Bis(oxazoline)copper Complexes Covalently Bonded to Insoluble Support as Catalysts in Cyclopropanation Reactions

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Chiral bis(oxazolines) are readily dialkylated in the methylene bridge, opening the way to immobilization at that position, keeping the C_2 symmetry of the chiral ligand. Bis(oxazolines) functionalized with two allyl or vinylbenzyl groups are easily grafted onto mercaptopropylsilica. Another approach to immobilization is the polymerization of the ligands bearing vinylbenzyl groups to yield insoluble polymers. The $Cu(OTf)_2$ complexes of the immobilized ligands promote the enantioselective cyclopropanation reaction between styrene and ethyl diazoacetate. The results depend on the nature of the support and the method of immobilization. With regard to the type of solid, the best results, which are similar to or even better than those obtained with the corresponding dibenzylated homogeneous catalysts, are obtained with homopolymers. With regard to the bis(oxazoline), that bearing indan groups leads to good results both onto silica and polymers, whereas with the ligand bearing *tert*-butyl groups good enantioselectivities are only obtained with homopolymeric catalysts. Some of the heterogeneous catalysts can be easily recovered and reused, as much as five times, with the same yield and stereoselectivities.

Introduction

The study of enantioselective reactions promoted by chiral catalysts constitutes a research area of great interest.[1] In this regard, the development of new heterogeneous catalysts to promote enantioselective reactions is important in connection with the application of heterogeneous catalysis in the industrial synthesis of fine chemicals and specialities.[2] There are several strategies available to obtain chiral heterogeneous catalysts, but the grafting of a chiral complex onto an insoluble support is the most widely used. It is known that both the method used to immobilize the complex and the nature of the support have a decisive influence on the catalytic activity and the enantioselectivity of a given system.[3,4] However, very few studies have been undertaken to compare the immobilization of the same complex on different supports and through different strategies.

To undertake such a study, we selected bis(oxazolines), a well-known family of chiral ligands that has been used in a large number of enantioselective reactions.[5] Recently, we showed that cationic complexes bearing bis(oxazoline) ligands can be immobilized onto anionic supports and we studied the scope and limitations of these solids as catalysts in enantioselective cyclopropanation[6] and Diels−Alder reactions.[7] Bis(oxazoline)copper complexes have also been noncovalently immobilized onto Y zeolite and used as catalysts for aziridination reactions.[8] In a preliminary paper, we reported that bis(oxazolines) can be immobilized onto organic supports through a copolymerization process[9] and that the copper complexes

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of these immobilized ligands are efficient catalysts in cyclopropanation reactions. Members of a related family of chiral ligands, azabis(oxazolines), have been attached to soluble organic polymers and used in enantioselective reactions.[10] Very recently, the grafting of bis(oxazolines) onto soluble polymers[11] and the immobilization by copolymerization[12] have been also described. However, no precedents exist concerning covalent immobilization of these kinds of chiral ligands onto inorganic supports.[13] In this paper we compare the immobilization of bis(oxazoline) ligands by different methods: grafting onto silica using two different spacers, and immobilization onto organic supports by both grafting and copolymerization. The corresponding copper-complexes are tested in the benchmark cyclopropanation reaction of styrene with ethyl diazoacetate, one of the reactions in which these ligands form excellent soluble catalysts.[14]

Results and Discussion

Immobilization of Bis(oxazolines) by Grafting onto Silica. Methylenebis(oxazolines) **1** are easily modified by alkylation of the central methylene bridge in the presence of strong bases. Thus, the reactions of bis(oxazolines) with allyl bromide in the presence of methyllithium lead to bis(oxazolines) **2**, which contain two allyl substituents. In this way the C_2 symmetry of the original ligand is maintained. These bis(oxazolines) were immobilized by reaction with mercaptopropylsilica (**3**) in the presence of azoisobutyronitrile (AIBN)[15] following two different strategies (Scheme 1). In the first strategy (route A), the chiral ligand was immobilized and the complex with $Cu(OTf)_2$ was then formed. In the second approach (route B), the complex was formed in solution prior to the immobilization process. Table 1 gathers the results obtained from the analysis of the different immobilized chiral ligands and catalysts.

Surprisingly, the results obtained with the immobilized catalysts strongly depend on the method of grafting used. On using route A, although the immobilization of the bis(oxazoline) ligand takes place with moderate to high yield (Table 1, solids **4**), the complexation with copper leads to solids **6** with very low degree of functionalization. This effect may be due to diffusion limitations imposed by the situation of the ligand in nonaccessible sites, as shown by the drastic decrease in surface area from 475 $m^2\ g^{-1}$ in the original silica to 200−225 $m^2\ g^{-1}$ in solids **4** and **6**.

In an attempt to overcome this limitation we tried to immobilize the copper complex itself (Scheme 1, route B). On using this approach a higher functionalization in copper, at nearly 50%, was achieved (Table 1).

The catalytic performances of the solids **6**, prepared by both strategies, were compared in the benchmark cyclopropanation reaction between styrene and ethyl diazoacetate (Scheme 2) with the corresponding analogous homogeneous catalysts (Table 2, entries 1−8). The reaction conditions were not optimized and equimolecular amounts of both reagents were used only for comparison purposes. In all cases, total conversion of ethyl diazoacetate was observed, with formation of diethyl fumarate and maleate as main side products. With regard to catalytic activity, the solids obtained by route B (Table 2, entries 6−8) gave similar yields to those obtained with the homogeneous catalysts (Table 2, entries 1−3). However, the yields are lower with the catalysts obtained by route A (Table 2, entries 4 and 5), which may be due to the diffusion limitations mentioned above. All of these catalysts led to similar trans/cis selectivity, but the immobilization gives rise to a noticeably decrease in the enantioselectivity (Table 2, entries 1−3 vs 4−8). Surprisingly, the asymmetric induction also depends on the immobilization method, with the solids prepared by route A (Table 2, entries 4 and 5) being more enantioselective than those prepared by route B (Table 2, entries 6 and 7). This different behavior could be associated with differences in the structure of the catalytic site.

To shed some light on this area, we carried out a comparative study of the IR spectra of the homogeneous and the immobilized systems. As can be seen in Figure 1, the bis(oxazoline) ligand **2b** and the homogeneous complex **5b** show a C═N band near 1650 cm^{-1} and a series of weaker bands in the region 1400−1525 cm^{-1}. These bands are also observed in the ligand immobilized by route A (**4b**). Complexation of **4b** with copper does not modify the spectrum (not shown), a fact that is not unexpected given the very low degree of copper functionalization. However, the catalyst immobilized by route B (**6b**) shows a marked reduction of the C═N band, indicating the partial loss of the oxazoline structure. Complexation with $Cu(OTf)_2$, a Lewis acid, increases the electrophilic character of the C═N bond and favors its reaction with different nucleophiles present on the solid surface, such as thiol and silanol groups or residual water.

In an attempt to improve the results, we tried to increase the size of the spacer between the bis(oxazoline) and the support. This was achieved by using *p*-vinylbenzyl instead of allyl group (Scheme 1). In view of the results discussed above it was decided to test only route A. As can be seen from the results in Table 1, the chiral ligands **7** are grafted with good yields (solids **8**) but once again the complexation with copper (solids **9**) leads to very low degrees of functionalization. The solids **9** were tested in the same cyclopropanation reaction and the results were compared with the corresponding homogeneous systems (Table 2, entries 9−14). The nature of the substituents in the methylene bridge has a noticeable influence on the results obtained with homogeneous catalysts. This fact can be seen by comparing the results for ligands **2** and **10**. The presence of a benzyl instead of an allyl group leads to a reduction in enantioselectivity

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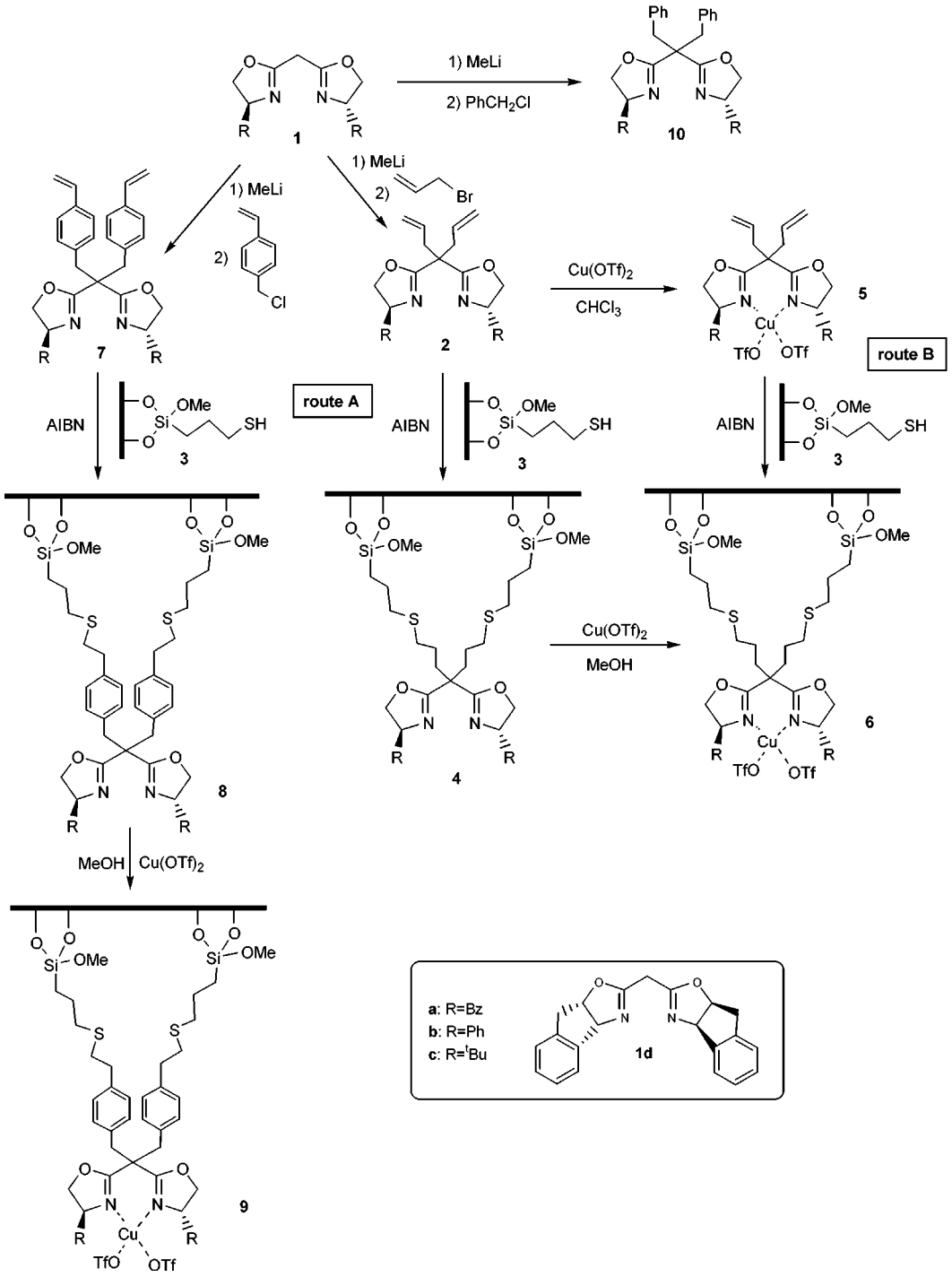
Scheme 1. Immobilization of Bis(oxazoline)copper Complexes onto Silica



with bis(phenyloxazoline) (**2b** and **10b**), despite the use of a larger amount of catalyst **10b**-$Cu(OTf)_2$. On using bis(*tert*-butyloxazoline) (**2c** and **10c**), the normal trans preference of the cyclopropanation is reversed to a cis preference. The enantioselectivities are also modified, with a slight decrease and increase in trans and cis isomers, respectively. As far as the heterogeneous catalysts are concerned, the use of a longer spacer does not significantly influence the cyclopropanation results (Table 2, entries 5 and 12). The best results are obtained with **9d**, which arises from the grafting of **7d**, in agreement with the results obtained in homogeneous phase with ligands **10**. Compound **9c**, on the other hand, leads to disappointingly low enantioselectivities. After the results described by Rechavi and Lemaire,[13] the immobilized ligand **8c** was treated with *N*-trimethylsilylimidazole and then with $Cu(OTf)_2$. This catalyst showed the same results than the nonsililated material, excluding in this way the role of the free silanol groups of the silica support in the poor results of this ligand.

The IR spectra of the different solids **8** do not show noticeable differences, and so analysis of the solids was carried out by Raman spectroscopy, a useful method for the study of organic molecules immobilized on different supports.[4] The Raman spectra (Figure 2) show bands corresponding to the bis(oxazoline), in particular the C=N band near 1600 cm^{-1}. However, solid **8c** also shows a band at 1631 cm^{-1}, which can be assigned to a C=C deformation and it is present in the Raman spectrum of **7**. This band is not present in the spectra of the rest of

Table 1. Analysis of the Ligands and Catalysts Immobilized onto Silica[a]

solid	route	S[b] (mmol/g)	N[b] (mmol/g)	Cu[c] (mmol/g)	% DF[d]
3		1.09			
4a	A	0.97	0.58		60
4b	A	0.91	0.84		92
6a	A	0.88	0.52	0.08	18
6b	A	0.83	0.75	0.10	24
6a	B	0.92	0.44	0.23	49
6b	B	0.93	0.48	0.22	48
6c	B	0.92	0.47	0.22	48
8b	A	0.89	0.72		82
8c	A	0.91	0.68		75
8d	A	0.90	0.66		74
9b	A	0.88	0.70	0.04	5
9c	A	0.89	0.67	0.07	8
9d	A	0.87	0.64	0.04	5

[a] Silica has a surface area of 475 $m^2\ g^{-1}$, which decreases upon grafting of the complexes. All the silicas obtained have surface areas in the range 200−225 $m^2\ g^{-1}$. [b] Determined by elemental analysis. [c] Determined by plasma emission spectroscopy. [d] Degree of functionalization in ligand or copper referred to the thiol functionalization.

Scheme 2. Cyclopropanation Reaction between Styrene and Ethyl Diazoacetate

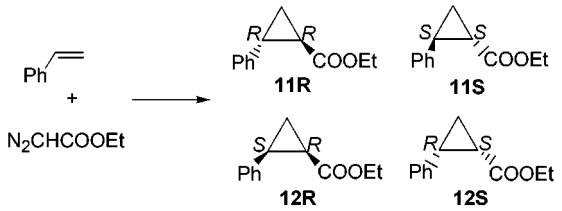


Table 2. Results Obtained from the Cyclopropanation Reaction between Styrene and Ethyl Diazoacetate Catalyzed by Silica-Based Catalysts[a]

			yield[b]		ee[c] (%)	
entry	catalyst	diazo/Cu	(%)	trans/cis[b]	trans[d]	cis[e]
1	**2a**-$Cu(OTf)_2$	100	40	62:38	29	33
2	**2b**-$Cu(OTf)_2$	100	36	68:32	60	50
3	**2c**-$Cu(OTf)_2$	100	58	67:33	80	72
4	**6a** (route A)	100	29	62:38	15	18
5	**6b** (route A)	100	28	64:36	29	31
6	**6a** (route B)	100	36	63:37	9	14
7	**6b** (route B)	100	37	66:34	10	10
8	**6c** (route B)	100	47	68:32	26	27
9	**10b**-$Cu(OTf)_2$	10	32	70:30	50	40
10	**10c**-$Cu(OTf)_2$	50	46	33:67	70	79
11	**10d**-$Cu(OTf)_2$	125	49	58:42	83[f]	86[g]
12	**9b**	1720	24	62:38	33	32
13	**9c**	983	19	60:40	6	12
14	**9d**	1720	35	47:53	52[f]	65[g]

[a] Using equimolecular amounts of styrene and ethyl diazoacetate at room temperature. [b] Determined by GC. Total conversion of ethyl diazoacetate. [c] Determined by GC with a Cyclodex-B column. [d] **11R** is the major isomer. [e] **12R** is the major isomer. [f] **11S** is the major isomer. [g] **12S** is the major isomer.

the silica-immobilized ligands. The presence of this band indicates that the bis(oxazoline) is bound to the support, at least in part, by only one benzyl arm. This change in the structure of the immobilized ligand may account for the difference observed in copper functionalization and enantioselectivity.

In view of the limitations found in grafting onto silica, we turned our attention toward the use of organic supports.

Immobilization of Bis(oxazolines) onto Organic Polymers. The grafting of the bis(oxazoline) **1b** onto an organic support was carried out using the same general strategy as described above, namely alkylation in the methylene bridge. However, in this case a chloromethylated polystyrene-divinylbenzene resin (1% cross-linking, 1 mmol Cl g^{-1}) was used as the alkylating agent (Scheme 3). The IR spectrum of the resulting solid (**13b)** shows the absence of the C−Cl band at 1265 cm^{-1} and the presence of the C=N band at 1655 cm^{-1}. The amount of ligand, 0.54 mmol g^{-1} determined by nitrogen analysis, is consistent with double alkylation of most of the bis(oxazoline) ligand. In contrast with silica-supported bis(oxazolines), ligand **13b** is able to complex the expected amount of copper (Table 3). However, this immobilized complex is less active and less enantioselective (Table 4, entry 3) than the corresponding homogeneous system. It is also important to note that the polymer-grafted catalyst **13b**-$Cu(OTf)_2$ leads to lower enantioselectivity than the analogous catalyst grafted on silica (**9b)** (Table 2, entry 11).

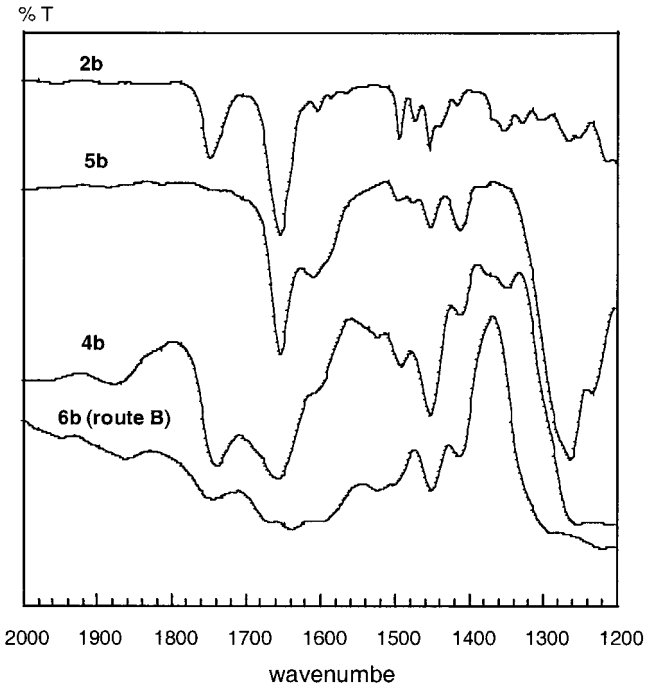


Figure 1. Infrared spectra of ligand **2b**, complex **5b**, and solids **4b** and **6b** (method B).

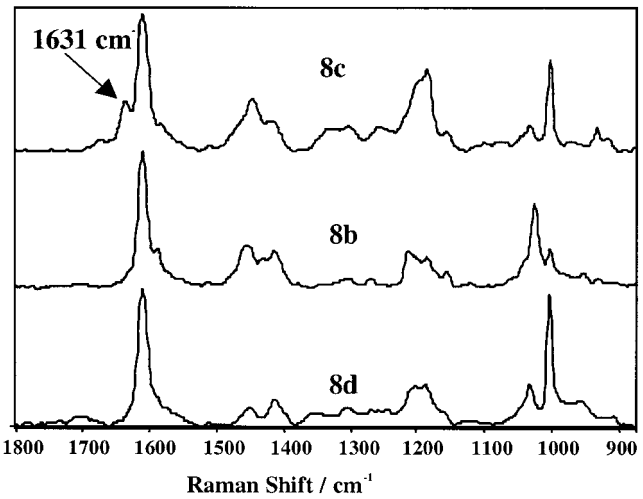
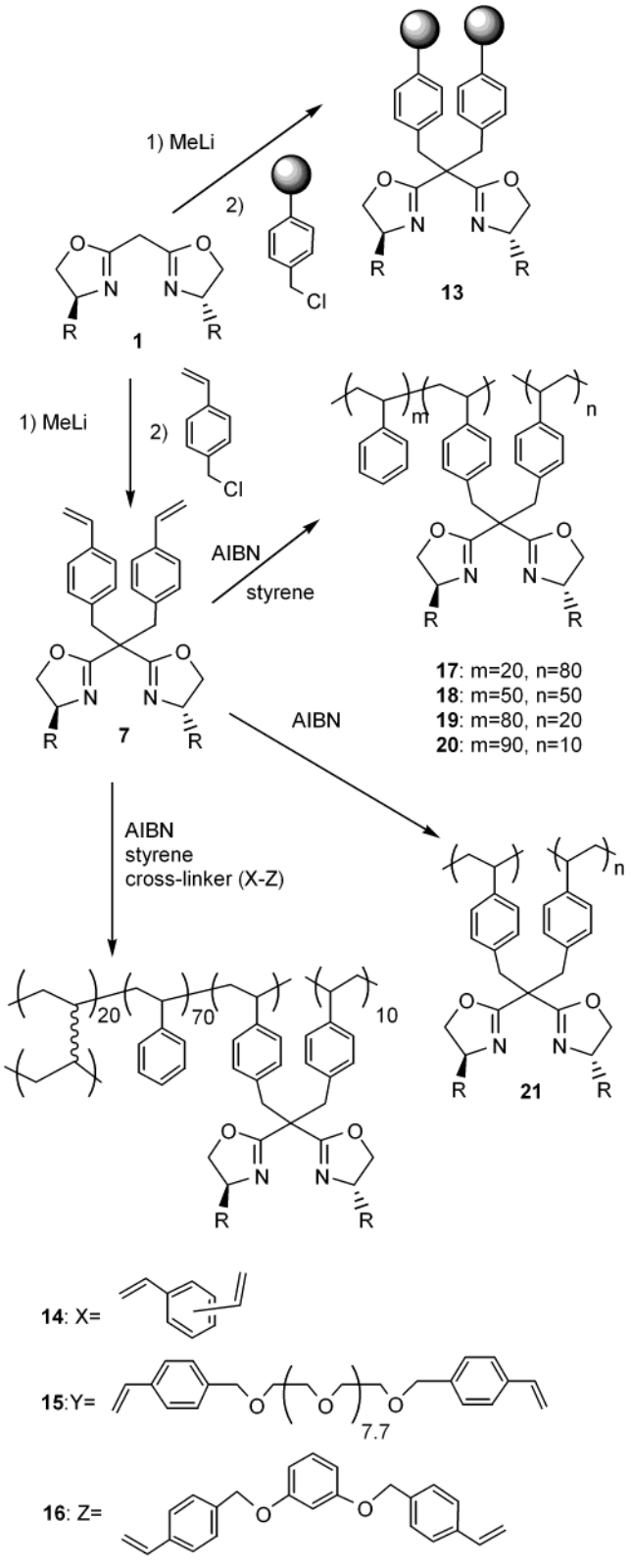


Figure 2. Raman spectra of solids **8b**−**d**.

Scheme 3. Preparation of Polymeric Bis(oxazoline) Ligands by Grafting and Polymerization



In the preparation of polymer-supported enantioselective catalysts, polymerization has provided, in some cases, better results than grafting,[4,16] so we decided to use bis(oxazolines) **7** to prepare copolymers.[17] Monomers were copolymerized with styrene and different cross-linking agents by following the protocol for the preparation of monolithic resins developed by Frechet.[18] To

Table 3. Solids Obtained by Grafting onto Chloromethylated Polystyrene-Divinylbenzene (13) or Polymerization with the Chiral Monomers 7b−d and 22c (Schemes 3 and 4)[a]

	composition of the mixture				
polymer	chiral monomer	styrene	cross-linker[b]	Cu (mmol g^{-1})	% DF[c]
13b		(grafted)		0.44	98
14b	10 (**7b**)	70	20 (X)	0.19	36
15b	10 (**7b**)	70	20 (Y)	0.18	51
16b	10 (**7b**)	70	20 (Z)	0.04	9
17b	80 (**7b**)	20	0	0.16	15
18b	50 (**7b**)	50	0	0.09	9
19b	20 (**7b**)	80	0	0.11	14
20b	10 (**7b**)	90	0	0.39	64
21b	100 (**7b**)	0	0	0.14	13
21c	100 (**7c**)	0	0	0.08	7
21d	100 (**7d**)	0	0	0.03	3
23c	10 (**22c**)	0	90 (X)	0.08	16
24c	10 (**22c**)	40	50 (X)	0.08	15
25c	10 (**22c**)	70	20 (X)	0.07	13

[a] At 80 °C using 60% (w/w) of a mixture toluene/dodecanol (1/5 w/w) as a porogen and 1% AIBN. Quantitative yields of the polymers were obtained in all cases. [b] In parentheses the cross-linker used: X = divinylbenzene; Y = di(vinylbenzyl)polyethyleneglicol; Z = O,O′-di(vinylbenzyl)resorcinol. [c] Degree of functionalization in copper referred to the ligand content.

Table 4. Results Obtained from the Cyclopropanation Reaction between Styrene and Ethyl Diazoacetate Catalyzed by Polymeric Catalysts[a]

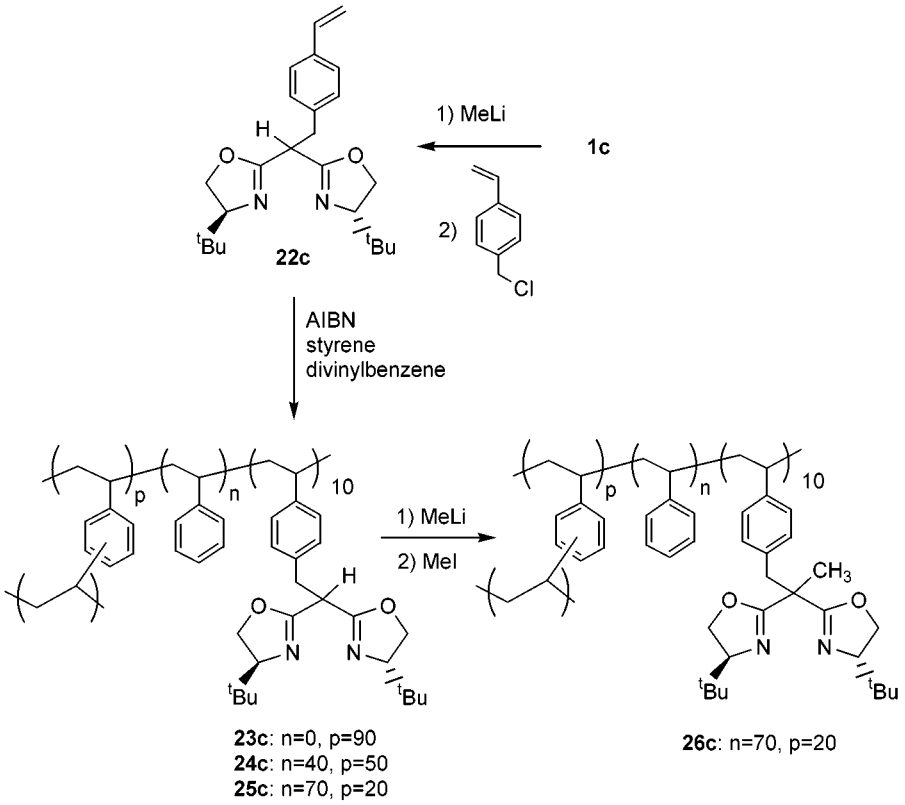
						ee[c] (%)	
entry	ligand	diazo/Cu	run	yield[b] (%)	trans/cis[b]	trans[d]	cis[e]
1	**10b**	10	1	32	70:30	50	40
2	**10c**	50	1	46	33:67	70	79
3	**10d**	125	1	49	58:42	83[g]	86[h]
4	**13b**	122	1[f]	18	66:34	26	21
5	**14b**	176	1[f]	11	71:29	18	18
6	**15b**	95	1[f]	32	67:33	8	8
7	**16b**	428	1	12	58:42	50	46
8	**17b**	208	1	26	57:43	56	51
9	**18b**	371	1	18	57:43	57	51
10	**19b**	304	1	20	60:40	46	42
11	**20b**	86	1	28	60:40	46	42
12			2	24	60:40	43	41
13	**21b**	510	1	40	52:48	57	53
14			3	19	53:47	47	49
15	**21c**	796	1	36	37:63	78	72
16			3	33	36:64	75	72
17	**21d**	2630	1	35	44:56	69[g]	75[h]
18			2	22	44:56	69[g]	75[h]
19	**23c**	417	1	11	58:42	28	33
20	**24c**	417	1	15	56:44	45	44
21	**25c**	477	1	21	57:43	29	34
22	**26c**	550	1	16	60:40	23	22

[a] Using equimolecular amounts of styrene and ethyl diazoacetate. Reaction carried out at room temperature unless otherwise indicated in the table. The catalysts were prepared by treatment of the ligand with $Cu(OTf)_2$. [b] Determined by GC. Total conversion of ethyl diazoacetate. [c] Determined by GC with a Cyclodex-B column. [d] **11R** is the major isomer. [e] **12R** is the major isomer. [f] At 60 °C. [g] **11S** is the major isomer. [h] **12S** is the major isomer.

(16) (a) Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J. M. J. *J. Org. Chem.* **1990**, *55*, 304−310. (b) Kamahori, K.; Tada, S.; Ito, K.; Itsuno, S. *Tetrahedron*: *Asymmetry* **1995**, *6*, 2547−2555.

(17) Copolymerization could not be carried out with allylic monomers **2** because they have a polymerization rate very slow in comparison with that of styrene.

Scheme 4. Preparation of Polymers with Bis(oxazoline) Ligands in the Main Chain



compare different polymerization conditions, initial experiments were carried out with bis(oxazoline) **7b**. Table 3 shows the conditions used for the synthesis of each polymer. Catalysts were obtained by treatment of the polymeric ligand with $Cu(OTf)_2$ and the data for copper incorporation are also given in Table 3.

It is important to note that all the polymers are cross-linked because the bifunctionalization of the chiral monomer makes it act as a cross-linker. In general the incorporation of copper is low, probably as a consequence of the high degree of cross-linking. Typical values for the copper content are in the range 0.04−0.16 mmol g^{-1}, corresponding to 7−15% of the maximum copper functionalization. This situation occurs even with polymer **19b**, which contains only 20% of chiral monomer as a cross-linking agent. There are two possible explanations for this low degree of copper incorporation. One possibility would be the result of a high reactivity of the chiral monomer, which could then be incorporated in the inner part of the polymer particles and lead to low accessibility. The other possibility involves a distorted disposition of the majority of the chiral ligand due to the double bonding to the polymer. Such a situation could prevent the formation of a chelate complex, with the copper being washed out in the catalyst preparation process. Exceptions to this trend include polymers **14b** and **15b**, which contain other cross-linking agents. In these cases, the copper content is not markedly higher, but it represents a higher proportion in comparison with the maximum functionalization. Finally, polymer **20b**, with only 10% cross-linking by its own chiral monomer, is the only catalyst with high copper content in both absolute (0.39 mmol g^{-1}) and relative terms. Higher accessibility and greater flexibility could account for the higher copper content in this case.

All the immobilized catalysts were tested in the cyclopropanation reaction between styrene and ethyl diazoacetate. The results in Table 4 show that, in the case of polymers containing a nonchiral cross-linker, both the activity and enantioselectivity strongly depend on the nature of the cross-linker. The use of a longer cross-linker seems to lead to a more enantioselective catalyst, as deduced from the comparison between **14b** and **16b** (Table 4, entries 4 and 6). However, polymer **15b** leads to low values of enantiomeric excess (Table 4, entry 5). In this case, the presence of a poly(ethylene glycol) chain, which is able to form nonchiral complexes with copper, accounts for this result. This hypothesis is also consistent with the unexpectedly high relative copper content in this polymer. This result is in strong contrast with the high enantioselectivities obtained when bis(oxazolines)[11] or azabis(oxazolines)[10] are bonded to soluble PEG.

The polymers prepared with the chiral bis(oxazoline) as the only cross-linker (**17b**−**20b**) are more active and give rise to enantioselectivities (Table 4, entries 8−11) that are similar to those obtained with the analogous homogeneous catalyst (Table 4, entry 1). The catalysts can be recovered and reused, as demonstrated with polymer **20b** (Table 4, entries 11 and 12). A particularly interesting result concerns the enantioselectivities. These values increase as the amount of bis(oxazoline) in the polymer increases. In view of this fact, we decided to explore the use of homopolymers, obtained using bis(oxazolines) **7** as the sole monomers. Despite the low copper content, polymers **21b**, **21c**, and **21d** efficiently

(18) (a) Svec, F.; Fréchet, J. M. J. *Chem. Mater.* **1995**, *7*, 707−715. (b) Svec, F.; Fréchet, J. M. J. *Science* **1996**, *273*, 205−211. (c) Xie, S.; Svec, F.; Fréchet, J. M. J. *Chem. Mater.* **1998**, *10*, 4072−4078. (d) Svec, F.; Fréchet, J. M. J. *Ind. Eng. Chem. Res.* **1999**, *38*, 34−48. (e) Hird, N.; Hughes, I.; Hunter, D.; Morrison, M. G. J. T.; Sherrington, D. C.; Stevenson, L. *Tetrahedron* **1999**, *55*, 9575−9584.

promote the cyclopropanation reaction and lead to enantioselectivities that are similar to, or even better than, their homogeneous counterparts (Table 4, entries 1 and 2 vs 13 and 15). Moreover the catalysts are recyclable, particularly catalyst **21c**, which does not show any loss of activity or selectivity. In the conditions of equimolecular amounts of reagents, the catalysts show a decline in activity after the third run because of the coordination of byproducts detected by IR. The life of the catalysts can be enlarged by using a 5-fold excess of styrene in the cyclopropanation reaction, leading to higher yields, in the range of 55−75%, and stability during five runs. It is important to note the reversal of the trans/cis selectivity with the homogeneous system with **10c** and the related polymeric catalyst from **21c**. This behavior was not observed with the silica-immobilized catalyst **9c** (Table 2, entry 13) and it is difficult to find a simple explanation. The trans/cis selectivity is also reduced with the dibenzylated bis(oxazoline) **10d** derived from indan and a reversal is observed with the polymer **21d**. Polymeric catalysts derived from **7b** gave rise to a similar trend and a reduction in the trans preference was observed. However, reversal of the trans/cis selectivity is not seen in this case. These results show the importance of the bulkiness of the substituents in the methylene bridge and in the oxazoline rings for the stereoselectivity of the cyclopropanation reaction.

Despite the good results obtained, the polymeric catalysts suffer from the drawback of low copper content. This fact must be related to the situation of the chiral ligand in places that are difficult to access, i.e., corresponding to cross-linking points, despite of the fact that a porogen is used. To overcome these problems, we tried to obtain polymers in which the chiral ligand is situated in the main chain by using monofunctionalized bis(oxazolines) (Scheme 4). This strategy was applied to the chiral ligand that led to the best enantioselectivity. However, this methodology was not found to improve the incorporation of copper into polymers **23**−**25**, as can be seen from the results in Table 3. The results obtained in the cyclopropanation reaction depend on the composition of the polymerization mixture. A higher yield was obtained with the less cross-linked polymer (**25c**), but it is difficult to find a clear relationship between composition and enantioselectivity. Polymer **25c** was treated with methyllithium and methyl iodide in order to obtain a polymer **26c** with bis(oxazoline) moieties with two substituents in the central methylene bridge placed in the main chain of the polymer. However, the results obtained in the cyclopropanation reaction (entry 22 in Table 4) are even slightly worse than those obtained with **25c**.

Conclusions

Bis(oxazolines) can be readily immobilized on silica and organic polymers by means of appropriate functionalization of the methylene bridge. Copper complexes of the immobilized chiral bis(oxazolines) can act as catalysts of the cyclopropanation reactions. The results obtained with the catalysts grafted onto mercaptopropylsilica depend on both the spacer used (allylic or benzylic) and the immobilization method. With regard to organic polymers, monolithic polymerized catalysts are better than those grafted onto flexible polymers. The composition of the mixture of monomers has an enormous influence on the results. The best results in terms of activity, enantioselectivity and recoverability were observed for homopolymers **21b**, **21c** and **21d**. With these polymers enantioselectivites up to 78% e.e. were obtained with a catalyst that can be reused five times with the same results. Although some chiral ligands must be situated in inaccessible sites, the use of doubly functionalized bis(oxazolines) is advantageous, probably due to the conservation of the C_2 symmetry in the immobilized catalyst.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra ($CDCl_3$, δ (ppm), J (Hz)) were obtained at 300 and 75 MHz, respectively, in a Varian Unity 300 and a Bruker ARX 300 apparatus. Specific rotations were measured with a Perkin-Elmer 241MC polarimeter. Quantitative elemental analyses were performed in duplicate on a Carlo Erba EA1108 CHNS-O instrument. Copper analyses were carried out by plasma emission spectroscopy on a Perkin-Elmer Plasma 40 emission spectrometer. Transmission FTIR spectra of self-supported wafers of silica-based solids evacuated ($<10^{-4}$ Torr) at 50 °C were obtained with a Mattson Genesis series FTIR spectrometer. FTIR spectra of KBr pellets of the polymers were recorded on a Perkin-Elmer 2000 FTIR spectrometer. Surface area was measured by BET method[19] on a Micromeritics Flowsorb 2300 apparatus. Raman spectra of polymers and silicas were obtained on the Raman accessory FT-Raman Perkin-Elmer Na:YAG Laser PSU for the same instrument. Gas chromatography was carried out on two Hewlett-Packard 5890 chromatographs, equipped with FID detector and cross-linked methyl silicone (25 m × 0.2 mm × 0.33 μm) and Cyclodex B (30 m × 0.25 mm × 0.25 μm) columns.

Preparation of the Modified Chiral Ligands. 2,2′-(1-Allylbut-3-enylidene)bis[(4*S*)-4-benzyl-4,5-dihydro-2-oxazole] (2a). Methyllithium (2.2 mmol) was added to a solution of 2,2′-methylenebis[(4*S*)-4-benzyl-4,5-dihydro-2-oxazole] (**1a**) (1 mmol) in anhydrous THF at −55 °C under argon atmosphere, and the resulting solution was stirred for 1 h. Allyl bromide (2.2 mmol) was then added dropwise, and the reaction was stirred at −10 °C for 3 h. The mixture was washed with a saturated NH_4Cl solution, the organic layer was dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography using an end-capped silica[20] and *n*-hexane/diethyl ether (9:1) as an eluent. Yield: 87%. ^{1}H NMR: 7.4−7.2 (m, 10H), 5.63 (m, 2H), 5.11 (m, 4H), 4.40 (m, 2H), 4.15 (dd, 2H, $J_1 = 7.5$, $J_2 = 7.5$), 3.98 (dd, 2H, $J_1 = 7.5$, $J_2 = 7.4$), 3.13 (dd, 2H, $J_1 = 12.0$, $J_2 = 3.8$), 2.71 (d, 4H, $J = 7.3$), 2.59 (dd, 2H, $J_1 = 12.0$, $J_2 = 3.8$). ^{13}C NMR: 167.6, 138.5, 133.5, 130.0, 129.2, 127.1, 119.3, 72.5, 67.9, 42.3, 38.1, 31.6. Anal. Calcd for $C_{27}H_{30}N_2O_2$: C, 78.2; H, 7.3; N, 6.8. Found: C, 78.4; H, 7.2; N, 7.0. $[\alpha]_D = -95.1$ (*c* 1.045, $CHCl_3$).

2,2′-(1-Allylbut-3-enylidene)bis[(4*S*)-4-phenyl-4,5-dihydro-2-oxazole] (2b). Using the same procedure from 2,2′-methylenebis[(4*S*)-4-phenyl-4,5-dihydro-2-oxazole] (**1b**). Yield: 85%. ^{1}H NMR: 7.3−7.2 (m, 10H), 5.82 (m, 2H), 5.22 (dd, 2H, $J_1 = 10.1$, $J_2 = 7.7$), 5.13 (m, 4H), 4.64 (dd, 2H, $J_1 = 10.1$, $J_2 = 8.4$), 4.09 (dd, 2H, $J_1 = 8.4$, $J_2 = 7.7$), 2.87 (d, 4H, $J = 7.9$). ^{13}C NMR: 168.0, 142.2, 132.9, 128.7, 127.6, 126.8, 118.9, 75.2, 69.7, 46.1, 37.7. Anal. Calcd for $C_{25}H_{26}N_2O_2$: C, 77.7; H, 6.8; N, 7.2. Found: C, 77.9; H, 7.0; N, 7.1. $[\alpha]_D = -107.0$ (*c* 1.06, $CHCl_3$).

2,2′-(1-Allylbut-3-enylidene)bis[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (2c). Using the same procedure from 2,2′-methylenebis[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (**1c**). Yield: 79%. ^{1}H NMR: 5.71 (m, 2H), 5.08 (m, 4H), 4.12 (dd, 2H, $J_1 = 9.9$, $J_2 = 8.4$), 3.99 (dd, 2H, $J_1 = 8.4$, $J_2 = 7.8$), 3.82 (dd, 2H, $J_1 = 9.9$, $J_2 = 7.8$), 2.76 (dd, 2H, $J_1 = 12.3$, $J_2 = 8.0$), 2.65 (dd, 2H, $J_1 = 12.3$, $J_2 = 8.0$), 0.82 (s, 18H). ^{13}C NMR:

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166.2, 133.2, 118.5, 75.5, 68.6, 45.7, 37.4, 33.8, 25.8. Anal. Calcd for $C_{21}H_{34}N_2O_2$: C, 72.8; H, 9.9; N, 8.1. Found: C, 72.6; H, 10.0; N, 7.9. $[\alpha]_D = -101.5$ (*c* 0.4, $CHCl_3$).

2,2′-(1-Benzyl-2-phenylethylidene)bis[(4*S*)-4-phenyl-4,5-dihydro-2-oxazole] (10b). Methyllithium (2.2 mmol) was added to a solution of 2,2′-methylenebis[(4*S*)-4-phenyl-4,5-dihydro-2-oxazole] (**1b**) (1 mmol) in anhydrous THF at −55 °C under argon atmosphere, and the resulting solution was stirred for 1 h. Benzyl chloride (2.2 mmol) was then added dropwise, and the reaction was heated under reflux for 4 h. The mixture was washed with a saturated NH_4Cl solution, the organic layer was dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography using an end-capped silica[17] and *n*-hexane/ethyl acetate (10:1) as an eluent. Yield: 88%. ^{1}H NMR: 7.25 (m, 20H), 5.04 (t, 2H, J = 9.4), 4.50 (t, 2H, J = 8.7), 3.88 (t, 2H, J = 8.7), 3.40 (m, 4H). ^{13}C NMR: 167.4, 136.3, 136.2, 136.0, 130.6, 128.3, 127.2, 126.6, 125.9, 74.9, 69.4, 48.7, 38.8. Anal. Calcd for $C_{33}H_{30}N_2O_2$: C, 81.5; H, 6.2; N, 5.8. Found: C, 81.6; H, 6.3; N, 5.7.

2,2′-(1-Benzyl-2-phenylethylidene)bis[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (10c). Using the same procedure from 2,2′-methylenebis[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (**1c**). Yield: 76%. ^{1}H NMR: 7.25 (m, 10H), 4.06 (dd, 2H, J_1 = 9.9, J_2 = 8.4), 3.97 (dd, 2H, J_1 = 8.4, J_2 = 7.5), 3.78 (dd, 2H, J_1 = 9.9, J_2 = 7.5), 3.44 (d, 2H, J = 14.1), 3,15 (d, 2H, J = 14.1), 0.82 (s, 18H). ^{13}C NMR: 166.2, 137.1, 130.5, 127.9, 126.5, 75.6, 68.3, 53.4, 39.3, 33.9, 25.8. Anal. Calcd for $C_{29}H_{38}N_2O_2$: C, 80.0; H, 8.6; N, 6.3. Found: C, 79.8; H, 8.5; N, 6.2.

[3a*R*-[2(3′a*R,8′a*S**),3′aα,8′aα]]-2,2′-(1-Benzyl-2-phenylethylidene)bis[3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole] (10d).** Using the same procedure from [3a*R*-[2(3′a*R**,8′a*S**),3′aα,8′aα]]-2,2′-methylenebis[3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole] (**1c**). Yield: 86%. ^{1}H NMR: 7.5−6.9 (m, 18H), 5.59 (d, 2H, J = 8.0), 5.28 (dd, 2H, J_1=8.0, J_2=6.7), 3.32 (dd, 2H, J_1=18.5, J_2=6.7), 3.23 (d, 2H, J = 14.4), 3,06 (d, 2H, J = 14.4), 3.05 (d, 2H, J = 18.5). ^{13}C NMR: 167.1, 141.5, 139.8, 136.0, 130.2, 128.4, 127.7, 127.5, 126.3,125.9, 125.1, 83.4, 76.4, 47.5, 39.3, 38.0. Anal. Calcd for $C_{35}H_{30}N_2O_2$: C, 82.3; H, 5.9; N, 5.5. Found: C, 82.6; H, 6.1; N, 5.4.

2,2′-[2-(4-Vinylphenyl)-1-(4-vinylbenzyl)ethylidene]bis-[(4*S*)-4-phenyl-4,5-dihydro-2-oxazole] (7b). Using the same procedure described for **10b** with 4-vinylbenzyl chloride as the alkylating agent. The product is easily polymerizable and only a small amount was purified for analytical identification. ^{1}H NMR: 7.3−7.1 (m, 14H), 6.84 (m, 4H), 6.61 (dd, 2H, J_1 = 17.7, J_2 = 10.6), 5.70 (d, 2H, J = 17.7), 5.15 (d, 2H, J = 10.6), 5.07 (t, 2H, J = 9.4), 4.52 (t, 2H, J = 8.7), 3.89 (t, 2H, J = 8.7), 3.41 (m, 4H). ^{13}C NMR: 167.4, 141.5, 136.3, 136.2, 130.6, 130.4, 128.3, 127.2, 126.6, 125.9, 113.5, 74.9, 69.5, 48.7, 38.9. Anal. Calcd for $C_{37}H_{34}N_2O_2$: C, 82.5; H, 6.4; N, 5.2. Found: C, 83.0; H, 6.5; N, 5.0.

2,2′-[2-(4-Vinylphenyl)-1-(4-vinylbenzyl)ethylidene]bis-[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (7c). Using the same procedure described for **10c** with 4-vinylbenzyl chloride as the alkylating agent. The product is easily polymerizable and only a small amount was purified for analytical identification. ^{1}H NMR: 7.33 (d, 4H, J = 8.0), 7.25 (d, 4H, J = 8.0), 6.71 (dd, 2H, J_1=17.8, J_2=10.9), 5.74 (d, 2H, J = 17.8), 5.22 (d, 2H, J = 10.9), 4.10 (dd, 2H, J_1=9.9, J_2=8.8), 3.99 (dd, 2H, J_1=8.8, J_2=7.8), 3.85 (dd, 2H, J_1=9.9, J_2=7.8), 3.48 (d, 2H, J = 14.1), 3,19 (d, 2H, J = 14.1), 0.87 (s, 18H). ^{13}C NMR: 165.6, 136.5, 135.6, 130.4, 125.9, 125.6, 113.0, 75.5, 68.3, 48.2, 39.1, 33.9, 25.8. Anal. Calcd for $C_{33}H_{42}N_2O_2$: C, 79.5; H, 8.5; N, 5.6. Found: C, 79.9; H, 8.5; N, 5.4.

[3a*R*-[2(3′a*R,8′a*S**),3′aα,8′aα]]-2,2′-[2-(4-Vinylphenyl)-1-(4-vinylbenzyl)ethylidene]bis[3a,8a-dihydro-8*H*-indeno-[1,2-*d*]oxazole] (7d).** Using the same procedure described for **10c**, from **1d** with 4-vinylbenzyl chloride as the alkylating agent. The product is easily polymerizable and only a small amount was purified for analytical identification. ^{1}H NMR: 7.7−7.5 (m, 8H), 7.12 (d, 4H, J = 10.9), 6.93 (d, 4H, J = 10.9), 6.78 (dd, 2H, J_1 = 17.8, J_2 = 10.7), 5.86 (d, 2H, 7.3), 5.85 (d, 2H, J = 17.8), 5.54 (t, 2H, J = 7.2), 5.41 (d, 2H, J = 10.7), 3.59 (dd, 2H, J_1 = 18.7, J_2 = 7.1), 3.52 (d, 2H, J = 15.2), 3.32 (d, 2H, J = 18.7), 3.29 (d, 2H, J = 15.2). ^{13}C NMR: 167.4, 141.7, 140.0, 136.8, 135.9, 135.7, 130.5, 128.6, 127.7, 126.0, 125.7, 125.4, 113.2, 83.8, 76.7, 47.9, 39.6, 38.9. Anal. Calcd for $C_{39}H_{34}N_2O_2$: C, 89.2; H, 6.1; N, 5.0. Found: C, 89.5; H, 6.0; N, 5.0.

2,2′-[2-(4-Vinylphenyl)ethylidene]bis[(4*S*)-4-*tert*-butyl-4,5-dihydro-2-oxazole] (22c). Using the same procedure described for **7c** but only 1.1 mmol of methyllithium and 4-vinylbenzyl chloride were used. The product is easily polymerizable and only a small amount was purified for analytical identification. ^{1}H NMR: 7.32 (d, 2H, J = 8.9), 7.23 (d, 2H, J = 8.9), 6.62 (dd, 1H, J_1 = 18.5, J_2 = 11.7), 5.65 (d, 1H, J = 18.5), 5.16 (d, 1H, J = 11.7), 4.09 (dd, 4H, J_1 = 29?, J_2 = 21?), 3.99 (t, 1H, J = 9.0), 3.82 (dd, 2H, J_1 = 20?, J_2 = 10?), 3,21 (t, 2H, J = 9.0), 0.82 (s, 9H), 0.81 (s, 9H). ^{13}C NMR: 163.8, 163.4, 137.7, 136.4, 135.7, 129.0, 125.9, 113.1, 75.4, 68.4, 41.2, 35.5, 33.5, 25.7. Anal. Calcd for $C_{24}H_{34}N_2O_2$: C, 75.3; H, 8.9; N, 7.3. Found: C, 75.2; H, 8.9; N, 7.4.

Immobilization on Silica Gel. Synthesis of Mercaptopropylsilica (3). To a suspension of 4 g of silica gel (Merck 60, 63−200 nm, dried at 140 °C under vacuum) in anhydrous toluene (25 mL) under argon atmosphere were added dropwise dry pyridine (6 mL) and 3-mercaptopropyltrimethoxysilane (2.75 g, 14 mmol). The suspension was heated under reflux for 40 h, and the solid was separated by filtration and washed with toluene, THF, and *n*-hexane. After drying, the content of sulfur (1.09 mmol g^{-1}) was determined by elemental analysis.

Immobilization of Functionalized Bis(oxazolines) by Route A (4a,b, 8b−d). To a suspension of mercaptopropylsilica (**3**) (1 g, 1.09 mmol) in chloroform (15 mL) under argon atmosphere were added 1.09 mmol of the corresponding bis(oxazoline) (**2a**,**b**, **7b**−**d**) and 0.08 mmol of azoisobutyronitrile. The suspension was heated under reflux for 40 h, and the solid was separated by filtration and washed with dichloromethane and toluene. The method was repeated once. After drying, the content of chiral ligand (Table 1) was determined by elemental analysis.

Preparation of Immobilized Copper Complexes (6 and 9). To a suspension of the immobilized bis(oxazoline) (**4** or **8**) a solution of $Cu(OTf)_2$ (stoichiometric amount) in anhydrous methanol (approximately 1 M) was slowly added. The mixture was stirred at room temperature for 24 h. The solid was separated by filtration, washed with methanol, and dried under vacuum at 50 °C. The copper content (Table 1) was determined by plasma emission spectroscopy.

Immobilization of Bis(oxazoline)copper Complexes by Route B. A mixture of bis(oxazoline) (**2**) (1.09 mmol) and $Cu(OTf)_2$ (1.09 mmol) in anhydrous chloroform (5 mL) was stirred at room temperature under argon atmosphere until complete solution. This solution was added to a suspension of mercaptopropylsilica (**3**) (1 g, 1.09 mmol) in chloroform (10 mL), and finally 0.08 mmol of azoisobutyronitrile was also added. The suspension was heated under reflux for 40 h, and the solid was separated by filtration and washed with dichloromethane. After drying, the content of chiral ligand was determined by elemental analysis and copper content by plasma emission spectroscopy (Table 1).

Preparation of Polymeric Catalysts. Preparation of Polymer-Grafted Bis(oxazoline) (13b). The method described for the synthesis of **10b** was followed but using 0.3 g of a chloromethylated resin (polystyrene-divinylbenzene, 1% cross-linking, 1.04 mequiv g^{-1}) as the alkylating agent. The mixture was heated under reflux for 40 h, and the solid was separated by filtration and thoroughly washed with THF, dichloromethane, and methanol and dried under vacuum at 50 °C. The content of chiral ligand was determined by elemental analysis (Table 3).

Immobilization of Bis(oxazolines) by Polymerization (14−25). A mixture of monomers (composition in Table 3), toluene, and 1-dodecanol (ratio 40:10:50 w/w) was placed in a glass mold and purged with nitrogen in the presence of azoisobutyronitrile (1% w/w). The mold was closed and heated at 80 °C for 24 h. The mold was broken, and the polymer was extracted with THF in a Soxhlet apparatus. The content of chiral ligand was determined by elemental analysis (Table 3).

Preparation of Polymeric Catalysts. To a suspension of the polymer (**14** to **25**) in methanol was added a solution of $Cu(OTf)_2$ (stoichiometric amount) in the same solvent. The mixture was stirred at room temperature for 24 h. The solid was separated by filtration, washed with methanol, and dried under vacuum at 50 °C. The copper content (Table 3) was determined by plasma emission spectroscopy.

Cyclopropanation Reactions. To a suspension of the corresponding catalyst in a solution of styrene (358 mg, 3.44 mmol) and *n*-decane (150 mg, internal standard) in dichloromethane (3.5 mL) at room temperature under argon atmosphere was added ethyl diazoacetate (196 mg, 1.72 mmol) in the same solvent (0.5 mL) during 2 h using a syringe pump. Reactions at 60 °C were carried out in 1,2-dichloroethane. The reaction was monitored by gas chromatography, and after consumption of the diazoacetate, a second portion of this reagent was added in the same way (the diazoacetate/Cu ratio is given in Tables 2 and 4). After the reaction was finished, the catalyst was separated by filtration, washed with dichloromethane, and air-dried. Some catalysts were reused under the same conditions. The results were determined by gas chromatography as described elsewhere.[6,9]

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