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ORGANOMETALLIC CATALYSIS IN ASYMMETRIC SYNTHESIS

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Abstract - Asymmetric reactions involving organometallic catalysis are briefly reviewed. Recent developments in the field include the discovery of a few new asymmetric catalytic reactions and the improvement of the enantiomeric excess of already known reactions. The factors determining type and extent of asymmetric induction are considered and the difficulties encountered in the attempts to identify the origin of asymmetric induction in organometallic asymmetric catalysis are discussed.

1. Introduction

The most efficient way to utilize chiral (*)compounds in asymmetric synthesis is to use them as catalysts (1). The broad field of asymmetric catalysis includes catalysis by organic compounds (including enzymes), by inorganic compounds as well as by organometallic compounds which have received increasing attention since 1970.

In this brief overview we shall confine ourselves to the consideration of homogeneous organometallic catalysis by transition metals, i.e., catalytic reactions involving as intermediates compounds containing metal-to-carbon bonds between the catalytic system and the substrate or its transformation products (including π-olefins and π-allyl metal complexes). We have previously reviewed the field in 1977 (2) and 1979 (3) and an interesting review on the same subject has appeared recently (4). Therefore we shall consider mainly the progress in this field in the last three years discussing mainly reactions in which high e.e.'s have been obtained.

2. Main achievements in asymmetric homogeneous catalysis with transition metal complexes

Table 1 lists the most relevant asymmetric catalytic reactions involving homogeneous organometallic catalysis. The reactions are classified, when possible, according to the new chiral center forming bond which is originated during the catalytic reaction. For each reaction, the compounds are classified according to which functional group is involved in the asymmetric reaction and, for each type of compound, the substrate is indicated for which the highest enantiomeric excess is reported. At the bottom of the table are listed some miscellaneous reactions in which the formation of the new chiral center is due to reactions involving bonds not included in the chirality center; in these reactions differentiation between enantiotopic groups takes place. When only optical yields are reported in the literature the e.e. value is given in parenthesis.

From the Table 1 it appears that the large prevalence of the results concerns reactions in which the substrate becomes chiral because of the formation of a new $\rangle$C-H or $\rangle$C-C$\langle$ bond; however there are reports for reactions in which the new chirality center is originated by the formation of $\rangle$C-N$\langle$ $\rangle$C-O-, $\rangle$C-Br or $\rangle$C-Si$\langle$ bonds. Hydroformylation and hydrosilylation appear in two sections of the table, since the origination of the chiral center in the catalytic reaction can involve either the formation of a $\rangle$C-H bond (e.g. the case of 1,1-disubstituted ethylenes) or of a $\rangle$C-C$\langle$ or a $\rangle$C-Si$\langle$ bond (e.g. the case of monosubstituted ethylenes).

Only for epoxidation the evidence for metal-carbon bonds participating in the reaction is small although in some cases olefin-complexes of molybdenum have been postulated to be intermediates (36). The most spectacular results in asymmetric epoxidations concern allylic alcohols (30) and in this case it is assumed (37) that the olefinic substrate is bound to the metal through a M-O-C- bond and the present conception of this catalytic reaction, is that it does not involve, strictly speaking, organometallic intermediates.

The asymmetric Diels-Alder reaction (4) is not mentioned in the table, as it is catalyzed by main group elements.

Table 2 reports transition metal catalyzed kinetic resolutions. Also in this case some reactions are listed (Reactions 9, 13, 14, 15, 17) for which -C-M bonds in the intermediates have not been ascertained. Besides the enantiomeric excess, the conversion is reported in order to make it possible to calculate the ratios between the reaction rate constants for the two antipodes ($k_{(S)}/k_{(R)}$). Only in the case of epoxidation have results been obtained

(*) As in previous reviews (2,3) we use the expression "chiral" compound to indicate a chiral non-racemic compound.

Table 1. Asymmetric Reactions Involving Organometallic Catalysis Classified According to the Bond Involved in the Formation of the New Chirality Center

Entry	Reaction Type	Catalyst	Asymmetric ligand[a)]	Substrate(s)	e.e. %	Ref.
			C*—H			
1	Hydrogenation	[Rh(COD)(Dipamp)] BF_4	Dipamp	(Z)-$C_6H_5CH=C(COOH)NHCOCH_3$	95	5
2	Hydrogenation	$[Rh(NBD)Cl]_2$	Diop	2-$C_{10}H_7COCH_2N(C_2H_5)_2$	95	6
3	Hydrogenation	$[Rh(NBD)(Diop)]ClO_4$	Diop	$C_2H_5(CH_3)C=NCH_2C_6H_5$	(22)	7
4	Hydroformylation	$[Rh(NBD)Cl]_2$	Chiraphos	i.$C_3H_7(CH_3)C=CH_2$	(21.8)	8
5	Hydrocarbonylation	$PdCl_2(C_6H_5CN)_2$	Diop-dbp	$C_6H_5(CH_3)C=CH_2$	(69)	9
6	Hydrosilylation	$NiCl_2$	BzMePhP	$C_6H_5(CH_3)C=CH_2$	(20.9)	10
7	Hydrosilylation	$[Rh(COD)Cl]_2$	Thiazolidine[b)]	$C_6H_5COCH_3$	87.6	11
8	Hydrosilylation	$[Rh(C_2H_4)_2Cl]_2$	Diop	$C_6H_5(CH_3)C=NCH_2C_6H_5$	65	12
9	Isomerization	$RhH(CO)(PPh_3)_3$	Diop	$C_2H_5CH=C(CH_3)CH_2OH$	(4)	13
10	Isomerization	$[Rh(COD)(Binap)]ClO_4$	Binap	(E)-$(CH_3)_2C=CH(CH_2)_2C(CH_3)=CHCH_2N(C_2H_5)_2$	96	14
11	Displacement	$Pd(Sal)_2$	Sal[c)]	(i.$C_4H_9)_3Al/C_6H_5(C_2H_5)C=CH_2$	(26.6)	15
			C*—C			
12	Hydroformylation	$PtCl_2/SnCl_2$	Diop-dbp	$C_6H_5CH=CH_2$	(79.8)	16
13	Hydrocarbonylation	$Pd(OOCCF_3)_2$	Ph_2P(Neomenthyl)	$C_6H_5CH=CH_2$	52	17
14	Hydrovinylation	$[\eta^3-C_3H_5NiCl]_2/Et_3Al_2Cl_3$	i.PrP(Menthyl)$_2$	Norbornene	(80.6)	18
15	Cross-Coupling	$PdCl_2$	PPFA	$C_6H_5(SiMe_3)CHMgBr/CH_2=CHBr$	95[g]	19
16	Allylation	$NiCl_2$	Chiraphos	Cyclohexenylphenylether/C_2H_5MgBr	(97.7)[h]	20
17	Polymerization	$Ti(OR)_4/Al_2Et_6$	R=Menthyl	$CH_3CH=CH-CH=CH_2$	n.d.	21
18	Cyclooligomerization	$Ni(COD)_2$	Phospholane[d)]	$CH_2=CH-CH=CH_2$	(35)	22
19	Rearrangement	$Ni(COD)_2$	Phospholane[e)]	cis-Divinylcyclobutane	(22)	23
20	Carbenoid Reaction	Cu(Sal)	Sal[f)]	$Cl_3CCH_2CH=C(CH_3)_2/N_2CHCOOC_2H_5$	91	24
21	Hydrocyanation	$Pd(Diop)_2$	Diop	Norbornene	(35)	25

22	Cross-addition	$Ni(COD)_2$	BzMePhP	Norbornadiene/Methylenecyclopropane	n.d.	26
			C*—N			
23	Amination of Dienes	$Pd(OOCCH_3)_2$	Dipamp	CH_2=CH-CH=CH_2/($\underline{i}$.C_3H_7)$_2$NH	15.1	27
			C*—O			
24	Cyclization	(η^3-Pinenyl)$Pd(OOCCH_3)$	β-Pinene	o-(3-methylallyl)phenol	(19.5)	28
25	Allylic Esterification	Cu(L-Prolinato)$_2$	L-Prolin	Cyclohexene	(16.5)	29
26	Epoxidation	Ti($O\underline{i}$.Pr)$_4$	Diethyltartrate	(E)-$C_9H_{19}CH_2CH$=$CHCH_2OH$	>95	30
			C*—Br			
27	Addition of $BrCCl_3$	$[Rh(CO)_2Cl]_2$	Diop	C_6H_5CH=CH_2	(32)	31
			C*—Si			
28	Hydrosilylation	$PdCl_2$	PPFA	C_6H_5CH=CH_2	(52)	32
		Asymmetric reaction not involving bonds at the chirality center				
29	Dehydrogenation of Diols	Ru_2Cl_4(Diop)$_3$	Diop	$HOCH_2CH_2CH(\underline{i}.C_3H_7)CH_2CH_2OH$	15.2	33
30	Hydrogenation of Anhydrides	Ru_2Cl_4(Diop)$_3$	Diop	2-Phenylglutaricanhydride	20.0	34
31	Dehydrohalogenation	Co(3,5-Cl-Sal)	CHXDA	$ClCH_2CH(OH)CH_2Cl$	(67)	35

a) For the formulas of the chiral ligands refer to the original literature. b) 2-[2-pyridyl]-4-methoxycarbonyl-thiazolidine. c) N-[1-methylpropyl]salicylaldimine. d) 2-$\underline{t}$.butyl-4,5-diethoxycarbonyl-1,3,2-dioxaphospholane. e) 2-$\underline{t}$.butyl-4,5-dimethoxyethoxycarbonyl-1,3,2-dioxaphospholane. f) N-[1-methyl-2,2-bis(2-octyloxy-5-$\underline{t}$.butylphenyl)-3-oxypropyl]-salicylaldimine. n.d. = not determined. g) The Grignard reagent is chiral racemic; due to its rapid racemisation, however, it is possible to obtain a single antipode of the product. h) The racemic reagent gives an organometallic intermediate in which the η^3-allylic moiety is achiral. Therefore enantiomer discrimination of the reagent does not influence the optical yield of the reaction.

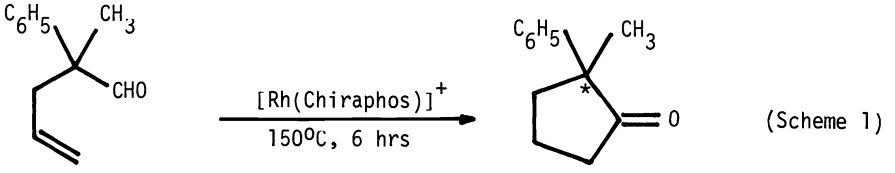
Table 2. Antipodes Differentiating Reactions (Kinetic Resolutions) Involving Organometallic Catalysis

Entry	Reaction Type	Catalyst	Asymmetric ligand [a]	Substrate	e.e. % [b]	Conversion %	Ref.
1	Rearrangement	Rh(Diop)Cl	Diop	1-methyl-2,2-diphenylbicyclo [1.0.0] butane	35	73	38
2	Isomerization	$Ni[P(OEt)_2Ph]_4$	MePhPrP	$C_2H_5CH(CH_3)CH=CH_2$	(22)	50	39
3	Cannizzaro Reaction	$H_4Ru_4(CO)_8(Diop)_2$	Diop	$C_2H_5CH(CH_3)CHO$	(0.2)	37	40
4	Cross-coupling	$NiCl_2$	Valphos	exo-2-norbornylmagnesium chloride	(15)	38	41
5	Allylation	$NiCl_2$	Chiraphos	$C_6H_5OCH(CH_3)CH=CH_2/C_6H_5MgBr$	(5)	45	20
6	Hydrogenation	$[Rh(COD)Cl]_2$	Diop	$C_2H_5CH(CH_3)C(CH_3)=CH_2$	(22)	46	8
7	Hydroformylation	$RhH(CO)(PPh_3)_3$	Diop	$t.C_4H_9CH(CH_3)CH=CH_2$	(14.0)	49	8
8	Hydrocarbonylation	$PdCl_2$	Diop	$C_2H_5CH(CH_3)CH=CH_2$	(1.2)	50	42
9	Epoxidation	$Ti(Oi.Pr)_4$	Diisopropyltartrate	$C_4H_9CH(OH)C(CH_3)=CH_2$	>96	55	43
10	Hydrovinylation	$[\eta^3-C_3H_5NiCl]_2/Et_3Al_2Cl_3$	$i.PrP(Menthyl)_2$	2-Bornene	(13.3)	40	18
11	Hydrosilylation	$[Rh(1,5-HD)Cl]_2$	Diop	$C_6H_5COCH(CH_3)N(CH_3)_2$	23	40	44
12	Polymerization	$Ni(OOCR)_2/Bu_3P$	$R=C_2H_5(CH_3)CH$	γ-Benzylglutamate N-carboxy-anhydride	(11.6) [c]	28	45
13	Hydrolysis	L-HistidineCo(II)	L-Histidine	Leucinemethylester	n.d. [d]	n.d. [d]	46
14	Acetoxylation	$Li^+[Co(Sal)_2CHXDA]^-$	CHXDA	Propylene oxide	(4.8)	29.8	47
15	Isomerization	$Li^+[Co(Sal)_2CHXDA]^-$	CHXDA	Propylene oxide	(6.2)	8.3	48
16	Dehydrogenation	$RuCl_2(NMDP)_3$	$Ph_2P(Neomenthyl)$	$C_6H_5CH(CH_3)OH$	(4.8)	81.2	49
17	Dehydrohalogenation	$Li^+[Co(Sal)_2CHXDA]^-$	CHXDA	$CH_3CHClCH_2OH$	(18.7)	40.3	50

a) See corresponding footnote in Table 1. b) The e.e.'s refer to the recovered substrates. The e.e.'s are related with the conversion to the ratios between the rate constants for each antipode (see, for instance, Ref.37). c) Calculated from the values of the e.e. of the reaction products and from the conversion, assuming no interfering reactions. d) A maximum k_L/k_D value of 1.42 is reported.

which have a significance for asymmetric organic synthesis. Some other results are interesting, as they give some information (8) about the mechanism of the catalytic reactions.

Only two new asymmetric reactions that fit within the scope of this review have appeared since 1979, one being the addition of hydrogen cyanide to double bonds in the presence of $Pd(Diop)_2$ as the catalyst precursor(25) and the second, the cyclization of an unsaturated aldehyde catalyzed by $[Rh(Chiraphos)]^+$ (51) (Scheme 1)(see addendum).



(Scheme 1)

In the first case an e.e. of 35% was reported (Table 1, reaction 21), while in the second case an e.e. of 50% for the 2-methyl-2-phenylcyclopentanone was obtained.

The main progress in asymmetric catalysis in the last four years was the remarkable improvement of the e.e. in already known reactions. There are now ten asymmetric catalytic reactions (Table 1, ractions 1, 2, 7, 10, 12, 14, 15, 16, 20, 26) in which with particular substrates e.e.'s of 80% or more have been achieved. Of the six substrates which gave e.e.'s of 95% or more, four have, besides the reacting group, a second (Reactions 2 and 26) or even two other (Reactions 1 and 10) functional groups which could interact with the metal atom. The substrates in the reactions having e.e.'s around 80% (Reactions 8, 12 and 14) do not contain additional polar groups, but two of them contain phenyl groups, which might interact (67) with the aromatic groups of the asymmetric ligands. These data indicate that functional groups suitably located in the substrate may have an enhancing effect on e.e., but this effect should not be overemphasized, as shown by reactions 14, 15, 16 and 20.

Concerning the structure of the ligands, in only one case (reaction 14) was a high e.e. obtained using a monophosphine as the chiral ligand. However, the reaction was carried out at very low temperature. In all the other cases ligands forming chelate rings with the metal present in the catalyst were used. In the catalyst precursors a five member chelate ring was present in three and a seven member ring in four cases. In two cases the catalyst was prepared in situ (reactions 7 and 26) and it can be assumed that a chelation ring is present in the catalytic species.

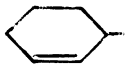
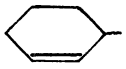
In most cases the stereoselectivity of the catalytic systems is very strongly dependent on the nature of the substrate and small changes in the structure of the substrate usually cause dramatic changes in the enantiomeric excess (Table 3). For hydrogenation and hydrosilylation attempts have been made to find a rationale for the above changes in e.e. The very large change in e.e. observed in the hydrogenation of the methylesters of methylenebutanedioic acid and of 2-methylenepentanedioic acid (Table 3, entries 8 and 9) has been attributed to the differences in abilities of the carbomethoxy group far from the double bond to interact with the metal atom in the π-complex (5). The low e.e. found for itaconic acid in comparison with its diester (Table 3, entries 5 and 8) was related to the tendency of the acid to form intermolecular hydrogen bonding, thus decreasing the interactions between carboxylic groups and the metal atom of the catalyst. In the hydrogenation of aminoketones (Table 3, entries 10, 11 and 12) both electronic effects and specific interactions (55) of the -OH group of the chiral ligand and of the catalyst with the carbonyl group of the substrate can be considered.

Concerning the hydrosilylation of ketoesters (Table 3, entries 13 and 14), the high e.e. obtained in the case of butyl pyruvate has been ascribed to an attractive interaction between the carbonyl of the ester group and the metal (56); this interaction should be less favored in butyl acetoacetate.

No clear explanation has been given for the surprising results obtained in allylation (Table 3, entries 1 and 2), whereas differences in the cross-coupling reactions(entries 3 and 4) most probably arise from the differences in structures of the species which alkylate the chiral catalyst (53).

This large substrate selectivity is a well known feature in asymmetric catalysis and is one of the main factors hindering progress in its applications to organic synthesis. In fact, predictions in the case of new substrates are very uncertain and a time consuming screening of different catalytic systems is necessary in general because of lack of reasonable criteria for the design of suitable catalytic precursors.

Table 3. Some Examples of the Influence of Changes in the Substrate Structure on Enantiomeric Excess.

Entry	Reaction Type	Substrate(s)	Catalytic System	Optical yield (%) and absolute configuration	Ref.
1	Allylation	 OC_6H_5 + CH_3MgBr	[(S,S)-Chiraphos]$NiCl_2$	4.8 (S)	16,52
2		 OC_6H_5 + C_2H_5MgBr		97.7 (R)	
3	Cross-Coupling	C_6H_5Br + $C_2H_5(CH_3)CHMgBr$	[(R)-Phenphos]$NiCl_2$	50.0 (R)	53
4		C_6H_5Cl + $C_2H_5(CH_3)CHMgCl$		18.5 (R)	
5	Hydrogenation	$H_2C=C(COOH)CH_2COOH$	[Rh(COD)(R,R)-Dipamp]BF_4	38 (R)	5,54
6		$H_2C=C(COOH)CH_2COOCH_3$		55 (R)	
7		$H_2C=C(COOCH_3)CH_2COOH$		88 (R)	
8		$H_2C=C(COOCH_3)CH_2COOCH_3$		88 (R)	
9		$H_2C=C(COOCH_3)CH_2CH_2COOCH_3$		2.8 (n.r.)	
10	Hydrogenation	$C_6H_5COCH_2NH_2 \cdot HCl$	[Rh(HD)Cl]$_2$ + BPPFOH	52 (R)	55
11		$p.HOC_6H_4COCH_2NH_2 \cdot HCl$		69 (R)	
12		$3,4-(HO)_2C_6H_3COCH_2NH_2 \cdot HCl$		95 (R)	
13	Hydrosilylation	$CH_3COCOOC_4H_9$ + 1-NpPhSiH_2	[Rh(COD)Cl]$_2$ + (S,S)-Diop	83 (S)	56
14		$CH_3COCH_2COOC_4H_9$		24 (S)	

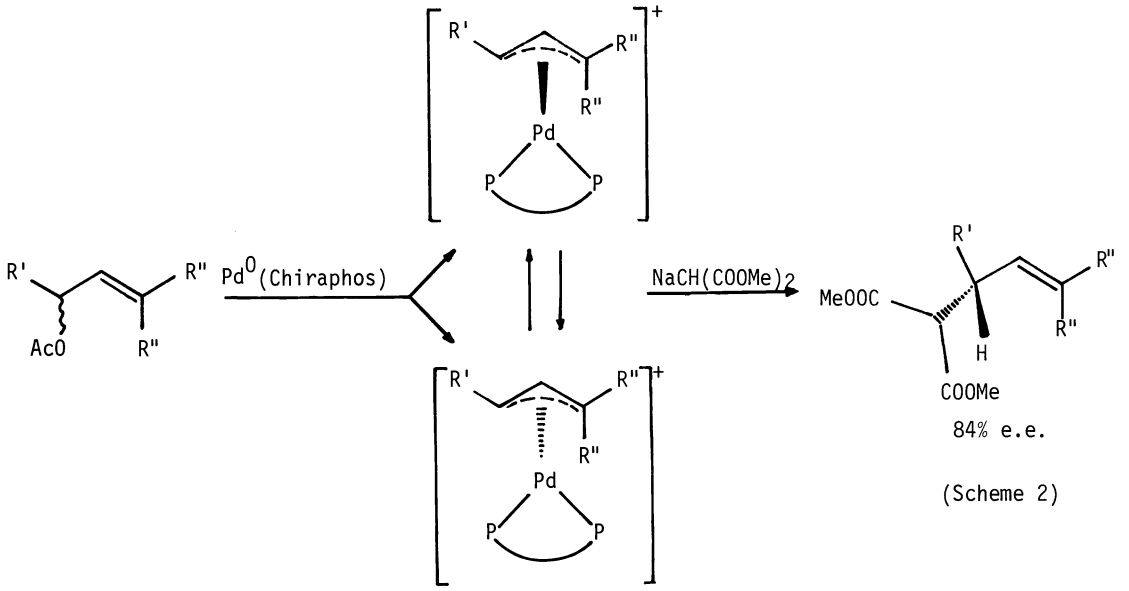
3. Present state of the knowledge about the factors determining the sign and the extent of asymmetric induction in homogeneous catalysis.

The present knowledge about asymmetric homogeneous catalysis does not allow, for a given substrate-catalyst pair, the prediction of the sign and, even less, of the extent of asymmetric induction. Therefore it is still not possible to rationally plan a catalytic system suitable to convert a given substrate with high e.e..

As it is known (57) in one step kinetically controlled asymmetric reactions the sign and the extent of asymmetric induction depend on sign and value of the difference between the energies of the two transition states ($\Delta G^{\ddagger}$) leading to the (R) or to the (S) antipode respectively. The main difficulties in this case are to envisage the structures of the two transition states and to identify the differences in the attractive and the repulsive interactions between the reacting moieties in each of the two activated complexes. The regularities observed with different substrates and the conformational analysis of the interacting moieties in the diastereomeric transition states are the basis for some rules which allow for some asymmetric reactions a somewhat reasonable prediction of the antipode which should prevail in the reaction product (e.g. Prelog's and Cram's rules (58)).

In general asymmetric catalytic processes are multistep reactions, and in order to use an approach similar to that mentioned for non catalytic asymmetric reactions, it is obvious that one must find the step of the catalytic cycle after which no equilibration between the diastereomeric intermediates leading to either antipodes takes place (*). This requires a sufficient knowledge of the mechanism of the catalytic reactions and a series of experiments directed either to isolate each intermediate (59) and to determine the rate of its transformation into the succesive one (60) or to obtain the above information from the composition of the reaction products obtained from suitably chosen substrates (8,42). In any case the isolation and the determination of the structure of the intermediate is essential to a conception of the structure of the transition states involved in the catalytic processes. A further complication is given by the possibility that the first irreversible step of the catalytic reaction can change, depending on the reaction conditions (e.g., on temperature and on H_2-pressure as shown in a hydrogenation reaction (60)) and on the substrate.

For the reactions in which e.e.'s of at least 80% have been reached, the first irreversible step has been established experimentally only in the hydrogenation of (Z)-methyl α-acetamidocinnamate with the catalytic systems $[Rh(Chiraphos)]^+$ or $[Rh(Dipamp)]^+$ (60). Good indirect indications concerning the first irreversible step have been obtained in the hydroformylation of the three linear butenes with the catalytic systems Rh/Diop, Rh/Chiraphos, Rh/EtDiop, Rh/CyDiop (61), Pt/Diop and Pt/Chiraphos (8,62) and in the hydrocarbalkoxylation of the same substrates and of 2-methyl-1-butene (42) with the catalytic system $PdCl_2$/Diop.



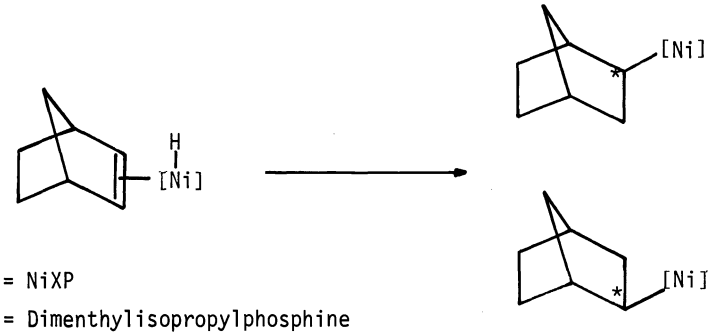
84% e.e.

(Scheme 2)

(*) This step is often the first irreversible step of the catalytic reaction; in the literature it is also indicated as the rate determining step; however it is not necessarily the step with the smallest rate constant.

Good evidence has also been obtained in some allylic alkylations of non cyclic compounds where there is an equilibrium between the two diastereomeric π-allyl intermediates (Scheme 2) and the nucleophilic attack by the carbanion to the π-allyl-group should be considered as the irreversible step which determines the e.e. (63).

No experimental data are available to determine the first irreversible step in other reactions with e.e.'s of 80% or higher. However some reasonable hypotheses have been proposed. For the hydrovinylation of norbornene (18), the insertion of the double bond of norbornene into a M-H bond is believed to be the first irreversible step in which asymmetric induction takes place (Scheme 3).

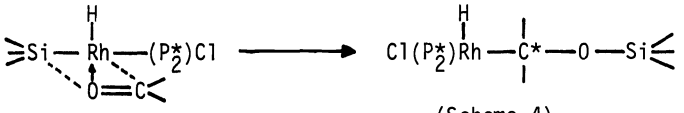


(Scheme 3)

[Ni] = NiXP

P = Dimenthylisopropylphosphine

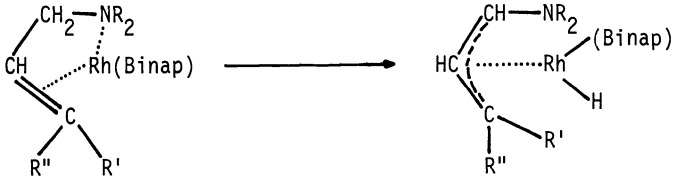
The insertion reaction of the C=O group in a M-Si≤ bond is believed to be the step in which the e.e. is determined (56) in the hydrosilylation of ketones (Scheme 4).



P^*_2 = BMPP or DIOP

(Scheme 4)

As far as the enantioselective hydrogen migration of allylamines (14) is concerned, it has been conclusively shown that there is a stereospecific 1,3-hydrogen migration and an η-allyl-hydride-Rh-complex has been postulated to be the reactive intermediate (64). The oxidative addition (Scheme 5) of a -C-H group to the metal atom may be assumed to be the step that determines the asymmetric induction.



(Scheme 5)

Empirical rules to predict the chirality of the prevailing antipode in the products based on the steric interaction between incoming substrate and catalytic complex have been formulated for the hydrogenation of olefinic compounds and for hydrosilylation of ketones. In the few cases investigated this gives relatively good results (65). Satisfactory results in the predictions of prevailing antipode in the products have been also obtained in terms of steric approach control for the hydrogenation of the acrylic derivatives on the basis of the steric hindrance around the metal atom of the catalytic complex, deduced from X-ray data on some catalyst precursors (66). Also in this case, predictions are restricted to a relatively narrow class of olefins. The reliability of these empirical rules, for some of which no theoretical basis exists, does not contribute per se to the knowledge of the structure of the catalytic complexes or of the reaction mechanisms. However, the rules show that, notwithstanding the relatively low absolute value of the differences between the energies of the diastereomeric transition states determining the e.e., some regularities might be found which, combined with the knowledge of the structure of the reaction intermediates, could contribute to a better understanding of asymmetric catalysis.

The results obtained in the asymmetric carbonylation of olefins seem to confirm this point of view. In this case, the knowledge about the mechanism of the reaction and about the step which in the case of the hydrocarbonylation of the linear butenes determines the asymmetric

induction has been used to propose a simple stereochemical model based on repulsive interactions between approaching substrate and catalysts (8,42). This model, given the type of antipode obtained in the hydroformylation of (Z)-2-butene, allows the prediction of the prevailing antipode produced with the same catalytic system when not only internal olefins but also mono- and 1,1-disubstituted ethylenes are used. This stereochemical model has been tested with 111 different substrate-catalyst systems involving 23 substrates and 15 catalytic systems; it gives a correct prediction in 81% of the cases examined and allows also the correct prediction of the prevailing isomer in 88% of the cases. Interestingly enough, 65% of the wrong predictions for the prevailing antipode and 70% of the wrong predictions for the prevailing isomer involve substrates having a phenyl group conjugated with the double bond undergoing hydroformylation; further exceptions concern substrates in which a heteroatom (e.g. -O- or -N<) is present in α-position with respect to the double bond. These results might indicate that the stereochemical model which is based exclusively on repulsive interactions fails when attractive interactions or electronic effects are superimposed on the repulsive interactions. Further experiments are in progress to investigate the nature of the interactions which cause the prediction by the model to be wrong. While a prediction on the percent of e.e. is far beyond the possibilities of the above oversimplified model, the approach to the problem seems to be promising, at least for suggesting further interesting experiments.

4. Final remarks

The difficulties discussed concerning the attempts to identify the origin of the asymmetric induction in the second part of this paper clearly show that in the near future results of practical importance in the field organometallic asymmetric catalysis will be mainly obtained empirically, combining for a given substrate chemical intuition with the systematic variation of the components of the catalytic system and of the reaction conditions.

A rational planning of a catalytic system, given the structure of the substrate, requires a much better knowledge of the mechanism of catalytic reactions including the investigation of the structure of the intermediate catalyst-substrate complexes and of the step that determines the asymmetric induction. Particularly relevant are the attempts to investigate the geometry of the transition states for the above steps. This type of investigation has been carried out till now on organic reactions and should be extended to organometallic reactions, where interactions between organic molecules and organometallic complexes take place.

The nature of organometallic catalysis and particularly its stereospecificity excludes the possibility for general rules for planning efficient catalytic systems disregarding the nature of the substrates and of the intermediates; however an improvement in the methods for investigating weak attractive interactions and geometry of the transition states could greatly contribute to the synthesis of tailor-made catalysts and to a greater use of asymmetric metallorganic catalysis in organic synthesis.

5. Addendum

After this review was written, the following three new asymmetric reactions appeared in the literature:

a) the cyclocondensation of aldehydes with siloxydienes catalyzed by tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato]europium (III); best reported e.e. 58%. (M.Bednarski, C.Maring and S.Danishefsky, Tetrahedron Lett., 24, 3451 (1983)).
b) the addition of diethylzinc to arylaldehydes catalyzed by bis[(-)-camphorquinone-α-dioximato]-cobalt (II) and -palladium (II) complexes; best reported e.e. 57.7%. (N.Oguni, T.Omi, Y.Yamamoto and A.Nakamura, Chem.Lett., 841 (1983)).
c) the cis-dihydroxylation of alkenes catalyzed by bovine serum albumin-[2-phenylpropane-1,2-diolato]-dioxo-osmium (VI) complex; best reported e.e. 68%. (T.Kokubo, T.Sugimoto, T.Uchida, S.Tanimoto and M.Okano, J.Chem.Soc., Chem.Comm., 769 (1983)).

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