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The Asymmetric (Enantioface Differentiating) Hydrogenation of the C=O Double Bond with Modified Raney Nickel. XXIX.

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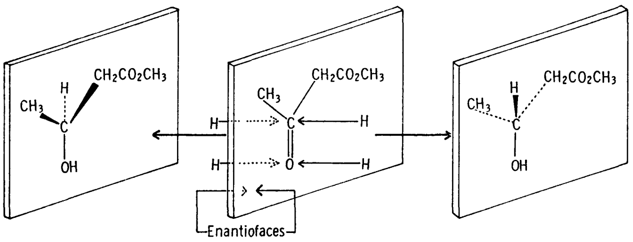
In the asymmetric (enantioface differentiating) hydrogenation of methyl acetoacetate with modified Raney nickel catalysts, the effects of the modifying pH on the amounts of the modifying reagents adsorbed and the enantioface differentiating abilities of the catalysts were studied using glycolic acid, mandelic acid, and 2-hydroxy-3-phenylpropionic acid as the modifying reagents. The results indicate that the modifying pH governs the adsorption mode of the modifying reagent. Thus, the change in the adsorption mode of the modifying reagent with the change in the modifying pH results in changes in the amount of the modifying reagent adsorbed and in the enantioface differentiating ability of the catalyst.

The asymmetric hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate has been previously studied by our research group[1,2] in the presence of Raney nickel catalysts modified with optically active 2-amino or 2-hydroxy acid (modifying reagent). This reaction can be classified as an enantioface differentiating reaction,[2,3] because in this reaction process the catalyst differentiates between the two sides of the enantiotopic plane (the enantiofaces) of methyl acetoacetate. The enantioface differentiating hydrogenation of methyl acetoacetate is shown in Fig. 1. In the course of our studies, it was found that the enantioface differentiating ability of the catalyst[4] and the amount of the modifying reagent adsorbed on the catalyst were both strongly affected by the pH of the aqueous solution of the modifying reagent (the modifying pH.)[5,6] In order to understand the change in the enantioface differentiating ability of the catalyst with the change in the modifying pH, it is essential to clarify the relationship between the enantioface differentiating ability of the catalyst and the amounts of the modifying reagent adsorbed at various modifying pH values.



(*S*)-Isomer Methyl acetoacetate (*R*)-Isomer

Fig. 1. Enantioface differentiating hydrogenation of methyl acetoacetate.

In the present work, the effects of the modifying pH on the amount of the modifying reagent adsorbed and on the enantioface differentiating ability of the catalyst were investigated by means of catalysts modified with 2-monohydroxy monocarboxylic acids, such as glycolic acid, mandelic acid, and 2-hydroxy-3-phenylpropionic acid.

Results and Discussion

The modified Raney nickel catalysts were prepared with glycolic acid, DL-mandelic acid, and L-2-hydroxy-3-phenylpropionic acid at various modifying pH values.

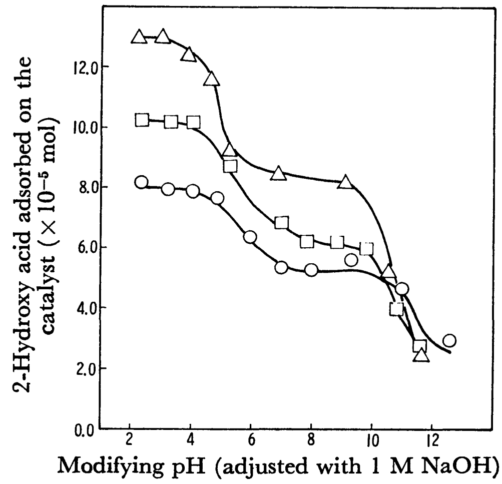


Fig. 2. Effects of the modifying pH on the amounts of the modifying reagents adsorbed.

△: glycolic acid

○: DL-mandelic acid

□: L-2-hydroxy-3-phenylpropionic acid

An amount of 1.5 g of Raney alloy (Ni: Al=42: 58) was used for each preparation of the catalyst.

Modifying solution: 100 ml of a 1% aqueous solution of the modifying reagent.

Plots of the amounts of the modifying reagent adsorbed against the modifying pH are shown in Fig. 2.

The amount of the modifying reagent (RCH(OH)-COOH) adsorbed at each modifying pH depends on the nature of the R group. However, on modification with these compounds, the changes in the amounts show a similar figure with the change in the midifying pH, regardless of the drastic changes in the R groups (*i.e.* H to phenyl). That is, the amounts of these compounds adsorbed are constant below pH 4 and at pH 6(7)—9, while they vary steeply at pH 4—6(7) and above pH 9. These observations indicate that the curve can be divided into four segments; that is, below pH 4(A), pH 4—6(7)(B), pH 6(7)—9(C), and above pH 9(D).

The enantioface differentiating abilities of the catslysts modified with L-2-hydroxy-3-phenylpropionic acid and L-mandelic acid were studied at various modifying pH values; the results are shown in Fig. 3. The enantioface differentiating abilities of the catalysts and the amounts of the modifying reagents adsorbed change in a fashion similar to each other with the change in the modifying

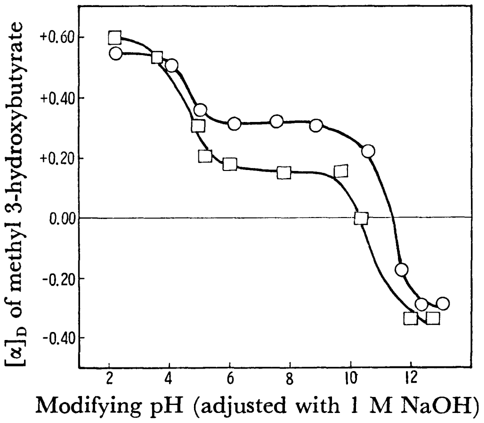


Fig. 3. Effects of the modifying pH on the enantioface differentiating abilities of the catalysts.

○: L-mandelic acid[a)]

□: L-2-hydroxy-3-phenylpropionic acid[b)]

a) The hydrogenation of 3.5 ml of methyl acetoacetate was carried out with the catalyst prepared from 0.3 g of Raney alloy (Ni: Al=42: 58).

b) The hydrogenation of 17.5 ml of methyl acetoacetate was carried out with the catalyst prepared from 1.5 g of the alloy.

pH. That is, the ability of the catalyst does not change in A and C, but does change drastically in B and D. However, the ratio of the enentioface differentiating ability in A to that in C is dependent on the nature of the R group, while the ratio of the amount of the modifying reagent adsorbed in A to that in C is independent of the nature of the R group, as is shown in Tables 1 and 2. From the data in Tables 1 and 2, it is clear that the ratio of the enantioface differentiating ability of the catalyst in A to that in C cannot be interpreted simply on the basis of the amount of the modifying reagent adsorbed. However, the similarity between the modifying pH dependence of the amount of the modifying reagent adsorbed and that of the enantioface differentiating ability of the catalyst suggests that there are some common factors which control both of them. The present author introduces the term of the adsorption mode to account for these common factors. Thus, the modifying pH governs the adsorption mode of the modifying reagent; the change in the adsorption mode results in the change in the amount of the modifying reagent adsorbed and that in the enentioface differentiating ability of the catalyst. The adsorption mode is determined by the adsorption species and the conditions of the catalyst surface.

Furthermore, on modifications with L-2-hydroxy-3-phenylpropionic acid and L-mandelic acid the direction of the optical rotation ($[\alpha]_D$) of the hydrogenation product is (−) above pH 12, while it is (+) below pH 10. These findings also support the dependence of the adsorption mode on the modifying pH.

The modifying pH dependence of the enentioface differentiating abilities observed with the catalysts modified with other 2-monohydroxy monocarboxylic acids can be explained in the same way, since our research group has obtained similar results with L-3,3-dimethyl-2-hydroxybutyric acid[7)] and L-2-hydroxy-3-methylbutyric acid.

Studies of the absorption modes of the modifying reagent in A, B, C, and D are in progress and will be reported soon.

Experimental

The preparation of the modified Raney nickel catalyst, the hydrogenation of methyl acetoacetate, and the measurement of the enantioface differentiating ability of the catalyst were carried out by the procedures described in the previous paper.[8)]

The modification of the catalyst was carried out at 0 °C for 90 min. During the modification, the mixture of the modifying solution and the catalyst was shaken every 15 min. After the midification, the catalyst was washed once with 10 ml of deionized water and then with three 50 ml portions of methanol.

Elution of the Modifying Reagent from the Catalyst Surface. A mixture of the modified Raney nickel and 10 ml of M sodium hydroxide was allowed to stand for 2 hr at 100 °C in a 50 ml, round-bottomed flask fitted with a condenser. The catalyst was removed by filtration and washed with deionized water. The filtrate and the washings were then combined and diluted accurately to 50 ml with deionized water. This solution was used for the determination of the modifying reagent adsorbed on the catalyst.

The Determination of L-2-Hydroxy-3-phenylpropionic Acid and

TABLE 1. THE AMOUNTS OF THE MODIFYING REAGENTS ADSORBED ON THE CATALYSTS IN A AND C[a)]

Modifying Reagent	A_a[b)] (midifying pH)	C_a[b)] (modifying pH)	C_a/A_a
Glycolic acid	14 $\times 10^{-5}$ (2.2)	8.6×10^{-5} (6.9)	0.61
DL-Mandelic acid	8.2×10^{-5} (2.3)	5.3×10^{-5} (7.0)	0.64
L-2-Hydroxy-3-phenylpropionic acid	10 $\times 10^{-5}$ (2.3)	6.0×10^{-5} (7.8)	0.60

a) The catalyst was prepared from 1.5 g of Raney nickel alloy (Ni: Al=42: 58). Modifying solution: 100 ml of a 1% aqueous solution of the modifying reagent. b) A_a (C_a): the amount (expressed in mole) of the modifying reagent adsorbed on the catalyst in A(C).

TABLE 2. THE ENANTIOFACE DIFFERENTIATING ABILITIES OF THE CATALYSTS MODIFIED IN A AND C

Modifying reagent	A_e[a)] (modifying pH)	C_e[a)] (modifying pH)	C_e/A_e
L-Mandelic acid	+0.55[b)] (2.4)	+0.32[b)] (7.5)	0.58
L-2-Hydroxy-3-phenylpropionic acid	+0.60[c)] (2.3)	+0.15[c)] (7.8)	0.25

a) A_e(C_e): The enantioface differentiating ability of the catalyst modified in A(C). b) The hydrogenation of 3.5 ml of methyl acetoacetate was carried out with the catalyst prepared from 0.3 g of Raney nickel alloy (Ni: Al=42: 58). c) The hydrogenation of 17.5 ml of methyl acetoacetate was carried out with the catalyst prepared from 1.5 g of the alloy.

DL-*Mandelic Acid.* These compounds were determined by the measurement of the absorbance at 258 nm, using a reagent blank as the reference.

The Determination of Glycolic Acid. The glycolic acid was determined by the procedure of Sasakawa *et al.*, using 2,7-dihydroxynaphthalene.[9]

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