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Enantio-Differentiating Hydrogenation of Methyl acetoacetate over Asymmetrically Modified Reduced Nickel Catalysts: The Effects of the Coverage of the Modifiers on the Enantio-Differentiating Ability

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Abstract In order to investigate the factors for attaining a high enantio-differentiating ability (e.d.a.) for the enantio-differentiating hydrogenation of methyl acetoacetate over a tartaric acid pre-modified reduced nickel catalyst, the relation between the coverage of the modifiers on a nickel surface and e.d.a. was investigated. A Ni773 or Ni1373 (the reduced nickel catalyst prepared from a nickel oxide which was calcined at 773 K or 1,373 K, respectively) was used for the preparation of a modified catalyst. It was revealed that the tartaric acid coverage of about 0.2, the appropriate surface for the enantio-differentiation, such as the conditioned surface of Ni1373, and the inhibition of the hydrogenation on non-enantio differentiating sites by Br^-, were all important for attaining a high e.d.a. This would be interpreted that only when tartaric acid is adsorbed as an isolated molecule on the appropriate surface, the acid exerts its intrinsic e.d.a.

Keywords Enantio-differentiating hydrogenation · Reduced nickel catalyst · Tartaric acid coverage

1 Introduction

The tartaric acid (TA)-NaBr-modified nickel is a solid catalyst, which hydrogenates β-ketoesters and 2-alkanones with a high enantio-selectivity [1–6]. Many types of base nickel catalysts for preparing modified catalysts have been investigated; that is, Raney nickel, supported nickel, nickel obtained by the reduction of nickel oxide (reduced nickel), nickel obtained by the decomposition of nickel formate, nickel powder, and intermetallic catalysts. The characteristics of the resulting modified nickel catalyst depend on its base nickel catalyst. For example, a modified Raney nickel catalyst has a high hydrogenation activity and a high enantio-differentiating ability (e.d.a.) [6, 7]. The modified reduced nickel catalyst has a higher e.d.a. than that of the modified Raney nickel catalyst [8]. However, it was demonstrated that the e.d.a. of the modified reduced nickel catalyst was influenced by the nickel oxide manufacturers [9–11]. In order to clarify the factors determining the e.d.a. of the modified reduced nickel catalyst, we prepared nickel oxide from nickel hydroxide at 773 K or 1,373 K (which was denoted NIO773 or NIO1373) and used it for the preparation of the modified nickel catalyst, because the preparation details of the commercial nickel oxides are scarcely known [12]. It was revealed that the modified nickel catalyst prepared from NIO1373 had a higher e.d.a. than that prepared from NIO773, and that NIO1373 had a low non-stoichiometric oxygen [13].

The studies of the TA coverage on a nickel surface for the enantio-differentiating hydrogenation have been carried out by Keane. Keane reported the relation between the TA coverage and the e.d.a. of Ni/SiO_2 prepared at various calcination temperatures [14] and modification pH's [15]. Although the reported e.d.a. values were not high (below 30%), the TA coverage of about 0.2 gave the highest e.d.a.

It is known that the e.d.a. of the catalyst pre-modified in an aqueous solution decreased after a few repeated uses of the recovered catalyst [16]. This fact suggests that the quantity and coverage of the modifier on the catalyst

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surface decreased to negligible values after a few repeated uses of the catalyst.

During the course of the studies investigating the reason why the modified nickel catalyst prepared from NIO1373 had a high e.d.a., the relation between the coverage of the modifiers on the modified catalyst prepared from NIO773 or NIO1373 and e.d.a. was examined in the present study. The coverage of the modifiers during the repeated use of the pre-modified catalyst was also studied.

2 Experimental

The GLC determination of the conversion and enantiomer excess (e.e.) of the products were carried out using Hitachi 263-30 and Shimadzu GC-18A gas chromatographs, respectively. The optical rotations were measured using a JASCO DIP-1000 polarimeter. The BET surface area was measured using a Micromeritics Gemini 2375 by N_2 adsorption at 77 K. The amounts of the adsorbed tartaric acid on the nickel surfaces were measured by an ion chromatograph using a Metrohm 761 Compact IC.

2.1 *Nickel Oxide*

Nickel oxide was prepared by the calcination of nickel hydroxide (Wako Pure Chemical Industries, Ltd., lot KLL4435) under a stream of nitrogen (40 ml/min) and oxygen (10 ml/min) for 3 h at 773 K or 1,373 K.

2.2 *Reduced Nickel Catalyst*

Nickel oxide (0.5 g, which corresponds to 0.39 g of Ni after the reduction with H_2) was reduced at 623 K in a hydrogen stream for 1 h. Ni773 and Ni1373 denote the resulting Ni prepared from NIO773 and NIO1373, respectively.

2.3 *Modification of the Reduced Ni Catalyst*

Modification of the reduced nickel catalyst was carried out by a pre-modification method [17]. The reduced nickel catalyst prepared from 0.5 g of nickel oxide (corresponding to 0.39 g of nickel) was immersed in a solution (39 cm^3 of H_2O) of *(R,R)*-TA (0.39 g) and NaBr (0 or 3.9 g) at pH 3.2 and 373 K for 1 h. The pH of the modification solution was adjusted by 1 mol cm^{-3} NaOH before the modification. These modification conditions are typical for the pre-modification method. After the modification, the modified catalyst was successively washed with 10-cm^3 of deionized water, two 15-cm^3 portions of methanol, and two 15-cm^3 portions of THF.

2.4 *Enantio-Differentiating Hydrogenation of Methyl Acetoacetate*

The reaction mixture of methyl acetoacetate (5 g), THF (10 cm^3) and acetic acid (0.1 g) was subjected to hydrogenation over the modified reduced nickel catalyst. The hydrogenation was carried out at 373 K and the initial hydrogen pressure was 9 MPa. The conversion was determined by GLC analyses (5% Thermon 1,000 on Chromosorb W (AM-DMCS) 2 m, at 373 K). For the repeated use of the catalyst, the used catalyst was recovered and washed with two 20-cm^3 portions of THF and then used for the next run under the same reaction conditions except for the absence of TA and NaBr.

2.5 *Determination of e.d.a.*

The e.d.a. of the catalyst was evaluated using the optical purity of the hydrogenated product determined by polarimetry.

e.d.a. (%) = ($[\alpha]_D^{20}$ of methyl 3-hydroxybutyrate/$[\alpha]_D^{20}$ of pure enantiomer) × 100

The $[\alpha]_D^{20}$ of methyl 3-hydroxybutyrate was calculated using its specific gravity; $d_{20} = 1.058$. The specific optical rotations $[\alpha]_D^{20}$ of the optically pure (*R*)-methyl 3-hydroxybutyrate is $[\alpha]_D^{20} = -22.95°$ (neat) [17]. When the purity of the methyl 3-hydroxybutyrate after distillation was >90% (in the case of the low conversion), the e.d.a. was evaluated by the e.e. determined by GLC. Acetylation of the sample was carried out using acetyl chloride and pyridine. A portion of the acetylated sample was subjected to the analysis using a chiral capillary gas chromatograph equipped with a CP Chirasil DEX-CB (0.25 mm × 25 m). The e.e. was calculated from the peak integration of the corresponding enantiomers.

2.6 *Measurement of the Coverage of TA*

The modified catalyst was washed with deionized water (a 10-cm^3 portion), methanol (two 15-cm^3 portions), and THF (two 15-cm^3 portions). After the measurement of the weight of the catalyst (0.2 g) in deionized water, the catalyst was suspended in 15 cm^3 of a 1 mol dm^{-3} NaOH solution at 373 K to remove the TA from the surface to the solution. The supernatant was collected by decantation, and the remaining catalyst was washed three times with 10 cm^3 of water. After the combining of the supernatant and the washings, the solution was filled to 50 cm^3 using deionized water. The amount of TA was determined by an ion chromatograph equipped with a Shodex KC-811 (8 mm ID × 300 mm) at 313 K. The eluent was 1 mmol dm^{-3} perchloric acid.

The coverage of TA on the surface was calculated by the following equation;

Coverage $(\theta_{\mathrm{TA}}) = N_{\mathrm{TA}} \times \mathrm{S}_{\mathrm{TA}}/S_{\mathrm{BET}}$ N_{TA} : Number of the adsorbed TA (g^{-1}), S_{TA} : size of TA molecule (3.13×10^{-19} m^2) [18], $\mathrm{S}_{\mathrm{BET}}$: Surface area of the catalyst (m^2 g^{-1}).

2.7 *Measurement of the Coverage of Br$^-$*

The determination of Br$^-$ was carried out by the phenol red method [19]. A 0.1 g portion of the modified catalyst was decomposed with 0.5 cm^3 of conc. $\mathrm{HNO_3}$. After the adjustment of the pH to 4.7 with sodium acetate, the solution was made up to 50-cm^3 with water to produce the sample solution. To a 5-cm^3 portion of the sample solution, 0.2 cm^3 of acetate buffer (pH 4.7), 0.2 cm^3 of phenol red solution (10.5 mg/50 cm^3), and 0.05 cm^3 of Chloramine T solution (62.5 mg/25 cm^3) were added and the mixture was stored for 30 min at 303 K. After 30 min, the reaction was stopped with the addition of 2 cm^3 of sodium thiosulfate (2 mol dm^{-3}) and the absorbance at 590 nm was measured.

The coverage of Br$^-$ on the surface was calculated by the following equation; Coverage $(\theta_{\mathrm{Br}}) = N_{\mathrm{Br}} \times \pi R_{\mathrm{Br}}^2 / S_{\mathrm{BET}} N_{\mathrm{Br}}$: Number of the adsorbed Br$^-$(g^{-1}), R_{Br} : Radius of Br$^-$ (1.82×10^{-10} m), S_{BET} : Surface area of the catalyst (m^2 g^{-1}).

3 Results and Discussion

3.1 Effects of the Modification Conditions on θ_{TA}, θ_{Br}, and e.d.a

In this study, the modification was carried out by the pre-modification method, in which a base nickel catalyst was modified in a solution of TA and, if necessary, NaBr before the hydrogenation. The typical modification condition, such as pH 3.2 at 373 K was used. The condition of pH 3.2 and 373 K was often used for the modification of a Raney nickel catalyst. Under this condition, as well as the adsorption of the modifiers, the corrosion (conditioning) of the nickel surface by a weakly acidic solution of TA provided an appropriate surface for the enantio-differentiation [17].

As the catalysts used in this study are non-supported Ni catalysts prepared by the reduction of nickel oxide, the entire surface area can principally exhibit the hydrogenation activity. The adsorption of TA on the nickel surface creates “enantio-differentiating active sites” (e.d. sites) at which optically active compounds are produced. The sites where no TA is adsorbed are called “non-enantio-differentiating sites” (non-e.d. sites) and produce racemic products. Concerning the addition of the auxiliary modifier NaBr, it was proposed that Br$^-$ ions would be adsorbed on the non-e.d. sites and hinder the hydrogenation for producing racemic products and hence increase the e.d.a. [20]. The BET surface area divided by the projected area of a TA molecule determines the maximum number of enantio-differentiating active sites. The TA coverage (θ_{TA}) is expressed by the ratio of the number of adsorbed TA molecules to the maximum number of enantio-differentiating active sites. The studies of the relation between the θ_{TA} and the e.d.a. would help to elucidate the problem of which type of TA-adsorption is more suitable for attaining a high e.d.a., isolated or contiguous TA-adsorption.

Table 1 shows the effects of the modification conditions on the TA coverage (θ_{TA}), Br$^-$coverage (θ_{Br}) and e.d.a., when 0.39 g of TA (1 g of TA for 1 g of the base Ni catalyst) and 0.0 or 3.9 g of NaBr were added to the modification solution. In the case of the modification with TA alone (0.39 g, Entries 1 and 2), both the modified Ni773 and modified Ni1373 had almost the same θ_{TA} of about 0.6. When Ni was modified with TA 0.39 g and NaBr 3.9 g (Entries 3 and 4), the θ_{TA} values were about 0.2. Much TA is liable to be adsorbed (θ_{TA}: 0.55–0.63) when the modification was carried out using only TA. The addition of NaBr to the modification solution resulted in the adsorption of Br$^-$ (θ_{Br}: 0.13) and decrease in θ_{TA} to 0.17–0.25. An e.d.a. attained with the modified Ni1373 was higher than that with the modified Ni773 for each

Table 1 The effects of the modification conditions on θ_{TA}, θ_{Br}, and e.d.a

Entry	Base nickel catalyst	Modification				Surface area[a]/m^2 g^{-1}	e.d.a./%	θ_{TA}[b]	θ_{Br}[b]
		pH	Temperature/K	TA/g	NaBr/g				
1	Ni773	3.2	373	0.39	0	5.3	13	0.55	0
2	Ni1373	3.2	373	0.39	0	2.8	51	0.63	0
3	Ni773	3.2	373	0.39	3.9	5.9	52	0.17	0.13
4	Ni1373	3.2	373	0.39	3.9	3.3	88	0.25	0.13

[a] surface area after the modification

[b] the coverage determined before the hydrogenation

modification conditions. These results would indicate that Ni1373 has an appropriate surface for the enantio-differentiation with the aid of TA. An 88% e.d.a. was attained with Ni1373 modified with TA and NaBr.

When particles are adsorbed on a metal surface consisting of ordered sites, some of the particles exist as isolated adparticles and some as contiguous ones. Miyazaki calculated the probability of the adsorption of the isolated particle on the metal surface [21]. He reported that, when the metal surface is large enough, the probability that a metal site is occupied and isolated is a maximum at about 0.15–0.2 of the surface coverage of the particle (Fig. 1).

In order to apply Miyazaki's results to our experiments, we shall assume the following points; (1) the enantio-differentiating hydrogenation is carried out at the site where TA is adsorbed, and (2) the formation of a surface complex between the TA and the substrate results in the enantio-differentiation. The relation between the θ_{TA} (area of TA adsorbed/BET surface area) and the number of isolated TA molecules would be similar to that shown in Fig. 1. The results that θ_{TA} of about 0.2 gave the high e.d.a. suggest that the isolated TA molecule is suitable for the effective enantio-differentiation.

Based on the above results, we can claim that the following three points are necessary for attaining the high e.d.a. using the pre-modified reduced Ni catalyst, (1) an appropriate nickel surface such as the conditioned Ni1373, (2) θ_{TA} of about 0.2, and (3) hydrogenation on the area where TA is not adsorbed is hindered by the adsorbed Br^-.

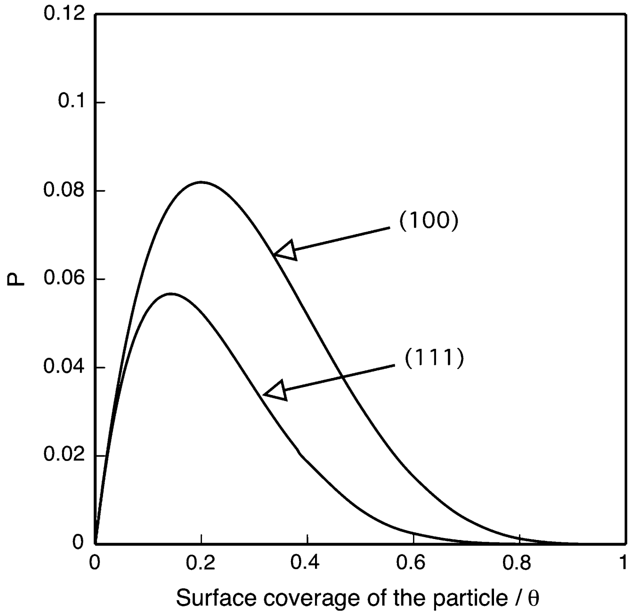

Fig. 1 The relation between the surface coverage of the particle and the probability that a site is occupied and isolated (*P* the probability that a site is occupied and isolated; *calculated from the equation in reference) [21]

Table 2 The relation between e.d.a. and θ_{TA} during the repeated runs

Run	e.d.a./%	θ_{TA}
Before the reaction	–	0.24
1	84	0.07
2	83	0.02[a]
3	46	–[a,b]

[a] θTA determined after the corresponding run

[b] the amount of adsorbed TA was below the limit of detection

3.2 Change in the Coverage of TA During the Repeated Use of the Catalyst

As mentioned in the preceding section, the modified catalyst with a moderate to high e.d.a. has the θ_{TA} of about 0.2. This would be due to the fact that TA was adsorbed as an isolated molecule on the nickel surface at that θ_{TA}.

It is known that the e.d.a. of the catalyst pre-modified in an aqueous solution decreased after a few repeated uses of the recovered catalyst [16]. Table 2 shows the relation between the e.d.a. and θ_{TA} during the repeated use of the recovered modified catalyst. The θ_{TA} was 0.24 before the 1st run, and 0.07 and 0.02 after the 1st and 2nd runs, respectively. After the 3rd run, almost no TA was adsorbed. As the e.d.a. of the 2nd run was 83%, about an 80% e.d.a. was attained when TA was adsorbed with a θ_{TA} of at least 0.02–0.07. We reported that the hydrogenation rate of the e.d. sites is higher than that of the non-e.d. sites [22]. Even when the θ_{TA} was 0.02–0.07, the high e.d.a. was attained, because the hydrogenation of methyl acetoacetate would be faster on the e.d. sites than on the non-e.d. sites. For the θ_{TA} of less than 0.02, the hydrogenation on the non-e.d. sites would not be ignored and the e.d.a. decreased. These results that a small coverage of TA (θ_{TA}: 0.02–0.07) produced a high e.d.a. would support the fact that the isolated TA on the surface was important for attaining a high e.d.a.

4 Conclusion

For the enantio-differentiating hydrogenation of methyl acetoacetate over a TA-NaBr^- pre-modified reduced nickel catalyst, the TA coverage of about 0.2 on the nickel surface, the appropriate surface for the enantio-differentiation, such as the conditioned surface of Ni1373, and the inhibition of the hydrogenation on non-e.d. sites, are all important for attaining a high e.d.a. This would be explained on the basis of the idea that only when TA is adsorbed as an isolated molecule on the appropriate surface would TA exert its intrinsic e.d.a.

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