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PyDipSi: A General and Easily Modifiable/Traceless Si-Tethered Directing Group for C−H Acyloxylation of Arenes

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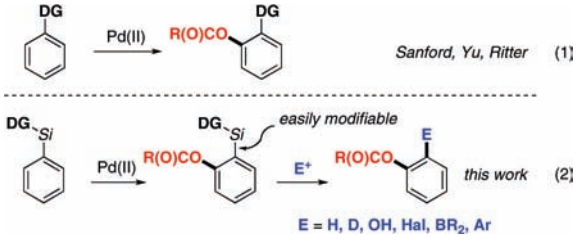
Palladium-catalyzed, ligand-directed C−H functionalization has emerged as a powerful tool for the direct conversion of arenes into a variety of valuable products.[1] Among these transformations, Pd-catalyzed directed acetoxylation reactions of aromatic C−H bonds[2,3] are particularly attractive because they allow the direct formation of oxygenated arenes.[4] A variety of directing groups, such as pyridine,[3a,c,g] pyrimidine,[3e,j] pyrazole,[3e] oxazoline,[3d,e] amide,[3f,k] and oxime ether,[3d] have been shown to be efficient in these reactions. However, despite the achieved high yields and selectivities, the acyloxylation reactions somewhat lack generality, as the majority of the directing groups, which are necessary for the selective transformation, often cannot easily be removed from the products, thus limiting these methodologies to particular types of substrates (eq 1). Herein we report the use of the pyridyldiisopropylsilyl (PyDipSi) group as a new silicon-tethered directing group that allows for efficient acetoxylation/pivaloxylation of aromatic C−H bonds. Most importantly, this directing group can efficiently be removed or converted into a variety of other functional groups (eq 2).



Our approach to the design of the removable directing group was based on the employment of a temporary silicon tether to connect a good metal-coordinating group for C−H activation with an aromatic substrate of interest. We thought that employment of a silicon-tethered directing group[5,6] would bring a certain advantage, since it is easily removable from the products of C−H functionalization. We chose pyridine as a platform for our new group design because it is known to be superior in coordinating palladium in directed C−H activation processes.[1j] To this end, we aimed at establishing a suitable silicon tether for the pyridine group. Accordingly, substrate **A** containing a pyridyldimethylsilyl directing group (Figure 1), which was previously developed by Yoshida[5] for the highly regio- and stereoselective Pd-catalyzed Heck arylation of vinylsilanes,[5b] was tested first. However, the reaction with $PhI(OAc)_2$ in the presence of 10 mol % $Pd(OAc)_2$ in PrCN at 80 °C[3a] resulted in total decomposition of the starting arylsilane **A** with no formation of the desired product (Table 1, entry 1). To further optimize the silicon tether, the silacyclopentane (**B**) and diisopropylsilyl (**1a**) derivatives were synthesized (Figure 1). Similarly to **A**, compound **B** appeared to be unstable as well (Table 1, entry 2). However, we were pleased to find that the diisopropylsilyl derivative **1a** was more stable

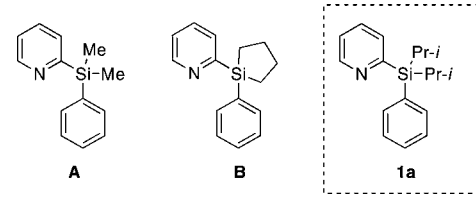
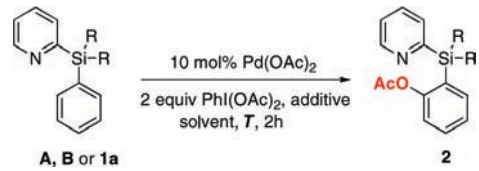


Figure 1. Substrates for optimization of the silicon tether.

toward $PhI(OAc)_2$ at 80 °C, producing the desired product **2a** in 15% yield (entry 3). Increasing the temperature to 100 °C led to a slight improvement in the reaction outcome (entry 4). Addition of a stoichiometric amount of $Cu(OAc)_2$ gave only traces of product (entry 5). Surprisingly, employment of 1 equiv of AgOAc[7] resulted in a dramatic improvement in the reaction, affording the desired **2a** in 70% yield. Furthermore, performing the reaction at slightly higher temperature (100 °C) resulted in a better yield of **2a** (80%, entry 7). Finally, switching the solvent to dichloroethane (DCE) provided the highest yield of the product (85%) at lower temperature (80 °C) (entry 8).

Table 1. Optimization of the Ortho Acetoxylation Reaction Conditions



entry	substrate	additive (equiv)	solvent	*T* (°C)	yield (%)[a]
1	**A**	none	PrCN	80	—[b]
2	**B**	none	PrCN	80	—[b]
3	**1a**	none	PrCN	80	15 (**2a**)[b]
4	**1a**	none	PrCN	100	30 (**2a**)[b]
5	**1a**	$Cu(OAc)_2$ (1)	PrCN	100	trace (**2a**)
6	**1a**	AgOAc (1)	PrCN	80	70 (**2a**)
7	**1a**	AgOAc (1)	PrCN	100	80 (**2a**)
8	**1a**	AgOAc (1)	DCE	80	85 (**2a**)

[a] NMR yield. [b] Decomposition of the starting arylsilane was observed.

It should be mentioned that the synthesis of arylsilanes containing the PyDipSi directing group is straightforward (Scheme 1). First, pyridyldiisopropylsilane is obtained in excellent yield from commercially available 2-bromopyridine and diisopropylsilyl chloride. Next, the hydride-substitution reaction in pyridyldiisopropylsilane with in situ-generated aryllithium reagents affords arylsilanes **1** in high yields (Scheme 1).

With the optimized conditions in hand, the generality of the Pd-catalyzed acyloxylation reaction of PyDipSi-containing arenes **1** was examined (Table 2). To our delight, it was found that

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Scheme 1. Synthesis and Installation of the PyDipSi Directing Group

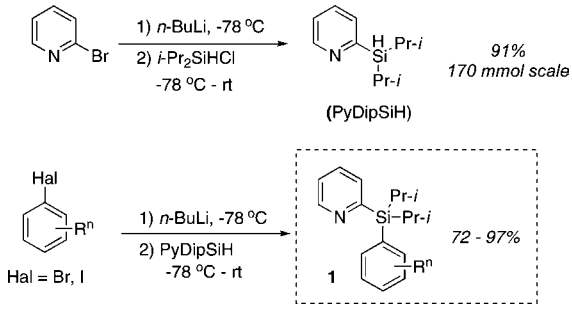
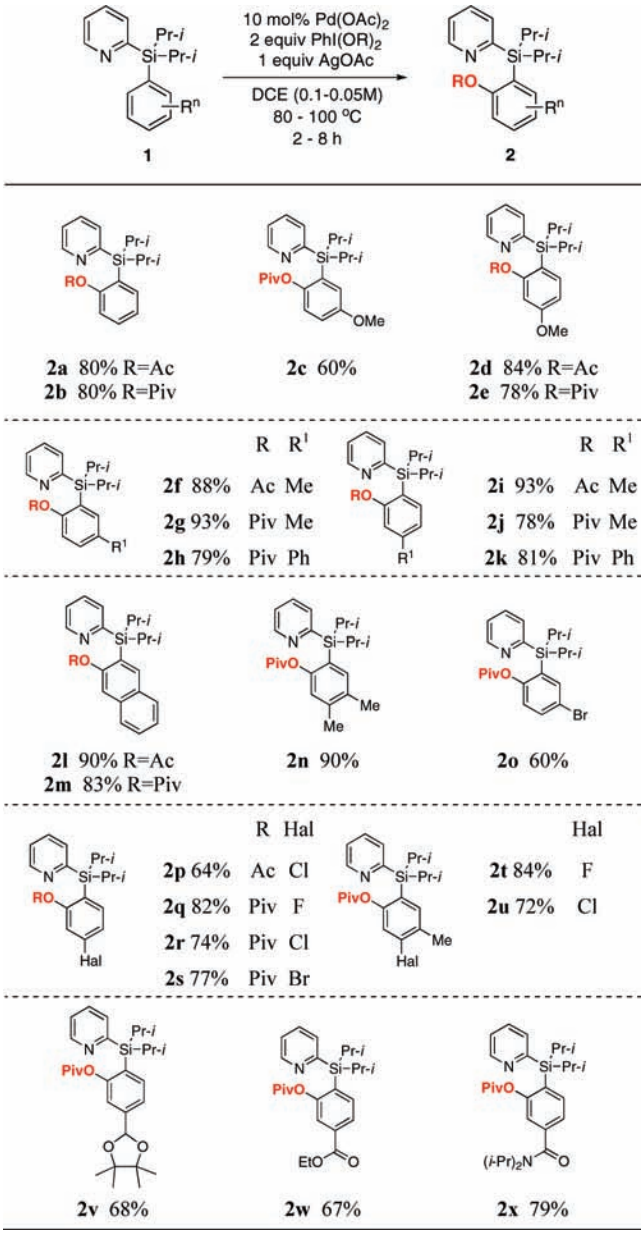


Table 2. Pd-Catalyzed Ortho Acyloxylation of Arylsilanes[a,b]

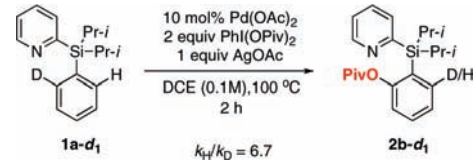


[a] Isolated yields. [b] See the Supporting Information for details.

this transformation is highly efficient for the exclusive monoacyloxylation of a wide range of substrates. Thus, arylsilanes **2a**−**x** possessing the acetoxy group[8] and the even more synthetically valuable pivaloxy group[9] were synthesized in good to excellent yields. A variety of functional groups, including OMe (entries **2c**−**e**), F (entries **2q** and **2t**), Cl (entries **2p**, **2r**, and **2u**), Br (entries **2o** and **2s**), pinacol-protected aldehyde (entry **2v**), CO_2Et (entry **2w**), and $CON(i\text{-}Pr)_2$ (entry **2x**), were perfectly tolerated under these reaction conditions. Notably, substrates containing meta substituents displayed excellent regioselectivity in both the acetoxylation and pivaloxylation reactions, producing the corresponding oxygenated products as single regioisomers in high yields (**2c**, **2f**−**h**, **2n**, **2o**, **2t**, **2u**). Remarkable site selectivity was also observed in acetoxylation and pivaloxylation of 2-naphthyl derivatives, yielding the desired compounds as sole isomers (entries **2l** and **2m**).

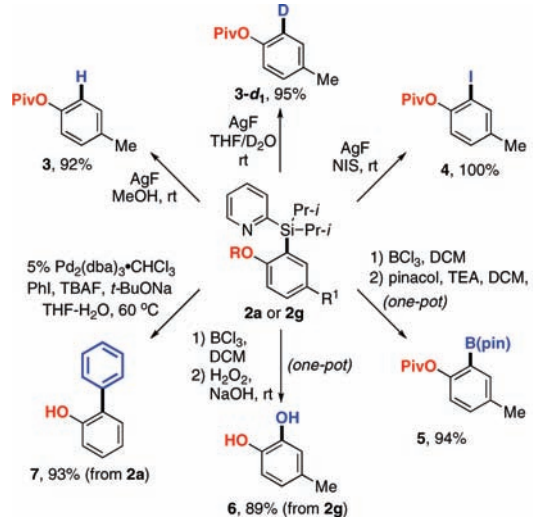
Our initial mechanistic studies indicated that electron-rich arenes were acyloxylated more rapidly than electron-deficient ones.[10,11] In addition, the substantial value of k_H/k_D (6.7) was observed in intramolecular kinetic isotope effect (KIE) studies of the pivaloxylation reaction of **1a-*d*$_1$** (Scheme 2).[12] It is believed that the present Pd-catalyzed acyloxylation reaction follows the C−H activation pathway.[3b,e,h,i,13]

Scheme 2. Intramolecular Kinetic Isotope Effect Studies



Naturally, after the development of the efficient directed C−H acyloxylation of arylsilanes, we explored further transformations of the PyDipSi group of the product **2g** (Scheme 3). First, it was found that the reaction of **2g** with AgF[14] in methanol resulted in efficient deprotection of the directing group, affording tolylpivalate (**3**) in 92% yield. Moreover, treatment of **2g** with AgF in tetrahydrofuran (THF)/D_2O produced the deuterated tolylpivalate **3-*d*$_1$** in 95% yield. Remarkably, use of a combination of AgF and *N*-iodosuccinimide (NIS) resulted in quantitative conversion of the PyDipSi group into an iodide functionality. The latter transformation, taken together with the installation and pivaloxylation steps, represents a formal three-step ortho oxygenation of 3-iodotoluene.[15] Furthermore, **2g** was converted into the synthetically valuable arylboronate **5**[16] in 94% yield via a one-pot sequence involving borodesilylation with

Scheme 3. Further Transformations of the PyDipSi Group



BCl_3followed by protection with pinacol.[17] In addition, borodesilylation of **2g** followed by oxidation in the presence of H_2O_2/NaOH produced substituted catechol **6** in excellent yield. Finally, it was found that the acetoxy derivative **2a** underwent an efficient Hiyama−Denmark cross-coupling[18] with phenyl iodide and subsequent hydrolysis of the acetoxy group, providing 2-phenylphenol (**7**) in 93% yield (Scheme 3).

In summary, we have shown that the PyDipSi group can serve as new, general directing group for the Pd-catalyzed acyloxylation of arenes, providing access to a variety of acetoxylated and pivaloxylated aromatic compounds in good yields. Most importantly, it was shown that this newly designed directing group could efficiently be cleaved or converted into other valuable functional groups such as iodide and boronate. Finally, borodesilylation of this directing group under oxidative conditions allowed for the preparation of a substituted catechol, whereas Hiyama−Denmark cross-coupling provides direct access to *o*-hydroxybiphenyl.

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Supporting Information Available: Detailed experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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