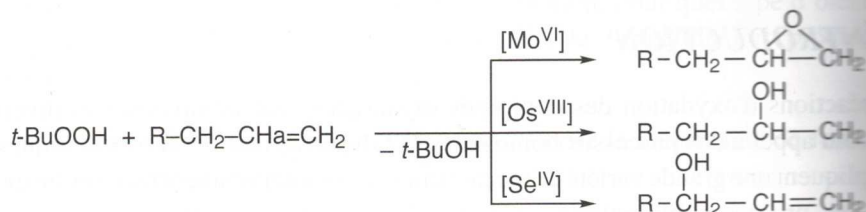


cumyle, $\text{PhC}(\text{CH}_3)_2\text{OOH}$ (précurseur du phénol), d'éthylbenzène, $\text{PhCH}(\text{CH}_3)\text{OOH}$ (précurseur du styrène) et de tertiobutyle, $t\text{-BuOOH}$ ^{16.1,16.2} (agent industriel d'époxidation des oléfines, voir ci-après).

Les grands procédés catalytiques tels que l'oxydation du butane en acide acétique, du *p*-xylène en acide téréphthalique et de l'éthylène en acétaldéhyde ont vu le jour vers la fin des années 1950. Ils nécessitent une catalyse basée sur les métaux de transition. A l'échelle du laboratoire, les catalyses de réactions d'oxydation à l'aide de l'hydroperoxyde de tertiobutyle sont variées :

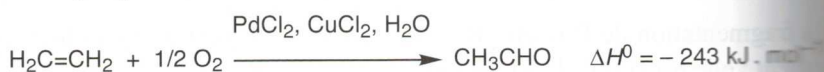


Plus récemment, les recherches sur la catalyse des réactions d'oxydation ont émergé d'une part de la chimie bioinorganique avec les modèles de cytochrome P-450 à structure porphyrinique et de méthane monooxygénase à structure non porphyrinique, et d'autre part de la chimie organique avec les réactions d'époxydation et de dihydroxylation asymétrique.

L'oxydation des alcanes et des arènes est traitée dans le chap. 17. L'activation biologique des alcanes (ainsi que l'activation C-H) par les enzymes mono oxygénases est discutée dans le chap. 19, § 4 et les transformations des hydrocarbures, y compris saturés par les catalyseurs hétérogènes, sont détaillées dans le chap. 20.

2. OXYDATION DE L'ÉTHYLÈNE EN ACÉTALDÉHYDE : PROCÉDÉ WACKER

Le procédé Wacker (1953) conduit actuellement à la production de 4 millions de tonnes d'acétaldéhyde par an :



La réaction stœchiométrique d'oxydation de l'éthylène en acétaldéhyde par PdCl_2 a été découverte par F. C. Phillips dès 1894 :



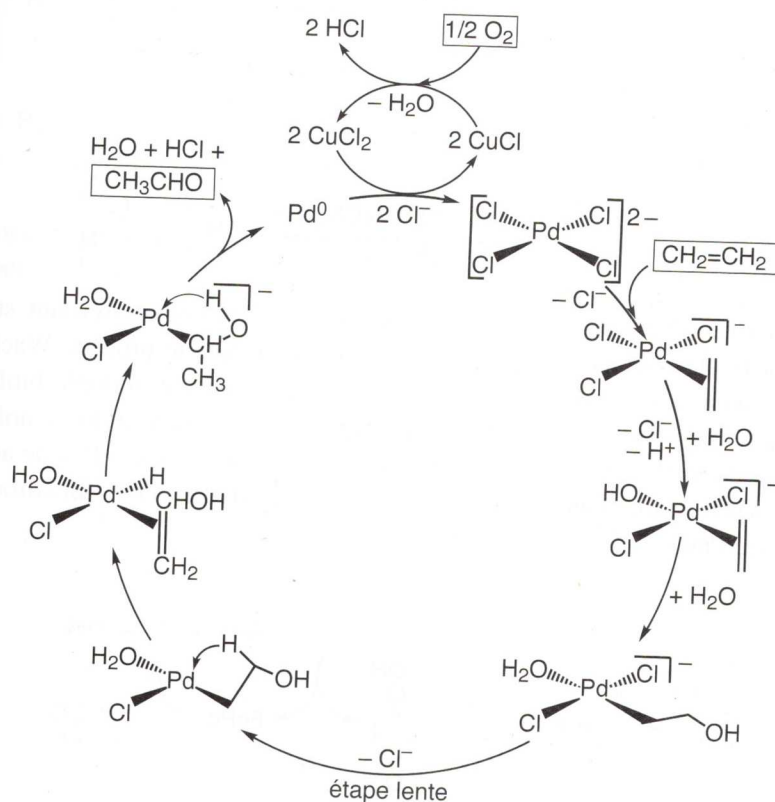
En milieu aqueux, PdCl_2 se présente en fait sous la forme de $[\text{PdCl}_4]^{2-}$. Le mécanisme détaillé n'a été proposé qu'en 1979 par Bäckwall et Stille ^{16.3,16.6} (voir cycle p. 407). L'isomérisation du ligand hydroxyéthyle par β -élimination et ré-insertion avant la décomposition en acétaldéhyde a été démontrée par le fait que l'addition de

D_2O , connue pour deutérer un énol, ne conduit pas ici à l'incorporation de deutérium dans l'acétaldéhyde. La loi de vitesse est :

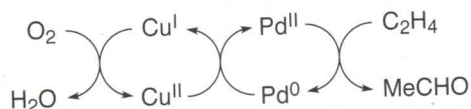
$$v = d(CH_3CHO)/dt = k([PdCl_4]^{2-})(C_2H_4)/(Cl^-)^2(H^+)$$

On en déduit que l'étape lente de la réaction implique, dans son état de transition, un complexe de palladium contenant une molécule d'éthylène et ayant perdu deux ligands chlorures et un proton.

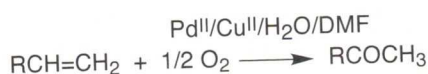
Dans cette réaction stœchiométrique, le palladium précipite sous forme de palladium colloïdal. En présence d'oxygène, la thermodynamique est favorable à la réoxydation de Pd^0 en Pd^{II} . Cependant, la formation de colloïde est trop rapide et les transformations structurales exigées sont trop importantes. La cinétique est donc défavorable. C'est l'introduction de $CuCl_2$ comme co-catalyseur qui a permis de rendre le processus catalytique opérationnel dans le procédé Wacker. En effet, $CuCl_2$ peut ré-oxyder Pd^0 en $PdCl_2$ rapidement grâce à un transfert de ligand Cl par sphère interne (c'est-à-dire par l'intermédiaire d'un pont Cl entre Cu et Pd) et $CuCl$ formé peut être ré-oxydé en $CuCl_2$ par O_2). Le système rédox Cu^I/Cu^{II} fonctionne comme catalyseur rédox de façon tout à fait analogue aux nombreuses catalyses rédox effectives dans les systèmes biologiques. Le couplage entre la catalyse par coordination et la catalyse rédox est un concept biochimique. Le cycle complet s'établit comme suit :



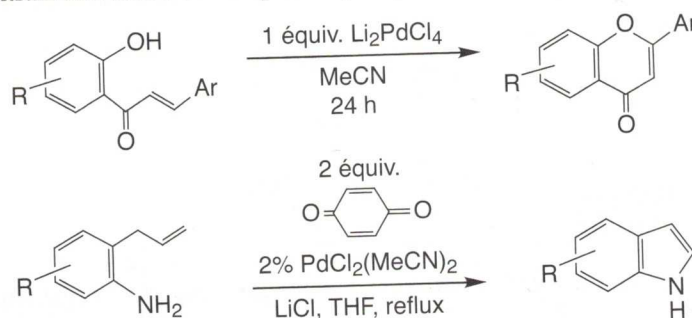
ou, en résumé :



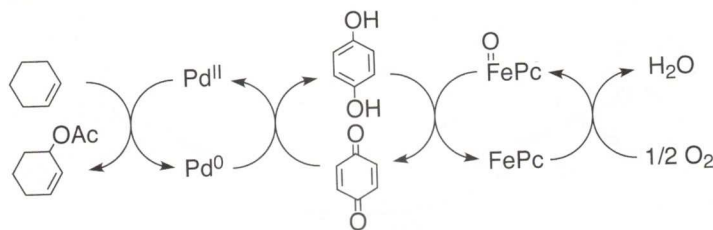
Le procédé Wacker a aussi été appliqué à la cétonisation des oléfines terminales. Bien que ces applications soient compliquées par l'isomérisation des oléfines, de bonnes sélectivités sont maintenant obtenues, en particulier si l'on ajoute du DMF, et la réaction est couramment utilisée en synthèse organique au laboratoire^{21.17}.



Pour cette cétonisation, *t*-BuOOH s'avère aussi supérieur à O₂ en terme de sélectivité. Par exemple, l'oct-1-ène est oxydé dans ces conditions par *t*-BuOOH dans le benzène en octane-1-one à 98% en 10 minutes à 20 °C. L'oxydation des oléfines internes est impossible sauf si elles sont conjuguées avec un carbonyle. Il est aussi possible d'utiliser un alcool ou une amine au lieu de l'eau comme nucléophile, ce qui conduit à un éther ou à une amine. Cette version, particulièrement utile pour la formation intramoléculaire de composés cycliques, est illustrée ci-dessous.



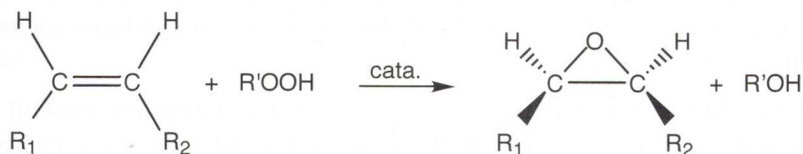
Dans le dernier exemple, la benzoquinone est utilisée comme oxydant stœchiométrique à la place du cuivre qui, lui, est catalytique dans le procédé Wacker. En mettant au point une catalyse multiple inspirée de la catalyse multiple biologique, Bäckwal a réussi à utiliser stœchiométriquement l'oxygène de l'air bien moins coûteux comme donneur d'oxygène pour acétoxyler le cyclohexène par l'acide acétique. Les catalyseurs rédox sont la phthalocyanine de fer (FePc) et la dihydroquinone couplés avec PdCl₂ :



Il existe de nombreuses variantes de systèmes catalytiques pour la cétonisation des oléfines terminales, par exemple avec le catalyseur de Wilkinson-Osborn $[\text{RhCl}(\text{PPh}_3)_3]$. Il est souvent possible de se passer également de cuivre en utilisant ce dernier catalyseur avec PPh_3 comme co-substrat ou avec $[\text{Pd}(\text{OAc})_2]$ en utilisant H_2O_2 comme oxydant. Cependant, ces systèmes catalytiques ont un mécanisme éloigné de celui du procédé Wacker et font intervenir des entités catalytiques métal-oxo ou métal-peroxo aux propriétés remarquables que nous allons examiner dans la suite de ce chapitre (voir chap. 18, § 5).

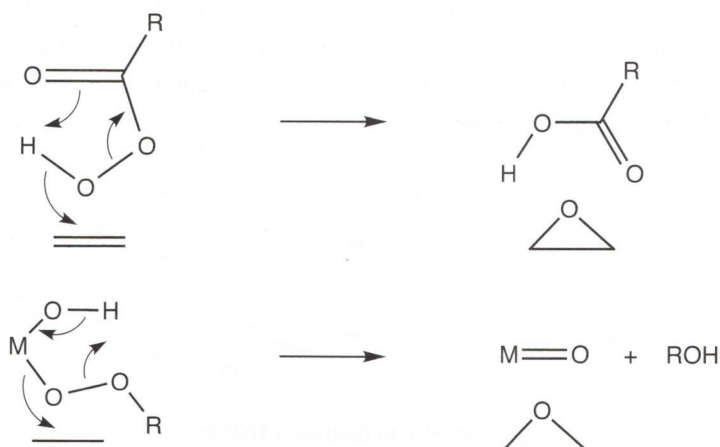
3. EPOXYDATION DES OLÉFINES

L'époxydation des oléfines a été découverte par un chimiste russe, N. Prileschajew, en 1909 en utilisant les peracides RCO_3H . Cette réaction a été longtemps utilisée. Cependant, les peracides sont souvent dangereux (explosifs) et donc à éviter impérativement. Les chimistes emploient maintenant une catalyse métallique et les hydroperoxydes ROOH (le plus souvent $\text{R} = t\text{-Bu}$, c'est-à-dire en abrégé le TBHP) dont le premier exemple a été découvert par Hawkins en 1950 avec $[\text{V}_2\text{O}_5]$ comme catalyseur. Les catalyseurs sont le plus souvent des complexes d^0 , avec un métal oxophile acide de Lewis capable de se lier à un oxygène de l'hydroperoxyde.



$\text{R}' = \text{RCO}$ (peracide), R (hydroperoxyde) ou H (eau oxygénée)

L'analogie mécanistique entre la réaction utilisant un peracide et celle utilisant un hydroperoxyde et un catalyseur métallique a été soulignée par Sharpless ^{16.7} :

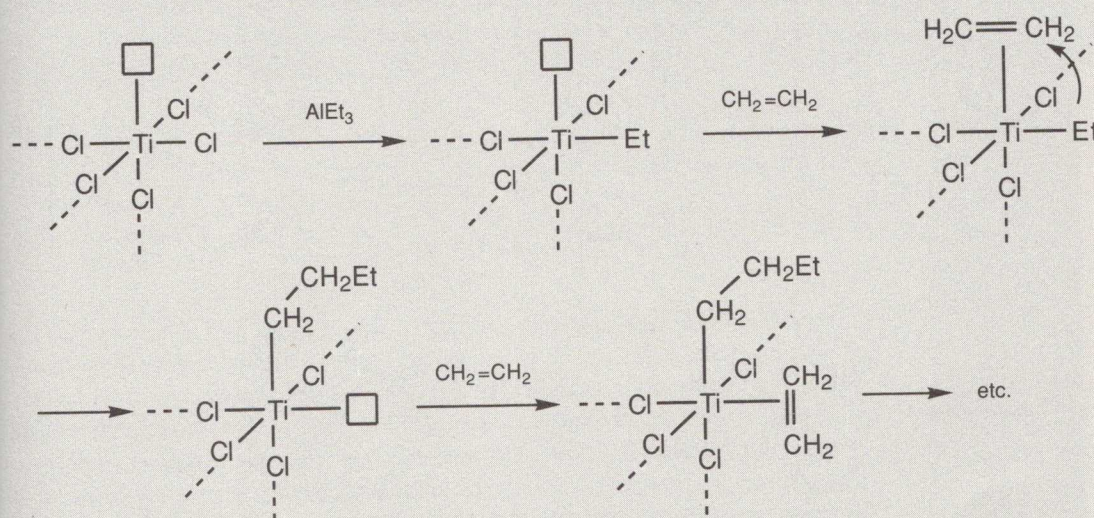


Ziegler-Natta polymerization

During experiments to synthesize long chain aluminium alkyls by treating aluminium triethyl with ethene under pressure ('Aufbau reaction'), K. Ziegler noted that transition metal halides have a dramatic effect on the course of the reaction. Whereas nickel salts led to the dimerization of ethene to butene, TiCl_4 catalysed its polymerization to give a relatively high melting linear polymer. G. Natta applied this catalyst to the stereospecific polymerization of propene. The polymerization of alkenes with metal halides activated by aluminium alkyls (**Ziegler-Natta catalysis**) is now one of the most important industrial processes.

$\text{TiCl}_4/\text{AlEt}_3$ mixtures as used by Ziegler react to give polymeric TiCl_3 , a solid with a layer structure and octahedrally coordinated Ti, in finely divided form, that is the catalyst is heterogeneous. Catalysis occurs at crystal defect sites where the metal is coordinatively unsaturated. The surface structure is also thought to be responsible for the stereoregular propene polymerization by imposing steric constraints on the way the monomer can coordinate to the metal prior to insertion into the metal-alkyl bond. It is now commonly accepted that the polymerization follows the principles laid out above, that is the active species is a metal alkyl with a vacant coordination site *cis* to the alkyl ligand (**Cossee-Arlman mechanism**).

The Nobel prize for Chemistry in 1963 was awarded jointly to K. Ziegler and G. Natta.

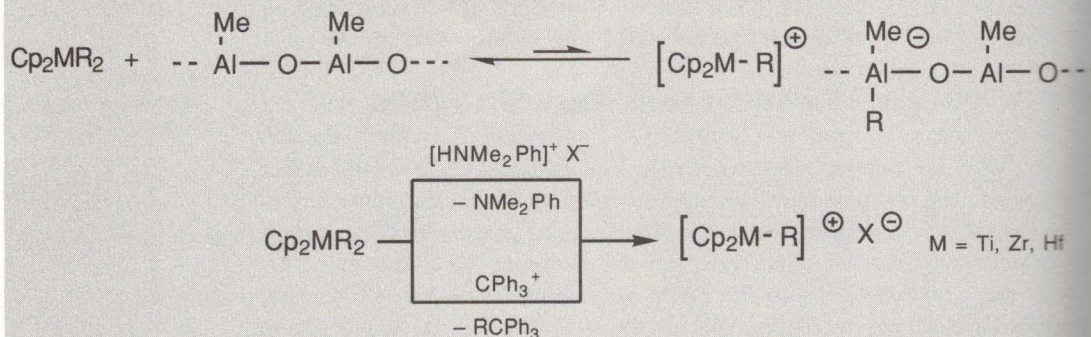


Metallocene dihalides Cp_2MCl_2 ($\text{M} = \text{Ti}, \text{Zr}, \text{Hf}$) in the presence of aluminium alkyls give highly active *homogeneous* Ziegler-Natta catalysts; the most effective activator is methylaluminoxane (MAO, $[\text{MeAlO}]_n$), a polymeric substance with, on average, one methyl group per aluminium atom.

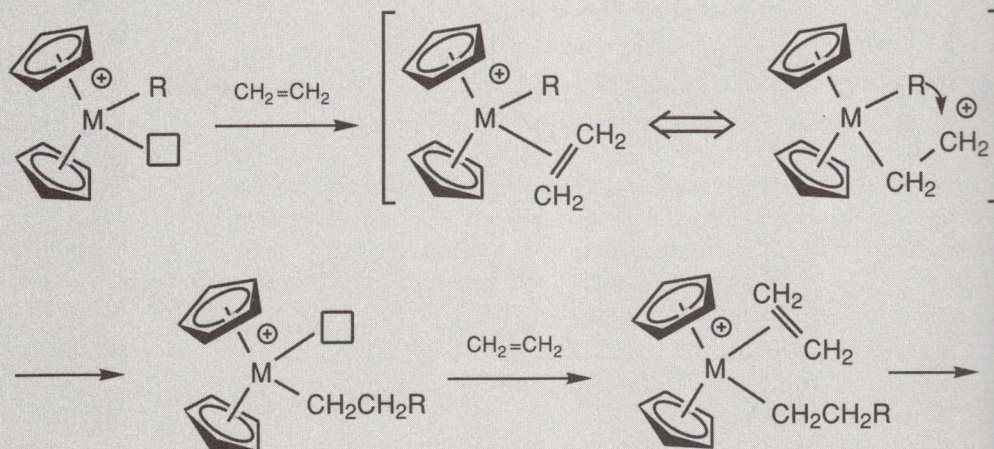
The function of the aluminium alkyl is to:

- alkylate the transition metal;
- act as a Lewis acid and create a vacant coordination site by abstracting a halide or alkyl ligand from the transition metal.
- act as a cleaning role, by mopping up impurities from the monomer and the reaction medium.

Cationic 14 VE alkyl complexes $[\text{Cp}_2\text{M-R}]^+$ have been identified as the active species. The same cationic complexes are obtained in the absence of aluminum alkyls from metallocene dialkyls by protolysis or R^- abstraction with CPh_3^+ . With non-coordinating counterions such as $\text{B}(\text{C}_6\text{F}_5)_4^-$ these cationic catalysts show very high activity. A number of ligand stabilized complexes $[\text{Cp}_2\text{MR}(\text{L})]^+$ have been isolated ($\text{L} = \text{THF}, \text{RCN}, \text{PR}_3$) which catalyse alkene polymerizations only if dissociation of L is facile.

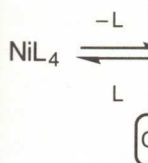


The mechanism of polymer chain propagation is similar to that for heterogeneous catalysts. In either case two coordination sites are required: one for the alkyl group, and one for binding of the unsaturated substrate.



The activity increases in the series $\text{M} = \text{Ti} \ll \text{Hf} < \text{Zr}$.

Why are these catalysts so highly active? Catalysis only occurs if the metal is in oxidation state IV (d^0); so stabilization of the intermediate olefin adduct by back-bonding is not possible. The d -orbitals of early transition metals are high in energy and, if occupied, would lead to substantial back-bonding stabilization which would greatly increase the activation barrier of the alkyl migration step. For this reason the d^2 complex $\text{Cp}_2\text{NbEt}(\text{C}_2\text{H}_4)$, which structurally resembles the intermediate ethene adduct above, resists alkyl migration to the $\text{C}=\text{C}$ double bond, even under forcing conditions.



Whether or dimerization or dimerization in the absence of the elimination of the transition state for polymerization propagation

M—

If $k_t \approx k_p$, Suitable choice made selective ethylene. With not a facile scandium, yttrium which exhibit

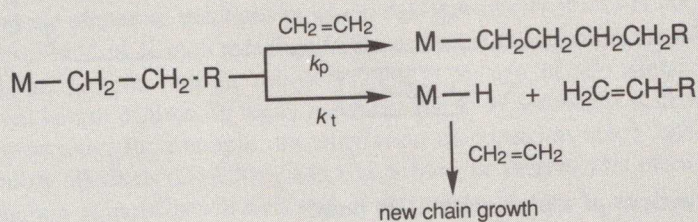
Reactions with Attack of a nucleophile

R—M

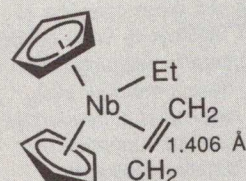
The reaction functionalization

The hydrophobic precursor molecule phosphine complex electron-withdrawing presence of H₂ to illustrate the

Whether or not a metal complex acts as a polymerization, oligomerisation or dimerization catalyst, depends on the likelihood of chain termination. In the absence of hydrogen, alkyl chain growth is usually terminated by β -H elimination (if aluminium alkyls are present, transfer of the polymer chain from the transition metal to aluminium can also take place). Successful polymerization therefore depends on two kinetic parameters: the rate of chain propagation k_p , and the rate of termination k_t .



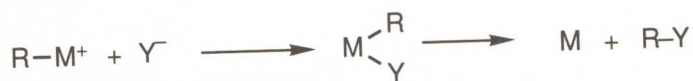
If $k_t \approx k_p$, ethene is dimerized to butene (using $\text{NiX}_2/\text{AlEt}_3$ mixtures). Suitable choice of ligands is important: for example, nickel catalysts can be made selective for the dimerization, oligomerization and polymerization of ethylene. With d^0 complexes $[\text{Cp}_2\text{MR}]^+$ ($\text{M} = \text{Ti}, \text{Zr}, \text{Hf}$) β -H elimination is not a facile process: $k_p \gg k_t$. Similarly, there are isoelectronic neutral scandium, yttrium and lanthanide complexes $\text{Cp}'_2\text{MR}$ ($\text{Cp}' = \text{C}_5\text{H}_5, \text{C}_5\text{Me}_5$) which exhibit high polymerization activity for the same reasons.



Back-bonding stabilization becomes less important with decreasing d -orbital energy from left to right of the periodic table, and coordinatively unsaturated alkyls of cobalt and nickel are indeed able to polymerize ethene, although the activity is substantially lower than with d^0 systems.

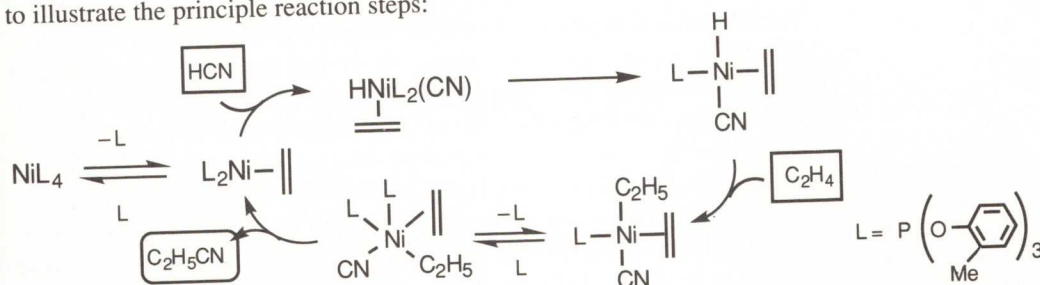
Reactions with nucleophiles

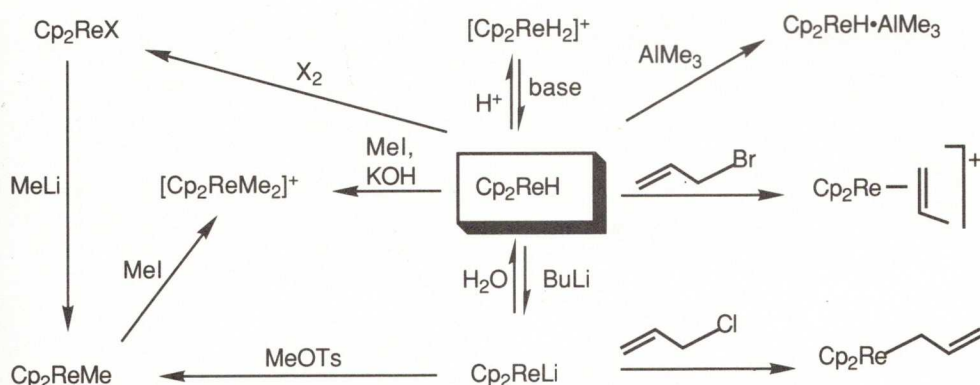
Attack of a nucleophile on a metal alkyl often induces reductive coupling.



The reaction is frequently part of a catalytic cycle and leads in effect to the functionalization of alkenes. An example is the hydrocyanation of alkenes.

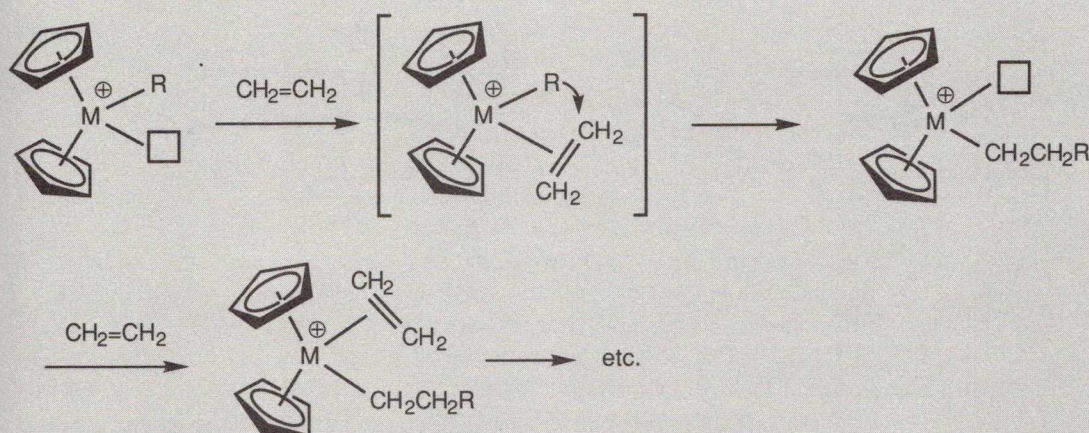
The hydrocyanation of butadiene with HCN gives adiponitrile, a nylon precursor monomer. It is catalysed by nickel phosphite complexes. While phosphine complexes would react irreversibly to give $\text{Ni}(\text{CN})_2\text{L}_2$, the more electron-withdrawing phosphite ligands stabilize Ni^0 species even in the presence of HCN. Ethene reacts similarly to propionitrile; the reaction serves to illustrate the principle reaction steps:





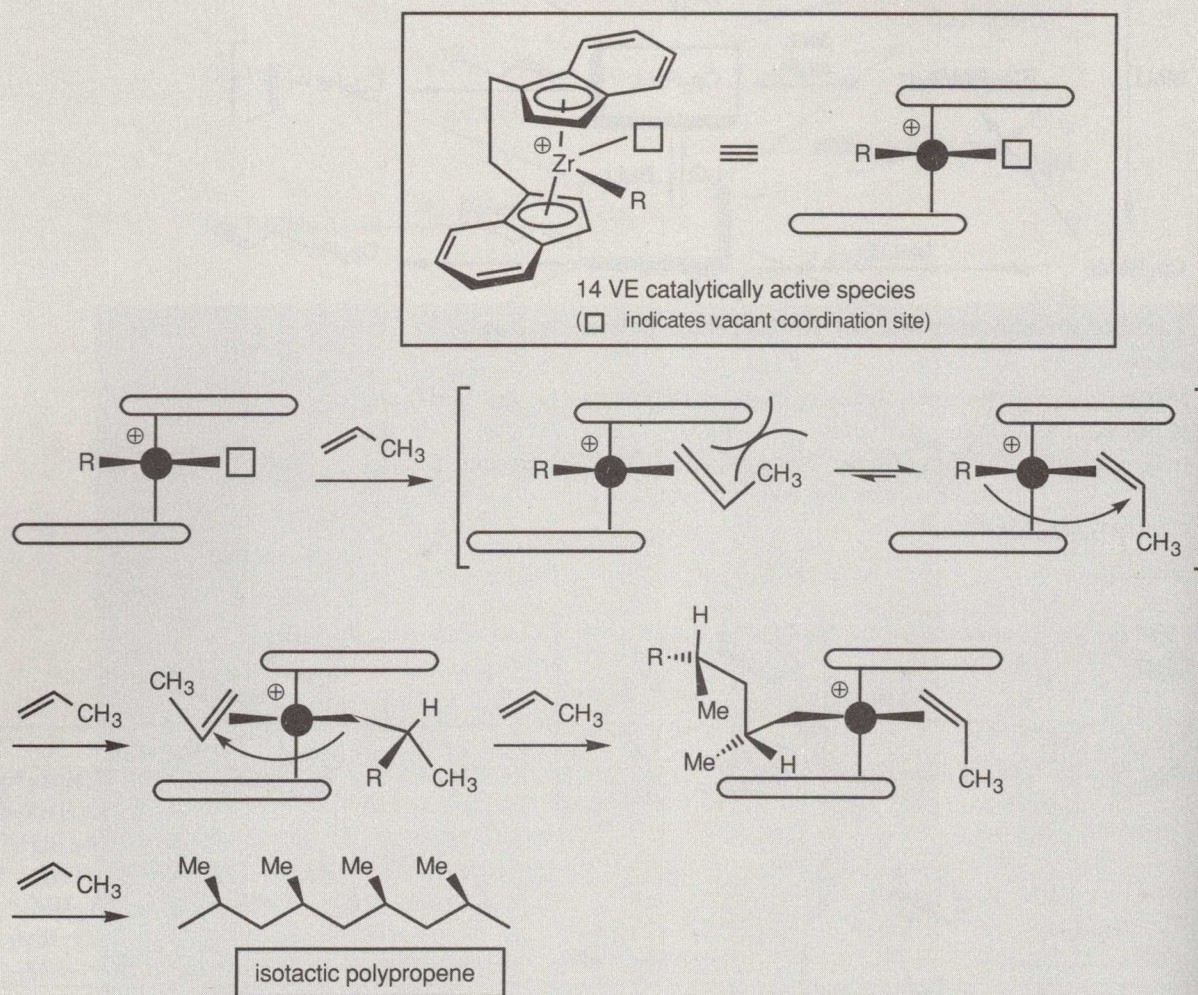
Tailored metallocenes and the stereospecific polymerization of 1-alkenes

Mixtures of metallocene dihalides of group IV metals (Ti, Zr, or Hf) and aluminium alkyls as activators are highly active catalysts for the polymerization of olefins (Ziegler–Natta polymerization; see *Organometallics* 1, p. 69 ff.). The active species is a coordinatively unsaturated cationic alkyl complex, $[\text{Cp}_2\text{M}-\text{R}]^+$:

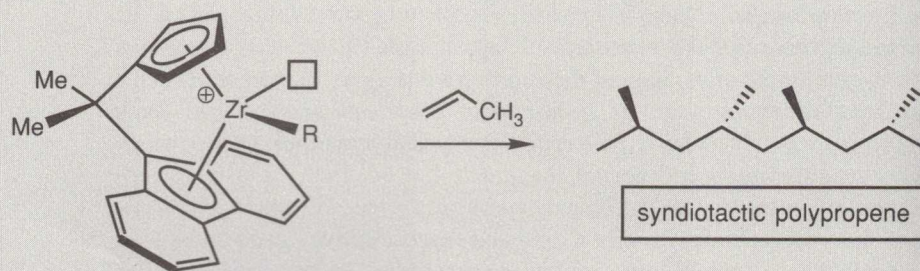


The polymerization of 1-alkenes such as propene with such a catalyst would lead to a polymer with randomly oriented alkyl side-chains. However, since cyclopentadienyl ligands are easily modified by substituents and can be tailored to suit particular requirements, appropriate ligand design has been used to control the orientation of the coordinated propene monomer in such a way that either isotactic or syndiotactic polymers must result. Such stereoregular polymers have quite different physical properties, such as much higher melting points and greater toughness. For example, in bis-(indenyl) complexes the rotation of the ligands can be prevented by connecting them via a $-\text{CH}_2-\text{CH}_2-$ bridge, to give a rigid and stereoselective ligand framework (a so-called *ansa*-metallocene, from *ansa* = handle). Catalysts containing this ligand orient the methyl group of the incoming propene monomer away from

the indenyl ligand prior to the insertion step to give highly isotactic polypropene:



Similarly, a ligand system in which a large, raft-like Cp analogue such as fluorenyl is combined with a small C_5H_5 ligand leads, via an analogous mechanism, to the chain growth of syndiotactic polypropene.



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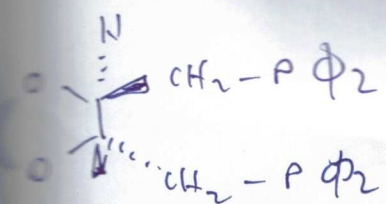
Midland and Preston, 1982; Jadhav, Brown, et al., 1986; Brown et al., 1986) and boronic and borinic esters (Matteson, 1986) have also been utilized in a wide range of enantioselective reactions.

Reductions with Chiral Complex Hydrides

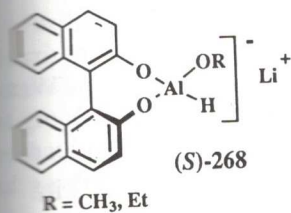
A massive effort has been invested in the search for chiral hydride reagents that might afford good levels of enantioselection in the reduction of ketones and aldehydes. Much of this has centered on lithium aluminum hydride modified by the attachment of chiral ligands, including diols, amines, diamines, aminoalcohols, and diaminocarbinols (Haubenstock, 1983; Grandbois et al., 1983; Matteson and Asami, 1985; ApSimon and Collier, 1986; Nogradi, 1987; Tomita, 1987). The attainment of reasonable levels of enantioselectivity has on the whole been limited to a narrow range of substrate structures (aryl alkyl ketones and aldehydes), while the properties of many of the early reagents often varied with time and temperature. The binaphthyl derivative, "BINAL-H" (268) (BINAL = 2,2'-dihydroxy-1,1'-binaphthyl, and ethanol), which is available as either enantiomer (Noyori et al., 1979; Noyori, 1981), and similar compounds obtained from biphenyl (Suda et al., 1984) and 9,9'-phenanthryl derivatives (Yamamoto et al., 1984) provided excellent results, however, and 95–100% enantiomeric excesses have been obtained from the reduction of a reasonable range of ketones (Fig. 12.162). Differentiation between R^1 and R^2 depends on the electronic rather than the steric properties of these substituents and requires that one of them is unsaturated (in the present case this is designated as R^1). Poor enantiomeric excesses are obtained when both are simple alkyl groups (Noyori et al., 1984). The stereochemical outcome can be rationalized by considering four likely transition state structures ($A^\ddagger$ – $D^\ddagger$). Two of these ($A^\ddagger$ and $B^\ddagger$) were discounted because of the severe nonbonded interaction between the alkyl group R and one of the ortho hydrogen atoms of the binaphthyl residue. The $C^\ddagger$ transition state was then rejected because of the repulsion between the nonbonding orbital of the naphthyloxy oxygen and the π orbital of the axial R^1 substituent. Thus, the favored reaction pathway based on (S)-BINAL proceeds via $D^\ddagger$ to afford the (S)-carbinol.

Hydride transfer from boron in chiral boranes and boranes rendered chiral by complexation with chiral amines has been studied for possible utility in enantioselective reductions, but the outcomes have not been encouraging (Midland, 1983). While hydride transfer from carbon ligands, as in the reactions of "chiral borane" (Ipc.BBN) 269 (Midland et al., 1977; Midland and Nguyen, 1982; also Midland et al., 1984), has furnished high enantiometric excesses (77–98%) with deuterio aldehydes and acetylenic ketones (Fig. 12.163), sluggish reactions with other ketones may allow dissociation and, as a consequence, lower levels of enantioselectivity. The problem may be partly ameliorated by performing the reaction at high pressure (Midland and McLoughlin, 1984) or with neat reagents (Brown and Pai, 1982), but diisopinocampheylchloroborane, (Ipc)₂BCl, appears to be the reagent of choice for a wide range of ketones, including sterically hindered derivatives (Chandrasekharan, Brown, et al., 1986; Brown et al., 1986b).

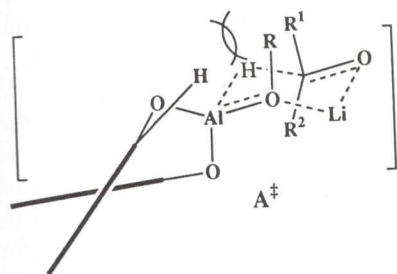
Modified borohydrides have been comparatively neglected, but may provide



Enantioselective Syntheses



R ¹	R ²	R	ee (%)
C ₆ H ₅	CH ₃	Et	95
C ₆ H ₅	Et	Et	98
C ₆ H ₅	Pr	Et	100
C ₆ H ₅	iPr	Et	71
C ₆ H ₅	CH ₃	CH ₃	84
n-BuC≡C	CH ₃	CH ₃	90
n-BuC≡C	n-C ₅ H ₁₂	CH ₃	90



B[‡] = A[‡] with R¹ and R² interchanged

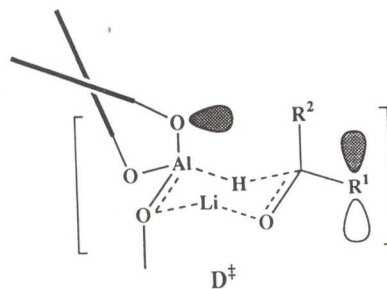
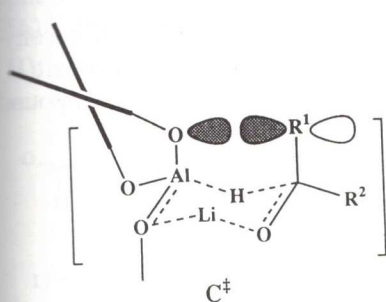


Figure 12.162. An effective reagent for the enantioselective reduction of ketones is BINAL-H 268.

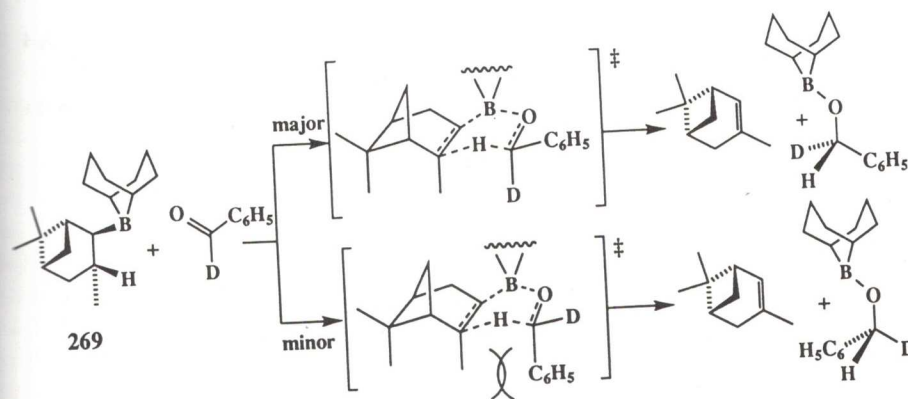


Figure 12.163. Enantioselective reduction of α-deutero benzaldehyde with Alpine borane 269.

1:1 ratio of the two diastereomeric adducts **287** and **288**, respectively (by NMR spectroscopy), corresponded quantitatively to the enantiomeric ratio of products. This observation led to the conclusion that the stereodifferentiation had occurred at this stage and that the product was formed from the observed major diastereomer (Brown and Chaloner, 1978). However, a detailed kinetic study

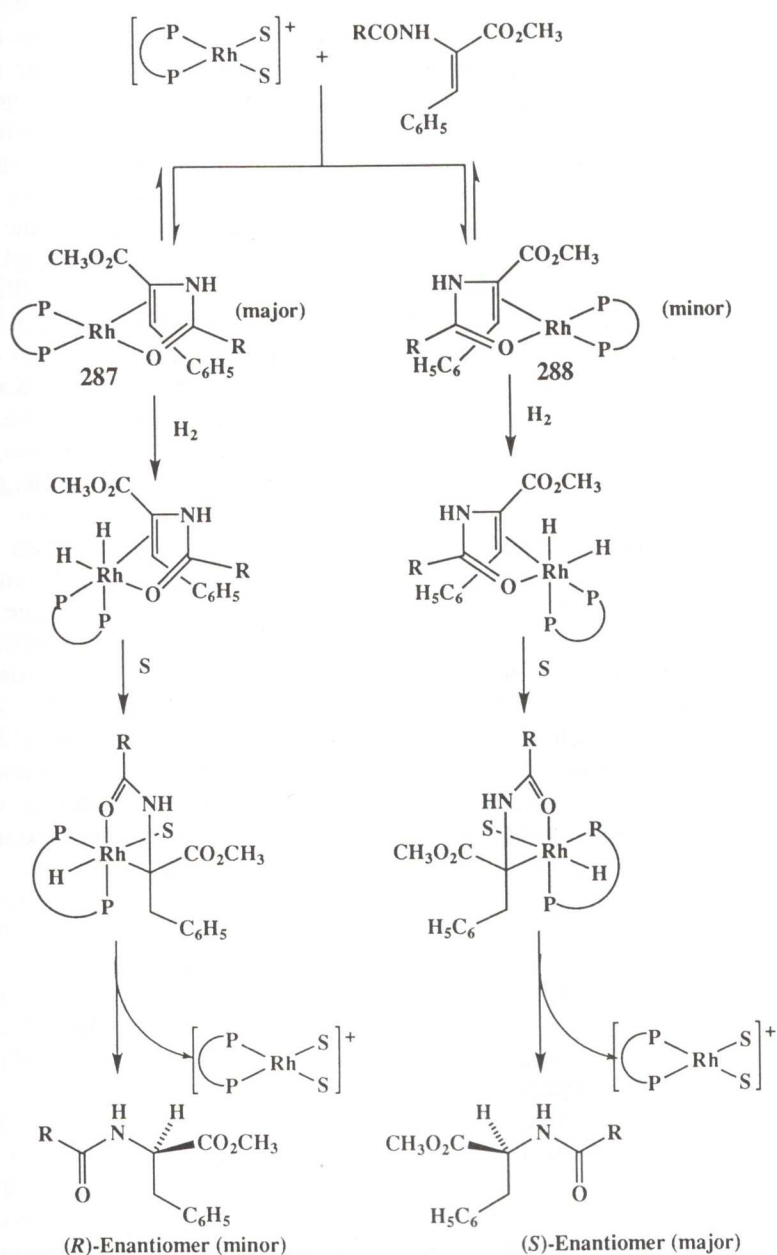
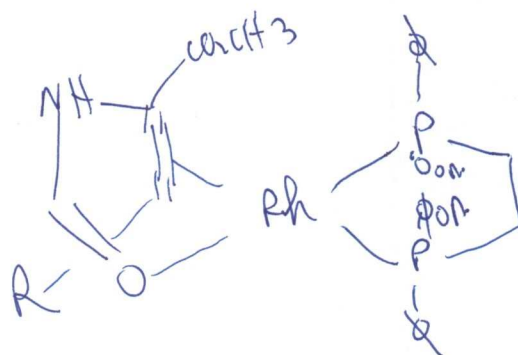
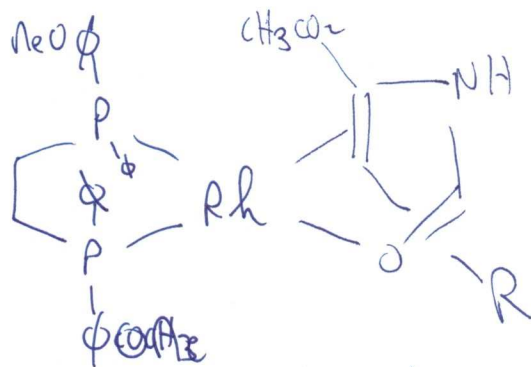
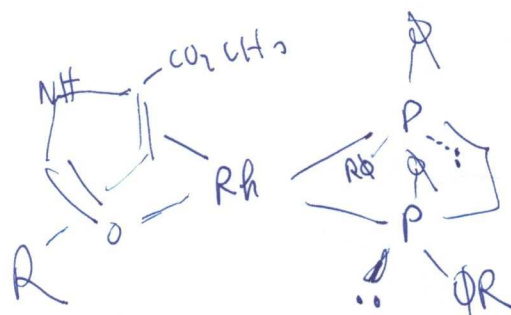
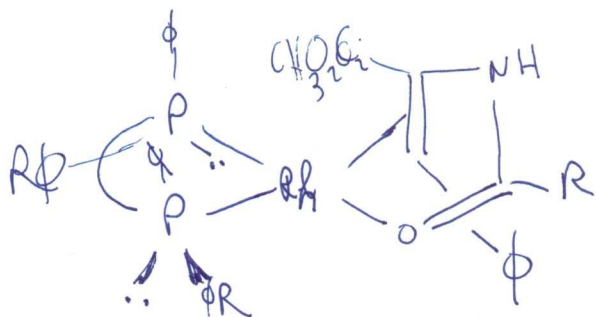
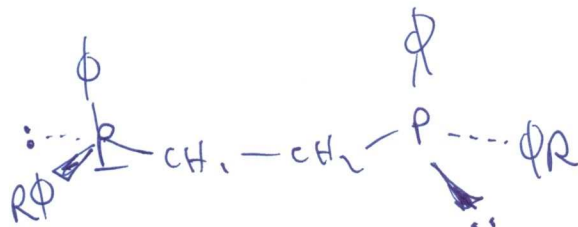
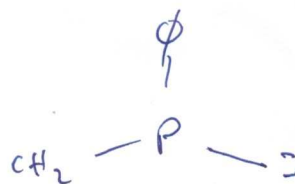
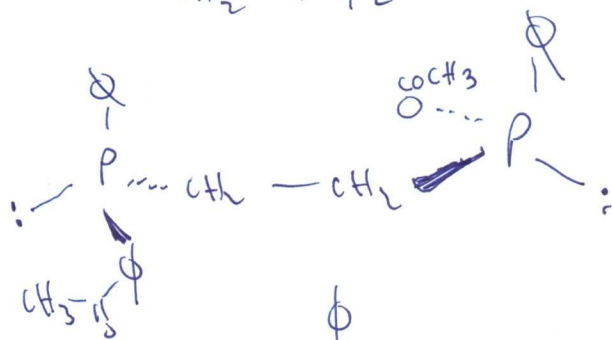
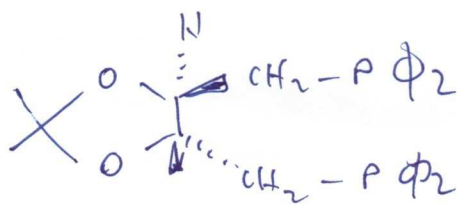


Figure 12.174. Mechanism for the enantioselective hydrogenation of α -amidocinnamic esters, where $S = CH_3OH$.



stereocentres catalyse
1) réduction des cétones

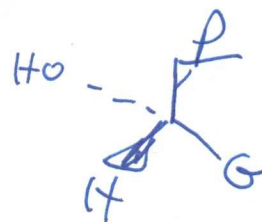
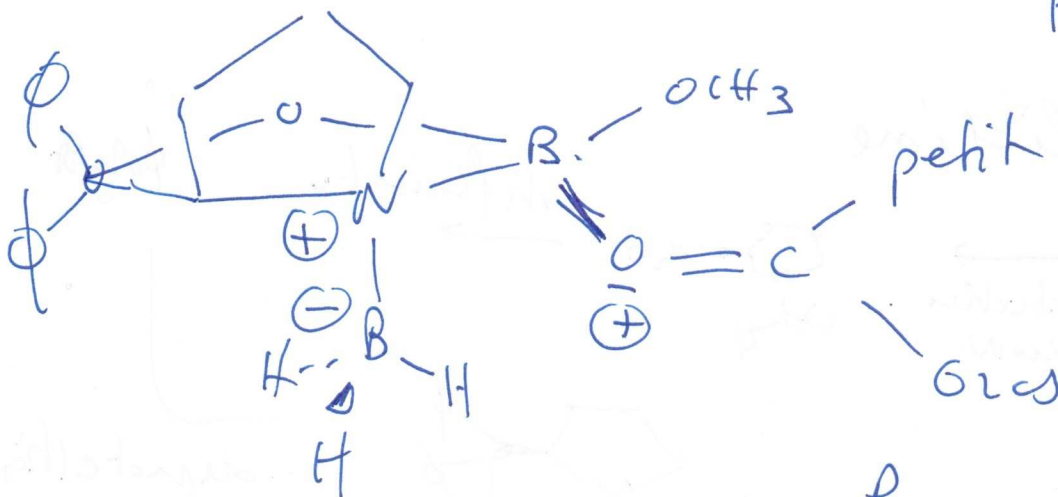
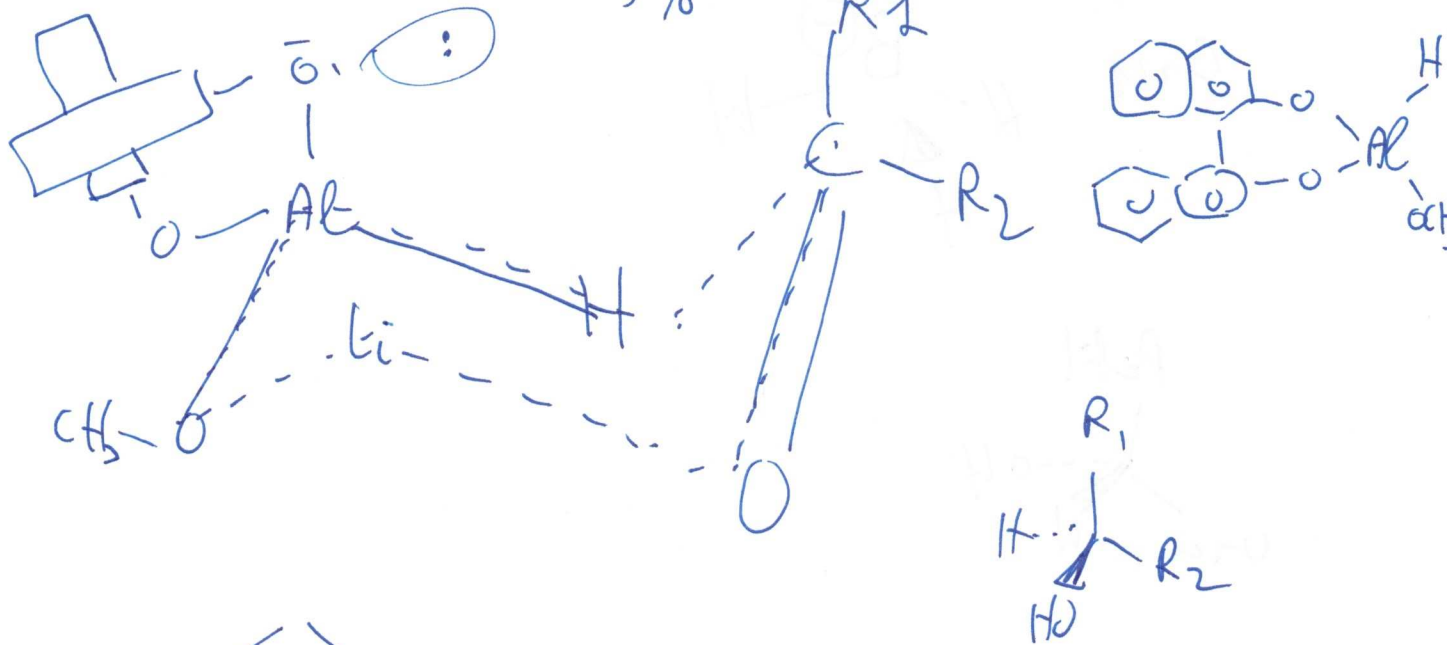
réduction énantiosélective

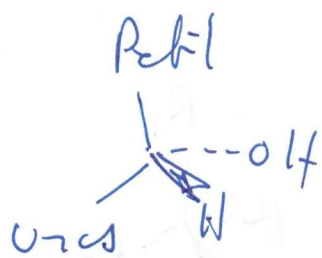
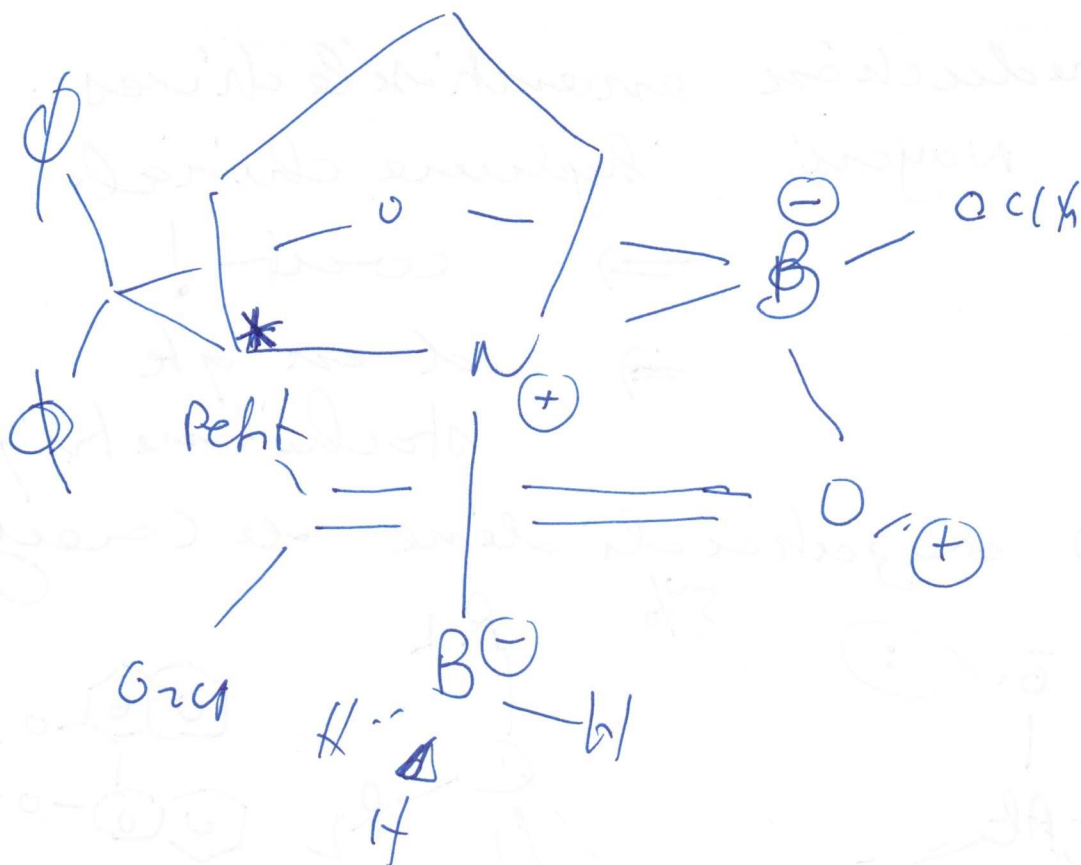
Noyau hydrure chiral.

$\Rightarrow$ coût !

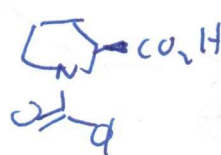
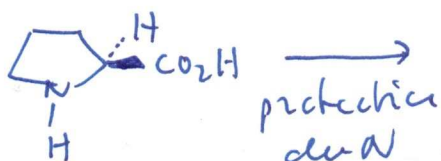
$\Rightarrow$ red en gte
stochimétrique.

$\Rightarrow$ oxazabicyclique de Corey
5%

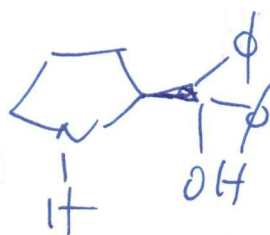




oxazabicyclidine



erhöhen



deprotection



2.) annulation de
Robinson.

catalysée par la proline

3.) hydrogénation
catalytique.

catalyseurs chiraux
(knoes).

→ hydratation alcène catalysée ms c'est pas le cata qui gouverne

→ Plutôt catalyse homogène

→ Procédé ~~W~~Wacker p 408
(mentionner)
ms pas expliquer

Astruc
Chimie organométallique
et catalyse

→ p 85 - 86 Régiosélectivité / effet trans.
↳ du côté N pas P.

ouverture époxyde avec ac de Lewis — pb récup ac de Lewis
ap hydrolyse
- proport° stoechiométrique

Sélectivité cata

1) Réduction des cétones

énantiosélective

Brückner

ou Atkinson

(stereoselective synthesis)

Noyori hydrure chiral

↳ livre rouge 942-943
inconvenant coût

cata en quantité
stoechiométrique

↳ justification: as livre rouge

2) ~~oxazabone~~ oxazabonolide de Corey

↳ dernière

énantiosélectivité dep de
la cétone

< =

faiblesse dessin YT
dep de R₁ & R₂

* Corey cf Y.T.

réducteur BH_3 $\Rightarrow$ bcp $\ominus$ cher

qte cata = 5%.

$\downarrow$ Brückner

2) Annelat° de Robinson

JCE

~~pp~~ paldine $\Rightarrow$ énantioselective
cycle $\rightarrow$ nommer chaque étape

3) Hydrogenation catalytique Knowles

$\hookrightarrow$ livre rouge - 951

(+) YT on a un schéma complé.

role phénol au dessous
empêcher la cétone
de se mettre en dessous

cétone au dessus

$\Rightarrow$ conduit nul
part

phényl au dessus
on évite $\perp$ C $\equiv$
de plus...

- fabriqué ap.
de la paldine
YT

$\downarrow$
si paldine
naturelle

= pas
cher

~~polymère~~