Communication

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Rhodium-Catalyzed Asymmetric Synthesis of Silicon-Stereogenic Dibenzooxasilines via Enantioselective Transmetalation

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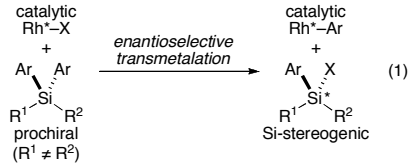
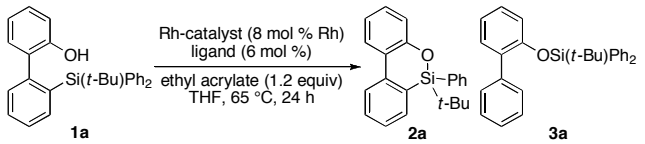
ABSTRACT: A rhodium-catalyzed asymmetric synthesis of silicon-stereogenic dibenzooxasilines has been developed. High enantioselectivities have been achieved by employing (*S*,*S*)-Me-Duphos as the ligand through "enantioselective transmetalation".

Transmetalation is one of the key elemental steps for a wide variety of transition metal-catalyzed processes involving organometallic reagents such as palladium-catalyzed cross-coupling reactions[1] and rhodium-catalyzed conjugate addition reactions.[2] Although this elemental step also often appears as part of the catalytic cycle for various asymmetric catalyses, "enantioselective transmetalation" that constructs a stereogenic center at the metal(loid) of the transmetalating reagent has never been reported as far as we are aware.[3,4] In this context, here we demonstrate the first example of such enantioselective transmetalation using prochiral organosilicon compounds under the catalysis of a chiral rhodium(I) complex, leading to the formation of silicon-stereogenic organosilanes with high enantioselectivity (eq 1).[5,6]



To realize this mode of asymmetric catalysis, we chose hydroxy-tethered tetraoragnosilanes bearing two of the same aryl groups as the transmetalating reagent in combination with an electron-deficient olefin as the electrophile in the presence of a chiral rhodium complex.[7] As a starting point, we decided to employ 2'-(*tert*-butyl)diphenylsilylbiphenyl-2-ol (**1a**) as a model substrate and conducted several reactions to find a set of conditions that could effectively promote the formation of silicon-stereogenic dibenzooxasiline **2a**[8] with high ee through enantioselective transmetalation (Table 1). Thus, high yield of **2a** with 91% ee was obtained along with a minute amount of byproduct **3a** by conducting the reaction of **1a** with ethyl acrylate (1.2 equiv) in the presence of a catalyst generated from $[Rh(OH)(coe)_2]_2$[9] (8 mol % Rh) and (*S*,*S*)-Me-Duphos[10] (6 mol %) in THF at 65 °C (entry 1). It is worth noting that the phenyl group cleaved from **1a** ended up on ethyl acrylate in the forms of ethyl 3-phenylpropionate (1,4-adduct; 3% of Ph on **1a**), ethyl cinnamate (Heck-type product; 11% Ph), and ethyl 3,3-diphenylpropionate (1,4-adduct of the cinnamate; 72% Ph) under these conditions. The rhodium/ligand ratio and the choice of rhodium complex were found to be critically important in the present reaction. No reaction took place when the reaction was conducted without any added phosphine ligands (entry 2), and the use of excess (*S*,*S*)-Me-Duphos (10 mol %; 1.25 equiv to Rh) gave product **2a** in 95% yield but with complete loss of enantioselectivity (entry 3).[11] We tentatively attribute this loss of ee to the partial formation of a Rh((*S*,*S*)-Me-Duphos)$_2$ complex,[12] which displays much higher catalytic activity with no enantioinduction. The reaction also proceeded well by using $[Rh(OH)(cod)]_2$ instead of $[Rh(OH)(coe)_2]_2$ in combination with (*S*,*S*)-Me-Duphos, but **2a** was obtained only with 10% ee (entry 4). This observation can be explained by the slower ligand exchange between 1,5-cyclooctadiene (cod) and (*S*,*S*)-Me-Duphos and by the fact that $[Rh(OH)(cod)]_2$ alone can promote the formation of **2a** as a racemate (93% yield). In contrast, the use of $[RhCl(coe)_2]_2$ completely shut down the reaction (entry 5), which is presumably because a chloro-rhodium complex cannot undergo ligand exchange with **1a** to form an aryloxorhodium species for successive transmetalation to take place (vide infra). Other chiral bisphosphine ligands such as (*R*)-Binap, (*R*)-H_8-Binap, (*R*)-Segphos, and (*S*,*S*)-Chiraphos were inferior to (*S*,*S*)-Me-Duphos, giving product **2a** with lower enantioselectivity (5–62% ee; entries 6–9).

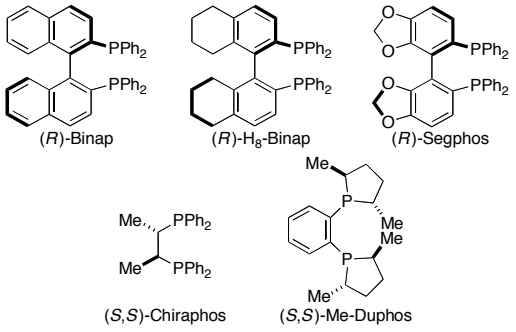
Table 1. Rhodium-Catalyzed Asymmetric Synthesis of Dibenzooxasiline 2a from 1a



1a **2a** **3a**

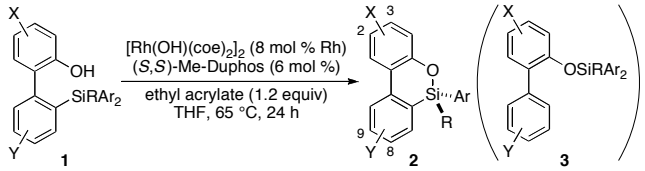
entry	Rh-catalyst	ligand	yield (%)[a]	**2a**/**3a**[b]	ee of **2a** (%)[c]
1	$[Rh(OH)(coe)_2]_2$	(*S*,*S*)-Me-Duphos	89	98/2	91 (*R*)
2	$[Rh(OH)(coe)_2]_2$	—	0	—	—
3[d]	$[Rh(OH)(coe)_2]_2$	(*S*,*S*)-Me-Duphos	95	>99/1	0
4	$[Rh(OH)(cod)]_2$	(*S*,*S*)-Me-Duphos	90	>99/1	10 (*R*)
5	$[RhCl(coe)_2]_2$	(*S*,*S*)-Me-Duphos	0	—	—
6	$[Rh(OH)(coe)_2]_2$	(*R*)-Binap	20	95/5	5 (*R*)
7	$[Rh(OH)(coe)_2]_2$	(*R*)-H_8-Binap	88	99/1	17 (*S*)
8	$[Rh(OH)(coe)_2]_2$	(*R*)-Segphos	51	99/1	56 (*S*)
9	$[Rh(OH)(coe)_2]_2$	(*S*,*S*)-Chiraphos	94	99/1	62 (*R*)

[a] Combined isolated yield of **2a** and **3a**. [b] Determined by ^{1}H NMR. [c] Determined by chiral HPLC on a Chiralpak AD-H column with hexane/2-propanol = 500/1. [d] 10 mol % of ligand was used.



Under the reaction conditions described in Table 1, entry 1, various substituted dibenzooxasilines **2** are effectively prepared with high enantioselectivity as summarized in Table 2, entries 2–8 (87–92% ee), including an example of benzonaphthooxasiline **2d** (entry 4). In addition, substrates **1** having two of the same substituted phenyl groups on the silicon atom are also converted to the corresponding dibenzooxasilines **2** with high efficiency (88–92% ee; entries 9–12). Unfortunately, the use of substrates having a less bulky alkyl group such as cyclohexyl group on the silicon shows lower reactivity and enantioselectivity in the present catalysis (entry 13).[13] The absolute configuration of product **2e** in entry 5 was determined to be *R* by X-ray crystallographic analysis with Cu-Kα radiation after recrystallization from hexane at –20 °C (Figure 1).[14]

Table 2. Rhodium-Catalyzed Asymmetric Synthesis of Dibenzooxasilines 2: Scope



entry	**2** (X, Y, R, Ar)	yield (%)[a]	**2**/**3**[b]	ee of **2** (%)[c]
1	**2a** (H, H, *t*-Bu, Ph)	89	98/2	91
2	**2b** (2-Me, H, *t*-Bu, Ph)	80	96/4	90
3	**2c** (2-F, H, *t*-Bu, Ph)	96	97/3	88
4	**2d** (2,3-(CH=CH)$_2$, H, *t*-Bu, Ph)	96	98/2	91
5	**2e** (H, 8-Me, *t*-Bu, Ph)	77	96/4	87
6	**2f** (H, 8-F, *t*-Bu, Ph)	97	>99/1	92
7	**2g** (H, 9-OMe, *t*-Bu, Ph)	70	98/2	90
8	**2h** (H, 9-CF$_3$, *t*-Bu, Ph)	92	>99/1	90
9	**2i** (H, H, *t*-Bu, 4-MeOC$_6$H$_4$)	87[d]	98/2	92
10	**2j** (H, H, *t*-Bu, 4-MeC$_6$H$_4$)	90	98/2	91
11	**2k** (H, H, *t*-Bu, 4-PhC$_6$H$_4$)	82[d]	98/2	88
12	**2l** (H, H, *t*-Bu, 3-MeC$_6$H$_4$)	85	98/2	90
13[e]	**2m** (H, H, Cy, Ph)	59	93/7	71

[a] Combined isolated yield of **2** and **3** unless otherwise noted. [b] Determined by ^{1}H NMR. [c] Determined by chiral HPLC with hexane/2-propanol. [d] Isolated yield of **2**. [e] The reaction was conducted in dioxane at 80 °C.

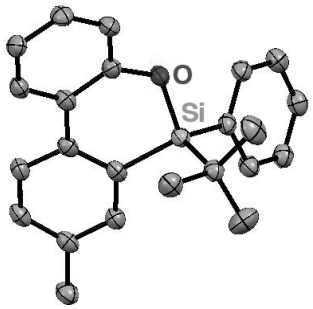
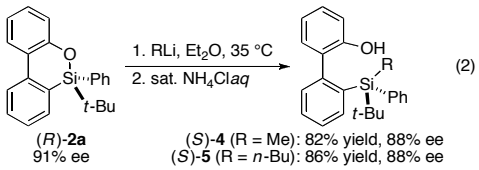


Figure 1. X-ray crystal structure of (*R*)-**2e** (Flack parameter = 0.01(4); hydrogen atoms are omitted for clarity).

We have also begun to explore the derivatization of silicon-stereogenic dibenzooxasilines **2** obtained in the present catalysis. In our preliminary experiments, we found that the reaction of (*R*)-**2a** (91% ee) with methyllithium proceeds with retention of configuration at the silicon stereocenter[15] to give ring-opened tetraorganosilane (*S*)-**4** in 82% yield with 97% enantiospecificity (eq 2). Similarly, the reaction of (*R*)-**2a** with *n*-butyllithium gives (*S*)-**5** in 86% yield with 97% enantiospecificity. It is worth noting that these compounds exist as a 1:1 mixture of inseparable (interconvertible) atrop isomers in solution at room temperature, but only one atrop isomeric form with *S* configuration around the axis is obtained in a solid state upon recrystallization of (*S*)-**4** from hexane as shown in Figure 2 with the dihedral angle of 79–86° (cf. dihedral angle for **2e** in Figure 1 is 18°).[14]



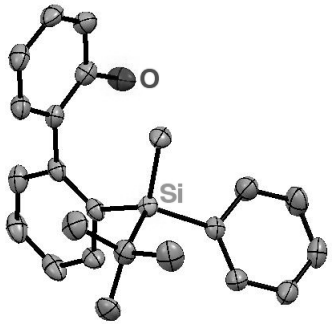
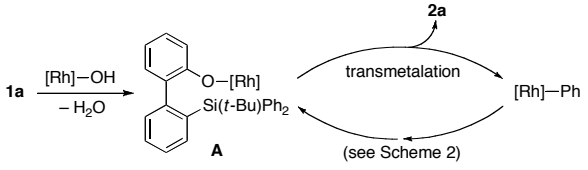


Figure 2. X-ray crystal structure of (*S*)-**4** (Flack parameter = –0.02(2); only one out of two independent molecules in the unit cell is shown and hydrogen atoms are omitted for clarity).

A proposed catalytic cycle for the reaction of **1a** to give **2a** is illustrated in Scheme 1.[2,7d] Initial ligand exchange of hydroxorhodium complex with substrate **1a** gives aryloxorhodium species **A**. This then undergoes enantio-discriminating transmetalation intramolecularly to give phenylrhodium species with the release of silicon-stereogenic **2a** as the product. The resulting phenylrhodium species undergoes the following processes to regenerate aryloxorhodium **A** on the basis of the fate of the phenyl group described for Table 1, entry 1. Thus, at the early stage of catalysis, insertion of ethyl acrylate to the phenylrhodium takes place to give oxa-π-allylrhodium **B**, which mostly leads to the formation of a rhodium hydride and ethyl cinnamate through β-hydrogen elimination (Scheme 2a).[16] The rhodium hydride presumably reacts with another molecule of ethyl acrylate, followed by protonolysis of resulting intermediate **C** with **1a**, provides aryloxorhodium **A** along with ethyl propionate. On the other hand, at the late stage of catalysis where most of ethyl acrylate has been converted to ethyl cinnamate and ethyl propionate, insertion of ethyl cinnamate to the phenylrhodium species occurs to give intermediate **D**, and protonolysis of this intermediate with substrate **1a** leads to the formation of aryloxorhodium **A** and ethyl 3,3-diphenylpropionate (Scheme 2b).

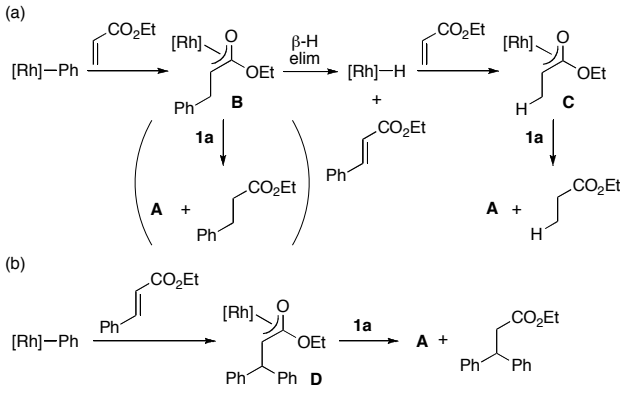
Scheme 1. Proposed catalytic cycle for the reaction of 1a to give 2a ([Rh] = Rh((*S*,*S*)-Me-Duphos))



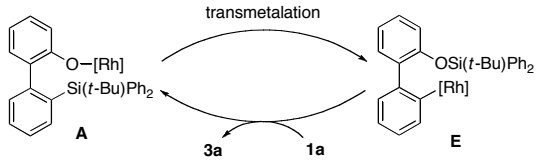
The formation of minor byproduct **3a** can be rationalized by the following pathway as illustrated in Scheme 3. Instead of

undergoing transmetalation between aryloxorhodium and one of the phenyl groups on the silicon from intermediate **A**, transmetalation with the cleavage of the biphenyl–silicon bond gives arylrhodium species **E**, protonolysis of which with **1a** provides **3a** along with regeneration of aryloxorhodium **A**.

Scheme 2. Proposed pathways for the conversion of [Rh]–Ph to aryloxorhodium A: (a) early stage of the catalysis, (b) late stage of the catalysis



Scheme 3. Proposed reaction pathway for the reaction of 1a to give 3a



In summary, we have developed a rhodium-catalyzed asymmetric synthesis of silicon-stereogenic dibenzooxasilines through enantioselective transmetalation of prochiral organosilanes. High enantioselectivities have been achieved by employing (*S*,*S*)-Me-Duphos as the ligand, successfully demonstrating the proof-of-principle for "enantioselective transmetalation". Future studies will explore further expansion of the scope of the present catalysis as well as development of related asymmetric reactions.

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SUPPORTING INFORMATION. Experimental procedures and compound characterization data (PDF) and X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) The same trend was observed for (*S*,*S*)-Chiraphos when 10 mol % (1.25 equiv to Rh) was used, giving compound **2a** in 91% yield with 0% ee (see Table 1, entry 9 for comparison), but no significant change of ee was observed for (*R*)-Binap, (*R*)-H_8-

Binap, and (*R*)-Segphos (see Table 1, entries 6–8 for comparison).
(12) We currently have no good understanding for the structure, reactivity, and stereoselectivity of this species. For preliminary ^{31}P NMR studies on Rh/(*S*,*S*)-Me-Duphos complexes, see the Supporting Information.
(13) The use of even smaller R groups (e.g., R = Me) results in formation of complex product mixture.
(14) CCDC-893230 and CCDC-893231 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See also the Supporting Information for details.
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