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Catalytic Enantiodifferentiating Hydrogenation with Commercial Nickel Powders Chirally Modified by Tartaric Acid and Sodium Bromide

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The chirally modified nickel catalysts for the enantiodifferentiating hydrogenation of β-ketoesters are prepared conventionally by immersing hydrogen-activated metallic nickel into an aqueous solution of enantiopure tartaric acid, in which the preactivation of nickel is essential. Herein, we revealed that even commercially available nickel powders without any pretreatment can catalyze the enantiodifferentiating hydrogenation of β-ketoesters to give the corresponding β-hydroxyesters in quantitative yield and high enantioselectivity (up to 91%) under optimized conditions. The immediate use of commercially available nickel powders and the reproducible high chemical and optical yields not only expand the scope of heterogeneous asymmetric catalysis but also pave the way for the practical application and industrial use of chirally modified nickel catalysts.

Introduction

Optically active compounds are the key elements of natural systems such as living organisms.[1] Therefore, the production of such compounds is of prime importance, especially in the fields of pharmaceuticals, agrochemicals, and so on. Furthermore, novel and emerging approaches to supramolecular chemistry, nanoscience, biomimetics, and sensing also require optically active molecules of high enantiopurity. Several methods, such as optical resolution and catalytic and enzymatic asymmetric syntheses, have been developed thus far to obtain enantiomeric compounds. Of these approaches, heterogeneous chiral catalysis is one of the most promising techniques for the large-scale production of enantiopure compounds, featuring facile preparation, simple separation, and easy recovery and reuse of the catalyst, as well as the time- and cost-saving, environmentally benign methods.[2] Practically, there are two most effective heterogeneous catalytic systems for enantiodifferentiating hydrogenation: (1) cinchona alkaloid-modified metallic platinum and palladium catalysts[3–5] and (2) tartaric acid (TA)-modified nickel catalysts.[6–9] Both catalysts give high enantioselectivities for specific prochiral substrates. The platinum-based chiral catalysts hydrogenate activated ketones, such as α-ketoesters, ketopantolactones, pyrrolidinetriones, α-ketoacetals, α-ketoethers, α-diketones, and other related compounds, in 95–98% *ee*,[10–18] whereas the modified palladium catalysts reduce α,β-unsaturated carboxylic acids and alkene derivatives in 90–94% *ee*.[19–22] In contrast, the TA-modified nickel catalysts prepared in the presence of NaBr reduce β-ketoesters and 2-alkanones and give the corresponding alcohols in up to 98[23] and 85% *ee*,[24] respectively.

In the preparation of TA-modified nickel catalyst, activated metallic nickel powders, such as Raney nickel,[25–28] reduced nickel (prepared by the reduction of nickel oxide),[29] supported nickel,[30–32] and activated commercial nickel powder,[33,34] are commonly used. The commercially available nickel powder is usually activated through treatment with hydrogen stream at an elevated temperature, which is followed by the chiral modification by immersing the activated nickel powder into an aqueous solution containing TA and NaBr.[33,34] The hydrogen pretreatment is not necessary if the commercial nickel powder is used as a nickel base,[35] because the modification solution (containing TA and NaBr) is adjusted to pH 3.2 and thus it can remove the oxidized material from the nickel surface. Thus, the TA-NaBr solution plays dual roles of cleaning and modifying the nickel surface to afford a smooth surface structure appropriate for the enantiodifferentiation by removing defects.[9] This risk-free surface activation without using the hydrogen pretreatment is an important step toward the large-scale production and application of chirally modified nickel catalysts in industry.

Herein, to establish the protocol for preparing highly efficient TA/NaBr-modified nickel catalysts without preactivation,

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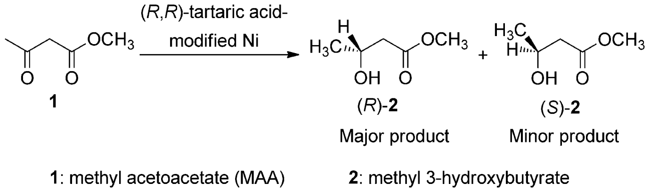

Scheme 1. Enantiodifferentiating hydrogenation of MAA.

the parameters for chiral modification and subsequent hydrogenation were optimized by using commercially available nickel powders as a nickel source and methyl acetoacetate (MAA; Scheme 1) as a benchmark substrate for assessing the hydrogenation and enantiodifferentiation abilities.

Results and Discussion

The overall effectiveness and enantioselectivity of the catalytic hydrogenation are generally affected by the conditions used in the following three major stages: (1) the preparation and activation of metallic nickel, (2) the chiral modification, and (3) the hydrogenation reaction. The previous comprehensive studies to optimize the conditions enabled us to establish the best protocol for each step of the catalytic hydrogenation with the chirally modified Raney nickel catalyst.[25,27,28] In contrast, the direct use of commercially available nickel powders in chiral hydrogenation does not appear to have been explored intensively,[33–35] although they are more suitable for the industrial use from the economic and environmental points of view. Our experience with the chirally modified Raney nickel catalyst was proven to be useful in optimizing the conditions used in the three major steps of heterogeneous hydrogenation with chirally modified nickel powders.

Choice and pretreatment of nickel powders

The effects of the source and type of nickel powders as well as the activation of the nickel surface on the overall hydrogenation efficiency and enantioselectivity were examined with commercially available nickel powders of different sizes.

Source and type of nickel powders

The performance of TA/NaBr-modified nickel catalyst significantly depends on the nature of metallic nickel used, for example, the particle size and morphology of the commercial nickel powder to be activated[33] and the source of nickel oxide to be reduced.[36] Therefore, the commercially available nickel powders of different sizes were first characterized morphologically by using SEM and then were examined for the effects of the source and type of nickel powders on the catalytic activity and enantioselectivity.

The analysis of SEM images of the commercial nickel powders of different sizes (Figure 1) revealed that the 3 μm and 5 μm nickel powders were aggregates of sharp-edged particles of similar morphology whereas the other nickel powders were appreciably different in shapes and surface structures. Thus, the 100 nm and submicrometer nickel powders, which were also aggregates, had smoother surfaces and more spherical shapes. The 150 μm nickel powder appeared to be positioned morphologically in between these two extrema, which had smoother surfaces than those of the 3 μm and 5 μm nickel powders but less round shape than that of the 100 nm and submicrometer nickel powders. Such a distinction is apparently due to the use of different preparation methods.

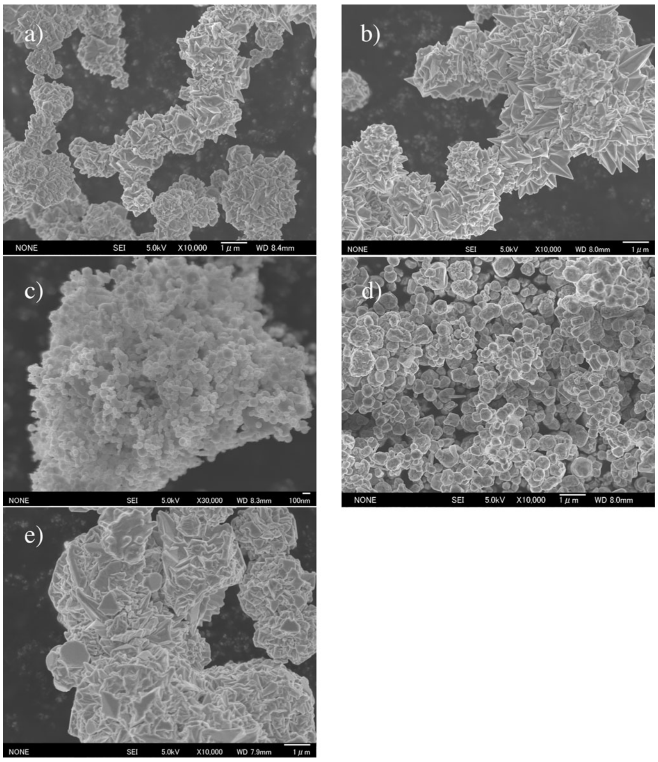

Figure 1. SEM images of commercial nickel powders of different sizes: a) 3 μm nickel (magnification: ×10000); b) 5 μm nickel (×10000); c) 100 nm nickel (×30000); d) submicrometer nickel (×10000); e) 150 μm nickel (×10000). Scale bars: 1 μm (a,b,d,e), 100 nm (c).

In the chiral modification, the optimum amount of NaBr in the modification solution varies with the type of nickel source used.[36] Thus, the effect of the amount of NaBr added on enantioselectivity was examined for each type of nickel powder (with a fixed amount of TA as 0.5 g). As shown in Figure 2, all types of nickel powders, except the submicrometer nickel powder, afforded the hydrogenation product in high enantioselectivities (ranging from 84 to 91% *ee*) at the optimized NaBr concentration; the best *ee* value was obtained with the 5 μm nickel powder after the addition of 2 g of NaBr. The poorer *ee* values obtained with the submicrometer nickel powder may be related to its different shape and surface structure (Figure 1), which apparently discourage the adsorption of the TA–MAA complex on the nickel surface in right conformation—an essential condition for achieving high *ee*.[9]

The conversion of MAA in the same reaction was also a critical function of the amount of NaBr added as well as the type

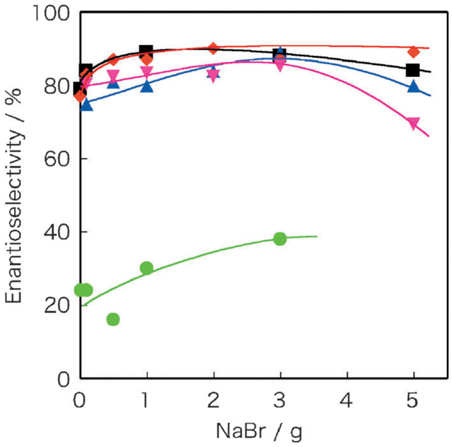

Figure 2. Effects of the amount of NaBr added to the modification solution containing (*R*,*R*)-TA on the enantioselectivity of methyl 3-hydroxybutyrate obtained upon hydrogenation with chirally modified nickel powders of different sizes: 5 μm (◆); 3 μm (■); 100 nm (▲); 150 μm (▼); submicrometer (●). Modification: TA (0.5 g); pH 3.2; temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen pressure 9 MPa; temperature 373 K.

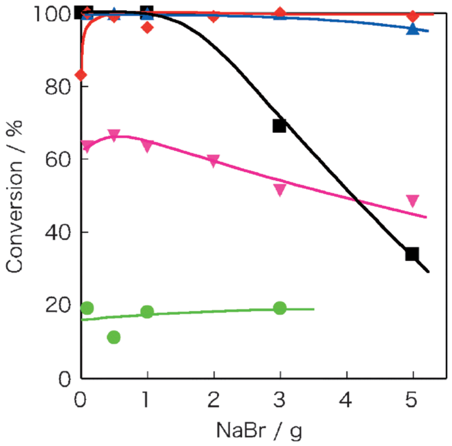

Figure 3. Effects of the amount of NaBr added to the modification solution containing (*R*,*R*)-TA on the conversion of MAA upon hydrogenation with chirally modified nickel powders of different sizes: 5 μm (◆); 3 μm (■); 100 nm (▲); 150 μm (▼); submicrometer (●). Modification: TA (0.5 g); pH 3.2; temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen pressure 9 MPa; temperature 373 K.

of nickel powder used (Figure 3). The 100 nm and 5 μm nickel powders achieved nearly quantitative conversions over the entire range of NaBr concentration used, except the case of 0 g of NaBr for the latter catalyst, which nevertheless gave 83 % conversion. The 3 μm nickel powder was sensitive to the overdose of NaBr, which led to a significant decrease in conversion upon the addition of 3 and 5 g of NaBr. This decrease is due to the excessive adsorption of NaBr on the nickel surface that blocks the access of the substrate to the catalyst. The 100 nm nickel powder showed a much weaker but a similar tendency upon the addition of 5 g of NaBr. The 150 μm and submicrometer nickel powders gave modest and low conversions, respectively, regardless of the amount of NaBr added, which indicates their low hydrogenation activities. Judging from the aforementioned results, we selected 5 μm and 100 nm nickel powders for further experiments to establish the optimized hydrogenation conditions.

Nonessentiality of hydrogen activation before chiral modification

The pretreatment of nickel powder with hydrogen at an elevated temperature (to reduce nickel oxides on the surface[33,34]) is a common, apparently indispensable, method in the standard protocol for preparing a highly efficient TA-modified nickel catalyst. Hence, the effects of pretreatment temperature on conversion and enantioselectivity were examined for the 100 nm nickel powder at 473–633 K, and the results are illustrated in Figure 4. The conversion was consistently quantitative throughout the temperature range examined. In contrast, the enantioselectivity increased appreciably from 84 to 89 % *ee* with the increase in the temperature from 473 to 573 K owing to accelerated reduction by hydrogen; however, heating above this temperature gradually decreased the *ee* to 86 % at 633 K, probably owing to the sintering of the nickel powder (vide infra).

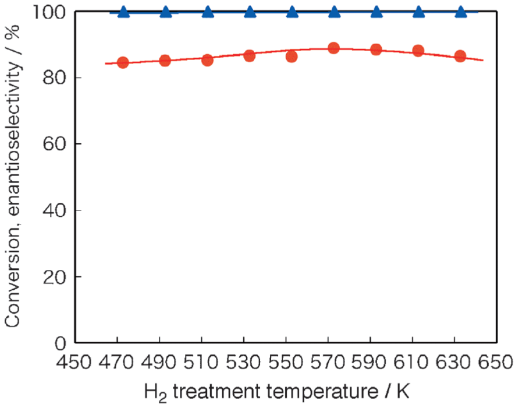

Figure 4. Effects of the temperature for hydrogen pretreatment on the conversion (▲) and enantioselectivity (●). Nickel powder: 100 nm. Modification: TA (0.5 g); NaBr (3.0 g); pH 3.2; temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen pressure 9 MPa; temperature 373 K.

The catalyst prepared with the 5 μm nickel powder was much more sensitive to temperature, and the conversion and enantioselectivity decreased steadily with temperature, which reached 48 % conversion and 15 % *ee* at 573 K (Figure 5) owing to more pronounced sintering (vide infra).

The analysis of SEM images taken before and after the hydrogen activation at 573 K (Figures 6 and 7) revealed that the pretreatment caused sintering with the corresponding morphological changes in nickel particles, which were more significant for the 5 μm nickel powder than for the 100 nm nickel powder. In addition, the different degree of sintering may affect the crystal structure. The XRD analyses of the two samples indicated that the pretreatment at 573 K augmented the mean crystallite size of the 100 nm nickel powder from 85 to 109 nm and that of 5 μm nickel powder from 103 to > 200 nm.

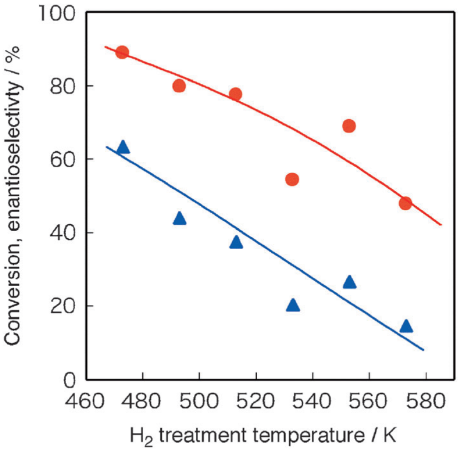

Figure 5. Effects of the temperature for hydrogen pretreatment on the conversion (▲) and enantioselectivity (●). Nickel powder: 5 μm. Modification: TA (0.5 g); NaBr (2.0 g); pH 3.2; temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen pressure 9 MPa; temperature 373 K.

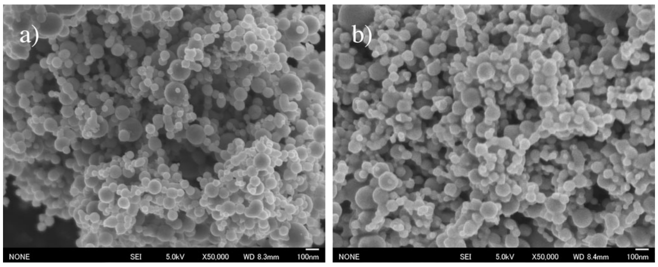

Figure 6. SEM images of the 100 nm nickel powder a) before and b) after hydrogen pretreatment at 573 K (magnification: ×50 000). Scale bars: 100 nm (a,b).

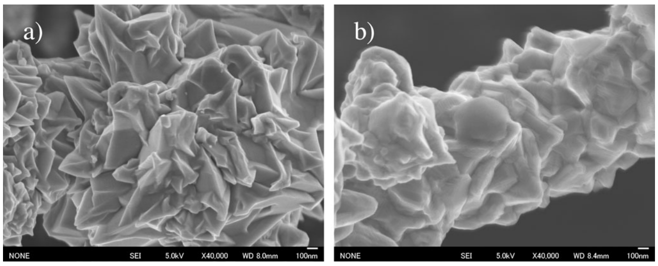

Figure 7. SEM images of the 5 μm nickel powder a) before and b) after hydrogen pretreatment at 573 K (magnification: ×40 000). Scale bars: 100 nm (a,b).

The significant increase in the crystallite size of the 5 μm nickel powder could be one of the reasons for the observed decrease in hydrogenation activity, although the detailed mechanism is yet to be clarified.

Although the chirally modified nickel with preactivation with hydrogen can give the hydrogenation product in high enantioselectivities of up to 89 % *ee* and quantitative yield under optimized conditions, we wanted to avoid the effects of sintering and simplify the protocol for preparing the chirally modified nickel catalyst, for example, by skipping the potentially hazardous hydrogen activation process. The nickel catalysts prepared by directly immersing the commercial 100 nm and 5 μm nickel powders into the modification solution possessed equally high hydrogenation and enantiodifferentiation abilities as did those with hydrogen preactivation, which afforded 86 % *ee* (100 % conversion) and 90 % *ee* (99 % conversion), respectively. These results confirm our observation with the 3 μm nickel powder that the hydrogen activation of nickel before chiral modification is not necessarily indispensable to achieve high enantioselectivity and conversion, as the modification solution at pH 3.2 can activate the nickel surface by removing nickel oxides.[35] This finding is crucial from a practical application point of view because other nickel sources require hydrogen activation. The direct use of commercially available nickel powders without any pretreatment eliminates the potential risk of using hydrogen at elevated temperatures and facilitates the large-scale production of optically active compounds.

Optimization of the modification conditions

As the chiral modification of metallic nickel is an essential part of the enantiodifferentiating hydrogenation, a considerable portion of our study has thus far been devoted to the optimization of major modification parameters, such as pH, temperature, immersion period, and solvent.[25,27,28,37] Of these factors, the pH of the modification solution and the amounts of TA and NaBr are the two most important parameters to be optimized.

Optimization of the solution pH

The above experiments have shown that both the 100 nm and 5 μm nickel powders are equally suitable for the preparation of TA/NaBr-modified nickel catalysts without hydrogen activation, but the latter is much less expensive. Thus, we used the 5 μm nickel powder in our further endeavor to optimize the pH of the solution for higher conversion and enantioselectivity.

The chiral modification of the 5 μm nickel powder was performed at pH values varying from 2.0 to 6.5 without changing other parameters or methods to show modest pH dependences. The conversion increased quickly with the increase in pH and reached approximately 100 % at $pH > 3.0$, whereas the enantioselectivity maximized at pH 3.0–3.2 and attained the highest *ee* value (91 %), which decreased to 80 % at higher pH values (Figure 8). This trend and the *ee* values are identical to those reported for Raney nickel, reduced nickel, and fine nickel powders with hydrogen pretreatment.[25,38,39] This finding indicates the same chiral modification mechanism for all types of nickel catalysts, which is controlled by two major counterbalancing factors: surface corrosion and TA adsorption.[9] At $pH < 4.5$, TA exists as a monoacid and/or a diacid (pK_{a2} of $TA = 4.25$) and corrodes the nickel surface to provide a fresh surface suitable for chiral modification, whereas at $pH > 3.0$ (pK_{a1} of $TA = 2.95$), TA is adsorbed on the nickel surface as a monosodium salt, which is the effective chiral species that induces high enantioselectivity.[9] Counterbalancing these two conflicting

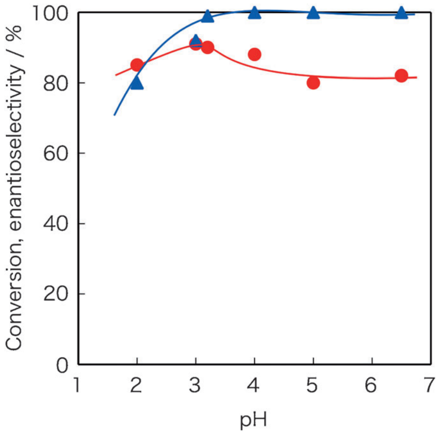

Figure 8. Effect of the pH of the modification solution on the conversion (▲) and enantioselectivity (●). Nickel powder: 5 μm. Modification: TA (0.5 g); NaBr (2.0 g); temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen 9 MPa; temperature 373 K.

factors is essential to maximize the enantioselectivity, which was achieved at pH 3.0–4.0, or more specifically at 3.0–3.2, in the present case. In this context, it is reasonable that all the chirally modified nickel catalysts attain the best enantioselectivity and 100% conversion in this particular pH region, irrespective of the nickel source used.

To better understand the origin of the pH effect, we performed the X-ray photoelectron spectroscopy (XPS) analyses of the chirally modified nickel catalysts prepared at different pH values to characterize the surface composition. Preliminary results of the pH dependence were reported in Ref. [40]. The content of metallic versus oxidized nickel is important to evaluate the catalyst properties, and the 2p region of nickel is the most suitable for this purpose, as the composition of the metallic and oxidized forms of nickel can be assessed quantitatively (Figure 9). Thus, the $Ni^0/(Ni^{2+}+Ni^{3+})$ ratios of 17:83, 43:57, and 35:65 were obtained for the modified nickel catalysts prepared at pH 2.0, 3.2, and 6.5, respectively. These results are consistent with our earlier report that the modification at pH 3.2 activated the nickel surface by removing the oxidized material from the surface.[35] Although the TA solution has the highest ability to remove the oxidized nickel species by corroding the surface at pH 2.0 of all the pH values examined, it also has the highest ability to produce nickel tartrate on the surface. Therefore, the surface modified at pH 2.0 had the lowest proportion of Ni^0. In contrast, the surface modified at pH 6.5 had a moderate amount of Ni^0, as the TA solution at pH 6.5 has the lowest activity of corrosion and negligible ability to produce nickel tartrate because the pK_{a2} of TA is 4.25, which indicates that disodium tartrate is the dominant species at pH 6.5. Because of these two incompatible processes, the modification at pH 3.2 afforded the highest Ni^0 content. This observation is reasonable because the TA solution at pH 3.0–3.2, which contains both diacid and monosodium salts of TA at pH close to the pK_{a1} value (2.95), is active enough to remove the oxidized species from the surface of the nickel particles and modify the surface with the monosodium salt of TA.

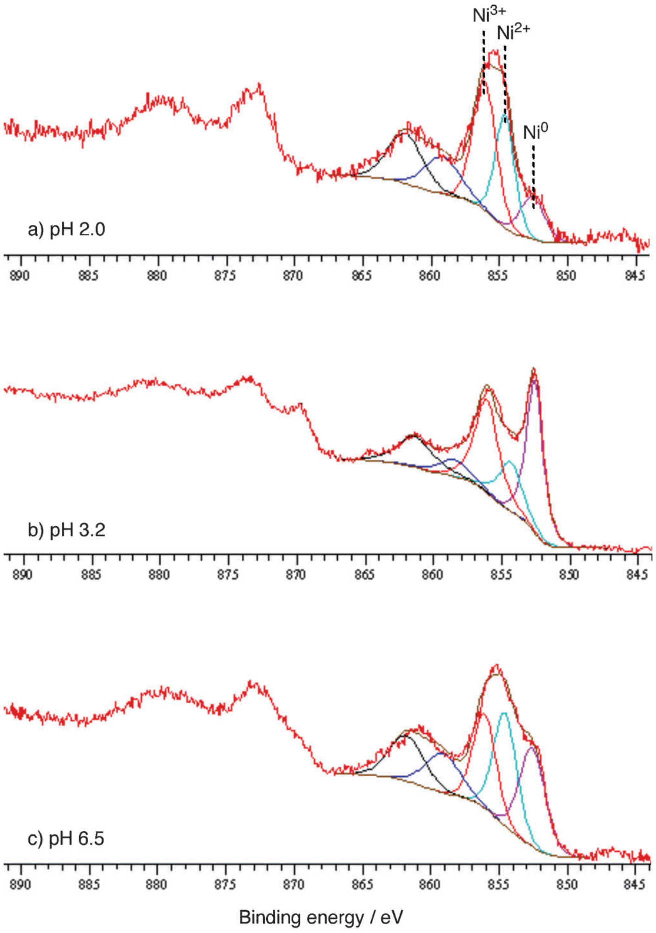

Figure 9. Effects of the pH of the modification solution on the XPS spectra of the 5 μm nickel powder: a) pH 2.0; b) pH 3.2; c) pH 6.5.

Optimization of the amounts of TA and NaBr

The amounts of TA and NaBr in the modification solution are also crucial parameters that need to be optimized to attain high enantioselectivity and conversion.[25,28,41] Although the absolute configuration of TA is directly responsible for the chiral nature of the hydrogenation product obtained, NaBr is an auxiliary modifier to increase the enantioselectivity by blocking the non-enantio-differentiating sites (a nickel domain in which the racemic products are produced).[42] The effects of the amounts of TA and NaBr on enantioselectivity and conversion, with the use of the 5 μm nickel powder without hydrogen pretreatment as a catalyst base, are summarized in Table 1.

Table 1. Effects of the amounts of TA and NaBr on enantioselectivity and conversion (with the use of 5 μm nickel powder).

TA	Amount of NaBr, Enantioselectivity [%] (Conversion [%])					
[g]	0 g	0.5 g	1 g	2 g	3 g	5 g
0.25			86 (100)	86 (100)	89 (100)	91 (93)
0.5	77 (83)	87 (99)	87 (96)	90 (99)	87 (100)	89 (99)
1.0	77 (89)	89 (83)	90 (87)	90 (69)	90 (77)	90 (74)
2.5			90 (82)	89 (66)	90 (73)	89 (58)

As can be observed from Table 1, both the enantioselectivity and conversion were moderately affected by the amounts of TA and NaBr. Thus, the addition of NaBr (0.5–5 g) increased the product's *ee* from 77 to 86–91 %, whereas the highest conversions of 96 % or more were achieved in a narrower region of the TA–NaBr matrix, that is, the region with 0.25–0.5 g of TA and 0.5 g or more of NaBr. A closer examination of the data reveals a sort of competition between TA and NaBr. Thus, the *ee* value of 89 % or more was achieved upon addition of 3 g of NaBr in the presence of 0.25 g of TA whereas only 0.5 g of NaBr was needed to obtain the same level of *ee* in the presence of 1 g of TA. In contrast, the use of smaller amounts of TA and NaBr led to higher conversions and the overdose decreased the conversion and it reached 58 % at the largest amounts of TA (2.5 g) and NaBr (5 g). This finding seems reasonable because TA and NaBr competitively block the active sites of the nickel surface. Considering the two conflicting factors, we used the modification solution containing 0.5 g of TA and 2 g of NaBr to obtain high enantioselectivity and nearly quantitative conversion in the case of the 5 μm nickel powder.

Unexpectedly, the 100 nm nickel powder (without hydrogen pretreatment) modified with TA and NaBr under identical conditions behaved differently upon hydrogenation. As shown in Table 2, the conversion was consistently quantitative in most examined cases, except the low TA/high NaBr case, whereas the enantioselectivity was modest (59–81 % *ee*) at low amounts of TA and NaBr but increased gradually with an increase in the amounts of TA and NaBr and attained the highest *ee* value (91 %) upon modification with a solution containing 2.5 g of TA and 3 g of NaBr. Notably, the two nickel powders of different sizes afford the same optimized enantioselectivity of 91 %, which indicates that they share the same coordination geometry around the active hydrogenation site on the nickel surface despite significant differences in size and morphology (see Figure 1 b and c). Notably, the 100 nm nickel particles, possessing larger surface areas, show higher hydrogenation activity and require larger amounts of TA and NaBr to achieve the full coverage of the surface.

Table 2. Effects of the amounts of TA and NaBr on enantioselectivity and conversion (with the use of 100 nm nickel powder).

TA	Amount of NaBr, Enantioselectivity [%] (Conversion [%])					
[g]	0 g	0.5 g	1 g	2 g	3 g	5 g
0.5		81 (100)	80 (100)	84 (100)	88 (100)	80 (96)
1.0	72 (100)		81 (100)		85 (100)	87 (100)
2.5	59 (100)		83 (100)		89 (100)	89 (100)
5.0			82 (100)	87 (100)	91 (100)	87 (100)

From a practical application point of view, the cost of the nickel source is another important factor to be taken into account. In the catalytic asymmetric hydrogenation of MAA, the hydrogenation ability assessed by the conversion in a given reaction period is appreciably higher for the 100 nm nickel powder (100 %) than for the 5 μm nickel powder (93 %) under the condition that affords the highest enantioselectivity (91 % *ee*) in each case. However, the 100 nm nickel powder is considerably more expensive than the 5 μm nickel powder, which prompted us to use the modified 5 μm nickel powder (without hydrogen pretreatment) to optimize the conditions for the final hydrogenation step.

Optimization of the hydrogenation conditions

The factors affecting the hydrogenation step include solvent, substrate concentration, additive and its concentration, temperature, and hydrogen pressure.[9,43–45] However, the solvent and the substrate concentration have already been optimized for the catalytic hydrogenation of MAA in the previous studies,[43,44] and thus the remaining influential factors, that is, temperature and pressure, were studied in detail here.

Effect of the hydrogenation temperature

The examinations of the results of foregoing studies on the catalytic hydrogenation of MAA with chirally modified nickel catalysts[44,46–48] revealed that the temperature-dependent behavior varies with the catalyst and/or the phase used. For example, an optimum temperature to obtain the highest *ee* existed in the liquid phase hydrogenation at 0.1[46] or 10 MPa[44] whereas the enantioselectivity was independent of the temperature in the liquid phase hydrogenation at 9 MPa,[47] but it decreased with increasing temperature in the gas phase hydrogenation at 0.1 MPa.[48] Although some of the results are puzzling and not readily explainable, it is clear that the hydrogenation temperature has to be optimized for each catalyst.

The catalytic hydrogenation of MAA with the 5 μm nickel powder (without hydrogen pretreatment) modified with 0.5 g of TA and 2.0 g of NaBr at pH 3.2 was performed at temperatures ranging from 353 to 393 K and at a hydrogen pressure of 9 MPa. The enantioselectivity increased gradually with temperature and reached the highest value of 89 % *ee* at 373 K and decreased quickly thereafter and reached 77 % *ee* at 393 K (Figure 10), which indicated structural deformation and/or de-

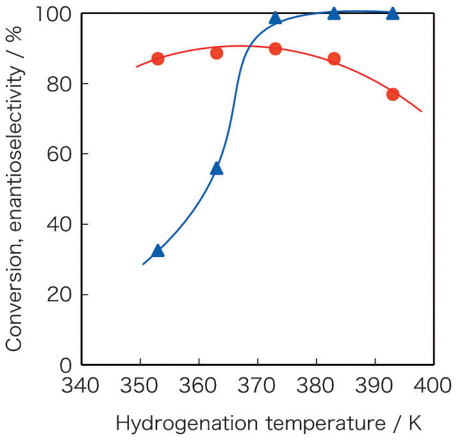

Figure 10. Effects of the hydrogenation temperature on the conversion (▲) and enantioselectivity (●). Nickel powder: 5 μm. Modification: TA (0.5 g); NaBr (2.0 g); temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); hydrogen pressure 9 MPa.

tachment of the adsorbed TA at higher temperatures. In contrast, the conversion was rather low (<40%) at 353 K or lower temperatures but it suddenly increased to 98–100% at 373 K and higher temperatures, which reflected the increased hydrogenation ability of the nickel surface. This result indicates that the favorable adsorption of MAA on the nickel surface producing (*R*)-alcohol is followed by the rate-limiting hydrogenation step.[49]

Effect of the hydrogen pressure

Some conflicting results have been reported for the effect of hydrogen pressure on the hydrogenation of MAA with supported and Raney nickel catalysts. Nitta et al. reported that the enantioselectivity decreased with increasing hydrogen pressure (0.1–13 MPa) upon hydrogenation with the chirally modified Ni/SiO_2 catalyst under conditions in which the rate was controlled by the surface reaction.[50] Kukula and Cerveny reported that the enantioselectivity increased slightly with increasing pressure (1–12 MPa) upon hydrogenation with the chirally modified Raney nickel catalyst.[44] Some of us reported that the enantioselectivity was constant at 1–9 MPa but decreased significantly below 0.5 MPa upon hydrogenation with the chirally modified Raney nickel catalyst.[51] These apparent discrepancies may arise from the different nature of the chiral catalysts prepared with various nickel sources under various conditions and presumably from the use of different types of reactors.

Hence, we performed the catalytic hydrogenation of MAA with our own nickel catalyst at hydrogen pressures varying from 6 to 11 MPa to obtain the pressure-dependence profiles of the *ee* and conversion (Figure 11). The enantioselectivity increased appreciably with pressure and reached the highest *ee* value (91%) at 10 MPa. Similar to the temperature-dependence profile (Figure 10), the conversion increased from 36% at 7 MPa to a plateau of 94–99% at 9–11 MPa in the pressure-dependence profile. The contrasting behaviors of conversion and *ee* indicate that the hydrogenation rate does not affect the enantioselectivity at hydrogen pressures varying from 6 to 11 MPa.

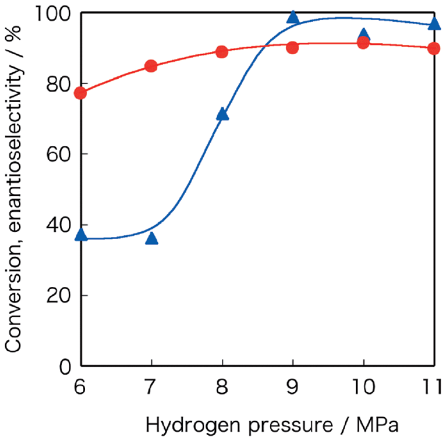

Figure 11. Effects of the hydrogen pressure on the conversion (▲) and enantioselectivity (●). Nickel powder: 5 μm. Modification: TA (0.5 g); NaBr (2.0 g); temperature 373 K. Hydrogenation: additive acetic acid (0.1 g); temperature 373 K.

Effect of the amount of acetic acid added to the reaction medium

The addition of acetic acid to the reaction medium is necessary to achieve the high enantioselectivity for which the accelerated hydrogenation on the enantiodifferentiating sites is responsible.[52] Therefore, in all the aforementioned experiments, we performed the catalytic hydrogenation of MAA in the presence of 0.1 g of acetic acid as a default value, the amount of which was finally optimized to give the results shown in Figure 12.

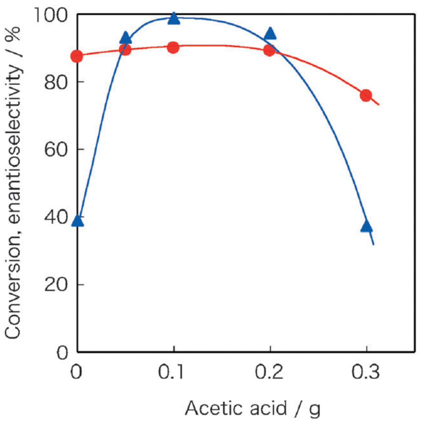

Figure 12. Effects of the amount of acetic acid in the reaction mixture on the conversion (▲) and enantioselectivity (●). Nickel powder: 5 μm. Modification: TA (0.5 g); NaBr (2.0 g); temperature 373 K. Hydrogenation: hydrogen pressure 9 MPa; temperature 373 K.

The enantioselectivity was not much affected by the addition of acetic acid at least up to 0.2 g, which afforded 88–90% *ee*, but it decreased appreciably to 76% *ee* upon addition of 0.3 g of acetic acid. The conversion was a critical function of the amount of acetic acid, which increased appreciably upon the addition of 0.05–0.2 g of acetic acid but decreased significantly at a higher dose of 0.3 g. This behavior is a result of the delicate role played by acetic acid in stabilizing the MAA–TA complex formed on the chirally modified nickel surface through hydrogen bonding–electrostatic interactions, which are essential to give the hydrogenation product in high *ee*. However, the excess amount of acetic acid weakens the MAA–TA complex on the surface because of the competition between TA and acetic acid.

Conclusions

The chiral nickel catalysts modified with tartaric acid and NaBr were prepared from commercially available nickel powders of different particle sizes without any pretreatment (such as activation with hydrogen) under various conditions. Their hydrogenation and enantiodifferentiation abilities were assessed to optimize the parameters for chiral modification and subsequent hydrogenation by using the enantiodifferentiating hydrogenation of methyl acetoacetate as a benchmark reaction. Of the nickel powders examined, 5 μm and 100 nm nickel powders (both from Aldrich) gave the best results in terms of the enantioselectivity and conversion, which are comparable to those obtained with the conventional chirally modified catalysts prepared from the activated nickel powder. The highest enantioselectivity (91 %) was attained with quantitative conversion with the 5 μm nickel powder without hydrogen pretreatment under optimized conditions. The direct use of commercially available nickel powders, as well as the high enantioselectivity and conversion values, will promote the practical application of the heterogeneous chiral nickel catalysts as a promising route to enantiopure compounds in industry.

Experimental Section

Materials

All the chemicals used were available commercially and used as received. The nickel powders of different diameters (< 100 nm, submicrometer, 3 μm, 5 μm, and 150 μm) were purchased from Aldrich.

Chiral modification of metallic nickel

Nickel powders with and without hydrogen activation were used for comparison purpose. For hydrogen activation before chiral modification, nickel powder (0.5 g) was exposed to a stream of hydrogen at 473–573 K for 0.5 h. Chiral modifications were performed at 373 K by immersing the activated and nonactivated nickel powders in an aqueous solution (50 cm^3) containing varying amounts of (*R*,*R*)-TA and NaBr, pH of which was preadjusted to 3.2 with an aqueous NaOH solution (1 м), unless noted otherwise. After 1 h of immersion, the modification solution was removed through decantation and the catalyst was washed successively once with deionized water (10 cm^3), twice with methanol (25 cm^3), and twice with THF (10 cm^3).

Enantiodifferentiating hydrogenation with the chirally modified nickel catalyst

A typical method for the hydrogenation reaction used was as follows. The modified catalyst was added to a mixture of MAA (5 g), acetic acid of varying amounts, and THF (10 cm^3) placed in an autoclave equipped with a magnetically coupled mechanical stirrer. The hydrogenation was performed for 20 h at 373 K and at a varying initial pressure of hydrogen. The hydrogenation product, a mixture of methyl (*R*)-3-hydroxybutyrate and methyl (*S*)-3-hydroxybutyrate, was isolated from the reaction mixture through distillation. The conversion was determined from gas–liquid chromatography (GLC) analysis with a Hitachi Model 263-30 equipped with a packed column of 5 % Thermon 100 on Chromosorb W (2 m) at 363 K or with a GL Sciences Model GC4000 equipped with a CP-Chirasil-Dex CB capillary column (0.25 mm × 25 m) at 363 K.

Determination of the enantioselectivity

The enantioselectivity was determined from chiral GLC analysis after the acetylation of the reaction product with acetyl chloride and pyridine. A portion of the acetylated sample was subjected to chiral GLC analysis on a CP-Chirasil-Dex CB column (0.25 mm × 25 m) operated at 363 K. The *ee* value was calculated from the peak integration of the corresponding enantiomer peaks. The reproducibility of the *ee* value was found to be within ± 2 %.

Characterization of the catalyst

The powder XRD spectra were recorded with a Bruker D8 DISCOVER high-resolution X-ray diffractometer with CuK_α radiation. The nickel crystallite size was calculated with the Scherrer equation. SEM was performed at a beam voltage of 5 kV with a JEOL JSM-6700F scanning electron microscope.

XPS was performed on an ULVAC-PHI ESCA 5800 with a MgK_α source. The samples for the measurements were prepared under air at ambient temperature and then placed into the chamber. The XPS spectra obtained were processed with the CasaXPS software (version 2.3.1.15). The carbon (1 s) line was used for calibration at 284.8 eV. For the XPS measurement, the washed sample after chiral modification was dried under vacuum (4.0 kPa) at 323 K for 18.5 h and stored under argon in a sealed glass ampoule. The stored dry catalyst was used for the measurement immediately after opening the ampoule.

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