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Reusable chiral bis(oxazoline)–copper complexes immobilized by donor–acceptor interactions on insoluble organic supports

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ABSTRACT

Heterogeneous asymmetric Diels–Alder reactions between cyclopentadiene and 3-but-2-enoyl-oxazolidin-2-one were efficiently promoted by reusable chiral bis(oxazoline)–copper catalysts, immobilized through charge transfer interactions with trinitrofluorenone, that was covalently grafted on Merrifield resins. The modified support was also used for the synthesis of both enantiomers of the target product, thanks to the non-covalent anchoring of the catalyst that allowed its easy removal and exchange.

1. Introduction

Extensive work has been devoted to the catalyzed synthesis of enantio-enriched valuable synthons by chiral bis(oxazoline) complexes [1]. Associated to various metals, these ligands were particularly efficient for the enantioselective formation of carbon–carbon bonds, although these transformations generally suffered from a high catalyst loading. The costs of both precious metal and optically pure ligand that are required to achieve satisfactory yields of the expected products are dissuasive for an economical development of these processes. To overcome these constraints, several methods have been proposed towards an easy recovery and reuse of the chiral catalysts [2]. These procedures are mainly based on the heterogenization of the complex by a structural modification of the bis(oxazoline) ligand. Its subsequent grafting on an insoluble (organic [3] or inorganic [4]) support allows the catalytic reaction to be performed under heterogeneous conditions and the catalyst, recovered by simple filtration, is further reused. Some examples have also been reported in which the structure of the ligand is modified so that it can be polymerized, creating an insoluble catalyst with the chirality present in the pendant groups or in the main chain of the polymer [5]. Bis(oxazolines) have also been covalently grafted onto soluble polymers [6], or used in non-conventional solvents such as ionic liquids [7] or fluorous phases [8]. Other methodologies that generally do not imply a drastic modification of the ligand's structure concern non-covalent electrostatic interactions of the charged complexes with ionic supports [9].

We have reported the efficient reuse of chiral bis(oxazoline)–copper catalysts in Diels–Alder reactions by their precipitation as charge-transfer complexes (CTC) [10]. Several bis(oxazoline) ligands were substituted *via* a short methylene linker by an anthracene moiety. The corresponding copper complexes were prepared and charge-transfer complexes were synthesized by the addition of trinitrofluorenone (TNF) as electron deficient moiety (Fig. 1). At the end of the catalytic transformation promoted by these complexes, pentane was added to the reaction mixture leading to the precipitation of the catalysts. Removal of the products solution for analysis was then followed by addition of new substrates to the catalysts in the same reaction vessel for convenience. The efficiency of this procedure was demonstrated in a Diels–Alder reaction [11] between cyclopentadiene and 3-acryloyl-oxazolidin-2-one to reach the expected *endo* product as major isomer (up to 97% de and 94% ee): the catalyst was used 12 times without loss of either activity or selectivity.

The efficient use and recycling of these modified bis(oxazoline) complexes is satisfying but the method should be improved to avoid the addition of pentane for the precipitation of the complex in a batch procedure. The ultimate goal of our work is to develop a fixed-bed reactor for a continuous flow process, as the best way towards an economic and environmentally friendly production of enantio-enriched valuable products [12]. We thus report here our preliminary results for the immobilization of bis(oxazoline) complexes through charge-transfer interactions with trinitrofluorenone covalently grafted on solid supports and their use in

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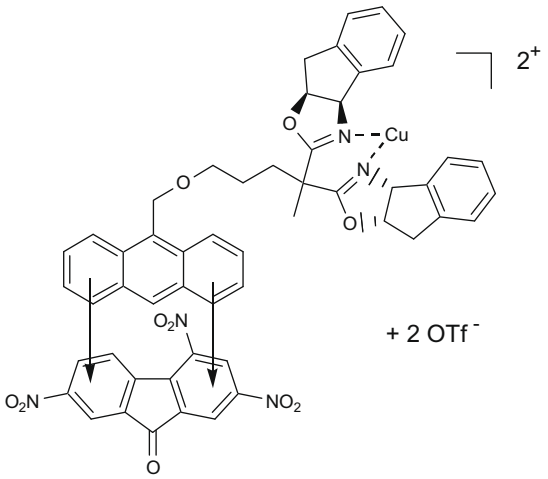


Fig. 1. Charge-transfer complex structure for bis(oxazoline)–copper catalyst's recycling.

heterogeneous asymmetric catalysis. Our methodology involving both a solid support, for a direct filtration without the need of an additional precipitation procedure, and non-covalent donor–acceptor interactions, for a reversible anchoring of targeted asymmetric complexes, should allow the implementation of various processes for a wide range of applications. Usually, indeed, the same batch of heterogenized material, often prepared through long and fastidious procedures, is only useful for one reaction type. To overcome this difficulty, we propose to test a new immobilization strategy based on non-covalent reversible interactions of type charge transfer, between the support and the chiral organometallic complex. This methodology should allow the facile exchange of various catalysts on the support for a broad use in numerous enantioselective transformations.

2. Experimental section

2.1. General methods and materials

All reactions were carried out under argon in oven-dried glassware with magnetic or mechanic stirring. Solvents were distilled before use: toluene and CH_2Cl_2 from calcium hydride, THF from sodium metal/benzophenone ketyl. Cyclopentadiene was distilled by cracking dicyclopentadiene over calcium hydride. Bis(oxazoline) **3** was prepared as described in Ref. [10a].

^{1}H NMR spectra were recorded on a Bruker AM 200 (200 MHz) or AM 250 (250 MHz) as $CDCl_3$ solutions and data are reported in ppm relative to the solvent (7.27 ppm). ^{13}C NMR spectra were recorded on a Bruker AM 250 (62.5 MHz) as $CDCl_3$ solutions and data are reported in ppm relative to the solvent (77.0 ppm). Optical rotations were measured as solutions in 10 cm cells at the sodium D line, using a PERKIN ELMER 241 polarimeter. Mass spectra were recorded on a Finnigan MAT 95 S spectrometer. HPLC analyses were carried out on a PERKIN–ELMER chromatograph equipped with a diode array UV detector using a WHELK column. Elemental analyses were performed by the CNRS. Service of Microanalyses in Gif-sur-Yvette (France) for C, H, N.

2.2. Hydrazine resin (see Ref. [13])

PS-**A**: The Merrifield resin leading to TNF-PS-**A** was synthesized in the Laboratoire de Catalyse et Synthèse Organique (ICBMS, UMR 5246, Lyon) that is gratefully acknowledged for a gift. It is prepared from Amberlite XAD1180 (Rohm & Haas Company) leading to a loading in chlorine of 1.89 mmol Cl/g. 10 eq. of hydrazine monohydrate (1.90 mL, caution toxic compound) was slowly added to 2 g of this Merrifield resin (1.89 mmol Cl/g) in 12 mL of ethanol at ambient temperature. At the end of the addition, the mixture was mechanically stirred for 24 h at 60 °C. The resin was then filtered, washed with water then with ethanol.

PS-**B**: A Merrifield polymer resin commercially available from Acros Organics was used (2% crosslinked with DVB, 2.0–2.2 mmol Cl/g, 200–400 mesh) for the synthesis of TNF-PS-**B**. 10 eq. of hydrazine monohydrate (1.95 mL, caution toxic compound) was slowly added to 2 g of Merrifield resin (2.00 mmol Cl/g) in 12 mL of ethanol at ambient temperature. At the end of the addition, the mixture was mechanically stirred for 24 h at 60 °C. The resin was then filtered, washed with water then with ethanol.

2.3. TNF-PS-A

1.35 g of trinitrofluorenone (4.3 mmol) was dissolved in 57 mL of toluene and 5.7 mL of acetic acid, then 2 g of hydrazine resin (PS-**A**) was added. The mixture was mechanically stirred for 3 days at room temperature. The resin was washed for 3 days with toluene in a soxhlet, then with pentane and was dried. Anal. Found: C 79.48; H 7.25; N 3.53. The loading capacity was based on the TNF mass balance and nitrogen elemental analysis and was found to be 0.5 mmol/g.

2.4. TNF-PS-B

1.29 g of trinitrofluorenone (4 mmol) was dissolved in 46 mL of toluene and 4.6 mL of acetic acid, and then 2 g of hydrazine resin (PS-B) was added. The mixture was mechanically stirred for 3 days at room temperature. The resin was washed for 3 days with toluene in a soxhlet, then with pentane and was dried. Anal. Found: C 77.51; H 6.53; N 5.76. The loading capacity was based on the TNF mass balance and nitrogen elemental analysis and was found to be 0.8 mmol/g.

2.5. Bis(oxazoline)-ent-3 (according to Ref. [10a])

A 50 mL flask was charged with diethyl-malonimidate dihydrochloride (185 mg, 0.80 mmol), (1*S*,2*R*)-1-amino-2-indanol (250 mg, 1.67 mmol), and dry CH_2Cl_2 (18 mL). The mixture was heated under reflux overnight. The resulting suspension was cooled to room temperature, washed with water and extracted with CH_2Cl_2 (3×20 mL). The combined organic phases were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by recrystallization in propan-2-ol, giving the corresponding bis(oxazoline) as a white solid (235 mg, 0.71 mmol, 89% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.48–7.46 (m, 2H), 7.30–7.28 (m, 6H), 5.58 (d, 2H, J = 8.2 Hz), 5.39–5.34 (m, 2H), 3.40 (dd, 2H, J = 7.0 Hz, J = 17.7 Hz), 3.29 (s, 2H), 3.18 (dd, 2H, J = 17.7 Hz, J = 1.7 Hz). HRMS (ESI): calcd for $C_{21}H_{18}O_2N_2Na$ ($M + Na^+$): 353.1260, found: 353.1269.

A Schlenk tube was charged with dry THF (2 mL), TMEDA (161 μL, 1.07 mmol) and *i*Pr_2NH (120 μL, 0.85 mmol). *n*-BuLi (445 μL, 1.6 M in hexanes) was added at −20 °C, and the mixture was stirred at this temperature for 1 h. The above synthesized bis(oxazoline) (235 mg, 0.71 mmol) was dissolved in THF (2 mL) and LDA, prepared *ex situ*, was added at −20 °C to this solution. The mixture was stirred for 3 h, then methanesulfonic acid 3-(anthracen-9-ylmethoxy)-propyl ester (see Ref. [1]) (245 mg, 0.71 mmol) in THF (10 mL) was added at −20 °C. The mixture was heated at 60 °C during 24 h. The solution was cooled, washed with NH_4Cl_{sat} and extracted with AcOEt (3×30 mL). The combined organic phases were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash

chromatography (cyclohexane/AcOEt: 1/2, then AcOEt 100%), giving the expected anthracene-substituted bis(oxazoline) as a white solid (52 mg, 0.09 mmol, 13% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.28 (d, 2H, J = 9.3 Hz), 7.98 (d, 2H, J = 9.3 Hz), 7.48–7.43 (m, 6H), 7.26–7.18 (m, 6H), 5.51 (d, 2H, J = 7.8 Hz), 5.28–5.23 (m, 4H), 3.52 (t, 2H, J = 6.3 Hz), 3.50–3.25 (m, 3H), 2.99 (d, 2H, J = 19.1 Hz), 1.97–1.91 (m, 2H), 1.51–1.46 (m, 2H). HRMS (ESI): calcd for $C_{39}H_{34}O_3N_2Na$ ($M + Na^+$): 601.2462, found: 601.2486.

A Schlenk tube was charged with dry THF (2 mL), TMEDA (23.5 μL, 0.16 mmol) and iPr$_2$NH (11 μL, 0.08 mmol). n-BuLi (97 μL, 1.6 M in hexanes) was added at −20 °C, the mixture was stirred at -20 °C for 1 h and was added at −20 °C to a solution of the anthracene-substituted bis(oxazoline) (45 mg, 0.08 mmol) in THF (2 mL). The mixture was stirred for 3 h. Then, MeI (15 μL, 0.24 mmol) was added at −20 °C. The mixture was heated at 60 °C during 24 h. The solution was cooled, washed with NH_4Cl_{sat} and extracted with AcOEt (3 × 10 mL). The combined organic phases were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (cyclohexane/AcOEt: 1/2), giving 46 mg of compound *ent*-**3** (0.08 mmol, 96% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.31 (d, 2H, J = 9.3 Hz), 7.99 (d, 2H, J = 9.3 Hz), 7.48–7.46 (m, 6H), 7.26–7.12 (m, 6H), 5.51–5.47 (m, 2H), 5.29 (s, 2H), 5.27–5.16 (m, 2H), 3.53–3.50 (m, 2H), 3.27–3.18 (m, 2H), 2.94–2.78 (m, 2H), 2.01–1.88 (m, 2H), 1.45–1.41 (m, 2H), 1.39 (s, 3H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 169.0, 141.9, 139.6, 139.5, 131.7, 131.2, 128.9, 128.5, 127.6, 126.4, 125.8, 125.5, 125.1, 124.9, 124.5, 83.4, 76.6, 70.8, 64.6, 39.9, 32.7, 24.5, 20.9. $[\alpha]_D$ −122 (c = 1, $CHCl_3$).

2.6. Diels–Alder reaction between cyclopentadiene and 3-(but-2-enoyl)-oxazolidin-2-one

A Schlenk tube was charged with $Cu(OTf)_2$ (0.033 mmol) and the ligand (**3** or *ent*-**3**) (0.036 mmol), dissolved in CH_2Cl_2 (650 μL), was added dropwise. The solution was stirred for 1 h. Then, the newly formed complex was added to the resin TNF-PS (0.144 mmol) and the mixture was stirred for 4 h. Then, 3-but-2-enoyl-oxazolidin-2-one (0.33 mmol, 51 mg) was added as a solution in CH_2Cl_2 (650 μL) via syringe. Immediately thereafter, cyclopentadiene, freshly cracked, (200 μL, 2.4 mmol) was added via syringe. The resulting mixture was stirred at room temperature for the specified amount of time. When the reaction was finished, the products solution was removed by syringe from the Schlenk, washed with NH_4Cl_{sat} and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (toluene/ethylacetate: 80/20) and analyzed by HPLC for the determination of the de and ee (see below). The resin in the Schlenk was washed twice with pentane and dried under reduced pressure. New substrates were then added in dichloromethane for a new run of the catalytic asymmetric Diels–Alder reaction. For removing the organometallic complex immobilized on the resin, the resin is additionally washed three times with toluene (15 mL) prior to the introduction of a new catalyst.

2.7. General procedure for HPLC analyses

The ee for the major *endo* isomer was determined by HPLC analysis using a WHELK column (flow rate = 0.8 mL/min; 99% hexane, 1% ethanol, λ = 215 nm), which resolves the two diastereoisomers (*exo*$_1$ t_r = 35.4 min, *exo*$_2$ t_r = 36.8 min, *endo*$_1$ t_r = 40.3 min, *endo*$_2$ t_r = 42.8 min). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.38 (dd, 1H, J = 5.8 Hz, J = 3.4 Hz), 5.82 (dd, 1H, J = 5.8 Hz, J = 3.4 Hz), 4.40 (t, 2H, J = 7.8 Hz), 4.03–3.87 (m, 2H), 3.55–3.47 (m, 1H), 3.29 (bs, 1H), 2.55 (bs, 1H), 2.13–2.09 (m, 1H), 1.73–1.70 (m, 1H), 1.48–1.45 (m, 1H), 1.16 (d, 3H, J = 6.3 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 175.3, 154.0, 138.7, 132.2, 62.6, 50.8, 47.0, 43.8, 43.5, 43.4, 30.1.

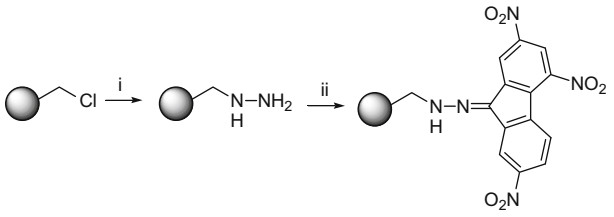
3. Results and discussion

Trinitrofluorenone-modified polystyrene resins (TNF-PS) were synthesized according to a procedure described by Lemaire's group [13]. The Merrifield resin was first treated with hydrazine monohydrate in ethanol and trinitrofluorenone was then introduced as a toluene/acetic acid solution (Scheme 1). The resin was finally washed with toluene by soxhlet extraction to yield the expected TNF-PS. A thorough washing of the resin is of major importance for the complete removal of hydrazine, as it can reduce Cu(II) to Cu(I), [14] an unreactive catalyst in the Diels–Alder reaction. Two modified supports were prepared arising from different sources of polystyrene beads (see Section 2.2.). A first batch of resin (TNF-PS-**A**) was synthesized possessing a loading in TNF of 0.5 mmol/g and a particle size lower than 50 mesh, and another batch was prepared (TNF-PS-**B**) with a higher loading in TNF (0.8 mmol/g) and smaller particles (200–400 mesh).

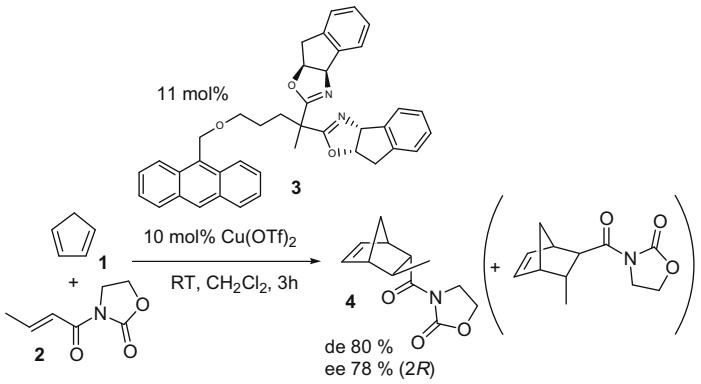
To check our new immobilization procedure, we have tested the anthracene-modified bis(oxazoline) ligand **3** derived from enantiomerically pure (1*R*,2*S*)-1-amino-2-indanol associated to copper triflate. The test reaction under homogeneous conditions implied the cycloaddition between 3-but-2-enoyl-oxazolidin-2-one **2** and cyclopentadiene **1** at room temperature in dichloromethane and the chiral copper complex provided the desired *endo* product **4** with both a high diastereoselectivity (80%) and enantioselectivity (78%, Scheme 2) [10a]. These values are in good accordance with those reported in the literature with similar ligands. This transformation was indeed run under analogous operating conditions with the ligand (3a*S*,3a′*S*,8a*R*,8a′*R*)-2,2′-(cyclopropane-1,1-diyl)bis(8,8a-dihydro-3aH-indeno[1,2-d]oxazole), developed by Sibi and his group [15]. They obtained at room temperature the expected major *endo* product with 83% ee and 78% de. By comparing these results with ours, we assume that the introduction of the anthracene group is not detrimental to the progress of the catalytic transformation.

The chiral copper-**3** complex was then tested as catalyst to perform the same transformation in the presence of the TNF-PS resins. According to the TNF loading, the resins were used in a four-molar excess compared to the copper catalyst (10 mol%). The evaluation of the global loading in TNF is based on the TNF mass balance and elemental analysis. As the exact amount of accessible TNF on this resin is not easily measurable, we chose to use our recoverable support in excess compared to the stoichiometry required for the CTC formation.

The organometallic copper-**3** complex was prepared *ex situ* from ligand **3** and $Cu(OTf)_2$ in dichloromethane as a green solution before its addition on the resin. Stirring was then pursued for 4 h and both the acyloxazolidinone **2** and freshly distilled cyclopentadiene **1** were added in DCM. After completion of the reaction, the



Scheme 1. Synthesis of the TNF-PS resins. Reagents and conditions: (i) NH_2–NH_2, EtOH, 60 °C, 24 h; (ii) TNF, CH_3COOH, toluene, RT, 3 days.



Scheme 2. Diels–Alder reaction between cyclopentadiene and 3-but-2-enoyl-oxazolidin-2-one in the presence of copper-**3** under homogeneous conditions.

solution was removed for products analysis and the resin was washed twice with pentane. New substrates were then added in DCM on the resin for the next run. The results obtained for the catalysis in the presence of TNF-PS-**A** are collected in Table 1. The first use of the immobilized copper-**3** complex allowed the synthesis of the expected *endo* product as major compound with an excellent isolated yield (91%) and enantioselectivity (76%) in 18 h reaction time. The recorded activity and enantioselectivity values are comparable to those obtained under homogeneous conditions. Part of the catalytic transformation probably occurred in solution for this first run since 46 h were further necessary to obtain a high conversion in the second run. Yet, product **4** was again obtained with the expected high selectivity. The third run was also carried out with a high efficiency as a proof of concept for this new immobilization strategy of bis(oxazoline)-based catalysts. The chiral copper-complex associated to the resin by donor–acceptor interactions was used again for three successive runs. Nevertheless its reuses proceeded every time with a loss of activity indicating a partial leaching of the catalyst. The selectivity values also decreased, probably due to a competitive racemic, non-catalyzed, transformation of the substrates.

Some blank tests were performed to evaluate the exact role of the CTC formation for the reuse of the chiral organometallic complex. The catalysis was for example run under exactly similar conditions, but in the presence of a Merrifield resin that was not modified with an electrodeficient compound. The first run of the reaction led, as expected to the desired product with an efficiency similar to that obtained under homogeneous conditions (>95% conversion, 78% ee). The same recycling procedure was performed and the Merrifield support was subjected again to the introduction of new substrates. After 20 h reaction time, only 50% of 3-but-2-enoyl-oxazolidin-2-one was transformed and the desired product was isolated with 65% ee, indicating thus a slight adsorption of the catalyst on the resin. A third run allowed only the formation of **4** as traces. By comparison with results reported in Table 1, and the steady formation of the enantio-enriched *endo* product **4** at the 6th run, the contribution of the CTC complex to maintain the chiral copper-complex at a close proximity of the surface is here verified.

However, the undeniable partial leaching of the catalyst via these reversible CTC interactions could also be verified as follows. A dichloromethane solution of ligand **3** with an equimolar amount of added $Cu(OTf)_2$ was stirred at room temperature for 4 h with TNF-PS-**B**. The solution was then separated from the beads and both substrates **1** and **2** were added to this filtrate. After 20 h reaction time, product **4** was isolated with 78% ee, albeit with only 28% yield. Thus, under our conditions, leaching of the catalyst from the beads is obvious and the CTC interaction has still to be improved.

Another set of experiments was conducted by using TNF-PS-**B** resin and immobilizing firstly copper-*ent*-**3** complex, prepared from (1*S*,2*R*)-1-amino-2-indanol, by charge-transfer interactions (see Table 2). Product **4** possessing the expected (2*S*) configuration was isolated in the two first runs with high yield and enantioselectivity. The subsequent reuse of the catalyst in the next 3rd and 4th run was accompanied with a significant loss of efficiency. To illustrate the possible use of the TNF-modified support with different chiral catalysts thanks to the reversible grafting on the solid, copper-*ent*-**3** catalyst was removed after the 4th run by simple washing of the resin with toluene, a competitive solvent for the formation of CTC with electrodeficient molecules. The same TNF-PS-**B** batch reacted then with copper-**3** complex. After addition of the substrates in a 5th reaction run, product **4** possessing the opposite configuration (2*R*) was isolated with the same enantiomeric excess value than in the first catalytic run. The recycling of the new catalyst followed then the same trend than its enantiomer analogue. These experiments proved the validity of this new concept for the successive non-covalent immobilization of different

Table 1
Heterogeneous Diels–Alder reaction between **1** and **2** with copper-**3** complex immobilized by CTC interactions on TNF-PS-**A**.

Run	*t* (h)	Conv (%)[a]	Yield (%)	de (%)[b]	ee **4** *endo* (%)[b]
1st	18	100	91	74	76 (2*R*)
2nd	46	82	80	73	71 (2*R*)
3rd	45	100	82	74	73 (2*R*)
4th	46	81	67	70	63 (2*R*)
5th	45	33	22	69	37 (2*R*)
6th	45	47	28	68	39 (2*R*)

[a] Determined by ^{1}H NMR analysis.
[b] Determined by HPLC chromatography (Whelk column, hexane/ethanol).

Table 2
Heterogeneous Diels–Alder reaction between **1** and **2** with copper-**3** and copper-*ent*-**3** complexes in the presence of TNF-PS-**B**.

Run	*t* (h)	Conv (%)[a]	Yield (%)	de (%)[b]	ee **4** *endo* (%)[b]
*Copper-ent-**3** catalyst*					
1st	46	100	82	76	73 (2*S*)
2nd	46	100	81	76	74 (2*S*)
3rd	72	79	62	73	62 (2*S*)
4th	72	59	32	67	30 (2*S*)
*Copper-**3** catalyst*					
5th	46	84	72	78	73 (2*R*)
6th	46	95	86	76	72 (2*R*)
7th	72	96	79	73	61 (2*R*)
8th	72	92	72	73	52 (2*R*)

[a] Determined by ^{1}H NMR analysis.
[b] Determined by HPLC chromatography (Whelk column, hexane/ethanol).

chiral catalysts on the same modified support. As far as we know, such reuse of a support for performing another catalytic reaction, here affording the opposite enantiomer, has never been described. Our procedure could be interestingly evaluated as a new system to perform asymmetric catalysis in a fixed-bed reactor, suitable for different transformations. However and as very often observed by using reversible interactions, some leaching of the catalyst could not be avoided after several runs.

4. Conclusion

We have described a new procedure for the recovery of chiral bis(oxazoline)-based catalysts, involving the formation of charge-transfer complexes with insoluble organic supports. Some valuable preliminary results have been obtained for the promotion of the Diels–Alder reaction. Work is still in progress to improve the resin structure and optimize the charge-transfer interaction for a better recycling of the system after several batches. For instance, new (organic and inorganic) supports are being prepared in which the acceptor moiety is placed far away from the solid to favour its accessibility. Furthermore, the inversion of the CTC interactions is currently under progress, namely the introduction of the electron poor moiety covalently on the active chiral organometallic site and the use of an electron rich support, to study the catalyst leaching under those conditions.

To the best of our knowledge, this study is the first report of a procedure involving the preparation of immobilized chiral catalysts via reversible linkage for which the same batch of support is suitable for the synthesis of different enantio-enriched compounds.

Acknowledgements

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