

Robust and Recyclable Self-Supported Chiral Nickel Catalyst for the Enantioselective Michael Addition

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Received: January 20, 2016; Revised: March 2, 2016; Published online: June 2, 2016

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201600083.

Abstract: A simple chemical modification of a chiral diamine ligand may produce a robust and recyclable enantioselective catalyst. Metallopolymers based on chiral cyclohexyldiamine-containing ditopic ligands and nickel(II) complexes have been readily prepared and applied in catalytic enantioselective Michael additions of 1,3-dicarbonyl compounds to nitroalkenes. High yields and good enantioselectivities have been recycled up to 11 times without loss of either activity or enantioselectivity at a low catalyst loading of 0.75 mol%. Moreover, the nickel metallopolymers were found to be air- and moisture-stable, which ena-

Introduction

The preparation of enantiomerically pure products is a continuous demand in particular in the fragrance and pharmaceutical industry. Although the asymmetric synthesis or the synthesis of racemic compounds followed by chiral separation remain predominant in the production of these compounds, the enantioselective catalysis offers significant potential advantages over these classical procedures. A chiral catalyst, being continually regenerated, can produce many molecules of chiral product. Indeed, enantiopure molecules are produced in nature by such a chirality transfer from enzymatic catalysts and today some chiral catalytic processes have been applied on an industrial scale. However, most of the chiral homogeneous systems frequently show activities that are not sufficient for a valuable scale-up application and they suffer from two main drawbacks which are the possible product contamination and the inability to reuse the chiral catalyst.

For all these reasons, the development of recoverable enantioselective catalytic systems is nowadays considered as an important objective.^[1,2] Various stratbled this chemistry to be carried out on the bench without the use of any air-free techniques and with non-degassed solvents. Finally, the nature of the catalyst was studied by non-linear effect experiments, giving a negative non-linear effect (NLE) as a consequence of an *in situ* decrease in the *ee* of the active species consistent with the trapping of homochiral aggregates.

Keywords: catalyst recycling; diamine ligand; enantioselective catalysis; Michael addition; multitopic ligands

egies have been investigated; however none of them has been completely satisfactory. For example, the immobilization of the catalyst on a solid support or the use of non-conventional media have demonstrated good performances but very few are really competitive with their homogeneous analogues.^[3]

In this context, the dynamic self-supported catalysts which aim to combine the advantages of both techniques (homogeneous and heterogeneous) are attractive.^[4] The system remains aggregated – and possibly heterogeneous – at its resting state and is dissolved in the reaction medium at its catalytically active state (release-and-capture strategy, Figure 1). Such dynamic self-supported catalysts may be achieved by the combination of a multitopic ligand and a metal salt pre-



Figure 1. Principle of dynamic self-supported catalysts.

Adv. Synth. Catal. 2016, 358, 1982-1988

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Figure 2. Structures of chiral nickel complexes: Evans catalyst (R=Bn: 1) and self-supported catalyst (R=Bn: 4; R = p-OMe-Bn: 4_{OMe}).

cursor. In this area, highly symmetrical bis(oxazoline) ligands have proved to be interesting tools to develop such self-supported chiral catalysts.^[5,6] They have been applied with success in several copper-based catalytic reactions such as cyclopropanation,^[7] allylic oxidation,^[8] α -hydrazination,^[9] benzoylation^[10] or Henry reaction.^[10,11]

In this work, we demonstrate that the dynamic selfsupported catalyst approach in not limited to copper salts and oxazoline-based ligands. In 2007, chiral bis-(cyclohexyldiamine)-based Ni(II) [NiL₂] complexes have been reported by Evans and co-workers as highly efficient catalysts for the enantioselective Michael addition of 1,3-dicarbonyl substrates to nitroalkenes.^[12] Mechanistic studies suggested that the substrate displaces a diamine ligand thus generating an active catalyst [NiL] that contains only one diamine ligand. With these observations, we successfully designed a chiral ditopic cyclohexyldiamine-based ligand that generates a dynamic self-supported catalyst with nickel(II) (Figure 2). Our investigations showed that the self-supported catalyst is robust and air stable and could be recycled up to 11 times without any loss of activity and enantioselectivity.^[13]

Results and Discussion

Synthesis and Characterization of the Catalyst

A very easy and straightforward procedure has been developed for the synthesis of the chiral ditopic cyclohexyldiamine-based ligands (Scheme 1). (1R,2R)-cis-N-Boc-1,2-cyclohexanediamine was treated with 0.5 equiv. of terephthalaldehyde in dry methanol giving the corresponding bis-imine product (87% yield) which was then treated with sodium borohy-



Scheme 1. Preparation of the chiral ditopic ligands and their corresponding complexes. *Reagents and conditions:* (i) terephthaldehyde (0.5 equiv.), MeOH, 4 h, room temperature (87%); (ii) NaBH₄, MeOH, 4 h, 0°C to room temperature (93%); (iii) TFA, CH₂Cl₂, 1 h (quant.); (iv) benzaldehyde, MeOH, 4 h, room tremperature, followed by NaBH₄, MeOH, 4 h, 0°C to room temperature (70–92%); (v) NiBr₂, CH₃CN reflux, 5 h (79–80%).

dride to obtain the 1,4-phenylenebis(methylene) derivative (2) in 93% yield. TFA deprotection followed by benzaldehyde, *p*-anisaldehyde or *p*-nitrobenzaldehyde condensation and reduction with sodium borohydride gave the expected ditopic ligands 3, 3_{OMe} , 3_{NO2} in 70–92% yield. The overall yields for the sequence range from 57% yield for 3_{OMe} and 74% for 3_{NO2} .

The preparation of nickel(II) complexes was done by reaction of the desired ditopic ligand **3** and **3**_{OMe} with one equiv. of NiBr₂ in refluxing acetronitrile. After cooling to room temperature, an off-white solid could be filtered, washed with diethyl ether and dried which correspond to metallopolymer **4** and **4**_{OMe}, respectively.^[14] The 1:1 ligand-to-metal stoichiometry consistent for a metallopolymer was confirmed by elemental analysis. Note that the mononuclear nickel complex Ni(II)-bis[(*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine]Br₂ (**1**) has been synthesized and used for



comparison purpose, since it is structurally similar to the polytopic ligands developed in our study.

Catalytic Properties of the Catalyst

As a test reaction we examined the activity of our catalysts in the enantioselective Michael addition of diester malonates to nitroalkenes. From the literature, the nickel mononuclear catalyst (1) displays a good activity and enantioselectivity in THF, EtOAc, dichloromethane or toluene as solvent, the latter being the best choice.^[12]

The reaction of nitrostyrene with dimethyl malonate was used as reference reaction and some representative results are presented in Table 1. All catalytic tests were conducted in air with non-degassed reagent-grade solvents. The metallopolymer (4) was found to be completely insoluble in toluene or ethyl acetate and accordingly no conversion was observed when carrying the reaction in such a solvent (entries 1) and 2). On the other hand, good enantiomeric excesses and activities were observed in THF or dichloromethane (83% ee and 85% ee, respectively; entries 3 and 4), which is consistent with a good solubility of the pre-catalyst. Under the same experimental conditions in CH_2Cl_2 , the Evans catalyst (1) afforded 89% ee with a poorer activity [8 h to go to completion vs. 3 h with (4)]. The use of the *p*-methoxy-containing metallopolymer (4_{OMe}) did not improve the activity and enantioselectivity, as displayed in entry 5. Finally, a decrease of the reaction temperature to 4°C result-

Table 1. Enantioselective Michael addition of dimethyl malonate to nitrostyrene.^[a]

CH ₂ (CO ₂ Me) ₂ + Ph) ₂ (Cat. 0.75 mol%		MeO ₂ C CO ₂ Me	
Entry	Cat.	Solvent	Temp.	Time [h]	Conv. [%]	ee [%]
1	(4)	toluene	r.t.		no reac-	
2	(4)	EtOAc	r.t.		tion no reac- tion	
3	(4)	THF	r.t.	5	95	83
4	(4)	CH_2Cl_2	r.t.	3	98	85
5	(4_{OMe})	CH_2Cl_2	r.t.	5	97	71
6	(1)	CH_2Cl_2	r.t.	8	99	89
7	(4)	THF	4°C	16	99	91
8	(4)	CH_2Cl_2	4°C	16	99	92

[a] Experimental conditions: 0.75 mol% based on Ni. Conversion determined by ¹H NMR. Enantiomeric excesses were determined by HPLC using a Chiracel AD-H column.

ed in an increase in enantiomeric excess up to 92% (entries 7 and 8); we thus fixed these experimental conditions for further studies: 0.75 mol% Ni, CH_2Cl_2 as solvent at 4°C.

We next studied the possibility of recycling the catalyst (4). The results are summarized in Table 2. For the catalyst recycling, diethyl ether was added to the reaction media at the end of each run, leading to the instantaneous precipitation of the catalytic system. The solid was then recovered, washed with diethyl ether, dried and then used again for another catalytic run. First, only one catalytic run could be conducted with the monomeric Evans catalyst (1), since the catalytic system could not be recovered at the end of the reaction. Notably using the metallopolymer (4), we could perform up to 6 cycles for the reaction of nitrostyrene with dimethyl malonate with no significant alteration in enantioselectivity and yield (92% ee, 99% conversion for each run; entry 1). The seventh and eighth sequences displayed a slight decrease of enantioselectivity (89% ee and 76% ee, respectively). Interestingly, the number of cycles was increased (up to 11 cycles) while running the reaction at room temperature rather than at 4°C albeit with a lower enantioselectivity (83-85% ee and conversion >96% for all catalytic runs; entry 2). Finally, good results were demonstrated for a series of 5 substrates (entries 3–7). Quantitative conversions and good enantiomeric excesses (90-92% ee on average) could be obtained and a minimum of 5 consecutive runs could be performed



Figure 3. Pictures of a) metallopolymer (4); b) Evans catalyst (1) and after exposition to air; c) metallopolymer (4) after 2 weeks; d) (1) Evans catalyst after 2 days (scale bar: 5 mm).



(4) Cat NO_2 NO_2 (0.75 mol% Ni) ĊOR' recycling Entry Product Rrun ee conv NO_2 ee^[b] MeC conv.[b] ĊO₂Me ee FtC conv. ĊO₂Et C₆H₄Br ee NO-[c] MeC conv. ĊO₂Me Ph ee NO_2 EtO conv. ĊO₂Et Ph ee 6^[d] NO_2 conv ĊO₂Me ee NO-7^[e] conv. ĊO₂t-Bu

Table 2. Enantioselective Michael addition catalyzed by (4) and evaluation of the recycling.^[a]

^[a] *Experimental conditions:* 0.75 mol% cat. (based on Ni), 16 h, 4°C in CH₂Cl₂. Conversion determined by ¹H NMR. Enantiomeric excesses were determined by HPLC using a Chiracel AD-H column.

^[b] Room temperature.

^[c] $C_6HBr: para-bromophenyl.$

^[d] dr = 1.05:1 (determined by ¹H NMR), *ee* of the minor diastereomer given in the Supporting Information.

[e] dr=3.5:1(determined by ¹H NMR), ee of the minor diastereomer given in the Supporting Information.

in all cases without any loss of activity and enantioselectivity.

An important feature of the nickel metallopolymer (4) is its high air and moisture stability, which enable this chemistry to be carried out on the bench without use of any air-free techniques and with non-degassed solvents. Indeed, the metallopolymer (4) is air-stable and can be stored exposed to air at room temperature indefinitely. Figure 3 shows images of the metallopolymer (4) and the Evans catalyst (1) when exposed to air. After two weeks exposure, no change was ob-

served for the compound (4) (images **a** and **c**) whereas exposition to air of the mononuclear nickel complex (1) lead to an oily green compound after only two days (images **b** and **d**). Moreover, the exposed catalyst (1) displays very poor catalytic activity (38% conversion, 0% *ee*) whereas no change of activity and enantioselectivity was observed for exposed catalyst (4) (91% conversion, 91% *ee*) and also one month later.

Evans and co-workers studied the non-linear effects (NLE) in the reaction of diethyl malonate and nitro-



styrene catalyzed by the nickel catalyst (1) and they found a linear relationship between the enantiomeric excess of the product and the enantiomeric excess of the catalyst.^[12] The authors concluded that the active species might be a monomeric species, a suggestion that is also consistent with further kinetic studies. We anticipated that this behavior could be different while using our dynamic self-supported catalyst (4) since the active species might be in equilibrium with polymeric inactive entities (i.e., reservoir effect).^[15] Indeed, a significant negative non-linear relationship between the ee of the product and that of the ligand was found as shown in Figure 4. The above asymmetric depletion is a consequence of an *in situ* decrease in the *ee* of the active catalyst consistent with a trapping of a homochiral aggregate. The shape of the curve may be the result of complex mixtures of mononuclear species, oligomers and polymers, which could not be modelled by the simple mathematical models developed by Kagan.^[16] As another evidence for the presence of equilibrium between an active monomeric species and catalytically inactive metallopolymer, a slower reaction rate (and unchanged enantioselectivity) was observed when an excess of ditopic ligand was added in the reaction media [1 equiv. of (3) based on Ni, see the Supporting Information]. This can be





Figure 4. Enantiomeric excess of the product as function of the enantiomeric excess of the chiral auxiliary (4) showing a negative nonlinear effect.

ascribed to a decrease of complexed substrate by biasing the equilibrium in favor of diamine complexes.

Conclusions

In summary, we have described that a simple chemical modification of a chiral diamine ligand may produce a highly efficient, robust and recyclable enantioselective catalyst. The reaction of the chiral ditopic diamine ligand with NiBr₂ precursor generated a metallopolymer which could be stored in air at room temperature indefinitely. This system was able to act as an efficient self-supported catalyst in the Michael additions of 1,3-dicarbonyl compounds to nitroalkenes with very easy operational simplicity on the bench with non-degassed reagent-grade solvents and a low catalyst loading. Easy recovery of the catalyst has been demonstrated in up to 11 cycles without loss of activity or enantioselectivity. Finally, the nature of the active catalyst has been studied by non-linear experiments revealing that the mechanism most likely involves equilibrium between an active monomeric species and a catalytically inactive homochiral metallopolymer. Future efforts will be directed to extend the scope of the metallopolymer to related nickel-based catalytic asymmetric reactions.^[17]

Experimental Section

General Considerations

All reactions (except catalytic runs) were performed under an inert atmosphere of argon or nitrogen using standard Schlenk line techniques. Solvents were purified and degassed by standard procedures. All reagents were used without further purification. (1*R*,2*R*)-trans-*N*-Boc-1,2-cyclohexanediamine was synthesized according a reported procedure.^[18] ¹H and ¹³C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVANCE 300 spectrometer using the residual solvent peak as reference (CDCl₃: $\delta_{\rm H}$ =7.26 ppm; $\delta_{\rm C}$ =77.16 ppm) at 298 K. HR-MS ESI analyses were performed on a microTOF, Bruker Daltonics. HPLC analyses were performed on a Gilson apparatus (UV-VIS156/321 PUMP) with Chiralcel Daicel columns using *n*hexane/*i*-PrOH eluents.

Synthesis of Di-*tert*-butyl [(1*R*,1'*R*,2*R*,2'*R*)-{[1,4-Phenylene-bis(methylene)]-bis(azanediyl)}-bis(cyclohexane-2,1-diyl)]dicarbamate (2)

(1R,2R)-trans-N-Boc-1,2-cyclohexanediamine (300 mg, 1.4 mmol, 2 equiv.) was dissolved in dry methanol (10 mL). Terephthaldehyde (0.7 mmol, 94 mg) was added and the reaction mixture was stirred at room temperature for 4 h. The resulting precipitate was collected by filtration. The solid was then dissolved in methanol (20 mL) and the mixture was cooled to 0 °C. Sodium borohydride (100 mg) was added

Adv. Synth. Catal. 2016, 358, 1982-1988



portion wise and the mixture was stirred at 25 °C for 4 h. After evaporation of the solvents, water was added and the mixture was extracted with CHCl₃ (3×15 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed under vacuum to give a brown solid; yield: 345 mg (93%); $[\alpha]_{D}^{20}$: -117.3 (*c* 1.14, CHCl₃). MS (ES⁺): m/z=531.13 [M+H]⁺; ¹H NMR (400 MHz, CDCl₃): δ =7.19 (s, 4H, H_{arom}), 4.42 (br, 2H, -NH), 3.81 [d, ¹*J*=13 Hz, 2H, -NH(*CH*₂)], 3.59 [d, ¹*J*=13 Hz, 2H, -NH(*CH*₂)], 3.59 [d, ¹*J*=13 Hz, 2H, -NH(*CH*₂)], 3.25 [m, 2H, -NHboc(*CH*)], 2.18 [m, 2H, -NH(*CH*₂)], 2.08–2.02 (m, 2H, H_{Cy}), 2.01–1.97 (m, 2H, H_{Cy}), 1.68–1.57 (m, 4H, H_{Cy}), 1.37 (s, 18H, H_{t-Bu}), 1.28–1.12 (m, 4H, H_{Cy}), 1.10–1.06 (m, 2H, H_{Cy}), 1.05–0.98 (m, 2H, H_{Cy}); ¹³C NMR (100 MHz, CDCl₃): δ =156.0 (C=O), 139.4 (-C_{arom}),128.1 (-C_{arom}), 79.2 (C_{t-Bu}), 60.4 [-NH(CH)], 55.3 [-NHboc(*CH*)], 50.2 [-NH(*CH*₂)], 32.9 (C_{Cy}), 31.6 (C_{Cy}), 28.4 (C_{t-Bu}), 25.6 (C_{Cy}), 24.8 (C_{Cy}).

General Procedure for (3)

2 (300 mg, 0.56 mmol) was dissolved in dichloromethane (5 mL) and trifluoroacetic acid (5 mL) was added. The reaction mixture was stirred for 1 h at room temperature. Then the excess of reagent and solvent were removed under vacuum. The resulting oil was neutralized by potassium hydroxide (2N), extracted with dichloromethane $(5 \times 10 \text{ mL})$, and dried over sodium sulfate. After evaporation, the oil was dissolved in anhydrous methanol (5 mL), the corresponding aromatic aldehyde (in excess) was added and the reaction mixture was stirred for 4 h at room temperature. To the reaction mixture, sodium borohydride (8.0 equiv.) was added. After 4 h, the solvent was evaporated and water was added and the mixture extracted with chloroform (3 ×15 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed under vacuum. The crude mixture was dissolved in a small amount of DCM and the dropwise addition of HCl (36% in diethyl ether solution) provided a white precipitate. This solid was filtered and washed with diethyl ether to provide the pure hydrochloride amine salt derivatives as a white solid, while the benzylic alcohol (by-product) remained in solution.

(1*R*,1*'R*,2*R*,2*'R*)-*N[']*,*N[']*-[1,4-Phenylenebis(methylene)]bis(*N*²-benzylcyclohexane-1,2-diamine) (3): The compound 3 was obtained from benzaldehyde according to the general procedure as a white solid; yield: 131 mg (85%); $[\alpha]_D^{20}$: -164.6 (*c* 1.14, CHCl₃). IR (CH₂Cl₂): ν =3297 (N–H), 3022, 2918, 2852, 1496, 1450, 1112, 730 cm⁻¹; MS (ES⁺): *m/z*= 511.37 [M+H]⁺; ¹H NMR (400 MHz, CDCl₃): δ =7.31–7.12 (m, 14H, H_{arom}), 3.84 [d, ¹*J*=7 Hz, 2H, -NH(*CH*₂)], 3.80 [d, ¹*J*=7 Hz, 2H, -NH(*CH*₂)], 3.59 [d, ¹*J*=8 Hz, 2H, -NH(*CH*₂)], 3.56 [d, ¹*J*=8 Hz, 2H, -NH(*CH*₂)], 2.16–2.23 [m, 4H, -NH(*CH*)], 2.12–2.05 (m, 4H, H_{Cy}), 2.01 (br, 4H, -NH), 1.70–1.62 (m, 4H, H_{Cy}), 1.20–1.09 (m, 4H, H_{Cy}), 1.04– 0.92 (m, 4H, H_{Cy}); ¹³C NMR (100 MHz, CDCl₃): δ =140.9 (C_{arom}), 139.3 (C_{arom}), 128.3 (C_{arom}), 128.12 (C_{arom}), 128.10 (C_{arom}), 126.8 (C_{arom}), 60.85 [-NH(CH)], 60.81 [-NH(CH)], 50.8 [-NH(CH₂)], 50.5 [-NH(CH₂)], 31.4 (C_{Cy}), 25.0 (C_{Cy}). (**1***R***,1***'R***,2***R***,2***'R***)-***N[']***,***N^{''}***-[1,4-Phenylenebis(methylene)]-**

(1*R*,1*'R*,2*R*,2*'R*)-*N'*,*N'*-[1,4-Phenylenebis(methylene)]bis[*N*²-(4-methoxybenzyl)cyclohexane-1,2-diamine] (3_{0Me}): The compound 3_{0Me} was obtained from anisaldehyde according to the general procedure as a red solid; yield: 120 mg (70%); $[\alpha]_{20}^{20}$: -91.3 (*c* 1.14, CHCl₃). MS (ES⁺): $\begin{array}{l} m/z = 571.40 \quad [\rm M+H]^+; \ ^1\rm H \ NMR \ (400 \ MHz, \ CDCl_3): \ \delta = \\ 7.19-7.13 \ (\rm m, \ 8H, \ H_{arom}), \ 6.78-6.74 \ (\rm m, \ 4H, \ H_{arom}), \ 3.80 \ [\rm d, \ ^1J = 13 \ Hz, \ 2H, \ -\rm NH(\mathit{CH}_2)], \ 3.73 \ [\rm d, \ ^1J = 13 \ Hz, \ 2H, \\ -\rm NH(\mathit{CH}_2)], \ 3.71 \ (\rm s, \ 6H, \ -\rm OCH_3), \ 3.57 \ [\rm d, \ ^1J = 13 \ Hz, \ 2H, \\ -\rm NH(\mathit{CH}_2)], \ 3.51 \ [\rm d, \ ^1J = 13 \ Hz, \ 2H, \ -\rm NH(\mathit{CH}_2)], \ 2.20-2.14 \ [\rm m, \ 4H, \ -\rm NH(\mathit{CH})], \ 2.10-2.04 \ (\rm m, \ 4H, \ H_{\rm Cy}), \ 1.73 \ (\rm br, \ 4H, \ -\rm NH), \ 1.67-1.61 \ (\rm m, \ 4H, \ H_{\rm Cy}), \ 1.18-1.10 \ (\rm m, \ 4H, \ H_{\rm Cy}), \ 1.01- \\ 0.89 \ (\rm m, \ 4H, \ H_{\rm Cy}); \ ^{13}\rm C \ NMR \ (100 \ MHz, \ CDCl_3): \ \delta = 158.46 \ (\rm C_{arom}), \ 139.5 \ (\rm C_{arom}), \ 133.3 \ (\rm C_{arom}), \ 129.2 \ (\rm C_{arom}), \ 128.1 \ (\rm C_{arom}), \ 113.7 \ (\rm C_{arom}), \ 60.9 \ [-\rm NH(\rm CH)], \ 60.8 \ [-\rm NH(\rm CH)], \ 55.3 \ (-\rm OCH_3), \ 50.7 \ [-\rm NH(\rm CH}_2)], \ 50.3 \ [-\rm NH(\rm CH}_2)], \ 31.6 \ (\rm C_{\rm cy}), \ 25.1 \ (\rm C_{\rm cv}). \end{array}$

(1*R*,1*R*,2*R*,2*'R*)-*N*^{*I*},*N*^{*I*}-[1,4-Phenylenebis(methylene)]bis[*N*²-(4-nitrobenzyl)cyclohexane-1,2-diamine] (3_{N02}): The compound 3_{N02} was obtained from *p*-nitrobenzaldehyde according to the general procedure as a yellow solid; yield: 168 mg (92%); $[\alpha]_{D}^{20}$: -106.8 (*c* 1.14, CHCl₃). MS (ES⁺): *m*/*z* = 601.34 [M+H]⁺; ¹H NMR (400 MHz, CDCl₃): δ = 8.11–8.03 (m, 4H, H_{arom}), 7.43–7.36 (m, 4H, H_{arom}), 7.20–7.17 (m, 4H, H_{arom}), 3.90 [d, ¹*J* = 14 Hz, 2H, -NH(*CH*₂)], 3.84 [d, ¹*J* = 14 Hz, 2H, -NH(*CH*₂)], 3.70 [d, ⁻¹*J* = 14 Hz, 2H, -NH(*CH*₂)], 3.57 [d, ¹*J* = 14 Hz, 2H, -NH(*CH*₂)], 2.25–2.15 [m, 4H, -NH(*CH*)], 2.09–2.00 (m, 4H, H_{Cy}), 1.93 (br, 4H, -NH), 1.70–1.62 (m, 4H, H_{Cy}), 1.21–1.12 (m, 4H, H_{Cy}), 1.03– 0.91 (m, 4H, H_{Cy}); ¹³C NMR (100 MHz, CDCl₃): δ = 149.0 (C_{arom}), 146.9 (C_{arom}), 61.3 [-NH(CH)], 61.0 [-NH(CH)], 50.7 [-NH(CH₂)], 50.3 [-NH(CH₂)], 31.7 (C_{Cy}), 31.5 (C_{Cy}), 25.0 (C_{Cy}).

Synthesis of Metallopolymer (4)

A mixture of NiBr₂ (64 mg, 0.3 mmol) and **3** (150 mg, 0.3 mmol) in acetonitrile (5 mL) was refluxed for 5 h. After solvent removal, the residue was washed with ether (3× 10 mL) to afford the expected compound as a microcrystalline pale grey powder; yield: 80%. IR: ν =3256 (N–H), 2932, 2854, 1450, 1440, 1089, 913, 874, 736, 695 cm⁻¹; elemental analysis calcd. (%) for C₃₄H₄₆Br₂N₄Ni: C 56.00, H 6.36, N 7.68; found: C 56.00, H 6.44, N, 7.47.

Synthesis of (4_{OMe})

A mixture of NiBr₂ (64 mg, 0.3 mmol) and 3_{OMe} (150 mg, 0.3 mmol) in acetonitrile (5 mL) was refluxed for 5 h. After solvent removal, the residue was washed with ether (3× 10 mL) to afford the expected compound as a microcrystalline pale yellow powder; yield: 79%. IR: $\nu = 3256$ (N–H), 2932, 2854, 1450, 1440, 1089, 913, 874, 736, 695 cm⁻¹; elemental analysis calcd. (%) for C₃₆H₅₀Br₂N₄NiO₂: C 54.78, H 6.38, N 7.10; found: C 54.82, H 6.49, N, 7.04.

General Procedure for the Enantioselective Reactions and Recycling (Table 1, entry 1)

The metallopolymer (4) (2.3 mg, 0.003 mmol), dimethyl malonate (69 mg, 0.52 mmol) and (*E*)-nitrostyrene (65 mg, 0.43 mmol) were added in a vial with dichloromethane (1.0 mL) under air. The mixture then was stirred at 4°C. After 16 h, diethyl ether was added and a precipitate was instantly formed. The organic phase was isolated, concentrated and the product was purified by flash chromatography



(AcEt/cyclohexane 1:4) to give a white solid; yield: 99%; 92% ee).

The catalyst recovered by centrifugation was washed with diethyl ether, dried and reused in a renewed catalytic run.

Acknowledgements

The authors gratefully acknowledge the CNRS and the University of Strasbourg.

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