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Asymmetric palladium-catalyzed hydrosilylation of styrenes using efficient chiral spiro phosphoramidite ligands

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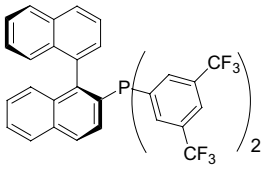
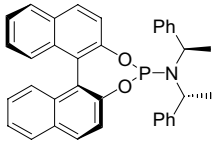
Abstract—Asymmetric hydrosilylation of styrene derivatives with trichlorosilane in the presence of palladium complexes of chiral spiro phosphoramidites provided 1-aryl-1-silylalkanes as single regioisomers in high yields, which have been oxidized with hydrogen peroxide to give the corresponding chiral alcohols in up to 99.1% ee.

1. Introduction

Catalytic asymmetric functionalization of alkenes has been recognized as one of the most useful methods for the preparation of optically active alcohols.[1] In particular, the asymmetric palladium-catalyzed hydrosilylation of olefins with trichlorosilane is a highly potent example of hydrometallation reactions that display excellent regioselectivities and enantioselectivities for alkyl-substituted terminal alkenes, styrene derivatives and the other alkenes.[2] In this hydrosilylation reaction, palladium can provide only one coordination site to the ligand, so monophosphorus ligands are essential for achieving high reactivities and enantioselectivities. Many well-known chelating diphosphine ligands, such as BINAP and CHIRAPHOS, cannot be used in this reaction.[1,2a] Despite the palladium-catalyzed hydrosilylation of alkenes being a facile method for the synthesis of chiral alcohols, only a few monophosphorus ligands have been applied in this reaction. Efficient ligands include Hayashi's MOP ligands[2] and Feringa's MONOPHOS ligands[3] based on axially chiral biaryl backbones and MOPF ligands[4] based on planar chiral ferrocene backbones. The most enantioselective ligands so far reported for the palladium-catalyzed hydrosilylation of alkenes are ligands **1**[2] and **2**,[3] which afforded the alcohols upon oxidation in up to 98% ee and 99% ee, respectively.



(*R*)-**1**



(*S*,*R*,*R*)-**2**

Recently, we designed a novel class of chiral monophosphoramidite ligands (SIPHOS) **3** and **4**[5] containing a 1,1′-spirobiindane scaffold and demonstrated that these ligands were highly efficient for the Rh-catalyzed asymmetric hydrogenation of functionalized olefins[5a,b] and the Cu-catalyzed conjugate addition of Et_2Zn to α,β-unsaturated ketones.[5c] These results stimulated us to further extend the application of these spiro monophosphorus ligands in transition metal-catalyzed reactions. Herein, we report the asymmetric palladium-catalyzed hydrosilylation of styrene derivatives using phosphoramidite ligands **3** and **4**, providing 1-aryl-1-silyalkanes and the corresponding alcohols in high yields with excellent enantioselectivities (up to 99.1% ee).

2. Results and discussion

Asymmetric hydrosilylation of styrene **5a** with trichlorosilane was carried out without solvent at room temperature in the presence of 0.25 mol% of catalyst generated in situ by mixing $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and chiral

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Table 1. Palladium-catalyzed hydrosilylation of styrene **5a** using chiral spiro monodentate phosphoramidite ligands **3** and **4**[a]

Entry	Ligand	Sub./$HSiCl_3$	Time (h)	Yield (%)[b]	Ee (%)[c]
1	(*R*)-**3a**	1:2	20	91	62 (*R*)
2	(*R*)-**3b**	1:2	45	61	46 (*R*)
3	(*R*)-**3c**	1:2	30	42	51 (*S*)
4	(*R*,*R*,*R*)-**4**	1:2	2	99	97 (*R*)
5	(*S*,*R*,*R*)-**4**	1:2	2	99	55 (*S*)
6	(*R*,*R*,*R*)-**4**	1:1.2	2	97	96 (*R*)
7	(*R*,*R*,*R*)-**4**	1:4	2	99	96 (*R*)
8[d]	(*R*,*R*,*R*)-**4**	1:2	2	97	97 (*R*)
9[e]	(*R*,*R*,*R*)-**4**	1:2	72	64	90 (*R*)

[a] All reactions were conducted without solvent with **5a**/$HSiCl_3$/[Pd(η^3-C_3H_5)Cl]$_2$/ligand, 1/2/0.00125/0.005 at room temperature (15–20 °C), unless otherwise stated.
[b] Isolated yield of silane by distillation.
[c] Ee of alcohol determined by chiral GC on a Suplco β-DEX™ 120 column. Absolute configurations were determined by comparison of specific rotations with literature data.
[d] 0.1 mol% Pd was used.
[e] 0.025 mol% Pd was used.

spiro phosphoramidite ligands **3** or **4** (Pd/L = 1:2). The results are summarized in Table 1. It was found that the reactivities and enantioselectivities of hydrosilylation were strongly dependent on the alkyl groups on the nitrogen atom of the ligand. Ligand (*R*)-**3a**, which had a dimethylamino group, provided 91% of silane product **6a** in 20 h. The oxidation of silane **6a** under Tamao conditions[6] produced alcohol **7a** in 62% ee with an (*R*)-configuration (entry 1). Ligands (*R*)-**3b** and (*R*)-**3c**, having pyrrolinyl and diisopropylamino groups, gave sluggish hydrosilylation reactions, with low yields and enantioselectivities (entries 2 and 3). It is interesting to note that the alcohol obtained with ligand (*R*)-**3c** had an (*S*)-configuration, which is opposite to those obtained with ligands (*R*)-**3a** and (*R*)-**3b**. Ligand (*R*,*R*,*R*)-**4**, derived from (*R*)-1,1′-spirobiindane-7,7′-diol and bis[(*R*)-1-phenylethyl]amine, was found to be the ligand of choice, which afforded hydrosilylation products (*R*)-**6a** in 99% yield with 97% ee (entry 4). The reactivity of (*R*,*R*,*R*)-**4**-Pd catalyst is noteworthy as the reaction was complete within 2 h.[7] However, the diastereomeric ligand (*S*,*R*,*R*)-**4** had a much lower enantioselectivity (55% ee) (entry 5). These results clearly indicate that ligand (*R*,*R*,*R*)-**4** has matched configurations. The configurations of the products were determined by the configuration of 1,1′-spirobiindane scaffold. The amount of $HSiCl_3$ used in the hydrosilylation was found to have no obvious effect on the rate and enantioselectivity of reaction (entries 6 and 7 vs 4). When the catalyst loading was lowered to 0.1 mol%, the reaction still gave satisfying result. Reducing the catalyst loading further to 0.025 mol% led to a very slow reaction with a dramatic decrease in the enantioselectivity (entry 9).

A variety of styrene derivatives can be efficiently hydrosilylated with a Pd complex of (*R*,*R*,*R*)-**4**. As shown in Table 2, most of the substituted styrenes can react completely with $HSiCl_3$ within 10 h at room temperature, affording the corresponding hydrosilylation products in high yields and excellent enantioselectivities. The highest enantioselectivity (99.1% ee) was achieved in the hydrosilylation of 2-chlorostyrene (entry 4). The hydrosilylations of 4-methoxylstyrene **5g** and 3-bromostyrene **5i** are two exceptions; the former gave the lowest enantioselectivity while the latter had a slow reaction

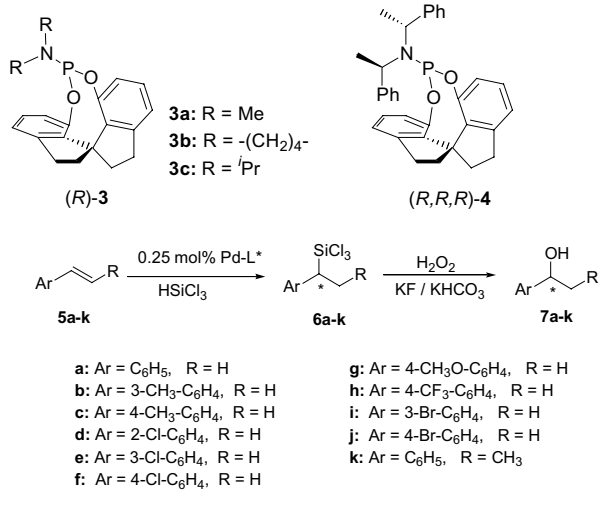


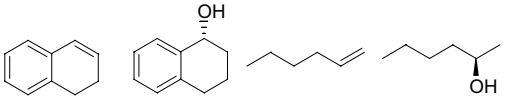
Table 2. Asymmetric hydrosilylation of styrene derivatives catalyzed by Pd complex of (*R*,*R*,*R*)-**4**[a]

Entry	Substrate	Time (h)	Yield (%)[b]	Ee (%)[c]
1	**5a**	2	99	97 (*R*)
2	**5b**	3	90	97 (*R*)
3	**5c**	4	91	98 (*R*)
4	**5d**	7	88	99.1 (*R*)
5	**5e**	9	86	95 (*R*)
6	**5f**	3	90	96 (*R*)
7[d]	**5g**	3	84	82 (*R*)
8	**5h**	4	94	96 (*R*)
9	**5i**	45	75	97 (*R*)
10	**5j**	7	93	95 (*R*)
11	**5k**	36	86	95 (*R*)

[a] All reactions were conducted without solvent with **5**/$HSiCl_3$/[Pd(η^3-C_3H_5)Cl]$_2$/(*R*,*R*,*R*)-**4**, 1/2/0.00125/0.005 at room temperature (15–20 °C), unless otherwise stated.
[b] Isolated yields of silane by distillation.
[c] Ee of alcohol determined by chiral GC on a Suplco β-DEX™ 120 column. Absolute configurations were determined by comparison of specific rotations with literature data.
[d] Reaction performed at 0 °C.

rate (entries 7 and 9). The low enantioselectivity (82% ee) obtained in the hydrosilylation of **5g** showed that the strong electron-donating group on the phenyl ring of the substrate was unfavourable for achieving high enantioselectivity. However, the reason for the slow reaction rate observed in the hydrosilylation of **5i** remains unknown. β-Methylstyrene **5k** can also be hydrosilylated in high yield and high enantioselectivity (95% ee), albeit slowly (entry 11).

To extend the range of substrates in the hydrosilylation catalyzed by Pd complex of (*R*,*R*,*R*)-**4**, we next investigated the hydrosilylation of cyclic substrate 1,2-dihydronaphthalene **8**. The hydrosilylation of **8**, proceeded at room temperature in the presence of 1 mol% of catalyst for 5 days and provided alcohol **9** upon oxidation in 61% yield with 85% ee (*R*). Increasing the catalyst loading to 5 mol% improved the yield (80%) as well as the enantiomeric excess (88% ee) of alcohol **9**. The catalytic asymmetric hydrosilylation of simple 1-alkenes was much more difficult with only the Hayashi's MOP ligand giving satisfactory results.[2a,8] We performed the hydrosilylation of 1-hexene **10** in benzene in the presence of 1 mol% (*R*,*R*,*R*)-**4**-Pd catalyst at 40 °C for 72 h. The hydrosilylation product was oxidized under Tamao conditions giving the corresponding alcohol **11** in 35% yield with 68% ee (*R*).



8 **9** **10** **11**

3. Conclusion

We have demonstrated that the chiral spiro monophosphoramidite (*R*,*R*,*R*)-**4** containing a 1,1′-spirobiindane scaffold is a highly effective ligand for the palladium-catalyzed asymmetric hydrosilylation of styrene derivatives, producing the chiral silanes and alcohols upon oxidation in high yields and excellent enantioselectivities (up to 99.1% ee). This novel ligand has a higher activity and comparable enantioselectivity to monophosphoramidite ligand **2** derived from BINOL. Further applications of this ligand in other transition metal-catalyzed asymmetric reactions are currently under investigation.

4. Experimental

4.1. General

All moisture-sensitive reactions were carried out under a dried nitrogen atmosphere. Reagents were purchased and used without further purification. Ligands **3** and **4** were synthesized according to the previous method.[5c] Enantiomeric excesses were determined by chiral GC performed on Hewlett Packard 6890 with a Suplco β-DEX™ 120 column (30 m × 0.25 mm i.d., 0.25 μm, fused silica capillary column) and chiral HPLC performed on a Hewlett Packard 1100 with Chiralcel OB column (25 cm × 0.46 cm i.d.). All spectral data of products were in accordance with those reported in the literature.[9]

4.2. General procedure for asymmetric hydrosilylation

A dried Schlenk tube containing a stirbar was charged with allylpalladium chloride dimer (1.5 mg, 0.0041 mmol), the phosphoramidite ligand (*R*,*R*,*R*)-**4** (8.3 mg, 0.0164 mmol) and styrene **5a** (341 mg, 3.28 mmol). After 20 min stirring at room temperature, trichlorosilane (0.66 mL, 6.56 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 2 h. The product was purified by distillation to yield 778 mg (99%) of **6a**. The results for the asymmetric hydrosilylations of styrene derivatives **5b**–**k** are summarized in Table 2.

4.3. General procedure for oxidation of silanes

The silane **6a** (177 mg, 0.741 mmol), KF (258 mg, 4.446 mmol), $KHCO_3$ (445 mg, 4.446 mmol), MeOH (15 mL) and THF (15 mL) were transferred to a 50-mL flask. H_2O_2 (0.89 mL, 30%) was added and the mixture stirred for 16 h before quenching with 4 mL saturated $Na_2S_2O_3$ solution. After stirring for an additional 1 h, the reaction mixture was extracted with Et_2O (3 × 30 mL), and the combined organic phases dried over $MgSO_4$, filtered and concentrated in vacuum. The crude residue was purified by flash column chromatography on silica gel (pentane/ethyl acetate, 90/10), affording the alcohol **7a** (76 mg, 99%) with 97% ee (*R*). The results for the oxidation of silanes **6b**–**k**, are summarized in Table 2.

Acknowledgements

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