Tetrahedron: *Asymmetry* 24 (2013) 769–775

Contents lists available at SciVerse ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# π-Stacking interactions at the service of [Cu]-bis(oxazoline) recycling

Dorian Didier [a], Emmanuelle Schulz [a,b,*]

[a] *Equipe de Catalyse Moléculaire, Univ Paris-Sud, ICMMO, UMR 8182, Orsay F-91405, France*
[b] *CNRS, Orsay F-91405, France*

ARTICLE INFO

*Article history:*
Received 29 April 2013
Accepted 15 May 2013

ABSTRACT

Anthracene- and pyrene-tagged bis(oxazoline) ligands have been prepared and immobilized on charcoal, fullerene, and single-walled carbon nanotubes through π–π interactions. The corresponding copper complexes have been evaluated for their propensity to promote heterogeneous asymmetric Henry and ene reactions. The best results, in terms of activity, selectivity, and stability toward the recycling procedure have been obtained with the pyrene/SWCNT system, as the first example demonstrating the usefulness of such reversible interactions for the asymmetric formation of new C–C bonds.



## 1. Introduction

Asymmetric catalysis is the most atom economic and efficient method to produce valuable complex molecules with high selectivities.[1–3] In this context, numerous efforts have been performed in order to determine a simple procedure for the easy recovery and reuse of precious chiral catalysts.[4] Anchoring the catalyst onto a solid support in order to facilitate its capture by filtration is one of these successful methods. It often requires structural modifications on the chiral ligand to allow its specific covalent or non-covalent binding onto the chosen material. A covalent link is a guarantee of strength during recycling, whereas a non-covalent one may give rise to catalyst leaching to some extent. In this last case however, the recovery of the support to be used in other transformations with other chiral catalysts is also interesting in terms of economic value. In this context García et al.[5] have studied and compared the covalent grafting of a chiral vanadyl salen complex on various supports, to promote the enantioselective cyanosilylation of aldehydes. They were able to perform the transformation on different scaffolds including silica, room-temperature ionic liquids, single-walled carbon nanotubes, or activated carbon and to compare with results obtained in the homogeneous phase. Direct immobilization of metal(II) bis(oxazoline) complexes via non covalent interactions onto silica or carbon supports has been described by Hardacre et al.,[6] by using an ionic liquid without modification of the ligand structure. Carbon nanotubes have also been used to support Pt nanoparticles.[7] Upon subsequent modification with (−)-cinchonidine, these catalysts proved their efficiency for the asymmetric hydrogenation of α-ketoesters showing high catalytic activity and a ligand acceleration effect. The deposit of Pd on $TiO_2$ coated multi-walled carbon nanotubes followed by reduction of Pd nanoparticles was studied by Szőllősi et al.[8] in the presence of cinchonidine as a chiral modifier for the enantioselective hydrogenation of α,β-unsaturated carboxylic acids. More recently, Li et al.[9] have described the use of carbon nanotube channels as nanoreactors for asymmetric catalysis, leading to greatly enhanced activity and enantioselectivity for asymmetric hydrogenations.

Pyrene moieties interact with carbon supports through π–π stacking. These reversible interactions have already been used for various applications: the easy removal of stannane derivatives possessing a 3-pyrenylpropyl side chain on activated carbon has been described for simplifying tin removal and product isolation after radical reactions or Stille couplings;[10,11] proteins have been immobilized through those non-covalent interactions on carbon nanotubes;[12] for catalytic purposes and specifically for $H_2$ evolution and uptake, nickel-based nanomaterials have been anchored onto multiwalled carbon nanotubes through π–π stacking to produce robust electrocatalytic complexes;[13] Reiser et al. have prepared carbon coated cobalt nanoparticles to non-covalently maintain a pyrene-modified palladium complex on the carbon shell to perform the hydroxycarbonylation of aryl halides in water.[14,15] A pyrene-tagged ruthenium carbene was also immobilized via π–π stacking on single-walled carbon nanotubes to achieve stable and recyclable catalytic species to promote ring-closing metathesis reactions.[16] To the best of our knowledge, this strategy was used only once to perform asymmetric catalysis. Zhou et al.[17] modified the enantiomerically pure Pyrphos ligand by a covalent pyrene link and proceeded to carry out the rhodium-catalyzed heterogeneous asymmetric hydrogenation of α-dehydroamino esters.

We have previously described the synthesis of anthracene-tagged bis(oxazoline) ligands and demonstrated their efficient use and recycling in various copper-catalyzed asymmetric reactions.[18–20] The recovery of the asymmetric catalysts occurred easily through the formation of non-covalent charge transfer interactions

* Corresponding author. Fax: +33 169154680.
*E-mail address:* emmanuelle.schulz@u-psud.fr (E. Schulz).

0957-4166/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetasy.2013.05.008

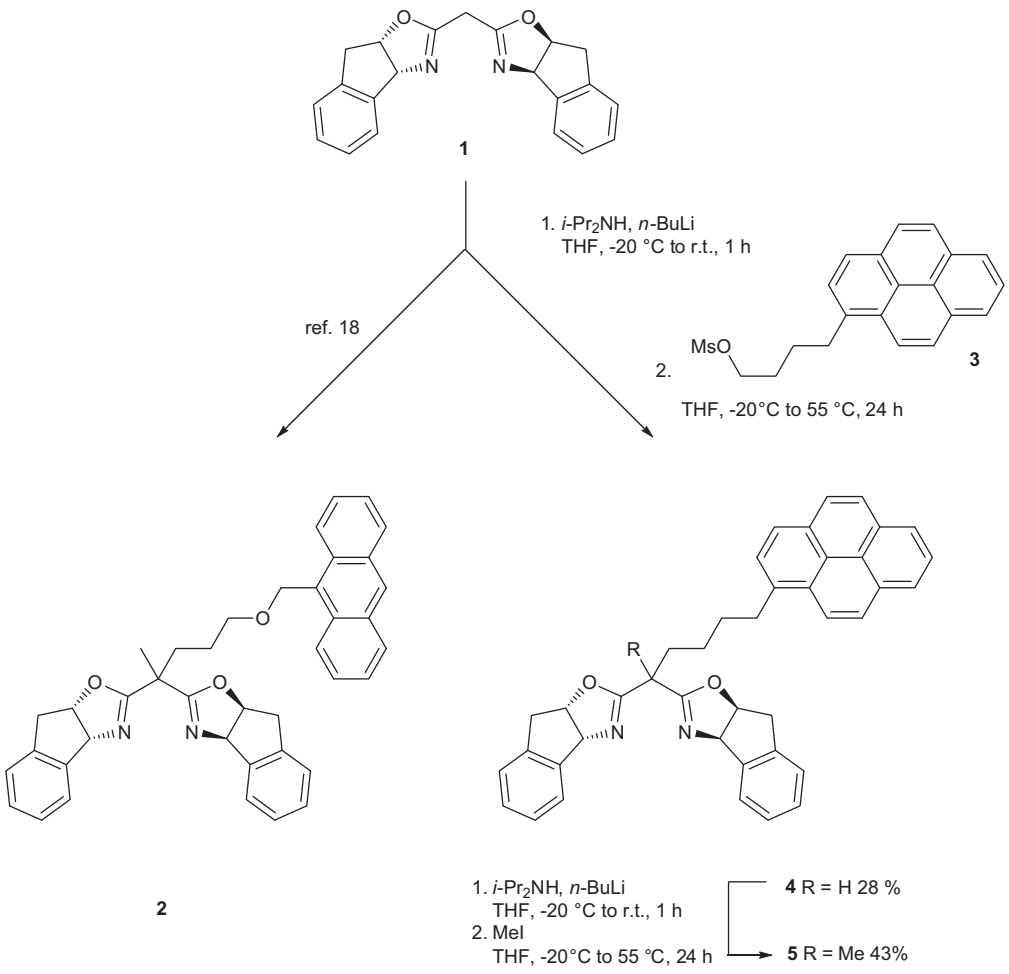
with trinitrofluorenone additives, subsequent precipitation in pentane, and finally by filtration. Direct heterogeneous catalysis could also be performed by covalently anchoring the electron-deficient molecule either on a polystyrene support[21] or on amorphous silica.[22] Recently we demonstrated the efficiency of TNF-tagged bis(oxazolines) in their recycling for the enantioselective Diels–Alder transformation.[23] Herein we report the use of activated carbon, fullerene, and single-walled carbon nanotubes as supports for non-covalent immobilization via $\pi$–$\pi$ stacking of the anthracene-tagged bis(oxazoline) ligand and its pyrene-modified analogue. Copper complexes have been prepared and the thus obtained heterogenized asymmetric catalysts have been tested for their ability to promote asymmetric nitroaldol and ene reactions.

## 2. Results and discussion

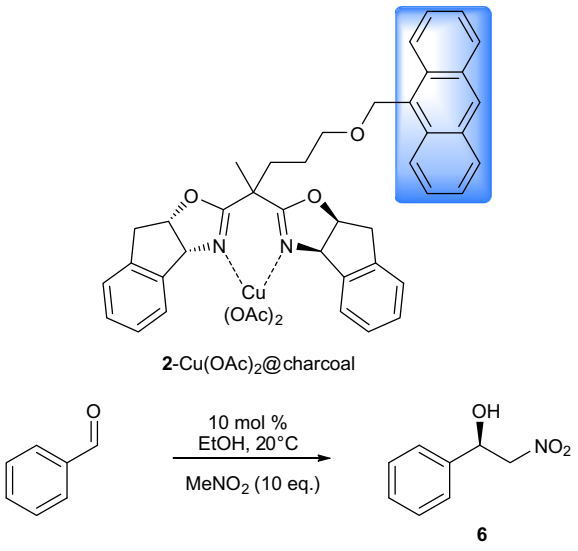
The synthesis of bis(oxazoline) ligand **2** bearing an anthracene moiety has already been reported (Scheme 1),[18] and the corresponding pyrenyl-tagged bis(oxazoline) **5** was prepared by following the same synthetic strategy. The intermediate ligand **4** was obtained after deprotonation of bis(oxazoline) **1** with freshly prepared LDA and subsequent addition of the mesylate derivative **3** synthesized from commercially available 4-(pyren-1-yl)butan-1-ol. Subsequent deprotonation of compound **4** allowed the introduction of the methyl moiety to give the targeted ligand **5** in a moderate global yield (Scheme 1).

Ligands **2** and **5** were then used in the presence of copper salts for their ability to promote two asymmetric catalytic transformations; the Henry reaction between benzaldehyde and nitromethane, and the ene reaction with $\alpha$-methylstyrene and ethylglyoxylate, as test reactions. Special attention was given to the recovery and further reuse of the catalysts via non-covalent immobilization on activated carbon, fullerene, and single-walled carbon nanotubes.

Ligand **2** was first associated to $Cu(OAc)_2 \cdot H_2O$ to furnish a catalyst for the Henry reaction. Analogous classic bis(oxazoline) ligand based on the indanol framework was indeed proved, in the presence of copper salts gave the targeted nitroalcohol in high yield and with up to 94% ee.[24] We have already described the efficiency of the copper catalyst derived from **2** in this transformation,[22] which showed no loss of activity or enantioselectivity despite the change in the ligand structure. In a typical reaction between benzaldehyde and nitromethane, ligand **2** mixed with copper acetate in a 1:1 ratio in ethanol yielded 2-nitro-1-phenyl-ethanol in 89% isolated yield and 90% ee. Activated carbon was chosen as a support to interact through non covalent interactions with the anthracene part of ligand **2** to give a new catalyst, anthracene-tagged bis(oxazoline)@activated carbon. The transformation was performed in ethanol as the best solvent and gave high selectivities under homogeneous conditions. The copper complex **2**–$Cu(OAc)_2$ diluted in ethanol was thus mixed in the presence of charcoal (500 mg per catalyst mmol). The mixture was stirred for further 3 h at room temperature under an argon atmosphere, while the supernatant,




**Scheme 1.** Synthetic procedure for the synthesis of bis(oxazoline) ligands **2** and **5**.




**Scheme 2.** Nitroaldol reaction in the presence of **2**–$Cu(OAc)_2$@charcoal.

**Table 1**
Henry reaction between benzaldehyde and nitromethane promoted by **2**–$Cu(OAc)_2$@charcoal[a]

| Run | *t* (h) | Yield **6**[b] (%) | ee **6**[c] (%) |
|---|---|---|---|
| 1 | 24 | 68 | 69 (*R*) |
| 2 | 24 | 63 | 50 (*R*) |
| 3 | 24 | 30 | 61 (*R*) |
| 4 | 24 | 33 | 59 (*R*) |
| 5 | 24 | 26 | 60 (*R*) |
| 6 | 24 | 28 | 41 (*R*) |
| 7 | 120 | 56 | 40 (*R*) |

[a] 10 equiv $MeNO_2$, 20 °C, 10 mol % cat.
[b] Isolated yield.
[c] Determined by chiral HPLC, see Experimental.

which was initially a green solution, became colorless. The substrates (benzaldehyde and nitromethane) were then added for the reaction to proceed (see Scheme 2 and Table 1).

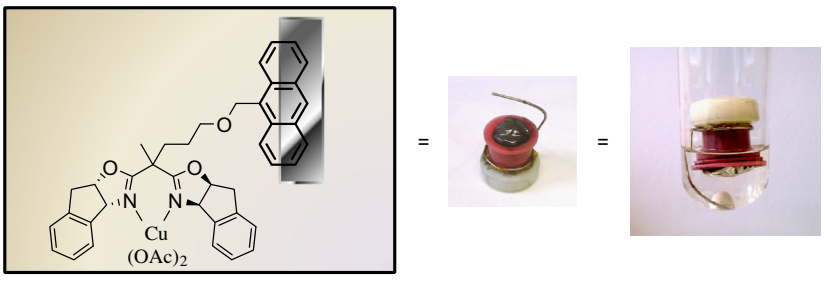
For the first run in the Henry reaction, after 24 h, the targeted product **6** could be isolated in 68% yield with 69% ee. This selectivity value is significantly lower compared to the ee achieved under homogeneous conditions, indicating that the support may play, in this case, a harmful role, disturbing the approach of the substrates to the complex. Trace amounts of the elimination product arising from loss of water were also found, probably due to the non-negligible acidity of the support. The catalyst recovery was performed through centrifugation and further filtration of the reaction mixture after pentane addition. This procedure was repeated six times, delivering product **6**, albeit with important variations in both its yield and enantiomeric purity. At the seventh use of the catalyst, the targeted product was recovered in 56% yield after a five day reaction, with an enantioselectivity value reaching only 40% ee. A release of the complex into the product solution under these conditions is undeniable. This could indeed be proven by a test experiment, which was conducted after the formation of **2**–$Cu(OAc)_2$@charcoal. The supernatant solution was removed and used to test its reactivity in a catalytic nitroaldolization between both substrates. Under these conditions, after 24 h, a conversion of 73% into **6** could be observed, and it was isolated in 74% ee, as a proof for the important leaching of the enantioselective copper complex **2**–$Cu(OAc)_2$ in solution. The higher enantioselectivity obtained in this last case may also be indicative of copper leaching to some extent, which has been already reported for bis(oxazoline) complexes,[25] for transformations performed in ethanol.[26]

Encouraged by the 'tea-bag' procedure described by Bellemin-Laponnaz and Gade,[27] and as an attempt to improve the recyclability of complex **2**–$Cu(OAc)_2$@charcoal, this supported catalyst was trapped within membrane bags made from a commercially available dialysis membrane (see Fig. 1). The asymmetric Henry reaction was performed under these conditions, but the reaction mixture had to be diluted five times to ensure the best contact between the substrates and the immobilized catalyst. The results arising from the transformation between benzaldehyde and nitromethane are reported in Table 2.

The reaction time was increased to obtain high conversions in the diluted reaction mixture. The first catalyst use gave product **6** in 53% isolated yield and with a very modest ee value (31%) after 48 h (Table 2, run 1). The product formed from a crotonization reaction could also be detected in a non-negligible amount (22%, NMR yield). The supernatant was directly collected after the indicated reaction time without any further processing and the supported catalyst was engaged in a second run without being rinsed or dried. The reaction time was extended to 96 h allowing the isolation of the nitroalcohol with 73% yield and 55% ee. The catalyst was reused for 6 additional runs, and each time gave the product with a relatively good maintenance of the enantioselectivities, in comparison with the aforementioned procedure. The ratio of crotonization product/Henry product was stabilized at approximately 10/90 all along the procedure.

Charcoal was thus demonstrated to be a potential support for anthracene-tagged bis(oxazoline) copper derivatives. Some reuses were performed by direct filtration or caging in a dialysis membrane, but significant catalyst leaching could not be avoided under these reaction conditions. In order to evaluate the scope of application of such heterogenization methodologies, the efficiency of the copper **2**–@charcoal catalyst was further tested in another transformation, the ene reaction.

The ene reaction was described for the first time by Evans et al. This reaction was promoted by chiral bis(oxazoline) copper triflate salts between olefins and activated aldehydes, delivering the corre-




**[ 2-Cu(OAc)$_2$ @ charcoal ]**

**Figure 1.** **2**–$Cu(OAc)_2$@charcoal in a 'tea bag' procedure.

**Table 2**
Henry reaction between benzaldehyde and nitromethane promoted by **2**–Cu(OAc)$_2$@charcoal in a 'tea-bag' procedure[a]

| Run | *t* (h) | Yield **6**[b] (%) | ee **6**[c] (%) |
|---|---|---|---|
| 1 | 48 | 53 | 31 (*R*) |
| 2 | 96 | 73 | 55 (*R*) |
| 3 | 120 | 76 | 62 (*R*) |
| 4 | 120 | 75 | 57 (*R*) |
| 5 | 120 | 36 | 51 (*R*) |
| 6 | 120 | 60 | 51 (*R*) |
| 7 | 120 | 54 | 47 (*R*) |
| 8 | 120 | 60 | 46 (*R*) |

[a] 10 equiv $MeNO_2$, 20 °C, 10 mol % cat.
[b] Isolated yield.
[c] Determined by chiral HPLC, see Experimental.

**Table 3**
Ene reaction between ethyl glyoxylate and α-methylstyrene promoted by **2**–Cu(OTf)$_2$@charcoal[a]

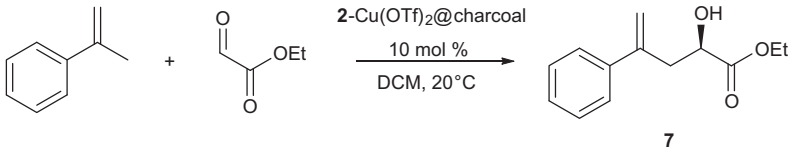
| Run | Yield **7**[b] (%) | ee **7**[c] (%) |
|---|---|---|
| 1 | 85 | 70 (*R*) |
| 2 | 91 | 67 (*R*) |
| 3 | 89 | 70 (*R*) |
| 4 | 84 | 62 (*R*) |
| 5 | 86 | 57 (*R*) |
| 6 | 80 | 55 (*R*) |
| 7 | 76 | 52 (*R*) |

[a] 18 h, 2 equiv ethyl glyoxylate, 20 °C, 10 mol % cat.
[b] Isolated yield.
[c] Determined by chiral HPLC, see Experimental.

sponding alcohol derivatives in very high yields and selectivities.[28] Singh et al. published later the efficiency of bis(oxazoline) ligands based on the indanol framework in the presence of Cu(OTf)$_2$ to catalyze the transformation between ethyl glyoxylate and α-methylstyrene, to produce 2-hydroxy-4-phenyl-pent-4-enoic acid ethyl ester **7** in 64% yield and with 71% ee.[29] We have proved[20] that **2**–Cu(OTf)$_2$ catalyzed this reaction with a similar efficiency, since **7** could be isolated under the same conditions in 89% yield with 67% ee. Although the enantioselectivity achieved for this transformation is rather modest under homogeneous conditions, it represents a noteworthy test for the preparation of functionalized compounds in another solvent. Consequently **2**–Cu(OTf)$_2$@charcoal was tested to promote this reaction under heterogeneous conditions (Scheme 3).

Compound **2**–Cu(OTf)$_2$@charcoal was prepared via the same procedure as that described from the copper acetate salt and it was used in the first reaction run with both substrates to furnish **7** after an 18 h reaction, with 85% yield and 70% ee (Table 3). These results match perfectly with those obtained in the presence of the analogous homogeneous catalyst. The catalyst was directly recovered after the first transformation through filtration with prior pentane addition. It was then reengaged in six supplementary runs following the same procedure and compound **7** was isolated each time with high yield and selectivity, although in this case again, a slight but steady drop in these values was observed during the recycling. In order to ensure the major role of the anthracene moiety involved in the interactions with the support, the classical *inda*Box ligand diMe-**1**, lacking this aromatic substituent on the methylene bridge, was tested as a ligand in the presence of the charcoal support. The corresponding copper(II) complex for its first use gave product **7** in 82% isolated yield and with 61% ee. After reaction completion and pentane addition, the supernatant was filtered, the remaining solid was dried, and a new substrate batch was added. The second use of the charcoal showed a substantial drop in performance since **7** was isolated in only 20% yield and with 35% ee, indicating the very inefficient recovery of the non-tagged bis(oxazoline)-based catalyst. The anthracene-charcoal interaction was thus demonstrated to allow chiral catalyst recovery for two different asymmetric transformations. Some efficient re-uses could be performed with this procedure but partial leaching of the catalyst and the metal could not be avoided.

Analogous ligand **5**, bearing a pyrene moiety, was therefore investigated to take advantage of its high potential to generate




**Scheme 3.** Ene reaction between ethyl glyoxylate and α-methylstyrene in the presence of **2**–Cu(OTf)$_2$@charcoal.

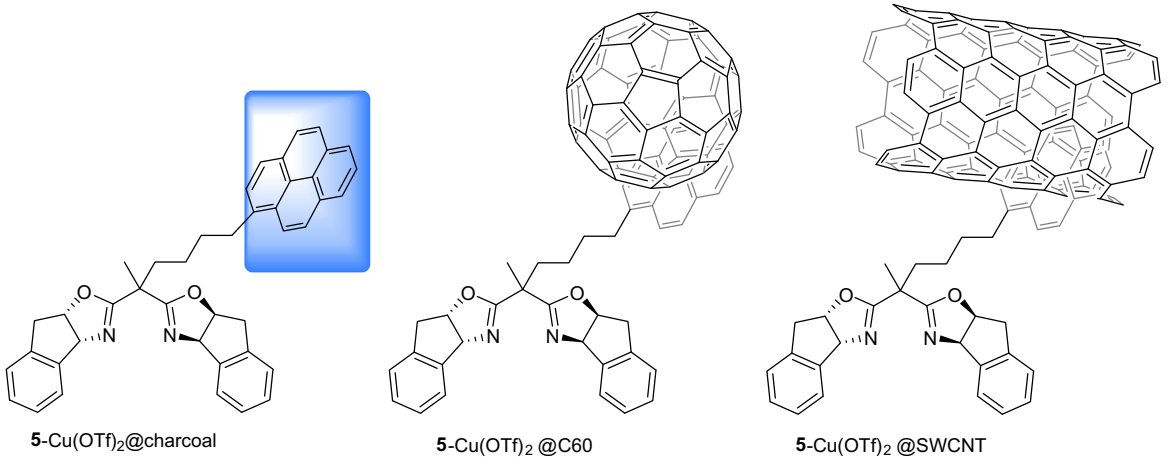
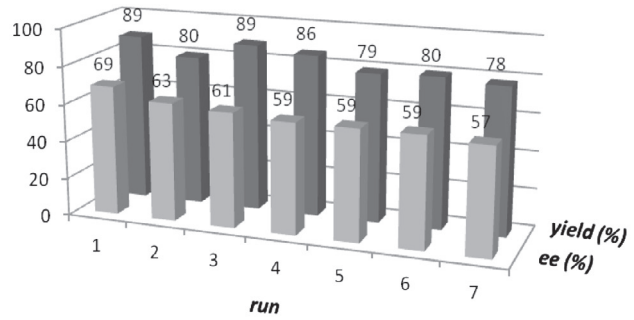
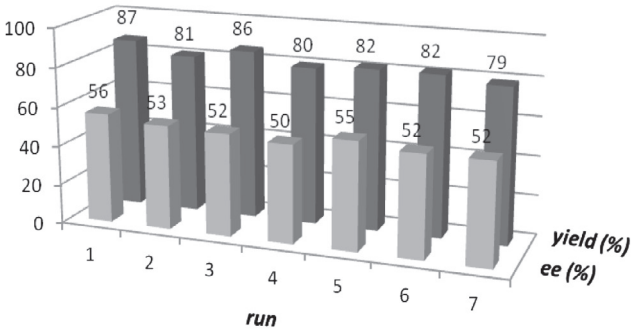


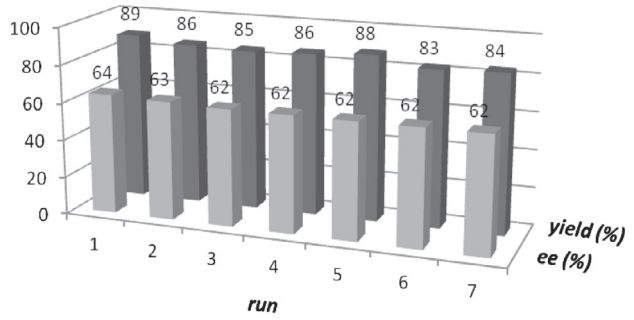

**Figure 2.** **5**–Cu(OTf)$_2$@charcoal, **5**–Cu(OTf)$_2$@fullerene, **5**–Cu(OTf)$_2$@SWCNT chiral catalysts.




**5**-Cu(OTf)$_2$@charcoal




**5**-Cu(OTf)$_2$@fullerene




**5**-Cu(OTf)$_2$@SWCNT

**Figure 3.** The ene reaction between ethyl glyoxylate and α-methylstyrene at 20 °C for 16 h in the presence of the supported catalysts (10 mol %) [formation of (*R*)-**7** as the main product].

strong π–π interactions to improve upon the bis(oxazoline) copper catalyst recyclability.[30] Activated charcoal was examined as a support, as were fullerene and single-walled carbon nanotubes, since such procedures are rarely described in the literature (Fig. 2).

The ene reaction between ethyl glyoxylate and α-methylstyrene was used as a test transformation for evaluating and comparing the efficiency of the three supported catalytic systems; the results are shown in Fig. 3. All complexes were insoluble in dichloromethane; the recycling procedure involved in each case the addition of pentane and subsequent filtration of the supernatant after 16 h of reaction, at room temperature, drying of the catalyst, and renewed addition of the substrates.

The three anchored catalysts gave product **7** in high yield for the first catalyst runs. In each case, **7** could be isolated with approximately 89% yield. Differences were however undoubtedly noted concerning the selectivities of the transformations; **5**–Cu(OTf)$_2$@charcoal produced **7** with the highest enantioselectivity of 69%, whereas only 56% ee could be achieved in the presence of **5**–Cu(OTf)$_2$@fullerene as a promoter. A mean value of 64% was obtained when the product was synthesized through **5**–Cu(OTf)$_2$@SWCNT catalysis. Seven cycles were performed for every supported catalyst. The use of charcoal as a support behaved similarly with ligand **5** compared to results obtained in the presence of ligand **2** (see Table 3), with similar average values in terms of yield and enantioselectivity. A slight but undeniable decrease of these values proved the release of trace amounts of the catalyst in the product solution all along the recycling procedure, also with the bis(oxazoline) ligand bearing a pyrene functionality. Catalysis performed in the presence of **5**–Cu(OTf)$_2$@fullerene provided more stable results, particularly concerning the enantioselectivity values. However, the average value achieved in this case was only 53% ee, which is a notable decrease compared to the efficiency of the corresponding homogeneous species. In this case, the structure of the fullerene probably modified complex intermediate leading to lower selectivities. The interaction between the pyrene moiety and the fullerene is however strong enough, ensuring robust anchorage of the chiral catalyst at the support surface for an efficient steady recycling procedure. The best support proved to be the single-walled carbon nanotubes since both the enantioselectivity and yield values remained high and constant during all catalytic cycles. The seventh use of **5**–Cu(OTf)$_2$@SWCNT in this case nearly perfectly matched the results obtained in the presence of fresh promoter.

## 3. Conclusion

We have thus demonstrated that bis(oxazoline) ligands modified by anthryl- or pyrenyl-based tags can be efficiently immobilized through non-covalent π–π interactions on various supports. The catalysis of the Henry reaction conducted in the presence of charcoal led to the desired product and numerous catalyst reuses could be performed although some leaching of the active chiral complex could not be avoided in ethanol. Some improvements in terms of stability of the activity and selectivity values were achieved by capturing the heterogenized catalyst in a benzoylated dialysis membrane. The strength of the interactions is certainly reduced under the very polar reaction conditions (ethanol and excess nitromethane) necessary to drive the Henry reaction. The ene reaction between α-methylstyrene and ethylglyoxylate was successfully performed in the presence of a pyrene-tagged bis(oxazoline), non-covalently anchored onto the three supports. Specifically, fine-tuning the procedure with the use of SWCNT allowed the synthesis of product **7** with enantioselectivity values perfectly matching those obtained under homogeneous conditions. The catalyst was recovered and reengaged in six other catalytic runs with new substrate batches. No decrease in the selectivity or activity values could be observed, indicating the very efficient recovery of the chiral catalyst by this procedure. To the best of our knowledge, this example is the first demonstration of the efficient formation of new chiral C–C bonds, by a catalyst immobilization involving π–π interactions with fullerene or SWCNT as solid supports. This facile methodology may be transposed to other asymmetric catalytic transformations, leading to the preparation of valuable chiral synthons, allowing both, the recycling of the precious organometallic complexes, and also the recovery of the support.

## 4. Experimental

### 4.1. General

All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Solvents were distilled before use from calcium hydride or sodium/benzophenone. Ligand **1**, 4-(py-

ren-1-yl)butan-1-ol and the substrates used for the nitroaldol and ene reactions were purchased and used as received. The synthesis of ligand **2**[18] and 4-(pyren-1-yl)butyl methanesulfonate **3**[31] has already been described. Activated charcoal, NORIT SA II was commercially available from Acros Organics, the benzoylated dialysis membrane was received from Sigma–Aldrich. Fullerene C60 and carbon nanotubes (single walled) were purchased from Aldrich. The HRMS analyses were performed with a MicroTOFq (quadrupole coupled with TOF analyzer).

### 4.2. (3a*R*,3a′*R*,8a*S*,8a′*S*)-2,2′-(5-(Pyren-1-yl)pentane-1,1-diyl)bis-(8,8a-dihydro-3aHindeno[1,2-d]oxazole) 4

In a dried Schlenk tube, TMEDA (114 μL, 0.76 mmol) and diisopropylamine (159 μL, 1.14 mmol) were mixed in 3 mL of THF and the solution was cooled to −20 °C. A lithium diisopropylamide solution was then obtained by the slow addition of *n*BuLi (605 μL, 1.6 M in hexane, 1.51 mmol) over 30 min at −20 °C. The colorless solution was then allowed to stir at rt. After 1 h, the solution of LDA was transferred into a second Schlenk containing Box-**1** (250 mg, 0.76 mmol) in 8 mL of THF and the mixture was stirred at rt for 2 h. Mesylate **3** (293 mg, 0.83 mmol) in 4 mL of THF was then added to the previous solution and the mixture was heated to 55 °C and stirred for 24 h. Water was then added to the solution and the aqueous layer was extracted with ethylacetate (3 × 15 mL). The combined organic layers were washed with a saturated solution of $NH_4Cl$, dried over $MgSO_4$, and then concentrated. The crude product was purified on silica gel (cyclohexane/ethylacetate = 1:1) to afford the pure product **4** as a yellow solid (124 mg, 28% yield). $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ (ppm) 1.38–1.45 (m, 2H), 1.66–1.71 (m, 1H), 1.75–1.84 (m, 2H), 2.12–2.19 (m, 2H), 2.84 (dd, 2H, $J$ = 17.6 Hz and $J$ = 5.4 Hz), 3.17–3.30 (m, 4H), 5.27–5.36 (m, 2H), 5.54–5.58 (m, 2H), 7.17–7.28 (m, 6H), 7.48–7.51 (m, 2H), 7.78 (d, 1H, $J$ = 7.9 Hz), 7.98–8.20 (m, 8H). $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ (ppm) 23.0, 30.2, 31.4, 33.3, 35.2, 39.4, 71.8, 84.7, 123.5, 124.6, 124.8, 125.0, 125.1, 125.6, 125.7, 126.5, 127.1, 127.2, 127.4, 127.5, 128.5, 128.6, 129.7, 130.9, 131.4, 136.9, 139.6, 141.2, 141.9, 166.9. HRMS (EI): calcd for $C_{41}H_{35}N_2O_2^+$: 587.2693, found: 587.2681.

### 4.3. (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(6-(Pyren-1-yl)hexane-2,2-diyl)bis-(8,8a-dihydro-3aHindeno[1,2-d]oxazole) 5

In a dried Schlenk tube, TMEDA (86 μL, 0.59 mmol) and diisopropylamine (81 μL, 0.59 mmol) were mixed in 1.5 mL of THF and the solution was cooled to −20 °C. A lithium diisopropylamide solution was then obtained by the slow addition of *n*BuLi (513 μL, 1.6 M in hexane, 0.77 mmol) over 30 min at −20 °C. The colorless solution was then allowed to stir at rt. After 1 h, the solution of LDA was transferred into a second Schlenk containing Box-**4** (250 mg, 0.43 mmol) in 8 mL of THF and the mixture was stirred at RT for 2 h. Next, MeI (36 μL, 0.59 mmol) was then added dropwise to the previous solution and the mixture was heated to 55 °C and stirred for 24 h. Water was then added to the solution and the aqueous layer was extracted with ethylacetate (3 × 15 mL). The combined organic layers were washed with a saturated solution of $NH_4Cl$, dried over $MgSO_4$, and then concentrated. The crude product was purified on silica gel (cyclohexane/ethylacetate = 1:1) to afford the pure product **5** as a yellow powder (110 mg, 43% yield). $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ (ppm) 1.29–1.32 (m, 2H), 1.43 (s, 3H), 1.69–1.76 (m, 2H), 1.98–2.03 (m, 2H), 3.00 (dd, 2H, $J$ = 178 Hz and $J$ = 6.0 Hz), 3.08–3.23 (m, 2H), 3.30–3.61 (m, 2H), 5.20–5.30 (m, 2H), 5.56 (t, 2H, $J$ = 7.9 Hz), 7.23–7.34 (m, 4H), 7.50–7.58 (m, 2H), 7.75 (d, 1H, $J$ = 8.0 Hz), 7.80–8.20 (m, 10H). $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$(ppm) 20.8, 24.0, 31.7, 33.3, 35.9, 39.6, 42.1, 76.3, 83.0, 123.5, 124.6, 124.8, 125.1, 125.6, 125.7, 126.5, 127.0, 127.1, 127.4, 127.5, 128.4, 128.5, 128.6, 129.7, 130.9, 131.4, 136.9, 139.6, 141.9, 142.1, 168.6. HRMS (EI): calcd for $C_{42}H_{37}N_2O_2^+$: 601.2850, found: 601.2842. $[\alpha]_D^{20}$ + 99.4 (*c* 1.20, $CHCl_3$).

### 4.4. Procedure for the Henry reaction with 2–Cu(OAc)$_2$@charcoal

Ligand **2** (33 mg, 0.055 mmol), dissolved in EtOH (2 mL) was added to $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol) and the blue–green solution was stirred for 1 h at rt. Next, the mixture was directly introduced into a tube containing charcoal (180 mg, NORIT SA II). After 1 h of additional stirring, nitromethane (270 μL, 5.0 mmol) was introduced dropwise, followed by the addition of benzaldehyde (51 μL, 0.5 mmol) and the mixture was stirred for the appropriate time at 20 °C. The suspension was then filtered after pentane addition and the supported catalyst dried to be reengaged in the following transformation. The solution containing products was then evaporated in vacuum; the residue was purified by preparative thin layer chromatography (pentane/ether = 4:1) and analyzed by HPLC for determination of the ee.

### 4.5. Tea-bag procedure for the Henry reaction with 2–Cu(OAc)$_2$@charcoal

Ligand **2** (33 mg, 0.055 mmol), dissolved in EtOH (2 mL) was added to $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol) and the blue–green solution was stirred for 1 h at rt. Next, it was directly introduced into a flask containing charcoal (180 mg, NORIT SA II). The solvents were removed in vacuum and the resulting powder was enclosed in a cellulosic membrane (1 cm$^3$). Next, EtOH (10 mL) was added and after 1 h of additional stirring, nitromethane (270 μL, 5.0 mmol) was introduced dropwise, followed by the addition of benzaldehyde (51 μL, 0.5 mmol) and the mixture was stirred for the appropriate time at 20 °C. The supernatant was then directly removed via a pipette and the supported catalyst was reengaged in the following transformation. The solution containing products was then evaporated in vacuum and the residue purified by preparative thin layer chromatography (pentane/ether = 4:1) and analyzed by HPLC for the determination of the ee.

### 4.6. (*R*)-(−)-2-Nitro-1-phenylethanol 6

$^1$H NMR: ($CDCl_3$, 250 MHz) $\delta$ (ppm) 2.99 (br s, 1H), 4.53 (dd, 2H, $J$ = 13.3 Hz and $J$ = 3.5 Hz), 4.64 (dd, 1H, $J$ = 13.3 Hz and $J$ = 9.3 Hz), 7.38–7.45 (m, 5H). $^{13}$C NMR: ($CDCl_3$, 250 MHz) $\delta$ (ppm) 71.1, 81.3, 126.1, 129.0, 129.1, 138.3. HPLC: IB (hexane/iPrOH = 9:1, 1.0 mL min$^{-1}$, 215 nm) t*R* (major) = 11.42 min, t*S* = 13.37 min.

### 4.7. Ene-reaction; immobilization of ligand-2 on charcoal

Ligand **2** (33 mg, 0.055 mmol) dissolved in DCM (2 mL) was added to $Cu(OTf)_2$ (18 mg, 0.05 mmol) and the blue–green solution was stirred for 1 h at rt. Next, it was directly introduced into a tube containing charcoal (180 mg, NORIT SA II). After 1 h of additional stirring, α-methylstyrene (65 μL, 0.5 mmol) was added to the previous suspension and the homogeneous mixture was then stirred for 10 additional minutes at 20 °C. Ethyl glyoxylate (510 μL, 2.5 mmol) was then introduced dropwise and the mixture was stirred for 12 h. The suspension was then filtered after pentane addition and the supported catalyst dried to be reengaged in the following transformation, after the addition of DCM (2 mL). The solution containing products was evaporated in vacuum, and the residue was purified by preparative thin layer chromatography (pentane/ether = 4:1) and analyzed by HPLC for determination of the ee.

### 4.8. Ene-reaction; immobilization of ligand-5 on charcoal, $C_{60}$ or SWCNT

Ligand **5** (33 mg, 0.055 mmol) dissolved in DCM (2 mL) was added to $Cu(OTf)_2$ (18 mg, 0.05 mmol) and the blue-green solution was stirred for 1 h at rt. Next, it was directly introduced into a tube containing charcoal (180 mg, NORIT SA II), $C_{60}$ (40 mg, 0.055 mmol) or SWCNT (40 mg). After 1 h of additional stirring, α-methylstyrene (65 μL, 0.5 mmol) was added to the previous suspension and the homogeneous mixture was then stirred for 10 additional minutes at 20 °C. Ethyl glyoxylate (510 μL, 2.5 mmol) was then introduced dropwise and the mixture was stirred for 12 h. The suspension was then filtered after pentane addition and the supported catalyst dried to be reengaged in the following transformation, after the addition of DCM (2 mL). The solution containing products was evaporated in vacuum and the residue was purified by preparative thin layer chromatography (pentane/ether = 4:1) and analyzed by HPLC for the determination of the ee.

### 4.9. (*R*)-(−)-Ethyl 2-hydroxy-4-phenylpent-4-enoate 7

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (ppm) 1.25 (t, 3H, $J$ = 7.1 Hz), 2.70 (br s, 1H), 2.86 (dd, 1H, $J$ = 14.7 Hz and $J$ = 7.5 Hz), 3.09 (dd, 1H, $J$ = 14.7 Hz and $J$ = 4.4 Hz), 4.02–4.17 (m, 2H), 4.28 (dd, 1H, $J$ = 7.5 Hz and $J$ = 4.4 Hz), 5.23 (s, 1H), 5.42 (s, 1H), 7.28–7.45 (m, 5H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ (ppm) 14.1, 40.5, 61.6, 69.1, 116.2, 126.4, 127.7, 128.4, 140.3, 143.6, 174.4. HRMS (ESI+): calcd for $C_{13}H_{16}O_3Na^+$: 243.0992, found: 243.0984. HPLC: OJ-H (hexane/iPrOH = 9:1, 0.5 mL min$^{-1}$, 254 nm) t*S* = 19.67 min, t*R* (major) = 27.27 min.

### Acknowledgments

CNRS, MESR and the program 'Chimie et Développement Durables' du CNRS are acknowledged for the financial support. The Labex Charmmmat is thanked for support.

### References

1. Temkin, O. N.; Pozdeev, P. P. In *Homogeneous Catalysis with Metal Complexes: Kinetic Aspects and Mechanisms*; Wiley-VCH: Weinheim, 2012.
2. Mikami, K.; Lautens, M. In *New Frontiers in Asymmetric Catalysis*; Wiley-VCH: Weinheim, 2007.
3. Desimoni, G.; Faita, G.; Jørgensen, K. A. *Chem. Rev.* **2011**, *111*, 284–437.
4. Fraile, J. M.; García, J. I.; Mayoral, J. A. *Coord. Chem. Rev.* **2008**, *252*, 624–646.
5. Baleizão, C.; Gigante, B.; García, H.; Corma, A. *Tetrahedron* **2004**, *60*, 10461–10468.
6. Goodrich, P.; Hardacre, C.; Paun, C.; Ribeiro, A.; Kennedy, S.; Lourenço, M. J. V.; Manyar, H.; Nieto de Castro, C. A.; Besnea, M.; Pârvulescu, V. I. *Adv. Synth. Catal.* **2011**, *353*, 995–1004.
7. Xing, L.; Du, F.; Liang, J.-J.; Chen, Y.-S.; Zhou, Q.-L. *J. Mol. Cat. A: Chem.* **2007**, *276*, 191–196.
8. Szőllősi, G.; Németh, Z.; Hernádi, K.; Bartók, M. *Catal. Lett.* **2009**, *132*, 370–376.
9. Chen, Z.; Guan, Z.; Li, M.; Yang, Q.; Li, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 4913–4917.
10. Stien, D.; Gastaldi, S. *J. Org. Chem.* **2004**, *69*, 4464–4470.
11. Gastaldi, S.; Stien, D. *Tetrahedron Lett.* **2002**, *43*, 4309–4311.
12. Chen, R. J.; Zhang, Y.; Wang, D.; Dai, H. *J. Am. Chem. Soc.* **2001**, *123*, 3838–3839.
13. Tran, P. D.; Le Goff, A.; Heidkamp, J.; Jousselme, B.; Guillet, N.; Palacin, S.; Dau, H.; Fontecave, M.; Artero, V. *Angew. Chem., Int. Ed.* **2011**, *50*, 1371–1374.
14. Wittmann, S.; Schätz, A.; Grass, R. N.; Stark, W. J.; Reiser, O. *Angew. Chem., Int. Ed.* **2010**, *49*, 1867–1870.
15. For a related use of pyrene-tagged dendritic catalysts in Suzuki couplings see Keller, M.; Collière, V.; Reiser, O.; Caminade, A.-M.; Majoral, J.-P.; Ouali, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 3626–3629.
16. Liu, G.; Wu, B.; Zhang, J.; Wang, X.; Shao, M.; Wang, J. *Inorg. Chem.* **2009**, *48*, 2383–2390.
17. Xing, L.; Xie, J.-H.; Chen, Y.-S.; Wang, L.-X.; Zhou, Q.-L. *Adv. Synth. Catal.* **2008**, *350*, 1013–1016.
18. Chollet, G.; Rodriguez, F.; Schulz, E. *Org. Lett.* **2006**, *8*, 539–542.
19. Chollet, G.; Guillerez, M.-G.; Schulz, E. *Chem. Eur. J.* **2007**, *13*, 992–1000.
20. Didier, D.; Schulz, E. *ChemCatChem* **2011**, *3*, 1880–1884.
21. Chollet, G.; Didier, D.; Schulz, E. *Catal. Commun.* **2010**, *11*, 351–355.
22. Didier, D.; Magnier-Bouvier, C.; Schulz, E. *Adv. Synth. Catal.* **2011**, *353*, 1087–1095.
23. Didier, D.; Schulz, E. *Synlett* **2012**, *23*, 1309–1314.
24. Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692–12693.
25. Fraile, J. M.; García, J. I.; Herrerías, C. I.; Mayoral, J. A.; Reiser, O.; Socuéllamos, A.; Werner, H. *Chem. Eur. J.* **2001**, *10*, 2997–3005.
26. Rasappan, R.; Olbrich, T.; Reiser, O. *Adv. Synth. Catal.* **2009**, *351*, 1961–1967.
27. Gaab, M.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Eur. J.* **2009**, *15*, 5450–5462.
28. Evans, D. A.; Burgey, C. S.; Paras, N. A.; Vojkovsky, T.; Tregay, S. W. *J. Am. Chem. Soc.* **1998**, *120*, 5824–5825.
29. Pandey, M. K.; Bisai, A.; Singh, V. K. *Tetrahedron Lett.* **2006**, *47*, 897–900.
30. For the use of graphitised carbon for purification of compounds through π–π interactions, see: Brown, A. R.; Irving, S. L.; Ramage, R. *Tetrahedron Lett.* **1993**, *34*, 7129–7132.
31. Cicchi, S.; Pierangelo, F.; Ghini, G.; Brandi, A.; Foggi, P.; Marcelli, A.; Righini, R.; Botta, C. *Chem. Eur. J.* **2009**, *15*, 754–764.