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An efficient phosphorous-containing oxazoline ligand derived from *cis*-2-amino-3,3-dimethyl-1-indanol: application to the rhodium-catalyzed enantioselective hydrosilylation of ketones

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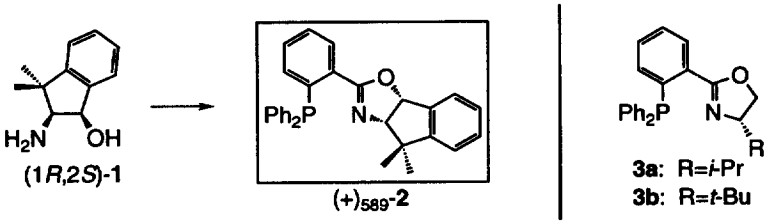
Abstract: Enantiopure 2-[2-(diphenylphosphino)phenyl]oxazoline, derived from a non-natural amino alcohol, *cis*-2-amino-3,3-dimethyl-1-indanol, was found to be an efficient ligand for the rhodium-catalyzed enantioselective hydrosilylation of ketones. © 1997 Elsevier Science Ltd

In the course of our studies concerning the development of non-natural chiral auxiliaries and their application to asymmetric syntheses,[1] phosphorus-containing oxazoline **2**, derived from *cis*-2-amino-3,3-dimethyl-1-indanol **1**,[2] was found to be a more efficient ligand than **3** for the palladium-catalyzed enantioselective allylic amination reaction.[3] Encouraged by this successful result, we next tried to apply **2** as a ligand in the enantioselective rhodium-catalyzed hydrosilylation of ketones.



The transition metal-catalyzed hydrosilylation of ketones, followed by hydrolysis of the resulting silyl ethers, is a useful method for obtaining alcohols from ketones, since in this reaction the use of a water- and air-sensitive metal hydride and explosive pressurized hydrogen gas can be avoided and since the application of an optically active ligand in the reaction results in the production of enantioenriched chiral alcohols.[4] Recently, Newman *et al.* and Langer *et al.* reported that valinol-derived phosphorus-containing oxazoline **3a** is an effcient ligand in the rhodium-catalyzed hydrosilylation of ketones.[5,6]

The reaction conditions for the present enantioselective hydrosilylation were optimized by using acetophenone and α-tetralone as substrates (Scheme 1, Table 1). The reactions were carried out at room temperature using a catalyst, which was prepared *in situ* from 1 mol% $[Rh(cod)Cl]_2$ and $(+)_{589}$-**2**. First, the solvent effect was examined using 2.4 mol% $(+)_{589}$-**2** (entries 1 to 4). When the hydrosilylation of acetophenone was carried out without solvent using 10 eq. of Ph_2SiH_2, the enantioselectivity was only moderate. In contrast, excellent enantioselectivity for the hydrosilylation of acetophenone was observed, when the reaction was carried out in toluene using 2 eq. of Ph_2SiH_2 (entry 4). However, the enantioselectivity for the hydrosilylation of α-tetralone was unsatisfactory, even when the reaction was carried out in toluene. In order to improve the selectivity, we next examined the amount of $(+)_{589}$-**2**; when the amount of $(+)_{589}$-**2** was increased from 2.4 mol% to 4 mol%, remarkable improvement of the selectivity was achieved (entry 5). Further increasement of the amount of $(+)_{589}$-**2** did not affect the selectivity (entry 6). Concerning the reaction temperature, these reactions did not proceed at all at

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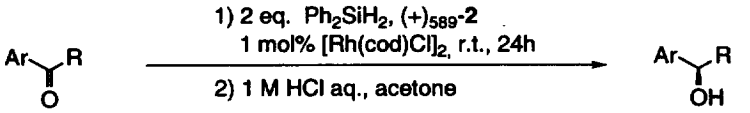
0°C. The use of $[Rh(cod)_2]^+BF_4^-$ or $[Ir(cod)Cl]_2$ in the place of $[Rh(cod)Cl]_2$ resulted in deterioration of the selectivity. Thus, we deduced that the optimum reaction conditions were those for entry 5.



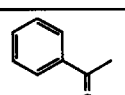
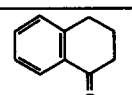
Scheme 1.

Under the optimized conditions, the hydrosilylation of various prochiral ketones was carried out (Scheme 2, Table 2). Good to excellent enantioselectivity was observed in the hydrosilylation of aralkyl ketones (entries 1 to 5). The hydrosilylation of dialkylketones was also successful (entries 7 and 8); 87% e.e. was accomplished in the reaction of cyclohexyl methyl ketone. These results are much better than those reported using **3a** as a ligand.[5,6] However, disappointingly low selectivity was observed for the reaction of benzalacetone (entry 6). It is noteworthy that both enantiomers of this ligand are readily available and consequently both enantiomers of the desired alcohol are equally obtained (entries 4 and 5).

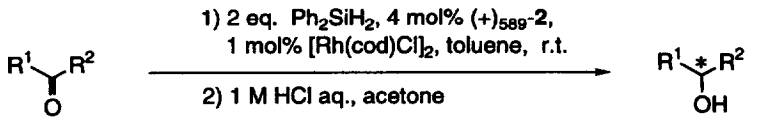
The absolute configurations of the alcohols, produced using $(+)_{589}$-**2** as a ligand, are all *R*, the same as those obtained using **3a** as a ligand. Therefore, the chiral induction mechanism of the present reaction using $(+)_{589}$-**2** would be similar to that of the reaction using **3a**. Newman *et al.* and Langer *et al.* reported that **3a** (valinol-derived) is a much more efficient ligand than **3b** (*t*-leucinol-derived).[5,6] Their results indicate that the selectivity is anti-proportional to the bulkiness of the substituent at the 4-position of the oxazoline moiety of the ligand. However, the chiral induction ability of $(+)_{589}$-**2** is anomalously high, even though the conformationally fixed two methyl substituents of $(+)_{589}$-**2** are considered to be more bulky than a *t*-Bu substituent. In order to clarify these apparently conflicted phenomena, further investigations concerning the mechanism of rhodium-catalyzed hydrosilylation and concerning the structures of the intermediates are required.

The general procedure for the enantioselective hydrosilylation is as follows. To a mixture of $[Rh(cod)Cl]_2$ (6.2 mg, 0.013 mmol) and $(+)_{589}$-**2** (22.4 mg, 0.0501 mmol) in toluene (0.5 mL), which has been pre-stirred at rt for 30 min, was added a solution of a ketone (1.25 mmol) in toluene (1.0 mL). Then, Ph_2SiH_2 (0.5 mL, 2.5 mmol) was added at −78°C, and the resultant solution was stirred at rt for 24 h. After being cooled to 0°C, 1M HCl aq. (3 mL) and acetone (5 mL) were successively

Table 1.

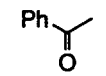
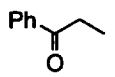
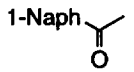
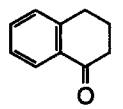
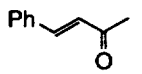
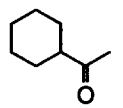
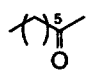
entry	solv.	$(+)_{589}$-2 /mol%				
			yield/%	% e.e.[a]	yield/%	% e.e.[a]
1	none[b]	2.4	64	76	–	–
2	THF	2.4	76	85	68	43
3	ether	2.4	80	91	–	–
4	toluene	2.4	76	93	76	59
5		4	84	94	89	89
6		10	–	–	84	89

[a]Determined by chiral HPLC analysis (Daicel Chiralcel OB). [b]The reaction was carried out using 10 equimolar amounts of Ph_2SiH_2.



Scheme 2.

Table 2. Enantioselective hydrosilylation of various ketones[a]

entry	ketone	yield/%	% e.e. (config)
1		84	94[c] (*R*)
2		91	91[c] (*R*)
3		90	92[c] (*R*)
4		89	89[c] (*R*)
5[b]		97	92[c] (*S*)
6		83	22[c] (*R*)
7		85	87[d] (*R*)
8		90	52[e] (*R*)

[a]The reaction was carried out in toluene in the presence of 1 mol% $[Rh(cod)Cl]_2$, 4 mol% $(+)_{589}$-2, and 2 eq. of Ph_2SiH_2 at rt. [b]As a ligand, $(-)_{589}$-2 was used. [c]Determined by chiral HPLC analysis (Daicel Chiralcel OB). [d]Determined by GC analysis of the corresponding (+)-MTPA ester. [e]Determined by chiral HPLC analysis (Daicel Chiralcel OD) of the corresponding 2-naphthoate.

added to the solution, and the mixture was stirred for 2 h at rt. After usual workup, purification by column chromatography gave the corresponding alcohol. The absolute configuration of the alcohol was deduced by comparison of the sign of its specific rotation with that in the literature.

In summary, 2-[2-(diphenylphosphino)phenyl]oxazoline **2**, derived from *cis*-2-amino-3,3-dimethyl-1-indanol **1**, was found to be an efficient ligand for the rhodium-catalyzed enantioselective hydrosilylation of ketones.

Acknowledgements

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