Asymmetric Hydrogenation with Modified Raney Nickel. V. Studies on the Modified Hydrogenation Catalyst. VI

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In previous papers of this series, the asymmetric hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate using Raney nickel catalysts modified with various optically active compounds, such as amino acids and hydroxy acids, has been reported.[1-4]

In the present work, the asymmetric activity of Raney nickel catalysts modified with (+)-2-methylglutamic acid* or (+)-2-benzylglutamic acid* was tested to study the role of a substituent at the asymmetric α-carbon atom in an α-amino acid. The asymmetric activities of these catalysts were compared with that of the catalyst modified with L-glutamic acid.

2-Methyl- and 2-benzylglutamic acid are characterized by the lack of a hydrogen atom on the asymmetric α-carbon atom, and thus have the structure, $HOOCCH_2CH_2(R)C(NH_2)$-COOH, where R is a methyl or a benzyl group. L-Glutamic acid however has an α-hydrogen atom on the α-carbon. It is interesting to find out whether a methyl or a benzyl group on the asymmetric α-carbon in an amino acid takes part in the mechanism of the asymmetric hydrogenation.

Results

The Effect of the pH of the Modifying Solution. — Measurements were made of the asymmetric activities of the catalysts modified at 0°C with solutions of (+)-2-methylglutamic acid, (+)-2-benzylglutamic acid or L-glutamic acid,[1] the pH's of which had been adjusted to specified values. The results are shown in Fig. 1.

As shown in Fig. 1, the catalyst modified with (+)-2-methylglutamic acid produced

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

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

[3] S. Tatsumi, M. Imaida, Y. Fukuda, Y. Izumi and S. Akabori, ibid., 37, 846 (1964).

[4] Presented at the 3rd International Congress on Catalysis, Amsterdam, July, 1964.

* The preparation of this amino acid was reported recently by the present authors, This Bulletin, in press.

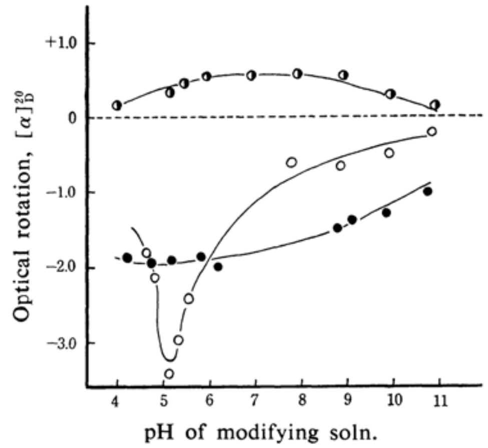

Fig. 1. Effect of modifying pH (modifying temp. at 0°C).
-○- L-Glutamic acid
-●- (+)-2-Methylglutamic acid
-◐- (+)-2-Benzylglutamic acid

levorotatory methyl 3-hydroxybutyrate and that modified with (+)-2-benzylglutamic acid produced the dextrorotatory form. With these amino acids, the asymmetric activities of both modifications of the catalyst were less influenced by the pH of the modifying solution than that of the catalyst modified with L-glutamic acid, and the optimum pH range for asymmetric activity was pH 5—8. This pH range approximately corresponds to the pH jumping region of the neutralization curves of these *α-C*-substituted glutamic acids. Thus, the two activity curves were alike in character except for the direction of their optical rotation. However, the asymmetric activity of the catalyst modified with L-glutamic acid was much influenced by the pH of the modifying solution. The greatest asymmetric activity was observed at pH 5.1 and there was considerable diminution in activity at both higher and lower pH values.

The effects of the pH values of modifying solutions at 100°C on the asymmetric activities of the modified catalysts are shown in Fig. 2.

Optimum asymmetric activities were observed when catalysts were modified with solutions of the three amino acids at pH 7—9.5. On modifications with (+)-2-methyl- and (+)-2-benzylglutamic acid, the asymmetric activity curves showed tendencies similar to those shown on modification at 0°C. In the case of modification with L-glutamic acid, however, the dextrorotatory product was obtained below pH 5.4 or above pH 11 and the levorotatory product in the intermediate range.

The Effect of the Modifying Temperature.—The effect of the temperature of the modifying solution was studied at pH 5.2; the results are shown in Fig. 3.

As shown in Fig. 3, the asymmetric activity of the catalyst modified with (+)-2-methylglutamic acid was greater than that of the catalyst modified with (+)-2-benzylglutamic acid and both activities increased with elevation of the modifying temperature. On modification with L-glutamic acid, however, the activity was characteristically different from those obtained on modification with the other two amino acids; the highest activity was obtained by modification at 0°C and the asymmetric

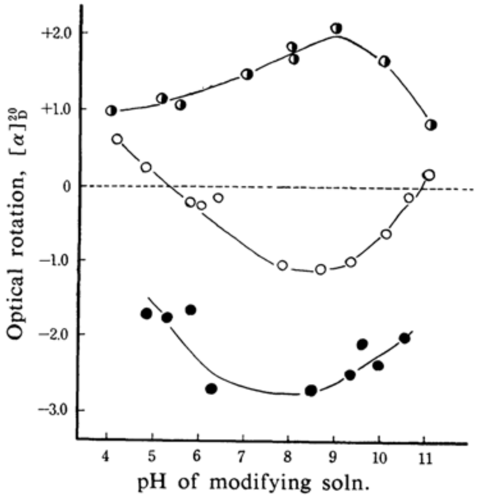

Fig. 2. Effect of modifying pH (modifying temp. at 100°C).
-○- L-Glutamic acid
-●- (+)-2-Methylglutamic acid
-◐- (+)-2-Benzylglutamic acid

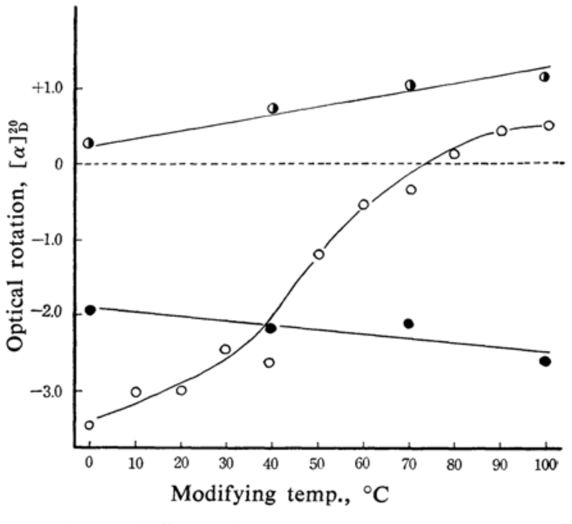

Fig. 3. Effect of modifying temperature.
-○- L-Glutamic acid (pH 5.2)
-●- (+)-2-Methylglutamic acid (pH 5.2)
-◐- (+)-2-Benzylglutamic acid (pH 5.2)

activity decreased at higher temperatures. If the catalyst was treated with the same modifying solution at temperatures higher than 80°C, the hydrogenation products showed reverse optical rotations.

Discussion

Two kinds of asymmetric hydrogenation catalyst are obtained by modification with L-glutamic acid. One has the asymmetric capacity to hydrogenate methyl acetoacetate predominantly to levorotatory methyl 3-hydroxybutyrate and the other has the capacity to produce the dextrorotatory product. On the other hand, only one asymmetric catalyst is obtained by modification with (+)-2-methylglutamic acid or (+)-2-benzylglutamic acid under a variety of modifying conditions as shown in Figs. 1, 2 and 3.

These results show that on modification with L-glutamic acid, at least two types of asymmetric center are produced on the surface of the modified catalyst; but only one type is formed, or this type is in excess on modification with α-*C*-substituted glutamic acid under all modifying conditions.

The difference between glutamic acid and α-*C*-substituted glutamic acid is caused by the substituent on the asymmetric α-carbon atom. The steric hindrance of the substituent on the α-carbon atom regulates the adsorption of α-*C*-substituted glutamic acid on Raney nickel catalyst and permits the formation of only one or mainly one type of asymmetric center. The relationship between the bulk of the substituent on the α-carbon atom of the modifying reagent and the optical direction of the asymmetric activity of the modified catalyst will be discussed after the absolute configuration of (+)-2-methylglutamic acid and (+)-2-benzylglutamic acid have been confirmed.

Experimental

The preparation and modification of the Raney nickel catalyst, the hydrogenation of methyl acetoacetate and the measurement of the asymmetric activity of the catalyst were performed as described in a previous paper.[1]

Summary

1) The asymmetric activities of Raney nickel catalysts modified with (+)-2-methylglutamic acid or (+)-2-benzylglutamic acid have been formed to be quite different from that of the catalyst modified with L-glutamic acid.

2) Levorotatory methyl 3-hydroxybutyrate is obtained by the catalyst modified with (+)-2-methylglutamic acid, and the dextrorotatory product by the catalyst modified with (+)-2-benzylglutamic acid. With the catalyst modified with L-glutamic acid, however, the direction of optical rotation of the hydrogenation product is much influenced by the pH and by the temperature of the modifying solution.

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