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# Structural and configurational relationships 'metal complex – substrate – product' in asymmetric catalytic hydrogenation, hydrosilylation and cross-coupling reactions

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**Abstract. The present-day published data on the relationships between the structures of rhodium, iridium, ruthenium, nickel and cobalt catalytic complexes and substrates in homogeneous asymmetric hydrogenation, hydrosilylation and cross-coupling reactions are systematised. The optimum ratio between the number of coordination vacancies in the complex and the number of functional groups of the substrate has been characterised in terms of a criterion of maximum enantioselectivity of the catalytic complex. The relationships between the configurations of the complexes and the products formed in the reactions are analysed. In the case of $C_2$-symmetrical chiral diphosphine complexes as catalysts (some structural elements of their ligands represent an incomplete turn of a helix surrounding the central metal atoms), substrates of the same kind form the products having definite configurations characteristic of the particular orientation of the helix. For example, rhodium complexes with ligands that form an incomplete *P*-helical turn around metal atoms catalyse the formation of (*R*)-amino acids from the corresponding precursors. If the ligands contain fragments of *M*-helices around rhodium atoms, it is (*S*)-amino acids that are formed. The bibliography includes 234 references.**

## I. Introduction

Considerable recent interest in asymmetric synthesis is explained not only by the objective logic of organic chemistry, but also by the fact that in the past decade the pharmaceutical industry has largely concentrated on the preparation of drugs in an enantiomerically pure form. Therefore, a search for relatively simple and inexpensive techniques for separation of enantiomers or the synthesis of compounds in the form of individual enantiomers has become a very urgent problem. In this respect, priority is given to asymmetric catalysis, which allows one-step synthesis of products (or intermediates) from prochiral compounds with high enantiomeric excess (*ee*). The latter is expressed in per cent as the ratio of the difference in the yields of two enantiomers to their total yield (the terms 'optical yield' and 'enantiomeric purity' are also used to describe stereoselectivity). The costs of enantiomeric products are sometimes close to those of racemates, since the concentrations of expensive chiral metal complex catalysts in the reaction mixture are usually low and the substrate : catalyst ratios are rather high (up to 70 000).

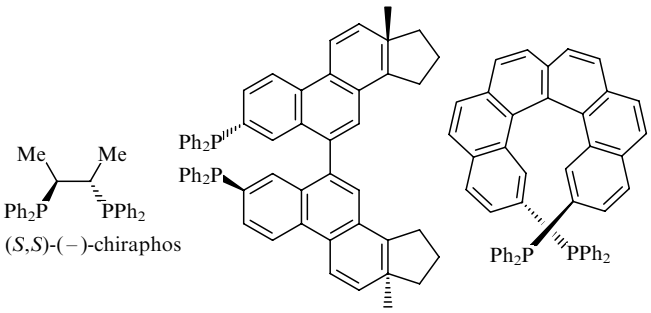
The progress in asymmetric metal complex catalysis has been documented in numerous publications (see the monographs [1–4] and the reviews [5–19]), and their number is steadily increasing. However, the 'catalyst – substrate – product' structural and configurational relationships remain relatively little-studied. Analysis of these relationships is the first step in the elucidation of the mechanism of a transfer of asymmetry from the catalyst to the reactive substrate, *i.e.*, asymmetric induction.

Most probably, the crucial role in asymmetric induction belongs to chiral ligands of metal complexes. It is these ligands that determine the chiral environment of metal atoms [20] in the catalyst. Therefore, special attention in the analysis of general regularities of 'catalyst – substrate – product' structural and configurational relationships should be given to reactions where the greatest number of different ligands have been used. These reactions include hydrogenation, hydrosilylation and cross-coupling. These were chosen for two additional reasons. First, in these reactions very high enantiomeric excesses of the products have been achieved. Second, this minimum set of reactions allows one to obtain chiral products with the largest number of functional groups (*e.g.*, alcohols, amines, organic acids, amino alcohols, amino acids, hydroxy acids and hydrocarbons), which is of considerable value in the synthesis of drugs and synthons.

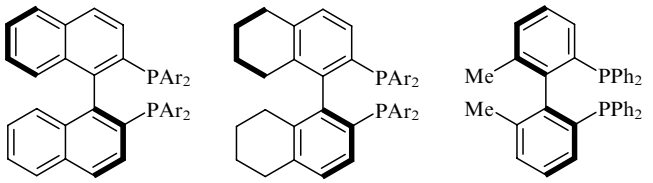
By now, a vast variety of ligands, which represent components of $C_1$- and $C_2$-symmetrical chiral complexes (see, *e.g.*, reviews [20–32]), have been synthesised and analysed in these and some other reactions. Configurational relationships of chiral complexes having $C_2$ symmetry axes can be systematised most easily. Complexes with five- and seven-membered chelate cycles formed by bis(diphenylphosphine) ligands (from the simplest [33] to exotic [34, 35]) shown below manifest the highest enantioselectivities.

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Substrates, such as α-acetamidocinnamic acid, which allow coordination by metals in the catalytic complexes both at the double bonds and at two additional functional groups, are especially suitable for the synthesis of chiral products by hydrogenation. Thus the *ee* of the hydrogenation product reaches 99% (see Ref. 36). The enantioselectivity of this reaction decreases dramatically upon removal of at least one functional group. Ruthenium complexes with atropoisomeric diphosphine ligands of the binap type are most suitable reagents for hydrogenation of such substrates.[37–41]




Ar = Ph: (*S*)-binap
Ar = *p*-$MeC_6H_4$: (*S*)-Tolbinap

(*S*)-$H_8$-binap

(*S*)-biphemp

In the presence of these complexes, the maximum value of *ee* exceeds 99.5% (see Ref. 40). The enantioselectivity of hydrogenation of substituted ketones in the presence of these complexes is at the same level.[42–50]

Asymmetric hydrosilylation of ketones[3,4]

$$R^1R^2C{=}O + HSiR_3 \xrightarrow{ML_n^*} HR^1R^2COSiR_3 \xrightarrow{H_3O^+} R^1R^2CHOH + HOSiR_3$$

M = Rh, Ir, Ru; $L_n^*$ = P*,  ; the chiral fragment or the asymmetric atom is marked with an asterisk

can be regarded as a variant of their asymmetric hydrogenation, since the silyl ether formed can be hydrolysed into an alcohol with retention of the configuration of the asymmetric carbon atom.[51–53] Very often, the same catalysts manifest similar efficiencies in both reactions, which also suggests their similarity.[54] However, specific hydrosilylation catalysts are known[55–57] which result in a maximum *ee* of 97.6% (see Ref. 58).

Asymmetric cross-coupling of organometallic compounds ($R^1M'X$) with alkenyl or aryl halides and related compounds ($R^2Y$)

$$R^1M'X + R^2Y \xrightarrow{ML_n^*} (R^1{-}R^2)^*$$

M′ = Mg, Zn *etc.*; X = Hal; M = Ni, Pd; Y = Hal, OR, OH, *etc.*;

$L_n^*$ = P*, 

results in the formation of a C*−C bond in the product; its enantiomeric purity reaches 95%. In terms of enantioselectivity, this reaction is somewhat inferior to hydrogenation and hydrosilylation, however, cross-coupling combined with allylic alkylation arouses considerable interest,[59–63] since it gives rise to chiral hydrocarbons.

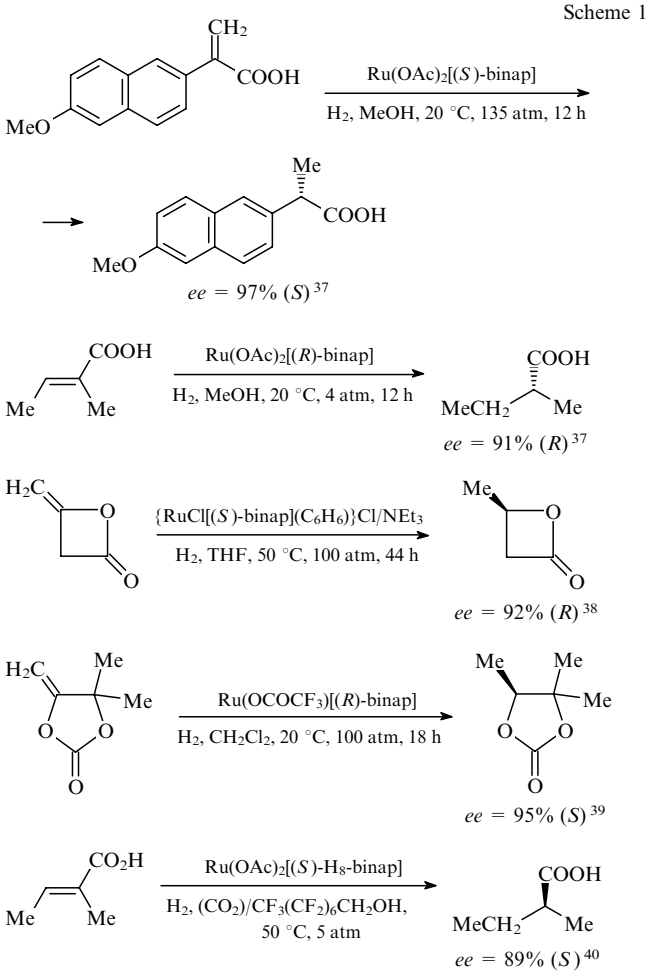
## II. Catalyst – substrate structural relationships

In a search for the most suitable substrates for performing their conversions on metal complexes containing structurally different ligands, enantiomeric purity of the product serves usually as the main criterion. Asymmetric hydrogenation on rhodium – phosphine complexes is certainly one of the most extensively studied reactions of this kind.

The *ee* values of hydrogenation products of various substrates depending on the structures of the ligands of the catalytic complexes are listed in Table 1. As can be seen from these examples, any substitution of the alkyl radical for the coordination-active substituent at the double bond results in a drastic decrease in the reaction enantioselectivity. Hence, the double bond should contain at least two groups of the type NHCOR or $CO_2R$. However, if a catalytic complex contains the bppm ligand, which can be coordinated by three groups (also in the presence of $Et_3N$), replacement of the acetamido group in the substrate by a group with weaker coordination ability has a smaller effect on the enantioselectivity in comparison with reactions catalysed by complexes with bidentate ligands. Similarly, the number of coordination-active groups in the substrate can be reduced to one (with the exception of C=C) on going from the planar Rh(I) complexes to the octahedral Ru(II) complexes containing ligands of the binap type (Scheme 1).†

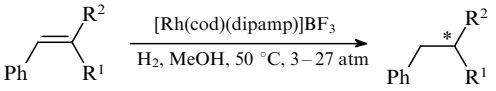
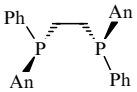
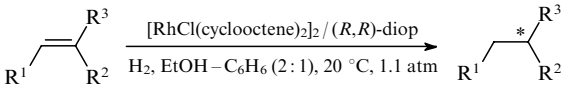
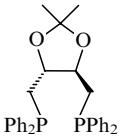
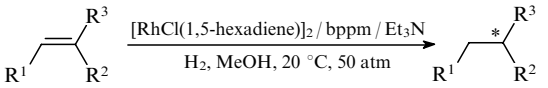
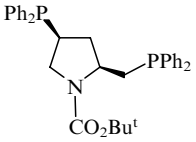
† Hereinafter we give the best or close to best parameters cited in the relevant publications.

Scheme 1

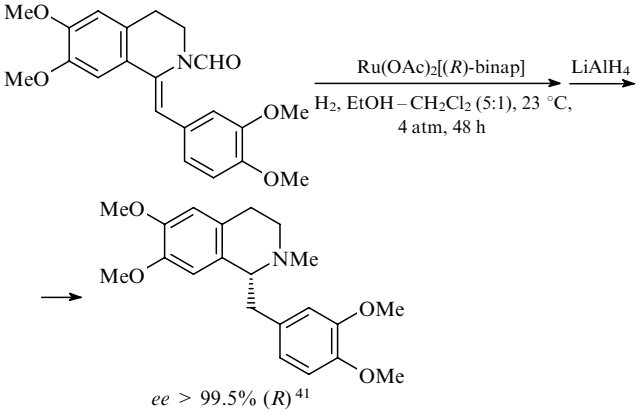



(CO2) is supercritical $CO_2$, $T_c$ = 31.0 °C, $p_c$ = 72.9 atm,

**Table 1**. The dependence of enantiomeric excesses of hydrogenation products of various substrates on the ligand structure of the catalytic complex.

| Ligand | $R^1$ | $R^2$ | $R^3$ | *ee* (%) | Ref. |
|---|---|---|---|---|---|
|  | | | | | |
|  dipamp | NHCOMe | $CO_2H$ | | 94 (*S*) | 64 |
| | $CO_2H$ | NHCOMe | | 47 (*S*) | 64 |
| | NHCOMe | $CO_2Me$ | | 96 (*S*) | 64 |
| | $CO_2Me$ | NHCOMe | | 23 (*S*) | 64 |
| | NHCOPh | $CO_2H$ | | 93 (*S*) | 64 |
| | $CO_2H$ | NHCOPh | | 39 (*S*) | 64 |
| | NHCOPh | CN | | 89 (*S*) | 64 |
| | NHCOMe | Me | | 51 (*R*) | 64 |
| | Me | NHCOMe | | 9 (*R*) | 64 |
| | Me | $CO_2H$ | | 1 (*R*) | 64 |
| | $CO_2H$ | Me | | < 1 (*R*) | 64 |
|  | | | | | |
|  (*R*,*R*)-diop | H | NHCOMe | $CO_2H$ | 73 (*R*) | 65 |
| | Ph | NHCOMe | $CO_2H$ | 82 (*R*) | 66 |
| | $Pr^i$ | NHCOMe | $CO_2H$ | 22 (*R*) | 65 |
| | H | Ph | $CO_2H$ | 63 (*S*) | 67 |
| | H | Ph | Et | 24.5 (*S*) | 67 |
| | H | OAc | $CO_2Et$ | 27 (*R*) | 68 |
| | H | OAc | $CF_3$ | 0 | 68 |
|  | | | | | |
|  bppm | Ph | NHCOMe | $CO_2H$ | 83 (*R*) | 69 |
| | H | OAc | $CO_2Et$ | 67 (*R*) | 68 |
| | H | $CF_3$ | $CO_2Et$ | 10 (*S*) | 68 |

**Note**. Hereinafter, hydrogen pressure ($pH_2$) is included, among other factors, into the description of reaction conditions. Abbreviations: cod is cycloocta-1,5-diene; An is *o*-$MeOC_6H_4$.



*ee* > 99.5% (*R*) [41]

These and some other data [70–73] suggest that high enantioselectivity of hydrogenation of substrates, such as tiglic acid in the presence of complexes of the $Ru(OAc)_2$[binap] type is provided by only one coordination group, which is located in the α-position relative to the double bond. Interestingly, hydrogenation of α-acetamidocinnamic acid on such catalysts is less enantioselective than that in the presence of rhodium complexes with binap ligands.[74] Thus for ruthenium complexes, the presence of two coordination-active groups at the double bond of the substrate is excessive and does not favour maximum enantioselectivity.

Simple ketones $R^1COR^2$ ($R^1$ = Ar, Alk, $R^2$ = Alk) are hydrogenated on chiral rhodium diphosphine complexes with low enantioselectivities. This can be improved by addition of an acid or a base to complexes which have proved to be efficient in asymmetric hydrogenation of enamide substrates. Thus in the presence of Rh/camp/$Pr^iCO_2H$, where camp is the ligand synthesised from camphor, *ee* = 12% (*R*) (see Ref. 75) and in the presence of Rh/(*S*,*S*)-diop/$Et_3N$, *ee* = 68% (*R*) (see Ref. 76). An alternative approach to increase enantioselectivity consists in the introduction of groups into α- or β-positions of ketones which can coordinate the metal. For example, hydrogenation of the ketone $ArCOCH_2NEt_2$ proceeds with high enantioselectivity without any base [in the presence of Rh/(*S*,*S*)-diop, *ee* = 93% (see Ref. 77)].

Presumably, complexes with bidentate diphosphine ligands (or diamino ligands in hydrogen-transfer hydrogenation reactions) do not provide a sufficiently high level of 'chiral recognition' of simple ketones due to small molecular sizes of the latter, nor do they favour their enantioselective hydrogenation. The results of hydrogenation of various ketones on such complexes

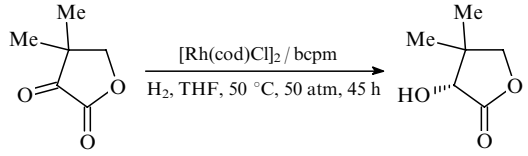
**Table 2**. Asymmetric hydrogenation of simple and β-substituted ketones on chiral diphosphine and diimine metal complexes.

| Catalyst | Ph(C=O)Me | | Ph(C=O)CH$_2$NBu$^t$ | | Ph(C=O)CH$_2$NR$^2$ | | R(C=O)CH$_2$(C=O)OEt | |
|---|---|---|---|---|---|---|---|---|
| | *ee* (%) | Ref. | *ee* (%) | Ref. | *ee* (%) | Ref. | *ee* (%) | Ref. |
| Rh-(*S*,*S*)-diop | 3 – 54 (*R*) | 78 – 82 | 35 (*R*) | 83 | 93(+) (R = Et) | 77 | – | – |
| Rh-(*R*)-binap | – | – | 6 (*R*) | 83 | – | – | – | – |
| Ru-(*R*)-binap | 30 – 74 (*S*) | 42 | 78 (*R*)[a] | – | – | – | 85 (*S*) (R = Ph) | 45 |
| Ru-(*S*)-binap | – | – | – | – | 95 (*S*) (R = Me) | 42 | – | – |
| Ru(OAc)$_2$[(*R*)-binap] | – | – | – | – | – | – | 4 (*S*) (R = Me) | 45 |
| RuCl$_2$[(*R*)-binap] | – | – | – | – | – | – | 99 (*R*) (R = Me) | 45 |
| RuCl$_2$(C$_6$H$_6$)/[(*S*)-binap] | – | – | – | – | – | – | 99 (*R*) (R = CH$_2$Cl$_2$) | 84 |
| RuCl$_2$(C$_6$H$_6$)/[(*R*)-binap] | – | – | – | – | – | – | 99 (*S*) (R = CH$_2$Cl$_2$) | 84 |
| Rh-(1*R*,2*R*)-*N*,*N*′-dibenzylidene-1,2-diaminocyclohexane | 48 (*S*) | 85 | – | – | – | – | – | – |
| Ir-(1*S*,2*S*)-*N*,*N*′-dibenzylidene-1,2-diaminocyclohexane | 55 (*R*) | 85 | – | – | – | – | – | – |

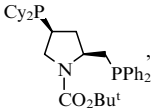
[a] Our data obtained with {Ru$_2$Cl$_4$[(*R*)-binap]$_2$}NEt$_3$.

are presented in Table 2. It can be seen that the enantioselectivity increases considerably with an increase in the size of the fragment of the substrate involved in coordination. If an additional coordination-active group of a ketone is blocked by a bulky substituent, *e.g.*, NHBu$^t$, or cannot compete with an achiral ligand of the catalytic complex for vacancies (*e.g.*, in the presence of the β-ester group in the substrate and the carboxyl ligand in the Ru(AcO)$_2$. .[binap] complex), the enantioselectivity of this reaction at room temperature approximates a level characteristic of unsubstituted ketones [*ee* = 4% (*S*)]; however, at high temperatures the situation is different.[48] The introduction of an additional coordination-active group into a ketone can change both the value and the sign of enantioselectivity (as in reactions of ruthenium catalysts with the binap ligands (see Table 2), which points to the change in the mechanism of asymmetric induction.

Enantioselectivity can be increased by using complexes with ligands coordinated to metals by three groups.[86]

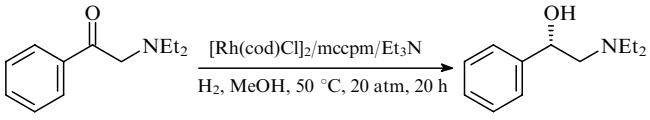



*ee* = 92% (*R*),[86]

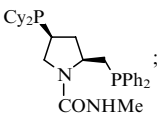
bcpm = 

, Cy is cyclohexyl.

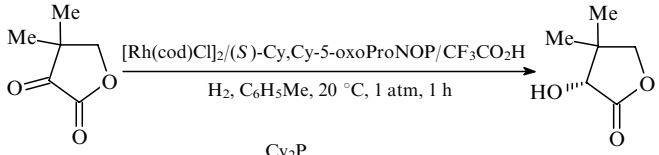
And, finally, the maximum enantioselectivity is achieved through a combined use of all the methods described above.



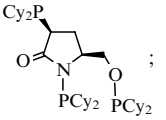

*ee* = 97% (*S*),[87]

mccpm = 

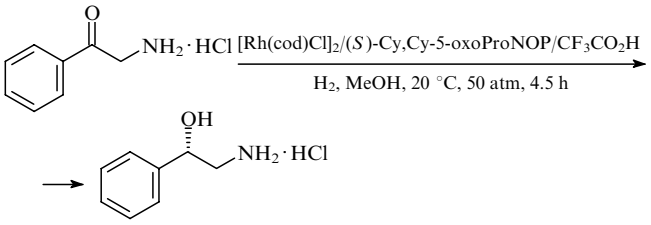
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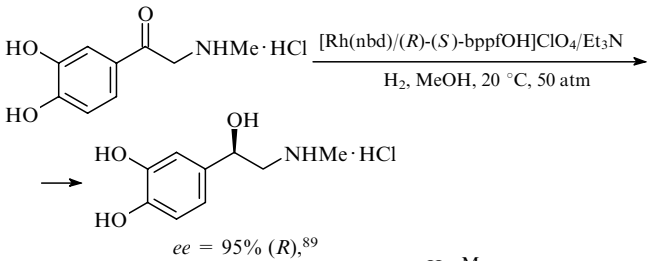

*ee* = 97.7% (*R*),[88]

(*S*)-Cy,Cy-5-oxoProNOP = 

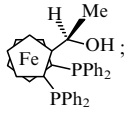
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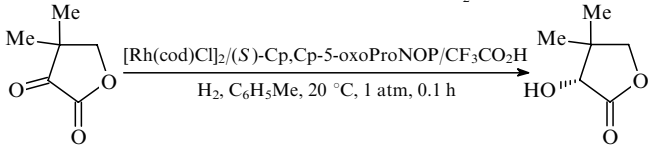

*ee* = 93% (*S*);[88]



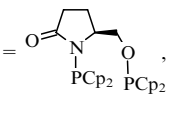

*ee* = 95% (*R*),[89]

nbd is norbornadiene, (*R*)-(*S*)-bppfOH = 

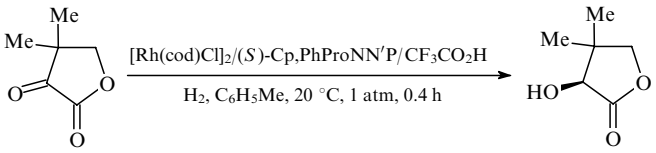
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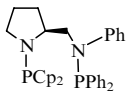

*ee* = 98.7% (*R*),[88]

(*S*)-Cp,Cp-5-oxoProNOP = 

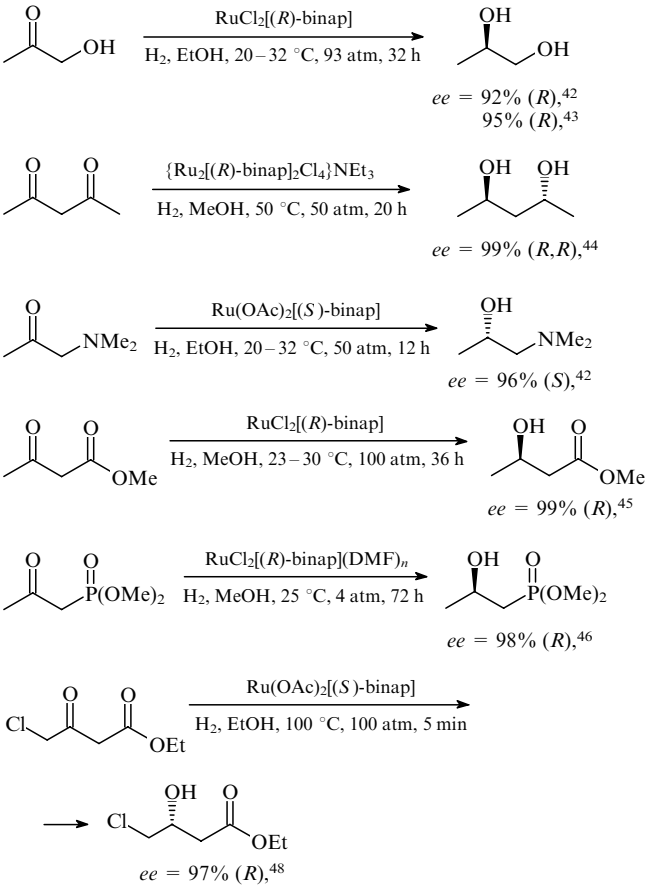
, Cp is cyclopentyl;

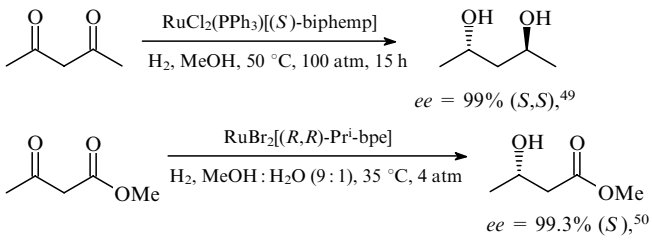



(*S*)-Cp,PhProNN′P =



As in the hydrogenation of substrates containing C = C bonds, the use of octahedral ruthenium complexes with such ligands as binap, biphemp, *etc*., is advantageous for an increase in the enantioselectivity of hydrogenation of ketones possessing coordination-active groups in the β-positions relative to carbonyl group.




bpe is bis(phospholano)ethane.

Special mention should be made of a group of highly enantioselective catalytic complexes, which are active at atmospheric pressure of $H_2$. These complexes have the *in situ* composition $\{RuCl_2[binap(or\ biphemp)]\}_2 \cdot MeCOMe$ and are used for hydrogenation of β-oxo esters,[91] β-oxo phosphonates, β-oxo thiophosphonates[92] and phenylthio ketones.[93] Other catalytic complexes of this kind are also known.[34,94–100] The hydrogenation of α- and γ-substituted ketones occurs less enantioselectively.[101–103]

Ruthenium complexes with tri- and tetradentate ligands, such as the ligands **1**–**8** and the complex **9**, are used as catalysts for increasing the enantioselectivity of hydrogen-transfer hydrogenation of simple ketones.

The effects of these complexes on the enantioselectivities of different hydrogenation reactions are demonstrated in Table 3 in the example of acetophenone.

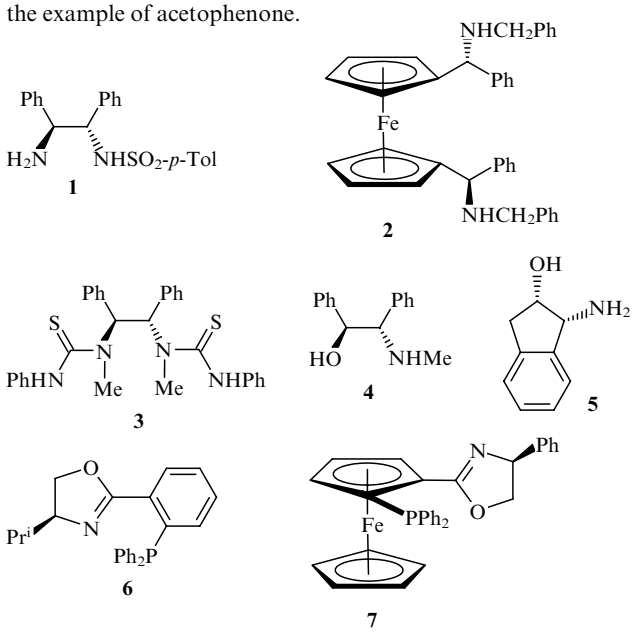


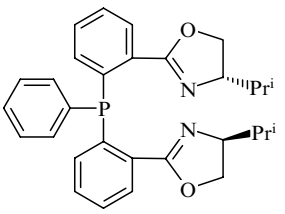

**Table 3**. Hydrogen-transfer hydrogenation of acetophenone on chiral ruthenium complexes.

| Precursor of the complex or the complex | Ligand | Base | *T* /°C | Conversion (%) | *ee* (%) | Ref. |
|---|---|---|---|---|---|---|
| $[RuCl_2(1,3,5\text{-}Me_3C_6H_3)]_2$ | **1** | KOH | 20 | 95 | 97 (*S*) | 104 |
| $[RuCl_2(1\text{-}Me\text{-}4\text{-}Pr^iC_6H_4)]_2$ (see [a]) | **2** | KOH | −30 | 91 | 90 (*R*) | 105 |
| $[RuCl_2(1\text{-}Me\text{-}4\text{-}Pr^iC_6H_4)]_2$ | **3** | $Bu^tOK$ | – | 98 | 87 (*S*) | 106 |
| $[RuCl_2(\eta^6\text{-}C_6Me_6)]_2$ | **4** | KOH | 28 | 94 | 92 (*S*) | 107 |
| $[RuCl_2(1\text{-}Me\text{-}4\text{-}Pr^iC_6H_4)]_2$ | **5** | KOH | 20 | 70 | 91 (*S*) | 108 |
| $RuCl_2(PPh_3)_3$ | **6** | NaOH | 82 | 24 | 94 (*R*) [b] | 109 |
| | **6** | NaOH | 82 | 83 | 73 (*R*) [c] | 109 |
| $RuCl_2(PPh_3)_3$ | **7** | $Pr^iOK$ | 28 | 80 | 97 (*R*) | 110 |
| | **7** | $Me_2CHOK$ | 80 | 87 | 88 (*R*) [c] | 110 |
| $[RuCl_2(C_6H_6)]_2$ | **8** | NaOH | 80 | 72 | 79 (*R*) | 111 |
| **9** | | $Me_2CHOK$ | | 93 | 97 (*R*) | 112 |

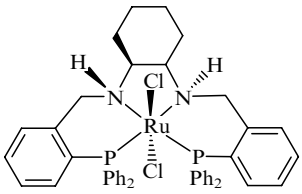
[a] 1-Acetylnaphthalene was used as a substrate. [b] The reaction time was 5 min. [c] The decrease in *ee* at higher levels of conversion is attributed to the reversibility of the hydrogen transfer reaction.[113]

**Table 4**. Hydrosilylation of acetophenone on chiral rhodium complexes.

| Complex precursor | Chiral ligand (L) | L : Rh | Achiral ligand | Solvent | $T$ /°C | Yield (%) | *ee* (%) | Ref. |
|---|---|---|---|---|---|---|---|---|
| $[Rh(cod)Cl]_2$ | **10** | 5 | – | – | 0 | 83 | 48.1(*R*) | 114 |
| | **11** | 8 | – | $CCl_4$ | −5 | 90 | 64.0 (*R*) | 115 |
| | **12** | 8 | – | $CCl_4$ | −5 | 84 | 65.0 (*R*) | 115 |
| | **13** | 9 | – | – | −15 | 98 | 86.7 (*R*) | 116 |
| | **14** | 13 | – | – | −20 | 99 | 97.6 (*R*) | 58 |
| | **14** | 2 | – | – | 0 | – | 75.6 (*R*) | 58 |
| $RhCl_3$ | **15** | 4 | $2AgBF_4$ | – | 0 | 94 | 95.0 (*S*) | 117, 118 |
| | **16** | 4 | $AgBF_4$ | THF | 5 | 98 | 90.0 (*S*) | 119 |

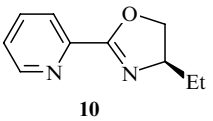



**8**

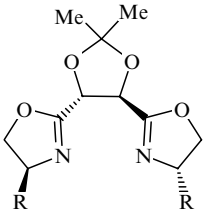



**9**

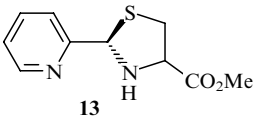
In order to achieve maximum enantioselectivity of hydrosilylation, bi-, tri- or tetradentate ligands should be taken in 2–13-fold excess with respect to the metal. This is sufficient to provide the substitution of at least four coordination vacancies in a catalytic complex. But even in this case achiral ligands should sometimes be added. The necessary ratios of the chiral ligands **10**–**16** to rhodium in catalysts for acetophenone hydrosilylation are shown in Table 4.



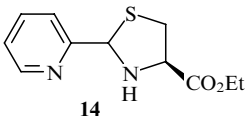

**10**



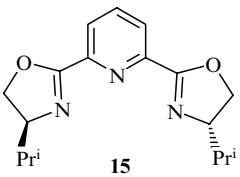

**11**: R = Pr$^i$
**12**: R = Bu$^t$



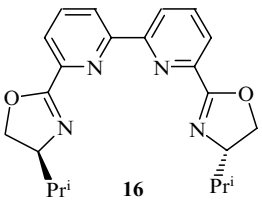

**13**




**14**




**15**




**16**

Thus, the maximum enantioselectivity will be provided by catalysts which ensure the minimum degree of freedom in the coordination of substrates in the intermediate complexes.

The dependence of enantioselectivity on the ligand structures of catalytic complexes is well studied and is not considered in this review. Until very recently, most of the studies devoted to asymmetric metal complex catalysis were aimed at obtaining maximum enantiomeric excesses of reaction products by simple search for all possible variants of ligand structures. A great body of evidence has been accumulated in this field, the effect of such structural parameter of a complex as symmetry deserves special mentioning.

Apparently, it is the difference in the symmetries of structurally related complexes, *viz*., {Rh[(*S,S*)-chiraphos](nbd)}$ClO_4$ (**I**) and {Rh[(*R*)-prophos](nbd)}$ClO_4$ (**II**), that can explain different enantioselectivities of hydrogenation in the presence of these catalysts (Table 5).

**Table 5**. The enantiomeric excess of the product in asymmetric hydrogenation of enamides on complexes (**I**) and (**II**).[33, 120, 121]

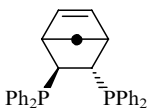
| Substrate (S) | **I** (S : Rh = 100) | | **II** (S : Rh = 250) | |
|---|---|---|---|---|
| | THF | EtOH | THF | EtOH |
| AcΔPhe | 74 (*R*) | 89 (*R*) | 91 (*S*) | 90 (*S*) |
| AcΔTyr | 80 (*R*) | 88 (*R*) | 92 (*S*) | 89 (*S*) |
| AcΔDOPA | 80 (*R*) | 83 (*R*) | 89 (*S*) | 87 (*S*) |
| AcΔLeu | 100 (*R*) | 93 (*R*) | 87 (*S*) | 87 (*S*) |
| BzΔPhe | 99 (*R*) | 95 (*R*) | 93 (*S*) | 91 (*S*) |
| BzΔLeu | 87 (*R*) | 72 (*R*) | 87 (*S*) | 87 (*S*) |

**Note**. Hereinafter, the following designations were used: AcΔPhe is (*Z*)-α-acetylaminocinnamic acid; BzΔPhe is (*Z*)-α-benzoylaminocinnamic acid; AcΔTyr is *N*-acetyldehydrotyrosine; AcΔDOPA is 2-*N*-acetyl-β-(4-hydroxy-3-methoxyphenyl)-α-dehydroalanine; AcΔLeu is *N*-acetyldehydroleucine; BzΔLeu is *N*-benzoyldehydroleucine.

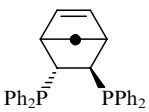
As can be seen from the table, the enantioselectivities achieved with the asymmetric complex **II** are less prone to variation than with the $C_2$-symmetrical chiral complex **I**. The *ee* value in the reactions catalysed by the former is virtually independent of the solvent or the nature of the substituent in the substrate.

## III. Catalyst – product configurational relationships in reactions on $C_2$-symmetrical chiral metal complexes

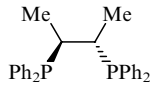
A search for relationships between configurations of catalytic complexes and products of asymmetric reactions is best carried out for complexes with ligands of the same type. Chiral bis(diphenylphosphine) ligands which form $C_2$-symmetrical complexes or $C_2$-symmetrical chelate rings (without substituents) meet these requirements.



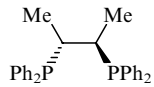

(*S,S*)-norphos



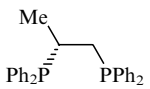

(*R,R*)-norphos



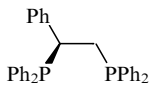

(*S,S*)-chiraphos



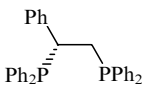

(*R,R*)-chiraphos



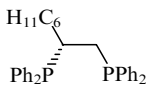

(*R*)-prophos



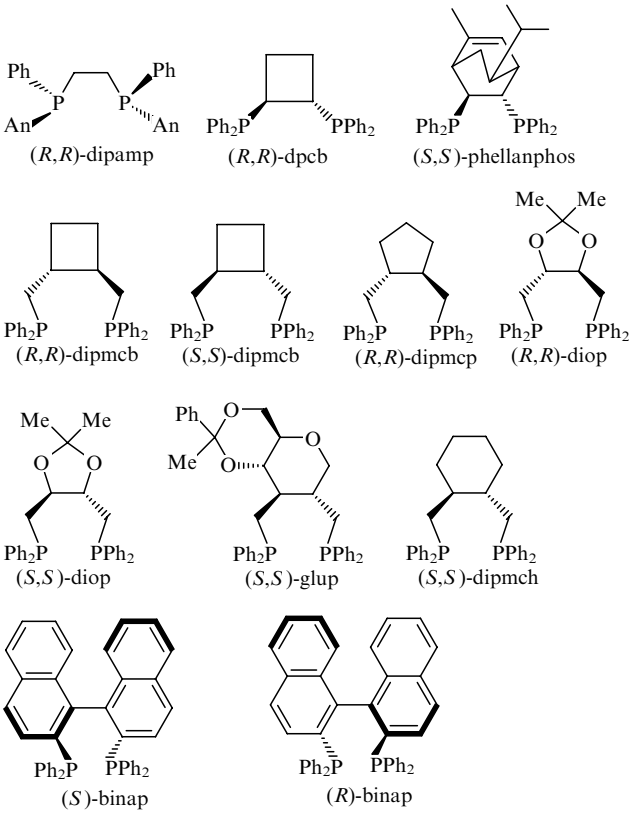

(*S*)-phenphos



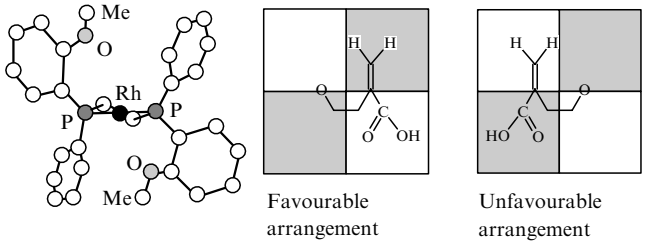

(*R*)-phenphos




(*R*)-cycphos

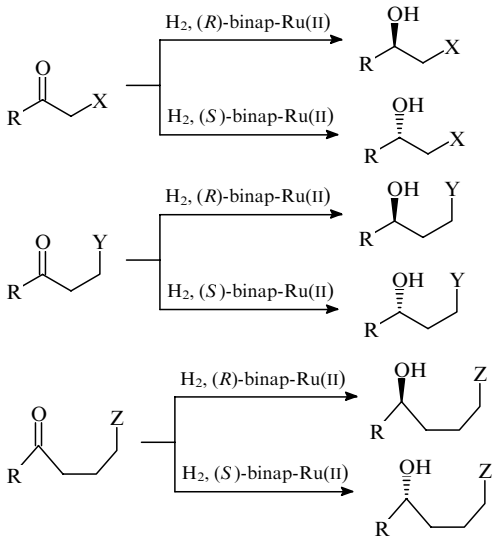



Regular relationships between the configurations of products and catalytic complexes in hydrogenation reactions on rhodium – phosphine catalysts have been established only for complexes with $C_2$-symmetrical chelate rings. Formal configurational relationships between catalysts and products are not always related to concrete reaction mechanism. A mnemonic dependence was proposed by Knowles in 1983.[122]




This dependence follows the 'quadrant rule' ‡ which relates the structure of the rhodium complex containing the dipamp ligand to the orientation (or coordination) of the substrate in the intermediate complex. It is assumed that the substituents occupying the hatched quadrants (*i.e.*, those blocked by the phenyl groups edge facing the viewer; the metal atom is located in the centre of the coordinates), experience larger steric hindrances. Therefore, the bulky carboxy group occupies preferably the unhatched quadrant. It is in this orientation that the formation of a particular enantiomer is experimentally observed. These graphical representations were used to describe the enantioselective behaviour of binap [14] and duphos [bis(phospholano)benzene] [124] complexes in asymmetric hydrogenation reactions.

The use of such graphical representations implies that the asymmetric induction step coincides with the coordination of the substrate in the intermediate complex. However, this conclusion demands further verification. The scheme proposed for the description of catalyst – product configurational relationships in the hydrogenation of α-, β- and γ-substituted ketones on ruthenium complexes containing binap ligands is even more formal. The configuration of the product depends exclusively on the configuration of the complex, rather than on the position of the functional group in the ketone.[14]

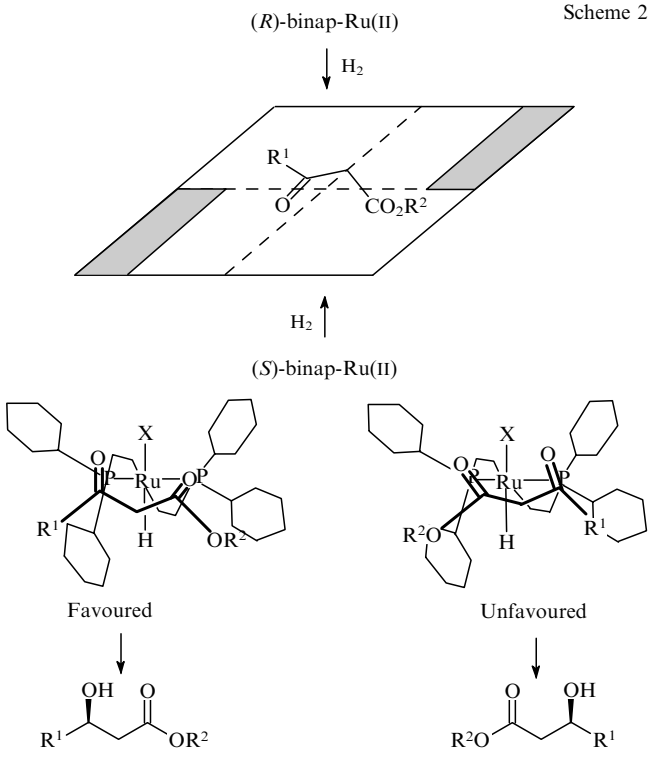



where X, Y, Z are N, O or Hal.

This has led to the development of a formal scheme for the formation of an intermediate complex using hydrogenation of a β-oxo ester as an example (Scheme 2).

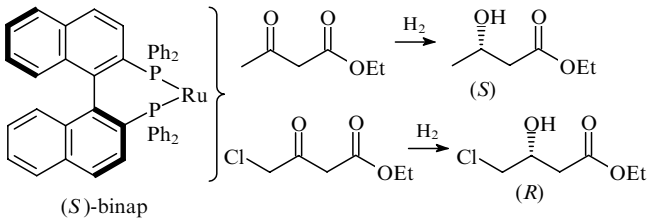
A similar scheme of configurational relationships has been proposed for hydrogenation of substituted β-oxo esters.[125] The configuration of the product does not depend on the nature of the substituent at the carbonyl group, whereas the change in the order of priority changes the configuration symbol.

Scheme 2

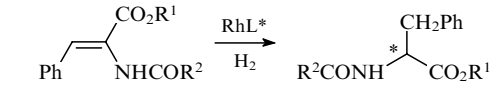


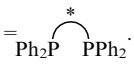

X = Hal.

‡ For the first time, this structural approach in the form of the 'octant rule' has been used to describe the chiral environment of carbonyl groups in steroids.[123]



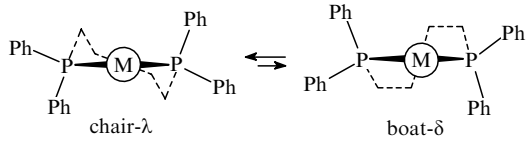

A large body of evidence has been gained concerning the application of rhodium complexes with these ligands as catalysts in hydrogenation of the same kind of substrates, *viz*., α-acetamidocinnamic acid derivatives.




L* = 

Earlier, it was suggested that enantioselective effects of such complexes are related to chiral arrangements of the phosphine phenyl groups.[120] We suppose that the arrangement of phenyl groups forming the chiral environment of the metal atoms can be related to the sign of helicity or the conformation of the chelate complex (Scheme 3) (view from the side of the metal atom; the chelate complex without substituents is shown by a dotted line). The schematic representations of the helix turns are shown in the right part of the Scheme, where the *P*-helix moves off clockwise, while the *M*-helix moves off anti-clockwise.

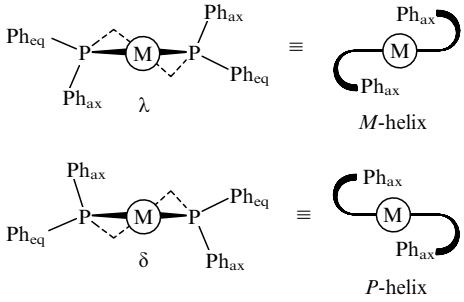
The analysis of molecular models has demonstrated that the conformations of λ- or δ-five-membered chelate complexes can be distorted to some extent, but their interconversions are either impossible (*e.g*., for chelates based on cyclic 1,2-diphosphines, such as norphos, phellanphos, dpcb, *etc*.) or result in the formation of chelate complexes with unfavourable axial positions of substituents [126–128] (*e.g*., prophos, chiraphos, cycphos, phenphos, *etc*.). In the case of seven-membered chelate complexes, a change in the sign of chirality in the orientation of the phenyl groups is also accompanied by the transition from the favourable chair-λ (or -δ) conformation to the unfavourable boat-δ (or -λ) conformation. However, in this case the advantage is less apparent.



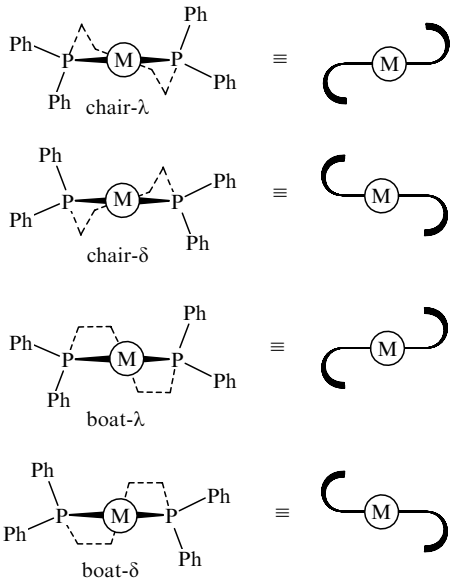

A correlation between the conformations of five-membered chelate rings of rhodium catalytic complexes with bis(diphenylphosphine) ligands and the configurations of the hydrogenation products of acetamidocinnamic acid and its derivatives was found in 1982 simultaneously and independently by two groups of authors (see Refs 129–131 and 132).§ The λ-conformation of the

§ There are many examples of simultaneous publications by different research groups of experimental results concerning asymmetric hydrogenation on rhodium phosphine catalysts in which the same catalyst (ligand) was used or, as in our case, the same regularity of the reaction was established (see, *e.g*., Refs 133 and 134; 135,136 and 137; 138 and 139, *etc*.).

Five-membered chelate complexes Scheme 3

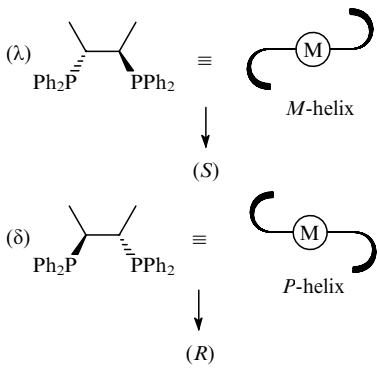



Seven-membered chelate complexes




chelate complex determines the formation of (*S*)-, whereas the δ-conformation determines the formation of (*R*)-products. Quite naturally, this effect is directly related to the chiral positions of the phosphine phenyl groups corresponding to these conformations rather than to the conformations themselves. The conformations and the conformational rigidities of chelate rings in catalytic complexes play a crucial role in stabilisation of chiral positions or helical chiralities of the phosphine phenyl groups.

In a simplified form, this regularity may be described by the formula: λ-(*S*), δ-(*R*).[140,141] Another representation of this rule appears to be more complete:




Some known ligands of rhodium complexes and the results of hydrogenation of α-acetylamidocinnamic acid derivatives in the presence of these complexes are shown in Table 6.

As can be seen, the results of hydrogenation in the presence of five-membered chelate rhodium complexes obey the λ-(*S*), δ-(*R*) rule [140,141] irrespective of whether the $C_2$ symmetry axis is inherent

**Table 6**. Arylphosphine ligands forming five-membered rhodium chelate complexes and hydrogenation of α-acetylaminocinnamic acid and its derivatives in the presence of these complexes.

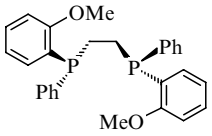
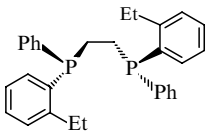
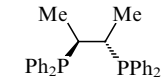
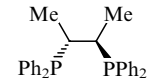
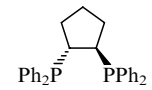
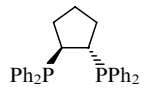
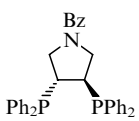
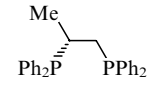
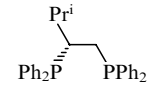
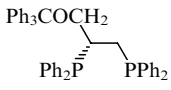
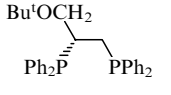
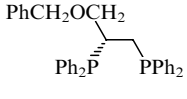
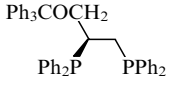
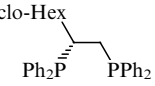
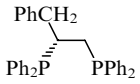
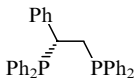
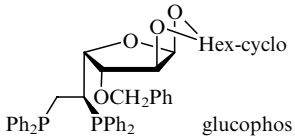
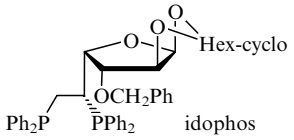
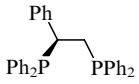
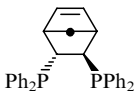
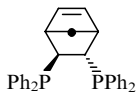
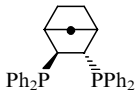
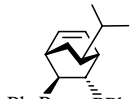
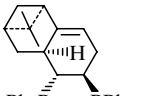
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes | | | | | | | | |
|  (*R*,*R*)-(−)-dipamp | λ (*M*) | AcΔAla | 90 (*S*) | C | M | 50 | 3 | 142 |
| | | AcΔPhe | 94 (*S*) | C | M or E | 50 | 3 | 64,[a] 143 |
|  | δ (*P*) | AcΔAla | 93 (*R*) | C | E | 50 | 3 | 144 [a] |
| | | AcΔPhe | 90 (*R*) | C | $Pr^i$ | 50 | 3 | 144 [a] |
|  (*S*,*S*)-(−)-chiraphos | δ (*P*) | AcΔAla | 91 (*R*) | C | E | 20 | 1 | 33 |
| | | AcΔPhe | 89 (*R*) | C | E | 20 | 1 | 33 |
|  (*R*,*R*)-(+)-chiraphos | λ (*M*) | AcΔAla | 91 (*S*) | C | E | 20 | 1–4 | 145 |
| | | AcΔPhe | 88 (*S*) | C | E | 20 | 1–4 | 145 |
| | | BzΔPhe | 94 (*S*) | C | E | 20 | 1–4 | 145 |
|  (*R*,*R*)-(+)-dpcp | λ (*M*) | AcΔPhe | 91 (*S*) | N | M – B | 30 | 1 | 125 |
|  (*S*,*S*)-(−)-dpcp | δ (*P*) | AcΔPhe | 90 (*R*) | N | M – B | 30 | 1 | 125 |
| | | BzΔPhe | 98 – 100 | N | M – B | 30 | 1 | 146 |
| | | BzΔPheOMe | 98 – 100 | N | M – B | 30 | 1 | 146 |
|  | λ (*M*) | AcΔPhe | 99 (*S*) | C | M | 20 | 40 | 36 |
| Ligands forming chiral $C_2$-symmetrical complexes (without substituents in the chelate rings) | | | | | | | | |
|  (*R*)-(+)-prophos | λ (*M*) | AcΔPhe | 90 (*S*) | C | E | 25 | 1 | 120 |
| | | BzΔPhe | 91 (*S*) | C | E | 25 | 1 | 120 |
| | | AcΔPhe | 83 (*S*) | N | M | 20 | 1 | 147 |
| | | BzΔPhe | 88 (*S*) | N | M | 20 | 1 | 147 |
|  (*R*)-(+)-valphos | λ (*M*) | BzΔPhe | 95 (*S*) | N | E | 20 | 1 | 148 |
| | | AcΔAla | 88.6 (*S*) | N | E | 20 | 1 | 148 |
|  | λ (*M*) | AcΔPhe | 85 (*S*) | C | E | 20 | 1 | 149 |
| | | AcΔAla | 78 (*S*) | C | E | 20 | 1 | 149 |
|  | λ (*M*) | AcΔPhe | 86 (*S*) | C | E | 20 | 1 | 150 |
| | | AcΔAla | 92 (*S*) | C | E | 20 | 1 | 150 |
|  | λ (*M*) | AcΔPhe | 87 (*S*) | C | E | 20 | 1 | 150 |
| | | AcΔAla | 91 (*S*) | C | E | 20 | 1 | 150 |
| | | AcΔPhe | 86 (*S*) | C | E | 20 | 1 | 149 |
| | | AcΔAla | 75 (*S*) | C | E | 20 | 1 | 149 |
|  | δ (*P*) | AcΔAla | 78 (*R*) | C | E | 20 | 1 | 149 |

**Table 6** (continued).

| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes (without substituents in the chelate rings) | | | | | | | | |
| cyclo-Hex  (*R*)-(+)-cycphos | λ (*M*) | AcΔPhe | 84 (*S*) | N | M | 20 | 1 | 147 |
| | | AcΔAla | 93 (*S*) | N | M | 20 | 1 | 147 |
| | | BzΔPhe | 90 (*S*) | N | M | 20 | 1 | 147 |
|  (*R*)-(+)-phephos | λ (*M*) | AcΔPhe | 99 (*S*) | C | E – B (2 : 1) | 20 | 20 | 148 |
| | | AcΔAla | 84.5 (*S*) | C | E – B (2 : 1) | 20 | 20 | 148 |
|  (*R*)-(–)-phephos | λ (*M*) | AcΔPhe | 79 (*S*) | N | M | 20 | 1 | 147 |
| | | AcΔPheOMe | 88 (*S*) | N | M | 20 | 1 | 147 |
| | | AcΔAla | 82 (*S*) | N | M | 20 | 1 | 147 |
| | | BzΔPhe | 84 (*S*) | N | M | 20 | 1 | 147 |
|  glucophos | λ (*M*) | AcΔPhe | 54 (*S*) | C | T | 20 | 1 | 151 |
| | | AcΔPheOMe | 41 (*S*) | C | T | 20 | 1 | 151 |
|  idophos | δ (*P*) | AcΔPhe | 56 (*R*) | C | T | 20 | 1 | 151 |
| | | AcΔPheOMe | 27 (*R*) | C | T | 20 | 1 | 151 |
|  (*S*)-(+)-phenphos | δ (*P*) | AcΔPhe | 78 (*R*) | C | T | 30 | 1 | 152 |
| | | AcΔPhe | 82 (*R*) | C | T | 30 | 1 | 152 |
| | | AcΔPheOMe | 8 (*R*) | C | T | 30 | 1 | 152 |
| | | BzΔPhe | 84 (*R*) | C | T | 30 | 1 | 152 |
| | | BzΔPhe | 76 (*R*) | C | T | 30 | 1 | 152 |
| | | AcΔPheOMe | 76 (*R*) | C | T | 30 | 1 | 152 |
|  (*R*,*R*)-(–)-norphos | λ (*M*) | AcΔPhe | 95 (*S*) | C | E | 20 | 1 | 153 [a] |
| | | AcΔAla | 90 (*S*) | C | E | 20 | 1 | 153 [a] |
|  (*S*,*S*)-(+)-norphos | δ (*P*) | AcΔPhe | 97 (*R*) | C | M | 20 | 1 | 153 |
|  (+)-renophos | δ (*P*) | AcΔPhe | 95 (*R*) | C | M | 20 | 1 | 154 |
| | | AcΔAla | 95 (*R*) | C | M | 20 | 1 | 154 |
|  (*S*,*S*)-phellanphos | δ (*P*) | AcΔPhe | 95 (*R*) | C | E | 25 | 1 | 155, 156 |
|  (*R*,*R*)-nopaphos | λ (*M*) | AcΔPhe | 80 (*S*) | C | E | 25 | 15 | 155 |
| | | AcΔAla | 81 (*S*) | C | E | 25 | 15 | 155 |

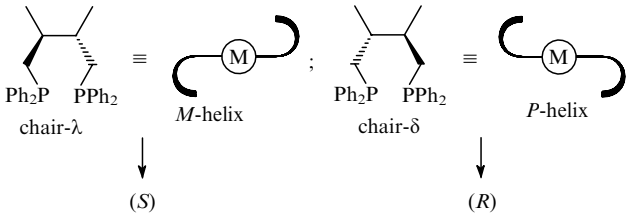
**Note**. Hereinafter, the following designations are used. For the substrate: AcΔPheOMe is (*Z*)-α-acetylaminocinnamic acid methyl ester; AcΔAla is α-acetylaminoacrylic acid; for the type of the catalytic complex: N is neutral including that formed *in situ*; C is cationic; for the solvent: M is methanol; E is ethanol; B is benzene; T is tetrahydrofuran.

[a] Data from X-ray diffraction analysis.

in the whole complex or in its chelate ring without substituents. The implementation of this rule is not influenced by the nature of substituents and experimental conditions. The situation is more complicated in the case of seven-membered ¶ chelate rhodium complexes in which the conformational transitions chair-λ – boat-δ and chair-δ – boat-λ are possible (other intermediate conformations have also been described [158]). Such transitions change the helicity sign of the phosphine phenyl groups, as a result of which the configuration of the product also changes. Unfortunately, X-ray diffraction analysis does not provide any unambiguous information about the conformations of the corresponding molecules in solution and especially in the intermediate catalytic complex, since the factors involved in crystal formation are stronger than those inducing conformational changes. Indeed, the conformations acquired by the diop ligand in Ir[(*S*,*S*)-(+)-diop](cod)Cl [159] and [(*R*,*R*)(−)-diop]$NiCl_2$ [160] crystals differ from the more favourable ideal conformations chair-λ and chair-δ. In the case of [(*R*,*R*)(−)-diop]$NiCl_2$, the distortions are so great that the position of the phenyl groups relative to the metal becomes close to symmetrical. If such conformations were maintained in solution, this would contradict the Curie – Pasteur principle ('there is no asymmetry without asymmetry') and would be in conflict with the very logic of asymmetric catalysis. The same complex, *viz*., [(*R*,*R*)-(−)-diop]$NiCl_2$, manifests high enantioselectivity in various cross-coupling reactions;[161] hence, its phenyl groups occupy chiral positions relative to the metal.

Therefore, the opposite statement, *viz*., if the λ-(*S*), δ-(*R*) rule is observed, the true conformations of the ligands in the complexes are close to the predictable chair conformation, seems to be more applicable to seven-membered chelate rhodium complexes.

Some examples of fulfilment of the chair-δ-(*R*), chair-λ-(*S*) rule are given in Table 7,[130, 140] *viz*.:




It is easy to ascertain that in the case of both seven-membered chelate complexes with second-order symmetry axes and complexes where only chelate rings without substituents possess $C_2$ symmetry the chair-λ-(*S*), chair-δ-(*R*) rule [or the boat-λ-(*S*),

¶ Six-membered chelate complexes have been studied relatively little, apparently due to their low efficiencies in asymmetric reactions resulting from conformational labilities of six-membered compounds. However, one such complex, *viz*., Rh(*S*,*S*)-skewphos [skewphos is 2,4-bis(diphenylphosphino)pentane], manifests high enantioselectivity [AcΔPhe, 93% (R)].[157]

**Table 7**. Arylphosphine ligands forming seven-membered rhodium complexes for which the chair-λ-(*S*), chair-δ-(*R*) rule holds.

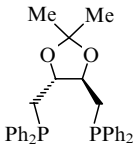
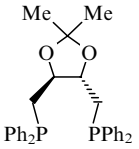
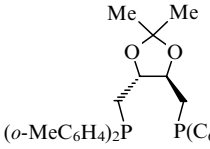
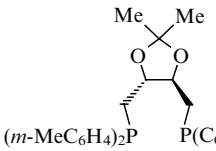
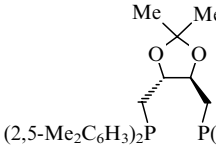
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 82 (*R*) | N | E – B (2 : 1) | 20 | 1.1 | 65, 66 |
| | | *Ac*ΔAla | 73 (*R*) | N | E – B (2 : 1) | 20 | 1.1 | 65, 66, 159 [a] |
| $Ph_2P$ $PPh_2$ | | | | | | | | |
| (*R*,*R*)-(−)-diop | | | | | | | | |
|  | chair-λ (*M*) | AcΔPhe | 81 (*S*) | N | E – B (2 : 1) | 20 | 1.0 | 162, 163 |
| $Ph_2P$ $PPh_2$ | | | | | | | | |
| (*S*,*S*)-(+)-diop | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 27 (*R*) | N | E – B (2 : 1) | 20 | 1.0 | 164 |
| $(o\text{-}MeC_6H_4)_2P$ $P(C_6H_4Me\text{-}o)_2$ | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 87 (*R*) | N | E – B (2 : 1) | 20 | 1.1 | 164 |
| $(m\text{-}MeC_6H_4)_2P$ $P(C_6H_4Me\text{-}m)_2$ | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 44 (*R*) | N | E – B (2 : 1) | 20 | 1.1 | 164 |
| $(2,5\text{-}Me_2C_6H_3)_2P$ $P(C_6H_3Me_2\text{-}2,5)_2$ | | | | | | | | |

**Table 7** (continued).

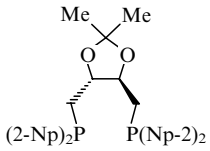
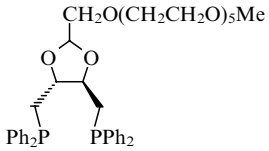
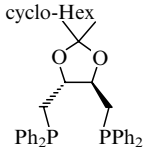
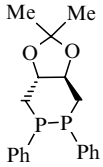
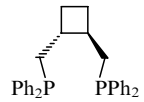
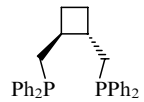
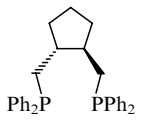
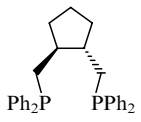
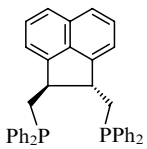
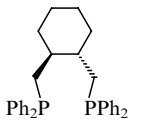
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes | | | | | | | | |
|  $(2\text{-Np})_2P$ $P(Np\text{-}2)_2$ | chair-δ (*P*) | AcΔPhe | 83 (*R*) | N | E–B (2 : 1) | 20 | 1.1 | 164 |
|  $Ph_2P$ $PPh_2$ | chair-δ (*P*) | AcΔPhe | 64 (*R*) | C | E | 25 | 1.1 | 165 |
| cyclo-Hex  $Ph_2P$ $PPh_2$ | chair-δ (*P*) | AcΔPhe | 77.5 (*R*) | N | E–B (1 : 2) | 20 | 1.1 | 164 |
|  | chair-δ (*P*) | AcΔPhe | 71 (*R*) | N | E–B (1 : 2) | 20 | 1.1 | 166 |
|  $Ph_2P$ $PPh_2$ (*R*,*R*)-(−)-dipmcb | chair-δ (*P*) | AcΔPhe<br>AcΔAla<br>AcΔPhe | 86 (*R*)<br>72 (*R*)<br>91 (*R*) | N<br>N<br>N | E – B (2 : 3)<br>E – B (2 : 3)<br>E – B (1 : 2) | 25<br>25<br>25 | 1.0<br>1.0<br>1.1 | 167<br>167<br>168 |
|  $Ph_2P$ $PPh_2$ (*S*,*S*)-(+)-dipmcb | chair-λ (*M*) | AcΔPhe | 87 (*S*) | C | E – B (1 : 1) | 20 | 1.0 | 169 |
|  $Ph_2P$ $PPh_2$ (*R*,*R*)-(−)-dipmcp | chair-δ (*P*) | AcΔPhe<br>AcΔAla | 63 (*R*)<br>72 (*R*) | N<br>N | E – B (1 : 2.3)<br>E – B (1 : 2.3) | 25<br>25 | 1.0<br>1.0 | 167<br>167 |
|  $Ph_2P$ $PPh_2$ (*S*,*S*)-(+)-dipmcp | chair-λ (*M*) | AcΔPhe<br>AcΔAla | 73 (*S*)<br>68 (*S*) | N<br>N | E – B (2 : 1)<br>E – B (2 : 1) | 25<br>25 | 1.0<br>1.0 | 168<br>168 |
|  $Ph_2P$ $PPh_2$ | chair-λ (*M*) | AcΔPhe<br>AcΔAla | 81 (*S*)<br>52 (*S*) | N<br>N | E – B (2 : 1)<br>E – B (2 : 1) | 25<br>25 | 1.0<br>1.0 | 168<br>168 |
|  $Ph_2P$ $PPh_2$ | chair-λ (*M*) | AcΔPhe | 35 (*S*) | N | E – B (1 : 2.3) | 25 | 1.0 | 170 |

**Table 7** (continued).

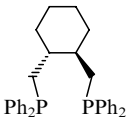
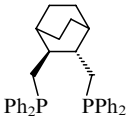
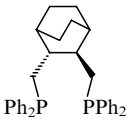
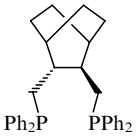
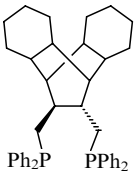
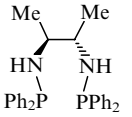
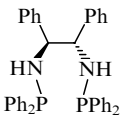
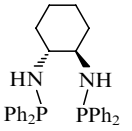
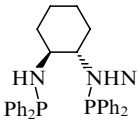
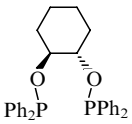
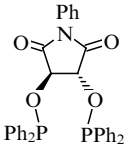
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | $T$ /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 36 (*R*) | N | E – B (2 : 1) | 25 | 1.0 | 168 |
| | | AcΔAla | 39 (*R*) | N | E – B (2 : 1) | 25 | 1.0 | 168 |
|  | chair-λ (*M*) | AcΔPhe | 81 (*S*) | N | E – B (2 : 1) | 25 | 1.0 | 168 |
|  | chair-δ (*P*) | AcΔAla | 74 (*R*) | N | E – B (2 : 1) | – | 1.0 | 169 |
|  | chair-δ (*P*) | AcΔPhe | 79.5 (*R*) | N | E – B (2 : 1) | 20 | 1.1 | 171 |
|  | chair-λ (*M*) | AcΔPhe | 35 (*S*) | N | E | 25 | 1.0 | 171 |
|  | chair-λ (*M*) | AcΔPhe | 45 (*S*) | C | E | 20 | 1.0 | 137, 172 |
|  | chair-λ (*M*) | AcΔPhe | 93.8 (*S*) | C | E | 25 | 1.0 | 173 |
|  | chair-δ (*P*) | AcΔPhe | 49 (*R*) | C | E | 20 | 1.0 | 136 |
| | | AcΔPhe | 41 (*R*) | C | E | 20 | 1.0 | 137 |
| | | AcΔPhe | 47 (*R*) | C | E | 20 | 1.0 | 135 |
|  | chair-λ (*M*) | AcΔPhe | 41 (*S*) | C | E | 20 | 8.0 | 137 |
|  | chair-λ (*M*) | AcΔPhe | 68 (*S*) | N | E | 20 | 50 | 174 |
| | | AcΔAla | 79 (*S*) | N | E | 20 | 50 | 174 |
|  | chair-λ (*M*) | AcΔPhe | 36 (*S*) | N | M | 20 | 50 | 175 |

**Table 7** (continued).

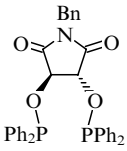
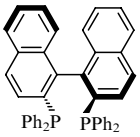
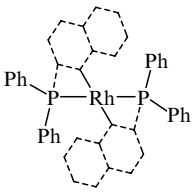
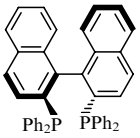
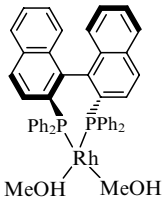
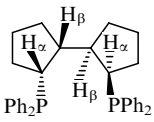
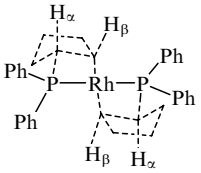
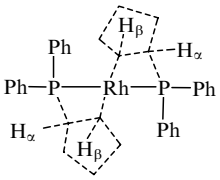
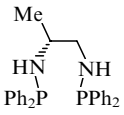
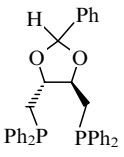
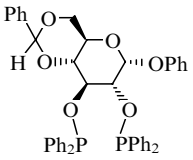
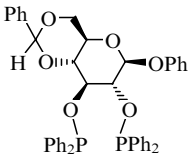
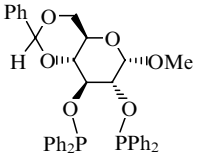
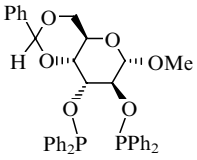
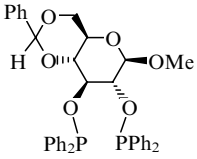
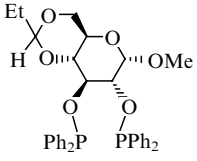
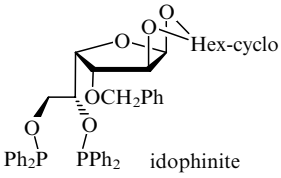
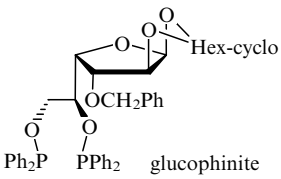
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | $T$ /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes | | | | | | | | |
|  | chair-λ (*M*) | AcΔPhe | 16 (*S*) | N | M | 20 | 1.0 | 176 |
|  (*R*)-(+)-binap |  boat-λ (*M*) | BzΔPhe | 100 (*S*) | C | E | 20 | 3–4 | 175 |
|  (*S*)-(−)-binap | boat-δ (*P*) | AcΔPhe | 84 (*R*) | C | E | 20 | 3–4 | 178 |
| | | AcΔAla | 67 (*R*) | C | E | 20 | 3–4 | 177 |
| | | AcΔPhe | 84 (*R*) | C | E | 20 | 3–4 | 177 |
| | | BzΔPhe | 96 (*R*) | C | E | 20 | 3–4 | 177 |
|  | boat-δ (*P*) | BzΔPhe | 98 (*R*) | C | E | 20 | 1.0 | 179 |
|  (*R*,*R*)-bicp |  boat-λ, favourable conformation (*M*) | AcΔPhe | 89 (*S*) | C | T | 20 | 1.0 | 180 |
| | | BzΔPhe | 99 (*S*) | C | T | 20 | 1.0 | 180 |
| |  boat-δ, unfavourable conformation (see [b]) | | | | | | | |
| Ligands forming chiral $C_2$-symmetrical complexes (without substituents in the chelate rings) | | | | | | | | |
|  | chair-δ (*P*) | AcΔPhe | 28 (*R*) | C | E | 20 | 1.0 | 136 |
|  | chair-δ (*P*) | AcΔPhe | 79.5 (*R*) | N | B–E | 20 | 1.0 | 163 |

**Table 7** (continued).

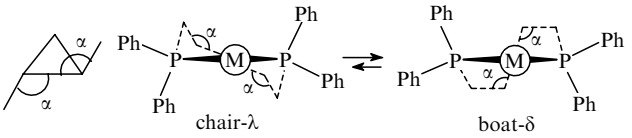
| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | $T$ /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| Ligands forming chiral $C_2$-symmetrical complexes (without substituents in the chelate rings) | | | | | | | | |
|  Ph-α-glup | chair-λ (*M*) | AcΔPhe | 54 (*S*) | C | M | 25 | 1.0 | 181 |
| | | AcΔPhe | 60.5 (*S*) | N | M | 25 | 1.0 | 181 |
|  Ph-β-glup | chair-λ (*M*) | AcΔPhe | 96 (*S*) | C | M | 25 | 1.0 | 181 |
| | | AcΔPhe | 87 (*S*) | N | M | 25 | 1.0 | 181 |
|  | chair-λ (*M*) | AcΔPhe | 61 (*S*) | C | E | 25 | 1.0 | 182 |
| | | AcΔPhe | 73 (*S*) | C | M | 25 | 1.0 | 181 |
| | | AcΔPhe | 75 (*S*) | C | E | 0 | 1.0 | 183 |
|  | chair-δ (*P*) | AcΔPhe | 70 (*R*) | C | E | 0 | 1.0 | 182 |
|  | chair-λ (*M*) | AcΔPhe | 91 (*S*) | N | E | 30 | 1.0 | 184 |
| | | AcΔAla | 91 (*S*) | N | E | 30 | 1.0 | 184 |
|  | chair-λ (*M*) | AcΔPhe | 80 (*S*) | N | M | −25 | 50 | 185 |
|  idophinite | chair-λ (*M*) | AcΔPhe | 54 (*S*) | C | T | 20 | 1.0 | 151 |
|  glucophinite | chair-δ (*P*) | AcΔPhe | 40 (*R*) | C | T | 25 | 1.0 | 151 |

[a] Data from X-ray diffraction analysis. [b] The positions of the phosphine phenyl groups characteristic of the boat-δ conformation (in this case, boat-λ and boat-δ cannot be mutually interconverted without the bond cleavage) is associated with considerable steric hindrances.

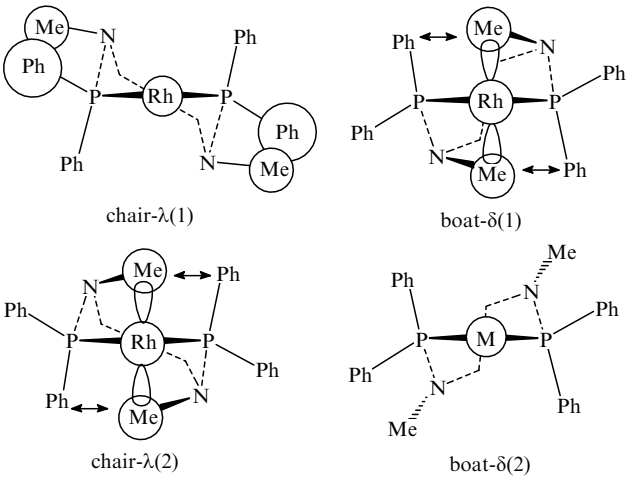
boat-δ-(*R*) for the atropoisomeric binap ligands] is obeyed.[140, 141] Thus, the intermediate catalytic complexes have predominantly the chair-λ and chair-δ conformations in solution. In the chelate complexes, the atropoisomeric ligands binap exist in the only possible boat-λ, boat-δ conformation.

The ligands which form complexes with seven-membered chelate rings, but do not formally follow the chair-λ-(*S*), chair-δ-(*R*) rule are shown in Table 8.

Let us consider molecular models. In the ligands based on *trans*-disubstituted cyclopropane, the α-angles between the planes of the rings and the substituents are close to 123°.




The boat-δ conformation of the chelate ring based on this ligand is preferable to the chair-λ conformation, since the α-angles are closer to 123°, and the λ-(*S*), δ-(*R*) rule is not violated in this case. The structures of the following four ligands, *viz*.:

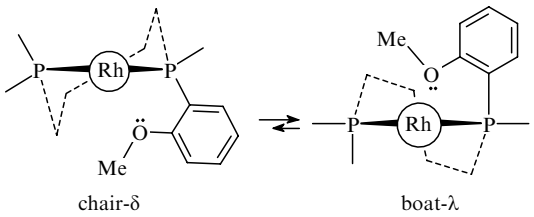



are of the same kind. In our opinion,[140] these ligands can theoretically have four conformers, *viz*., chair-λ(1), boat-δ(1), chair-λ(2) and boat-δ(2), owing to the well-known ability of pyramidal nitrogen atoms to invert.

Of the four possible conformers of the ligand (*S*,*S*)-Mediop(N), the boat-δ(2) conformer is the most sterically favourable. The chair-λ(1) conformation is characterised by spatial proximity of the Ph and Me groups, whereas in the chair-λ(2) and boat-δ(1) conformations non-bonding interactions of the methyl groups with the apical orbitals of rhodium atoms in planar-square complexes are observed.

Another disadvantage of the chair-λ(2) and boat-δ(1) conformations is the interaction of Me and Ph groups (they are marked by bidirectional arrows). We have carried out a series of non-empirical quantum-chemical calculations for the interactions of isolated fragments of these structures.[140] It was found that the boat-δ(2) conformation (or its mirror-opposite boat-λ(2) conformation) is more favourable for NMe-ligands taking into account the interaction between the Me and Ph groups. In the presence of complexes with these conformations of ligands, the reaction should proceed according to the δ-(*R*) [or λ-(*S*)] rule as is actually the case in experiment.

Formally, the *o*-$MeOC_6H_4$-phosphine diop analogue does not conform to this rule, which can also be explained by stabilisation of the 'unfavourable' conformation. The conformational equilibrium in complexes containing this ligand seems to be shifted towards the boat conformation due to the interactions of the electron pairs of the methoxy group oxygens with the apical orbitals of the rhodium atoms.




The existence of similar coordination bonds between the *o*-$MeOC_6H_4$ groups and rhodium atoms in complexes with dipamp ligands has been confirmed by X-ray diffraction analysis.[64] The boat-λ conformation is geometrically more fit for the formation of such bonds than the chair-δ conformation. It can therefore be assumed that the λ-(*S*), δ-(*R*) rule is also applicable to the rhodium complex with this ligand. The catalytic system containing the phosphinite ligand $[Rh(nbd)_2]ClO_4/CuCl$ (see Table 8) cannot be considered as an exception to this rule, since it is possible that it is a bimetallic cluster or a complex where the necessary stereochemistry that manifests the catalytic activity under the reaction conditions is violated.

Examination of molecular models of the other two ligands leads to a conclusion that only the boat-λ conformation in the strained bridged structure of 9,10-dihydro-9,10-ethanoanthracene enables the formation of seven-membered chelate complexes with a metal, *viz*., in this case, the λ-(*S*) rule is fulfilled. In the case of 1,4-bisdiphenylphosphino-(2*S*,3*S*)-diphenylbutane, the boat-δ conformation of the chelate complexes, in which both phenyl rings occupy equatorial positions and thus give an additional gain in energy, is more favourable.[127] Therefore, the λ-(S), δ-(R) rule holds true for complexes containing this ligand.

Five-membered chelate rhodium complexes based on alkylphosphine ligands with second-order symmetry axes (Table 9), conform also to this rule,† however, in its basic 'helical' form.

It is impossible to isolate the helical component of the rhodium complex with the (***S***,*S*)-Pr$^i$-cnrphos ligand without recourse to X-ray diffraction analysis. However, the *P*-helical structure can be predicted from the configuration of the hydrogenation product.

The data presented in Table 9 suggest that the product configuration is determined by the helical component present in all complexes with alkylphosphine ligands.

Sometimes, the enantioselectivity of reactions in the presence of bisdiphenylphosphine complexes is associated with chirality, which is determined by a definite inclination of the planes of the phenyl groups relative to one another.[194] However, the values and the signs of enantioselectivity in complexes with alkylphosphine ligands,[124, 191–193] cyclodiop [166] and Cydiop,[195] which are devoid of such chirality, do not differ from the corresponding parameters of complexes with bisdiphenylphosphine ligands. Therefore, the helical component makes the main contribution.

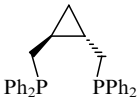
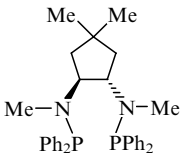
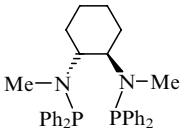
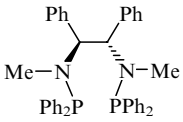
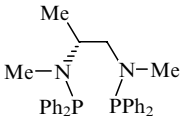
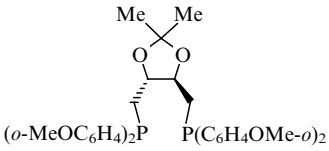
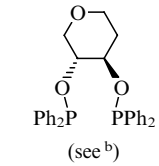
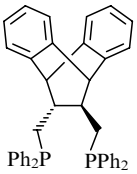
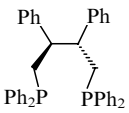
An experimental proof of the effect of the helical component on enantioselectivity follows from the enantioselective properties of the complex the achiral ligands in which form helices around the metal ions.[196]

The ligands forming eight- and nine-membered chelate complexes with $C_2$ symmetry axes (with the exception of atropoisomeric non-substituted aminophosphines [197–200]) are not very effective in the majority of asymmetric hydrogenation reactions. Enantioselectivity can be increased either through the use of bimetallic complexes or through a decrease in reaction temperature.

There is no reason to suppose that the above-considered rule concerning the conformation of five- or seven-membered bis(diphenylphosphine) chelate complexes with the $C_2$ symmetry axes is only applicable to hydrogenation reactions. Presumably, similar rules exist for other reactions, too. Indeed, the hydrosilylation of acetophenone by diphenylsilane in the presence of rhodium complexes proceeds in accordance with the λ-(*S*), δ-(*R*) rule (Table 10).

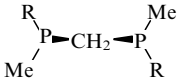
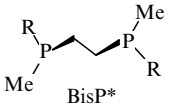
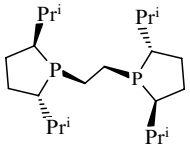
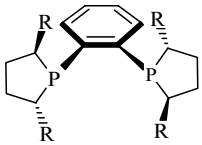
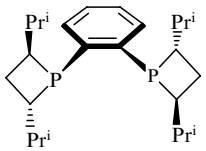
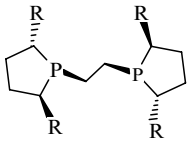
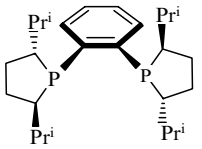
† In our opinion, the critical attitude [190] to the conformational expression of this rule, *viz*., λ-(*S*), δ-(*R*), is too formal.

**Table 8**. Arylphosphine rhodium complexes with seven-membered chelate rings which do not formally obey the chair-δ(*S*), chair-δ(*R*) rule.

| Ligand | Conformation [a] (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
|  | boat-δ<br>(*P*) | AcΔPhe<br>AcΔAla | 15 (*R*)<br>23 (*R*) | N<br>N | E – B (2 : 1)<br>E – B (2 : 1) | 25<br>25 | 1.0<br>1 | 167<br>167 |
| <br>(*S*,*S*)-Mediop(N) | boat-δ(2)<br>(*P*) | AcΔPhe | 30 (*R*) | C | E – B | 20 | 1 | 186 |
|  | boat-λ(2)<br>(*M*) | AcΔPhe<br>AcΔAla | 92 (*S*)<br>89 (*S*) | C<br>C | E<br>E | 25<br>20 | 1<br>1 | 187<br>136 |
|  | boat-δ(2)<br>(*P*) | AcΔPhe<br>AcΔAla | 68.4 (*R*)<br>86.3 (*R*) | C<br>C | E<br>E | 25<br>25 | 5<br>5 | 135, 173<br>135, 173 |
|  | boat-λ(2)<br>(*M*) | AcΔPhe | 70 (*S*) | C | E | 20 | 1 | 136 |
|  | boat-λ<br>(*M*) | AcΔPhe<br>AcΔPheOMe<br>AcΔAla | 31 (*S*)<br>71 (*S*)<br>8 (*S*) | C<br>C<br>C | M<br>M<br>M | 20<br>20<br>20 | 1<br>1<br>1 | 188<br>188<br>188 |
| <br>(see [b]) | – | AcΔPhe | 90 (*S*) | C | E – B | −15 | 1.48 | 189 |
|  | boat-λ<br>(*M*) | AcΔPhe | 50 (*S*) | N | E | 25 | 1 | 171 |
|  | boat-δ<br>(*P*) | AcΔPhe<br>AcΔAla | 54 (*R*)<br>61 (*R*) | C<br>C | E<br>E | 25<br>25 | 1<br>1 | 173<br>173 |

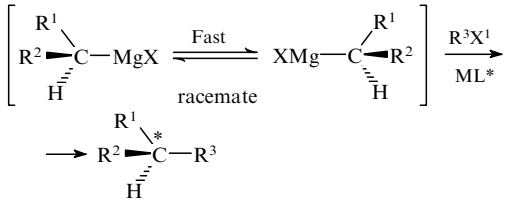
[a] The favourable conformation is indicated (see text). [b] The catalytic system $[Rh(nbd)_2]ClO_4$/CuCl was studied using this ligand.

**Table 9**. Alkylphosphine ligands forming five-membered chelate rhodium complexes and hydrogenation of α-acetylaminocinnamic acid and its derivatives in the presence of these complexes.

| Ligand | Conformation (helix) | Substrate | *ee* (%) | Type of the catalytic complex | Solvent | *T* /°C | $p_{H_2}$ /atm | Ref. |
|---|---|---|---|---|---|---|---|---|
| *P*-helix | | | | | | | | |
|  (*R*,*R*)-miniphos | $Bu^t$ | AcΔPhe | 97 (*R*) | C | M | 20 | 1 | 191 |
| | $Bu^t$ | AcΔAla | > 99.9 (*R*) | C | M | 20 | 1 | 191 |
| | cyclo-$C_6H_{11}$ | AcΔAla | 99.1 (*R*) | C | M | 20 | 1 | 191 |
| | $Pr^i$ | AcΔAla | 98 (*R*) | C | M | 20 | 1 | 191 |
| | Ph | AcΔAla | 26 (*R*) | C | M | 20 | 1 | 191 [a] |
|  BisP* | $Bu^t$ | AcΔPhe | 98.4 (*R*) | C | M | 20 | 2 | 192 |
| | $Et_3C$ | AcΔPheOMe | 94.7 (*R*) | C | M | 20 | 2 | 192 |
| | 1-Adamantyl | AcΔPheOMe | 99.9 (*R*) | C | M | 20 | 2 | 192 |
| | cyclo-$C_5H_9$ | AcΔPheOMe | 43.0 (*R*) | C | M | 20 | 2 | 192 |
| | cyclo-$C_6H_{11}$ | AcΔPheOMe | 47.1 (*R*) | C | M | 20 | 2 | 192 [a] |
|  (*R*,*R*)-$Pr^i$-bpe | – | AcΔPheOMe | 93 (*R*) | C | M | 20 | 2 | 124 |
| | – | AcΔAlaOMe | 96.4 (*R*) | C | M | 20 | 2 | 124 [a] |
|  (*S*,*S*)-R-duphos | Me | AcΔPheOMe | 98 (*R*) | C | M | 20 | 2 | 124 |
| | Me | AcΔAlaOMe | 99 (*R*) | C | M | 20 | 2 | 124 |
| | Et | AcΔPheOMe | 99 (*R*) | C | M | 20 | 2 | 124 |
| | Et | AcΔAlaOMe | 99.4 (*R*) | C | M | 20 | 2 | 124 |
| | $Pr^n$ | AcΔPheOMe | > 99 (*R*) | C | M | 20 | 2 | 124 |
| | $Pr^n$ | AcΔAlaOMe | 99.8 (*R*) | C | M | 20 | 2 | 124 |
|  (*S*,*S*)-$Pr^i$-cnrphos | – | AcΔPheOMe | 74 (*R*) | – | – | – | – | 193 |
| *M*-helix | | | | | | | | |
|  | Me | AcΔPheOMe | 85 (*S*) | C | M | 20 | 2 | 124 |
| | Me | AcΔAlaOMe | 91.4 (*S*) | C | M | 20 | 2 | 124 |
| | Et | AcΔPheOMe | 93 (*S*) | C | M | 20 | 2 | 124 |
| | Et | AcΔAlaOMe | 98.1 (*S*) | C | M | 20 | 2 | 124 |
| | $Pr^n$ | AcΔPheOMe | 92 (*S*) | C | M | 20 | 2 | 124 |
| | $Pr^n$ | AcΔAlaOMe | 97.7 (*S*) | C | M | 20 | 2 | 124 |
|  (*R*,*R*)-$Pr^i$-duphos | – | AcΔPheOMe | 87 (*S*) | C | M | 20 | 2 | 124 |
| | – | AcΔPheOMe | 95.4 (*S*) | C | M | 20 | 2 | 124 |

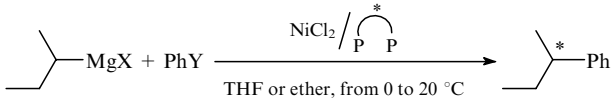
[a] Data from X-ray diffraction analysis.

The cross-coupling reaction has been most studied for secondary alkyl or arylalkyl Grignard reagents which react in the following way:[59]



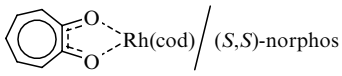
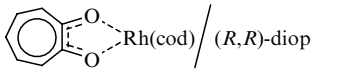
(1)

The cross-coupling of $Bu^s MgX$ with PhY in the presence of bis(diphenylphosphine) nickel complexes:



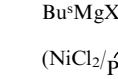
obeys the rule λ-(*R*), δ-(*S*) (Table 11).

**Table 10**. Hydrosilylation of acetophenone by diphenylsilane on chiral rhodium complexes.

| Catalytic system | Conformation of the complex | Ref. | Enantiomeric excess | |
|---|---|---|---|---|
| | | | *ee* (%) | Ref. |
| $[Rh(cod)Cl]_2$/(*S*,*S*)-norphos | δ | 153 | 15 (*R*) | 201 |
| $[Rh(cod)Cl]_2$/(*S*,*S*)-chiraphos | δ | 202, 203 | 3 (*R*) (see [a]) | 53 |
|  (*S*,*S*)-norphos | δ | 153 | 5.4 (*R*) | 204 |
| $[Rh(cod)Cl]_2$/(*S*,*S*)-diop | chair-λ | 159, 176 | 28 (*S*) | 52 |
| | | | 23 (*S*) | 53 |
| $[Rh(cod)Cl]_2$/(*R*,*R*)-diop | chair-δ | 159, 176 | 31 (*R*) | 205 |
| | | | 22.5 (*R*) | 206 |
| | | | 55 (*R*) (see [b]) | 51 |
| $[Rh(cod)Cl]_2$/(*S*,*S*)-glup | chair-λ | 159, 176, 200 | 47 (*S*) | 207 |
| $[Rh(cod)Cl]_2$/(*S*,*S*)-cyclo-Hex·diop | chair-δ | 159, 176 | 24 (*R*) | 208 |
|  (*R*,*R*)-diop | chair-δ | 159, 176 | 32.7 (*R*) | 204 |

[a] Hydrosilylation of propiophenone. [b] Hydrosilylation with α-$NpPhSiH_2$.

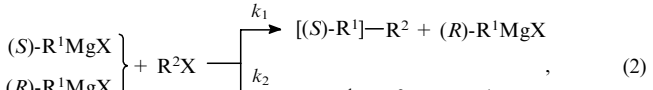
**Table 11**. The optical yields of asymmetric cross-coupling products of $Bu^sMgX$ with PhY in the presence of nickel complexes.

($NiCl_2$/).

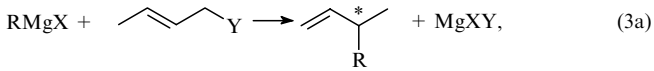
|  | Conformation of the complex | Ref. | Optical yield (%) | | |
|---|---|---|---|---|---|
| | | | X = Y = Cl | X = Y = Br | Ref. |
| (*R*,*R*)-dipamp | λ | 34 | 4.5 (*R*) | 4.2 (*R*) | 209 |
| (*R*)-prophos | λ | 210 | 14.4 (*R*) | 39.9 (*R*) | 209 |
| | λ | 210 | 21.0 (*S*) [a] | 44.0 (*R*) | 212 |
| (*R*)-cycphos | λ | 213 | 14.4 (*R*) | 45.8 (*R*) | 209 |
| (*R*)-phenphos | λ | 214 | 18.5 (*R*) | 50.0 (*R*) | 209 |
| (*S*,*S*)-chiraphos | δ | 213, 215 | 14.5 (*S*) | 43.1 (*S*) | 209 |
| (*R*,*R*)-norphos | λ | 216 | 26.7 (*R*) | 50.7 (*R*) | 209 |
| (*R*,*R*)-(−)-diop | chair-δ | 214, 217 | 10.9 (*R*) | – | 161 |
| | chair-δ | 214, 217 | – | 17.0 (*R*) [b] | 218 |

[a] Presumably, the (*S*) conformation is indicated erroneously, since more recent studies by the same authors [209, 211] suggest the formation of (*R*)-products in analogous experiments. [b] In this case, X = Br, Y = Cl.

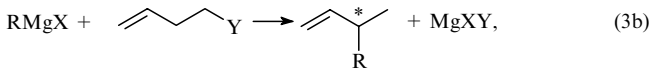
The following catalytic reactions also represent cross-coupling:



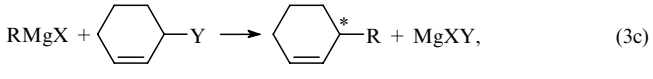
$$(S)\text{-}R^1MgX,\ (R)\text{-}R^1MgX + R^2X \xrightarrow{k_1} [(S)\text{-}R^1]\text{—}R^2 + (R)\text{-}R^1MgX \quad (2)$$
$$\xrightarrow{k_2} [(R)\text{-}R^1]\text{—}R^2 + (S)\text{-}R^1MgX$$



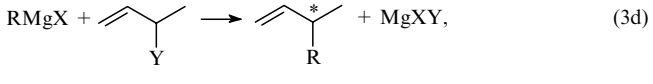
$$RMgX + \text{—}CH=CH\text{—}CH_2Y \longrightarrow \text{—}CH=CH\text{—}C^*HR + MgXY, \quad (3a)$$



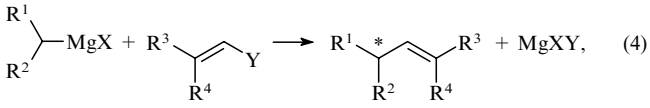
$$RMgX + CH_2=CH\text{—}CH_2Y \longrightarrow CH_2=CH\text{—}C^*HR + MgXY, \quad (3b)$$



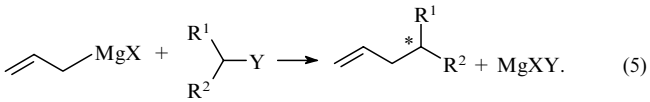
$$RMgX + \text{cyclohexenyl-}Y \longrightarrow \text{cyclohexenyl-}C^*HR + MgXY, \quad (3c)$$



$$RMgX + \text{—}CH=CH\text{—}CHY\text{—} \longrightarrow \text{—}CH=CH\text{—}C^*HR\text{—} + MgXY, \quad (3d)$$



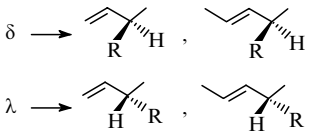
$$R^1R^2CHMgX + R^3CH=CHCH_2Y \longrightarrow R^1R^2C^*HCH=CHCH_2R^3 + MgXY, \quad (4)$$



$$CH_2=CHCH_2MgX + R^1R^2CHY \longrightarrow CH_2=CHC^*HR^1R^2 + MgXY. \quad (5)$$

The reaction of a vinyl halide with a non-racemisable Grignard reagent also belong to the type of reaction (2).[218–220] In this case, the resolution of the racemic Grignard reagent occurs due to different reactivities of the enantiomers of the racemate in the presence of chiral catalysts (kinetic resolution). This enantioselective reaction results in the enrichment of the non-consumed Grignard reagent with one of the enantiomers.

The results obtained in the study of reaction (3c) are given in Table 12. The data concerning reactions (3a), (3b) and (3d) (Table 13) illustrate the applicability of this rule:



δ → 

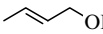
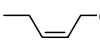
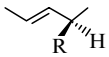
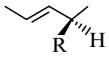
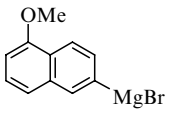
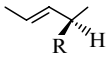
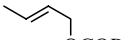
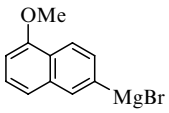
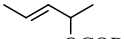
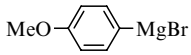
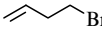
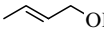
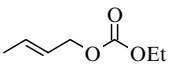
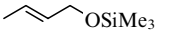
λ → 

**Table 12**. The optical yields of 2-ethylcyclohexane in asymmetric cross-coupling of EtMgBr with cyclohexene derivatives in the presence of bisdiphenylphosphine nickel complexes.

($NiCl_2$/).[211]

|  | Conformation of the complex | Substituent in cyclohexene | Optical yield (%) |
|---|---|---|---|
| (*R*)-phephos | λ | OH | 28.4 (*S*) |
| (*S*,*S*)-chiraphos | δ | OH | 49.5 (*R*) |
| (*R*)-phephos | λ | OPh | 26.5 (*S*) |
| (*S*,*S*)-chiraphos | δ | OPh | 51.2 (*R*) |
| (*R*)-prophos | λ | OPh | 29.7 (*S*) |
| (*R*)-cycphos | λ | OPh | 16.2 (*S*) |
| (*R*,*R*)-norphos | λ | OPh | 48.1 (*S*) |
| (*R*,*R*)-dipamp | λ | OPh | 11.2 (*R*) |

**Table 13**. Asymmetric cross-coupling of Grignard reagents ($R^1MgX$) with allylic alcohols, ethers and esters ($R^2Y$) on chiral nickel complexes at room temperature.

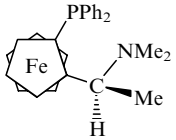
| $R^2Y$ | $R^1MgX$ | Complex | Conformation | Product | Optical yield (%) | Ref. |
|---|---|---|---|---|---|---|
|  | EtMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 22 (*S*) | 221 |
|  | PhMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 58 (*R*) | 221 |
|  | EtMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 17 (*S*) | 221 |
|  | PhMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 58 (*R*) | 221 |
|  | MeMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 15 (*R*) | 222 |
|  | MeMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 8.5 (*R*) | 222 |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 68 (*R*) | 223 |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 89 (*R*) | 223 |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 68 (*R*) | 223 |
|  | PhMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 6 (*R*) | 224 |
|  | PhMgBr | $NiBr_2$[(*R*,*R*)-dpcp] | λ |  | 41 (*S*) | 225 |
|  | PhMgBr | $NiBr_2$[(*R*,*R*)-dpcp] | λ |  | 53 (*S*) | 225 |
|  | PhMgBr | $NiBr_2$[(*R*,*R*)-dpcp] | λ |  | 52 (*S*) | 225 |
|  | PhMgBr | $NiBr_2$[(*R*,*R*)-dpcp] | λ |  | 67 (*S*) | 225 |

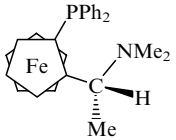
Tables 11 and 12 each contain one entry where the λ-(*S*){(*R*)}, δ-(*R*){(*S*)} regularities are not fulfilled. These examples may be regarded as the exceptions that corroborate the rule.

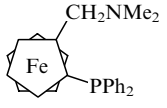
More generally, if we consider the helical structure of a ligand around the central metal atom rather than the conformation of the chelate complex, this rule can be formulated as follows.[125] In homogeneous asymmetric catalytic hydrogenation, hydrosilylation and cross-coupling reactions $C_2$-symmetrical chiral complexes with ligands in the form of an incomplete turn of a helix around the central metal atom catalyse, from the same kind of substrates, the formation of products having strictly specific configurations characteristic of this particular helicity sign, the metal and the reaction. For example, (*R*)-amino acids are the products of hydrogenation of amino acid precursors on rhodium complexes in which the ligands form incomplete turns of *P*-helices around the rhodium atoms. If the ligands in such complexes form a part of *M*-helices around the rhodium atoms, (*S*)-amino acids are formed.

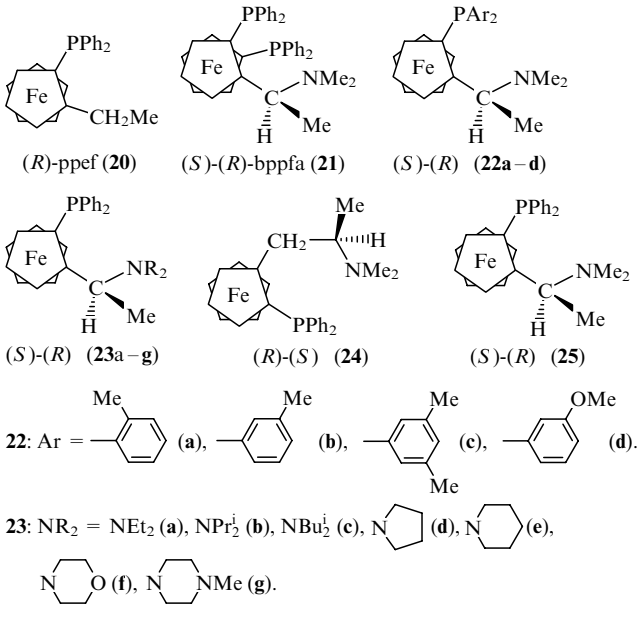
## IV. Catalyst – product configurational relationships in reactions on asymmetric metal complexes

With respect to asymmetric catalytic reactions catalysed by chiral complexes devoid of any symmetry elements (with the exception of $C_1$), the regular catalyst – product configurational relationships have been gained exclusively in the cross-coupling reactions catalysed by nickel ($NiCl_2$/L*) and palladium ($PdCl_2$/L*) complexes with ferrocene-based (amino)diphenylphosphine ligands (L). The structural formulae of such complexes are given below.


(*S*)-(*R*)-ppfa (**17**)


(*R*)-(*R*)-ppfa (**18**)


(*S*)-fcpn (**19**)




Examination of the cross-coupling reaction (1) (Table 14) demonstrates that the configurations of the products obtained on nickel and palladium complexes containing the same ligand are identical. Moreover, even the value of enantioselectivity virtually does not change. The introduction of *ortho*-substituted aryl radicals at the phosphorus atoms into the ligands decreases the enantioselectivity in comparison with complexes with non-substituted (phenyl) or *meta*-substituted radicals. The absence of amino groups in the ligands, the introduction of bulkier (in comparison with methyl) substituents at the nitrogen atoms and removal of the amino functional groups at a distance of one $CH_2$ group from the ferrocenyl ring decrease drastically the optical yields of the target products. Therefore, any disturbances in the optimum structures of ligands in catalytic complexes have negative effects on the enantioselectivity of the reaction.

**Table 14**. Asymmetric cross-coupling of 1-PhEtMgCl with vinyl bromide on chiral nickel and palladium complexes.[226–228]

| Ligand | Yield (%) | *ee* (%) | Ligand | Yield (%) | *ee* (%) |
|---|---|---|---|---|---|
| (*S*)-(*R*)-ppfa | >95 | 61 (*R*) | **22c** | 90 | 65 (*R*) |
| (*R*)-(*S*)–ppfa | >95 | 68 (*S*) | **22d** | >95 | 57 (*R*) |
| **17** | 62 | 52 (*R*) | **23a** | 65 | 35 (*R*) |
| **17** (Pd) | 82 | 61 (*R*) | **23b** | 49 | 7 (*S*) |
| **18** | >95 | 54 (*R*) | **23c** | 50 | 15 (*S*) |
| **19** | >95 | 65 (*S*) | **23d** | >95 | 62 (*R*) |
| **20** | 86 | 5 (*S*) | **23e** | 43 | 42 (*S*) |
| **21** | 73 | 65 (*R*) | **23f** | 68 | 17 (*R*) |
| **21** (Pd) | 93 | 61 (*R*) | **23g** | >95 | 65 (*R*) |
| **22a** | 79 | 33 (*R*) | **24** | 88 | 15 (*S*) |
| **22b** | >95 | 65 (*R*) | **25** | 95 | 57 (*R*) |

Reaction (4), which proceeds in the presence of (amino)-diphenylphosphine nickel and palladium complexes, is a somewhat more complicated version of reaction (1). The corresponding experimental data ‡ are presented in Table 15. The coincidence of configurations and optical yields of reaction

‡ The catalyst – product configurational relationships have not been analysed in Refs 219, 220, 227–231.

**Table 15**. Cross-coupling reactions catalysed by nickel and palladium complexes with ferrocene-based ligands ($0 < T < 25$ °C).

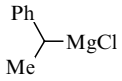
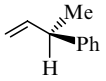
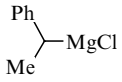
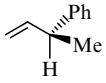
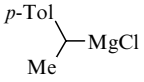
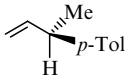
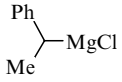
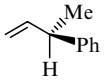
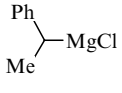
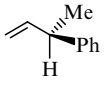
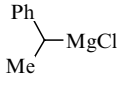
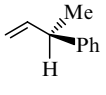
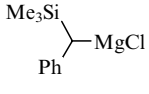
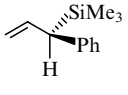
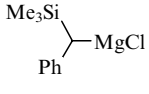
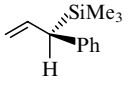
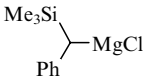
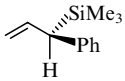
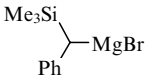
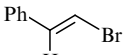
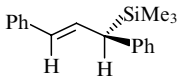
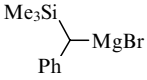
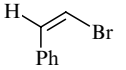
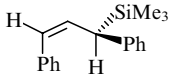
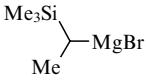
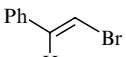
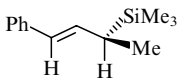
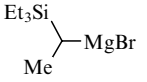
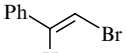
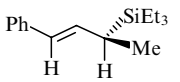
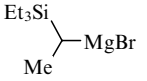
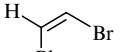
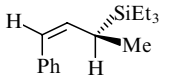
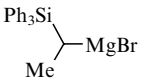
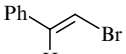
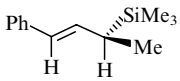
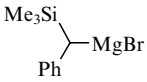
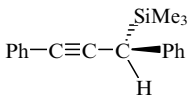
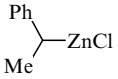
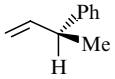
| Entry | Ligand | Grignard reagent | Alkenyl (alkynyl) halide | Configuration of the product | Optical yield (%) | Ref. |
|---|---|---|---|---|---|---|
| Nickel complexes | | | | | | |
| 1 | (*S*)-(*R*)- ppfa |  | $CH_2=CHBr$ |  | 66 (*R*) (see [a]) | 228 |
| 2 | (*R*)-(*S*)-ppfa |  | $CH_2=CHBr$ |  | 68 (*S*) (see [a]) | 228 |
| 3 | (*S*)-(*R*)-ppfa |  | $CH_2=CHBr$ |  | 66 (*R*) | 219, 220 |
| 4 | (*S*)-(*R*)-ppfa |  | $CH_2=CHBr$ |  | 61 (*R*) | 227 |
| Palladium complexes | | | | | | |
| 5 | (*S*)-(*R*)-ppfa |  | $CH_2=CHBr$ |  | 61 (*R*) | 227 |
| 6 | (*S*)-(*R*)-bppfa |  | $CH_2=CHBr$ |  | 61 (*R*) | 227 |
| 7 | (*R*)-(*S*)-ppfa |  | $CH_2=CHBr$ |  | 56 (*R*) (see [b]) | 219, 220, 229 |
| 8 | (*R*)-(*S*)-bppfa |  | $CH_2=CHBr$ |  | 21 (*R*) (see [b]) | 219, 220, 229 |

**Table 15** (continued).

| Entry | Ligand | Grignard reagent | Alkenyl (alkynyl) halide | Configuration of the product | Optical yield (%) | Ref. |
|---|---|---|---|---|---|---|
| 9 | (*R*)-(*S*)-ppfa |  | $CH_2=CHBr$ |  | 95 (*R*) | 219, 220, 229 |
| 10 | (*R*)-(*S*)-ppfa |  |  |  | 95 (*R*) | 219, 220, 229 |
| 11 | (*R*)-(*S*)-ppfa |  |  |  | 13 (*R*) | 219, 220, 229 |
| 12 | (*R*)-(*S*)-ppfa |  |  |  | 71 (*S*) | 219, 220, 229 |
| 13 | (*R*)-(*S*)-ppfa |  |  |  | 93 (*S*) | 219, 220, 229 |
| 14 | (*R*)-(*S*)-ppfa |  |  |  | 14 (*S*) | 219, 220, 229 |
| 15 | (*R*)-(*S*)-ppfa |  |  |  | 36 (*S*) | 219, 220, 229 |
| 16 | (*R*)-(*S*)-ppfa |  | $Ph-C\equiv C-Br$ |  | 18 (*S*) | 230 |
| 17 | (*R*)-(*S*)-ppfa |  | $CH_2=CHBr$ |  | 85 (*S*) | 231 |

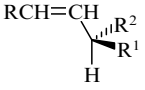
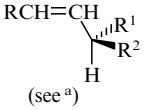
[a] At −20 °C. [b] At 50 °C.

products in the presence of catalytic complexes $NiCl_2$/(*S*)-(*R*)-ppfa and $PdCl_2$/(*S*)-(*R*)-ppfa (entries 4 and 5), $PdCl_2$/(*S*)-(*R*)-ppfa and $PdCl_2$/(*S*)-(*R*)-bppfa (entries 5 and 6) as well as $NiCl_2$/(*S*)-(*R*)-ppfa (entries 1 and 3), prompt a conclusion about the same type of their structures. Thus the bppfa ligand is coordinated through a metal atom (Ni, Pd) to the $PPh_2$ and $NMe_2$ groups belonging to the same five-membered ring of ferrocene (the second $PPh_2$ group in bppfa is hardly involved in coordination). The palladium catalyst $PdCl_2$/(*R*)-(*S*)-ppfa can be used for the synthesis of optically active allylsilanes (entries 7–15), being much more enantioselective than the $PdCl_2$/(*R*)-(*S*)-bppfa complex (entry 8). In the presence of $PdCl_2$/(*R*)-(*S*)-ppfa, the (*E*)-isomers of alkenyl bromides generate products of higher optical purity than the (*Z*)-isomers (entries 10, 11, 13 and 14). Substitution of the phenyl group for the methyl group in the Grignard reagent $Me_3Si(PhCH)MgBr$ (entries 7–11 and 12–15) has no effect on the configuration of the product, since substitution of the (*S*) symbol for the (*R*) symbol reflects the changes in the order of priority of the substituents only.

The actual configurations of products do not change in reactions involving vinyl bromide and phenylethynyl bromide (entries 7 and 16). The substitution of zinc for magnesium in the Grignard reagent does not affect the product configuration either (entries 2 and 17).

The analysis of configurational relationships between the catalytic complex and the product (Table 16) shows that the Ni- and Pd-complexes with ferrocenyl(amino)diphenylphosphine ligands belonging to the (*S*)-(*R*) and (*R*)-(*S*) configurational series catalyse the formation of enantiomeric products or products with different actual configurations in reactions (3) and (4).

**Table 16**. Catalyst–product configurational relationships in cross-coupling reactions catalysed by ferrocenyl nickel and palladium complexes.[219, 220, 224, 227–231]

| Configuration of the ligand | Configuration of the product [a] | Configuration of the ligand | Configuration of the product |
|---|---|---|---|
| Reaction (3b) | | Reaction (4) | |
| (*S*)-(*R*) | (*S*) | (*S*)-(*R*) |  |
| (*R*)-(*S*) | (*R*) | (*R*)-(*S*) |  (see [a]) |

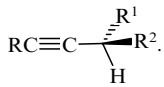
[a] One of the experiments yielded .

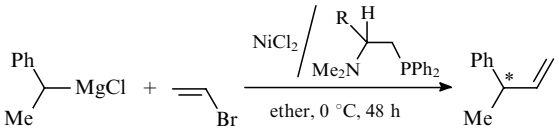
**Table 17**. Enantioselectivity of the cross-coupling reaction catalysed by nickel complexes with aminophosphine ligands prepared from amino acids.

| Ligand | R | *ee* (%) |
|---|---|---|
| (*S*)-alaphos | Me | 38 (*S*) |
| (*S*)-leuphos | $Bu^i$ | 57 (*S*) |
| (*S*)-phephos | Bn | 71 (*S*) |
| (*R*)-phglyphos | Ph | 70 (*R*) |
| (*S*)-valphos | $Pr^i$ | 81 (*S*) |
| (*S*)-ilephos | $Bu^i$ | 81 (*S*) |
| (*R*)-chglyphos | cyclo-Hex | 77 (*R*) |
| (*R*)-*t*-leuphos | $Bu^t$ | 83 (*R*) |
| | | 94 (*R*) [a] |

[a] The optical yield is adjusted for the optical purity of the ligand.

Reaction (5) has been studied relatively little. In this reaction, asymmetric catalytic effects are produced by complexes (*R*)-(*S*)-$C_5H_5FeC_5H_3(CHMeNMe_2)$·(SR)$PdCl_2$, where R = Me, $Pr^i$, Ph, *p*-Tol, 4-$ClC_6H_4$. The optical purity of the product does not depend on the nature of the radical R (*S*-configuration, *ee* = 26%, 22%, 18%, 25% and 16%, respectively).[232]

Interesting relationships were found between the configurations of the metal complexes and the products as well as between the enantioselectivities and the structures of complexes for cross-coupling under the action of chiral nickel complexes with aminophosphine ligands based on amino acids (Table 17).[233, 234]




In this reaction, the configurations of the products depend on the configuration of the ligand. Special mention should be made of the stable tendency of enantioselectivity to increase with an increase in the molecular size of the radical R in the ligand.

Reaction (2) of a vinyl halide with a non-racemisable Grignard reagent proceeds with low enantioselectivity [218–221, 234] and does not present special interest from the standpoint of configurational relationships.

## V. The structure of the intermediate complex

Knowing the configurations of the catalytic complexes and the products in cross-coupling reactions of Grignard reagents with allylic derivatives, one can conjecture upon the structure of the intermediate complex.[125]

Cross-coupling of Grignard reagents with allyl phenyl ethers gives rise to an intermediate compound.[221]

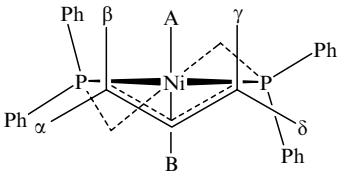
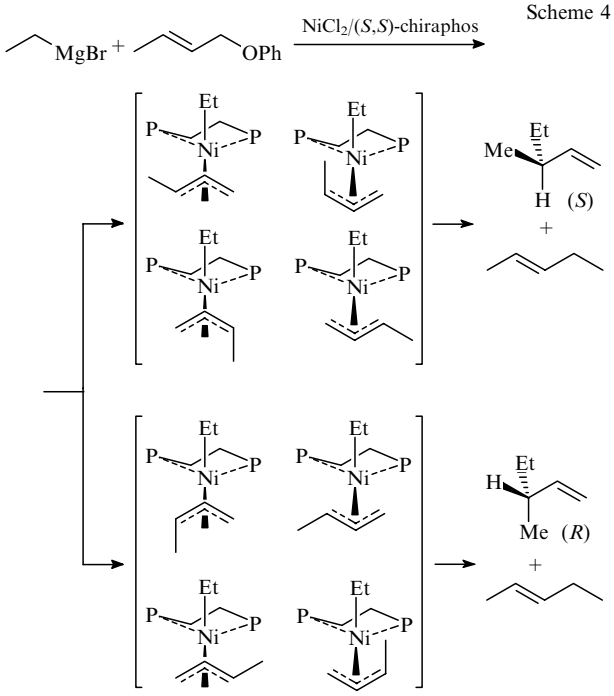
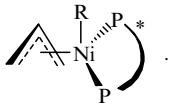



**Figure 1.** The intermediate compound in the cross-coupling reaction (see Scheme 4), a view from the side of the coordinated allylic group.

Scheme 4




Thus the formation of eight intermediates may be expected resulting in two enantiomers of the product (Scheme 4).

Figure 1 shows a structural scheme for the intermediate compound with a fixed position of the allylic fragment (a view from the side of the coordinated $\eta^3$-allylic group). The four positions of the methyl substituent in the allyl group are marked by the letters α, β, γ and δ, whereas the two positions of the apical radical at the nickel atom are designated by the letters A and B (in total, eight possible intermediates).

All these variants as applied to different reactions of the same kind and analysed in terms of their stereochemical properties have been compared with the known experimental data. The α-position of the Me group is unfavourable at any position of the apical substituent at the nickel atom (A and B), because of the unfavourable ('eclipsed') position of this radical relative to the phosphine equatorial phenyl group. Position β is also unfavourable due to the spatial proximity of the Me group to the phosphine axial phenyl group; if a radical of the Grignard reagent occupies position A, this is proximal to the Me group, too. Position γ is unfavourable only in the case where the apical substituent at the nickel atom occupies position A. And, finally, position δ is favourable at any position (A or B) of the apical radical. Thus only three out of eight intermediates are theoretically more or less preferred. An attack of the radical R(Et) from A or B at the nickel atom on the prochiral allylic carbon atom results in the formation of products with (*S*)-, or (*R*)- and (*S*)-configurations, respectively. In general, a small preference (2/3) goes to the (*S*)-configuration, which is consistent with the experimental data.[221] This simple analysis demonstrates a good coincidence with experimental results, which, in turn, corroborates the correctness of the statement about the structure of the intermediate complex (*cf.* Table 18).

**Table 18**. Relationships between the experimentally determined product configurations of cross-coupling reaction of alkyl (aryl) Grignard reagents with allylic compounds and those predicted from stereochemical models.

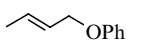
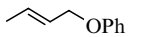
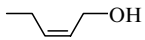
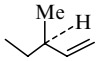
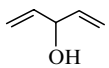
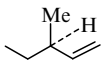
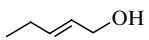
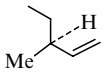
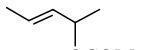
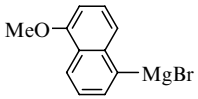
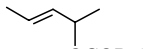
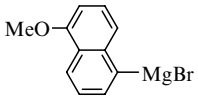
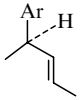
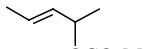
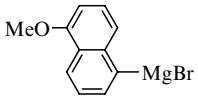
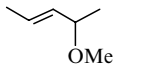
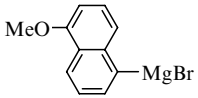
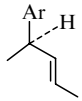
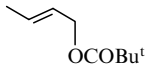
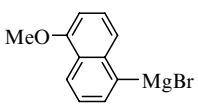
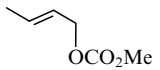
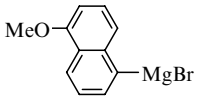
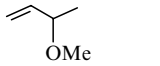
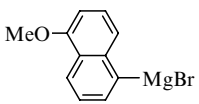
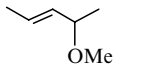
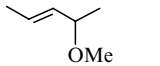
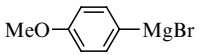
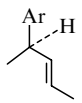
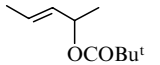
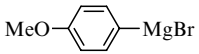
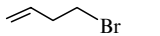
| Experimental results | | | | | | | Preferential intermediates and configurations of reaction products predicted using the model shown in Fig. 1 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alkene | Grignard reagent | Catalytic system | Conformation of the complex | Product | *ee* (%) | Ref. | A | B | α | β | γ | δ | C | PC |
|  | EtMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 22 (*S*) | 221 | Et | – | H | H | H | Me | *S* | *S* |
| | | | | | | | – | Et | H | H | Me | H | *R* | |
| | | | | | | | – | Et | H | H | H | Me | *S* | |
|  | PhMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 58 (*R*) | 221 | Ph | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ph | H | H | Me | H | *S* | |
| | | | | | | | – | Ph | H | H | H | Me | *R* | |
|  | EtMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 17 (*S*) | 221 | Et | – | H | H | H | Me | *S* | *S* |
| | | | | | | | – | Et | H | H | Me | H | *R* | |
| | | | | | | | – | Et | H | H | H | Me | *S* | |
|  | PhMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 58 (*R*) | 221 | Ph | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ph | H | H | Me | H | *S* | |
| | | | | | | | – | Ph | H | H | H | Me | *R* | |
|  | MeMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 15 (*R*) | 222 | Me | – | H | H | H | Et | *R* | *R* |
| | | | | | | | – | Me | H | H | Et | H | *S* | |
| | | | | | | | – | Me | H | H | H | Et | *R* | |
|  | MeMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 8.5(*R*) | 223 | Me | – | H | H | H | Et | *R* | *R* |
| | | | | | | | – | Me | H | H | Et | H | *S* | |
| | | | | | | | – | Me | H | H | H | Et | *R* | |
|  | MeMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 1 (*S*) | 223 | Me | – | H | H | H | Et | *R* | *R* |
| | | | | | | | – | Me | H | H | Et | H | *S* | |
| | | | | | | | – | Me | H | H | H | Et | *R* | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 68 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 67 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 41 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |

**Table 18** (continued).

| Experimental results | | | | | | | Preferential intermediates and configurations of reaction products predicted using the model shown in Fig. 1 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alkene | Grignard reagent | Catalytic system | Conformation of the complex | Product | *ee* (%) | Ref. | A | B | α | β | γ | δ | C | PC |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 58 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 89 (*R*) | 223 | Ar | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ar | H | H | Me | H | *S* | |
| | | | | | | | – | Ar | H | H | H | Me | *R* | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 64 (*R*) | 223 | Ar | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ar | H | H | Me | H | *S* | |
| | | | | | | | – | Ar | H | H | H | Me | *R* | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 67 (*R*) | 223 | Ar | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ar | H | H | Me | H | *S* | |
| | | | | | | | – | Ar | H | H | H | Me | *R* | |
|  | PhMgBr | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 47 (*R*) | 223 | Ph | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ph | Me | H | H | Me | *R*[a] | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 30 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |
|  |  | $NiCl_2$/(*S*,*S*)-chiraphos | δ |  | 68 (*R*) | 223 | Ar | – | Me | H | H | Me | *R*[a] | *R* |
| | | | | | | | – | Ar | Me | H | H | Me | *R*[a] | |
|  | PhMgBr | $NiCl_2$/(*R*,*R*)-diop | chair-δ |  | 6 (*R*) | 224 | Ph | – | H | H | H | Me | *R* | *R* |
| | | | | | | | – | Ph | H | H | Me | H | *S* | |
| | | | | | | | – | Ph | H | H | H | Me | *R* | |

**Note**. Designations: C is configuration of the product formed from the intermediate (Fig. 1); PC is predicted preferential configuration of the product.

[a] The introduction of Ar into the allylic positions (α,β) is less favourable, being sterically more hindered than that into positions (γ,δ) [eclipsed conformation of the C(α,β) – Ar and the P – Ph bonds of the ligand].

## VI. Conclusion

The analysis of experimental data presented in this review suggests that the highest enantiomeric excess of the target product can be reached if an optimum correlation is established between the number of coordination vacancies on the metal complex catalyst accessible to the substrate and the number of coordination-active functional groups of the substrate.

Presumably, the nature of asymmetric catalysis is such that high enantioselectivity is ensured with the minimum degree of freedom of the substrate where the latter is coordinated to the catalyst through all of its functional groups. For example, high enantioselectivity in asymmetric hydrogenation of acetamidocinnamic acid, which contains coordination-active groups in addition to the double bond, is attained with rhodium catalytic complexes with bidentate ligands. In hydrogenation of simple ketones, which are coordinated exclusively through one carbonyl group, this is insufficient and catalytic systems with tridentate ligands should be used which produce a chiral catalytic complex devoid of any symmetry elements other than $C_1$, where one of the vacancies is additionally blocked by an achiral monodentate ligand (*e.g.*, $Et_3N$, $CF_3CO_2H$, $PriCO_2H$, *etc.*). But even in such complicated catalytic systems, the most enantioselective hydrogenation is observed for ketones possessing additional coordination-active groups in the α- or, which is better, the β-position relative to the carbonyl.

The ratios of coordinating and coordination-active vacancies of the catalyst and the substrate should be an optimum. For example, substrates of the tiglic acid type, which contain only one coordination-active group (in addition to C=C), are hydrogenated with much higher enantioselectivity on $Ru(OAc)_2$[binap] complexes than on Rh complexes containing the binap ligand. Contrariwise, the hydrogenation of α-acetamidocinnamic acid occurs with higher enantioselectively in the presence of rhodium complexes. If the hydrogenation is carried out on octahedral ruthenium complexes with the binap ligand, substrates with two coordination-active groups seem to be less optimal as regards enantioselectivity than those with only one coordination-active group.

A similar situation is observed in hydrosilylation reactions where rhodium complexes with tri- and tetradentate ligands manifest the maximum enantioselectivity in hydrosilylation of simple ketones.

Simple graphical dependences between the structures of catalytic complexes and the configurations of the reaction products can be useful for predicting the configurations of reaction products at the design stage of asymmetric catalytic synthesis. The relationships between the configurations of reaction products and the signs of the helical components of the complexes seem to suggest the similarity of asymmetric induction mechanisms of all reactions which obey these regularities.

The analysis of putative structures of intermediate complexes based on stereochemical concepts further corroborates the similarity of asymmetric induction mechanisms of certain reactions. This approach, which enables one to predict the configuration of the product, differs from the graphical plots mentioned above. In this case, we deal with the actual structures of the intermediates.

The analysis of stereochemical relationships between chiral metal complex catalysts, substrates and products in asymmetric homogeneous catalytic hydrogenation, hydrosilylation and cross-coupling reactions illustrates the important role of steric factors in asymmetric catalysis. Additional evidence for the extreme importance of asymmetric catalysis can be derived from the fact that the three leading specialists in asymmetric homogeneous catalysis, *viz.*, W S Knowles, K B Sharpless and R Noyori, were awarded the Nobel Prize for Chemistry in 2001.

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