

Chapter 4

HYDROGENATION ON CATALYSTS BASED ON Ni AND BIMETALS

Abstract

This Chapter summarizes more than 250 works of new types of metal catalysts, based on nickel and other metals including bimetals, which are active in the enantioselective heterogeneous hydrogenation of *beta*-keto carboxylic acid esters to *beta*-hydroxy carboxylic acid esters, and also are important in the production of monomers for chiral biodegradable polyesters. Cited are works mainly by groups working since the 1950's, which were published from the initial period of discovery up to the present time. Over 30 monographs and reviews on the elaboration of Ni-dissymmetric systems characterize the steps of development of this field from the first modest attempts at asymmetric hydrogenations up to the current excellent effective catalytic systems which produce optical yields of hydroxyesters up to 98% and are comparable to the effectiveness of homogeneous chiral metal-complex catalysts. But unlike them the preparation of heterogeneous metal catalysts are very simple and involve only readily available starting materials like Raney catalysts and tartaric acid as a modifier.

Chapter 4 contains the background of the development of effective modified Ni catalysts, discusses the methods of preparation of different types of stable and active metal catalysts, and discusses the selection of effective modifiers and the most suitable substrate molecules having practical interests. On the basis of these studies a reaction mechanism for the new effective catalytic systems was suggested and experimentally examined. The Chapter discusses the preparation variables for the development of this new type of effective chiral modified Ni catalyst, the supported metal catalysts, the chiral modified bimetal and multimetal catalysts including rare earth metals, and the new chiral modified nickel-ruthenium and palladium catalysts. Attempts are undertaken to elucidate the mechanism of enantioselectivity and to reveal the general regularities of asymmetric actions.

4.1. Background and elaboration of Ni catalysts modified with amino and hydroxy acids

Studies of heterogeneous enantioselective hydrogenation of 2-oxocarboxylic acid esters over chirally modified Ni catalysts were developed first in the early 60's by Izumi's group (Osaka, Institute of Protein Researches) and by Klabunovskii's group (Moscow, Zelinskii Institute of Organic Chemistry) and have been summarized in monographs and reviews¹⁻³¹. Later, experiments were continued by the groups of Smith (SIU Carbondale), Sachtler (Leiden, Evanston), Yasumori (Tokyo), and Wells (Hull). Then during the 70-80's experimental and theoretical works were developed toward improving Ni catalytic systems^{32-41,109-113}, involving the elaboration of methods of chiral modification of catalysts^{42-60,120}; searching for the best suitable substrate

molecules besides the 2-oxo-systems^{61-66,117-119}, and elaborating new methods for increasing enantioselectivity in modified catalysts^{67-70,115,116,218-222,235-253}, including the search of new bimetal and multimetal modified catalysts based on nickel^{120-183,193-198} and supported catalysts¹⁹⁸⁻²⁰⁶. Mechanistic studies were reported^{75-79,84-112,184-187,208-217,223-234}. Methods of enhanced durability of modified catalysts and their use in practice (see also Chapter 7) were considered in other reports^{71-74,80-83,188-192}.

A well known fact was that some inorganic and organic compounds, that possess strong complexing ability, can affect the stability and selectivity of metallic catalysts. The effect of non-reacting compounds (so called *modifiers*), on the rates of hydrogenation of unsaturated compounds have been shown by Balandin²³⁴. He found that the rates depend not only on the nature of the solvent but also on the nature of added compounds that are not able to react under the reaction conditions. Such compounds can modify the catalyst surface and strongly influence the rate and selectivity. If such compounds possess chiral characteristics they might influence the asymmetric action of the catalyst. Probably the earliest example of the combination of a chiral modifier (fructose) and a heterogeneous catalyst (ZnO) was described by Erlenmeyer (see Chapter 5). Certain, but very small enantioselective actions of heterogeneous metal catalysts in the presence of optically active compounds were observed during the hydrogenation of 2-methylcinnamic acid over Raney Ni in a solution of D-glucose resulting in the formation of optically active product with an *ee* of not more than 0.5%. This combination also produced optically active (+)-*N*-phenylalanine from the hydrogenation of 2-acetamidocinnamic acid⁹.

The original details of the influence of optically active additives on catalytic reactions were reported by Isoda et al.^{32,33}. Hydrogenation of C=O and C=N bonds in diethyl 2-oxoglutarate and diethyl 2-oximinoglutarate were carried out in the presence of modifier compounds (camphor, borneol, amino acids) *in situ* at elevated hydrogen pressures and temperatures.

The most characteristic data are summarized in Table 4.1. and show very striking results: optical yield reached 24% in the presence of several compounds (camphor, borneol) that are not inclined to complex-formation with nickel surface.

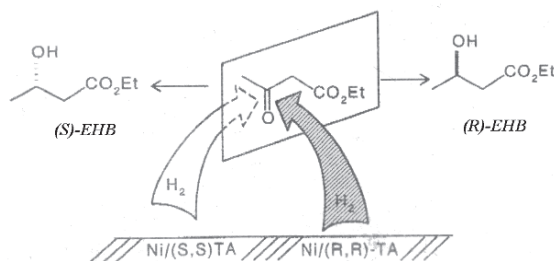
The higher optical yields were achieved with the addition of L-amino acids to the reaction mixtures. The addition of L-tyrosine resulted in the formation of phenylalanine with an *ee* of 50%. Unfortunately, these data were not noticed for some time and only in 1963 did the group of Akabori and Izumi³⁵⁻⁴¹ attempt to reproduce these results; however, the first results were of modest success even using other methods of preparation of the catalysts.

In the early studies of Izumi's group (Osaka)¹⁻⁸ the new method of modification of Raney Ni by preliminary treatment of the catalyst with modifier solution was elaborated.

Modifier	Reaction conditions			Product <i>ee</i> %
	°C	bar	solvent	
Diethyl 2-oxoglutarate				
(+)-Camphor	80	63		24.4
(+)-Camphor	100	60		6.7
(+)-Camphor	75	60	Hexane	7.0
(+)-Camphor	50	60	Ethanol	7.0
(+)-Borneol	100	10	Hexane	1.1
(+)-Borneol	80	10	AcOEt	1.1
(-)-Borneol	80	60	AcOEt	23.3
L-Tyrosine	70	74		7
L-Glu	80	56		6
L-Leu	85	30		2.5
L-Phe	85	16		5
Diethyl 2-oximinoglutarate				
(+)-Camphor	120	20	AcOEt	1.1
(+)-Borneol	120	20	AcOEt	1.1
L-Tyr	60	70		3
2-acetamidocinnamic acid				
L-Tyr	50	80		50
L-Tyr	60	80		36
L-Tyr	65	74		18

Table 4.1. Enantioselective hydrogenation of the C=O bond in diethyl 2-oxoglutarate to diethyl 2-hydroxyglutarate, of the C=N bond in diethyl 2-oximinoglutarate to diethyl glutamate, and of the C=C bonds in 2-acetamidocinnamic acid to phenylalanine on Raney nickel catalysts, modified with optically active ketones, alcohols and amino acids (according to mainly Isoda et al.^{32,33}).

The first results showed that optically active amino acids are not very effective as modifiers and showed that the most effective modifiers are hydroxycarboxylic acids, such as tartaric and malic acids. Also, it was found that the treatment of Raney Ni catalysts with these modifying solutions diminished the catalytic activity for the hydrogenation of the C=O bonds in *beta*-keto esters but not for the hydrogenation of C=C bonds in olefinic substrates (Scheme 4.1.).



Scheme 4.1. Formation of a chiral center from a prochiral center.

Balandin and Klabunovskii's group (Moscow)^{9,10,113} and Smith's group (Carbondale)^{220-222,263} examined this type of chiral catalysts using the new method of preliminary modification of the catalysts in solutions of optically active compounds and confirmed that these catalysts produce the hydrogenation products; however, they possess very small optical activities if modifiers are amino acids or amino alcohols [for example (-)-ephedrine or (-)-1-(4-nitrophenyl)-2-aminopropan-1,3-diol], and they found good results using ethyl acetoacetate instead of methyl acetoacetate as the substrate.

The next important finding was that: the best catalyst is Raney Ni modified with tartaric acids (TA) rather than amino acids (AA) using the esters of 2-oxocarboxylic acid (mainly methyl acetoacetate, MAA) as model substrates. Using RNi-TA produced MHB with an *ee* above 50% from the hydrogenation of MAA in the liquid phase at higher temperatures, 50-70°C, and higher hydrogen pressure, 50-100 bar.

A very important discovery was that enantioselective hydrogenation can be realized only with *beta*-keto-esters rather than *alpha*-keto esters. The asymmetric hydrogenation of *alpha*-keto esters demands other types of chiral catalytic systems (see Chapter 5). Hydrogenation of monoketones or 2,3-diketones over RNi-TA gave only modest results, whereas hydrogenation of 2,4-diketones, e.g. acac, gave good results.

Preparation of catalysts

Because catalytic activity and enantioselectivity of modified metal catalysts strongly depend on their preparation procedures, some examples of the preparation procedures of Raney Nickel catalysts modified with TA (MRNi-TA-NaBr) or AA and of supported Ni catalysts (HNi-AA-aerosil) are described below.

Smith and Musoiu^{218,264} prepared RNi-TA catalyst by leaching 0.3g Ni-Al alloy at 100-105°C for 2-3h with 15 mL of 20% aqueous NaOH solution. The prepared catalyst was centrifuged, washed with water (7x30ml) with shaking each time for 5-10 min. Modification was carried out by soaking the catalyst in 100 mL of 2% aqueous solution of TA at a pH of 5.0-

5.1. After modification the catalyst was centrifuged, washed with water (2x2ml), and methanol (2x2ml).

Groenewegen and Sachtler²¹¹ prepared supported Ni catalyst using two methods: impregnation and precipitation. The impregnation of the aerosil support was carried out with a solution of nickel nitrate followed by drying at 100°C, heating at 500°C and, finally, reduction in flowing hydrogen at 300-500°C. In the precipitation method, aerosil was mixed with an aqueous solution of Ni-salt and ammonia was added slowly at such a rate that with increasing pH the metal precipitated on the surface of support rather than in the solution. The resulting precipitated catalyst was heated at 500°C and reduced in flowing hydrogen at 300-400°C. By these preparation methods, catalysts containing 17% Ni on aerosil were prepared. Modifications of catalyst were carried out by subliming the appropriate optically active amino acids in vacuum at 100°C.

An efficient RNi-TA-NaBr catalyst was prepared by Harada and Izumi¹⁰⁵ according to the following method: 1.9g of pulverized Ni-Al alloy (42:58) was added in small portions into a solution of 4.5g NaOH in 20 mL water over a 2 min period. The resulting mixture was heated at 110°C for 1h. The liquid was decanted, and the resulting catalyst was washed 15 times with 30 mL of water. Modification was carried out with a solution of 1g TA and 10g NaBr in 100 mL of water. The pH of the solution was adjusted to 3.2 by the addition of 1N NaOH. Modification of 0.8g of Ni was carried out by soaking in this solution, then heating at 100°C for 1 h. The resulting modified catalyst was washed with 10 mL of water. This process was repeated three times. Then the catalysts was washed with methanol (2x50ml) and then with 25 mL of methyl propionate. The hydrogenation of MAA was carried out with this catalyst in a solution of methyl propionate with small amounts of acetic acid. The reaction rate was 8.5 mol/h/g Ni, the optical yield of MHB reached 88.6% (without addition of AcOH; under these conditions the *ee* was only 39.2%). Hydrogenation of acetylacetone (acac) on this catalyst resulted in a diol with an *ee* of almost 100%.

A very effective Ni catalyst was prepared from Ni-acetylacetonate supported on crystallized *alpha*-alumina (Japanese origin "Sumico Rundum") and modified with (2*R*,3*R*)-tartaric acid + NaBr solution. A maximum *ee* of 87% was obtained from the hydrogenation of MAA^{110,111,256}.

The effectiveness of enantioselective hydrogenations on chiral modified RNi catalysts depends on many factors. It is influenced by variables of modification procedure, pH of solution modifier, structure of modifier, concentration of modifier, temperature of solution, period of action of modified solution, and presence of additional components. In the case of modifier (2*R*,3*R*)-tartaric acid, it proved very important to add NaBr into the modifying solution. The amount of TA adsorbed on the catalyst determined the effectiveness of the resulting MRNi catalyst.

Modification variables

Enantioselective hydrogenation of MAA to MHB was studied as a model reaction and it was found that the hydroxy-dicarboxylic acids, like tartaric acid, were the most effective modifiers. 2-Methyltartaric acid was a very effective modifier, the *threo*-acid showed the best results in this case: RNi catalyst modified with this acid at pH 5.0 resulted in producing MHB with an *ee* of 51%, while the *erithro*-acid had almost no effect⁴².

Much attention was spent on the problem of the influence of the nature of alkali cations when adjusting the pH value of the modifying solution. For the hydrogenation of MAA on RNi-TA only NaOH produced good results when used in the TA modifying solution to adjust to a definite pH value (mostly 5.2 for the modification with TA). Using KOH, LiOH or RbOH diminished *ee* values of the resulting MHB. It was suggested that the Na cation in the solution reacts with the free COOH group of tartaric acid during the process of modification, whereas the other COOH group and the OH group are coordinated with the surface of the nickel catalyst. The nature and amounts of other amines or alkalis added to the TA modifying solution exhibited small effects on the *ee*'s of the resulting MHB. On the other hand, modifications of RNi with mono-hydroxycarboxylic acids are not sensitive to the nature of the alkali cation in the modifying solution, which indicates that the cation does not take part in the adsorption of these modifiers. A similar behavior was observed when RNi was modified with amino acids⁵⁵. From these data the following conclusion was drawn: in acidic modifying solutions one COOH group of the modifying dicarboxylic acid is linked with the Ni surface and the other is connected to the alkali cation in the solution.

The temperature, concentration, and pH of the modifying solution have strong influences on the effectiveness of the resulting modified catalyst. Increasing the time of modification and the concentration of modifier at optimal temperature and pH enhances enantioselectivity of the catalyst up to an optimal value due to corrosion of the nickel surface with formation of nickel-tartrate chelates coming into the solution. Therefore, for the best enantioselective effect the amounts of TA on the surface of Ni must reach an optimal value.

Instead of the conventionally used modification by pre-immersion of the catalyst in a solution of modifier, Osawa et al.^{58,255} used an *in situ* modification during the enantioselective hydrogenation of MAA. Fine nickel powder modified with (2*R*,3*R*)-tartaric acid was used and sodium salt was added to the reaction media. By this method the optical yield was increased up to an *ee* of 79%. Improvement of this method²⁵⁷ consists in modification *in situ* of finely reduced Ni-powder by addition of (2*R*,3*R*)-tartaric acid and NaBr to the reaction media. In this case, an *ee* of 89% was obtained in the hydrogenation of MAA. The addition of small amounts of NaBr to the reaction media increased both the *ee* and the reaction rate, while, in contrast, the rate decreased with the addition of NaBr to the modification solution in

the conventional modification method. Addition of NaBr to the reaction media for the *in situ* modification would have both of the following roles:

- i) Na⁺ increases *ee* and rate
- ii) Br⁻ increases *ee* and decreases rate.

According to Osawa et al.²⁵⁸ the *in situ* modified and reduced Ni catalyst showed high durability during repeated use in enantioselective hydrogenation of MAA. In comparison with Raney Nickel used earlier, reduced Ni from nickel-oxide and fine Ni powder were the best precursors for the preparation of effective catalysts. Nickel hydroxide and nickel carbonate were used as the precursors of the nickel oxide²⁶². They were calcined to nickel oxides, then reduced to nickel metal, and finally modified with Tart-NaBr modifiers. The temperature of calcination of the precursors was an important variable for attaining high *ee* values in the hydrogenation of methyl acetoacetate. 1100°C was found to be the best calcination temperature, at which the nickel was produced with crystalline sizes of 40-70nm. One of the possible reasons for the lower durabilities of the conventionally pre-modified Ni catalyst with repeated use could be desorption of tartaric acid from the catalyst surface during repeated hydrogenations.

Structure of modifier molecule

Among many classes of organic compounds the best results were obtained with the following combination: a dihydroxy-dicarboxylic acid as modifier and a *beta*-ketocarboxylic acid ester (or *beta*-diketone) as substrate.

Further investigations showed that the means of improving enantioselectivity consists not in searches for new modifier structures but in elaboration of the stereochemical mechanism of reaction based on concepts of 'dual sites', the existence of chiral modified and non-stereospecific centers, on the surface of catalysts (see, Sachtler²⁰⁹⁻²¹⁷, Klabunovskii⁹⁻¹⁵, Smith²⁶³⁻²⁶⁵).

Effect of solvents and additives

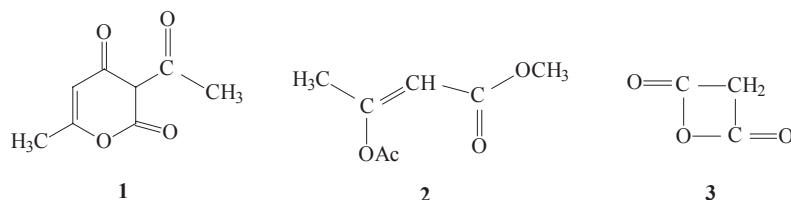
The solvents and additives employed in the reaction system exert a significant influence on optical yield and reaction rate. In the early works (see Lipgart et al.¹²⁰) it was reported that the use of a polar solvent such as methanol, ethanol, or isopropyl alcohol increased *ee*'s in the hydrogenation of EAA on RNi-TA in comparison with hydrogenation of neat EAA. Addition of water to the ethanol solvent in the amounts of 25% and 50% diminished the *ee* values of EHB from the original 16% to 4.4% and 0.4%, respectively¹²⁰. But it was found later that aprotic solvents increased the *ee* of MHB and; that either THF or methyl propionate proved to be the most suitable solvents^{8,105}. On the other hand a pronounced effect of additives containing carbonyl groups, carboxylic groups or unsaturations was noted. Moreover Ninomiya^{63,65} and Higashi et al.⁶⁴ found that the addition of water or reducible components to the reaction mixture exert significant influences on *ee* during the hydrogenation of MAA.

Thus Higashi ⁶⁴ observed that increasing the amounts of added water to the reaction mixture during the hydrogenation of MAA on MRNi, modified with L-amino acids like Ala, Glu and Val, resulted in (*R*)-(-)MHB with *ee* values from 0.4 to 17%. Besides, the addition of a very small amount of water sharply diminished the *ee* and even changed the configuration of the MHB: instead of the (*R*)-(-)-enantiomer the (*S*)-(+)-MHB was formed. But when RNi was modified with (*2R,3R*)-tartaric acid, no significant drop of *ee* was observed after addition of water, and the inversion of the configuration of MHB was not found ⁶⁵.

The studies resulted in the conclusion that water affects the asymmetric center of the catalyst rather than the keto-enol tautomerism of MAA.

It is of interest to point out that in the enantioselective hydrogenation of ethyl pyruvate on a Pt-alumina-cinchonidine system (see Chapter 5, Wehrli ⁴⁸) the presence of water improved the asymmetric effect, which indicates a quite different enantioselective mechanisms in that case.

As mentioned above, the presence of additives containing carbonyl or carboxyl groups in the reaction mixture exert large effects on enantioselectivity. Ninomiya ⁶³ found that dehydroacetic acid (**1** in Scheme 4.2.), methyl (*E*)-3-acetoxycrotonate (**2**) and diketene (**3**) were always present in small amounts as impurities in commercial MAA. These impurities affected the *ee* values of the MHB during hydrogenations of MAA with MRNi catalysts. For example, the addition a small amount (4%) of dehydroacetic acid to the reaction mixture during the hydrogenation of MAA on MRNi, modified with L-Glu or L-Val, resulted in an increase in the *ee* of MHB from 20.9% up to 32.7%.



Scheme 4.2.

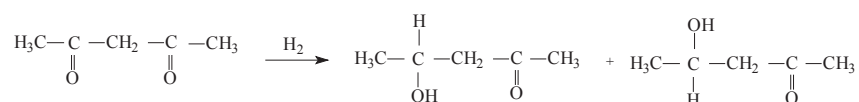
Temperature effect

It is very difficult to draw general conclusions about the influence of temperature factors on *ee* because the reaction temperature affects the *ee* of MHB in different ways depending on the nature of the modifier. For example, when MRNi is modified with L-amino acids (Glu,Val), the *ee* values of the resulting MHB reached a zero value at 40°C and the configuration changed from (*R*)-(-)-MHB to (*S*)-(+)-MHB as a function of temperature, whereas when MRNi is modified with (*2R,3R*)-tartaric acid, the resulting MHB showed a maximum *ee* value at 40°C (Osaki ^{56,102}).

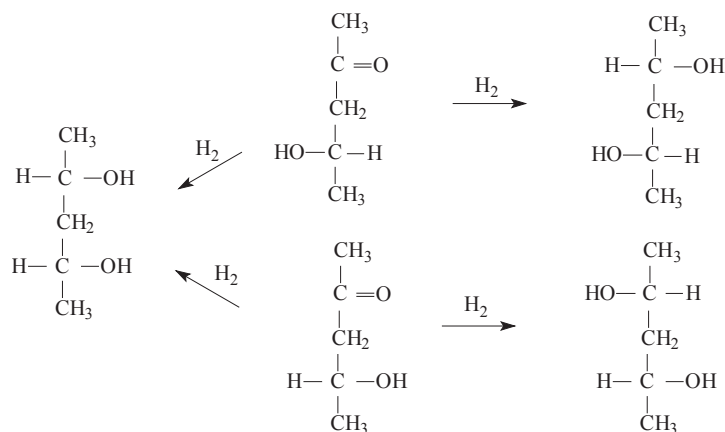
Effects of the structure of substrates

As mentioned above, the best substrate in the enantioselective hydrogenation on modified Ni catalysts proved to be *beta*-keto esters and *beta*-diketones, compounds that are capable of forming an intermediate six-membered chelate with a Ni atom, or a 'Ni-center' on the surface. Optical yields drop drastically if a monoketone substrate is used.

Besides the acetoacetic acid esters, many studies were devoted to enantioselective and diastereoselective hydrogenation of ketones, especially alkan-2-ones^{70,78-80,87} and diketones, such as pentan-2,4-dione (acetylacetone, *acac*). The latter reaction consists of two steps, the first is the formation of a hydroxyketone, 4-hydroxypentan-2-on (Scheme 4.3.)

**Scheme 4.3.**

The second step is the desorption of the hydroxyketone into solution. It is followed by its readsorption and the final hydrogenation into the diol. During the hydrogenation of *acac* the chiral (*2R**,*4R**)-pentan-2,4-diol and the achiral *meso*-diol can also be formed (Scheme 4.4.).

**Scheme 4.4.**

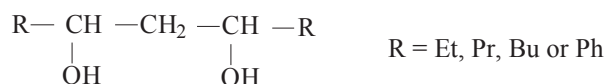
If the reaction is not selective, the product contains the hydroxyketone, the achiral *meso*-diol, and the chiral (*2R**,*4R**)-pentan-2,4-diol with different optical activities. On chiral catalysts, the first step, the formation of the 4-hydroxypentan-2-one, can proceed enantioselectively, and the second step can

proceed diastereoselectively, which can explain the high effectiveness of the enantioselective hydrogenation of *beta*-diketones.

Acac is a strong complex-forming reagent, therefore, a part of the Ni catalyst is corroded and transformed (even up to 75%) into the solution as the [Ni(acac)₂] complex. Saturation of Ni with hydrogen and also modification with TA diminishes the solubility of Ni and its ability to form complexes with *acac*. These facts support theoretical suggestions about the formation of the triple complex [Ni - Modifier - Substrate] on the surface of modified Ni catalyst as the reaction proceeds^{9,113}.

Tanabe⁹¹ hydrogenated *acac* over RNi modified with L-Glu and (2*R*,3*R*)-TA and found that the reaction proceeded according to Scheme 4.3. and Scheme 4.4. A very effective hydrogenation of *acac* on RNi catalyst modified with TA + NaBr gave the diol with high optical yield, 87%, with a 65% chemical yield. After one recrystallization from ether the optically pure pentane-2,4-diol was obtained.

A similar method was applied to the preparation of a number of optically pure diols (Scheme 4.5.) (Ito et al.⁸⁸).

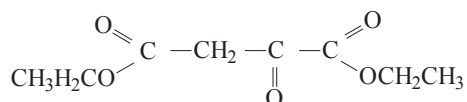


Scheme 4.5.

In general the enantioselective hydrogenations of monoketones are less effective than the enantioselective hydrogenation of diketones, but Osawa et al.⁷⁹ found special conditions under which methyl-ketones, such as acetone, butan-2-one and 3,3-dimethylbutan-2-one, produced optical yields of 74%, when they were hydrogenated on RNi-TA-NaBr at 100 bar hydrogen pressure and 100°C in a solution of THF, to which pivalic acid has been added.

Hydrogenation of octan-2-one proceeded with an *ee* of 80% at 40°C^{71,70,87} and hydrogenation of 2,6-dimethylheptan-3,5-dione gave the corresponding (3*S*,5*S*)-2,6-dimethylheptan-3,5-diol with an *ee* of 99.5% and a 29% chemical yield after three recrystallizations⁷¹.

It is of interest that diethyl oxalacetate (Scheme 4.6.), that can be considered both as an *alpha*- and a *beta*-keto ester, cannot be hydrogenated on the RNi-TA catalyst. This demonstrated that small changes in the groups around the carbonyl group may result in difficulties in asymmetric hydrogenation (Tanabe et al.⁹²).



Scheme 4.6.

4.2. Preparation variables for new nickel catalysts modified with tartaric acid

The important question of the effect of the composition of the original Ni-Al alloys on enantioselective ability was not studied in detail. But Zubareva et al.¹¹⁹ studied samples of Ni catalysts prepared from commercially available Ni-Al alloys with different contents of intermetallic NiAl₃ and Ni₂Al₃ with results shown in Table 4.2. An increase of NiAl₃ in the alloy facilitated etching of the alloy and diminished the contents of Al in the resulting Ni catalysts.

Sample No.	Chemical analysis (%)			Phase analysis (%)			
<i>Ni-Al alloys</i>							
	Ni	Al	Cr + Ti	NiAl ₃	Ni ₂ Al ₃		
1	50	50	-	10.0	90.0		
2	15.2	51.2	3.6	25.1	74.9		
3	38.3	59.7	2.0	51.2	48.8		
<i>RNi catalysts</i>							
	Ni	Al	Cr + Ti	Rest	Ni	Al	Bayerite
2	70.6	15.8	2.8	10.8	91.6	5.4	3.0
3	73.0	6.8	0.12	20.1	97.9	0.0	2.1

Table 4.2. Chemical and phase compositions of Ni-Al alloys and RNi-catalysts (according to Zubareva et al.¹¹⁹).

RNi No. 3, prepared from the commercial NiAl alloy No. 3, containing 2% Cr+Ti and small amounts of other additives, contained 6.8% Al, approximately half of the Al in RNi sample No. 2, which was prepared from the NiAl alloy No. 2. Impurities during the preparation of RNi No. 3 were almost completely removed. Table 4.2. and Fig. 4.1. show that decreasing the Ni₂Al₃ phase in the alloy and increasing the contents of NiAl₃, promoted an increase in both the general activity and the enantioselectivity of the resulting RNi catalysts.

Harada et al.¹⁰³ have found that the presence of traces of aluminium or Al-compounds in Ni catalysts are unfavorable for enantioselective activity. Therefore the use of Ni catalyst prepared by

reducing nickel oxide instead of etching Ni-Al alloy resulted in a MHNi that exhibited optical yields up to 85%.

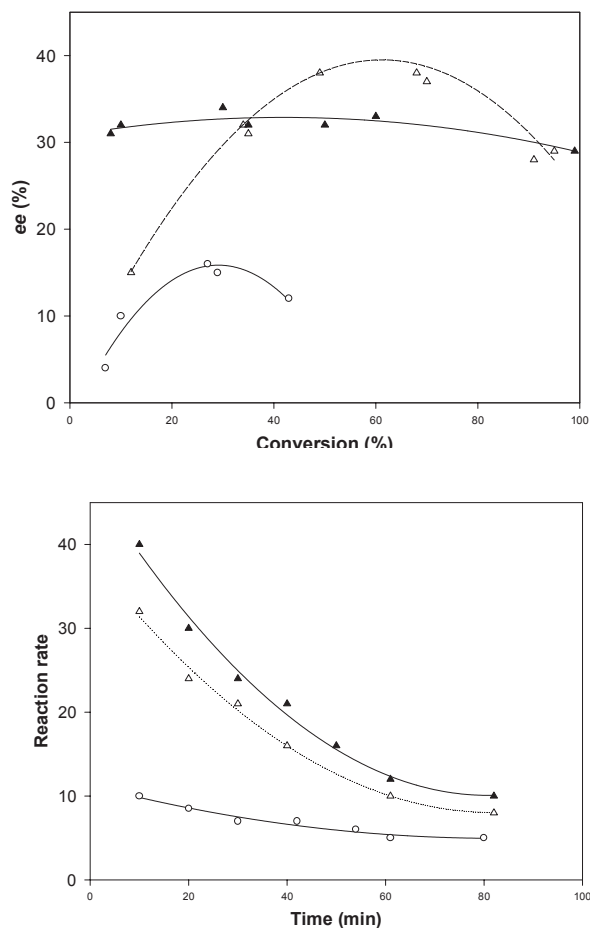


Figure 4.1. Influence of the composition of Ni-Al alloy on the catalytic properties of RNi catalysts, modified with (2*R*,3*R*)-tartaric acid, in the enantioselective hydrogenation of ethyl acetoacetate. Sample numbers 1(o), 2(Δ) and 3(\blacktriangle) are in Table 4.2. (according to Zubareva et al. ¹¹⁹).

It was found that the addition of 1-2% AcOH to the reaction mixture is very favorable. Table 4.3. shows that commercially available NiO reduced for 1 h at 350°C in flowing hydrogen gives the best results (81.6% *ee*) in the hydrogenation of MAA.

Source of Activated Ni	Reaction Temperature	Solvent	Optical Yield of MHB
Raney Ni	60	neat	44
Ni-formate	100	neat	54.8
NiO	120	THF + AcOH	68
NiO	120	THF + AcOH	81.6

Table 4.3. Effect of different kinds of activated nickel catalysts modified with tartaric acid in the enantioselective hydrogenation of MAA (adapted from ¹⁰³).

The catalytic activity and enantioselectivity of the catalysts depend on the mode of preparation of RNi from the original alloy. According to Gross and Rys ²²³ etching the Ni-Al (1:1) alloy with 20% NaOH aqueous solution under different conditions (temperature, time, concentration of alkali solution) results in RNi with different activities and stabilities. The catalysts prepared at a low etching temperature showed higher hydrogenation activities and aluminium contents than catalysts prepared at a high etching temperature; moreover, after modification with TA solution the low etching catalysts produced higher *ee* values in the hydrogenation of MAA. Most catalytically active catalysts, such as W-6, exhibit high activities but low enantioselectivities, while one of the least active catalysts, W-1, exhibits high *ee* values. It follows that Ni catalysts that are least contaminated with remaining Al (or with other components) may provide catalysts with high enantioselectivities. Therefore the nickel catalysts prepared by decomposition of nickel salts exhibited higher enantioselectivities than Raney Ni catalysts.

Vedenyapin et al. ¹¹⁶ used mild reduction conditions in the preparation of HNi catalysts by heating Ni-nitrate in flowing He at 450°C followed by reduction of the resulting NiO in a H₂-He mixture (1:10) at 280°C. Eight grams of the resulting Ni was modified in air with 100 mL of 0.5% solution of (2*R*,3*R*)-(+)-tartaric acid at pH 5.1 and 50°C for 1h. Hydrogenation of EAA (neat) with 0.5g of this Ni at 100°C and 100 bar gave (-)-EHB with an *ee* of 71%, a value that exceeded an earlier value ²¹⁸.

In general, nickel catalysts prepared by reduction of NiO are very sensitive to preparation variations, even to the mode of manufacture of commercial NiO (*ee* of obtained MHB can change from 68 to 86%). Modifications of HNi with tartaric acid + NaBr solution were presented in Figures 4.2.-4.4. This catalyst was characterized by high *ee*'s but exhibited the disadvantage of slow reaction rates; therefore, the reaction had to be performed at temperatures above 100°C, in which case by-products were formed.

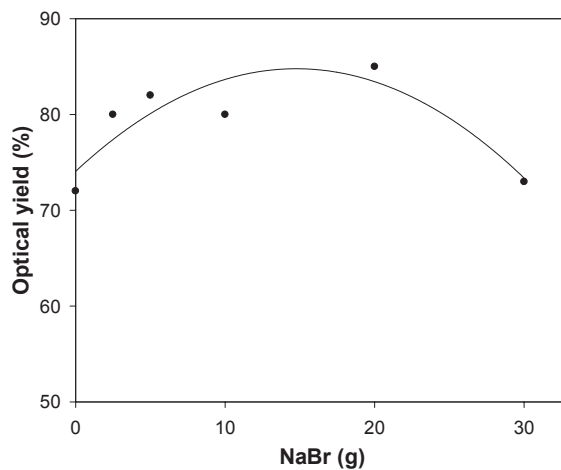


Figure 4.2. Relationship between the amounts of NaBr in the modifying solution and the optical yield of MHB on MNi-Tart-NaBr (conditions are the same as in Figure 4.4.)⁵⁹.

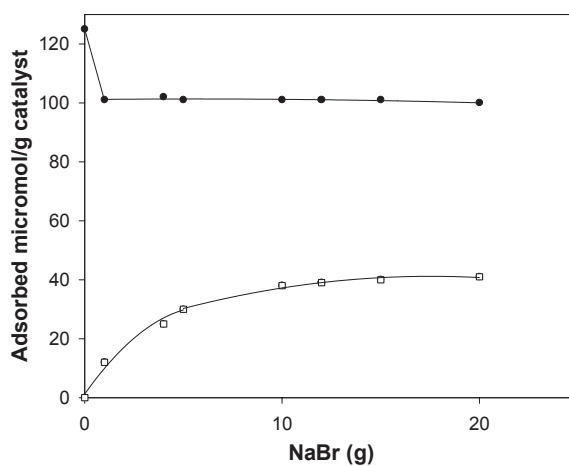


Figure 4.3. Relationship between the amounts of NaBr (◻) and adsorbed tartaric acid (●) in solutions modifying activated Ni (conditions are the same as in Figure 4.4.) (adapted from^{59,103}).

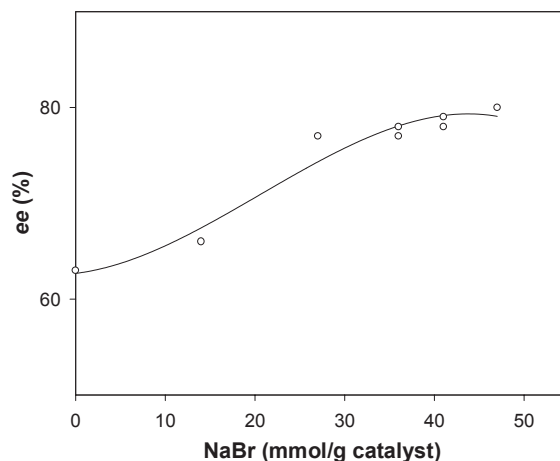


Figure 4.4. Relationship between the amount of adsorbed NaBr on the surface of Tart-NaBr-MRNi catalyst and *ee* in the hydrogenation of methyl acetoacetate.

Conditions: 110 bar, 100°C and the ratio of volumes of MAA to solvent to AcOH are 11.5 : 23 : 0.2 (Harada ⁵⁹).

As has been shown in Figures 4.2.-4.4., adsorption of NaBr on non-specific Ni-centers can enhance *ee* in this hydrogenation as a result of blocking of "racemic" centers, which produce racemic MHB and result in increases in optical yields ⁵⁹.

Inorganic salts	No. of modification procedures	Optical yield of (<i>R</i>)-MHB
None	1	39.2
NaBr	1	83.1
NaBr	2	86.1
NaBr	3	88.6
NaCl	1	72.1
Na ₂ SO ₄	1	56.4

Table 4.4. Effects of inorganic salts, added to the (*2R,3R*)-tartaric acid modifying solution, on enantioselectivity in the hydrogenation of MAA on MRNi (mainly according to Harada ¹⁰⁵).

It was frequently noticed that addition of water and some other reducible additives to the reaction system during the reaction have a significant effect on *ee*⁶³⁻⁶⁵. Also it was found that during the preparation of MRNi, addition of some inorganic salts to the modifying solution sharply increased enantioselectivity during the hydrogenation of MAA. Table 4.4. summarizes the effect of addition of different salts. The greatest effect occurred with the addition of NaBr. This mode of modification with (2*R*,3*R*)-tartaric acid + NaBr was used in further studies by Izumi's group¹⁻⁸.

The basic modification procedure consisted of the following: 10g of Raney Ni were soaked in the modifying solution at 100°C. The mixture was kept for 1h with shaking, the solution was removed by decantation and the residue was washed with 10 mL of deionized water, then the catalyst was washed with 50 mL of methanol and with 25 mL of methyl propionate. This procedure was repeated two or three times (results seen in Table 4.4.).

Hydrogenation was carried out after removal of the solvent by decantation, suspending the MRNi in 23 mL of MAA, followed by hydrogenation in an autoclave at 90 bar and 100°C with shaking until hydrogen uptake ceased (about 10h).

Another method of improving enantioselectivity of modified Ni was reported by Tai et al.⁶⁷⁻⁶⁹.

The idea of the existence of two kinds of centers on the surface of modified Ni catalysts, MRNi, was realized by using ultrasound irradiation in the treatment of the catalyst *before* its modification^{67,68}. A sample of W-1 type RNi (according to Rys²²³) was prepared from 38 g of Raney Ni-Al alloy (Ni:Al=42:58). This alloy was etched in 20% NaOH solution followed by further washing with 400 mL deionized water. Then a suspension of the catalyst was subjected to ultrasound irradiation in an ultrasonic generator (118W, 48kHz) for 3 min and the turbid supernatant suspension was separated by decantation from paramagnetic Ni-powder with a magnet. This operation was repeated several times to afford RNi-U catalyst. The particles in the supernatant were collected by centrifugation. Sixty-nine mg of particles (0.3% of the original 38 g RNi alloy) were obtained. The same procedure was repeated with HNi catalyst for preparation of HNi-U. Modifications of the catalysts were performed in a solution of 24 g (2*R*,3*R*)-tartaric acid + 240 g NaBr in 2400 mL water.

Table 4.5. compares results using traditional MRNi catalysts as references and results using catalysts treated with ultrasound. The new catalysts were characterized by an increase in reaction rates, by factors of 2 to 4, and an increase in *ee* of 5-8%. The highest *ee*, 94%, was obtained in the preparation of (*R*)-methyl 3-hydroxytetradecanoate (No.13). In the hydrogenation of MAA, a new catalysts proved to be very efficient for the large scale production (10 kg) of (*R*)-MHB with an *ee* of 79% (No.4). It is important to note that ultrasound treatment should be used before the modification procedure. When RNi was ultrasonicated in a modification

solution, the resulting catalysts showed poor enantioselectivity (No.5, *ee* 58.6%) and the solution thereby contained was contaminated with aluminium tartrate, which had originated from aluminium in the Ni-Al alloy. The use of MHNi instead of MRNi resulted in no significant changes from the ultrasonic treatment (No.6 and No.7). This fact indicated that the ultrasonic treatment is only effective on the fragile aluminium contaminations in Raney Nickel catalysts.

Sample No.	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2\text{CO}_2\text{CH}_3$ R	Catalyst	Reaction time (h)	Method	<i>ee</i> (%)	Chemical yield,% ⁶⁹
1.	Me	MRNi-U	2.5	A	83.9	70(>98)
2.	Me	MRNi	5.0	A	78	
3.	Me	MRNi-U	3.0	B	83.9	
4.	Me	MRNi-U	12	C	79	
5.	Me	MRNi-U	3	A	58.6	
6.	Me	MHNi-U	20	A	81	
7.	Me	NiHNi	20	A	81	
8.	Et	MRNi-U	4	A	92	
9.	CH ₃ (CH ₂) ₆	MRNi-U	36	A	89	79 (>98)
10.	CH ₃ (CH ₂) ₆	MRNi	144	A	83	
11.	CH ₃ (CH ₂) ₈	MRNi-U	48	A	91	80 (100)
12.	CH ₃ (CH ₂) ₈	MRNi	192	A	86	
13.	CH ₃ (CH ₂) ₁₀	MRNi-U	48	A	94	81(>98)
14.	CH ₃ (CH ₂) ₁₀	MRNi	192	A	86	
15.	CH ₃ (CH ₂) ₁₂	MRNi			87	82
16.	Me	MRNi			83	

Table 4.5. Enantioselective hydrogenations of methyl 3-oxoalkanoates over ultrasonicated (U) and untreated Tart-NaBr-MRNi and Tart-NaBr-MHNi catalysts at 100 bar and 100°C (adapted from Tai⁶⁷⁻⁶⁹).
 Reactant A (10 g), catalyst (1.9 g), EtCO₂Me (20 mL), AcOH (0.2 mL),
 Reactant B (200 g), catalyst (10 g), EtCO₂Me (200 mL), AcOH (2 mL),
 Reactant C (10 kg), catalyst (100 g), EtCO₂Me (10 L), AcOH (15mL).

Ultrasonicated catalyst, RNi-U, proved to be very effective besides the hydrogenation of 3-oxoalkanoates, in the enantioselective hydrogenation of 1,3-diketones (pentan-2,4-dione, 2,3-dimethylheptan-3,5-dione) into diols, too, with *ee*'s of 86-91%. For example, this new type of catalyst was used for the preparation of optically pure (*R*)- and (*S*)-methyl 3-hydroxyalkanoates after hydrogenation in high enantioselectivity followed by crystallization of their dicyclohexylammonium salts⁶⁹ (see Table 4.5, Chemical yields).

Recently Tai's group⁶⁶ demonstrated a new example of high efficacy of enantioselective hydrogenation in heterogeneous catalysis, which is

comparable to the best cases of the enantioselective reactions of homogeneous chiral metal-complex catalysts. The MRNi-TA-NaBr catalyst was treated with ultrasonic irradiation in water, then it was modified with a solution of tartaric acid + NaBr at 100°C and at pH 3.2 (the pH of the solution was adjusted with NaOH) for 1h. A series of *beta*-keto esters was hydrogenated on this catalyst at 100°C and 60°C. The results showed that the higher *ee*'s were obtained at the lower temperatures. The hydrogenation reactions were carried out both on untreated and on ultrasonicated catalysts (Table 4.6.).

	untreated catalyst <i>ee</i> (%)	ultrasonicated catalyst <i>ee</i> (%)
methyl (3-oxobutanoate)	86	86
methyl (3-oxopentanoate)	91	94
methyl (4-methyl-3-oxopentanoate)	88	96
methyl (5,5-dimethyl-3-oxohexanoát)	84	96

Table 4.6. Hydrogenation of methyl (3-oxoalkanoates) on untreated and ultrasonicated MRNi-TA-NaBr catalyst.

The most important result was that the highest *ee* value was obtained in the hydrogenation of methyl (3-cyclopropyl-3-oxopropanoate) into the optically very pure prospective synthon, methyl (3-cyclopropyl-3-hydroxypropanoate). The starting material was shaken in 4g of THF and 0.2 mL of AcOH at 100 bar hydrogen in an autoclave with 0.9g ultrasonicated MRNi-TA-NaBr and resulted in producing (*S*)-(+)-methyl (3-cyclopropyl-3-hydroxypropanoate) with 100% chemical yield. In one experiment the optical yield was found to be 96% at 100°C and 98% at 60°C. In other experiments reproducibilities of the *ee*'s of the (*S*)-(+)-hydroxyester at 60°C were 98.1%, 98.3% and 98.6%. It is clear that hydrogenation under the same conditions with a catalyst modified with (2*S*,3*S*)-tartaric acid gives (*R*)-(-)-methyl (3-cyclopropyl-3-hydroxypropanoate) with an *ee* of 98%. This was the maximum optical yield received in enantioselective hydrogenations on heterogeneous metal catalysts based on Raney Ni.

The idea of two kinds of centers on the surface of nickel in the modified MRNi catalysts was strengthened by results from the treatment of catalyst *before* its modification with ultrasound irradiation^{67,68}. Theoretically though, a more effective method might be selective poisoning of the non-enantioselective centers in chirally modified catalysts.

According to the model of active surfaces of modified catalysts two kinds of centers, selective and non-selective, exist. It may be possible to improve enantioselectivity of hydrogenation if non-modified centers producing racemic MHB can be blocked with a poison, while modified centers are being protected with tartaric acid modifier and therefore are not poisoned. The effect of poisoning depends on the strength of adsorption of

the poison in comparison with that of the modifier and ester to be hydrogenated. Yasumori²²⁵ attempted to increase the *ee* in enantioselective hydrogenation of MAA on MRNi-Tart by adding catalytic poisons to the reaction. Figure 4.5. shows the effects of added poisons on the resulting *ee* of MHB.

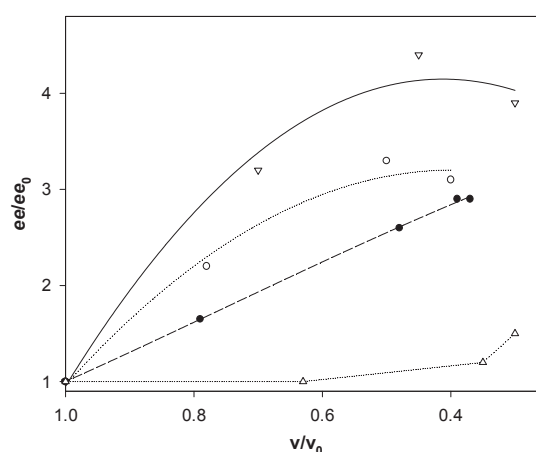


Figure 4.5. The effect of poisoning on enantioselectivity in the hydrogenation of MAA at 80°C on Tart-MRNi catalysts.

The plot represents the relative optical yields, ee/ee_0 , versus the relative reaction rates, v/v_0 , where v_0 and ee_0 (11%) are the rate and *ee* for the unpoisoned catalyst. Poisons are butylamine (∇), triethylamine (o), ammonia (\bullet) or pyridine (Δ) (mainly according to Yasumori²²⁵).

Poisons applied in²²⁵ were butylamine, triethylamine, ammonia and pyridine, all of which diminished the reaction rate but increased the optical yield.

Another method was elaborated by Chernysheva et al.¹⁸⁶. They studied the enantioselective hydrogenation of EAA (neat) on MRNi-Tart in the liquid phase at 75°C and 1 bar, using two methods of poisoning.

The first method started with modification and it was followed by poisoning (M-P),

The second method started with poisoning, and was followed by modification (P-M).

Poisons were thiophene and pyridine. In method P-M, the addition of thiophene *prior* to modification, inhibited the most active racemic EHB producing centers of the catalyst, resulting in the increase of *ee* from 11% to 15% at the 20% conversion level. Addition of pyridine by the same method, increased the *ee* from 2.35% to 13.5% at 10% conversion. However, upon further hydrogenation the *ee* decreased.

In method M-P the addition of thiophene after modification increased the *ee* value from 6.8 to 11% at 10% conversion. Thus the inhibition effect of the poison in the P-M process appears to be more effective than in the M-P process. This suggests that in the latter case all of the active centers are already occupied by the tartaric acid modifier molecules, which is more easily displaced from the less active chiral sites than from the racemic sites.

It was found that the relative adsorption coefficients (poison/EAA), calculated according to Balandin's theory of hydrogenation²³⁴, are 25 for pyridine and 14.6 for thiophene (in the M-P process), while in the P-M process they are much higher (1400).

4.3. Bimetallic and multimetallic modified hydrogenation catalysts

4.3.1. Supported Ni catalysts promoted with noble metals

In 1976 Orito et al.¹⁹³⁻¹⁹⁷ discovered that nickel catalysts deposited on Kieselguhr (Kg) (1:1), alloyed with 1% noble metals, and modified with (2*R*,3*R*)-tartaric acid exhibited an exceptionally high enantioselectivity in the hydrogenation of MAA to (*R*)-(-)-MHB. According to Orito¹⁹⁷ the optical yield of MHB reached an extremely high value, 99.4%, using Ni-Pd-Kg catalyst. However, Orito's group at that time determined the value of *ee* using polarimetric measurements and adopted the specific rotation value of 20.9° for the optically pure MHB (neat). But as it was later established, the specific rotation of neat MHB is 22.95° (Harada et al.¹⁰⁵), therefore the highest value of *ee* in the above studies should have been reported as 79.9-90.5 %, which are still extremely high values. The importance of these results led us to examine methods of preparation of the catalysts, the methods of carrying out experiments on the hydrogenation of MAA¹⁹³, and discuss the reason of such high enantioselectivity.

Kieselguhr (manufactured by the National Chemical Laboratory, Japan) was used without any additional purification or treatment (according to the personal communication by Prof. Orito in 1980 to one of the authors of this book, E.K.) in the solution of nickel nitrate and a platinum metal salt such that the ratios of Ni : Pt : Kg = 100 : 1 : 100 were attained. The mixture was allowed to stand for 1h and then was treated with a solution of sodium carbonate. The precipitate was thoroughly washed and dried for 24 h at 110°C. The resulting 3g of catalyst was heated by quartz lamp in a stream of hydrogen (7 L/h) up to 300°C for 1h (formation of alloy?), after which it was cooled and added to 100 mL of a 1.5% aqueous solution of (2*R*,3*R*)-tartaric acid at pH 4.1 under bubbling nitrogen. The temperature of the solution gradually increased to 85°C. The catalyst was then centrifuged and washed initially twice with water (with 25 mL in each case), then with methanol, and finally with the solvent in which the hydrogenation was to be carried out. The reaction was performed in an autoclave with stirring under a hydrogen

pressure of 60-80 bar with a substrate to catalyst ratio of 14:1. The reaction temperature was raised from 20°C to the required level at a rate of 0.7° per min. When the hydrogen uptake was complete, the catalyst was filtered off and the product distilled. The compilation of data in Table 4.7 is based on references 193-197 and shows the maximal optical yields of MHB under different conditions (the *ee* values were corrected in accordance with the 22.95° specific rotation of MHB¹⁰⁵).

By carrying out the reaction in THF and by adding small amounts of carboxylic acids into the reaction mixture the *ee* values of the products can be increased by 6-10%.

The method of synthesis of MHB with an *ee* of up to 90.6% was developed for the Ni-Pd-Kg catalyst, on which modification with tartaric acid is carried out at pH 4.1-4.5 and 84°C. Before reaction, the catalyst must be treated for 4h in THF without stirring, having added 1.5% of acetic acid at 109°C and maintaining a hydrogen pressure of 55 bar (Table 4.7., experiment No. 10). The reaction mixture (MAA in 44 mL of THF to which 1 mL of AcOH has been added) is kept initially without stirring for 1h at the same temperature and pressure and is then stirred for 10-20 h. The optical yield of MHB thus obtained reached a maximum value of 90.6% (Table 4.7., experiment No. 11). Instead of acetic acid, formic or benzoic acid may be added. The optical yield of the product could be increased if the added monocarboxylic acid has a pK_a , lower than that of the modifying agent, (2*R*,3*R*)-tartaric acid ($pK_a = 2.89$).

It follows from Table 4.7. that alloying of the nickel catalyst with platinum metals significantly increases enantioselectivity and the overall rate of the reaction. The deposited Ni-Ru-Kg catalyst is more effective (producing an *ee* of 50%) than the Raney catalysts, RNi-Ru, without a support, on which *ee*'s of only 4% and 17% were achieved, for the MAA and EAA hydrogenations, respectively⁹. An increase in the temperature of the modifying TA solution from 20°C to 80-90°C helps to increase the *ee* values of MHB. When the reaction is carried out in alcohol solutions, the *ee*'s of MHB diminish but the overall rate of reaction increases. The best solvents proved to be THF and ethyl acetate with addition of a carboxylic acid (acetic, formic or benzoic). The antiparallel changes of *ee* and the overall reaction rate observed earlier by Orito¹⁹⁴⁻¹⁹⁷ were confirmed by Klabunovskii and Vedenyapin⁹. Amongst the supports investigated (activated charcoal, alumina, silica gel, Kieselguhr) the best results were obtained with Kieselguhr (but only according to the data of Orito's group because, unfortunately, there are no literature data on the reproducibility of these results). Nevertheless, a question arises concerning the reason for the high enantioselectivity of nickel catalysts alloyed with other metals and especially concerning the specific role of supports. Bimetallic catalysts based on nickel and copper with added platinum metals (ruthenium, palladium), according to the reference 9, did not

exhibit an appreciable enantioselectivity in the EAA hydrogenation reaction (see next Parts of this Chapter 4 and references 9 and 238).

Number of experiment	Catalyst	Solvent	Rate	$[\alpha]_D^{20}$	<i>ee</i> (%)
1 ^a	Ni-Kg	none	5.9	12.20	53.2
2	Ni-Rh-Kg	none	7.8	13.75	59.9
3	Ni-Pt-Kg	none	9.7	14.20	61.9
4 ^b	Ni-Pt-Kg	THF	4.7	15.00	65.4
5 ^c	Ni-Pt-Kg	THF	7.2	18.05	78.6
6 ^d	Ni-Pd	none	3.8	9.15	39.8
7	Ni-Pd-Kg	none	8.7	14.65	63.8
8 ^c	Ni-Pd-Kg	THF	6.9	18.22	79.4
9 ^c	Ni-Pd-Kg	THF	2.8	20.10	87.6
10 ^c	Ni-Pd-Kg	THF	2.5	20.44	89.1
11 ^e	Ni-Pd-Kg	THF	2.5	20.79	90.6
12 ^f	Ni-Pd-Kg	THF	2.6	20.49	89.3
13	Ni-Pd-C	none	5.6	13.02	56.7
14	Ni-Pd-Al ₂ O ₃	none	5.2	11.13	48.5
15	Ni-Ir-Kg	THF	4.9	16.50	71.9
16 ^b	Ni-Ru-Kg	none	8.8	11.35	49.5
17	Ni-Ru-Kg	none	7.8	12.35	53.8
18 ^g	Ni-Ru-Kg	none	9.3	12.05	52.5
19 ^c	Ni-Ru-Kg	THF	6.7	16.75	73.0
20 ^h	Ni-Ru	none	1.6	4.10	17.0

Table 4.7. Rate of formation of (*R*)-(-)-MHB (mmol h⁻¹ g⁻¹) and *ee* values in the enantioselective hydrogenation of methyl acetoacetate on deposited nickel-kieselguhr catalysts, promoted with 1% noble metals and modified with (2*R*,3*R*)-tartaric acid (according to summarized data of Orito et al.¹⁹³⁻¹⁹⁷).

Composition: Ni:Pt:Kieselguhr = 100:1:100

Samples: 2.3g catalyst, 2.3g MAA, 44 mL solvent

Modification: 1.5% aqueous solution of TA, at pH 4.3 and 84°C

Hydrogenation: 55 bar H₂, temperature 21-130°C

(a) Ni:Kg = 1:1; (b) catalyst was modified at 20°C; (c) 1 mL AcOH

was added; (d) Ni:Pd = 100:1; (e) 0.05g HCOOH was added;

(f) 0.5g PhCOOH was added; (g) Ni:Ru:Kg = 100:1:100;

(h) Ni:Ru = 100:1.

Modification conditions: pH 4.5, 20°C. Samples: 0.2g of the catalyst, 41 mL ethyl acetoacetate. The hydrogenation was carried out at 60°C (these data are given for comparison, according to Klabunovskii⁹)

Nitta et al.²⁰⁵ investigated in details modified nickel catalysts deposited on different supports including Kieselguhr. They exhibited high enantioselectivities in many cases, but Kieselguhr as a support revealed no special properties. Apparently the addition of small amounts of noble metals to the

nickel catalyst preparation stage promotes a more complete reduction of nickel salt and the formation of nickel crystallites of optimum size²⁰⁵. The NiO reduction process is influenced significantly by Cl⁻ and Br⁻ anions. The addition of PdCl₂ to the initial NiO-SiO₂ system promotes the reduction of NiO but has little influence on enantioselectivity²⁰⁵.

Contrary to the data of Orito¹⁹³⁻¹⁹⁷, the deposition of nickel on Kieselguhr of the Japanese origin, "Shimalite brand" or on alumina with subsequent modification by (2*R*,3*R*)-tartaric acid does not make it possible to attain a value of *ee* in excess of 54-68% from the hydrogenation of MAA, even in the presence of high metal contents on the support (see Harada et al.⁵⁹). Similar *ee* values were also obtained when nickel was deposited on TiO₂ (*ee* of 70%) and ZrO₂ (*ee* of 68%) at 90 bar hydrogen pressure and 20°C⁵⁹.

The higher *ee* values attained by Orito¹⁹³⁻¹⁹⁷ appear to be partly accounted for by the high nickel content on the support (50%), which actually converts the deposited catalyst into nickel black catalyst and also by the especially favorable conditions for formation of the catalyst created by the addition of platinum metals. It is also possible that the Kieselguhr employed in the above studies contained promoting but unknown admixtures. Nitta²⁰⁵ concluded that the high effectiveness of the nickel catalysts¹⁹³⁻¹⁹⁷ may be accounted for by the special condition in catalyst formation. According to Nitta²⁰⁵, the introduction of 1% Pd into the Ni-SiO₂ catalyst during the reduction stage of the NiCO₃-SiO₂ precursor promotes the reduction of the salt, allowing for a decrease in the process temperature, and forms larger nickel crystallites. To better understand the reason for the high enantioselectivity of noble metal-promoted nickel-support catalysts detailed studies of the preparation process of modified nickel catalysts will be needed.

Conditions	Nitta et al.			Orito et al.
	A	B	C	
Ni(NO ₃) ₂ : Na ₂ CO ₃	1	1.2	0.83	1
Deposition temperature (K)	348	358	273	298
Ageing time (min)	15	30	5	60
Drying temperature (K)	383	393	323	383
Drying time (h)	24	45	20	24
NiCO ₃ content in deposit (%)	35-40	7-10 ^a	60-65	-

^a Ni(OH)₂ content

Table 4.8. Conditions of preparation methods of Ni-SiO₂-TA catalysts for the hydrogenation of MAA (ratio of Ni:SiO₂ = 1:1) adopted from Nitta et al.²⁰⁵ and Orito et al.¹⁹³.

Nitta²⁰⁵ attempted to reproduce the data of Orito¹⁹³⁻¹⁹⁷. The Ni-SiO₂ catalysts were prepared by three methods differing in the condition of deposition of catalyst and its reduction. The role of Kieselguhr (60-200 mesh) as a support

and the influence of the introduction of Pd on the formation of the catalysts and on their enantioselectivity were also investigated.

Table 4.8. presents the conditions for the preparation of nickel catalysts described by Nitta²⁰⁵ and, for comparison, the conditions quoted by Orito¹⁹³. In that work²⁰⁵ Nitta used silica gel with a specific area of 600 m²/g and Kieselguhr with a specific area of 5.7 m²/g supplied by the Japanese company Yoneyama Yakuhin Co. The suspension of the support was impregnated with a solution of nickel nitrate and precipitated with a solution of carbonate at 75°C. After drying at 100°C the catalytic mass was reduced in a stream of hydrogen for 1h at 500°C. In order to obtain the Ni-Pd-SiO₂ system, PdCl₂ was added to the catalytic mass before its reduction. The Pd was introduced in amounts to prepare a ratio of Ni:Pd:support =100:1:100²⁰⁵. As can be seen from Table 4.8., methods A and C differ in the severity of the conditions during the deposition and treatment of the catalyst mass. The catalyst obtained by method C contained an excess of NiCO₃. Method A is distinguished by milder conditions, similar to those adopted in Orito's experiments¹⁹³⁻¹⁹⁷.

Preparation method ^a	Catalyst ^b	T _r (K)	D (nm)	ee (%)
A	Ni-Kg	523	31	32.5
A	Ni-Pd-Kg	523	16	26.3
A	Ni-Kg ^c	573	31	12.1
A	Ni-SiO ₂	573	-	23.8
		673	9	50.6
A	Ni-Pd-SiO ₂	573	-	27.8
		673	12	41.6
B	Ni-SiO ₂	673	4	29.8
B	Ni-Pd-SiO ₂	673	5	20.1
C	Ni-SiO ₂	573	13	43.4
C	Ni-Pd-SiO ₂	573	13	30.1
C	Ni-SiO ₂ ^c	573	13	36.8
C	Ni-Pd-SiO ₂ ^c	573	13	34.6
C	Ni-Pd-Kg	573	12	27.7
	Ni-Pd-Kg ^c	573	-	63.8 ^d
	Ni-Pd-Kg	573	-	89.1 ^e

Table 4.9. The influence of the catalysts preparation method, the nature of the support, the reduction temperature (T_r) and the added palladium on enantioselectivity in the hydrogenation of methyl acetoacetate (MAA) to (*R*)-(-)methyl hydroxybutyrate (according to Nitta et al.²⁰⁵).

(a) see Table 4.8.; (b) Ni-Pd/support =100:1/100, modification with (2*R*,3*R*)-tartaric acid at pH 5.1; (c) modification at pH 4.1 (adapted mainly from Orito¹⁹³).

Method B affords a deposit containing less effectively reduced $\text{Ni}(\text{OH})_2$, the reduction of which gives rise to large crystallites, even in the presence of palladium ²⁰⁵. Depending on the composition of the initial mixture, the catalysts differ significantly in their enantioselectivity in hydrogenation of MAA in AcOEt at 60°C and a hydrogen pressure of 10 bar. It was shown ²⁰⁵ that nickel catalyst with added Pd, deposited on silica gel or Kieselguhr are usually less effective than the catalyst without added Pd, which conflicts with the data of Orito's group ¹⁹³. Admittedly, the introduction of palladium into the catalyst obtained by method A promoted some increase in enantioselectivity as a consequence of the increase in the average size of the nickel crystallites (see Table 4.9).

The use of Kieselguhr did not increase but actually somewhat decreased *ee*'s even when modification was carried out by the method of Orito ¹⁹³ at pH 4.1. The reaction rate on all samples of Ni-SiO₂-TA catalysts were similar and amounted to 1.4 - 0.8 mmol/min/g Ni. The introduction of Pd decreased somewhat the average size of the crystallites, which increased the rate of reaction, but did not increase *ee*'s. However, according to Orito ¹⁹³ the catalysts on Kieselguhr with added Pd are more active (the rates of the reactions were 2.5-8.7 mmol/min/g Ni) and more enantioselective, with *ee*'s 63.8 - 89.1%. Thus, contrary to Orito's data ¹⁹³⁻¹⁹⁷ the introduction of Pd and the use of Kieselguhr as a support does not lead to the formation of especially effective catalysts ²⁰⁵.

Increasing the Ni content above 25% in the fraction of NiCO₃ during the preparation method increased the average size of the nickel crystallites (Figure 4.6.).

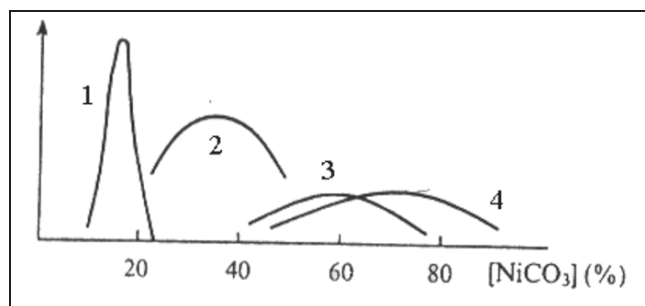


Figure 4.6. Influence of NiCO₃ content in the initial catalytic mass (catalyst reduction temperature 400°C) on the average size of the nickel crystallites.

Relative amounts of crystallites with 3.5 (1), 8.0 (2), 16.0 (3), and 18.0 (4) nm average size, respectively (according to Nitta ²⁰³).

The optical yield passed through a maximum corresponding to the catalyst obtained from the catalyst mass containing 37% of NiCO₃ and reduced at

500°C. Increasing the fraction of NiCO_3 to 58% makes it possible to lower the reduction temperature to 300°C. This leads to an increase in mean diameter of crystallites, D , to 15 nm, which promotes an increase in *ee*. Hence, it follows that the studied enantioselective hydrogenation of MAA is a structure-sensitive reaction and may be used even as a method for the monitoring of the distribution of nickel crystallites. Figure 4.7. presents the variations of the catalytic activity and the optical yields from MAA hydrogenations on Ni-SiO_2 with the fraction of NiCO_3 in the catalytic mass.

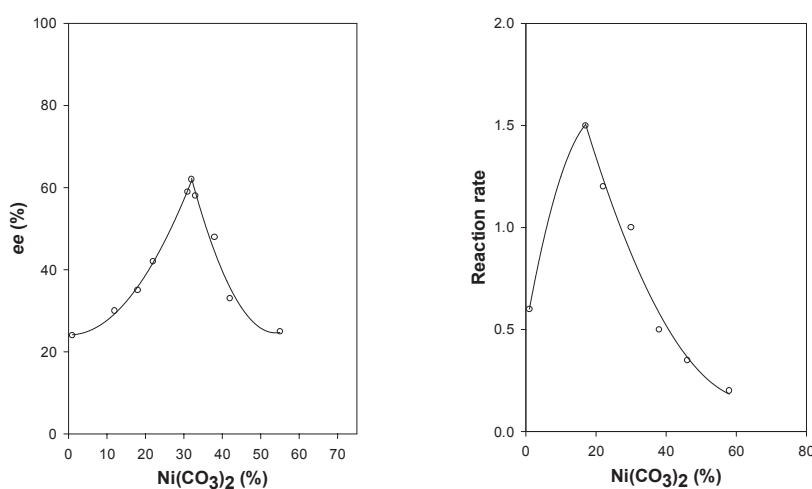


Figure 4.7. The effect of the NiCO_3 content in the initial catalytic mass (catalyst reduction temperature 400°C) on the optical yield of MHB (left) and the catalytic activity ($\text{mmol MHB min}^{-1} \text{gNi}^{-1}$) (right) on Ni-SiO_2 -TA catalyst in the hydrogenation of MAA (adapted from Nitta ²⁰³).

Studies have shown ^{201,203} that the formation of the catalyst is greatly influenced by the additives, the nature of the initial salts, and the reduction conditions. The high effectiveness of the bimetallic catalysts deposited on Kieselguhr may therefore be caused by the precise influence of these factors on the formation of the structure of the catalytic surface and primarily on the size of the nickel crystallites ^{198,199,200-203}.

The introduction of Pd into the catalyst apparently affects the degree of reduction of nickel which occurs at lower temperatures. This influence depends greatly on the nature of the initial salts; the presence of Pd promotes the reduction of NiCO_3 , which is formed on precipitation with Na carbonate, but has little effect on the reduction of Ni(OH)_2 . The presence of the support accelerates the partial transformation of NiCO_3 into Ni(OH)_2 , but reduction of the hydroxide requires more severe conditions.

According to Orito ¹⁹³⁻¹⁹⁷, the addition of AcOH significantly increases *ee* in the hydrogenation of MAA on Ni-Pd-Kg catalyst. The addition of certain salts into the modifying solution of tartaric acid also helps to increase *ee*.

The nature of the anion plays an important role, and NaBr proved to be the most effective modifying additive to RNi-TA catalyst preparations (Harada et al.¹⁰⁵). High concentrations of halide salts in the modifying TA solution have a negative effect on the rate of reaction and on *ee* (see Sachtler ²⁰⁹), but the addition of NaI or KI at very low concentrations tends to increase the optical yield. It has been found that NaI reduces *ee* sharply at a concentration of just 0.002%, whereas NaBr is effective even at higher concentrations by a factor of 100. This is associated with the fact that the iodide is adsorbed on nickel much more strongly than the bromide. Thus the anion affects *ee* much more than the cation ¹⁰⁵.

The nature of cation is important in the etching of the Ni-Al alloys and in the establishment of a suitable pH for the modifying tartaric acid solution. Best results were achieved when Na⁺ ions were employed at a NaBr concentration of 8% and a tartaric acid concentration of 1%. The optical yield in the hydrogenation of MAA was 70.2%. On the other hand, Li⁺ and Rb⁺ ions hardly affect *ee*. The cations are coordinated to the oxygens in the TA and MAA molecules adsorbed on the nickel. Sodium and potassium participate in the octahedral coordination which intensifies the template effect in the stereochemical interaction of TA with MAA (or MHB). The anions are by themselves incapable of showing the template effect, particularly at high salt concentrations; their function consists of fixing the appropriate amounts of cation on the catalyst surface needed for coordination to the TA-MAA (or MHB) complex. The influence of NaBr is also manifested by the fact that the salt is a weak poison for the nickel catalysts. It blocks the most active centers on the nickel surface increasing the fraction of selective centers and thereby intensifying the enantioselective effect of the modified centers (see, Sachtler et al.²⁰⁹⁻²¹⁷).

According to Nitta ²⁰⁵ the introduction of chlorides or bromides into the catalyst salt mass during the formation of deposited catalyst, promotes an increase in *ee* by virtue of the increase in D, but the overall rate of the reaction decreases under these conditions. Additions of NiCl₂, NaCl, FeCl₂, and NaBr or of HCl or HBr to the catalyst precursor mass prepared by method A (see Table 4.8.) increases *ee* from 36.1% to 49.7-57.5%, and also increases D from 13 to 20-30 nm while narrowing the size distribution of the nickel crystallites ²⁰⁵.

The increase in *ee* after the addition of NiCl₂ during the preparation process is of interest. The introduction of 29.8% of this salt into the catalyst mass prepared by methods A, B, and C (see Table 4.8.) sharply diminishes the specific surface of the reduced metal, which indicates an increase in D. Depending on the method employed, the *ee* increased from 36.1% to 54.7% in

method A, from 19.3% to 51% in method B, and from 39.4% to 53.2% in method C. The sharp decrease in the specific surface area indicates not only the growth of D but also the presence of surface chloride residues, which hinder the adsorption of hydrogen during reaction. At the same time, the Cl⁻ ions remaining on the catalyst surface after its reduction may act as promoting additives; that is, they may behave similarly to NaBr in the modifying solution (Harada, Izumi¹⁰⁵).

According to these authors, the RNi-TA-NaBr catalyst was prepared by leaching the Ni-Al alloy (42:58) at 100°C. The catalyst was washed with portions of deionized water 15 times and was modified with an 1% aqueous solution of (2*R*,3*R*)-tartaric acid, containing 10g NaBr, at 100°C for 1h. After modification, the catalyst was washed again with water and then with methanol. MAA was hydrogenated in a solution, containing EtCOOMe + 0.2 mL AcOH at a hydrogen pressure of 90 bar and a temperature of 10°C. The reaction rate was 0.2 mmol/min/g.Ni. A threefold repetition of the modification procedure increased *ee* from 83.1% to 88.6%. Under the same conditions, but without the addition of NaBr and AcOH, the *ee* was only 31.2%. The introduction of NaBr at a concentration of 0.01-0.04 mmol/g Ni, did not affect the degree of adsorption of TA on nickel and the optical yield increased in proportion with the NaBr concentration. This has been attributed to the presence of two types of centers on the surface of the modified catalyst⁹: selective centers, modified with TA on which the (*R*)-(-)-MHB is formed, and nonselective centers on which the racemic MHB is produced. This method of co-modification with NaBr in addition to tartaric acid also has its negative aspects. For example, NaBr diminishes the activity of the nonselective centers and lowers the overall reaction rate. In order to compensate this effect, it is necessary to increase the pressure and temperature of the reaction, and this entails a decrease in regioselectivity and the appearance of side products, in particular the methyl (5-hydroxy-3-methyl-4-oxoheptanoate).

The behaviour of the deposited nickel catalysts are somewhat different from that of the Raney catalysts. The presence of residual amounts of Cl⁻ ions in the Ni-SiO₂ catalyst imparts stability during repeated hydrogenations. On the other hand, the Ni-SiO₂ (1:1) catalyst modified with TA with added NaBr is not quite so effective²⁰⁵ as RNi¹⁰⁵. The modification by NaBr increases *ee* in the MAA hydrogenation reactions from 36.1% to 46.0%, but after repeated hydrogenations on the same portion of the catalyst, the *ee* fell to 11.0%, while the catalyst promoted by the addition of NiCl₂ to the catalyst mass before reduction retained its stability in three consecutive experiments (chemical yields are 90%; 79%, and 81% and *ee*'s are 52.7%, 55.0%, and 54.9%, respectively). This can be explained not only by the presence of residual amounts of the halogen on the nickel surface, but also by a more uniform size distribution of the nickel crystallites. Promotion by halides (nickel chloride) of the initial catalyst mass increased the degree of

reduction of NiO to metal²⁰⁵. This effect is manifested to a particularly notable extent in reduction of the catalyst mass obtained by method B (Table 4.8.) and containing Ni(OH)₂, which is reduced with difficulty as a consequence of the strong interaction with the support. As a result of this, the catalyst obtained has higher activity but lower enantioselectivity.

The low enantioselectivity of the Ni-alumina catalyst, in the preparation of which NaOH is used for the hydroxide preparations, can be accounted for by the strong interaction of the metal with the support and the formation of Ni-Al compounds on the surface. However, similar catalysts formed under circumstances which rule out the formation of small nickel crystallites, have the same enantioselectivity as Ni-SiO₂ (Zubareva et al.¹⁶³).

A series of studies of Izumi's group^{1-4,103,105} were devoted to the development of methods for increasing the enantioselectivity of the RNi-TA catalysts in the hydrogenation of MAA. Increasing the leaching temperature of the Ni-Al alloy increases optical activity of the product, presumably due to the decrease in the residual amount of Al present in the catalyst as aluminium hydroxide. The OH groups present in TA and Al(OH)₃ compete with one another for the formation of hydrogen bonds with MAA and thereby reducing *ee*. Elimination or blocking of the aluminium-enriched nickel centers increases the fraction of chiral centers and increases *ee*. This view is confirmed by the fact that the nickel catalyst, HNi-TA, obtained from reduction of NiO in a stream of hydrogen (8 L/h) at 350°C and modified with a 1% solution of TA at 85°C and pH 4.1, exhibits higher enantioselectivity than the RNi-TA Raney catalyst. The overnight hydrogenation of MAA (11.5 mL) in a solution of EtCOOMe (23ml) + AcOH (0.2 mL) at 110 bar initial hydrogen pressure and 120°C, leads to the formation of (*R*)-(-)-MHB with an *ee* of 81.6%, whereas the optical yield on the RNi-TA catalyst under approximately the same conditions leads to only an *ee* of 44-46%^{55,103}.

4.3.2. Enantioselective lanthane-nickel intermetallic compounds

Multicomponent metallic hydrogenation catalysts, based on intermetallic compounds (IMC) of rare-earth elements with nickel, copper, cobalt, and other *d*-metals and their hydrides are of interest for asymmetric catalysis as models of clusters quite similar to bimetallic systems. Most studies were devoted to two structural systems LnM₃ and LnM₅, where Ln = La, Sm, Gd, Ce, Pr, and Nd and M = Ni (see Klabunovskii, Konenko's group^{13,28,171-183,251,252}). Comparison of LnNi₅ catalysts with Ni catalysts supported on oxides of Ln, show higher activities of the IMC's and their hydrides in hydrogenation of propene (100°C, 1 bar), where LaNi₅ proved to be the most active catalyst¹⁷³.

Specific activities of hydrides of IMC, such as LaNi₅ or LaCo₅, are ten times higher, than activities of supported catalysts, such as 5% Ni-CeO₂¹³.

Originally intermetallic compounds and their hydrides like LaNi₅H₆ and La_{1/2}Pr_{1/2}Ni₅H₅ treated with aqueous solution of (2*R*,3*R*)-tartaric acid at pH

4.8, produced *ee*'s in the hydrogenation of EAA into (*R*)-(-) EHB at 80°C and 100 bar hydrogen pressure of not more than 9.8 and 5.7%, respectively (Konenko et al.¹⁷¹). Using the catalyst 5% Ni-CeO₂ produced the same result: (*R*)-(-)EHB with an *ee* of 5.7%. This fact probably indicates that the responsible component for enantioselectivity in the IMC's is Ni, which as the result of segregation, enriched the surface of the IMC's and formed during the process of modification with tartaric acid chiral clusters. However, it was found that after modification the IMC LaNi₃ produced an *ee* of 11.9% in spite of the fact that segregation in this sample became difficult or even impossible (Konenko¹⁷⁵). Substitution of the fraction of Ni atoms for other metals, such as Cu in LaNi_(5-x)Cu_(x) increased the stability of IMC and its hydrides (Starodubtseva et al.^{174-176,252}).

In accordance with Balandin's multiplet theory of heterogeneous catalysis²³⁴ the best catalytic activity will occur in catalytic systems with optimal bond energies between catalyst substrate molecules. Indeed, most catalytic and enantioselective activities in a series of IMC's of the general formula LaNi_(5-x)Cu_(x) reveal LaNi₃Cu₂H_{2.7} producing an *ee* of 15.6% and occupying a position of stability between LaNi₅ and LaNiCu₄¹⁷⁴. Thus isostructural substitution of one or two atoms of Ni with Cu in LaNi₅ leads to more effective chiral catalysts; so with a content of Cu 28.7 atomic % in LaNi₃Cu₂, an *ee* of 17% was accomplished¹⁷⁴. This fact indicated that the catalytic and enantioselective properties of IMC resulted from the whole system rather than from the segregation of Ni into a separate phase on the surface of the IMC's¹³.

The influence of tartaric acid modifying solution pH on the *ee*'s of products from hydrogenation also influence the catalytic activity of the entire IMC cluster. Thus for IMC's of the type LaNi₄Cu, the optimal pH is 5, whereas for SmNi₄Cu and GdNi₄Cu the optimal pH is 9. In accordance with values of stability constants of complexes of Ln-TA, modification at pH 9 of the IMC of composition LnNi₃Cu₂, where Ln = La, La_(0.5)Sm_(0.5), and Sm_(0.5)Gd_(0.5), lead to increasing optical yield: 4.4% to 6.1% and 9.9%, respectively. Hydrogen pressure and reaction temperature also influence the value of *ee*. The most effective catalyst, LaNi₄Cu H_{6.2}, produced *ee* values of 11.5% at 80°C and 40 bar hydrogen pressure, 27% at 80°C and 80 bar, and 9.7% at 40°C and 80 bar¹³.

Thus chiral properties of intermetallic catalysts are determined both by the ratio of Ni to Cu in the crystalline lattice of the hydride and by the nature of the atoms of different rare earth elements in the clusters.

Most effective catalysts were prepared by introducing cobalt into the matrix of the hydride of LaNi₅^{13,178}. These catalysts revealed increased enantioselectivity and catalytic activity in comparison with LaNi_{5-x}Cu_x. For LaNi₄CoH_{3.5} an *ee* of 26.6% was obtained. This value is twice the value obtained with IMC catalysts containing Cu.

Figure 4.8. shows the dependence of *ee* and conversion on the amounts of cobalt atoms in $\text{LaNi}_{5-x}\text{Co}_x$. For comparison, the data of IMC's containing Cu are also shown. As can be seen from Figure 4.8. for both types of IMC's the *ee* and conversion of EAA depends on the number of Co or Cu introduced into the intermetallic LaNi_5 ¹³.

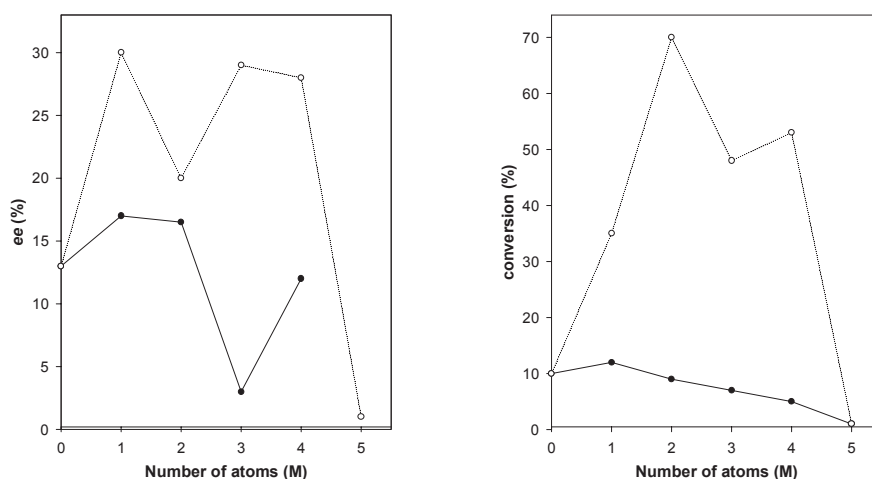


Figure 4.8. Dependence of optical yield (left) and conversion (right) in the enantioselective hydrogenation of EAA into EHB on the number of atoms (M) in the crystalline lattice of $\text{LaNi}_{(5-x)}\text{M}_{(x)}$. M = Co (white circles) and Cu (black circles), pH 4.5. EAA hydrogenated at 80°C, 80 bar, 7h (according to Klabunovskii¹³).

Upon introduction of Cu into LaNi_5 , *ee* value did not exceed 17%, but upon introduction of Co, *ee* increased to 30%, and after modification of intermetallic LaNi_3Co_2 with a solution of tartaric acid at pH 4.5 with addition of trimethylacetic acid, *ee* increased to 45% (Figure 4.9.)¹³. It is interesting to note that the introduction of NaBr in the modifying solution of tartaric acid was very effective for the preparation of modified RNi catalysts, but had no influence in the modification of IMC's¹³.

Introducing into the IMC other metals like Mn, Cr, Ti, V, or Al instead of Co, LaNi_5 , increased its stability for forming hydrides, but decreased enantioselectivity. Only in the case of $\text{LaNi}_4\text{MnH}_2$ and $\text{LaNi}_4\text{CrH}_{2.5}$ were moderate enantioselectivities obtained with *ee*'s of 20% and 16%, respectively¹³.

Interesting results were obtained from partial substitution of Co for Cu in $\text{LaNi}_{5-x}\text{Co}_x\text{H}_n$ ¹³. In general both the catalytic activity and the enantioselectivity decreased in the hydrogenation of EAA, and the $\text{LaNi}_3\text{Co}_2\text{H}$ system produced a rather high *ee* of 52% as shown in Table 4.10. (Starodubtseva et al.¹⁸⁰).

Intermetallic catalyst	Conversion (%)	<i>ee</i> (%)
LaNi ₃ Co ₂ H _{3.5}	100	52
LaNi ₂ CoCu H _{2.7}	96	9
LaNi ₂ Co ₂ Cu H	20	27
LaNi ₂ CoCu ₂ H _{3.8}	30	17
LaNiCo ₂ Cu ₂ H _{3.8}	12	13

Table 4.10. Conversion and *ee* values on different intermetallic catalysts.

Intermetallic catalysts without Ni exhibited low activity, successive and complete substitution of Ni for Co leads to sharp decrease in catalytic activities and the enantioselectivity. Partial introduction of Cu atoms into LaCo₃ did not give increasing activities¹³.

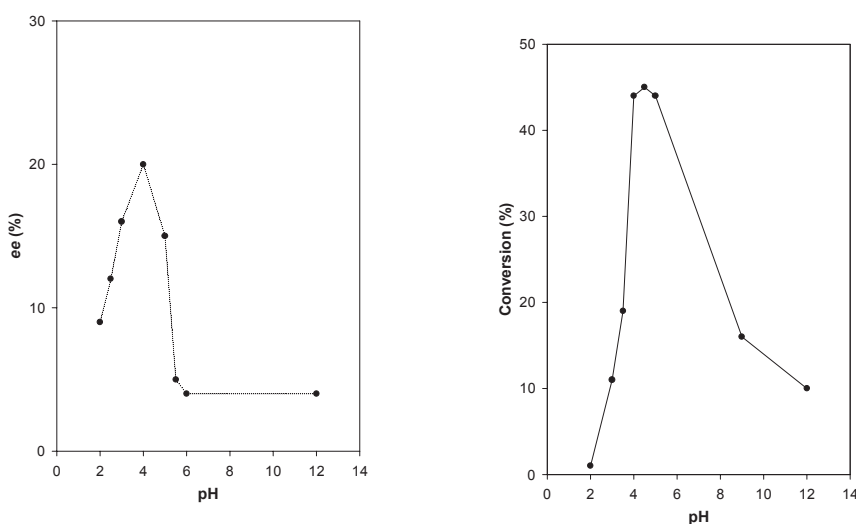


Figure 4.9. Dependence of optical yield (left) and degree of conversion (right) on the pH of the modifying solution of (2*R*,3*R*)-(+)-tartaric acid in the LaNi₃Co₂H_{3.5} catalyzed hydrogenation of EAA^{13,177}.

The greatest enantioselectivity, *ee* = 60%, was observed on the system LaNi_(5-x-y)Co_(x)Cu_(y) which can be explained by the formation of mixed complexes [LaCo_(x)Cu_(y)-TA]¹³. Such behavior of intermetallic catalysts based on systems LaNi_(5-x-y)M_(x)M_(y) is significantly different from Ni-Co catalysts modified in the same way as IMC; on binary Ni-Co catalysts, the *ee* values continuously increased with increasing Ni content of the catalysts.

Klabunovskii et al.¹⁴⁶ have been shown that in the hydrogenation of EAA and acetylacetone into ketol and diol, enantioselectivities are diminished upon using a series of metal catalysts, like Ni, Cu, Co, modified with TA or amino acids and in the case of Co-Ni the *ee* was not above 5-8%. But IMC's contained La, Ni, Co components were much more active and stereospecific than binary Ni-Co catalysts, which can be explained by the nature of clusters that involved atoms of three different elements: La, Ni and Co (or Cu) (see Starodubtseva et al.¹⁷⁷).

Modifying at the optimal range of pH, intermetallic catalysts were more stable during the course of catalytic reactions, than was suggested by their ferromagnetic properties (Faraday method). Thus the higher *ee*'s corresponded to the less degradable hydrides during the modification and catalytic processes. The catalytic properties of intermetallic catalysts depend also on the strength of IMC-hydrogen interaction. Therefore the introduction of Co in IMC increases the strength of the IMC - H bond and increases the stability of the hydride. This behavior is especially characteristic for the catalyst LaNi_3Cu_2 , for which the maximal values of magnetic moments corresponds to the maximal density of hydrogen atoms in lattice of hydride and optimal values of bond energies IMC -H (Konenko et al.¹⁷⁸).

For intermetallic catalysts the dependence of *ee* on pH of the modifying TA solution results in the same extrenal character and effect as exhibited by the modification of Cu and Co catalysts¹³.

For the hydrogenation of EAA, Figure 4.8. shows the extrenal dependence of *ee* and degree of conversion on the initial value of pH of the modifying TA solution with a maximum at pH 4.5 for the catalyst $\text{LaNi}_3\text{Co}_2\text{H}_{3.5}$. The high catalytic activity of the IMC's containing Co is connected to the stability of the original hydrides. The isotherms of adsorption of hydrogen by the IMC's showed that replacing Ni for Co diminishes their stability¹⁷⁷. Comparing the stability of the two IMC's, $\text{LaNi}_{(5-x)}\text{Co}_x\text{H}_n$ and $\text{LaNi}_{(5-x)}\text{Cu}_x\text{H}_n$, showed that hydrides in the lattice containing Co are more stable than those containing Cu. This indicates the formation of chiral complexes involving tartrate on the surface of the catalysts⁹.

Composition of intermetallides (%)	La	Ni	Co	Cr
IMC, original	14.7	60.0	15.8	9.5
IMC-hydride	17.5	64.6	7.9	10.0
IMC $\text{H}_{4.2}$, after modification at pH 4.5	8.3	65.2	7.8	18.7
IMC $\text{H}_{4.2}$, after modification at pH 7.0	22.3	44.5	12.2	21.2
Bulk composition of IMC original hydride: $\text{LaNi}_3\text{CoCrH}_{4.2}$	32.3	40.9	13.7	12.1

Table 4.11. Composition of surface layers of intermetallic compounds.

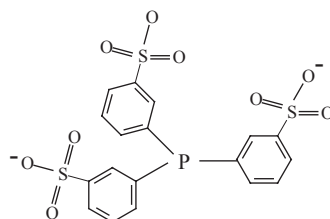
In addition to the enantioselective effect from complex formation, also observed was the enhancement effect of pH and the evolution of hydrogen during modification of the hydrides of the IMC's. During these processes the presence of components (especially La) in the modifying solution resulted in enrichment of IMC surface Ni. Data on Table 4.11. from X-ray photoelectronic spectra show the composition of surface layers of a number of IMC's¹³.

The substitution of La for Sm or Gd in the $\text{LaNi}_3\text{CoCr-H}_{4.2}$ IMC resulted in a sharp decrease in catalytic and enantioselective activity, which indicates an involvement of the rare-earth metals in chiral clusters besides the involvement of the *d*-metals¹⁷². This decrease of *ee* values can be attributed to the increased stability of the tartrate complexes in the case of IMC's containing Sm or Gd in comparison with IMC's containing La¹³. Substitution of La in the LaNi_5H_4 IMC¹³ by other rare-earth metals like Pr, Sm, and Gd, also leads to decreases in stability of the hydrides¹⁸³ and this forces an increase in hydrogen pressure during the preparation of IMC-hydrides. In contrast, substitution of Ni for other metals in LaNi_5 -hydride increases the IMC-H bond strength. Therefore, catalysts based on the most stable hydrides like LaNi_4M (M=Al,Ti,V) exhibit high catalytic activity, but low enantioselectivity¹³. Table 4.12. summarizes some intermetallic hydride's catalytic activities in the hydrogenation of EAA^{13,177,179,181,182}.

As can be seen from Table 4.12., using multimetallic IMC catalysts with 5 and 6 components do not exhibit any preferences for enantioselective hydrogenation compared to the simpler structures.

Chiral intermetallic, heterogeneous and heterogenized catalysts were put to practical use; for example in the diastereoselective hydrogenation of D-fructose into mannitol and sorbitol^{13,192,251}.

Inulin, a polysaccharide containing one D-glucose and 10-50 D-fructose units, when hydrolyzed and hydrogenated in a one pot approach, would be an attractive D-mannitol feedstock. With this goal in mind, the hydrogenation was studied^{192a} with fructose as a model compounds using a water soluble catalyst, $[\text{Ru}(\text{TPPTS})_2]$ (where TPPTS is the tris(3-sulphonatophenyl)phosphine ligand, Scheme 4.7.), at 90°C. The addition of HCl increased selectivity and activity in the preparation of D-glucitol and D-mannitol.



Scheme 4.7. The TPPTS ligand.

Intermetallic hydride	conversion (%)	ee (%)
LaNi ₅ -H _{6.0}	14.90	12.7
LaNi ₄ Co-H _{4.8}	48.80	26.6
LaNi ₃ Co ₂ -H _{3.7}	100.00	20.0
LaNi ₂ Co ₃ -H _{3.9}	52.90	28.0
LaNi ₂ Co ₂ Cu-H _{3.9}	10.00	21.0
LaNiCo ₄	0.00	0.0
LaCo ₄ Cu	19.30	3.5
LaCo ₃ Cu ₂	14.40	0.0
LaCo ₂ Cu ₃ -H _{3.0}	0.00	0.0
La _{0.5} Sm _{0.5} Ni ₄ Co	27.70	19.7
Sm _{0.5} Gd _{0.5} Ni ₄ Co	0.00	0.0
CeCo ₃	5.60	0.0
20% Ni-80% Co	22.00	11.0
LaNi ₄ Al-H _{4.0}	60.90	6.3
LaNi ₄ Ti-H _{3.5}	93.40	1.1
LaNi ₄ V-H _{3.5}	95.4	5.2
LaNi ₄ Cr-H _{4.0}	96.0	16.3
LaNi ₄ Mn-H _{5.0}	40.70	23.4
LaNi ₄ Cu-H _{5.8}	17.50	17.0
LaNi ₃ Cu ₂ -H _{3.7}	13.30	15.6
LaNi ₂ Cu ₃ -H _{3.5}	9.50	4.3
LaNi ₃ CoCr-H _{4.2}	58.20	13.5
LaNi ₃ CuCr-H _{3.9}	64.70	16.0
LaNi ₄ Co _{0.5} Cu _{0.5} -H _{4.2}	10.30	0.0
LaNi ₃ CrMn-H _{3.9}	48.20	3.8
LaNi ₃ Co _{0.5} Cu _{0.5} Cr _{0.5} Mn _{0.5} -H _{4.2}	36.60	6.8
LaNi ₂ Co _{2.5} Mn _{0.5} -H _{5.3}	65.40	20.9
LaNi ₂ Co ₂ Mn-H _{3.5}	77.80	7.2

Table 4.12. Dependence of conversions and optical yields in the hydrogenation of ethyl acetoacetate on intermetallic catalysts (at 80°C and 80 bar for 7h) on the composition of hydrides of IMC, modified with (2*R*,3*R*)-(+)-tartaric acid at pH 4.5 ^{13,177, 179,181,182}.

Veksler et al.^{192 b} found that to accomplish selective hydrogenation of D-fructose to the preferential formation of mannitol, the pH of the modifying solution of TA is important. This process was studied using RNi modified with (2*S*,3*S*)-TA > L-Glu > (2*R*,3*R*)-TA > RNi ^{192b}. RNi-(*SS*)-Tart proved to be the best catalyst among the other modified catalysts. Hydrogenation of an

aqueous solution of fructose at 80°C and 90 bar hydrogen resulted in D-glucitol with a yield of 65.7% and a ratio of sorbitol to mannitol of 1:9.

For this process a number of isostructural IMC's, LaNi_3Co_2 , LaNi_3Cu_2 , and $\text{LaNi}_3\text{M}'\text{M}''$ were used, where $\text{M}'\text{M}''$ are CoCu, CoCr, MnCr, or $\text{Co}_{0.5}\text{Cu}_{0.5}\text{Cr}$, modified with (2*R*,3*R*)-(+)-TA. It was found that the crucial significant factors for catalyst selectivity were the pH values of the modification process.

At pH 7-8 for the intermetallic catalysts LaNi_5 , LaNi_3Co_2 , and LaNi_3Cu_2 and at pH's 4.5-5.5 for the catalyst LaNi_3CoCr at 80-90°C and 50 bar hydrogen pressure the excess of D-mannitol was found to be 46% and of D-glucitol 39% with the optimal catalyst being LaNi_3Co_2 -TA. The study of the mechanism of this reaction showed that mainly the *alpha*-D-fructopyranose and *alpha*-D-fructofuranose stereomers were responsible for the formation of D-mannitol,¹³

It is of interest that the above mentioned IMC's, based on La, Ni, and Co, are very stable and active catalysts for the vapour phase decomposition of methanol into hydrogen and carbon monoxide (Klabunovskii et al.^{188,189}).

4.4. Modified nickel and bimetallic catalysts

In general, chirally modified bimetallic catalysts exhibited low to moderate enantioselectivity in the hydrogenation of EAA. A number of studies were carried out by Klabunovskii's group to investigate new metal catalysts, modified mainly with tartaric acid and amino acids, which were active in enantioselective hydrogenation of ethyl acetoacetate and acetylacetone.

They were catalysts containing Cu^{140,141,143-148,150,184,242,246,247}, Co^{114,140-142,146,161,162, 184,239,242, 247}, Ru^{121-124,,235,243,244} or Pd^{157,160,190,220,221,250,253}, and bimetallic catalysts containing Ni-Cu^{149-160,245,249}, Ni-Co^{140,142,163-165,183}, Ni-Ru^{133,134,235}, Ni-Pd^{170,193-197,253}, Cu-Ru^{133-139,169,235,245,250}, or Cu-Pd^{166-170,190,250}, and multimetallic catalysts based on intermetallide Ln-Ni^{13,171-183,188,189,251,252}. The mechanism of the reaction on bimetallic catalysts was studied in^{9,14-19,21-30,145,146,184-187,238}.

4.4.1. Nickel - Copper Catalysts

Chiral Ni-Cu powder catalysts without support^{149-160,245,249} were rather active in the liquid phase hydrogenation of EAA. These catalysts were prepared by three procedures used by Chernysheva et al.^{159,248}:

- a) by reduction of mixed oxides of Ni and Cu ("Ni-Cu-1")
- b) by reduction of their hydroxides ("Ni-Cu-2")
- c) by reduction of their carbonates ("Ni-Cu-3").

Changes in the nature of the original salt led to different phases and surface compositions of the catalysts and to different relationships of the reduced and remaining non-reduced forms of the metal compounds, which influenced the activities and enantioselectivities of catalysts after their modification with TA.

Table 4.13. demonstrates the effect of various methods of preparation on the phase composition of Ni-Cu catalysts modified with tartaric acid and on their catalytic and enantioselective properties during hydrogenation of EAA (according to Zubareva et al.¹⁵⁴).

As can be seen from Table 4.13., the Ni-Cu-1 catalyst consists of two phases of solid solutions, Ni-Cu enriched with Ni or Cu and small quantities of NiO. This catalyst is characterized by high *ee*'s but low catalytic activities. In the 'precipitated' catalysts, Ni-Cu-2 and Ni-Cu-3, copper and nickel separated as phases resulting in sharp increases in hydrogenation activities but lower enantioselectivities. Reduction of precursors of these three catalysts in flowing gas (hydrogen + nitrogen) produced catalysts that gave enantiomeric excesses of 50.0, 14.4, and 21.3%, respectively, in the hydrogenation of EAA.

Catalyst	S (m ² /g)	Rate (mmol/ m ² · min)	Optical yield (%)	Phase I		Phase II		Cu	Ni	NiO	CuO
				Cu	Ni	Cu	Ni				
Ni-Cu-1	9.3	0.6	50.0	23.3	76.7	79.4	20.6	-	-	5.1	-
Ni-Cu-2	1.5	8.5	14.4	-	-	-	-	49.8	26.0	22.4	1.8
Ni-Cu-3	1.3	11.8	21.3	23.3	76.7	85.4	14.6	23.0	35.2	-	1.6

Table 4.13. The effect of preparation methods on the catalytic and enantioselective properties and phase compositions of Ni-Cu catalysts modified with tartaric acid in the hydrogenation of EAA (according to Zubareva et al.¹⁵⁴).

Apparently, the presence of small amounts of NiO on the surface of Ni-Cu-1 was favorable for increasing complex formation with TA and hence for increasing optical yields; however, a further increase in the amounts of NiO or CuO in the Ni-Cu-2 and Ni-Cu-3 catalysts led to diminishing *ee*'s.

In order to further elucidate the reasons for higher enantioselectivities, consideration will be given below to the x-ray photoelectronic spectra of the TA modified Ni which proved to be enantioselective in the hydrogenation of MAA in the gas phase, see Figure 4.10. (according to Yasumori²²⁵).

The electronic state of the Ni catalyst surfaces of different natures were studied by x-ray photoelectron spectroscopy in which binding energies were calibrated with those of 4f_{5/2} and 4f_{7/2} from peaks of Au taken as the standard.

Spectrum (a) for the modified surface exhibits a characteristic peak 1 at 852.7 eV, which is close to that for the Ni film at 852.5 eV. Peaks 2 and 4 correspond to Ni₂O₃ and peak 3 at 858.5 eV corresponds to the satellite peak in the spectrum of a Ni film. None of the Ni surfaces covered with adsorbed oxygen and oxides gave rise to any peaks near peaks 1 and 3. In the spectra of Ni-tartrate (c) and Ni-oxide coated with TA (d) peak 1 did not appear. In

the modified surface there are two peak maxima at 1.1 and 1.2eV which indicate that the modified surface is protected from oxidation by TA.

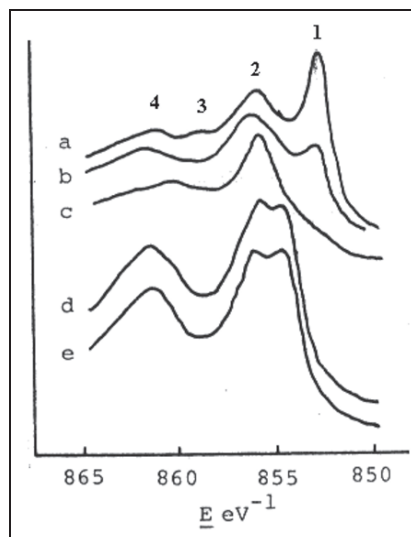


Figure. 4.10. X-ray photoelectron spectra of Ni $2p_{3/2}$. The plots of intensity (I) of characteristic peaks (1, 2, 3, and 4) versus binding energy (E). (a) modified Ni, (b) unmodified Ni, (c) nickel tartrate, (d) Ni-oxide modified with TA, (e) Ni-oxide (according to Yasumori ²²⁵).

Zubareva et al.¹⁵⁴ studied the X-ray photoelectron spectra of a Cu-Ni-TA catalysts (Table 4.13.) in the region of Ni3p and Cu3p of the original Ni-Cu-1 catalyst (Figure 4.11., a, curve 1). The ratio of surface concentrations of Ni:Cu was near 1.5. In the Ni-Cu-2 catalyst the surface layer was enriched with Cu⁰ (curve 2). After modification of both catalysts with TA, their surfaces became enriched with Ni in such a way that for Ni-Cu-1 the Ni:Cu ratio was 1.3 and for Ni-Cu-2 this ratio was 2. Spectra of Ni2p and Cu2p in Ni-Cu-1 (Figure 4.11., b and c) showed that Cu and Ni are in the reduced state. And from Figure 4.11., b, curve 3, it follows that a portion of Ni in the modified Ni-Cu-1 catalyst was transformed into the Ni²⁺ oxidized state, which corresponds to the NiO state.

Thus maximal enantioselectivity of catalyst Ni-Cu-1 (Table 4.13.) can be explained by the presence of NiO, CuO, and Ni²⁺ centers on the surface. These conclusions were confirmed with data of Nitta et al.¹⁹⁹ for Ni-silica catalysts modified with TA that were active in the enantioselective hydrogenation of MAA and showed ¹⁹⁹ that centers of Ni and Ni²⁺ are on the surface of the catalysts.

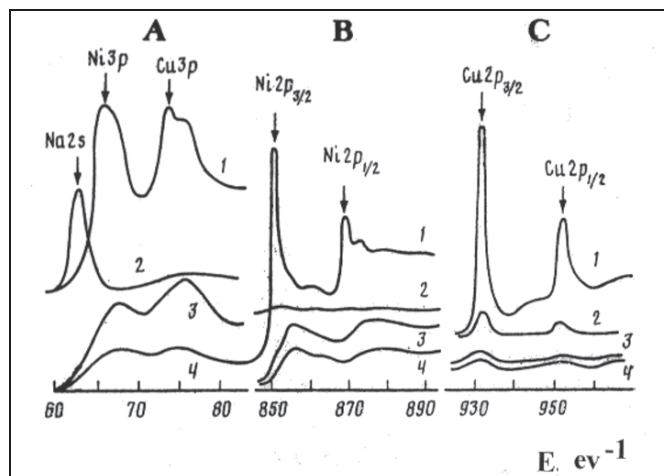


Figure 4.11. X-ray photoelectronic spectra of Ni3p and Cu3p (a), Ni2p (b) and Cu2p (c) of different Ni-Cu catalysts.

(1) original Ni-Cu-1 catalyst; (2) original Ni-Cu -2 catalyis;
 (3) Ni-Cu-1 modified with TA; (4) Ni-Cu-2 modified with TA
 (according to Zubareva et al.¹⁵⁴).

The data on differential thermal desorption spectra of the reduction of NiO and CuO proved to be very important. Despite the differences in reduction temperatures of individual oxides (320°C and 270°C), a maximum *ee* was observed at that reduction when mixture of oxides were reduced at a lower temperature, 220°C, because Ni-Cu catalysts contain two phases: a Cu phase and a Cu-Ni-alloy phase. With increase of the copper content, the Ni-Cu phase is enriched in the bulk with Ni and on the surface with Cu. According to Klabunovskii et al.¹⁵¹ the Ni-Cu (70:30) catalyst is five times more active than the pure Cu catalyst, but after modification of this catalyst with TA, its enantioselectivity in the hydrogenation of EAA was lower than either the modified pure Cu catalyst (*ee* 50%) or pure Ni-TA catalyst (*ee* 33%) under the same conditions. Thus the bimetallic Ni-Cu catalysts revealed synergism in catalytic activity but not in enantioselectivity.

Increasing the copper content of the mixed Ni-Cu, inactivates the catalysts, because copper, as an inactive component and dilutes the Ni centers responsible for enantioselectivity. The specific activity related only to the Ni-Cu alloy phase in the concentration range of 20-80 mol% Cu (Figure 4.12.), so the *ee* and the specific rate remained constant corresponding to the constancy of the surface concentration of the active component in the Ni-Cu catalysts.

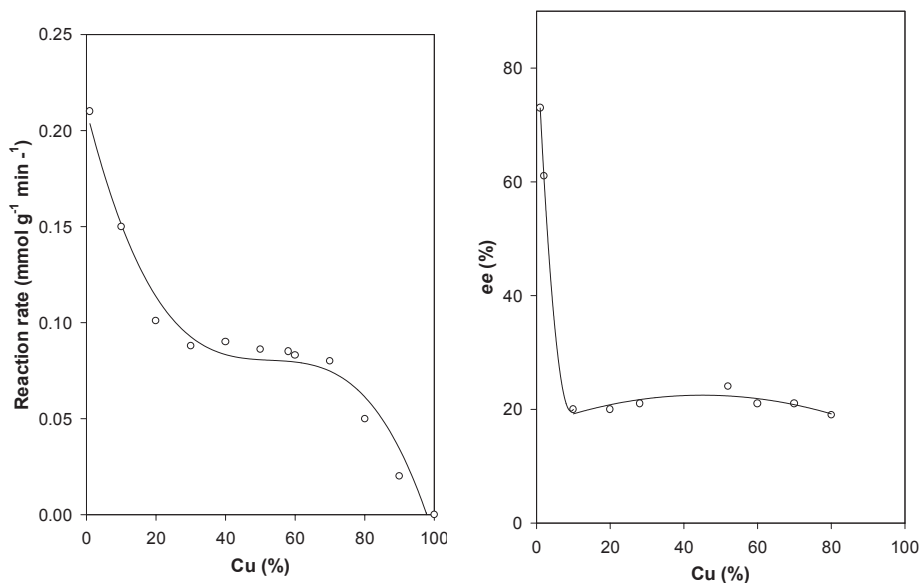


Figure 4.12. Effect of the composition of Ni-Cu catalysts, modified with TA, on the reaction rate (left) and on the *ee* (right) in the hydrogenation of EAA¹³.

Increasing the fraction of Ni in the Ni-Cu catalysts leads to segregation of Ni on the surface, which was confirmed by Chernysheva et al.¹⁴⁹ in the hydrogenation of EAA on Ni-Cu catalysts modified with (*S*)-phenylalanine, *S*-Phe. Indeed, on the Cu-*S*-Phe catalyst the product (*S*)-(+)-EHB was obtained, whereas on the Cu-Ni catalyst, (90:10) modified with *S*-Phe, another enantiomer, the (*R*)-(-)-EHB, was obtained. The latter product was also observed on Ni-*S*-Phe. This fact confirmed that Ni was segregated on the surface of the Ni-Cu catalysts with the maximum Ni contents of 20-40% (see Figure 4.13.)¹³

The effect of modifying solution pH on the *ee* during hydrogenation on Ni and Ni-Cu catalysts was displayed by the appearance of two *ee* maxima at pH 6 and pH 10.5 (Figure 4.14.). For the pure Ni-TA catalyst the resulting *ee*'s were 57% and 71% at pH's of the modifying solutions of 5 and 10, respectively. However, for the Ni-Cu-TA catalyst *ee* values were 20% at pH 5 and 22% at pH 10 (Figure 4.14.).

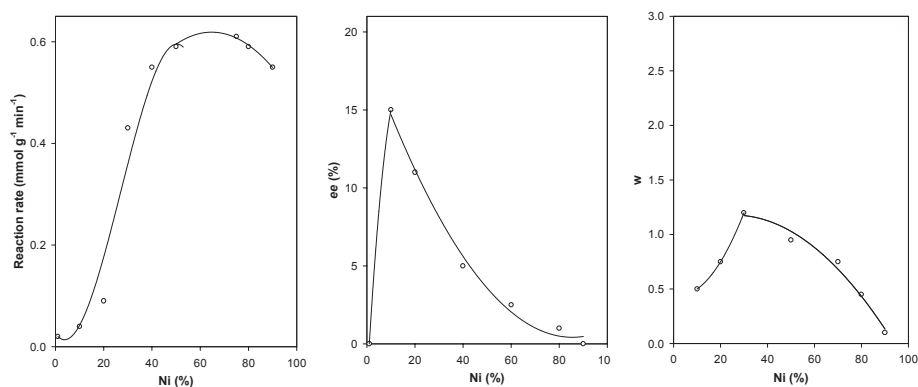


Figure 4.13. Dependence of reaction rate (left) and optical yield (middle) and the rate of formation of the excess of (-)-enantiomer (w) ($w = v \times ee$) (right) on the composition of Ni-Cu catalysts, modified with *S*-phenylalanine (according to Chernysheva et al.¹⁴⁹).

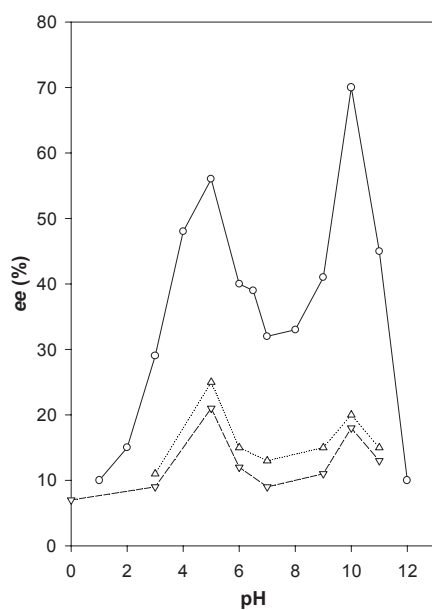


Figure 4.14. Dependence of ee of (-)-EHB on the pH of the modifying solution of (2*R*,3*R*)-(+)-tartaric acid. Catalysts are Ni (o), Cu-Ni (50:50) (Δ), Cu-Ni (20:80) (Δ) (according to Klabunovskii¹³).

Such dependence of *ee* on the pH of the modifying solution was significantly different from data obtained on Ni¹⁴⁹, over which only one maximum was found, indicating the formation of two kinds of complexes on the catalyst surface.

Introduction of 10-15% Cu into a Ni-TA catalyst, sharply diminished the degree of conversion and *ee*. This indicates that Cu is not an indifferent support but can influence the catalytic properties. Probably the high Cu content in the catalyst destroys the chiral clusters, consisting mainly Ni¹³, which are responsible for asymmetric effects.

It was found that tartaric acid as a modifier forms complexes on the surface of Ni-silica and Cu-silica catalysts in which IR spectra reveal quite close coordination between the COOH groups. This is confirmed by similar values of *ee* in which Ni-silica catalysts are modified at pH 5 and pH 10. The similarity of the effect of pH of the modifying solution on Ni and Ni-Cu catalysts indicate that the structure of chiral clusters on the surface of both catalysts remained unchanged. Probably additional introduction of copper into Ni-Cu catalyst did not produce any ligand effect and did not change the behaviour of chiral clusters, but only changed the number of such clusters ('cluster effect').

The dependences of *ee* and rate of hydrogenation of EAA on the composition of Ni-Cu catalysts indicate that the centers of enantioselective hydrogenation contain four times more chiral species (atoms and clusters) than centers of "racemic" hydrogenation leading to racemic EHB.

4.4.2. Cobalt and cobalt-nickel catalysts

Informations provided by chiral cobalt catalysts modified with tartaric acid and amino acids are very important for the theory of enantioselective hydrogenation.

Neupokoev et al.^{161,242} prepared Raney cobalt catalyst modified with tartaric acid and found that the active catalyst can be prepared by etching the Co-Al alloy with 20.3% Co content. Hydrogenation of EAA gave product with only an *ee* of 4%. However, Raney cobalt catalyst (RCo) prepared from Co-Al alloy with 35.5% Co content and modified with amino acids was more active in the hydrogenation of EAA and acetylacetone. Hydrogenation with an RCo-S-Leucine catalyst resulted in EHB with an *ee* of 8.8%¹⁶².

Zubareva et al.¹⁶⁵ found that some chiral bimetallic Raney Ni-Co catalysts modified with TA in hydrogenation of EAA also produced relatively low enantioselectivities, *ee* of only 5-8%. It is of interest that intermetallic catalysts (IMC) based on LaNi₅ M'M" (see Parts 4.3. and 4.5.), containing additional metals, M' and M" and modified with TA, revealed significant enantioselectivities after building the cobalt component into this catalyst. In this case *ee* increased up to 52%¹⁸⁰.

Cobalt assisted the segregation of Ni and increased its concentration on the surface of IMC's. In order to elucidate the reasons for such enhanced enantioselectivity of the Ni-Co catalysts, samples of powdered Ni-Co catalysts modified with TA were prepared by decomposition of acetates or nitrates of Ni and Co at 450°C followed by reduction of the resulting oxides in a stream of hydrogen or a mixture of hydrogen + helium at 350°C. Modifications with tartaric acid were carried out at pH 4.5-5.0 (see Zubareva et al.^{164,179}). Hydrogenations of EAA were carried out at 20-80°C and 25-100 bar hydrogen in AcOEt solution containing AcOH. Under these conditions the Co-catalyst did not produce any enantioselectivity; however, after introduction of 20% Ni, the *ee* reached 3.6% and after addition of 80% Ni the *ee* reached 15%¹⁷⁹. Changes of the catalyst composition and the reaction conditions resulted in an increase in *ee* of up to 46-50% with Ni-Co (50:50)-TA catalyst. Under the same conditions RNi-TA catalyst resulted in a 65% *ee*. This indicated that the main component responsible for enantioselectivity is the Ni component, and its increasing concentration in the Ni-Co catalyst sharply increased the *ee* values. Thus, these catalysts, based only on Ni-Co components, significantly differ from IMC catalysts, which include La, Ni, and Co components, in that the increasing content of Co rather than Ni (e.g. in LaNi₃Co₂-LaNi₂Co₃ systems) leads to increasing *ee*'s in the hydrogenation of EAA.

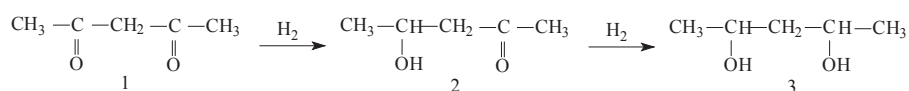
Chiral Ni-Co catalysts were examined in an industrially important reaction, in the hydrogenation of the equilibrated mixture of menthone and isomenthone (70:30) into menthol stereoisomers. The use of the Ni-Co-(90:10)-TA catalyst resulted in an optical yield of 54% (Klabunovskii et al.¹⁸³). On an RCo-TA catalyst the unavailable neoisomenthol was obtained with a yield of 80% (Zubareva et al.¹⁴²).

4.4.3. Supported nickel-copper and nickel catalysts

Supported chiral Ni and Ni-Cu catalysts^{149-160,245,248,249} are of special interest because they allow the elucidation of the nature of the metal-support interaction and the asymmetric adsorption of modifier and substrate molecules by use of the IR spectra of adsorbed molecules.

In general, supported metal catalysts are less effective than Raney metal modified catalysts, and the enantioselectivities of supported catalysts are near to those of the Raney catalysts only in the cases when large amounts of metal are found on the surface of the support^{198,200}. This can be explained, at least in the cases of bulk metal catalysts, as a consequence of an increase in crystallite sizes^{207,208} and diffusion of the tartaric acid modifier into the pores during modification of the catalyst (Sachtler²⁰⁹). Detailed consideration of this problem is in discussed in Chapter 5.

The supported chiral catalyst, Ni-Cu-TA, was supported on aerosil²⁸, and proved to be active in the hydrogenation of acetylacetone (acac) (**1**) into hydroxyketone (**2**) and diol (**3**) (Scheme 4.8).



Scheme 4.8.

Under the conditions used (*R*)-(-)-4-hydroxypentan-2-one (**2**) was produced chemoselectively with an *ee* of 9.1% without production of diol (**3**).

The Ni-Cu-TA-aerosil and Ni-TA-aerosil catalysts were also compared in the enantioselective hydrogenation of EAA²⁸. It was found that increasing amounts of metals on the surface of the support, increases *ee* and conversion. Increased also were the rate of formation of the excess (-)-enantiomer, *w*, (where $w = v \text{ times } ee$) and the rate of formation of racemic EHB ($v_r = v - w$), which goes through a maximum (Figure 4.15.).

This can be explained by an increase of Ni on the surface of the support accompanied by an increase in the general surface of the unmodified part of the metallic phase.

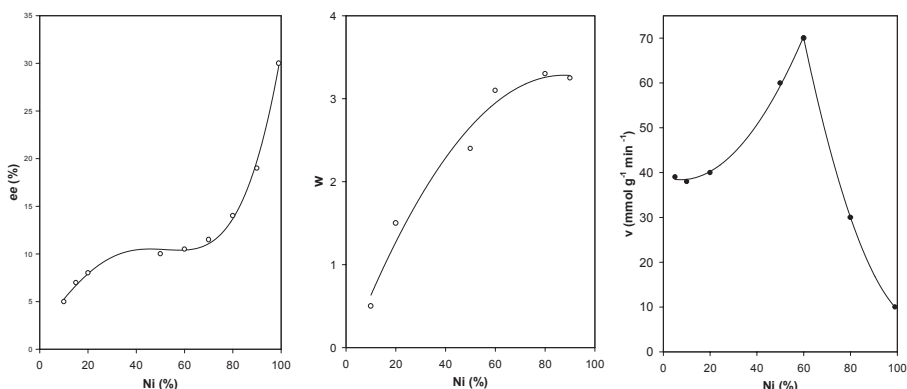


Figure 4.15. The effect of Ni content on the surface of the support on the optical yield (left), on the rate of formation of excess (-)-EHB (*w*) (middle) and on the rate of formation of racemic EHB (*v*) (left) in the hydrogenation of ethyl acetoacetate²⁸.

With the increase of Ni content the surface area begins to decrease as a result of consolidation of small Ni crystallites into larger Ni particles that are less active in enantioselective hydrogenation.

This process was shown both for Ni¹⁹⁸ and for Ru-TA catalysts⁹. Thus the optical yield, which was not very high in the case of diluted supported catalysts, increased with increasing metal content on the surface of

the supports¹⁹⁹. This explained the high effectiveness of catalysts with large amounts of metal on the supports.

The nature of the support also exerts a very strong influence on enantioselectivity of the supported catalysts¹⁹⁹. Thus in the enantioselective hydrogenation of MAA over a series of catalysts in which the Ni to support ratio was 1:1, diminishing optical yields (*ee* %) were exhibited in the following series: Ni without support (57) > SiO₂ (56.2) > zeolite (45.6) > Al₂O₃ (43.7) > kieselguhr (29.1) > MgO (6.1) > TiO₂ (3.1). A probable explanation is that the degree of interaction of Ni with these supports increases in this series and inhibits the growth of large Ni crystallites during the catalyst preparation process by means of an interaction that does not occur in the case of the Ni-aerosil¹⁹⁹.

Keane et al.²⁵⁴ have found that the gas phase hydrogenation of butan-2-one to butan-2-ol can be accomplished with an *ee* of 31% at 70°C over a 2.2% Ni-Zeolite Y catalyst modified with 0.008 mol/L solution of L-tartaric acid. The optimum particle size of the catalyst was found to be 3 nm (this size seems to be important in catalysis²⁶³). Modification of catalysts with solutions of L-Val or L-Glu had a negative results on enantioselectivity.

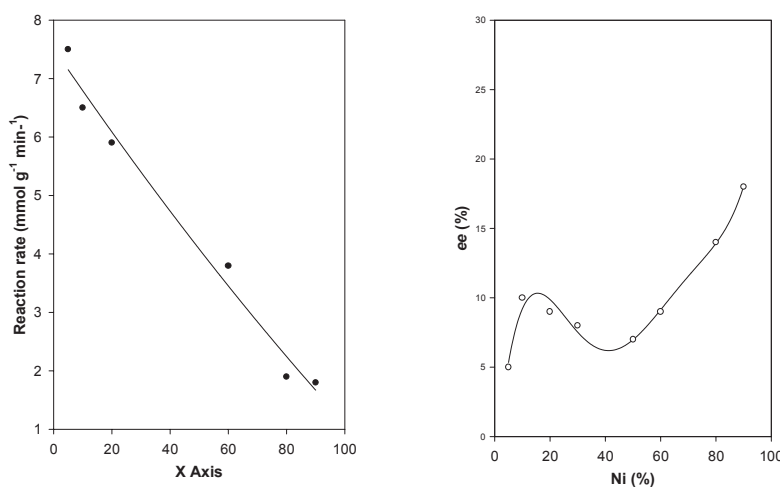


Figure 4.16. The effect of Ni content on the reaction rate (left) and *ee* values (right) in the hydrogenation of EAA on Ni-TA-aerosil catalyst (according to Vedenyapin et al.¹⁵⁵).

Vedenyapin et al.¹⁵⁵ studied catalysts prepared by soaking supports like silica, aerosol, and kieselguhr with solutions of Ni salts followed by reduction in flowing hydrogen at 380°C. The enantioselectivity of such catalysts after modification with TA depended on the nature of the support and diminished in the series of supports: aerosil > kieselguhr > silica gel. In this series the

mean size of crystalline particles decreased as 22, 17, and 12 nm, respectively. Five percent copper in the 5% Ni-aerosil catalyst resulted in a decrease of crystalline size to 2.3 nm and a concomitant decrease of *ee* from 4.1% to 3.3%. Increasing Ni content on the support from 10 to 60% increased the mean crystalline size from 8-11 to 12 nm and upon further increase of Ni the *ee* value increased but the reaction rate fell (Figure 4.16.).

Under the same reaction conditions, powdered Ni-TA catalyst produced *ee* values above 50-60%, which showed the complicated character of the dependence of enantioselectivity; therefore, the increase of *ee* can not be connected only with the increase of Ni crystallite size. Ni supported on aerosils produced higher dispersions of the metallic phase and decreasing *ee* values. Such inhibiting influence of the support was observed up to 80% Ni content.

In the case of Ni-Cu-aerosil catalysts *ee*'s and reaction rates underwent sharp decreases upon adding small amounts of copper into a Ni catalyst. Infrared spectra of supported 20% (Ni-Cu)-TA catalysts of different Ni-Cu compositions showed the interaction of the Ni-Cu phase with both COOH groups of tartaric acid but in different states depending on the ratios of Ni:Cu. A lower covalent character of binding of the TA with metals was observed for Ni-Cu catalysts of composition 1:1¹⁵⁰.

4.4.4. Modified ruthenium and ruthenium-copper catalysts

Chirally modified Ru^{121,130,132,134,192,235,243,244} and Ru-Cu^{133-139,169,235,245,250} catalysts, active in the enantioselective hydrogenation of EAA, were studied for the first time in a number of papers by the Klabunovskii's group¹²¹⁻¹³⁹. A Ru-silica catalyst modified with TA at pH 5.5 produced only an *ee* of 3% in the hydrogenation of EAA at 75°C and 80 bar¹²². A skeletal Ru catalyst modified with an aqueous solution of TA was used in the hydrogenation of EAA in the liquid phase at 80°C and 100 bar. The optical yield was only 2%¹²¹. On these Ru-TA catalysts it was observed for a first time that the optical yield depends on the crystallite size of Ru (see the details in Chapter 5).

The Ru-Cu catalysts modified with TA also proved to be not very effective. Skeletal Cu-Ru catalysts (1:1) were prepared by leaching a Cu-Ru-Al alloy (15:15:70) at 60°C with a 20% aqueous NaOH solution. Modification of the Cu-Ru (1:1) catalyst was carried out in a 4% aqueous solution of (2*R*,3*R*)-tartaric acid at pH 4.4. Hydrogenation of EAA was carried out without solvent at 30°C and 140 bar for 5h. For comparison the hydrogenation of EAA using skeletal Ru and Cu catalysts were also examined under the same conditions. Results are summarized in Table 4.14.

Catalyst	Conversion (%)	Rate (mmol/min)	ee (%)
Cu-Ru	78	102	3.5
Cu-Ru	91	120	2.3
Cu-Ru	100	130	2.4
Cu	6	7.9	19.6
Ru	100	130	1.4

Table 4.14. Catalytic and enantioselective activities of Raney Cu-Ru, Cu and Ru catalysts in the hydrogenation of ethyl acetoacetate (according to Kuznetsova et al.¹³⁷)

Promotion of Ru -TA catalyst with Cu, preserved the high overall reaction rate characteristic for pure Ru catalyst and somewhat increased the *ee* from 1.4% to 3.3% for Cu-Ru catalysts. This revealed a synergism in the action of mixed bimetal catalysts.

In other conditions the *ee*'s of 17-20% for pure Cu-TA catalyst dropped to an *ee* of 0.6% after introduction 0.5% Ru into the catalyst and then increased after further increasing Ru content up to an *ee* of 2.5%, which is characteristic for the pure Ru-TA catalyst.

Studies of the hydrogenation of EAA at 90°C and 100 bar using supported 10% (Cu-Ru)-aerosil-TA catalysts with different Cu-Ru compositions showed that there is an antiparallel dependence between the optical yield and the reaction rate. This was especially true at the 4 to 6 Ru:Cu ratio, in which the *ee* dropped from the 4% of the Ru-Cu catalyst to almost zero, while the rate increased linearly^{135,136}.

It is very interesting that under these conditions the Cu-TA catalyst were not active in the enantioselective hydrogenation of EAA, while the skeletal Cu-TA produced an *ee* of 17%¹⁴⁸, and enantioselectivity occurred at the Cu-Ru-aerosil catalyst with a composition of Cu to Ru of 4:6, indicating synergism in the Cu-Ru-TA catalysts as a results of activation of the Cu in mixed bimetal catalysts. This suggestion for the origin of the enantioselective properties exerted by Cu atoms in the Cu-Ru catalysts corresponds to the characteristic properties of skeletal Cu-Ru catalysts in their dependence of *ee* on the pH of the modifying TA solution because optically active (*R*)-(-)-EHB with an *ee* of 12% is obtained only in the pH interval of 3-7, and the best results were at pH 5¹⁵³. It is of interest that for Cu-Ru-TA and for Ni-TA catalysts the resulting *ee*'s depend on the general content of the metal on the support. Increasing Cu-Ru content from 5% to 15% diminished *ee* from 25% to 4% and then to zero; however, a constant and rather high reaction rate was maintained. These data indicate that on the surface of bimetal catalysts there are two kinds of Cu-metal centers; one is less active catalytically but

enantioselective, while the other is highly reactive but non-stereoselective. Despite the absence of mutual solubilities of Cu and Ru in supported catalysts, both metals are in close interaction, probably in the form of bimetallic clusters.

In skeletal Cu-Ru-TA catalysts, Cu affects the Ru but the reverse action of Ru affecting Cu was not observed, a fact that can be explained by the difference of structures in supported and skeletal catalysts. In the latter case there are the structures of Cu phase covered with Ru phase. After etching of the Ru-Al alloy in the preparation of Raney Ru catalyst, some admixtures of bayerite were found in the resulting catalyst. Ru atoms interacted with the hydrated form of alumina, which provided high dispersion of Ru and presented the possibilities of chiral interaction with the modifier¹²⁸ when the Ru-alumina catalyst could not be modified chirally¹³. These conclusions were confirmed by studies of hydrogen spillover on skeletal Ru catalyst^{131,132}. Indeed, in skeletal catalysts a more homogeneous distribution of the metal particles and OH groups were found and their interaction were higher than in supported catalysts.

4.4.5. Palladium, palladium-copper and palladium-nickel catalysts

Palladium^{157,160,190,220,221,253}, palladium-copper^{166-170,190,250} and palladium-nickel¹⁷⁰ catalysts were studied in a number of papers.

Orito et al.¹⁹³⁻¹⁹⁷ found that small amounts (1%) of noble metal additives, like Ru, Pt, or Pd, in Ni catalysts supported on Kieselguhr significantly increased enantioselectivity in the liquid phase hydrogenation of MAA. Therefore, it was of interest to study bimetallic catalysts based on Pd and mixed with Cu and Ni with greater concentrations of Pd than 1% (see works of Klabunovkii's group^{166-170,250}).

Skeletal Cu-Pd of different compositions were prepared¹⁹⁰. Catalysts were obtained by etching Cu-Pd-Al alloys (70% Al). The prepared catalysts contained Cu and Pd phases and their solid solutions and up to 40-58% bayerite. Linearly increasing the contents of Pd in the catalysts from 5 to 100%, increased the rate of hydrogenation of EAA at 100°C and 100 bar. More complicated dependence on concentrations of Pd was found below 5%. In the interval of 1-5% Pd the *ee* values went through a maximum and at 2% Pd in Cu-Pd the optical yield reached the maximal value of 4-5%¹⁶⁸. Vedenyapin et al.^{167,238,250} used an electrochemical method and found decreasing adsorption of hydrogen on Cu-Pd with Pd contents less than 10%. This can be explained¹⁶⁷ by the involvement of a fraction of the Pd phase (or Cu-Pd alloy) in the Cu phase and was confirmed with the results of enantioselective hydrogenation of EAA. Indeed, only the catalysts containing less than 5% Pd produced enantioselectivity and at increasing concentrations of Pd from 1 to 5% the *ee* falls from 9 to 1%.

In hydrogenations over a Cu-Pd-TA containing 2.7% Pd two optimal pH values of 4 and 8 were found for the TA modifying solution¹⁶⁸; these produced (*R*)-(-)-EHB's with 4.1 and 4.6% *ee*'s, respectively (Figure 4.17.).

Likewise, as was the case with the Cu-Ru catalysts, the violation from additivity was observed upon the introduction of small amounts of Pd into the Cu catalyst. At 5% Pd the specific rate related to m² of surface area of the Pd phase increased up to 150 times the rate of hydrogenation on the pure Pd catalyst. This indicated sharp changes of the properties of copper in bimetallic catalysts after mixing it with palladium.

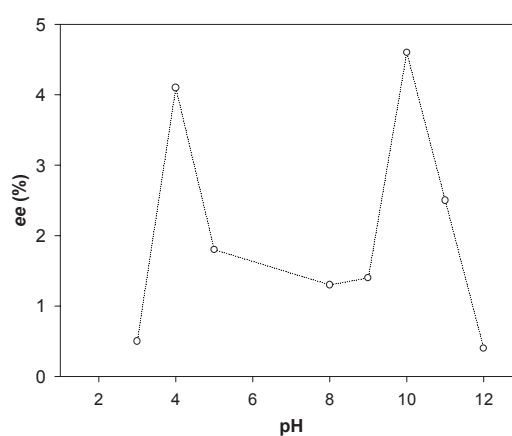


Figure 4.17. Effect of the pH of the (*2R,3R*)-tartaric acid modifying solution on the optical yield of (*R*)-(-)-EHB on Cu-Pd (97.3:2.7) catalyst (according to Vedenyapin et al.¹⁶⁸).

Comparison of the chiral bimetallic catalysts, Cu-Pd-TA and Cu-Ru-TA, showed significant differences. In the case of Cu-Ru-TA catalyst, introducing 0.1-0.5% Ru into Cu-TA leads to almost complete loss of enantioselectivity, while in the cases of Cu-Ru and Cu-Pd catalysts such chiral deactivation proceeds only after introduction of more than 5% Pd. The general catalytic activity of the Cu-Ru-TA catalysts increased with increasing Ru content, while the Cu-Pd catalysts exhibited a synergism of catalytic activity, which was explained by a peculiar structure of the active center and by invoking a ligand effect^{167,168}. A similar effect for skeletal Cu-Ru-TA catalysts was observed.

Because Cu did not adsorb hydrogen, the exposed surface of Ru in Cu-Ru catalysts can be determined by adsorption of hydrogen using galvanostatic and potentiodynamic measurements in KOH and H₂SO₄ media¹³.

Comparison of the properties of Cu-Ru-TA and Cu-Pd-TA catalysts using electrochemical methods showed that the strength of adsorption of

hydrogen on these catalysts diminished with a weakening of the Ru-H and Pd-H bonds as a result of a ligand effect found by Vedenyapin et al.¹⁶⁹. Unlike the sandwich structure of the Cu-Ru-TA catalysts (the surface of Cu-Ru catalyst is covered with a layer of Ru atoms), electrochemical data show the Cu-Pd catalysts' surfaces are enriched with copper below 5% Pd¹⁶⁸, and this causes a synergistic catalytic action resulting from a ligand effect. In this way the special behavior of the Cu-Pd catalysts and their peculiar dependence of optical yield on the pH's of the TA modifying solutions can be explained.

Supported Cu-Pd and Ni-Pd catalysts were prepared by impregnation of aerosil and alumina supports with solutions of Cu and Ni salts followed by reduction of these precursors in flowing a hydrogen-helium mixture (1:10) at 360°C and modified with a solution of TA + PdCl₂ at pH 5. The Ni-Pd-silica catalyst produced an optical yield of 7% from the hydrogenation of EAA. Table 4.15. shows the results¹⁷⁰.

Catalyst	Optical yield (%)	Rate mmol/min g.cat
10% Pd-SiO ₂	0.0	18
10% Ni-SiO ₂ -TA	7.1	9
(2:8) Pd-Cu-SiO ₂	0.0	5
(1:10) Pd-Cu-SiO ₂ -TA	1.0	5
(1:9) Pd-Ni-SiO ₂ -TA	7.0	8
(1:10) Pd-Ni-SiO ₂ -TA	4.6	11

Table 4.15. Reaction rate and enantioselectivities of Cu-Pd and Ni-Pd supported catalysts in the hydrogenation of ethyl acetoacetate (according to Kuznetsova et al.¹⁷⁰).

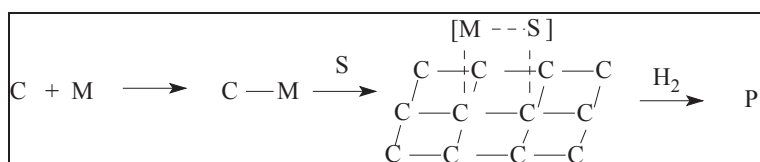
Under the conditions studied it was found that the supported Ni catalysts also produced low enantioselectivities, and changing the silica support for alumina completely inhibited enantioselectivities.

4.5. Mechanism of enantioselective hydrogenation

4.5.1. Enantioselectivity as a function of the bond strength in intermediate surface complexes

Balandin, Klabunovskii et al.^{9,28,113} published the first ideas about the structure of the intermediate complexes in enantioselective hydrogenation. According to their idea, the reaction proceeds through an intermediate complex, consisting of atoms of the catalyst on the surface (C) or an active center of the catalyst (C-C-C), the amino acid or hydroxyacid chiral modifier

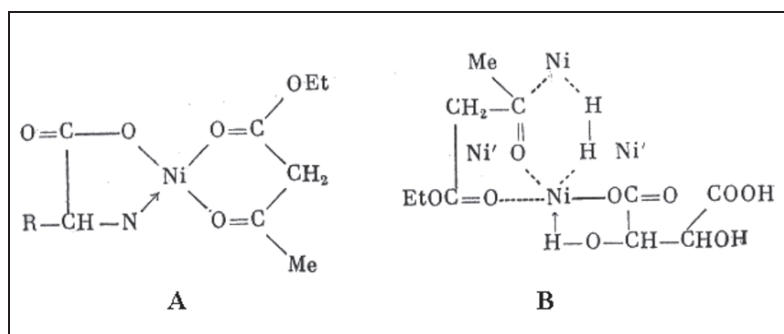
molecule (M), and the prochiral substrate molecule (S), (predominantly carbonyl-compounds, such as 3-oxocarboxylic acid esters or *beta*-diketones) which can also coordinate to the metallic catalyst, and after addition of two hydrogen atoms produces the hydrogenated product (P) (Scheme 4.9.).



Scheme 4.9.

Scheme 4.9. does not give the detailed picture of the intermediate complex and does not precisely delineate the structure of catalytic center. But after modification, this scheme was applied to the hydrogenation of ethyl acetoacetate on Ni catalyst modified with an amino acid (Scheme 4.10.a.) and (2*R*,3*R*)-(+)-tartaric acid (Scheme 4.10.b.) (Klabunovskii et al.^{25-28,153,184})

Scheme 4.10. corresponds to the "doublet" scheme of the multiplet theory of catalysis by Balandin²⁰⁴ but the Ni' centers should not be applied as centers of the multiplet theory but used in accordance with the principle of microscopic reversibility^{28,204}.



Scheme 4.10. Possible structures of the intermediate complexes in the enantioselective hydrogenation of ethyl acetoacetate on Ni, modified with an amino acid (A) or with tartaric acid (B)^{9,28}.

The general idea that the enantioselective reaction proceeds through a triple complex, including the catalytic center (C), the modifier (M) and the substrate molecules (S) was elaborated in several models about the intermediate complex formation on the catalyst surface.

Klabunovskii et al.²⁸ suggested that hydrogenation of EAA or acetylacetone would be performed through reaction of a heteroligand complex

which was composed of the intermediate produced from the substrate and the modifier adsorbed on the catalyst as shown in Scheme 4.10.

The conformations of EAA or acetylacetonone (acac) in the complex were studied by means of circular dichroism and magnetic rotatory dispersion spectra (Faraday effect) of the complexes prepared from modeling the species formed on the surface of the catalysts^{239,247,260}. There was good agreement between the carbonyl ligand conformation and the results of enantioselective hydrogenation. The model is presented in Figure 4.18., in which the complex is disposed on the edge of crystalline catalyst particle modified with (2*R*,3*R*)-tartaric acid (a) or an amino acid (b) (Klabunovskii, Vedenyapin⁹, Ollis³¹). According to Balandin^{234,259} the Ni catalysts revealed a peak height of 1 nm.

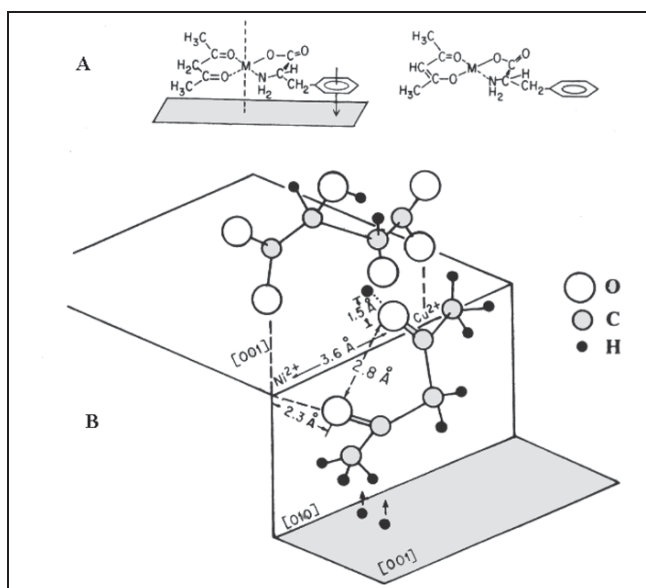
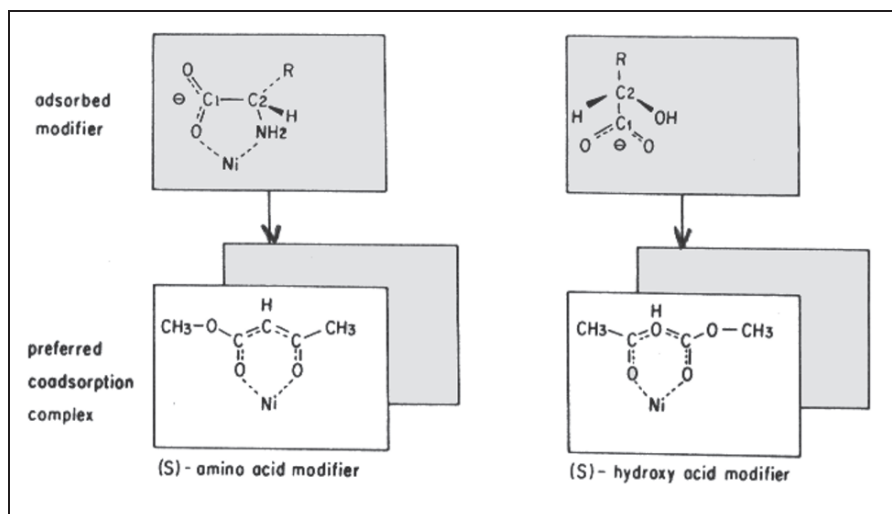
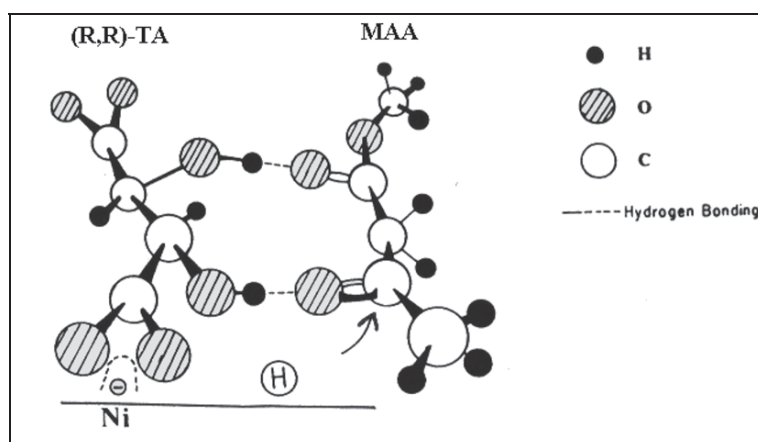


Figure 4.18. Stereochemical models of intermediate complexes in the hydrogenation of ethyl acetoacetate on crystalline Ni modified with (2*R*,3*R*)-tartaric acid (a) and with amino acid (b) (according to Klabunovskii, Vedenyapin⁹).

Using IR spectroscopy Sachtler et al.²⁰⁸⁻²¹⁷ developed models of the intermediates for the adsorption of complexes on Ni-silica catalysts that are modified with amino acids and hydroxyacids and active in the gas phase hydrogenation of MAA. These are presented in Schemes 4.11. and 4.12.



Scheme 4.11. Preferred arrangements of the coadsorbed MAA molecules on Ni-silica catalysts, modified with amino acids and hydroxyacids (according to Sachtler, Yasumori^{209-217,224-226}).



Scheme 4.12. Stereochemical model of the interaction of the modifier, TA, with the substrate, MAA (according to Sachtler, Yasumori^{209-217,224-226}).

They proposed the models shown in Schemes 4.11. and 4.12., based on the interaction of MAA with amino acids and hydroxyacid with MRNi, in which each atom of Ni tetracoordinated with TA. One of the remaining two coordination sites of Ni participates in the hydrogenation, and the structure of

the Ni complex acts as a template. The hydrogen used for the reaction is supplied from the Ni metal surface by a spillover transport via the tartaric acid ligand.

Inoue et al.²²⁶ studied X-ray photoelectron spectra of MAA and coordinated (*2R,3R*)-tartaric acid, (*S*)-aspartic acid, and (*S*)-alanine as modifiers of nickel surfaces, prepared by decomposition of nickel formate, DNi (Figure 4.19.).

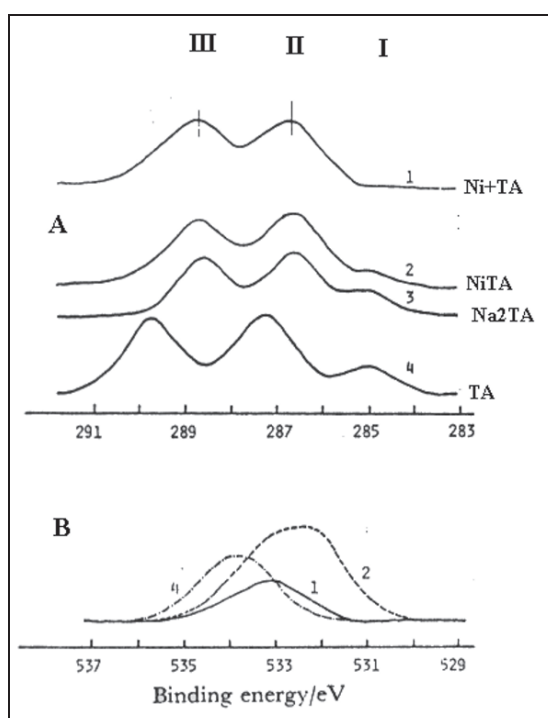


Figure 4.19. XPS spectra in the C1s (a) and O1s (b) regions. Difference spectrum between unmodified Ni and TA modified Ni, at pH 5 (1), nickel tartrate (2), sodium tartrate (3) and tartaric acid (4) (according to Inoue et al.²²⁵).

Figure 4.19.a. shows two peaks, III and II, that have been assigned to the C atom of the carboxy group and to the *alpha*-C-atom of the tartrate molecule. A small peak at 285 eV (I) is the carbon peak of a contaminant. The binding energies of peaks III and II for adsorbed TA (288.7 and 286.7 eV) are much closer to those for NiTA (288.7 and 286.7 eV) and Na₂TA (288.6 and 286.6 eV) than those for free TA (287.3 eV and 287.3 eV).

Figure 4.19.b. shows the O1s peak for TA, adsorbed on Ni (1) which appears at ca. 533 eV. The peak for NiTA (2) appears at a binding energy

lower than that of adsorbed TA, whereas the peak for free TA (4) appears at a higher binding energy. The broad O1s peak for TA was assigned to OH and COOH groups in the formation of the Ni complex, since the C1s spectrum for TA, adsorbed on Ni, is similar to that for NiTA and Na₂TA, while the O1s spectrum of TA, adsorbed on Ni, differs from that of NiTA. Therefore, the OH probably is not in contact with the surface of Ni.

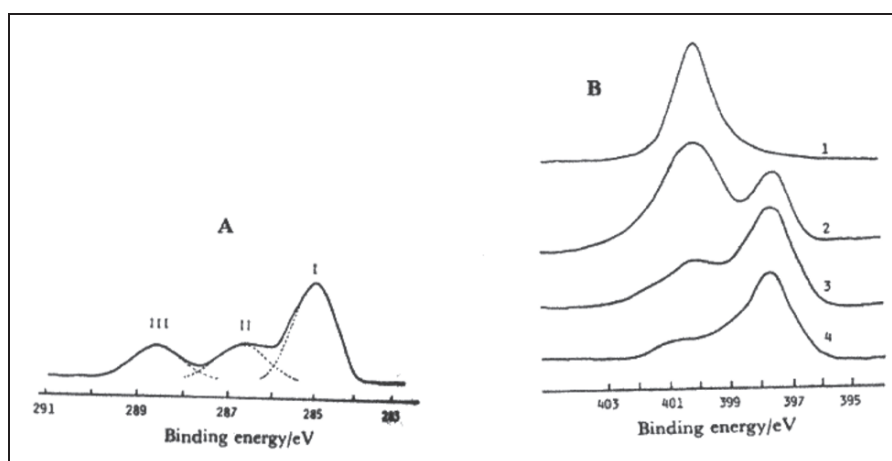


Figure 4.20. XPS spectra in the C1s region of MAA, adsorbed at room temperature on nickel surface (a), and in the N1s region of adsorbed amino acids (b).

- (1) aspartic acid, evacuated at room temperature
- (2) aspartic acid, exposed to 0.008 bar of H₂ at 90°C
- (3) alanine, exposed to 0.013 bar of H₂ at 100°C
- (4) aspartic acid, exposed to 0.008 bar of H₂ at 280°C (according to Inoue et al.²²⁵).

The XPS method was also applied to the study of adsorption of aspartic acid and alanine on Ni, and the conclusion was made that amino acids were coordinated on Ni in a manner similar to the corresponding Ni chelate complex²²⁶. Figure 4.20.a. shows the N1s spectra of adsorbed amino acids. The adsorption of MAA at RT on a clean Ni surface provides three peaks in the C1s region (285.0, 286.6 and 288.6 eV). Peak III can apparently be assigned to C atoms of a carbonyl group, whereas peak I is associated with C atoms of a hydrocarbon chain, and peak II is due to the carbon atom in the methoxy group. Peaks II and III originates from the keto-form of MAA and should provide the intensity ratio of 1:2, so the observed equal intensity is derived on the basis of the assumption that about half of the adsorbed MAA is in the enol-form, which is confirmed by IR spectra²²⁴. Figure 4.20.b. confirm a

model (Sachtler²¹¹ and Hatta¹⁰⁶) in which the amino acid is linked to a surface Ni atom through both amino and carbonyl groups.

Yasumori et al.²²⁴⁻²²⁶ proposed a stereomodel of the interaction of MAA with HNi on the surface of a nickel catalyst prepared by the reduction of NiO (marked as "HNi") based on IR spectra data which showed that the hydrogen on C₂ in MAA had been replaced by deuterium during the deuteriumation of MAA on HNi in the gas-phase reaction.

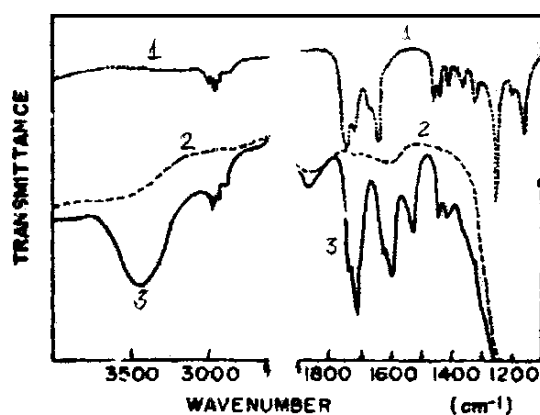


Figure 4.21. IR spectra of gaseous and adsorbed methyl acetoacetate on Ni catalyst. Gaseous MAA (1), Ni supported on silica gel (2), MAA adsorbed on Ni (3), (according to Yasumori et al.²²⁴).

IR spectra of Ni supported on silica gel before and after adsorption of MAA are shown in Figure 4.21. The band at 3100-3200 cm⁻¹ was assigned to the stretching vibration of the enolic hydroxyl group and the two adsorption bands at 1740 and 1710 cm⁻¹ were attributed to *beta*-carbonyl and carboxyl groups, respectively. The band at 1620 cm⁻¹ is indicative of the interaction of the C atom of carbonyl group with Ni. Therefore, it was concluded²²⁴ that the adsorbed form of MAA is in the enol form, a fact that was confirmed by deuterium exchange experiments.

Kishi et al.^{104,106} also found adsorption bands of *acac* on Ni which are similar to forms in Ni(*acac*)₂ chelate in which it is considered that *acac* adsorbs in the enol form probably with formation of a pseudo-aromatic ring (according to UV spectra^{107,261,263}).

Thus, according to Yasumori²²⁴, reaction in gas phase proceeds through the enol form of MAA. But this scheme probably does not apply to liquid phase reactions because enantioselective hydrogenation can be accomplished with 2,2-dimethyl-3-oxobutyrate, which cannot have an enol form.

Enantioselective hydrogenation of 2,2-dimethyl-3-oxobutyrate resulted in an *ee* of 30% (modified at a pH of 5.0 at 0°C with the reaction at

60°C and 80 bar) compared to the hydrogenation of MAA in solution, which gave an *ee* of 38% (according to Smith et al. ²¹⁸). Thus the enol formation does not play an exclusive role in liquid phase enantioselective hydrogenation in systems like MAA-MNi. Analysis of the experimental data from hydrogenations of MAA, EAA, and *acac* on Ni, Cu, and Co catalysts that have been modified with chiral amino acids and hydroxyacids, revealed the regularities connecting enantioselectivity with the stabilities of the intermediate complex [C-M-S] formed on the surface of the catalyst during reaction.

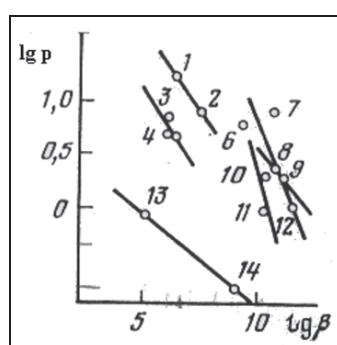


Figure 4.22. Dependence of optical yield ($\lg p$) on stability constants ($\lg \beta$) in the hydrogenation of methyl acetoacetate on Ni, modified with amino acids. (1) Glu, (2) Asp, (3) Phe, (4) Leu, (6) Lys, (7) Trp, (8) Meth, (9) Cyst, (10) Thr, (11) Ser, (12) Pro, (13) Arg, (14) Hist.

As can be seen from Figure 4.22., data on the hydrogenation of MAA on RNi modified with chiral amino acids published mainly by Izumi's group (see Izumi ¹⁻⁸) show the linear dependences between enantioselectivities ($\ln p$) and stability constants, $\lg \beta$, of the complex [Ni-amino acid] formed on the surface of the catalyst according to equation (1):



Figure 4.22. shows good correlation of the experimental data as a number of curves unite the amino acid modifiers of similar structures.

The next step in the evaluation of correlations of enantioselectivity with stability constants of the intermediate complex was made when the bond strength of substrate molecule [S] with chiral surface complexes [C-M], was measured by the constant K_{CM-S} in accordance with equation (2), where AA are amino acids.



In the large interval of changes of constants, the dependence of $\lg p$ on $\lg K_{\text{CM-S}}$ resulted in a curve similar to the "volcano-shape" of multiplet theory (Figure 4.23.).

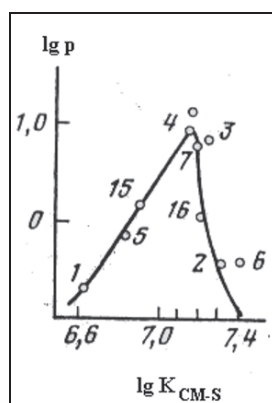


Figure 4.23. Dependence of optical yield ($\lg p$) on stability constant, $K_{\text{CM-S}}$, in the hydrogenation of ethyl acetoacetate on Cu modified with amino acids, (1) Glu, (2) Asp, (3) Phe, (4) Leu, (5) Ala, (6) Lys, (7) Trp, (15) Val, (16) Tyr.

For the correlations of EAA and acetylacetone (*acac*) data were used from the hydrogenations of EAA and *acac* on Cu and Co catalysts modified with amino acids (AA).

In the case of the cobalt catalyst, only a linear dependence was obtained, which can be considered as one branch of the same extreme dependence "volcano shape" curve²⁰⁴.

A more general approach was developed by Vedenyapin, Fridman, and Klabunovskii¹⁴⁴⁻¹⁴⁶ in which the measure of complex stability the coproportional constant, K_d , was taken for the reaction:



In this approach, equilibration on the surface of catalyst was taken as equilibration in the reaction mixture between the complexes that can form from homoligand complexes in solution, and then the connection of ee (p) with K_d was obtained¹⁴⁴⁻¹⁴⁶

$$\text{Lg } p = nK_d + C \quad (4)$$

These data were summarized in Figure 4.24.

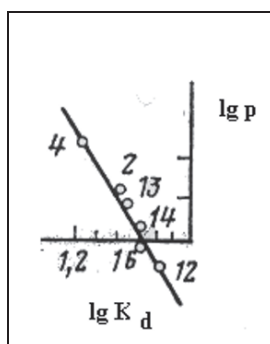


Figure 4.24. Dependence of optical yield ($\lg p$) on coproportional constant, K_d , in the hydrogenation of ethyl acetoacetate on Co, modified with amino acids. (2) Asp, (4) Leu, (12) Pro, (13) Arg, (14) Hist, (16) Tyr.

Instead of optical yield in such calculation, it is more correct to use the value of "enantioselectivity", E , equal to the relation of enantiomers $[R] / [S]$. (The connection of p with E has linear character only at small values of p and E and in general reveal a complicated dependence).

The general equations were given¹⁴⁴⁻¹⁴⁶ for the connection of E with the stability constant K_{CM-S} and with constant co-proportionation, K_d according to equations (5) and (6):

$$\lg E = a + \beta \lg K_{CM-S} \quad (5)$$

$$\lg E = b + 2 \beta (\delta - 1) \lg K_d \quad (6)$$

where coefficient β characterizes the degree of asymmetrizing action of the modifier molecule and δ -accounts the degree of influence of modifier on the strength of the C-S bond, the metal atom in the catalyst with the substrate molecule, involved in the heteroligand complex $[M-C-S]$.

Values of coefficients for eqs. (5), (6) and (7) were calculated from the experimental data (Table 4.16.).

Value $[\epsilon]$ is sensitive to changes of the bond strengths of both ligand S (MAA, EAA, acac) with complex $[C-AA]$ and AA with $[C-S]$. With the diminishing of bond strengths CM-S and CS-M, there is a trend of increasing of $[\epsilon]$ as the differential value of the induced Cotton effect in the absorbance band of the chromophore of the substrate molecule.

Complexes	a	β	b	δ	A	B
[Cu-AA-EAA] (AA = Glu, Ala, Val, Trp, Leu, Tyr, Phe)	0.065	0.14	0.09	3.1	0.093	0.036
[Cu-AA-acac] (AA = Glu, Val, Phe)	0.01	0.003	-0.60	1.32	-	-
[Ni-AA-MAA] (AA = Glu, Val, Ala, Ser, Leu, Pro, Asp, Tyr)	-0.035	-0.15	0.005	4.41	0.086	0.085
[Co-AA-EAA] (AA = Glu, Pro, Leu, Tyr, Arg, Hist)	-0.012	-0.03	-0.036	1.33	0.032	0.018

Table 4.16. Coefficients for equations (5), (6), and (7) for different amino acids (AA) and ligand (EAA, MAA, and acac) complexes (according to Klabunovskii²⁸).

Electronic interaction in chelate knots of complexes and elucidation of the nature of bonds Cu-N and Co-N in chelates [Cu(AA)(acac)] and [Co(AA)(acac)], were studied using circular dichroism and Faraday effect spectra, in which AA = tyrosine (Tyr), triptophane (Trp) and phenylalanine (Phe).

Table 4.17. presents experimental data showing a good correlation between the conformation of the AA ligand and the configuration of the hydrogenation products MHB (or EHB) and ketol (in the hydrogenation of *acac*). All *ee* values were determined only for the initial stage of the reaction and were taken into consideration only at a definite degree of conversion. For Cu and Ni catalysts the correlation λ -S was observed and for the Co catalyst correlation δ -R was observed.

It is of interest that the values of differential dichroic absorbance coefficients correlated with optical yield and enantioselectivity, E, according to equation (7) (A and B values are in Table 4.16.).

$$\lg E = A + B \lg([\varepsilon]) \quad (7)$$

Thus a quantitative evaluation of chirodiastaltic interactions inside the intermediate complexes [CMS] was made during the asymmetric hydrogenation of carbonyl compounds and correlations were found that characterizes this processes.

Catalysts	Modifier	°C	$\Delta[\epsilon]$	Substrate	Conform.	Product	Config.	ee (%)
Ni	R-Tyr	100	0.150	acac	δ	ketol	R	2.3
Ni	R-Trp	100	0.900	acac	δ	ketol	R	3.2
Co	S-Phe	100	4.150	acac	δ	ketol	R	1.0
Co	R-Tyr	100	0.163	acac	λ	ketol	S	0.4
Co	R-Trp	100	2.275	acac	λ	ketol	S	0.7
Co	S-Phe	100	0.172	EAA	δ	EHB	S	1.3
Co	R-Tyr	100	0.074	EAA	λ	EHB	R	0.5
Co	R-Trp	100	0.112	EAA	λ	EHB	R	3.4
Cu	S-Phe	20	0.24	acac	λ	ketol	S	1.2
Cu	R-Tyr	20	0.20	acac	δ	ketol	R	0.2
Cu	S-Trp	20	0.35	acac	λ	ketol	S	1.4
Cu	S-Phe	20	0.21	EAA	λ	EHB	S	0.93
Cu	R-Tyr	20	0.42	EAA	δ	EHB	R	3.4
Cu	S-Trp	20	0.65	EAA	λ	EHB	S	7.1

Table 4.17. Relationship between the conformation of the dicarbonyl-compounds in their heteroligand complexes with amino acids and the configuration of the hydrogenation products.

°C: modification temperature; $\Delta[\epsilon]$: differential dichroitic absorption coefficient; conform.: conformation of the substrate; config.: configuration of product.

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