

Enantio-differentiating hydrogenation of methyl acetoacetate over fine nickel powder with in situ modification

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Abstract

Enantio-differentiating hydrogenation of methyl acetoacetate (MAA) was carried out using fine nickel powder (FNiP) by adding tartaric acid (TA) and sodium salts to the reaction media (in situ modification) instead of using a conventionally modified nickel catalyst. This catalyst prepared by the in situ modification gave an optical yield up to 79%. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

The tartaric acid (TA)-modified nickel catalyst is one of the most promising and intensively studied enantio-differentiating heterogeneous catalysts. This catalyst attained 80–95% optical yield in the hydrogenation of β -ketoesters [1,2] and alkanones [3,4]. The preparation of this catalyst is very simple. It can be easily prepared by immersion in an aqueous solution of TA and NaBr. However, it has not been easy to scale up the reactions with this conventional catalyst to industrial production. One of the main reasons is the generation of a large amount of waste solution involving nickel ions during the modification procedure prior to the hydro-

genation. Nickel was dissolved in the modification solution and the solution turned green after the modification. The wastes containing nickel ions can cause environmental problems. If the modification procedure prior to the hydrogenation is excluded from the entire enantio-differentiating hydrogenation process, the process would be extremely simple and the problems of the waste solution would be solved, because few nickel ions would be produced in the organic reaction mixture during the hydrogenation.

In situ modification (modifier is directly added to the reaction media) is a general method for the enantio-differentiating hydrogenation with cinchona-modified Pt [5,6] or Pd [7] catalysts. However, only a few studies about in situ modification have been reported in the case of TA-modified nickel systems. An optical yield of

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32% was reported for the Ni–Ce oxide catalysts [8].

In this paper, we will first clarify the indispensable species on the catalyst surface for the effective enantio-differentiation in the hydrogenation of methyl acetoacetate (MAA) using the TA-modified nickel fine powder catalysts prepared by the conventional modification process. We will then present the in situ modification systems for the enantio-differentiating hydrogenation by directly adding these species to the reaction media. This paper would contribute to the industrial application of this catalyst system for the production of optically active chemicals.

2. Experimental

All the chemicals except sodium 2-ethylhexanoate were used as received. Sodium 2-ethylhexanoate was obtained by neutralization of 2-ethylhexanoic acid by NaOH solution. The GLC measurement of the products was carried out using a Hitachi 263-30 gas chromatograph. The optical rotations were measured with a JASCO DIP-1000 polarimeter.

2.1. Enantio-differentiating hydrogenation using conventionally modified fine nickel powder (FNiP)

One gram of commercially available FNiP (Vacuum Metallurgical, Chiba, Japan, mean particle diameter: 20 nm, specific surface area: 43.8 m²/g, bulk density: 0.19 g/ml) was treated in a hydrogen stream at 280°C for 0.5 h. The activated FNiP was immersed in a 100-ml solution containing 1 g of (*R,R*)-TA at 0°C. The pH of the modification solution was adjusted in advance to the given value with 1 mol/dm³ NaOH solution. After the modification, the solution was removed by decantation and the resulting catalyst was successively washed once with 20 ml of distilled water, twice with 25 ml of methanol, and twice with 25 ml of tetrahydrofu-

ran (THF). The modified catalyst was employed for the hydrogenation of MAA (10 g) in THF (20 ml) in an autoclave. The initial hydrogen pressure was 9 MPa and the reaction temperature was 100°C. The hydrogenation products were obtained by simple distillations and had a chemical purity of more than 98% (GLC analyses: 90°C, 5% Thermon 1000 on Chromosorb W).

2.2. Enantio-differentiating hydrogenation by in situ modification method

One gram of FNiP was treated in a hydrogen stream at 280°C for 0.5 h. The enantio-differentiating hydrogenation of MAA by activated FNiP was carried out using the following two types of reaction mixtures at 100°C under an initial hydrogen pressure of 9 MPa. (i) MAA (10 g), THF (20 ml), acetic acid (0.2 g), and the stated amount of monosodium tartrate monohydrate. (ii) MAA (10 g), THF (20 ml), acetic acid (0.2 g), the stated amount of TA, and sodium salts.

2.3. Determination of optical yield

The optical purity of methyl 3-hydroxybutyrate was determined by polarimetry.

Optical purity (%)

$$= \frac{[\alpha]_D^{20} \text{ of hydrogenation product}}{[\alpha]_D^{20} \text{ of optically pure methyl 3-hydroxybutyrate}} \times 100$$

The specific optical rotation of optically pure (*R*)-methyl 3-hydroxybutyrate is -22.95° (neat) [9].

3. Results and discussion

3.1. Essential species for the effective enantio-differentiation

In the studies of a conventional TA-modified nickel catalyst, various modification parameters, which affect the optical yield, were investigated

using Raney nickel catalysts (RNi). However, when a nickel–aluminum alloy is used as the starting material for the preparation of the modified nickel catalyst, aluminum cannot be completely removed from the catalyst and residual aluminum decreases the optical yield [9]. Furthermore, it is unavoidable that alkaline solution used for the development of a nickel–aluminum alloy affects the modification procedure. That is, a small portion of the alkaline ions remains on the RNi catalysts even after a thorough washing of the RNi with distilled water. Therefore, for precise investigation of the indispensable species for the effective enantio-differentiation, we used pure FNiP as the starting material in this study.

It is known that adsorbed species on the nickel surface change according to the modification pH [10]. Fig. 1 shows the effect of the modification pH on optical yield, when FNiP was used. Although a small amount of acetic acid was commonly added to the reaction mixture using conventional modified RNi, the mixture of only MAA and THF was used in this experiment in order to avoid the complexity caused by acetic acid (adsorption of acetic acid on the surface, dissolution of the adsorbed species from the surface by the action of acetic acid). It was revealed that pH 3.2 gave the maximum optical yield. This means that the

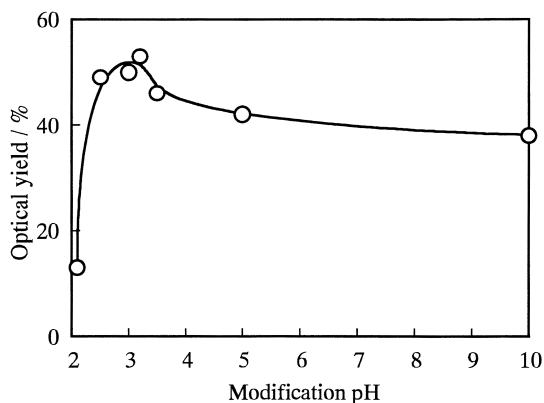


Fig. 1. Effect of modification pH on optical yield (modification temperature: 0°C).

adsorbed species from the pH 3.2 modification solution (TA is partially neutralized by NaOH) is indispensable for the effective enantio-differentiation. This result was similar to that obtained using the RNi catalysts [9]. When the conventional modification method was used, the appropriate adsorbed species for the effective enantio-differentiation on the modified FNiP were almost the same as that on the modified RNi catalyst.

3.2. Enantio-differentiating hydrogenation by *in situ* modification

We then tried to develop the enantio-differentiating hydrogenation system without modification of the catalyst prior to the hydrogenation but with the direct addition of the indispensable species for the enantio-differentiation to the reaction media (*in situ* modification). A preliminary experiment of adding only TA (200 mg) to the reaction media gave a 6% optical yield. This result supports the result shown in Fig. 1. The catalyst modified with the solution containing only TA (the solution without adjusting pH using NaOH solution) gave a low optical yield. Both TA and sodium ions are indispensable for attaining a high optical yield. Two kinds of experiment were carried out in order to introduce sodium ions to the reaction media. One was the addition of monosodium tartrate, and the other was the addition of TA and sodium salts (not the salts of TA) to the reaction media. Fig. 2 indicates the effect of monosodium tartrate added to the reaction media on the optical yield. The addition of monosodium tartrate increased the optical yield and the addition of more than 30 mg (0.16 mmol) attained more than a 50% optical yield. In order to examine the effect of the types of sodium salt on the optical yield, various sodium salts were added to the reaction media in the presence of TA. (Table 1) The addition of both TA and sodium salts increased the optical yield compared with the experiment without sodium salts (optical

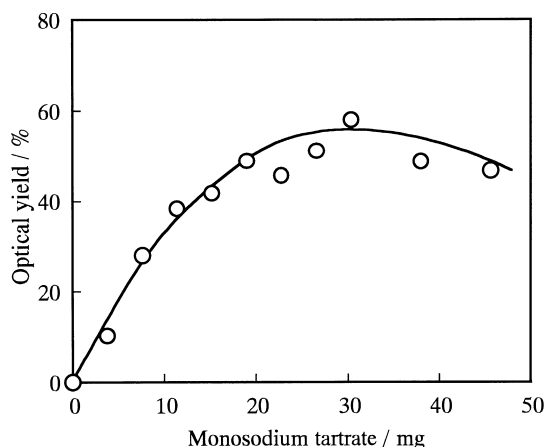


Fig. 2. Effect of the amount of monosodium tartrate added to the reaction media on optical yield.

yield 6%). When sodium 2-ethylhexanoate (2 mg, 0.01 mmol) was added to the reaction media, the amount of TA from 30 mg (0.2 mmol) to 200 mg (1.3 mmol) did not affect the optical yield (Nos. 1–4). The addition of 3.3–6.6 mg of sodium acetate (0.04–0.08 mmol) also gave moderate optical yield (Nos. 5 and 6). The addition of a small amount of sodium ions (0.01–0.08 mmol) was effective in increasing the optical yield when TA and sodium salts (not sodium tartrate) were added to the reaction media. It is known that NaBr is an effective co-

modifier that increases the optical yield using a conventional modification procedure [11]. NaBr would be adsorbed at the nonenantio-differentiating site and retards the production of racemic products [12]. The direct addition of 1 mg of NaBr (0.01 mmol) to the reaction mixture gave a 67% optical yield (No. 7). This value was higher than that obtained by the addition of sodium 2-ethylhexanoate. The addition of 4 mg of NaBr (0.04 mmol) gave the highest optical yield up to 79% (No. 8). This value is comparable to that attained by TA–NaBr-modified FNiP prepared by the conventional modification method (No. 10). The addition of 8.4 mg of NaBr decreased the optical yield (No. 9). The present study shows that the direct addition of NaBr to the reaction media is also effective increasing the optical yield. Bostelaar and Sachtler also demonstrated that the addition of NaBr to the reaction media increased the optical yield. They reported that the optical yield was enhanced from 28% to 55% by the addition of NaBr using the TA-modified Ni/SiO₂ catalyst prepared by the conventional modification procedure [13]. When RNi was used instead of FNiP, only a 36% optical yield was attained (No. 11). The addition of 200 mg of TA retarded the hydrogenation activity (not shown in the table). Therefore, concerning the in situ

Table 1

Effects of the addition of TA and Na salts to the reaction media on optical yield (OY)

	Catalyst	Optically active compounds /mg	Sodium salts /mg	OY /%
1	FNiP	TA /30	Na 2-ethylhexanoate /2.0	47
2	FNiP	TA /50	Na 2-ethylhexanoate /2.0	43
3	FNiP	TA /100	Na 2-ethylhexanoate /2.0	48
4	FNiP	TA /200	Na 2-ethylhexanoate /2.0	46
5	FNiP	TA /200	Na acetate /3.3	55
6	FNiP	TA /200	Na acetate /6.6	53
7	FNiP	TA /200	NaBr /1.0	67
8	FNiP	TA /200	NaBr /4.0	79
9	FNiP	TA /200	NaBr /8.4	57
10	TA–NaBr–MFNiP ^a	–	–	68
11	RNi	TA /50	NaBr /4.2	36

^aFNiP was modified in a 100-ml solution containing 1 g of (*R,R*)-TA and 0.5 g of NaBr at 100°C. Reaction mixture contains MAA (10 g), THF (20 ml), and acetic acid (0.2 g).

modification, FNiP behaved differently from RNi, and FNiP was the most important material to attain a high optical yield.

During the conventional modification process, 137 mg of nickel was dissolved in the 100-ml modification solution [9] and the modification solution turned green after the modification. The in situ modification presented in this study would produce no remarkable nickel ions during the entire process of enantio-differentiating hydrogenation, because no remarkable change in the color (colorless, transparent) of the organic reaction mixture was observed before and after the hydrogenation.

4. Conclusions

In conclusion, the use of FNiP and the addition of TA and a sodium salt to the reaction media attained up to a 79% optical yield. This in situ modification system generates no significant nickel ions during the entire process of the enantio-differentiating hydrogenation. This system would contribute the application of the TA modified nickel to the industrial process.

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