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Mechanisms of asymmetric induction in catalytic hydrogenation, hydrosilylation and cross-coupling on metal complexes

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Abstract. The current state of studies on the mechanisms of asymmetric hydrogenation, hydrosilylation and cross-coupling induced by metal complexes is considered. The possibilities for the identification of stages of catalytic reactions involving asymmetric induction are analysed. The classification of the types of asymmetric induction according to the differences in these stages is proposed. In most cases, asymmetric induction occurs in the stage of substrate coordination by catalytic complexes (the key – lock interaction). Evidence is presented in favour of the assumption that the asymmetric carbon atom is formed in the product in the stages of transformations of the asymmetric intermediate, even though the starting chiral catalytic complex is C_2-symmetric. The bibliography includes 118 references.

I. Introduction

Asymmetric catalytic reactions involving prochiral substrates on chiral metal-complex catalysts proceed through the interaction of these species to form diastereomeric intermediate complexes. The rational description of the phenomenon of asymmetric induction (or diastereoselectivity) † in asymmetric synthesis can be given using empirical stereochemical rules and models [1] analogous to those proposed by Prelog, Cram, Cornforth, *et al*. Asymmetric induction can take place either in the stage of interaction (coordination) of a metal-complex catalyst with a substrate to form an intermediate complex or in the course of subsequent transformations of the resulting complex. The first alternative is sometimes called the steric control or the 'key – lock' interaction (the terms 'chiral recognition' and 'chiral discrimination' are also used).

For the reaction

$$A + B \longrightarrow [AB]^1 \longrightarrow [AB]^2 ... \longrightarrow \text{product},$$

where A is the substrate and B is the reagent (catalyst), the following general classification of the types of asymmetric induction is proposed:

(1) prior to the reaction (due to a chiral medium);

(2) the stage involving the interaction of A with B (coordination of the substrate by the catalyst);

(3) transformations of the first ($[AB]^1$), second ($[AB]^2$) and subsequent intermediates already involving the coordinated substrate;

(4) nonbonded diastereomeric interactions analogous to those existing between enantiomers in racemates.

Asymmetric induction of the first type is observed in reactions performed in a chiral matrix [for example, in cholesteric liquid crystals (CLC) in the mesophase temperature range, where a chiral helical structure is formed] or in a chiral solvent and, probably, under the combined action of the electric and magnetic fields.[2, 3] Asymmetric induction of the second type takes place in asymmetric metal-complex catalysis, in particular, on hydrogenation and hydrosilylation of aromatic ketones. Asymmetric induction occurring in the course of transformations of the first and second intermediates (the third type) has been examined in detail for catalytic allylic alkylation.[4] The nature of asymmetric induction, which is caused by interactions between enantiomers in racemates (the fourth type) and due to which the racemates differ from the constituent individual enantiomers in some chemical and physical properties, is poorly known.

Asymmetric induction, if considered as a way of communicating stereochemical information, involves two components, *viz*., static discrimination due to steric hindrance and dynamic discrimination resulting from kinetic or thermodynamic factors.[5]

Hydrogenation, hydrosilylation and cross-coupling are of importance from the practical standpoint because they comprise a minimal set of reactions, which provide the preparation of chiral products bearing many functional groups involved in pharmaceuticals.[6] Because of this, the present review deals with the mechanisms of asymmetric induction occurring in these three reactions.

II. Asymmetric induction prior to the catalytic reaction

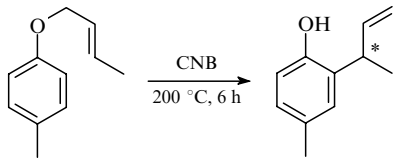
Asymmetric induction prior to the reaction should be considered as a manifestation of the chiral action of a medium both on the catalyst, which in this case can be achiral, and the prochiral substrate. Asymmetric reactions can proceed in a CLC medium

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† The enantioselectivity can be considered as a measure of asymmetric induction in asymmetric catalysis where the enantiomeric product is isolated from a diastereomeric intermediate complex.

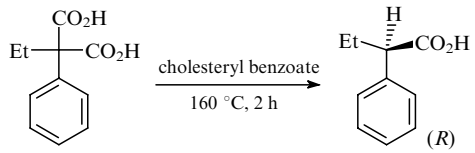
in the mesophase temperature range where a chiral helical structure is formed (for more detailed arguments in favour of asymmetric induction prior to the reaction, see below). However, the published data on asymmetric synthesis in a CLC medium as a chiral matrix are contradictory. The enantioselective Claisen rearrangement performed in a CLC mesophase has been reported:[7]



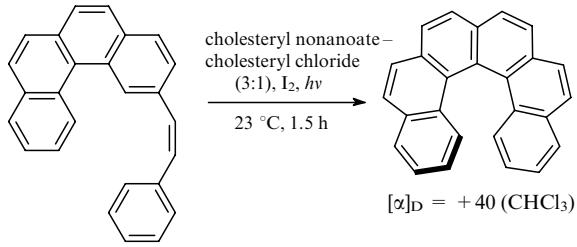
CNB is cholesteryl *p*-nitrobenzoate.

The authors judged the enantioselectivity of the reaction from the CD spectra of the product.

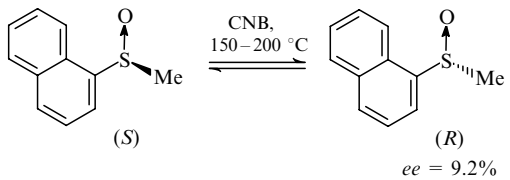
Ethyl(phenyl)malonic acid was decarboxylated in a CLC mesophase in an optical yield (*p*) of 18%:[8]

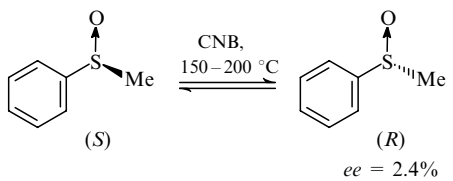


In the photochemical synthesis of hexahelicene performed in CLC within the mesophase temperature range of 20–25 °C, the enantioselectivity of the process was 1%, which was confirmed by the presence of a CD maximum in the absorption band of the hexahelicene obtained.[9]



However, photocyclisation of α-(*N*-methylanilino)styrene into *N*-methyl-2-phenylindoline in various CLC mesophases afforded a racemic product.[10] When studying thermochemical interconversions of sulfoxides in a cholesteryl *p*-nitrobenzoate mesophase, a small enantiomeric excess (*ee*) of the product was observed.[11]





It was concluded [10,11] that asymmetric transformations in cholesteric mesophases, like those in standard chiral solvents, proceed in low optical yields. However, the authors of the cited papers noted that exceptions are possible in the case of strong specific interactions between the dissolved compound and CLC.

In another study,[12] even the theoretical possibility of the manifestation of the asymmetric effect in a CLC mesophase was denied because the helical step of CLC (300–400 nm) is incompatible with the molecular sizes of standard reagents. These molecules do not 'notice' the helical structure of CLC, much as people do not notice the curvature of the earth's surface. Nevertheless, CLC, owing to the chirality of their molecules, can exert a slight asymmetric effect on chemical reactions, if only as optically active solvents.

The asymmetric influence of the magnetic field is poorly known.‡ Pasteur was the first to take an interest in this problem. He believed that if the magnetic field can induce rotation of the polarisation plane of light in the case of achiral compounds (the Faraday effect), it can generate the disymmetry analogous to that possessed by chiral molecules. Kelvin reasoned that this idea is in error because the magnetic rotation does not possess the right- or left-handed quality, *i.e.*, it is not chiral. However, P Curie noted that the magnetic field parallel to the electric field can induce chirality because the mirror operation (which provides interchangeability of components) is applicable to the parallel and antiparallel molecular arrangements in this combined field.[14] The above-considered enantiomorphism and the enantiomorphism of chiral molecules are distinguished as the 'false' and 'true' chirality, respectively.[2,3] This raises the question of whether the 'false' chiral effect can cause asymmetric induction. It is known that the symmetry is broken at the level of elementary particles. It is assumed that the 'false' chiral effect can induce analogous symmetry distortions in chemical reactions. Changes in the symmetric (in the absence of this effect) energy barriers in the path of formation of enantiomers of the product can lead to differences between the rate constants of formation of enantiomers in the chemical reaction away from the equilibrium.[2,3]

This theoretical reasoning has been supported experimentally. Thus Gerike [15] discovered the enantiomeric enrichment (although small and irregular) of the product (*ee* < 1%) in alkylation of prochiral ketones with Grignard reagents, the addition of bromine at the double bond and some other reactions using various combinations (parallel, antiparallel and orthogonal mutual arrangements) of the electric (15–8100 V cm^{-1}) and magnetic (constant and alternating, $8 \times 10^3 - 1.17 \times 10^5$ A m^{-1}, 0–50 Hz) fields. It was reported that reduction of ketones with Grignard reagents and lithium aluminium hydride in a constant magnetic field proceeded with high enantioselectivity.[16] However, this conclusion was disproved by one of the authors.[17] It is agreed [2,3] that the concept of the asymmetric influence of the constant magnetic field is reasonable, but this influence can serve only as a 'starter' and must be combined with a chiral autocatalytic process. Apparently, this problem calls for further careful experimental investigation.

We also examined asymmetric induction in catalytic reactions proceeding in a liquid-crystal chiral matrix [18,19] by studying hydrogenation of α-acetamidocinnamic acid (ACA) in the presence of achiral Wilkinson's catalyst $RhCl(PPh_3)_3$ possessing a substantial molecular volume (this fact is of importance in imparting the helical ordering of the CLC molecules to the molecules of the catalyst). Since $RhCl(PPh_3)_3$ and ACA are insoluble in a CLC melt, *viz.*, in cholesteryl tridecanoate (CTD), the reaction was carried out in a CTD–Bu^nOH–C_6H_6 mixture. In this solution, the molecules of CTD, the substrate (ACA) and the catalyst $RhCl(PPh_3)_3$ have helical ordering at the mesophase temperature of 60–70 °C. This is evidenced by the fact that the CD spectra show maxima of induced circular dichroism of the same sign in the absorption bands of the substrate and the catalyst. Probably, the same sense of helical ordering of the substrate and catalyst molecules facilitates discrimination between the *Re*- and *Si*-sides of the C=C bond in the substrate coordinated to the catalyst in an intermediate complex. Actually, a moderate temperature-dependent enantioselectivity was observed in the reaction under consideration (Fig. 1).

‡ The non-asymmetric influence of the magnetic field on chemical reactions has long been known (see, for example, the review [13]).

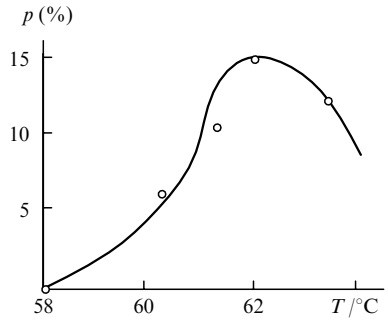


Figure 1. Temperature dependence of the optical yield of *N*-acetylphenylalanine in hydrogenation of ACA.

The dependence has a maximum in the middle of the temperature range of the CTD mesophase where the cholesteric liquid crystal is helically ordered. This effect could also be attributed to the effect of CLC as a chiral solvent. However, the fact that the maximum of enantioselectivity coincides with the middle of the temperature range of the liquid crystal mesophase counts in favour of the former explanation.

With the aim of investigating the effect of a combination of the electric and constant magnetic fields on chemical reactions, we§ used a solenoid.[20] Acid- and base-catalysed mutarotation of D-glucose in water was examined. In the mutarotation of monosaccharides, the equilibrium was established between the α and β forms, which are diastereomers. In the initial stage, the reaction was far from the equilibrium (this is a necessary condition for the magnetic field to exert the asymmetric effect [2, 3]). The reaction was carried out in a temperature-controlled polarimetric tube placed in a solenoid and its course was followed from the change in the optical rotation. The rate constant of mutarotation k was calculated according to the first-order equation. The magnetic field strength (H) was calculated from the magnetic rotation of the polarisation plane of light under the action of water at $\lambda = 589$ nm. The direction of magnetic field was judged from the direction of the observed rotation of the plane of polarisation induced by water. To obtain a more accurate estimate of the dispersion of the rate constants, some experiments were repeated several times at the same temperature. The results are given in Table 1.

Presently, one cannot give an unambiguous answer to the question of how the rate constant is changed depending on the direction of magnetic field. However, the reaction at low temperatures in the field with (+)-α_D H_2O proceeds somewhat more rapidly than that in the field with (−)-α_D H_2O. At the same time, it can be said with reasonable confidence that the effect of a constant magnetic field (without combining with the electric field) is absent. The results of the investigation of D-glucose mutarotation in water in a constant magnetic field demonstrated that the changes in the rate constants depending on the direction of the magnetic field are comparable in value to the errors of the measurements (Table 2).

Table 1. Rate constants of mutarotation of D-glucose at different temperatures depending on the direction of magnetic field in a solenoid.[20]

T /°C	H /G	$10^3 k$ /min^{-1}		$10^3\Delta k$ /min^{-1}
		(+)-α_D H_2O	(−)-α_D H_2O	
6.2	1266	3.73 ± 0.04	3.69 ± 0.02	+0.04
		3.74 ± 0.03	3.42 ± 0.08	+0.32
10.2	1265	6.01 ± 0.02	5.65 ± 0.03	+0.36
		5.81 ± 0.04	5.59 ± 0.02	+0.22
		6.02 ± 0.01	5.50 ± 0.04	+0.52
20	1262	16.68 ± 0.05	16.72 ± 0.05	−0.04
		16.80 ± 0.03	16.82 ± 0.06	−0.02
30	1259	43.57 ± 0.29	41.57 ± 0.08	+2.00
		42.50 ± 0.39	43.10 ± 0.20	−1.60
38.3	1256	90.87 ± 0.49	83.58 ± 0.62	+7.29

§ The experiment was carried out in collaboration with E I Klabunovskii.

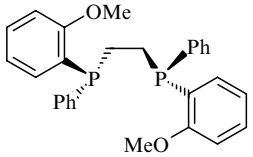
Table 2. Rate constants of mutarotation of D-glucose at 20 ± 0.1 °C depending on the direction of constant magnetic field (H = 7490 G).

$10^3 k$ /min^{-1}		$10^3\Delta k$ /min^{-1}
(+)-α_D H_2O	(−)-α_D H_2O	
13.73 ± 0.85	14.67 ± 0.29	−0.94 ± 0.85
14.84 ± 0.26	15.03 ± 0.07	−0.19 ± 0.26
14.17 ± 0.41	15.19 ± 0.23	−1.02 ± 0.41
15.14 ± 0.56	14.85 ± 0.11	+0.29 ± 0.56
15.00 ± 0.42	15.07 ± 0.11	−0.07 ± 0.42

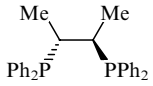
III. Asymmetric induction in the stage of substrate coordination by catalytic complexes

The elucidation of the nature of asymmetric induction and the identification of the stage where it takes place are closely related to the investigation of the general mechanism of asymmetric reactions. For the latter problem to be solved, it is necessary to reveal individual elementary stages, determine their rates, detect and characterise intermediates (including the establishment of their absolute configurations) and, finally, identify the key stage of asymmetric induction. If asymmetric induction occurs in the stage of substrate coordination by a chiral catalytic complex, this fact can be established using rather simple logical approaches considered below.

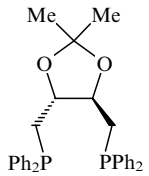
The mechanism of hydrogenation of the C=C bond in substrates was studied using rhodium phosphine catalysts, involving such ligands as dipamp,[21–25] chiraphos,[26–29] diop,[21,29] bppm,[30,31] dioxop [32,33] and BisP*.[34]



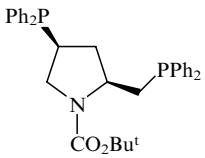
(*R*,*R*)-(−)-dipamp



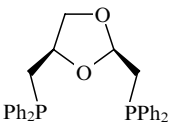
(*S*,*S*)-(−)-chiraphos



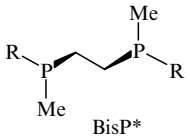
(*R*,*R*)-(−)-diop



bppm



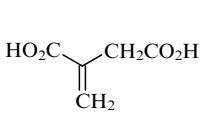
dioxop



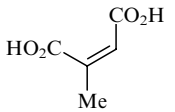
BisP*

R = Bu^t, Et$_3$C, cyclo-C_5H_9, cyclo-C_9H_{11}, 1-adamantyl

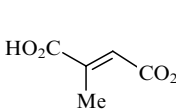
In studies on hydrogenation of itaconic, citraconic and mesaconic acids in the presence of $[Rh(bppm)]^+$ giving rise to 2-methylsuccinic acid, an attempt was made to reveal the stage involving asymmetric induction (the optical yields of the products are given below the formulae of the acids).[35]



85.3% (*S*)

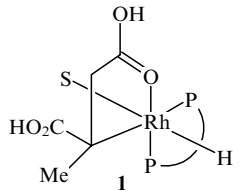


22.0% (*S*)



50.9% (*S*)

In the event that the enantioselectivity of the reaction is controlled by intermediate **1** common to all the three substrates (which follows from Halpern's theory discussed below), the optical yields must be close, which is contradictory to the experimental data considered above. Hence, it was concluded that asymmetric induction occurred in the stage of substrate coordination (the 'key – lock' interaction).



1

S is the solvent

It should be noted that the chiral catalytic complex with the bppm ligand does not possess symmetry elements (except for C_1) and, hence, asymmetric induction in the stage of substrate coordination is performed by the asymmetric complex.

The hydrogen pressure influences the enantioselectivity of hydrogenation of acetyl- and benzoylaminocinnamic acids and their esters in the presence of rhodium complexes with the bppm, diop or dipamp ligands (with NEt_3 and without it). To explain this fact, Ojima *et al.*[35] offered the hypothesis that two reaction pathways compete with each other:

Path *A*

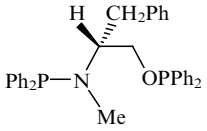
$$\overset{*}{\mathrm{Rh}} + (\mathrm{C{=}C}) \rightleftharpoons \overset{*}{\mathrm{Rh}}(\mathrm{C{=}C}) \xrightarrow{\mathrm{H_2}} \overset{*}{\mathrm{Rh}}(\mathrm{C{=}C})\mathrm{H_2} \longrightarrow (S/R)\text{-product}$$

Path *B*

$$\overset{*}{\mathrm{Rh}} + \mathrm{H_2} \rightleftharpoons \overset{*}{\mathrm{RhH_2}} \overset{(\mathrm{C{=}C})}{\rightleftharpoons} \overset{*}{\mathrm{RhH_2}}(\mathrm{C{=}C}) \longrightarrow (R/S)\text{-product}$$

Paths *A* and *B* are favourable at low and high hydrogen pressures, respectively. Path *B* has been found previously in the studies of hydrogenation of alkenes on Wilkinson's catalyst. The authors of the cited study postulated[35] that paths *A* and *B* afforded different enantiomers. Hence, an elevation of the pressure, which facilitates path *B*, would be expected to decrease the enantioselectivity up to the inversion of the configuration. It is this situation that was experimentally observed. Interestingly, the addition of triethylamine weakened the influence of the hydrogen pressure on the enantioselectivity. The anion, which is generated upon the addition of NEt_3 to acid (the substrate), has a much higher tendency to form an adduct with the rhodium phosphine complex than the corresponding acid. Consequently, the contribution of path *B* in the presence of a base is insignificant, which agrees with the experimental evidence that the enantioselectivity remained virtually unchanged at different hydrogen pressures. Hence, the hypothesis under consideration provides an adequate explanation for the effect of the hydrogen pressure and the influence of the addition of a base on the enantioselectivity.

However, this scheme, as applied to the hydrogenation of derivatives of amidocinnamic acid, does not allow one to reveal the stage responsible for asymmetric induction due to a lack of detailed stereochemical information on two competitive reaction pathways. Nevertheless, the hypothesis for two competitive reaction pathways is fruitful. It was found[36–39] that the enantioselectivity of hydrogenation of ACA in the presence of the [Rh((*R*)-PheNOP)(cod)]ClO_4 complex



(*R*)-PheNOP

depends on the hydrogen pressure, the temperature, the ratio of the concentrations of ACA and the complex and the dielectric constant of the solvent (Fig. 2). These dependences can readily be explained within the framework of the above-considered concept. The contribution of the reaction path *B* becomes more significant and, correspondingly, the higher enantiomeric excess of the product adopting a certain configuration, *viz.*, (*S*)-AcPhe, is achieved as the hydrogen pressure is elevated, the concentration of the substrate with respect to the catalyst is decreased, the temperature is lowered and the dielectric constant of the solvent decreases. The role of the first two factors follows directly from the schemes of the reaction paths *A* and *B*. The influence of the two last-mentioned factors is in agreement with the observations made in the study.[35] The proposed explanation is also confirmed by the fact that rhodium hydride was observed in the reaction mixture at low temperature (−20 °C).[37]

Upon hydrogenation of the enamide substrate on complexes with bppm and PheNOP, asymmetric induction occurs during the transformation of an asymmetric intermediate.

The pure dihydride mechanism (path *B*), which is realised even at low temperature and hydrogen pressure, was considered in the study[34] devoted to hydrogenation of methyl α-acetamidocinnamate (AcΔPheOMe) on a rhodium complex containing (*S*,*S*)-1,2-bis(*tert*-butylmethylphosphino)ethane (Scheme 1).

Asymmetric induction takes place during substrate coordination by the dihydride complex (major intermediate) present in an

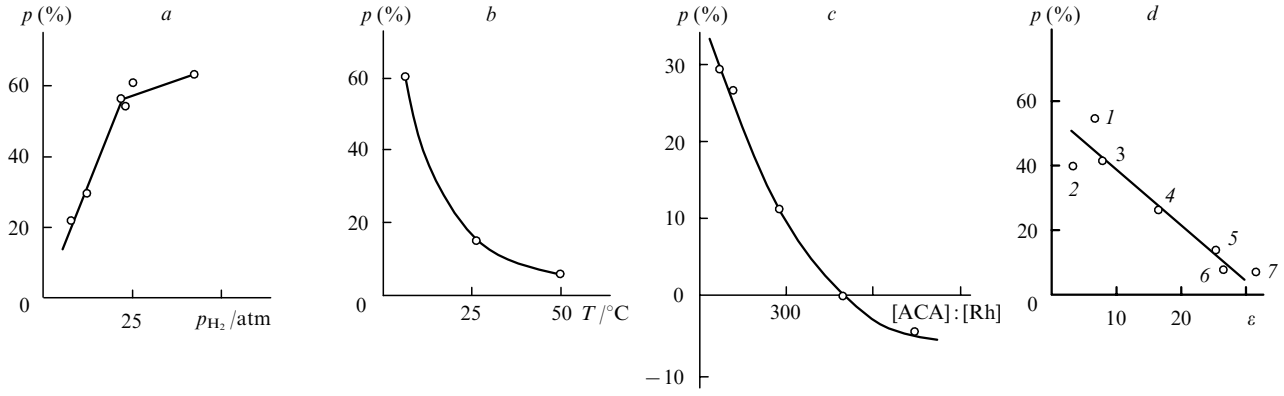
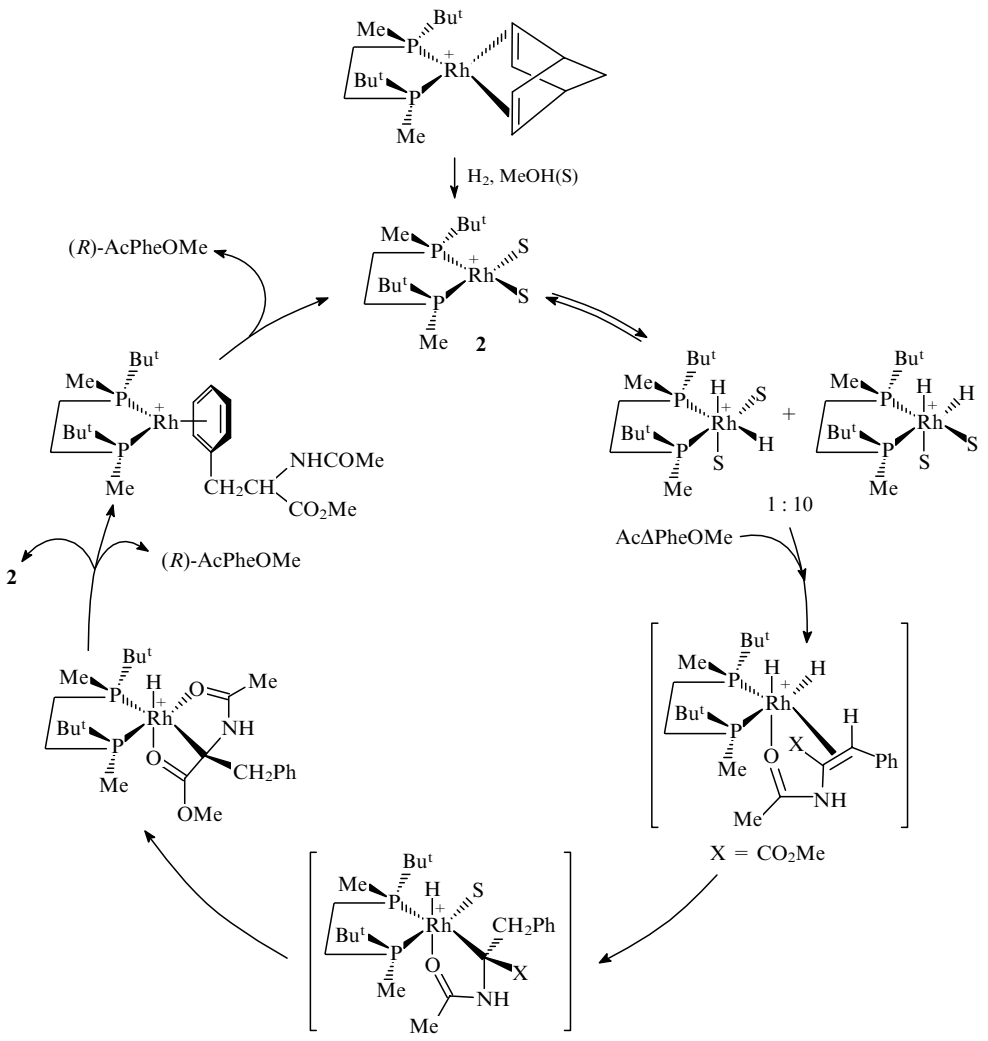


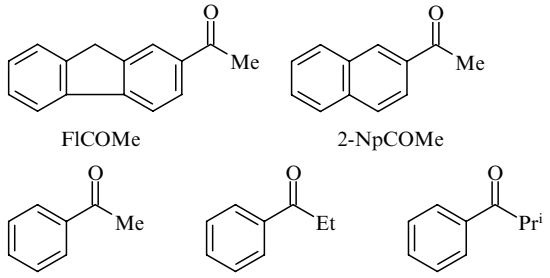
Figure 2. The optical yield of the product (*S*)-AcPhe in hydrogenation of ACA *vs.* the hydrogen pressure (*a*), the reaction temperature (*b*), the ratio of the concentrations of ACA and the catalytic complex (*c*) and the dielectric constant of the solvent (*d*).
The reaction conditions: (*a*) — T = 20 °C, [ACA] : [Ph] = 100 : 1, C_6H_6 – MeOH (1 : 1); (*b*) — p_{H_2} = 1 atm, [ACA] : [Ph] = 100 : 1, C_6H_6 – MeOH (1 : 1); (*c*) — T = 50 °C, p_{H_2} = 1 atm, Pr^iOH; (*d*) — T = 25 °C, p_{H_2} = 1 atm, [ACA] : [Ph] = 100 : 1, the solvent: (*1*) DMF; (*2*) dioxane; (*3*) THF (*4*) EtOH – C_6H_6; (*5*) MeOH – C_6H_6; (*6*) EtOH; (*7*) MeOH.

Scheme 1

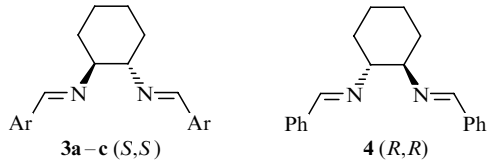


excess. As can be seen from Scheme 1, this intermediate is devoid of symmetry elements, *i.e.*, the asymmetric carbon atom is generated in the product in the stage of the transformation of the asymmetric intermediate although the starting chiral catalytic complex **2** possessed the symmetry C_2.

The mechanism of asymmetric induction was investigated for hydrogen-transfer hydrogenation of aromatic ketones R^1COR^2



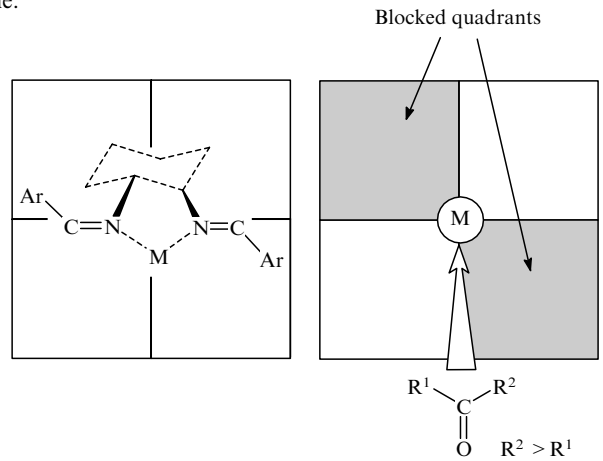
on rhodium and iridium complexes, which were generated *in situ* and contained Schiff bases, *viz.*, derivatives of (*S*,*S*)- (**3a**–**c**) and (*R*,*R*)-1,2-diaminocyclohexane (**4**).[40]



3: Ar = Ph (**a**), C_6H_4OMe-*o* (**b**), Np-2 (**c**).

In all cases, the configuration of the product was determined by the configuration of the ligand and was independent of the nature of the metal atom. If ketones as substrates of this reaction are arranged in order of decreasing difference between the molecular volumes of two substituents (Fig. 3), it can be seen that *ee* tends to decrease in the series FlCOMe > 2-NpCOMe > PhCOMe > PhCOEt > $PhCOPr^i$. In the case of rhodium complexes with the ligand **3a**, the corresponding series is as follows: FlCOMe > 2-NpCOMe ≈ PhCOMe ≈ PhCOEt ≈ $PhCOPr^i$.

The most pronounced difference in *ee* is observed for FlCOMe and PhCOMe. This fact can be interpreted using the quadrant rule.



The metal atom in the C_2-symmetric chelate chiral complex (the catalyst) is oriented toward the intersection point of the

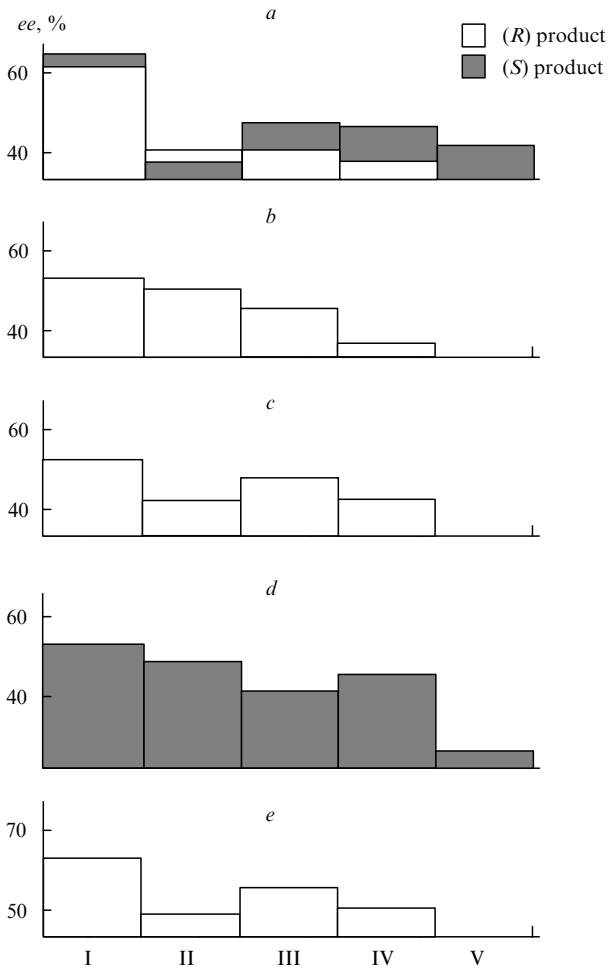
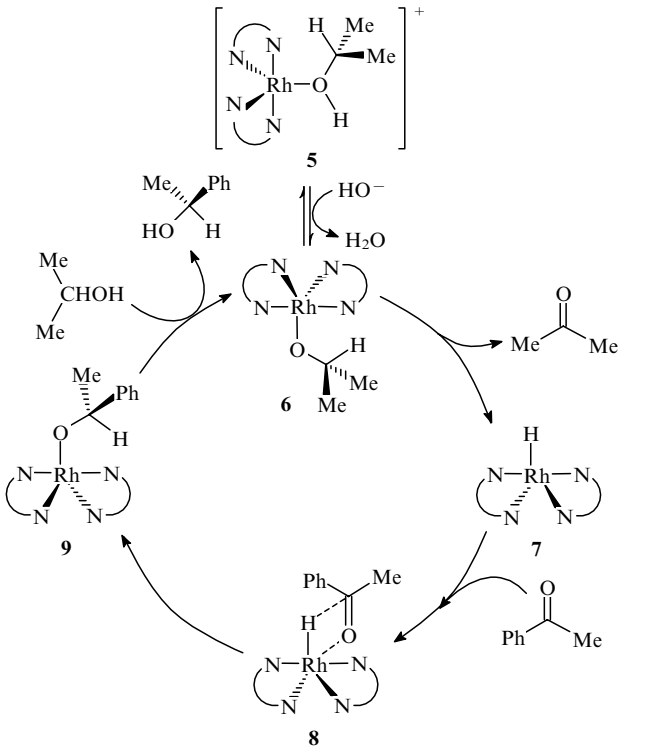


Figure 3. Influence of the difference between the molecular volumes of the substituents R^1 and R^2 in ketone R^2COR^1 ($R^2 > R^1$) on the enantioselectivity of hydrogenation.
(The catalytic system: (*a*) Rh/**3a**, Rh/**4**; (*b*) Rh/**3b**; (*c*) Rh/**3c**; (*d*) Ir/**4**; (*e*) Ir/**3b**. Ketone: (I) FlCOMe; (II) 2-NpCOMe; (III) PhCOMe; (IV) PhCOEt; (V) PhCOPr^i.

quadrants and the C_2-symmetrically arranged aryl substituents fall in the quadrants related by the symmetry C_2 (left upper and right lower), thus 'blocking' them. The larger the difference between the molecular volumes of the substituents in the ketone involved in the intermediate complex (the average of two possible positions, which can occupy the ketone in the intermediate, is indicated by an empty arrow), the higher the probability of the bulky substituent of the carbonyl group of the ketone being located in the free quadrant and, correspondingly, the larger the chiral discrimination and, consequently, the higher the enantioselectivity. It is this situation that was experimentally observed and, hence, the data obtained can be considered as an argument in favour of the fact that asymmetric induction (chiral recognition) takes place in the stage of substrate coordination in an intermediate complex.

Other authors also support the idea that asymmetric induction in hydrogenation with the hydrogen transfer catalysed by rhodium and iridium complexes occurs in the stage of ketone coordination. Thus the following catalytic cycle (Scheme 2) was proposed [41] for hydrogen-transfer hydrogenation of acetophenone catalysed by (*S*)-(+)-3-*sec*-butyl-, (*S*)-(−)-3-(1,2,2)-trimethylpropyl- or (*S*,*S*)-(+)-3,8-di-*sec*-butyl-1,10-phenanthroline complexes of rhodium(I) in a Pr^{i}OH – KOH medium.

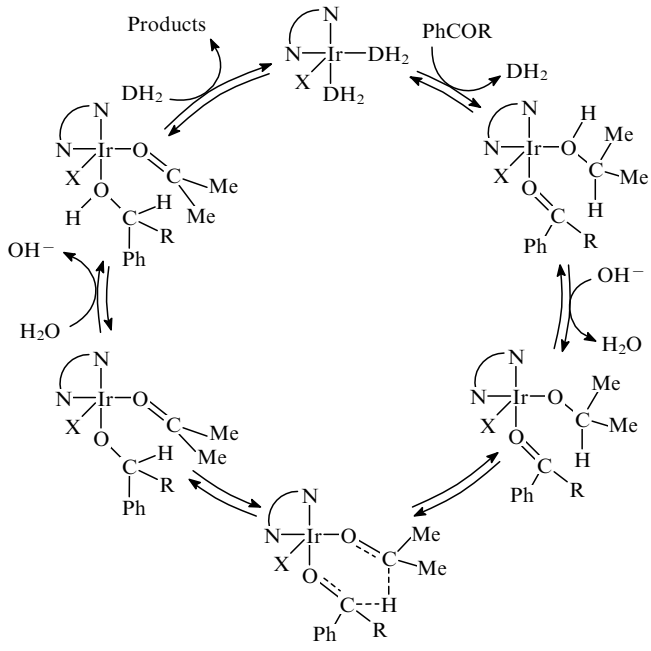
Scheme 2



As can be seen from Scheme 2, asymmetric induction occurs upon substrate coordination by asymmetric intermediate **7**. However, this mechanism of hydrogenation needs additional evidence.

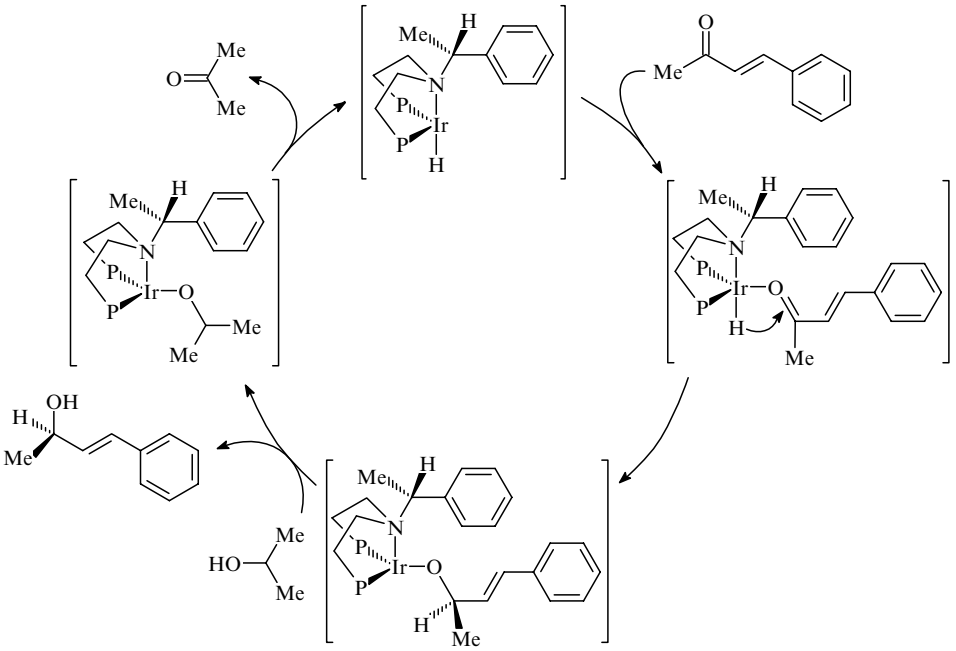
For the reactions catalysed by iridium complexes with Schiff bases, which were prepared from pyridine-2-carbaldehyde and α-phenylethylamine, a mechanism was proposed according to which asymmetric induction takes place in the stage of the hydrogen transfer from the donor (isopropyl) group to the acceptor molecule (ketone subjected to hydrogenation) in the cyclic transition state (Scheme 3).[42,43]

Scheme 3



DH_2 is propan-2-ol; X = DH_2, OH^-; R = Me, Et, Pr^n, Pr^i.

Scheme 4



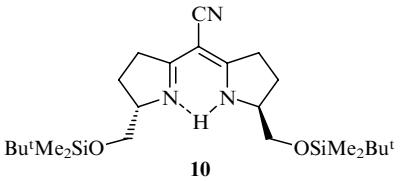
P = PPh_2.

The catalytic cycle proposed [44] for hydrogenation of benzylideneacetone in the presence of the HIr[(*R*)-Ph.CH(Me)N($CH_2CH_2PPh_2$)$_2$] complex is shown in Scheme 4. The structure of the intermediate was established by X-ray diffraction analysis. According to this scheme, asymmetric induction occurs in the stage of coordination of the ketone by the asymmetric complex.

Scheme 3 involves direct hydrogen transfer, whereas Scheme 4 implies that the transfer proceeds with the participation of metal hydride.[44] Both schemes are to a large extent conventional, but the latter scheme seems to be better justified ¶ because the hydride intermediate was found experimentally.[44]

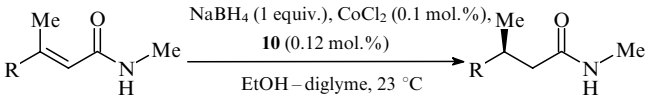
Therefore, there is some evidence that asymmetric induction takes place in the stage of ketone coordination by an asymmetric intermediate complex, which lost the symmetry C_2 (if it was present in the starting catalytic complex).

The complex, which is formed *in situ* based on $CoCl_2$, semicorrin ligand **10** and $NaBH_4$ in alcohol, serves as an efficient catalytic system for asymmetric reduction.[46, 47]

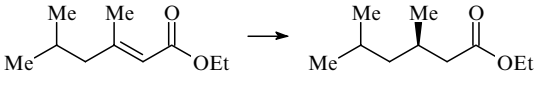


10

Amides and esters of α,β-unsaturated acids are reduced by this system with high enantiomeric excess (*ee* = 90% – 99%).



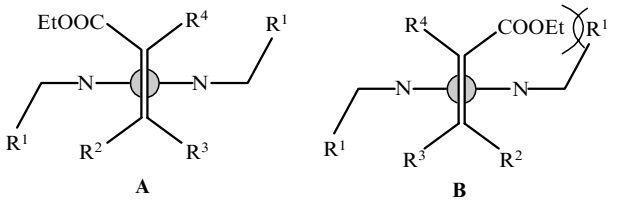
ee = 98.7% (R = $(CH_2)_2$Ph), 98.9% (R = C_6H_{11}), 92.4% (R = Ph);



ee = 96%

¶ At the same time, Scheme 4 ignores the reversibility of the reaction involving the hydrogen transfer from isopropanol [45] and, hence, Scheme 3 seems to be preferable.

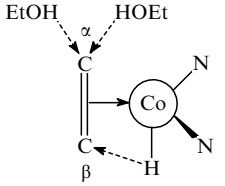
The investigation of the reaction mechanism followed with the use of $NaBH_4$ in an EtOD – DMF medium or using $NaBD_4$ in an EtOH – DMF medium demonstrated that borohydride and EtOH serve as sources of hydrogen atoms at the β- and α-carbon atoms of the product, respectively.[47] Hydrogenation of substrates bearing a prochiral carbon atom in the α-position proceeds non-enantioselectively with respect to this atom.[47, 48] The assumed structure of the intermediate complex is shown in Fig. 4.



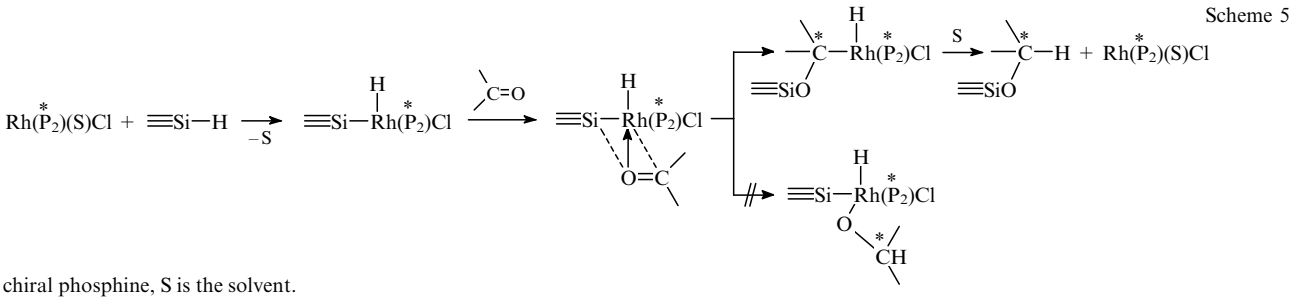
A **B**

Figure 4. Possible structures of the intermediate complex in reduction reactions on a cobalt-containing catalyst (the cobalt – hydride bond is omitted for clarity).[47]

The involvement of the coordinated alkene in structure **B** is sterically hindered so that the transition state **A** is more favourable. Unfortunately, the authors did not indicate the Co – H bond, whereas the latter, probably, provides an explanation for the fact that the asymmetric carbon atom is generated only in the β-position of the alkene and hydrogen is generated from $NaBH_4$. Actually, the experimental observations mentioned above can readily be explained by assuming that the alkene containing the non-equivalent α- and β-carbon atoms is coordinated to the cobalt atom (whose hydride ion is, undoubtedly, generated from $NaBH_4$) as shown below

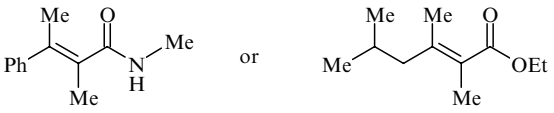


Scheme 5



* P is chiral phosphine, S is the solvent.

Reduction of the C = C bond in substrates of the types

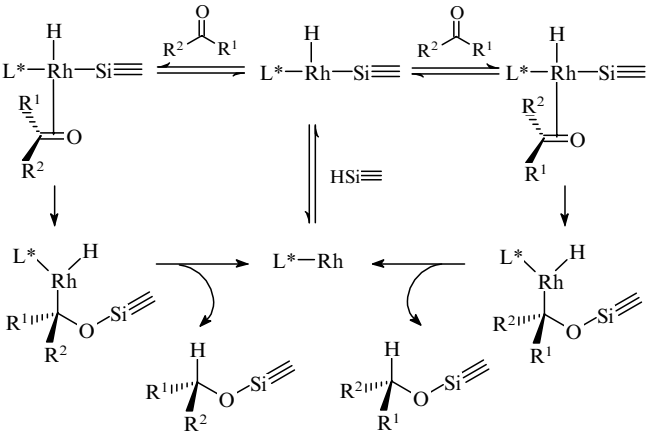


involves the enantioselective addition of the hydride ion at the C_β atom, which is controlled by an asymmetric Co hydride complex, whereupon the intact chiral C_2-symmetric metal complex fragment, apparently, cannot ensure the enantioselective attack on the α-carbon atom. This explanation agrees well with the conclusion made previously that asymmetric induction is realised in the stage of the transformation of an asymmetric intermediate. Hence, turning back to Fig. 4, it can be said that asymmetric induction takes place in the stage of coordination of alkene by the asymmetric monohydride complex of cobalt.

The mechanism of asymmetric hydrosilylation has been studied less thoroughly than the mechanism of asymmetric hydrogenation. It was suggested [49] that the enantioselectivity results from the competition between diastereomeric silyloxyalkyl(aryl)-rhodium intermediates (Scheme 5).

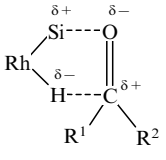
According to another assumption, asymmetric induction takes place in the stage of the addition of ketone to an intermediate complex [50, 51] (Scheme 6).

Scheme 6



L* is (*S*,*S*)-(+)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane [(*S*,*S*)-(+)-diop].

This scheme is similar to that proposed in the study [52] where the following structure of the five-membered transition state was assumed



In all the above-considered cases, asymmetric induction is realised in the stage of substrate coordination by an asymmetric intermediate.

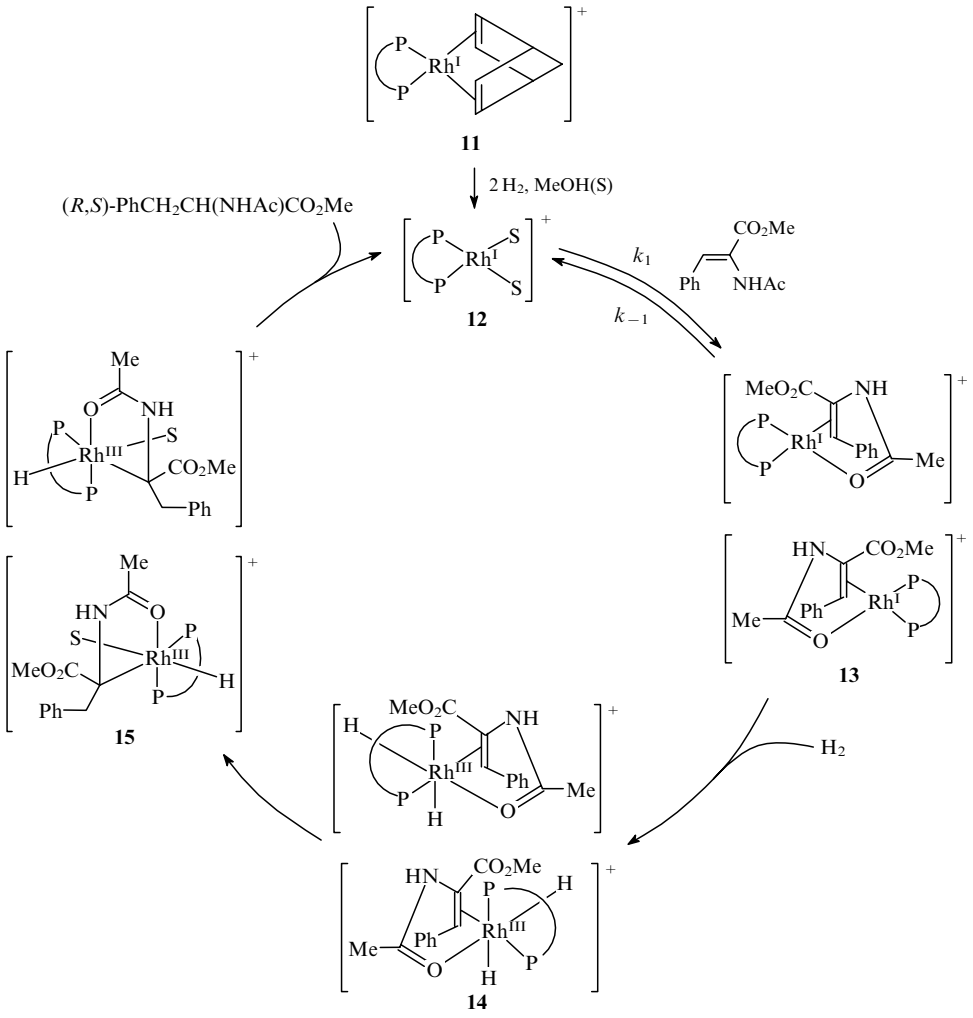
IV. Asymmetric induction in the course of transformations of the first or subsequent intermediates of the catalytic reaction

Research on the mechanism of catalytic hydrogenation of substrates like (*Z*)-α-acetamidocinnamic acid in the presence of rhodium phosphine complexes was started with the detailed investigation of the kinetics of hydrogenation of methyl (*Z*)-α-acetamidocinnamate catalysed by a rhodium complex containing achiral diphosphine, *viz*., 1,2-bis(diphenylphosphino)ethane (diphos).[27, 53–55] The catalytic cycle of this reaction is shown in Scheme 7. The precursor of the catalytic complex, *viz*., an ionic adduct of diene with a catalyst (**11**), is involved in the catalytic cycle after reduction of the diene. The structure of complex **12** was determined by ^{31}P NMR spectroscopy [53] and the structure of complex **13** was established by ^{31}P, ^{13}C and ^{1}H NMR spectroscopy and X-ray diffraction analysis.[24] At room temperature, the oxidative addition of hydrogen to the complex **13** is the rate-limiting step of the reaction, whereas reductive elimination of the product becomes the rate-limiting step at −40 °C. As a result, alkyl hydride complex **15** at −75 °C was accumulated in a concentration sufficiently high for analysis by ^{31}P, ^{13}C and ^{1}H NMR spectroscopy.[29, 54]

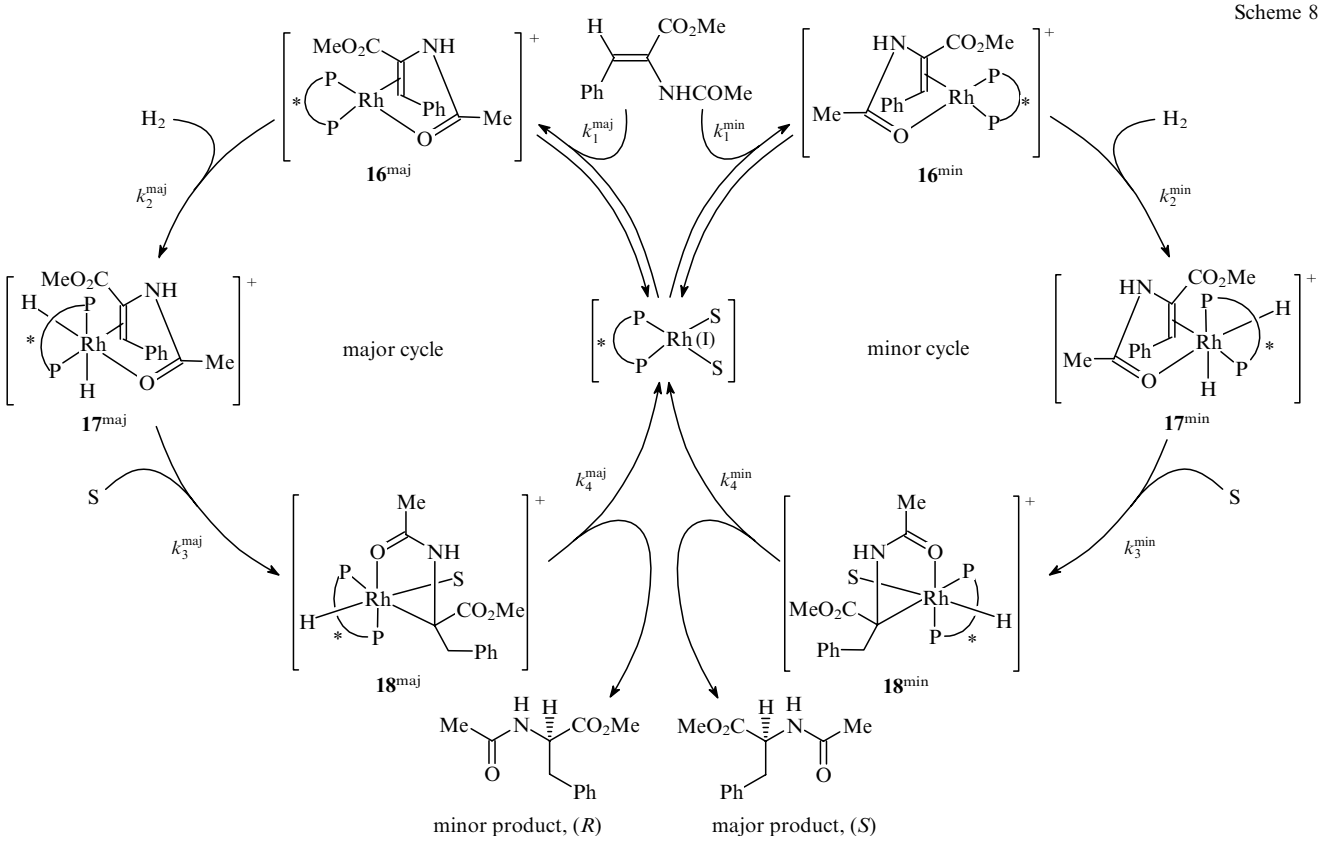
Of compounds presented in Scheme 7, only intermediate **14** was not identified and its structure was proposed 'by analogy'.[56, 57] Later on, the dihydride intermediate was found experimentally.[58] The intermediates **13**, **14** and **15** as well as the reaction product are racemates (both enantiomers of these intermediates are shown in Scheme 7).

The catalytic cycle of hydrogenation of the same substrate catalysed by {Rh[(*R*,*R*)-dipamp]}$^+$ is shown in Scheme 8. In this catalytic cycle, the corresponding intermediates are diastereomers and it is reasonable that the reactions involving these intermediates proceed at different rates.[59] An analogous catalytic cycle was proposed [26, 27] for hydrogenation in the presence of {Rh[(*S*,*S*)-chiraphos]}$^+$. In both cases, ^{31}P NMR spectroscopic studies demonstrated [26, 29, 55, 59] that one of the diastereomers (**16**^{maj}) was present in a high excess with respect to the other diastereomer (**16**^{min}). The structure of the major diastereomer (**16**^{maj}) obtained in the reaction in the presence of {Rh[(*S*,*S*)-chiraphos]}$^+$ was established by X-ray diffraction analysis [26] and circular dichroism spectroscopy.[27] However, the configuration of the resulting product was opposite to that, which would be expected to be realised if the reaction proceeds through this intermediate.[23, 26, 60, 61] Hence, it was suggested [26, 55] that the enantioselectivity is associated with the difference between the constants k_2^{min} and k_2^{maj} ($k_2^{min} \gg k_2^{maj}$, see Scheme 8) due to which the reaction proceeded predominantly through the intermediate **16**^{min} whose concentration was small compared with that of **16**^{maj}. In the case of hydrogenation of methyl (*Z*)-α-acetamidocinnamate in the presence of {Rh[(*R*,*R*)-dipamp]}$^+$ at 0 °C, the ratio of the constants $k_2^{min} : k_2^{maj} \approx 1000$.[59] Halpern [55] assumed that this situation follows the Curtin – Hammet principle according to which

Scheme 7



Scheme 8



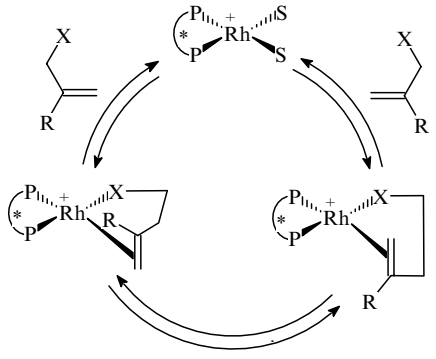
the ratio of the products depends only on the difference between the free energies of the transition states and is independent of the ratio of the conformers (intermediates). According to Halpern's theory, the chiral recognition (asymmetric induction) takes place in the transformation **16** → **17** involved in the catalytic cycle. Unfortunately, no explanation was offered for the differences in stability and reactivity of the intermediates **16**^{maj} and **16**^{min}, which could allow an understanding of the reason for the substantial difference in the rates of their transformations.

Halpern's theory provides an explanation for the effects of hydrogen pressure and temperature on the enantioselectivity of the reaction. It was demonstrated [35] that the enantioselectivity decreased and even the configuration of the product was changed as the hydrogen pressure was increased. According to Halpern's mechanism (see Scheme 8), the formation of the intermediates **17** is accelerated as the hydrogen pressure is increased. At some time, this step ceases to be rate-limiting and the process is controlled by the reversible formation of the diastereomeric adduct **16**, *i.e.*, the enantioselectivity is determined by the ratio $k_1^{min} : k_1^{maj}$. Since $k_1^{maj} > k_1^{min}$, another catalytic cycle, which affords an opposite isomer of the product, becomes more favourable and the enantioselectivity is decreased. It is this situation that was experimentally observed.

The formation step of adduct **16** is characterised by a substantially higher enthalpy of activation than the next step of the addition of hydrogen (in the presence of [Rh-dipamp]$^+$ as the catalyst, 18.3 and 6.3 kcal mol^{-1}, respectively). What this means is the rate of the first step is decreased much more rapidly than that of the second step as the temperature is decreased and, consequently, the first step can become rate-limiting. Hence, the enantioselectivity would be expected to decrease with decreasing temperature. This situation was observed in reactions involving some phosphine catalysts.[32, 35]

Since Halpern's theory provides an explanation for many experimental observations, it was commonly accepted in the 1980s.[62–65] However, this theory has a number of drawbacks.

1. According to Scheme 8, the coordination mode of enamide is not changed (*Re–Si*) and, consequently, the balance between the major and minor catalytic cycles remains unchanged on going from the planar-square complex **16** containing the C_2-symmetric chiral (diphosphine)Rh(I) fragment to the octahedral complex **17** containing the asymmetric (diphosphine)Rh(III)H_2 fragment.

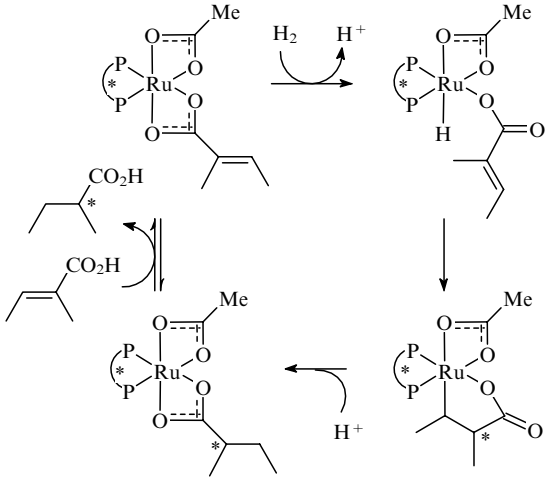


However, the real situation may be different. Moreover, intramolecular interconversions of the complex **16** are quite possible and even (see Ref. 66) the energy barrier for these interconversions is low. It is conceivable that the interconversion *Re–Si* occurs in the step **16** → **17**, in which case the major enantiomer is formed in the major catalytic cycle.

2. Most likely, Halpern's theory is inapplicable in the case of rhodium complexes serving as catalysts of hydrogenation of enamides with *ee* = 99.0%–99.9%. In this case, with the generally observed ratio between the major and minor intermediates (10 : 1), the ratio of the rate constants $k^{min} : k^{maj}$ must be even several orders of magnitude larger than that in the case of the rhodium complex with the chiraphos ligand (*ee* = 88%, $k^{min} : k^{maj} \approx 1000$). This difference in the rate constants of the transformations of diastereomeric intermediates seems to be unlikely. For the reaction involving the rhodium complex with the BisP* ligand, another mechanism was proposed [34] (see above).

3. Halpern's scheme provides no explanation for some experimental evidence, for example, for the difference in enantioselectivity of hydrogenation of the *E* and *Z* isomers.[67, 68] The enantioselectivities of hydrogenation of (*Z*)- and (*E*)-α-benzoylaminocinnamic acids using the Rh/(*S*,*S*)-diop system differ not only in magnitude but also in sign.[69] This may be associated with the different modes of coordination of the above-mentioned substrates by the rhodium atom (the *E* isomer is coordinated through the carboxy carbonyl group, whereas the *Z* isomer is coordinated through the amide carbonyl fragment).[70] Apparently, the *Re*- or *Si*-side of the coordinated double bond of the substrate may also be changed. Halpern's theory provides no explanation for the influence of bases on the value of *ee* in the reactions performed in the presence of catalysts for which this theory has been initially proposed.[35] Thus according to Halpern's hypothesis, the enantioselectivity of hydrogenation in the presence of diphosphine catalysts decreases as the temperature is decreased; however, this is not necessarily the case. Thus in hydrogenation of dehydroamino acids in the presence of rhodium complexes with the prophos, cycphos or diop ligands, the optical yields decreased as the temperature was raised.[42, 71] Apparently, Halpern's mechanism is only a special case.

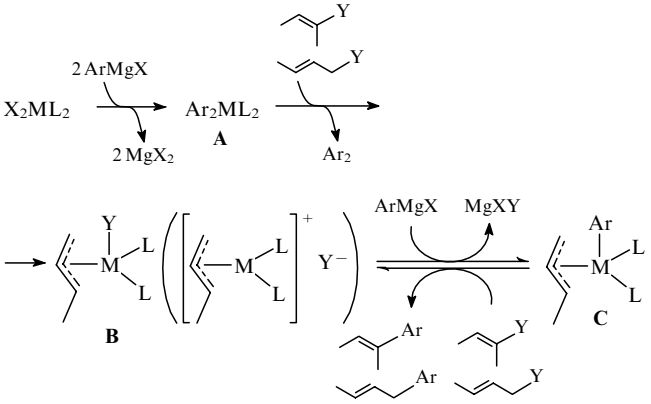
The mechanism of hydrogenation of substrates, such as tiglic acid, catalysed by the $Ru(OAc)_2$[binap] complex has been studied in sufficient detail. It was demonstrated that hydrogenation proceeded through the formation of a ruthenium monohydride complex.[72] The mechanism of hydrogenation of tiglic acid on this catalyst was detailed in the study.[73]



The bis(carboxylato)ruthenium complex involving a substrate performs the heterolytic splitting of H_2 giving rise to a hydride. The hydride ion reduces the C=C bond in the coordinated substrate to form the chelate which contains the chiral product in the half-hydrogenated state. Protonolysis of the newly formed Ru–C bond affords the target product. According to this scheme, asymmetric induction takes place in the formation of the chelate complex with the substrate hydrogenated, *i.e.*, in the step of the transformation of the intermediate devoid of symmetry elements (except for C_1). An analogous mechanism for hydrogenation of tiglic acid on the catalytic methallyl complex [binap]Ru.[η^3-$(CH_2)_2$CHMe]$_2$ was proposed in the study.[74] In the cited study, it was also assumed that asymmetric induction occurs in the step of the transformation of the asymmetric intermediate, which already involves the substrate in the coordination sphere.

Asymmetric cross-coupling of Grignard reagents with alkenes has been less well studied. According to the presently accepted mechanism, the reaction proceeds through the formation of the intermediate π-allyl(aryl)ML_2 (Scheme 9).[75–79]

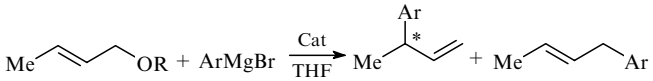
Scheme 9



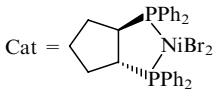
X = Hal; M = Ni, Pd; L_2 = P_2, P⌒P;

Y = Br, OH, OPh, COMe, $OSiMe_3$, CO_2Me.

The stages **A** → **B**, **B** → **C** or **C** → products may be responsible for asymmetric induction. With the aim of elucidating this problem, we studied the reaction of arylmagnesium bromides with derivatives of crotyl alcohol under the action of a nickel catalyst by increasing successively the molecular volume of the leaving group (OR):[80]



R = H, Ph, CO_2Et, $SiMe_3$;

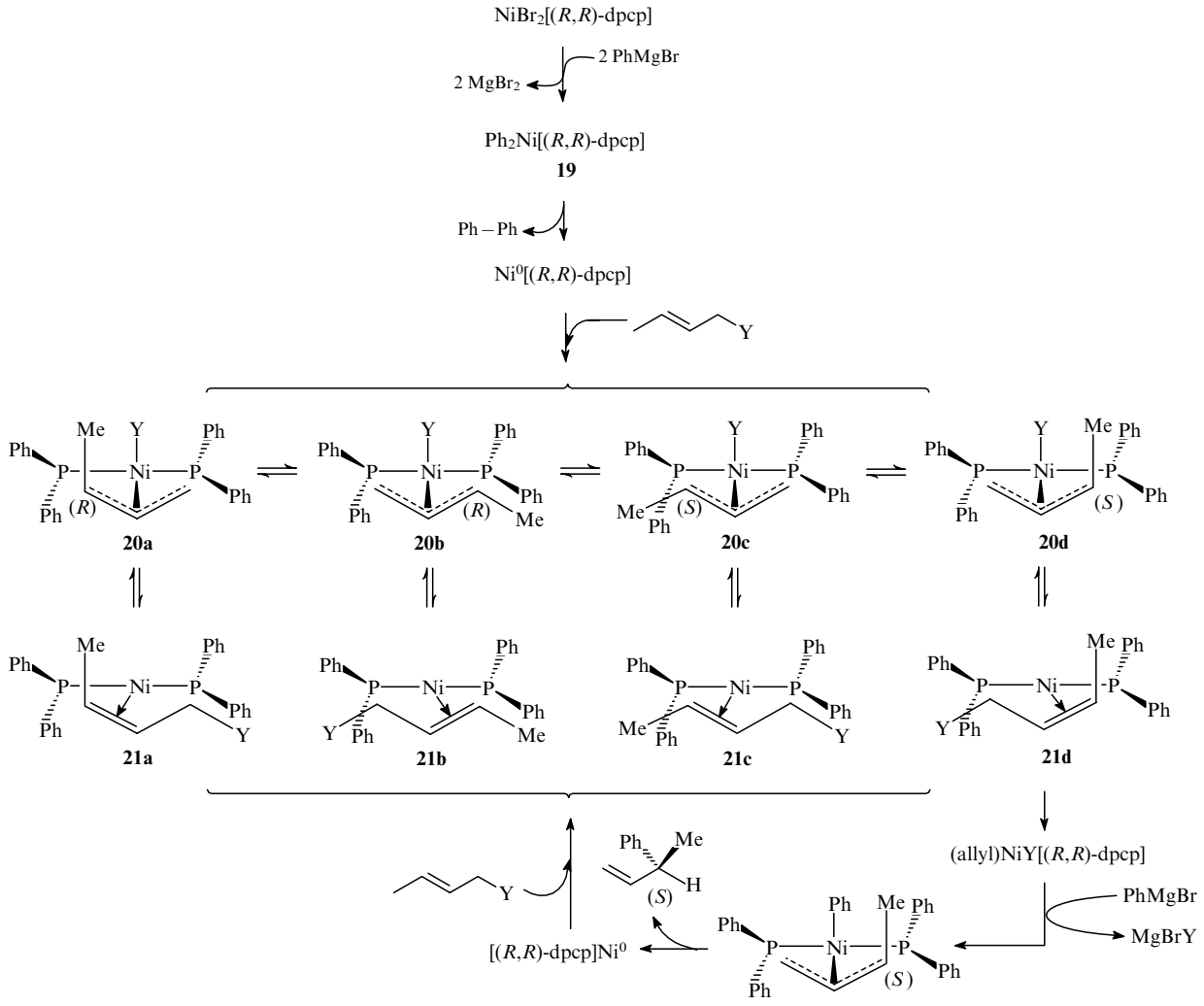


{(−)-$NiBr_2$[(*R*,*R*)-dpcp]}.

Among the intermediates which confirmed the general reaction mechanism proposed previously, species involving π-coordinated alkene (the substrate) were identified by ^{31}P NMR and CD spectroscopy. Probably, these intermediates, which exist in the equilibrium with intermediates **20**, are involved in the overall reaction (Scheme 10).

The chiral arrangement of the phosphine phenyl groups of the coordinated dpcp ligand presented in Scheme 10 is based on the results of X-ray diffraction analysis of the complex[81] (the cyclopentane ring of the dpcp ligand is omitted). The crotyl ligands in the intermediates **20a**–**20d** involve the stereogenic[82] carbon atom whose configurations are symbolised as (*R*) and (*S*). The π-coordinated crotyl ligand of this type can be subjected both to the (*R*)–(*S*)-inversion of the π-allylic chirality and the *syn*–*anti* transformation according to the π–δ–π mechanism.[83–85] Hence, it can be assumed that all possible forms of the intermediate **20** (**a**–**d**) exist in the equilibrium. In turn, each intermediate can exist in equilibrium with the intermediates **21a**–**21d**. The interconversion **20d** ⇌ **21d** experiences the smallest of steric

Scheme 10

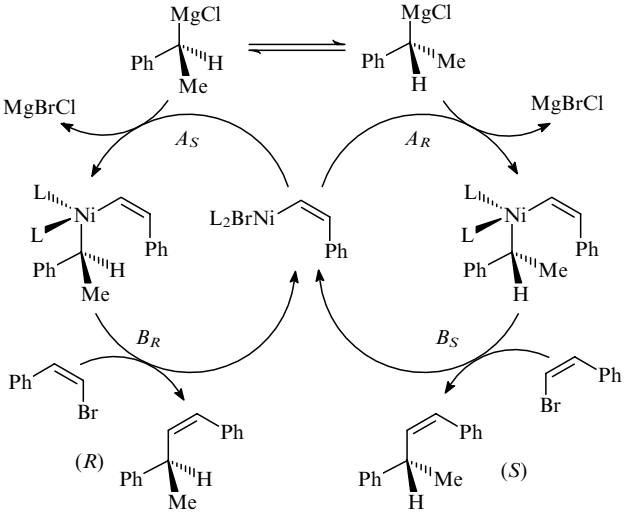


hindrances. The reaction proceeding through these intermediates affords a product whose configuration is identical with that observed experimentally. The larger the molecular volume of the leaving group, the more favourable this path and the higher the expected enantioselectivity. This fact was confirmed experimentally. Hence, asymmetric induction in the reaction under consideration takes place in the stage of the interconversion of the asymmetric intermediates **20(a – d)** $\rightleftharpoons$ **21(a – d)**.

This mechanism allows one to explain rather readily the characteristic features of the reaction observed experimentally, *viz*., the dependence of the enantioselectivity on the molecular volume of the leaving group (the larger the molecular volume, the more favourable the path through the intermediate **21d** and the higher the enantioselectivity) and the fact that the enantiomeric excess of the product is independent of the temperature (because the equilibrium can be established even at low temperatures). Both intermediates responsible for asymmetric induction already involve the coordinated substrate and are asymmetric.

Another type of cross-coupling, for example, the reaction of a racemic mixture of 1-phenylethylmagnesium chloride with (*Z*)-β-bromostyrene catalysed by nickel complexes (the dynamic kinetic resolution) can be represented by Scheme 11.[86]

Scheme 11

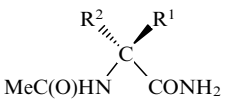


Asymmetric induction can take place both in steps *A* and *B* (in both cases, the intermediates are asymmetric).

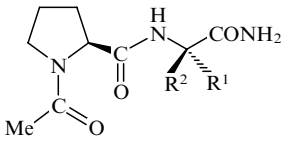
V. Asymmetric induction caused by nonbonded diastereomeric interactions

Solutions containing one enantiomer or a mixture of enantiomers (a racemate) may differ in physical properties. Thus the NMR spectra of the racemate differ from those of the optically active compounds comprising this racemate.[87,88] Analogous effects were also observed in calorimetric studies. These effects are attributable to diastereomeric interactions between enantiomers in solutions.[89,90]

The enthalpies of interactions of amide derivatives of L- and D-alanine as well as of dipeptides containing the terminal L- and D-alanine residues in aqueous solutions are given in Table 3.



(*S*)-**22**: R^1 = Me, R^2 = H;
(*R*)-**22**: R^1 = H, R^2 = Me.

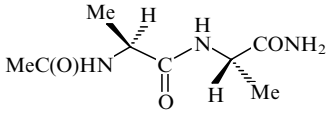


(*S*,*S*)-**23**: R^1 = Me, R^2 = H;
(*S*,*R*)-**23**: R^1 = H, R^2 = Me.

Table 3. Enthalpies of interactions of peptide fragments containing the terminal L- and D-alanine residues.[91]

Solution A	Solution B	H_{AB} /J kg mol^{-2} (see [a])
(*S*)-**22**	(*S*)-**22**	269 ± 5
(*R*)-**22**	(*R*)-**22**	277 ± 5
(*R*)-**22**	(*S*)-**22**	337 ± 10
(*S*,*S*)-**24**	(*S*)-**22**	488 ± 17
(*S*,*S*)-**24**	(*R*)-**22**	578 ± 9
(*S*,*S*)-**23**	(*S*)-**22**	769 ± 49
(*S*,*S*)-**23**	(*R*)-**22**	748 ± 16
(*S*,*R*)-**23**	(*S*)-**22**	803 ± 22
(*S*,*S*)-**23**	(*S*,*S*)-**23**	1629 ± 24
(*S*,*R*)-**23**	(*S*,*R*)-**23**	1399 ± 8
(*S*,*S*)-**23**	(*S*,*R*)-**23**	1515 ± 43

[a] This dimension was used by the authors of the cited study.[91]



(*S*,*S*)-**24**

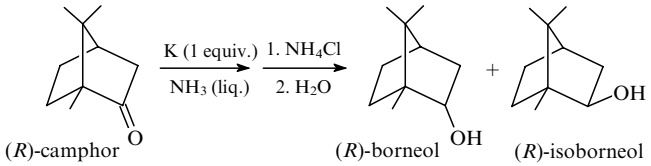
The observed differences in *H* are indicative of the presence of nonbonded interactions between enantiomers in solutions, such as monomer – monomer, monomer – dimer and dimer – dimer containing the terminal L- and D-alanine residues.[91]

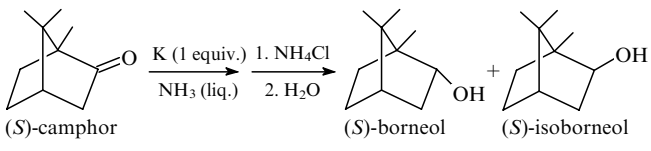
An impressive example of the separation of an enantiomer and a racemate by fractional distillation was reported.[92] It appeared that the boiling point of the racemate of trifluorolactic acid differs from that of its enantiomers. This is indicative of the presence of strong nonbonded diastereomeric interactions. However, this effect was not observed for the ester of lactic acid. The differences in the physical properties of enantiomers and the racemate in solutions are generally rather small,† but they are sufficiently large for these substrates to exhibit different chemical activities.[94]

The following general principle was stated: the reaction rate for a chiral compound and the ratio of the resulting products depend, among other things, on the enantiomeric composition of the starting compound.[95] The following reactions can be distinguished:

$R + R \longrightarrow RR$ (enantiomeric recognition),
$S + S \longrightarrow SS$ (enantiomeric recognition),
$R + S \longrightarrow RS$ (antipode interaction).

Below examples are given of reactions where one of the nonbonded interactions (or all these interactions taken together) leads to different compositions of the products.

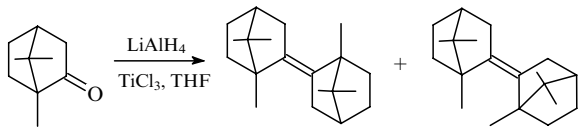




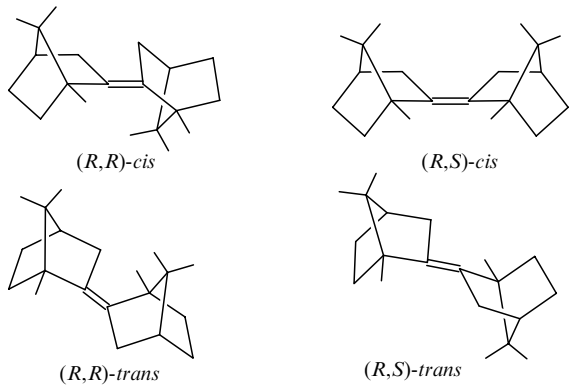
† Differences in the physical properties of the enantiomers and the racemate in crystals have long been known and were described in handbooks (for example, see Ref. 93). These differences are due primarily to the differences in the molecular packings in the crystals.

If (*R*)- or (*S*)-camphor was used as the starting substrate, the excess of borneol in the resulting mixture was insignificant. However, the reaction starting from racemic camphor afforded borneol as the major product.[96] In contrast, reduction of (*R*)-camphor with $LiAlH_4$ gave rise predominantly to isoborneol, whereas borneol was obtained as the minor product (90.2% and 9.8%, respectively).[95,97] A somewhat different composition of the mixture was obtained in the reaction starting from (*R*,*S*)-camphor (88.7% and 11.3%, respectively).

Reductive dimerisation of camphor

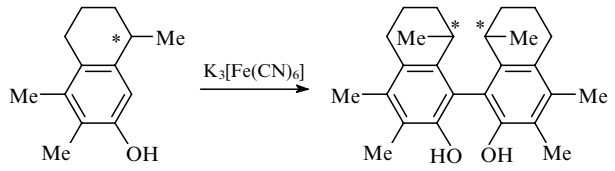


afforded a mixture of isomers

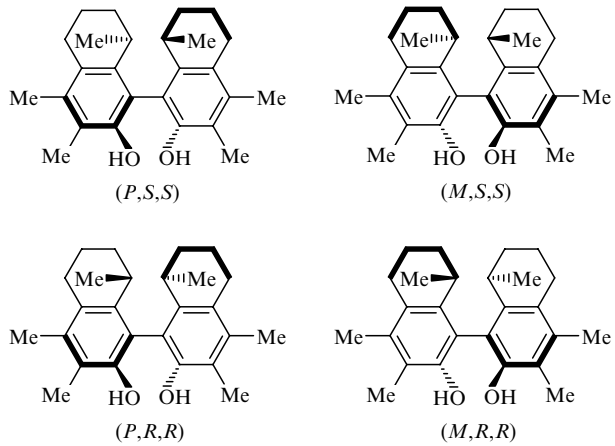


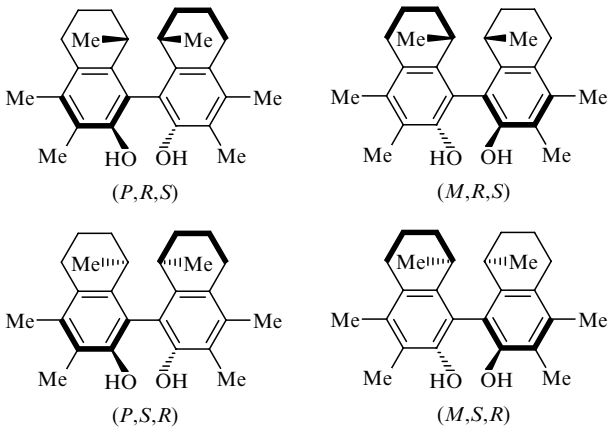
The reaction involving the (*R*)-monomers of camphor gave rise to the (*R*,*R*)-*cis* and (*R*,*R*)-*trans* dimers in a ratio of 34.8 : 65.2. In the product obtained from the racemate of camphor, (*R*,*S*)-*cis* [(*R*,*R*,*S*,*S*)-*cis*] and (*R*,*S*)-*trans* [(*R*,*R*,*S*,*S*)-*trans*] isomers were present in a ratio of 37.4 : 62.6.[95]

Oxidative dimerisation of the (*S*)-monomer of a phenol derivative

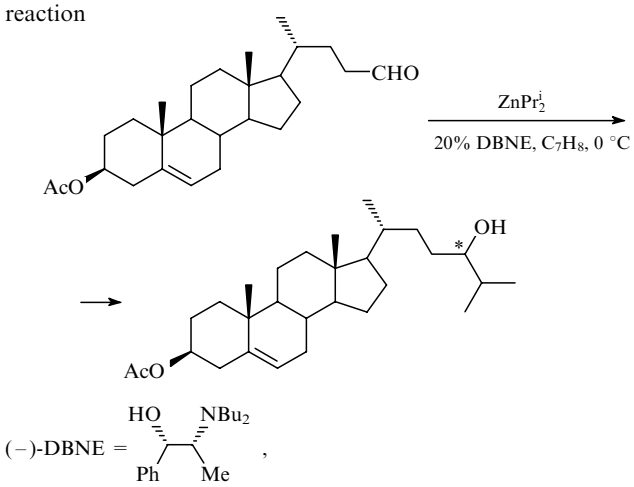


afforded the (*P*,*S*,*S*) and (*M*,*S*,*S*) diastereomers in a yield greater than 97.5%.[95] The racemic monomer can, in principle, give eight diastereomers:





However, dimerisation of this monomer produced a mixture of the (*P*,*S*,*S*), (*M*,*S*,*S*), (*P*,*R*,*R*) and (*M*,*R*,*R*) diastereomers (*trans* dimers) in 66% yield, whereas the theoretically possible yield is 50%. This inconsistency can be considered as an argument in favour of active interactions between the enantiomers. The reaction



catalysed by chiral aminoalcohol yielded a chiral compound bearing an asymmetric centre in the terminal fragment.[98] (–)-Aminoalcohol catalysed the formation of (*R*)-alcohol with the diastereomeric excess *de* = 97% independently of its enantiomeric purity (100% and 21%), whereas the (*S*) product with *de* = 87% was obtained in the presence of (+)-aminoalcohol (*ee* = 100%). This result is attributable to nonbonded diastereomeric interactions between the chiral substrate and the aminoalcohol.

The non-linearity of the changes in the optical and enantiomeric purities, which was observed in some cases, is accounted for by similar reasons.

The effect of the non-linear dependence of the enantiomeric excess of the product on the enantiomeric (or diastereomeric in the case of a diastereomer) purity of the catalyst (the reagent) can be manifested in asymmetric catalysis [99] (in asymmetric synthesis and in stereoselective reactions [100]) if a chiral catalyst (or a reagent) can form a dimeric diastereomeric complex with one of the reagents of the catalytic (or non-catalytic) reaction.

Possible dependences of the enantiomeric excess of the product on the enantiomeric excess of the catalyst (the reagent) are shown in Fig. 5. A wide range of such reactions is presently known.[99,100] These effects are attributed to the differences in the reactivity of homochiral and heterochiral dimeric complexes.

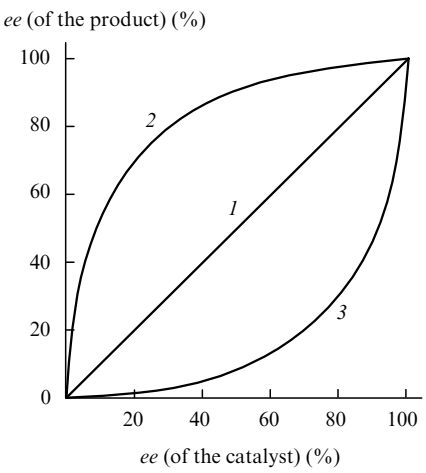
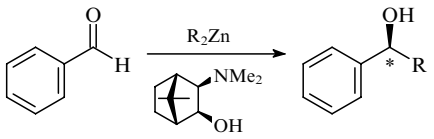
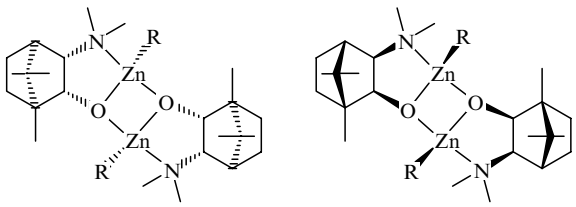


Figure 5. Possible deviations from the linear dependence of *ee* of the product on *ee* of the catalyst.
(*1*) the linear dependence, (*2*) the positive non-linear effect, (*3*) the negative non-linear effect.

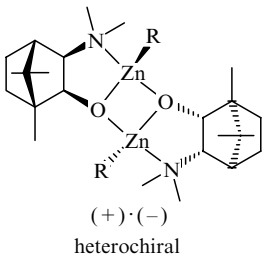
For example, in the reaction



the homochiral (−)·(−) dimer



is 1200 times more active than the heterochiral dimer,



which gives rise to the positive non-linear effect.[101–103]

VI. Conclusion

Recent investigations demonstrated that the enantioselectivity of some metal-complex catalysts approaches 100%. Ligands for complexes, which ensure the record-breaking enantiomeric purity of the products in various reactions, are given in Table 4. All the listed ligands are conformationally rigid and possess a pronounced helical component bearing bulky groups at the ends of an incomplete helical turn.[6]

The investigation into the mechanism of hydrogenation of enamides in the presence of one of such complexes (the octahedral asymmetric rhodium dihydride complex containing the BisP* ligand) demonstrated that asymmetric induction takes place in the stage of substrate coordination by the complex. The high enantioselectivity of this catalytic reaction (99.9%) is determined by the 99.95% probability of the coordination of enamide by one side {the *Re*-side in the case of the Rh[(*S*,*S*)-BisP*] complex}.[106] This is indicative of a large difference between the free activation energies of substrate coordination through the favourable and unfavourable sides. The probability of the substrate being coordinated through a particular side is, evidently, determined by the helical component of the conformationally rigid ligand of the complex bearing bulky groups at the ends of the incomplete turn of the helix.

As an alternative mechanism for improving the diastereomeric purity of an adduct of a dihydride complex with enamide, intramolecular isomerisation is less probable due to the high reactivity (short lifetime) of this intermediate (such an isomerisation is more likely in the case of an adduct of the starting complex with the substrate,[66] which is not involved in the catalytic cycle [34]).

Table 4. Ligands involved in catalytic complexes, which are used in various reactions.

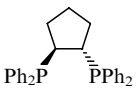
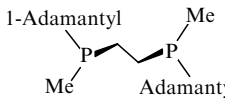
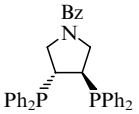
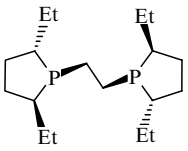
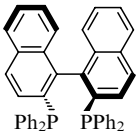
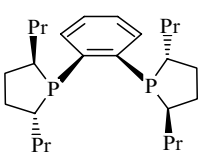
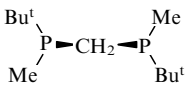
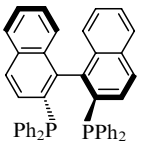
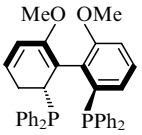
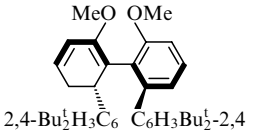
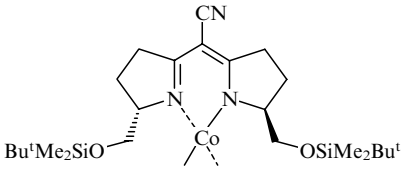
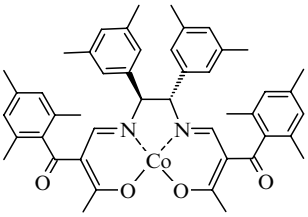
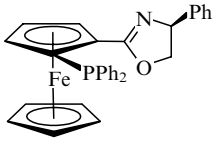
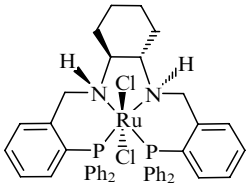
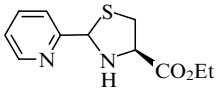
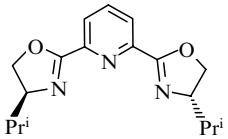
Ligand, complex	*ee* (%)	Ref.	Ligand, complex	*ee* (%)	Ref.
Hydrogenation of enamides catalysed by rhodium complexes			Hydrogenation of enamides catalysed by rhodium complexes		
	98 – 100	20, 81		99.9	107
	99	104		98.1	108
	100	105		99.8	108
	> 99.9	106			

Table 4 (continued).

Ligand, complex	*ee* (%)	Ref.
Hydrogenation of ketones, ketoesters and aminoketones catalysed by ruthenium complexes		
	99 – 100	109, 110
	98	111
	97.8	112
Reduction of enamides and imines catalysed by cobalt complexes		
	98.9	40, 47
	98	113

Ligand, complex	*ee* (%)	Ref.
Hydrogen-transfer hydrogenation of ketones catalysed by ruthenium complexes		
	97	114
	97	115
Hydrosilylation of ketones catalysed by rhodium complexes		
	98	116
	95	117, 118

The relationship between the sense of the helical component of a ligand in a rhodium complex involved in hydrogenation of enamides and the configuration of the product [6] either results from asymmetric induction taking place in the stage of substrate coordination or is a consequence of an alternative mechanism, which is most likely common to the overall series of reactions in which this regularity is observed.

The available experimental data indicate that the reactions proceeding under the action of chiral C_2-symmetric metal-complex catalysts generate the asymmetric carbon atom in the product in a step involving an asymmetric intermediate. Apparently, the Curie – Pasteur principle, which states that there is 'no asymmetry without asymmetry', has a literal sense.

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