



## Asymmetric cyclopropanation catalysed by cationic bis(oxazoline)–Cu<sup>II</sup> complexes exchanged into clays

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**Abstract:** Several clays, exchanged with cationic bis(oxazoline)–Cu<sup>II</sup> complexes, have been tested as catalysts in the benchmark cyclopropanation reaction of styrene with ethyl diazoacetate. Either the catalytic activity or the enantioselectivity are improved with regard to the same complexes when used in homogenous phase. The solvent used to carry out the cationic exchange has a decisive influence on the enantioselectivity and the same is true with regard to the solvent used in the homogeneous reaction. The clay-catalysed reactions lead to an increase in the amount of *cis*-cyclopropanes. These catalysts are recoverable and retain most of their catalytic activity. © 1997 Elsevier Science Ltd

### Introduction

The development of new heterogeneous catalysts able to promote enantioselective organic reactions is a field of growing interest.<sup>1,2</sup> From an industrial point of view, heterogeneous catalysts have the advantages of easier handling and separation, and in some cases they can be recovered and reused, retaining a great deal of their initial catalytic activity.

Several approaches are used for the preparation of chiral heterogeneous catalysts, and a good number of examples are related to the use of metal complexes immobilised by binding onto organic or inorganic supports. In most cases, the immobilisation is achieved through a covalent bond between the ligand and the support. From a practical point of view, the immobilisation through physical adsorption or entrapping is simpler, because it very often avoids the necessity of functionalising the complex.<sup>1,3</sup>

As far as this latter strategy is concerned, the intercalation of transition metal complexes into lamellar solids is a valuable method to easily support metal complexes with catalytic activity. Clays with cation exchange capacity can be used to support cationic complexes by electrostatic interactions with aluminosilicate sheets.<sup>4</sup> This strategy has only been used in asymmetric hydrogenation reactions promoted by clay-supported rhodium–chiral phosphine complexes.<sup>5</sup>

Most of the work on heterogeneous enantioselective catalysis has been carried out in reduction (mainly hydrogenation) and oxidation reactions.<sup>1,2</sup> Carbon–carbon bond formation reactions have been studied much less, and interest in this area has mainly been focussed on addition to carbonyl compounds,<sup>6</sup> and in hydroformylation.<sup>7</sup> Cycloaddition reactions have scarcely been studied, and only some isolated examples dealing with cyclopropanation reactions,<sup>8</sup> and more recently with Diels–Alder reactions, have been reported.<sup>9</sup>

To the best of our knowledge, there are no precedents regarding the use of complexes intercalated into lamellar solids as catalysts for C–C bond formation reactions. The complex must fulfil two conditions. First of all, it must be cationic. Furthermore, the cationic character of the complex must be maintained throughout the reaction, in order to avoid leaching of the neutral species from the solid.

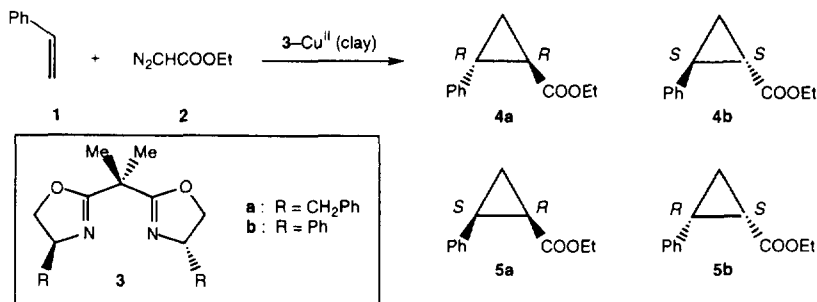
In this regard, the catalytic enantioselective cyclopropanation of alkenes, using copper–bis(oxazoline) complexes as catalysts,<sup>10</sup> is a very interesting possibility. In this communication

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we present the results of our preliminary study with two of the simplest chiral bis(oxazoline)-Cu<sup>II</sup> complexes.

### Results and discussion

Chiral bis(oxazolines) (**3a**, **3b**) were prepared from dimethylmalonyl chloride and the corresponding amino alcohols, following the procedure described by Pfaltz and co-workers.<sup>11</sup> The specific rotation of each compound was in agreement with previous data.<sup>12</sup> The chiral complexes were obtained using an equimolecular amount of CuCl<sub>2</sub> in methanol (340 ml mmol<sup>-1</sup>) or nitroethane (20 ml mmol<sup>-1</sup>). The cation exchange was carried out by stirring a suspension of the non-activated clay (1 g) in a solution of the complex (2 mmol) in methanol or nitroethane. The homogeneous and heterogeneous catalysts were tested in the benchmark reaction of styrene (**1**) with ethyl diazoacetate (**2**) (Scheme 1).



Scheme 1.

Table 1 shows the results obtained in these reactions. As can be seen, if the reactions carried out in methylene chloride are compared, homogeneous and heterogeneous catalysts behave in a very different way. Clay-catalysts lead, in general, to higher selectivities with regard to styrene, which is somewhat surprising if the acidic character of the supports is taken into account. Heterogeneous catalysts also lead to higher conversions than their homogeneous counterparts, in spite of the use of an equal or lower styrene:copper ratio (1 mmol of copper per 100 mmol of styrene in the homogeneous phase and 3 g of clay per 100 mmol of styrene in the heterogeneous reactions), which indicates that the clay does not impose any diffusional limitation to the reaction. The selectivity with regard to diazoacetate is also higher with the clays, which again is in agreement with a lack of diffusional restrictions. As previously described with non-chiral heterogeneous catalysts,<sup>13</sup> a lower *trans* preference is observed. Finally, most of the heterogeneous catalysts lead to higher enantioselectivities.

Several factors could account for these differences. Firstly, it is possible that the complexes in solution and those exchanged into the clay are different in nature. Although this possibility cannot be completely discarded, the complexes give similar IR spectra, both in solution and exchanged into the clays, and the elemental analyses show that the exchanged complexes have a 1:1 stoichiometry [the nitrogen excess in the case of the bentonite may be due to the interaction of non-coordinated bis(oxazoline) with the acidic centres of the clay]. A second reason may be related to a different microenvironment induced by molecules of the solvent used in the cationic exchange, which are not completely eliminated by washing the solid. Indeed, the solvent used in the exchange noticeably influences the enantioselectivity, with the best results obtained with nitroethane. In order to confirm this hypothesis, we carried out the homogeneous reaction in nitroethane and higher enantioselectivities were obtained. However, the results obtained in this reaction indicate that the solvent is not responsible for the changes in catalytic activity and *trans/cis* selectivity. The influence of the solvent on the asymmetric induction of a hetero-Diels–Alder reaction promoted by **3a**-Cu(OTf)<sub>2</sub> has been described.<sup>14</sup> However, in this case, the use of nitromethane leads to a decrease in the asymmetric induction with regard to methylene chloride.

**Table 1.** Results obtained in the reactions promoted by the bis(oxazoline)-Cu<sup>II</sup> complexes in CH<sub>2</sub>Cl<sub>2</sub> (1 ml/mmol of 1)

Ligand	Clay <sup>a</sup>	Cu (mmol g <sup>-1</sup> )	2N/Cu	1:2	t (h)	%Conv.	%Sel. (1)	%Sel. (2)	%ee <sup>c</sup>		
									4:5 <sup>b</sup>	4 <sup>d</sup>	5 <sup>e</sup>
<b>3a</b>	—	—	—	1	13	31	26	10	2.3	4	6
<b>3a<sup>f</sup></b>	—	—	—	1	23	13	70	9	1.8	45	40
<b>3b</b>	—	—	—	1	26	33	56	18	2.3	3	7
<b>3a</b>	Lmm	0.29	1.10	2	18	28	61	34	1.4	16	16
				1	19	47	60	29	1.4	15	16
<b>3a</b>	Lnn	0.37	1.60	2	16	24	62	29	1.2	32	25
				1	17	56	48	26	1.3	29	25
<b>3a</b>	Lmn	0.30	1.15	2	16	23	61	28	1.2	34	27
				1	17	37	65	27	1.2	31	26
				1	40	39	67	26	1.2	31	26
<b>3a</b>	Lmn <sup>f,g</sup>	0.13	1.15	2	16	25	49	25	1.2	35	26
				1	40	47	56	26	1.3	30	26
<b>3a</b>	Lmn <sup>f,h</sup>	0.13	1.00	2	16	26	45	22	1.3	28	24
				1	38	41	55	22	1.3	28	24
<b>3a</b>	Bmn	0.12	2.40	2	15	26	48	25	0.9	10	11
				1	38	46	52	24	1.1	10	5
<b>3b</b>	Lmm	0.45	0.70	2	17	30	66	40	1.4	6	0
				1	18	55	69	38	1.4	7	0
<b>3b</b>	Lnn	0.36	1.15	2	16	20	64	25	0.9	46	3
				1	21	44	60	27	0.9	45	11

<sup>a</sup> L and B stand for laponite and bentonite, m and n stand for methanol and nitroethane, the first letter indicating the solvent used to obtain the complex, and the second the solvent used to carry out the cationic exchange. <sup>b</sup> Determined by gas chromatography, using *n*-decane as the internal standard. <sup>c</sup> Determined by gas chromatography using a Cyclodex-B chiral column. <sup>d</sup> (1*R*,2*R*) is the major enantiomer. <sup>e</sup> (1*R*,2*S*) is the major enantiomer. <sup>f</sup> Reaction carried out in nitroethane. <sup>g</sup> Recovered catalyst <sup>h</sup> Catalyst recovered twice.

The third possibility lies in the influence of the counter-ion, namely the change from chloride to the negatively charged sheets of the clay. Evans and co-workers have shown that the nature of the counter-ion noticeably influences both the catalytic activity and the enantioselectivity of these reactions.<sup>15</sup> Therefore, we believe that this is one of the main reasons for the behaviour of the clay-supported catalysts.

The changes in *trans/cis* selectivity are not easy to explain. We speculate that these changes may be due to the isolation of the catalytic sites or to the changes in the dimensionality that take place on changing from a homogeneous to a heterogeneous phase.

The nature of the clay also influences the selectivities, and higher asymmetric inductions are obtained with the more easily swelled laponite, in comparison with bentonite.

Finally, the influence of the nature of the chiral auxiliary was also considered by using **3b** instead of **3a**. It is generally accepted that **3b** is a better chiral auxiliary than **3a**, and hence better enantioselectivities in *trans*-cyclopropanes are obtained in the reactions catalysed by **3b**-Cu<sup>II</sup>. However, surprisingly, the selectivity in the *cis*-cyclopropanes is very low in the same reactions. With this catalyst, a slight *cis* preference is observed experimentally.

One of the main advantages of heterogeneous catalysts is the possibility for their recovery and reuse. This possibility was explored with one of the solids which led to the best results, namely a laponite exchanged with **3a**-Cu<sup>II</sup> in nitroethane. The results obtained indicate that after the first reaction, the recovered catalyst shows a significant degree of leaching of copper, but that this has no influence on either the catalytic activity or on the selectivities when this recovered catalyst is used in a second reaction. The catalyst recovered after the second reaction does not show further leaching of copper, and the slight decrease in the catalytic performance may be due to the formation of coke, which probably consists of styrene polymers.

To summarise, exchanged clays show interesting catalytic properties in cyclopropanation reactions, and these properties are related to the changes in the microenvironment (solvent, negatively charged

sheets, site isolation, dimensionality) of the bis(oxazoline)-Cu<sup>II</sup> complex, caused by the clay. These catalysts can be recovered and reused, retaining most of their catalytic activity.

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