ASYMMETRIC CATALYSIS BY CHIRAL RHODIUM COMPLEXES IN HYDROGENATION AND HYDROSILYLATION REACTIONS

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ABSTRACT

The preparation of optically active molecules needs a chiral auxiliary. It is important to use the minimum amount of this auxiliary, and from that point of view asymmetric catalysis is much more advantageous than stoichiometric asymmetric synthesis. Some homogeneous catalysts prepared from chiral complexes have become during the past few years a useful tool in asymmetric synthesis. The complexes L_2RhCl where L_2 is a family of chiral diphosphines were prepared and used in asymmetric reduction. DIOP is a readily available ligand prepared from tartaric acid. Many of its derivatives were obtained as well as other types of chiral phosphines.

General syntheses of optically active α-amino acids, amines or acids are described. Optical yields as high as 90 per cent could be attained. The same complexes can catalyse the hydrosilylation of ketones and imines, giving rise after hydrolysis to optically active alcohols and amines. To improve the usefulness of asymmetric catalysis a supported chiral catalyst was prepared starting from a Merrifield resin. It was used both in reduction and in hydrosilylation. The mechanism of the reactions and the origin of the asymmetric induction will be discussed.

The creation of optical activity is an important problem from both theoretical and practical points of view. For many useful chiral compounds it is only one enantiomer which is desired, as is the case with pharmaceuticals, food additives, perfumes.... Total synthesis is one of the processes which is becoming important on the route to such compounds. It is then an interesting goal for organic chemists to devise efficient methods of generating optical activity. Almost all the methods take advantage of using a chiral auxiliary which can be recovered at the end of the process.

In a *resolution* only 0.5 mole of the desired enantiomer is at best obtained (for each one mole of the auxiliary chiral material). In an *asymmetric synthesis* one mole can be prepared, and thanks to an *asymmetric catalysis* (where the catalyst is chiral) an unlimited amount of optically pure compound should be, in principle, synthesized.

Asymmetric catalysis will become operative if the two following objectives are to be reached: high stereospecificity and good catalytic activity, i.e. high substrate/catalyst ratio. In recent years, the utilization of chiral soluble complexes as catalysts has given a new life to the field of asymmetric catalysis (for

some recent reviews see refs 1, 2). We will describe the main results that we obtained in this area using optically active rhodium complexes and we deal with several types of reaction.

When we started to investigate asymmetric catalysis with soluble complexes there were only a few reports which were not very encouraging since only small asymmetric induction could be observed. In order to take a rational approach in constructing a chiral catalyst we looked for a reaction where the mechanism was reasonably well known and where there is some sensitivity to steric hindrance. We selected the efficient catalyst system described by Wilkinson[3] where the catalyst is a rhodium complex. A feature of rhodium complexes is ability to pass easily from oxidation state I to oxidation state III (and the reverse). A covalent molecule X_2 for example, can be cleaved and added to a rhodium (I) complex by an oxidative addition(*Figure 1*). The

$$L_3Rh^{I}X + X_2 \longrightarrow L_3Rh^{III}X_3$$

Oxidative addition

$$L_3Rh^{III}X_3 \longrightarrow L_3Rh^{I}X_2$$

Reductive elimination

Figure 1

reverse process is called a reductive elimination. If L is a phosphine and $X_2 = H_2$ we have the basis of the catalyst system studied in great detail by Wilkinson[3] in 1966 (*Figure 2*). The complex $RhClL_2S$ (where S is a presumed coordinated solvent molecule) can be generated from the precursors $RhClL_3$ or $(RhClL_2)_2$. The oxidative addition of hydrogen followed by displacement of S by an olefin gives the crucial complex [$RhClL_2HHolefin$] wherein both

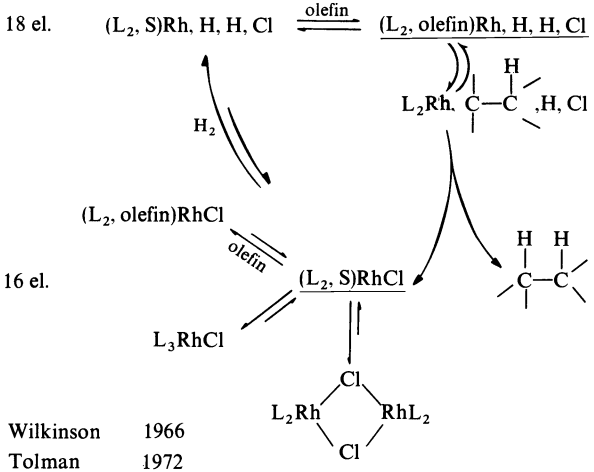


Figure 2

hydrogen atoms and substrate are present. Dihydrido complexes were studied and it seems that the two hydrogens are *cis* to each other. The reduction occurs then by two consecutive internal hydrogen transfers. For a *cis* addition, the second step must occur with retention of configuration at the carbon atom of the alkylrhodium intermediate. The kinetic details of the system have given rise to many studies and, especially during the last two years several publications have appeared (Tolman, Halpern, De Aguirre). The main pathway takes place via the hydride route, with a part of the reaction occurring through the dimer $(RhClL_2)_2$ which can fix one hydrogen molecule. The unsaturate route, oxidative addition of hydrogen on [Rh, Cl, L_2, olefin] is not very effective. The catalyst is very sensitive to steric hindrance, tetrasubstituted double bonds are not reduced. Many types of carbon–carbon double bonds are reducible, in contrast to carbonyl or imine groups.

How should one use the Wilkinson catalyst in order to reduce prochiral double bonds asymmetrically? It is necessary to introduce chiral ligands L. We prepared the chiral catalyst by a general method (*Figure 3*) which starts

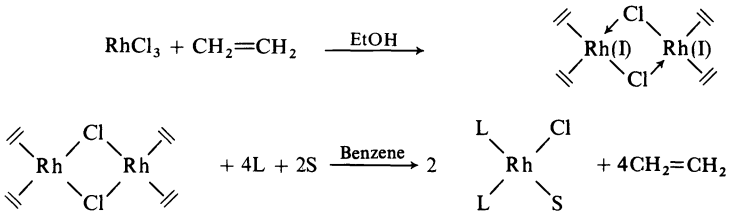


Figure 3

from $(RhClOlefin_2)_2$, a stable complex easily obtained from $RhCl_3$. The addition of ligands such as phosphines gives a displacement of olefins. The new species is usually not isolated and is the catalyst.

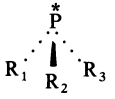
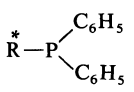
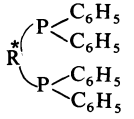
Phosphines	Authors	Advantages	Disadvantages
	Horner *et alii* Knowles *et alii*	Inducing chiral centre close to the complex	Difficulty in the synthesis and resolution
	Morrison *et alii*	Facility in the synthesis, no resolution	Inducing chiral centre far from the complex
	Dang and Kagan	Facility in the synthesis, no resolution, good chelating properties	Inducing chiral centre far from the complex

Figure 4. Chiral phosphines as ligand

To prepare chiral phosphines many approaches can be envisaged (*Figure 4*). Several teams have worked on the problem[4–6]. We used phosphines $R—P(C_6H_5)_2$ where R is chiral. In order to improve the steric control introduced by R we chose[7] to use diphosphines with the idea of decreasing the flexibility around the R→P bond. To give an equivalent character to the diphenyl-phosphino groups we first selected molecules with a twofold axis of symmetry. It is essential to start from a cheap material, with both the enantiomers available. We chose tartaric acid and prepared several phosphinated derivatives. One possibility is to use the carbon atoms of the carboxylic groups after protection of the diol system. We prepared a dimethoxydiphosphine (*Figure 5*) which was not very efficient in asymmetric catalysis. To reduce

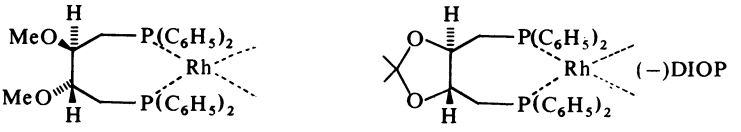


Figure 5

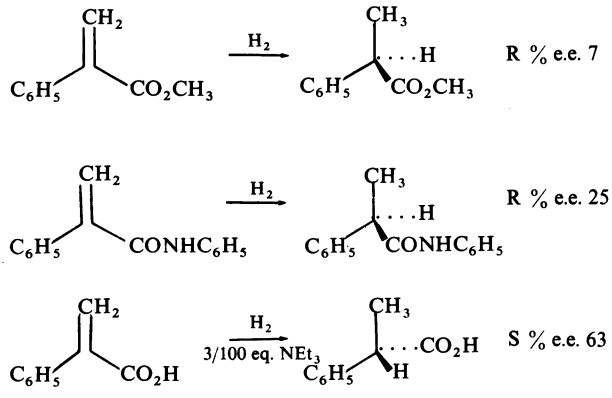
the flexibility of the chelate seven-membered ring we fused it with a dioxolan ring. The *trans* configuration between them distorts the heptagonal ring thanks to a large dihedral angle. This acetonid diphosphine is a crystallized compound easy to purify and to store, and was called DIOP[7]. (−)DIOP is derived from (+) tartaric acid. It is with DIOP and its derivatives that we obtained results which are among the best known in asymmetric catalysis.

In our standard conditions we generally use a substrate to catalyst ratio of 100, and all the experiments were performed at room temperature under atmospheric pressure. The more convenient solvent is a mixture benzene–ethanol (1/2), with a substrate concentration of 0.3 M.

REDUCTION OF CONJUGATED ACIDS

Our first experiments were conducted on atropic acid and its derivatives (*Figure 6*). DIOP induced asymmetric reduction with a moderate enantiomeric excess (% e.e.), but an optical yield as high as 63 per cent could be attained in the specific case of the free acid with addition of a small amount of triethylamine. It is interesting to notice that the absolute configuration is reversed with respect to the methyl ester. It is possible that the carboxylate function is coordinated to the rhodium atom during the reduction (*Figure 7*), giving a new steric situation (with respect to the ester reduction).

Many unsaturated acids were reduced by the system Rh/DIOP, the optical yields are often high and strongly related to the E—Z isomerism around the double bond[8]. Among the conjugated acids which can give rise to an asymmetric reduction, the α-*N*-acylaminoacrylic acids will be specially considered since they are precursors of the important class of α-amino acids.



Catalyst: $\frac{1}{100}$ eq. Rh/(−)DIOP

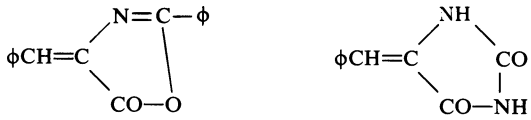
Figure 6

Figure 7

ASYMMETRIC SYNTHESIS OF α-AMINO ACIDS

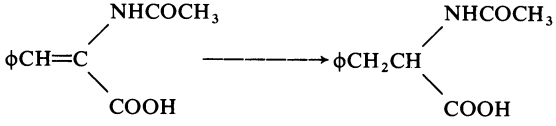
To test the possibilities of the system Rh/DIOP we first investigated[7] several potential precursors of phenylalanine. The corresponding azlactone and hydantoin are not reduced, but all the other compounds of *Figure 8* react easily. The optical yields are quite high, (R)-amino acids are obtained if (−)DIOP is used. Of course we prepared too natural (S)-amino acids by taking (+) DIOP. Many amino acids were synthesized in this way (*Figure 9*), the chemical yields being almost quantitative. We were surprised to see that substituents on the phenyl ring of the *N*-acetylphenylalanine precursor enhance significantly the optical yield (72 per cent for phenylalanine, 80–83 per cent for DOPA or tyrosine). We recently found that this is not a substituent effect. Indeed the specific rotation described in the literature for *N*-acetylphenylalanine (used also by us[7]) is in error. The value is too high.

We could demonstrate this fact by v.p.c. analysis on *t*-butyl-*N*-lauroyl valine as the chiral phase, according to a Gil-Av procedure[9]. The crude *N*-acetylamino acid is treated with diazomethane and is then directly analysed by v.p.c. The two enantiomers are nicely separated (column 1.5 m, 150°C), and from the area of the peaks an enantiomeric excess of 83 per cent was calculated for *N*-acetylphenyalanine which is very close to the value in DOPA and tyrosine syntheses.

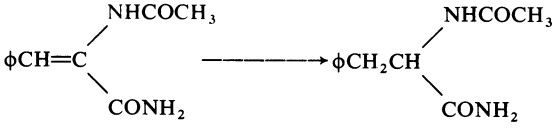


%e.e.

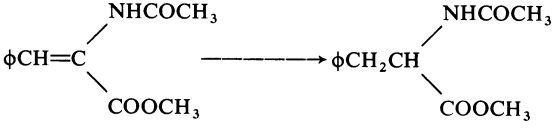
64 [R]



73 [R]

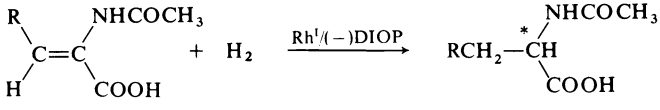


71 [R]



55 [R]

Figure 8



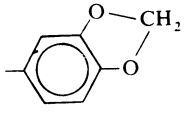
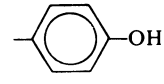
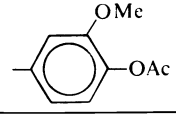
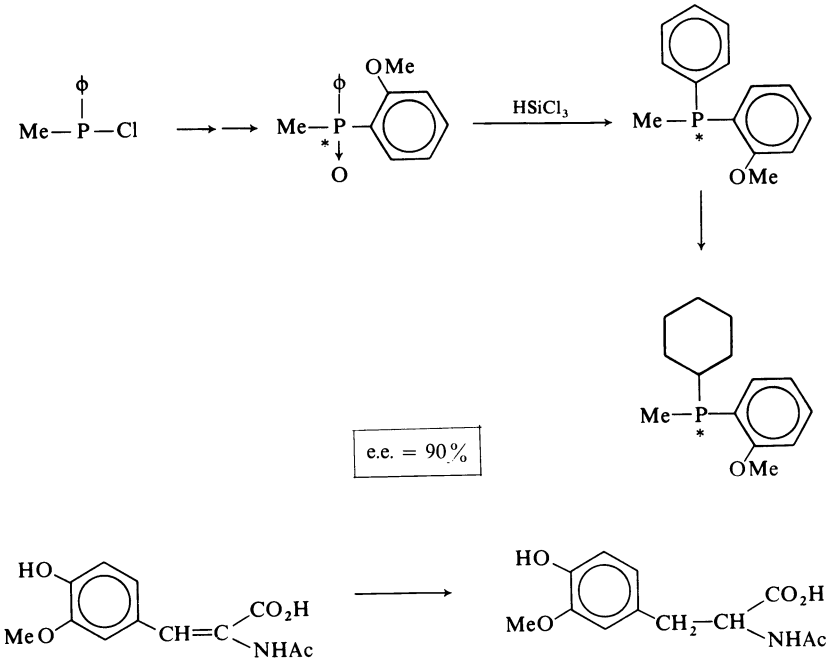
	yield %	% e.e.	Amino acid
R = H	96	73	Alanine
R = C_6H_5	95	(72)	Phenyl alanine
R = 	87	79	→ DOPA
R = 	97	80	Tyrosine
R = 	95	83	→ DOPA

Figure 9

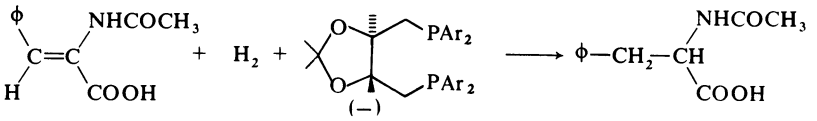


Knowles *et al.*, *Chem. Commun.* 10 (1972)

Figure 10

Many chiral phosphines, in which phosphorus is an asymmetric centre, were prepared by Knowles[5], and some gave amino acids of high optical purity. In *Figure 10* is indicated the best result of Knowles: asymmetric synthesis of a DOPA derivative with 90 per cent enantiomeric excess. The chiral ligand is obtained by a multistep synthesis (starting from a chloro phenyl alkyl phosphine) which includes a resolution step.

In order to compete with this interesting result we prepared several *modified DIOP* with the hope of altering the optical yield. In *Figure 11* are summarized the effects of methyl substitution in each phenyl ring of DIOP. A meta methyl group increases both optical yield and rate of reduction. *N*-acetylphenylalanine of 88 per cent enantiomeric purity was thus obtained. It is interesting to notice that the classical catalyst with triphenyl phosphine as ligand is less active than DIOP in this type of reduction. The DOPA synthesis was improved too (*Figure 12*); an optical yield of 90 per cent was observed. This type of research demonstrates that it is possible to progressively improve the efficiency of asymmetric catalysis and to adjust the structure of the chiral ligands to the asymmetric synthesis of a specific amino acid. We have here a ligand engineering where the tartaric acid is the chiral starting material. If the structural changes are not gradual some surprises can occur. For example, we prepared an analogue of DIOP where phenyl rings were ortho-linked to give a



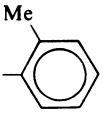
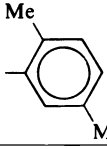
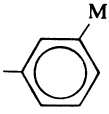
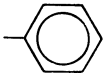
Phosphine (Ar)	% e.e.	Config.	Relative rates
	27	R	0.025
	44	R	0.094
	88	R	5
	82	R	1
Rh. Cl. S. $2P(C_6H_5)_3$			0.12

Figure 11

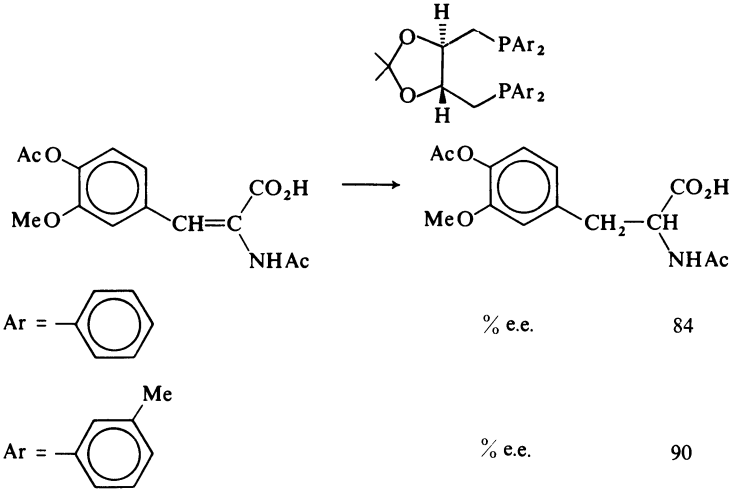
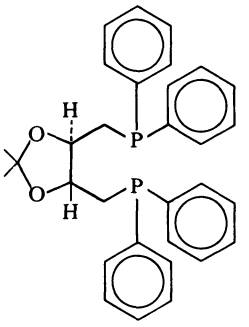
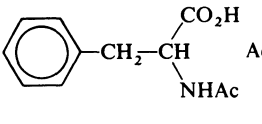
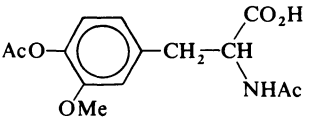


Figure 12

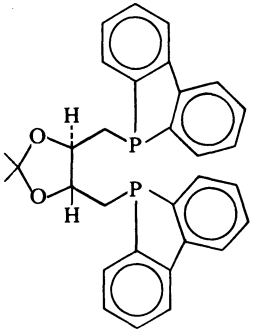






e.e. 82%R

84%R



e.e. 28%S

14%S

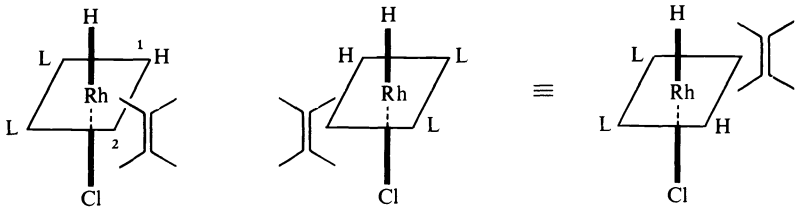
Figure 13

phosphole system as shown in *Figure 13*. The catalytic activity is greatly reduced, and there is a reverse of stereospecificity. It is an interesting situation where with the same chiral skeleton (derived from a natural product) it is possible to prepare ligands of opposite stereospecificity.

DISCUSSION OF THE MECHANISM

To be able to devise the structure of good chiral ligands it is essential to understand and analyse accurately the mechanism of asymmetric catalysis. In our case it is impossible to give a simple picture of the reaction. Many parameters have to be taken into account. For example, we found that the E—Z isomerism around the double bond of some amino acid precursors is of importance for asymmetric induction. In the experiments of *Figures 7* and *8* the olefins contain the usual Z configuration. We prepared the E isomer of *N*-benzoyl α-amino cinnamic acid, and there was a strong decrease in the optical yield[10].

Another complication arises by the nature of the catalytic species which is believed[3] to be octahedral with two hydrogens in a *cis* relationship. It is clear by looking at *Figure 14* that the complex is chiral even if the ligands are achiral. If the ligands become chiral then the olefin has the choice between two complexing sites which are diastereotopic, and of different reactivities. Therefore the chiral ligands induce the preferential formation of one asymmetric rhodium atom, and afterwards the prochiral olefin is preferentially complexed



L Achiral — Positions 1 and 2 are Enantiotopic

L Chiral — Positions 1 and 2 are Diastereotopic

Figure 14

by one of its faces. Actually the discussion is more complicated since the kinetic framework of the catalytic cycle has to be taken into account. The relative rate constants of all the competitive reactions in *Figure 15* need to be known. If there is a slow rate of interconversion between the two complexes which differ by bonding at re or si faces of the olefin, then the origin of asymmetric induction is related to the relative stabilities of the two complexes. But if the equilibrium is fast with respect to the first hydrogen transfer the free energy difference between the two competing transition states for hydrogen transfer is the decisive factor.

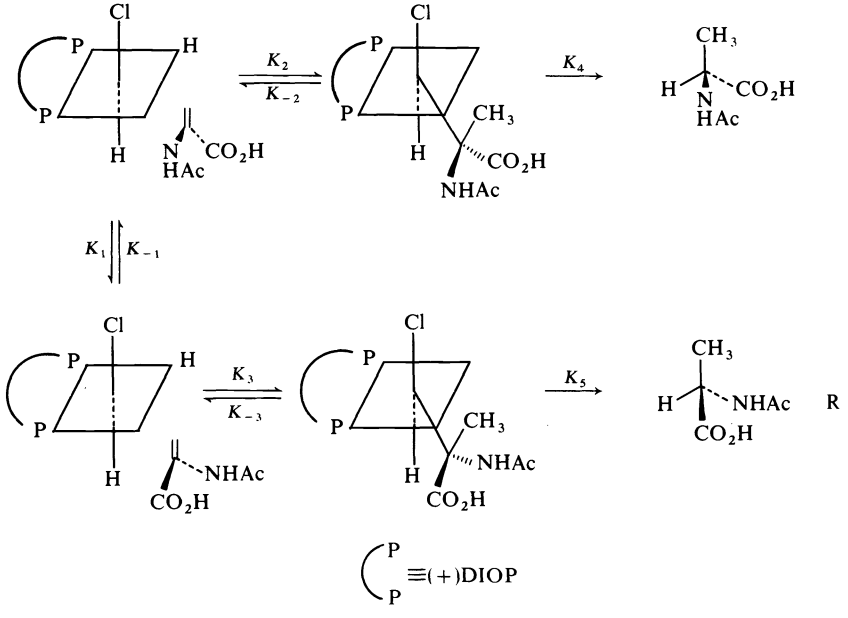
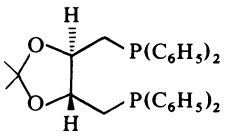
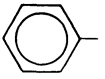
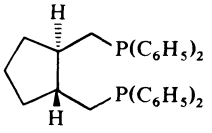
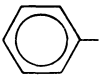


Figure 15

To propose a scheme of asymmetric induction it is not only important to gain more information from kinetic studies, but it is necessary to know if the oxygen atoms of DIOP are helpful for high asymmetric inductions and what is the DIOP conformation when complexed.

To check the effect of oxygen atoms in DIOP we removed it by preparing[8] a cyclopentane analogue (*Figure 16*). The optical yields are lower but still

Diphosphine	R substrate	Optical yield absolute configuration
	H—	73 R
		82 R
	H—	72 R
		63 R

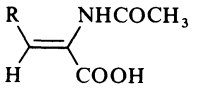
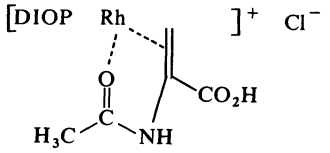
Hydrogenation of 

Figure 16.

good, and the absolute configurations of amino acids are identical (when DIOP and its analogue are of the same configuration). We can conclude that steric factors play a key role in the asymmetric reduction. In order to determine the DIOP conformation we prepared and isolated several stable cationic complexes such as Rh DIOP $B(C_6H_5)_4$ or Rh COD DIOP ClO_4. They are good catalysts, giving the same optical yield as the *in situ* Rh/DIOP catalyst. But unfortunately the crystals were not suitable for x-ray analysis. We succeeded with Ir DIOP Cl, and very recently we got the first results[11] of an x-ray structural study (*Figure 17*). The DIOP acts, as expected[7], as a bidentate ligand. The heptagonal ring of chelation is a distorted twisted chair, which is chiral by itself. The phenyl rings on each phosphorus are orthogonal to each other. The double bonds of COD are in a dissymetric arrangement with respect to the two systems of aromatic rings. We have here an interesting model for an octahedral catalytic species if we imagine one hydrogen atom in the apical position and another hydrogen atom replacing one double bond.

More information is needed before putting forward a model of asymmetric induction. It is important to find out if the α-aminoacrylic derivatives act as a mono- or bidentate ligand. From *Figure 8* it appears that the free carboxylic function is not crucial, since its methyl ester or amide also give asymmetric reduction. But there remains the chance that the amide group will react with the rhodium atom by substituting chlorine, the catalyst being a

cationic complex 

To test this idea we prepared prochiral molecules where the carboxylic group had been removed and the amide group was retained.

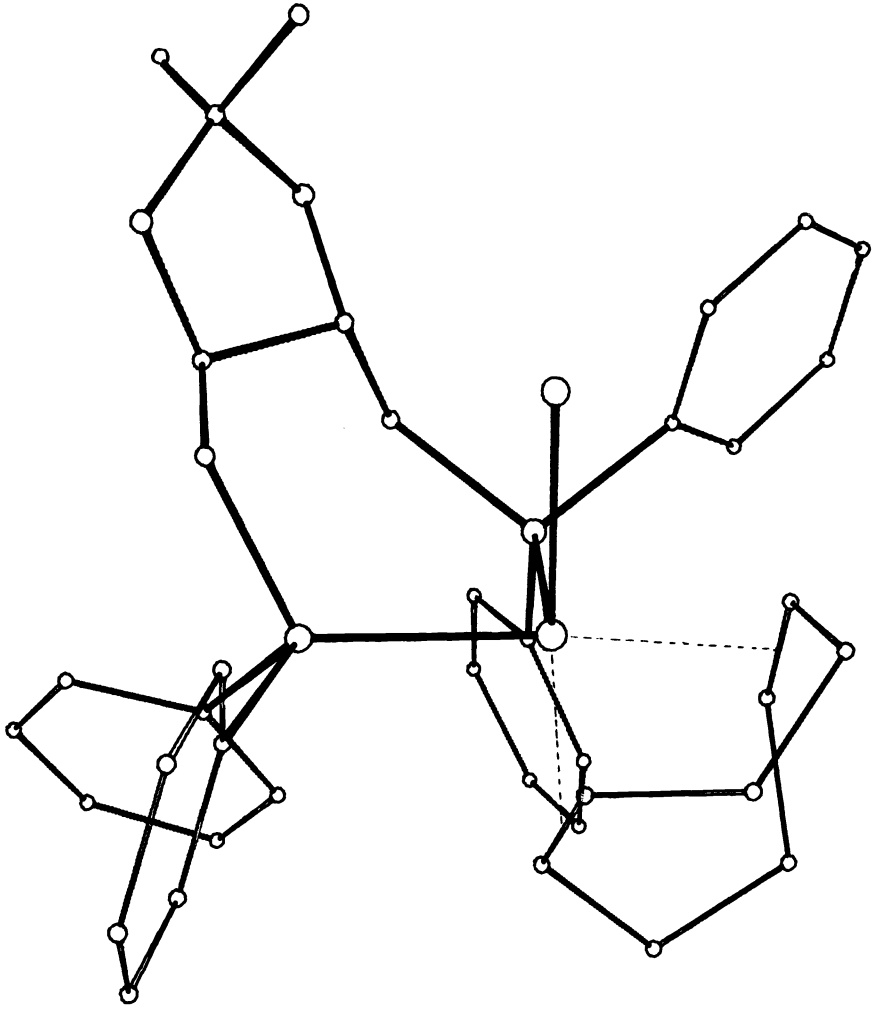


Figure 17. Ir DIOP COD Cl

ASYMMETRIC REDUCTION OF ENAMIDES

We found that enamides are good prochiral substrates for the asymmetric synthesis of optically active amides and amines[12]. Since enamides are less well known than enamines we summarized in *Figure 18* some preparations of these compounds. From the many results that we obtained only the specific case

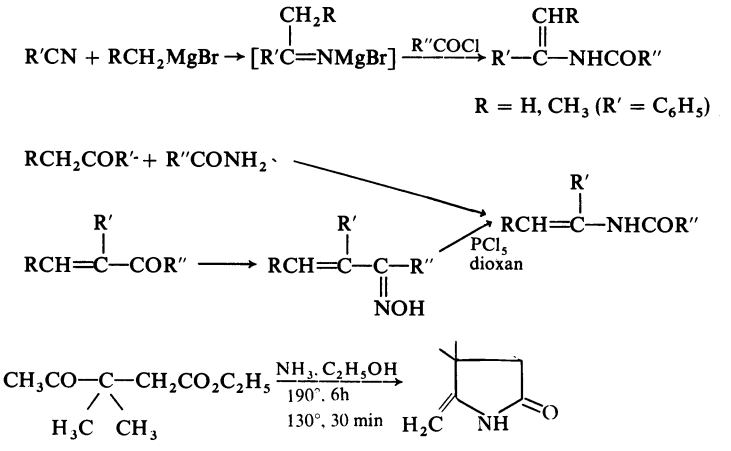
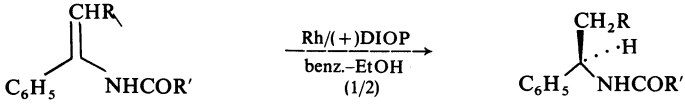


Figure 18

of asymmetric synthesis of α-arylalkylamines will be detailed (*Figure 19*). In some examples the optical yields are as good as in the amino acid synthesis, for example *N*-acetyl α-phenylpropylamine could be prepared with 83 per cent enantiomeric excess. We made a very interesting discovery during asymmetric synthesis of *N*-acetyl α-phenylethylamine. Experiments were, as usual, performed in the mixture benzene/ethanol (1/2). If the solvent composition is modified, there is a striking effect on the asymmetric synthesis. In pure benzene with (+)DIOP the optical yield is still 44 per cent, but the amide has the reverse configuration (S instead of R). We could follow the progressive change in the asymmetric induction according to the solvent composition. A possible explanation of this phenomenon could be a mechanistic change. In



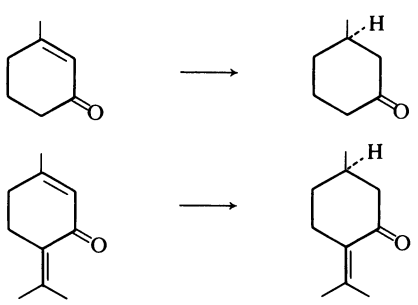
	% e.e.	
R=H, R'=CH3:	45	(R)
R=R'=CH3:	83	(R)

Figure 19

pure benzene the enamide would be coordinated by its double bond. Addition of ethanol would help the dissociation of Rh—Cl bond, giving a cationic species which can then interact with both the double bond and the amide group of enamides. If our hypothesis is valid there would be a delicate balance between two competing situations which are controlled by solvent and substituents. It is then difficult to decide at the moment what is the actual mechanism in the reduction of amino-acid precursors. We are studying para-substituted α-*N*-benzoylamino cinnamic acids in order to obtain information on the role of the amide group during the reduction.

Besides conjugated acids or enamides we looked for the asymmetric reduction of other substrates. *Conjugated ketones* can be precursors of chiral ketones, the Rh/DIOP catalyst is able to catalyse the selective reduction of conjugated ketones[13]. Methyl-3 cyclohexanone or pulegone could be synthesized, but optical yields are low (*Figure 20*). We still have to find the appropriate chiral ligand for these substrates.

Wilkinson catalysts cannot reduce carbonyl and imine groups unless some special conditions prevail. We found that asymmetric hydrosilylation can be used as a general method to prepare chiral alcohols and amines.



T. P. Dang and H. Kagan (1974)

Figure 20

ASYMMETRIC HYDROSILYLATION

Hydrosilylation of ketones or carbon–carbon double bonds is known to be catalysed by rhodium complexes. The mechanism is more or less similar to that of hydrogenation where the oxidative addition of H—H is replaced by oxidative addition of H—Si. With a ketone as substrate the primary product is a siloxane. *Figure 21* describes the catalytic hydrosilylation of acetophenone with the Rh/(+)DIOP catalyst. We do not isolate the siloxane which is hydrolysed to the alcohol, obtained with excellent yield. The reaction is carried out for a few hours at room temperature in benzene solution, under argon. We selected dihydrosilanes as active reagents, and we found[14] that the optical yield depends strongly on the nature of the silane. Enantiomeric excess up to 58 per cent could be obtained in the reduction of acetophenone

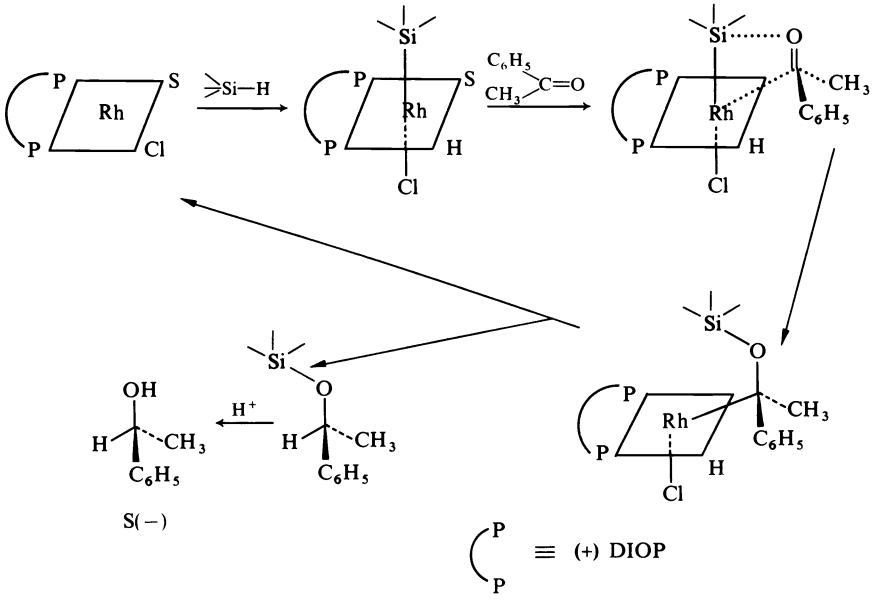
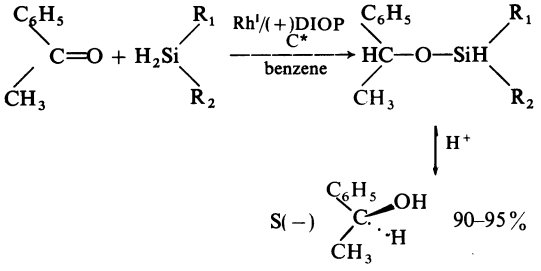


Figure 21

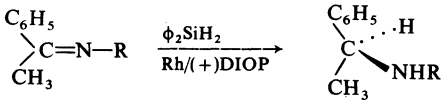
by phenylnaphthylsilane (*Figure 22*). Recently Rh DIOP Cl S was used by Ojima and Kogure[15] in the catalytic hydrosilylation of some pyruvic esters, a lactic ester of 80 per cent enantiomeric purity was prepared when phenylnaphthylsilane was the reagent.

The Rh/DIOP catalyst is useful too in the asymmetric synthesis of *chiral silicon atoms.* Corriu[16] investigated the asymmetric reduction described in *Figure 22* for the specific case of phenylnaphthyl silane. This silane is prochiral, and the intermediate siloxane has two asymmetric centres (one of which



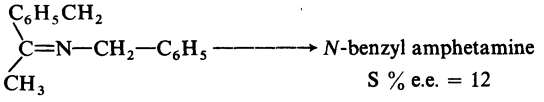
$R_1=R_2=C_6H_5$	% e.e. 13
$R_1=CH_3$, $R_2=C_6H_5$	% e.e.27
$R_1=C_6H_5$, $R_2=\alpha$—Naphthyl	% e.e. 58

Figure 22



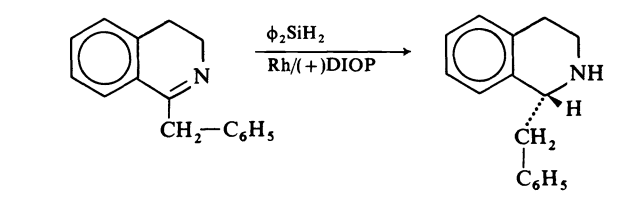
1 R=$CH_2\phi$ S % e.e. = 50

1'R=ϕ S % e.e. = 40

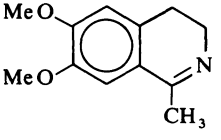


	t°C	% e.e.	
1:	60	27.5	
	40	33	
	24	50	$\Delta\Delta H^{\neq} = -3$ kcal/mole
	2	65	$\Delta\Delta S^{\neq} = -8$ e.u.

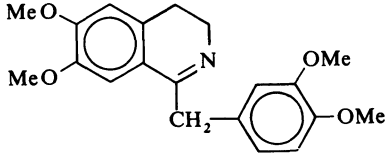
Figure 23



% e.e. 22



Salsolidine R — 6



Tetrahydro papaverine R — 38

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Figure 24

is silicon). By suitable reactions this siloxane was transformed into a chiral silane. Asymmetric induction in the creation of the asymmetric silicon is about 32 per cent. By starting from achiral ketones Corriu prepared silanes $R_1R_2R_3$ SiH with enantiomeric excess between 30 and 45 per cent.

We applied hydrosilylation to the *imines*. This reaction was unknown when we started this work[17]. We found that amine synthesis is performed in excellent conditions by the same procedure used for ketones. In addition, if we consider prochiral imines, asymmetric hydrosilylation occurs with an efficiency very often better than that for the related ketones. In *Figure 23* details are given for the asymmetric reduction of some imines. A temperature effect was found in the hydrosilylation of **1**. A linear relation between logR/S and $1/T$ allows us to estimate $\Delta\Delta H^{\neq}$ and $\Delta\Delta S^{\neq}$. By decreasing the temperature an enantiomeric excess of 65 per cent was reached, which is one of the best results so far in the synthesis of amines by asymmetric catalysis. The reaction was extended to dihydroquinolines and (*Figure 24*) allowed us to prepare alkaloids such as salsolidine or tetrahydropapaverine[12].

Asymmetric hydrosilylation is at the present time evolving fast and should be a smooth and useful tool for preparing chiral amines and alcohols of high optical purity, since both catalyst and silane can be submitted to various structural transformations for optimization of optical yield.

SUPPORTED CATALYSTS

A problem, which is vital if industrial syntheses are considered, will now be discussed.

How can we minimize the amount of the catalyst which contains an expensive metal and sophisticated ligands? It is necessary to find very active catalysts and, in addition, to try to recover them. Unfortunately the separation of the catalyst from the reaction products requires special treatment which may well destroy it. This is why efforts have been made for several years to prepare supported catalysts which are generally fixed to a polymer. We looked, too, at this question with the goal of constructing an insoluble chiral diphosphine which would retain the main features of DIOP. We decided to choose as starting point a commercial polymer well known for its mechanical properties. A Merrifield resin was modified as indicated in *Figure 25*, and a supported chiral rhodium catalyst was easily prepared[14, 18]. This catalyst was inactive in the reduction of amino acid precursors, but it catalyses the reduction of several apolar olefins if benzene is taken as solvent.

Recently[12] we succeeded in reducing an enamide, α-*N*-acetylaminostyrene, which was previously studied in *Figure 19*. The reaction is much slower than in homogeneous conditions, but the enantiomeric excess (31 per cent S) is not too far from the value found in solution (43 per cent S). This result is interesting and allows some hope that polymers with suitable and useful hydrophilic properties could be found in the future for preparation of catalysts for reduction of polar substrates. Hopefully we discovered[14] a useful application of our supported catalyst in the hydrosilylation reaction. It is very active in the hydrosilylation of ketones. A detailed study was made for acetophenone and phenylnaphthylsilane (*Figure 26*). (S) phenylmethylcarbinol was prepared with an excellent yield and 58 per cent enantiomeric

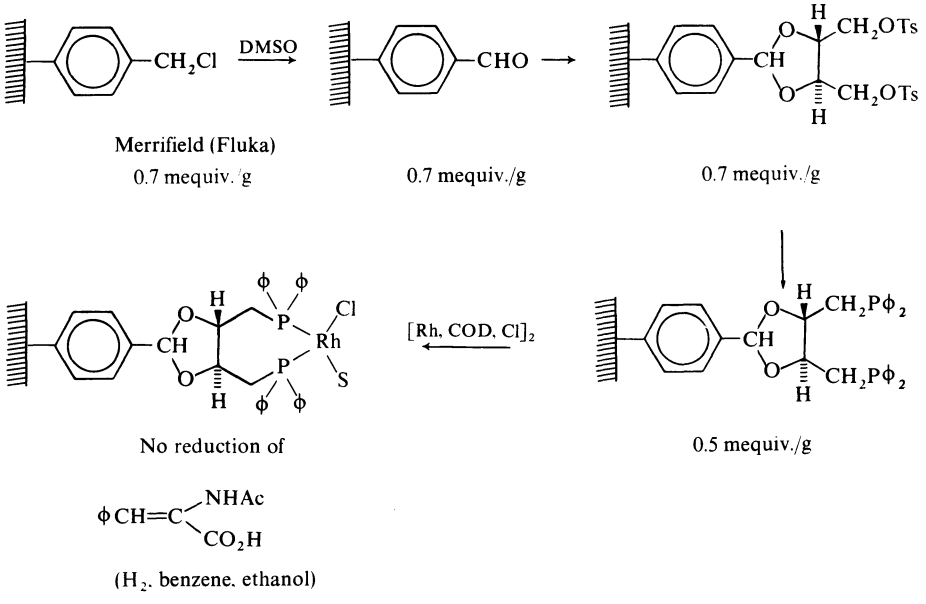
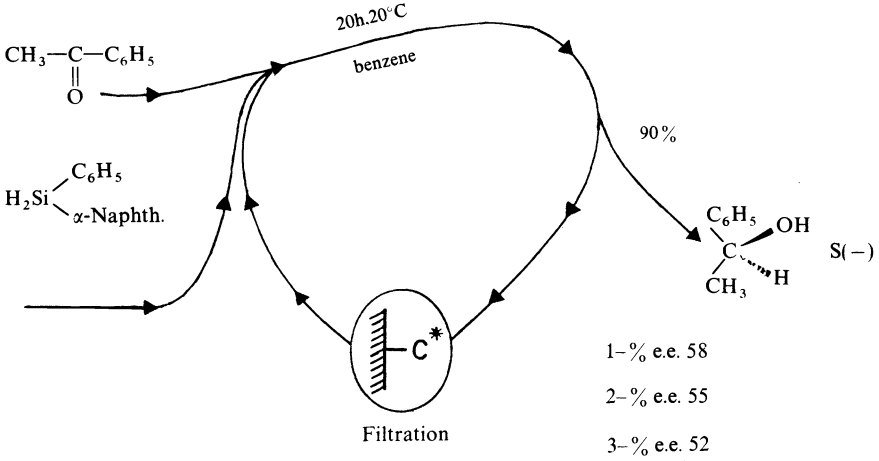


Figure 25



Dumont, Poulin, Dang and Kagan
J. Amer. Chem. Soc. **95**, 8295 (1973).

Figure 26

excess, as in the homogeneous reaction. The catalyst was reused several times after filtration. The slight decrease in optical yield must be attributed to a very slow oxidation of the catalyst by atmospheric oxygen during the filtration leading to another catalytic species. In general the first asymmetric hydrosilylation gives results quite similar to those of the homogeneous reaction (*Figure 27*). This seems to mean that the steric course of the catalysis is not drastically changed by the neighbourhood of the polymer. The diminution of reactivity must be related to the difficulty of access for the reactants to the catalytic sites.

Ketone	Silane	% e.e. Heterogeneous	Homogeneous
PhCOMe	$H_2SiPhMe$	12	13
	—	8	
PhCOMe	H_2SiPh_2	29	28
	—	22.5	
PhCOMe	$H_2SiPhNp$	58.5	58
	—	55	
	—	52	
PhCOiPr	$H_2SiPhMe$	6.5	20
PhCOiPr	H_2SiPh_2	28	35

Figure 27. Heterogeneous hydrosilylation

It is interesting to point out that our experiments show that the polymer has two helpful actions: the catalyst is much less sensitive to air oxidation than in solution and it is active independently of the Rh/DIOP ratio. In solution it is quite critical to use a Rh/DIOP ratio < 2, otherwise the catalytic activity strongly decreases [presumably by formation of $Rh(DIOP)_2^+ Cl^-$]. The supported catalyst retains its activity whatever may be the Rh/DIOP ratio[14]. In *Figure 28* are given some data on the reduction of acetophenone by diphenylsilane. It is known[19] that the polymeric chains in a phosphinated Merrifield resin two per cent crosslinked exhibit some flexibility. It is then possible to coordinate a rhodium atom to several phosphines located on different chains. In our case a rhodium atom is

Diphosphine/Rh	Yield %	% e.e.
1	80	20.5
2	82	29.5
4	86	23.0

Figure 28. Heterogeneous hydrosilylation of $C_6H_5COCH_3$ by $(C_6H_5)_2SiH_2$

complexed by the two phosphorus atoms afforded by the DIOP moiety. It must be difficult to form the equivalent of $Rh(DIOP)_2^+$ because of the geometrical requirements. But a likely possibility (*Figure 29*) is the formation of a RhP_3 complex (P being a phosphorus atom) which can dissociate to the active species RhP_2.

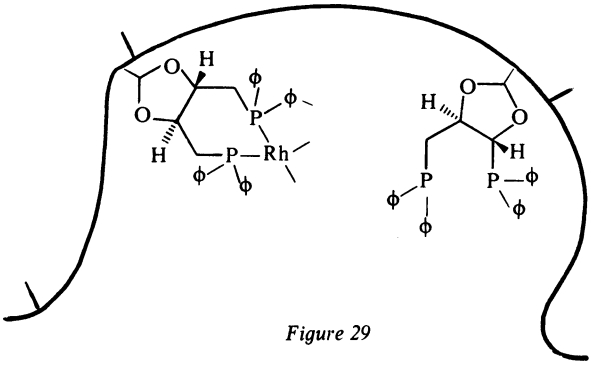


Figure 29

CONCLUSION

Some concluding remarks seem appropriate: (i) The rhodium catalysts can accommodate chelating diphosphines in which the chiral centres are far from the metal atom. Good asymmetric induction can often be observed during reduction or hydrosilylation, presumably due to the predominant chiral conformation of the chelated ring. Other rhodium catalysts than RhCl diphosphine can be utilized in asymmetric reduction and can extend the scope of chiral phosphines. For example, $HRh(DIOP)_2$ was recently prepared by James[20] and, like ClRh(DIOP), catalyses the asymmetric reduction of α-*N*-acetamidoacrylic acid, although with a lower optical yield. We found that clusters such as $Rh_6(CO)_{16}$ are good catalysts for the reduction if six equivalents of DIOP are added[13]. The interesting point is the reverse stereospecificity [with respect to RhCl(DIOP)] which we observed in the reduction of aminoacid precursors. We do not know which is the active species but we can exclude $RhH(DIOP)_2$ which gives asymmetric induction in the same direction as RhCl(DIOP).

(ii) DIOP is a good chiral ligand which was recently utilized by several laboratories in a great variety of asymmetric reactions such as hydroformylation[21] with rhodium catalysts, hydrocarboxylation and asymmetric alkylation with nickel and palladium catalysts. In order to have at hand catalysts which could be adjusted to specific prochiral substrates we are developing the synthesis of chiral diphosphines derived from DIOP, particularly those without a twofold axis of symmetry.

(iii) The future of the asymmetric catalysis is closely related to the diversification of chiral ligands. In order to avoid the resolution step it is particularly important to start from cheap natural compounds. We are preparing several new types of mono- and diphosphines derived from natural products other than tartaric acid (amines, sugars . . .).

A better understanding of the mechanisms of reactions is important too; it will help in devising appropriate structural changes in the ligands.

We started our researches at a time when it was impossible to estimate the potential of asymmetric catalysis with chiral complexes since no examples with optical yields higher than ten per cent had been described. It is clear now that values of 90 per cent can be reached if good asymmetric ligands are available. Is it possible to do better? Why not, we are making efforts in this direction and hope to approach enzymatic stereospecificity.

As pointed out at the beginning, the great advantage of asymmetric catalysis is the good balance between the amount of synthesized compound with respect to the auxiliary chiral material. In our case this number can be as high as 10^4 for the aminoacid synthesis[22]. If now we can anticipate being able to use a supported chiral catalyst this last number should be increased considerably. The future of asymmetric catalysis as a preparative method appears promising but much effort remains to be made to develop general methods, and to improve and to predict the stereospecificity.

All the work described is due to my co-workers Drs Dang, Dumont, Langlois, Gelbard and Poulin.

I thank CNRS, DGRST and the French Institute of Petroleum for financial support.

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