Recent Progress in the Asymmetric Hydrosilylation of Ketones and Imines

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Abstract: The asymmetric hydrosilylation of ketones and imines has seen significant advances in the last decade. The discovery of new highly efficient catalysts has turned this catalytic process into an attractive method for practical applications. Impressive chemical yields and enantioselectivities have been attained employing newly designed catalytic systems based on rhodium, copper, zinc and iron with suitable bidentate chiral ligands.

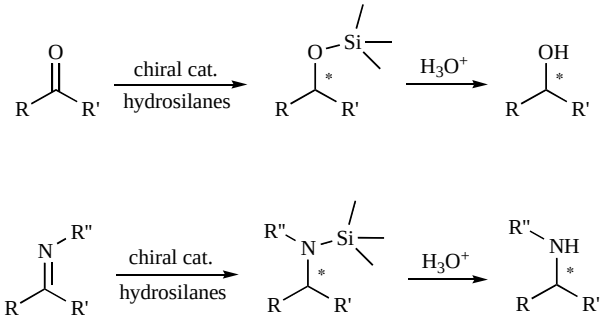
This mini review will focus on the most recent and successful developments in this area.

Keywords: Asymmetric catalysis, hydrosilylation, alcohols-amines, ketones, amines.

I. INTRODUCTION

Enantiomerically pure alcohols and amines are important intermediates for the synthesis of many active pharmaceuticals and agrochemicals [1]. In the recent years, the catalytic asymmetric reduction of prochiral ketones and imines has attracted growing attention as an economic and environmentally friendly method for the production of these classes of compounds [2].

Although catalytic asymmetric hydrogenation proved to be a successful strategy to optically active alcohols and amines [3-6], asymmetric hydrosilylation of carbon-heteroatom bonds catalyzed by transition-metal complexes (Scheme **1**) emerged as desirable alternative to asymmetric hydrogenation owing to the mild reaction conditions and manipulative simplicity [7].



Scheme 1. Catalytic asymmetric hydrosilylation of carbonyl and imino groups. Hydrolysis of the silyl ether and silyl amine gives the corresponding chiral alcohol or amine.

Intensive studies have been focused on the development of efficient hydrosilylation chiral catalysts and in the last few years impressive chemical yields and enantioselectivities have been attained [8].

Rhodium(I) complexes with chiral diphosphines were first used to promote hydrosilylation of ketones [9]. Since then, several chiral rhodium complexes with numerous homo- and heterobidentate ligands have been explored and some of them showed high selectivity for the reduction of prochiral ketones and imines [10]. Nevertheless, the high cost of rhodium-based chiral catalyst and the low substrate-to-catalyst ratio have precluded practical applications of this method to date. Because of this limitation, in the last few years, many researchers have turned their attention to the development of less expensive catalysts [11]. New, more effective catalysts based on various transition metals such as copper, iron, titanium, zinc have been discovered.

Copper-based catalysts along with safe and inexpensive reducing silylating agents afforded promising results. These systems offer economic advantages and could be potentially useful for large-scale industrial applications.

II. RHODIUM CATALYSTS

Chiral rhodium complexes have been widely used as catalysts in asymmetric hydrosilylation of ketones and imines owing to their high catalytic activity.

The performance of rhodium catalysts proved to be strongly dependent on the nature of silane. Usually, diarylsilanes such as diphenylsilane and phenyl(1-naphtyl)silane furnished the best results. Although rhodium-catalyzed hydrosilylations give higher stereoselectivities at lower temperature, some Rh-catalysts which display unusual temperature dependence have been observed [12-15].

At the first time, neutral or cationic rhodium(I) complexes with chelated chiral diphosphines were employed exclusively as catalysts for the reduction of many ketones. Later on, it was established that the nitrogen atom present in chiral bidentate ligands produced better results than the phosphorus atom. Thus, a large number of P,N and N,N ligands were designed. Among them, phosphino-oxazolines, **1** [16,17], "planar chiral" heterocycle **2** [18] and bis(oxazoline)pyridine, **3** [19] ligands depicted in Fig. (**1**) are some of the most successful ligands for rhodium catalyzed asymmetric hydrosilylations of ketones and imines.

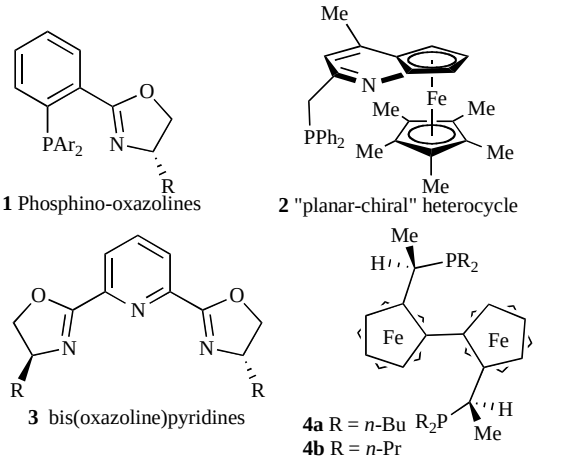


Fig. (1). Some of the most successful ligands for Rh-catalyzed asymmetric hydrosilylation of ketones and imines.

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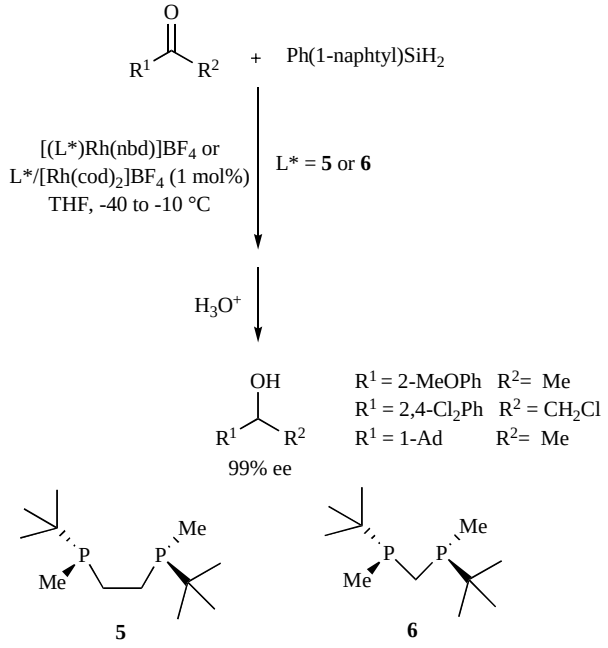
1570-193X/09 $55.00+.00

Many P,N- and N,N-Rh chiral catalytic systems for asymmetric hydrosilylation have been extensively reviewed and therefore this article will focus only on the most recent developments on this area [7, 8, 10, 11].

Most of the diphosphine ligands gave rise low to moderate ee's in the rhodium-catalyzed asymmetric hydrosilylation of ketones and imines, except for ferrocene-based trans-chelating chiral diphosphines [(*R*,*R*)-(*S*,S)-AlkylTRAPs], (Fig. (**1**), **4**) developed by Ito and co-workers [20].

Using the combination of $[Rh(COD)_2BF_4]$ with *n*BuTRAP, **4a** and *n*PrTRAP, **4b** values over 90% ee were reached in the hydrosilylation of simple ketones.

Recently, Imamoto *et al.*, [21] achieved very high enantioselectivities (99% ee) in the Rh-catalyzed hydrosilylation of 2-methoxyphenyl methyl ketone and 2,2',4'–trichloroacetophenone, using the cis-chelating P-chiral diphosphine (*S*,*S*)-1,2-bis(*tert*-butylmethylphoshino)ethane, **5** in the presence of phenyl(1-naphtyl)silane as a reducing agent. Moderate selectivities up to 87% were reached for dialkyl ketones except for the reduction of 1-adamantyl methyl ketone. The corresponding alcohol was obtained with 99% ee when (*R*,*R*)-bis(*tert*-butylmethylphosphino)methane, **6** was employed as chiral ligand (Scheme **2**).



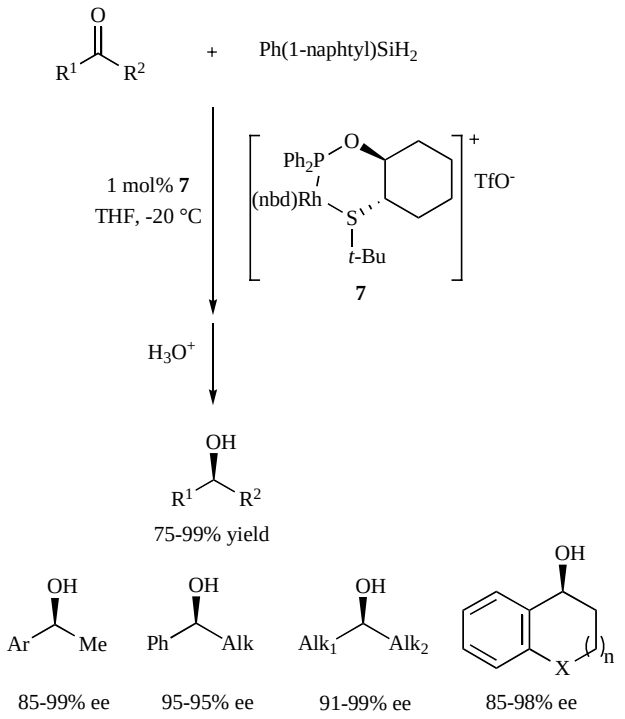
Scheme 2. P-chiral diphosphines/Rh catalyzed asymmetric reduction of ketones with phenyl(1-naphtyl)silane.

The authors proposed a plausible mechanism for this process. The sense of the stereoselection was rationalized considering that the enantioselection occurs at the migratory insertion step.

A chiral mixed phosphorus/sulphur ligand was successfully tested by Evans and co-workers [14] in the hydrosilylation of ketones. The catalyst complex **7** afforded high enantioselectivities for a wide range of aryl alkyl and dialkyl ketones. An important feature of the catalyst **7** is that the ee values over 90% were attained for the reduction of challenging dialkyl ketones (Scheme **3**).

In the last years, the most impressive results in the rhodium catalyzed hydrosilylation of ketones have been obtained by using the chiral N-heterocyclic carbenes (NHC) as ligands. NHC are flexible ligands that have been developed rapidly in the last decade owing to their air and moisture stability [22].

The NHC-rhodium complexes were early assayed in asymmetric hydrosilylation of methyl ketones by Enders *et al.* [23].



Scheme 3. Reduction of aryl alkyl and dialkyl ketones with penyl(1-naphtyl)silane catalyzed by cationic P,S rhodium complex **7**.

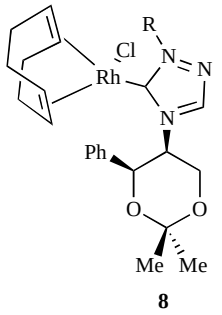


Fig. (2). The first carbene-rhodium complex used in asymmetric hydrosilylation by Enders (1997).

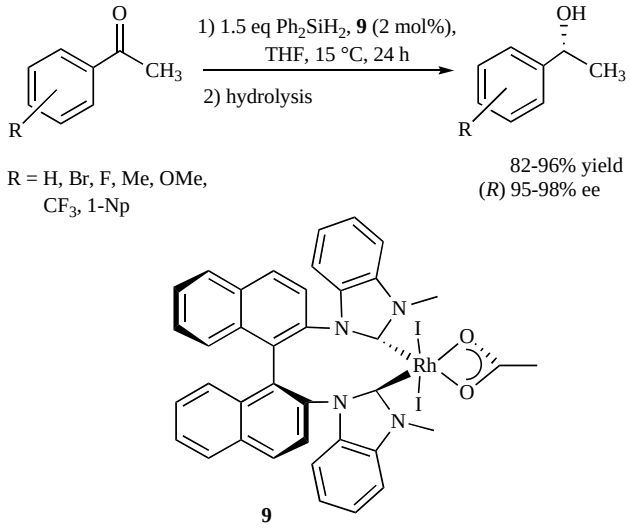
The monocarbene rhodium(I) complexes (Fig. (**2**), **8**) displayed a good catalytic activity even if the enantioselectivities were quite modest (20-43%).

Excellent asymmetric induction in the enantioselective hydrosilylation of various aryl methyl ketones were reached by Shi and co-workers [24] using the axially chiral BINAM NHC-Rh(III) complex **9** derived from 1,1'-binaphtalenyl-2,2'-diamine (BINAM) (Scheme **4**).

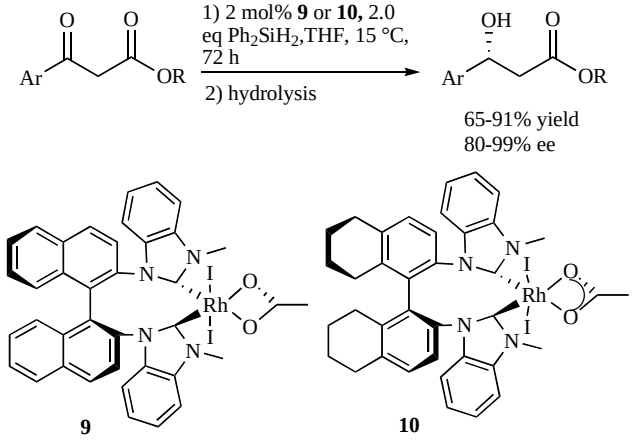
The rhodium carbene complex **9** was prepared as major product by reaction of dibenzimidazolium salt with $[Rh(COD)Cl]_2$ in the presence of sodium acetate and potassium iodide.

Recently, BINAM-NHC-Rh(III) complexes **9** and **10** were applied to the asymmetric hydrosilylation of β-ketoesters. Various 3-oxo-3-arylpropionic acid methyl or ethyl esters were reduced with diphenylsilane with enantioselectivities of up to 99% (Scheme **5**) [25].

Remarkable selectivity was reported in the asymmetric hydrosilylation of unsymmetrical dialkyl ketones by Gade, Bellemin-Laponnaz and Cesar [26] who developed a very efficient oxazolinyl carbene-rhodium complex. A library of ten different oxazolinyl



Scheme 4. Asymmetric hydrosilylation of methyl ketones catalyzed by BINAM NHC-Rh(III) complex **9**.

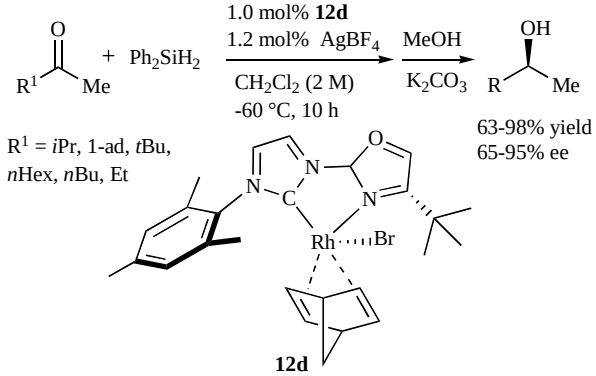


Scheme 5. BINAM NHC-Rh complexes catalyzed asymmetric hydrosilylation of 3-oxo-3-arylpropionic acid alkyl esters.

carbene ligands was obtained the reaction of the 2-bromo-4(*S*)-*tert*-butyl and 2-bromo-4(*S*)-isopropyl oxazoline with various N-substituted imidazoles in THF (Scheme **6**).

Reaction of the imidazolium salt **11** with [{Rh(μ-O*t*Bu)(nbd)}$_2$] (nbd = nobornadiene) generated in situ from KO*t*Bu and [{RhCl(nbd)$_2$}], gave the corresponding N-heterocyclic carbene rhodium complexes **12a-j** [27]. The most selective catalyst **12d** was identified after an initial screening of carbene complexes **12a-j** in the enantioselective hydrosilylation of acetophenone with diphenylsilane with a catalyst loading of 1 mol% in the presence of $AgBF_4$. The treatment of complexes **12a-j** with silver salt is a crucial step for the formation of the active cationic square- planar catalysts.

Although the cationic catalyst derived from complex **12d** hydrosilylated the 2-naphtyl methyl ketone in 99% yield and with 92% ee, the asymmetric inductions for most aryl alkyl ketones were found to be somewhat below those of the most effective rhodium diphosphine catalysts. Nevertheless, the reduction of unsymmetrical dialkyl ketones using the complex **12d** afforded enantioselctivities comparable and even superior to the best results previously reported for prochiral non aromatic ketones. A remarkable 95% ee value was obtained in the case of *tert*-butyl methyl ketone (Scheme **7**).

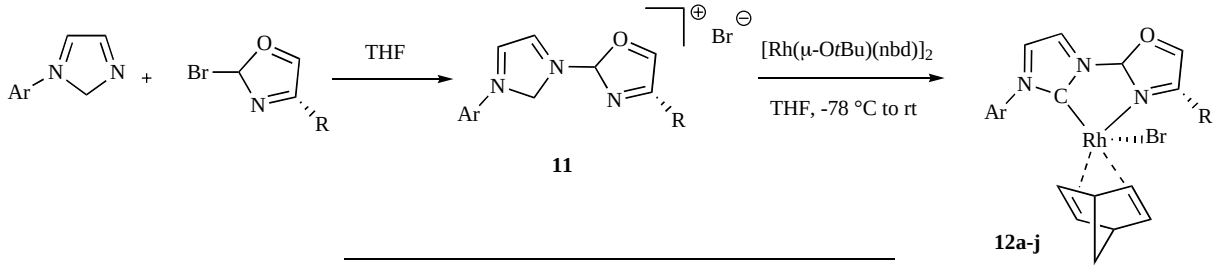


Scheme 7. Asymmetric reduction of alkyl methyl ketones with diphenylsilane catalyzed by complex **4d**.

The challenging linear chain n-alkyl methyl ketones such as 2-octanone an 2-butanone were also reduced with good asymmetric induction reaching enantiomeric excesses of 79% and 65% respectively.

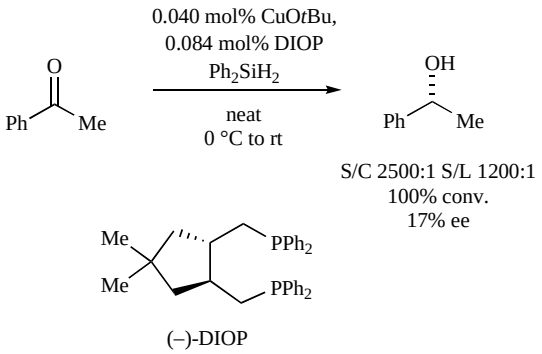
III. COPPER CATALYSTS

The first copper(I)-catalyzed asymmetric reduction of ketones using diphenylsilane as reducing agent was reported by Brunner *et al.* in 1984 [28]. The in situ formed (-)-DIOP-copper hydride re-



	Ar	R		Ar	R
12a	Ph	*t*Bu	**12f**	2-*t*BuC$_6$H$_4$	*t*Bu
12b	o-tol	*t*Bu	**12g**	CH_2Ph	*t*Bu
12c	mes	*i*Pr	**12h**	$CHPh_2$	*t*Bu
12d	mes	*t*Bu	**12i**	fluorenyl	*t*Bu
12e	2,6-(iPr)$_2$Ph	*t*Bu	**12j**	CH(napht)$_2$	*t*Bu

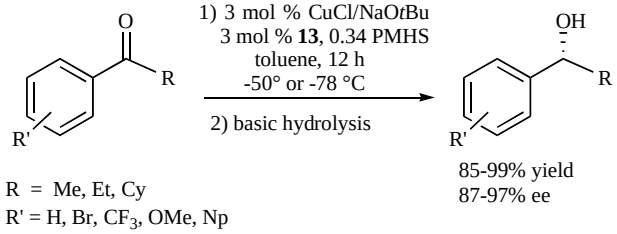
Scheme 6. Synthesis of the mixed oxazoline-carbenes rhodium complexes **12a-12j**.

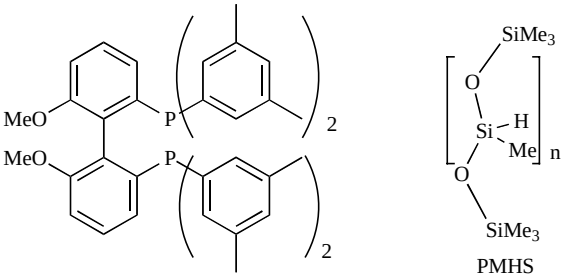


Scheme 8. The first example of copper catalyzed asymmetric reduction of a ketone using diphenylsilane as reducing agent.

duced the acetophenone with a high substrate-to-catalyst ratio but the enantiomeric excess was rather low (Scheme **8**).

A considerable breakthrough in this field was made by Lipshutz's group in 2001 who applied Buchwald's protocol for conjugate reduction to the asymmetric hydrosilylation of aromatic ketones [29]. Catalytic quantities of diphosphine copper hydride generated *in situ* from CuCl, NaO*t*Bu, and Roche's (*R*)-3,5-xyl-MeO-BIPHEP **13** in the presence of safe and inexpensive polymethylhydrosiloxane (PMHS) as a source of hydride allowed the reduction of the aryl ketones with excellent yields (up to 99%) and enantiomeric excessess (up to 97%) (Scheme **9**).





Scheme 9. (*R*)-3,5-xyl-MeO-BIPHEP/Cu catalyzed enantioselective reduction of ketones with polymethylhydrosiloxane (PMHS).

It is noteworthy that this catalytic system could be used at remarkably high substrate-to-ligand ratios (S/L>20.000) without significant loss of enantioinduction.

After these preliminary studies, a wide variety of bidentate ligands were screened and Takasago's (R)-(-)-DBTM-SEGPHOS (Fig. (**3**), **14**) was found to display the best performance [30].

Using this chiral ligand, acetophenone and cyclohexyl phenyl ketone were reduced with higher rates and ees than those observed employing ligand **13** (Scheme **10**).

Interestingly, these "ligand accelerated" hydrosilylations were performed with very high substrate to ligand ratios (S/L>100.000) at temperature betweens -50° and -78 °C.

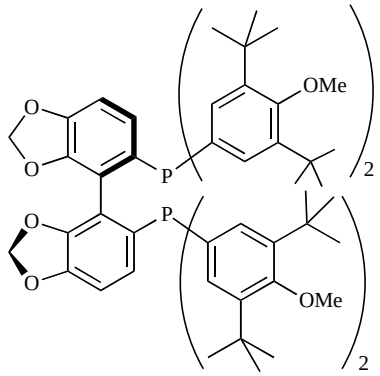
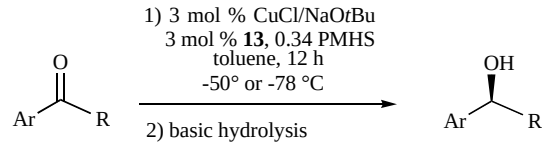
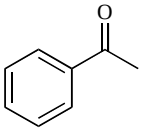
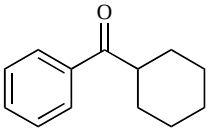


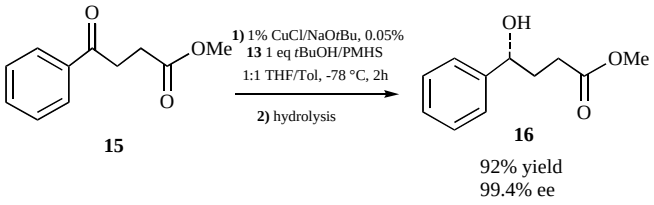
Fig. (3).



Ketone	Ligand	Time (h)	ee (%)
	**13**	5	94
	14	<1	96
	**13**	10	88
	14	<1	93

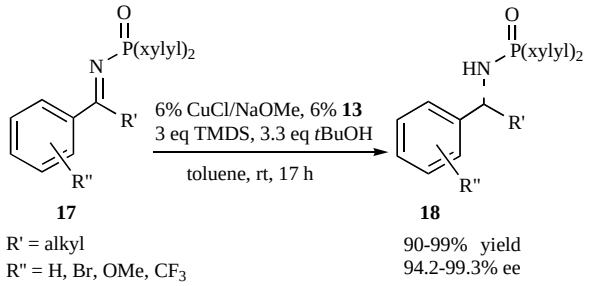
Scheme 10. Asymmetric reduction of aryl ketones with PMHS: comparison of (R)-3,5-Xyl-MeO-BIPHEP- and (R)-DTBM-SEGPHOS ligands.

More recently several functionalized aryl ketones, precursors useful in the synthesis of known-physiologically active compounds, were reduced to the corresponding non racemic alcohols in very high yields, ee's and turnover numbers [31]. For example, using a catalytic quantity of (R)-(-)-DTBM-SEGPHOS·CuH and stoichiometric PMHS with ketoester **15**, an important precursor in the synthesis of antidepressant fluoxetine (prozac), and in the presence of *t*BuOH (1 eq) alcohol **16** could be isolated in 92% yield and with 99.4% ee (Scheme **11**).



Scheme 11. Asymmetric hydrosilylation of a ketoester, precursor to fluoxetine.

The highly chemo- and enantioselctive hydrosilylation of aryl ketimines was another significant result achieved by Lipshutz and Shimizu [32]. The combination of CuCl/NaO*t*Bu/(R)-(-)-DTBM-SEGPHOS and tetramethyldisiloxane (TMDS) as a hydride source reduced the *N*-phosphinylimines **17** at room temperature with high levels of enantioselectivitiy (94-99%) and complete conversion (90-99%) in the presence of *t*-BuOH as additive (Scheme **12**).

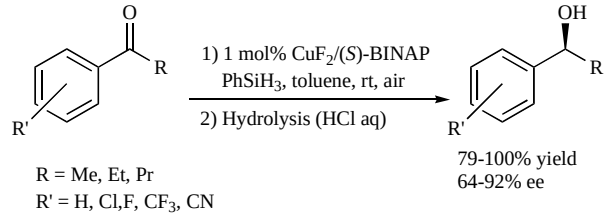


Scheme 12. Cu/(*R*)-DTBM-SEGPHOS catalyzed asymmetric reduction of N-phospinylimines with tetramethyldisiloxane (TMDS).

The resulting products **18** can easily be hydrolyzed to desired amines [33].

The development of an efficient easy-to-handle catalyst system for asymmetric hydrosilylation is of great significance in view of practical applications.

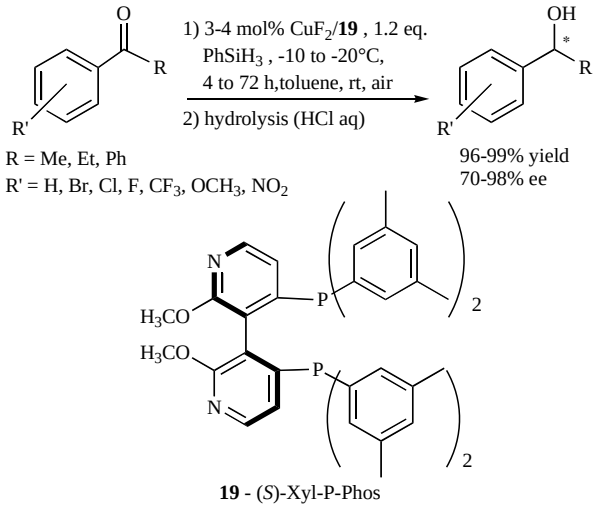
Riant *et al.* [34] reported a base-free and air accelerated CuF_2/(*S*)-2,2'-bis(diphenylphosphino)-1,1'-binaphtyl/$PhSiH_3$ system which catalyzes the hydrosilylation of several aryl alkyl ketones affording the corresponding secondary alcohols in quantitative yields and ee values up to 92% at S/L ratios of 100-200 (Scheme **13**).



Scheme 13. Air-accelerated copper catalyzed hydrosilylations of aryl ketones.

The air stability and mild reaction temperatures are the most interesting features of this catalyst.

More recently, Chan and co-workers [35] found that the combination of pyridyl phosphine ligand **19**, copper difluoride and the silylating agent $PhSiH_3$ is a remarkably reactive free-base catalyst system (S/L ratio up to 100.000) for air-accelerated enantioselective hydrosilylation of a broad spectrum of aryl alkyl ketones at mild temperatures (room temperature to -20°C) and compatible with traces of moisture (Scheme **14**).

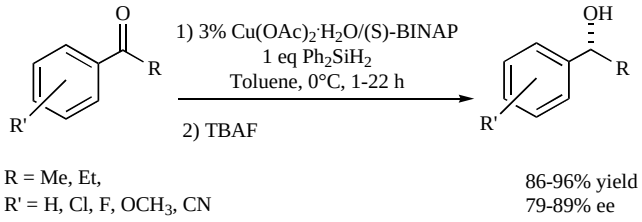


Scheme 14. Air- accelerated asymmetric hydrosilylation of aryl ketones catalyzed by CuF_2 and dipyridylphosphine **19**.

Chan's system achieved levels of enantioselectivities up to 97% ee for hydrosilylation of *meta*- and *para*- substituted acetophenones. Moreover, this P-Phos catalyst system was found to be higly effective in the asymmetric hydrosilylation of some ortho-substituted benzophenones with good to excellent ee values (up to 98%).

In the above described copper(II) systems, the fluoride in the copper salt appears to be crucial for the generation of the active catalyst. Although the role of fluoride still remains elusive, some tests carried out by Riant's group allowed suggested that it activates the Si-H bond to generate a copper hydride species [34].

During their search to find different easy-to-handle copper sources, Yun and Lee [36] showed that the air and moisture stable copper(II) salt $Cu(OAc)_2 \cdot H_2O$ could be successfully used in the asymmetric hydrosilylation of ketones (Scheme **15**).



TBAF = Tetrabutylammonium fluoride

Scheme 15. Asymmetric reduction of aryl ketones with diphenylsilane using copper(II) acetate.

The active catalytic species Cu(I)-H is quickly generated by direct transmetallation with the hydrosilylating reagent itself. This Cu-H generation protocol has some advantages over existing methods such as the absence of base additivies and formation of salts in the reaction medium.

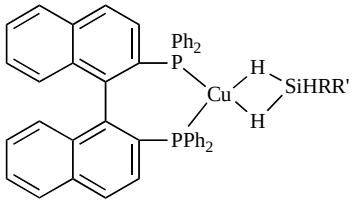
Copper(II) acetate was also employed by Lipshutz and Frieman to prepare the hydrosilylation catalyst [{(R)-(-)-DTBM-SEGPHOS}CuH] which is especially stable at room temperature when kept under inert atmosphere and was introduced as a storable "CuH in a bottle" [37].

Recently, Bellemin-Laponnaz, Dagorne and Issenhuth have shown that enantioselectivity of the asymmetric reduction of ketones catalyzed by (R)-BINAP/Cu(I)-silane system is highly dependent on the nature of the silane [38]. The best combination of phenyl(methyl)silane with the (*R*)-BINAP/CuCl/*t*BuONa system hydrosilylated various aryl alkyl ketones with enantiomeric excesses up 99%.

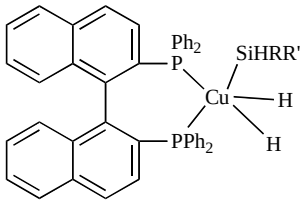
Although some research group have proposed a plausible mechanism for the copper-catalyzed asymmetric hydrosilylation [39-41], the role and importance of silane in the stereodifferanting step still remains unclear [30]. On the basis of kinetic studies, the Bellemin-Laponnaz group proposed two plausible mechanisms to explain the silane effect. The first involves the oxidative addition of the silane to the copper(I)-hydride complex generating a copper(III) intermediate **A**, the second one includes the formation of a pentacoordinate silicon intermediate **B** (Fig. (**4**)).

These silyl-hydrido cuprate species would be able to react with the prochiral ketone.

The numerous advantages of heterogeneous catalysis, such as simplicity of catalyst separation, recyclibility of catalysts and minimization of residual metal in the product [42], prompted some research groups to explore the use of the heterogeneous catalysts in the asymmetric hydrosilylations. Lipshutz's group recently reported a heterogeneous copper catalyst for asymmetric hydrosilylation of several fuctional groups [43].



Intermediate A



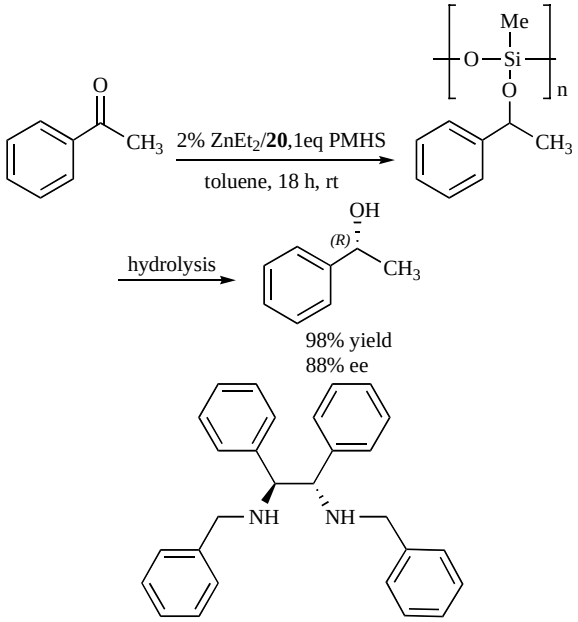
Intermediate B

Fig. (4). Possible copper intermediates that accounts for the silane effect.

Copper(II) immobilized on charcoal (Cu/C) ligated by catalytic amounts of (*R*)-DTBM-SEGPHOS and NaOPh in the presence of poly(methylhydrosiloxane), generate a chiral copper(I) hydride reagent. This species efficiently hydrosilylated some aromatic ketones and *N*-phosphinylimines affording the corresponding reduced products in high yields (up tp 95%) and with excellent ee values (up to 94%).

Detailed studies ruled out the leaching of copper into the solution therefore the catalytic process occurred in a heterogeneous fashion.

Kantam's group used the nanocrystalline copper oxide and (*S*)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphtyl ligand in the presence of phenylsilane for the asymmetric reduction of aryl alkyl ketones. The corresponding chiral secondary alcohols have been obtained with good yields and excellent enantioselectivity (up to 99% ee). Catalyst recycling experiments carried out using acetophenone as model substrate, have shown that the nano-CuO catalyst can be reused for several cycles without loss of activity and selectivity [44].



20 - (*S*,*S*)-*N*,*N*'-dibenzyl-1,2-diphenyl-1,2-ethanediamine

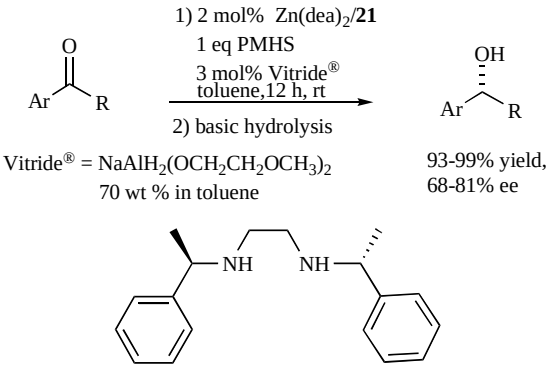
Scheme 16. Diamine/Zn-catalyzed hydrosilylation of acetophenone.

IV. ZINC-CATALYSTS

The first efficient and economic chiral zinc catalysts for the asymmetric hydrosilylation of simple ketonic substrates were described by Mimoun *et al.* in the late nineties [45, 46].

The organometallic zinc precursor, $ZnEt_2$ with a chiral diimine or diamine and PHMS as reducing agent was initially tested in the enantioselective reduction of acetophenone. The best results were obtained using the chiral secondary diamine (*S*,*S*)-*N*,*N*'-dibenzyl-1,2-diphenyl-1,2 ethanediamine **20** (Scheme **16**).

A soluble zinc carboxylate along with a hydride reducing agent such as Vitride® can be also efficiently used as zinc precursor. Moreover, this economic route has been carried out for many aryl ketones employing (*R*,*R*)-*N*,*N'*-ethylenebis(1-phenylethylamine) **21** as chiral ligand on a kilogram scale with recovery of the chiral ligand (Scheme **17**).

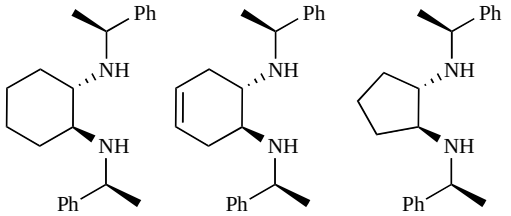


21- *(R.R)- N,N'*-ethylenbis(1-phenylethylamine)

Scheme 17. Diamine/Zn catalyzed hydrosilylation of ketones carried out on a 1 kg scale.

Further developments in the Zn/diamine-catalyzed asymmetric hydrosilylation of ketones have been reported by other groups.

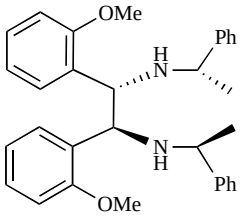
The Walsh group observed that chiral diamines **22-24** having both chiral backbone and N,N' substituents generated Zn catalysts that exhibit high enantioselectivitiy with PMHS o $(EtO)_3Si$ as reducing silylating agents (Fig. (**5**)) [47].



22 90% yield 84% ee

23 99% yield 84% ee

24 95% yield 83% ee



25

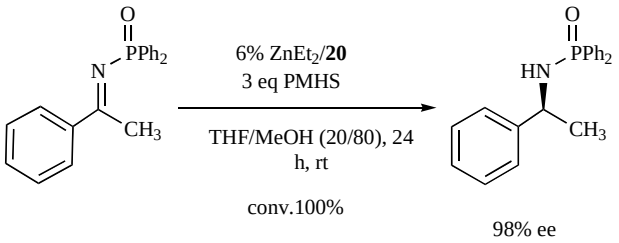
66% yield
91% ee

Fig. (5). Chiral diamines for Zn catalyzed enantioselective reduction of prochiral ketones by PMHS.

Carpentier *et al.* described a new chiral diamine ligand **25** achieving ee values up to 91% in the reduction of acetophenone with PMHS [48].

Recently, Yun *et al.* [49] have shown that chiral Zn/diamine systems can be efficiently used as catalysts for enantioselective hydrosilylation of *N*-phosphinylimines.

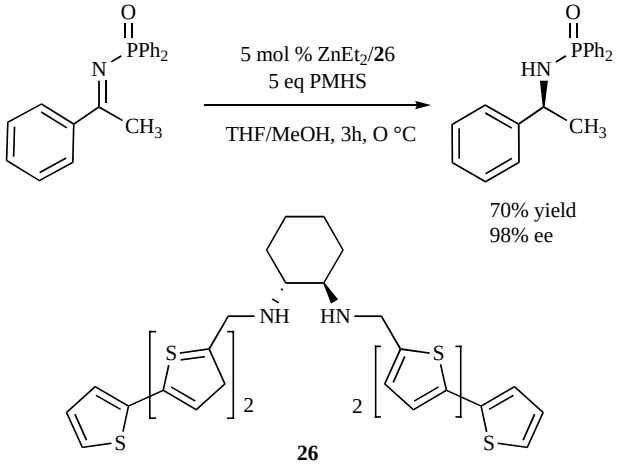
A series of chiral diamines derived from 1,2-diphenyl-1,2 ethanediamine was tested at room temperature and the best enantioselctivity value (98% ee) was obtained in the reduction of phenyl methyl *N*-diphenylphosphinylimine by employing **20** with PHMS as stoichiometric reducing agent in a 20:80 THF:MeOH solvent mixture (Scheme **18**).



Scheme 18. Diamine/Zn-catalyzed enantioselective reduction of N-phosphinylimines with PMHS.

Lately, Brandi, Umani-Ronchi and coll. [50] applied a new readily accessible chiral diamino-bis(*tert*-tiophene) ligand **26** to the Zn-catalyzed PMHS based reduction of aryl alkyl ketones and the phenyl methyl *N*-diphenylphosphinylimine.

The in situ formed (*R*,*R*)-**26**-$ZnEt_2$ complex hydrosilylated a series of aryl alkyl ketones with good yields and ee up 83% showing a good tolerance respect to substituents on the ring as well as in the aliphatic chain. Remarkably, the *N*-phosphinylimine was also reduced with 70% isolated yield and ee of 97% after only 3h reaction time (Scheme **19**).

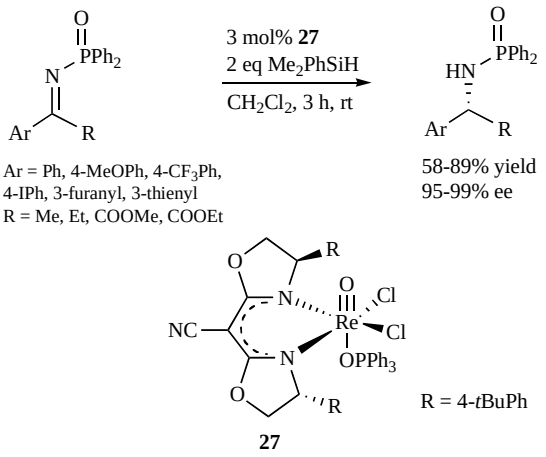


Scheme 19. Enantioselective reduction of imines catalyzed by **26**-Zn complex.

V. MISCELLANEOUS CATALYSTS

Many chiral catalysts based on the other transition metals have been explored to promote hydrosilylation of C=O and C=N groups. High chemical yields and enantioselectivities have been attained in the asymmetric reductions of ketone and imines by chiral titanocene complexes [51-54]. This topic was recently reviewed [55] and since then significant improvements have not been reported.

An interesting "open-flask" reduction of imines that used a chiral high-oxidation Re-dioxo complex was recently developed by Toste and co-workers [56]. The air and moisture stable cyano-bis(oxazoline)rhenium(V)-oxo complex **27** reduced various aromatic, heteroaromatic imines and α-iminoesters in the presence of dimethylphenylsilane as the hydride source with levels over 90% ee (Scheme **20**).

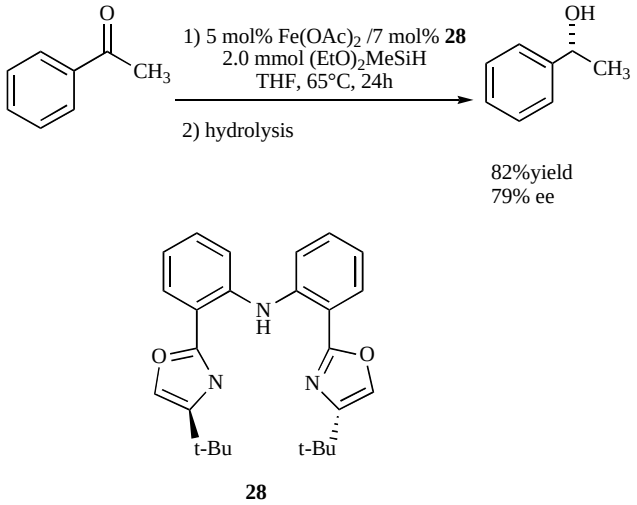


Scheme 20. Enatioselective imine reduction catalyzed by Re-complex **27**.

This enantioselective process is one of the rare examples of a transformation that makes use of a chiral rhenium complex.

Use of an inexpensive and environmentally friendly metal such as iron in the catalytic asymmetric reduction have recently attracted much interest.

Nishiyama and Furuta first examined [57] the combination of ferrous acetate $Fe(OAc)_2$ and multi-nitrogen based ligands in the standard asymmetric hydrosilylation of acetophenone (Scheme **21**).

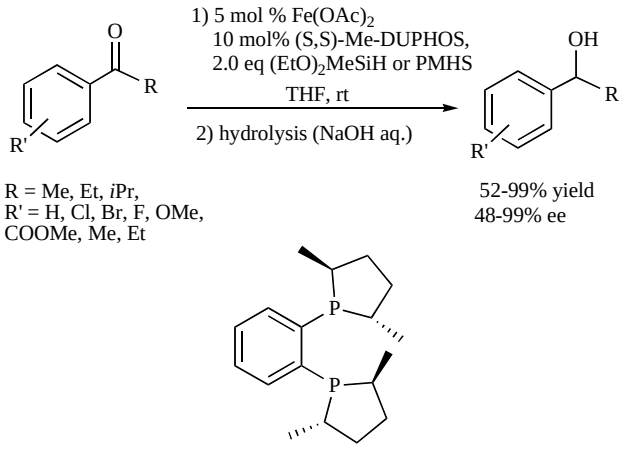


Scheme 21. First iron-catalyzed reduction of ketones with diethoxymethylsylane.

Using the chiral tridentate bisoxazoline ligand **28** and diethoxymethylsylane as reducing agent enantioselectivities of up to 79% have been reached.

Very recently, Beller *et al.* obtained high yields and ee values (up to 99%) in the Fe-catalyzed hydrosilylation of ketones employing $Fe(OAc)_2$ in the presence of diphosphine ligand (*S*,*S*)-Me-DUPHOS (Scheme **22**).

Several aryl ketones were reduced and the best enantioselectivities were obtained for sterically hindered aryl ketones [58].



Scheme 22. Asymmetric hydrosilylation of aryl ketones using (*S*,*S*)-Me-DUPHOS/Fe catalyst.

Multi-substrate screening has been used by Kemp *et al*. demonstrating a novel (*R*,*R*)-DIOP/nickel catalytic system for hydrosilylation of aryl alkyl ketones [59]. Interestingly, this Ni(0)-catalyst gave higher asymmetric induction than the corresponding Rh-catalyst. Mechanistic studies allowed to optimize the Ni catalyst and improve the ee values by around 20% (up to 71%).

VI. CONCLUSIONS

Since the pioneering work carried out over thirty years ago by Kagan, the asymmetric hydrosilylation of ketones and imines has seen significant advances. In the last decade, the development of more efficient catalytic systems which are attractive from economically and environmentally sustainable point of view, has generated the possibility to employ this catalytic process for fine chemical production. Altough the recently discovered catalysts show moderate functional group tolerance and a limited application range, the competitive cost ratio and efficiency achieved in this chemical transformation has opened up new perspectives.

The very recent discovery of inexpensive and environmentally benign iron catalysts for asymmetric hydrosilylation of aryl ketones might encourage the development of an successful methodology for sustainable chemistry.

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Received: April 01, 2008 Revised: March 03, 2009 Accepted: March 10, 2009