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Asymmetric Hydrogenation of C=O Double Bond with Modified Raney Nickel. XIII.*1 Modification with Peptides

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Previous papers of this series have reported that Raney nickel catalysts (R-Ni) modified with optically-active α-amino acids or α-hydroxy acids asymmetrically catalyze the hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate. The relationship between the asymmetric hydrogenation activity of a modified R-Ni catalyst and the structure of its modifying reagent has also been studied in previous papers.[1)]

On the other hand, the silk-palladium asymmetric catalyst prepared as an enzyme model was studied prior to the modified R-Ni catalyst by one of the present authors.[2)] Investigations of R-Ni catalysts modified with peptides have a great importance in elucidating the mechanisms for the substrate specificity of the enzyme action and for the asymmetric hydrogenation of a silk-palladium catalyst. However, no modifications with peptides have been attempted. The influence of the peptide structure used as a modifying reagent on the asymmetric activity of the catalyst was studied, with focussed attention on several leucyl-peptides in the present work. In additionl the asymmetric activity of the catalyst modified with glycyl-L-aspartic acid was tested. The results of the present work are listed in Table 1.

TABLE 1. THE OPTICAL ROTATION OF THE PRODUCTS ON THE MODIFICATIONS WITH DIPEPTIDES

Modifying reagent	Modifying conditions		$[\alpha]_D^{20}$ of methyl 3-hydroxybutyrate
	pH	Temp. °C	
L-Leucine	7.32	0	−1.10*
L-Leucyl-glycine	5.72	0	+1.12
	5.80	40	+1.03
	5.75	70	+0.92
Glycyl-L-leucine	5.70	0	−0.41
	5.55	40	−0.37
	5.50	70	−0.65
L-Leucyl-L-leucine	5.85	0	−0.42
	5.70	40	−0.50
	—	70	−0.46
L-Leucyl-D-leucine	5.80	0	+1.20
	5.80	40	+0.75
	5.80	70	+0.60
L-Aspartic acid	4.65	0	−1.10[3)]
Glycyl-L-aspartic acid	—	0	−1.47
	—	100	−1.09

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

L-Leucyl-glycine (L-Leu-Gly) gives the catalyst a higher asymmetric yield*4 than glycyl-L-leucine (Gly-L-Leu) and the reverse asymmetric direction to Gly-L-Leu or L-leucine as a asymmetric modifying reagent. The asymmetric direction of the catalyst modified with Gly-L-Leu is the same as that with L-leucine, and the asymmetric yield of the former

*1 The previous title of the papers of this series, I-X, was "Asymmetric Hydrogenation with Modified Raney Nickel."

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1) H. Fukawa, Y. Izumi, S. Komatsu and S. Akabori, This Bulletin, **35**, 1703 (1962); Y. Izumi, M. Imaida, H. Fukawa and S. Akabori, *ibid.*, **36**, 21 (1963); Y. Izumi, M. Imaida, H. Fukawa and S. Akabori, *ibid.*, **36**, 155 (1963); S. Tatsumi, M. Imaida, Y. Fukuda, Y. Izumi and S. Akabori, *ibid.*, **37**, 846 (1964); Y. Izumi, S. Akabori, H. Fukawa, S. Tatsumi, M. Imaida, Y. Fukuda and S. Komatsu, Proc. of the 3rd Int. Cong. on Catalysis, Vol. 2, 1364 (1964); Y. Izumi, S. Tatsumi, M. Imaida, Y. Fukuda and S. Akabori, This Bulletin, **38**, 1206 (1965); Y. Izumi, S. Tatsumi, M. Imaida, Y. Fukuda and S. Akabori, *ibid.*, **39**, 361 (1966); Y. Izumi, S. Tatsumi and M. Imaida, *ibid.*, **39**, 2223 (1966); S. Tatsumi, *ibid.*, **41**, 409 (1968); Y. Izumi, T. Tanabe and S. Yajima, *ibid.*, **41**, 941 (1968); Y. Izumi, K. Matsunaga, S. Tatsumi and M. Imaida, *ibid.*, **41**, 2515 (1968); Y. Izumi, M. Imaida, T. Harada, T. Tanabe, S. Yajima and T. Ninomiya, *ibid.*, **42**, 241 (1969); Y. Izumi, S. Tatsumi and M. Imaida, *ibid.*, **42**, 2373 (1969).

2) S. Akabori, Y. Izumi, Y. Fujii and S. Sakurai, *Nature*, **178**, 323 (1956); S. Akabori, Y. Izumi, Y. Fujii and S. Sakurai, *Nippon Kagaku Zasshi*, **77**, 1374 (1956); **78**, 168 (1957).

*4 The "asymmetric activity" of a catalyst involves two factors. One is the direction of the asymmetric activity, which is expressed as the direction of the specific rotation, (+) or (−), of the hydrogenated product. The other is the degree of asymmetric activity, which is usually presented as the asymmetric yield.

is considerably weaker than that of the latter. It can be expected from the results that the peptide bond existing at the carboxy group of amino acid residue reverses the effect of the asymmetric center of the amino acid itself on the asymmetric direction of the catalyst, and that the peptide bond existing at the amino group of amino acid reduces the effect of the asymmetric center of amino acid on the asymmetric yield of the catalyst.

Since glycine has no asymmetric center, the deviation of the asymmetric activity of the catalyst modified with L-Leu-Gly or Gly-L-Leu from that with L-leucine is considered to occur mainly as a result of the peptide structure.

If the simple additional regulality in the structure of the peptide can be found in the asymmetric activity of the catalyst, it should be possible to calculate the asymmetric activity of the catalyst modified with L-leucyl-L-leucine (L-Leu-L-Leu) or L-leucyl-D-leucine (L-Leu-D-Leu) from those with L-Leu-Gly and Gly-L-Leu. The asymmetric activities of the catalysts modified with L-Leu-L-Leu and L-Leu-D-Leu at 0°C are calculated as follows, respectively;

$$(+1.12) + (-0.41) = +0.71$$

and

$$(+1.12) - (-0.41) = +1.53$$

However, our results, shown in Table 1, are quite far from the above expectations.

Within the limited number of experiments of the present work, the effect of the structure of the peptides as the asymmetric modifying reagent are not simple; there are two possible reasons, either there are two types of adsorption states of peptide on the catalyst surface, as is shown in Fig. 1, or the effect of the structure of the leucine residue is different from that of the glycine residue in the peptide structure as a modifying reagent.

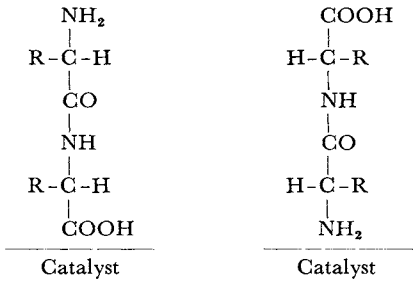

Fig. 1. Adsorption formulas of dipeptide on the catalyst surface.

Although the relationship between the structure of the dipeptide used as a modifying reagent and the asymmetric activity of the catalyst seems to be rather complicated, the following experimental regularity can be presented as the conclusion of the present work. The asymmetric direction of the catalyst modified with dipeptide is ruled by asymmetric center in C-terminal amino acid and has the same sign as the asymmetric direction of the catalyst modified with C-terminal amino acid itself. The glycine residue at the C-terminal reverses the effect of the asymmetric center of N-terminal amino acid itself on the asymmetric direction of the catalyst.