NOTES

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

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In the course of the investigation of the asymmetrically modified R-Ni catalyst, it was found that catalysts modified with α-amino or α-hydroxy dicarboxylic acids have higher asymmetric hydrogenation activities than do those modified with α-amino or α-hydroxy monocarboxylic acids. That is, the asymmetric activity of the catalyst modified with aspartic acid, glutamic acid, or malic acid is higher than that of the catalyst modified with alanine, butyrine, norvaline, or lactic acid.[1-6]

The expectation that the excellent property of α-amino or α-hydroxy dicarboxylic acid as a modifying reagent will greatly depend on the ω-carboxyl group is also supported by the fact that the optimum asymmetric activity of the catalyst modified with α-amino or α-hydroxy dicarboxylic acid is produced by the modification at pH 5, which is the point where the ω-carboxyl group is neutralized. The contribution of the ω-carboxyl group to the increase in the asymmetric activity of the catalyst may be ascribable to its ionic and steric effects and to its electronegativity. Therefore, it can be expected that more acidic, more electronegative, and bulkier substituents than the carboxyl group, such as the sulfonyl group, will increase the asymmetric activity of the catalyst.

In the present work, the abilities of L-α-hydroxy-β-sulfopropionic acid, L-homocysteic acid, and L-cysteic acid as modifying reagents were tested at various modifying pH values in order to test the expectation mentioned above. The results are shown in Figs. 1 and 2, where they are compared with those obtained with aspartic acid and malic acid.

As may be seen in Figs. 1 and 2, unexpected results were obtained. The asymmetric activities of the catalyst modified with the sulfonic acids were considerably lower than those of the catalysts modified with

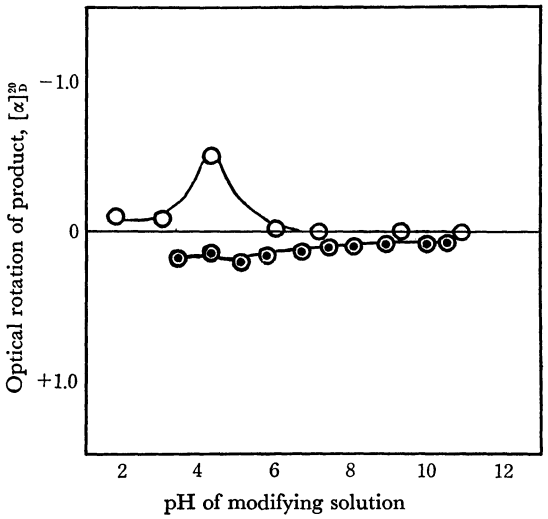

Fig. 1. Modifications with L-cysteic acid and L-homocysteic acid (Modified at 0°C).

—⊙— L-Cysteic acid $HO_3SCH_2\underset{\underset{NH_2}{|}}{C}HCO_2H$

—○— L-Homocysteic acid $HO_3SCH_2CH_2\underset{\underset{NH_2}{|}}{C}HCO_2H$

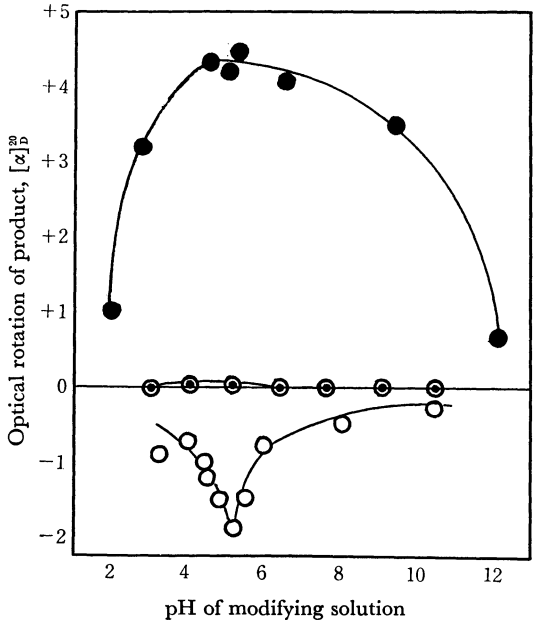

Fig. 2. Modifications with L-malic acid and L-aspartic acid and L-α-hydroxy-β-sulfopropionic acid.

-●- L-malic acid $HOOCCH_2\underset{\underset{OH}{|}}{C}HCO_2H$

-○- L-aspartic acid $HOOCCH_2\underset{\underset{NH_2}{|}}{C}HCO_2H$

-◎- L-α-hydroxy-β-sulfopropionic acid $HO_3SCH_2\underset{\underset{OH}{|}}{C}HCO_2H$

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

4) Y. Izumi, T. Tanabe, S. Yajima, and M. Imaida, *ibid.*, **41**, 941 (1968).

5) Y. Izumi, K. Matsunaga, S. Tatsumi, and M. Imaida, *ibid.*, **41**, 2515 (1968).

the α-amino or α-hydroxy dicarboxylic acids. Scarcely no effect of the modifying pH is found in the case of modifications with cysteic acid and α-hydroxy-β-sulfopropionic acid, although a slight effect was found in the case of modification with homocysteic acid.

The asymmetric directions of the catalysts modified with L-homocysteic acid and L-α-hydroxy-β-sulfopropionic acid come under the general rule of the relation between the absolute configuration of the modifying reagent and the asymmetric direction of the catalyst —the catalysts modified with L-α-amino acids or D-α-hydroxy acids at 0°C produce predominantly methyl D-3-hydroxybutyrate in the hydrogenation of methyl acetoacetate. However, cysteic acid gives a catalyst which has an asymmetric direction, contrary to the general rule, as was also found in the case of the catalyst modified with serine, cysteine, and threonine.[7]

From the results described above, the regular correlations between the asymmetric activities of the catalysts modified with sulfonic acids and the ones modified with amino dicarboxylic acids were difficult to be found, from the simple view point of ionic effect, electronegativity or steric hindrance of the β- or γ-substituent.

As it was reported in the previous paper that the modifying reagent might be adsorbed on the catalyst surface with the chelate formation,[8] the contribution of the sulfonyl group to the chelate formation must be discussed. In connection with the sulfonyl group, however, it is generally known that, as the dissociation constant of the sulfonic acid is much larger than that of the carboxylic acid, the ability of the chelate formation with the metal ion is considerably weaker than that of the carboxyl group.

Accordingly, it is hard to accept the idea that the unexpected results obtained with the catalysts modified with the β- or γ-sulfonyl substituted amino and hydroxy acids are brought about by the different types of adsorption of the modifying reagent.

Therefore, it can be expected that the amino acids or hydroxy acids which have a sulfonyl group on the β- or γ-carbon are adsorbed by amino and carboxyl groups or by hydroxy and carboxyl groups.

As a conclusion of the present work, it was made clear that the electronegativity and bulkiness of the sulfonyl group on the β- or γ-carbon of the amino or hydroxy acid did not simply affect the asymmetric activity of the catalyst, and that the other new effect of the sulfonyl group overcame the effects of the electronegativity and bulkiness of the sulfonyl group.

The new effect of the substituent will be discussed in detail in This Bulletin in the near future.

The L-α-hydroxy-β-sulfopropionic acid was prepared from L-cysteic acid and was successively purified as benzidine and dicyclohexylamine salts.

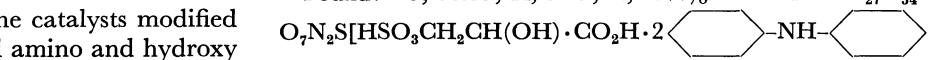
Experimental

The asymmetric activity of the catalyst was measured by a method reported in a previous paper.[6]

Preparation of the Dicyclohexylamine Salt of L-α-Hydroxy-β-sulfopropionic Acid. In 150 m*l* of 10% hydrochloric acid, 18.7 g of L-cysteinic acid monohydrate was dissolved. Into this solution, 50 m*l* of isoamyl nitrite was vigorously stirred, drop by drop, at room temperature, and then the reaction mixture was stirred continuously overnight. The isoamyl alcohol thus separated was removed, and the aqueous layer was washed thoroughly with ether. The aqueous solution was evaporated to a syrup, and the resulting syrup was taken up in a small amount of water and again evaporated. This syrup gave, quantitatively, benzidine salt in an alcohol solution; mp 260°C.

Found: C, 50.54; H, 4.71; N, 7.88%. Calcd for $C_{15}H_{18}O_6N_2S$: C, 50.85; H, 5.12; N, 7.91%.

To 17 g of syrup dissolved in 100 m*l* of acetone, was added 35 g of dicyclohexylamine, drop by drop, with ice cooling. The dicyclohexylamine salt thus precipitated was collected and washed with acetone. Two recrystallizations from ethanol-ether (1:5) gave 29.5 g (53.6%); mp 260°C.

Found: C, 58.83; H, 9.59; N, 5.22%. Calcd for $C_{27}H_{54}O_7N_2S[HSO_3CH_2CH(OH)\cdot CO_2H\cdot 2$  $\cdot H_2O]$: C, 59.00; H, 9.82; N, 5.09%. $[\alpha]_D$ −8.57 (*c* 2.3 EtOH).

Preparation of a Modifying Solution of L-α-Hydroxy-β-sulfopropionic Acid. In 30 m*l* of water, 5.36 g of the dicyclohexylamine salt was dissolved. The dicyclohexylamine was removed using a column of Amberite IR 120(400—600 mesh, 1×18 cm), and with water. The total volume of the eluted solution was adjusted to 100 m*l*. The specific rotation $[\alpha]_D$ −13.3 (*c* 1.65, H_2O) for L-α-hydroxy-β-sulfopropionic acid was calculated from the α_D of the solution obtained. An attempt to isolate the free acid failed.

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6) Y. Izumi, S. Tatsumi, and M. Imaida, *ibid.*, **42**, 2373 (1969).

7) Proline, hydroxyproline, and alanine all produced catalysts which have an asymmetric direction, thus contradicting the general rule. However, proline and hydroxyproline are special amino acids which have a pyrrole ring, and the modification with alanine is very sensitive to the modifying condition, so such results are reasonable even according to the general rule. The details of the asymmetric activity of the catalyst modified with alanine will be discussed in This Bulletin in the near future.

8) Y. Izumi and T. Ninomiya, This Bulletin, **43**, 579 (1970).