

## MECHANISM OF ENANTIOFACE DIFFERENTIATING HYDROGENATION ON MODIFIED NICKEL SURFACES

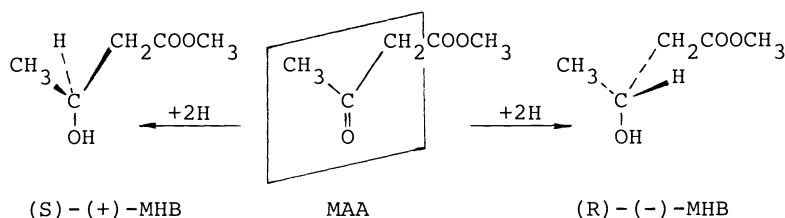
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**Abstract** - Recent studies on the mechanism of enantioface differentiation are described for the hydrogenation of methyl acetoacetate (MAA) over nickel surfaces modified with optically active molecules. Detailed investigations of the reaction using MAA vapor and tartaric acid as a modifier prove that the differentiation is controlled by the oriented adsorption of MAA which is caused by the attractive interaction between MAA and the modifier molecules. The influence of the conditions of reaction and the added poisons on the asymmetric yield is discussed on the basis of the proposed mechanism.

### INTRODUCTION

The enantioface differentiating activity of nickel catalyst, when the surface is modified with optically active molecules such as hydroxy acids or amino acids, was discovered by Izumi and his collaborators for the asymmetric hydrogenation of methyl acetoacetate (MAA) to give methyl 3-hydroxybutyrate (MHB) (Ref. 1).



After this pioneering work in 1963, the subject has been extensively studied to accumulate information about the catalytic properties of the modified surfaces, and some empirical rules on the functions of the modifiers have been derived from the results (Ref. 2). The precise pathway of the reaction and the mechanism of this enantioselective control, however, have not been verified yet though several models of the modified surface have been proposed to interpret the activity. Such functions of the modifiers or, in general, preadsorbed species as surface templates have become an important subject of recent research in heterogeneous catalysis, since the development of analytical technique has enabled us to reveal the structures of catalyst surfaces and the states of adsorbed species (Ref. 3 & 4).

The purpose of this paper is to show new approaches to revealing the mechanism of enantioface differentiating hydrogenation and to point out the problems to be solved before the complete understanding and control of this fine catalysis can be obtained.

### MECHANISM OF THE HYDROGENATION OF METHYL ACETOACETATE IN VAPOR PHASE

The hydrogenation has been studied conventionally by using the reactant, MAA, in the liquid phase with suspended catalyst under hydrogen of high pressure such as  $10^7$  Pa. These reaction conditions are not convenient for the

physicochemical analysis of the mechanism. Accordingly, the mixture of MAA vapor and hydrogen was used as the reactant and a nickel powder catalyst was chosen instead of Raney nickel in order to reduce the complexities of the reaction conditions (Ref. 5).

#### Adsorbed states of reactants

The nickel powder catalyst was prepared by decomposing nickel formate at 573 K and was reduced with hydrogen of  $2.7 \times 10^3$  Pa at the same temperature for 3 h.

The surface area of the catalyst was estimated at  $17.3 \text{ m}^2 \text{ g}^{-1}$  by means of BET method using nitrogen at 77 K. The catalyst was modified by immersing it into an aqueous solution of D<sub>5</sub>-tartaric acid (TA) of which pH was varied from 2.0 to 7.0. After the modification, the surface area decreased to  $16.6 \text{ m}^2 \text{ g}^{-1}$  and the maximum number of adsorbed acid molecules was 30% of that of surface nickel atoms.

The adsorption of hydrogen was studied in a pressure range of  $1 \times 10^2$ –  $3 \times 10^3$  Pa at 300 K. The obtained isotherm fitted with the Langmuir equation for dissociative adsorption and the monolayer capacity was estimated at  $2 \times 10^{18}$  molecule  $\text{m}^{-2}$ . The capacity was not much altered in the case of the modified surface. The state of MAA adsorbed on nickel dispersed on silica at 5 wt. % was investigated at 300 K by infrared spectroscopy. The observed strong bands at 3450, 1600 and  $1530 \text{ cm}^{-1}$  were assigned to O-H, C=O and C=O or C=C stretching vibrational frequencies respectively and these results indicate that the adsorbed MAA molecule takes partly an enol form.

#### Kinetics of the reaction

The kinetics of the reaction was studied by use of an apparatus consisting of an MAA evaporator, a reaction cell containing the catalyst and a trap cooled at 77 K in order to collect product, MHB, and unreacted MAA. Hydrogen of  $1 \times 10^4$ –  $5 \times 10^4$  Pa bubbled up through the evaporator to carry MAA vapor of 25– 150 Pa, passed on the catalyst heated at 310– 373 K, entered the trap and then circulated again. The reaction was followed by the decrease in the hydrogen pressure. The asymmetric yield of the product was evaluated from the concentration of the product and the angle of rotation measured with a Zeiss polarimeter. The results of the kinetic studies are summarized in Table 1.

TABLE 1. Kinetic parameters for the hydrogenation of MAA and MDA on nickel catalyst at 323 K

Catalyst	Unmodified	Modified with			
		Aqueous solution of TA (pH=5.0)		Alcoholic solution of TA	
Reactant	MAA	MAA	MDA <sup>a</sup>	MAA <sup>b</sup>	MAA
Number of adsorbed TA <sub>2</sub> (molecule $\text{m}^{-2}$ )	0		$3.0 \times 10^{18}$		$6.0 \times 10^{17}$
Activation energy <sub>-1</sub> (kJ mol <sup>-1</sup> )	44.3±2.5	43.9±2.0	26.9±2.0	44.0±2.0	43.1±2.0
MAA or MDA order	1.0±0.1	0.8±0.1	1.1±0.1	0.2–0.3	1.1±0.1
Hydrogen order	0.0±0.1	0.0±0.1	0.1±0.1	1.0±0.1	0.0±0.1
Asymmetric yield (%)	0	17.8±1.0	0.3±1.0	36.7±1.0	2.8±1.0

a: MDA represents methyl 2,2-dimethylacetoacetate.

b: The liquid phase or methanolic solution of MAA.

The orders of the reaction with respect to MAA vapor and hydrogen and the

values of activation energy are respectively much the same in both cases of the modified and unmodified catalysts. However, the slight decrease in the MAA order for the modified catalyst suggests that MAA is adsorbed more strongly on the modified surface than on the unmodified one.

The results of the reaction of MAA with gaseous deuterium and the hydrogen exchange reaction between the product, MHB, and deuterium molecules showed that the addition of deuterium to the carbonyl group at 3-position of MAA was accompanied by the replacement of hydrogen atoms in the methylene group at 2-position of MAA by deuterium, while those atoms in the methylene group of MHB were not exchanged with deuterium.

By using catalysts modified with TA under various conditions, it was found that the observed asymmetric yield was proportional to the amount of adsorbed TA in the form of divalent tartrate anion.

#### Interaction between adsorbed MAA and TA on the catalyst surface

In order to obtain information about the interaction between MAA and TA on the surface, the thermal desorption technique was applied to the catalysts which adsorbed MAA. For this study, an apparatus consisting of an adsorption cell, a pressure gauge and a mass spectrometer was used and was evacuated continuously so that the partial pressure of desorbed molecules on heating was proportional to the rate of desorption. MAA vapor was introduced into the cell containing the catalyst in a pressure range of 25- 150 Pa at 297 K and the cell was cooled to 273 K and was evacuated for 0.3 h. The saturated amount of adsorbed MAA was estimated at  $2.4 \times 10^{18}$  molecule  $m^{-2}$ . The heating rate was  $0.21 K s^{-1}$ . Figure 1 shows the desorption spectra of MAA. No desorbed molecules were observed up to 373 K on the modified surface without adsorbed MAA.

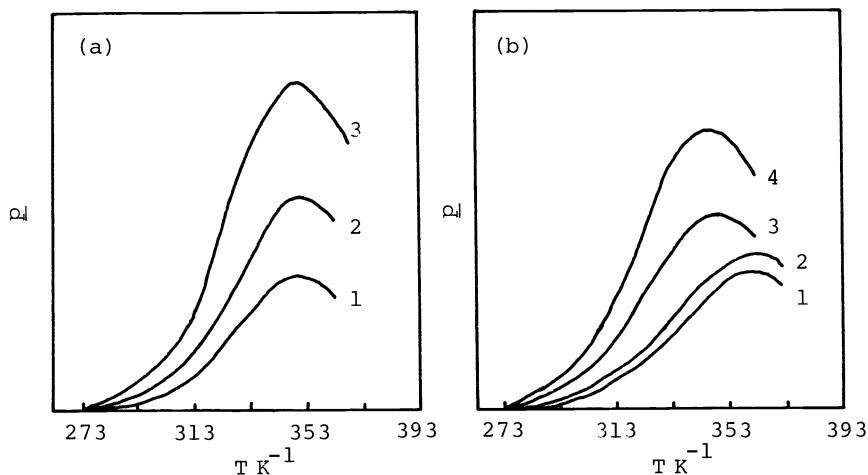


Fig. 1. Thermal desorption spectra of methyl acetoacetate. The plots of the partial pressure,  $p$ , versus the catalyst temperature,  $T$ . (a) Unmodified catalyst. The temperature at the peak maximum,  $T_m = 349 \pm 1$  K. (b) Modified catalyst.  $T_m = 364 \pm 1$  K (Curves 1 and 2),  $T_m = 348 \pm 1$  K (Curves 3 and 4).

In the case of the unmodified catalyst, the temperature at the peak maximum did not shift irrespective of the adsorbed amount of MAA in the range of  $1.2$ - $3.8 \times 10^{17}$  molecule  $m^{-2}$ . This finding shows that the desorption is a first order process, that is, the adsorbed species is in a molecular form. The results of mass spectroscopic analysis support this view by indicating that the desorbed molecule is only MAA. In the case of the modified catalyst, however, the position of peak maximum was shifted to higher temperature by 16 K and did not change until the adsorbed amount increased to  $1.7 \times 10^{17}$  molecule  $m^{-2}$ . This shift shows that the adsorbed MAA is stabilized to some extent by TA coordinated on the surface. For the amount of adsorption above this

value, the position of peak maximum became the same as that for the unmodified catalyst. In both regions, the desorption was of first order. By assuming the frequency factor of desorption rate constant to be  $1 \times 10^{13} \text{ s}^{-1}$ , this shift was found to be equivalent to an increase in the heat of adsorption by  $4 \text{ kJ mol}^{-1}$ .

#### Electronic state of the catalyst surface

The electronic states of the catalyst surfaces were examined by X-ray photoelectron spectroscopy. The spectra were measured with a Hewlett-Packard 5950A spectrometer and the observed values of binding energies were calibrated with those of  $4f_{5/2}$  and  $4f_{7/2}$  peaks of gold taken as standard. Figure 2 illustrates the  $2p_{3/2}$  spectra of nickel for various catalyst surfaces.

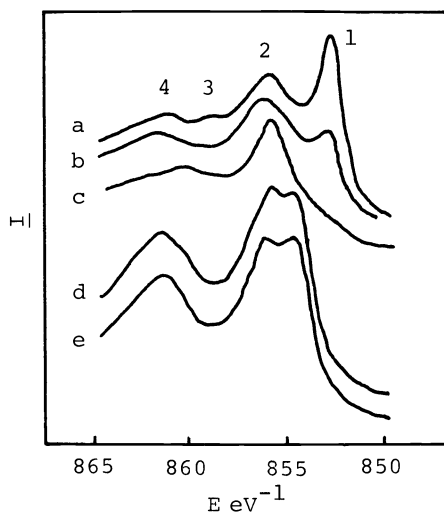


Fig. 2. X-ray photoelectron spectra of nickel  $2p_{3/2}$ . The plots of the intensity,  $I$ , versus the binding energy,  $E_{3/2}$ . (a) Modified nickel, (b) Unmodified nickel, (c) Nickel tartrate, (d) Nickel oxide modified with TA, (e) Nickel oxide.

The spectrum (a) for the modified surface exhibits a characteristic peak 1 at  $852.7 \text{ eV}$  which is close to that for a sputtered nickel film,  $852.5 \text{ eV}$  (Ref. 6). Peaks 2 and 4 in the spectrum correspond to those in the spectrum of dinickel trioxide and peak 3 at  $858.5 \text{ eV}$  is the same as the satellite peak appearing in that of the nickel film. None of the nickel surfaces covered with adsorbed oxygen and oxides such as dinickel trioxide and nickel oxide gave rise to any peak near the positions of peaks 1 and 3. When the modified surface was exposed to air, the intensity of peak 1 remained almost unchanged. A new peak of higher binding energy appeared at  $853.1 \text{ eV}$  in the spectrum of a fresh unmodified surface (b) and was attributed to the presence of adsorbed oxygen. This peak vanished quickly in open air because of the formation of oxide layer.

In the spectra of nickel tartrate (c) and nickel oxide coated with TA (d), peak 1 did not appear. The valence band spectrum of the modified surface was also examined. Two peak maxima were observed at the binding energies of  $1.1$  and  $3.2 \text{ eV}$  below Fermi level. The former peak corresponds to the emission from the characteristic d-band of metallic nickel and the latter is like that from the d-band of nickel oxide and was also observed in the spectrum of unmodified nickel surface exposed to air. Therefore, it is apparent that the modified surface is protected from oxidation to some extent by the presence of the modifier (Ref. 7).

#### Reaction scheme of the hydrogenation

By taking the adsorbed states of MAA and hydrogen as described above into consideration, a reaction scheme of the hydrogenation is proposed as shown in Fig. 3. Since deuterium atoms on the surface cannot replace the hydrogen atoms in the methylene group at 2-position of MHB, it is easily concluded that step 2 is rate controlling. Accordingly, it is possible to derive a rate

equation which agrees with the observed one, on the assumption that the strong dissociative adsorption of hydrogen is not competitive with the weak adsorption of MAA on the catalyst surface. This scheme also predicts that the enantioface differentiating step lies prior to step (2).

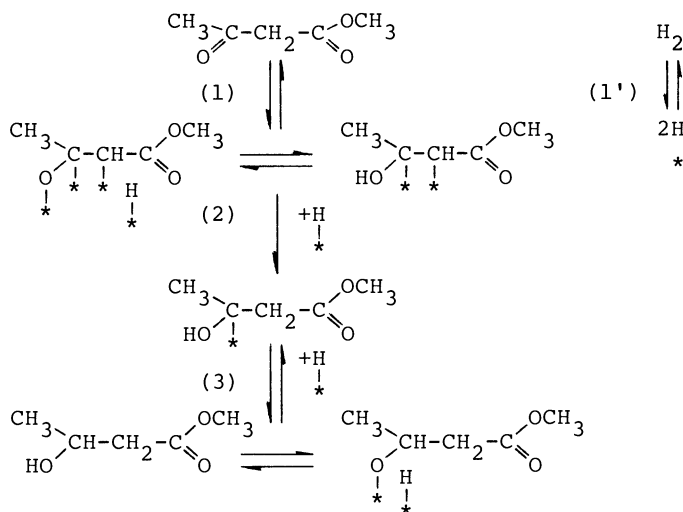


Fig. 3. Reaction scheme of the hydrogenation of MAA.

#### Mechanism of enantioface differentiation

The results of the above-mentioned studies lead to the conclusions that the enantioface differentiation occurs at the step of the oriented adsorption of MAA before the addition of hydrogen and that the attractive interaction such as hydrogen bond between MAA and the divalent tartrate anion is responsible for this orientation control. Subsequently, it seems reasonable to assume a model of the interaction as shown in Fig. 4. This model conforms with the

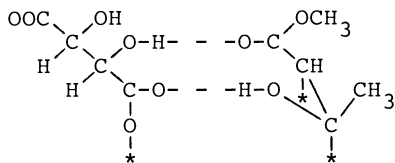


Fig. 4. Configuration for the enantioselective control.

observed trend of asymmetric hydrogenation: thus formed, two hydrogen bonds fix the orientation of adsorbed MAA molecule uniquely with the result that the surface hydrogen atoms are added to the carbon atoms of MAA to give the product having correct optical activity, (R)-(-)-MHB. Alternative orientations of the modifier lead to the results contradicted to the observed one: if the tartrate anion adsorbed with both the carboxyl groups, the adsorbed MAA molecule would give an oppositely asymmetric product by the interaction with the modifier. Similarly, when the catalyst surface is modified with  $L_5^-$  tartaric acid instead of  $D_5^-$  isomer, a large steric hindrance by the remaining part of the anion may occur on the surface in order to obtain the product molecule having the observed optical activity.

As is shown above, the oriented adsorption of MAA should take an enol form on the surface. Therefore, the enantioface differentiation is not expected for the hydrogenation of 2,2-dimethyl derivative of MAA (MDA) which can hardly take the form. In fact, the hydrogenation of this compound gave a negligibly small asymmetric yield as shown in Table 1. The activation energy is lower than that for the hydrogenation of MAA and the hydrogen exchange of the product with gaseous deuterium occurs only at the hydroxyl hydrogen of the molecule. Accordingly, the reaction path of this hydrogenation is different

from that of MAA and the addition of hydrogen to the carbon atom at 3-position of adsorbed MDA is the rate determining process.

A recent electron diffraction study of amino acids adsorbed on a nickel (100) surface has shown that L-glutamic acid molecule is adsorbed on the surface with a carboxyl oxygen atom close to the amino group, leaving the other carboxyl group far from the surface. The carboxyl oxygen and the amino nitrogen atoms near the surface are used to form two hydrogen bonds with the neighboring molecules and to fix the orientation of the acid molecule (Ref. 8). This configuration of glutamic acid is similar to that of tartaric acid assumed in the present study and gives a support on the proposed mechanism of the enantioface differentiation.

Several other models have been proposed to interpret the mechanism of the asymmetric hydrogenation by the modified catalysts. One of these models assumes that the incompletely reduced nickel surface is effective for the activity by forming the pairs of nickel cations coordinated properly with the TA modifier, the reactant MAA and hydrogen atoms (Ref. 9). The validity of this model was examined by using a nickel oxide catalyst modified with TA and a nickel catalyst covered with nickel tartrate. It was found that the rates of hydrogenation by these catalysts were quite low and the asymmetric yields were also negligible. In addition, this model includes the difficulty that the pair of nickel cations must be removed from the surface to bring the reactant and the modifier molecules in their proper positions of coordination.

Another model is based on the infrared spectroscopic studies of adsorbed reactant and modifier molecules (Ref. 10). The adsorbed MAA molecule is assumed to coordinate to a surface nickel atom with two carbonyl oxygen atoms making a six-membered ring such as that of coordinated acetylacetonate. Alpha-amino acid molecule is supposed to form a five-membered ring consisting of a carbonyl group, the carbon atom at 2-position, the amino nitrogen atom and a surface nickel atom, while hydroxy acid molecules form surface carboxylates. Since both MAA and the modifier molecules stand side by side on the surface, the preferred orientation of MAA for the enantioface differentiation is one of four possible configurations. This orientation may be brought about by forming a hydrogen bond between the hydroxyl group of the adsorbed hydroxy acid and the methoxy oxygen of MAA or by the steric hindrance occurring between the methyl group of MAA and the bulky substituted group attached to the carbon atom at 2-position of the coordinated amino acid. This model is similar to the present one in some points such as the assumption of hydrogen bond formation. However, the adsorbed hydrogen atoms in this model must be added to the carbon atoms of MAA at 2- and 3-positions, therefore, far from the nickel surface. It is necessary to assume the presence of the vertical hydrogen spill-over in order to avoid this difficulty and the validity of this assumption will be the subject of further investigation.

#### EFFECT OF POISONING ON THE ASYMMETRIC YIELD

According to the proposed model of the modified surface, the hydrogenation of MAA takes place simultaneously on the sites controlled by the modifier and on the uncontrolled sites which are distant from those of adsorbed modifiers. Therefore, it will be possible to improve the asymmetric yield, if the uncontrolled sites are selectively poisoned, while the controlled sites are protected by the preadsorbed reactant or product molecules from poisoning.

The choice of the poison suitable for the purpose depends on the adsorption strength of the poison relative to that of the reactant or product molecule. The results of trials using various kinds of poisons are shown in Fig. 5. Though all of the used poisons decreased the hydrogenation activity linearly with increasing adsorption, the poisoning by amines was effective for the purpose and butylamine exhibited the most excellent effect of increasing the yield. The detailed analysis of the obtained curves shows, however, that such a simple idea of preferential poisoning as described above cannot explain the initial high increase in the yield. Some additional roles of the poisons should be taken into consideration. Recently, it was found that the introduction of amine ligand to bis(acetylacetonato)palladium(II) complex turned over the orientation of one of the acetylacetonate ligands by breaking the chelate bonds between oxygen atoms and the metal cation and by forming the carbon-metal bond (Ref. 11). As is already shown, the oriented adsorption of MAA with the carbon atom at 2-position is important to the enantioface differentiation and therefore this fact is encouraging in order to understand the functions of the poisons.

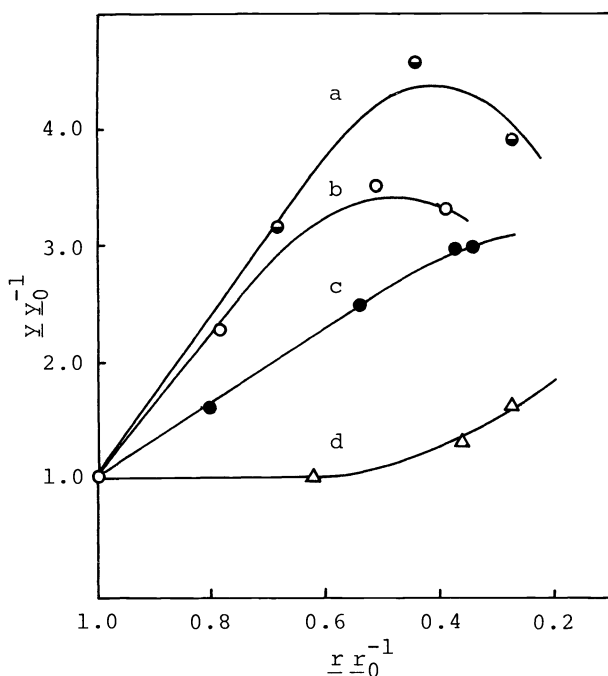


Fig. 5. The effect of poisoning on the asymmetric yield. The plots of the relative yield,  $\underline{y} \underline{y}_0^{-1}$ , versus the relative rate of hydrogenation,  $\underline{r} \underline{r}_0^{-1}$ .  $\underline{r}_0$  and  $\underline{y}_0$  represent the rate of hydrogenation and the asymmetric yield for the unpoisoned catalyst modified with TA respectively. Reaction temperature,  $T = 353$  K and  $\underline{y}_0 = 11\%$ . (a) Butylamine, (b) Triethylamine, (c) Ammonia, (d) Pyridine.

#### FEATURE OF THE REACTION IN LIQUID PHASE

It is pointed out that the feature of the reaction in liquid phase is quite different from that in vapor phase. The obtained kinetic parameters listed in Table 1 show evidently that the catalyst surface is almost saturated with MAA but scarcely covered with adsorbed hydrogen because of the virtual high concentration of MAA and the poor solubility of hydrogen in the liquid phase. The asymmetric yields in the liquid phase reactions are generally higher than those in the vapor phase ones and the yield increases to 50% as the pressure of hydrogen is raised from  $1 \times 10^5$  to  $2 \times 10^6$  Pa in the case of reaction using the modified catalyst with TA. The decrease in the activation volume due to the attractive interaction between the modifier and MAA molecules may partly contribute to the positive pressure dependence of the asymmetric yield. It seems that the rearrangements in the positions and orientations of the modifier and reactant molecules on the surface are more important in this situation of the reaction.

The temperature dependence of the asymmetric yield in the liquid phase reaction is also remarkable: in the case of the modified catalyst with TA, the yield shows a maximum at 333 K, while the yields change their signs with increasing temperature for the catalysts modified with optically active amino acids (Ref. 12). These findings may reflect the variety of interactions between the modifiers and the adsorbed MAA: as temperature increases, MAA molecules on the surface modified with TA will be agitated to take easily the suitable orientation for the enantioface differentiation, but this preferred orientation will be disturbed at higher temperature. The modified surfaces with amino acids may give two different orientations of adsorbed MAA which lead to the respective products having opposite optical activities and the fractions of molecules in these states will be relatively changed with increasing temperature. It was found that the asymmetric yield in the liquid phase reaction depends on the extent of conversion and the procedures of development and modification of Raney nickel as the catalyst (Ref. 13 and 14).

It will be noted that the asymmetric yield of 20- 30 % observed on the hydrogenation of methyl 2,2-dimethylacetoacetate (MDA) in liquid phase presents a striking contrast to the case of vapor phase reaction using the same catalyst modified with TA (Ref. 15). This finding also suggests that the orientation of reactant molecule on the surface is different from that in the vapor phase reaction.

Aside from these studies on the mechanism, there have been several attempts to improve the asymmetric yield of the reaction by the use of liquid reactant suspending the catalyst modified with D<sub>s</sub>-tartaric acid. The products of more than 85 % excess in (R)-isomer of MHB have been obtained by using nickel powder catalyst prepared from nickel oxide instead of Raney nickel (Ref. 16) and a nickel- 1wt.% palladium mixed catalyst dispersed on kieselguhr (Ref. 17). A recent study has proved that the latter catalyst is the most effective one for the enantioface differentiating hydrogenation of MAA dissolved in a liquid mixture of tetrahydrofuran and organic acids (Ref. 18).

#### CONCLUDING REMARKS

The present situation of research in the mechanism of enantioface differentiating hydrogenation on nickel surface modified with optically active molecules has been briefly outlined. It is expected that research concerning the mechanism of the catalysis for the reaction in vapor phase will be extended to examine the microscopic structures of catalyst surfaces where the suitably oriented adsorption of reactant and modifier molecules occurs. As for the liquid phase reaction, the analysis of the mechanism is rather in a primitive stage of investigating the kinetic behavior of adsorbed reactants which may be strongly influenced by the reactant and solvent molecules in bulk phase. Since the simple analogy of the vapor phase reaction is not valid for this case, new techniques must be developed in order to get insight into the complicated nature of liquid phase reaction under high pressure. Thus obtained understanding on the mechanism of this catalysis will surely provide a good approach to simulating the functions of enzyme.

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