Organic Letters
Letter
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Palladium-Catalyzed Desilylative Acyloxylation of Silicon−Carbon Bonds on (Trimethylsilyl)arenes: Synthesis of Phenol Derivatives from Trimethylsilylarenes

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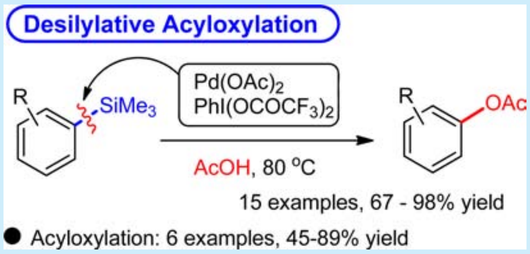
Supporting Information

ABSTRACT: A strategy for desilylative acetoxylation of (trimethylsilyl)arenes has been developed in which (trimethylsilyl)arenes are converted into acetoxyarenes. The direct acetoxylation is performed in the presence of 5 mol % of $Pd(OAc)_2$ and $PhI(OCOCF_3)_2$ (1.5 equiv) in AcOH at 80 °C for 17 h. The acetoxyarenes are obtained in good to high yields (67−98%). The synthetic utility is demonstrated with a one-pot transformation of (trimethylsilyl)arenes to phenols by successive acetoxylation and hydrolysis. Furthermore, desilylative acyloxylation of 2-(trimethylsilyl)naphthalene using several carboxylic acids has been conducted.



Silyl groups are important functional groups in organic synthesis and widely used for protection of OH and NH groups,[1] the Peterson olefination,[2] the Tamao−Fleming oxidation,[3] and the Hiyama coupling.[4] Recently, the use of a silyl group as a directing group in Pd-catalyzed C−H functionalization reactions is reported[5] where the silyl group can be removed by some reagents to introduce a new functionality.

Among the above reactions, the Tamao−Fleming oxidation is the most important reaction for converting organosilicon compounds to alcohols,[3] i.e., transformation of C−Si bonds to C−O bonds. Various alcohols can be prepared using the Tamao−Fleming oxidation. However, the silyl groups used for the Tamao oxidation are limited to those where the silicon atom has a heteroatom or hydrogen. Similarly, in the Fleming oxidation the aryl group of arylsilanes is in situ converted to hydrogen by protonolysis and then oxidized to alcohols. Therefore, these oxidations have not been applied to the oxidation of arylsilanes for the synthesis of phenols. Recently, the Fleming oxidation was applied to the synthesis of phenol derivatives, but this only occurred when strained siletanes were used.[6] In addition, the conversion of arylsilanes to phenols has been reported,[7] but the silyl groups necessarily contain heteroatoms or hydrogen. The outline concerning the Tamao−Fleming oxidation (a) and phenol synthesis from arylsilanes (b and c) is shown in Scheme 1.

Although the trimethylsilyl group is a readily available and popular functional group and widely used in organic synthesis,[8] it has not been applied to such oxidations giving phenols due to the stability of trimethylsilyl group. Therefore, direct transformation of an easily available trimethylsilyl group into the corresponding C−O bond is an important reaction in organic synthesis and is still challenging (Scheme 1, d).

Catalytic activation of the C−Si bond of arylsilanes has been widely studied in the cross-coupling reactions with aryl derivatives affording biaryls, where such conversions take place only in the cases of activated silyl groups such as pentafluorosilicate,[9] trialkoxysilyl,[10] triallylsilyl,[11] and aryl[2-hydroxymethyl]phenyldimethylsilanes.[12] The cross-coupling of arenes with (trimethylsilyl)arenes is very limited.[13] On the other hand, the Pd-catalyzed acetoxylation of C−H bonds of arenes has been recently studied as the synthesis of oxygenated arenes.[14] However, there are no examples that (trimethylsilyl)arenes are converted into the oxygenated arenes. Thus, we started to explore a novel and direct transformation of trimethylsilyl-substituted arenes into phenol derivatives and succeeded in the transformation by using $Pd(OAc)_2$ as a catalyst and $PhI(OCOCF_3)_2$ as an oxidant. Here we wish to report the palladium-catalyzed reaction transforming trimethylsilyl group into acyloxy groups as the first example.

First, we chose 1-fluoro-4-(trimethylsilyl)benzene (**1a**) as a model substrate, which is suitable for monitoring the reaction by ^{19}F NMR. Before optimizing the reaction conditions for the $Pd(OAc)_2$-catalyzed acetoxylation of **1a**, we examined several solvents using $PhI(OAc)_2$ as an oxidant, since $PhI(OAc)_2$ has been recently received much attention as an excellent, terminal oxidant in the Pd-catalyzed reactions.[15] We found that AcOH was the best solvent giving the product, 4-fluorophenyl acetate (**2a**), in 32% yield (Scheme 2). Product **2a** was not formed in other solvents such as DMF, MeCN, DCE, THF, and DME. Addition of Ac_2O in AcOH decreased product **2a** to 16%. The details are given in the Supporting Information.

As we obtained **2a** in 32% yield in the reaction with $PhI(OAc)_2$ as an oxidant in AcOH, we next examined the

Received: August 11, 2015
Published: September 24, 2015

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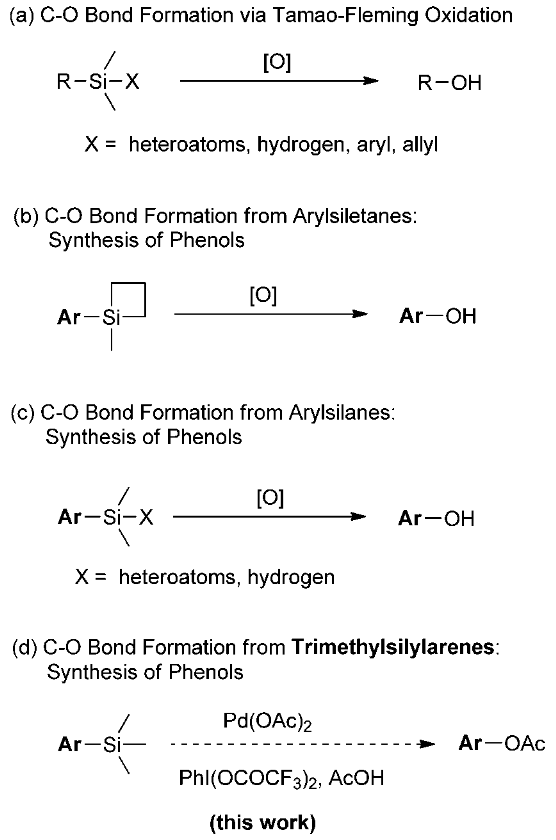
DOI: 10.1021/acs.orglett.5b02336
Org. Lett. 2015, 17, 4778−4781

Scheme 1. C−O Bond Formation from Arylsilanes



Scheme 2. Desilylative Acetoxylation of 1a Using PhI(OAc)$_2$

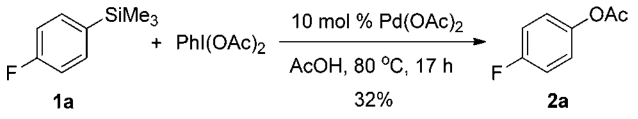
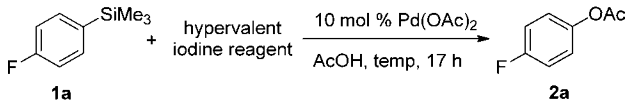


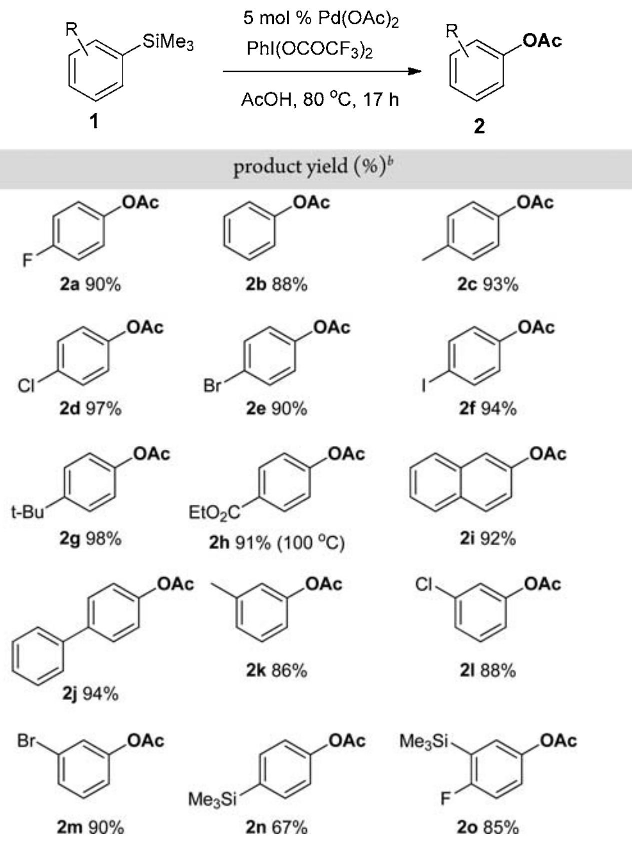
Table 1. Acetoxylation of 1a by Pd-Catalyzed Reaction[a]



entry	hypervalent iodine reagent	temp (°C)	yield[b] (%)
1	PhI(OAc)$_2$	80	32
2	PhI(OAc)$_2$	100	67
3	PhI(OAc)$_2$	120	81
4	PhI(OAc)$_2$[c]	100	69
5	PhI(OAc)$_2$[d]	100	78
6	PhI(OH)OTs	80	24
7	PhIO	80	33
8	PhI(OCOCF$_3$)$_2$	80	80
9	PhI(OCOCF$_3$)$_2$[c]	80	>99
10	PhI(OCOCF$_3$)$_2$[c,e]	80	>99
11	PhI(OCOCF$_3$)$_2$[c,f]	80	91
12	**3**	80	>99

[a] Conditions: **1a** (0.2 mmol), hypervalent iodine reagent (0.2 mmol), Pd(OAc)$_2$ (0.02 mmol), solvent (1 mL), 80 °C, and 17 h. [b] Yield was determined by ^{19}F NMR using hexafluorobenzene as an internal standard. [c] A hypervalent iodine reagent (0.3 mmol) was added. [d] A hypervalent iodine reagent (0.4 mmol) was added. [e] Pd(OAc)$_2$ (5 mol %) was used. [f] Pd(OAc)$_2$ (1 mol %) was used.

Table 2. Acetoxylation of 1 by Pd-Catalyzed Reaction[a]



[a] Conditions: **1** (0.4 mmol), PhI(OCOCF$_3$)$_2$ (0.6 mmol), Pd(OAc)$_2$ (0.02 mmol), AcOH (1 mL), 80 °C, and 17 h. [b] Isolated yield from column chromatography on silica gel.

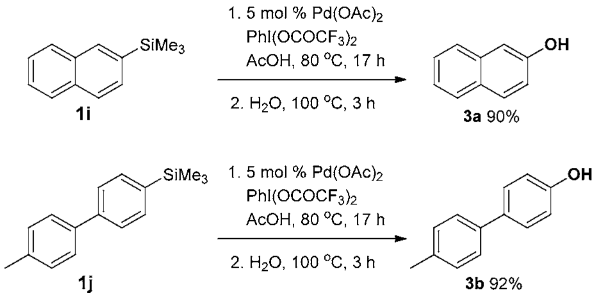
reaction temperature. The results are given in Table 1. When the reaction was conducted at 100 °C, the yield of **2a** was increased to 67% (entry 2). Furthermore, the yield was reached to 81% by elevating the temperature to 120 °C (entry 3). The amount of PhI(OAc)$_2$ was increased in the reaction at 100 °C, but the yield of **2a** was not improved (entries 4 and 5). Other hypervalent iodine reagents such as Koser's salt, PhI(OH)OTs, and PhIO were tested for this acetoxylation at 80 °C, but we found that these reagents were not effective (entries 6 and 7). Surprisingly, the use of bis(trifluoroacetoxy)iodobenzene PhI(OCOCF$_3$)$_2$ much improved the yield of **2a** under the mild conditions (80 °C), giving **2a** in 80% yield (entry 8). The increase of the amount of PhI(OCOCF$_3$)$_2$ provided **2a** in a quantitative yield (entry 9). Even in the cases of less loading Pd(OAc)$_2$ catalyst (5 and 1 mol %), product **2a** was formed in high yields (entries 10 and 11). Similarly, μ-oxo-bridged reagent, μ-oxodiphenylbis(trifluoroacetato-*O*)diiodine [[PhI(OCOCF$_3$)]$_2$O] (**3**), played an excellent role and gave **2a** in a quantitative yield (entry 12). Among the hypervalent oxidants, we adopted PhI(OCOCF$_3$)$_2$ as the terminal oxidant because it was easily available.

With the optimized conditions in hand, we examined a variety of (trimethylsilyl)arenes to determine the scope of this acetoxylation reaction. The results are given in Table 2. Various (trimethylsilyl)arenes **1** bearing alkyl groups and halogens at the *para* position underwent the desilylative acetoxylation reaction to give the corresponding *p*-acetoxyarenes **2** in high yields (88−98%). It is noteworthy that iodo and bromo substituents are inert under the optimized conditions.

(Trimethylsilyl)arene **1h** with an electron-withdrawing ethoxycarbonyl group showed less reactivity but gave *p*-acetoxyarene **2h** in 91% yield when the reaction was conducted at 100 °C. This desilylative acetoxylation could be applied to naphthalene and biphenyl derivatives **1i** and **1j**, affording **2i** and **2j** in 92 and 94% yields, respectively. However, this desilylative acetoxylation could not be applied to strongly electron-rich 1-methoxy-4-(trimethylsilyl)benzene and 1-(dimethylamino)-4-(trimethylsilyl)benzene. The desilylative acetoxylation reaction efficiently proceeded in the cases of *meta*-substituted (trimethylsilyl)arenes. (Trimethylsilyl)arenes **1** bearing methyl, bromo, and chloro substituents at the *meta* position were converted into the corresponding *m*-acetoxyarenes **2** in high yields (86−90%). However, the presence of substituents (Ph, Cl, and F) at the *ortho* position inhibited the desilylative acetoxylation reaction completely. Furthermore, we examined synthesis of acetoxyarenes with trimethylsilyl group as a sensitive functional group since trimethylsilyl group can be transformed to various useful functional groups. Bis(trimethylsilyl)arenes (**1n** and **1o**) were used for the desilylative acetoxylation reaction. Only one of two trimethylsilyl groups was converted into acetoxy group to give acetoxyarenes **2n** and **2o** in 67 and 85% yields, respectively.

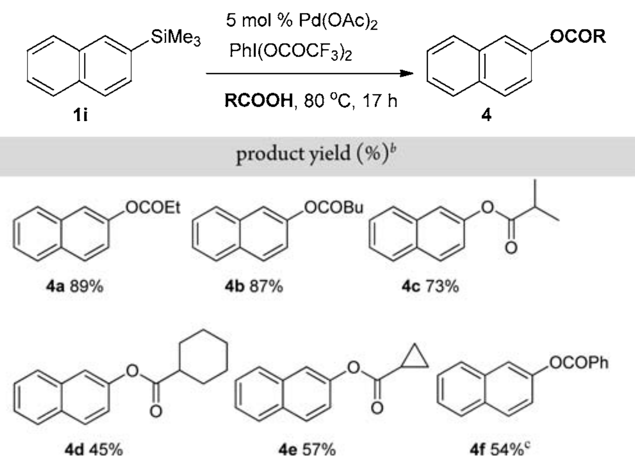
In order to examine the synthetic usefulness of acetoxylated products **2**, we tried to convert (trimethylsilyl)arenes **1** into phenols **3** directly. Since the acetoxy group of **2** is removed by hydrolysis, the acetoxylated products obtained in situ under the optimized conditions was refluxed in water after addition of water. Actually, phenols **3a** and **3b** were obtained in 90 and 92% yields, respectively, by the one-pot reactions (Scheme 3).

Scheme 3. One-Pot Transformation of Trimethylsilylarenes 1 to Phenols 3



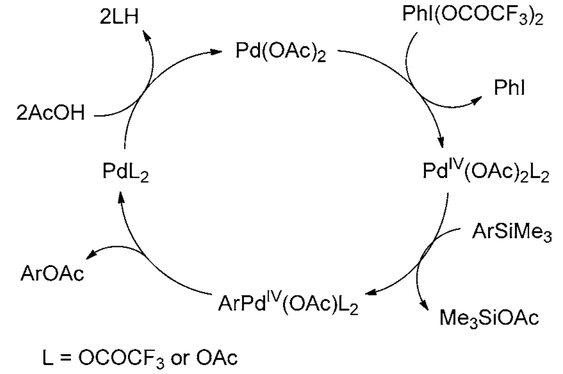
Furthermore, we explored the possibility for transformation of (trimethylsilyl)arenes **1** using other carboxylic acids. We examined the reaction of 2-(trimethylsilyl)naphthalene (**1i**) as a model substrate with various carboxylic acids under the optimized conditions. The results are given in Table 3. Propanoic acid, pentanoic acid, 2-methylpropanoic acid, cyclohexanecarboxylic acid, cyclopropanecarboxylic acid, and benzoic acid underwent the desilylative acyloxylation of **1i** to give the corresponding 2-acyloxynaphthalenes **4** in good to high yields. In the case of a sterically hindered pivalic acid, the desilylative acyloxylation reaction did not proceed.

Table 3. Desilylative Acyloxylation of 1i with Various Carboxylic Acids[a]



[a]Conditions: **1i** (0.4 mmol), $PhI(OCOCF_3)_2$ (0.6 mmol), $Pd(OAc)_2$ (0.02 mmol), RCOOH (1 mL), 80 °C, and 17 h. [b]Isolated yield from column chromatography on silica gel. [c]PhCOOH (0.5 g) and DCE (0.5 mL) were used instead of RCOOH.

Scheme 4. Possible Mechanism for Desilylative Acetoxylation of (Trimethylsilyl)arenes



The desilylative acetoxylation of a (trimethylsilyl)arene **1** using $Pd(OAc)_2$ as a catalyst and $PhI(OCOCF_3)_2$ as a terminal oxidant may be considered to proceed via Pd-induced C−Si bond activation generating an arylpalladium(IV) intermediate followed by reductive elimination, as shown in Scheme 4. This kind of mechanism involving a high oxidation state Pd(IV) species has been proposed for $Pd(OAc)_2$-catalyzed acetoxylation of C−H bonds of arenes with $PhI(OAc)_2$.[15] According to this mechanism, a (trimethylsilyl)arene is considered to undergo the C−Si bond cleavage by $Pd(OAc)_2$ to give an ArPd(II)OAc intermediate, which is oxidized by $PhI(OCOCF_3)_2$ to a ArPd(IV) intermediate. However, the Pd-catalyzed reaction of **1a** without $PhI(OCOCF_3)_2$ in AcOH did not proceed and **1a** was recovered unchanged. In addition, the reaction of **1a** with styrene or *tert*-butyl acrylate in the presence of $Pd(OAc)_2$ (5 mol % or 1 equiv) was conducted at 80 °C for 17 h in AcOH, but no coupling products were formed. These results suggest that the reaction of **1a** with $Pd(OAc)_2$ does not occur. Although the reaction mechanism for the desilylative acetoxylation is not clear at present, the ArPd(IV) species may be formed by oxidation of $Pd(OAc)_2$ with $PhI(OCOCF_3)_2$ followed by electrophilic substitution of $ArSiMe_3$. Recently, it has been reported that the Pd-catalyzed acetoxylation of pyrroles proceeds via phenyliodonium acetates.[14i] Although we conducted the reaction of **1a** with $PhI(OAc)_2$ or $PhI(OCOCF_3)_2$ in AcOH, we could not obtain diphenyliodonium salts in the reaction at 80 °C. In the present case, therefore, the possibility of the acetoxylation via phenyliodonium salts is ruled out.

In summary, we have demonstrated that desilylative acetoxylation of (trimethylsilyl)arenes proceeds efficiently in

DOI: 10.1021/acs.orglett.5b02336
Org. Lett. 2015, 17, 4778−4781

the presence of $Pd(OAc)_2$ (5 mol %) and $PhI(OCOCF_3)_2$ in AcOH at 80 °C. Various substituted (trimethylsilyl)arenes undergo the desilylative acetoxylation to give the corresponding acetoxyarenes in high yields. This acetoxylation is applied to one-pot synthesis of phenols from (trimethylsilyl)arenes. Furthermore, the possibility for acyloxylation using several carboxylic acids has been demonstrated. The use of "non-activated" (trimethylsilyl)arenes for acetoxylation or acyloxylation provides a practical and efficient synthesis of phenol derivatives. Therefore, further studies concerning the application and the mechanistic elucidation are future subjects.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02336.

Additional data and NMR spectra of the products (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (25410048).

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