains the main textural and physicochemical parameters of the solid used.

We selected amorphous silica since it is the most easily available solid, but we also include in the study *all silica*-ITQ-2 and *all silica*-MCM-41. ITQ-2 is a relatively novel delaminated zeolite [11], whose structure is formed by crystalline zeolite layers (25 Å depth). The main advantage of ITQ-2 is the large accessible surface area (see Table 1) and the presence of a significant population of OH groups located on the ring cups where anchoring can occur. In contrast to the ITQ-2 structure having a large external area and a reduced microporosity, the structure of MCM-41 encompasses a series of parallel hexagonal channels (38 Å diameter) and most of the total area corresponds to the internal mesopores [10,11]. The interior of the mesoporous channels of MCM-41 is available to substrates and products and is full of silanol groups that can be used to anchor the catalytic active complex.

The strategy to obtain chiral vanadyl salen complexes covalently anchored to the silica surface was the same for the three solids and is illustrated in Scheme 1.

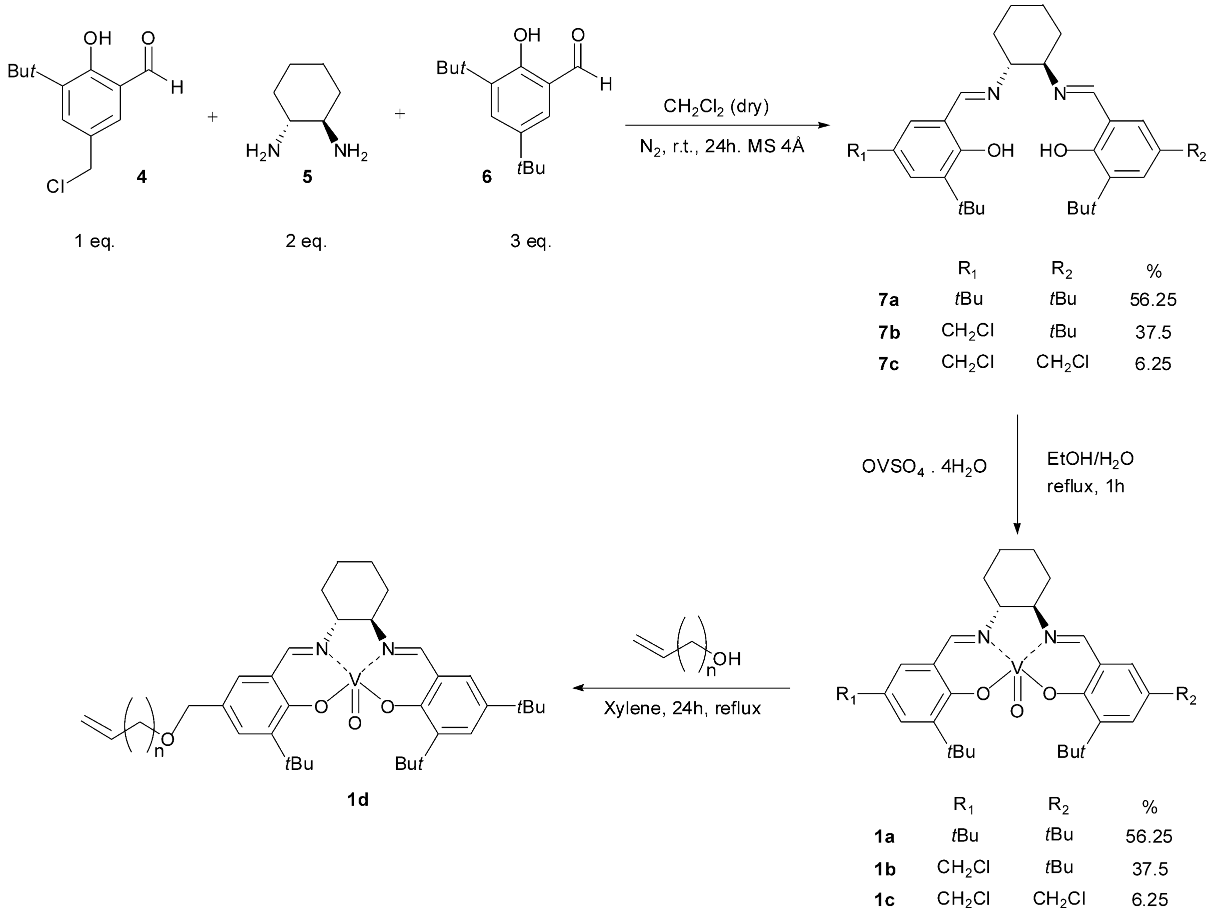
Basically the methodology consists in anchoring on the solid surface the 3-mercaptopropylsilyl groups followed by exhaustive silylation of the rest of the silanol groups. For the sake of comparison, one of the silica catalysts [$VO/SiO_2(OH)$] was prepared omitting the silylation step. This provides a valid comparison to establish the influence of the presence of residual silanol groups on the product enantioselectivity. The degree of silylation was determined by comparing the area of the OH stretching band in the IR for each solid before and after silylation. The results are also included in Table 1. To avoid the interference of coadsorbed water in the measurement of the silanol group population, before recording the IR, the solids were degassed at 100 °C under reduced pressure for 1 h. From these measurements it can be concluded that in the cases of ITQ-2 and MCM-41 part of the initial population of the silanol groups remains still unaltered after the silylation procedure. The residual silanol groups that have not been silylated could correspond to the fraction of OH groups located in nests or pockets where spatial restrictions preclude silylation. This residual population of OH groups was minimum for silica, but for this solid a catalyst [VO–SiO_2(OH)] containing OH was also studied. These data will become relevant when rationalizing the enantiomeric excesses obtained for each solid.

A major strength of our anchoring methodology is the independent preparation of vanadyl salen complex **1a–c** before anchoring to the solid surface. This allows the complete characterization of the complexes to be anchored onto the solid, thus ensuring the identity and purity of the catalytic active complex. To prepare the vanadyl complex we have followed a previous report in the literature [9] in which a statistical distribution of a mixture of salen ligands differing in the nature of the groups at the *para* position was obtained in a one-pot reaction (Scheme 2).

As is indicated in Scheme 2, preparation of the ligand was carried out by reacting *R,R*-1,2-cyclohexanediamine (**5**) with a mixture of unequivalent amounts of salicylaldehydes, **4** and **6**. This results in a distribution of three salen ligands in which the one having two *tert*-butyl groups at the *para* position (**7a**) cannot be anchored while ligands **7b** and **7c** having a chloromethyl functionality makes them suitable for covalent anchoring onto the mercapto groups of the solid after appropriate transformation into *ω*-terminated C=C double bond.

After preparation of the ligand, the vanadyl complex was formed by reacting **7a–c** with vanadyl sulfate using ethanol/water as solvent [7]. The last step before attaching the mixture of complexes to the support was the nuchleophilic substitution of benzylic chlorine by an *ω*-unsaturated linear long-chain alcohol [21]. The leading idea is to bind the complex to the solid surface by means of flexible tethers with different lengths, so to address the possible influence of the degree of freedom of the complex with respect to the solid surface. By varying the length of the chain it may be possible to address whether the proximity of the solid surface and the metallic center of the complex has a negative influence, restricting or making difficult the coordination of the substrate to the vanadium metal. This potential negative factor should be minimized by increasing the length of the tether anchoring the complex to the surface. The objective is to permit the complex to adopt conformations similar to those in the homogeneous phase, wherein large e.e. have been already achieved for this type of complex.

The actual anchoring of the vanadyl Schiff base complex to the modified solids was accomplished through a radical chain addition of a thiol to the terminal carbon–carbon dou-



Scheme 2.

ble bond using AIBN as radical initiator [8]. After the anchoring procedure the solid was thoroughly extracted to remove it from any adsorbed complex not properly anchored and, particularly, adventitious **1a** that is present predominantly in the complex mixture used for the preparation of the solid catalyst (see Scheme 2 for proportions). The actual loading of vanadyl complex is controlled by the density of mercaptopropylsilyl groups and the efficiency of the radical-promoted addition. This loading is independent of the density of silanol groups. It was maintained purposely low since the reaction under study works at a high substrate/vanadium ratio.

The solids were characterized by analytical and spectroscopy techniques. The loading of the complex was determined by vanadium analysis after the disaggregation of the solid. The data are contained in Table 1. The most salient feature from the analytical data is that the vanadium content of the three solids per weight is very similar, although obviously the loading differs considerably if the vanadium content per surface area is is the parameter considered. The density of complexes per surface area is more than double for VO/silica compared to the other two solids, which in turn have similar values of vanadyl complex considered either per weight or per surface area.

The presence of vanadium Schiff base complex anchored on the solids can be assessed spectroscopically. Thus, in the diffuse reflectance UV–visible spectra of the solids (Fig. 1) the characteristic metal–ligand band appearing at 360 nm is observed although with lower resolution than that for the transmission spectrum of the vanadium complex **1a** in solution. In the IR spectra of the solids (Fig. 2) the most characteristic band from the point of view of the structural identification is the presence of the metal salen complexes characteristic band appearing at 1536 cm^{-1}, which is absent for the ligand but can be clearly observed for the vanadium complexes either free or anchored on the solids. This band together with the optical spectra indicates that the complex **1d** has survived the anchoring procedure based on the radical addition under mild conditions of thiol groups to the terminated carbon–carbon double bond of the alkyl chain at the *para* position of the complex.

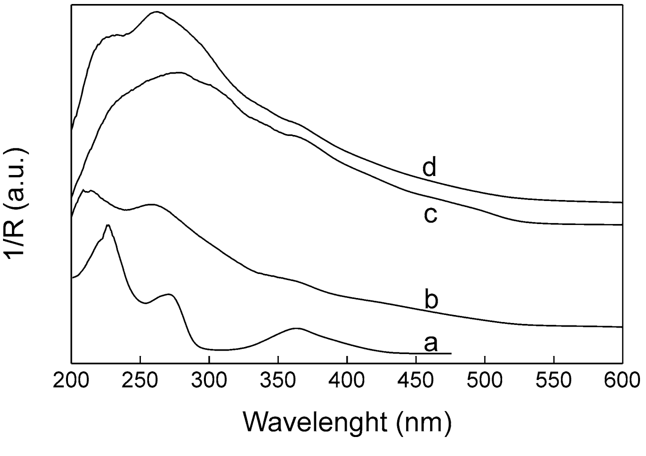


Fig. 1. Transmission UV–vis spectrum of homogeneous catalysts **1a** (a) and diffuse reflectance UV–vis spectra (plotted as the Kubelka–Munk function of reflectance; R) of VO/ITQ-2 (b), VO/MCM-41 (c), and VO/SiO_2 (d).

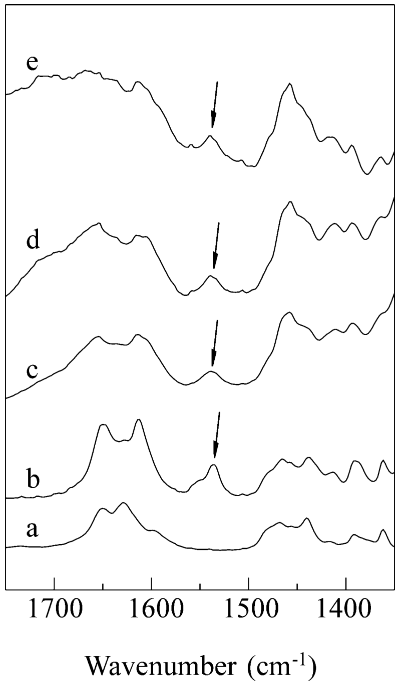


Fig. 2. IR spectra of the ligand mixture **7a–c** (a), the corresponding vanadyl complexes **1a–c** (b), catalyst VO/SiO_2 (c), catalyst VO/ITQ-2 (d), and catalyst VO/MCM-41 (e). The characteristic band of the metal salen complexes has been labeled with arrows. Spectra c, d, and e were recorded at room temperature in sealed cell after outgassing the water at 100 °C under 10^{-2} Pa for 1 h.

The solids were screened as enantioselective catalyst for the reaction of benzaldehyde with TMSCN using dichloromethane as solvent under the experimental conditions reported in the literature [14] and complex/substrate ratio of 0.24 mol%, somewhat higher than the ratio reported in the literature for this reaction (0.1 mol%) [14]. The results are summarized in Tables 2 and 3. A blank control using the modified solid (SiO_2/SHp) lacking vanadyl complex indicated that at even much longer reaction times this support exhibits a very low activity (Table 2), thus demonstrating that the activity of the solid catalyst is really due to the pres-

Table 2

Influence of the chain length linking the complex and the solid on the results of the catalytic addition of TMSCN to benzaldehyde in dichloromethane in the presence of vanadyl salen complex supported on silylated silica[a]

Catalyst	Chain length	Conversion (%)	e.e. (%)
SiO_2/SHp	–	8	0
VO–SiO_2	3	68	52
VO–SiO_2	6	66	56
VO–SiO_2	11	70	63

[a] Reactions were run at room temperature under N_2 atmosphere for 72 h: benzaldehyde (1.64 mmol), TMSCN (1.1 eq), heterogeneous catalyst (100 mg, 0.24 mol%), nitrobenzene (1.64 mmol), and CH_2Cl_2 (1.9 ml). No leaching was detected.

Table 3
Results of the catalytic addition of TMSCN to benzaldehyde in dichloromethane in the presence of vanadyl salen complex anchored to different supports[a]

Catalyst[b]	Time (h)	Conversion (%)	e.e. (%) [c]
VO/(1a)[c]	24	90	90
VO/SiO_2	72	70	63
VO/SiO_2(OH)[d]	72	70	48
VO/ITQ-2	72	53	58
VO/MCM-41	144	40	49

[a] Reactions were run at room temperature under N_2 atmosphere: benzaldehyde (1.64 mmol), TMSCN (1.1 eq), heterogeneous catalyst (100 mg, 0.24 mol%), nitrobenzene (1.64 mmol), and CH_2Cl_2 (1.9 ml). No leaching was detected.

[b] Carbon chain $n = 9$, in Scheme 1.

[c] 0.1 mol% used.

[d] Support without surface silylation. Carbon chain, $n = 9$.

ence of the anchored complex. No catalytically significant leaching of vanadium from the solid to the solution (which could catalyze the reaction in the homogeneous phase) was observed for any of the three supported catalysts. Thus, if some vanadium metal goes from the solid to the solution it has to be catalytically silent and below the analytic detection limits (nevertheless see deactivation of solids below). The most important data from Tables 2 and 3 are the e.e., which are significantly lower (maximum 63% e.e.) than that reported for the homogeneous reaction in solution (94%) [14]. In our hands, we repeated the reported reaction in dichloromethane using complex **1a** as catalyst and obtained an e.e. value of 90%, very close although somewhat lower than that reported. Therefore it can be concluded that anchoring of the complex on the solid surface has a negative influence on the asymmetric induction of the solid catalyst, even though the support has no significant activity in promoting the nonasymmetric product formation. To overcome this problem encountered also in related studies, we attempted to minimize as much as possible the solid surface–complex interaction by varying the linker length, protecting free silanol groups, and varying the nature of the solvent.

The influence of the chain length on the e.e. values of the product for the vanadyl salen complex anchored on silica is shown in Table 2. As can be seen there, the e.e. value increases progressively with the length of the tether linking the complex to the silica solid. These data demonstrate the beneficial influence of designing a complex with sufficiently large flexibility to allow the substrate–complex adduct to adopt a spatial disposition similar to that in the homogeneous phase. Molecular modeling indicates that the stretched conformation for the C11 linker should allow the complex to be as far as 46 Å from the solid surface.

Also we noted that there is an influence of the nature of the support in which the complex is anchored (Table 3). A likely explanation for this observation stems from correlating the decrease of the asymmetric induction ability of the complex with the presence of the free silanol groups on the support. As indicated in Table 1, the VO–MCM-41 is the solid in which the population of free silanol groups is higher, thus lowering the e.e. value. On the other hand, silica is the support with less residual OH groups and this may explain the higher e.e. value achieved for this solid. To support this assumption a vanadyl salen sample anchored on SiO_2 that was not submitted to silylation of the silanol groups was also used as catalyst (Table 3). The lower e.e. obtained for this unsilylated VO–SiO_2(OH) sample strongly supports our claim of a negative influence of the free silanol groups on the asymmetric induction ability of the solid catalyst. Concerning the unfavorable presence of free silanol groups, an alternative that could diminish the need of silylation would be to optimize the calcination procedure and synthesis conditions to reduce to the minimum possible level the population of free silanols.

In an attempt to increase the e.e. values for the reaction of benzaldehyde, we screened the activity of VO–SiO_2 for the same process and conditions using different solvents. The rationale behind this is that a variation of the polarity and hydrophilicity of the solvent could modify the activity of the complex by electrostatic interactions and by changes in the location of the complex at the solid–liquid interface. As a matter of fact, Table 4 shows that there is a large influence of the nature of the solvent on the e.e. values of the cyanohydrin derivative. Although there is not an obvious correlation between the polarity of the solvent and the e.e. achieved in the reaction product, it is clear from Table 4 that the solvent can dramatically vary the outcome of the reaction. The best solvent of the series was chloroform and when the reaction is carried out at low temperatures the e.e. is similar to that attained in solution with the homogeneous catalyst. Table 4 indicates that there probably are several factors influencing concurrently the reaction and that the interaction between the complex, solvent, and solid surface is not simple to understand. In addition, the lower asymmetric induction of the VO–ITQ-2 as compared to VO–SiO_2 was also reconfirmed under the optimum conditions.

Table 4
Results of the reaction of TMSCN with benzaldehyde using VO–SiO_2 as catalyst in the presence of different solvents[a]

Solvent	Electric dipole (debye)[b]	Time (h)	Conversion (%)	e.e. (%)
CH_2Cl_2	1.60	72	70	62
Hexane	0	24	71	32
Toluene	0.37	72	71	31
Ether	1.15	96	74	28
THF	1.75	96	43	22
CH_3CN	3.92	72	67	26
CCl_4	0	72	79	36
CCl_3CH_3	1.76	48	67	31
$CHCl_3$	1.04	48	73	72
$CHCl_3$[c]	1.04	120	78	85 (90)

[a] Reactions were run at room temperature under N_2 atmosphere: benzaldehyde (1.64 mmol), TMSCN (1.1 eq), VO/SiO_2 (100 mg, 0.24 mol%), nitrobenzene (1.64 mmol), and solvent (1.9 ml).

[b] Data taken from [22].

[c] TMSCN (3 eq), temperature 0 °C; mass balance 94%. The value in parentheses corresponds to the e.e. with homogeneous catalyst.

Table 5
Results of the recycling of the catalyst VO–SiO_2 in the reaction of TMSCN with benzaldehyde[a]

Used	Conversion (%)	Mass balance (%)	e.e. (%)
1	78	94	85
2	80	> 95	84
3	75	> 95	85
4	50	> 95	82
5	23	> 95	63

[a] Reactions were run at 0 °C under N_2 atmosphere for 120 h: benzaldehyde (1.64 mmol), TMSCN (3 eq), VO–SiO_2 (100 mg, 0.24 mol%), nitrobenzene (1.64 mmol), and $CHCl_3$ (1.9 ml).

With the optimum conditions from Table 4 (0 °C and $CHCl_3$ as solvent) we proceeded to study the reusability of the catalyst. The results are summarized in Table 5. After having used the solid catalyst in a reaction, the solid was recovered by simple filtration and used for a new batch with fresh reagents. As can be seen in Table 5, large changes in the activity and enantioselectivity are observed in the fourth use of the catalyst. The reason for the deactivation of the vanadium complex could be poisoning of the solid, loss of the vanadium metal, degradation of the ligand, or a combination of these possibilities. From the analytical data and the diffuse reflectance and IR spectra of the deactivated catalyst it can be concluded that some depletion in the vanadium content occurs upon repetitive use. Chemical analysis of the deactivated VO/SiO_2 catalyst after the fifth use indicates vanadium content of 0.02 mmol g^{-1}, which is significantly lower than that of the fresh catalyst. However it has to be remembered that the vanadium leached out of the solid is below the detection limit and thus does not contribute to the catalytic activity (see above and Table 3 for the leaching test).

Once the studies on the activity and recycling of the VO–SiO_2 were complete for the reaction with the benzaldehyde, we expanded the study to other aldehydes. The substrates, the conditions, and the results obtain are collected in Table 6. For the sake of comparison, the e.e. values achieved in chloroform solution using soluble **1a** as homogeneous catalyst are also included in Table 6. From these results it can be concluded that the vanadyl complex anchored through an 11-carbon tether on silylated silica is a general enantioselective catalyst for the cyanohydrin formation from aldehydes and promotes an enantioselectivity very similar (although lower) than the analogous complex in homogeneous catalysis under the same conditions.

Table 6
Results of the reaction of TMSCN with different aldehydes using VO/SiO2 as catalyst[a]

Aldehyde	Conversion (%)	Mass balance (%)	e.e. (%)[b]
Benzaldehyde	78	94	85 (90)
Benzaldehyde[c]	70	> 95	74 (90)
4-Fluorbenzaldehyde	80	> 95	75 (81)
4-Methoxybenzaldehyde	70	> 95	78 (85)
4-Methylbenzaldehyde	88	> 95	85 (89)
Citronenal	90	> 95	68 (74)

[a] Reactions were run at 0 °C under N_2 atmosphere for 120 h: aldehyde (1.64 mmol), TMSCN (3 eq), VO/SiO_2 (100 mg, 0.24 mol%), nitrobenzene (1.64 mmol), and $CHCl_3$(1.9 ml).

[b] The values in parentheses correspond to e.e. with **1a** as homogeneous catalyst.

[c] VO/ITQ-2 as catalyst.

4. Conclusions

Anchoring of a highly enantioselective complex on a solid surface, even if it is pure, may reduce its asymmetric induction capability, due to its interaction with the solid surface, but it is possible to increase the enantioselectivity of the anchored complex to the values obtained in solution. To achieve this goal, the tether linking the complex and the solid should be long enough to permit the complex to have a large conformational freedom and the solid surface has to be modified to reduce the presence of residual silanol groups. Finally the importance of the solvent on the asymmetric induction is consistent with variations in the location of the complex with respect to the solid–liquid interface and has to be considered when reporting the enantioselectivity of a heterogeneous catalyst.

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