Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 6, pp. 1599-1602, 1996

0957-4166/96 $15.00 + 0.00

PII: S0957-4166(96)00192-9

Catalytic Asymmetric Hydrosilylation of Ketones Using Rhodium-(I)-Complexes of Chiral Phosphinooxazoline Ligands

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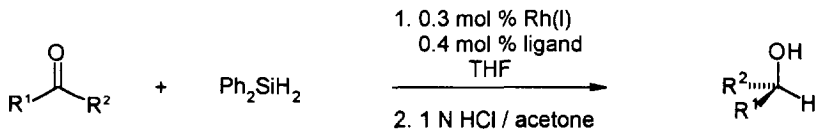
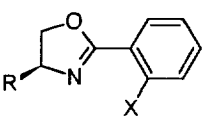
Abstract: (Phosphinooxazoline)rhodium(I) complexes, prepared in situ with ligand:Rh molar ratio of 1.3:1, were applied as catalysts in hydrosilylations of a variety of ketones to yield secondary alcohols with moderate to good enantioselectivities.

Enantioselective reduction of ketones to chiral alcohols is of great importance in preparative organic chemistry. For industrial applications, catalytic hydrogenation methods that avoid pressurized hydrogen are desired. Interesting alternatives are transfer hydrogenation, hydroboration and hydrosilylation. In the course of our investigations of oxazoline ligands, we have previously studied asymmetric hydrosilylations with Rh(I) complexes of bi- and bisoxazolines[1]. We have now extended this work[2] and want to report hydrosilylations with phosphinooxazolines as chiral ligands

Scheme 1



Ligands:



R = CH_3, iPr, tBu, CH_2Ph

X = PPh_2, P(1-Naphthyl)$_2$, SPh, SeP

(Scheme 1).

Hydrosilylation is efficiently promoted by rhodium complexes and known to be tolerant to a variety of functional groups in the substrate[3]. Continuous interest in this method is documented by recent publications[4]. Surprisingly, with respect to enantioselectivity, nitrogen-based ligands such as bis-

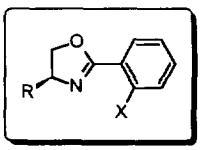
oxazolines or pyridyl-oxazolines proved so far superior to bidentate phosphine ligands. However, with N,N ligands high levels of enantioselectivity were only obtained if the ligand was applied in large excess with respect to the transition metal, *i.e.*, ratios of ligand:Rh of up to 10 were required. We hoped that with phosphinooxazolines one might combine the high degree of reactivity induced by phosphorus with excellent enantiofacial differentiation induced by the oxazoline moiety. A variety of phosphinooxazolines have been synthesized in this group[5] and this allowed a thorough investigation of the influence of the substituents R and X in these ligands. Results are summarized in Table 1.

With acetophenone as standard substrate, *conversion* in the range 80-97 % (entries 1-6, 8, 11, 13,14) was achieved with most ligands. However, low levels of conversion were found for ligands with bulky substituents, *i.e.*, a *t*-butyl or a dinaphthylphosphino group (entries 7, 12), and all ligands bearing sulfur in the side chain of the oxazoline (entries 9,10). With best suited ligands **2** and **9** reduction of acetophenone was nearly quantitative even at 0 °C. This demonstrates that the typical side reaction of enolizable ketones to form varying amounts of silyl enol ethers, which are reconverted to starting material upon hydrolysis, is not a serious problem with phosphinooxazolines.

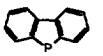
Rather typical for enantioselective catalysis, in tests with acetophenone as standard, the ligands that induced high turnover induced the highest level of *enantioselectivity*. Concerning the substituents R of the oxazoline moiety, best results were achieved with R = *i*-Pr, *i.e.*, ligands **2** and **9** (entries 2-6, 13-15). Ligands with larger (entries 7,8) as well as smaller substituents (entry 1) proved inferior. The soft donor group is also important. The diphenylphosphino group and the rigid dibenzophospholyl substituent proved almost equivalent (entries 2,11), but the sterically demanding dinaphthylphosphino group led to a low degree of enantioselectivity and reversal of the steric course of the reaction (entry 12). Substituting phosphorus for sulfur or selenium (entries 18, 19) gave rise to almost complete loss of selectivity. The same effect was observed with ligands containing sulfur in the side chain of the oxazoline moiety (entry 9,10). This is in contrast to results of Faller and co-workers who obtained up to 62 %ee (reduction of acetophenone) with the sulfur containing N,P chelate ligand cystphos[4g].

No significant increase in enantioselectivity could be achieved with the ligand in excess (entry 4). This has also been observed with other P,N-chelate ligands[4a-d]. (1-Naphthyl)-phenylsilane[6] as silylating reagent afforded slightly better enantioselectivity than diphenyl silane (entries 2,3); however, the advantage is not significant enough to warrant use of the latter silane which is not commercially available. Furthermore, lower reaction temperatures lead to improved ee-values (entries 2, 5, 6). However, at temperatures below 0 °C complete conversion was not achieved under the comparatively high substrate/catalyst ratio employed by us[7].

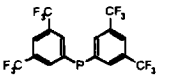
	R (X = PPh_2)
1	CH_3
2	iPr
3	tBu
4	CH_2Ph
5	$(CH_2)_2S\text{-}CH_3$
6	$C(CH_3)_2S\text{-}CH_2\text{-}iPr$



	X (R = iPr)
7	DBP
8	$P(1\text{-Naphthyl})_2$
9	BFP
10	$P(Cyclohexyl)_2$
11	SePh
12	SPh



DBP



BFP

Table 1. Asymmetric Hydrosilylation of Ketones with Phosphinooxazoline-rhodium(I) Complexes[8] (0.4 mol% of ligand, 0.3 mol% of Rh, 1 equiv of Ph_2SiH_2, THF, concn of ketone: 3.33 mol/l).

Entry	Substrate R^1	R^2	Ligand	Temp. [°C]	Conversion[a] [%]	% ee Config.)[a]
1	Ph	CH_3	1	rt	92	44 (*R*)
2	Ph	CH_3	2	rt	97	73 (*R*)
3	Ph	CH_3	2	rt	91	76 (*R*)[b]
4	Ph	CH_3	2	rt	96	76 (*R*)[c]
5	Ph	CH_3	2	10	94	81 (*R*)
6	Ph	CH_3	2	0	95	82 (*R*)
7	Ph	CH_3	3	rt	65	40 (*R*)
8	Ph	CH_3	4	rt	93	52 (*R*)
9	Ph	CH_3	5	rt	55	2 (*R*)
10	Ph	CH_3	6	rt	56	4 (*S*)
11	Ph	CH_3	7	rt	97	69 (*R*)
12	Ph	CH_3	8	rt	33	17 (*S*)
13	Ph	CH_3	9	rt	99	79 (*R*)
14	Ph	CH_3	9	10	94	85 (*R*)
15	Ph	CH_3	9	0	98	84 (*R*)
16	Ph	CH_3	9	-40	99	86 (*R*)[d]
17	Ph	CH_3	10[9]	rt	92	26 (*R*)
18	Ph	CH_3	11	rt	85	0
19	Ph	CH_3	12	rt	78	3 (*R*)
20	Ph	CH_2Cl	2	rt	71	58 (*R*)
21	1-Indanone		2	rt	85[e]	50 (*R*)
22	Dihydro-4,4-dimethyl-2,3-furandione		8	rt	68	37 (*S*)[b]
23	$H_3C\text{-}CO(CH_2)_2CO_2C_2H_5$		2	rt	66	52 (*R*)
24	Cyclohexyl methyl ketone		9	rt	97	37 (*R*)[f]

a) Conversion and enantioselectivity were determined by gas chromatography (GLC) (Chrompack Permethyl-β-CD, 50 m x 0.25 mm); retention times: acetophenone 8.9 min, (*R*)-1-phenylethanol 14.1 min, (*S*)-1-phenylethanol 17.9 min (100 °C); (*S*)-indanol 33.6 min, (*R*)-indanol 34.9 min, 110 °C; dihydro-4,4-dimethyl-2,3-furandione 9.9 min, (*R*)-pantolactone 22.0 min, (*S*)-pantolactone 25.9 min, 110 °C; α-chloroacetophenone 11.7 min, (*S*)-2-chloro-1-phenylethanol 20.1 min, (*R*)-2-chloro-1-phenyl-ethanol 21.9 min, 130 °C; ethyl levulinate 42.6 min, (*R*)-γ-valerolactone 34.3 min, (*S*)-γ-valerolactone 42.6 min, 90 °C. Absolute configurations were determined by comparing specific rotations of isolated alcohols with reference data from the literature.

b) $H_2SiPh(1\text{-Naphthyl})$ was used instead of diphenylsilane.

c) Ligand: 0.8 mol %.

d) Catalyst: 1.25 mol%.

e) Isolated yield.

f) Enantioselectivity was determined by gas chromatography (GLC) after conversion to the acetate (Chrompack Permethyl-β-CD, 50 m x 0.25 mm); retention times: (*S*)-1-cyclohexylethyl acetate 14.1 min, (*R*)-1-cyclohexylethyl acetate 17.9 min (100 °C).

The results presented above left little choice but to seek improvement by electronic tuning of the diphenylphosphino group. Preliminary experiments with derivatives of **2** indicate that acceptor substituents in the PAr_2 moiety are beneficial. Thus, with ligand **9** the standard test reduction with acetophenone required only *two* hours at rt to furnish complete conversion and 1-phenylethanol with 79 %ee. At 10 and 0 °C enantiomeric purities of 85 and 84 %ee, respectively, were achieved (entries 13-15).

In conclusion, (phosphinooxazoline)rhodium(I) complexes can efficiently catalyze hydrosilylations of aromatic as well as aliphatic ketones (entries 22-23) and tolerate a range of functional groups. Compared to N,N chelate ligands, phosphinooxazolines as ligands at Rh(I) induce a lower level of enantioselectivity but give rise to considerably enhanced reactivity. Our current work is directed at a thorough investigation of electronic tuning along the lines indicated above.

Acknowledgments: This work was supported by the Fonds der Chemischen Industrie and the Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie. DEGUSSA AG generously donated enantiopure amino acids, in particular *t*-leucine.

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8 *Typical procedure for hydrosilylation*: Under an atmosphere of argon, 0.013 mmol of ligand were added to a solution of 0.05 mmol of $[Rh(COD)Cl]_2$ in 1 ml of degassed, dry THF and the solution was stirred for 30 min. Then 3.33 mmol of the ketone and 3.66 mmol of diphenylsilane were added and the resultant solution was stirred for 70 h. For work-up 1 ml of 1 N aq. HCl was added and then acetone until a clear solution was obtained which was stirred for 1 h at room temp. The mixture was diluted with ether and extracted with aq. $NaHCO_3$, water and aq. NaCl, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to bulb-to-bulb distillation (0.2 mm Hg, 130-150 °C). In the case of ethyl levulinate as substrate, the reaction was maintained for 68 h at room temperature and stopped by addition of 2 ml of a 1% solution of p-toluenesulfonic acid in methanol. After further work-up as discribed above γ-valerolactone was obtained as product and was characterized.

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(*Received in UK* 23 *April* 1996)