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Asymmetric 1,4-Addition of Organosiloxanes to α,β-Unsaturated Carbonyl Compounds Catalyzed by a Chiral Rhodium Complex

Shuichi Oi,* Akio Taira, Yoshio Honma, and Yoshio Inoue*

Department of Materials Chemistry, Graduate School of Engineering, Tohoku University, Sendai 980-8579, Japan

oishu@aporg.che.tohoku.ac.jp

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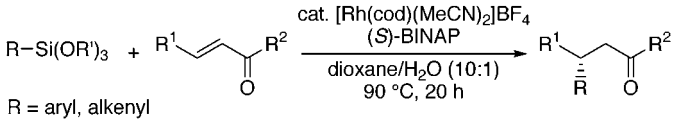
ABSTRACT



Highly enantioselective 1,4-addition of organosiloxanes to α,β-unsaturated carbonyl compounds was found to be catalyzed by a chiral rhodium complex generated from [Rh(cod)(MeCN)$_2$]BF$_4$ and (*S*)-BINAP. Both (*E*)- and (*Z*)-1-alkenyl groups as well as aryl groups can be introduced enantioselectively into the β-position of a variety of ketones, esters, and amides.

Transition-metal-catalyzed transformations using organometallic reagents are of great importance in modern organic chemistry.[1] In particular, an asymmetric carbon−carbon bond-forming process is being emphasized in advanced materials and pharmaceuticals. The asymmetric 1,4-conjugate addition of organometallic reagents to α,β-unsaturated carbonyl compounds is widely used for carbon−carbon bond formation with a new stereogenic center being introduced at the β-position of the formed saturated carbonyl compounds.[2] Hayashi and Miyaura proposed the highly useful rhodium-catalyzed asymmetric 1,4-addition of organoboron reagents with α,β-unsaturated ketones, esters, amides, and phosphonates.[3] Organosilicon reagents are playing a growing role in organic synthesis due to their low cost, low toxicity, ease of handling, tolerance to a variety of functional groups, and simplicity of byproduct removal.[4] A synthetical advantage is that the organosilicon reagents are readily prepared in one step by a variety of methods. For example, β-substituted (*E*)- and (*Z*)-vinylsilanes[5] and α-substituted ones[6] can be prepared by regio- and stereoselective hydrosilylation of alkynes, and acyl- alkyl-, vinyl-, and arylsilanes can be prepared by cross-coupling reaction of corresponding organic halides with disilanes[7] or hydrosilanes.[8] Regarding the

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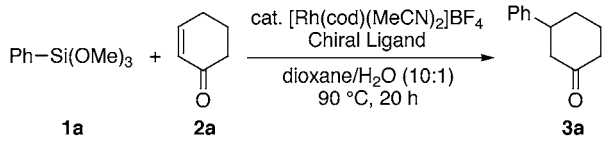
Table 1. Rhodium-Catalyzed Asymmetric 1,4-Addition of Phenyltrimethoxysilane (**1a**) to Cyclohexenone (**2a**)[a]



1a 2a 3a

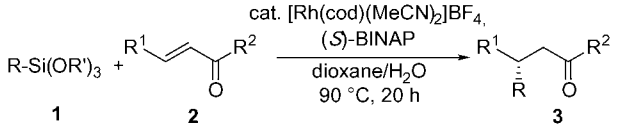
entry	ligand (mmol)	yield,[b] %	ee, %
1	(*S*)-(*R*)-BPPFA (0.02)	72	0
2	(*S*)-(*R*)-BPPFOAc (0.02)	33	0
3	(*R*)-DIOP (0.02)	77	0
4	(*S*)-Tol-BINAP (0.02)	59	12
5	(*S*)-BINAP (0.02)	88	25
6	(*S*)-BINAP (0.025)	75	35
7	(*S*)-BINAP (0.03)	58	97
8	(*S*)-BINAP (0.04)	38	97
9[c]	(*S*)-BINAP (0.03)	72	98
10[d]	(*S*)-BINAP (0.06)	76	98

[a] Common reaction conditions: **1a** (2.0 mmol), **2a** (1.0 mmol), $[Rh(cod)(MeCN)_2]BF_4$ (0.02 mmol), 2.2 mL of dioxane/H_2O (10:1), 90 °C, 20 h, N_2 atmosphere. [b] Isolated yield. [c] Reaction for 40 h. [d] 0.04 mmol of $[Rh(cod)(MeCN)_2]BF_4$ was used.

rhodium-catalyzed reaction of the organosilicon reagents, we reported addition of phenylmethyldifluorosilane to aldehydes.[9] Addition of diaryldichlorosilanes to unsaturated carbonyl compounds,[10] and addition of arylmethylsilanediols to unsaturated carbonyl compounds and aldehydes[11] also occur. The 1,4-addition of organotrialkoxysilanes to unsaturated carbonyl compounds was recently reported to be catalyzed by rhodium complexes.[12] In this paper, we wish to report a highly enantioselective 1,4-addition of aryl- and alkenyltrialkoxysilanes to α,β-unsaturated carbonyl compounds catalyzed by a BINAP−rhodium complex.

Initially, various chiral phosphine ligands were examined (P/Rh = 2) in the reaction of phenyltrimethoxysilane (**1a**) with cyclohexenone (**2a**) under the conditions reported before (Table 1, entries 1−5).[12a] Although ferrocene-based ligands (entries 1 and 2) and DIOP (entry 3) did not show any enantioselectivity, modest ees were obtained when binaphthyl-based ligands were used (entries 4 and 5). Then, other conditions were examined using (*S*)-BINAP as a ligand (Table 1, entries 6−10). The amount of BINAP affected both chemical and optical yields. When the amount of BINAP was increased to 0.025 mmol (P/Rh = 2.5) or 0.03 mmol (P/Rh = 3), the chemical yield decreased to 75 and 55%, respectively, and the optical yield increased to 35 and 97% ee, respectively (entries 5−7). Further addition of BINAP (0.04 mmol) caused the chemical yield to only decrease (entry 8). The chemical yield could be improved by lengthening the reaction time and by increasing the amount of catalyst loaded without loss of the optical yield (entries 9 and 10).

Table 2. Rhodium-Catalyzed Asymmetric 1,4-Addition of Organosiloxanes to α,β-Enones[a]



entry	1	2	yield, %[b]	ee, %[c]
1	$PhSi(OMe)_3$ (**1a**)	(**2a**)	76 (**3a**)	98 (*S*)
2	**1a**	(**2b**)	89 (**3b**)	94 (*S*)
3	**1a**	(**2c**)	90 (**3c**)	75 (*R*)
4	**1a**	(**2d**)	90 (**3d**)	75 (*R*)
5	**1a**	(**2e**)	87 (**3e**)	91
6	**1a**	(**2f**)	62 (**3f**)	98
7	*p*-$ClC_6H_4Si(OEt)_3$ (**1b**)	(**2a**)	56 (**3g**)	96
8	*p*-$MeOC_6H_4Si(OEt)_3$ (**1c**)	**2a**	73 (**3h**)	96
9	$Si(OEt)_3$ (**1d**)	**2a**	54 (**3i**)	96 (*S*)
10	Ph, $Si(OEt)_3$ (**1e**)	**2a**	85 (**3j**)	91 (*S*)
11	Ph, $Si(OEt)_3$ (**1f**)	**2a**	88 (**3k**)	87

[a] Common reaction conditions: 1 (2.0 mmol), 2 (1.0 mmol), $[Rh(cod)(MeCN)_2]BF_4$ (0.04 mmol), (*S*)-BINAP (0.06 mmol), 2.2 mL of dioxane/H_2O (10:1), 90 °C, 20 h, N_2 atmosphere. [b] Isolated yield. [c] Absolute configuration is shown in parentheses.

With the optimized reaction conditions (Table 1, entry 10), asymmetric 1,4-addition of various organosiloxanes to enones were examined. Results are summarized in Table 2. As in the reaction of cyclohexenone (**2a**, entry 1), cyclopentenone (**2b**) also underwent the asymmetric 1,4-addition of phenyltrimethoxysilane (**1a**) with high enantioselectivity affording the (*S*)-form product (**3b**) in good yield (entry 2). The reaction of **1a** with linear enones also proceeded enantioselectively, but afforded the (*R*)-form producs. Enantioselectivity and reactivity were affected by bulkiness of the substituent on the β-position of the enones. With the

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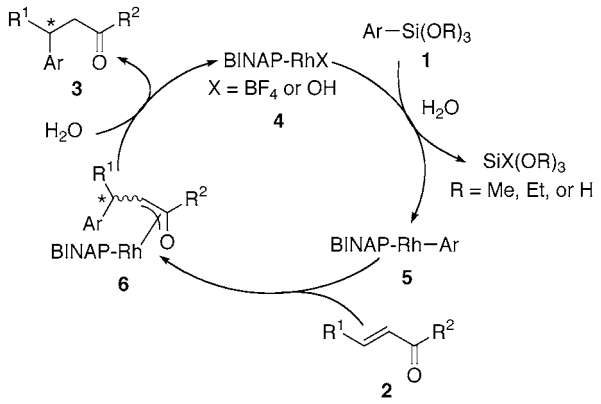
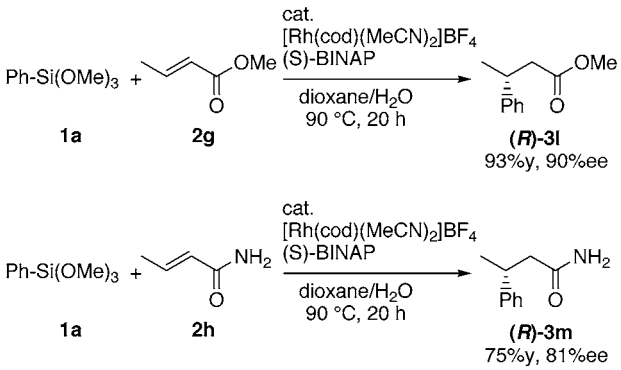
Scheme 1. Presumed Reaction Pathway



substituent on the β-position was changed from methyl (**2c**) to propyl (**2e**) and to isopropyl (**2f**), the optical yield increased from 75% to 91% ee, and then to 98% ee, while the chemical yield decreased from 90% to 87%, and then 67% (entries 3, 5, and 6). On the other hand, the substituent on the carbonyl carbon had no influence on either enantioselectivity or reactivity, in that methyl ketone **2c** and phenyl ketone **2d** gave similar results (entries 3 and 4). Aryltrialkoxysilanes bearing either an electron-donating or an electron-withdrawing group, **1b** and **1c**, also added to cyclohexenone (**2a**) enantioselectively affording the corresponding products of over 95% ee (entries 7 and 8). Asymmetric 1,4-addition of 1-alkenyltrialkoxysilanes was also successful. Vinylsilane **1d** added to **2a** to give (*S*)-3-vinylcyclohexanone (**3i**) in an excellent ee of 96%. The reaction of both *E*- and *Z*-styrylsilane, **1e** and **1f**, proceeded without isomerization of styryl moiety affording the products in good yield with high ees of 91% and 87%, respectively (entries 10 and 11).

To expand the scope of the reaction, the asymmetric addition of **1a** to α,β-unsaturated esters and amides was examined. As a result, the reactions with methyl crotonate (**2g**) and crotonamide (**2h**) proceeded as in the reaction of 3-penten-2-on (**2c**) giving the phenylated (*R*)-form adducts, **3l** and **3m**, in good yield with high enantioselectivity.



The reaction mechanism (Scheme 1) probably involves the generation of an organorhodium intermediate **5** by the transmetalation between the silicon reagent **1** and a rhodium complex **4** and the addition of the organorhodium intermediate **5** to the α,β-unsaturated carbonyl compound **2** as we reported.[12] The stereochemical pathway of the addition of the Rh−C bond to the enones should be similar to that in the asymmetric 1,4-addition of arylboronic acids reported by Hayashi and Miyaura.[3] We considered that the chiral rhodium species would be an 1:1 complex of rhodium and BINAP, although addition of 1.5-fold excess of BINAP was needed to obtain high enantioselectivity, which would be necessary to complete the complexation. The (*E*)-enones coordinates to the Rh−(*S*)-BINAP complex (Figure 1) on

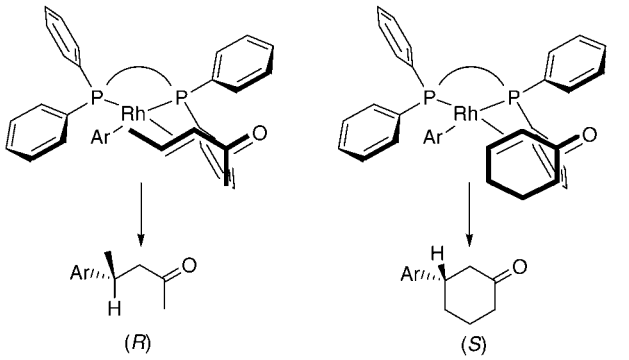


Figure 1.

their 2*re* face to avoid the steric interaction with the edges of two pseudoequatorial phenyl groups to afford the (*R*)-products. Cyclic enones, i.e., (*Z*)-enones, coordinate to the Rh−(*S*)-BINAP complex in the same manner but on their 2*si* face to afford the (*S*)-products.

In conclusion, highly enantioselective 1,4-addition of organosiloxanes to α,β-unsaturated carbonyl compounds was catalyzed by a chiral rhodium complex generated from [Rh(cod)(MeCN)$_2$]BF$_4$ and (*S*)-BINAP. Both (*E*)- and (*Z*)-1-alkenyl groups as well as aryl groups can be introduced enantioselectively into β-position of a variety of ketones, esters, and amides. Further studies to expand the scope and to clarify mechanistic details are underway.

Supporting Information Available: Experimental details and characterization data for **3a**−**m**. This material is available free of charge via the Internet at http://pubs.acs.org.

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