BCSJ

Ligand-Acceleration by a Chiral Modifier in the Enantioselective Hydrogenation of Methyl Acetoacetate on a Raney Nickel Catalyst: Effect of a Modifier Configuration

Takashi Sugimura,[*1] **Satoshi Nakagawa,**[2] **Naoya Kamata,**[1] **Takahiro Tei,**[1] **Takashi Tajiri,**[1]
Ryo-ichi Tsukiyama,[3] **Tadashi Okuyama,**[1] **and Yasuaki Okamoto**[1]

[1]Graduate School of Material Science, University of Hyogo, 3-2-1 Kohto, Kamigori, Ako-gun, Hyogo 678-1297

[2]Toyo Kasei Kogyo Co., Ltd., 2900 Sone, Takasago, Hyogo 676-0082

[3]Higashimaru Shoyu Co., Ltd., 100-3 Tominaga, Tatsuno, Hyogo 679-4193

E-mail: sugimura@sci.u-hyogo.ac.jp
Received: September 13, 2014; Accepted: October 24, 2014; Web Released: November 12, 2014

Reaction rate and enantioselectivity of asymmetric hydrogenation of methyl acetoacetate were studied over Raney nickel catalysts modified with (*R*,*R*)-tartaric acid, malic acid, or succinic acid to reveal the impacts of the modifier configuration. Catalysts comodified with two different acids were also examined to confirm the conclusions. From analysis of the enantiomer ratio of the hydrogenation product and initial reaction rate, tartaric acid (TA) was found to have dual functions as the modifier during the hydrogenation; effective suppression of the racemic catalysis on bare Ni surface and extensive enantiodifferentiating ligand acceleration by adsorbed TA. It was demonstrated that each adsorbed chiral modifier molecule independently takes part in the enantiospecific hydrogenation.

Enantiodifferentiating hydrogenation of prochiral ketones and olefins over chiral organic compound modified heterogeneous metal catalysts have recently received extensive attention from both scientific and practical points of view.[1–7] Since the first report on the hydrogenation of methyl acetoacetate (MAA)[8] over (*R*,*R*)-tartaric acid-modified Raney nickel (TA-MRNi) catalysts, this and analogous hydrogenation systems have been keenly investigated by many research groups to improve the optical yield,[1,9–15] that has recently reached 98% or even higher over MRNi catalysts doubly modified with TA and NaBr (TA-NaBr-MRNi)[16–19] as well as to obtain deeper insights into the nature of molecular events during enantiodifferentiating hydrogenation.[20–25] Since the enantiodifferentiation step of this system is the adsorption of the substrate prior to the rate-determining hydrogenation,[26–29] the kinetic effect by the chiral modifier is hidden behind the energy barrier of the total process, and thus the expression of the enantiodifferentiation mode is still controversial. In the present study, the reaction rate and enantioselectivity of asymmetric hydrogenation of MAA were systematically studied over Raney nickel catalysts modified with (*R*,*R*)-tartaric acid (TA), malic acid (MA), or succinic acid (SA) to reveal the effect of the modifier configuration.

Achievement of the high optical yield means that the active nickel surface for the hydrogenation is uniformly modified. TA molecules cover the nickel surface and the substrate is adsorbed on the catalyst where the interaction with the TA molecule is possible for enantiodifferentiation and for hydrogenation to take place. Thus, the uncovered nickel surface should remain around the TA molecule to keep the catalyst activity, although the uncovered surface is a potential source of a racemic product. Recently, it was suggested that the highest enantioselectivity was achieved at a 20% fractional coverage of TA over a Ni catalyst reduced at 1373 K[30] and Ni/SiO_2 supported catalysts.[31–33] Many researchers have tried to solve this basic issue, but no reasonable conclusion could be obtained.[9–14] In this report, we will show that the strict stereocontrol ability of TA-NaBr-MRNi is not due to a delicate balance of the covered and uncovered surfaces, but due to the dual functions of the TA modifier; minimization of the racemic catalysis on bare Ni surface and enantio-differentiating ligand acceleration by adsorbed TA.

To look into phenomena occurring prior to the transition state of the overall process, we have planned to construct two reaction sites on a catalyst by comodification with two kinds of modifier acids. When such a comodified catalyst is employed for the hydrogenation, kinetic effects of the adsorbed acids can be determined by the product analysis in the enantiomer ratio. This system is effective because the two kinds of enantiodifferentiating sites formed by the coexisting modifiers work under absolutely the same reaction conditions, and thus, the result is not affected by other factors including reproducibility of the catalyst.

Experimental

Catalyst Preparation. Raney nickel (RNi) was prepared from a Ni/Al alloy (42/58, Kawaken Fine Chemicals, Ltd. Japan) by W-1 type development followed by washing with water under ultrasonic irradiation.[16–18] 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 MRNi (0.4 g) by heating the RNi at 373 K for 1 h in a solution, including the modifier (TA, MA, or SA, 6.6 mmol) or a homo-stereochemical combination of the modifiers (TA–MA, TA–SA, or MA–SA, 3.3 mmol each) on comodification in the simultaneous presence of NaBr (5 g) in water (50 mL), after adjustment of the pH with NaOH at 3.2. After the modification, the solution was removed by decantation, followed by thorough washing with water, then with methyl alcohol, and finally with tetrahydrofuran (THF).[16–18] Unless otherwise noted, MRNi denotes RNi catalysts doubly modified with both the organic acid and NaBr hereafter. The BET surface area was determined by N_2-adsorption at a liquid N_2-temperature after evacuation at 393 K for 1 h ($<$ca. 10^{-5} Pa).

Analysis of Adsorbed Acid on the Catalyst. MRNi (0.4 g) was heated in a NaOH solution (1.25 M, 20 mL) at 373 K for 1 h. The water layer was collected by decantation. Amounts of the acids dissolved in this solution were determined by a Shimadzu LC-10AD organic acid analyzer with a Shim-pack SCR-102(H) column and a CCD-6A detector. Retention times eluted with 5 mM *p*-toluenesulfonic acid (0.4 mL min^{-1}) are 18.0 min for TA, 19.5 min for MA, and 22.7 min for SA.

Hydrogenation and Analysis of the Product. The catalyst (0.4 g) and a solution of methyl acetoacetate (MAA, 2 g) in THF (20 mL) were placed in a 100 mL autoclave. Hydrogen was charged into the autoclave under the initial pressure of 10 MPa, and the autoclave was heated to 333 ± 1 K under reciprocating shaking until the end of the hydrogen uptake. Aliquots of the reaction mixture were periodically withdrawn for analysis. When MAA was hydrogenated over the modified RNi catalysts, methyl 3-hydroxybutyrate was obtained in a quantitative yield. Enantiomeric ratios of (*R*)- and (*S*)-methyl 3-hydroxylbutyrates were determined by GLC equipped with a CP-Chirasil DEX CB capillary column (25 m, 0.25 mm id, GL Science, Japan, flow rate: 30 cm s^{-1}). After acetylation with acetic anhydride and pyridine, the retention times of the product (363 K) are 7.1 min for (*S*) and 7.5 min for (*R*). Enantio excess (ee) is defined here as

$$\text{ee (\%)} = 100([\mathrm{R}] - [\mathrm{S}])/([\mathrm{R}] + [\mathrm{S}]) \qquad (1)$$

where [R] and [S] denote the amounts of (*R*)- and (*S*)-methyl 3-hydroxylbutyrates.

Results and Discussion

The adsorbed acids on MRNi catalysts were extracted into a hot NaOH solution, and the amounts of the acids in the solution were directly determined by ion chromatography. This procedure is essentially the same used by Osawa et al.[30] Table 1 summarizes the adsorbed amounts of the modifiers thus determined as well as the BET surface areas. The surface area was decreased to 25–30% of the original RNi (102 $m^2\,g^{-1}$) by the modification with the organic acids. The TA amount adsorbed on TA-MRNi is 19 ± 2 μmol $(\text{g-cat})^{-1}$ or 0.66 ± 0.07 μmol m^{-2}. The adsorption mode of TA on Ni{111} surface, which is thermodynamically the most stable surface for Ni metal particles, was studied by Jones and Baddeley[25] by means of reflection absorption infrared spectroscopy (RAIRS) and scanning tunneling microscopy (STM) techniques, showing that monotartrate surface species is relatively stable at 300 K, while bitartrate species are predominantly formed at > 350 K. Furthermore, Humblot et al.[20] demonstrated with RAIRS and STM the formation of bitartrate surface species even at 300 K with Ni(110) surface. It was also reported that the presence of NaBr has no effect on the adsorption mode of TA.[22] In these studies using the surface science techniques, TA was adsorbed on Ni surface in a vacuum, in contrast to the modification of RNi with TA and NaBr in an aqueous solution. Taking into consideration the high dielectric constant of H_2O, it is reasonable to expect enhanced double deprotonation of TA to form bitartrate species on Ni metal. Since the modification temperature was 373 K in the present study, it is considered that TA molecules are adsorbed as bitartrate species with two bonding to the Ni metal surface of RNi and/or as monosodium bitartrate surface species (sodium nickel tartrate), that was originally proposed by Tai et al.[34] and later by Osawa et al.[13] to explain the positive effect of Na^+ ions. The molecular cross section of bitartrate surface species was calculated to be $0.68 \times 0.46\,nm^2$ or $0.31 \times 10^{-18}\,m^2$.[20] Assuming this cross section, the fractional coverage of TA molecules on TA-MRNi is estimated to be 0.12. With RNi catalysts prepared from a 42/58 Ni/Al-alloy as in the present study, Okamoto et al.[35] showed with XPS that the fraction of Ni in the surface was 0.7 when the alloy was activated at 373 K. It is then estimated that under the present modification conditions the coverage of TA on Ni metal surface is 0.17, the value which has been suggested to be optimum for the highest enantioselectivity.[30–33] This may be one of the reasons why the maximum selectivity (86% enantio excess) was achieved over the TA-MRNi catalyst in the present study (vide infra).

The amounts of adsorption of MA and SA are very close to that of TA, as presented in Table 1. The adsorption geometries of MA and SA on Ni metal surface have rarely been studied with spectroscopic techniques. With Cu(110) surface, RAIRS and STM studies showed that bisuccinate surface species were formed on the adsorption of SA at >350 K, as bitartrate species for TA/Cu(110),[36,37] with a subtle second-order effect of the OH groups on finer details of the self-assembled structure. Similarly, it was demonstrated with RAIRS, XPS, and STM that MA was adsorbed on Cu(110) surface to form bimalate structure.[38] Thus, it is evident that TA, MA, and SA form essentially the same bicarboxylate structure by double deprotonation on the adsorption on Cu(110). It is rational to assume that Ni metal adsorbs these organic acids to form similar surface bicarboxylate species with a different number of OH

Table 1. BET Surface Area of Raney Nickel Catalysts and the Adsorbed Amount of the Modifier[a)]

Modifier	BET surface area /$m^2\,g^{-1}$	Adsorbed amount of the modifier /μmol g^{-1}		
		TA	MA	SA
TA-NaBr	29	19		
MA-NaBr	33		18	
SA-NaBr	—			20
TA-MA-NaBr	23	7	9	
TA-SA-NaBr	23	7		10
MA-SA-NaBr	25		8	7

a) TA: tartaric acid, MA: malic acid, SA: succinic acid.

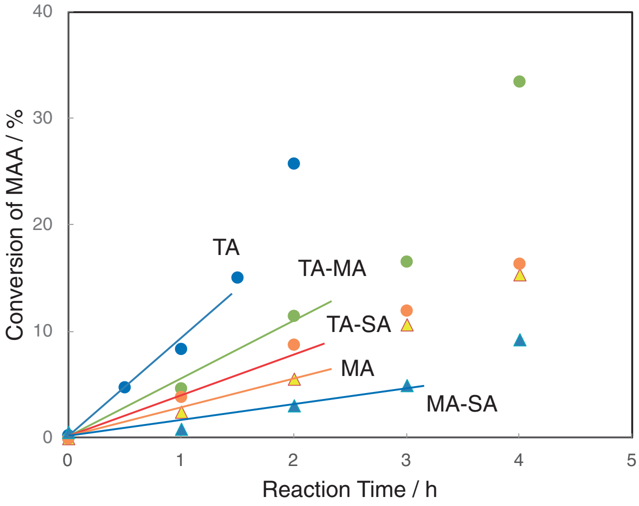

Figure 1. Conversions of methyl acetoacetate (MAA) as a function of the reaction time for the asymmetric hydrogenation of MAA over a Raney nickel catalyst (RNi) doubly modified with NaBr and (*R*,*R*)-tartaric acid (TA) (blue circle) or (*S*)-malic acid (MA) (yellow triangle) and over a RNi catalyst comodified with TA–MA (green circle), TA–succinic acid (SA) (orange circle), or MA–SA (blue triangle). Reaction conditions: 10 MPa of H_2 at 333 K.

groups. Thus, it is presumed that the fractional coverage of adsorbed MA (bimalate) and SA (bisuccinate) species on Ni metal surface of RNi are essentially the same as that of TA, around 20% on the basis of the molecular cross section.

Table 1 also summarizes the amounts of the adsorbed modifier for the comodified catalysts. A TA-SA-MRNi comodified catalyst was prepared by our standard procedure[18] except for the use of the modifying solution containing both TA and achiral SA in equimolar amounts. $7 \pm 1\,\mu\text{mol}\,\text{g}^{-1}$ of TA and $10 \pm 1.5\,\mu\text{mol}\,\text{g}^{-1}$ of SA are adsorbed on TA-SA-MRNi (Table 1). The total amount of TA and SA is $17\,\mu\text{mol}\,\text{g}^{-1}$ and approximately identical to the amount of the modifier adsorbed on TA-MRNi or SA-MRNi, showing that about half of the TA-adsorbed species on TA-MRNi is replaced by the SA-adsorbed species on TA-SA-MRNi and vice versa. With TA-MA- and MA-SA-MRNi catalysts, the total amounts of the adsorbed acids are 16 and $15\,\mu\text{mol}\,\text{g}^{-1}$, respectively, and comparable with the other catalysts including individually modified ones. It is concluded that the two acids in the comodified catalysts are competitively adsorbed on Ni metal surface and that the total fractional coverage is limited to about 20% in the present modification procedure. It appears that the modifier acids have a similar ability to modify the surface of RNi. However, scrutinizing the amount of each modifier on the co-modified MRNi catalysts in Table 1, it seems that the adsorbed amount of the modifier slightly decreases in the order SA > MA ≈ TA. This order may be due to the order of slightly increasing van der Waals cross section of the adsorbed modifier molecule and/or to a slightly different self-assembled surface structure.

Figure 1 shows the conversion of MAA as a function of reaction time for the enantioselective hydrogenation over the modified RNi catalysts. As apparently exemplified by the reaction over TA-MRNi, the conversion reaction time relation is described as a more or less concave curve, that is, the incremental increase in the conversion is enhanced as the reaction proceeds. In addition, it is evident that the curvature is enlarged as the increase in the initial reaction rate (the linear lines in Figure 1); TA > TA-MA > TA-SA ≈ MA > MA-SA. Such reaction behavior is reasonably understood on the basis of a Langmuir–Hinshelwood (L–H) formalism; the reaction rate r can be expressed as, assuming that the substrate MAA and hydrogen are competitively adsorbed on the Ni surface and that the first addition of a hydrogen atom to adsorbed MAA is the rate-determining step of the hydrogenation,

$$r = k^0 K_S C_S {K_H}^{1/2} {P_H}^{1/2}/(1 + K_S C_S + {K_H}^{1/2} {P_H}^{1/2})^2 \qquad (2)$$

where k^0 is a real rate constant, K_S and K_H the adsorption constants of MAA and H_2, C_S the concentration of MAA, and P_H the pressure of H_2. When K_S is large and/or the concentration of MAA is high ($K_S C_S \gg 1 + {K_H}^{1/2}{P_H}^{1/2}$), r can be reduced to

$$r = k^0 {K_S}^m {C_S}^m {K_H}^{1/2} {P_H}^{1/2} \quad (-1 < m < 0) \qquad (3)$$

When K_S is not very high and/or C_S is relatively low, m in eq 3 is positive. Keane[39] reported that $m = 0.3$ at 343 K over TA-NaBr-Ni/SiO_2. However, the concave curve in Figure 1 clearly shows that the reaction order m is negative with respect to the substrate MAA under the present reaction conditions (333 K, 10 MPa, 0.86 M of MAA). It is deduced from the L–H rate equation that the negative order is caused by relatively strong adsorption of MAA on the modified catalysts and that the adsorption strength of MAA increases in the order, SA < MA–SA < MA ≈ TA–SA < TA–MA < TA. It is noteworthy that the initial reaction rate increases as the adsorption strength or the adsorption amount of MAA on the MRNi catalyst increases. With the reaction on SA-MRNi (not shown in Figure 1), the conversion of MAA linearly increased up to 55% after 45 h reaction time, indicating that the reaction is zeroth order ($m = 0$) with respect to MAA over SA-MRNi. It is deduced that MAA is more weakly adsorbed on SA-MRNi than on TA-MRNi or MA-MRNi.

To evaluate the hydrogenation activity of MRNi catalysts, the initial reaction rate (r $\text{mmol}\,\text{h}^{-1}\,\text{g}^{-1}$) was calculated from the initial conversion (<10%) of MAA and reaction time as presented in Figure 1. Table 2 compares the initial reaction rate and ee of the enantioselective hydrogenation of methyl acetoacetate (MAA) over a Raney Ni catalyst modified with TA, MA, or SA. The reaction rate r can be divided into two components, r_R and r_S corresponding to the formation rates of (*R*)- and (*S*)-configurations, respectively.

$$r = r_R + r_S \qquad (4)$$

$$\text{ee } (\%) = 100(r_R - r_S)/(r_R + r_S) \qquad (5)$$

The values of r_R and r_S were calculated using the reaction rate and selectivity, enantiomeric excess (ee). Table 2 summarizes r, r_R, and r_S for the relevant catalyst systems.

The initial reaction rate r of the MAA hydrogenation over MA-MRNi is 4.1 fold increased relative to that on SA-MRNi. While no enatiodifferentiating hydrogenation is observed with SA-MRNi as expected, enantioselectivity is induced to the hydrogenation to provide 60% ee by replacing SA with MA,

Table 2. Enantioselectivities and Initial Reaction Rates of the Hydrogenation of MAA over Modified Raney Nickel Catalysts

Modifier[a)]	TA-NaBr	MA-NaBr	SA-NaBr	TA-MA-NaBr	TA-SA-NaBr	MA-SA-NaBr
ee/%[d)]	86	60	0	81 (79)	86 (78)	50 (52)
r_R/r_S	13	4.0	1	9	13	3
r/mmol h^{-1} g^{-1} [b)]	4.3	1.2	0.29	2.4 (2.5)	1.7 (1.9)	0.73 (0.73)
r_R/mmol h^{-1} g^{-1}	4.0	0.96	0.15	2.2	1.6	0.55
r_S/mmol h^{-1} g^{-1}	0.31	0.24	0.15	0.24	0.12	0.18

a) Abbreviation of the modifiers; TA: tartaric acid, MA: malic acid, SA: succinic acid. b) Values in parentheses are calculated assuming independent contributions from the respective modified sites.

which has a single hydroxy group as a chiral origin. That is, r_R is increased 6.4-fold compared to that of SA-MRNi, while r_S only 1.6-fold. A comparison of r_R and r_S between MA-MRNi and SA-MRNi reveals that the modification of Ni metal surface with MA obviously induces "ligand acceleration"[40,41] in the hydrogenation of MAA over chiral-modified Ni catalysts. Keane[39] noted a promotion of the reaction rate as well as a decrease in the activation energy in the enantioselective hydrogenation of MAA (ee $<$ 30%) by the modification of Ni/SiO_2 with TA.

It is clearly demonstrated in Table 2 that TA-MRNi exhibits even more significant ligand acceleration effects than MA-MRNi. The initial reaction rate r is 15-fold increased by replacing SA with TA. In particular, r_R is 27-fold enhanced with respect to SA-MRNi, while r_S is only doubled, resulting in the very high enantioselectivity, 86% ee. When compared with MA-MRNi, the value of r is 3.6-fold increased. r_R is 4.2-fold enhanced by replacing MA with TA, while r_S is only slightly increased. It is concluded that the enatiodifferentiating hydrogenation is induced not only by poisoning the racemic sites with the modifier molecules and NaBr but also more predominantly by a great increase of r_R by specific interactions of MAA with the surface chiral modifier, that is, by the ligand acceleration effects induced by the chiral modifier. In the above discussion on the relative magnitudes of r_R and r_S, a possible contribution of the reaction over non-enantioselective sites (N-sites) to the reaction rates is neglected, since the fraction of the reaction on the N-sites was previously estimated to be 4% over TA-MRNi.[18]

The ee greatly increases as the number of hydroxy groups of the chiral modifier increases: nil, one, and two for SA (0%), MA (60%), and TA (86%), respectively, as presented in Table 2. This is rationally accounted for in terms of the interaction modes between the hydroxy groups and MAA: two-point interaction mode or two pairs of hydrogen bonding between the surface bitartrate (possibly monosodium bitartrate surface species in the presence of NaBr)[13,34] and MAA for highly enantiodifferentiating reaction to occur and one-point interaction mode or a single hydrogen bonding between adsorbed bimalate and MAA, leading to less selective hydrogenation. From the kinetics analysis, r_R increases several times as the number of hydroxy group increases by one: 6.4-fold from nil to one and 4.2-fold from one to two (ligand acceleration). On the other hand, the corresponding r_S values increase only 1.6- and 1.3-fold, respectively. These increases in the reaction rates, which reflect both the true rate constant k^0 directly connected with the surface reactions and the adsorption constant K_S of MAA (eqs 2 and 3), are induced by the interactions between the surface modifier and the substrate. RAIRS and STM provided such direct interactions between surface bitartrate and MAA with Ni(110)[21] and Ni{111}.[24] It is surmised that the adsorption constant K_S increases as the number of the hydroxy groups increases from nil through two and thus as the interaction mode of MAA changes from van der Waals interaction with surface bisuccinate, one hydrogen-bonding interaction with surface bimalate, and two-point hydrogen-bonding interaction with surface bitartrate, resulting in the increase in the reaction rate. However, it is expected from the increase of r_S by replacing SA with TA that the increase of the reaction rate due to the increase of K_S is limited to, at most, twofold. Thus it is concluded that the great increase in r_R is due to the increase in k^0 induced by the interactions with deprotonated surface MA or TA molecules (ligand acceleration). It is evident that the increasing magnitude in the difference between r_R and r_S from SA through TA is induced by the increase in the intrinsic enantiodifferentiating ability, i,[11,42] due to the change in the modifier–substrate interaction modes from dipole or van der Waals interaction (SA), one-point hydrogen bonding (MA), and two-point hydrogen bonding (TA) interactions.[11,13] This was previously envisaged by the findings that the addition of pyvaric acid reduces the enantioselectivity of TA-MRNi for the enantioselective hydrogenation of various ketoesters and 2-octanone.[43] It is concluded that the increase in the number of the hydroxy groups of the modifier not only enhances the enantiodifferentiating ability of the chiral modifier but also causes a significant increase in the reaction rate (ligand acceleration) through the changes in the interaction mode and strength, accompanying the increase in the adsorption strength of the substrate. The interaction between the surface modifier and MAA is clearly evidenced by the findings in Figure 1 that the magnitude of the negative reaction order with respect to MAA, that is, the interaction strength increases in the order; SA $<$ MA $<$ TA.

As discussed above, the coverage of the modifier bicarboxylate on the Ni metal surface is estimated to be about 20% from the molecular cross section. In spite of rather low coverages of the modifiers, high ee values are observed, in particular with TA-MRNi, as presented in Table 2. It is proposed that the preadsorbed modifier molecules strongly suppress the hydrogenation activity by blocking the Ni metal ensemble sites required for racemic reactions but the preadsorbed modifier molecule having appropriate interactions with the substrate forms a novel ensemble site including Ni metals for highly enantiodifferentiating hydrogenation. The loss of the ensemble sites for the hydrogenation may result from surface reconstruction by the adsorption of modifier molecules and from the formation of ordered surface structure. Actually, Humblot et al.[20] showed with STM and DFT calculations for TA/Ni(110) that the formation of the surface bitartrate accompanies reconstruction of surface Ni atoms, the size of which amounts to $1.25 \times 1.55\,\mathrm{nm}^2$ or $1.9 \times 10^{-18}\,\mathrm{m}^2$, six times larger than the molecular cross section of bitartrate ($0.31 \times 10^{-18}\,\mathrm{m}^2$). Ordered adlayers of tartrate species are formed on Ni{111}, depending on the modification temperature.[25] Self-assembled structures of bisuccinate were observed for SA/Cu(110).[36]

We studied the enantioselective hydrogenation over comodified MRNi catalysts to confirm the reaction rates and ee results, obtained separately on the MRNi catalysts individually modified with TA, MA, or TA, and to obtain deeper insights, if possible, into the generation of enantiospecific hydrogenation on the chiral modified RNi. Table 2 summarizes the initial reaction rates and ee values for the comodified MRNi catalysts. The reaction rates and ee values on the comodified catalysts are intermediate between the values of the respective individually modified MRNi catalysts. It is reasonable to estimate the reaction rates and ee values from the adsorbed amounts of the modifiers in Table 1 and the reaction results in Table 2, assuming that the modifier molecules independently take part in the asymmetric hydrogenation. Table 2 compares the observed and thus estimated reaction rates and ee values. It is obvious that estimated values are essentially identical to the observed ones within experimental accuracy, confirming that the reaction rates and enantioselectivity in Table 1 have been measured accurately enough for the above discussion on the effects of the modifier configuration. The coincidence in Table 2 furthermore strongly indicates that the surface chiral modifier bicarboxylate species independently take part in the enantioselective hydrogenation of MAA. This suggests that with TA-MRNi, the formation of 1:1 surface interaction species between the bitatrate and MAA via two-point hydrogen-bonding interactions is a predominant origin to produce (*R*)-methyl 3-hydroxylbutyrate, as tentatively proposed by several research groups.[1,7,11]

Conclusion

The reaction rate and enantioselectivity of the asymmetric hydrogenation of MAA were studied over Raney nickel catalysts modified with (*R*,*R*)-tartaric acid, malic acid, or succinic acid to reveal the impacts of the modifier configuration. The surface coverage of the modifier was about 20% irrespective of the configuration. From the enantiomer ratio of the hydrogenation product and initial reaction rate, it is concluded that surface modifier molecules have dual functions during the hydrogenation; effective suppression of the racemic catalysis on bare Ni surface and extensive enantiodifferentiating ligand acceleration through the hydrogen-bonding interactions with the substrate molecule.

One difference in the three modifiers is the number of hydroxy groups. The adsorption of the modifier poisons much wider area of the nickel surface than the molecular cross section. Replacement of a proton on the adsorbed SA with a hydroxy group in making a chiral center on the modifier MA accelerates the hydrogenation 4.1-fold (ligand acceleration), and it is the origin of the enantiodifferentiation. A further replacement of the hydrogen of MA with a hydroxy group enhances more the rate by 3.6 times. It is concluded that the high enantiodifferentiating ability of TA-MRNi is induced by the high ligand acceleration effects due to the chiral modifier as well as effective poisoning of nonselective hydrogenation sites. The interaction strength between the surface modifier and MAA increases in the order; SA < MA < TA. MRNi catalysts comodified with two different acids were also examined to confirm the conclusions. It was demonstrated that each adsorbed chiral modifier molecule independently takes part in the enantiospecific hydrogenation.

The authors thank Professors Yoshiharu Izumi (Osaka University, Emeritus Professor) and Akira Tai (Himeji Technical University, Emeritus Professor) for their encouragement. They also thank Professor Yuriko Nitta for her helpful comments.

References

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

2 H.-U. Blaser, *Tetrahedron: Asymmetry* **1991**, *2*, 843.

3 A. Baiker, *J. Mol. Catal. A: Chem.* **1997**, *115*, 473.

4 H.-U. Blaser, H.-P. Jalett, M. Müller, M. Studer, *Catal. Today* **1997**, *37*, 441.

5 T. Mallat, E. Orglmeister, A. Baiker, *Chem. Rev.* **2007**, *107*, 4863.

6 F. Zaera, *J. Phys. Chem. C* **2008**, *112*, 16196.

7 G. Kyriakou, S. K. Beaumont, R. M. Lambert, *Langmuir* **2011**, *27*, 9687.

8 Y. Izumi, *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 871.

9 A. Tai, T. Harada, in *Tailored Metal Catalysis* in *Catalysis by Metal Complexes*, ed. by Y. Iwasawa, Springer, Dordrecht, **1986**, Vol. 7, pp. 265–324. doi:10.1007/978-94-009-5261-4_5.

10 T. Osawa, T. Harada, A. Tai, *Catal. Today* **1997**, *37*, 465.

11 T. Sugimura, *Catal. Surv. Jpn.* **1999**, *3*, 37.

12 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, Weinheim, **2000**, pp. 173–209. doi:10.1002/9783527613144.ch08.

13 T. Osawa, T. Harada, O. Takayasu, *Top. Catal.* **2000**, *13*, 155.

14 T. Osawa, T. Harada, O. Takayasu, *Curr. Org. Chem.* **2006**, *10*, 1513.

15 T. Osawa, I.-Y. S. Lee, S. Ikeda, T. Kitamura, Y. Inoue, V. Borovkov, *Appl. Catal., A* **2012**, *445–446*, 269.

16 S. Nakagawa, T. Sugimura, A. Tai, *Chem. Lett.* **1997**, 859.

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

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

19 T. Osawa, Y. Hayashi, A. Ozawa, T. Harada, O. Takayasu, *J. Mol. Catal. A: Chem.* **2001**, *169*, 289.

20 V. Humblot, S. Haq, C. Muryn, W. A. Hofer, R. Raval, *J. Am. Chem. Soc.* **2002**, *124*, 503.

21 T. E. Jones, A. E. Rekatas, C. J. Baddeley, *J. Phys. Chem. C* **2007**, *111*, 5500.

22 T. E. Jones, C. J. Baddeley, *J. Phys. Chem. C* **2007**, *111*, 17558.

23 A. G. Trant, C. J. Baddeley, *J. Phys. Chem. C* **2011**, *115*, 1025.

24 T. E. Jones, C. J. Baddeley, *Surf. Sci.* **2002**, *519*, 237.

25 T. E. Jones, C. J. Baddeley, *Surf. Sci.* **2002**, *513*, 453.

26 T. Harada, Y. Hiraki, Y. Izumi, J. Muraoka, H. Ozaki, A. Tai, Proc. 6th Int. Congr. Catal., London, **1976**, pp. 1024–1033.

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

28 Y. Nitta, S. Imanaka, S. Teranishi, *J. Catal.* **1983**, *80*, 31.

29 I. Yasumori, M. Yokozeki, Y. Inoue, *Faraday Discuss. Chem. Soc.* **1981**, *72*, 385.

30 T. Osawa, M. Kitano, T. Harada, O. Takayasu, *Catal. Lett.* **2009**, *128*, 413.

31 M. A. Keane, G. Webb, *J. Catal.* **1992**, *136*, 1.

32 M. A. Keane, *Catal. Lett.* **1993**, *19*, 197.

33 M. A. Keane, *Can. J. Chem.* **1994**, *72*, 372.

34 A. Tai, T. Harada, Y. Hiraki, S. Murakami, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1414.

35 Y. Okamoto, Y. Nitta, T. Imanaka, S. Teranishi, *J. Chem. Soc., Faraday Trans. 1* **1980**, *76*, 998.

36 V. Humblot, M. O. Lorenzo, C. J. Baddeley, S. Haq, R. Raval, *J. Am. Chem. Soc.* **2004**, *126*, 6460.

37 M. O. Lorenzo, V. Humblot, P. Murray, C. J. Baddeley, S. Haq, R. Raval, *J. Catal.* **2002**, *205*, 123.

38 C. Roth, D. Passerone, L. Merz, M. Parschau, K.-H. Ernst, *J. Phys. Chem. C* **2011**, *115*, 1240.

39 M. A. Keane, *Langmuir* **1997**, *13*, 41.

40 H. Ogawa, T. Mameda, T. Misaki, Y. Okamoto, T. Sugimura, *Chem. Lett.* **2013**, *42*, 813.

41 T. Mameda, K. Nakai, T. Misaki, Y. Okamoto, T. Sugimura, *Catal. Today*, in press. doi:10.1016/j.cattod.2014.03.075.

42 T. Harada, M. Yamamoto, S. Onaka, M. Imaida, H. Ozaki, A. Tai, Y. Izumi, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2323.

43 T. Sugimura, T. Osawa, S. Nakagawa, T. Harada, A. Tai, *Stud. Surf. Sci. Catal.* **1996**, *101*, 231.