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Asymmetric hydrogenation on metals

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ABSTRACT. The most recent findings in the field of asymmetric hydrogenation of prochiral compounds with C=C and C=O bonds on dissymmetric catalysts—bimetals and hydrides of intermetallic compounds modified with (*RR*)-(+)-tartaric acid and (*S*)-α-amino acids—are reviewed.

The bibliography includes 121 references.

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I. Introduction

Despite the well recorded progress made in recent years in carrying out asymmetric reactions with the use of chiral metal-complex catalysts, and primarily in the asymmetric hydrogenation of dehydroamino acids on rhodium phosphine complexes, there is continued interest in studies on dissymmetric metal hydrogenation catalysts modified with chiral ligands. This is mainly due to the ease in preparing them and the technological effectiveness of their application. Amongst the disadvantages of dissymmetric heterogeneous catalysts should be included the relatively narrow spectrum of their action; effective systems have so far only been found for the hydrogenation of the carbonyl bond in ketoesters and diketones. Attempts to extend the range of such reactions and substrates have so far not produced the required results, although there are individual reports of the successful asymmetric hydrogenation of prochiral compounds with C=C and C=N bonds.

A significant proportion of current research has been directed at improving dissymmetric metallic catalysts and the preparation of novel, including polymetallic, catalysts that are active in the asymmetric hydrogenation of the C=O bond, an elucidation of their structure, action mechanism, and the general characteristics that make it possible to predict their catalytic and enantioselective properties. In this review† the results of studies carried out over the last years are examined. Previous studies have been reviewed by Klabunovskii and Vedenyapin.[1]

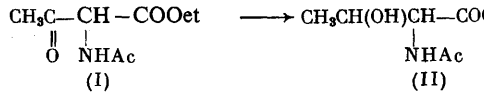
†In this review the following notation is used: Ni–TA is a catalyst modified with (*RR*)-(+)-tartaric acid; Ni-AA is a catalyst modified with an amino acid (Ala—alanine, Val—valine, Glu—glutamic acid, Phe—phenylalanine, Pro—proline, Ile—isoleucine); MAA is methyl acetoacetate; EAA is ethyl acetoacetate; MHB is methyl β-hydroxybutyrate, EHB is ethyl β-hydroxybutyrate, PEA is (*S*)-phenylethylamine.

II. Skeletal nickel catalysts

The skeletal catalysts also known as Raney catalysts have been extensively used in organic synthesis in the hydrogenation of unsaturated organic compounds because of the ease in preparing them and their high activity. Skeletal Ni catalysts exhibit high enantioselectivity in the hydrogenation of prochiral carbonyl compounds.

Skeletal Ni catalysts are obtained by leaching a Ni–Al alloy usually containing up to 50% Ni with a solution of NaOH on heating to 80–100 °C and washing the resulting Ni powder with water. The catalyst is then modified with optically active compounds. The modification process involves bringing into contact a previously reduced catalyst at a given temperature and pH with a solution of the modifying agent—an optically active hydroxyacid or amino acid.

In general, modification of catalysts with chiral compounds can help to increase the selectivity of hydrogenation. Thus ketoacid (I)—a precursor of threonine—can be hydrogenated on Ni–TA with 100% selectivity and with an overall yield of 82% on the *allo*-threonine derivative (II),[2] while hydrogenation of (I) on a skeletal Pd–Cu–TA catalyst containing 15.1% Pd at 75 °C and 50–100 atm results in the yield of *allo*-threonine increasing to 90% while the *threo* isomer is completely absent[3,4]



In the diastereoselective hydrogenation of *D*-fructose to a mixture of sorbitol and mannitol, a catalyst such as the hydride of the intermetallic compound $LaNi_3Co_2$ proved effective only after it was modified with (*RR*)-(+)-tartaric acid.[5]

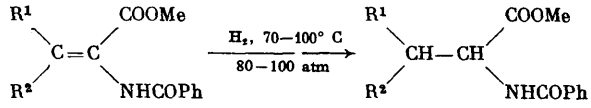
Attempts have been made to use modified Ni catalysts for the synthesis of optically active compounds of practical importance. Thus, for example, optically pure (3*S*,5*S*)-2,6-dimethylheptane-3,5-diol[6] and (*R*)-(−)-3-hydroxytetradecanoic acid (an endotoxin component) were obtained on Ni modified with (*RR*)-(+)-tartaric acid.[7] Modified catalysts were also studied in the synthesis of α-amino acids of practical importance. One of the methods used to synthesise them is hydrogenation of C=C or C=N bonds to the corresponding precursor compounds. However, enantioselective hydrogenation of the C=N bond was ineffective. For example the optical yield‡ of the product derived from hydrogenation of

‡The optical yield (*p*, %) that characterises the enantioselectivity of the reaction is determined from the following equations:

$$p = \frac{([R] - [S])}{([R] + [S])} \times 100 = \frac{[\alpha]^t_{exp}}{[\alpha]^t_{lit}} \times 100\%.$$

acetophenoxime to PEA is only 3.5%,[8] whereas diastereoselective hydrogenation of azomethines is very successful.[9]

A more promising method is the enantioselective hydrogenation of the C=C bond in the (*E*) and (*Z*)-methyl esters of *N*-benzoylaminoacrylic acids in methanol of Ni–(*S*)-AA.[10,11]



(III, a): R^1 = Me, R^2 = Et; (III, b): R^1 = Et, R^2 = Me.

On a Ni–(*S*)-Phe catalyst, Ile containing 70% as the *erythro* form and 30% as the *threo* form is obtained from (*Z*)-(III, a), while Ile containing 60% as the *erythro* isomer and 40% as the *threo* isomer is obtained from (*E*)-(III, b). In the latter case p = 15%.[12] Replacement of Ni–(*S*)-Phe by a Ni–(*S*)-Pro catalyst resulted in an optical purity of p = 8%, while when a Ni–(*R*)-Pro catalyst was used the value of p was only 1.5%. Other amino acids such as Ala, Val, GluOme proved ineffective as modifying agents.

It was recently reported[13] that enantioselective hydrogenation of the C=C bond in (*E*)-PhCH=C(Ph)COONa (30 °C, 1 atm., absolute ethanol) can be carried out on Ni–TA with p = 17.03%. Hydrogenation of the (*Z*)-isomer is less effective.

The poor efficiency of modified Ni–Ta catalysts in a number of cases has been attributed by Harada et al.[14] to the residual content of Al in the skeletal catalysts impairing their enantioselective properties as a result of the formation of considerable quantities of Al_2O_3 or bayerite after leaching of the metal–aluminium alloy. Thus, metals deposited on Al_2O_3, such as Ru/Al_2O_3 modified with (+)-TA did not exhibit enantioselectivity in the hydrogenation of EAA[15] most likely because the formation of highly dispersed X-ray-amorphous metal on the surface of the catalyst.

Studies by Nitta et al.[16] carried out recently showed that only when there is a sufficiently high nickel content (50% or more) deposited on Al_2O_3 can the catalyst be effective in enantioselective hydrogenation.

It was shown by Zubareva et al.[17] that in a 2% Ni/Al_2O_3 catalyst the metal phase cannot be detected by X-ray phase analysis (XPA) because of the formation of an X-ray-amorphous phase. An increase in the content of metal deposited on the surface helps to increase the size of crystallites, and starting with 8% Ni on Al_2O_3 the catalyst modified with TA by now has the ability to cause asymmetric hydrogenation of ethyl acetoacetate (EAA) to ethyl β-hydroxybutyrate (EHB) with p = 3%.

$$\underset{\text{(EAA)}}{CH_3COCH_2COOEt} \xrightarrow{\text{Ni.(+)-TA}} \underset{\text{(}R\text{(−)-EHB)}}{CH_3CH(OH)CH_2COOEt}$$

On increasing the percentage of Ni on Al_2O_3 to 50% (reduction temperature 500 °C, current of $H_2:N_2$ = 1:1, modified with tartaric acid at pH 4.7) the optical yield of (*R*)-(−)-EHB increased to 19.5%.[17] On changing the conditions for preparing the Ni/Al_2O_3 catalyst (reduction temperature 400 °C, current of H_2, modification with TA at 83 °C, pH 4.2) and the hydrogenation (135 °C, 100 atm., ethyl acetate as solvent, EAA:catalyst = 8:1) the composition of the catalyst was found to be 20% Ni/Al_2O_3, and by using it the value of p could be increased to 66–76% with, however, a low degree of conversion (~10%). On increasing the degree of conversion (y) of EAA to 98%, the value of p decreased to 50%.[17]

It was to be expected that the powdered catalysts that are obtained by decomposition of metal salts by the Sabatier method would prove effective in asymmetric hydrogenation processes. Thus, highly effective Ni–TA is obtained by decomposition of Ni nitrate in a current of He with subsequent decomposition of the resulting Ni oxides in a current of H_2 + He (1:10) at 280 °C and modification at 50 °C in a 0.5 solution of TA at pH 5.1.[18] It was not necessary in this case to introduce also into solution NaBr, which is known[19] to increase the enantioselectivity of hydrogenation. Hydrogenation of EAA at 100 °C and 100 atm takes place at a high rate on this catalyst, the rate of formation of excess (*R*)-(−)-EHB (w) being 20.5 mmol (g Ni)$^{-1}$ h^{-1} ($w = pv$). It should be noted that, according to Smith and Misoiu,[20] the optical yield in the hydrogenation of EAA is usually lower than in the hydrogenation of methyl acetoacetate (MAA) under the same conditions, so the optical yield of p = 63–71% obtained on this catalyst may be regarded as quite high.

It was found by XPA of samples of skeletal Ni–(+)-TA catalysts which actively hydrogenate EAA,[21,22] obtained from Ni–Al alloys containing 50.0, 45.2, and 38.3% Ni, that with an increase in the fraction of Ni in the alloy the content of the $NiAl_3$ phase increases, assisting a more effective removal in the leaching of Ni–Al alloys and an increase in the optical purity of EHB. During the reaction the value of p passes through a maximum, which occurs at a degree of conversion of the initial EAA of y = 30–60%. In a number of cases of asymmetric hydrogenation, in particular on Ni catalysts, an antibatic variation of p and y occurred, i.e., the enantioselectivity of reaction decreased as the overall rate of hydrogenation increased.[1] Often during the reaction the initially constant value of p starts to decrease after significant degrees of conversion are reached.[23] This is possibly due to the adsorption inhibition of reaction by both the initial substrate (a fall in p in the hydrogenation of EAA on Ni–TA when the initial concentrations of EAA are increased has been recorded by Lipgart et al.[24]) and the reaction product. In the latter case it is to be expected that this inhibition will differ according to whether a racemic or optically active reaction product interacts with the chiral centre of the catalyst.

For a quantitative determination of this interaction, Chernysheva et al.[25] studied the degree of inhibition of the asymmetric hydrogenation of EAA by the reaction product EHB on a Ni–TA catalyst, and the relative adsorption coefficients were determined by the method of Balandin,[26] according to the equation

$$\frac{1}{v} = \frac{b_2/b_1}{k}\frac{C_2}{C_1} + \frac{1}{k},$$

where k is the rate constant of the reaction, b_1 and b_2 are the adsorption coefficients of the initial EAA and reaction product EHB (or inhibitor) C_1 and C_2 are their concentrations.

It was found that the hydrogenation of EAA is markedly inhibited when even small quantities of EHB are added to the initial EAA. Moreover, some variation in the rates of hydrogenation also occurs when the (−)-enantiometer of EHB instead of racemic EHB is added to the initial mixture. Inhibition by the raction product does not have a significant effect on the ratio of the adsorption coefficients—b_{EHB}/b_{EAA} is usually 0.2–0.3. However, when other compounds, such as thiophene or pyridine, which strongly inhibit the catalyst are added to the initial EAA, b_{EHB}/b_{EAA} varies considerably—from 15 to 25. This ratio increases even more (up to 1400) if the catalyst is first treated with thiophene and then modified with TA. At the initial stages of the reaction when the degrees of

conversion of EAA are no greater than 10%, the introduction of pyridine has a favourable effect on the optical yield of yield—the value of p increases from 2.35 to 13.5%. This suggests that introduction of strongly absorbing compounds which poison the most active unmodified catalyst sites (at small degrees of conversion) increases the proportion of modified sites and thus increases the optical yield.

Similar results were obtained by Yasumori[27] in the hydrogenation of MAA on Ni–TA in the presence of pyridine and also NH_3, Et_3N, $BuNH_2$, whereby with an increase in the amounts of poison the rate of hydrogenation decreased by a factor of 2–3 while the optical yield increased from 11% (without introduction of poison) to 17, 33, 39, and 50% respectively.

According to the results given by Klabunovskii and Vedenyapin,[1] an optically active site must contain an array consisting of regularly ordered metal atoms and molecules of modifying agent and substrate. Hence an enantioselective reaction, according to Budar, is classed as a structurally sensitive reaction and the enantioselectivity should vary in relation to the surface structure. In fact, as was first found for Ru–TA–SiO_2 catalysts,[1] the value of p in the hydrogenation of EAA increased to a given limit with the increase in size of crystallites of Ru (up to 4.5 μm). This observation was subsequently confirmed for Ni–TA/SiO_2 and Pt–quinine/Al_2O_3 catalysts.[28]

The idea[1] that two types of site—optically selective and non-selective—exist on the surface of dissymmetric catalysts was applied in an electrochemical study of the mechanism of the modification of skeletal Ni catalysts with (+)-tartaric acid.[29] The assumption that a selective site is a ternary heteroligand complex of the type metal–modifying agent–substrate, which was first stated by Petrov et al.[30] was subsequently supported in two studies.[29,31]

It was found[32] that modification of Ni catalysts with solutions of chelates such as Ni[(*S*)-Ala]$_2$ and Ni[(*S*)-Glu]$_2$ in the hydrogenation of MAA gives the product MHB with p = 3.7 and 17.4% respectively [these values of p are similar to those obtained on Ni–Ala and Ni–Glu catalysts (p = 4.7 and 15.1%)].

Correlation of the rates of hydrogenation of acetylacetone (AA) and EAA with the hydrogenation of their chelates with Cu, Ni, Co, and Zn on skeletal Ni and Ni–TA showed[33] that both at atmospheric pressure and at 100 atm the rate of hydrogenation of the chelates is lower than the rate of hydrogenation of pure AA and EAA, but the composition of the products is the same, with the rate of hydrogenation decreasing in the series of chelates Cu–Ni–Zn–Co in accordance with the values of the stability constants of the acetylacetonate complexes of these metals. Hydrogenation of Co, Zn, Cu, and Ni acetylacetonates on a Ni–TA catalyst gives an optically active pentanediol with similar values of p, equal to 9.6, 11.1, 10.6, and 12.4% respectively. The difference between the rates of hydrogenation of EAA and Ni(EAA)$_2$ is not so large as for AA and Ni(AA)$_2$, which is due to the lower stability of the Ni(EAA)$_2$ complex compared to Ni(AA)$_2$.

The formation of a ternary complex on the surface of the catalyst was studied by means of IR spectroscopy of the adsorbed molecules.[34–36] It was found that (+)-TA, AA, and Ni^{2+} in solution form a ternary complex in which, according to the IR spectra, the AA molecule experiences an effect from (+)-TA. Comparison of the absorption bands for AA in this complex with the absorption bands for AA adsorbed on the surface of Ni–TA/SiO_2 showed that an AA molecule forming part of an adsorbed complex assumes a shape which is different to that of the pure heteroligand complex in solution. There is an increase in the asymmetry of the substrate molecule as a result of a surface effect, i.e., in this case an achiral factor assists a chiral process.

The steric model of the surface complex proposed previously[1] is supported by IR spectroscopic data on the adsorption of CO on a Ni–TA/SiO_2 catalyst, which show that TA adsorbed on the faces of a Ni crystal inhibits the adsorption of CO. This conclusion is based on the absence of an absorption band at 1940 cm^{-1} that characterises the bridged form of CO adsorption and on the decrease in intensity of the absorption band in the region of 2050 cm^{-1}.[36]

The high enantioselectivity of powdered Ni–TA catalysts in the hydrogenation of EAA is not corroborated during electrocatalysis.[37] Electroreduction of EAA in a monolayer, carried out on Ni–TA deposited on a Pt electrode, took place with 100% conversion but with a low optical yield (p = 8–12%). According to the charge curves, modification of the Ni catalyst reduces the surface area by a factor of 10 (from 4 to 0.4 m^2). In the region of the hydrogen overvoltage the conversion of EAA was 10–25% and p = 8–10%. During electrocatalysis, those sections of the surface (edges and apexes of the crystals) where the intensity of the electrical field is highest would appear to be the most active; however, these sections are least suitable for enantioselective hydrogenation because of the steric hindrance towards orientation of chiral clusters, which require quite an extensive area.[1]

At the same time, in the electroreduction of phenylglyoxylic acid in the presence of strychnine,[38] for example, it would appear that in a double electrical layer asymmetric synthesis occurs with considerable efficiency ($p \sim 20\%$).

III. Dissymmetric bimetallic catalysts

Dissymmetric bimetallic catalysts are of considerable interest both from the practical viewpoint (the possibility of synergism occurring for catalytic and enantioselective properties) and from the theoretical point of view, since the possibility arises for studying the influence of their phase state, cluster, and ligand effects on the catalytic and dissymmetric properties of these catalysts.

Bimetallic and modified dissymmetric catalysts were first studied in the case of Cu–Ru catalysts.[1] Systems based on Ni were subsequently developed.[39]

Dissymmetric Ni–Cu powdered catalysts without a support, modified with TA, displayed high enantioselectivity in the asymmetric hydrogenation of EAA. Their efficiency depends to a significant extent on their genesis and the reaction conditions.

Zubareva et al.[39–42] studied the hydrogenation of EAA in the presence of powdered Ni–Cu–TA catalysts which were prepared by reduction of mixtures of Ni and Cu oxides (nickel–copper catalyst, NCC-1), hydroxides (NCC-2), or carbonates (NCC-3) in hydrogen or a mixture of H_2 + N_2. It was established that varying the nature of the initial salts leads to a change in the phase and surface composition of the catalysts obtained, and the ratio of reduced to non-reduced forms of the phases of Ni compounds in an NCC is a factor that affects the magnitude of the optical yield. As is shown in Table 1, the NCC-1 catalyst consists of phases of solid Ni–Cu solutions enriched with Ni or Cu and a small quantity of NiO (~5%). In precipitated NCC-2 and NCC-3 catalysts, Cu and Ni form separate phases, as a result of which there is a sharp increase in the total hydrogenating activity of these catalysts. For catalyst samples that were reduced in a current of pure H_2, in which Ni, according to the XPA data, occurred in a reduced state, the value of p did not exceed 20–24% and did not depend on the

nature of the initial compounds used to prepare the catalysts. With reduction in a current of $H_2 + N_2$ the optical yield for NCC-1, NCC-2, and NCC-3 was 50.0, 14.4 and 8.4% respectively. The fact that a small quantity of NiO is contained on the surface of NCC-1 [up to 10% according to the results of X-ray photoelectron spectroscopy (XPES)] evidently assists complexation with TA. However, the presence of fairly large quantities of NiO in NCC-2 and NCC-3 leads to a reduction in p.

Table 1. Effect of conditions of formation on the catalytic and enantioselective properties and phase composition of nickel–copper catalysts (NCC) modified with (*RR*)-(+)-tartaric acid in the hydrogenation of EAA.[41]

Catalyst*	H_2/N_2**	S_{sp}, $m^2 g^{-1}$	$A \times 10^2$, (mmol m^{-2} min^{-1})	p, %	Composition of NCC from X-ray phase analysis, wt. %							
					Phase 1		Phase 2		Cu	Ni	NiO	CuO + Cu_2O
					Cu	Ni	Cu	Ni	the rest consists of phases 1 and 2			
NCC-1	0.1	9.3	0.6	50.0	23.3	76.7	79.4	20.6			5.1	–
NCC-2	1	1.3	10.6	24.2					48.2	48.2	–	3.6
	0.1	1.5	8.5	14.4					49.8	26.0	22.4	1.8
NCC-3	1	1.3	11.8	21.3	23.3	76.7	85.4	14.6	23	35.2	–	1.6
	0.1	0.7	24.3	8.4	–	–	86.0	14.0	39	20	27.5	–

* Catalysts NCC-1, NCC-2, and NCC-3 were obtained by reduction of Ni and Cu oxides, hydroxides, and carbonates respectively.

** Composition of gas flow during reduction of catalysts.

According to the XPES data[41] (in the region of Ni3p and Cu3p) the ratio of surface concentrations of Ni/Cu is close to 1.5 in the initial NCC-1 (Fig. 1*a*, curve *2*). In NCC-2 the surface layer is enriched with copper in the form of Cu^0 (curve *2*). After modification of both catalysts their surface is enriched with nickel—for NCC-1 the ratio of Ni/Cu is 1.3 while for NCC-2 the ratio of Ni/Cu is equal to 2. From the spectra in the region of Ni2p and Cu2p (Fig. 1*b* and 1*c*) it follows that the Cu and Ni atoms in NCC-1 are in a reduced state (with a small quantity of NiO). Moreover, it follows from the shift in Ni2p lines (Fig. 1*b*, curve *3*) that a certain proportion of Ni in modified NCC-2 changes to the Ni^{2+} oxidation state, which is consistent, according to the results of Balandin,[26] with the spectrum of nickel oxide NiO modified with TA. Thus, on the surface of NCC-1, which displays the highest enantioselectivity, Ni^0, Cu^0, and Ni^{2+} sites occur.[42] This conclusion is consistent with the results obtained by Zubareva et al.[42] for Ni–TA/SiO_2 catalysts, for which the presence of Ni^0 and Ni^{2+} sites on the surface of the catalyst has been demonstrated.[43]

The effect of the conditions for reducing Cu and Ni oxides obtained by decomposition of the nitrates on the enantioselectivity of these mixed catalysts modified with (+)-TA in the hydrogenation of EAA (100 °C, 100 atm) was studied by Klabunovskii et al.[44] According to differential thermal analysis data, the reduction of NiO and CuO occurs at the same time in the mixture, despite the difference in reduction temperatures of the individual oxides (320 and 270 °C respectively). It was established that the value of p does not depend on the time of reduction of the catalyst if modification is carried out at 50 °C and pH 5.0 but it increases slightly with an increase in time of reduction from 51 to 65% when modification is conducted at pH 10.0. Reduction at higher temperatures results in more complete alloying and homogenisation of the alloy.[45] However, the maximum value of p is reached when the oxides are reduced at 220 °C. It was established[46] that Ni–Cu catalysts contain two phases—a Cu phase and a Ni–Cu alloy phase. With an increase in the Cu content in the catalyst, the Ni–Cu alloy phase is enriched with nickel in bulk and with copper on the surface. According to the results of Klabunovskii et al.,[47] the hydrogenating activity of (70% Ni–30% Cu) catalysts is 5 times higher than that of a pure nickel catalyst, while the activity of the latter is 5 times higher than the activity of a Cu catalyst. However, the enantioselectivity of a (70% Ni–30% Cu) catalyst proved to be lower than that of Cu–TA (p = 50%) and Ni–TA (p = 33%) catalysts. Thus, in bimetallic Ni–Cu catalysts synergism occurs in the total catalytic activity but not in the enantioselectivity.

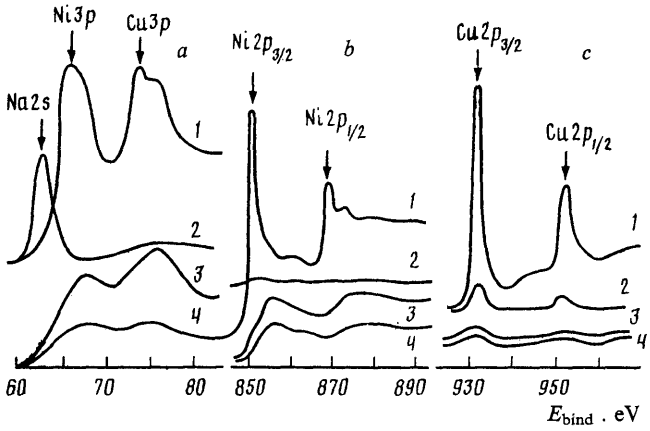


Figure 1. X-Ray photoelectron spectra of nickel–copper catalysts[41] in the region of Ni3p and Cu3p (*a*), Ni2p (*b*), and Cu2p (*c*). *1*, Initial NCC-1; *2*, initial NCC-2; *3*, NCC-1 modified with (*RR*)-(+)-tartaric acid; *4*, NCC-2 modified with (*RR*)-(+)-tartaric acid.

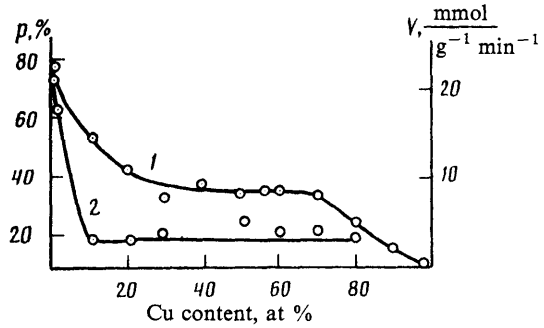


Figure 2. Dependence of the rate of hydrogenation of EAA (curve *1*) and optical yield (curve *2*) on the composition of dissymmetric Ni–Cu catalysts modified with (*RR*)-(+)-tartaric acid.[44]

Increasing the Cu content in a mixed Ni–Cu catalyst deactivates the catalyst, since Cu as an inactive component dilutes the Ni sites[44] that are responsible for the enantioselectivity of reaction. If the specific activity is attributed solely to the Cu–Ni alloy phase over the range 20–80% Cu (Fig. 2), the value of p and the specific rate remain constant, which is an indication of the constant magnitude of the surface concentration of the active component in a Ni–Cu catalyst. The value of p is little affected by both the phase state and the total hydrogenating capacity of Ni–Cu catalysts, in contrast to pure Ni catalysts, in which the enantioselectivity is strongly dependent on these factors.

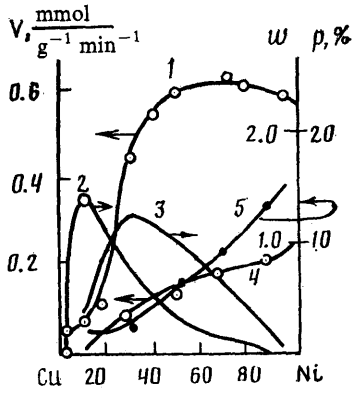


Figure 3. Dependence of the rate of hydrogenation v (curves *1* and *4*), the optical yield p (curves *2* and *5*), and rate of formation w of excess (–)-enantiomer (curve *3*) on the composition of Ni–Cu catalysts modified with (*S*)-phenylalanine (curves *1*, *2*, and *3*) and (*RR*)-(+)-tartaric acid (curves *4* and *5*) in the hydrogenation of EAA.[48]

The fact that on increasing the proportion of Ni in a Ni–Cu catalyst the latter segregates on the surface is apparently supported by data[48] on the hydrogenation of EAA on a Ni–Cu catalyst modified with (*S*)-phenylalanine (Fig. 3, curves *1–3*). In fact, whereas (*S*)-(+)-EHB is formed on Cu–(*S*)-Phe, the other enantiomer, (*R*)-(–)-EHB, is formed on Ni–Cu–(*S*)-Phe even with a Ni content of 10–15%, as on a Ni–(*S*)-Phe catalyst. The conclusion that Ni segregates on the surface of a Ni–Cu catalyst is also supported by the correspondence of the maxima on the curves plotting the change in w and the content of surface H_2 in Cu–Ni catalysts, which according to Takai[49] have a Ni content in the Ni–Cu catalysts ranging from 20 to 40%. The effect of the pH of the modifying solution of TA on the value of p for Ni and Ni–Cu catalysts for all compositions[44,50] is evident in the appearance of two maxima for p at pH 6 and 10.5.[50] For a pure Ni–TA catalyst p is equal to 57% (pH 5) and 71% (pH 10), while for a Ni–Cu–TA catalyst p = 20% (pH 5) and p = 22% (pH 10) (Fig. 4). This type of dependence of p on the pH of the modifying solution is substantially different from that reported previously for Ni,[1,48] when only a single maximum for p was found.

The introduction of just 10–15% Cu into Ni–TA sharply reduces the values of y and p. This demonstrates that Cu cannot be regarded as simply an inert component of the catalyst. It would appear that when there is a large content of Cu, it breaks up the dissymetric clusters[50,51] that are responsible for asymmetric hydrogenation and which consist of several surface atoms of Ni in a different valence state.

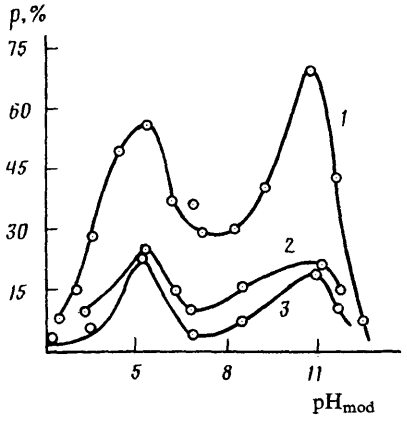


Figure 4. Dependence of the optical yield of (–)-EHB on the pH of the modifying solution of (*RR*)-(+)-tartaric acid.[44] Catalysts: *1*, Ni; *2*, Cu(50%)–Ni(50%); *3*, Cu(20%)–Ni(80%).

It was shown by Vedenyapin et al.[36] that tartaric acid forms complexes on the surface of Ni/SiO_2 and Cu/SiO_2 catalysts, and the value of ν_{COO^-} in the region of ν_{as} at 1600 cm^{-1} and ν_s at 1400 cm^{-1} for Ni/SiO_2 and Cu/SiO_2 catalysts modified with TA at pH 5 and 10 does not differ by more than 10 cm^{-1}, which suggests that there is a similar type of coordination of the COO^- group in TA. This is supported by the fact that for Ni/SiO_2 catalysts modification at pH 5 and 10 leads to the highest and approximately equal values of p. It should be noted that a change in the temperature of modification and concentration of TA solution has no effect on the type of adsorption of TA on Ni and Cu.[36] The same type of effect of the pH of the modifying solution of TA on p for Ni and Cu–Ni catalysts supports the assumption that the structure of the dissymmetric sites remains unchanged on introduction of different quantities of Cu to the composition of the catalyst. When both acidic and alkaline modifying solutions are used, two types of dissymmetric clusters having similar enantioselective properties are formed on the surface of the catalyst. It can be assumed from this that copper does not exhibit a ligand effect in Cu–Ni catalysts and the properties of the dissymmetric clusters do not change; its introduction only changes the number of such clusters.

According to Klabunovskii and Vedenyapin,[1] a dissymmetric cluster is located on specific sites of the surface, which makes it possible for contacts to occur between the metal, modifying agent, and substrate with the minimum steric hindrance. These sites can be steps on the crystallographic faces of the metal, which accounts for the high sensitivity of asymmetric hydrogenation to the structure of the active surface of the catalyst and in particular the size of the metal crystallites. This is supported by the dependence of p on

reaction temperature and on the concentration of hydrogen in the reducing atmosphere in the reduction of oxides (a decrease in the ratio of H_2:He increases p from 11 to 19%), since these factors affect the rate of formation of a Ni–Cu metal catalyst, its phase composition, the structure of the surface, the size of the metal particles, and hence the steric hindrance and magnitude of the optical yield.

It follows from the dependence of p, v, and w on the composition of Ni–Cu catalysts that the sites of enantioselective hydrogenation contain 4 times more active formations (atoms, clusters) than sites of non-selective hydrogenation.[52] It is assumed in this case that only one enantiomer is formed on the enantioselective sites.

Dissymmetric Ni–Co catalysts have been investigated in a number of studies.[53,54] On a skeletal Co catalyst modified with TA, the optical yield in the hydrogenation of EAA did not exceed 5–8%.[1] At the same time, it was found that intermetallic compounds (IMC) (for example, $LnNi_5$) modified with TA display considerable enantioselectivity in this reaction only after the introduction of cobalt into their composition (in this case the value of p reaches 52% or more).[55] It was to be expected that the introduction of Co would assist the segregation of Ni on the surface of the IMC, thus increasing the enantioselectivity of the catalyst. Therefore it was of interest to study the effect of genesis of Ni–Co–TA catalysts of different compositions on their enantioselective properties in the hydrogenation of EAA. In order to do this, a study was made of powdered Ni–Co catalysts obtained by decomposition of Ni and Co acetates or nitrates at 450 °C and by reduction of the resulting mixed oxides at 350 °C in a current of H_2 or H_2 + He for 1.5 h. Modification was carried out with a 5% solution of TA at pH 4.5–5.0.[56,57] Hydrogenation of EAA was carried out at 20–80 °C and 25–100 atm in a solution of ethyl acetate with added acetic acid.[56] Under these conditions a Co–TA catalyst did not exhibit enantioselectivity, but when 20% Ni was introduced into the catalyst the optical yield reached 3.6%, introduction of 50% Ni gave p = 6.3%,[53] and introduction of 80% Ni gave p = 9–15%.[57] A variation in the conditions for preparing the catalysts did not result in any improvement in their enantioselective properties whereas a change in the pH of modification and the nature of the solvent used in hydrogenation had a considerable effect on the values of p and y.

The conditions were found (120 °C, 110 atm) at which an increase in the content of Ni in Ni–Co catalysts to 50% increased the optical yield to 46–50% [58] (for Ni–TA catalysts under these conditions p = 65%, with a conversion of EAA close to 100%). This shows that, as in the case of Ni–Cu catalysts, the Ni component of the catalyst is mainly responsible for asymmetric hydrogenation, so that even a small increase in its content in Ni–Co catalysts markedly increases their enantioselectivity.

Thus, a Ni–Co system is considerably different in terms of its enantioselective action to the corresponding IMCs based on La, Ni, and Co, in which, on the other hand, an increase in the content of Co rather than Ni [for example, in the series $LaNi_3Co_2$–$LaNi_2Co_3$, which correspond to the systems 67% (60% Ni–40% Co)/La and 67% (40% Ni–60% Co)/La]§ results in an increase in optical yield in the hydrogenation of EAA.

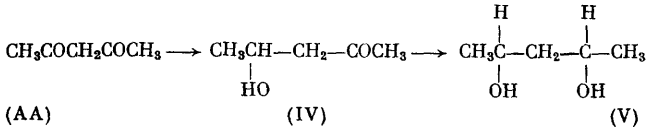
Ni–Co catalysts were tested in the practically significant reaction involving hydrogenation of an equilibrium mixture of menthone–isomenthone (70:30) to isomeric menthols. On unmodified Ni, Co, and Ni–Co catalysts the reactions occur most effectively in an aqueous medium, the conversion reaching 99%.[59] The maximum yield of racemic menthol (40–44%) was obtained on Ni and Ni–Co catalysts in an alkaline medium. Modification of these catalysts with a solution of TA reduced the rate and selectivity of the reaction, although in the hydrogenation of EAA the samples of modified catalysts exhibited high enantioselectivity—p = 65% on Ni–TA and p = 54% on (90% Ni–10% Co)–TA.[60]

In the hydrogenation of the same mixture on a Co–TA catalyst it was possible to obtain up to 80% of neoisomenthol,[61] which is difficult to prepare, whereas on Ni, Pd, Rh, and copper chromite catalysts, neoisomenthol was not formed during hydrogenation in the gaseous and liquid phases.[62]

Supported dissymmetric catalysts based on Ni are of definite interest since they make it possible to study the asymmetric adsorption of the modifying agent and substrate on the surface of the catalyst by means of IR spectroscopy of the adsorbed molecules and to elucidate a number of questions concerning the theory of a strong interaction between metal and support. As has been demonstrated above, supported dissymmetric catalysts are less effective than skeletal ones,[1] especially when Al_2O_3 is the support, and only by increasing the content of metal on the support (up to 50% for Ni)[16,63] or by selecting special conditions of preparation (see below) is it possible to obtain an enantioselective catalyst.[17]

This may be due, as in the case of bulk catalysts, to the effect of an increase in the size of the crystallites[63] or to the diffusion of TA into the pores during modification of the catalyst.[64] For a clear demonstration of the effect of crystallite size on the enantioselectivity it is necessary to vary the size of the crystallites when there is a constant degree of covering the surface of the support with metal. In addition, it is known that, apart from the average dimensions of the crystallites, their distribution in size plays an important part, since crystallites of a smaller size are responsible for a greater activity but a lower enantioselectivity.

A bimetallic Ni–Cu–TA catalyst deposited on an Aerosil support that was active in the asymmetric hydrogenation of acetylacetone (AA) was first reported by Klabunovskii.[65] The conditions were found at which hydrogenation occurred selectively with the formation of only the (*R*)-(−)-ketol (IV) with p = 9.1% without the presence of diol (V).[65]



(AA) (IV) (V)

(Ni–Cu–TA)/Aerosil and Ni–TA/Aerosil catalysts were also studied in the hydrogenation of EAA.[65] It was found that with an increase in Ni content on the support the optical yield and rate of formation (w) of excess (−)-EHB increased, while the rate of formation of EHB racemate v_r ($v_r = v - w$) passed through a maximum (Fig. 5). This occurs because the increase in Ni content on the support is accompanied by an increase in the total surface of the unmodified part of the metal phase. On increasing the Ni content, the surface area starts to diminish as a result of the enlargement of Ni particles from small crystallites of Ni that are inactive in asymmetric hydrogenation. This was demonstrated for both Ni[66] and Ru–TA catalysts.[1] Thus, the optical yield (small in the case of dilute catalysts) increases with an increase in metal content on the surface of the support.[43] This may account for the

§ This representation of the catalyst composition denotes a 67% metal content (60% Ni and 40% Co) on the surface of La.

high efficiency of catalysts with a large content of metal on the support.[16] The nature of the support also has a considerable effect on the enantioselective action of the catalyst. Thus, it was found for Ni/support (1 : 1) catalysts that were active in the enantioselective hydrogenation of MAA that there was a decrease in optical yield in the following series of supports (p in brackets, %): no support (57) > SiO_2 (56.2) > zeolite Y (45.6) > Al_2O_3 (43.7) > kieselguhr (29.1) > MgO (6.1) > TiO_2 (3.1). In the same series the degree of interaction between Ni and the support increases, which during reduction of the catalyst inhibits the growth of the large crystallites which increase the enantioselectivity of the process.[43]

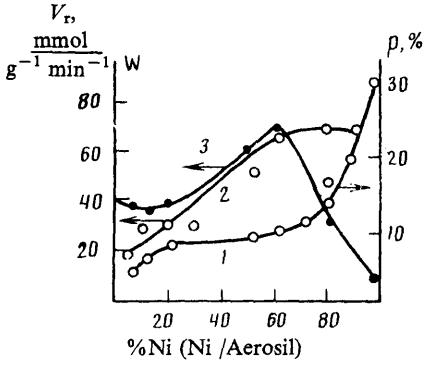


Figure 5. Dependence of the optical yield p (*1*), the rate of formation w of excess (−)-EHB (*2*), and the rate of formation v_r of the racemate of EHB (*3*) on the content of Ni in Ni−TA/Aerosil catalysts during the hydrogenation of EAA.[65]

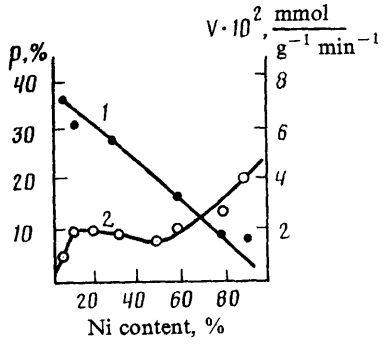


Figure 6. Dependence of the rate of hydrogenation (curve *1*) and optical yield (curve *2*) on content of Ni on the support in the hydrogenation of EAA on a Ni−TA/Aerosil catalyst.[67]

Vedenyapin et al.[67] studied catalysts obtained by impregnating supports [silica gel, Aerosil (120 m^2 g^{-1}), and kieselguhr (7.8 m^2 g^{-1})] with a solution of salts and then reduced in a current of H_2 at 380 °C. It was established that the enantioselectivity of these catalysts depend on the nature of the support, decreasing from 9% to zero in the following series: Aerosil > kieselguhr > silica gel. The average diameter of the particles ($\overline{D}$) decreases in the same series: 22, 17, and 12 nm respectively. Introduction of only 5% Cu into a 5% Ni/Aerosil catalyst leads to a decrease in $\overline{D}$ to 2−3 nm, which causes a reduction in p from 4.1 to 3.3%.

On increasing the Ni content on the support from 10 to 60% the value of $\overline{D}$ increases from 8−11 to 120 nm. This increase in $\overline{D}$ has hardly any effect on p, but with a further increase in Ni content, p increases while the rate of hydrogenation falls (Fig. 6). The fact that powdered Ni metal catalysts under these conditions give EHB with p = 50−60% demonstrates the complex nature of the dependence of p, whose increase cannot be solely related to the growth of the Ni crystallites. The depositing of Ni on a support results in an increase in the degree of dispersion of the metal phase and a reduction in p. This "inhibiting" effect of the support (Aerosil) occurs with a Ni content of up to 80%.

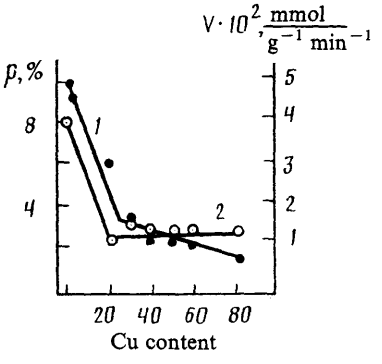


Figure 7. Dependence of the total rate of hydrogenation (curve *1*) and the optical yield (curve *2*) in the hydrogenation of EAA on Ni−Cu−TA/Aerosil catalysts on their Cu content.[67]

For Ni−Cu/Aerosil catalysts (Fig. 7) the values of p and v fall sharply when even small quantities of Cu are introduced. This effect had been observed previously[68] for bulk (powdered Ni−Cu−TA catalysts. This may occur because Cu under these conditions is inactive in the hydrogenation of EAA, but assists an increase in the degree of dispersion of the metal phase. From IR spectroscopic studies of supported Ni−Cu−TA catalysts it was possible to obtain information about the coordinate interaction between the metal phase and the molecule of modifying agent. IR spectra of adsorbed TA and AA on 20% (Ni−Cu)/Aerosil catalysts with a varying composition of Ni−Cu showed that in the interaction between TA and the Ni−Cu phase adsorption of both COOH groups of tartaric acid occurs, but to an unequal degree. This follows from the dependence of the spectroscopic characteristics of the Ni−Cu catalysts on their composition, and the bond between TA and metal which has the least covalent character occurs for Ni−Cu catalysts of composition 1 : 1.[36,69,70] The proximity of the COO^- vibration frequencies in the regions of 1600 and 1400 cm^{-1} for catalysts that are modified at pH 5 and 10 indicates the similar nature of the coordination of COO^- with the metal phase in both cases, which also results in similar values of p (in the hydrogenation of EAA, for example).[68] Substantial differences in the spectra of TA adsorbed on

Ni (1751 and 1275 cm^{-1}) occur if the surface of Ni is treated with TA in the presence of NaBr, in the latter case TA is adsorbed in the form of carboxylate ions (1416 and 1257 cm^{-1}).[71]

Supported dissymmetric bimetallic catalysts based on ruthenium have been the subject of a number of studies.[72-77] It was in the case of skeletal Cu–Ru catalysts modified with TA that the possibility of using bimetallic dissymmetric catalysts in enantioselective hydrogenation was first demonstrated.[72]

Since Cu does not adsorb hydrogen, the magnitude of the surface area of Ru in these catalysts could be determined electrochemically from the charge curves for H_2 adsorption by galvanostatic and potentiodynamic methods in KOH and H_2SO_4.[73]

Hydrogenation of EAA in the liquid phase on Cu–Ru–TA occurs enantioselectively, but p falls from 17–20% for pure Cu to 0.6% when even 0.5% Ru is introduced into the catalyst and then increases to 2.5% on a Ru–TA catalyst (with an increase in H_2 pressure the value of p increases slightly).[74] As the Ru content increases, the size of the crystallites first increases then diminishes, the specific surface increasing at the same time.[75] The effect of the size of crystallites of a metal catalyst on enantioselectivity was first demonstrated by these experiments,[1] and this was confirmed subsequently in a number of studies.[28,66]

A study of supported 10% (Cu–Ru)/Aerosil catalysts with a variable ratio of Cu:Ru in the liquid-phase hydrogenation of EAA (90 °C, 100 atm) showed that an antibatic relationship occurs between v and p, whereby when Ru:Cu = 4:6 falls from 4% to almost zero, while at the same time v increases linearly.[76,77] Under these conditions a Cu–TA/Aerosil catalyst does not hydrogenate EAA asymmetrically [whereas a skeletal Cu–TA catalyst gives (–)-EHB with p = 17%] [78] and only Cu–Ru–TA catalysts with Ru:Cu = 4:6 exhibit enantioselectivity, which suggests that there is synergism in the enantioselective action of Ru–Cu catalysts as a result of the activation of Cu in a mixed catalyst over a given Cu–Ru composition range.

This assumption about the enantioselective activity of just the Cu atoms in Cu–Ru/Aerosil catalysts is consistent with a dependence of p on pH of the modifying solution that is typical for a skeletal Cu–TA catalyst. Optically active (*R*)-(–)-EHB with p = 12% is obtained in the modification of a Cu catalyst only in the region of pH 3–7 with a maximum value of p at pH 5.[68]

A characteristic feature of Cu–Ru catalysts is that the value of p, as in the case of Ni–TA catalysts, depends on the total metal content on the support (with a constant Ru:Cu ratio, equal to 2:8). An increase in metal content from 5% (Cu+Ru) to 15% reduces p from 25 to 4%, and with a further increase in metal content p falls to zero, while retaining, however, quite a high overall rate of hydrogenation. The results obtained can be regarded as an indication that there are two types of sites on the surface of a bimetallic catalyst—inactive but stereospecific Cu sites and highly active but non-stereospecific Ru sites. Despite the lack of mutual solubility between these two metals, Cu and Ru are in close contact in supported catalysts, according to Sachtler,[79] possibly in the form of bimetallic clusters.

In skeletal Cu–Ru–TA catalysts Cu has an effect on Ru but the reverse action of Ru on Cu does not occur, which is attributed to the difference in the structures of supported and skeletal catalysts. In the latter a structure is formed that assumes the covering of the Cu phase by the Ru phase. Correlation of data obtained for Ru/SiO_2 and Ru/Al_2O_3 catalysts indicates the effect of supports on the activity of catalysts and their adsorbing capacity relative to hydrogen.

In a study of skeletal Ru that contained a small quantity of bayerite [$Al(OH)_3$] after leaching of a Ru–Al alloy, it was established that metallic Ru interacts with hydrated Al_2O_3, the Ru atoms being located close to the OH groups of bayerite, thus achieving a high degree of dispersion of Ru and the possibility of chiral modification of the catalyst when it is treated with TA,[80] whereas Ru/Al_2O_3 undergoes virtually no chiral modification.[1] These conclusions were based on a study of the spill-over of hydrogen on these catalysts. In skeletal ruthenium catalysts a more uniform distribution of metal particles and OH groups is achieved, and their interaction is more intimate than with supported catalysts. The possibility of chiral modification of the former has been attributed to this.[80]

Because of the small asymmetrising activity detected in bimetallic catalysts based on ruthenium, it was of interest to study other bimetallic systems containing Group VIII metals, in particular, palladium.

Skeletal Cu–Pd catalysts of different compositions were obtained and studied in the hydrogenation of EAA. The catalysts were obtained by leaching of a Cu–Pd–Al alloy (70% Al), and they contained Cu and Pd phases, their solid solution, and bayerite (about 40–58%). An increase in Pd content from 5 to 100% additively increase the rate of hydrogenation of EAA (100 °C, 100 atm).[81] A more complex relationship between activity and enantioselectivity occurs when there are small quantities of Pd present (up to 5% Pd). In the region of 1–5% Pd the values of w and p pass through a maximum.[82] From an electrochemical study of the catalysts using charge curves and $i\varphi$ curves it was possible to determine the quantity of hydrogen adsorbed on the catalyst. The curve showing the dependence of the ratio of H:(Pd + Cu) on the content of Pd (%) for catalysts with a Pd content of less than 10% deviates from linearity, displaying a decrease in adsorption of hydrogen on catalysts with this composition. This is attributed[81] to a screening of the Pd phase (or Cu–Pd alloy) by the Cu phase, which is supported by the results of enantioselective hydrogenation. Only catalysts containing less than 5% Pd exhibit enantioselectivity in the hydrogenation of EAA, and when the content of Pd is increased from 1 to 5 at.%, p decreases from 9 to 1%.

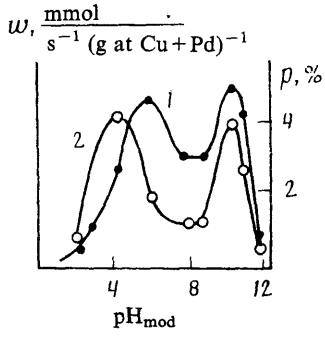


Figure 8. Dependence of the rate of formation of excess (*R*)-(–)-EHB (curve *1*) and optical yield (curve *2*) on the pH of a solution of (+)-tartaric acid during modification of a Pd(2.7%)–Cu(97.3%).

Two optimum regions of pH of the modifying solution were established by Vedenyapin et al.[82] At pH 5 and 10 the values of p were 4.1 and 4.6 % respectively in the hydrogenation of EAA on a Cu–Pd–TA catalyst containing 2.7% Pd (Fig. 8).

By carrying out the hydrogenation of EAA in ethanol solution it is possible to increase p slightly, as occurred for Co–TA catalysts.[83] However, this solvent effect proved insignificant for Cu–Pd–TA catalysts—p remained at a level of 2–3% and only the total rate of hydrogenation increased. It should be noted that, despite the results of Sachtler,[64] the rates of hydrogenation of pure EAA on modified and unmodified Cu–Pd catalysts proved to be similar, whereas the rate of hydrogenation of EAA in ethanol on a modified catalyst is higher than its rate of hydrogenation on an unmodified catalyst.

On changing the Pd content in Cu–Pd–TA catalysts, the values of p and w pass through a maximum at a level of 2% Pd (Fig. 9), while on changing from skeletal Cu–TA to Cu–Pd–TA p falls from 15 to 4–5%.

Thus, as in the case of Cu–Ru catalysts, a deviation from additivity occurs when small quantities of Pd are introduced into a Cu catalyst. With a Pd content of about 5% the specific rate, relative to 1 m^2 of surface of the Pd phase, increases by a factor of about 150 compared to the rate of hydrogenation on pure Pd. This may be regarded as evidence that in a bimetallic catalyst the properties of copper vary markedly when it is promoted by palladium, and it acquires a capacity to hydrogenate EAA and make a contribution to both the total rate and the rate of enantioselective hydrogenation.

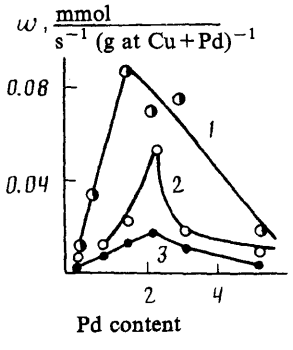


Figure 9. Dependence of the rate of formation of excess (*R*)-(−)-EHB on the composition of Pd–Cu catalysts in ethanol (curve *1*) and without a solvent (curves *2* and *3*) at pH_{mod} 4.5 (curves *1* and *2*) and pH_{mod} 10.5 (curve *3*) during hydrogenation of EAA.[82]

A comparison of different dissymmetric catalysts containing copper, such as Cu–Pd and Cu–Ru, reveals considerable differences between them. While the presence of only 0.1–0.5% Ru in the case of Cu–Tu–TA causes almost complete suppression of enantioselectivity, this suppression in Cu–Pd–TA catalysts only occurs when more than 5 at.% Pd is added. The total activity of Cu–Ru catalysts increases with an increase in Ru content, whereas on Cu–Pd synergism of catalytic action occurs, which may be due to a difference in structure of the active phase and dependent on a ligand effect.[81,82] A similar effect was detected for skeletal Cu–Ru–TA catalysts. Comparison of Cu–Pd and Cu–Ru catalysts by an electrochemical study of the adsorption of H_2 on them showed that with an increase in Cu content in the catalysts the strength of the Ru–H and Pd–H bonds decreases. The maximum on the $i\varphi$ curves is shifted to lower potential when copper is introduced into a Ru or Pd catalyst, which suggests that they interact electronically, i.e., there is a ligand effect.[84]

In contrast to the phase composition of Cu–Ru catalysts, for which a sandwich structure has been accepted (the surface is mainly covered with Ru atoms), the surface of Cu–Pd, according to electrochemical data,[82] is enriched with copper when Pd < 5%, which assists the formation of Cu–Pd clusters that provide synergism of catalytic action of such a catalyst through the ligand effect. This leads to a change in state of the Cu atoms, resulting in not only their high catalytic activity but also the distinctive dependence of p on the pH of modification.

Kuznetsova et al.[85] studied copper–palladium (CPC) and nickel– palladium (NPC) catalysts deposited on A-300 Aerosil and on γ-Al_2O_3. The catalysts were obtained by impregnation of the support with solutions of Cu^{2+} and Pd^{2+} or Ni^{2+} and Pd^{2+} salts, reduction in a current of H_2/He (1 : 10) at 360 °C, followed by modification at pH 5 and 50 °C with a solution of TA (method A) or by modification of reduced Cu/SiO_2 and Ni/SiO_2 catalysts with a solution of $PdCl_2$ + TA (method B).

Table 2. Activity and enantioselectivity of supported catalysts modified with TA in the hydrogenation of EAA.[85]

Catalyst	Optical Yield, p, %	Activity $A \times 10^2$ mmol (g cat)$^{-1}$ min^{-1}
10% Pd/SiO_2	0	18
10% Ni/SiO_2	7.1	9
(2% Pd–8% Cu)/SiO_2	0	5
(1% Pd–10% Cu)/SiO_2	1.6	5
(1% Pd–9% Ni)/SiO_2	7.0	8
(1% Pd–10% Ni)/SiO_2	4.6	11

It was established that asymmetric hydrogenation with p = 1.6% only occurred on the CPC obtained by method B and not by method A, which is apparently due to the presence of Pd^{2+} ions on the surface of the catalyst that can form a complex with TA. In the case of the NPC, regardless of the method of preparation (A or B), an enantioselective reaction occurred with p = 7 and 4.6% respectively. It should be noted that under these conditions a nickel catalyst—(10% Ni–TA)/SiO_2—also exhibited low enantioselectivity (Table 2), while in all cases replacement of SiO_2 by Al_2O_3 led to complete inhibition of the asymmetric activity of the catalyst.

IV. Dissymmetric intermetallic catalysts

Multicomponent hydrogenating metal catalysts—intermetallic compounds (IMCs) of rare earth elements (REEs) with Ni, Co, Cu, and other *d*-metals and their hydrides—are of interest for

asymmetric catalysis as cluster models, in a similar manner to bimetallic systems.

A study was made of two structural types of IMC enriched with nickel—LnM_3 and LnM_5.[65] Comparison of $LnNi_5$ catalysts (Ln = La, Sm, Gd, Ce, Pr, Nd) with Ni catalysts deposited on the oxides of the same REE demonstrated the high activity of IMCs and their hydrides in the hydrogenation of propylene, the greatest activity (1 atm, 100 °C) being exhibited by $LaNi_5$ [86] and the least activity by $CeNi_5$.[87] The specific activity of the hydrides of IMCs such as $LaNi_5$ and $LaCo_5$ is ten times higher than that of a supported 5% Ni/CeO_2 catalyst.[88] In this case the catalytic activity is higher the lower the equilibrium pressure of hydrogen in the system $IMC-H_2$, i.e., the more stable the hydride,[89] which was demonstrated for a $LnNi_5$ series of IMCs (Ln = La, Ce, Pr, Nd, Sm) and for $La_{1-x}Pr_xNi_5$.[89–91]

According to XPES data and magnetic measurements, segregation of Ni and its enrichment of the surface occurs on the IMC hydrides during the reaction, with the Ni:La ratio increasing from 5 to 6. However, conventional metal catalysts such as Ni/CeO_2, Ni metal, and skeletal Ni—have low activity under these conditions. This suggests that IMC hydrides may be regarded as a new class of hydrogenation catalysts with high activity, despite their small specific area.[87,92,93] The high activity of intermetallic REE compounds may be related to their ability to form hydrides with a high IMC–carbon bond energy that significantly exceeds the metal–C bond energy for Ni, Pt, and Pd catalysts. Calculated values of the bond energies of $(LnH_3)-C$ (for Ln = La, Pr, Gd, and Lu) according to the multiplet theory of catalysis[26] were 56.7, 34.3, 34.8, and 50.3 kcal mol^{-1} respectively.[94]

Replacement of a proportion of the Ni atoms by Co gives more stable hydrides with higher IMC–H bond energies, and the highest activity in the hydrogenation of propylene is exhibited by $LaNi_{5-x}Co_x$–hydride when $x = 2$. For this system the greatest density of hydrogen occurs in the $LaNi_3Co_2-H_4$ lattice. A similar pattern occurs for $LaNi_{5-x}Cu_x-H_4$, for which, according to the multiplet theory of catalysis,[26] the highest catalytic activity corresponds to the maximum hydride stability. The strength of the $IMC-H_x$ bond increases with an increase in x, and the free energy of the system ΔG decreases from 1.46 ($x = 1$) to −0.63 ($x = 3$); a further reduction in ΔG leads to a decrease in catalytic activity.[96] Other systems of $LaNi_{5-x}M_x$ and their hydrides, where Ln = La, Sm, Gd, and M = Al, Ti, V, Cr, Mn, are also active in the hydrogenation of propylene.[57]

It was found for the first time by Konenko et al.[97] that IMC hydrides such as $LaNi_5-H_6$ and $La_{1/2}$, $Pr_{1/2}Ni_5-H_5$ treated with a solution of (+)-tartaric acid at pH 4.8 exhibit enantioselectivity in the hydrogenation of EAA at 80 °C and 100 atm to (*R*)-(−)-EHB, with $p = 9.8$ and 5.7% respectively. However, a similar asymmetric effect ($p = 5.7\%$) was found for a 5% Ni/CeO_2 catalyst that was modified under the same conditions. This could suggest that the Ni which enriches the surface of the IMC as a result of segregation and forms dissymmetric clusters during modification with tartaric acid is responsible for the enantioselective properties of the catalyst. However, the fact that enrichment of an IMC with lanthanum, as in the case of La_3Ni, will hinder the segregation of Ni and affect the catalytic properties does not support this theory (partial replacement of La by Pr generally results in catalyst deactivation).[98] It is found that the initial La_3Ni, being modified with TA, achieves the asymmetric hydrogenation of EAA with $p = 11.9\%$, whereas a ferromagnetic sample with a specific magnetisation of saturation $\delta = 0.6-0.75$, in which considerable segregation of Ni has occurred as a result of the initial treatment of the sample, is inactive in enantioselective hydrogenation.[99]

Replacement of a proportion of the Ni atoms in $LaNi_5$ by other metals results in the formation of paramagnetic IMCs and their stabilisation. Thus, $LaNi_5$ forms the least stable hydride while an IMC of the type $LaNi_{5-x}Cu_x$ forms the most stable hydride.[99,100] According to the multiplet theory of heterogeneous catalysis, the catalytic system with the optimum energy values of the bonds between the catalyst and the atoms of the substrate molecule will have the highest catalytic activity. In fact, the highest catalytic and enantioselective activity in a series of $LaNi_{5-x}Cu_x$ IMCs was exhibited by $LaNi_3Cu_2-H_{3.7}$ ($p = 15.6\%$), which in terms of stability occupies a position between $LaNi_5$ and $LaNiCu_4$.[100] Thus, the isostructural replacement of one or two Ni atoms by Cu in $LaNi_5$ leads to more efficient dissymmetric catalysts. Similarly, in Ni–Cu catalysts modified with TA,[102] an increase in Cu content to 30 at.% gives a maximum value of p (in $LaNi_3Cu_2$ the Cu content is 28.7% and p reaches 17%).[100] This shows that it is the IMC hydrides as a whole, rather than the individual phase of Ni that separates out during segregation, which exhibit catalytic and enantioselective activity.[101]

The effect of pH of the modifying solution of TA on the value of p also confirms the participation of the whole IMC cluster, i.e., all of its components, in the formation of a complex with TA. Thus, for IMCs of the type $LaNi_4Cu$ the optimum value of pH is 5, whereas for $SmNi_4Cu$ and $GdNi_4Cu$ the optimum is pH 9. Modification of an IMC of composition $LnNi_3Cu_2$, where Ln = La, $La_{0.5}Sm_{0.5}$, and $Sm_{0.5}Gd_{0.5}$, at pH 9 leads, in line with the stability constants of Ln–TA complexes, to an increase in optical yield p from 4.4 to 6.1 and 9.9% respectively. The hydrogen pressure and reaction temperature also affect p. On the most active IMC of composition $LaNi_4Cu-H_{6.3}$, values of $p = 11.5\%$ at 80 °C and 40 atm, $p = 17\%$ at 80 °C and 80 atm, and $p = 9.7\%$ at 40 °C and 80 atm were obtained.[101]

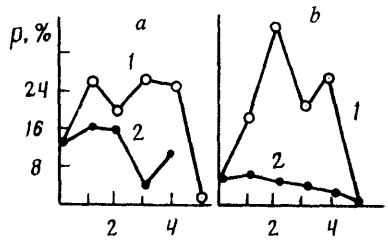


Figure 10. Dependence of the optical yield (*a*) and degree of conversion (*b*) in the hydrogenation of EAA on the number of atoms of M in the lattice of intermetallide $LaNi_{5-x}M_x$ [M = Co (*1*) and Cu (*2*), $pH_{mod} = 4.5$, hydrogenation conditions: 80 °C, 80 atm, 7 h].[103]

Thus, the dissymmetric properties of intermetallic catalysts are governed by both the ratio of Ni/Cu in the crystal lattice and the nature of the cluster that incorporates REE atoms of different types. The most effective catalysts were obtained[95,103] when cobalt was

introduced into the matrix of $LaNi_5$ hydride. These catalysts exhibit higher enantioselectivity and catalytic activity than that of $LaNi_{5-x}Cu_x$ catalysts. For the hydride $LaNi_4Co-H_{3.3}$ the value of p (26.6%) is more than twice that of $LaNi_5$ (p = 12%) and that of IMCs containing Cu.

The dependence of p on the number of Co atoms in an IMC of the type $LaNi_{5-x}Co_x$ is shown in Fig. 10. The corresponding $LaNi_{5-x}Cu_x$ are given for comparison. It is clear that for both types of catalysts there is an extremal dependence of the optical yield and degree of conversion of EAA on the number of Co or Cu atoms replacing Ni in $LaNi_5$.[103] While the optical yield did not exceed 17% when Cu was introduced into $LaNi_5$, when Co was introduced it increased to 30%, and with modification of $LaNi_3Co_2$ with a solution of TA at pH 4.5 with added trimethylacetic acid it rose to 45%.[104,105] It should be noted that the introduction into the modifying solution of NaBr, which is very effective for skeletal Ni,[18] has almost no effect in the case of IMCs, which is an indication once again of the special properties of IMC catalysts.[104]

When instead of Co other metals such as Mn, Cr, Ti, V, or Al are introduced into $LaNi_5$, the stability of the corresponding hydrides increases but their enantioselectivity is reduced. Only when Mn and Cr are introduced ($LaNi_4Mn-H_3$ and $LaNi_4Cr-H_{2.5}$) is there any appreciable activity (p = 20 and 16%).[104]

Interesting results were obtained in the partial replacement of Co by Cu in $LaNi_{5-x}Co_x-H_n$.[106] In this case both the total catalytic activity and enantioselectivity of the catalyst were reduced, the latter being greatest in $LaNi_3Co_2-H$ (p = 52%).[55]

Hydride of intermetallide	y, %	p, %
$LaNi_3Co_2$-$H_{3.5}$	100	52
$LaNi_3CoCu$-$H_{5.7}$	96	9
$LaNi_3Co_2Cu$-H	20	27
$LaNi_2CoCu$-$H_{3.8}$	30	17
$LaNiCo_2Cu_2$-$H_{3.6}$	12	13

Intermetallic catalysts that do not contain Ni have low activity. The successive and complete replacement of Ni by Co leads to a sharp decrease in catalytic and asymmetric activity. The partial introduction of Cu atoms into $LaCo_5$ does not lead to an increase in activity.[106]

The highest value of p (about 60%) was found for a $LaNi_{5-x}M_xM_y$ system containing Co and Cu. This asymmetrising effect is attributed to the formation of heterometallic complexes $[LaM_xM_y-TA]$.[107]

This behavioural feature essentially distinguishes intermetallic catalysts from bimetallic Ni–Co catalysts that are modified under the same conditions as IMCs and for which the value of p steadily increases with an increase in Ni content.

According to Klabunovskii et al.,[108] asymmetric activity in the hydrogenation of EAA and AA decreases in the following series of metal catalysts modified by TA and amino acids: Ni > Cu > Co, the value of p not exceeding 5–8% for Co. It was therefore to be expected that IMCs containing Ni and Cu would be more enantioselective than those containing Ni and Co. However, the results obtained indicate that, on the contrary, Ni–Co IMCs are more active than Ni–Cu IMCs. This may occur because Ni and Co are not segregated to any significant degree on the surface of an IMC, otherwise the enantioselectivity of the catalyst would be governed by the nature of the metal segregated on the surface of the catalyst. The catalytic and enantioselective activity of IMCs are determined rather by the nature of the cluster which contains the atoms of three different metals—La, Ni, and Co (or Cu).

Intermetallic catalysts that are modified in the optimum pH region decompose to a lesser degree during catalysis, which is supported by a test for their ferromagnetic properties) (test carried out by the Faraday method). Hence, a higher value of p is characteristic of those hydrides that decompose to a lesser degree during modification and hydrogenation. Moreover, the catalytic properties also depend on the strength of the IMC–H bond. Introduction of Co into an IMC increases the strength of the IMC–H bond and improves the stability of the hydride. This relates in particular to $LaNi_3Co_2$, for which maximum values of the magnetic moment, a maximum density of the hydrogen atoms in the hydride lattice, and optimum values of the IMC–H bond energy have been found.[95]

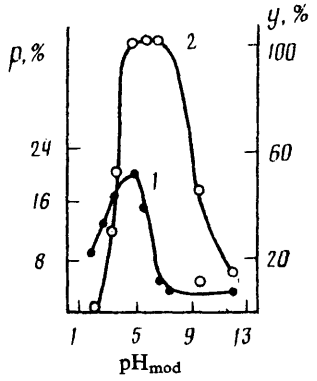


Figure 11. Dependence of the optical yield (*1*) and degree of conversion (*2*) on $LaNi_3Co_2-H_{3.5}$ on the pH of the modifying solution of (+)-tartaric acid.[103]

The dependence of p on the pH of the modifying solution of TA has the same extremal nature as the dependence for modified Cu and Co metal catalysts.[102,109] The dependence of p and y on the initial pH of the modifying solution of TA for $LnNi_3Co_2$ and $LaNi_4Cu$ catalysts is shown in Fig. 11.[103] This suggests the identity of the tartrate complexes of the metals contained in the dissymmetric site that are formed on the surface of the catalysts.[1]

The increase in pH of the solution of TA in the course of modification and the evolution of hydrogen during modification of the hydride also point to complexation on the surface of the IMCs during their modification, in addition to the asymmetric effect in hydrogenation. At the same time a proportion of components of a $LaNi_3CoCr-H_{4.2}$ catalyst passes into solution (especially La) and the surface of the IMC is enriched with Ni. Data on the

composition of the surface layer, obtained by using XPES,[13] are given below.

Hydride of intermetallide	La	Ni	Co	Cr
IMC (initial)	14.7	60.0	15.8	9.5
IMC hydride	17.5	64.6	7.9	10.0
IMC–$H_{4.2}$ after modification at pH 4.5	8.3	65.2	7.8	18.7
The same after modification at pH 7.0	22.3	44.5	12.2	21.2
Bulk composition of the initial hydride $LaNi_3CoCr-H_{4.2}$	32.3	40.9	13.7	12.1

Replacement of La in $LaNi_3CoCr-H_{4.2}$ by Sm or Gd results in a sharp fall in catalytic and enantioselective activity of the catalyst, which is an indication of the inclusion of REE atoms in addition to *d*-metals in the dissymmetric cluster.

The decrease in *p* may be related to the increase in strength of the tartrate complexes of IMCs containing Sm and Gd in comparison to IMCs based on La.[101] Replacement of La in $LaNi_5-H_4$ by other rare earth elements (Pr, Sm, Gd)[60] leads to a reduction in stability of the corresponding hydride, and this gives rise to the need for a considerable increase in the hydrogen pressure that is necessary for hydride formation in the preparation of an IMC hydride. On the other hand, replacement of Ni in $LaNi_5-H_4$ by atoms of other transition metals strengthens the IMC–H bond. Therefore, catalysts based on more stable hydrides, such as $LaNi_4M$ with M = Al, Ti, V, with a high overall catalytic activity exhibited low enantioselectivity.[110] Data on a number of polymetallic hydrides that have been studied are summarised in Table 3.[57,96,103,110–112]

Table 3. Dependence of the degree of conversion (*y*, %) and optical yield (*p*, %) in the hydrogenation of EAA on IMC catalysts (80 °C, 80 atm, 7 h) on the composition of IMC hydrides modified with (+)-tartaric acid (pH 4.5).[57,96,103,110–112]

Catalyst	*y*, %	*p*, %	Catalyst	*y*, %	*p*, %
$LaNi_5$-$H_{6.0}$	14.9	12.7	$LaNi_4Cu$-$H_{5.8}$	17.5	17.0
$LaNi_4Co$-$H_{4.8}$	48.8	26.6	$LaNi_3Cu_2$-$H_{3.7}$	13.0	15.6
$LaNi_3Co_2$-$H_{3.7}$	100	20.0	$LaNi_2Cu_3$-$H_{3.5}$	9.5	4.3
$LaNi_2Co_3$-$H_{3.9}$	52.9	28.0	$LaNi_3CoCr$-$H_{4.2}$	58.2	13.5
$LaNi_2Co_2Cu$-$H_{3.9}$	10.0	21.0	$LaNi_3CuCr$-$H_{3.9}$	64.7	16.0
$LaNiCo_4$	0	0	$LaNi_4Co_{0.5}Cu_{0.5}$-$H_{4.2}$	10.3	0
$LaCo_4Cu$	19.3	3.5	$LaNi_3CrMn$-$H_{3.9}$	48.2	3.8
$LaCo_3Cu_2$	14.4	0	$LaNi_3Co_{0.5}Cu_{0.5}Cr_{0.5}Mn_{0.5}$-$H_{4.2}$	36.6	6.8
$LaCo_2Cu_3$-$H_{3.0}$	0	0	$LaNi_2Co_{2.5}Mn_{0.5}$-$H_{5.3}$	65.4	20.9
$La_{0.5}Sm_{0.5}Ni_4Co$	27.7	19.7	$LaNi_2Co_2Mn$-$H_{3.5}$	77.8	7.2
$Sm_{0.5}Gd_{0.5}Ni_4Co$	0	0			
$CeCo_3$	5.6	0			
20% Ni – 80% Co	22.0	11.0			
$LaNi_4Al$-$H_{4.0}$	60.9	6.3			
$LaNi_4Ti$-$H_{3.5}$	93.4	1.1			
$LaNi_4V$-$H_{3.5}$	95.4	5.2			
$LaNi_4Cr$-$H_{4.0}$	96.0	16.3			
$LaNi_4Mn$-$H_{5.0}$	40.7	23.4			

It is evident from Table 3 that the use of catalysts based on polymetallic IMCs, especially 5- and 6-component systems, in asymmetric hydrogenation does not have any advantages over IMCs of a simpler composition. In certain cases the polymetallic systems generally proved inactive. However, for an understanding of the mechanism of action of these catalysts, the important conclusion that a change in the nature of all the components of the IMC, including the REEs, has a considerable effect on the catalytic and enantioselective properties of the catalysts follows from the data given.

This again provides confirmation that during the modification of IMC hydrides, heterometallic tartrate complexes contained in a catalytic cluster of asymmetric hydrogenation are formed on the surface. This cluster is similar to that which has been proposed for dissymmetric monometallic hydrogenation catalysts.[1]

Dissymmetric intermetallic catalysts were studied in the practically significant diastereoselective hydrogenation of fructose to mannitol and sorbitol.[113,114] Previously[112] the hydrogenation of *D*-fructose to sorbitol and mannitol had been optimised with respect to sorbitol by means of mathematical planning of the experiment. Skeletal Ni modified with (+)-tartaric acid proved to be the best catalyst. Hydrogenation of an aqueous solution of *D*-fructose at 80 °C and a hydrogen pressure of 90 atm gave sorbitol in 65.7% yield (sorbitol : mannitol = 1.9 : 1).

A number of isostructural IMC hydrides — $LaNi_3Co_2$ and $LaNi_3Cu_2$ and also $LaNi_3M'M''$, where M'M'' = CuCo, CoCr, MnCr, $Co_{0.5}Cu_{0.5}Cr$, modified with (+)-tartaric acid — were studied[113,114] for the diastereomeric hydrogenation of *D*-fructose. The task involved finding catalysts and optimising the hydrogenation of fructose to mannitol — a product of practical importance. It was found that the pH of the modifying solution of TA is of crucial importance for preparing the optimum catalyst. The maximum values of the degree of conversion of fructose were achieved by pH 7–8 for $LaNi_5$, $LaNi_3Co_2$, and $LaNi_3Cu_2$ and at pH 4.5–5.5 for $LaNi_3CoCr$. By varying the reaction conditions it was found that the highest yield and maximum diastereoselectivity could be attained when $LaNi_3Cu_2$ was used. The optimum conditions were: 1.5 g of catalyst, a 15% solution of fructose, 80–90 °C, a hydrogen pressure of 50 atm. It should be noted that by introducing up to 50% sorbital into the reaction mixture it was possible to increase substantially the diastereoselectivity of the reaction with respect to the formation of mannitol. The excess of mannitol was 46% and the total yield was 73%. The $LaNi_3Co_2$ catalyst was more selective towards formation of sorbital (39% excess of diastereoisomer and 70% yield).

Comparison of the selectivity of action of the catalyst with the content of the stereoisomeric forms of *D*-fructose in the reaction system showed that the stereoisomers of α-*D*-fructopyranose and α-*D*-fructofuranose are mainly responsible for the formation of *D*-mannitol.[113]

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The studies described above have not covered all aspects of research into asymmetric hydrogenation on metals. Questions relating to the reaction mechanism, which has recently been the subject of considerable attention in a number of studies, have remained untouched. Ideas have been developed concerning the decisive role in asymmetric hydrogenation of the coordination of metal ions on the surface of the catalyst with molecules of modifying agent — these are usually hydroxyacids or amino acids — and with

substrate ions—mainly readily complexing diketones and ketoesters. The previously advanced theories[1] about asymmetric hydrogenation occurring via the formation of an intermediate ternary complex of metal–modifying agent–substrate have received support in a number of studies.[26,31,64] The nature of the chirodiastaltic interaction between molecules of modifying agent and substrate (or semihydrogenated compound) in such complexes is evident in correlation[108] between the stability constants of complexes that simulate an intermediate complex on the surface of the catalyst and the enantioselectivity of the catalyst containing this complex.[65] By finding these correlations it is possible to predict the composition of effective dissymmetric catalysts and the nature of the modifying agent—in the metal series Ni–Cu–Co with (*S*)-α-amino acids as modifying agents. Additional correlations between the conformation of a ternary complex determined from circular dichroism spectra and the configuration of the hydrogenation product make it possible to establish the configuration of the product with sufficient reliability.[69,115]

The second aspect of asymmetric hydrogenation (which was only mentioned in two studies)[6,7] is the problem of the industrial development of asymmetric catalysis for the preparation of optically active compounds of practical importance. Considerable progress in the field of asymmetric metal-complex catalysis is known to have been achieved in this area. Chiral rhodium phosphine complexes proved very effective in the synthesis of a number of important optically active products, and only the complex nature of synthesising the ligands and the high cost of the processes have placed a restraint on their widespread application.[116,117] In certain cases these processes have had a practical application in the synthesis of high-cost products [for example, 3,4-dihydroxylphenylalanine (DOPA) for the treatment of Parkinson's disease, phenylalanine[117] for the production of the sweetener Aspartame, menthol[118] for the food and perfumery industries and medicine] on a large scale.

Modified heterogenous metal catalysts, because of the limited range of their action (on the whole it is only the C=O bond that is effectively hydrogenated), have so far found less applications, despite their evident technological advantages over metal-complex catalysts. However, there is an indication[119] that a Ni–TA catalyst has been used to obtain (2*R*,4*R*)- and (2*S*,4*S*)-pentanediol by hydrogenation of acetylacetone. (*S*)-Alkyl-β-hydroxybutyrates—important optically active synthons[120] that have already come on the market—have also been obtained in this manner. Thus, it is possible to look forward to a wider practical realisation of asymmetric hydrogenation on heterogeneous metal catalysts modified with optically active compounds.

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