

Enhanced Enantioselectivity Achieved at Low Hydrogen Pressure for the Asymmetric Hydrogenation of Methyl Acetoacetate over a Tartaric Acid NaBr-Modified Raney Nickel Catalyst: A Kinetic Study

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Received: March 12, 2019; Accepted: April 11, 2019; Web Released: May 31, 2019



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Abstract

To ensure high enantiopurity of the product, enantiodifferentiating hydrogenation of methyl acetoacetate over a (R,R)-tartaric acid-modified Raney nickel catalyst is normally performed under elevated H2-pressure (~10 MPa). In this study, higher enantioselectivity than previously reported for methyl acetoacetate was achieved (92% ee) under low H2pressure of 0.42 MPa. Effects of reaction conditions on the enantioselectivity and hydrogenation rate were investigated using a low-pressure reaction system (<0.5 MPa of H₂). It was found that impurities in the solvent greatly reduce the enantioselectivity of MAA. The low-pressure reaction system enabled a satisfactory kinetic approach. The reaction rate was well described by Langmuir-Hinshelwood formalism, verifying the previous assumption that the addition of adsorbed hydrogen to the substrate interacting with surface tartrate is a ratedetermining step.

Keywords: Low-pressure enantioselective hydrogenation | Modified Ni catalyst | Reaction kinetics

1. Introduction

(R,R)-Tartaric acid and NaBr-modified Raney nickel is known as an excellent catalyst for the asymmetric hydrogenation of β -ketoesters and ketones. This catalyst system has been intensively studied by various groups for a long time to enhance the enantiopurity of the hydrogenation products. Many aspects have been thoroughly investigated, including catalyst preparations, reaction conditions, substrate generality and reaction mechanism.^{1–15} The highest enantioselectivity ever



Scheme 1. Enantio-differentiating hydrogenation of methyl acetoacetate (MAA) under low pressure over a (R,R)-tartaric acid-NaBr-modified Raney nickel catalyst.

achieved was 98% ee (enantiomeric excess) when methyl 3cyclopropyl-3-oxopropanoate was used as a substrate.⁴ The hydrogenation of methyl acetoacetate (MAA), the simplest β ketoester, resulted in methyl 3-hydroxybutyrate (MHB) with enantiopurity of 86% ee (Scheme 1) over tartaric acid-NaBrmodified Raney nickel.⁵ Recently Osawa and co-workers reported higher ee values of 88% and 91% with tartaric acid-NaBr-modified reduced Ni¹⁴ and commercial Ni powder^{16,17} catalysts, respectively, at 9 MPa of H₂. Severe reaction conditions (10 MPa, 333 K) are mostly used to study this system to ensure high reactivity and enantioselectivity.^{1,2,5,18}

However, it would be much more favorable for industrial applications, particularly in terms of safety and atom economy of hydrogen, if the reaction could be conducted under low hydrogen pressure, preferably atmospheric pressure of hydrogen, while maintaining high enantioselectivity of the reaction.

The dependency of enantioselectivity of the asymmetric hydrogenation over tartaric acid-modified Ni catalysts on hydrogen pressure has been investigated previously by several groups (Figure 1). Lipgart et al.¹² reported that the enantiose-lectivity hardly changed under hydrogen pressure of 2.5–10 MPa for the hydrogenation of ethyl acetoacetate over a modified Raney nickel catalyst. The maximum enantioselectivity achieved was 17% ee. Ozaki and co-workers⁶ reported



Figure 1. Previous reports by several groups regarding the dependency of enantioselectivity on hydrogen pressure; Nitta et al.¹⁸ (filled circles), Kukula and Cerveny¹¹ (filled triangles), and Osawa et al.⁸ (filled and empty squares).

the maximum enantioselectivity of 39% ee for the hydrogenation of MAA under atmospheric pressure of hydrogen using a tartaric acid-modified Raney nickel catalyst. Nitta and coworkers¹⁸ studied the dependency of optical yields on hydrogen pressure for the hydrogenation of MAA over a tartaric acid NaBr-modified Ni/SiO₂ catalyst. It was shown that under vigorous stirring, by which diffusion limitation was assumed to be negligible, the enantioselectivity was slightly decreased and then remained constant as the hydrogen pressure increased from 0.5-13 MPa (333 K, 15% conversion). The maximum enantiopurity of the product achieved was 80% ee. According to Kukula and Červený,¹¹ the optical yield of the hydrogenation of MAA in THF at 333 K over a tartaric acid-NaBr-modified Raney nickel catalyst increased as the hydrogen pressure increased from 1 to 12 MPa. The maximum enantiopurity of the product was 83% ee at 12 MPa. More recently, Osawa and coworkers⁸ reported the hydrogen pressure-dependency of the optical yield over a tartaric acid-NaBr-modified Raney nickel catalyst for the hydrogenation of MAA in THF at 373 K using an autoclave equipped with a magnetic stirrer (1220 rpm). It was shown that the optical yield of the product remained almost constant under hydrogen pressure of 2-9 MPa, but decreased significantly as the pressure decreased below 1 MPa. At the low hydrogen pressure, a higher stirring rate was necessary to ensure sufficient hydrogen supply onto the catalyst surface to attain higher enantiopurity of the product. A maximum enantioselectivity of 82% was achieved under 0.2 MPa at 333 K at a high stirring rate (1630 rpm). Low-pressure asymmetric hydrogenation of MAA assisted by hydrogen atom transfer has also been reported using tartaric acid-NaBr-modified supported Ni.¹³ 2-Propanol, as a hydrogen transfer agent, was used as the solvent. A maximum enantioselectivity of 64% was attained when the hydrogenation reaction was conducted at 323 K under atmospheric pressure of H₂ using tartaric acid-NaBr-modified Ni/CeO₂.

In this study, we report the enhanced enantioselectivity for the hydrogenation of MAA over tartaric acid and NaBrmodified Raney nickel under low hydrogen pressure (0.05–0.42 MPa) using a reciprocating reactor, with the maximum enantiopurity, 92% ee, being achieved under 0.42 MPa, the highest ee value ever reported. A kinetic study was satisfactorily performed under the present low-pressure reaction system. It is shown that the reaction rate can be expressed by a Langmuir-Hinshelwood formalism assuming the first hydrogen addition to the substrate as a rate-determining step.

2. Experimental

2.1 Materials. Methyl acetoacetate (MAA) and acetic acid were purchased from Kishida Chemical Co., Ltd. and used as received. Ion exchanged water for the catalyst preparation was supplied from Kishida Chemical Co., Ltd. (R,R)-tartaric acid sodium salt was supplied from Nacalai Tesque, Inc. and used as received. Commercially available THF was distilled vigorously using sodium-potassium alloy and benzophenone prior to use as a solvent.

2.2 Catalyst Preparation. Raney nickel (RNi) was prepared from a Ni/Al allov (42/58, Kawaken Fine Chemicals, Ltd., Japan) by the W-2 type development method, followed by washing with water under ultrasonic irradiation. An aliquot of the alloy (1.0 g) was treated in an alkaline solution of NaOH (4.5 g) in deionized water (20 mL) at 373 K for 1 h. The modification was performed to prepare tartaric acid and NaBrmodified Raney nickel (TA-NaBr-MRNi) by heating RNi at 373 K for 1 h in a 50 mL aqueous solution of (R,R)-tartaric acid mono sodium salt as a chiral modifier (6.6 mmol) and NaBr (5 g) as an auxiliary. After the modification, the solution was removed by decantation, followed by washing with water $(50 \text{ mL} \times 2)$, then with methyl alcohol $(50 \text{ mL} \times 2)$, and finally with tetrahydrofuran (distilled THF) (50 mL \times 2) to prepare TA NaBr MRNi (400 mg).

2.3 Hydrogenation. To a 250 mL glass autoclave (Parr, Hydrogenation Apparatus, Model 3916) equipped with a thermocouple, heating mantle, temperature controller, pressure gauge, gas cylinder and reciprocal shaker, MAA was placed with THF (50 mL), acetic acid (0.2 mL) and TA-NaBr-MRNi (400 mg). The residual air in the reactor was replaced with hydrogen by performing a cycle of refill of H₂ at 0.5 MPa/ release at 0.1 MPa five times and then hydrogen was injected into the reactor for the reaction (total pressure, 0.13-0.50 MPa). Hydrogen pressure was kept constant during the hydrogenation reactions by use of a hydrogen reservoir. The partial hydrogen pressure was calculated assuming a Raoult's law for the solvent THF (ca. 0.08 MPa at 333 K). The autoclave was heated to 333 K and then reciprocating shaking was applied to initiate the catalytic reaction. The reciprocating cycle was 175 cycles per minute. The reaction was conducted for 16 h, 24 h, 32 h, 48 h or 96 h with TA-NaBr-MRNi. The reaction mixture was separated from the catalyst by decantation. NMR was used to determine the conversion of the substrate. Prior to determining enantioselectivity, the reaction products were acetylated with acetic anhydride and pyridine. Enantiomeric excess of the products was determined with gas chromatography (Shimadzu GC 17A equipped with a CP-Chirasil DEX-CB capillary column, 0.25 $mm \times 25 m$ with a helium flow in 32 cm/s) at 100 °C; Rt = 5.18 min for (S)- and 5.32 min for (R)-product. Analytical condition at different temperature has been reported elsewhere.⁴ Enantiomeric excess (%ee) is defined as,

$$\% ee = 100 \times ([R] - [S])/([R] + [S])$$
(1)

where [R] and [S] denote the amounts of the (*R*)- and (*S*)-products.

3. Results and Discussion

3.1 Effect of Solvent Impurities. Tetrahydrofuran has been known as the best solvent for asymmetric hydrogenation of β -ketoesters over TA-NaBr-MRNi resulting in the highest enantiopurity of the product.^{5,6} Thus, in the present study, THF was used as the solvent. However, commercially available THF contains impurities, such as 2,6-di-tert-butyl-4-methylphenol (250 ppm) and water (<0.05%), which may affect the hydrogenation reaction. Therefore, preliminary experiments were conducted to investigate the effect of impurities contained in THF on the asymmetric hydrogenation of MAA.

Table 1 summarizes the effect of impurities in THF on the hydrogenation reaction of MAA. When untreated commercially available THF was used as the solvent, the asymmetric hydrogenation of MAA resulted in 57% conversion after 24 h of reaction time, producing MHB in 78% ee (Entry 1). However, when commercially available THF was distilled prior to use (Entry 2), the conversion of MAA slightly increased to 61%. Moreover, surprisingly, the enantiopurity of the product significantly increased to 90% ee.

The addition of 1 mL H₂O into the distilled THF (50 mL) considerably decreased the total hydrogenation rate to almost one-third compared to that using distilled THF, accompanying a significant decrease in enantioselectivity to 60% ee (Entry 3). The production rate of (R)-MHB was decreased to almost onefourth by the addition of H₂O, while that of (S)-MHB slightly increased. This result is in agreement with the findings reported by Izumi¹ that water could act as an additive in the hydrogenation of MAA over amino acid-modified RNi catalysts to reduce the enantiopurity or, at a higher doping, even to reverse the configuration of MHB. It is probable that the deteriorating effect of H₂O in Table 1 is due to the formation of hydrogen bonding between water and, possibly, one hydroxy group of surface tartrate, leaving only one hydroxy group available for the interaction with MAA. In the presence of water-modifier interaction, it is considered that a part of MAA interacts with the surface modifier in the reversed position, in which the relatively bulky alkoxy group of MAA is positioned opposite from water due to steric hindrance, resulting in reversed enantioface prior to the hydrogenation reaction. The decrease in the hydrogenation rate of MAA in the presence of water might be explained by competitive adsorption between MAA and water on the active sites of the catalyst, which in consequence decelerate the hydrogenation of MAA. We have observed similar phenomenon in our previous studies where malic acid. having only one hydroxy group, was used as a modifier instead of tartaric acid.¹⁹ Malic acid-modified RNi resulted in a lower

selectivity and a lower reaction rate acceleration (a smaller ligand-acceleration effect). Based on this preliminary study, distilled THF was used as the solvent for further study on reaction kinetics.

3.2 Enantioselectivity of MAA-Hydrogenation under Low Hydrogen Pressure. With the current low-pressure reciprocating reactor, sampling was not possible during the reaction. Therefore, each reaction was conducted separately for different length of time in order to understand the reaction rate profile. Figure 2 shows the conversion of MAA against reaction time under two representative hydrogen pressures: 0.42 MPa and 0.05 MPa. These results indicate that the reproducibility of the catalyst preparation and reaction procedures is high enough for a kinetic study. The initial reaction rate was evaluated from the slope of the conversion-reaction time curve below 20% conversion.

The effect of MAA conversion on the enantioselectivity of MAA hydrogenation was also investigated under various hydrogen pressures. Figure 3 shows the enantioselectivity of MAA hydrogenation as a function of MAA conversion and hydrogen pressure ranging from 0.05 to 0.42 MPa. As shown in Figure 3, the enantioselectivity of the MAA hydrogenation slightly increases as the conversion increases; the degree of the increase being marginally enhanced as the hydrogen pressure increases from 0.12 to 0.42 MPa. The selectivity remains almost constant for the reaction under 0.05 MPa of H_2 .

Ozaki et al.⁶ reported a more extensive increase in the enantioselectivity of MAA hydrogenation over a tartaric acidmodified Raney nickel catalyst with increasing reaction time at 10 MPa (<40% ee). Kukula and Červený¹¹ also observed that



Figure 2. Methyl acetoacetate (MAA) conversion against reaction time at two representative hydrogen pressures: 0.42 MPa (red square) and 0.05 MPa (cross). (MAA 18.5 mmol, THF 50 mL, acetic acid 0.2 mL, TA-NaBr-MRNi 0.4 g, 333 K)

 Table 1. Effect of impurities in THF on the hydrogenation rate of methyl acetoacetate (MAA) and enantiopurity of methyl 3-hydroxybutyrate (MHB)^a

Entry	Solvent	Additive	ee (%)	$(\text{mol } h^{-1} \text{ g-cat}^{-1})$	$(\text{mol}h^{-1}\text{g-cat}^{-1})$	$(\text{mol}h^{-1}\text{g-cat}^{-1})$
1	THF ^b	-	78	1.09	0.97	0.12
2	Distilled THF		90	1.18	1.12	0.06
3	Distilled THF	H ₂ O 1 mL	60	0.41	0.32	0.08

^aMAA 18.5 mmol, THF 50 mL, acetic acid 0.2 mL, TA-NaBr-MRNi 0.4 g, 333 K, 0.42 MPa of H₂, 24 h-reaction time. ^bCommercially available THF was directly used without any pre-treatment.

the selectivity on the MAA hydrogenation increased as the reaction proceeded over a tartaric acid-NaBr-modified Raney nickel catalyst at 12 MPa (<83% ee). In contrast, Nitta and coworkers¹⁸ found with a tartaric acid-modified Ni-SiO₂ catalyst that the optical yield of MHB showed the maximum around 50% conversion of MAA at 1 MPa of H₂ (<60% ee). The reasons of the selectivity increase with increasing conversion are not clear enough at present. Ozaki et al.⁶ assumed that non-selective sites of the modified Raney nickel catalysts suffered from the loss of the hydrogenation activity caused by contamination by residual Al-compounds during the reaction, thereby causing the selectivity increase. In addition to the activity loss of the non-selective sites, it may be also possible to evoke a small contribution of pre-adsorbed hydrogen, which evolves during the catalyst preparation and remains on the resultant catalyst surface, in particular, on the unmodified or non-selective sites even after the chiral modification, to be responsible for the initial formation of racemic products and, probably, for the relatively lower selectivity at 0.05 MPa of H₂.

We investigated the enantioselectivity of the hydrogenation of MAA over TA-NaBr-MRNi using distilled THF as the solvent at 333 K under low H₂-pressures, ranging from (0.05-0.42MPa). Table 2 summarizes the enantioselectivity of the MAAhydrogenation as a function of the H₂-pressure.



Figure 3. Dependence of the enantioselectivity of the MAA hydrogenation on the MAA conversion under various H₂-pressures: 0.42 MPa (red square), 0.32 MPa (yellow triangle), 0.22 MPa (blue circle), 0.12 MPa (green diamond) and 0.05 MPa (cross). (18.5 mmol of MAA and 0.2 mL of acetic acid in 50 mL of THF at 333 K)

It is shown in Table 2 that, regardless of the reaction time, the enantioselectivity of MAA gradually increases as the hydrogen pressure increases from 0.05 to 0.42 MPa, with the maximum enantioselectivity (92% ee, the highest ee value ever reported for MAA) being achieved at 0.42 MPa. However, it decreases significantly to 82% ee for the reaction at subatmospheric pressure (0.05 MPa). The highest enantioselectivity, 86% ee, reported previously⁵ for the hydrogenation of MAA has been achieved at elevated pressure of H₂ by optimizing the catalyst preparation of TA-NaBr-MRNi and reaction conditions. The present research group greatly improved in 1994 the enantio-differentiating ability of the catalyst system from 80 to 86% ee for MAA hydrogenation at 10 MPa by applying ultrasonic irradiation during washing procedures after leaching.³ Since then, the selectivity of 86% ee has long been the highest and, then, the target selectivity for the asymmetric hydrogenation of MAA, a kind of a standard compound in the asymmetric hydrogenation of β-ketoesters over modified Raney nickel catalysts, although a higher selectivity of 91% ee was recently reported over a modified commercial Ni powder catalyst at 9 MPa of H₂.^{16,17} In addition, as noted in Introduction and Figure 1, the selectivity remains almost constant at a relatively high hydrogen pressure (2-10 MPa) but significantly decreases as the hydrogen pressure decreases, in particular, below 0.5 MPa. However, as summarized in Table 2, it is very noteworthy here that the selectivity of 92% ee is attained at as low as 0.42 MPa of H₂. This extraordinary enantiodifferentiating ability of TA-NaBr-MRNi resulted from the purification of the solvent used, as suggested above. A slight increase in the selectivity with increasing hydrogen pressure may be due to the increase in the ratio of the reaction rates over modified sites to unmodified sites. The fraction of the unmodified sites was estimated to be below 5%.² The present findings that the highest ever enantioselectivity is achieved even under a low hydrogen pressure will expand the industrial applications of modified Raney nickel catalyst systems for the asymmetric hydrogenation of β -ketoesters.

3.3 Reaction Kinetics of MAA Hydrogenation over TA-NaBr-MRNi. The initial hydrogenation rate was evaluated from Figure 1 below 20% conversion of MAA. Figure 4 shows the effect of hydrogen pressure on the hydrogenation rate of MAA at two representative MAA concentrations: (a) 0.71 mol/L and (b) 1.42 mol/L. It is apparent that the reaction rate increases with the hydrogen pressure, following a convex

Table 2. Enantioselectivity of asymmetric hydrogenation of MAA over TA-NaBr-MRNi at 333 K^a

Hydrogen pressure/MPa	Reaction time/h	Conversion/%	Enantioselectivity/%ee
0.05	24	25	82
0.12	16	28	87
0.12	24	45	87
0.22	16	42	89
0.22	48	91	89
0.22	16	33	88
0.52	24	63	90
0.42	24	59	91
0.42	48	93	92

^aReaction Conditions: 18.5 mmol of MAA and 0.2 mL of acetic acid in 50 mL of THF with 0.4 g of the catalyst.



Figure 4. Effect of hydrogen pressure on the hydrogenation rate of methyl acetoacetate (MAA) at concentration of MAA (a) 0.71 and (b) 1.42 mol/L. (0.2 mL of acetic acid in 50 mL of THF with 0.4 g of TA-NaBr-MRNi at 333 K). The dotted lines show the fittings by use of eq 2.



Figure 5. Dependency of MAA hydrogenation rate on the MAA concentration. $(0.2 \text{ mL acetic acid and } 0.4 \text{ g of TA-NaBr-MRNi at 333 K under } 0.42 \text{ MPa of } H_2 \text{ pressure})$. The dotted line shows the fitting by use of eq 2.

curve. When the dissolution rate of hydrogen into the reaction solution and/or the adsorption rate of hydrogen onto the catalyst surface through stagnant films control the reaction rate, the reaction rate is expected to increase linearly with the hydrogen pressure. Thus, it is considered that the reaction rate is determined by surface reactions under the present reaction conditions.

Figure 5 shows the effect of MAA concentration on the hydrogenation rate over TA-NaBr-MRNi. The hydrogenation rate increases as the MAA concentration increases and reaches a maximum at $[MAA] \sim 1 \text{ mol/L}$. We tried to describe the reaction rate of the asymmetric hydrogenation of MAA over TA-NaBr-MRNi by Langmuir-Hinshelwood formalism, assuming that the substrate and hydrogen are competitively adsorbed on the catalyst surface and that the first addition of adsorbed hydrogen to the adsorbed substrate is a rate-determining step. In the present study, we neglected the contribution of nonselective hydrogenation of MAA over unmodified sites, since it was shown previously that the fraction of the unmodified or non-selective sites was less than $5\%^2$ on finely prepared TA-NaBr-MRNi and that the enantioselectivity achieved here was considerably high, even at a low conversion of MAA (Figure 2 and Table 2, >86%ee), in spite of a low hydrogen pressure

(<0.5 MPa). Thus, when we focus on the initial reaction rate, the hydrogenation rate of MAA, r, can be expressed as,

$$\mathbf{r} = (\mathbf{k}^{0} \ \mathbf{K}_{\text{MAA}} \mathbf{C}_{\text{MAA}} \ \mathbf{K}_{\text{H}}^{1/2} \mathbf{P}_{\text{H}}^{1/2}) /(1 + \mathbf{K}_{\text{MAA}} \mathbf{C}_{\text{MAA}} + \mathbf{K}_{\text{H}}^{1/2} \mathbf{P}_{\text{H}}^{1/2})^{2}$$
(2)

where k^0 is a real rate constant, K_{MAA} and K_H the equilibrium adsorption constants of MAA and H₂, respectively, C_{MAA} the concentration (mol/L) of MAA, and P_H the pressure (MPa) of H_2 . We tried to fit the results in Figures 4 and 5 by assuming appropriate sets of kinetics parameters in eq 2. The best fitting curves are presented in these Figures. Satisfactory fittings of the kinetics data by eq 2 lead us, for the first time, to conclude that the asymmetric hydrogenation of MAA over the modified Raney nickel is represented by the Langmuir-Hinshelwood rate equation, assuming the first hydrogen attack to surface tartratesubstrate interaction species as a rate-determining step to form a half-hydrogenated intermediate. It is worth noting that precise reaction kinetic studies of the asymmetric hydrogenation can be facilitated only by the reactions under low pressure of hydrogen. Since asymmetric hydrogenations of β -ketoesters on modified-nickel catalysts have been conducted at high hydrogen pressure (e.g., 1-10 MPa) to keep the selectivity high, it would have been difficult to get information on the hydrogen pressure-dependency. Ozaki et al.⁶ tried kinetic analysis of the MAA-hydrogenation over modified Raney nickel at a fixed hydrogen pressure (0.1 MPa) using a Langmuir-Hinshelwood type equation. In their kinetics study of the hydrogenation of MAA over a tartaric acid modified Ni-SiO₂ catalyst under low hydrogen pressure (0.1-1 MPa), Nitta et al.¹⁸ also assumed a Langmuir-Hinshelwood rate equation with K_HP_H instead of $(K_H P_H)^{1/2}$ in eq 1. But, they only discussed the behavior of the selectivity as a function of hydrogen pressure and substrate concentration on the basis of their rate equation. In our previous study,19-21 we tentatively assumed eq 1 to describe the kinetics behavior of the reaction. The present results verify our previous assumptions.

The kinetics parameters used for the fittings in Figures 4 and 5 are 57 (mol h⁻¹ g-cat⁻¹), 1.1 (mol/L)⁻¹, and 4.5×10^{-8} (MPa)⁻¹ for k⁰, K_{MAA}, and K_H, respectively. It is obvious that $K_{\rm H}^{1/2}P_{\rm H}^{1/2} \ll K_{\rm MAA}C_{\rm MAA}$ under the present reaction conditions and even under a high H₂ pressure (e.g., 10 MPa) conventionally

used in previous studies.^{19–21} It is suggested that the adsorption of hydrogen involved in the reaction is much weaker than that of the substrate interacting with surface tartrate.

4. Conclusion

Enantioselective hydrogenation of MAA over TA-NaBr-MRNi has been intensively studied by various groups. Many aspects have been investigated in order to find the best reaction conditions to achieve excellent enantio-purity of the product.^{1–15} It was believed that severe reaction conditions, such as H₂-pressure of 10 MPa, were necessary in order to obtain high enantioselectivity. In the current study, enantioselective hydrogenation of MAA was successfully conducted under low hydrogen pressure (0.05–0.42 MPa). The highest enantioselectivity of the asymmetric hydrogenation of MAA. 92% ee, the highest value ever reported, was achieved by use of distilled THF even under low hydrogen pressure of 0.42 MPa. The present study on the asymmetric hydrogenation of MAA under low pressure enabled us, for the first time, to determine the precise dependency of the reaction rate on the hydrogen pressure and suggest the rate-determining step based on Langmuir Hinshelwood formalism. The present study under low hydrogen-pressure can expand industrial applications of modified-Raney nickel catalyst systems.

References

1 Y. Izumi, Adv. Catal. 1983, 32, 215.

2 A. Tai, T. Sugimura, in *Chiral Catalyst Immobilization and Recycling*, ed. by D. E. De Vos, I. F. J. Vankelecom, P. A. Jacobs, Wiley-VCH Verlag GmbH, **2000**, pp. 173–209. doi:10.1002/9783527613144.ch08.

3 A. Tai, T. Kikukawa, T. Sugimura, Y. Inoue, S. Abe, T.

Osawa, T. Harada, Bull. Chem. Soc. Jpn. 1994, 67, 2473.

4 T. Sugimura, S. Nakagawa, A. Tai, *Bull. Chem. Soc. Jpn.* 2002, 75, 355.

5 T. Sugimura, Catal. Surv. Asia 1999, 3, 37.

6 H. Ozaki, A. Tai, S. Kobatake, H. Watanabe, Y. Izumi, *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3559.

7 H. Ozaki, Bull. Chem. Soc. Jpn. 1978, 51, 257.

8 T. Osawa, M. Onogi, I.-Y. S. Lee, T. Harada, *React. Kinet. Mech. Catal.* **2011**, *103*, 443.

9 S. Nakagawa, T. Sugimura, A. Tai, *Chem. Lett.* 1998, 1257.

10 S. Nakagawa, A. Tai, T. Okuyama, T. Sugimura, *Top. Catal.* **2000**, *13*, 187.

11 P. Kukula, L. Červený, *Res. Chem. Intermed.* 2003, 29, 91.

12 P. Kukula, L. Červený, *J. Mol. Catal. A: Chem.* **2002**, *185*, 195.

13 T. Osawa, S. Kawajiri, A. Ishisaki, *React. Kinet. Mech. Catal.* **2016**, *119*, 195.

14 T. Osawa, Y. Tanabe, M. Fujiwara, *Catal. Lett.* **2017**, *147*, 686.

15 T. Osawa, M. Wakasugi, T. Kizawa, V. Borovkov, Y. Inoue, *Mol. Catal.* **2018**, *449*, 131.

16 T. Osawa, T. Kizawa, S. Ikeda, T. Kitamura, Y. Inoue, V. Borovkov, *Tetrahedron: Asymmetry* **2014**, *25*, 1630.

17 T. Osawa, T. Kizatsune, F. Takano, S. Ikeda, T. Kitamura, Y. Inoue, V. Borovkoy, *ChemCatChem* **2014**, *6*, 170.

18 Y. Nitta, T. Imanara, S. Teranishi, J. Catal. 1983, 80, 31.

19 T. Sugimura, S. Nakagawa, N. Kamata, T. Tei, T. Tajiri, R. Tsukiyama, T. Okuyama, Y. Okamoto, *Bull. Chem. Soc. Jpn.* **2015**, *88*, 271.

20 A. A. Choliq, E. Murakami, S. Yamamoto, T. Misaki, M. Fujita, Y. Okamoto, T. Sugimura, *Bull. Chem. Soc. Jpn.* **2018**, *91*, 1325.

21 A. A. Choliq, J. Watanabe, T. Misaki, Y. Okamoto, T. Sugimura, *Tetrahedron: Asymmetry* **2016**, *27*, 657.