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Improved method for immobilization of a chiral complex on PTA/alumina for asymmetric hydrogenation of a β-ketoester

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ABSTRACT

Ru-BINAP was immobilized on alumina using the well-known Augustine method with heteropoly acid (HPA) as the anchoring agent ("Augustine catalyst"). The supported catalyst was tested in a high-pressure reaction such as asymmetric hydrogenation of methyl acetoacetate (MAA). Since the activity of the supported catalyst was significantly lower than that of the homogeneous catalyst, the solvent used in preparing PTA/Al_2O_3 was changed from ethanol to a solution of HCl. The modified supported catalyst ("modified Augustine catalyst") exhibited higher conversion, better selectivity, and improved enantioselectivity compared with the catalyst prepared by the Augustine method. The modified Augustine catalyst also produced β-hydroxyesters with good yield and enantioselectivity in asymmetric hydrogenation of various β-ketoester derivatives. The modified Augustine catalyst was examined by FT-IR, XRD, NH_3-TPD, and ICP-AES, which revealed the existence of strong acid sites formed by HPA with a Keggin structure. These results were attributed to the effect of enhanced acidity on the modified Augustine catalyst.

1. Introduction

Chiral catalysts have received a great deal of attention due to the importance of obtaining pure enantiomers in the production of fine chemicals and pharmaceuticals. Among these processes, enantioselective hydrogenation with homogeneous catalysts is the most widely used approach, and there have been many attempts to develop such catalysts [1,2]. However, the use of these catalysts is limited due to recovery and recycling issues, which detract from their practical application. To overcome the disadvantages of homogeneous catalysts, a number of approaches have been taken to develop effective methods for the heterogenization of homogeneous catalysts [3–5]; however, in most cases, the activity and enantioselectivity of the supported catalysts has been significantly lower than that of the homogenous catalysts.

Augustine et al. reported a very dependable and widely applicable method [6–12] to avoid these problems. Specifically, they immobilized chiral or achiral metal complexes on supports modified with heteropoly acids as anchoring agents (herein referred to as the 'Augustine method'), and the resulting catalysts (herein referred to as 'Augustine catalysts') exhibited good performances in many reactions, including asymmetric hydrogenation of compounds with C═C bonds at moderate pressure [6–9]. Similarly, Ru-BINAP/PTA/alumina catalysts prepared by our group using the Augustine method exhibited good activity and enantioselectivity in asymmetric hydrogenation of DMIT [13]. However, there have been no reports to date on the application of Augustine catalysts in slower, high-pressure reactions, such as hydrogenation of compounds like β-ketoesters. The catalytic hydrogenation of methyl acetoacetate (MAA), a representative β-ketoester, is useful in preparing optically active β-hydroxy esters, which are important chiral building blocks for production of fine chemicals and pharmaceuticals [1].

In the present study, we attempted to apply Ru-BINAP/PTA/alumina prepared by the Augustine method to the hydrogenation of MAA. We also modified the step of supporting PTA in the Augustine method by using an acidic solvent instead of ethanol in an effort to enhance the activity of the Augustine catalyst. The catalytic performance of the newly prepared catalyst ('modified Augustine catalyst') was evaluated for the asymmetric hydrogenation of MAA and various β-ketoester derivatives. Catalysts were characterized by FT-IR, XRD, NH_3-TPD, and ICP-AES to examine the changes in the physical properties of the catalysts according to the immobilization method. The enhancement in the performance of the modified Augustine catalysts was evaluated in relation to the acid sites of the catalysts.

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2. Experimental

2.1. Materials

Prior to its use, γ-Al_2O_3 (activated, neutral, Brockmann I, 150 mesh, Aldrich), which was used as the support, was washed with ethanol to remove fine particles. Phosphotungstic acid (PTA), phosphomolybdic acid (PMA), silicotungstic acid (STA), and silicomolybdic acid (SMA), which were used as anchoring agents, were purchased from Aldrich and dehydrated at 110 °C prior to use. Ru-BINAP [$RuCl_2$((R)-BINAP)] was purchased from Strem Chemicals and used as received. Methyl acetoacetate (MAA) was obtained from Aldrich, and ethyl acetoacetate (EAA), methyl 3-oxovalerate (MOV), and *tert*-butyl acetoacetate (TBAA) were purchased from TCI; chemicals were degassed at reduced pressure with an aspirator for 1–2 h before use. EtOH (99%) was obtained from Merck and degassed at reduced pressure before use, and 0.5 M HCl was purchased from Riedel-de Haen and used without further purification.

2.2. Preparation of immobilized Ru-BINAP catalysts

2.2.1. Augustine method

All reactions used for catalyst preparation were performed using standard Schlenk techniques under an inert atmosphere. Nitrogen and hydrogen were purified by passing through columns packed with a molecular sieve (4 Å) and Ridox copper. All solvents were degassed with an aspirator prior to use.

A 250 mL glass reactor was charged with 4.5 g of pre-washed Al_2O_3, which was evacuated and refilled with dried nitrogen several times to remove air from the pores of the solid. Next, 40 mL of ethanol was added to the reactor using a cannula under positive nitrogen pressure. A phosphotungstic acid (PTA) solution (0.96 g in 30 mL of EtOH) was then added dropwise into the suspension of Al_2O_3 with stirring for 30 min. After completion of the addition, the mixture was stirred at room temperature for 4 h. The reaction mixture was then filtered and the resulting solid was washed five times with 20 mL of ethanol. The PTA/Al_2O_3 solid residue was subsequently dried at room temperature overnight under vacuum. Next, 3.5 g of the prepared PTA/Al_2O_3 was charged in a glass reactor and 40 mL of ethanol was added, followed by the slow dropwise addition of 0.1526 g (0.192 mmol) of Ru-BINAP dissolved in 40 mL of deoxygenated ethanol into the PTA/Al_2O_3 slurry with vigorous stirring. The resulting mixture was stirred at room temperature for 24 h, after which the reaction liquid was filtered and the remaining solid was washed with ethanol until no color was observed in the filtrate. Lastly, the obtained yellow solid was dried at room temperature overnight under vacuum to give the Ru-BINAP/PTA/Al_2O_3 catalyst, which was referred to as the Augustine catalyst.

2.2.2. Modified Augustine method

Preparation of PTA/Al_2O_3 was carried out under ambient atmosphere, which is different from that of the Augustine method described above. First, 0.875 g of PTA was charged in a 100 mL glass reactor. Next, 41 mL of 0.5 M HCl was added to the reactor to dissolve the PTA, followed by 4.5 g of Al_2O_3 after complete dissolution of PTA. The mixture was then stirred at room temperature for 4 h, and the reaction liquid was removed by heating at 80 °C under reduced pressure. Next, the remaining solid was dried at 110 °C overnight. The resulting PTA/Al_2O_3 solid residue was calcined at 400 °C for 4 h, and immobilization of Ru-BINAP was performed by the Augustine method as described previously. The immobilized Ru-BINAP catalyst that was prepared in this way was referred to as the modified Augustine catalyst.

2.3. Characterization

The metal contents of the immobilized Ru-BINAP catalysts were determined using an ICP-AES instrument (SPECTRO FLAME). The acid sites of the supports and supported catalysts were investigated by NH_3 TPD (Autochem 2920, Micromeritics, USA). Briefly, after pretreatment in He (500 °C, 50 mL/min, 2 h), 100 mg samples were exposed to 15% NH_3/He at 100 °C for 2 h and purged with helium. Next, the temperature was increased at a rate of 10 °C/min from 100 °C to 980 °C with He (30 mL/min), and the desorption of ammonia was monitored with a TCD detector.

FT-IR spectra of Al_2O_3 and PTA/Al_2O_3 were obtained with a Varian spectrophotometer in the range of 400–4000 cm^{-1} using KBr pellets. XRD patterns of Al_2O_3, PTA, and PTA/Al_2O_3 were also obtained using a Rigaku D/Max-2500 with Cu Kα radiation at 40 kV and 20 mA. A 2θ range from 2° to 50° was scanned at $2^\circ\ min^{-1}$.

2.4. Catalytic hydrogenation

Catalytic hydrogenation reactions were carried out in a 50 mL autoclave equipped with a magnetic bar. The reaction temperature was controlled by an electric heater and maintained at a set temperature. All reaction temperatures were 60 °C, and the hydrogen pressure was set at 40 bar. Prior to use, all substrates and solvents were degassed at reduced pressure with an aspirator. Under inert atmosphere conditions, catalyst, degassed solvent, and substrate were introduced sequentially into the reactor. The reactor was connected to a hydrogenation apparatus and purged with hydrogen (3 bar) five times before stirring was initiated. The reaction was initiated by introducing hydrogen at a pressure of 40 bar. Samples were obtained at predetermined time intervals from the reaction mixture to determine the reaction rate and enantioselectivity. The products were analyzed by gas chromatography (HP 6890) using a Rtx-1701 column. Enantiomeric excess was determined by GC using a Chiraldex G-TA column.

3. Results and discussion

3.1. Catalytic properties of the modified Augustine catalysts

The loading of active components on the support was analyzed by ICP-AES. Table 1 shows the result of ICP-AES analysis for Ru-BINAP/PTA/Al_2O_3. Ru and W were well deposited on alumina by both methods and the Ru loading and PTA content of the modified Augustine catalysts were slightly lower than those of the Augustine catalyst. ICP-AES analysis indicated that immobilization efficiency with the Augustine method was higher.

The properties of the prepared catalysts were tested by asymmetric hydrogenation of MAA. The main product from the asymmetric hydrogenation of MAA with Ru-BINAP/PTA/Al_2O_3 was methyl (R)-3-hydroxybutylate (MHB), while small amounts of methyl-3,3-diethoxybutanoate (ketal) and ethyl hydroxyl butylate (EHB) were obtained as well. Fig. 1 shows the changes in product distribution with time. It is notable that a ketal was formed in the initial stage, but disappeared in later stages.

Table 2 shows that the reaction catalyzed by Ru-BINAP/PTA/Al_2O_3 prepared by the Augustine method exhibited a much lower activity (28% conversion in 6 h), selectivity to MHB (52.5%), and enantioselectivity (80.8%) compared to the homogeneous Ru-BINAP catalyst (100% conversion in 6 h, 98% selectivity, and 99% enantioselectivity). This result was disappointing in the context of the superior performances of the Augustine catalyst for low-pressure hydrogenation of C=C bonds in previous reports [9,13]. Thus, it would appear that diffusion of the substrate within