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ENANTIOSELECTIVE HYDROSILYLATION OF ACETOPHENONE WITH RHODIUM / OXAZOLINES CATALYSTS

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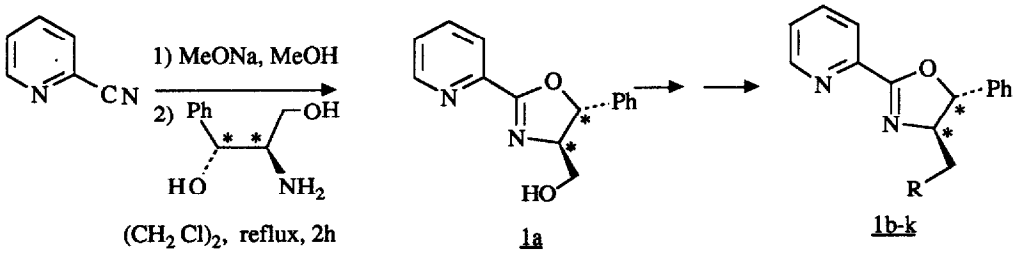
Abstract : N-chelate ligands based on chiral oxazolines are efficient co-catalysts in the enantioselective hydrosilylation of acetophenone with α-naphtylphenylsilane. Enantiomeric excess as up to 80% have been achieved.

Asymmetric synthesis by means of homogeneous catalysis with transition metal complexes associated to chiral ligands has been a subject of great topical concern during the recent years[2]. As phosphines are highly efficient ligands in many catalytic reactions, much effort has been devoted to design chiral phosphines and especially chelating diphosphines. On the other hand, transition metal complexes with nitrogen containing ligands such as phenantroline or bipyridine have been shown to have important and useful stereoelectronic properties. Many reactions mediated by these compounds have been reported. Even though several chiral nitrogen containing ligands have been already described[3], there is definitely a need for new and efficient ligands for asymmetric catalysis and also for the design of new transition metal complexes able to play a role in the field of molecular materials[4].

Brunner and coworkers have reported high enantioselectivity in asymmetric hydrosilylation of ketones using catalytic systems prepared *in situ* from a rhodium based precursor and (2-pyridine)thiazolidine[3].

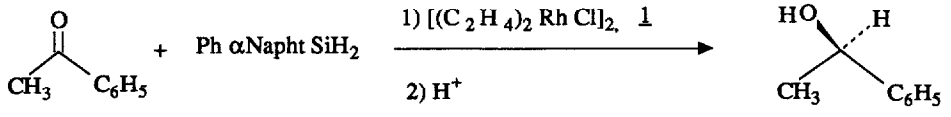
The successful use of chiral oxazolines in asymmetric synthesis[5] led us to believe that their use in enantioselective catalysis could be promising. Recent publications[6] related to our work prompt us to report our results on the asymmetric hydrosilylation of ketones using various chiral 2-pyridinyl-oxazolines.

The (4S,5S)-4-hydroxymethyl-5-phenyl-2-(2-pyridinyl)-1,3-oxazoline **1a** (scheme1) has been readily prepared on a hundred grams scale (83% yield), from cheap and commercially available 2-cyanopyridine and (1S,2S)-(+)-2-amino-1-phenyl-1,3-propanediol[7]. From this common intermediate **1a**, a large variety of chiral 2-(2-pyridinyl)-1,3-oxazolines **1b**,....,**1k** have been further elaborated[8] in order to shed light on the stereoelectronic effects of the ligands in the enantioselective rhodium catalyzed hydrosilylation of ketones.



scheme 1

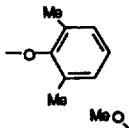
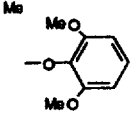
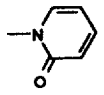
The efficiency of these new chelating ligands was tested in the model system acetophenone/ αnaphtylphenylsilane (scheme 2). A 0.6% of the bis-ethylene-Rhodium chloride dimer was used with a ratio ligand to metal of 8. In all cases the (R)-1-phenylethanol was obtained in excess after acidic hydrolysis (3N HCl, 0°C) of the intermediate silylether.



scheme 2

From the results presented in table I it appears that the enantioselectivity is highly dependent of both steric and electronic properties of the R group located at the 4 position of the oxazoline ring. In all examples, R group could be a third but temporary anchoring point for the metal center. When the coordinating properties of the R group are quite similar (entries b to g), a clear correlation between the enantioselectivity and the size of the R moiety appeared. The highest enantiomeric excess (80%), close to the best value reported under similar conditions[3c], was achieved in a quantitative chemical yield with the more bulky trityl ether **1g**. The introduction in R of an additionnal anchoring point with good coordinating properties (**1j**, **1k**) does not seem to be beneficial, probably owing to a mechanism involving other conformations or structures of the catalytic intermediates

TABLE I

entry[i]	R	% hydrosilylation[ii]	% ee (R configuration)[iii]
a	-OH	65	37
b	-OMe	64	11
c	$-OSO_2Me$	92	29.5
d	-OPh	93	61
e		92	74
f		91	70.3
g	$-OC(Ph)_3$	100	80
h		98	67
i	-OCO-CH=CH-Ph	89	56.2
j	-SH	60	11.2
k	-SPh	60	18.5

i) Typical procedure :
To a mixture of the catalyst $[Rh(C_2H_4)_2Cl]_2$ ($5x10^{-5}$mole) and the ligand **1** ($4x10^{-4}$mole) was added under argon $17.1x10^{-3}$mole of dry degassed acetophenone. To the cooled solution (0°C), the α–naphtylphenylsilane ($19x10^{-3}$mole) was added dropwise and the reaction was stirred for 3 days at 0°C. The workup is conducted as described earlier[3a] with in all cases a chemical yield over 80%.
ii) Determined by GC and ^1H NMR
iii) Determined by polarimetry (see ref.3a) and GC of the diastereoisomeric menthyl carbonate[11]

The influence of the structure of the reducing silane $Ar^1Ar^2SiH_2$ was then studied using the trityl ether **1g** as a chiral ligand, the results are presented in table II.

TABLE II

entry	Ar^1	Ar^2	% hydrosilylation	% ee (R)
l	Ph	Ph	96	63.2
m	α-Napht.	Ph	100	80
n	Mesityl.	Ph	28	57
o	α-Napht.	α-Napht.	93	24

Surprisingly, exchanging the α-naphtyl group with either a smaller group (phenyl, entry l) or a more sterically demanding one (mesityl entry m) resulted in both cases in a sharp decrease of the enantioselectivity.

Interestingly Brunner has reported[3] that with thiazolidine ligands, diphenylsilane was clearly superior to α-naphtylphenylsilane. The stereochemical course of this rhodium catalyzed hydrosilylation seems to be highly dependent of a good match in term of molecular recognition between the ligand and the silane.

Applications of oxazoline ligands in the design and the use of chiral transition metal complexes are under current investigation.

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7- Both enantiomers (1S,2S) and (1R,2R) of 2-amino 1-phenyl-1,3-propanediol are commercially avalaible.

8- All compounds **1a-1k** were fully characterized by elemental analysis and ^1H NMR spectroscopy.
The synthesis of **1a** followed the route in scheme 1[9,10] (87% yield, mp 172°C, $[\alpha]^D_{25} = +11.6°$ (c = 2.37, $CHCl_3$)).
Compounds **1b-1k** were readily obtained from **1a** by the following reactions:
1b: i) HNa, THF, **1a**, 30°C, 1h.; ii) MeI, 30°C, 15h.; 86% (oil, $[\alpha]_D^{25} = + 46.6°$ (c = 1.03, $CHCl_3$)).
1c: i) **1a**, CH_2Cl_2, NEt_3, -5°C; ii) $MeSO_2Cl$, -5°C, 3h; iii) H_2O; 92% (mp 87°C, $[\alpha]_D^{25} = + 13.6°$ (c = 1.365 ($CHCl_3$)).
1d,**1e**,**1f** and **1h** were obtained by the same procedure using different phenols: i) NaOH, H_2O, Aliquat 336, ArOH, RT, 0.5h; ii) **1c**, C_6H_6, reflux under argon, 24h. **1d** was obtained from PhOH; 80% (oil, $[\alpha]_D^{25} = -36.2°$ (c = 1.2,$CHCl_3$)). **1e** was obtained from 2,6-dimethylphenol; 78% (oil,$[\alpha]_D^{25} = -34.8°$ (c = 1.46, CHCl3)). **1f** was obtained from 2,6-dimethoxyphenol ; 68% (mp 88°C, $[\alpha]_D^{25} = -35.8°$ (c = 1.65, $CHCl_3$)). **1h** was obtained from 2-hydroxypyridine; 52% (mp 140°C, $[\alpha]_D^{25} = + 1.85$ (c = 1.09, $CHCl_3$)). (O-alkylated product was also obtained in 17%yield)
1g: i) **1a**, $(Ph)_3CCl$, DMAP, CH_2Cl_2, NEt_3, RT 12h; reflux 2h; ii) H_2O; 72% (mp 70°C,$[\alpha]_D^{25} = +14.0°$ (c=0.99, $CHCl_3$)).
1i: i) **1a**, CH_2Cl_2, Et_3N, DMAP, $C_6H_5CH{=}CHCOCl$, 0°C; RT 20h; reflux 2h; ii) H_2O; 54% (mp 72°C, $[\alpha]_D^{25} = -7.1$ (c= 1.02 $CHCl_3$)).
1j: i) **1c**, thiourea, EtOH, reflux, 3h; ii) NaOH, H_2O, reflux 3h; 32% (mp 204°C, $[\alpha]_D^{25} = +77.4°$ (c= 0.807, $CHCl_3$)).
1k: i) NaOH, H_2O, Aliquat 336, PhSH; ii) **1c**, C_6H_6, reflux 12h; 88% (mp 111°C $[\alpha]_D^{25} = +97.8°$ (c= 0.98, $CHCl_3$)).

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