NOTES

Asymmetric Hydrogenation with Modified Raney Nickel.*1 X. Effect of the β-Substituent of α-Amino Acid as a Modifying Reagent

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The asymmetric activities of Raney nickel catalysts modified with optically active α-amino acids in the hydrogenation of methyl acetoacetate have previously been reported on by the present authors.[1]

From the relation between the asymmetric activities of catalysts and the structures of the modifying reagents upon modification with α-amino acids at 0°C and at their isoelectric points, it was concluded that a catalyst modified with an α-amino acid, such as L-valine or L-isoleucine, which is replaced at the β-position by a methyl group shows a higher asymmetric activity than a catalyst modified with an α-amino acid which does not have a β-alkyl substituent.

The present paper will report on the asymmetric activities of catalysts modified with L-3-ethylnorvaline,*2 its acetyl derivative, and L-alloisoleucine. The specific rotation of the materials used in the present paper are as follows:

TABLE 1. OPTICAL ROTATIONS OF MODIFYING REAGENTS

Modifying reagent	Optical rotation, $[\alpha]_D^{20}$
L-3-Ethylnorvaline	+38° (*c* 1, 6 N HCl)
N-Acetyl-L-3-ethylnorvaline	+17° (*c* 2, EtOH)

The asymmetric activity of the catalyst was studied in the hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate, as has been described in previous papers.[2,3] In Fig. 1 the asymmetric activity of the catalyst modified with L-3-ethylnorvaline at the isoelectric point is shown as a function of the modifying temperature.

In Fig. 2 the asymmetric activities of the catalyst modified with *N*-acetyl-L-3-ethylnorvaline at 0°C and 100°C are shown. In comparison with L-3-ethylnorvaline, a decrease in the asymmetric activity of the catalyst was also found, as was also

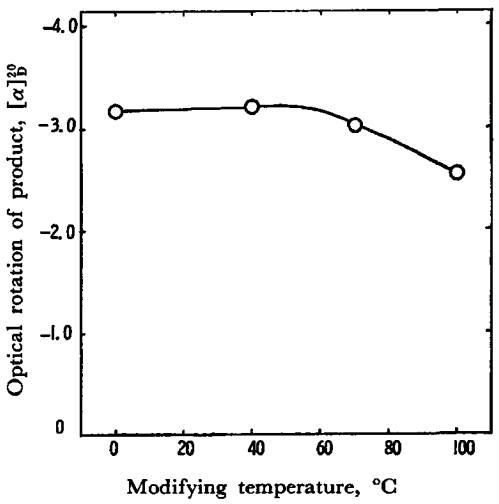

Fig. 1. Effect of modifying temperature modified with L-3-ethylnorvaline at the isoelectric point.

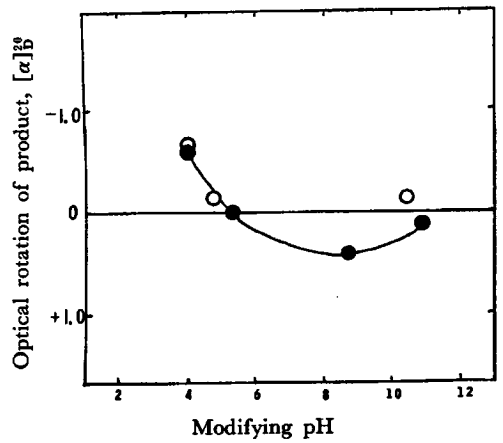

Fig. 2. Effect of modifying pH on the modifications at 0°C and 100°C with *N*-acetyl-L-3-ethylnorvaline.
● modified at 0°C, ○ modified at 100°C

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1) Y. Izumi, M. Imaida, H. Fukawa and S. Akabori, This Bulletin, **36**, 21 (1963).

*2 Details of the preparation of this material will be reported in this Bulletin in the near future.

2) Y. Izumi, M. Imaida, H. Fukawa and S. Akabori, *ibid.*, **36**, 155 (1963).

3) Y. Izumi, S. Tatsumi and M. Imaida, *ibid.*, **39**, 2223 (1966).

observed in the catalyst modified with the acetyl derivative of L-glutamic acid. On modification at 0°C, an inversion of the direction of asymmetric activity was observed at pH 5.0.

The asymmetric activities of catalysts modified with L-valine and L-aminobutyric acid at 0°C and at the isoelectric points, which were presented in the previous paper,[2] and those with L-3-ethylnorvaline and L-alloisoleucine in the present work are compared in Fig. 3. It may be seen from the figure that alloisoleucine gave a higher asymmetric a ctivity to the catalyst than did isoleucine, the diastereomer of alloisoleucine. As the threo configuration is more effective for the asymmetric activity of the catalyst than the erythro form, the (R)-configuration of the β-carbon in an L-α-amino acid increases the activity of the catalyst. The asymmetric activity of a catalyst modified with alloisoleucine is less than that of one modified with 3-ethylnorvaline, and the asymmetric activity caused by valine is intermediate between the asymmetric activities caused by *threo* and *erythro*-isoleucine.

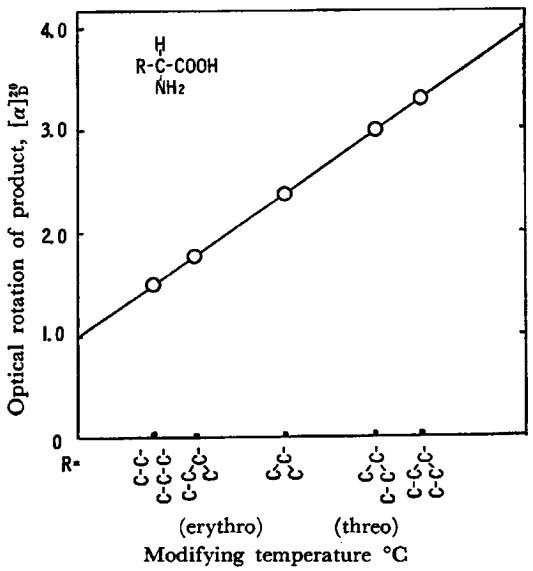
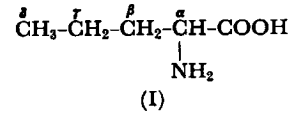
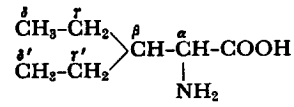


Fig. 3. Comparison of symmetric activities modified at 0°C and the isoelectric point.

As the catalysts modified with aminobutyric acid and with norvaline had the same asymmetric activity, the δ-carbon of *n*-alkyl amino acid (I) is not effective in increasing the asymmetric activity. Unlike as with *n*-alkyl amino acids, a catalyst modified with 3-ethylnorvaline has a higher asymmetric activity than one modified with valine. These facts show that the δ'-carbon of the β-side chain of β-alkyl amino acids (II) is effective in increasing the asymmetric activity.



(I)



(II)

The asymmetric activity caused by *threo*-isoleucine greatly differs from that caused by *erythro*-isoleucine. This shows that the relative conformations of the β-carbon to the α-carbon in the two isoleucines are different when they are adsorbed on the catalyst. Let us name the adsorbed conformations of an β-alkyl amino acid similar to those of the *threo*- and *erythro*-isoleucines threo- and erythro-type conformations, respectively. Valine and 3-ethylnorvaline allow at least these two types of adsorbed conformations on the catalyst, even though valine and 3-ethylnorvaline have the β-carbon, which is replaced symmetrically. Consequently, as a result of the difference between the stabilities of threo- and erythro-type conformations formed by valine or 3-ethylnorvaline, the threo- and erythro-types of the asymmetric centers may be supposed to exist in different proportions. According to the disproportion in the existent ratios of the two asymmetric centers, the observed asymmetric activity of the catalyst caused by valine or 3-ethylnorvaline can hardly be expected to show the arithmetical mean of each asymmetric activity of the two types of centers.

Because of the above reason, it is difficult to discuss the exact role of β-alkyl-substituents in the asymmetric activity of β-alkyl amino acids. A study of the asymmetric activity of a catalyst modified with 3-methylnorvaline, which may give further information on this point, will, however, be reported in this Bulletin in the near future.

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