Journal of Catalysis 334 (2016) 120–128

Contents lists available at ScienceDirect

Journal of Catalysis

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

Highly selective multifunctional nanohybrid catalysts for the one-pot synthesis of α,β-epoxy-chalcones

Dana-Georgiana Crivoi, Anna M. Segarra *, Francesc Medina *

Departament d'Enginyeria Química, Universitat Rovira i Virgili, Av. Països Catalans, 26, Campus Sescelades, Tarragona 43007, Spain
EMaS-Centro de Investigación en Ingeniería de Materiales y Micro/nanoSistemas, Campus Sescelades, Tarragona 4300, Spain

ARTICLE INFO

Article history:
Received 19 October 2015
Revised 27 November 2015
Accepted 28 November 2015
Available online 30 December 2015

Keywords:
One-pot reaction
Asymmetric catalysis
Nanohybrid
Poly-L-leucine
Hydrotalcite
Chiral α,β-epoxy-chalcone

ABSTRACT

An efficient one-pot heterogeneous process for producing chiral α,β-epoxy-chalcones from the corresponding aldehydes and ketones has been described. The nanohybrid materials based on poly-L-leucine immobilised into rehydrated hydrotalcites did not require any pre-activation and were easily recovered and recycled for four consecutive runs without losing their catalytic efficiency in terms of conversion, total selectivity towards the corresponding epoxy-chalcones and excellent enantioselectivity.

1. Introduction

Catalytic asymmetric synthesis is an important technique for the preparation of chiral epoxides in both academia and industry. These epoxides are versatile products that can easily undergo stereospecific ring-opening reactions to form multifunctional compounds. They are not only important chiral building blocks, but also key intermediates in the synthesis of more complex molecules with important bioactivity such as leukotriene, erythromycin, (+)-aurilol or brevetoxin B [1–3].

The main pathway to obtain the chiral epoxides consists in the epoxidation of olefins by either metal-catalysed reactions [2] or peptide-type reactions [4–6]. Even though metal-catalysed reactions gained much attention in the last years, they are not suitable to produce bioactive molecules due to some possible drawbacks: metal leaching, toxic effects of the metal used, etc. Thus, peptide-catalysed reactions represent a possible solution to these drawbacks.

In 1983 Colonna et al. introduced a triphasic catalytic system based on water–organic solvent–poly-amino acids which afforded optical active epoxides [7]. The long reaction time and the problems regarding the recovery of the catalyst were overcome by Roberts et al. who developed a biphasic system composed of an organic base and anhydrous urea-hydrogen peroxide and poly-amino acids on silica as catalyst [8].

To increase the yield of the epoxidation reaction, Geller et al. modified the triphasic protocol by adding tetrabutylammonium bromide (TBAB) as cocatalyst. Using this method and in the presence of poly-L-leucine, the reaction time was considerably decreased and the enantiomeric excess was improved [9].

Recently, our group developed a new catalyst based on poly-L-leucine immobilised into hydrotalcites able to catalyse the Juliá–Colonna epoxidation of *trans*-chalcone under triphasic conditions with good conversions and enantioselectivity [10].

Industry favours catalytic processes that require less workup and where intermediates are obtained *in situ*, avoiding unnecessary purification procedures. Various α,β-unsaturated ketones used in asymmetric epoxidation reactions require the preparation from the corresponding aldehydes and ketones, which can be troublesome according to the available procedures [11–13].

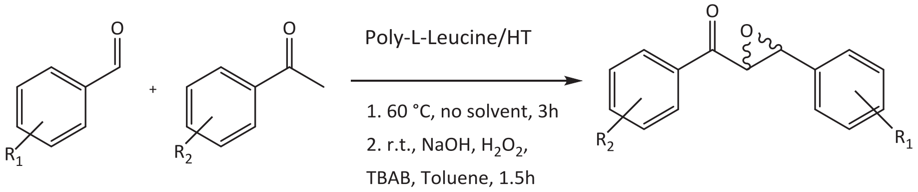
In the literature there are several homogeneous systems [14–17], but only two heterogeneous systems were able to carry out the Claisen–Schmidt condensation–asymmetric epoxidation reaction. Choudary et al. used nanomagnesium oxide (NAP-MgO), but the conversion and enantioselectivity obtained were moderate. Additionally, the catalytic system lost its activity by poisoning with the water formed during the condensation reaction [18]. Liu et al.

---

* Corresponding authors at: Departament d'Enginyeria Química, Universitat Rovira i Virgili, Av. Països Catalans, 26, Campus Sescelades, Tarragona 43007, Spain.

E-mail addresses: anamaria.segarra@urv.cat (A.M. Segarra), francesc.medina@urv.cat (F. Medina).

http://dx.doi.org/10.1016/j.jcat.2015.11.020
0021-9517/© 2015 Elsevier Inc. All rights reserved.



Scheme 1. One-pot synthesis of chiral epoxy-chalcones catalysed by immobilised poly-L-leucine (IPL).

carried out the first part of the reaction in homogeneous medium and added afterwards poly-L-leucine for the asymmetric epoxidation. Though they recycled the polymer, the system is not completely heterogeneous and the process requires longer reaction time [19].

Herein, we wish to report an efficient green one-pot way to synthesise chiral epoxy-chalcones from the corresponding aldehydes and ketones using poly-L-leucine immobilised into rehydrated hydrotalcites (Scheme 1).

2. Experimental

2.1. General

All chemicals and solvents were commercially available (Aldrich Chemical, Fluka) and used without further purification/drying unless otherwise mentioned.

XRD measurements were made using a Siemens D5000 diffractometer (Bragg–Brentano parafocusing geometry and vertical – goniometer) fitted with a curved graphite diffracted-beam monochromator and diffracted-beam Soller slits, a 0.06° receiving slit and scintillation counter as a detector. The angular 2θ diffraction range was between 1° and 70°. The sample was dusted onto a low background Si (510) sample holder. The data were collected with an angular step of 0.05° at 3 s per step and sample rotation. CuK radiation was obtained from a copper X-ray tube operated at 40 kV and 30 mA.

Thermogravimetric analyses coupled with MS and differential thermal analyses (TGA-MS/DTA) were performed on a SenSys Evo TG coupled with HiCube-Pfeiffer Vacuum system.

MALDI-TOF analyses were performed using a Voyager-DE STR MALDI mass spectrometer from Applied Biosystems equipped with a nitrogen laser using the following conditions: emission wavelength 337 nm, pulse duration 3 ns and 20 Hz repetition rate.

^{1}H NMR spectra were recorded on a Varian NMR System 400 spectrometer in $CDCl_3$. Chemical shifts (δ) are given in ppm and J values are given in Hz.

HPLC analyses were performed on a Shimadzu RID-10A (Refractive Index Detector) using CHIRALPACK IA column and heptane: ethanol 3:1 as mobile phase. Optical rotations were measured on a Perkin–Elmer 241 MC Polarimeter using Na-lamp and CH_2Cl_2 as solvent.

2.2. Synthesis of hydrotalcite materials (HTs)

Mg–Al HTs (molar ratio 2:1) were prepared by the co-precipitation method at room temperature and pH = 10. The appropriate amounts of $Mg(NO_3)_2{\cdot}6H_2O$ and $Al(NO_3)_3{\cdot}9H_2O$ were dissolved in 110 ml Milli-Q water and added dropwise into a vessel containing 150 ml of Milli-Q water. The pH was kept constant using 2 M NaOH solution. The suspension was stirred overnight at room temperature. The obtained solid was filtered and washed several times with water and dried under vacuum. The solids were calcined in air at 450 °C overnight to obtain the corresponding mixed oxides (HTc). HTr was obtained by the rehydration of HTc in inert atmosphere using decarbonated water and sonication for 30 min [10].

2.3. Synthesis of poly-L-leucine (PLL)

PLL was synthesised by the ring opening polymerisation method using trimethylamine as initiator, as previously reported [10]. The L-leucine-NCA (0.6 g) was dissolved in anhydrous 1,4-dioxane (11.4 ml) under Ar atmosphere and stirred at 60 °C. After 15 min the corresponding amount of trimethylamine (monomer/initiator ratio = 5) was added and the flask was closed with a freshly prepared $CaCl_2$ drying tube. The final mixture was left under stirring at 60 °C for 4 days. Milli-Q water was used as workup solvent and the mixture was stirred for another 2 h. The obtained solid was filtered and dried under vacuum. The polymer was characterised by MALDI-TOF spectroscopy.

2.4. Preparation of immobilised poly-L-leucine (IPL)

The poly-L-leucine synthesised using a monomer/initiator ratio of 5 at 60 °C was immobilised into Mg–Al HTr (molar ratio 2:1). In a typical procedure, 100 mg PLL was added over a mixture containing 300 mg HTr and 5 ml decarbonated water. The suspension was stirred for 1 h and subjected to ultrasound for another 30 min. The obtained material was washed with THF and dried at 40 °C under inert atmosphere. The nanohybrid materials were characterised by MALDI-TOF and XRD spectroscopy. The amount of PLL immobilised was determined by TGA analysis.

2.5. Standard conditions for the Claisen–Schmidt condensation

The Claisen–Schmidt condensation was performed in a 10 ml tube. The general procedure was as follows: acetophenone (0.19 mmol) and benzaldehyde (0.20 mmol) were added, along with the solvent – in some cases – over the catalyst (PLL, IPL, uncalcined HTs). The mixture was stirred for 3 h at different temperatures: 30 °C, 60 °C or 80 °C. The catalyst was recovered by centrifugation and washed several times with the solvent. The organic layer was dried over $MgSO_4$ and the solvent was removed by evaporation under reduced pressure. The products were identified by ^{1}H NMR.

2.6. Standard conditions for the one-pot Claisen–Schmidt condensation/Juliá–Colonna epoxidation reaction

The one-pot Claisen–Schmidt condensation/Juliá–Colonna epoxidation reaction was performed in a 10 ml tube. The corresponding ketones (0.19 mmol) and aldehydes (0.20 mmol) were added over IPL (100 wt% PLL with respect to ketone) and stirred for 3 h at 60 °C. In all the experiments the molar ratio ketone/aldehyde was 0.95. The reaction mixture was cooled at room temperature and TBAB (3.7 mg), H_2O_2 (169.7 µl), NaOH 2 M (245 µl) and 1 ml toluene were added. The reaction mixture was stirred at room temperature for another 1.5 h. The catalyst recovered by centrifugation was washed several times with toluene and water and reused without drying. The organic layer was dried over $MgSO_4$ and the solvent was removed by evaporation under reduced pressure. The products were identified by ^{1}H NMR. The ee% of the corresponding epoxide was determined by chiral HPLC. The