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Inducing chirality on ZnS nanoparticles for asymmetric aldol condensation reactions†

Cite this: DOI: 10.1039/c3ra41285g

Ekta Shah and Hemant P. Soni*

Received 18th March 2013,
Accepted 22nd July 2013

DOI: 10.1039/c3ra41285g

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L-Proline immobilized ZnS nanoparticles (NPs) were synthesized by a simple wet chemical method and characterized by XRD. The as-synthesized NPs were used as a catalyst for the direct asymmetric aldol reaction of several aldehydes with acetone to achieve chiral β-hydroxy carbonyl compounds in good yields and enantioselectivity at room temperature. The peculiarity of our strategy is that the reaction is carried out at room temperature and does not involve any co-solvent for solubility purposes. The selectivity of the developed heterogeneous catalyst leads to only (*R*)-β-hydroxy carbonyl compounds and restricts the reaction at the aldolization stage only, without any formation of dehydrated α,β-unsaturated product. The modified reaction mechanism, showing the involvement of surface Zn^{+2} ions, is proposed. The catalyst was recovered and reused several times without any significant lost in activity. This opens new avenues for surface engineering leading to green catalytic processes.

1 Introduction

The Aldol condensation reaction is one of the classical organic reactions that has contributed to the progress in the field of catalysis and organic synthesis, particularly in processes involving C–C bond formation.[1,2] Catalytic aldol reactions are also considered as a waste free method (100% atom economy) when carried out in the presence of a base or basic ion-exchange resins.[3] This reaction involves the condensation reaction between enolic and ketonic forms of the same (self condensation) or different carbonyl compounds (cross condensation). The stereoselectivity of the process depends on the way in which the electron donor–acceptor species react but requires systematic strategies. Many factors need to be controlled to achieve products with the desired stereochemistry, such as temperature, pH, mole ratio of the reactants, thermodynamic and kinetic control, geometry of the reacting species, catalysis, chiral auxiliaries involved in the reaction, hydrogen bonding, interactions between the solvent and reaction species *etc.*[4] For this purpose, different types of catalytic systems have been developed with the progress of the field. Most of these are either enzymatic[5,6] or involve non-transition metal Lewis acids (*e.g.*, tetramethylsilane (TMS), lithium diisopropylamide (LDA), alkyl boranes). However, in recent years, transition metal and rare earth metal-based complex compounds have also been reported as chiral catalysts for the condensation of silyl enol ethers with different aldehydes (the Mukaiyama reaction[7]) in aqueous media.[8] For example, Kobayashi *et al.* reported the copper(II) catalyzed Mukaiyama aldol reaction in an ethanol–water solution. In another work, the same authors also reported the application of lanthanide(III) trifluoromethane sulfonate (particularly yitterbium triflate), a substitute for traditional Lewis acids, in the Mukaiyama aldol reaction in the presence of water. They reported that a high yield and selectivity can be obtained at −15 to 0 °C in protic solvents, such as water. The same group of researchers also reported that the Fe(II) and Fe(III) salts also exhibited good activity for the Mukaiyama aldol reaction in aqueous THF.[9] Mlynarski and co-workers reported a C_2-symmetric cationic aqua complex of Fe(II)–pybox (bis(oxazolinyl)pyridine) as an effective Lewis acid catalyst for the same reaction in aqueous media. They obtained aldol products in good yield and 70% enantioselectivity.[10] Samarium diiodide and other lanthanide iodides are also very efficient Lewis acid catalysts for numerous reactions, such as Mukaiyama aldol and Michael reactions. Several excellent reviews are available which discuss the state of the art in asymmetric aldol reactions.[8,11] A few enantioselective aldolization processes involving a Lewis base as the catalyst have been reported. For example, Denmark *et al.* reported a Lewis base chiral phosphor amide catalyzed asymmetric aldol addition of trichlorosilyl enolates.[12] However, most of the above strategies involve homogenous catalysis. The benefits of heterogeneous catalysis[13] can be achieved if such 'microaldolase' type catalysts can be immobilized on some inert support or any other material which can not only enhance the catalytic activity by coordinating with the original catalyst but also drive the reaction towards a stereospecific pathway, resulting in products with a high enantiomeric excess. Research activities in this direction

Department of Chemistry, Faculty of Science, The Maharaja Sayajirao University of Baroda, Vadodara-390 002, Gujarat, India. E-mail: drhpsoni@yahoo.co.in; Tel: +91-0265-2795552

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3ra41285g

RSC Advances

PAPER

Cite this: *RSC Adv.*, 2015, **5**, 26291

Immobilization of *Thermomyces lanuginosus* lipase on ZnO nanoparticles: mimicking the interfacial environment†

Ekta Shah, Paramita Mahapatra, Ashutosh V. Bedekar and Hemant P. Soni*

Received 5th February 2015
Accepted 5th March 2015

DOI: 10.1039/c5ra02249e

www.rsc.org/advances

Thermomyces lanuginosus lipase (TL lipase) was immobilized covalently on ZnO nanoparticles (NPs) functionalized with small amino acid molecules, like glycine. Glutaraldehyde was used as a spacer between the ZnO/glycine Nps and the enzyme. This study is based on the observation that the favorable conformation of an enzyme (in which the catalytic lid is exposed to reactant molecules) can be obtained at the lipid/water interface and such an interfacial environment can be mimicked by properly designing the carrier used as the support for its immobilization. Glycine functionalized ZnO NPs were covalently bonded with glutaraldehyde and consequently TL lipase enzyme immobilization was carried out by a simple wet chemical method. The resulting assemblies were characterized by using techniques like XRD, UV absorption and photoluminescence spectroscopy. The particle size was determined by using Transmission Electron Microscopy (TEM). The immobilized TL lipase enzyme showed high activity for esterification of oleic acid (C-18) with methanol in an organic medium. The catalyst was recovered and reused several times without any significant loss of activity.

1. Introduction

With thousands of years of evolution nature has developed molecules called enzymes which can carry out specific biochemical conversions in the constrained environment of a cell. Chemically, enzymes are long chain polypeptides folded in such a way that unique reaction sites (pockets) are generated according to a predefined genetic program enabling them to act as catalysts. Highly selective and specific reactions occur at these reaction sites usually in a narrow range of temperatures and pH values in an aqueous medium. From an industrial point of view, enzymes can be manufactured or extracted from the cells and utilized for large scale production of high purity stereoisomers which would be difficult by conventional catalytic processes. However, the major drawbacks are (i) denaturation of enzymes when the temperature or pH of the reaction are drastically changed (ii) enzymes function mostly in an aqueous medium under homogeneous conditions (iii) enzymes are denatured sometimes and the reaction sites may be distorted/blocked at the end of a single reaction cycle during the recovery process. Such problems can be solved by immobilizing enzyme on a suitable support. By this way the reactions can be heterogenized and the immobilized enzyme can be recovered and recycled for several times maintaining the activity. This makes overall operation simple, efficient in both aqueous and non-aqueous medium, and of course, economically viable.

Lipase (triacylglycerol ester hydrolase EC 3.1.1.3) is an enzyme which catalyzes the hydrolysis of triacylglycerol to glycerol and fatty acids. It finds wide applications in diverse areas like dairy industry, specialty chemicals, organic synthesis and manufacture of enantiomerically pure pharmaceuticals. Immobilization of lipase is carried out by various techniques[1] such as (i) non-covalent adsorption on robust supports like polymeric beads,[2,3] films,[4,5] natural kaolin clay,[6] nanoparticles,[7] *etc.* (ii) entrapment of enzyme in a polymeric gel or on membranes by physical adsorption, inclusion or covalent bonding[8–11] (iii) covalent attachment with the supports like polymers[12] or nanoparticles[13] and (iv) cross-linking of an enzyme making it carrier free.[14] However, each method has its own drawbacks. For example, non-covalent adsorption of an enzyme may cause multilayers of unfavorable orientations on the support that hamper the activity.[15] Cross-linking may cause inactive enzyme aggregates, deteriorating the catalytic efficiency of preparation. Physical entrapment in gels or membranes also requires the trapping of enzyme in active orientation in the matrix which is laborious and demands a lot of experimentation. This may restrict the natural movement of the enzyme[16] diminishing the catalytic efficiency. The fact is that there is no universal method available for immobilizing the enzyme without restricting its activity.[17] Suitable selection of a carrier, reaction conditions and enzyme itself are the three major

Department of Chemistry, Faculty of Science, The Maharaja Sayajirao University of Baroda, Vadodara-390 002, Gujarat, India. E-mail: drhpsoni@yahoo.co.in; Tel: +91-0265-2795552

† Electronic supplementary information (ESI) available: FTIR spectra of immobilized enzyme at various stages, ^{1}H NMR, ^{13}C NMR and HPLC analysis of the product methyl oleate. See DOI: 10.1039/c5ra02249e

NJC

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c6nj00655h

EDTA capped iron oxide nanoparticles magnetic micelles: drug delivery vehicle for treatment of chronic myeloid leukemia and T_1–T_2 dual contrast agent for magnetic resonance imaging†

Ekta Shah,[a] Pratik Upadhyay,[b] Mala Singh,[c] Mohmmad Shoab Mansuri,[c] Rasheedunnisa Begum,[c] Navin Sheth[d] and Hemant P. Soni*[a]

Received (in Montpellier, France) 29th February 2016,
Accepted 24th September 2016

DOI: 10.1039/c6nj00655h

www.rsc.org/njc

Ethylene diamine tetra acetate (EDTA) capped Fe_3O_4 nanoparticles (NPs) have been synthesized and encapsulated using polymeric micelles. The synthesized Fe_3O_4/EDTA/P magnetic micelles are used as a vehicle to load the hydrophobic drug imatinib and transfect it in a bone marrow cell-line (K562) *in vitro* for the treatment of chronic myeloid leukemia. From FTIR spectroscopy it is established that EDTA coordinates bidentately with the surface Fe ions. From the vibrating sample magnetometry (VSM) study, the shape of the magnetization curve indicates superparamagnetic behavior in the presence of a magnetic field. The hydrodynamic diameter measured by dynamic light scattering (DLS) is found to be 440 nm within the upper limit (500 nm) required to transfect into the cell. An *in vitro* drug release kinetics study reveals that approximately 60% of the drug is released at the end of 196 h. Notably, the drug-loaded magnetic micelles display much lower liver accumulation compared to the bare drug, indicating prolonged circulation time and maximum availability at the bone marrow. *In vivo* magnetic resonance (MR) imaging conducted on nude mice bearing the synthesized magnetic micelle after *i.v.* administration reveals excellent imaging capabilities, in dual mode, especially 24 h post-injection. We propose that the longitudinal relaxation (T_1) of water protons can be induced by mimicking Gd-DTPA chelate chemistry while transverse relaxation (T_2) can be achieved by controlling the particle size.

1. Introduction

Nowadays, nanoscience and nanotechnology are a boon to the patients suffering from diseases like cancer, diabetes, alzheimers *etc.* Especially in the case of cancer, it requires early and explicit diagnosis followed by target specific treatment.[1,2] Traditional treatments like chemotherapy are vigorous and non-specific. Ideally, factors like psychology of the patients, efficacy of the drugs for the disease, immune response, competence of the patient toward drug dosage *etc.* should be considered before adopting any treatment for cancer. Established drugs (like *cis*-platin, taxol, paclitaxol *etc.*) available in the market, even though highly effective, cause many side-effects in patients due to non-specificity and insolubility in body fluids.[3,4] Many strategies have been developed for the purpose. For example, a drug can be entrapped in micro or nano cavities of carrier like cyclodextrin or micelles having a hydrophilic/hydrophobic surface.[5–8] However, this suffers from the disadvantage of enzymatic degradation of the vehicle on its way into target cells. Further, even if the vehicle with the loaded drug reaches the target cells, cell transfection remains a major issue.[9,10]

Surface engineered Super Paramagnetic Iron Oxide Nanoparticles (SPIONs) are the best option available for the purpose. The advantages of SPIONs as drug carriers over the traditional delivery vehicles are:[11,12] (1) the particle size, shape and surface charge can be tuned according to requirement. It was observed that particles with sizes larger than 200 nm are removed from the body by liver, spleen and reticuloendothelial system (RES) while those of less than 5 nm are rapidly excreted through the kidneys.[13] However, the circulation lifetime of particles (having a definite size) in the blood can be extended and tuned by varying the nature (hydrophilic/hydrophobic) of coating materials around the core. Various functionalities (drugs, plasmids, small organic molecules, antibodies *etc.*) can be anchored on to the

[a] Department of Chemistry, Faculty of Science, The Maharaja Sayajirao University of Baroda, Vadodara – 390 002, Gujarat, India. E-mail: drhpsoni@yahoo.co.in; Tel: +91-0265-2795552
[b] Department of Pharmaceutical Technology, L. J. Institute of Pharmacy, Ahmedabad, Gujarat, India
[c] Department of Biochemistry, Faculty of Science, The Maharaja Sayajirao University of Baroda, Vadodara – 390 002, Gujarat, India
[d] Department of Pharmaceutical Sciences, Saurashtra University, Rajkot, Gujarat, India

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c6nj00655h