Short Articles

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Specific Acceleration of the Hydrogenation of Methyl Acetoacetate on Enantio-Differentiating Sites of a Tartaric Acid-Modified Nickel Catalyst by the Addition of Acetic Acid to the Reaction Media

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The hydrogenation of methyl acetoacetate on enantio-differentiating sites of a tartaric acid-modified nickel catalyst was specifically accelerated by the addition of acetic acid to the reaction media to increase the enantio-differentiating ability of the catalyst.

The production of optically active compounds is an important issue in synthetic organic chemistry, especially in the fields of pharmaceutical, flavor- and aroma-chemicals, and agro-chemicals.[1] Enantio-differentiating solid catalysts for this purpose have attracted much attention because of their easy handling, that is, easy preparation, easy separation, easy recovery and reuse, and ease to scale up, compared with the homogeneous ones.

The tartaric acid-modified nickel catalyst is one of the most successful enantio-differentiating solid catalysts. The hydrogenation of β-ketoesters attained an enantio-differentiating ability (e.d.a.) of 90–98%,[2–4] and that of 2-alkanones attained an e.d.a. of 80–85%[4] over a tartaric acid-NaBr-modified nickel catalyst (Chart 1).

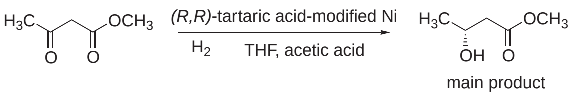

Chart 1.

Modified catalyst can be prepared by two methods, one is a pre-modification and the other is an in-situ modification. The pre-modification method has been typically studied for many years.[5] An activated nickel catalyst is soaked in an aqueous solution of tartaric acid (modifier) and NaBr (co-modifier, if necessary) at pH 3.2 and 373 K. A pre-modified nickel catalyst was prepared in a different vessel from the reactor before hydrogenation of the substrate. The in-situ modification was carried out in the reactor during the initial stage of the hydrogenation.[6] Here, tartaric acid (and if necessary, NaBr) was added to the reaction media. It was demonstrated that the tartaric acid-NaBr-in-situ-modified reduced nickel catalyst maintained about an 80% e.d.a. during 20 runs,[6] whereas the pre-modified nickel catalyst lost most of the virgin e.d.a. after only a few runs.

For both methods, many variables need to be optimized for attaining a high e.d.a. For example, the type of nickel catalyst and the method of activation, the type and amount of the modifier and co-modifier, the pH and temperature of the modification solution (for the pre-modification), and the reaction temperature and the additive to the reaction media.

During studies for optimizing the variables affecting the e.d.a., it was demonstrated that the addition of carboxylic acid to the reaction media increased the e.d.a. of the pre-modified catalyst.[2,7] During the hydrogenation of β-ketoesters, a small amount of acetic acid increased the e.d.a. by 10–20%. Harada et al. demonstrated that the added acetic acid converted the sodium nickel tartrate adsorbed on the "enantio-differentiating site" to nickel hydrogen tartrate, and that this increased the e.d.a. of the tartaric acid-NaBr-pre-modified nickel catalyst.[8]

In the present paper, we describe the effects of acetic acid added to the reaction media on the rate of the hydrogenation of methyl acetoacetate over the in-situ modified and unmodified nickel catalysts and on the e.d.a. of the in-situ modified catalyst.

A typical experimental procedure is as follows. Nickel oxide (Wako Pure Chemical Industries, Ltd., lot LDQ3413) was calcined in air at 1373 K for 6 h. The resultant nickel oxide was reduced at 623 K in a hydrogen stream for 1 h (40 cm^3 min^{-1}) to produce a reduced nickel catalyst. Methyl acetoacetate (5 g) was hydrogenated with the reduced nickel catalyst (0.5 g) in a mixture of THF (10 cm^3) and acetic acid. For hydrogenation over an in-situ modified catalyst, (*R*,*R*)-tartaric acid (1.7 mg) was added to the reaction mixture. Hydrogenation was carried out in a stirred autoclave at an initial hydrogen pressure of 9 MPa and at 373 K. To avoid mass diffusion control, the stirring rate and the amount of the catalyst were examined. A stirring rate of 1370 rpm and a catalyst amount of 0.5 g were the optimum conditions, which avoided mass diffusion control, and the apparent hydrogenation rate would represent the intrinsic rate of hydrogenation. The hydrogen pressure in the reactor was automatically recorded by a PC every one minute. The hydrogenation rate was expressed by the amount of hydrogen consumption during the reaction after the temperature of the autoclave reached the reaction temperature (373 K). After the reaction was completed, the reaction solution was separated by decantation from the catalyst, and then subjected to distillation. The e.d.a. of the catalyst was expressed by the optical purity of the methyl 3-hydroxylbutyrate determined by polarimetry.

Optical purity/% = ($[\alpha]_{\mathrm{D}}^{20}$ of methyl 3-hydroxybutyrate/$[\alpha]_{\mathrm{D}}^{20}$ of pure enantiomer) × 100. It was calculated using the value of $[\alpha]_{\mathrm{D}}^{20} = -22.95$ (neat) for the optically pure (*R*)-methyl 3-hydroxylbutyrate.[5]

Figure 1 shows the effect of the addition of acetic acid to the reaction media on the hydrogenation rate. In the absence of

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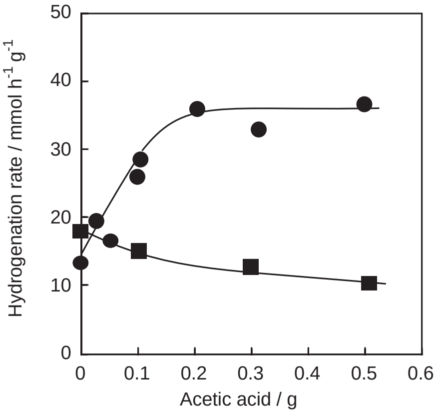

Fig. 1. Effect of the addition of acetic acid on the hydrogenation rate for the tartaric acid-modified and unmodified catalysts. Tartaric acid-modified catalyst (●) and unmodified catalyst (■).

acetic acid in the reaction media, the hydrogenation rates over the modified and the unmodified catalysts were similar to each other. The addition of acetic acid to the reaction media affected the rates over the two types of catalysts in different ways. For the hydrogenation over the unmodified catalyst, the hydrogenation rate gradually decreased with the increase in the amount of acetic acid. The acetic acid would competitively adsorb against the substrate on the nickel surface. However, the hydrogenation rate over the tartaric acid-modified nickel catalyst was significantly increased with the addition of a small amount of acetic acid, and remained constant with the addition of more than 0.2 g of acetic acid. The effect of the added acetic acid on the e.d.a. is shown in Fig. 2. The addition of acetic acid increased the e.d.a. of the in-situ modified catalyst, and the e.d.a. eventually reached a plateau with the addition of 0.2 g of acetic acid. The similarity between the rate- and e.d.a.-plots for the in-situ modified catalyst shown in Figs. 1 and 2 suggests that the acceleration of the hydrogenation rate and the increase in the e.d.a. arise from a common origin.

It has been reported that there are two types of active sites on the tartaric acid-modified nickel catalyst, that is, the "enantio-differentiating site" and the "non-enantio-differentiating site". The active site where tartaric acid is adsorbed and optically active compounds are produced is called the "enantio-differentiating site". The "non-enantio-differentiating site" is where tartaric acid is not adsorbed and racemic compounds are produced. Sodium bromide (co-modifier) is preferentially adsorbed on the "non-enantio-differentiating site" and inhibited the hydrogenation activity of the site to improve the e.d.a. of the modified catalyst.[2]

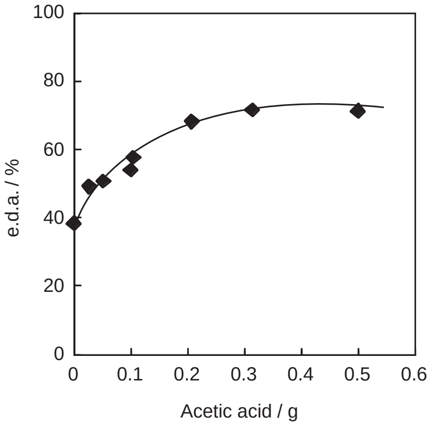

Fig. 2. Effect of the addition of acetic acid on the e.d.a. for the tartaric acid-modified catalysts.

The active sites of the unmodified catalyst are considered to be "non-enantio-differentiating sites", while the modified catalyst has both "enantio-differentiating sites" and "non-enantio-differentiating sites". All of the results mentioned above can be rationalized by the idea that the added acetic acid specifically accelerates the hydrogenation of methyl acetoacetate on the "enantio-differentiating sites". One of the reasons for the increase of the e.d.a. by the addition of acetic acid would be acceleration of the "enantio-differentiating site". Since the acceleration of the hydrogenation rate was not observed for the unmodified catalyst, this acceleration would be attributed to the interaction of acetic acid with the tartaric acid on the "enantio-differentiating site".

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