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Highly Enantioselective Hydrosilylation of Aromatic Alkenes

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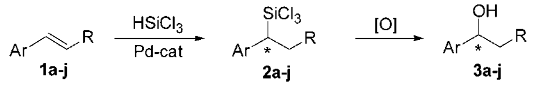
Catalytic asymmetric functionalization of alkenes continues to be one of the most important methods for constructing chiral units. The palladium-catalyzed hydrosilylation of alkenes is a highly potent example of a hydro-metalation reaction that displays excellent regioselectivity for aryl-substituted olefins (Scheme 1).[1] Addition of a hydrosilane in the presence of an optically active palladium-complex affords a chiral organosilane. The Tamao−Fleming oxidation is an important example of the numerous versatile transformations organosilanes can undergo.[2] Stereospecific oxidation affords a chiral alcohol with retention of configuration, making the overall reaction sequence equivalent to an enantioselective Markovnikov hydration of an olefin. Opposed to the hydroboration, the hydrosilylation can be conducted with very low catalyst loadings, applying cheap hydrosilanes as the stoichiometric reagent, making this process outstanding in terms of synthesizing chiral alcohols.

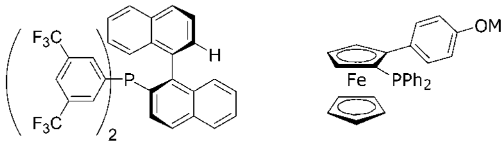
Scheme 1



1-3a: Ar=C_6H_5, R=H
1-3b: Ar=3-NO_2-C_6H_4, R=H
1-3c: Ar=2-Cl-C_6H_4, R=H
1-3d: Ar=3-Cl-C_6H_4, R=H
1-3e: Ar=2-CF_3-C_6H_4, R=H
1-3f: Ar=3-CF_3-C_6H_4, R=H
1-3g: Ar=2-CH_3-C_6H_4, R=H
1-3h: Ar=4-CH_3-C_6H_4, R=H
1-3i: Ar=2,4-$(CH_3)_2$-C_6H_3, R=H
1-3j: Ar=C_6H_5, R=CH_3

The development of highly enantioselective optically active palladium complexes for the hydrosilylation was troubled in its infancy by the lack of activity of palladium−bisphosphine complexes. Considering the excellent results obtained with C_2-symmetric bisphosphine ligands in asymmetric transition metal catalysis, the focus put on this ligand class is not surprising. However, with the discovery that some catalytical processes require a free coordination site on the metal to proceed, the importance of monophosphine ligands became clear. Despite several reports of novel monophosphine ligands, thus far only Hayashi's MOP ligands have displayed high efficiency with respect to reactivity and selectivity in the hydrosilylation of aryl-substituted alkenes.[3,4] Thus, palladium-catalyzed hydrosilylation of styrene **1a** with the MOP ligand **4** (Figure 1) affords upon oxidation 1-phenyl ethanol **3a** in excellent yield and 98% enantiomeric excess.

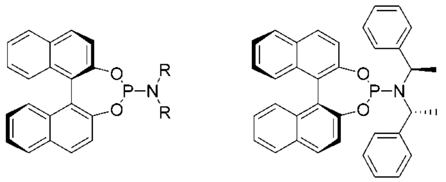
We became interested in the asymmetric hydrosilylation reaction in the course of developing a novel class of aryl-monophosphino ferrocene ligands (MOPF ligands).[5]



(*R*)-**4** (*S*)-**5**

Figure 1. Monophosphine ligands.

p-MeO−Ph-MOPF **5** (Figure 1) displayed the highest selectivity in the hydrosilylation of styrene, furnishing **3a** with 90% ee.[6] In our continued studies we focused on other possible ligands for the hydrosilylation.



(*R*)-**6** : R= Me
(*R*)-**7** : R= *i*-Pr
(S_A, R_C, R_C)-**8**

Figure 2. Phosphoramidite ligands.

Chiral phosphoramidite ligands represented by **6**−**8** (Figure 2) introduced by Feringa and co-workers are interesting candidates for application in the hydrosilylation.[7] They include the axially chiral BINOL structure in combination with a phosphorus−nitrogen bond. Furthermore, as ligand **8** demonstrates, additional chiral elements can be introduced, allowing facile structure modification.

Table 1. Palladium-Catalyzed Hydrosilylation of Styrene (**1a**) Using Phosphoramidite Ligands[a]

entry	ligand	conversion [%][b]	ee [%][c,d]
1	**6**	100	55 (*S*)
2	**7**	100	20 (*R*)
3	**8**	100	99 (*R*)
4[e]	**8**	100	99 (*R*)
5	**8′**[f]	100	60 (*S*)

[a] All reactions were conducted with **1a**/$HSiCl_3$/$[ClPd(C_3H_5)]_2$/ligand − 1/1.2/0.005/0.02 unless otherwise stated. [b] Conversion to **2a** determined by ^{1}H NMR. [c] Ee of **3a** determined by chiral HPLC on a OD-H column. [d] Absolute configuration determined by optical rotation and comparison with literature data. [e] 0.25 mol % Pd and 0.5 mol % ligand was applied. [f] Reaction performed with the diastereomeric (R_A,R_C,R_C)-**8′** ligand.

Initially, ligands **6**−**8** were tested in the hydrosilylation of styrene (Table 1).[8] The reactions proceeded smoothly at room temperature with 1 mol % of the catalyst affording 100% conversion to the product within 24 h. Upon oxidation under Tamao conditions, the alcohol **3a** was obtained in yields >80%. Notably, ligand **6** affords **3a** with (*S*)-configuration in 55% ee (entry 1), whereas **7** furnishes

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the product with opposite configuration (entry 2), albeit with low enantiomeric excess (20%). Ligand **8** also lead to the (*R*)-configured product, but with *99% enantiomeric excess, which is the highest selectivity ever observed in the hydrosilylation of styrene* (entry 3). Lowering the catalyst loading to 0.25 mol % did not affect the excellent selectivity displayed by ligand **8** (entry 4).

To evaluate the impact of the configuration of substituents on nitrogen, the diastereomeric ligand (R_A,R_C,R_C)-**8'** was applied in the reaction (entry 5). While retaining the activity of the Pd−ligand complex, the absolute configuration was inversed, accenting to the effect from the absolute stereochemistry of the binaphthol system. The relative low enantiomeric excess of **3a** (entry 5, Table 1) clearly demonstrates that this diastereoisomer (**8′**) has mismatched chiral elements.

Given the excellent performance of the Pd−**8** complex in the hydrosilylation reaction, we wanted to explore the scope of this reaction toward diversely functionalized styrenes. Table 2 summarizes the results obtained with substrates **1a**−**1j**.

Table 2. Catalytic Asymmetric Hydrosilylation of Aromatic Alkenes[a]

entry	substrate	reaction time [h]	conversion [%][b]	yield [%][c]	ee [%][d]
1[e]	**1a**	16	100	87	99 (*R*)
2[e,f]	**1b**	144	100	94	95 (*R*)
3[g]	**1c**	40	100	89	96 (*R*)
4[g]	**1d**	60	100	91	98 (*R*)
5[g]	**1e**	40	92	74	95 (*R*)
6[f,g]	**1f**	60	100	88	98 (*R*)
7[g]	**1g**	40	83	75	97 (*R*)
8[g]	**1h**	40	100	95	86 (*R*)
9[g]	**1i**	40	100	80	96 (*R*)
10[f,g]	**1j**	40	100	91	98 (*R*)

[a] All reactions were conducted with substrate/$HSiCl_3$/ $[ClPd(C_3H_5)]_2$/ ligand, 1/1.2/0.00125/0.005 at 20 °C, unless otherwise stated. [b] Conversion to silane determined by ^1H NMR. [c] Isolated yield of silane. [d] Absolute configuration determined by optical rotation. [e] Ee of alcohol determined by HPLC on a Chiralcel OD-H column. [f] Reaction performed at 40 °C. [g] Ee of alcohol determined by GC on a Chiralsil-Dex column.

Electron-withdrawing substituents prolong the reaction time (entry 2−6), but in all cases excellent yields and enantiomeric excess is achieved. The positioning of these substituents on the aromatic ring has no apparent effect on the outcome of the reaction. The weakly electron-donating methyl substituent affords comparable selectivity when positioned ortho to the vinyl group (entry 7). *p*-Methyl-substituted alcohol **3h** was obtained with the lowest ee (entry 8). However, reconstituting the 2-methyl group enhanced the selectivity to 96% (entry 9). β-Methyl-substituted styrene **1j** was an excellent substrate in the reaction, the silyl group was introduced exclusively at the benzylic position, and the product was obtained with 98% enantioselectivity (entry 10).

Herein we have presented a novel catalytic system for the asymmetric hydrosilylation of aromatic alkenes giving the products in high yields and with the highest enantioselectivity ever observed for this reaction. The reaction works efficiently for a variety of substituted aromatic alkenes, giving access to almost optically pure benzylic alcohols in high yields after Tamao oxidation.

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Supporting Information Available: Detailed experimental procedures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) General procedure for the hydrosilylation/oxidation sequence: A dried Schlenk tube containing a stirbar was charged with allylpalladium chloride dimer (1.5 mg, 0.0041 mmol, 0.25 mol % Pd), **8** (8.9 mg, 0.0164 mmol, 0.5 mol %) and 2-chlorostyrene (**1c)** (454 mg, 3.28 mmol). After 20 min stirring at room temperature, trichlorosilane (396 μL, 3.93 mmol) was added. The reaction mixture was stirred and heated for the time specified in Table 2. The product was purified by Kugelrohr distillation to yield 796 mg (89%) of **2c**. The silane (200 mg, 0.741 mmol), KF (6 equiv), $KHCO_3$ (6 equiv), 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 was stirred for 16 h before quenching with $Na_2S_2O_3$ (saturated 4 mL). After stirring for an additional hour the reaction mixture was extracted with Et_2O (3 × 30 mL), and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (pentane/ethyl acetate, 90/10), affording the alcohol **3c** in 86% yield and with 96% ee. All spectral data were in accordance with literature. See, e.g.: Doucet, H.; Fernandez, E.; Layzell, T. P.; Brown J. B. *Chem. Eur. J.* **2001**, *5*, 1320.

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