BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 1419—1420(1971)

Asymmetric Hydrogenation of C=O Double Bond with Modified Raney Nickel.[1] XIX

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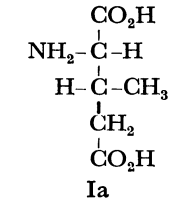
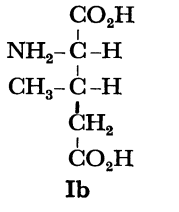
(Received October 20, 1970)

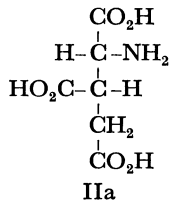
In the previous papers of this series,[2] it has been reported that, in the presence of the Raney nickel catalyst modified with optically-active α-amino or α-hydroxy acid, methyl acetoacetate is asymmetrically hydrogenated to methyl 3-hydroxybutyrate. Thereafter, the correlation of the asymmetric activity of the catalyst and the chemical and steric structures of the modifying reagent was studied.



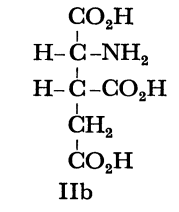
Ia



Ib



IIa



IIb

In the present paper, the asymmetric activities of catalysts modified with optically-active 3-methylglutamic acid[3] (Ia, Ib) and 2-aminotricarballylic acid[4] (IIa, IIb) are described, and the effect of the β-substituent of the modifying reagent on the asymmetric activity of the catalyst and the relationship between the asymmetric activities of the catalysts modified with the *thero* and the *erythro* isomers are discussed.

TABLE 1. OPTICAL ROTATIONS OF MODIFYING REAGENTS

Modifying reagent		Optical rotation, $[\alpha]_D$
3-Methylglutamic acid	Ia (2S, 3R)	+22 (*c* 2.2, 4N HCl)
	Ib (2S, 3S)	+42 (*c* 3, 4N HCl)
2-Aminotricarballylic acid	IIa (2R, 3S)	−49 (*c* 1, 5N HCl)
	IIb (2R, 3R)	−36 (*c* 1, 5N HCl)

Experimental

The preparation of the modified Raney nickel catalyst, the hydrogenation of methyl acetoacetate, and the measurement of the asymmetric activity of the catalyst were done as described in a previous paper.[5]

Results and Discussion

Measurements were made of the asymmetric activities of the catalysts modified with aqueous solutions of L-*threo*-3-methylglutamic acid (Ia), L-*erythro*-3-methylglutamic acid (Ib), D-2-aminotricarballylic acid ((2R, 3S), IIa), and D-2-aminotricarballylic acid ((2R, 3R), IIb), the pH of which had been adjusted to specified values with a sodium hydroxide solution; the results are shown in Figs. 1 and 2.

Correlation of the Asymmetric Activity of the Catalyst and the β-Configuration of the Modifying Reagent. As has been reported in the previous papers of this series, the direction of the optical rotation of the hydrogenation product, methyl 3-hydroxybutyrate, is decided by the α-configuration of the modifying reagent (for example, in the hydrogenation with the catalysts modified with D-glutamic acid and L-glutamic acid, the directions of

1) Presented in part at the 20th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1967.

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2) Part XV: T. Tanabe, T. Ninomiya, and Y. Izumi, This Bulletin, **43**, 2276 (1970). Part XVI: Y. Izumi, S. Yajima, K. Okubo, and K.K. Babievsky, *ibid.*, **44**, 1416 (1971). Part XVII: Y. Izumi, T. Harada, T. Tanabe, and K. Okuda, *ibid.*, **44**, 1418 (1971). Part XVIII: Y. Izumi, and K. Okubo, *ibid.*, **44**, 1330 (1971).

3) The diastereomeric mixture was obtained by the procedure of Morrison. [D. C. Morrison, *J. Amer. Chem. Soc.*, **77**, 6072 (1955).] The details of its separation into the diastereomers and the optical resolution of the isomers will be reported in This Bulletin, later.

4) The optically-active isomers were prepared by the procedure of Greenstein *et al.*, while the configurations of their α- and β-carbons were assigned by Kaneko *et al.* [J. P. Greenstein, N. Izumiya, M. Winitz, and S. M. Birnbaum, *J. Amer. Chem. Soc.*, **77**, 707 (1955). T. Kaneko, Y. Ariyoshi, S. Andō, and H. Katsura, This Bulletin, **37**, 324 (1964).]

5) Y. Izumi, T. Harada, T. Tanabe, and K. Okuda, This Bulletin, **44**, 1418 (1971).

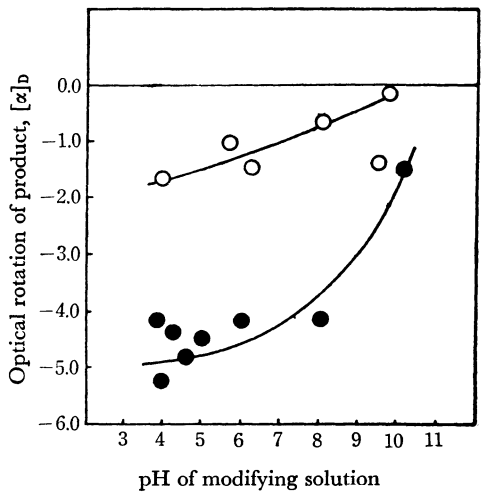

Fig. 1. Asymmetric activities of the catalysts modified with L-*threo*- and L-*erythro*-3-methylgulamic acids.
○ L-*erythro*-3-methylgutamic acid
● L-*threo*-3-methylglutamic acid

the optical rotations of the hydrogenation product were (+) and (−) respectively), and the β-configuration of the α,β-diasymmetric amino or hydroxy acid used as a modifying reagent greatly affects the asymmetric activity of the catalyst (for example, the asymmetric activity of the catalyst modified with the *threo* isomer of α,β-diasymmetric amino acid (2R, 3S) or (2S, 3R)) is higher than that of the catalyst modified with the corresponding *erythro* isomer ((2R, 3R) or (2S, 3S))). These differences in the asymmetric activities of the catalysts modified with the *erythro* and the *threo* isomers are ascribable to the disagreement of the β-configuration, which is distinguished mainly in terms of the bulkiness of the two β-alkyl substituents. As can be seen in Figs. 1 and 2, the catalyst modified with the *threo* isomer (Ia or IIa) had a higher asymmetric activity than the one modified with the corresponding *erythro* isomer (Ib or IIb). Accordingly, the similarlity between α,β-diasymmetric monoamino monocarboxylic acids and these β-substituted glutamic acids, in the correlation of the β-configuration of the modifying reagent and the asymmetric activity of the catalyst, suggests that the effect of the β-configuration of 3-methylglutamic acid and 2-aminotricarballylic acid is also due to the differences in bulkiness between a β-carboxymethyl group and either a methyl or a carboxyl group.

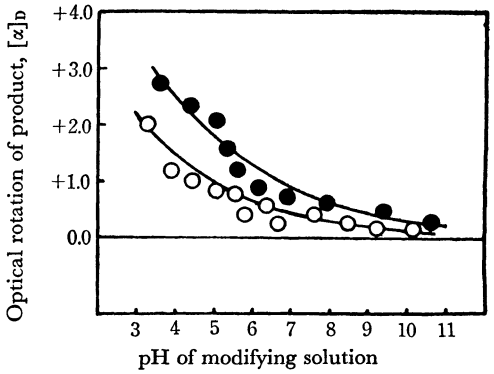

Fig. 2. Asymmetric activities of the catalysts modified with isomeric 2-aminotricarballylic acids.
● D-2-aminotricarballylic acid (2R, 3S)
○ D-2-aminotricarballylic acid (2R, 3R)

Correlation of the Asymmetric Activity of the Catalyst and the β-Substituent of the Modifying Reagent. As is shown in Figs. 1 and 2, the catalysts modified with Ia (*threo*) and Ib (*erythro*) had higher asymmetric activities than those modified with IIa (*threo*) and IIb (*erythro*) respectively.

As has been reported in a previous paper,[6] the asymmetric activity of the catalyst modified with monoasymmetric amino acid increases with an increase in the bulk of the α-alkyl substituent (R–CH–COOH), while that of the catalyst modified with monoasymmetric hydroxy acid decreases with an increase in the bulk of the α-alkyl substituent. From the facts that both *threo*- and *erythro*-3-methylglutamic acids are more effective asymmetric modifying reagents than the corresponding 2-aminotricarballylic acids, although a carboxyl group is bulkier than a methyl group, it seems that the asymmetric activity of the catalyst depends not only on the bulk of the β-substituent of the modifying reagent, but also on the electronic factor of the β-substituent. Similar effects of the β-substituents on the asymmetric activities of the catalysts can be found in the asymmetric activities of the catalysts modified with serine and threonine.[7]

6) Y. Izumi, T. Tanabe, S. Yajima, and M. Imaida, This Bulletin, **41**, 941 (1968).
7) Y. Izumi, M. Imaida, H. Fukawa, and S. Akabori, *ibid.*, **36**, 155 (1963).