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Novel nanohybrid materials based on L-leucine on hydrotalcite clays: Asymmetric epoxidation reaction of chalcona

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ABSTRACT

The assembly of biorgano-guest to laminar inorganic solids is of increasing interest to their versatile applications in biotechnology or catalysis. We synthesized two different biohybrid materials based on L-leu into the hydrotalcite rehydrated under ultrasound treatment (HT_{rus}), in which L-leu was immobilized by intercalation or by replacing of hydroxyl ions at the edge sites of HT_{rus}. Separately L-leu and HT_{rus} as catalysts showed very poor activity and lack of enantioselectivity in the epoxidation reaction of α,β-unsaturated ketones such as chalcone. Nevertheless, the catalysts presented high activity and even enantioselectivity towards the *trans*-(R,S)-epoxide depending on the L-leu location on the nanohybrid catalyst.

1. Introduction

Biohybrid nanostructured materials based on the combination of laminar inorganic solids such as hydrotalcites (HTs) and naturally occurring organo-molecules such as the amino acids (AAs) have received considerable attention due to their importance in catalysis, regenerative medicine, nanocomposite materials engineering etc. [1–3]. In addition, they find industrial interest since they are derived from abundant, cheap, and ecological sources. The biohybrid materials not only often exhibit highly complementary properties between their assembled components but also present new and interesting properties due to a synergistic effect [4–8]. These new and easily recovered materials may represent a big breakthrough in the pharmaceutical industry as they could replace current homogeneous catalysts which are difficult to separate and reuse. Particularly, hydrotalcite-like compound are widely used in the synthesis of bio-nanohybrids materials [2,9–15] because they possess suitable characteristics such as high surface area, swelling properties, high ion-exchange capacity and catalytic activity in several reactions. HTs are well known as anionic clay and layered double hydroxide compounds. The chemical composition of the HTs is $M_{1-x}^{2+}M_x^{3+}(OH)_2(A^{n-})_{x/n}.yH_2O$. The hydrotalcite-like compound structure consists of brucite-like layers [$Mg(OH)_2$] with edge-sharing hydroxyl octahedral occupied by bivalent (Mg^{2+}) and trivalent (Al^{3+}) cations. The positive charged of the layers is balanced by anions located in the interlayer which can be exchanged by other organic or inorganic anions [16]. These materials can reconstruct the original layered structure after being calcined by rehydration in a CO_2 free atmosphere. The rehydrated hydrotalcite also called meixnerite, contains interlayer OH^- anions which provide significant Brønsted basic properties [17,18].

The negatively charged AAs (formed in basic medium) are potential chiral biocatalysts suitable for being immobilized in layered double hydroxides compounds such as HTs. Different methodologies for immobilising AAs into HTs have been developed. The L-pro/HT biohybrid synthesized by co-precipitation method was used as asymmetric catalyst in C–C bond-forming reactions [15]. The authors suggested that the L-pro was mainly located at the edges of the hydrotalcite layers. The biohybrid catalyst resulted in a higher catalytic activity than pure L-pro, although asymmetric induction was lower. Hibino also used the co-precipitation method immobilising the AAs between the hydrotalcite layers [19]. Later, Pitchumani et al. also interspersed the L-pro but by ion-exchange [2]. This biohybrid catalyst improved the enantioselectivity of

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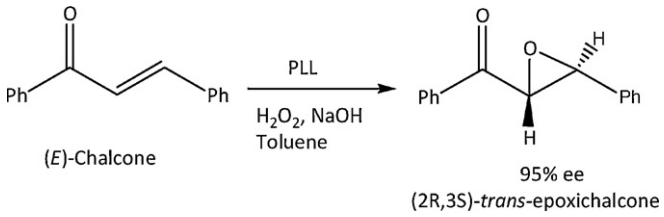

Scheme 1. Julia–Colonna asymmetric epoxidation of chalcone.

the not-immobilized L-pro in the Michael addition reaction of nitroalkenes with ketones. Furthermore, in some cases, the heterogenized catalyst presented an inversion in enantioselectivity compared to pure L-pro catalyst. To the best of our knowledge, all the reported protocols for synthesising AA-HT biohybrids require long time (>12 h).

Recently, our group has developed new protocols for synthesising nanolaminar hydrotalcite compounds using ultrasound treatment (HT_{rus}) which can incorporate highly efficient catalytic sites in the interlaminar space [20]. The properties of these HT_{rus} compounds make them a very attractive host structure for chiral molecules such as AAs which are able to catalyze the production of important chiral drugs. Several drugs such as Taxol (cancer chemotherapy) [21], (+)-Clausenamide (antiamnaesic agent) [22], Statin (cholesterol-lowering drug)[23] or (+)-Fenoprofen (rheumatoid arthritis) [24] are synthesized from chiral epoxide obtained by asymmetric epoxidation of α,β-unsaturated ketones. This reaction, known as Julià–Colonna, is catalyzed by the poly-L-leu (PLL) (Scheme 1) [25,26]. The PLL is synthesized by several steps and recovered after the reaction with difficulty.

Although the Julià–Colonna epoxidation mechanism is not at all clear, experiment and molecular modelling suggest that the helicity of the PLL determines the epoxide configuration through face-selective delivery of a hydroperoxide anion. Five L-leu residues were found to be sufficient to catalyze the Julià–Colonna epoxidation of chalcone with 96–98% ee [27]. In addition, the COOH-terminal group of the PLL does not seem to participate in the catalytic process.

Taking all this into consideration, we explored the possibility of developing new efficient synthetic protocols of different L-leu/HT_{rus} compounds where the combination of the layered materials and intercalation techniques offer new hybrid materials with desired properties. For first time, the L-leu/HT_{rus} biohybrids is used as catalysts in asymmetric Julià–Colonna epoxidation reaction, achieving higher activity and selectivity in the catalytic reaction of interest like the PLL.

2. Experimental

2.1. Synthesis of nanohybrid materials

2.1.1. Synthesis of rehydrated hydrotalcite (HT_{rus})

Mg–Al hydrotalcite (HT) with Mg/Al molar ratio = 2:1 containing nitrates as compensation anion was synthesized by the co-precipitation method at constant pH 10 [28]. Then, the HT was decomposed by thermal treatment at 450 °C during 15 h in air atmosphere and rehydrated in decarbonated water under ultrasound treatment according to the Medina et al. protocol [20]. Total rehydration of the HT was confirmed by ^{27}Al Magic-angle-spin (MAS) NMR. The obtained solid was denoted as HT_{rus}.

2.1.2. Synthesis of nanohybrid material

Nanohybrids were obtained using 20 ml of a solution of L-leu in decarbonated water at certain concentrations and HT_{rus} (500 mg). The immobilized process was performed employing two different methods. In the immobilization process by method A, the mixture was stirred for 30 min at room temperature under argon atmosphere. After immobilization process the obtained materials were separated by filtration, washed several times with decarbonated water and dried under argon. The variation in the concentration of the L-leu solution was performed to obtain different kind of materials which were denoted as L-leu/HT_{rus}-A_x, where x is the mmol of L-leu per mmol of Al^{3+} and correspond to 0.08, 0.22 and 0.44. In the immobilization process by method B, the mixture was stirred for 3 h at 80 °C under argon atmosphere. After immobilization process the obtained materials were separated by filtration, washed several times with decarbonated water and dried under argon. The nanohybrid material obtained was denoted as L-leu/HT_{rus}-$B_{1.09}$.

2.2. Characterization

The amount of L-leu immobilized onto HT_{rus} was determinate on a Shimatzu TOC-5000A in the combustion method at 953 K. Determination of the structural properties, material morphology and intercalation behaviour of the L-leu onto the HT layers were confirmed by powder XRD, FT-IR, ^{13}C and ^{27}Al MAS NMR and High-Resolution Transmission Electron Microscopy (HRTEM). Powder XRD measurements were performed on a Bruker-AXS D8-Discover diffractometer with 2θ angle ranging from 1° to 70°. FTIR spectra were recorded on a Nicolet Nexus Fourier Transform instrument provided with a DTGS KBr detector: for each spectrum 100 scans in the range 4000–400 cm^{-1} were recorded, resolution 4 cm^{-1}. HRTEM were performed with a JEOL 2010F instrument working at an acceleration voltage of 200 kV and equipped with a field emission source. The point-to-point resolution of the microscope was 0.19 nm and the resolution between lines was 0.14 nm. ^{13}C and ^{27}Al MAS-NMR spectra were obtained on a Varian Mercury VXR-400S spectrometer operating at 104.2 MHz with a pulse width of 1 ms. A total of 4000 scans were collected with a sweep width of 100 kHz and an acquisition time of 0.2 s. An acquisition delay of 1 s between successive accumulations was selected to avoid saturation effects.

2.3. Asymmetric Julià–Colonna epoxidation reaction

The asymmetric epoxidation reaction was performed in a tube of 10 ml where synthesized nanohybrid catalyst containing 0.44 mmol of L-leu (which corresponds to 458, 199, 125 and 80 mg of L-leu/HT_{rus}-$A_{0.08}$, L-leu/HT_{rus}-$A_{0.22}$, L-leu/HT_{rus}-$A_{0.44}$ and L-leu/HT_{rus}-$B_{1.09}$, respectively) tetrabutylammonium bromide (0.042 mmol), NaOH 5 M (0.43 ml) and hexane (3 ml) were mixed. Subsequently $H_2O_{2(aq)}$ (0.19 ml) and chalcone (1.44 mmol) were added. The mixture was stirred for 90 min at room temperature. To work-up the mixture, it was diluted in 1 ml of ethylacetate. The catalyst (solid phase) was washed several times with hexane and separated by centrifugation. The organic fraction was dried with $MgSO_4$. Then, the solvent in the organic phase was evaporated. The product was identified by ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.01 (s, 1H), 4.23 (s,1H), 7.32–7.45 (m,7H), 7.54 (d, 1H), 7.94 (d, 2H) ppm. The ee of *trans*-(2R,3S)-epoxy-1,3-diphenyl-propan-1-one formed by L-leu/HT catalyst was determinated by chiral HPLC using a ChiralPak IA column. The mobile phase was 25% hexane in ethanol, at a flow rate of 1 ml/min. The wavelength reading was 254 nm. The retention times were t_{major} = 7.6 min and t_{minor} = 10.6 min.

3. Results and discussion

3.1. Characterization results

In the present study, the immobilized amount of L-leu and the location of the AAs in the HT_{rus} were precisely controlled by changing the concentration of L-leu solution, the temperature and