BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 1418—1419 (1971)

Asymmetric Hydrogenation of C=O Double Bond with Modified Raney Nickel. XVII

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(Received June 8, 1970)

In the course of our studies of the asymmetric hydrogenation catalyst, it was found that the Raney nickel catalysts modified with various optically-active compounds catalyze asymmetrically the hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate; the relationship between the structure of the modifying reagent and the asymmetric activity of the catalyst has been studied in detail.[1] From the facts that *N*-substituted amino acids, *N*-cyanoethyl, *N*-benzoyl, and *N,N*-dimethyl derivatives of L-glutamic acid and L-aspartic acid, produce catalysts with much lower asymmetric activities than the original amino acids, it was concluded that a primary amino residue of amino acid is necessary for an effective modifying reagent.[2]

However, the role of the α-carboxyl group of the amino acid or hydroxy acid used as a modifying reagent for the asymmetric activity of the catalyst has not yet been made clear.

In the present paper, the asymmetric activities of the catalysts modified with optically-active 2-amino alcohols, $R\text{-}C^*H(NH_2)CH_2OH$, are examined in order to investigate the role of the α-carboxyl group.

The activities of the catalysts modified with amino alcohols are shown in Table 1, where they are compared with those of the catalysts modified with the corresponding amino acids. Also, the results of the adsorption-stability test of the modifying reagent on the catalyst are shown in Table 2.

Table 1. Asymmetric activities of the catalysts modified with optically active 2-amino alcohols, and 2-amino acids

Modifying reagent	Modifying conditions		$[\alpha]_D$ of methyl 3-hydroxybutyrate
	pH	Temp. °C	
L-Alaninol	11.6	0	−0.04
L-Leucinol	11.4	0	−0.25
L-Valinol	11.4	0	−0.15
L-Alanine	6.1	0	+0.45
L-Leucine	6.0	0	−1.65
L-Valine	5.9	0	−2.64

Table 2. The asymmetric activities of the catalysts after the contact with the substrate before use

Modifying reagent	Modifying temp., °C	$[\alpha]_D$ of methyl 3-hydroxybutyrate
L-Leucine	0	−1.40
L-Leucinol	0	−0.08

As is shown in Table 1, the catalyst modified with 2-amino alcohol has a lower asymmetric activity than that modified with the corresponding amino acid, and so it is evident that it is desirable for the modifying reagent to have an α-carboxyl group.

Moreover, the Raney nickel catalysts modified with L-leucine and L-leucinol were employed in the hydrogenation of methyl acetoacetate after contact with the substrate before use in order to study the adsorption stabilities of the modifying reagents on the catalysts in the presence of the substrate. As may be found in Table 2, the process of the contact with the substrate reduced the asymmetric activity of the catalyst modified with L-leucinol to about 30%, while the process did not result in any remarkable change in that of the catalyst modified with L-leucine. These facts show that the displacement of a carboxyl group by a hydroxymethyl group results in a considerable decrease in the adsorption stability on the catalyst, and that this poor adsorption stability of the amino alcohol in the presence of methyl acetoacetate causes the considerably lower asymmetric activity of the catalyst.

Materials

2-Amino Alcohols. These compounds were synthesized from the corresponding optically-active 2-amino acid ethyl esters by the method of Karrer and Naik.[3]

Experimental

Preparation of the Modified Raney Nickel Catalyst. Into a solution of 4.5 g of sodium hydroxide in 20 m*l* of deionised water, 1.5 g of Raney nickel alloy (Ni:Al=4:6) was added, in small portions, and then the solution was allowed to stand for 1 hr at 100°C. Then, the catalyst was washed with water until the pH of the washing was about neutral. The catalyst so obtained was added a 1—2% aqueous solution of the modifying reagent, and the mixture was allowed to stand at the specified temperature, with occasional shaking, for 1.5 hr. After the subsequent removal of the modifying solution by decantation, the catalyst was washed once with water and three times with methanol.

Hydrogenation. Methyl acetoacetate (17.5 m*l*, The Nippon Syntehtic Chemical Industry Co., Ltd.) was hydrogenated with a modified Raney nickel catalyst prepared from 1.5 g of the alloy under an initial hydrogen pressure of about 90 kg/cm^2 at 60°C in a shaking autoclave.

Adsorption-stability Test. The catalysts modified with L-leucine and L-leucinol, prepared by the procedure described above, were placed in contact with 20 m*l* of methyl aceto-

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[1] Part XIV: Y. Izumi, and T. Ninomiya, This Bulletin, **43**, 579 (1970). Part XV: T. Tanabe, T. Ninomiya, and Y. Izumi, *ibid.*, **43**, 2276 (1970). Part XVI: Y. Izumi, S. Yajima, K. Okubo, and K. K. Babievsky, *ibid.*, **44**, 1416 (1971).

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

[3] P. Karrer and A. R. Naik, *Helv. Chim. Acta*, **31**, 1617 (1948).

acetate at room temperature for 30 min, and then washed three times with methanol. The resulting catalyst was used for the hydrogenation of methyl acetoacetate.

Measurement of the Asymmetric Activity of the Catalyst. After the removal of the catalyst by filtration, the hydrogenation products were distilled under reduced pressure (bp 61—62°C/12 mmHg). The optical rotatory power of the distilled product was measured by a conventional polarimeter in a 1 dm tube without dilution. The optical rotatory power of methyl D-3-hydroxybutyrate, prepared by esterification with diazomethane of D-3-hydroxybutyric acid ($[\alpha]_D^{20} = -25.1$, *c* 10, H_2O), is $[\alpha]_D^{16}$ -22.05; literature value,[4] $[\alpha]_D^{20}$ -20.9.

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[4] P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **65**, 51 (1925).