Regioselective aromatic C–H silylation of five-membered heteroarenes with fluorodisilanes catalyzed by iridium(I) complexes†

Tatsuo Ishiyama,* Kazuaki Sato, Yukihiro Nishio, Takeaki Saiki and Norio Miyaura*

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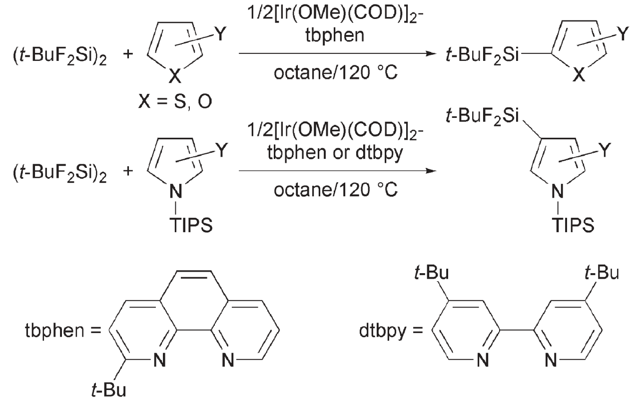
The aromatic C–H silylation of five-membered heteroarenes with 1,2-di-*tert*-butyl-1,1,2,2-tetrafluorodisilane regioselectively proceeded at 120 °C in octane in the presence of a catalytic amount of iridium(I) complexes generated from 1/2[Ir(OMe)(COD)]$_2$ and 2-*tert*-butyl-1,10-phenanthroline.

Transition metal-catalyzed aromatic C–H silylation of aromatic compounds is highly attractive as a convenient, economical, and environmentally benign process for preparing synthetically useful aromatic silicon compounds.[1] Although several studies on this type of transformation with disilanes[2] or hydrosilanes[2a,3] have been carried out, application of the protocol has been limited to the synthesis of less-reactive aromatic triorganosilicon derivatives. Recently, we found that iridium(I) complexes comprised of an air-stable, easily available 1/2[Ir(OMe)(COD)]$_2$ precursor and a simple, commercially available 2,2′-bipyridine (bpy) or 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy) ligand effectively catalyzed aromatic C–H silylation of neat arenes with 1,2-di-*tert*-butyl-1,1,2,2-tetrafluorodisilane (t-BuF$_2$Si)$_2$ at 120 °C to give the corresponding aryl fluorosilanes in high yields with high regioselectivities.[4,5] Also, the synthetic utility of the aryl fluorosilanes was demonstrated by their palladium-catalyzed cross-coupling[6] with aromatic electrophiles and rhodium-catalyzed 1,4-addition[7] to enones.[4] As an extension of our methodology to other aromatic substrates, we describe here the iridium(I)-catalyzed aromatic C–H silylation of five-membered heteroarenes with (t-BuF$_2$Si)$_2$ in octane at 120 °C (Scheme 1). Thiophene and furan derivatives were exclusively silylated at the α-position by using 1/2[Ir(OMe)(COD)]$_2$–(2-*tert*-butyl-1,10-phenanthroline)[8] (tbphen) catalysts. On the other hand, the reactions of 1-triisopropylsilylpyrrole and -indole catalyzed by 1/2[Ir(OMe)(COD)]$_2$–tbphen or –dtbpy complexes selectively yielded β-silyl products.



Scheme 1 C–H silylation of five-membered heteroarenes.

The silylation of 3-methylthiophene (60 mmol) with (t-BuF$_2$Si)$_2$ (1.0 mmol) in the presence of catalysts generated from [Ir(OMe)(COD)]$_2$ (0.015 mmol) and dtbpy (0.03 mmol) resulted in only a 38% yield of the silylated product after 16 h at 120 °C,[4] probably due to the high coordinating ability of the sulfur atom which retards the formation of a coordinatively unsaturated iridium species active for C–H activation.[9] This result prompted us to use an appropriate solvent inactive toward the C–H silylation. Indeed, a silylated product was obtained in 90% yield when 5.0 mmol of the substrate was diluted in 6 mL of octane. At that time, we expected formation of regioisomerically pure 5-silyl-3-methylthiophene, because previous studies on C–H silylation of alkylated arenes demonstrated that the reactions did not occur at sterically hindered *ortho* positions.[4] However, the present reaction gave a regioisomeric mixture of 5-, 4-, and 2-silylated products in a ratio of 69 : 3 : 28, indicating that the dtbpy-ligated iridium species was insufficient to recognize the steric environment of the substrate. Thus, we examined a sterically hindered 6,6′-di-Me-bpy ligand, but the reaction resulted in only an 8% yield. Presumably, twisting between two pyridyl units arising from steric hindrance around the iridium center leads to the low activity.[4] Based on this hypothesis, we investigated the reaction by using structurally rigid 1,10-phenanthroline (phen) derivatives as ligands for iridium (Table 1).

As we expected, phen ligands even having substituents at 2 and 9 positions displayed high reactivity. Although unsubstituted phen produced the desired 5-silylated products with 66% selectivity (Entry 1), the selectivity was improved to 81%, 91% and 93% when using 2,9-di-Me-phen, 2,9-di-*n*-Bu-phen and 2,9-di-*i*-Pr-phen, respectively (Entries 2–4). However, the use of sterically more hindered 2,9-di-*t*-Bu-phen led to no reaction (Entry 5). The result prompted us to examine monosubstituted phen derivatives. 2-*i*-Pr-phen resulted in a 72% selectivity (Entry 6), but 2-*t*-Bu-phen (tbphen) improved the selectivity to 98%, while its reactivity was low (Entry 7). Finally, we obtained the desired 5-silyl-3-methylthiophene in 96% yield with 99% regioselectivity when the reaction was carried out for 32 h by using 10 mmol of 3-methylthiophene (Entry 8).

Reactions of thiophene derivatives with (t-BuF$_2$Si)$_2$ catalyzed by the combination of 1/2[Ir(OMe)(COD)]$_2$ and tbphen at 120 °C in

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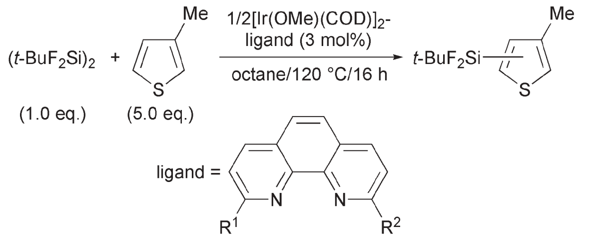
Division of Chemical Process Engineering, Graduate School of Engineering, Hokkaido University, Sapporo, 060-8628, Japan. E-mail: ishiyama@org-mc.eng.hokudai.ac.jp; Fax: +81 11 706 6562; Tel: +81 11 706 6562

† Electronic supplementary information (ESI) available: experimental procedures and spectral analyses of products. See http://dx.doi.org/10.1039/b511171d

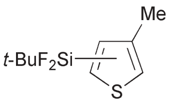
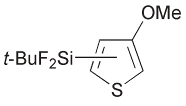
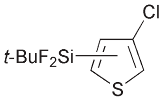
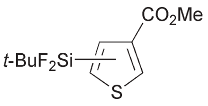
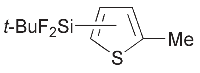
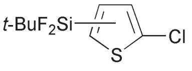
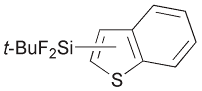
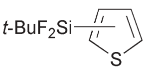
Table 1 Reaction conditions for 3-methylthiophene[a]



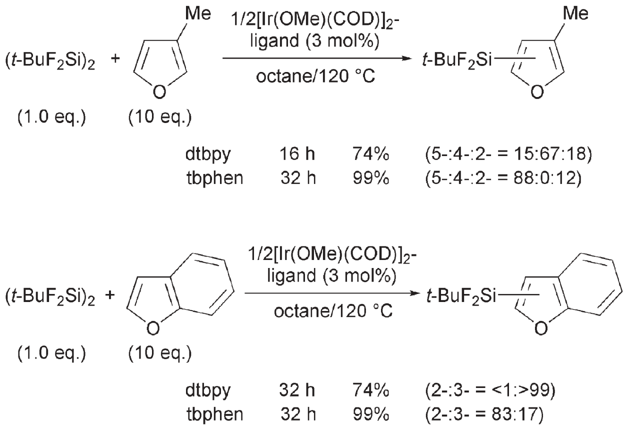
Entry	R^1	R^2	Yield (%)[b]	5- : 4- : 2- (%)[c]
1	H	H	99	66 : 4 : 30
2	Me	Me	85[d]	81 : 0 : 19
3	*n*-Bu	*n*-Bu	65	91 : 0 : 9
4	*i*-Pr	*i*-Pr	65	93 : 0 : 7
5	*t*-Bu	*t*-Bu	0	—
6	*i*-Pr	H	91	72 : 0 : 28
7	*t*-Bu	H	40	98 : 0 : 2
8	*t*-Bu	H	96[e]	99 : 0 : 1

[a] Reactions were carried out at 120 °C for 16 h by using $(t\text{-BuF}_2\text{Si})_2$ (1.0 mmol), 3-methylthiophene (5.0 mmol), $[\text{Ir(OMe)(COD)}]_2$ (0.015 mmol), ligand (0.03 mmol), and octane (6 mL). [b] GC yields based on $(t\text{-BuF}_2\text{Si})_2$. [c] Isomer ratios were determined by ^{1}H NMR. [d] 8 h. [e] 10 mmol of 3-methylthiophene, 32 h.

Table 2 C–H silylation of thiophene derivatives[a]

Entry	Product	Yield (%)[b]	Isomer ratio (%)[c]
1		96[d]	5- : 4- : 2- = 99 : 0 : 1
2		97	5- : 4- : 2- = 87 : 2 : 11
3		92	5- : 4- : 2- = 98 : 0 : 2
4		93	5- : 4- : 2- = 98 : 0 : 2
5		99[d]	5- : 4- : 3- = 95 : 5 : 0
6		88	5- : 4- : 3- = 95 : 5 : 0
7		98	2- : 3- = > 99 : < 1
8		96[d]	2- : 3- = 93 : 7

[a] Reactions were carried out at 120 °C for 48 h by using $(t\text{-BuF}_2\text{Si})_2$ (1.0 mmol), thiophenes (10 mmol), $[\text{Ir(OMe)(COD)}]_2$ (0.015 mmol), tbphen (0.03 mmol), and octane (6 mL). [b] GC yields based on $(t\text{-BuF}_2\text{Si})_2$. [c] Isomer ratios were determined by ^{1}H NMR. [d] 32 h.



dtbpy 16 h 74% (5-:4-:2- = 15:67:18)
tbphen 32 h 99% (5-:4-:2- = 88:0:12)

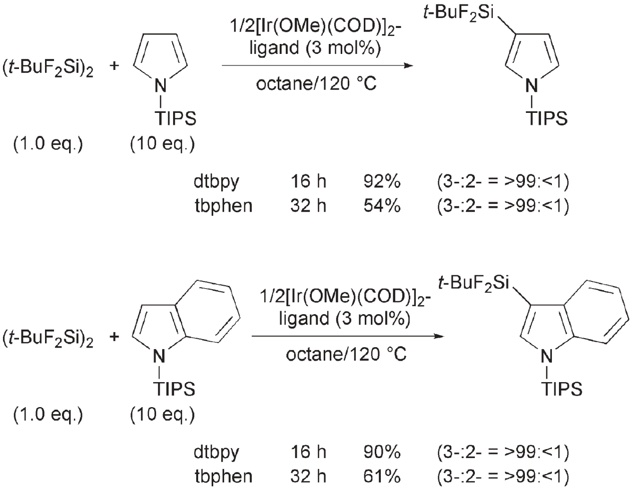
dtbpy 32 h 74% (2-:3- = <1:>99)
tbphen 32 h 99% (2-:3- = 83:17)

Scheme 2 C–H silylation of furan derivatives.

octane are summarized in Table 2. 3-Substituted (Entries 1–4), 2-substituted (Entries 5 and 6), benzo-fused (Entry 7), and unsubstituted (Entry 8) thiophenes were all viable substrates to produce the corresponding silylated products in excellent yields with high regioselectivities. The reactions were suitable for substrates possessing various functional groups, such as OMe, Cl, and CO_2Me or benzylic C–H bonds[10] (Entries 1–6). The regiochemistry was controlled by both electronic and steric effects. The electronegative sulfur atom caused the α-C–H bonds to be active,[11] and the substituents on thiophene blocked activation of the neighboring C–H bonds.[4] The low selectivity observed in the reaction of 3-methoxythiophene may be ascribed to the small steric hindrance of the MeO group (Entry 2).

Although furan derivatives also underwent smooth C–H silylation, the regiochemistry was perplexing. Reactions of 3-methylfuran and benzofuran using dtbpy as a ligand predominantly yielded unexpected 4-silylated and 3-silylated products, respectively. In such cases, use of a tbphen ligand resulted in the expected 5-silylated and 2-silylated products with 88% and 83% selectivities (Scheme 2).

The C–H silylation of unsubstituted pyrrole and indole by using either dtbpy or tbphen as a ligand produced complex mixtures probably due to the presence of an acidic hydrogen in the substrates, but the reactions of 1-triisopropylsilylpyrrole and -indole successfully gave silylated products. The silylation occurred only at the β-positions when using either dtbpy or tbphen because of the large steric hindrance of the TIPS group (Scheme 3).



dtbpy 16 h 92% (3-:2- = >99:<1)
tbphen 32 h 54% (3-:2- = >99:<1)

dtbpy 16 h 90% (3-:2- = >99:<1)
tbphen 32 h 61% (3-:2- = >99:<1)

Scheme 3 C–H silylation of pyrrole derivatives.

In summary, iridium complexes comprised of 1/2[Ir(OMe)(COD)]$_2$ and 2-*tert*-butyl-1,10-phenanthroline were found to be efficient catalysts for the regioselective aromatic C–H silylation of five-membered heteroarenes with 1,2-di-*tert*-butyl-1,1,2,2-tetrafluorodisilane. Further investigations to survey the scope and limitations of this C–H silylation, including that of other heteroarenes such as pyridines, as well as to elucidate the reaction mechanisms are in progress.

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