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Optically Active Phenanthrolines in Asymmetric Catalysis. IV. Enantioselective Hydrosilylation of Acetophenone by Rhodium/Chiral Alkyl Phenanthroline Catalysts.

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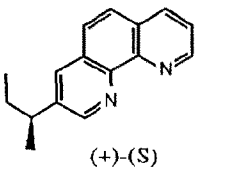
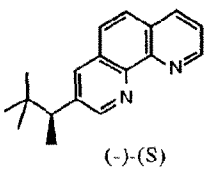
Abstract: The *in situ* catalysts prepared from $[Rh(Cod)Cl]_2$ (Cod = 1,5-cyclooctadiene) and chiral alkylphenanthroline ligands **1-6** display a remarkable activity in the asymmetric hydrosilylation of acetophenone affording, after hydrolysis, the expected 1-phenylethanol in high yield and complete selectivity. High enantioselectivities, up to 76%, were obtained in the presence of 2-substituted derivatives **5** and **6**, whereas 3-alkylphenanthrolines **1-4** gave e.e.'s not higher than 6%. High chemical yields, but modest enantioselectivities (10-20% e.e.) were recorded with the potentially terdentate ligands **7-10**. Chiral alkylphenanthrolines were poorly efficient ligands in the asymmetric Ni-catalysed cross-coupling of α-methylbenzylmagnesium chloride with vinyl bromide.

Optically active alkylphenanthrolines[1] and, to a lower extent, alkylbipyridines[2] have been shown to be efficient chiral modifiers in the rhodium catalysed asymmetric transfer hydrogenation of acetophenone. In 2-propanol solution and in the presence of KOH as a promoter, turnover rates up to 10,000 cycles-per-hour (c/h) have been attained at 83°C with the *in situ* catalyst obtained from $[Rh(Cod)Cl]_2$ and 3-alkylphenanthrolines **1** and **2**[3].Under these conditions, asymmetric inductions up to 65% and 35%, respectively, were recorded with the ligands **2** and **1**, whereas the C_2 symmetrical 3,8-disubstituted phenanthroline **4** produced a catalytic system of poor activity which gave rise to racemic product[3]. Lower reaction rates (up to 500 c/h) and 10-25% e.e.'s were recorded with 2-alkylphenanthrolines **5** and **6**[4] and with the related bipyridine **11**[2] under comparable conditions.



(+)-(S)

1



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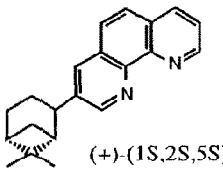
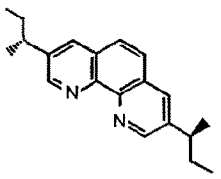


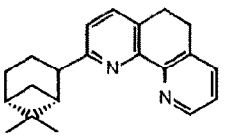
(+)-(1S,2S,5S)

3



(+)-(3S,8S)

4



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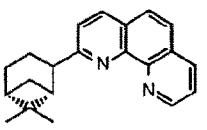
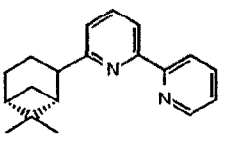
5



(+)-(1S,2S,5S)

6



(+)-(1S,2S,5S)

11

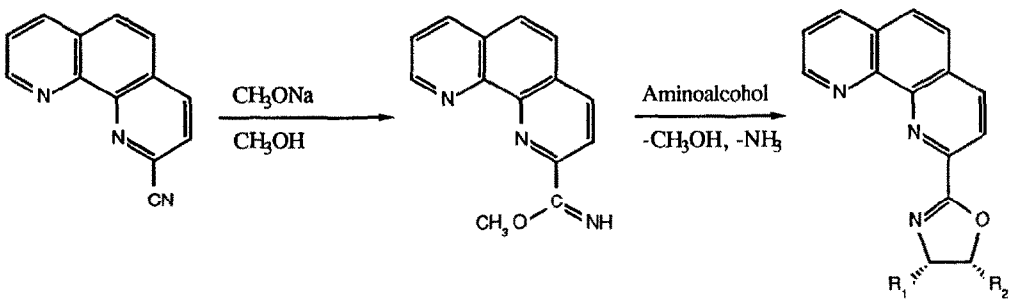
It has been suggested that the high stereoselectivity observed in this process with 3-alkylsubstituted derivatives is substantially determined by the chiral disposition of two phenanthroline ligands around the rhodium atom in a C_2 propeller-like assembly. This dissymmetric arrangement should account for the efficient transfer of the chiral information from the asymmetric carbon atom of the substituent in remote position to the reactive site of the catalyst.

The efficiency of chiral nitrogen ligands in the rhodium catalysed hydrosilylation of aryl alkyl ketones is well documented and the number of nitrogen derivatives that have been tested in this process is fairly large[5]. Chiral alkybipyridines were among these and an optical yield as high as 71.6% was recorded on acetophenone in the presence of ligand **11**[6]. Potentially terdentate nitrogen ligands have been also exploited in the hydrosilylation[7] and quite recently Japanese researchers have obtained good to excellent enantioselectivities on several prochiral ketones by the use of a C_2 symmetrical bis(oxazolinylpyridine)rhodium catalyst [8].

To expand the scope of chiral phenanthrolines in asymmetric catalysis, we have investigated the rhodium catalysed asymmetric hydrosilylation of acetophenone with diphenylsilane in the presence of ligands **1-6**. Additionally, in order to gain some more information on the efficiency of phenanthroline based ligands in this

process, we have synthesised a short set of potentially terdentate derivatives, **7-10**, substituted in position 2 with a chiral 2-oxazolinyl group. These derivatives have been prepared from readily available 2-cyanophenanthroline **12**[9] by condensation of the relevant methoxyimidate **13** with a suitable optically active β-aminoalcohol according to a reported procedure[10] (Scheme 1). Compounds **7-10** have been isolated as crystalline solids and gave spectroscopic and elemental analysis data in agreement with the expected structures.

SCHEME 1



12 **13** **7-10**

	R_1	R_2	Conf.
7	CH_3	H	4S
8	$CH_2CH(CH_3)_2$	H	4S
9	C_6H_5	H	4S
10	CH_3	C_6H_5	4S,5R

The results obtained in the enantioselective hydrosilylation of acetophenone in the presence of $[Rh(Cod)Cl]_2$ and chiral phenanthroline derivatives **1-10** are summarized in Table 1.

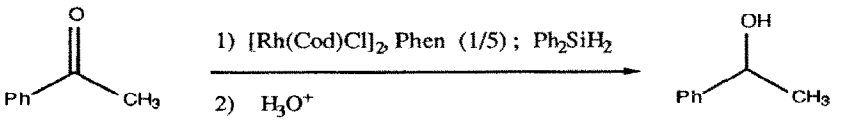
The *in situ* catalysts obtained from phenanthrolines are very effective: with ligand **1**, complete hydrosilylation of acetophenone was attained in 12 h at room temperature even at the relatively high substrate-to-catalyst ratio of 400:1. The reaction is quite chemoselective and no trace of enolsilylether could be detected in the reaction mixture at the end of the catalytic experiment. Thus, 1-phenylethanol could be recovered in almost quantitative yield after hydrolytic work up.

With bidentate phenanthrolines **1-6**, the enantioselectivity increases dramatically as the chiral substituent is moved closer to the nitrogen atom. The extent of this effect is quite high as pointed out from the comparison of the results obtained with ligands **3** and **6** (5.9% and 75.6% e.e., respectively) where the same chiral substituent is moved from the position 3 to the carbon atom adjacent to the nitrogen. Other structural factors like

the complexity of the chiral substituent (compare entries 1-3) or a higher degree of flexibility (compare entries 5 and 6) seem much less important. A reversal of the normal topicity of the reaction is observed with the C_2 symmetrical disubstituted phenanthroline **4**, but in this case also the enantioselectivity remains low.

TABLE 1

ENANTIOSELECTIVE HYDROSILYLATION OF ACETOPHENONE BY RHODIUM(I)/CHIRAL PHENANTHROLINE CATALYSTS ([Rh(Cod)Cl]$_2$ 0.02 mmol; [Phen]/[Rh] = 5; [S]/[Rh] = 200; [Ph_2SiH_2]/[S] = 1; toluene 2 ml; 0°C, then warm to room temperature; 18 h).



Ligand	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
e.e.[a]	2.4	3.7	5.9	4.2	69.8	75.6	8.3	10.8	20.1	8.1
Conf.	R	R	R	S	R	R	S	S	S	R

a) Determined by GLC of the corresponding *t*.butylurethane on a 50m Chirasil-L-Val capillary column[10].

The catalysts prepared from the oxazolinyl derivatives **7-10** displayed a good activity and chemoselectivity, but the asymmetric inductions were only modest and much lower than the ones obtained with the 2-substituted phenanthrolines **5** and **6**. Monosubstituted oxazolines **7-9** of (S) configuration produced (S)-1-phenylethanol, the enantioselectivity roughly increasing with the bulkiness of the substituent. The introduction of a second chiral center at C-5 of the oxazoline ring results in an inverse enantioselection with respect to the corresponding monosubstituted ligand (compare entries 7 and 10).

Making allowance for the direction of the asymmetric induction, which is opposite, and for its extent which is more pronounced in the previous case, these trends are quite similar to those observed with the pyridinyloxazoline ligands[10] with the same substitution pattern. This raises some doubts about the possibility that phenanthrolinyloxazolines **7-10** are coordinated in a tridentate fashion all the time during the catalytic cycle.

The results obtained in this study demonstrate that chiral alkylphenanthrolines can promote the formation of a highly efficient catalytic system for the asymmetric hydrosilylation of acetophenone in the presence of rhodium complexes. In the hydrosilylation, the coordination of the ligand to the metal does not seem inhibited by the presence of rather bulky substituent on the carbon adjacent to the nitrogen and, thus, the enantioselective ability of these catalysts is particularly pronounced when the ligands bear the chiral substituent as close as possible to the reactive site of the catalyst

Differently from the behaviour displayed by the same phenanthrolines in the rhodium catalysed transfer hydrogenation of the same substrate, in this case the proximity effect holds and stiffening the heterocyclic framework or changing the structure of the chiral target in remote position have only minor effects on the outcome of the process. Contrary to what happens in the rhodium catalysed transfer hydrogenation, in the hydrosilylation the use of phenanthroline derivatives in place of the corresponding bipyridine affords only a slight improvement in the enantioselectivity of the reaction (75.6 vs. 71.6 obtained with ligands **6** and **11**, respectively), without affecting at all the catalytic activity and the direction of the asymmetric induction.

Finally, a short set of experiments has been carried out in order to test the efficiency of alkylphenanthrolines in the nickel catalysed cross-coupling of Grignard reagents. The reaction of α-methylbenzylmagnesium chloride (60 mmoles) with vinyl bromide (30 mmoles) was carried out according to a reported procedure[11] at 0°C in the presence of a 1/1 $NiCl_2$/phenanthroline catalyst prepared *in situ*. Chemical yields consistently lower than 20% and e.e.'s of 2.7%, 8.5% and 4.3% were recorded with the ligands **1**, **5** and **6**, respectively. Thus it is concluded that this kind of nitrogen ligands are not well suited for this catalysis.

EXPERIMENTAL

Melting points were determined on a Büchi melting point apparatus and are uncorrected. GLC Analyses were performed on a Hewlett Packard 5890A instrument equipped with a 30 m SP 1000 or SP 2100 capillary column. ^{1}H NMR Spectra were recorded on a Varian VXR 300 spectrometer at 300 MHz in deuterochloroform solution with tetramethylsilane as internal standard (δ=0). Optical rotations were determined with a Perkin Elmer 241 polarimeter in 95% ethanol solution (c 1). Elemental analyses were performed with a Perkin Elmer Elemental Analyzer 240B.

Commercial chemical reagents were used as received. 2-Cyano-1,10-phenanthroline **12** was prepared from phenanthroline 1-oxide according to ref. 9 and was converted into the corresponding methyl carboxyimidate **13** following a reported method[12]. Catalytic hydrosilylations and determinations of the chemo- and enantioselectivities were carried out as described in ref. 10.

Preparation of phenanthrolinyloxazolines **7-10**. *General procedure.*-

A solution of methyl carboxyimidate **13** (1.9 g; 8 mmol) in anydrous benzene containing the appropriate aminoalcohol (8 mmol) and a few milligrams of *p*.toluenesulfonic acid was slowly distilled under nitrogen atmosphere until all the substrate was reacted (1-2 h). The solvent was removed and the residue was directly crystallised (**9** and **10**) or filtered through silica (acetone) prior to crystallization (**7** and **8**).

(S)-(-)-4-Methyl-2-(2-phenanthrolinyl)-2-oxazoline, **7**: from (S)-(+)-2-amino-1-propanol; 30% yield; m.p. 85-6°C (benzene); $[\alpha]_D^{25}$ -13.7. ^{1}H-NMR: 9.22 (1, dd, 9H), 8.35 (2, dd, 3H and 4H), 8.24 (1, dd, 7H), 7.84 (2, dd, 5H and 6H), 7.65 (1, dd, 8H), 4.71 (1, dd, Ox-5H), 4.52 (1, m, Ox-4H), 4.18 (1, dd, Ox-5H), 1.43 (3, d, CH_3). (Found: C, 70.30; H, 5.39; N, 15.58. $C_{16}H_{13}N_3O{\cdot}0.5\ H_2O$ requires: C, 70.57; H, 5.18; N, 15.43).

(S)-(+)-4-(2-Methylpropyl)-2-(2-phenanthrolinyl)-2-oxazoline, **8**: from (S)-(+)-2-amino-4-methyl-1-pentanol; 25% yield; m.p.83-4°C (MeOH-H_2O); $[\alpha]_D^{25}$ +11.4. ^{1}H-NMR: 9.22 (1, dd, 9H), 8.32 (2, dd, 3H and 4H), 8.27 (1, dd, 7H), 7.84 (2, dd, 5H and 6H), 7.66 (1, dd, 8H), 4.70 (1, dd, Ox-5H), 4.49 (1, m, Ox-4H), 4.19 (1, dd, Ox-5H), 1.95 (1, m, CH_2), 1.80 (1, m, CH_2), 1.42 (1, m, CH), 1.00 (6, dd, CH_3). (Found: C, 74.03; H, 6.76; N, 13.60. $C_{19}H_{19}N_3O{\cdot}0.5\ H_2O$ requires: C, 74.48; H, 6.58; N, 13.71).

(S)-(+)-4-Phenyl-2-(2-phenanthrolinyl)-2-oxazoline, **9**: from (S)-(+)-2-amino-2-phenylethanol; 84% yield; m.p.196-7°C (MeOH-H_2O); $[\alpha]_D^{25}$ +129.3. ^{1}H-NMR: 9.26 (1, dd, 9H), 8.55 (1, d, 3H), 8.36 (1, d, 4H),

8.27 (1, dd, 7H), 7.86 (2, dd, 5H and 6H), 7.67 (1, dd, 8H), 7.37 (5, m, C_6H_5), 5.55 (1, dd, Ox-5H), 5.03 (1, dd, Ox-4H), 4.53 (1, dd, Ox-5H). (Found: C, 73.75; H, 4.85; N, 11.99. $C_{21}H_{15}N_3O \cdot H_2O$ requires: C, 73.45; H, 4.99; N, 12.24).

(4S,5R)-(+)-4-Methyl-5-phenyl-2-(2-phenanthrolinyl)-2-oxazoline, **10**: from (1S,2R)-(+)-norephedrine; 85% yield; m.p.105°C (MeOH-H_2O); $[\alpha]_D^{25}$ +213.2. ^{1}H-NMR: 9.22 (1, dd, 9H), 8.40 (2, dd, 3H and 4H), 8.28 (1, dd, 7H), 7.88 (2, dd, 5H and 6H), 7.68 (1, dd, 8H), 7.36 (5, m, C_6H_5), 5.98 (1, d, Ox-5H), 4.83 (1, m, Ox-4H), 0.99 (3, d, CH_3). (Found: C, 72.39; H, 5.61; N, 11.50. $C_{22}H_{17}N_3O \cdot 1.5\ H_2O$ requires: C, 72.11; H, 5.50 N, 11.47).

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