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

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A series of studies of the asymmetric hydrogenation of methyl acetoacetate with the catalysts prepared from Raney nickel catalyst by modifications with aqueous solutions of various optically-active compounds has already been reported by the present authors.[1–11] The effect of the structure of the modifying reagent on the asymmetric activity of the catalyst has been extensively discussed. However, the relationship between the structure of the substrate and the asymmetric yield in the hydrogenation has not yet been reported. In order to clarify the mechanism of asymmetric hydrogenation with a modified Raney nickel catalyst, various substrates were examined with catalysts modified with D-tartaric acid, L-glutamic acid, and some other amino acids. In the present paper, a part of the accumulated results of this study will be given as a basis for future discussion.

TABLE 1.

No.	Substrate	Amount of R-Ni (as alloy) g	Modification				Optical rotation of product $[\alpha]^{20}_{D}$	Absolute config.	Asymmetric yield %
			Modifying reagent	Temp. °C	pH	Time hr			
1	Methyl ethyl ketone 0.2 mol	1.5	1%-D-Tartaric acid	100	5.10	1.5	+1.0	–S[a]	7.7
2	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	4.62	1.5	−0.05	–R	0.4
3	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	4.89	1.5	−0.09	–R	0.7
4	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	5.05	1.5	−0.11	–R	0.8
5	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	5.20	1.5	−0.06	–R	0.5
6	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	7.85	1.5	−0.10	–R	0.8
7	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	100	4.79	1.5	−0.09	–R	0.7
8	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	5.00	1.5	−0.29	–R	2.2
9	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Glutamic acid	0	8.80	1.5	−0.21	–R	1.6
10	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Alanine	0	6.2	1.5	+0.15	–S	1.1
11	Methyl ethyl ketone 0.15 mol	1.5	2%-L-Alanine	100	—	1.5	+0.27	–S	2.1

[*1] Papers I–X were entitled "Asymmetric Hydrogenation with Modified Raney Nickel."

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2) Y. Izumi, M. Imaida, H. Fukawa and S. Akabori, *ibid.*, **36**, 21 (1963).

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

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7) Y. Izumi, S. Tatsumi, M. Imaida, Y. Fukuda and S. Akabori, *ibid.*, **39**, 361 (1966).

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9) S. Tatsumi, *ibid.*, **41**, 409 (1968).

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11) Y. Izumi, K. Matsunaga, S. Tatsumi and M. Imaida, *ibid.*, to be published.

12	Methyl ethyl ketone 0.4 mol	1.5	2%-L-Phenylalanine	—	—	1.5	0.22	—	1.7
13	Acetophenone 0.15 mol	1.5	2%-L-Glutamic acid	0	5.16	1.5	+0.93	R[b]	2.1
14	Diacetyl 0.18 mol	1.5	2%-D-Tartaric acid	0	5.0	1.5	−0.06	R[c]	0.5
15	Ethyl pyruvate 5 g	0.5	D-Tartaric acid	0	5.0	1.5	+0.26	L–S[d]	2.5
16	α-Ketoglutaric acid 0.5 mol	1.5	2%-L-Glutamic acid	0	5.1	1.5	0	—	—
17	Diethyl α-ketoglutarate 10 g	1.5	2%-L-Glutamic acid	100	5.2	1.5	0	—	—
18	Diethyl α-ketoglutarate 10 g	1.5	2%-D-Tartaric acid	100	5.0	1.5	0	—	—
19	Ethyl acetoacetate 0.15 mol	1.5	2%-D-Tartaric acid	0	5.1	1.5	−2.97	D–R[e]	18
20	Ethyl acetoacetate 0.15 mol	1.5	2%-D-Tartaric acid	100	5.1	1.5	−4.30	D–R	27
21	*n*-Propyl acetoacetate 0.15 mol	1.5	2%-D-Tartaric acid	0	5.1	1.5	−2.28	D–R	16
22	Isopropyl acetoacetate 14 g	1.5	2%-D-Tartaric acid	0	4.0	2.0	−0.58	D–R	4
23	Isopropyl acetoacetate 14 g	1.0	2%-D-Tartaric acid	0	5.0	2.0	−0.76	D–R	5
24	Isopropyl acetoacetate 14 g	1.0	2%-D-Tartaric acid	100	5.1	2.0	−1.58	D–R	11
25	Ethyl benzoylacetate 0.065 mol	1.0	L-Glutamic acid	0	5.12	0.4	+1.90	D–R	8.3[f]
26	Acetylacetone 0.2 mol	1.5	D-Tartaric acid	0	5.0	1.5	−14.83	—	—[g]
27	DL-2-Pentanol-4-on 5 g	1.5	2%-D-Tartaric acid	0	5.0	1.5	−1.15	—	—[g]
28	Diacetonealcohol 13 g	1.5	2%-L-Glutamic acid	0	5.0	1.5	0	—	—
29	Levulinic acid 3 g	1.5	D-Tartaric acid	0	3.5	1.5	0	—	—
30	Methyl levulinate 10 g	1.0	D-Tartaric acid	0	5.2	1.5	−0.40	D–R	3.1[h]
31	Methyl levulinate 10 g	1.0	D-Tartaric acid	100	6.5	1.5	−0.44	D–R	3.4
32	Methyl levulinate 10 g	1.0	L-Glutamic acid	0	5.1	1.5	0	—	0
33	Methyl levulinate 10 g	1.0	L-Glutamic acid	100	5.4	1.5	+0.12	L–S	0.9
34	Methyl 3-acetoxy-crotonate 14 g	1.5	D-Tartaric acid	0	5.2	1.5	Decomposed	—	—
35	Ethyl 3-ethoxycrotonate 15 g	1.5	D-Tartaric acid	0	5.0	1.5	NO-H_2-uptake at 60°C	—	—

a) J. Kenyon, H. Phillips and V. P. Pittman, *J. Chem. Soc.*, **1935**, 1077.
b) J. A. Mills, W. Hyne, "Progress in Stereochemistry," Vol. 1, Butterworth, London (1954), p. 187.
c) K. Freudenberg, *Ber.*, **47**, 2027 (1914).
d) A. F. McKay, R. H. Meen and G. F. Wright, *J. Am. Chem. Soc.*, **70**, 430 (1948).
e) The asymmetric yield was calculated from the conversion of methyl 3-hydroxybutyrate to the corresponding ester.
f) G. Senter, A. M. Ward, *J. Chem. Soc.*, **125**, 2142 (1924). The product was hydrolyzed and the asymmetric yield was measured in alcohol.
g) The product is 2,4-pentanediol and the optical resolution of it is in progress.
h) Pure methyl levulinate could not be obtained and the asymmetric yield was calculated by induction of the product to γ-valerolactone.

Experimental

The procedures for the preparation of modified Raney nickel catalyst and for the hydrogenation of the substrate were the same as have been reported in previous papers. The hydrogenation products were purified by distillation, and the optical rotations of the products were measured without dilution in a 1-dm tube. Esters of acetoacetic acid were prepared from diketene and the corresponding alcohols.[12]

Results and Discussion

The modifying conditions and the results are shown in Table 1. In general, it will be seen that better results are obtained in the asymmetric hydrogenation of β-ketoesters or β-diketone, such as esters of acetoacetic acid, ethyl benzoylacetate, and acetylacetone, the enol isomers of which are fairly stable. On the other hand, the asymmetric yields are very low in the hydrogenation of ketones without a β-carbonyl group and, hence, without the stable enol isomer, ketones such as mono-

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[12] A. Treibs and K. Hintermeier, *Chem. Ber.*, **87**, 1163 (1954).

ketone, ethyl pyruvate, diethyl α-ketoglutarate, methyl levulinate and diacetyl.

In the asymmetric hydrogenation of monoketone, the effect of the modifying pH on the asymmetric activity of the catalyst shows a tendency similar to that observed in the asymmetric hydrogenation of methyl acetoacetate. In the hydrogenation of the esters of acetoacetic acid, those esters with a bulkier alkoxyl moiety gave lower asymmetric yields of the products, the esters of 3-hydroxybutyric acid.

Recently, Petrov *et al.*[13] have reported the asymmetric hydrogenation of ethyl acetoacetate, following the methods of our studies with methyl acetoacetate and using a catalyst prepared by our method. Some of their results agree with those included in the present table, confirming that our results are reproducible.

More detailed results and a discussion of the mechanism of the asymmetric hydrogenation of the carbonyl group will be presented in this Bulletin in the near future.

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[13] Yu. I. Petrov, E. I. Klabnovskii and A. A. Balandin, *Kinetika i Kataliz*, **8**, 814 (1967).