PAA-supported Hantzsch 1,4-dihydropyridine ester: an efficient catalyst for the hydrogenation of α,β-epoxy ketones

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ABSTRACT

A new type of water-soluble polymer-supported NADH co-enzyme model-PAA (polyacrylic acid)-supported Hantzsch 1,4-dihydropyridine ester (PAA–HEH) was designed and synthesized. Catalytic amount of the supported reagent was used in the hydrogenation of α,β-epoxy ketones to the corresponding β-hydroxy ketones and showed great catalytic efficiency in the reduction reaction. This PAA–HEH was an optimal potential for recycling use.

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NAD(P)H co-enzyme is a kind of oxidoreductase co-enzyme with great importance. It participates in more than 400 kinds of important biological redox reactions in vivo. NAD(P)H coenzyme is also a kind of natural organic hydride compound. Based on the active core, 1,4-dihydropyridine ring, of NAD(P)H, a series of model compounds have been synthesized to mimic the reductive performance of NADH coenzyme in vitro, such as BNAH, HEH, and AcrH2. Some of these models synthesized, like Hantzsch ester, accompanied with some small-molecule organocatalysts, were applied in the reductive reactions of aldehydes, ketones, activated olefins, and the hydrogenation of β-unsaturated aldehydes, α,β-epoxy ketones, imines, and showed great reductive activities and selectivities. However, the separating operation of these reactions is complicated. To simplify the separation process and promote the extensive use of the models, they have been immobilized on the surface of some supports, which combines the advantages of both the models and the supports. In the past few decades, the supports of the NADH coenzyme model compounds have experienced the Merrifield resin, SiO2, polysiloxane, water-soluble polymer like PEG, ferrocene, carbon nanotubes, magnetic nano like Fe3O4, graphene, etc.

Considering our group’s experience in the synthesis, application, and characterization of NADH coenzyme model compounds, herein we chose Hantzsch 1,4-dihydropyridine ester as the co-enzyme model and water-soluble polymer polyacrylic acid (PAA) as the support and they were connected to form a novel water-soluble polymer-supported reagent. The synthesis of the PAA-supported Hantzsch ester was presented herein as well as the application of the reagent in the hydrogenation of the α,β-epoxy ketones in homogeneous reaction system.

Polyacrylic acid-supported Hantzsch ester was synthesized according to the following protocol (Scheme 1). PAA was directly purchased and the Hantzsch 1,4-dihydropyridine ester was prepared according to the literature. HEH was co-valently connected with the carboxyl group of PAA through amide bond. Firstly, the mixture of formaldehyde, ethyl acetoacetate, and ammonium acetate was dissolved in ethanol and refluxed then to get Hantzsch 1,4-dihydropyridine ester. At the same time, the polyacrylic acid 3000 was treated with thionyl dichloride in DMF to obtain the corresponding partly chloride-PAA, which was then refluxed with the Hantzsch ester synthesized in DMF to get the PAA-partly-supported Hantzsch ester which was a light milky solid at room temperature and could be dissolved in water easily. The supported-reagent was characterized by elemental analysis and the loadings of PAA–HEH were 0.34 mmol/g.

To examine the reducibility and application of the PAA–HEH, we herein present the use of the supported-reagent in the reduction of a series of α,β-epoxy ketones. According to our previous work, all of the reactants including the phenyl(3-phenyloxy-ran-2-yl)methanone, the supported-reagent, Na2S2O4 (3 equiv), Na2CO3 (5 equiv) were mixed together and dissolved in mixed AcOEt/H2O (v:v = 1:1) solvent in one tube. The solution was irradiated with a 450 W high-pressure mercury lamp at room temper-
Scheme 1. The synthetic protocol of the PAA–HEH.

Table 1
The hydrogenation of \(\alpha,\beta\)-epoxy ketones to \(\beta\)-hydroxy ketones

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