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Synthesis of Acylsilanes by Palladium-catalyzed Cross-coupling Reaction of Thiol Esters and Silylzinc Chlorides

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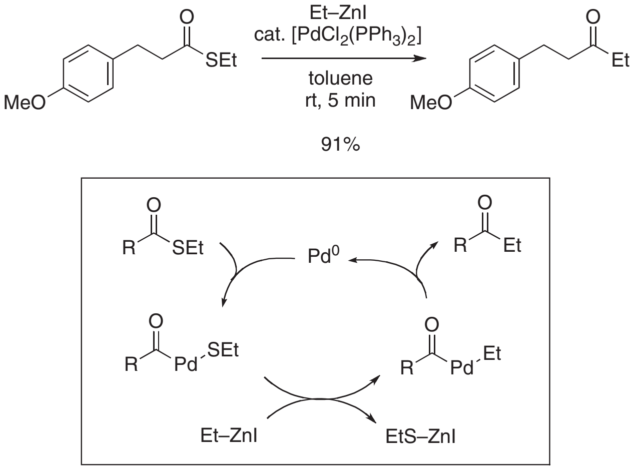
An acylsilane synthesis by a Pd-catalyzed cross-coupling reaction of thiol esters and silylzinc chlorides was developed. *S*-Phenyl thiol esters with a variety of functional groups were converted to corresponding acylsilanes.

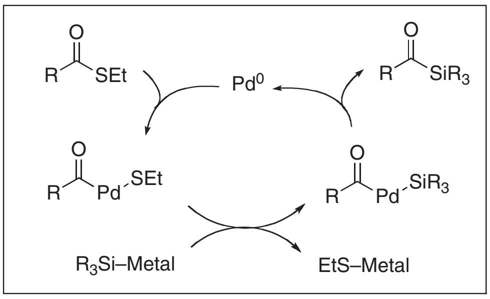
Since acylsilanes possess a variety of unique reactivities,[1] their synthesis has been an important research topic in organic chemistry.[1p–1r,2–4] Brook[2a] and Corey[2b] independently reported representative methods to prepare acylsilanes by silylation of a lithiated dithiane followed by removal of dithiane. Acylsilanes are also synthesized by 1,2-addition of silyllithium to aldehydes followed by oxidation according to a procedure of Reich.[5] However, both methods have only limited functional group compatibility since they use strong bases such as *n*-BuLi. To circumvent these problems, palladium-catalyzed cross-coupling of acid chlorides with disilane[4a–4d] or stannylsilane[4e] has recently been reported. These methods, however, are unsatisfactory because they require harsh conditions such as heating at high temperature without solvent. On the other hand, thiol esters are a suitable substrate for cross-coupling reactions based on oxidative addition of a transition-metal catalyst to the C–S bond.[6,7] Under this background, we initiated a study of the transformation of thiol esters to acylsilanes. Herein, we report a mild synthesis of acylsilanes by palladium-catalyzed cross-coupling of thiol esters and silylzinc chlorides.

Based on the proposed reaction mechanism for the palladium-catalyzed cross-coupling reaction of thiol esters with organozinc reagent (Scheme 1), we considered a working hypothesis for transformation of thiol esters to acylsilanes as shown in Scheme 2. Oxidative addition of palladium(0) to the C–S bond of the thiol ester gives acyl palladium species which should be transformed to the acylsilane via transmetalation with a silyl metal reagent followed by reductive elimination with regeneration of Pd(0).

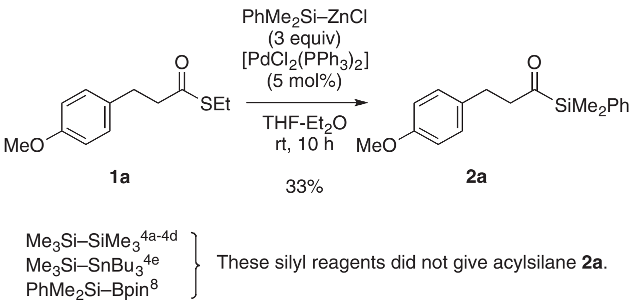
With this idea in mind, we explored a suitable silyl metal reagent for the expected cross-coupling reaction. Using thiol ester **1a** as the model substrate, various silyl metal reagents[4,8] were tested for ketone synthesis using $[PdCl_2(PPh_3)_2]$. However, silylating reagents, which act as silyl anion sources, did not provide the desired acylsilane (Scheme 3). Eventually, we found that the cross-coupling reaction proceeded when using $PhMe_2Si–ZnCl$[9,10] although the yield was low.



Scheme 1. Palladium-catalyzed ketone synthesis.



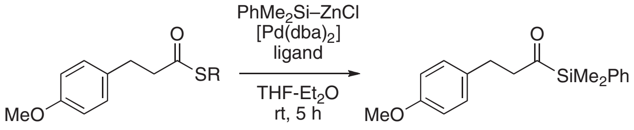
Scheme 2. Working hypothesis for acylsilane formation.



Scheme 3. Reaction using various silyl metal reagents.

This promising result prompted us to optimize the process regarding thiol ester substrate, ligand, and catalyst. First, we observed a significant structure effect on the reaction rate in a comparison of thiol esters **1a**, **1b**, and **1c** (Table 1). Thus, the reaction of **1a** or **1b** using a combination of $[Pd(dba)_2]$ and Ph_3P provided the desired acylsilane **2a** in 33–34% yield with recovery of a substantial amount of thiol esters (Entries 1 and 2). In contrast, the use of thiol ester **1c** derived from benzenethiol resulted in rapid conversion (Entry 3).[11] Then we carried out ligand screening using **1c** as a substrate. Yield of acylsilane **2a** strongly depended on the choice of ligand. Thus, the reaction using tricyclohexylphosphane gave the best yield (Entries 3–6). The bulky and electron-rich trialkylphosphane ligand would

Table 1. Effects of thiol ester and phosphorus ligand



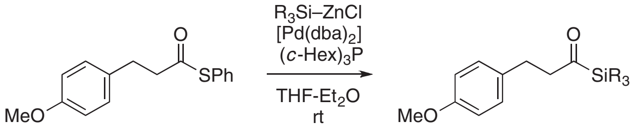
1a: R = Et
1b: R = Me
1c: R = Ph

2a

Entry^a	R	Ligand	**1**/%	**2a**/%
1	Et	Ph_3P	19^b	34^b
2	Me	Ph_3P	15^b	33^b
3	Ph	Ph_3P	1^b	31^b
4	Ph	(*c*-Hex)Ph_2P	—^{c}	37^d
5	Ph	(*c*-Hex)$_2$PhP	1^b	58^b
6	Ph	(*c*-Hex)$_3$P	—^{c}	91^d
7^e	Ph	—	73^d	0^d

^{a}PhMe$_2$Si–ZnCl (3 equiv), [Pd(dba)$_2$] (10 mol %), ligand (20 mol %). ^{b} ^{1}H NMR yield. ^{c}Not detected by ^{1}H NMR. ^{d}Isolated yield. ^{e}In the absence of [Pd(dba)$_2$] and a phosphorus ligand.

Table 2. Cross-coupling reaction with silylzinc chlorides



1c **2b-c**

Entry^a	$R_3SiZnCl$	Time/h	Yield/%^{b}
1	$Me_3SiZnCl$	1	69
2	$Ph_3SiZnCl$	10	83

^{a}R$_3$Si–ZnCl (3 equiv), [Pd(dba)$_2$] (10 mol %), (*c*-Hex)$_3$P (20 mol %). ^{b}Isolated yield.

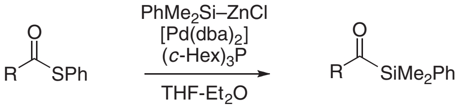
accelerate smooth reductive elimination. A control experiment without the palladium catalyst and ligand did not provide **2a** excluding a mechanism via a simple 1,2-nucleophilic addition of the silylzinc chloride to carbonyl carbon of the thiol ester (Entry 7).

The optimized reaction conditions were also feasible for trimethylsilylzinc chloride and triphenylsilylzinc chloride to give the corresponding acylsilanes in good to excellent yields (Table 2, Entries 1 and 2).

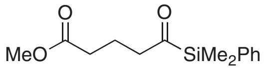
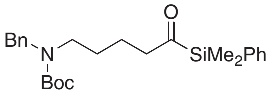
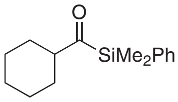
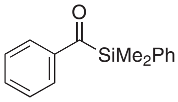
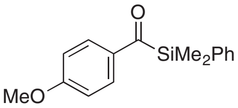
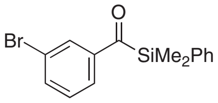
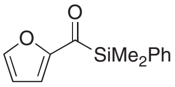
We then investigated the scope of thiol esters using PhMe$_2$SiZnCl (Table 3). Ester and the protected amino group remained untouched under the reaction conditions (Entries 1 and 2). The reaction was applied to the hindered substrate to give the desired acylsilane in excellent yield (Entry 3). *S*-Phenyl thiobenzoates were smoothly converted to the corresponding acylsilanes, which is quite superior to the recently reported method for preparing acylsilanes from morpholine amide and silyllithium species,[12] since the use of aryl morpholine amides resulted in low yield due to the Brook rearrangement (Entries 4–6). The reaction conditions were also compatible with the furyl group (Entry 7).

In summary, we developed a novel synthesis of acylsilanes by palladium-catalyzed cross-coupling reaction of thiol esters and silylzinc chlorides. Due to the mildness of the reaction conditions, this methodology would allows for the versatile preparation of highly functionalized acylsilanes. In addition, use of thiol esters should be advantageous over the reaction of acid chloride due to its relatively high stability even with various functional groups and its easy accessibility from the corresponding carboxylic acids.

Table 3. Substrate scope of thiol esters



3a-g **4a-g**

Entry^a	Product	Time/h	Yield/%^{b}
1		2	59
2		0.5	86
3		10	87
4		2	73
5		2	71
6^c		2	45
7^c		12	53

^{a}R$_3$Si–ZnCl (3 equiv), [Pd(dba)$_2$] (10 mol %), (*c*-Hex)$_3$P (20 mol %). ^{b}Isolated yield. ^{c}[Pd(dba)$_2$] (20 mol %), (*c*-Hex)$_3$P (40 mol %).

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