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Iridium-Catalyzed Silylation of Five-Membered Heteroarenes: High Sterically Derived Selectivity from a Pyridyl-Imidazoline Ligand

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Abstract

The steric effects of substituents on five-membered rings are less pronounced than those on six-membered rings because of the difference in bond angles. Thus, the regioselectivities of reactions that occur with selectivities dictated by steric effects, such as the borylation of C-H bonds, have been poor in many cases. We report that the silylation of five-membered ring heteroarenes occurs with high sterically derived regioselectivity when catalyzed by the combination of [Ir(cod)(OMe)]$_2$ and a phenanthroline ligand or a new pyridyl-imidazoline ligand that further increases the regioselectivity. The silylation reactions with these catalysts produce high yields of heteroarylsilanes from functionalization at the most sterically accessible C–H bonds of these rings under conditions that the borylation of C–H bonds with previously reported catalysts formed mixtures of products or products that are unstable. The heteroarylsilane products undergo cross-coupling reactions and substitution reactions with *ipso* selectivity to generate heteroarenes that bear halogen, aryl and perfluoroalkyl substituents.
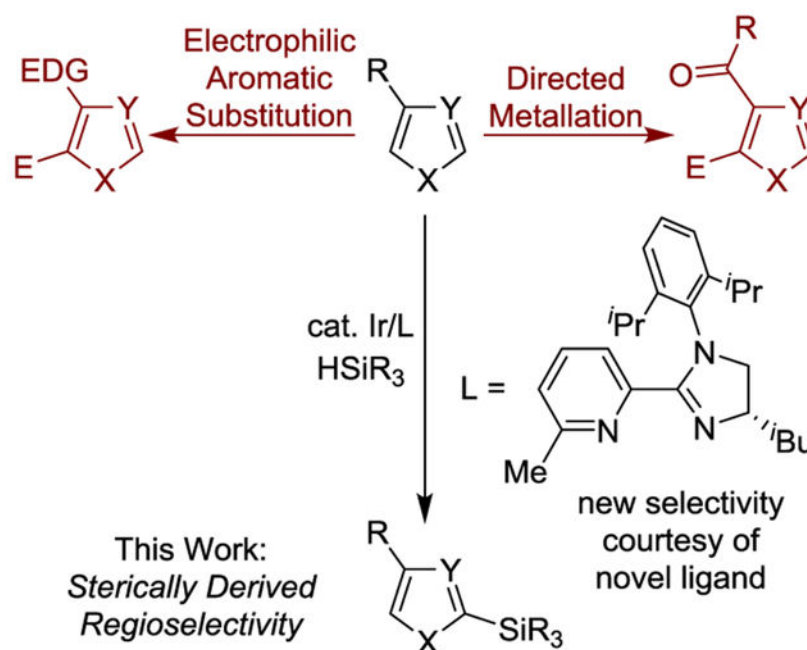
Graphical Abstract

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The silylation of five-membered heteroarenes occurs with high sterically derived regioselectivity when catalyzed by the combination of [Ir(cod)(OMe)]₂ and a novel pyridyl-imidazoline ligand. The silylation reactions with this catalyst produce high yields of heteroarylsilanes under conditions in which the borylation of C–H bonds with previously reported catalysts formed mixtures of products or products that are unstable.

Keywords

Silylation; Heteroarenes; C-H Functionalization; Iridium Catalysis

Introduction

The application of C-H bond functionalization to synthetic chemistry requires the selective activation of a single C–H bond among multiple C–H bonds that possess different steric and electronic properties.[1], [2] A common strategy for controlling the selectivity of catalytic reactions that functionalize the C–H bonds of arenes is to incorporate a functional group on the arene that coordinates to a transition-metal catalyst and directs the reaction to C–H bonds that are ortho, meta or para to that functional group.[3]

Undirected functionalizations of the C–H bonds of arenes occur with selectivities that are determined by the steric and electronic properties of the various types of C–H bonds.[4] The most classical undirected functionalizations include uncatalyzed or Lewis-acid catalyzed electrophilic aromatic substitution (EAS) processes. In general, these reactions occur at the most electron-rich C–H bonds, and the steric properties of the groups impart a secondary influence on selectivity.[5]

In contrast, the silylations and borylations of the C–H bonds of arenes catalyzed by iridium complexes of bipyridine or phenanthroline ligands generally occur at the most sterically accessible and acidic C–H bonds.[6] The regioselectivity of these reactions is almost exclusively determined by the steric properties of the arene; these catalysts selectively functionalize C–H bonds that are distal to functional groups in preference to C-H bonds that are more acidic, but proximal to functional groups. Thus, symmetrical 1,2-disubstituted or unsymmetrical 1,3-disubstituted or 1,2,3-trisubstituted arenes undergo borylation at the C–H meta to the nearest substituent (Figure 1).

The regioselectivity of the functionalization of heteroarenes is more complex than that of 6-membered rings because the more acute bond angles in 5-membered rings cause the distances between the substituents to be longer than those in 6-membered rings. This difference in distances between substituents in 5- and 6-membered rings makes the influence of steric properties on the selectivity of the functionalization of 5-membered heteroarenes less pronounced (Figure 1). Thus, catalytic functionalization of a single C–H bond in a five-membered ring heteroarene with high regioselectivity derived from steric effects is rare due to the distinct electronic properties of the positions of heteroarenes and the weaker steric influence in five-membered ring structures.

Consistent with this trend, the functionalization of these rings is limited by the poor selectivity of iridium-catalyzed borylation reaction, the low activity of catalysts for silylation reactions, and the requirement of special reagents for silylation. In particular, the current borylations of five-membered heteroarenes, in many cases, form isomers from the functionalization of sites ortho to small or medium-sized substitutents and product from diborylation,[7] even with the recently developed catalyst of Smith and Maleczka that contains a novel N-N ligand and with excess of thiophene.[8] Iridium-catalyzed silylations of these rings reported by Ishiyama and Miyaura with a phenanthroline bearing a large substituent in the 2-position occurred with several 3-substituted thiophenes and one furan with high sterically derived regioselectivity, but the low activity of this catalyst caused the reactions to require a large excess of heteroarene and high temperatures, and the tetrafluoro disilane used in this process is not commercially available and requires three steps to prepare.[9] Finally, neither the work of Ishiyama nor Smith describes the functionalization of heteroarenes containing multiple heteroatoms, even though these structures are among the most prevalent heteroarenes in medicinal and agrochemical chemistry.[10]

The identification of reactions that functionalize C-H bonds in five-membered-ring heteroarenes containing one or multiple heteroatoms regioselectively is important because these structural motifs are common in pharmaceuticals, electronic materials, agrochemicals, and natural products.[11] The regioselective silylation and borylation of heteroarenes would be particularly useful because silylarenes and aryl boronic esters undergo hydroxylation,[12] etherification,[13] amination,[14] cyanation,[15] halogenation,[16] and arylation,[17] and analogous derivatization of heteroarenes would provide an array of heteroarenes with substitution patterns that are derived from the catalytic system. The silylation of heteroarenes can be particularly valuable because the heteroarylsilanes are often more stable than the corresponding heteroarylboronates.[18]

We report silylations of five-membered heteroarenes catalyzed by an iridium complex that contains a pyridyl-imidazoline ligand, and also silylations catalyzed by a recently disclosed complex of 2,9-Me$_2$-phenanthroline (Me$_2$phen). We demonstrate that reactions with these catalysts produce high yields of products that are formed from functionalization of the most sterically accessible C–H bonds of five-membered heteroarenes under conditions in which borylation reactions produce mixtures of products. We also illustrate the versatility of the heteroarylsilanes by developing conditions for ipso substitution reactions to produce the corresponding five-membered-ring heteroarenes bearing halogen, aryl and perfluoroalkyl substituents.

Results and Discussion

1. Reaction Development

To achieve the undirected functionalization of five-membered heteroarenes with regioselectivity that is dictated by steric effects, we investigated reactions catalyzed by iridium complexes of a series of ligands that contain nitrogen donors. Two of the ligands, **L1** and **L2**, are based on pyridyl oxazoline structures, and two of the ligands, **L3** and **L4**, are based on pyridyl imidazoline structures. Ligand **L4** is new, and none of the ligands have been reported for the borylation or silylation of aromatic C–H bonds. We included pyridyl imidazoline structures in our study because the nitrogen atoms should be more electron donating than those in the pyridyl oxazoline structures, and substituents on the nitrogen in the imidazoline could influence the structures of these ligands.

To create a benchmark for our studies on the silylation of five-membered ring heteroarenes, we first measured the yield and selectivity of the borylation of 3-chlorothiophene that was catalyzed by the previously reported combination of [Ir(COD)(OMe)]$_2$ and 4,4'-di-tert-butylbipyridine (dtbpy).[19] Under standard conditions, the products from functionalization at positions both proximal and distal to the chlorine substituent formed, and the major product resulted from diborylation (Scheme 1). Similarly, the silylation of 3-chlorothiophene under the conditions recently reported by our group with 2,9-dimethylphenanthroline as ligand formed a mixture of products from silylation at both the 2 and 5-positions.

In contrast, the silylation of 3-chlorothiophene that was catalyzed by the combination of [Ir(COD)(OMe)]$_2$ and **L2** was selective for functionalization at the 5-position of the heteroarene. This regioselectivity was even higher when the reaction was catalyzed by [Ir(COD)(OMe)]$_2$ and the imidazoline ligand **L3** and was the highest when catalyzed by [Ir(COD)(OMe)]$_2$ and imidazoline ligand **L4**, which contains a 2,6-^{i}Pr-phenyl group on the imidazoline nitrogen. The silylation of 3-chlorothiophene, when catalyzed by iridium and **L3**, formed the product from functionalization at the 5-position in 74% yield, and the silylation of this thiophene, when catalyzed by iridium and **L4**, formed the product from functionalization at the 5-position in 90% yield with a 9:1 selectivity for this isomer over others and the product from di-functionalization.

We note that this regioselectivity for silylation and chemoselectivity for monosilylation is obtained with limiting heteroarene. The regioselectivity is similar to that reported for the borylation or silylation of the same substrate, but our silylation reaction occurs with the

thiophene as limiting reagent. The results on borylation or silylation were obtained with an excess of thiophene, and high selectivity for mono-borylation of such a thiophene with the heteroarene as limiting reagent has not been reported with any catalyst.[8-9]

2. Reaction Scope

Having identified a ligand that greatly increases the sensitivity of the iridium-catalyzed silylation of thiophenes to the steric environment of the C–H bonds, we studied the selectivity of this catalyst for the silylation of thiophenes that contain varied functional groups. We conducted silylation reactions with the catalyst that contains **L4** and cyclohexene as hydrogen acceptor, silylations with the catalyst that contains Me$_2$Phen and norbornene as hydrogen acceptor, and borylations with the catalyst that contains dtbpy (Scheme 2) without any hydrogen acceptor. These combinations of catalyst and acceptor for the silylations were used because the yields of silyl arenes from reactions conducted with the catalyst that contains Me$_2$Phen and cyclohexene were low, and only traces of silyl arenes were detected from reactions conducted with **L4** and norbornene.[19c] 5-Silyl-thiophenes that contain methyl, methoxy, phenyl, ester, boryl, bromide and iodide substituents in the 3-position were obtained with perfect selectivity for the monosilylation product, with perfect regioselectivity, and in yields ranging from 44% to 100% from reactions catalyzed by the combination of iridium and **L4**. The ethyl ester of **5** and the nitrile of **6** were tolerated; no products from reduction of these functional groups were observed. Thiophene **6**, which contains a small cyano substituent, was converted to the corresponding silylarene with 85:12:3 selectivity for functionalization at the 5-position of 3-cyanothiophene to functionalization at the 2-position to di-silylation. Likewise, heteroarylsilanes that contain halogen substituents were obtained from the corresponding arenes (**7-9**) in moderate (3-iodo) to high (3-bromo and 3-chloro) yield and without proto-dehalogenation. The reactions of the larger of the three halides gave a single product; the reactions of the 3-chloro isomer gave 94:1 regioselectivity and 95:5 selectivity of monosilylation to disilylation.

Results from the silylations catalyzed by the complex of Me$_2$Phen and the borylations catalyzed by the complex of dtbpy in Scheme 2 show the value of the silylation of the catalyst that contains **L4** for obtaining high regioselectivity. The silylation of thiophenes that contain smaller substituents occurred with low selectivity for functionalization at the 5-position (**1, 6, 7**) when catalyzed by the combination of iridium and Me$_2$phen. The borylations of these heteroarenes with iridium and dtbpy also produced mixtures of products. Silylations of thiophenes that contain larger phenyl, boryl, ester, bromide, and iodide substituents (**3-5, 8, 9**) and that were catalyzed by iridium and Me$_2$phen occurred with complete selectivity for functionalization at the 5-position of the heteroarene, but the yields were much lower than those catalyzed by iridium and **L4**. Likewise, borylation with dtbpy was highly selective for the 5-position of 3-phenylthiophene and ethyl 3-thiophenecarboxylate. However, the borylation of all the other thiophenes in Scheme 2 occurred with low selectivity for the 5-position. These results demonstrate that the catalyst formed from the combination of iridium and **L4** is more active and more selective for the functionalization of the least sterically hindered position of thiophenes than previously reported catalysts.

The analogous silylation and borylation reactions of furans and pyrroles are shown in Scheme 3. The silylations of 3-substituted furans and pyrroles catalyzed by iridium and imidazoline ligand **L4** occurred with perfect selectivity and in good yield (**11-15**, 60% to 100% yield). The silylation of 3-bromofuran (**10**) occurred with greater than 80% selectivity for the 5-position. In contrast, the silylation or borylation of 3-bromofuran under previously reported conditions led to the formation of large amounts of products from functionalization at the 2-position. In addition, the silylations of furans or pyrroles that contain esters at the 3-positions produced significant amounts of products from functionalization at the 2-position when the catalyst contained Me_2phen. The borylations of these nitrogen or oxygen-containing heterocycles occurred with universally poor selectivity for the least sterically hindered C–H bonds.

Five-membered ring heterocycles that contain multiple heteroatoms also underwent silylation in good yield and with high selectivity (Scheme 4). In these cases, the reactions occurred in the highest yields when catalyzed by [Ir(COD)(OMe)]$_2$ and Me_2phen. In all cases, the regioselectivity with which the silyl-azole products formed was high. The regioselectivity was dictated by steric effects with electronic effects influencing selectivity when potentially reactive C–H bonds were present in similar steric environments.

Three examples of the silylation of pyrazoles are provided in Scheme 4. The reactions of 1,3-dimethylpyrazole **16**, in which the two aromatic C–H bonds are in similar steric environments was completely selective for the 5-position, and this selectivity was consistent with the high preference for functionalization α to heteroatoms observed for the functionalization of thiophenes, furans and pyrroles. However, the silylation of pyrazoles that contain larger *tert*-butyl carbonate or tosyl substituents on nitrogen occurred distal to the nitrogen that bears that substituent. These results indicate that the silylation of pyrazoles occurs with a selectivity that is determined primarily by the steric environment of the C–H bonds, with electronic effects imparting a secondary influence.

The silylations of the thiazoles occurred at the position that is most sterically accessible. One might expect that the reaction would occur at the position more distal to the basic nitrogen because borylations of pyridines were shown previously not to form products from reaction at the position alpha to a basic nitrogen atom.[20] However, the silylation reaction formed a stable product from reaction at the 2-position of 4-substituted thiazoles due to the steric congestion at the 5-position, even if the substituent at the 4-position was as small as a methyl group.

The silylations of heteorarenes containing multiple nitrogen atoms also formed stable products in good yield. The silylation of imidazole **21** containing substituents at the 1 and 2 positions gave a single product from reaction at the 4 position. The imidazole unit of caffeine gave a stable product from reaction at the only available aromatic C–H bond. Silylation of the 1,2,3- and 1,2,4-triazoles also occurred at the sterically more accessible of the two heteroaryl C–H bonds to form stable products albeit with 5 mol % catalyst.

The borylations of **16**, **18** and **21**-**23** occurred with high selectivity to form the products indicated in Scheme 4, but the borylated products were unstable. The borylations of **16-18**,

21, and **22** gave the functionalized product in only 37-74% yields, and reactions of **19**, **20**, and **24** gave no borylated product, as determined by evaluating the crude reaction mixtures. Moreover, the amounts of borylated products from the reactions of **16** and **18** were lower after the reaction mixtures were filtered through silica, and no borylated products were present from reactions of **21**, **22** and **23** after the reaction mixtures were filtered through silica. Thus, consistent with prior literature, the products from the borylation of azoles are, in many cases, unstable to air and, in most cases, unstable to silica.[18, 20] In contrast, the products from the silylation of azoles **16-23** were isolated by silica gel chromatography, and the largest difference in yield of isolated silyl-azole products and yield determined from the crude reaction mixture was only 12%. The silyl-azole products are stable to air, moisture from solvents stored on the benchtop, and silica. The greater stability of silyl-azoles than of boryl-azoles renders the silylation of the C–H bonds of azoles particularly useful.

3. Functionalization of Heteroarylsilanes

To demonstrate the utility of C–H silylation to the preparation of functionalized heteroarenes, we assessed the ability to convert the silyl heteroarenes to heteroarenes that are functionalized with halogens or with aryl or trifluoromethyl groups (Scheme 5, right). In addition, we compared the products one would obtain from the combination of silylation and functionalization to those from more classical processes (Scheme 5, left). The silylation of ethyl 3-furan carboxylate, followed by functionalization with *N*-chlorosuccinimide in the presence of AgF formed ethyl 2-chloro-4-furancarboxylate **25** in 63% yield over two steps. In contrast, directed metalation of the related 3-furancarboxylate, followed by quenching with hexachloroethane, is known to produce 2-chloro-3-furancarboxylate.[21] The silylation of 3-chlorothiophene, followed by functionalization with *N*-bromosuccinimide and AgF, formed bromide 2-bromo-4-chlorothiophene **26** in 72% yield over two steps. In contrast, the direct bromination of 3-chlorothiophene with NBS has been reported to form 2-bromo-3-chlorothiophene.[22] Likewise, the sequential silylation and iodination of 3-methoxythiophene formed 2,4-functionalized product **27**, whereas direct iodination of the unfunctionalized arene is known to form the 2,3 functionalized product.[23] Heteroarylsilanes also undergo coupling reactions to form arylated products. The silylation of 3-methoxythiophene at the 5-position followed by Hiyama cross-coupling in the presence of a palladium catalyst furnished 5-arylated product **28** in 58% yield over 2 steps. Previous literature reported that the direct arylation of 3-methoxythiophene, when catalyzed by rhodium or palladium complexes, leads to arylation with high selectivity for the 2-position, [24] although direct arylation of 3-methoxythiophene at the 5- position does occur with diaryliodonium salts in the presence of a Cu/Fe catalyst.[25] The 5-arylated product **29** formed in 67% yield over two steps by the sequential silylation and cross-coupling of ethyl 3-furancaryboxylate. In contrast, ethyl 3-furancarboxylate is known to undergo direct arylation at the 2-position in the presence of Pd(PPh$_3$)$_4$ as catalyst and undergoes arylation at the 5-position with a modest 3 to 1 selectivity in the presence of Pd/C.[26]

Finally, the silylation of 3-methylthiophene, followed by coupling (phen)CuCF$_3$ under an atmosphere of oxygen, formed the product from trifluoromethylation of the 5-position of the thiophene. In contrast, the direct addition of trifluoromethyl radical is known to occur at the 2-position of 3-methylthiophene.[27] Due to the volatility of 2-trifluoromethyl-4-

methylthiophene, this product, was characterized by the ^{19}F NMR of the crude reaction mixture. However, to form an isolable analog, the silylation of 3-octylthiophene and coupling of the silyl thiophene with a source of trifluoromethyl group was studied, and 2-trifluoromethyl-4-octylthiophene was formed by this process in 61% yield by NMR spectroscopy and 37% isolated yield. These results demonstrate that the silylations of heteroarenes with high sterically derived regioselectivity, followed by functionalizations of the resulting heteroarylsilanes, generate products that are distinct from those accessible from the direct functionalization of the same heteroarenes.

The silyl-azoles presented in Scheme 4 are more electron-deficient than the silyl-thiophenes and silyl-furans in Scheme 5. To determine whether silyl-azoles are nucleophilic enough to undergo transformations that are similar to those of other silyl-arenes and heteroarenes, we conducted a series of derivatizations of silyl pyrazole **31** (Scheme 6). The reaction of **31** with NCS in the presence of AgF formed chloropyrazole **32** in 52% yield. Similarly, the reaction of **31** with NBS formed bromopyrazole **33** in 81% yield. Silyl-pyrazole **31** also coupled with 3,5-(MeO)$_2$-phenyl triflate to form biaryl **34** in 70% yield when catalyzed by Pd$_2$dba$_3$·CHCl$_3$ and BINAP. The identification of that catalyst system is discussed in greater detail below. In addition, **31** coupled with (phen)CuCF$_3$ under an atmosphere of oxygen to form 1-Ts-3-Me-4-CF$_3$-pyrazole (**35**) in 50% yield. These results demonstrate that the silylation of azoles, followed by the functionalization of the product, also can lead to products containing a diverse array of functional groups.

Suzuki couplings are widely used, in part, because the aryl boronic acid and ester reagents are stable to air and moisture and can be stored. However, as discussed, the boronic acids or esters of azoles are often unstable. Therefore, coupling of the more stable silyl derivatives of five-membered heteroarenes would be valuable. We found that the silyl-thiophenes and silyl-furans that result from the silylation of C–H bonds couple with aryl iodides in the presence of AgF and catalytic amounts of Pd(P^{t}Bu$_3$)$_2$. However, under similar conditions, only 10% of the product from the reaction of the silyl thiazole 2-silyl-4-thiazolecarboxylate methyl ester formed from coupling the representative partner *m*-Cl-iodobenzene (Scheme 7). After conducting reactions with a series of fluoride additives and phosphine ligands, we found that a high yield of biaryl product (85%) was obtained from reactions with CsF as activator and the combination of Pd$_2$dba$_3$·CHCl$_3$ and BINAP as catalyst. The 2-silyl-4-thiazolecarboxylate methyl ester also coupled with heteroaryl bromides catalyzed by the same system to form biaryls **37** and **38** in 76% and 50% yield. Although bithiazole **39** formed in a modest 22% yield from the same coupling of the silyl thiazole with 2-bromothiazole, this reaction has not been accomplished previously by Suzuki coupling of the analogous boronate, presumably due to the instability of this boronate. As noted in the previous paragraph, these conditions were also suitable for the coupling of the silyl-pyrazole **31** to form 3-aryl pyrazole **34**. Thus, the combination of CsF activator and BINAP-ligated palladium is an effective system to catalyze the coupling of silylazoles with aryl halides under mild conditions.

4. Origin of Regioselectivity

To determine the elementary steps controlling the high selectivity for the silylation of unhindered C–H bonds of heteroarenes catalyzed by complexes of **L4**, we conducted studies on the reactions of deuterated silane with 3-chlorothiophene (**7**). The reactions of an excess of **7** with deuterated silane catalyzed by iridium and Me$_2$phen or L4 exchanged deuterium between the silane Si–D bond and the 2-positions and 5-positions of the heteroarene to form deuterated products **7c** and **7d**, respectively. This reaction occurred in concert with the formation of silylated products **7a** and **7b**. After 15 min at 65 °C, the amounts of deuterated products **7c** and **7d** were greater than the amounts of silylated products **7a** and **7b** by factors of about 2:1 and 6:1 for the catalysts containing ligands Me$_2$phen and **L4**, respectively. This incorporation of deuterium into the heteroarene reactant indicates that cleavage of the C–H bond is reversible.

The ratio of deuterated products was distinct from the ratio of silylated products. The reaction catalyzed by the complex of Me$_2$phen formed deuterated products **7c** and **7d** in a ratio of 1.5:1 but formed the silylated products **7a** and **7b** in a higher ratio of 2.9:1 (Scheme 8). The reaction catalyzed by a complex of **L4** formed the deuterated products **7c** and **7d** in a ratio of only 1.1:1 but formed the silylated products **7a** and **7b** in a high ratio of 14:1. Thus, the cleavage of C–H bonds by the catalyst that contains **L4** is less regioselective than that of the catalyst that contains Me$_2$phen, but the formation of silylated products by the catalyst that contains **L4** occurs with much greater regioselectivity than that of the catalyst that contains Me$_2$phen. These results demonstrate that the regioselectivity of these two catalysts for the silylation of C–H bonds does not reflect the propensity of the catalysts to cleave C–H bonds. Rather, the selectivity of the silylation reaction is controlled by the relative rates of formation of the carbon-silicon bond from 2- or 5-heteroaryliridium intermediates that are formed reversibly. These experimental results resemble the computations reported by Sakaki for the selectivity of the borylations of β over α C–H bonds in THF, as well as the experiments and computations our group reported previously on the origins of selectivity of Rh-catalyzed borylations and silylations of primary over secondary alkyl C–H bonds.[28]

Conclusion

In summary, we have developed a method for the silylation of heteroaromatic compounds with high sterically derived regioselectivity. In many cases, these high selectivities are achieved with a new pyridyl-imidazoline ligand **L4.** The selectivity of this silylation to form functionalized products from reaction at the least sterically hindered position of five-membered heteroarenes is much higher than that of previously reported borylations of these heteroarenes, and the products formed are much more stable than the analogous boronates. Moreover, functionalizations of the heteroarylsilanes form products with substitution patterns that are orthogonal to those that have been reported by traditional methods and other catalytic processes. Mechanistic studies showed that the rates of formation of the carbon-silicon bond from isomeric heteoaryliridium complexes influences the selectivities of the silylation reactions more than the rates of the cleavage of carbon-hydrogen bonds to form these complexes and that the selectivities from the reactions catalyzed by the combination of iridium and the pyridyl-imidazoline ligand **L4** result almost exclusively from the rates of

formation of the carbon-silicon bond. Additional studies on the mechanism and origin of high selectivity of the silylation reaction with catalysts that contain imidazoline ligands are ongoing in our laboratory.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.
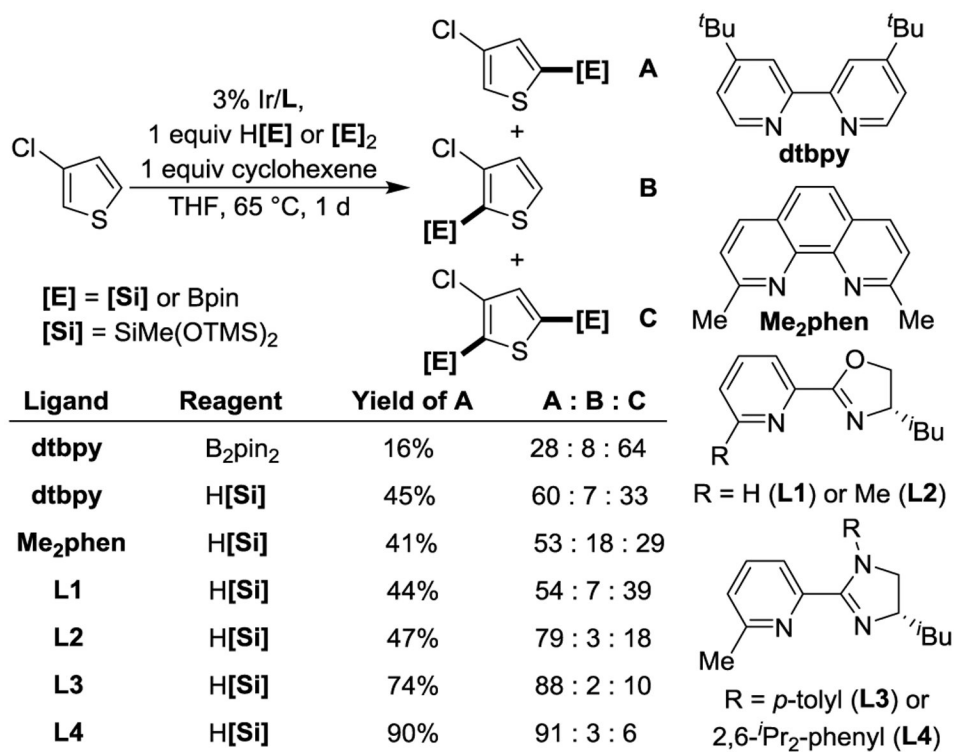
Acknowledgements

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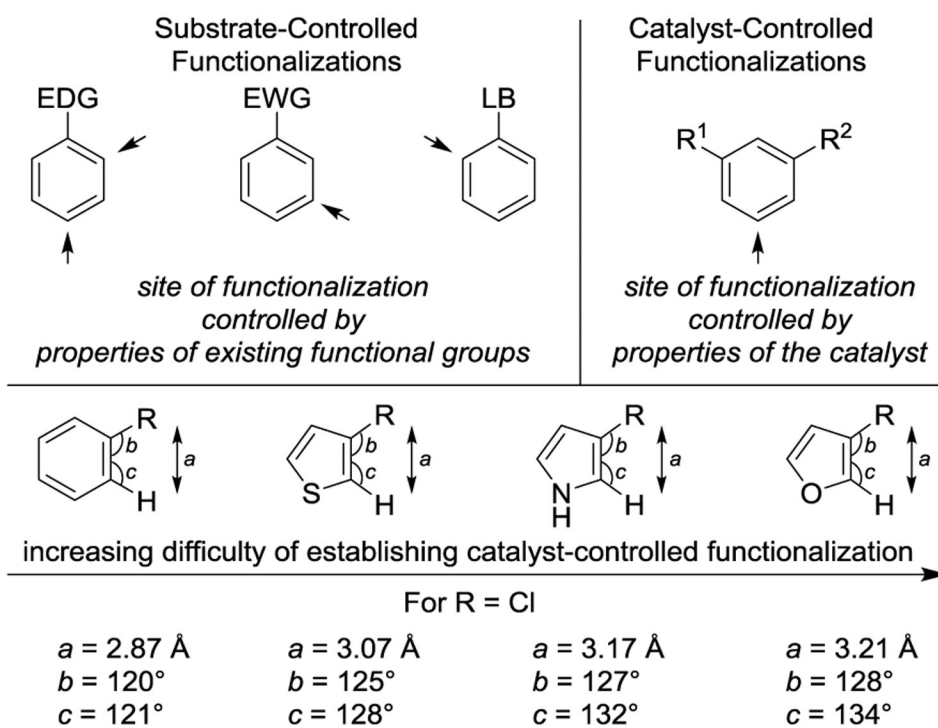
Figure 1.
EDG = Electron donating functional group. EWG = electron withdrawing functional group
LB = Lewis basic functional group.

Scheme 1.
Effect of Ligand on Selectivity[a]
[a]See SI for detailed procedures

Condition 1 (C1): 3% Ir/L4
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv cyclohexene
Condition 2 (C2): 3% Ir/Me$_2$phen,
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv norbornene
Condition 3 (C3): 3% Ir/dtbpy,
0.6 equiv B$_2$pin$_2$

THF, 65-80 °C, 18-26 h

[E] = SiMe(OTMS)$_2$ or Bpin

L4   Me$_2$phen   dtbpy

1, C1: 94%
C2: 40% (61:4:36)
C3: 33% (37:8:55)

2, C1: 90%
C2: 78% (94:0:6)
C3: 18% (39:30:30)

3, C1: 100%
C2: 26%
C3: 24%

4, C1: 85%
C2: 60%
C3: 13% (18:0:82)

5, C1: 100%
C2: 79%
C3: 84%

6, C1: 57% (85:12:3)
C2: 22% (26:28:46)
C3: 26% (30:31:39)

7, C1: 93% (94:1:5)
C2: 54% (60:10:30)
C3: 50% (52:16:32)

8, C1: 92%
C2: 30%
C3: 37% (60:12:28)

9, C1: 44%
C2: 42%
C3: 24% (90:0:10)

Scheme 2.

C-H Silylation of Thiophenes[a]

[a]See SI for detailed procedures. Yields correspond to ^{1}H NMR yield of desired product
(desired product : undesired, mono- : undesired, di-)

Condition 1 (C1): 3% Ir/**L4**
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv cyclohexene
Condition 2 (C2): 3% Ir/Me$_2$phen,
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv norbornene
Condition 3 (C3): 3% Ir/dtbpy,
0.6 equiv B$_2$pin$_2$

THF, 65-100 °C, 16-20 h

[E] = SiMe(OTMS)$_2$ or Bpin

10, C1: 86% (82:14:4)[b]
C2: 30% (34:46:20)[b]
C3: 41% (55:8:37)[b]

11, C1: 100%
C2: 99%
C3: 87% (90:0:10)

12, C1: 100%
C2: 100%
C3: 18% (19:6:75)

13, C1: 83%
C2: 53% (78:0:22)
C3: 17% (34:4:62)

14, C1: 60%
C2: 43%
C3: 48% (64:36:0)

15, C1: 90%
C2: 48% (75:18:7)
C3: 64% (76:16:8)
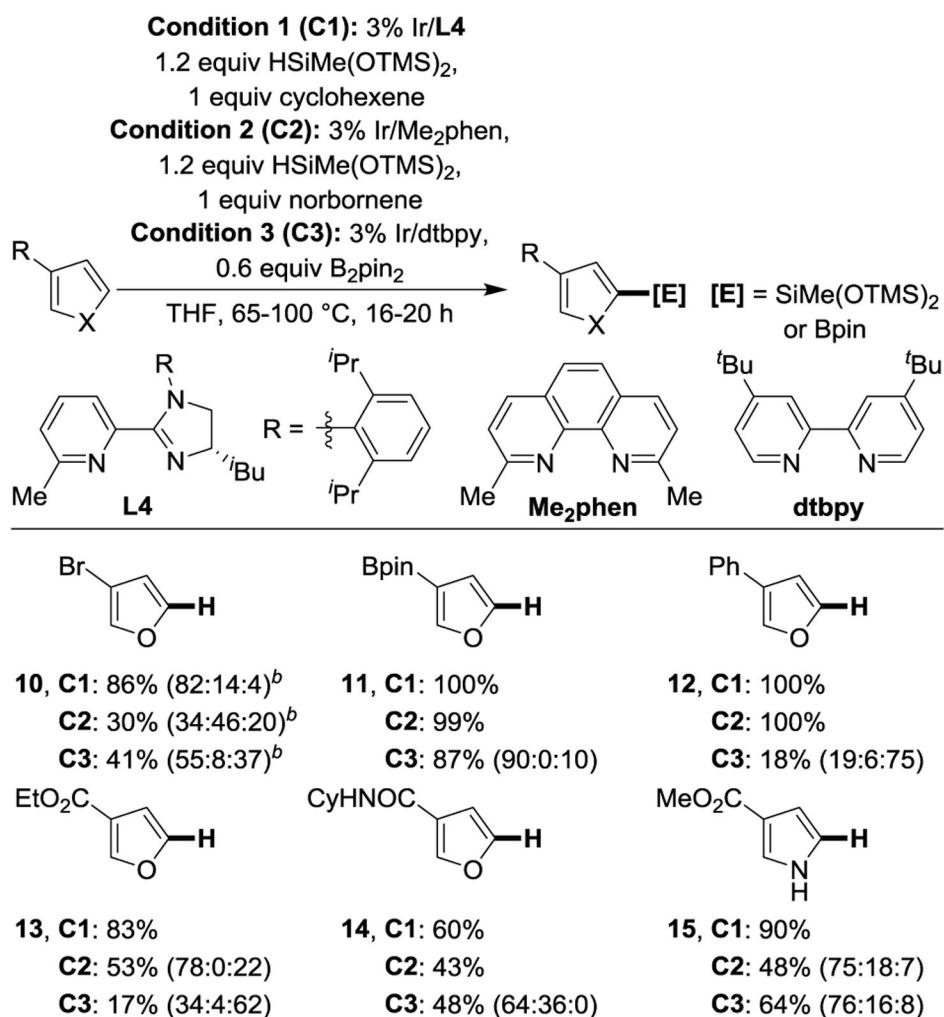
Scheme 3.

C-H Silylation of Furans and Pyrroles[a]

[a]See SI for detailed procedures. Yields correspond to ^{1}H NMR yield of desired product (desired product : undesired, mono- : undesired, di-). [b]4 °C, 5 d.

Condition 1 (C1): 3% Ir/**L4**
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv cyclohexene
Condition 2 (C2): 3% Ir/Me$_2$phen,
1.2 equiv HSiMe(OTMS)$_2$,
1 equiv norbornene
Condition 3 (C3): 3% Ir/dtbpy,
0.6 equiv B$_2$pin$_2$

THF, 80-120 °C, 13-24 h

[E] **[E]** = SiMe(OTMS)$_2$
or Bpin

L4 **Me$_2$phen** **dtbpy**

16, C1: 27%
  C2: 38%, 99%[b]
  C3: 37% [26%]

17, C1: 21%
  C2: 70%
  C3: 74% [72%]

18, C1: 9%
  C2: 85%
  C3: 68% [20%]

19, C1: trace product
  C2: 75% (93:7:0)
  C3: no product

20, C1: trace product
  C2: 72%
  C3: no product

21, C1: 53%
  C2: 82%
  C3: 64% [no product]

22, C1: trace product
  C2: 68%
  C3: 72% [no product]

23, C1: 17%[b]
  C2: 62%[b]
  C3: 73% [no product]

24, C1: 20%
  C2: 30%, 87%[b]
  C3: no product
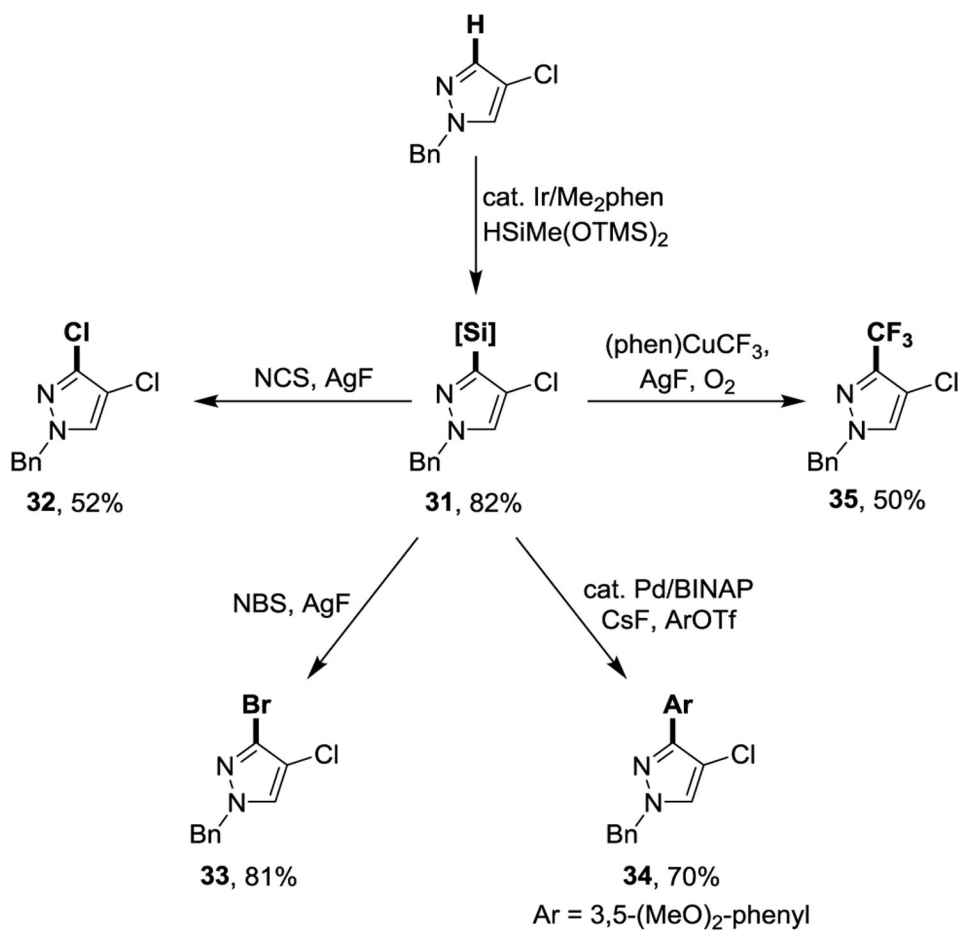
Scheme 4.

C-H Silylation of Azoles[a]

[a]See SI for detailed procedures. Yields correspond to ^{1}H NMR yield of desired product (desired product : undesired, mono- : undesired, di-), [yield after filtration through silica].
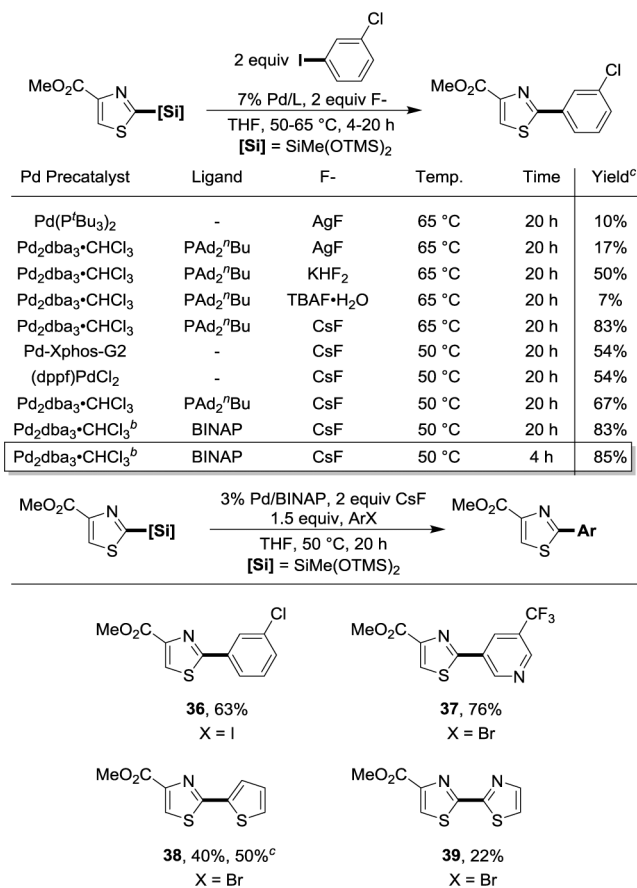
[b]5% Ir/L and 2 equiv. HSiMe(OTMS)$_2$.
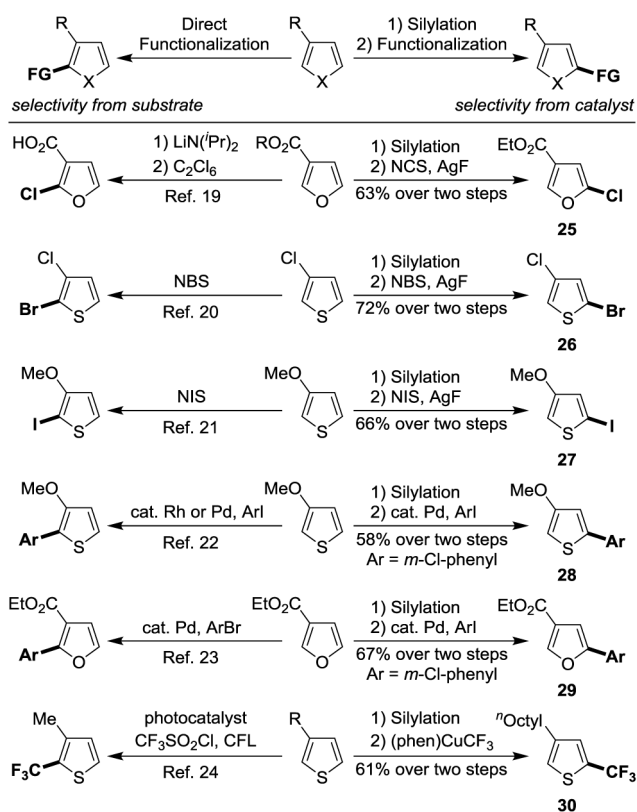
Scheme 5.

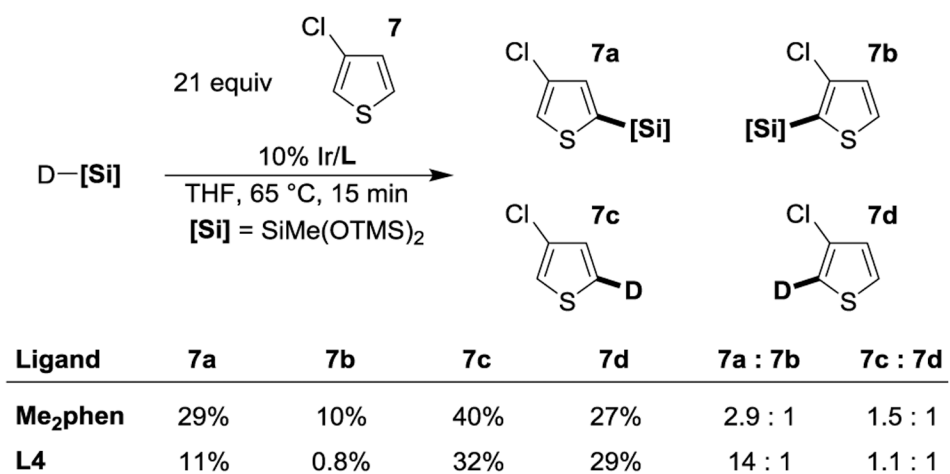Regio-Divergent Functionalization of Heteroarenes[a]

[a]See SI for detailed procedures.

Scheme 6.
Transformations of Silyl-Pyrazole[a]

[a]See SI for detailed procedures.

Scheme 7.

Hiyama Coupling of Silyl-Azoles[a]

[a]See SI for detailed procedures. [b]3% Pd/L. [c]Determined by ^{1}H NMR spectroscopy with dibromomethane internal standard.

Scheme 8.
Reactions of Deuterated Silane with Excess Arene[a]

Ligand	7a	7b	7c	7d	7a : 7b	7c : 7d
Me₂phen	29%	10%	40%	27%	2.9 : 1	1.5 : 1
L4	11%	0.8%	32%	29%	14 : 1	1.1 : 1