

# Enantioselective catalysis of Diels–Alder reactions by heterogeneous chiral bis(oxazoline) catalysts

Dalit Rechavi, Marc Lemaire\*

*Laboratoire de Catalyse et de Synthèse Organique (U.C.B.L.-C.P.E.), Inst. de Rech. sur la Catalyse, Université C. Bernard Lyon CPE, 43 bld du 11 Novembre 1918, 69622 Villeurbanne Cedex, France*

Received 6 July 2001; accepted 22 October 2001

## Abstract

We report here two heterogenization methods of a chiral bis(oxazoline) (BOX) ligand: (a) by grafting onto an inorganic (silica) surface, and (b) by its polymerization as a polyurethane chain polymer. The activity and enantioselectivity of both polymers as catalysts for the Diels–Alder reaction were checked, and it was shown that under certain conditions enantioselectivities similar to those of the homogeneous catalyst are reached. It has also been shown that under the same conditions the catalyst can be recycled without loss of activity or selectivity. © 2002 Elsevier Science B.V. All rights reserved.

*Keywords:* Asymmetric heterogeneous catalysis; Enantioselective Diels–Alder reactions; Chiral bis(oxazoline) ligands

## 1. Introduction

Chiral bis(oxazoline) (BOX) ligands and their application as catalysts have been the subject of extensive research during the last decade [1]. Ligands of this type show excellent enantioselectivities for a wide range of reactions [1]. In particular, they are enantioselective for Diels–Alder reactions [2–4], with enantioselectivities of up to 90–99% ee.

One of the disadvantages of the BOX catalysts, however, is that a large catalyst to substrate ratio is needed to accomplish most reactions. It is clear that for such catalysts to be practically useful they should be recycled, and this can best be done by their heterogenization. A successful heterogenization will also lead to a cleaner process, which will not leave

any catalyst (ligand or metal) contamination in the products of the reaction.

Recently, several heterogenizations of BOX ligands were reported in the literature. Chronologically, non-covalent heterogenizations were reported first. Mayoral and co-workers report the immobilization of BOX ligands by cationic exchange on clays and on nafion or nafion–silica nanocomposites, and their use in cyclopropanation reactions. They achieve good enantioselectivities in some cases, but recycling is often difficult, probably due to leaching of the active species [5–8]. Hutchings and co-workers report a modification of copper-exchange zeolite Y with BOX ligands, which gives only moderate enantioselectivities in aziridination of alkenes [9–13]. And very recently Fraile et al. attempted to perform enantioselective Diels–Alder reactions, using the same systems they used for the cyclopropanation reaction, but obtaining only 11% ee [14].

Covalent heterogenizations were first published in the year 2000. Burguete et al. functionalized the bridge

\* Corresponding author. Tel.: +33-4-72-43-14-07;  
fax: +33-4-72-43-14-08.  
E-mail address: marc.lemaire@univ-lyon1.fr (M. Lemaire).

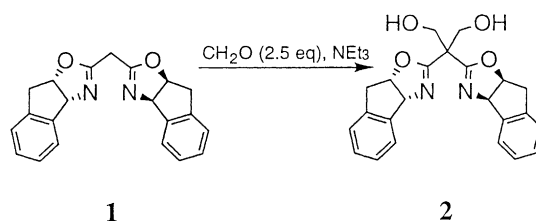
of BOX ligands with two styrene moieties, which were then homopolymerized or copolymerized with styrene. They tried these polymers in the cyclopropanation reaction, obtaining an interesting inversion of the *cis*–*trans* selectivity, even if their enantioselectivities were not as high as those of other heterogeneous systems for the same reaction [15].

Two works have been published recently which use polyethylene glycol (PEG) functionalized BOX ligands. The reactions in this case were performed in a homogeneous environment, and the polymers were then precipitated by the addition of a suitable solvent. Glos and Reiser introduced polyethylene glycol chains on the nitrogen bridge of aza-bis(oxazolines), and used the resulting polymers in cyclopropanation reactions, obtaining good enantioselectivities, and showing their ability to recycle the polymers over 15 cycles [16]. And very recently Annunziata et al. describe the immobilization of BOX ligands on PEG polymers, which were then tested in cyclopropanation reactions and in ene-reactions, giving good enantioselectivities, and also in the Diels–Alder reaction, giving only moderate enantioselectivities (up to 45%) [17].

We present here two heterogenizations of a BOX ligand: (a) by grafting onto an inorganic surface (silica) [18], and (b) by polymerization as part of the main chain of a polyurethane backbone. We apply these heterogenized catalysts to the Diels–Alder reaction, and obtain good enantioselectivities.

## 2. Results and discussion

We chose to heterogenize indaBOX (**1**) since due to its rigidity it gives especially good enantioselectivities for several reactions, and especially for the Diels–Alder reaction [4,19–21]. It was prepared according to a known procedure [4]. In order to achieve heterogenization, the ligands were functionalized on the carbon bridge between the two oxazoline moieties, in a way that will neither disturb the C<sub>2</sub> symmetry of the ligand, nor interfere with the catalytic site. The simplest way to introduce polymerizable functional groups seemed to be the double addition of formaldehyde to the active carbon, as shown in Scheme 1. We were inspired for this reaction by Guzaev [22], who reacted  $\beta$ -diketones with formaldehyde to obtain the same functionalization. We managed to obtain **2** by



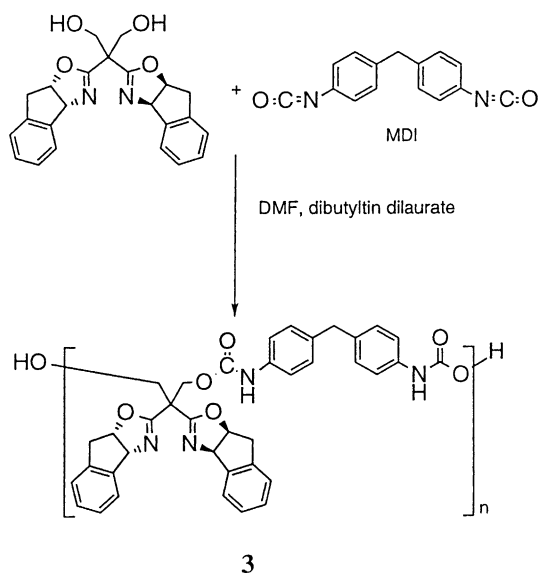
Scheme 1.

a facilitated version of this procedure, using solid formaldehyde instead of a freshly prepared formaldehyde solution (20% in water). IndaBOX-diol (**2**) was obtained in 75–85% yield.

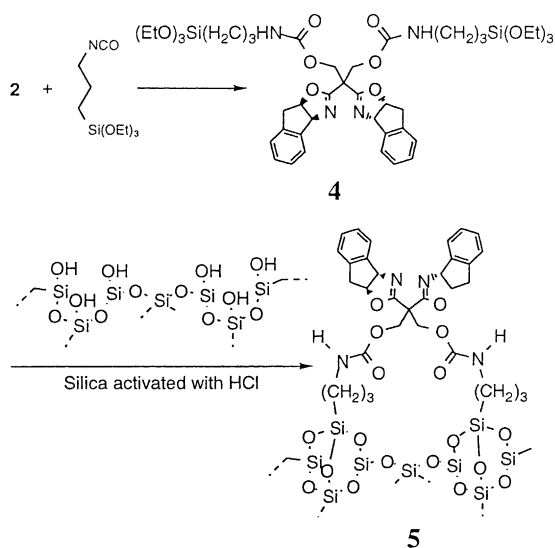
We then compared two strategies of heterogenization: polymerization as a polyurethane, and grafting onto an activated silica surface.

Reaction of diol **2** with MDI, catalyzed by dibutyltin dilaurate, gave polyurethane **3**, with a yield of 65% (Scheme 2).

Grafting on silica was done in a similar manner, by the reaction of 3-(isocyanatopropyl)triethoxysilane with **2** [23]. The resulting **4** was not purified—it was reacted directly with a silica (Matrex<sup>®</sup> Si-60 from Millipore, particle size 70–200  $\mu$ m) activated previously with HCl, to obtain **5**, with a degree of



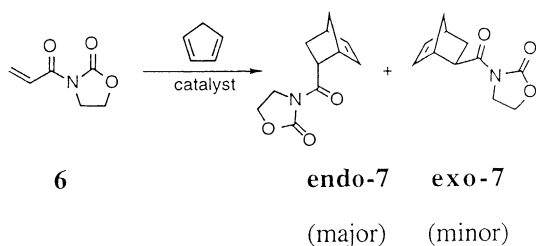
Scheme 2.



Scheme 3.

functionalization of 0.24–0.25 mmol ligand/g **5** (Scheme 3). The overall yield for the last two steps is 71–75% (determined by microanalysis).

We chose to test both polymers as catalysts of the well-known Diels–Alder reaction of 3-acryloyl-2-oxazolidinone (**6**) with cyclopentadiene (CPD), shown in Scheme 4 [24]. Polymer **3** (8 mol% relative to **6**) was mixed with  $\text{Cu}(\text{OTf})_2$  in  $\text{CH}_2\text{Cl}_2$  for 1–4 h, then cooled to  $-78^\circ\text{C}$ . 3-Acryloyl-2-oxazolidinone and CPD were then added one after the other, and the reaction was left 4 h at  $-78^\circ\text{C}$ , then allowed to warm to room temperature slowly overnight. The first three reaction cycles gave 51–56% ee, with quantitative yield, and about 90% selection towards the endo enantiomer (entries 1–3 in Table 1). The fourth cycle showed a complete loss of enantioselectivity (entry 4, Table 1).



Scheme 4.

Table 1  
Recycling of catalyst **3**, using  $\text{Cu}(\text{OTf})_2$  as metal precursor<sup>a</sup>

Entry	Cycle	Conversion (%)	Endo (%)	ee (%) <sup>b</sup>
1	1	100	89	51
2	2	99	90	56
3	3	99	90	56
4	4	99	87	0

<sup>a</sup> Temperature:  $-78^\circ\text{C}$  to RT.

<sup>b</sup> %ee of the endo isomer. The ee was determined by HPLC on Chiralcel-OD column with 95 heptane:5 isopropanol as the eluant. Absolute configuration: (+)-2R [2,25].

In addition, the polymer's appearance changed, and it looked worn-out. IR spectra also indicated that the polymer's composition had changed.

The catalyst grafted on silica (**5**) gave 87% ee at  $-78^\circ\text{C}$  (entry 1, Table 2). Even at a higher temperature ( $0^\circ\text{C}$ ) it gave better enantioselectivities (65–70% ee) than **3** at  $-78^\circ\text{C}$ . But here too the enantioselectivity went down on the fourth reaction cycle (entries 2–5, Table 2).

It occurred to us at this point that the reason for the unsatisfactory enantioselectivities after several recycling sessions may be the reaction's high sensitivity to water: both the polyurethane and the silica are hygroscopic by nature. Ghosh et al. have recently shown that, when  $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  is used as the metal precursor, the reaction is not sensitive to water [19]. We therefore used this as the metal in our system. The silica grafted **5** was mixed with the metal overnight at ambient temperature. The dienophile was added, and mixed for 30–60 min, cooled to  $0^\circ\text{C}$ , and treated with freshly cracked CPD. As opposed to the previous experiments, no efforts were made to keep the catalyst **5** dry: the reaction was conducted in  $\text{CH}_2\text{Cl}_2$ , not redistilled and not under inert atmosphere, and at the end of the reaction the catalyst was washed with the same solvent, and used as is for the next cycle, not dried. We obtained much better results with this system, with improved enantioselectivities, which did not diminish after four cycles (entries 6–9, Table 2).

It has previously been shown that in some cases protecting the free silanol groups of the silica with silanes increases the activity and the enantioselectivity of the reaction (e.g. for the addition of  $\text{Et}_2\text{Zn}$  to aldehydes catalyzed by amino alcohol ligands [26]). We therefore modified the silica surface using *N*-trimethylsilylimidazole (TMSIM) [27]. The protection



Table 3

The influence of protection of silanol groups, of ligand to metal ratio, and of temperature on enantioselectivity when  $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  is used to form the catalyst<sup>a</sup>

Entry	Catalyst	Equivalence of $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (eq.)	Temperature (°C)	Time (h)	Endo (%)	ee (%)
1	<b>5</b>	1	RT	1	85	65
2	<b>5'</b>	1	RT	1	86	71
3	<b>5''</b>	1	RT	1	86	81
4	<b>5''</b>	1	−78	3	86	92
5	<b>5</b>	2	RT	1	88	54
6	<b>5'</b>	2	RT	1	88	39

<sup>a</sup> The conversion is of 99–100% for all reactions.

unprotected silica **5** gave 54% ee (entry 5, Table 3), about 10% less than the ee obtained when a ratio of 1:1 was used. Under the same conditions (a 2:1 ratio), silica **5'** gave only 39% ee (entry 6, Table 3), 30% less than it gave under normal conditions, i.e. the protected silica is more sensitive to an excess of metal. The metal in the system can be located in three places: (1) coordinated to the ligand; (2) coordinated by the silanol groups; (3) free in the solution. The first case is the only one which catalyzes the reaction in an enantioselective manner. The second case is less accessible to the substrates, and therefore will catalyze the unwanted non-enantioselective reaction less than the third case. This explains why silica **5'** is more sensitive than silica **5** to an excess of metal: the free silanol groups on silica **5** coordinate with the excess metal, and therefore its catalytic activity is slow.

The difference in the enantioselectivities of catalysts **5** and **5''** can be explained either by the presence of the free silanol groups of the silica in **5**, which act as a non-enantioselective catalyst and reduce the enantioselectivity, or by a change in the environment of the catalyst in **5''** due to the presence of the protecting TMS groups. We checked whether the first explanation is sufficient by conducting simultaneously two experiments with the *homogeneous* ligand **1**, adding non-functionalized silica to one of the flasks but keeping all other conditions identical. The enantioselectivity of the reaction in the flask which contained the silica was much lower (66.5% ee) than that of the reaction in the flask which did not contain any silica (80.5% ee). Indeed, the results obtained are surprisingly similar to those of entries 1 and 3 in Table 3. The difference in enantioselectivities between **5** and **5''** can thus be explained mainly on the basis of

competitive racemic catalysis of the reaction by complexes involving the silanol groups of the silica.

When working with  $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  we usually worked with 10 mol% catalyst to substrate (entry 1, Table 4). Using 20 mol% catalyst does not improve the enantioselectivity (entry 2, Table 4), but reducing it to 5 mol% has surprisingly little effect on the enantioselectivity (entry 3, Table 4). It is known that the homogeneous indaBOX ligand gives 98% ee (at −78 °C) for the same reaction as long as 10 mol% of the catalyst are used [19], but that it goes down to 92% ee when only 5 mol% of the catalyst are used. It can be concluded that the major impediment to an increase in the enantioselectivity of our system is the accessibility of the silica-grafted ligand.

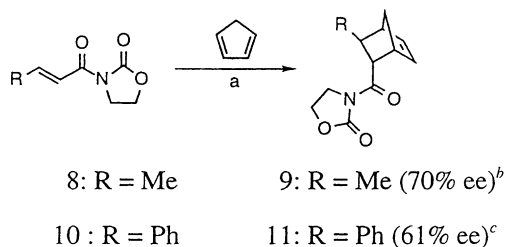
We tried using different metal precursors in the same model reaction, but they did not produce good results:  $\text{Sc}(\text{OTf})_3$  and  $\text{Yb}(\text{OTf})_3$  gave no enantiomeric excess, whereas  $\text{Co}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  gave a product of 16% ee, and  $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  gave only 11% ee.

In order to show the general nature of the reaction, several other substrates were tried. The results are presented in Scheme 6. For substrate **8** [28] an ee of 70% was observed, compared with 84% ee for the homogeneous ligand [19]. Substance **11** [28] was formed

Table 4  
The influence of the catalyst to substrate ratio

Entry	Catalyst (mol%) <sup>a</sup>	Conversion (%)	Endo (%)	ee (%)
1	10	>99	86	71
2	20	>99	89	71
3	5	>99	88	68

<sup>a</sup> Catalyst **5'** was used at RT.



<sup>a</sup> 1 Sili-indaBOX: 1 Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (10 mol%); CH<sub>2</sub>Cl<sub>2</sub>, rt. <sup>b</sup> after 3 hr.: 70% yield (GC), 96% endo, 70% ee (2R) (HPLC on chiralcel OD, 10% isopropanol in heptane). <sup>c</sup> reacted for 50 hr.; isolated on silica column with 0 to 25% EA in pentane. 63% Isolated yield; 79% endo, 61% ee (2S), calculated according to  $\alpha_D$  in CCl<sub>4</sub> (measured  $\alpha_D = 109^\circ$ ), by comparison with the literature.[29],[30].

Scheme 6.

with 61% ee (no experiments with the parallel homogeneous system are reported in the literature; however, when Cu(OTf)<sub>2</sub> was used with the homogeneous ligand and only 35% ee were obtained [4]).

### 3. Conclusion

We have shown in this paper that indaBOX (**1**) can be heterogenized either as part of a chain polyurethane polymer or by grafting onto silica. The silica grafted catalyst gave better enantioselectivities than the polyurethane catalyst. The obtained catalyst can then be efficiently recycled if Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O is used as the metal precursor. In this case the catalyst is very robust. Best results were obtained when the silanol groups of this silica catalyst were protected by TMS groups. In this case we obtain 81% ee at room temperature, and 92% ee at  $-78^\circ\text{C}$ . These results, although not quite as good as those obtained by the homogeneous system, are better than any achieved so far with heterogeneous BOX ligands for the Diels–Alder reaction. We suggest that this may be because (a) our ligand is symmetrically functionalized on the bridge, leaving the ligand with a pseudo C<sub>2</sub> symmetry, and not causing asymmetrical distortions in the active site, (b) our ligand is grafted onto the solid surface in a way that forces the active site to face away from the surface, and (c) the chains linking the ligand with the silica are long enough, leaving the ligand far enough from the surface and enabling relatively good accessibility to the ligand. Our system has the advantage

of being compatible with air humidity, and reactions as well as filtrations can be easily performed with no need for special conditions. The catalyst is ready for reuse directly after filtration. Other ways of heterogenizing the functionalized ligand **2** as well as other applications of this system to reactions such as cyclopropanation and aziridination are currently being explored in our laboratory.

### 4. Experimental

NMR spectra were taken using a Bruker AC 200 or 300 MHz. Peaks are given in ppm, and *J* is in Hz. Melting points were measured with a Kofler heating system (type WME). Elemental analysis was obtained from the Service Central d'Analyse of the CNRS (Solaize, France). IR spectra were taken with a Perkin-Elmer "Spectrum 1" spectrometer.

Preparation of indaBOX-diol (**2**): 2.843 g of indaBOX (**1**) (1 eq.) and 0.647 g of paraformaldehyde (2.5 eq.) were weighed into a 100 ml flask. CH<sub>2</sub>Cl<sub>2</sub> (34 ml) was added, a CaCl<sub>2</sub> tube was adjusted, and the suspension was stirred. Dioxane (8.6 ml) and H<sub>2</sub>O (1.6 ml) were added, followed by a solution of Et<sub>3</sub>N (3.4 ml) in THF (24.5 ml), which was added over a period of 1–3 h. The solids dissolved gradually during the period of the addition. The solution was mixed for 3 days at RT, then poured into 150 ml of pentane. A precipitate appeared at once. It was filtered, washed with pentane, water, and pentane again, and left to dry in the air. Compound **2** was obtained in 75–85% yield.

IR (cm<sup>-1</sup>): 3649, 3174 (br), 1652, 1479, 1459, 1372, 1210, 1195, 1167, 1080, 1016, 855, 746, 713, 650.

NMR (peaks in ppm, *J* in Hz): 7.45 (2H, m), 7.30 (6H, m), 5.54 (2H, d, *J* = 8), 5.27 (2H, dd, *J*<sub>1</sub> = 8, *J*<sub>2</sub> = 4), 3.96 (4H, AA' system, *J* = 12), 3.38 (2H, dd, *J*<sub>1</sub> = 7, *J*<sub>2</sub> = 18), 3.03 (2H, d, *J* = 18), 1.65 (2H, br s (OH)).

Microanalysis: Anal. Calcd.: C, 70.75%; H, 5.68%; N, 7.17%; O, 16.39%. Found: C, 68.76%; H, 5.72%; N, 7.02%; mp 169 °C, corrected by comparison to benzimidazole (mp 163 °C).

Preparation of PU-indaBOX (**3**): **2** (0.125 g, 1 eq.) and MDI (0.0642, 1 eq.) were dissolved in dry DMF (1.8 ml), under Ar. Dibutyltin dilaurate (15–30 μl) was added and the reaction was heated to 80 °C for 24 h, then poured into MeOH (20 ml). A white solid formed at once. It was cooled, filtered, and washed with ca. 30 ml of MeOH. We obtained **3** in 66% yield. Drying in vacuum does not remove all the water, which can be observed in the NMR spectrum. The NMR spectrum is too complex to give clear assignments, but the IR spectrum shows an absorption around 1650 cm<sup>-1</sup>, typical of a BOX motive, and an absorption at 1510 cm<sup>-1</sup>, typical of the carbamate moiety present in polyurethanes.

IR (cm<sup>-1</sup>): 3360, 3025, 2913, 1648, 1610, 1509, 1412, 1308, 1231, 1200, 1018, 997, 812, 751.

NMR in DMSO (peaks in ppm, *J* in Hz): 6.7–7.4 (aromatic protons, m), 4.9–5.5 (oxazoline CH protons, m), 3.4–3.9 (CH<sub>2</sub>-OCN protons + CH<sub>2</sub> of MDI protons, m), 2.9–3.4 (CH<sub>2</sub>-Ar of BOX, in superposition with H<sub>2</sub>O).

Microanalysis: Found: C, 75.4%; H, 5.7%; N, 9.97%.

IR after use: 3348–2925 (br), 2336, 1779, 1697, 1598, 1537, 1509, 1412, 1279, 1227, 1165, 1029, 759, 639.

Preparation of activated silica: Silica (Matrex<sup>®</sup> Si-60 from Millipore, particle size 70–200 μm, ca. 13 g) was refluxed with HCl (33%, 50 ml) for ca. 2 h. It was filtered and washed with water. After drying (vacuum, 70–80 °C, 24 h), about 10–11 g of activated silica were obtained.

Preparation of catalyst **5** —grafting of ligand **2** onto silica: The functionalized ligand **2** (1.5 mmol, 0.5857 g) was dissolved in dry DMF (approximately 7 ml) and dry Et<sub>3</sub>N (0.75 ml, 5 mmol), under Ar. 3-(Isocyanatopropyl)triethoxysilane (3.3 mmol,

0.8175 g, 0.82 ml) was added over a period of 10–20 min, at RT. The solution was stirred for ca. 48 h. A polystyrene-NH<sub>2</sub> resin (0.8715 g of 1.1 mmol NH<sub>2</sub>/g resin) was added in order to capture the excess isocyanate. The mixture was stirred for another hour, following which the amine resin was filtered off and washed with CH<sub>2</sub>Cl<sub>2</sub>. The solvents (including most of the DMF) were evaporated, and the resulting oil was added to a suspension of activated silica (4.00 g) in toluene (30 ml). The suspension was refluxed overnight, then filtered through a sinter and washed with toluene followed by ethyl acetate and CH<sub>2</sub>Cl<sub>2</sub>. After drying overnight in vacuum, 4.6720 g of the resulting catalyst were obtained.

IR (cm<sup>-1</sup>): 3429, 2981 (very small), 1648 (oxazolines), 1095 (very br), 800, 476.

IR taken after use for catalysis of the reaction of **6** with CPD, using Cu(OTf)<sub>2</sub> or Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O—essentially the same (sometimes small peaks at 1780, 1700 indicated the presence of some product or substrate which were not entirely washed away).

Microanalysis: Found: C, 9.65%; H, 1.72%; N, 1.41%; Si, 38.85% (O: the rest = 48.37%).

Since there are exactly four nitrogen atoms per ligand and the ratio mmol ligand/g **5** can be calculated as follows:

$$0.0141 \times \frac{\text{g N to g } \mathbf{5}}{14.007 \text{ g N to mol N} \times 4 \text{ mol N to mol ligand}} \times 1000 \text{ mmol/mol} = 0.252 \text{ mmol ligand/g } \mathbf{5}$$

Weight of silica recuperated	4.5016 g.
Overall mmol of indaBOX	1.13 mmol.
Yield from indaBOX-diol	(1.13/1.5) × 100 = 75.5%.

Catalyst **5'**: protecting the silanol groups of catalyst **5**. Catalyst **5** (1 g) was mixed in TMSIM (4.7 ml, 0.032 mol) for 1 h. It was filtered and washed with MeOH (5 × 20 ml). After drying in vacuum overnight the catalyst weighed 1.0125 g, and was analyzed: C, 12.36%; H, 2.06%; N, 1.41%; Si, 37.40%, i.e. 0.252 mmol ligand/g **5'**.

IR (cm<sup>-1</sup>): 3434 (smaller than the same peak for **5**, indicating less OH groups), 2964 (CH<sub>3</sub>), 1655 (oxazolines), 1091 (very br), 845, 802, 758, 474.

Catalyst **5''** was prepared in a similar manner, but mixing for 72 h.

Microanalysis: C, 12.69%; H, 2.22%; N, 1.22%; Si, 35.33%, i.e. 0.217 mmol ligand/g **5''**.

IR: similar to that of **5'**, but the peak of CH<sub>3</sub> is relatively bigger.

%Cu before use of the silica (calculated from amounts of catalyst **5''** and Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O put at 1/1 molar ratios): 1.46%.

%Cu according to elemental analysis after use: 1.21%, i.e. ratio of Cu to ligand after use is 1.46/1.21 = 1.21. This is the molar ratio usually used for homogeneous catalysis.

Products **6**, **8**, **10** were prepared according to the literature.

Preparation of **7**—test of catalytic activity of **3**: as a first try we took **3** (0.0379 g) and Cu(OTf)<sub>2</sub> (0.0205 g, 8 mol%), in 10 ml CH<sub>2</sub>Cl<sub>2</sub>, and mixed for 3.5 h at RT. The polymer swelled, and became slightly brown, then yellow-green, then green. The reaction mixture was cooled to ca. -78 °C, and dienophile **4** (0.1000 g, 0.7086 mmol, 1 eq.) was added, followed by freshly cracked cyclopentadiene (0.24 ml, 5 eq.). The reaction was left to mix overnight, at which time it was allowed to warm to RT. The reaction mixture was filtered and washed with CH<sub>2</sub>Cl<sub>2</sub> to give a brown powder weighing 0.0342 g, about 90% of the weight of the polymer used. The filtrate (0.1919 g) was green.

Catalytic tests of silica-grafted BOX with Cu(OTf)<sub>2</sub>: Catalyst **5** (0.0567 mmol, 8 mol%, 0.3626 g) was mixed with Cu(OTf)<sub>2</sub> (0.0567 mmol, 8 mol%, 0.0205 g) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 ml) overnight under Ar. The appropriate dienophile (1 eq., 0.7086 mmol) was added, and mixing was continued for 1 h. The mixture was brought to the appropriate temperature and freshly cracked CPD (5 eq., 3.54 mmol, 0.293 ml) was added over about 1 h. The reaction was sampled and analyzed by HPLC, GC. When conversion stopped increasing, workup was performed by filtration or by addition of CH<sub>2</sub>Cl<sub>2</sub>, centrifuging and removal of the solvent (repeated three times). The remaining silica was then dried in vacuum before recycling.

Catalytic tests of silica-grafted BOX with Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O: Catalysts **5** (or **5'**, or **5''**) (0.0567 mmol, 10 mol%, 0.2495 g) were mixed with Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (10 mol%, 0.0193 g) in CH<sub>2</sub>Cl<sub>2</sub> overnight. The appropriate dienophile (1 eq., 0.628 mmol) was added, and mixing was continued for 1 h. The mixture was brought to the appropriate temperature and freshly cracked CPD (5 eq., 3.14 mmol, 0.259 ml)

was added over about an hour. The reaction was sampled and analyzed by HPLC, GC. When conversion stopped increasing, workup was performed by filtration or by addition of CH<sub>2</sub>Cl<sub>2</sub>, centrifuging and removal of the solvent (repeated three times).

## References

- [1] A.K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymm.* 9 (1998) 1.
- [2] E.J. Corey, N. Imai, H.-Y. Zhang, *J. Am. Chem. Soc.* 113 (1991) 728.
- [3] D.A. Evans, S.J. Miller, T. Lectka, *J. Am. Chem. Soc.* 115 (1993) 6460.
- [4] A.K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron Lett.* 37 (1996) 3815.
- [5] J.M. Fraile, J.I. García, J.A. Mayoral, T. Tarnai, *Tetrahedron: Asymm.* 8 (1997) 2089.
- [6] J.M. Fraile, J.I. García, J.A. Mayoral, T. Tarnai, *Tetrahedron: Asymm.* 9 (1998) 3997.
- [7] J.M. Fraile, J.I. García, J.A. Mayoral, T. Tarnai, M.A. Harmer, *J. Catal.* 186 (1999) 214.
- [8] P.J. Alonso, J.M. Fraile, J. García, J.I. García, J.I. Martínez, J.A. Mayoral, M.C. Sánchez, *Langmuir* 16 (2000) 5607.
- [9] C. Langham, P. Piaggio, D. Bethell, D.F. Lee, P. McMorn, P.C.B. Page, D.J. Willock, C. Sly, F.E. Hancock, F. King, G.J. Hutchings, *Chem. Commun.* (1998) 1601.
- [10] G.J. Hutchings, *Chem. Commun.* (1999) 301.
- [11] C. Langham, S. Taylor, D. Bethell, P. McMorn, P.C.B. Page, D.J. Willock, C. Sly, F.E. Hancock, F. King, G.J. Hutchings, *J. Chem. Soc., Perkin Trans.* 2 (1999) 1043.
- [12] C. Langham, D. Bethell, D.E. Lee, P. McMorn, P.C.B. Page, D.J. Willock, C. Sly, F.E. Hancock, F. King, G.J. Hutchings, *Appl. Catal. Gen.* 182 (1999) 85.
- [13] Y. Traa, D.M. Murphy, R.D. Farley, G.J. Hutchings, *Phys. Chem. Chem. Phys.* 3 (2001) 1073.
- [14] J.M. Fraile, J.I. García, M.A. Harmer, C.I. Herreras, J.A. Mayoral, *J. Mol. Catal. Chem.* 165 (2001) 211.
- [15] M.I. Burguete, J.M. Fraile, J.I. García, E. García Verdugo, S.V. Luis, J.A. Mayoral, *Org. Lett.* 2 (2000) 3905.
- [16] M. Glos, O. Reiser, *Org. Lett.* 2 (2000) 2045.
- [17] R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi, M. Pitillo, *J. Org. Chem.* 66 (2001) 3160.
- [18] D. Rechavi, M. Lemaire, *Org. Lett.* 3 (2001) 2493.
- [19] A.K. Ghosh, H. Cho, J. Cappiello, *Tetrahedron: Asymm.* 9 (1998) 3687.
- [20] I.W. Davies, R.J. Deeth, R.D. Larsen, P.J. Reider, *Tetrahedron Lett.* 40 (1999) 1233.
- [21] I.W. Davies, L. Gerena, L. Castonguay, C.H. Senanayake, R.D. Larsen, T.R. Verhoeven, P.J. Reider, *J. Chem. Soc., Chem. Commun.* (1996) 1753.
- [22] A. Guzaev, H. Lönnberg, *Synthesis* (1997) 1281.
- [23] P. Hesemann, J.J.E. Moreau, *Tetrahedron: Asymm.* 11 (2000) 2183.
- [24] D.A. Evans, S.J. Miller, T. Lectka, P. von Matt, *J. Am. Chem. Soc.* 121 (1999) 7559.



- [25] S. Kanemasa, Y. Oderaotoshi, S.-I. Sakaguchi, H. Yamamoto, J. Tanaka, E. Wada, D.P. Curran, *J. Am. Chem. Soc.* 120 (1998) 3074.
- [26] S.J. Bae, S.W. Kim, T. Hyeon, B.M. Kim, *Chem. Commun.* (2000) 31.
- [27] K.D. McMurtrey, *J. Liq. Chromatogr.* 11 (1988) 3375.
- [28] D.A. Evans, K.T. Chapman, J. Bisaha, *J. Am. Chem. Soc.* 110 (1988) 1238.
- [29] S. Kobayashi, H. Ishitani, I. Hachiya, M. Araki, *Tetrahedron* 50 (1994) 11623.
- [30] G. Manickam, G. Sundararajan, *Tetrahedron: Asymm.* 10 (1999) 2913.