



Enantioselective Catalysis 94.¹

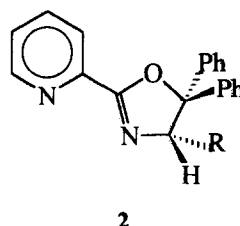
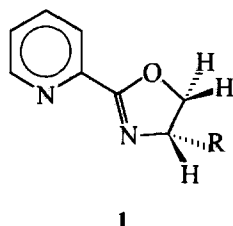
The "Diphenyl Effect" in the Enantioselective Hydrosilylation of Acetophenone with Diphenylsilane Using Rh/5,5-Diphenyl-2-(2-pyridinyl)oxazoline Catalysts

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Abstract: The 5,5-diphenyl-2-(2-pyridinyl)oxazolines **2a-e** give ee values 9.6 - 34.2 % higher than their unsubstituted counterparts **1a-e** in the Rh-catalyzed enantioselective hydrosilylation of acetophenone with diphenylsilane.

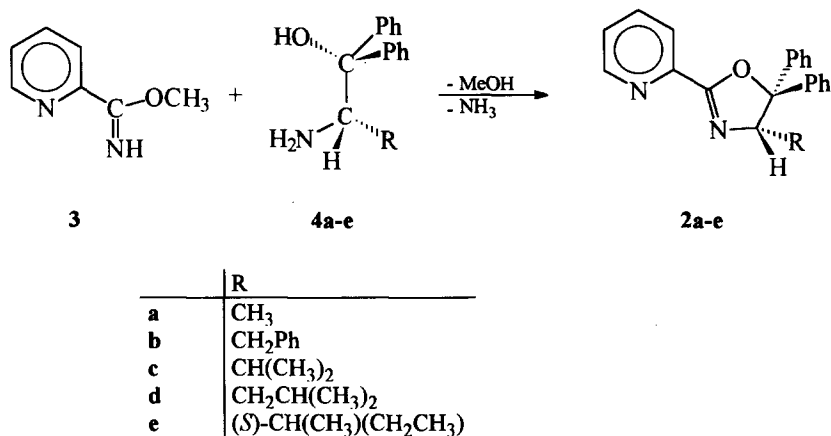
In 1986, we introduced 2-(2-pyridinyl)oxazolines **1** as optically active ligands in the Cu-catalyzed enantioselective monophenylation of diols.² Later on, 2-(2-pyridinyl)oxazolines **1** turned out to be suitable cocatalysts in the Rh-catalyzed enantioselective hydrosilylation of acetophenone with diphenylsilane.³⁻⁵ An extension of the 2-(2-pyridinyl)oxazolines **1** was the development of the Pybox ligand types, containing oxaline substituents in 2- and 6-position of the pyridine system.⁶ In the present paper we report on the synthesis and characterization of 5,5-diphenyl-2-(2-pyridinyl)oxazolines **2**, which give better optical inductions in the Rh-catalyzed hydrosilylation of acetophenone with diphenylsilane than the parent compounds **1** unsubstituted at the 5-position.



Results and Discussion

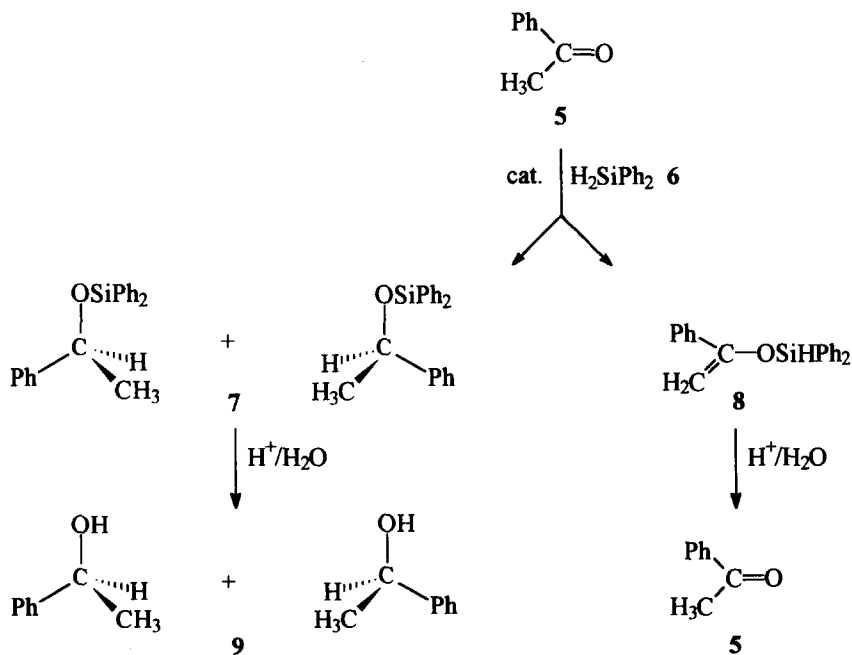
Optically active aminoalcohols can be prepared by LiAlH_4 reduction of aminoacid esters. Similarly, the optically active diphenyl derivatives **4a-e** are obtained by reacting the corresponding aminoacid esters with phenyl Grignard.⁷ Condensation of methyl pyridine-2-carboximidate **3** with the amino alcohols **4a-e** according to Scheme 1 gives the optically active 5,5-diphenyl-2-(2-pyridinyl)oxazolines **2a-e** as colorless crystals after recrystallization from CH_2Cl_2 .

Scheme 1



In the catalytic hydrosilylation of acetophenone **5** with diphenylsilane **6** the enantiomers of the silylether **7** are formed, which are subsequently hydrolyzed to give the enantiomers of 1-phenylethanol **9**. A by-product is the silylenol ether **8**, which on hydrolysis regenerates acetophenone **5** (Scheme 2).

Scheme 2



The catalytic reaction, the work-up of the reaction mixture and the product analysis were carried out as described.⁴ Prior to hydrolysis, the reaction mixture contains the starting materials **5** and **6** and the products **7** and **8**. On the basis of the ¹H-nmr intensities of these components the degree of hydrosilylation HS (formation of **7** and **8**)⁸ and the chemical yield CY (formation of **7**, which on hydrolysis gives 1-phenylethanol)⁹ could be calculated. The enantiomeric excess of 1-phenylethanol was determined after derivatization with tert-butylisocyanate by gc using a chirasil-L-val column of 50 m length.⁴

The hydrosilylation of acetophenone with diphenylsilane was carried out in CCl₄, which had turned out to be the best solvent.⁵ The standard system was obtained by mixing the catalyst components [Rh(cod)Cl]₂ (10 mg, 0.04 mmol Rh) and a fivefold excess of the optically active ligand (relative to Rh) and by adding the solvent CCl₄ (2 ml) and acetophenone (1 ml, 8 mmol). The catalysis was started at 0 °C by addition of diphenylsilane (1.5 ml, 8 mmol). The reaction mixture was allowed to warm to room temperature for analysis and work-up.

In Table 1 the results are summarized obtained for the unsubstituted cocatalysts **1a-e** and their 5,5-diphenyl counterparts **2a-e**. A comparison shows that the phenyl derivatives **2a-e** give ee values 9.6 - 34.2 % higher than the unsubstituted compounds **1a-e**. The reaction rates are a little slower for catalysts containing **2** with respect to **1**, as indicated by the smaller degree of hydrosilylation HS and chemical yield CY. The best optical induction with 89.1 % ee obtained with the valine-derived ligand **2c** compares favorably with the 62.2 % ee obtained with its unsubstituted analogue **1c**.

Table 1

Hydrosilylation of acetophenone (1 ml, 8 mmol) with diphenylsilane (1.5 ml, 8mmol) in CCl₄ (2 ml); catalyst [Rh(cod)Cl]₂/ligand (10 mg, 0.04 mmol Rh)/(0.2 mmol). HS=degree of hydrosilylation,⁸ CY=chemical yield.⁹

	HS [%]	CY [%]	ee [%]	reaction time [h]	number of experiments
2a	71	58	74.9±0.5	114	3
2b	91	77	83.1±0.4	18	3
2c	94	80	89.1±0.3	18	3
2d	78	66	81.2±0.4	114	3
2e	94	72	82.3±0.5	18	3
1a	87	80	40.7±1.9	18	2
1b	98	95	62.4±0.4	18	2
1c	98	85	62.2±0.6	18	2
1d	94	89	71.6±0.9	18	2
1e	78	67	69.8±0.5	18	2

Recently, oxazoline derivatives, such as bis(oxazolines),¹⁰ methylene-bis(oxazolines),¹⁰ triphenylphosphine ortho-substituted with an oxazolynyl group¹¹ etc., were used as cocatalysts in transition metal catalyzed enantioselective reactions. We plan to synthesize the corresponding 5,5-diphenyl substituted derivatives and to compare their performance with the unsubstituted counterparts in enantioselective catalyses, including allylic alkylation, cyclopropanation reactions and so on.

Synthesis of the 5,5-diphenyl-2-(2-pyridinyl)oxazolines 2a-e

Aminoalcohol (80 mmol), methyl pyridine-2-carboximidate (10 ml, 80 mmol) and one drop of conc. HCl were dissolved in 50 ml of chlorobenzene. The reaction mixture was kept at 80 °C for 48 h, while removing the volatile components in a stream of nitrogen. After removal of the solvent, the residue was dissolved in 50 ml of ether and filtered. The ether solution was extracted two times with 10 ml of 10 % HCl and dried with MgSO₄. Evaporation of the ether gave an oily product which became a solid by stirring in petroleum ether. Recrystallization from CH₂Cl₂.

Example: (*S*)-(-)-Methyl-5,5-diphenyl-2-(2-pyridinyl)oxazoline (**2a**). Aminoalcohol: (*S*)-(-)-(1,1-diphenyl)alaninol from L-alanine. - Colorless crystals, mp. 99 °C, yield 41 %. - ¹H-nmr (CDCl₃, i-TMS, 250 MHz): δ = 1.11 (d, 3 H, J = 7.0, CH₃), 5.12 (q, 1H, 4-H), 7.15-7.62 (m, 11H, arom. H, Py-5-H), 7.81 (m, 1H, Py-4-H), 8.13 (m, 1H, Py-3-H), 8.80 (m, 1H, Py-6-H). - MS (EI): m/z (%) = 314 M⁺ (68), 208 (66), 132 (100), 105 (45), 79 (63), 78 (33).

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