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# The Pyridyldiisopropylsilyl Group: A Masked Functionality and Directing Group for Monoselective *ortho*-Acyloxylation and *ortho*-Halogenation Reactions of Arenes

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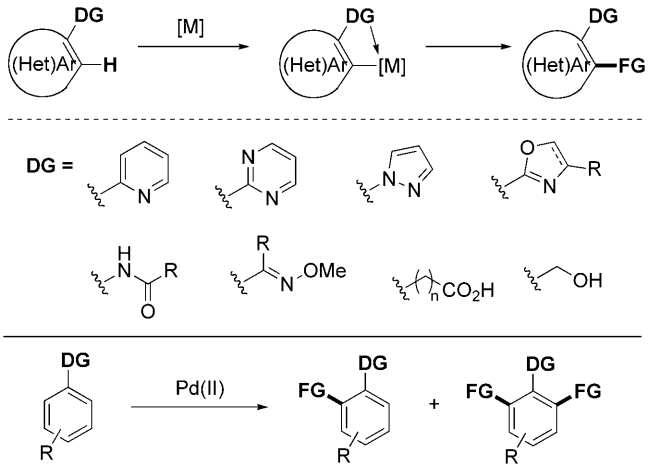
**Abstract:** A novel, easily removable and modifiable silicon-tethered pyridyldiisopropylsilyl directing group for C–H functionalizations of arenes has been developed. The installation of the pyridyldiisopropylsilyl group can efficiently be achieved *via* two complementary routes using easily available 2-(diisopropylsilyl)pyridine (**5**). The first strategy features a nucleophilic hydride substitution at the silicon atom in **5** with aryllithium reagents generated *in situ* from the corresponding aryl bromides or iodides. The second milder route exploits a highly efficient room-temperature rhodium(I)-catalyzed cross-coupling reaction between **5** and aryl iodides. The latter approach can be applied to the preparation of a wide range of pyridyldiisopropylsilyl-substituted arenes possessing a variety of functional groups, including those incompatible with organometallic reagents. The pyridyldiisopropylsilyl directing group allows for a highly efficient, regioselective palladium(II)-catalyzed mono-*ortho*-acyloxylation and *ortho*-halogenation of various aromatic compounds. Most importantly, the silicon-tethered directing group in both acyloxylated and halogenated products can easily be removed or efficiently converted into an array of other valuable functionalities. These transformations include protio-, deuterio-, halo-, boro-, and alkynyldesilylations, as well as a conversion of the directing group into the hydroxy functionality. In addition, the construction of aryl-aryl bonds *via* the Hiyama–Denmark cross-coupling reaction is feasible for the acetoxylated products. Moreover, the *ortho*-halogenated pyridyldiisopropylsilylarenes, bearing both nucleophilic pyridyldiisopropylsilyl and electrophilic aryl halide moieties, represent synthetically attractive 1,2-ambiphiles. A unique reactivity of these ambiphiles has been demonstrated in efficient syntheses of arylenediyne and benzosilole derivatives, as well as in a facile generation of benzyne. In addition, preliminary mechanistic studies of the acyloxylation and halogenation reactions have been performed. A trinuclear palladacycle intermediate has been isolated from a stoichiometric reaction between diisopropyl(phenyl)pyrid-2-ylsilane (**3a**) and palladium acetate. Furthermore, both C–H functionalization reactions exhibited equally high values of the intramolecular primary kinetic isotope effect ($k_H/k_D = 6.7$). Based on these observations, a general mechanism involving the formation of a palladacycle *via* a C–H activation process as the rate-determining step has been proposed.

**Keywords:** acyloxylation; catalysis; C–H activation; halogenation; palladium; silicon

## Introduction

Transition metal-catalyzed direct C–H functionalizations of arenes have emerged recently as one of the most powerful strategies for a rapid and atom-economical construction of a variety of bioactive molecules, pharmaceutical targets, and materials.[1,2] Despite several advantages achieved in this field, a selective functionalization of a particular C–H bond of interest remains challenging. One of the possible solutions involves the employment of directing groups,[3] which, by coordination to a metal catalyst, enable a selective activation of proximal C–H bonds *via* a cyclometalation process. Accordingly, a variety of di-

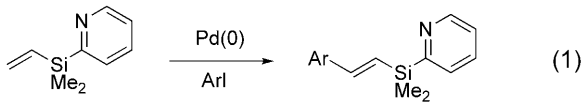
  




**Scheme 1.** Commonly used directing groups for C–H activations.

recting groups, such as pyridine,[2n,3a–f] pyrimidine,[2n,3a,g] pyrazole,[2r,3h] oxazoline,[3i–l] amide,[2j,m,3m–p] oxime ether,[3i,q] carboxylic acid,[2i,3r–t] and hydroxy group,[3u,v] have been developed for these transformations (Scheme 1). Despite the efficiencies achieved in the directed *ortho*-selective C–H functionalizations, the employment of the above-mentioned directing groups limits these transformations to particular types of substrates. Moreover, a control of reaction selectivities toward mono- versus bis-functionalization products for most directing groups is still problematic (Scheme 1, bottom).[2h,3p,w,4] Furthermore, a removal or conversion of these directing groups into other functionalities often represents a quite challenging synthetic task, and in many cases cannot be achieved at all.[5]

Employment of a silicon-tethered[6] directing group seems as a viable solution to this problem. Originally, this concept was applied by Yoshida for the highly regio- and stereoselective Pd-catalyzed Heck reactions of vinylsilanes [Eq. (1)].[7] Later, the same group




demonstrated further applications of the pyridyldimethylsilyl directing group to a variety of highly efficient and regioselective transformations, including carbomagnezation,[8] Pauson–Khand reaction,[9] directed *ortho*-metalation,[10] Stille cross-coupling,[11] and carbonyl allylation.[12]

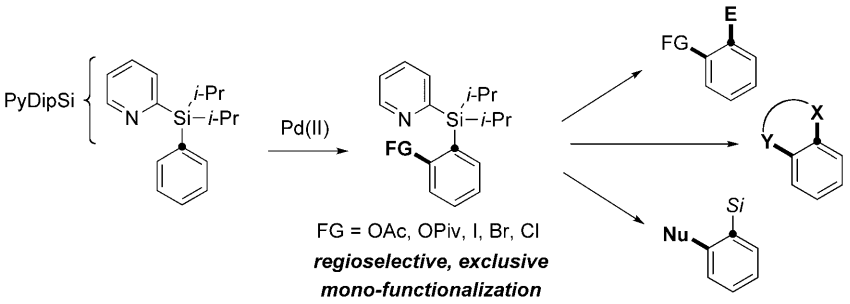
Along this line, we have recently communicated a traceless/modifiable silicon-tethered pyridyldiisopropylsilyl (PyDipSi) directing group for the Pd-catalyzed *ortho*-acyloxylation[13] and *ortho*-halogenation[14] reactions of aromatic and heteroaromatic C–H bonds (Scheme 2). These transformations allowed for efficient syntheses of the corresponding PyDipSi-arenes in a highly regioselective mono-functionalization fashion. Most importantly, in contrast to the directing groups mentioned above, the PyDipSi group could efficiently be removed or converted into a variety of other synthetically valuable functionalities.

Herein, we report an expanded scope of the Pd-catalyzed *ortho*-acyloxylation and *ortho*-halogenation reactions of arenes and heteroarenes; further applications of the corresponding functionalized PyDipSi-arenes for facile syntheses of a variety of synthetically valuable building blocks and products, including *ortho*-functionalized boronates, phenols, polyhaloaromatic compounds, catechols, benzosiloles, benzofuran, diarylenediynes, and the generation of arynes; mechanistic studies; as well as a new, mild, and a highly functional group-tolerant method for the installation of the PyDipSi directing group.

## Results and Discussion

### Design of a Removable Directing Group

Our design of a removable directing group was based on the following criteria: (a) the group should be capable of coordinating a Pd catalyst; (b) synthesis and installation of the directing group onto aromatic rings should be highly efficient and straightforward; (c) the group should be sufficiently stable under typical Pd-catalyzed C–H activation reaction conditions, involving the use of oxidants, electrophilic metals and re-

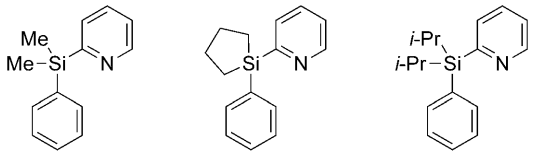



**Scheme 2.** Pd(II)-catalyzed PyDipSi-directed C–H functionalizations of arenes.

agents at elevated temperatures; yet, (d) it should remain labile enough to allow for its easy removal from the products of a C–H functionalization. Considering that pyridine is among the best coordinating ligands for Pd complexes in the directed C–H activation transformations,[1q,3a] we chose pyridine as the coordination site of our removable directing group. We envisioned that the employment of a temporary silicon linker to connect pyridine with an aromatic substrate would fulfill the above requirements for a general removable directing group. To this end, we aimed at establishing a suitable silicon tether for the pyridine group by tuning different substituents at silicon. Accordingly, substrates **1**, **2** and **3a** were synthesized and examined under the Pd-catalyzed C–H activation conditions (Figure 1).

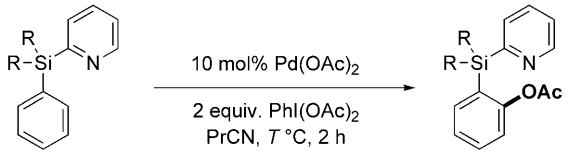
To this end, we decided to test our substrates in the Pd-catalyzed directed C–H acetoxylation[2f,3a,c,e,g,i,m,n,15] reactions first. These transformations are particularly important as they allow for a direct and selective preparation of oxygenated arenes.[16] Besides, typical Pd(II)-catalyzed *ortho*-acetoxylation reactions involve the employment of strong oxidants, such as $PhI(OAc)_2$, in acidic or neutral media at elevated temperatures. Unfortunately, arylsilane **1**, bearing Yoshida's pyridyldimethylsilyl directing group, appeared to be unstable under the common acetoxylation reaction conditions (Table 1, entry 1).[15] Likewise, an attempted acetoxylation of the silacyclopentane **2** led to a complete decomposition of the starting material only (entry 2). Promisingly, the employment of the PyDipSi-benzene **3a** under these reaction conditions provided a 15% NMR yield of the desired product **4a** (entry 3). Further increase of the reaction temperature to 100 °C allowed for a slight improvement of the reaction outcome (entry 4). At this point, it became apparent that the PyDipSi-directing group is sufficiently stable under oxidative conditions of C–H functionalizations. Thus, we turned our attention to the development of practical and general methods for the installation of the PyDipSi group onto arenes and heteroarenes.




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

**Figure 1.** Substrates for silicon tether screen.

**Table 1.** Optimization of silicon-tethered directing group under the *ortho*-acetoxylation reaction conditions.




**1**, **2**, **3a** **4**

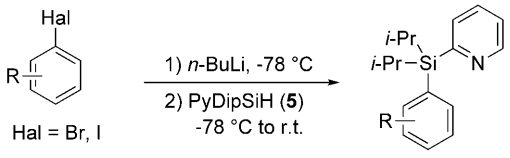
| Entry | Substrate | $T$ [°C] | Yield [%][a] |
|---|---|---|---|
| 1 | **1** | 80 | –[b] |
| 2 | **2** | 80 | –[b] |
| 3 | **3a** | 80 | 15 (**4a**) |
| 4 | **3a** | 100 | 30 (**4a**) |

[a] NMR yield.
[b] Decomposition of starting arylsilane was observed, no desired product was formed.

## Installation of the PyDipSi-Directing group onto Aryl and Heteroaryl Halides

### Nucleophilic Substitution (Method A)

The most common strategy for the installation of a silyl group onto an aromatic ring involves a nucleophilic substitution reaction between the corresponding chloro- or hydrosilane and aryl organometallic reagent. Accordingly, we chose to use a more stable PyDipSi hydride (**5**) for this purpose. Indeed, treatment of PyDipSiH (**5**) with phenyllithium smoothly produced the desired product **3a** in 92% yield. Next, installation of the PyDipSi group on halogenated arenes **6** was accomplished in a one-pot fashion *via* a nucleophilic hydride substitution in PyDipSiH with aryllithium reagents generated *in situ* from the corresponding aryl bromides or iodides [Eq. (2)]. It was

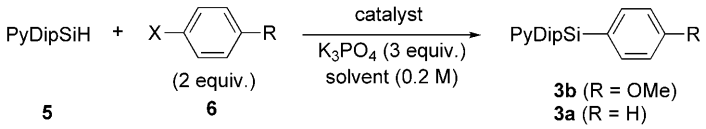



**6** **3** (2)

shown that an array of PyDipSi-arenes **3** could be accessed *via* this route (Table 3, method A). Bromo-substituted substrates **3f** and **3t** were obtained *via* a selective monolithiation of the corresponding 1,3- and 1,4-dibomobenzenes. Substrates **3i′** and **3o**, bearing ester and amide functional groups, were synthesized by a subsequent lithiation/quenching with an electrophilic reagent sequence from **3f**. In addition, a number of heterocycles, such as benzofuran, indole, benzoxazole, and carbazole were compatible with the organolithium reagents and afforded PyDipSi-heteroarenes (**3ao–3ar**) in good to excellent yields (entries 41–44).

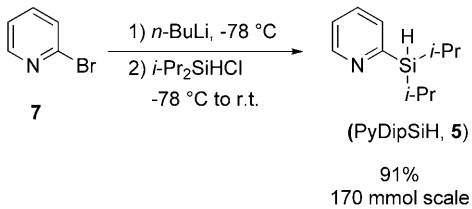
**Table 2.** Optimization of a direct coupling of haloarenes with PyDipSiH.[a]




| Entry | Catalyst | (%) | X/R | Solvent | T [°C] | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 | $Pd_2(dba)_3$·$CHCl_3$[c] | 1.5 | I/OMe | NMP | r.t. | dec |
| 2 | $Pd(dba)_2$[d] | 5 | I/OMe | NMP | 100 | dec |
| 3 | $Pd(OAc)_2$[e] | 4 | I/OMe | NMP | r.t. | dec |
| 4 | $PtO_2$[f] | 5 | I/OMe | NMP | 70 | dec |
| 5 | $[Rh(COD)_2]BF_4$[g] | 5 | I/OMe | NMP | r.t. | 13 |
| 6 | $[Rh(COD)_2]OTf$ | 5 | I/OMe | NMP | r.t. | 25 |
| 7 | $[Rh(OH)(COD)]_2$ | 5 | I/OMe | NMP | r.t. | 16 |
| 8 | $[Rh(OMe)(COD)]_2$ | 5 | I/OMe | NMP | r.t. | 19 |
| 9 | Rh(acac)(COD) | 5 | I/OMe | NMP | r.t. | dec |
| 10 | $[Rh(COD)(MeCN)]BF_4$ | 5 | I/OMe | NMP | r.t. | 19 |
| 11 | $[RhCl(COD)]_2$ | 5 | I/OMe | NMP | r.t. | 27 |
| 12 | $[RhCl(NBD)]_2$ | 5 | I/OMe | NMP | r.t. | 55 |
| 13 | $[RhCl(NBD)]_2$ | 5 | I/OMe | DMF | r.t. | 54 |
| 14 | $[RhCl(NBD)]_2$ | 5 | I/OMe | THF | r.t. | 74 |
| 15 | $[RhCl(NBD)]_2$ | 5 | I/OMe | MeCN | r.t. | 70 |
| 16 | $[RhCl(NBD)]_2$ | 5 | I/OMe | dioxane | r.t. | 96 |
| **17** | **$[RhCl(NBD)]_2$[h]** | **2.5** | **I/OMe** | **dioxane** | **r.t.** | **(98)** |
| 18 | $[RhCl(NBD)]_2$[h,i] | 1 | I/OMe | dioxane | r.t. | 79 |
| 19 | $[RhCl(NBD)]_2$[h] | 2.5 | Br/H | dioxane | 100 | 51 |
| 20 | $[RhCl(NBD)]_2$[h,j] | 2.5 | Br/H | dioxane | 100 | 40 |
| 21 | $[RhCl(NBD)]_2$[h] | 2.5 | Cl/H | dioxane | 100 | 1 |
| 22 | $[RhCl(NBD)]_2$[h,j] | 2.5 | Cl/H | dioxane | 100 | 0 |
| 23 | $[RhCl(NBD)]_2$[h] | 2.5 | OTf/H | dioxane | 100 | 2 |
| 24 | $[RhCl(NBD)]_2$[h,j] | 2.5 | OTf/H | dioxane | 100 | 30 |

[a] *Reaction conditions:* PyDipSiH (0.1 mmol), aryl halide (0.2 mmol), catalyst, $K_3PO_4$ (0.3 mmol), and solvent (0.5 mL) were stirred overnight at the indicated temperature.
[b] GC yields, isolated yields are in parenthesis.
[c] The reaction was carried out in the presence of 6 mol% of P(*o*-tol)$_3$ as a ligand, (*i*-Pr)$_2$NEt (3 equiv.) as a base, 22 h.
[d] KOAc (2 equiv.) was used as a base, 4 h.
[e] Pyridine (2.5 equiv.) was used as a base and LiCl (4 equiv.) as an additive, 4 h.
[f] NaOAc (2 equiv.) was used as a base, 29 h.
[g] The reaction time was 48 h.
[h] The reaction was run on a 0.2-mmol scale. Amounts of aryl halide or triflate were reduced to 1.1 equiv., 8 h.
[i] 72 h.
[j] TBAI (1.1 equiv.) was used as an additive.

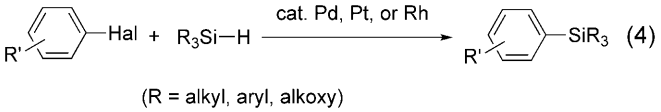
Finally, it is worth mentioning that PyDipSiH was made in an excellent yield from a commercially available chlorodiisopropylsilane and 2-bromopyridine on a 170-mmol scale [Eq. (3)].




(3)

## Rh(I)-Catalyzed Cross-Coupling (Method B)

Although method A is quite efficient for the preparation of PyDipSi-arenes, it suffers from low functional group compatibility owing to a requisite use of strong organolithium reagents. In contrast to the methods relying on strong organometallic reagents, the transition metal-catalyzed cross-coupling reaction of aryl halides with hydrosilanes is a well-precedented functional

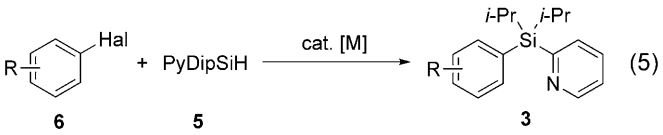



(4)

group-compatible strategy for the installation of alkyl, aryl, or alkoxysilyl groups onto arenes [Eq. (4)].[17] However, there are no reports on a direct coupling of haloarenes with hydrosilanes possessing a heterocyclic substituent. Thus, we envisioned that the development of the cross-coupling approach for the introduction of the PyDipSi group onto aryl and heteroaryl halides **6** would allow for a better functional group tolerance, thus complying with the requirements for our directing group design [Eq. (5)].

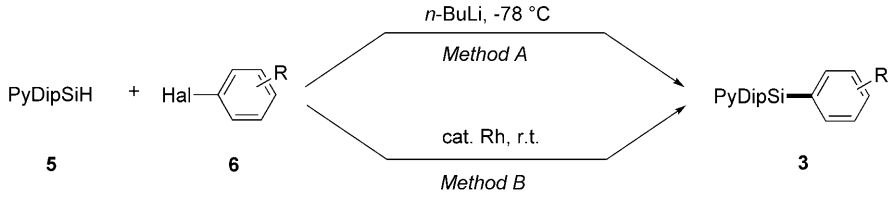
Accordingly, known Pd-,[17a–i] Pt-,[17j] and Rh-catalyzed[17k,l] methods for the coupling of hydrosilanes with aryl halides were tested in the reaction of PyDipSiH with 4-iodoanisole (Table 2, entries 1–5). It was found that employment of Pd- and Pt-based catalytic systems led to a decomposition of PyDipSiH (entries 1–4), whereas the use of the Rh(I) catalyst provided the desired product **3b** in a very low yield (entry 5). Further optimization of the Rh(I)-catalyzed



(5)

reactions (entries 6–12) revealed $[RhCl(NBD)]_2$ as a feasible catalyst for this transformation (entry 12).[18] Notably, switching the solvent to 1,4-dioxane dramatically improved the product yield to 96% (entry 16). Finally, decreasing both catalyst loading and amount

**Table 3.** Installation of the PyDipSi group on haloarenes.[a]



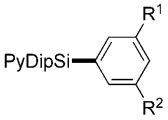
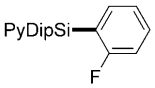
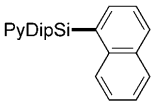
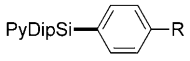
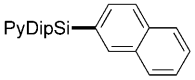
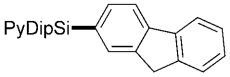
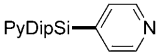
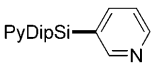
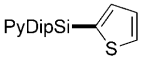
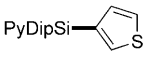
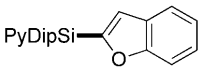
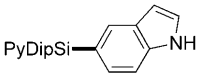
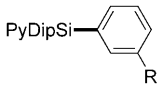
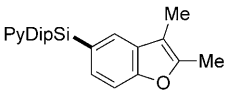
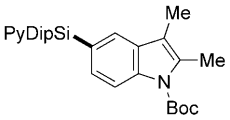
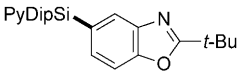
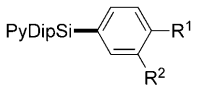
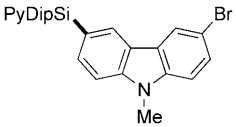

| Entry | Product | | Yield [%][b] A | B | Entry | Product | | Yield [%][b] A | B |
|---|---|---|---|---|---|---|---|---|---|
| 1 | | **3a** (H) | 92 | >99 | 28 |  | **3ab** ($R^1=R^2=F$) | – | 99 |
| 2 | | **3b** (OMe) | 92 | 98 | 29 | | **3ac** ($R^1=R^2=Cl$) | – | 78 |
| 3 | | **3c** (Me) | 91 | 98 | 30 | | **3ad** ($R^1=F$, $R^2=Me$) | – | 69 |
| 4 | | **3d** (F) | 73 | 85 | | | | | |
| 5 | | **3e** (Cl) | 87 | 95 | 31 |  | **3ae** | 31 | 73 |
| 6 | | **3f** (Br) | 72 | 84 | | | | | |
| 7 | | **3g** (CN) | 33 | 94 | 32 |  | **3af** | – | 88 |
| 8 |  | **3h** (COMe) | -[c] | >99 | | | | | |
| 9 | | **3i** ($CO_2Me$) | - | >99 | 33 |  | **3ag** | 97 | – |
| | | **3i'** ($CO_2Et$) | 53[d] | – | | | | | |
| 10 | | **3j** (CHO) | – | 93 | | | | | |
| 11 | | **3k** ($NO_2$) | – | 72 | 34 |  | **3ah** | – | 69 |
| 12 | | **3l** ($NH_2$) | – | 94 | 35 |  | **3ai** | 30 | 84[f] |
| 13 | | **3m** (Ph) | 95 | – | 36 |  | **3aj** | 36 | 99[f] |
| 14 | | **3n** (PIN)[e] | 95 | – | 37 |  | **3ak** | – | >99 |
| 15 | | **3o** [CON($i$-Pr)$_2$] | 71[d] | – | 38 |  | **3al** | – | >99 |

**Table 3.** (Continued)

| Entry | Product | | Yield [%][b] A | B | Entry | Product | | Yield [%][b] A | B |
|---|---|---|---|---|---|---|---|---|---|
| 16 | | **3p** ($CF_3$) | 67 | 77 | 39 |  | **3am** | – | 75[f] |
| 17 | | **3q** ($CO_2Et$) | – | 92[f] | 40 |  | **3an** | – | 93 |
| 18 |  | **3r** ($NO_2$) | – | 70 | | | | | |
| 19 | | **3s** (F) | – | >99 | 41 |  | **3ao** | 95 | – |
| 20 | | **3t** (Br) | 50 | 90 | | | | | |
| 21 | | **3u** (Ph) | 93 | – | | | | | |
| 22 | | **3v** (Me) | 94 | 96 | 42 |  | **3ap** | 77 | – |
| 23 | | **3w** (OMe) | 91 | 95 | | | | | |
| 24 | | **3x** ($R^1=R^2=Me$) | 58 | 96 | 43 |  | **3aq** | 87 | – |
| 25 |  | **3y** ($R^1=Me$, $R^2=F$) | 86 | 75 | | | | | |
| 26 | | **3z** ($R^1=F$, $R^2=Me$) | 96 | – | 44 |  | **3ar** | 50 | – |
| 27 | | **3aa** ($R^1=Cl$, $R^2=Me$) | 97 | – | | | | | |

[a] *Reaction conditions:* method A: aryl bromide or iodide (1 equiv.), *n*-BuLi (1 equiv.), THF (0.7 M), −78 °C; then PyDipSiH (1 equiv.), −78 to −30 °C; method B: PyDipSiH (1 equiv.), aryl iodide (1.1 equiv.), $[RhCl(NBD)]_2$ (2.5 mol%), $K_3PO_4$ (3 equiv.), and dioxane (0.2 M), room temperature.[18]

[b] Isolated yields.

[c] The reaction was not performed.

[d] Combined yield for two steps *via* intermediate **3f**.

[e] PIN = 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl.

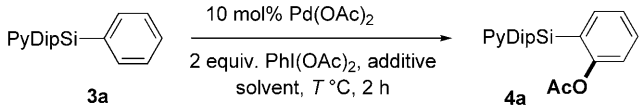
[f] Reaction was performed at 80 °C.

of aryl iodide to 2.5 mol% and 1.1 equivalents, respectively, allowed for the highest isolated yield of **3b** (entry 17). The catalyst loading could further be reduced to 1 mol% at the expense of both product yield and the reaction time (entry 18). Aryl iodides were notably more reactive in this transformation than the corresponding bromides, chlorides, and triflates (entries 19–24). Addition of stoichiometric amounts of tetrabutylammonium iodide (TBAI), known to enhance the reactivity of the latter electrophiles,[17k] however, showed no improvement of the reaction outcome for phenyl bromide and chloride (entries 20 and 22), while a slight increase of the product yield was observed for phenyl triflate (entry 24).

Next, the generality of this protocol toward the installation of the PyDipSi group on differently substituted aryl iodides was examined (Table 3, method B). To our delight, it was found that this transformation worked equally well for both electron-rich and electron-deficient arenes. Notably, in most cases, a direct method B appeared to be even more efficient than the method A. Expectedly, the functional group tolerance of the method B was much better compared to that of the method A, which required the employment of organolithium reagents. Thus, in addition to F, Cl, Br, $CF_3$, and OMe, a variety of other functional groups, such as ketone (**3h**), ester (**3i**), nitrile (**3g**), nitro (**3k** and **3r**), and even aldehyde (**3j**) and amino group (**3l**), were perfectly tolerated under these reaction conditions, providing PyDipSi-arenes in high to quantitative yields. Moreover, arylsilane **3i**, whose analogue **3i′** was previously synthesized *via* a two-step sequence involving intermediate **3f**, could be accessed directly in one step and in an excellent yield using method B (Table 3, entry 9). Furthermore, employment of the method B allowed for an efficient coupling of PyDipSiH with different heteroaryl iodides, such as iodopyridine, iodothiophene, iodobenzofuran, and iodoindole derivatives, affording the desired products **3ai**–**3an** in excellent yields (Table 3, entries 35–40, method B).

**Table 4.** Further optimization of the *ortho*-acetoxylation reaction conditions.




3a 4a

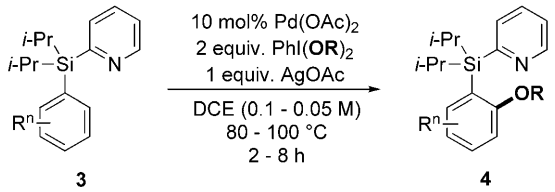
| Entry | Additive (equiv) | Solvent | $T$ [°C] | Yield [%][a] |
|---|---|---|---|---|
| 1 | none | AcOH | 100 | –[b] |
| 2 | $Cu(OAc)_2$ (1) | PrCN | 100 | trace |
| 3 | AgOAc (1) | PrCN | 80 | 70 |
| 4 | AgOAc (1) | PrCN | 100 | 80 |
| 5 | AgOAc (1) | DCE | 80 | 85 |

[a] NMR yield.
[b] Decomposition of starting arylsilane was observed, no desired product was formed.

## Pd-Catalyzed *ortho*-Acyloxylation of Arylsilanes

With two efficient and general methods for the installation of the PyDipSi-directing group onto arenes and heteroarenes in hand, the Pd-catalyzed *ortho*-acetoxylation reaction of the PyDipSi-arenes **3** was optimized further (Table 4). Thus, it was found that performing the reaction in acetic acid resulted in a rapid decomposition of **3a** (Table 4, entry 1). Similarly, the employment of a stoichiometric amount of $Cu(OAc)_2$ gave only traces of the product (entry 2). Gratifyingly, the use of 1 equivalent of AgOAc additive afforded the desired **4a** in 70% yield (entry 3). Performing the reaction at a slightly higher temperature (100 °C) provided a better yield of **4a** (80%, entry 4). Finally, switching the solvent to 1,2-dichloroethane (DCE) furnished **4a** with the highest yield (85%) at lower (80 °C) temperature (entry 5).

**Table 5.** Pd-catalyzed *ortho*-acyloxylation of arylsilanes.




3 4

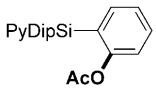
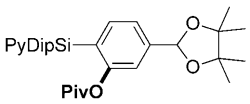
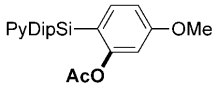
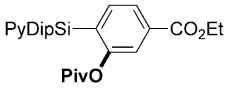
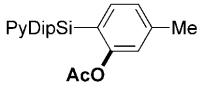
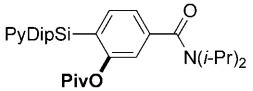
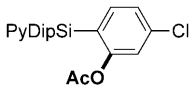
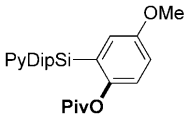
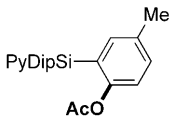
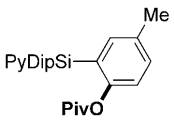
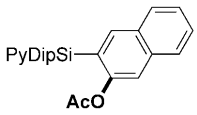
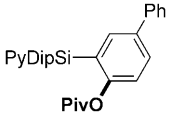
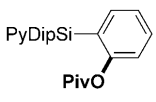
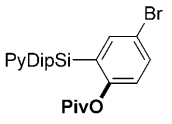
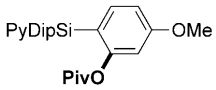
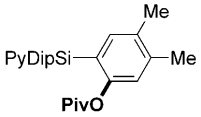
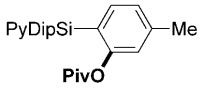
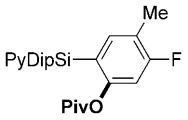
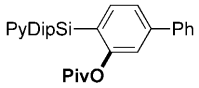
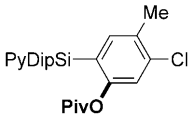
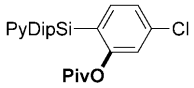
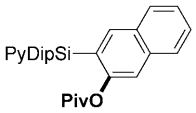
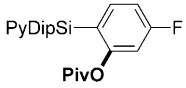
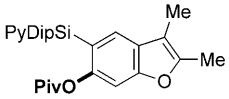
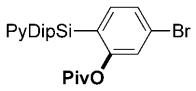
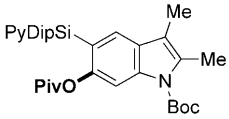
| Entry | Product | | $t$ [h] | Yield [%][a] | Entry | Product | | $t$ [h] | Yield [%][a] |
|---|---|---|---|---|---|---|---|---|---|
| 1 |  | **4a** | 2 | 80 | 14 |  | **4n** | 5 | 68 |
| 2 |  | **4b** | 2 | 84 | 15 |  | **4o** | 4 | 67 |
| 3 |  | **4c** | 2 | 93 | 16 |  | **4p** | 4 | 79 |
| 4 |  | **4d** | 7 | 64 | 17 |  | **4q** | 5 | 60 |
| 5 |  | **4e** | 2 | 88 | 18 |  | **4r** | 5 | 93 |
| 6 |  | **4f** | 3 | 90 | 19 |  | **4s** | 1 | 79 |
| 7 |  | **4g** | 3 | 80 | 20 |  | **4t** | 5 | 60 |

**Table 5.** (Continued)

| Entry | Product | | *t* [h] | Yield [%][a] | Entry | Product | | *t* [h] | Yield [%][a] |
|---|---|---|---|---|---|---|---|---|---|
| 8 |  | **4h** | 7 | 78 | 21 |  | **4u** | 5 | 90 |
| 9 |  | **4i** | 5 | 78 | 22 |  | **4v** | 8 | 84 |
| 10 |  | **4j** | 1 | 81 | 23 |  | **4w** | 2 | 72 |
| 11 |  | **4k** | 8 | 74 | 24 |  | **4x** | 8 | 83 |
| 12 |  | **4l** | 8 | 82 | 25 |  | **4y** | 1.5 | 80 |
| 13 |  | **4m** | 8 | 77 | 26 |  | **4z** | 1.5 | 70 |

[a] Isolated yields.

Next, the scope of the Pd-catalyzed *ortho*-acetoxylation reaction was examined (Table 5). It was found that this reaction was quite general and allowed for an efficient introduction of an acetoxy group into a variety of PyDipSi-arenes **4a–4f** (entries 1–6). Likewise, *ortho*-pivaloxylation reaction was efficiently achieved under similar reaction conditions by switching the oxidant to $PhI(OPiv)_2$. In contrast to the known directed *ortho*-acyloxylation reactions, a remarkable monoselectivity for most of the substrates was observed in both acetoxylation and pivaloxylation reactions.[19] In addition, a variety of functional groups, including OMe (**4b**, **4h**, **4q**), F (**4l**, **4v**), Cl (**4d**, **4k**, **4w**), Br (**4m**, **4t**), acetal (**4n**), ester (**4o**), and amide (**4p**), remained intact under these reaction conditions. Notably, *meta*-substituted substrates underwent the acyloxylation reaction providing the corresponding acyloxylated products **4e, 4q–4t** as single regioisomers, where acyloxy groups were installed at the less hindered *ortho*-position. In addition, the 2-naphthyl derivative (entires 6 and 24) was acyloxylated exclusively at the C-3 position. The C-5-substituted PyDipSi-heterocycles, such as benzofuran and indole derivatives (entries 25 and 26), under the standard acyloxylation reaction conditions produced the C-6 pivaloxy-functionalized heterocycles as sole regioisomers in high yields. Notably, a selective preparation of these C-6 hydroxy derivatives of heterocycles is a quite challenging synthetic task requiring a multistep synthesis. Using the PyDipSi-directed C–H acyloxylation reaction, these derivatives now can easily be synthesized in high yields from the corresponding readily available C-5 haloheterocyclic precursors. Finally, it is worth mentioning that the introduction of these acyloxy groups into aromatic substrates is a highly important transformation as they can serve as directing groups in the Pd-catalyzed C–H arylation reactions,[20] as well as electrophilic partners in the Ni-catalyzed cross-coupling reactions.[21]

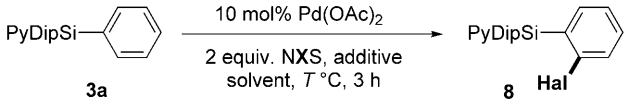
## Pd-Catalyzed *ortho*-Halogenation of Arylsilanes

Halogenated arenes are very useful building blocks in synthetic organic chemistry.[22] Thus, considering the immense synthetic potential of aryl halides as electrophilic reagents, we next aimed at the development of the Pd-catalyzed C–H halogenation reaction[1q,2h,23] of PyDipSi-arenes. Accordingly, PyDipSi-benzene **3a** was tested under various *ortho*-halogenation reaction conditions in the presence of $Pd(OAc)_2$ catalyst (Table 6).

First, the bromination reaction of **3a** using 2 equivalents of *N*-bromosuccinimide (NBS) in PrCN at 80 °C

**Table 6.** Optimization of reaction conditions for PyDipSi-directed *ortho*-halogenation.




3a 8

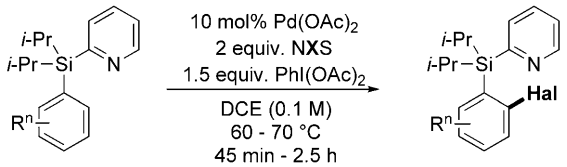
| Entry | Additive (equiv.) | Hal | Solvent | $T$ [°C] | Yield [%][a] |
|---|---|---|---|---|---|
| 1 | none | Br | PrCN | 80 | 50 |
| 2 | none | Br | PrCN | 100 | 65 |
| 3 | HOAc (50) | Br | PrCN | 80 | 15 |
| 4 | $Cu(OAc)_2$ (1) | Br | PrCN | 100 | trace |
| 5 | $PhI(OAc)_2$ (1.5) | Br | PrCN | 80 | 80 |
| 6 | $PhI(OAc)_2$ (1.5) | Br | PrCN | 100 | 65 |
| **7** | **$PhI(OAc)_2$ (1.5)** | **Br** | **DCE** | **60** | **85** |
| **8** | **$PhI(OAc)_2$ (1.5)** | **I** | **DCE** | **65** | **95** |
| 9 | $PhI(OAc)_2$ (1.5) | Cl | DCE | 65 | 42 |

[a] NMR yield.

provided 50% yield of the desired product **8x** (Table 6, entry 1, Hal = Br). Increasing the reaction temperature to 100 °C led to a slight improvement of the product yield (entry 2). Addition of 50 equivalents of acetic acid, commonly used in Pd-catalyzed C–H functionalization processes,[23a,b] resulted in a significant decrease of the reaction yield (entry 3). The employment of 1 equivalent of $Cu(OAc)_2$ additive provided only traces of the brominated product (entry 4). Remarkably, addition of 1.5 equivalents of $PhI(OAc)_2$ facilitated the bromination reaction, furnishing product **8x** in 80% yield (entry 5). However, performing the reaction at the elevated temperature (100 °C) lowered the yield of **8x** (entry 6). Notably, switching the solvent to DCE allowed for a higher reaction yield (85%) at lower temperature (60 °C; entry 7). Next, halogenating reagents other than NBS were also tested. Thus, the employment of *N*-iodosuccinimide (NIS) under these reaction conditions furnished the *ortho*-iodinated PyDipSi-benzene (**8a**) in an excellent 95% yield (entry 8; Hal = I). However, the employment of *N*-chlorosuccinimide (NCS) afforded the corresponding chlorinated product in a moderate yield only (entry 9; Hal = Cl).

Subsequently, the scope of the Pd-catalyzed *ortho*-halogenation reaction of the PyDipSi-arenes was examined under the optimized reaction conditions (Table 7). It was found that the *ortho*-iodination reaction displayed a high efficiency for a variety of substrates, which allowed for the preparation of mono-io-

**Table 7.** Pd-catalyzed *ortho*-halogenation of arylsilanes.




3 8

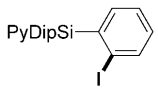
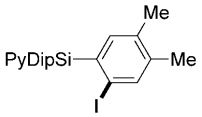
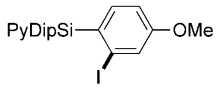
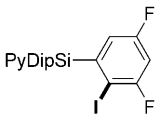
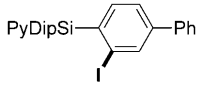
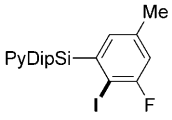
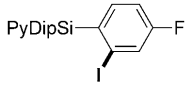
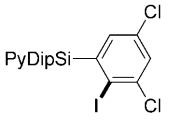
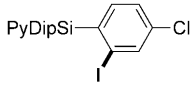
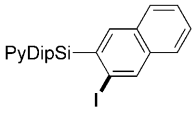
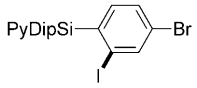
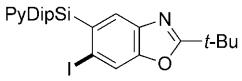
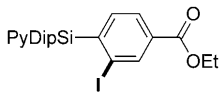
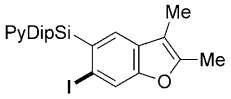
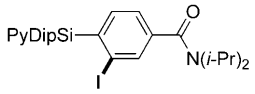
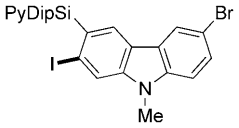
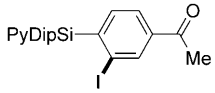
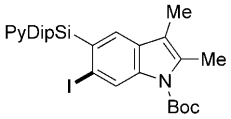
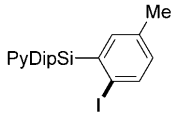
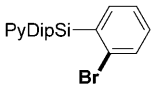
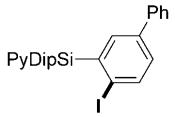
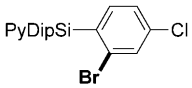
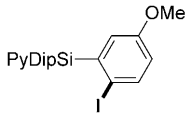
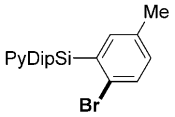
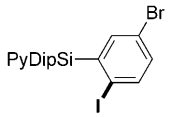
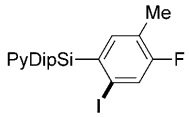
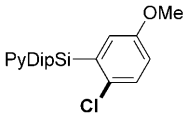
| Entry | Product | | $t$ [h] | Yield [%][a] | Entry | Product | | $t$ [h] | Yield [%][a] |
|---|---|---|---|---|---|---|---|---|---|
| 1 |  | **8a** | 0.75 | 91 | 15 |  | **8o** | 2 | 86 |
| 2 |  | **8b** | 1 | 70 | 16 |  | **8p** | 2 | 78 |
| 3 |  | **8c** | 1.5 | 88 | 17 |  | **8q** | 2 | 78 |
| 4 |  | **8d** | 2.5 | 87 | 18 |  | **8r** | 5 | 68 |
| 5 |  | **8e** | 1.2 | 84 | 19 |  | **8s** | 1.5 | 87 |

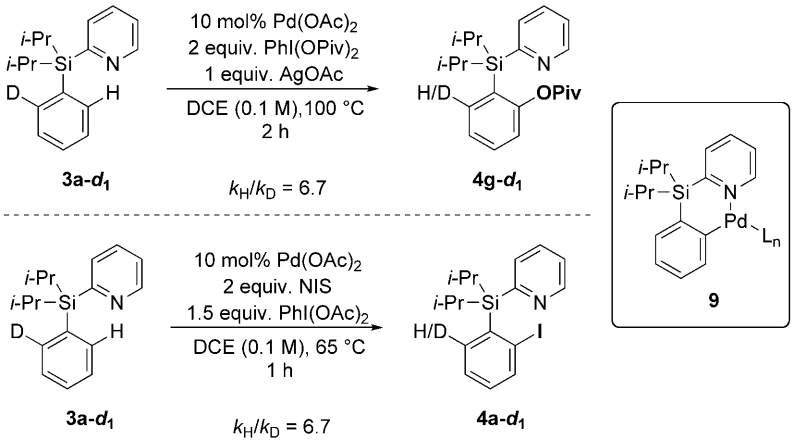
**Table 7.** (Continued)

| Entry | Product | | *t* [h] | Yield [%][a] | Entry | Product | | *t* [h] | Yield [%][a] |
|---|---|---|---|---|---|---|---|---|---|
| 6 |  | **8f** | 1.2 | 75 | 20 |  | **8t** | 5 | 72 |
| 7 |  | **8g** | 2 | 76 | 21 |  | **8u** | 1.5 | 77 |
| 8 |  | **8h** | 2 | 78 | 22 |  | **8v** | 2 | 69 |
| 9 |  | **8i** | 2 | 70 | 23 |  | **8w** | 1.5 | 74[b] |
| 10 |  | **8j** | 1 | 93 | 24 |  | **8x** | 3 | 80 |
| 11 |  | **8k** | 1.5 | 90 | 25 |  | **8y** | 3.5 | 75 |
| 12 |  | **8l** | 1.2 | 85 | 26 |  | **8z** | 3 | 91 |
| 13 |  | **8m** | 2 | 88 | | | | | |
| 14 |  | **8n** | 2 | 84 | 27 |  | **8aa** | 4 | 69[c] |

[a] Isolated yields.
[b] Reaction was performed without $PhI(OAc)_2$ and with 1 equivalent of NIS.[c] Reaction was performed in PrCN at 100 °C.

dinated arylsilanes in good to excellent yields. A variety of functional groups, such as OMe (**8b**, **8l**), F (**8d**, **8n**, **8p**, **8q**), Cl (**8e**, **8r**), Br (**8f**, **8m**, **8v**), ketone (**8i**), ester (**8g**), and amide (**8h**), were perfectly tolerated under the halogenation reaction conditions. Moreover, *meta*-substituted substrates demonstrated excellent site selectivity in the halogenation reaction, providing mono-iodinated compounds as sole regioisomers (entries 10–13). In addition, *ortho*-iodination of multisubstituted arylsilanes (entries 14–18) and 2-naphthyl derivative (entry 19) occurred smoothly furnishing the desired products as single regioisomers in high yields. Likewise, the bromination reaction allowed for an efficient synthesis of *ortho*-brominated arylsilanes, tolerating both electron-rich and electron-deficient substrates (entries 24–26). Notably, the chlorination reaction of electron-rich PyDipSi-arene **3w** was more efficient than that of electron-neutral **3a**, providing **8aa** in 69% yield. Finally, the iodination reactions of PyDipSi-heterocycles, such as benzoxazole (**8t**), benzofuran (**8u**), carbazole (**8v**), and indole (**8w**), occurred exclusively at the C-6 positions. Similarly to the C-6 acyloxylated heterocyclic derivatives described above, a selective preparation of the C-6 halogenated heterocycles is a challenging task. Now, these compounds can easily be accessed *via* the PyDipSi-directed C–H halogenation reactions of the C-5 PyDipSi-derived heterocycles, which are accessed from the corresponding easily available C-5 halogenated heterocyclic precursors.



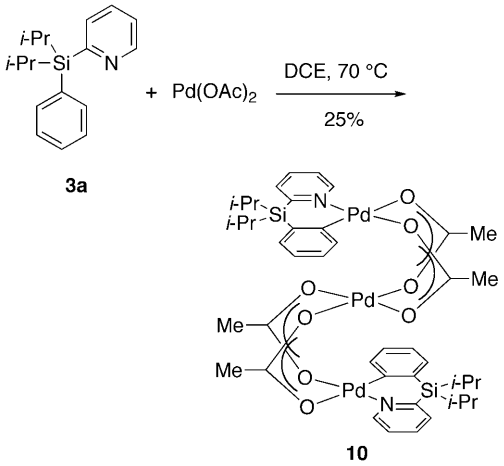

**Scheme 3.** Intramolecular kinetic isotope effect studies of pivaloxylation and halogenation reactions.

## Mechanistic Considerations

To shed light on possible reaction mechanisms of the Pd-catalyzed *ortho*-acyloxylation and *ortho*-halogenation reactions, intramolecular primary kinetic isotope effect (KIE) measurements have been performed first. Substantial $k_H/k_D$ values of 6.7 were found for both C–H functionalization reactions (Scheme 3). Observation of equally high values of KIEs for both transformations suggested that these reactions proceed *via* similar C–H activation pathways involving the formation of palladacycle **9** as a reactive intermediate. In addition, relative rate measurements indicated that the electron-rich arene (**3v**) underwent the pivaloxylation reaction more rapidly than electron-deficient **3p** ($k_{Me}/k_H = 1.37 \pm 0.04$; $k_H/k_{CF_3} > 100$). Only traces of the pivaloxylation product for *m*-$CF_3$-substituted substrate **3p** were observed, even when a full conversion was achieved for its unsubstituted analogue **3a**.

To further support a possible involvement of the palladacycle intermediate **9**, a stoichiometric reaction of **3a** with $Pd(OAc)_2$ in DCE solvent was performed next. A trinuclear palladacycle **10** was isolated in 25% yield [Eq. (6)], which was characterized by $^1H$ and $^{13}C$ NMR as well as HR-MS analyses. It is worth mentioning that using different ratios of **3a** and $Pd(OAc)_2$ did not provide any other palladium species and palladacycle **10** was isolated as the only complex in all cases. Similar trimetallic palladium species[24] were reported by Yu in the $Pd(OAc)_2$-catalyzed oxazoline-directed iodination of unactivated C–H bonds in the presence of IOAc[25] and in the oxygenation reaction of unactivated methyl groups in the presence of carboxylic acid anhydrides.[26]

Next, the palladacycle **10** was subjected to a stoichiometric reaction with $PhI(OPiv)_2$, however, no desired pivaloxylated product **4g** was formed under the standard pivaloxylation reaction conditions even at elevated temperature and upon a prolonged reaction



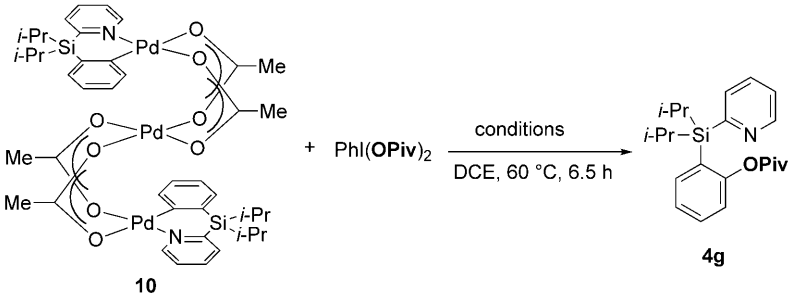

(6)

time (Table 8, entries 1 and 2). Recently, Ritter's group observed a "nitrogenous ligand effect"[27] during a mechanistic study of the Pd-catalyzed acetoxylation reaction of 2-phenylpyridine. According to this phenomenon, addition of 20 equivalents of starting material, 2-phenylpyridine, to the thermolysis reaction of the bimetallic Pd(III) complex[23c,27,28] resulted in a significant increase of the acetoxylated product yield. Similar to the above case, treatment of the trinuclear Pd(II) species **10** with $PhI(OPiv)_2$ in the presence of 20 equivalents of substrate **3a**, provided the desired product **4g** in 78% yield (entry 3). Furthermore, addition of 1 equivalent of AgOAc improved the yield to 87% (entry 4).[29]

Moreover, when substrate **3v** was used as a "nitrogenous ligand", the reaction of the palladacycle **10** with $PhI(OPiv)_2$ afforded two pivaloxylated products **4g** and **4r** in 35% and 30% GC yield, respectively [Eq. (7)]. Expectedly, when the reaction of the palladacycle **10** with $PhI(OPiv)_2$ was carried out in the presence of 20 equivalents of an unreactive *ortho*-methyl derivative **11**, no formation of **12** was observed, while **5g** was formed in 80% yield as a single

**Table 8.** Stoichiometric reactions of palladacycle **10** with $PhI(OPiv)_2$.




| Entry | Oxidant (equiv.) | Co-oxidant (equiv.) | Substrate (equiv.) | Yield [%][a] |
|---|---|---|---|---|
| 1 | $PhI(OAc)_2$ (4) | none | none | 0[b] |
| 2 | $PhI(OAc)_2$ (4) | AgOAc (2) | none | 0[b] |
| 3 | $PhI(OAc)_2$ (1.1) | none | **3a** (20) | 78 |
| 4 | $PhI(OAc)_2$ (1.1) | AgOAc (1) | **3a** (20) | 87 |

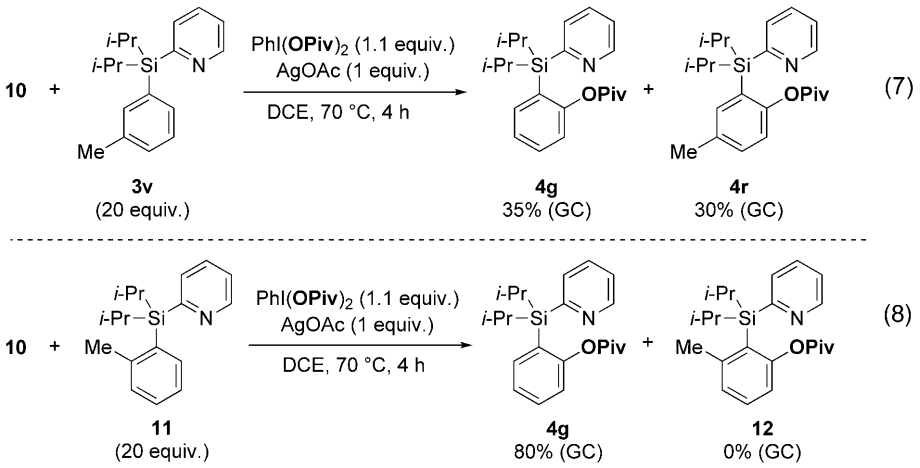
[a] GC yield, pentadecane was used as internal standard.
[b] The reaction mixture was heated up to 100 °C for 12 h.

product [Eq. (8)]. The above results can easily be explained by the release of reactive Pd(II) species upon the formation of **4g**, which can further catalyze the pivaloxylation reaction of **3v** to form **4r**. In contrast, in the case of an unreactive **11**, serving solely as a "nitrogenous ligand", the pivaloxylation reaction leading to **12** is suppressed, resulting in the formation of **4g** only. These observations strongly support the involvement of Ritter's "nitrogenous ligand effect" in the Pd-catalyzed pivaloxylation reaction of PyDipSi-arenes.

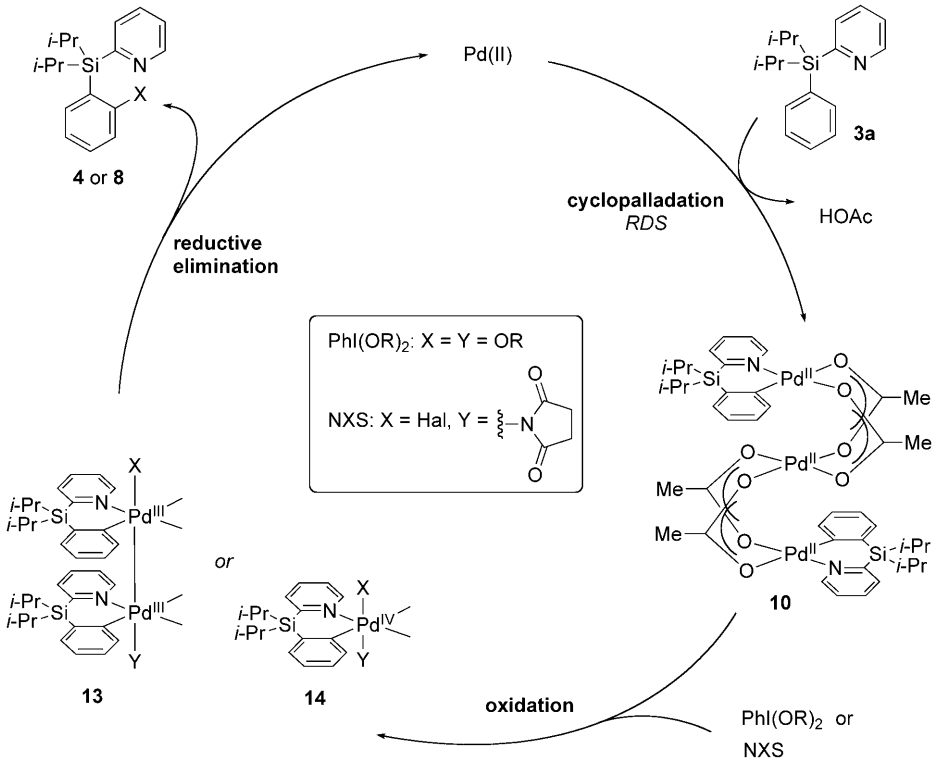
In light of these observations, a generalized mechanism for the PyDipSi-directed *ortho*-acyloxylation and *ortho*-halogenation reactions of C–H bonds is proposed (Scheme 4). According to it, palladium acetate first reacts with arylsilane **3** affording the trinuclear palladium(II) complex *via* a cyclopalladation process, which is a rate-limiting step based on the observed high values of the primary KIEs. A subsequent oxidation of Pd(II) in trinuclear species **10** with *N*-halosuccinimides or hypervalent iodine(III) reagents provides Pd(III) species **13** or Pd(IV) species **14**.[30] Finally, reductive elimination from **13** or **14** affords the observed functionalization products and regenerates the active Pd(II) catalyst.

## Further Transformations of Functionalized PyDipSi-Arenes

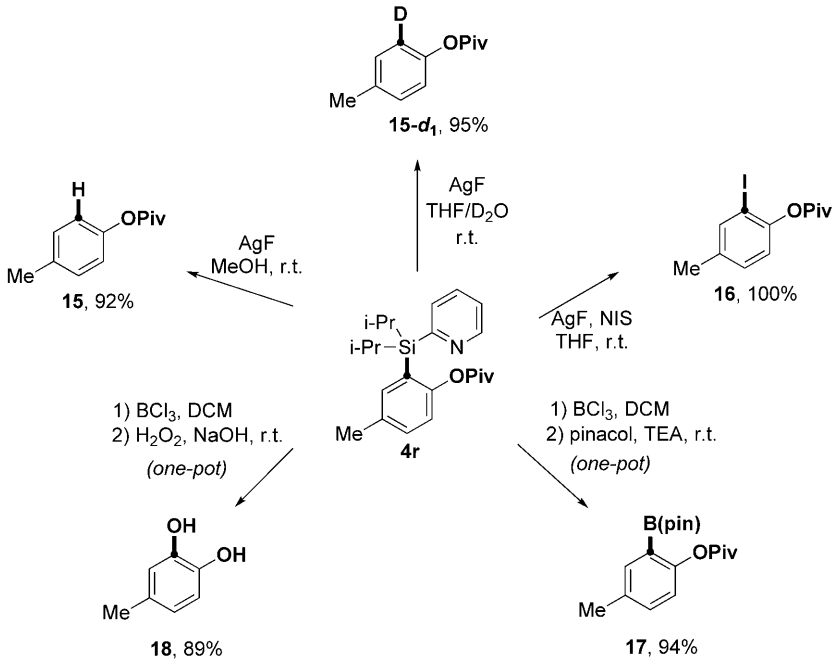
Next, we examined the synthetic usefulness of both acyloxylated and halogenated products. The cleavage of the PyDipSi directing group of the acyloxylated PyDipSi-arene **4r** was tested first (Scheme 5). Thus, the reaction of **4r** with AgF[11b,31] in methanol resulted in efficient removal of the PyDipSi directing group,





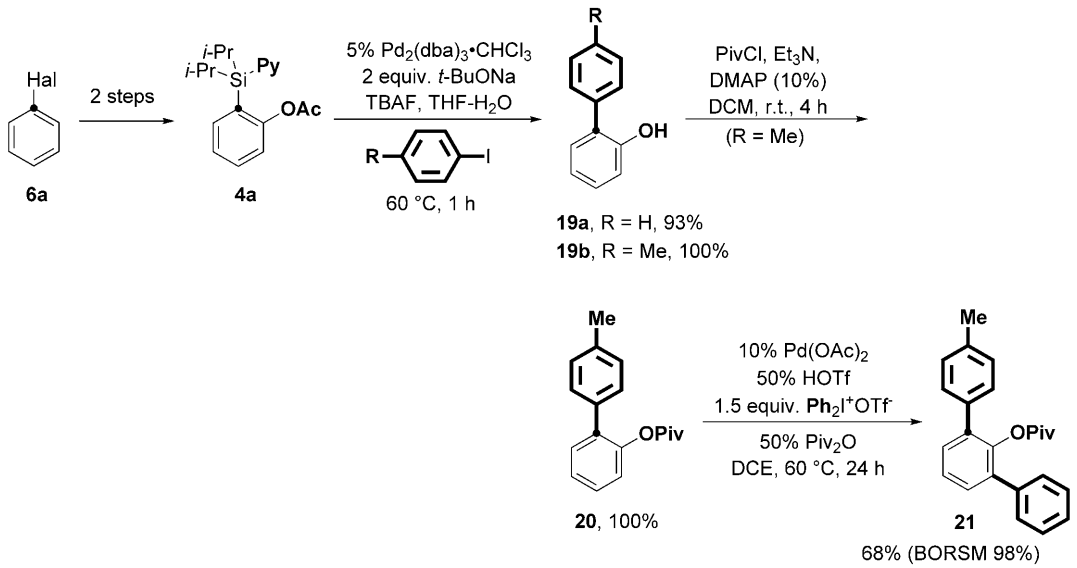

**Scheme 4.** Generalized mechanism for the Pd-catalyzed acyloxylation and halogenation reactions.




**Scheme 5.** Further transformations of the PyDipSi group in acyloxylated products.

producing tolyl pivalate **15** in 92% yield. In a similar manner, switching solvent to THF/$D_2O$, a deuterated tolyl pivalate **15-*d*$_1$** was produced in 95% yield. Remarkably, the reaction of **4r** in the presence of AgF and NIS in anhydrous THF led to iododesilylation product **16**, quantitatively. Of note, the overall three-step transformation of *m*-iodotoluene into pivaloxylated arene **16** constitutes a formal *ortho*-oxygenation of *m*-iodotoluene.[32] Moreover, borodesilylation of the PyDipSi group in **4r** with $BCl_3$, followed by the

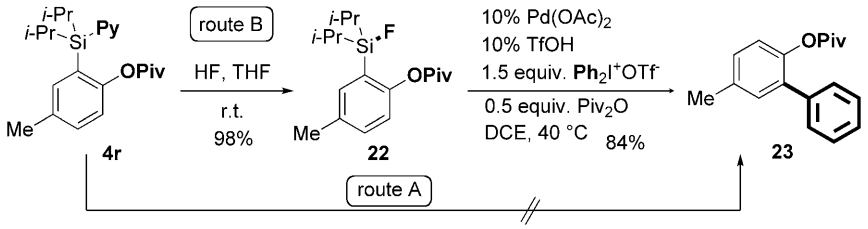
  




**Scheme 6.** Synthesis of unsymmetrically substituted 2,6-diarylphenol derivatives.

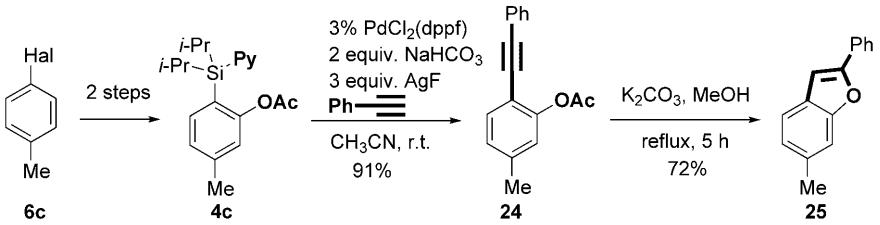
protection of the generated aryldichloroborane with pinacol under basic conditions,[7d,33] furnished a synthetically valuable arylboronate **17**[34] in an excellent yield. Likewise, a one-pot sequence involving the borodesilylation of **4r**, followed by the oxidation step in the presence of $H_2O_2$/NaOH, led to 4-methylcatechol (**18**) in 89% yield.

Furthermore, the Hiyama–Denmark cross-coupling[35] of the acetoxylated product **4a** proceeded smoothly with a concomitant acetoxy group hydrolysis, affording the *ortho*-arylated phenols **19** in excellent yields (Scheme 6). However, *ortho*-pivaloxylated PyDipSi-analogue **4g** remained intact under the same cross-coupling reaction conditions, suggesting that the hydrolysis of acetoxy group in **4a** into the corresponding phenoxide is required prior to the coupling step. As mentioned above, the pivaloxy group can serve as a directing group in the Pd-catalyzed *ortho*-arylation of arenes.[20] To test this reaction, 2-(4-tolyl)phenol **19b** was converted into the corresponding pivalate **20** quantitatively. The latter was subjected to the pivaloxy-directed *ortho*-arylation reaction conditions[20] furnishing the arylated product **21** in 68% (98% BORSM) yield (Scheme 6). The overall five-step transformation of haloarenes **6a** into **21** provides an easy entry into not so readily accessible unsymmetrically substituted 2,6-diarylphenol derivatives (Scheme 6). Next, the pivaloxy-directed arylation reaction was examined for substrate **4r**, however, no formation of the desired arylated product was observed (Scheme 7, route A). We reasoned that the relatively strong coordinating pyridyl moiety in the PyDipSi group might deactivate the Pd catalyst. To test this hypothesis, the pyridyl group was replaced with fluoride in almost quantitative yield by treatment of **4r** with aqueous HF in THF. Indeed, a subsequent pivaloxy-directed *ortho*-arylation reaction of pyridyl-free **22** occurred smoothly with a concomitant desilylation process, producing the arylated product **23** in 84% yield (Scheme 7, route B). Next, employment of the PyDipSi-arenes as nucleophilic aryl group donors for the functionalization of terminal acetylenes was examined. Thus, the reaction of PyDipSi-arene **4c** with phenylacetylene using the $PdCl_2$(dppf)/AgF catalytic system, previously developed for the alkynylation of aryltrimethoxysilanes,[36] allowed for the formation of the alkynylated cross-coupling product **24** in 91% yield. A subsequent saponification/cyclization cascade[37] afforded benzofuran derivative **25** in 72% yield (Scheme 8). The overall four-step sequence, in-

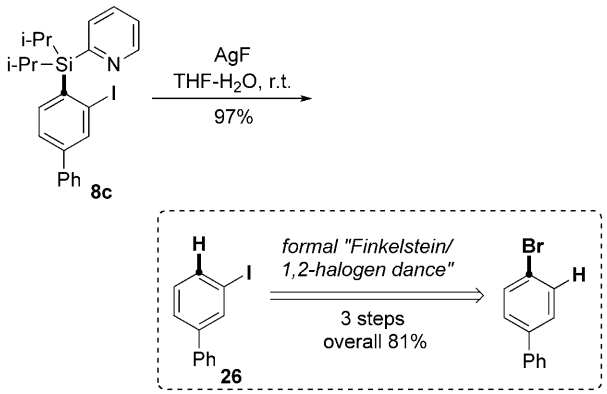



**Scheme 7.** Pd-catalyzed pivaloxy-directed *ortho*-arylation of PyDipSi-arene.




**Scheme 8.** Synthesis of benzofuran.



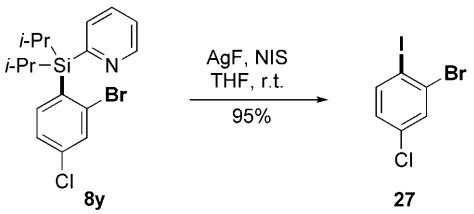

**Scheme 9.** Desilylation of iodinated PyDipSi-arene.

cluding the installation of the PyDipSi group and the Pd-catalyzed *ortho*-acetoxylation reaction, constitutes a powerful strategy for the synthesis of the polysubstituted benzofuran core from simple haloarenes.

As it was demonstrated above, the PyDipSi directing group could efficiently participate in a variety of reactions as a nucleophilic entity. Considering the electrophilic nature of haloarenes, *ortho*-halogenated PyDipSi-arene derivatives **8**, possessing both nucleophilic and electrophilic reactive sites, represent powerful 1,2-ambiphilic synthons,[38] which are traditionally accessed through a multistep synthesis.[39]

To this end, we decided to test possible reactions of the *ortho*-halogenated PyDipSi-arenes **8** as nucleophilic coupling partners first. Similarly to the reactions of *ortho*-acyloxylated PyDipSi-arenes, the same efficient removal or modification of the PyDipSi group was achieved. It was found that the removal of the silicon-tethered directing group in **8c** occurred smoothly in the presence of AgF in THF/$H_2O$ affording *m*-iodobiphenyl **26** in 97% yield (Scheme 9). *Interestingly, this transformation, taken together with the installation of the PyDipSi group and the Pd-catalyzed ortho-iodination steps, represents an example of a formal "Finkelstein/1,2-halogen dance" reaction!* Next, use of a combination of AgF and NIS in anhydrous THF allowed for an efficient iododesilylation of chlorobromoarylsilane **8y**, producing 1-chloro-3-bromo-4-iodobenzene **27** in 95% yield [Eq. (9)], a useful building block for a modular functionalization of the benzene ring. Moreover, *o*-iodoarylsilane **8j**, upon the borodesilylation with $BCl_3$, was efficiently converted into *o*-iodoarylboronate **28**,[40] another synthetically valuable ambiphile. Likewise, *o*-iodophenol **29** could be accessed *via* a similar one-pot sequence involving the borodesilylation reaction followed by the oxidation step with hydrogen peroxide (Scheme 10).

Next, coupling of the electrophilic aryl iodide functionality in PyDipSi-iodoarenes **8**, introduced by the C–H halogenation reaction, was examined. Thus, double alkynylation of the iodinated PyDipSi-benzene **8a** *via* a sequence involving Sonogashira reaction

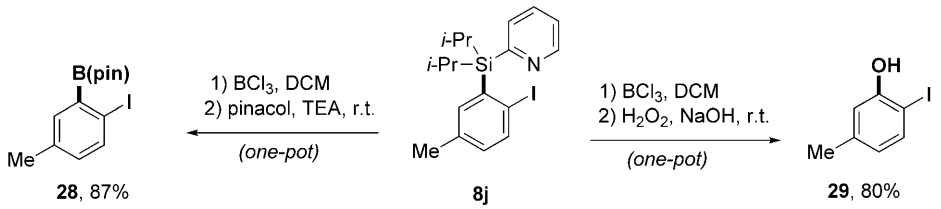



(9)

of the aryl iodide and a subsequent cross-coupling reaction of the PyDipSi group with phenylacetylene afforded diaryl enediyne **31** in good overall yield (Scheme 11). The latter is a common precursor for the construction of a variety of building blocks, for instance, benzofulvenes *via* a *5-exo-dig* radical cyclization[41] or naphthalene derivatives *via* the Bergman cyclization.[42]

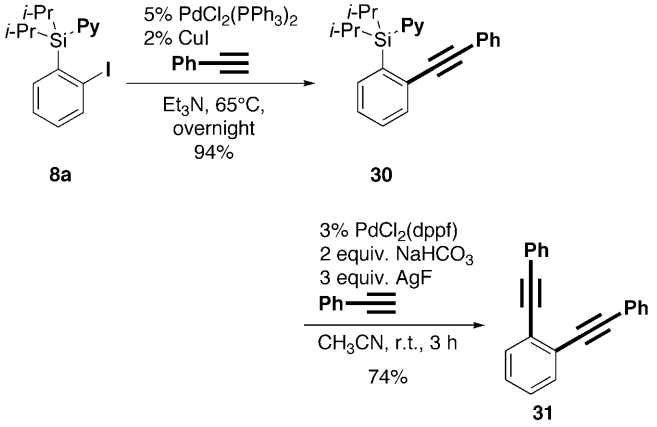
Recently, silole derivatives have received much attention as highly versatile organic optoelectronic materials.[43] We envisioned that a selective removal of the pyridyl moiety from the PyDipSi group and subsequent modifications of silicon and halogen handles could provide an easy access to silole derivatives from PyDipSi-haloarenes **8**. Thus, **8j** was subjected to a Sonogashira reaction with phenylacetylene to produce alkynylated PyDipSi-arene **32** in 69% yield. A subsequent selective substitution of the pyridyl moiety in the PyDipSi group with fluoride provided fluorosilane **33** in 90% yield.[44] Alternatively, fluorosilane **33** could be prepared with a similar efficiency *via* a sequence involving exchange of the pyridyl group to fluoride and Suzuki cross-coupling reaction[45] of the formed iodoarene **34** with potassium phenylethynyltri-



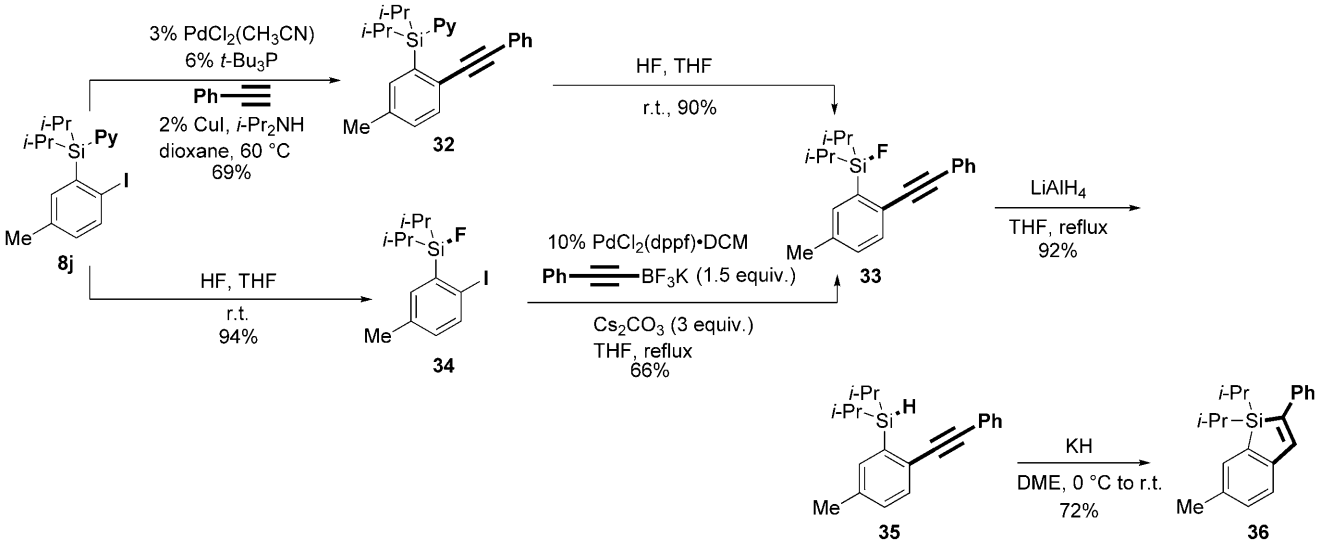

**Scheme 10.** Conversion of the PyDipSi group into boronate and phenol.

fluoroborate. A subsequent reduction of fluorosilane **33** with $LiAlH_4$ resulted in hydrosilane **35** in an excellent yield. Finally, unsymmetrically substituted benzo[*b*]silole **36** was obtained in 72% yield *via* a *5-endo-dig* cyclization of hydrosilane **31** in the presence of KH in DME (Scheme 12).[46] Dibenzosilole frameworks, as reported by Kawashima and Kobayashi, could efficiently be accessed from biphenylhydrosilanes *via* a sila-Friedel–Crafts reaction.[47a] In order to utilize this approach, biphenylsilane **37** was prepared in 89% yield by treating *o*-iodoarylsilane **8j** with 4-methoxyphenylboronic acid under the Suzuki cross-coupling reactions conditions. Synthesis of the key hydride **38** was achieved in 79% yield using a standard pyridyl/fluoride exchange followed by reduction with $LiAlH_4$. A subsequent treatment of biphenylhydrosilane **38** with $Ph_3CB(C_6F_5)_4$ under the sila-Friedel–Crafts reaction conditions provided unsymmetrically substituted dibenzosilole **39** in 71% yield (Scheme 13).[47]



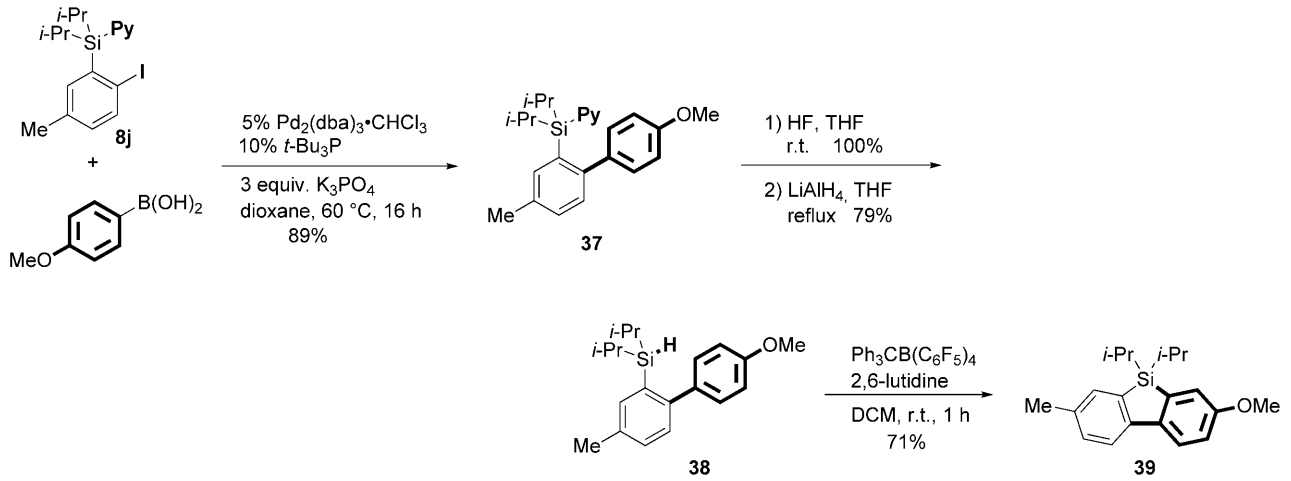

**Scheme 11.** Double alkynylation towards bis(ethynyl)arene.

Benzynes represent a highly important class of reactive intermediates widely used in organic synthesis.[48] Although a number of benzyne precursors have been disclosed,[49] structures of the most efficient and mild benzyne surrogates incorporate arylsilane moieties having a good leaving group adjacent to the silicon atom, such as in *o*-silylphenyl triflates and *o*-silylphenyliodonium salts. We thought that if the iodide functionality in the *ortho*-iodinated PyDipSi-arenes could serve as a good leaving group, benzynes could easily be generated from this precursor in one step. However, treatment of **8e** and furan with TBAF resulted only in desilylation product. Accordingly, the iodide functionality in iodoarene **8e** was converted into a better leaving iodonium group.[50] In order to prevent

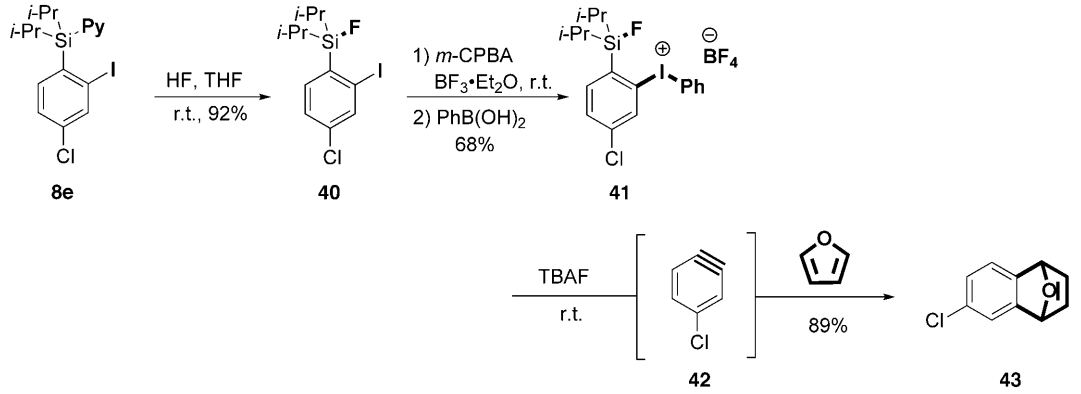



**Scheme 12.** Synthesis of benzosilole from *ortho*-iodinated PyDipSi-arene.




**Scheme 13.** Synthesis of unsymmetrically substituted dibenzosilole from iodinated PyDipSi-arene.




**Scheme 14.** Generation and trapping of benzyne.

oxidation of the pyridine core in the PyDipSi group, the pyridyl group was replaced with fluoride under standard reaction conditions to give **40** in an excellent yield. The latter silyl fluoride **40** was treated with *m*-CPBA and boron trifluoride-etherate complex followed by the addition of phenylboronic acid to produce the corresponding diaryliodonium tetrafluoroborate **41** (Scheme 14).[51] Treatment of **41** with excess amounts of furan in the presence of TBAF at room temperature afforded 1,4-epoxydihydronaphthalene **43** in 89% yield, suggesting a very efficient generation of benzyne **42** during the reaction course. Remarkably, the above sequence involving the *ortho*-iodination of PyDipSi-arenes, represents an unprecedented benzyne generation approach featuring a C–H activation strategy.

## Conclusions

In summary, we have developed an easily removable and modifiable silicon-tethered PyDipSi-directing group for C–H functionalization of arenes. Two complementary methods for the installation of the PyDipSi group onto haloarenes have been demonstrated. The first strategy involves a nucleophilic hydride substitution at silicon with organolithium reagents. The other approach features a very mild and highly functional group-compatible room temperature Rh(I)-catalyzed cross-coupling reaction. The PyDipSi directing group allows for a highly efficient mono- and regioselective Pd(II)-catalyzed *ortho*-acyloxylation and *ortho*-halogenation of arenes. Most importantly, the synthetic utility of the PyDipSi-directed C–H functionalization products was demonstrated in diverse transformations, involving protio-, deuterio-, halo-, boro-, alkynyldesilylations, and conversion of the
PyDipSi group into the OH functionality, as well as the formation of aryl-aryl bonds *via* Hiyama–Denmark cross-coupling reaction. Moreover, the *ortho*-halogenated PyDipSi-arenes represent synthetically attractive 1,2-ambiphiles. The unique reactivity of these ambiphiles was illustrated in efficient formation

of aryl enediyne, benzosilole derivatives, as well as in the efficient generation of benzyne. A general reaction mechanism involving a cyclopalladation process *via* a C–H activation at the rate-determining step for both acyloxylation and halogenation reactions has been proposed. Further studies on the application of temporary silicon tethers in directed transition metal-catalyzed transformations are underway in our laboratory.

## Experimental Section

### General Procedure for Rh(I)-Catalyzed Installation of PyDipSi Group on Arenes

An oven-dried 2.5-mL Wheaton V-vial, containing a stirring bar, was charged with 2-(diisopropylsilyl)pyridine (77.2 mg, 0.4 mmol), (hetero)aryl iodides (1.1 equiv.), $[RhCl(NBD)]_2$ (4.6 mg, 2.5 mol%), $K_3PO_4$ (254.0 mg, 3 equiv.), and dry 1,4-dioxane (2.0 mL) under an $N_2$ atmosphere. The reaction mixture was stirred at room temperature for 6–16 h until judged complete by GC/MS analysis. The resulting mixture was filtered through celite using EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (eluent: hexanes/EtOAc) affording the corresponding silylation product.

### General Procedure for Pd-Catalyzed *ortho*-Acyloxylation of PyDipSi-Arenes

An oven-dried 10-mL Wheaton V-vial, containing a stirring bar, was charged with 2-[diisopropyl-(aryl)silyl]pyridine (0.5 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), $PhI(OPiv)_2$ (406.3 mg, 1.0 mmol) or $PhI(OAc)_2$ (322.1 mg, 1 mmol), and AgOAc (83.5 mg, 0.5 mmol) under an $N_2$ atmosphere. Dry DCE (5–10 mL) or butyronitrile (10 mL) was added and the reaction vessel was capped with a pressure screw cap. The reaction mixture was heated at 80–100 °C for 2–8 h until judged complete by GC/MS analysis. The resulting mixture was cooled down to room temperature, quenched with $Et_3N$ (350 μL), and filtered through a layer of silica gel with the aid of EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on a silica gel (eluent: hexanes/EtOAc) affording the corresponding acyloxylated product.

### General Procedure for Pd-Catalyzed *ortho*-Halogenation of PyDipSi-Arenes

An oven-dried 10-mL Wheaton V-vial, containing a stirring bar, was charged with 2-[diisopropyl-(aryl)silyl]pyridine (0.5 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), $PhI(OAc)_2$ (241.6 mg, 0.75 mmol), and NIS (225 mg, 1 mmol) or NBS (178 mg, 1.0 mmol) or NCS (133.5 mg, 1.0 mmol) under an $N_2$ atmosphere. Dry DCE (5 mL) or butyronitrile (10 mL) was added and the reaction vessel was capped with pressure screw cap. The reaction mixture was heated at 60–70 °C (DCE) or 100 °C (PrCN) for 45 min to 4 h until judged complete by GC/MS analysis. The resulting mixture was cooled down to room temperature and filtered through a layer of silica gel with the aid of EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on a silica gel (eluent: hexanes/EtOAc = 1/10–1/2) affording the corresponding halogenated product.

## Acknowledgements

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