

Study on effects of modification conditions of powdered nickel–cobalt catalysts on enantioselectivity of hydrogenation of ethyl acetoacetate*

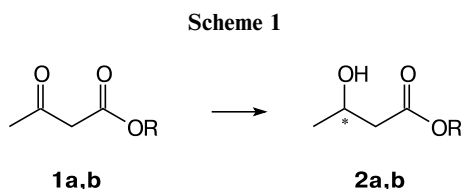
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An effect of modification conditions of powdered nickel–cobalt catalysts on enantioselectivity of hydrogenation of ethyl acetoacetate has been studied. Addition of NaBr to the modifying solution of *RR*-(+)-tartaric acid does not improve enantioselectivity of the catalyst. When the Ni–Co catalysts are modified with amino acids, the best results are obtained with *L*-β-phenylalanine (17% *ee*).

Key words: enantioselective catalytic hydrogenation, bimetallic Ni–Co catalysts, ethyl acetoacetate, modification, optically active ethyl hydroxybutyrate.

Asymmetric hydrogenation in the presence of heterogeneous catalysts is of interest for the synthesis of such products as pheromones and biodecomposable polymers. On hydrogenation of the C=O bond in β-keto esters (Scheme 1), nickel catalysts are the most active.



Hydroxy and amino acids (AA) are used as modifiers.^{1,2}

The efficiency of Ni catalysts in asymmetric hydrogenation is affected by addition of some salts to the modifying solution. The best results were obtained with NaBr. The highest optical yield (88.6% *ee*) was obtained on hydrogenating β-keto ester methyl acetoacetate (**1a**) into methyl (–)-β-hydroxybutyrate (**2a**)³ using a Raney Ni catalyst modified with *RR*-(+)-tartaric acid (TA) with addition of NaBr (RNi–TA–NaBr). The effect of NaBr on other Ni catalysts of various genesis, including those on various supports,^{4,5} has been also studied.

Earlier,^{6,7} we have shown that powdered Ni and Ni–Co catalysts obtained from acetates and modified with TA are active in the asymmetric hydrogenation

of the C=O bond of ethyl acetoacetate (**1b**) into ethyl (–)-β-hydroxybutyrate (**2b**). Nickel catalysts exhibited fairly high catalytic and asymmetry-inducing activity (the degree of conversion was 100%, the optical yield *ee* was 70%). For Ni–Co catalysts, both the extent of conversion and the optical yield decrease, but still they are active enough.

In the present work, we studied the effect of modification conditions of Ni and Ni–Co catalysts on their asymmetry-inducing properties in the reaction of asymmetric hydrogenation of compound **1b** into **2b**: some AA were used as the modifiers, as well as NaBr when the catalysts were modified using TA.

Experimental

Powdered Ni, Co, and Ni–Co catalysts were prepared by decomposition of cobalt and nickel acetates with subsequent reduction of oxides in the flow of hydrogen. Modification of the catalysts was carried out using solutions of *L*-amino acids or TA with NaBr additives or without them. More detailed procedure for the preparation, reduction, and modification of catalysts using TA is described in the works published earlier.^{6,7} To modify the catalysts with AA, they were treated with 0.5% aqueous solution of AA. The following α-amino acids were used: monoaminocarboxylic AA, *L*-α-alanine and *L*-β-phenylalanine, monoaminodicarboxylic AA, *L*-glutamic acid, as well as *L*-arginine and *L*-histidine.

Results and Discussion

Results on the hydrogenation of ethyl acetoacetate **1b** in the presence of Ni–Co–AA catalysts, as well as litera-

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Table 1. Hydrogenation of ethyl acetoacetate **1b** in the presence of Ni—Co catalysts (1 : 1) modified with amino acids^a

Amino acids	Formula	pH of modification	τ /h	Y (%)	ee (%)		
					I ^b	II ^c	III ^d
L- β -Phenylalanine (L-Phe)	Ph—CH ₂ —CH(NH ₂)—COOH	7.1 9.7 ^e	11.1	63 58	15 17	9.2 ⁸ —	— —
L- α -Alanine (L-Ala)	Me—CH(NH ₂)—COOH	9.4	14	63	1	2.4 ⁹	—
L-Arginine (L-Arg)	H ₂ NC(=NH)NH(CH ₂) ₃ —CH(NH ₂)—COOH	8.6	11	10	3	—	2.2 ¹⁰
L-Histidine (L-His)	C ₆ H ₉ N ₃ O ₂	7.5	11	25	1	2.1 ⁸	1.2 ¹⁰
L-Glutamic acid (L-Glu)	HOOC—CH ₂ —CH ₂ —CH(NH ₂)—COOH	7.0	14	1	0	21 ¹¹ 11.6 ¹²	3.0 ¹⁰

^a Modification conditions: 1 h 40 min in duration, 97 °C; hydrogenation conditions: ethyl acetate (12 mL) with AcOH (0.1 mL), 150 °C, P_{H_2} = 10 MPa.

^b Our data.

^c RNi—AA, **2a**.

^d RCo—AA, **2b**.

^e Aqueous alkali (4 mL) was added into the modifying solution.

ture data on *ee* for Raney RNi—AA and RCo—AA catalysts are given in Table 1.

As it can be seen from the Table, all the catalysts modified with AA tested (except of L-glutamic acid), possess the asymmetry-inducing properties. Using L- β -phenylalanine as an example, it was shown that the addition of an alkali during modification of the catalysts has low effect on both the degree of conversion and the optical yield of the reaction. Therefore, the rest of experiments with AA was carried out without adding alkali into the modifying solution. The most considerable optical yield (15—17% *ee*) was obtained with L- β -phenylalanine with the degree of conversion being 58—63%. This yield is higher by a factor of ~2 than the *ee* value in the case of hydrogenation of methyl acetoacetate **1a** on RNi—L-Phe (9.2% *ee*)⁸ and considerably higher when other AA were used. The degree of conversion with L- α -alanine is the same as with L- β -Phe (63%), but optical yield decreases

to 1%. In the case of L-histidine and L-arginine, both the degree of conversion (25 and 10%, respectively) and the optical yields (*ee* 1 and 3%, respectively) decrease. In contrast to hydrogenation of methyl acetoacetate **1a** on RNi—L-Glu,^{11,12} hydrogenation of ethyl acetoacetate **1b** in the presence of Ni—Co catalysts with L-glutamic acid virtually does not take place ($Y = 1\%$).

To sum up, the results on hydrogenation of compound **1b** in the presence of powdered Ni—Co catalysts modified with AA differ from the results obtained for individual Ni and Co catalysts. This is another evidence that asymmetric hydrogenation is a complicated reaction with optical yields being dependent on the genesis of dissymmetric catalysts.

The data on the study of effects of NaBr additives during modification of Ni and Ni—Co catalysts with TA on their asymmetry-inducing properties in hydrogenation of ethyl acetoacetate **1b** are given in Tables 2 and 3.

As it can be seen from Table 2, the optical yield of hydrogenation of compound **1b** without addition of NaBr

Table 2. Effect of NaBr additives during modification of Ni catalysts with *R,R*-(+)-tartaric acid on enantioselectivity of hydrogenation of ethyl acetoacetate **1b***

Catalyst	m_{NaBr} /g	P_{H_2} /MPa	$T/^\circ C$	τ /h	Y	<i>ee</i>
						%
Ni	0	11	140	13	100	71
	1	11	140	13	95	53
	3	11	140	13	97	65
	5	11	140	13	98	65
	3	10	130	13	22	7
	6.6	9	100	6	9	52
	6.6	9	130	6	40	39
	6.6	9	130	12	12	23
	6.6	12.5	150	6	9	19
	Co	0	11	140	13	90

* Modification conditions: 1 h 40 min in duration, 97 °C. hydrogenation conditions: ethyl acetate (12 mL) with AcOH (0.1 mL).

Table 3. Effect of NaBr additives during modification of Ni—Co catalysts (9 : 1) with *R,R*-(+)-tartaric acid on enantioselectivity of hydrogenation of ethyl acetoacetate **1b**^a

m_{NaBr} /g	P_{H_2} /MPa	$T/^\circ C$	Y	<i>ee</i>
				%
0	9	100	23	48
1	9	100	6	21
3	9	100	9	34
5	9	100	7	22
10	9	100	0	—
5	12.5	150	60 (14) ^b	22 (34) ^b

^a Modification conditions: 1 h 40 min in duration, 40 °C; hydrogenation conditions: ethyl acetate (12 mL) with AcOH (0.1 mL).

^b Modification temperature, 97 °C.

during modification is 71%, whereas with addition of NaBr (from 1 to 5 g), it is somewhat lower and does not exceed 65% under the same hydrogenation and modification conditions. The degree of conversion is not virtually changed and remains high. Under other hydrogenation conditions and on variation of amount of NaBr, a decrease in both the degree of conversion of compound **1b** and the optical yield is observed.

For Ni—Co catalysts (see Table 3) in the absence of NaBr, the optical yield is 48%, whereas with addition of the salt, both the degree of conversion of compound **1b** and the optical yield decrease with the value of the latter falling to 34%. When the temperature of hydrogenation of compound **1b**, the pressure of hydrogen, and the temperature of modification are elevated, the degree of conversion increases from 23 to 60%, but the *ee* value still does not exceed 34%.

Thus, the asymmetry-inducing properties of powdered Ni and Ni—Co catalysts can not be improved by addition of NaBr into the modifying solution of TA.

There are different opinions on the effect of NaBr on the catalytic activity and efficiency of Ni catalysts in asymmetric hydrogenation. Some authors³ believe that NaBr blocks racemic centers, since the efficiency in asymmetric hydrogenation of the catalysts increases followed treatment with NaBr (the optical yield in the hydrogenation of methyl acetoacetate **1a** increases). In this case, however, the degree of conversion decreases to lower level than in hydrogenation without addition of NaBr. At the same time, no considerable decrease in the degree of conversion was found during study of supported Ni contacts⁴. It was suggested⁴ that NaBr influences the formation of stereodiscriminating centers. For the Raney catalysts, the additional removal of aluminum metal, remaining after the leaching of the Ni—Al alloys is observed, The appearance of nickel ions necessary for the formation of stereodiscriminating centers on the surface is also described. These centers contain the metal in the reduced and nonreduced states, along with a substrate and a modifier.^{1,2}

The absence of a positive effect of NaBr on Ni and Ni—Co catalysts, possibly, is due to the presence of a sufficient amount of nickel and cobalt ions on their surface, which were detected¹³ during the study of the catalyst surface composition by XPS method. At the same time, the amount of stereodiscriminating centers, appar-

ently, decreases upon treatment of the catalysts with NaBr with the concentration of racemic centers remaining fairly high. For these reasons, the degree of conversion remains the same. Our data appear to favor the suggestion on effect of the salt additives for Ni catalysts on the formation of stereodifferentiating centers. For the Ni—Co contacts, the picture is even more complicated, since their surface is enriched with cobalt.¹³

In conclusion, in agreement with the published data,⁵ the addition of NaBr not always has a positive effect on the efficiency of Ni catalysts in asymmetric hydrogenation. This effect has a complicated mechanism, that still is not clear.

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