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ENANTIOFACE DIFFERENTIATING (ASYMMETRIC) HYDROGENATION OF METHYL ACETOACETATE WITH MODIFIED RANEY NICKEL

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Rate studies of the liquid phase hydrogenation of methyl acetoacetate were carried out on the Raney nickel catalyst modified with optically active substances.

The results are as follows ; 1) Both the optical yield of product and the rate of hydrogenation were controlled by the nature of modifying reagents but no direct correlation was present between them. 2) The apparent activation energy of hydrogenation was not varied with the change of modifying reagents.

The most probable rate-controlling process of hydrogenation was the surface reaction. The optical yield of product was not explained by the simple kinetic controlled differentiation. Details of differentiating process still remained equivocal.

Many distinctive features of asymmetric hydrogenations of C=O double bond with the Raney nickel modified with optically active substances have been made clear by the intensive studies based on chemical approaches.[1)]

These reactions are classified as an enantioface differentiating reaction[1,2)] because the formation of optically active product is achieved only when the catalyst possesses an ability to differentiate either face (enantioface) of the substrate. The enantioface differentiating hydrogenation of methyl acetoacetate, as a well established example, is shown in Fig. 1.

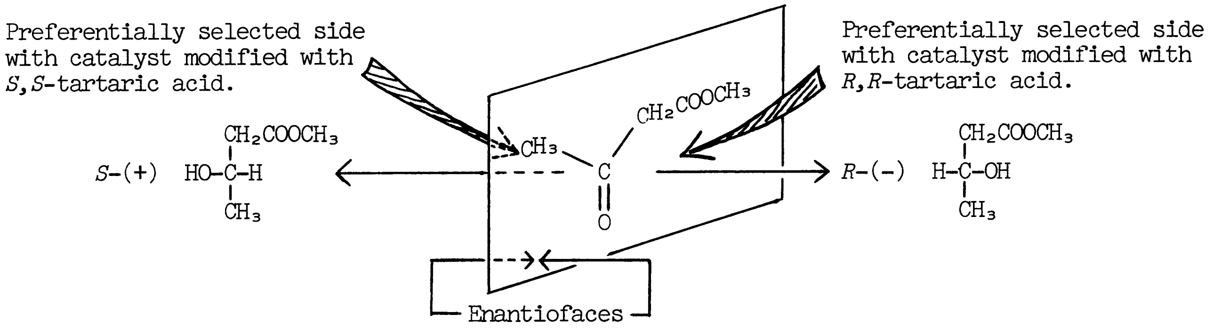

Fig. 1 Enantioface differentiating hydrogenation of methyl acetoacetate.

The present communication describes some kinetic features of the liquid phase hydrogenation of methyl acetoacetate with modified Raney nickel catalysts. Kinetic studies on the enantioface differentiating hydrogenation in gas phase have recently been undertaken by Okabe and co-worker.[3)]

To gain an insight into the mechanism of enantioface differentiating process in the reaction path, it is necessary to obtain reliable data on the relationship between activity of catalyst and optical yield of the reaction.[4] In the course of studies on hydrogenation with the catalyst originally presented by our research group,[5] it was found that while the reproducible results of the optical yield were obtained, the rates of each reaction were inconsistent. The systematic analysis of factors affecting the activity of catalyst has revealed that some modifications of the developing method of Raney nickel enabled us to prepare a favorable catalyst for the kinetic studies.[6] The values of rates and optical yields in Table 1. indicates the reproducibility of the data obtained by the hydrogenation of methyl acetoacetate with the new catalyst modified with *R,R*-tartaric acid.

With the new catalyst, several rate studies were attempted on the enantioface differentiating reaction. The rates and optical yields on the hydrogenation with the catalyst modified with *R,R*-tartaric acid and *S*-amino acids[7] are summarized in Table II.

Table I

Reproducibility of rate and optical yield of hydrogenation with new catalyst*.

No.	Rate**	Optical yield (%)
1	13.3	24.9
2	13.0	25.3
3	13.1	26.2
4	13.2	27.0

* Hydrogenation of methyl acetoacetate (0.15 mol) was carried out at 70°C under atmospheric pressure of hydrogen over 0.6g of catalyst modified with *R,R*-tartaric acid.

** Rate is expressed by hydrogen uptake in initial one hr. (mmol/hr)

Table II

Rate and optical yield of hydrogenation with modified catalyst*.

Modifying reagent	Rate**	Optical yield (%)
R,R-Tart	13.1	26.2
S-Ala	9.8	0.0
S-Val	10.2	13.3
S-Leu	10.3	4.3
S-Ileu	9.8	8.1
S-Glu	4.3	11.6
S-Orn	3.3	6.5
S-Lys	3.1	6.4

* Hydrogenation of methyl acetoacetate (0.15 mol) was carried out at 70°C under atmospheric pressure of hydrogen over 0.6g of catalyst.
** Rate is expressed by hydrogen uptake in initial one hr. (mmol/hr)

It is obvious in Table II that the rate decreases in the following order with respect to the modifying reagent; hydroxy acid > monoamino monocarboxylic acid > monoamino dicarboxylic acid > diamino monocarboxylic acid. It was found that the rate decreased with the increase of in number and electron-donating ability of substituents of the modifying reagent.

Each catalyst listed in Table II gave different optical yields as were expected from our earlier data.[8] However no correlation between the optical yield and rate was observed. The results suggested that the enantioface differentiation was independently controlled by the chiral environment which arised at the vicinity of catalyst surface by the adsorption of modifying reagent, irrespective of the nature of active area where hydrogenation of substrate undertook.

The effects of temperature upon the rate of reaction and the optical yield were investigated with three representative catalysts *i.e.* those modified with *R,R*-tartaric acid, *S*-valine, and *S*-glutamic acid. The results are listed in Table III.

The Arrhenius plots with respect to the rates of reactions gave straight lines with the same slope in each catalyst, and values for apparent activation energy were 8.5 ± 0.5 kcal/mol. The rates of reaction were expressed by 0.2 ~ 0.3th order (determined by the initial rate method) with respect to the concentration of substrate in all cases. Results described above excluded the possibility of the reaction of which rate is controlled by the diffussion of substrate or hydrogen to the active area of catalyst, and lead to the assumption that the rate of reaction was controlled by the surface reaction.

Table III

The effect of reaction temperature upon rate and optical yield of hydrogenation with modified catalyst*.

Modifying reagent	Reaction temperature	Rate**	Optical yield(%)
R,R-Tart	70°C	13.1	26.2
	50°C	6.6	37.8
	30°C	2.7	22.6
S-Val	70°C	10.2	13.3
	60°C	6.2	8.7
	40°C	2.6	2.6
S-Glu	70°C	4.3	11.6
	50°C	2.0	1.3
	30°C	0.85	0.0

* Hydrogenation of methyl acetoacetate (0.15 mol) was carried out under atmospheric pressure of hydrogen over 0.6g of catalyst.
** Rate is expressed by the hydrogen uptake in initial one hr. (mmol/hr)

The temperature dependence of optical yields was also investigated with the same catalysts as described above. As shown in Table III, there is no simple relationship between optical yields and temperatures in all cases. However, the tendency that optical yield increased with increasing the reaction temperature suggested that the entropy term takes important role in the enantio-face differentiation of substrate. The results are difficult to elucidate with a simple kinetic controlled differentiation usually claimed in literatures.[9)]

Since the supplying of substrate to the active area of catalyst is not the rate determining step, all substrates on the surface of catalyst would be placed in the chiral envilonment of modifying reagent and the enantioface of substrate (si-face or re-face) is eventually differentiated. Thus the optical yield of product would be controlled by the proportion of two differentiated enantiofaces being attacked by hydrogen.

Even though the mechanism of enantioface differentiation is hardly discussed from the observation presented in this paper, it is rather reasonable to assume that the optical yield of product is controlled by the interaction of substrate and modifying reagent prior to the rate determining addition of hydrogen. Nature of stereochemical interaction between substrate and modifying reagent in a cource of differentiation have not yet been visualized unequivocally. Work along this line is in progress.

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