doi:10.1246/cl.2012.374

Ruthenium-catalyzed Ortho-selective Aromatic C–H Silylation: Acceptorless Dehydrogenative Coupling of Hydrosilanes

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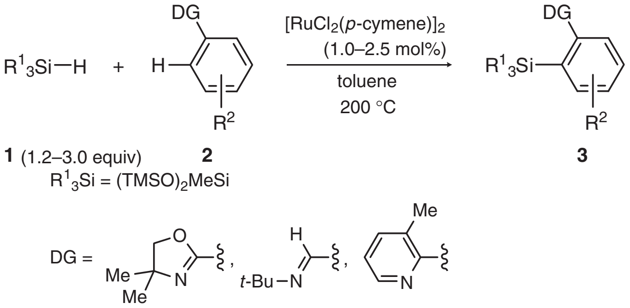
The intermolecular dehydrogenative coupling of 1,1,1,3,5,5,5-heptamethyltrisiloxane with aromatic compounds such as aryloxazolines and arylimines in the presence of a catalytic amount of [RuCl$_2$(*p*-cymene)]$_2$ gave the corresponding ortho-silylated products in good yields.

Since arylsilanes are versatile building blocks or reagents for modern organic synthesis, the development of transition-metal-catalyzed aryl C–Si bond-forming reactions has attracted considerable interest.[1] From an environmental and economic point of view, there is no doubt that the dehydrogenative silylation of ubiquitous C–H bonds of arenes with hydrosilanes is an ultimate goal.[2] However, examples of the C–H silylation with hydrosilanes bearing electronegative groups, such as halogen and alkoxy groups, on the silicon atom are still rare in spite of the significant synthetic value of produced arylsilanes.[3] Recently, we reported that 1,1,1,3,5,5,5-heptamethyltrisiloxane (**1**) promoted the platinum-catalyzed dehydrogenative coupling with arenes[4] and arylsiloxanes thus obtained exhibited good reactivity for converting the silicon functionality.[5]

During the past decade, much attention has been given to the control of regioselectivity in the catalytic C–H silylation.[6–9] Among the most promising strategies is utilization of a directing effect through heteroatom coordination to the catalyst.[6,7] As a representative example of regioselective silylation of aromatic C–H bonds with hydrosilanes, Murai and co-workers reported that the ruthenium-catalyzed reaction of benzene derivatives having an sp^2 nitrogen substituent afforded ortho-silylated products with complete regioselectively.[6a,6c] However, the silylating reagents were restricted to triorganosilanes, which provided less reactive aryl triorganosilanes as synthetic intermediates. It is the purpose of this paper, therefore, to present an alternative silicon source. We wish to report an ortho-selective C–H silylation of aromatic compounds **2**, such as aryloxazolines and arylimines, with **1**. (Scheme 1)



Scheme 1.

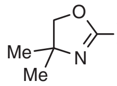
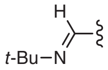
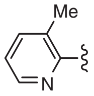
Table 1. Silylation of 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**2a**) with hydrosilanes[a]

Entry	Hydrosilane	Catalyst	Conv /%[b]	Yield /%[c]
1	**1**	[RuCl$_2$(*p*-cymene)]$_2$	98	92
2[d]	**1**	[RuCl$_2$(*p*-cymene)]$_2$	41	40
3	**1**	[RuCl$_2$(C$_6$H$_6$)]$_2$	92	85
4	**1**	[Ru$_3$(CO)$_{12}$]	80	61
5	**1**	[Cp*RuCl$_2$]$_2$	0	0
6	**1**	[Cp*RuCl]$_4$	5	5
7	(Me$_3$SiO)Me$_2$SiH	[RuCl$_2$(*p*-cymene)]$_2$	70	45[e]
8	Et$_3$SiH	[RuCl$_2$(*p*-cymene)]$_2$	65	61[f]
9	(EtO)$_3$SiH	[RuCl$_2$(*p*-cymene)]$_2$	0	0

[a]Reaction conditions: **1** (0.30 mmol), **2a** (0.25 mmol), catalyst (0.005 mmol of Ru), and toluene (0.5 mL), 200 °C, 16 h. [b]Conversions of **2a** were determined by GC. [c]GC yields of **3a** are based on **2a**. [d]The reaction was carried out in the presence of *tert*-butylethylene (1.0 mmol). [e]GC yield of 4,4-dimethyl-2-{2-[(trimethylsiloxy)dimethylsilyl]phenyl}-4,5-dihydrooxazole. [f]GC yield of 4,4-dimethyl-2-[2-(triethylsilyl)phenyl]-4,5-dihydrooxazole.

As a test for the optimization of reaction parameters, 4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (**2a**) was used as a substrate. The results are summarized in Table 1. When **2a** was treated with a slight excess of **1** (1.2 equiv) in the presence of 1.0 mol % of [RuCl$_2$(*p*-cymene)]$_2$ in toluene at 200 °C for 16 h, 92% yield of monosilylated product **3a** (DG: 4,4-dimethyl-4,5-dihydrooxazol-2-yl, R^2 = H) was obtained (Entry 1). The reaction is completely regioselective, introducing the silyl group to the ortho position of the benzene ring. Thus, the meta- and para-C–H bonds of **2a**, and toluene solvent did not participate in the present silylation. While dehydrogenative coupling of hydrosilanes with arenes often requires an added alkene as a hydrogen acceptor,[6,8] inclusion of *tert*-butylethylene (4 equiv) prevented the aromatic C–Si bond formation (Entry 2). Several ruthenium catalysts were tested, and the use of [RuCl$_2$(*p*-cymene)]$_2$ provided the best result (Entry 1). [RuCl$_2$(C$_6$H$_6$)]$_2$ also showed good catalytic activity affording **3a** in a similar yield (Entry 3), whereas the use of [Ru$_3$(CO)$_{12}$] complicated the reaction by the formation of side-products (Entry 4). [Cp*Ru] catalyst systems did not promote the present silylation reaction (Entries 5 and 6). Under our optimized conditions, the use of 1,1,1,3,3-pentamethyldisiloxane led to complex mixtures (Entry 7) and that of triethylsilane induced a lowering of the

Table 2. Ortho-selective aromatic C–H silylation of **2** with **1**[a]

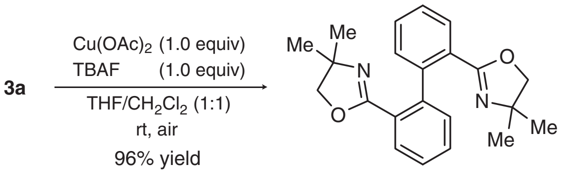
Entry	**2**		**3**	Yield/%[b]
	DG	R^2		
1		4-CF_3 (**2b**)	**3b**	89
2		4-Me (**2c**)	**3c**	88
3		4-OMe (**2d**)	**3d**	90
4[c]		3-Me (**2e**)	**3e**[d]	70
5		H (**2f**)	**3f**	94
6		4-OMe (**2g**)	**3g**	87
7		4-CO_2Me (**2h**)	**3h**	88
8[c]		H (**2i**)	**3i**	80

[a]Reaction conditions: **1** (0.30 mmol), **2** (0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 µmol), and toluene (0.5 mL), 200 °C, 16 h. [b]Isolated yields based on **2**. [c]Reaction conditions: **1** (0.75 mmol), **2** (0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (6.25 µmol), and toluene (0.5 mL), 200 °C, 48 h. [d]4,4-Dimethyl-2-{5-methyl-2-[bis(trimethylsiloxy)methylsilyl]phenyl}-4,5-dihydrooxazole.

reactivity (Entry 8). Furthermore, no reaction with triethoxysilane occurred (Entry 9). The present study demonstrates that **1** is an efficient silylating reagent for the aromatic C–H silylation.

The scope of this silylation using **1** was next explored (Table 2).[10] In the first part of this study, several aryloxazolines **2b**–**2e** were used as the substrates. In all cases, one of the aromatic C–H bonds ortho to the oxazolinyl groups was silylated. As shown in Table 2, para-substituted aryloxazolines were efficiently converted to the corresponding mono-silylated products **3b**–**3f** (Entries 1–3). The yields were almost independent of the electronic requirement; i.e., the differences in the yields among **2** having electron-withdrawing (Entry 1) or -donating groups (Entries 2 and 3) were not particularly large. In contrast to the para-substituted substrates, meta-substituted aryloxazoline **2e** was not sufficiently reactive under our standard conditions; i.e., the conversion and yield were low (29% GC yield). We found, however, 3 equiv of **1** and 2.5 mol % of $[RuCl_2(p\text{-cymene})]_2$ allowed the reaction to proceed to full conversion after 48 h (Entry 4). In the case of **2** bearing a methyl group at the 3-position of the aromatic ring, the C–Si bond formation took place only at the less hindered 6-position. The second portion of this work involves the application of this protocol to the silylation of aromatic aldimines **2f**–**2h** (Entries 5–7). These results also indicate that the present silylation is tolerant of both electron-donating and -withdrawing substituents on the aromatic ring (Entries 6 and 7). Furthermore, the pyridine ring could also be used as an ortho directing group (Entry 8).

We then tried to apply ortho-substituted 3-aryltrisiloxanes **3** thus obtained via the present silylation to C–C bond-forming reaction, as we have demonstrated that 3-aryltrisiloxanes underwent the transition-metal-catalyzed cross-coupling in the presence of TBAF.[4,5] It was found that $Cu(OAc)_2$ and TBAF promoted homocoupling of **3a** under aerobic conditions (Scheme 2). While the Cu(I)-catalyzed homocoupling of aryl(halo)silanes has been reported,[11] a catalytic amount of neither $Cu(OAc)_2$ nor CuI was totally effective. Unfortunately, we have no definitive explanation for the role of Cu(II) salt at present stage.



Scheme 2.

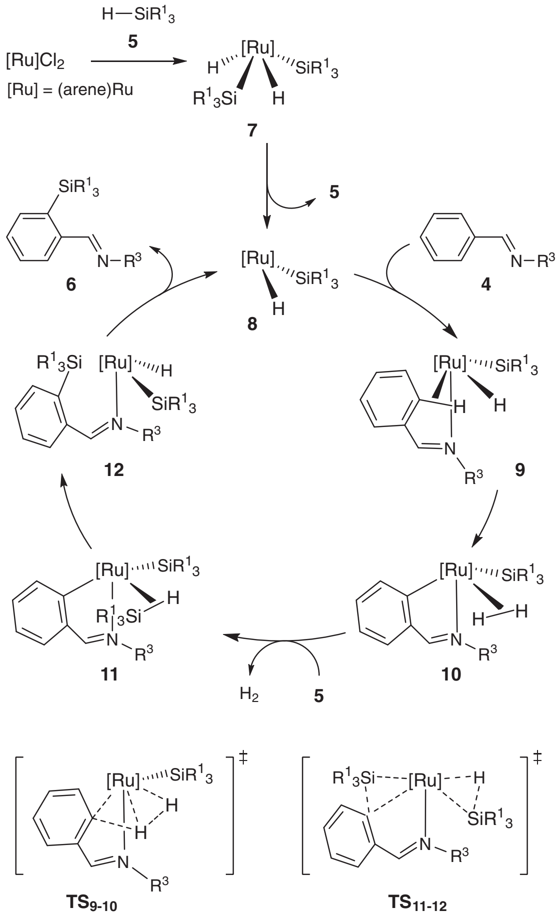


Figure 1. Plausible mechanism of ortho-selective aromatic C–H silylation.

Finally, we turned our attention toward the mechanism of this C–H silylation. The proposed catalytic cycle is illustrated in Figure 1. As Berry and co-workers have proven that $[(\eta^6\text{-arene})RuCl_2]_2$ reacted with $HSiR_3$ to give $[(\eta^6\text{-arene})Ru(H)_2(SiR^1{}_3)_2]$,[12] the first step in the proposed pathway involves the formation of the Ru(IV) dihydride bis(silyl) complex **7**. Indeed, the reaction between $[(p\text{-cymene})Ru(H)_2(SiEt_3)_2]$ and **2a** afforded the corresponding silylated product in quantitative yield.[13] The following process was computationally addressed by density functional theory (DFT) calculations.[10] We have adopted the reaction of phenylmethanimine (**4**, $R^3 = H$) with trimethylsilane (**5**, $R^1 = Me$) as a model reaction, and the p-cymene ligand was replaced by benzene in the computed structures. Although **7** potentially dissociates H_2, $HSiR^1_3$, or $Si_2R^1_6$, our calculations suggest that a hydride silyl complex **8** would form by elimination of **5**.[14] Then, after the coordination of both sp^2 nitrogen atom and ortho C–H bond of **4** to **8**, the σ-complex-assisted metathesis (σ-CAM) with the Ru–H bond takes place through a transition state $\mathbf{TS_{9–10}}$ to form an aryl silyl ruthenium **10**. A ligand substitution reaction includes dissociation of the H_2 ligand and coordination of **5** forming a σ-silane ruthenium **11**. Subsequently, oxidative addition of the coordinated Si–H bond and C–Si reductive elimination through a single transition state $\mathbf{TS_{11–12}}$ with no intermediates take place to give a hydride silyl complex **12** which contains a coordinated arylsilane **6**. Elimination of the silylated product **6** from **12** regenerates **8** and completes the silylation reaction. The activation barriers of the C–H bond activation and the C–Si bond-forming steps are 37.2 and 47.0 kcal mol^{-1}, respectively, indicating that the latter step is rate-determining for the proposed reaction mechanism.

The catalytic cycle initially proposed by Murai et al. involves a Ru(IV) intermediate via sequential oxidative addition both of C–H and Si–H bonds, although the potentiality for a σ-bond metathesis pathway has not been ruled out.[6c] As all attempts to locate the $[Ru(Ar)(SiR^1_3)(H)_2]$ intermediate as a stationary point were unsuccessful probably because of the energetically unfavorable high oxidation state, we believe that the above mechanism involving σ-CAM would be preferable to the oxidative addition pathway.

In conclusion, 1,1,1,3,5,5,5-heptamethyltrisiloxane (**1**) was found to promote the ruthenium-catalyzed intermolecular dehydrogenative coupling with aromatic compounds **2**, such as aryloxazolines, arylimines, and arylpyridines. The ortho-selective introduction of the silyl groups reported herein was achieved without hydrogen acceptors. Theoretical calculations suggest that the catalytic cycle involves the C–H bond activation via σ-CAM mechanism. Further studies are currently underway to obtain detailed mechanistic insights.

This work was partially supported by a Grant-in-Aid for Scientific Research from Japan Society for the Promotion of Science (JSPS). We thank Mr. Takashi Yamamoto for help in preparing this manuscript.

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13 A mixture of $[(p\text{-cymene})Ru(H)_2(SiEt_3)_2]$ (0.036 mmol) and **2a** (0.16 mmol) in toluene (0.2 mL) was stirred at 200 °C for 4.5 h. GLC analysis of the reaction mixture indicated formation of 4,4-dimethyl-2-(2-triethylsilylphenyl)-4,5-dihydrooxazole (95%).

14 The formation of bis(silyl) complex from **7** was proposed in the dehydrogenative silylation by Berry and co-workers (ref. 12). However, DFT calculations indicate that the formation of **8** is energetically favorable (ca. 10 kcal mol^{-1} lower than that of bis(silyl) or dihydride ruthenium complex).