

The first synthesis of organic–inorganic hybrid materials with chiral bis(oxazoline) ligands†

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Condensation of tetraethoxysilane with silane-functionalized bis(oxazolines) in the presence of dodecylamine leads to hybrid materials whose textural and catalytic properties depend on both the ligand and the spacer structure.

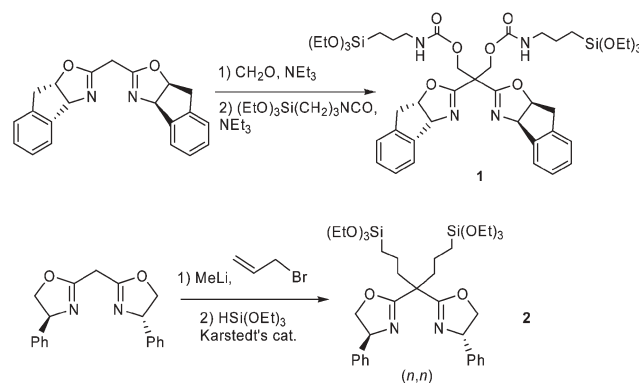
Organically modified silicas (ORMOSILS) are interesting materials for different fields given that they combine the properties of the organic polymers with higher thermal and chemical stability. In the case of catalysts, most such systems are prepared by grafting the organic moiety onto a preformed support.¹ This is particularly significant for enantioselective catalysts, whose chiral ligand is normally tethered to the silica surface.² In the case of purely organic supports, both the grafting of the chiral ligand onto a preformed polymer and the polymerization of a conveniently functionalized ligand are routinely applied strategies, with completely different results obtained with a good number of asymmetric catalysts.³ In analogy with the purely organic supports, the enantioselective silica-based catalysts could also be prepared by “inorganic polymerization” of a suitably functionalized chiral monomer. Although this strategy has been applied in the preparation of numerous non-chiral catalysts,⁴ the application of this approach to chiral catalysts is limited to some Rh–diamine complexes immobilized on low-surface area materials.⁵ Only recently has the preparation of high-surface area hybrid chiral materials been described, with the chiral groups either “hanging from”⁶ or “incorporated into”⁷ the silica walls. However, to date the catalytic results have been much poorer than those obtained with the grafted analogues, mainly with regard to enantioselectivity. One additional drawback of this approach is the low stability in aqueous solution of some of the most efficient families of chiral ligands, which is a clear limitation regarding the synthesis of siliceous materials. Bis(oxazolines) represent one of those families of highly efficient but water-sensitive chiral ligands and, for this reason, the development of strategies allowing their incorporation onto ORMOSILS is an attractive and interesting goal. Our group has been working on the immobilization of chiral bis(oxazoline)–metal complexes by different methods, including cationic exchange,⁸ ionic liquid solutions,⁹ polymerization,^{10,11} and grafting,^{11–13} with the aim of comparing the scope and limitations of the different methods. In this work we present our first results

on the synthesis of chiral ORMOSILS from chiral bis(oxazoline) ligands.

The bis(oxazoline) derived from indane was hydroxymethylated and reacted with 3-isocyanatopropyltriethoxysilane to obtain the precursor **1** (Scheme 1).¹³ However, the hydroxymethylation reaction was unsuccessful with the bis(oxazoline) bearing phenyl groups. The silanized precursor of this ligand (**2**) was prepared from the diallyl derivative¹¹ by hydrosilylation with HSi(OEt)₃ and Karstedt's catalyst¹⁴ (Scheme 1).

Bis(oxazoline) ligands are hydrolysis-sensitive in aqueous acidic media and Brønsted acids were therefore ruled out as catalysts for the sol–gel process. The ligands can also form strong complexes with a wide variety of Lewis acids and these were also unsuitable. Basic catalysis was preferred and the method using a long alkyl amine, which acts both as a catalyst and a template, was considered appropriate for our purpose. This method was initially developed for fully siliceous materials,¹⁵ although it has since been used for the preparation of organic–inorganic hybrid materials with simple (non-chiral) organic precursors.^{16–21} The chiral precursor was reacted with Si(OEt)₄ in a solution of dodecylamine in ethanol–water† (Scheme 2) in order to obtain a good dispersion of the ligand on the surface of the resulting material and give isolated catalytic sites. A white solid was immediately formed in all cases after the addition of the two silanes. After ageing, the solids were filtered off, washed and dried.

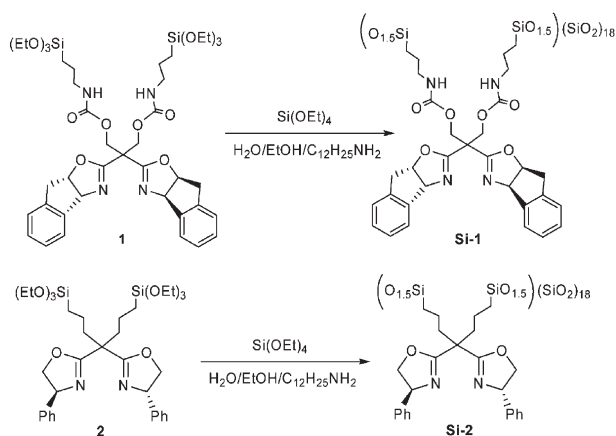
The presence of the ligand was detected by ¹³C-CP-MAS-NMR. The spectrum of **Si-1** is presented in Fig. 1. All the carbon atoms can be assigned in the spectrum, as shown in the figure. The presence of the imine and aromatic groups, together with the signals of the other carbon atoms in the oxazoline rings are key to demonstrating the integrity of the ligand.



Scheme 1 Synthesis of bis(oxazoline) precursors.

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† Electronic supplementary information (ESI) available: N₂ adsorption isotherms and pore size distribution of the three materials. See <http://dx.doi.org/10.1039/b507739g>



Scheme 2 Synthesis of the hybrid materials.

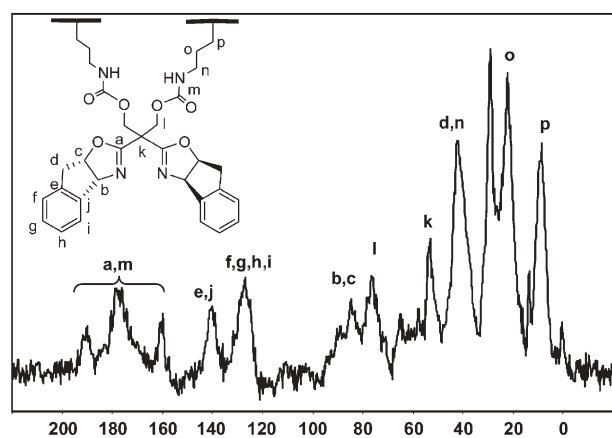


Fig. 1 ^{13}C -CP-MAS-NMR spectrum of **Si-1**.

SEM micrographs (Fig. 2) of the resulting materials show that the purely siliceous solid (Fig. 2A) presents large spherical particles of about $15\ \mu\text{m}$ together with aggregates of smaller particles (in the range $0.5\text{--}2\ \mu\text{m}$). These characteristics are consistent with the reported morphology for materials prepared by the same method.¹⁸ In contrast, the hybrid materials do not lead to the formation of such large particles, as shown in the micrograph of **Si-1** (Fig. 1B) and **Si-2** (not shown), and only aggregates of small ($<0.5\ \mu\text{m}$) primary particles can be observed. With regard to textural properties (Table 1), the purely siliceous material shows the expected high values of surface area and pore volume. The framework confined porosity ($0.70\ \text{cm}^3\ \text{g}^{-1}$, 37% of the total porosity) is in agreement with values reported by other authors, either in purely siliceous or in simple organic-inorganic hybrid materials.^{16,19} The large textural porosity is a consequence of a significant degree of particle intergrowth, as shown in the SEM micrographs. The bimodal character of the porosity is apparent from the pore size distribution (see ESI†). The maximum in the distribution at $20\ \text{\AA}$ must correspond to the framework porosity, and this is in good agreement with the results reported by other authors.^{16,19,20} The other maximum detected, in the range $800\text{--}900\ \text{\AA}$, may be due to the textural porosity.

These properties are drastically modified by the introduction of the chiral precursors and the final texture of the hybrid materials depends largely on the nature of the chiral bis(oxazoline). The

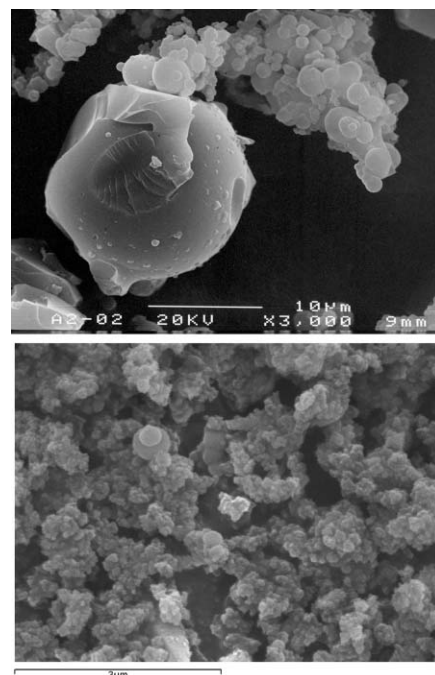


Fig. 2 SEM micrographs of the purely siliceous material (top) and **Si-1** (bottom).

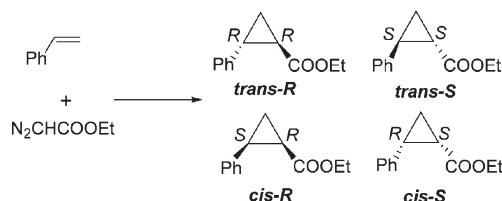
Table 1 Characterization of the hybrid materials^a

Solid	$S/\text{m}^2\ \text{g}^{-1}$	$V_p/\text{cm}^3\ \text{g}^{-1}$	$V_{\text{fp}}/\text{cm}^3\ \text{g}^{-1}$	$V_{\text{tp}}/\text{cm}^3\ \text{g}^{-1}$	$D_p/\text{\AA}$	Cu content/ $\text{mmol}\ \text{g}^{-1}$
Siliceous	1253	1.90	0.70	1.20	$20 + 850$	—
Si-1	40	0.14	0.05	0.09	—	0.076
Si-2	241	0.21	0.13	0.08	22	0.148

^a S = BET surface area. V_p = total pore volume (at $P/P_0 = 0.98$). V_{fp} = framework pore volume (at $P/P_0 < 0.5$). V_{tp} = textural pore volume ($V_{\text{tp}} = V_p - V_{\text{fp}}$). D_p = mean pore diameter (BJH).

material prepared from the indane-derived bis(oxazoline), **Si-1**, shows a very low surface area and porosity, as if the presence of this rather large precursor disturbs the formation of the micelles necessary to obtain framework porosity. The hybrid material **Si-2** presents completely different textural properties and has a moderate surface area ($240\ \text{m}^2\ \text{g}^{-1}$) and pore volume ($0.21\ \text{cm}^3\ \text{g}^{-1}$). However, the framework porosity contributes 62% of the total pore volume, a value much higher than in the other hybrid material, and the low textural volume is confirmed by the lack of a maximum in the distribution at large pore size. Another interesting feature is the slight, but significant, increase in the mean pore diameter to $22\ \text{\AA}$, in spite of the large organic moiety that must mainly be located in the framework pores. This result seems to indicate the good formation of micelles in the case of precursor **2**, which are even larger than in the case of the purely siliceous material. Finally, if we consider the copper loading obtained after complexation with $\text{Cu}(\text{OTf})_2$, it seems that the chiral ligand is much more accessible in **Si-2** than in **Si-1**, probably as a result of the larger surface area and pore size.

The copper(II) complexes were tested as catalysts in the benchmark cyclopropanation reaction between styrene and ethyl diazoacetate (Table 2). Both solids showed the same catalytic

Table 2 Catalytic results in the cyclopropanation reaction^a

Solid	Run	Yield (%)	trans : cis	ee trans (%) ^b	ee cis (%) ^b
Si-1	1	31	58 : 42	43 (88) ^c	51 (83) ^c
	2	3	59 : 41	9	14
Si-2	1	33	64 : 36	53 (60) ^d	45 (50) ^d
	2	30	62 : 38	50	43

^a Reaction conditions: catalyst (150 mg), styrene (5 mmol), dichloromethane (5 ml), slow addition of ethyl diazoacetate (5 mmol), room temperature. Results determined by GC. ^b The result in homogeneous phase with an analogous chiral ligand is given in parentheses. ^c The major isomers have *S* configuration in C1. ^d The major isomers have *R* configuration in C1.

activity and almost the same enantioselectivity. However, the enantioselectivity with Si-1-Cu, up to 51% ee, is still far from that obtained in the homogeneous phase with the dihydroxymethylated precursor (83–88% ee). This result confirms the general observation that lower enantioselectivities are obtained when the siliceous support is prepared with a silanized chiral precursor.^{5–7} In contrast, the enantioselectivity obtained with Si-2-Cu is close to that obtained in solution with the diallylated precursor. The most important difference between the two solids is probably the behaviour in terms of recycling. Unfortunately Si-1-Cu is not recoverable and loses both activity and enantioselectivity upon reuse. However, this deactivation is not due to copper leaching, a fact confirmed by the lack of activity for cyclopropanation in the final solution and also by elemental analysis. As in other heterogeneous catalysts,^{8–11} the deactivation may be ascribed to poisoning of the catalytic sites by irreversible coordination of the reaction by-products—namely maleate and fumarate derivatives from diazoacetate dimerization and subsequent reactions. Thus, Si-2 is the best support with regard to textural properties and catalytic performance.

In conclusion, we have demonstrated that it is possible to prepare organic-inorganic hybrid materials with silanized chiral precursors as hydrolysis-sensitive as bis(oxazolines). The textural properties and the catalytic performances of the resulting solids are dependent on the nature of both the substituents of the chiral ligand and the spacer. These results open the way for the synthesis of higher performance catalysts and further work is being carried out to obtain better solid supports for enantioselective catalysis.

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Notes and references

† Tetraethoxysilane (3.76 g, 18 mmol) and the bis(triethoxysilyl)-bis(oxazoline) (1 mmol) were added separately, but simultaneously, to a stirred clear solution of 1-dodecylamine (1.01 g, 2.5 mmol) in a mixture of ethanol (9.2 ml) and water (11 ml). The mixture was vigorously stirred for 18 h at room temperature. The solid was filtered off, thoroughly washed with ethanol, and dried under vacuum at 50 °C for 24 h. An analogous fully

siliceous material was prepared under the same conditions with only tetraethoxysilane (20 mmol) as the precursor.

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