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Immobilisation of bis(oxazoline)–copper complexes on clays and nanocomposites. Influence of different parameters on activity and selectivity†

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Bis(oxazoline)–copper complexes, immobilised by electrostatic interactions on Laponite and Nafion/silica nanocomposites, have been tested as catalysts in the cyclopropanation of styrene with ethyl diazoacetate. Several factors play a decisive role in the outcome of the reaction. Firstly, the nature of the solid counterion is important, with perfluorosulfonic solids being the best in this regard. Secondly, the nature of the solvent used has a marked influence as some solvents cause the solid support to modify the stereochemical course of the reaction. Finally, the nature of the chiral ligand is also very important, in particular the strength of its copper complex, in order to avoid the formation of non-chiral catalytic copper centres. This particular effect has been highlighted by using a ligand that is able to give strong complexation, namely an iminobis(oxazoline) ligand, and this leads to the best enantioselectivities being obtained for reactions using electrostatically immobilised catalysts.

Introduction

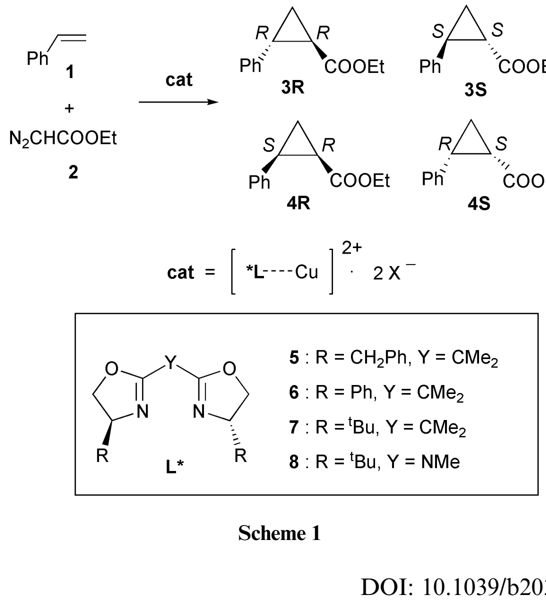
Homogeneous metal complexes with chiral ligands are widely used as enantioselective catalysts. However, from an industrial point of view, catalysts that are not soluble in the reaction medium are easier to handle and separate. Furthermore, in some cases they can be recovered and reused. One of the strategies most frequently used to prepare chiral heterogeneous catalysts is the immobilisation of the homogeneous complex.[1] Depending on the nature of the support, either an organic polymer or an inorganic solid, new organic or hybrid chiral materials can be obtained and these can be useful catalysts in enantioselective organic reactions.

In most cases, immobilisation is carried out by covalent bonding of the chiral ligand to an organic or inorganic support. The method used to form this covalent bond has a decisive influence on the catalytic activity and selectivity of the system. In particular, marked effects on the enantioselectivity have been described.[1] These changes are generally accounted for in terms of the conformational changes experienced by the ligand through its interaction with the support. In this regard, immobilisation without a covalent bond,[2] a process that avoids the chemical modification of the ligand, is an interesting alternative. However, very few studies have been undertaken to analyse the influence of different factors on the results of reactions promoted by these catalysts.

Bis(oxazoline)s are a well-known family of chiral ligands that are able to form stable complexes with a large variety of metals, and these complexes efficiently promote a large number of enantioselective organic reactions in the homogeneous phase.[3] Due to this fact, immobilised bis(oxazoline) complexes are, in principle, versatile chiral heterogeneous catalysts, which has led to increased interest in the immobilisation of such systems. Bis(oxazoline)s have been covalently bonded to insoluble inorganic[4,5] and organic[5–7] supports. Bis(oxazoline)–copper complexes, which are useful catalysts for several reactions,[3] are cationic in nature and, therefore, they can also be immobilised by formation of ion pairs with anionic supports.[7–9] In this paper we analyse the influence of several factors on the catalytic performance of the resulting solids. The factors investigated are the nature of the support, the structure of the chiral ligand, and the reaction conditions. In order to perform this investigation we selected the cyclopropanation of styrene (**1**) with ethyl diazoacetate (**2**) as the benchmark reaction (Scheme 1).

Results and discussion

Although bis(oxazoline) **7**, bearing *tert*-butyl groups, is the best ligand for Cu-catalysed cyclopropanation reactions, bis(oxazoline)s bearing other substituents (**5** and **6**) were tested in



Scheme 1

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Table 1 Characterisation of the bis(oxazoline)–Cu(II) complexes immobilized on Laponite[a]

Ligand	Cu/mmol g^{-1} as prepared	Cu/mmol g^{-1} after 1 run	2N : Cu	d_{001}/Å	Surface area/ m^2 g^{-1}
5	0.35	0.22	1.10	17.3	207
6	0.28	0.25	1.20	17.8	225
7	0.11	0.10	1.30	15.6[b]	218
—[c]	0.72	—	—	13.8	290

[a] Prepared by cation exchange of the bis(oxazoline)–Cu$(OTf)_2$ complex in methanol with the sodium form of the Laponite. [c] Non-chiral solid obtained by cation exchange of $CuCl_2$ in water. [b] Broad signal.

order to assess the generality of the immobilisation method prior to its application to different enantioselective reactions.

Previous studies using several clays as supports showed that Laponite leads to the best results.[8] Laponite is a poorly laminated clay and has a larger proportion of external exchange sites in comparison with other clays that may account for the better accessibility of the catalytic sites and hence for its better performance.

Bis(oxazoline)–Cu(II) complexes were immobilised on Laponite by cation exchange in methanol using the sodium form of the clay. Elemental analysis (Table 1) indicates that the amount of exchanged complex depends on the structure of the bis(oxazoline) and ranges from about 0.3 mmol g^{-1} with **5** and **6** to about 0.1 mmol g^{-1} with **7**. As a consequence of the Laponite structure, XRD patterns (Fig. 1) show very broad reflections and it is not easy to obtain conclusions from them. In spite of this, it seems that **5**– and **6**–Cu(II) show expanded basal spacings, which indicates that part of the complex is accommodated in the interlamellar space. The broad X-ray signal obtained after the exchange of **7**–Cu(II) does not allow us to draw any conclusions, although the lack of intercalation is also in agreement with the low copper content in **7**–Cu(Lap). The introduction of large cations accounts for the experimentally observed decrease in the surface area from values of around 300 m^2 g^{-1} in the starting and Cu-exchanged Laponites to 200–225 m^2 g^{-1} for the bis(oxazoline)–Cu exchanged Laponites (Table 1).

The structures of the exchanged complexes were confirmed by IR spectroscopy (Fig. 2). The spectra show the C=N band at around 1640 cm^{-1} for the **6**–Cu(II) complex. The structure of the **5**–Cu(II) complex in Laponite was also studied by EPR and EXAFS. The results of these experiments indicate that exchanged copper complexes are isolated species with an almost square planar structure. In this arrangement the surface of the clay acts as the counterion of the cationic complex, thus confirming that the complex is immobilised by electrostatic interactions with the anionic support.[10]

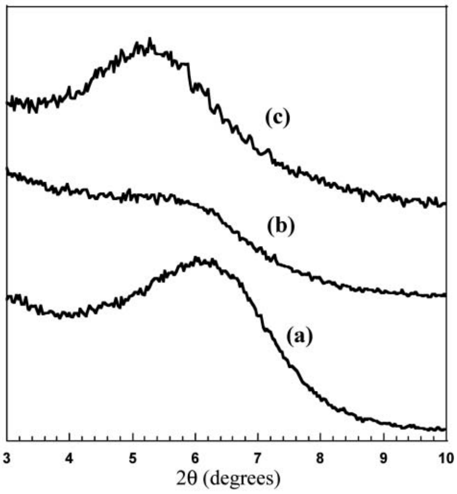

Fig. 1 Low-angle (2θ) X-ray diffraction patterns of (a) Laponite, (b) **7**–Cu(II) complex exchanged in Laponite, and (c) **6**–Cu(II) complex exchanged in Laponite.

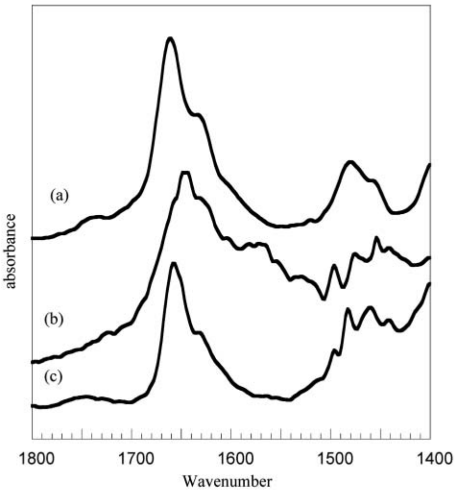

Fig. 2 IR spectra of the **6**–Cu(II) complex (a) in solution, (b) exchanged in Laponite, and (c) exchanged in SAC-40 Nafion/silica.

The Laponites containing the three different bis(oxazoline)–Cu(II) complexes were tested as catalysts in the benchmark cyclopropanation reaction. Table 2 compares the results obtained in these reactions with those observed using the respective homogeneous catalysts. In the homogeneous phase the **5**–Cu(II) complex (with triflate as the counterion) leads to 58% yield with a 2.1 : 1 *trans* : *cis* ratio and 59% and 53% enantiomeric excess (ee) in the *trans* and *cis* products, respectively. The same complex, when immobilised on Laponite, yields 25% of cyclopropane with equimolecular amounts of *trans* and *cis* products, and with only 24% and 19% ee, respectively. These values are even worse when the catalyst is recovered by filtration and reused. When bis(oxazoline) **6** is used as the chiral ligand in the homogeneous phase, a yield of 33% is obtained in a 2 : 1 *trans* : *cis* ratio and in 60% and 51% ee, respectively. The yield, *trans*/*cis* selectivity and ee in the *trans* product decrease only slightly in the reaction promoted by the corresponding Laponite-immobilised complex. On the other hand, the *cis*-cyclopropanes are obtained with only 24% ee. In this case the recovered catalyst leads to virtually the same results. In the homogeneous phase, the best results (72% yield, and 94% and 91% ee in the *trans*- and *cis*-cyclopropanes, respectively) are obtained with the **7**–Cu(II) complex. However,

Table 2 Results obtained from the cyclopropanation reaction at 25 °C with homogeneous and Laponite-supported catalysts[a]

Catalyst	Cu (%)[b]	*t*/h	Yield (%)[c]	*trans* : *cis* (**3** : **4**)[c]	Ee (%)[d] *trans*	Ee (%)[d] *cis*
5–Cu–$(OTf)_2$	10	7	58	2.1	59	53
5–Cu–(Lap)	1	22	25	1.0	24	19
5–Cu–(Lap)[e]	—[e]	22	32	1.1	14	12
6–Cu–$(OTf)_2$	10	5	33	2.1	60	51
6–Cu–(Lap)	0.84	21	30	1.6	49	24
6–Cu–(Lap)[e]	—[e]	24	28	1.4	43	19
7–Cu–$(OTf)_2$	10	7	72	2.4	94	91
7–Cu–(Lap)	0.33	39	30	1.8	69	64
7–Cu–(Lap)[e]	—[e]	88	26	1.4	43	37

[a] Reactions carried out in dichloromethane using a 1 : 1 styrene : diazoacetate ratio. [b] Proportion of Cu used in the reaction with regard to the reagents. [c] Determined by GC at total conversion of ethyl diazoacetate (ref. 9*b*). [d] Determined by GC using a Cyclodex-B column (ref. 9*b*); **3R** and **4R** are the major enantiomers. [e] Using recovered catalyst.

Table 3 Results obtained from the cyclopropanation reaction at 25 °C with homogeneous and Laponite-supported catalysts in different solvents[a]

Catalyst	Solvent	Yield (%)	*trans* : *cis* (**3** : **4**)	Ee (%)[c]		$\Delta\Delta G^{\ddagger d}$	
				trans	*cis*	*trans*	*cis*
6–Cu–(OTf)$_2$	CH_2Cl_2	33	2.1	60 (**3R**)	51 (**4R**)	—	—
6–Cu–(OTf)$_2$	Styrene	41	2.2	55 (**3R**)	42 (**4R**)	—	—
6–Cu–Cl$_2$	CH_2Cl_2	19	1.6	17 (**3R**)	13 (**4R**)	—	—
6–Cu–Cl$_2$	Styrene	59	1.6	11 (**3R**)	9 (**4R**)	—	—
6–Cu–(Lap)	CH_2Cl_2	30	1.6	49 (**3R**)	24 (**4R**)	0.63	0.29
6–Cu–(Lap)	Styrene	40	0.4	7 (**3R**)	34 (**4S**)	0.08	–0.42
6–Cu–(Lap)[b]	CH_2Cl_2	27	1.5	45 (**3R**)	22 (**4R**)	—	—
6–Cu–(Lap)	*n*-Hexane	10	0.4	3 (**3R**)	33 (**4S**)	0.02	–0.41
7–Cu–(OTf)$_2$	CH_2Cl_2	72	2.4	94 (**3R**)	91 (**4R**)	—	—
7–Cu–(Lap)	CH_2Cl_2	30	1.8	69 (**3R**)	64 (**4R**)	1.00	0.90
7–Cu–(Lap)	*n*-Hexane	9	1.0	27 (**3R**)	8 (**4R**)	0.33	0.10

[a] Reactions carried out in dichloromethane using a 1 : 1 styrene : diazoacetate ratio, except when styrene is used as the solvent. [b] Catalyst recovered from the reaction carried out in styrene. [c] Determined by GC using a Cyclodex-B column (ref. 9*b*). [d] $\Delta G_S^{\ddagger} - \Delta G_R^{\ddagger}$; values in kcal mol^{-1}.

the results are noticeably worse (30% yield, and 69% and 64% ee) when this complex is immobilised on Laponite. These values are even lower (26% yield, and 43% and 37% ee) on using the recovered catalyst. Analysis of the recovered catalysts shows that only in the case of **5**–Cu(II) is there a noticeable decrease in the copper content. After the addition of diazoacetate, the catalyst was separated by filtration and the reaction in the homogeneous phase did not continue, even when an additional amount of diazoacetate was added. This experiment clearly shows the heterogeneous character of the reaction.

The low yield obtained in the reaction is related to the concurrence of the carbene intermediate dimerization process, which affords maleate and fumarate. For this reason styrene is normally used either in excess or, in some cases, even as the solvent. In the homogeneous phase the use of styrene, rather than dichloromethane, as the solvent in the reaction catalysed by **6**–Cu(OTf)$_2$ increases the final yield without modifying either the *trans–cis* product distribution or the enantioselectivities (Table 3). The same effect is observed in the reaction catalysed by **6**–CuCl$_2$; in this case the enantioselectivities are lower as a result of the previously described effect of the counterion.[11] When styrene is used as the solvent in the presence of the Laponite catalyst, the yield increases from 30% to 40%, although a dramatic effect on the selectivities is also observed. Under these conditions the less stable *cis*-cyclopropane is obtained preferentially and the enantioselectivity in the *trans* products is noticeably reduced (from 49% to 7% ee). In addition, the direction of the asymmetric induction in *cis*-cyclopropanes is reversed in that it changes from 24% ee in **4R** to 34% ee in **4S**. When the catalyst used in styrene is recovered and reused in dichloromethane, the results are the same as those obtained originally, showing that the changes in selectivity are not due to the catalyst being permanently affected by the reaction.

In an attempt to analyse the origin of this effect, the reaction was carried out in hexane—a solvent of low polarity that is more similar to styrene than to dichloromethane. Under these conditions the yield decreases to 10%, but the *trans–cis* distribution and the enantioselectivities are the same as those obtained using styrene. Finally, we wondered if this effect was exclusive to ligand **6** and we therefore compared the results for the Laponite-containing complex **7**–Cu(II) in reactions carried out in dichloromethane and hexane. The results show the same trend as before; i.e. an increase in the amount of *cis*-cyclopropanes and in products **3S** and **4S**, but the greater steric interaction of the tert-butyl group precludes inversion of configuration in the major products.

The cyclopropanation reaction is catalysed by the bis(oxazoline)–Cu(I) complex, which is obtained by *in situ* reduction of the Cu(II) complex with the diazoacetate. From the Cu(I) complex the rate limiting step is the formation of a Cu(I)–carbene intermediate. This intermediate can either react with a diazoacetate molecule, leading to dimeric by-products, or the carbene can be directly inserted into the styrene double bond to yield the cyclopropanes. The stereochemical course of the reaction, *i.e.* the *trans–cis* distribution and enantioselectivities, is determined in this insertion step.[12] The four possible transition states, leading to four cyclopropanes, are schematically represented in Fig. 3 for the bis(oxazoline) **6**. In this projection, the carbene–Cu(I) complex (Cu=CH–COOEt) is represented by the central circle bonded to the ester group, E. The two oxazoline rings are almost coplanar and they have been represented as a line nearly perpendicular to the E–C$_\alpha$ bond. The phenyl groups correspond to the substituents of the oxazoline rings, with the relative stereochemistry calculated[12] for the intermediate. Finally, the figure represents the incoming styrene and shows the more important steric interactions either with the ester group (always present) or with the Laponite surface (present only in the heterogeneous phase). The selectivities reflect the relative energies of these transition states. In the homogeneous phase, the *trans*-preference (**3**) is explained by the higher energy of the *cis*-transition states as a consequence of the steric interaction between the phenyl group of styrene and the ester group of the carbene (Fig. 3). The preference for the **3R** and **4R** cyclopropanes over their enantiomers **3S** and **4S**, is due to the steric interaction between

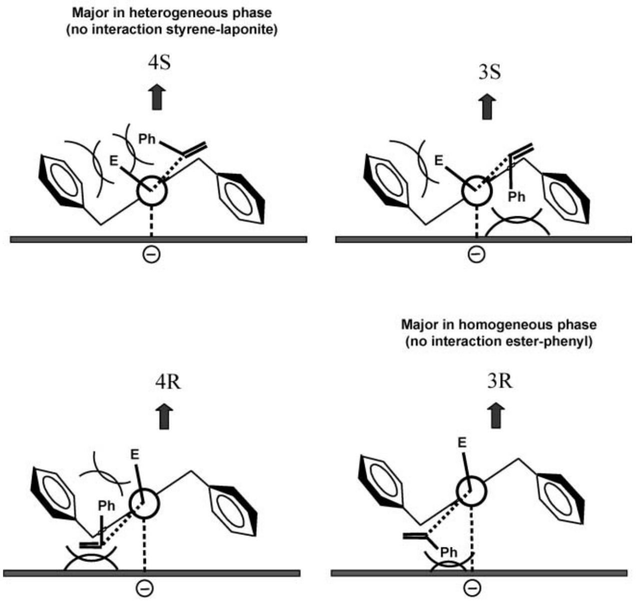

Fig. 3 Proposed model of the steric interactions responsible for the stereoselectivities observed both in homogeneous and heterogeneous phase reactions catalysed by the **6**–Cu(II) complex.

the ester group of the diazoacetate and the R-substituent of the bis(oxazoline), an interaction that is more important in the transition states leading to the **3S** and **4S** products. Similar behaviour is also observed with the Laponite-supported catalysts in dichloromethane. However, when the reaction is carried out in a solvent with a low relative permittivity, the electrostatic attraction between the cationic catalytic species and the clay support increases, meaning that the clay sheet is closer to the intermediate, playing an active role in the stereochemical course of the reaction. When the Cu(I)–carbene intermediate is close to the clay surface, the orientation in which the ester group points away from the surface will be favoured. As styrene approaches this intermediate, not only the previously mentioned steric interactions are important, but the interactions with the clay surface will also play a role. These latter interactions disfavour the formation of *trans*-cyclopropanes and they work in the opposite sense to the former interactions in asymmetric induction. Under these conditions the selectivity will depend on the balance between several sets of interactions. When R = Ph, the intermolecular interactions are weaker and the interactions with the surface dominate the stereochemical course of the reaction, leading to **4S** as the major product. On the other hand, when R = ^{t}Bu, the intermolecular interactions are stronger and the interactions with the surface cannot reverse the stereochemical course of the reaction, so that although the amount of **4S** is increased, it is not the major product. In order to compare the order of magnitude of these interactions, the difference in activation free energies ($\Delta\Delta G^\ddagger$) between the two *trans* and the two *cis* transition states are given in Table 3. When R = Ph, a change of solvent leads to a modification of the $\Delta\Delta G^\ddagger$ values in the range 0.55–0.70 kcal mol^{-1}. These changes are even more important when R = ^{t}Bu (0.67–0.80 kcal mol^{-1}), in spite of the fact that the stereochemical course of the reaction is not reversed. These results prove that the support plays an active role in the reaction and that the stereochemistry is modified when the reaction is carried out in the confined space of the clay.

Another important point to consider is the influence of the nature of the support on the course of the reaction. In the homogeneous phase, the nature of the counterion has a decisive influence on the enantioselectivity[11] and, in this regard, Laponite seems to be worse than triflate‡. Nafion, a perfluorosulfonic resin, has anionic groups similar to triflate but it also has a very low surface area. To overcome this drawback we used Nafion/silica nanocomposites—solids with acidic properties[13] that have also been used as supports for organometallic compounds.[14] These supports have a lower degree of functionalisation than Nafion, but they do have higher surface areas.[15] We used two different Nafion/silica nanocomposites with different degrees of functionalisation and surface areas. Catalysts were modified by cation exchange in methanol of the bis(oxazoline)–Cu(II) complex with the sodium form of Nafion.

Analyses of the resulting solids (Table 4) indicate that the immobilisation in SAC-40 (40 wt% Nafion/silica nanocomposite) leads to a catalyst with a higher copper content and surface area, a situation consistent with the higher degree of functionalisation and surface area of the support. The presence of the complex was demonstrated by IR spectroscopy (Fig. 2).

From our previously gained knowledge of the influence of the counterion, it is not unexpected that the use of SAC-13 (13 wt% Nafion/silica nanocomposite) increases the enantioselectivities of the reactions promoted by **5**–Cu(II) and **6**–Cu(II) (Table 5). In particular, the latter catalyst gives rise to enantioselectivities (57% and 46% ee) that are almost the same as those obtained in the homogeneous phase, and furthermore, it can be recovered and reused with the same results. On the other hand, when **5**–Cu(II) is supported on SAC-13, the recovered catalyst is less active and less enantioselective. Unfortunately, the use of ligand **7**, which gives the best results in the homogeneous phase, leads to very low enantioselectivities (23% and 19% ee). These results are even worse when the catalyst is recovered and reused. Elemental analyses of the mother liquors after catalyst synthesis suggest that the unexpectedly low enantioselectivity is due to the presence of non-chiral copper sites, which are able to promote a concurrent non-enantioselective reaction.

Table 4 Characterisation of the bis(oxazoline)–Cu(II) complexes immobilized on Nafion/silica

Catalyst[a]	Cu/ mmol g^{-1} as prepared	Cu/ mmol g^{-1} after 1 run	2N : Cu	Surface area/ m^2 g^{-1}
5–Cu–(SAC-13)	0.05	0.03	—[b]	82
6–Cu–(SAC-13)	0.08	0.08	—[b]	84
6–Cu–(SAC-40)	0.37	0.35	1.00	377
7–Cu–(SAC-13)	0.07	0.03	—[b]	88
7–Cu–(SAC-40)	0.27	0.26	0.37	395
8–Cu–(SAC-40)	0.31	0.29	1.43	370

[a] Prepared by cation exchange of the bis(oxazoline)–Cu(OTf)$_2$ complex in methanol with the sodium form of the Nafion/silica. [b] The N content is too low for a reliable determination.

Table 5 Results obtained from the cyclopropanation reaction at 25 °C with the Nafion/silica catalysts[a]

Catalyst	Cu (%)	*t*/h	Yield (%)	*trans* : *cis* (**3** : **4**)	Ee (%)[b] *trans*	Ee (%)[b] *cis*
5–Cu–(SAC-13)	0.30	21	34	1.6	49	47
5–Cu–(SAC-13)[c]		46	23	1.6	37	36
6–Cu–(SAC-13)	0.30	9	27	1.9	57	46
6–Cu–(SAC-13)[c]		9	27	1.9	56	45
6–Cu–(SAC-40)	2.2	9	28	1.8	62	50
6–Cu–(SAC-40)[c]		9	30	1.8	57	49
7–Cu–(SAC-13)	0.42	2	28	1.5	23	19
7–Cu–(SAC-13)[c]		2	30	1.6	14	14
7–Cu–(SAC-40)	1.6	2	37	1.5	18	16
7–Cu–(SAC-40)[c]		2	31	1.5	9	11
8–Cu–(SAC-40)[d]	0.93	24	20	2.1	90	84
8–Cu–(SAC-40)[c,d]		24	21	1.9	88	80
7–Cu–(SAC-40)[e]	0.42	24	20	1.9	91	88

[a] Reactions carried out in 1,2-dichloroethane (SAC-13) or dichloromethane (SAC-40) using a 1 : 1 styrene : diazoacetate ratio. [b] Determined by GC using a Cyclodex-B column (ref. 9*b*); **3R** and **4R** are the major enantiomers. [c] Recovered catalyst. [d] It is necessary to heat the reaction until the reduction of Cu(II) takes place. [e] After adding 0.042 eq. of **7**.

The use of SAC-40 as a support allowed us to confirm this hypothesis. Whereas the complex **6**–Cu(II), when immobilised on SAC-40, has the N : Cu ratio expected for a bis(oxazoline)–Cu complex, the immobilisation of **7**–Cu(II) on the same support led to a solid with a very low nitrogen content and a lower N : Cu ratio, a situation consistent with the presence of exchanged Cu(II) that is not complexed by the chiral ligand (Table 4). When these solids were tested as catalysts in the cyclopropanation reaction, the results obtained were found to be in agreement with this observation. The **6**–Cu(II) complex immobilised on SAC-40 gave the same yield and enantioselectivities (62% and 50% ee) as obtained in the homogeneous phase and, furthermore, the catalyst could be recovered and reused with the same results. In comparison with the same complex immobilised on SAC-13, the only advantage of the nanocomposite (with the higher degree of functionalisation and surface area) is a slightly better enantioselectivity. The **7**–Cu(II) complex immobilised on SAC-40 also led to low enantioselectivities (18% and 16% ee), again in agreement with the presence of more than 50% of non-chiral copper centres.

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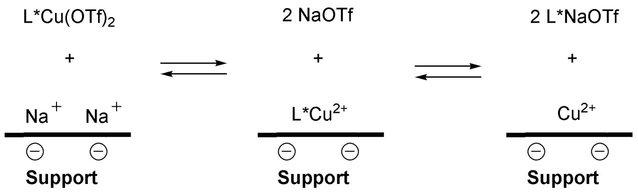
‡The IUPAC name for triflate is trifluoromethanesulfonate.



Scheme 2

Analyses of the SAC-immobilised catalysts after recovery do not show detectable leaching of copper. Furthermore, the above-described filtration experiment shows the absence of a homogeneous reaction.

The results obtained show that it is possible to successfully immobilise the **6**–Cu(II) complex by electrostatic interactions with anionic supports, but also that this strategy fails for the immobilisation of the **7**–Cu(II) complex. One possible explanation for this surprising result is that the formation constant of the **6**–Cu(II) complex is greater than that of the **7**–Cu(II) complex, meaning that all the chiral ligand remains bonded to the copper after cation exchange in the case of **6**. Scheme 2 shows a possible way in which the chiral ligand can leave the complex and pass into the solution. The equilibria will be shifted to right in the case of complexes with low formation constants, such as **7**–Cu(II).

Bearing this possibility in mind, we decided to explore the use of the iminobis(oxazoline) **8**. Given the donor character of the nitrogen atom in the central bridge, this ligand is expected to form a stronger complex with Cu(II) and it is known that these kinds of complexes efficiently promote the enantioselective cyclopropanation reaction in the homogeneous phase.[16] When the **8**–Cu(II) triflate complex was exchanged in methanol with the sodium form of SAC-40, the solid obtained had a 2N : Cu ratio near the theoretical value of 1.5 (Table 4). When this solid was used to promote the cyclopropanation reaction it was found that the rate was quite slow and it was necessary to heat the mixture to achieve the reduction of Cu(II) to Cu(I) by the diazoacetate. This characteristic of the reaction is consistent with strong complexation of the cation. Under these conditions the reaction yield is rather low (20%), but the enantioselectivities are very high (90% and 84% ee) and the recovered catalyst exhibits the same behaviour (Table 5).

Taking this result into account, it may be expected that the enantioselectivity obtained with the **7**–Cu(II) complex immobilised on SAC-13 and SAC-40 would increase if the reaction were carried out in the presence of an additional amount of chiral ligand in solution, in order to shift the equilibrium to the complex form. In fact, under these conditions the enantioselectivities observed are the same as those obtained in the homogeneous phase (91% and 88% ee), although the chemical yield decreases to 20%, a fact indicating that the non-complexed Cu(II) is more active than the bis(oxazoline)–Cu(II) complex. In order to confirm that this reaction is truly heterogeneous, the filtration experiment described above was carried out and further progress of the reaction was not observed in solution.

Conclusions

The results described show that bis(oxazoline)–copper catalysts can be successfully immobilised by the formation of ion-pairs with anionic supports. The results obtained depend on several factors. Firstly, the coordinating ability of the anionic solid is an important property and, in this regard, anions with low basicity seem to be better. Another significant factor is the nature of the chiral ligand, with the strength of complexation being particularly important to avoid the formation of non-chiral catalytic centres. The use of a more coordinating ligand, namely the iminobis(oxazoline), led to the best enantioselectivities found for this reaction with a supported catalyst. Finally, the nature of the solvent can modify the strength of the catalyst–support interaction, which not only modifies the catalytic activity but also the stereochemical course of the reaction as the support becomes closer to the catalytic centres.

In summary, we have shown that ion-pair formation is a suitable strategy to immobilise cationic chiral catalysts, provided that certain key factors are taken into account.

Experimental

2,2′-Isopropylidenebis[(4*S*)-4-benzyl-4,5-dihydro-1,3-oxazole] (**5**) and 2,2′-isopropylidenebis[(4*S*)-4-phenyl-4,5-dihydro-1,3-oxazole] (**6**) were obtained from (*S*)-phenylalaninol and (*S*)-phenylglycinol, respectively, as previously described.[17] 2,2′-Isopropylidenebis[(4*S*)-4-*tert*-butyl-4,5-dihydro-1,3-oxazole] (**7**) was purchased from Aldrich. Bis[(4*S*)-4-*tert*-butyl-4,5-dihydro-1,3-oxazol-2-yl]methylamine was prepared following the method previously described.[16] Laponite was obtained from Laporte Adsorbents. 13 wt% Nafion/silica nanocomposite (SAC-13) was prepared following a slight modification[9b] of the original method.[15]

Preparation of the 40 wt% Nafion/silica nanocomposite (SAC-40)

A mixture of tetramethoxysilane (204 g), distilled water (33 g) and 0.04 M HCl solution (3 g) was stirred for 45 min to give a clear solution. To a Nafion solution (containing 5 wt% Nafion in a mixed alcohol–water solution, from Aldrich) (1200 ml) was added 0.4 M NaOH (150 ml) with stirring. The addition was performed over 15 min and the resulting solution was stirred for an additional 15 min period. The silicon-containing solution was added rapidly to the stirred Nafion-containing solution and, after 10–15 min, the resulting solution gelled. The gel was placed in an oven and dried under a nitrogen flow for about 2 d. The hard glass-like product was ground slightly and passed through a 10-mesh screen. The material was then stirred with 3.5 M HCl (1 l), filtered and washed with water. This last process was repeated three times. The final solid was treated in HNO_3 (20 wt%) at 80 °C for 3 h, washed with water and then dried at 100 °C for 12 h.

The surface area, pore volume, and pore diameter were determined to be 468 $m^2\ g^{-1}$, 1.05 $cm^3\ g^{-1}$, and 8.9 Å, respectively.

Preparation of Laponite-exchanged catalysts

To a solution of bis(oxazoline) (1 mmol) in methanol (20 ml) was added Cu(II) triflate (1 mmol). Laponite (1 g) was slowly added to the above solution and the resulting suspension was stirred at room temperature for 24 h. The solid was separated by filtration, thoroughly washed with methanol and then with dichloromethane, and dried under a flow of air before use.

Preparation of Nafion/silica-exchanged catalysts

Prior to exchange, Nafion/silica nanocomposites were transformed into their sodium forms by passing a solution of 2 M NaCl through a column containing the solid until neutral pH was obtained. The solids were then washed with deionised water and dried under vacuum at 150 °C for about 4 h.

To a solution of bis(oxazoline) (1 mmol) in methanol (10 ml) was added Cu(II) triflate (1 mmol). To this solution was added the corresponding Nafion/silica (1.5 g) and the resulting suspension was stirred at room temperature for 24 h. The solid was separated by filtration, thoroughly washed with methanol and then with dichloromethane, and dried under vacuum.

Characterisation of the materials

Copper analyses were carried out by plasma emission spectroscopy on a Perkin-Elmer Plasma 40 emission spectrophotometer. Nitrogen analyses were carried out on a Perkin-Elmer 240 elemental analyser. Step-scanned X-ray diffraction patterns of oriented samples were collected at room temperature from 3° in 2θ up to 60°, using a D-max Rigaku system with a rotating anode. The diffractometer was operated at 40 kV and 80 mA, and the Cu-Kα radiation was selected using a graphite monochromator. Transmission FT-IR spectra of self-supported wafers evacuated ($<10^{-4}$ Torr) at 50 °C were recorded with a Mattson Genesis Series spectrophotometer. Surface areas were determined by N_2 adsorption (BET) using a Micromeritics ASAP 2000 apparatus.

Cyclopropanation reactions

To a suspension of the appropriate catalyst (amounts of Cu given in Tables 2 and 5) in a solution of styrene (5 mmol) and *n*-decane (100 mg, internal standard) in dichloromethane or *n*-hexane (5 ml), under an argon atmosphere, was added a solution ethyl diazoacetate (2.5 mmol) in the same solvent (0.5 ml) during 2 h using a syringe pump. The reaction was monitored by GC and, after complete consumption of the ethyl diazoacetate, a second portion of this reagent was added in the same way. After completion of the reaction, the catalyst was separated by filtration, washed, dried, and reused following the same method. The products of the reactions were identified by GC as described previously.[9b]

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