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An iterative approach to the synthesis of thiophene-based organic dyes

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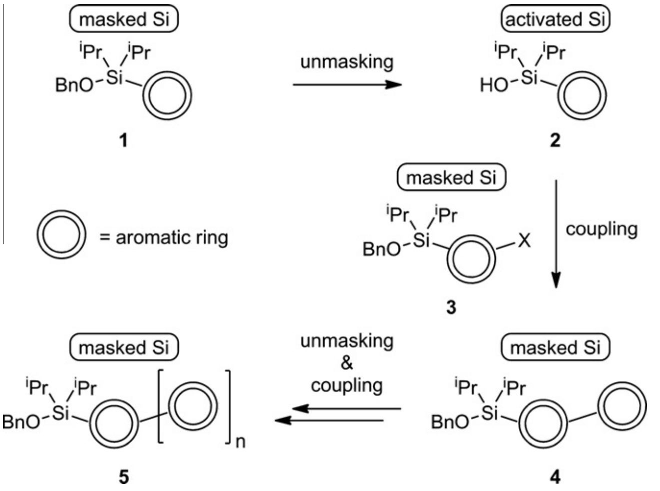
ABSTRACT

We developed an iterative synthetic method for oligo-aryl compounds using an organosilicon-based palladium-catalyzed cross-coupling reaction. Aryl compounds containing a benzyloxy(diisopropyl)silyl group (masked Si group) had sufficient chemical stability, and the unmasking step proceeded in a high yield under mild conditions. Both of the key unmasking/coupling steps required no strict anhydrous or degassed conditions. The developed procedure was used for the synthesis of thiophene-based organic dyes for dye-sensitized solar cells.

Thiophene-based organic dyes make up a very important class of compounds because they show promise as sensitizers for dye sensitized solar cells (DSSCs)[1–5] and as donor materials for small-molecule organic solar cells.[6,7] Palladium-catalyzed cross-coupling reactions (i.e., Suzuki–Miyaura,[8,9] Migita–Kosugi–Stille,[10–13] Kumada–Tamao,[14] Negishi,[15] Hiyama[16] coupling and so on[17]) are a particularly powerful tool for the preparation of thiophene-based dyes. Iterative palladium-catalyzed cross-coupling approaches[18–24] have garnered much attention because they can produce structurally diverse compounds from a somewhat-limited number of synthetic operations (activation/unmasking of unreactive groups and coupling), thus, this approach is suitable for laboratory automation.[24–29] It would be desirable for the development of an iterative approach to meet the following criteria: (**1**) that a readily available, non toxic, and environmentally benign substrate be employed with the generation of no toxic compound; (**2**) both the activation/unmasking and the coupling steps should have good yields and not require strict anhydrous and/or degassed conditions; and, (**3**) a substrate with an unreactive group should have enough stability so that the compound can be readily isolated and stored with the activation/unmasking step carried out under mild reaction conditions in one step. Hiyama, Nakao et al. reported an elegant silicon-based iterative palladium-catalyzed cross-coupling approach.[21] Organosilicon compounds are readily available, non toxic, and environmentally benign.

We have reported the combinatorial synthesis of aryl compounds based on palladium-catalyzed cross-coupling reactions in solution and in a solid phase.[30–32] Here, we wish to report the development of an iterative synthetic method for oligo-aromatic ring compounds using a silicon-based palladium-catalyzed cross-coupling reaction and its application to the synthesis of thiophene-based organic dyes for DSSC.

Denmark et al. reported a silicon-based cross-coupling reaction using dimethylsilanol[33] as an activating group. In the course of the solid-phase synthetic study using a silyl linker,[31,34–36] Showalter and co-workers ascertained that the benzyloxy(diisopropyl)silyl group can be converted into the corresponding diisopropylsilanol



Scheme 1. An iterative approach for the synthesis of oligo-aromatic ring compounds.

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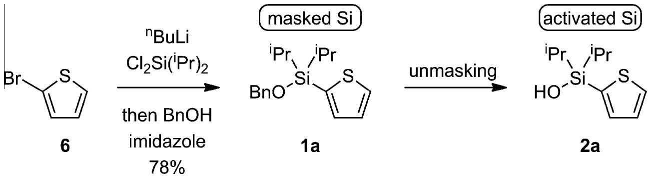
Table 1
Examination of the unmasking step to afford **2a** from **1a**



Entry	Reagent	Solvent	Yield[a] (%)
1	TBAF	THF	0%
2	TBAF	THF/H_2O	58%
3	TBAF	1,4-Dioxane/H_2O	72%
4	CsF	1,4-Dioxane/H_2O	No reaction
5	TFA	1,4-Dioxane/H_2O	0%
6	PPTS	MeOH/H_2O	39%
7	*p*-TsOH·H_2O	Acetone	37%
8	*p*-TsOH·H_2O	Acetone/H_2O	94%

[a] Isolated yield.

under mild reaction conditions (TBAF in THF).[37] According to suggestions in these reports, we developed the synthetic plan shown in Scheme 1. We anticipated that aromatic ring **1** with a benzyloxy(diisopropyl)silyl (masked Si) group would be sufficiently stable, in addition, it could be readily unmasked under mild reaction conditions in one step to afford compound **2** with a diisopropylsilanol (activated Si) group. We planned to couple compound **2** with aromatic ring **3** retaining both halogen and masked Si groups to afford the desired coupling product **4**. By repeating the unmasking and the coupling steps, the aimed oligo-aromatic ring compound **5** would be synthesized.

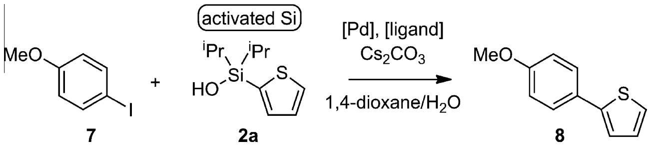
The unmasking step (**1a**–**2a**) was initially examined (Table 1). A one-pot, three-component coupling of 2-bromothiophene (**6**) and dichlorodiisopropylsilane with benzyl alcohol afforded 2-benzyloxy(diisopropyl)silyl-thiophene (**1a**) in a high yield.[38] The previously reported combination of TBAF in THF[37] did not afford the desired silanol **2a** and only the cleavage of the thiophene-Si bond was observed (entry 1). Interestingly, the addition of H_2O was effective in this reaction (entries 2 and 3). An excellent yield (94%) was observed from the combination of *p*-TsOH·H_2O in acetone/H_2O (entry 8). Again, the addition of H_2O was crucial to a high yield under these acidic conditions (entries 7 and 8).

We examined the key cross-coupling reaction of **2a** with 4-iodoanisole (**7**),[39] as shown in Table 2. According to a previous report,[33] combinations of $[allylPdCl]_2$ and ligands with Cs_2CO_3 in 1,4-dioxane/H_2O were examined (entries 1–12). Only the combination of 10 mol % $[allylPdCl]_2$ and $AsPh_3$ gave a satisfactory yield (entry 12). Various palladium reagents were examined in the presence of the $AsPh_3$ ligand (entries 12–19). However, an improvement in yield was not observed.[40]

The amount of H_2O influenced the results of the reaction (Table 3). A low yield was observed without the addition of H_2O (entry 1). The yield was improved by increasing the amount (1 equiv to 20 equiv) of H_2O (entries 1–6). However, the addition of a larger amount (80 equiv) of H_2O degraded the yield (entry 8). Thus, the optimal amount of H_2O was determined to be 20 equiv It should be noted that both the unmasking/coupling steps afforded reproducible results, and can be performed in the presence of H_2O, and neither required strict anhydrous nor degassed conditions.

The coupling reaction between **3a**, 3b,[41] and **2a**–**2c** was examined based on our developed procedure (Table 4). All the coupling products, **4a**–**4d** and **9**, were obtained in moderate to satisfactory yields.

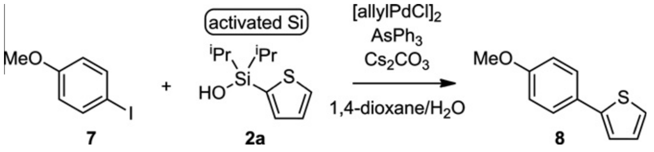
Table 2
Examination of the coupling step to afford **8** from **2a**



Entry	[Pd]	[Ligand]	Yield[a] (%)
1	$[AllylPdCl]_2$	PPh_3	12
2	$[AllylPdCl]_2$	PCy_3	25
3	$[AllylPdCl]_2$	P(2-furyl)$_3$	29
4	$[AllylPdCl]_2$	P(*o*-tolyl)$_3$	13
5	$[AllylPdCl]_2$	P(tBu)$_3$	34
6	$[AllylPdCl]_2$	dppe	11
7	$[AllylPdCl]_2$	dppp	28
8	$[AllylPdCl]_2$	dppb	37
9	$[AllylPdCl]_2$	dppf	19
10	$[AllylPdCl]_2$	Xantphos	19
11	$[AllylPdCl]_2$	Xphos	25
12	$[AllylPdCl]_2$	$AsPh_3$	65
13	$Pd(OAc)_2$	$AsPh_3$	6
14	$PdCl_2$	$AsPh_3$	21
15	$PdCl_2(MeCN)_2$	$AsPh_3$	8
16	$PdCl_2(PPh_3)_2$	$AsPh_3$	11
17	$PdCl_2$(dppf)	$AsPh_3$	12
18	$Pd(PPh_3)_4$	$AsPh_3$	9
19	$Pd_2(dba)_3·CHCl_3$	$AsPh_3$	8

[a] Isolated yield.

Table 3
Influence of H_2O amount on the coupling of silanol **2a** and 4-iodoanisole (**7**)



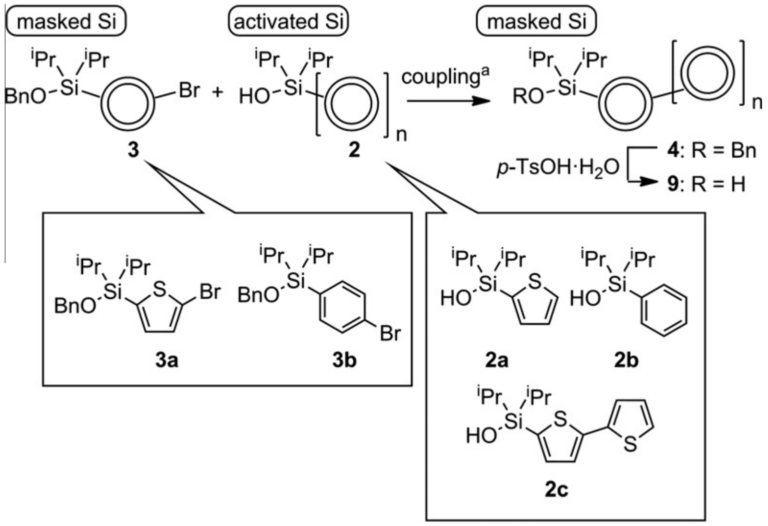
Entry	H_2O	Yield[a] (%)	Entry	H_2O	Yield[a] (%)
1	None	30	5	10 equiv	54
2	1 equiv	33	6	20 equiv	65
3	3 equiv	41	7	40 equiv	62
4	5 equiv	55	8	80 equiv	26

[a] Isolated yield.

The developed method was applied to the synthesis of thiophene-based dyes **15**[42–44] and **16**[45–48] for the dye-sensitized solar cell shown in Scheme 2. Both building block **2a** with an activated Si group and building block **3a** with masked Si- and bromo-groups were prepared from the common starting material, 2-benzyloxy(diisopropyl)silyl-thiophene (**1a**) in good yields. The palladium-catalyzed cross-coupling of **2a** with **3a** afforded the desired product **4a** in a 53% yield. A subsequent unmasking of benzyl silyl ether **4a** produced bithiophene **2c** in a 91% yield. Prepared monothiophene **2a** and bithiophene **2c** were coupled with 4-bromo triphenylamine (**10**) to afford the desired coupling products **11** and **12** in moderate yields. Formylation of compounds **11** and **12** by hexamethylenetetramine under microwave irradiation,[49] and the subsequent Knoevenagel condensation with *tert*-butyl cyanoacetate, all were carried out in one-pot reactions. Finally, the acid-mediated removal of *tert*-butyl groups proceeded smoothly to afford the desired thiophene-based dyes **15** and **16** in excellent yields. The developed synthetic scheme does not require strict anhydrous nor degassed conditions.

In conclusion, we have developed an iterative synthetic method for oligo-aryl compounds using an organosilicon-based palladium-catalyzed cross-coupling reaction. Aryl compounds containing a benzyloxy(diisopropyl)silyl group (masked Si group) have

Table 4
Palladium-catalyzed cross-coupling between **3a**,**b** and **2a**–**2c**



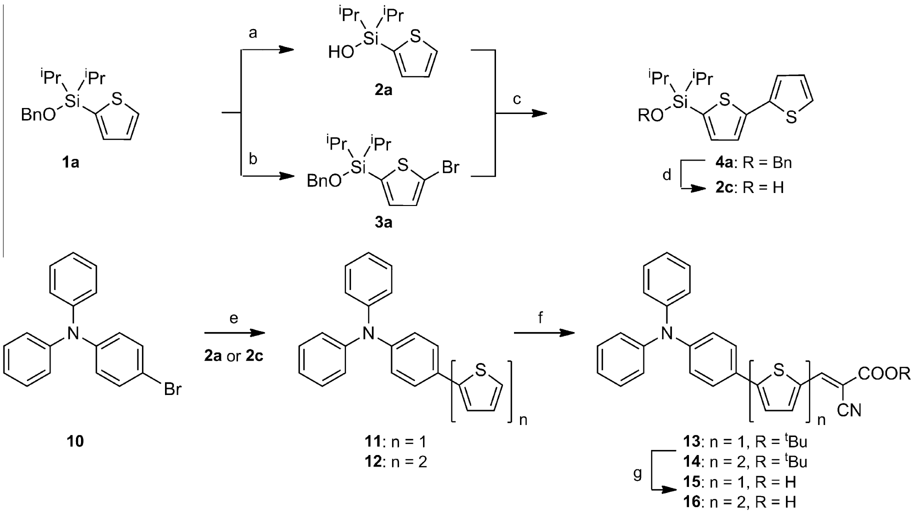
Entry	Sub	Sub	Pro	Yield[b] (%)
1	**3a**	**2a**	**4a**	53
2	**3a**	**2b**	**4b**	48
3	**3a**	**2c**	**9**	40[c] (67)[d]
4	**3b**	**2a**	**4c**	47
5	**3b**	**2b**	**4d**	50

Reagents and condition: 10 mol % $[allylPdCl]_2$, $AsPh_3$, Cs_2CO_3, 1,4-dioxane/H_2O, 90–100 °C, 12–24 h.

[b] Isolated yield.

[c] Overall yield from **2c**.

[d] Yield based on recovered **2c**.



Scheme 2. Synthesis of thiophene-based organic dyes **15** and **16** for DSSC based on our developed iterative synthetic approach. Reagents and conditions: (a) *p*-TsOH·H_2O, acetone/H_2O, rt, 8 h, 94% (b) NBS, K_2CO_3, CH_2Cl_2, rt, 4 h, 85% (c) 10 mol % $[allylPdCl]_2$, $AsPh_3$, Cs_2CO_3, 1,4-dioxane/H_2O, 90 °C, 12 h, 53% (d) *p*-TsOH·H_2O, acetone/H_2O, rt, 8 h, 91% (e) 10 mol % $[allylPdCl]_2$, $AsPh_3$, Cs_2CO_3, 1,4-dioxane/H_2O, 90 °C, 12 h (**11**: 49%, **12**: 38%) (f) hexamethylenetetramine, AcOH/H_2O, microwave irradiation, 150 °C, 1 h then *tert*-butyl cyanoacetate, NH_4OAc, 70 °C, 12 h {**13**: 67% (83% based on recovered **11**), **14**: 38% (81% based on recovered **12**)} (g) TFA, CH_2Cl_2, rt, 2 h, (**15**: 98%, **16**: 95%).

sufficient chemical stability, and the unmasking step proceeded in a high yield under mild acidic conditions. Both the key unmasking/coupling steps require no strict anhydrous and/or degassed conditions. The developed procedure was used for the synthesis of thiophene-based dyes **15** and **16**. Mono- and bi-thiophene compounds **2a** and **2c** were prepared in satisfactory yields. The coupling of thiophenes **2a** and **2c** with a triphenylamine moiety and our originally developed one-pot formylation/Knoevenagel condensation afforded the desired thiophene-based dyes. We want to again emphasize that this developed procedure requires no strict anhydrous or degassed conditions.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.04.059. These data include MOL files and InChiKeys of the most important compounds described in this article.

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