Stille Reaction on Pyridinium Cations

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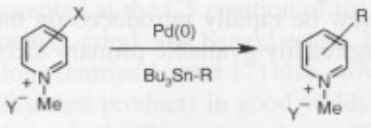
Abstract: A novel unit based on pyridinium cations has been synthesized by the Stille reaction and represents a model for development of molecular electronic devices.

Key words: heteroaromatic cations, Stille reaction, molecular electronic devices

The preparation of organic molecules with extended π-conjugation has attracted considerable attention because such materials exhibit interesting properties and can serve as models for the construction of nanoarchitectures. Molecular wires, electron-conducting devices and molecular machines are all fields of active investigation, to name a few examples.[1] Recent studies have shown that oligo(phenyleneethynylene)s containing nitro groups **1** (Figure 1) are good candidates for electronic switching and memory devices,[2] and attachment of terminal groups to one or both ends of the molecule could make them function as so-called molecular alligator clips.[3]

In this context, we considered that the presence of heteroaromatic cations in a π-conjugated system, such as **2** (Figure 1), could lead to a new class of compounds with potentially interesting properties such as electronic conductivity, electrochromism, and optical non-linearity, among others.[4]

With this target in mind, azinium cations were chosen as key building blocks and palladium coupling processes as methods to create the core units. Palladium-catalyzed reactions have emerged as powerful tools for C–C bond formation[5] and have been applied to a variety of heterocyclic substrates.[6] However, a coupling route involving heteroaromatic cations is a field that has received little attention. To our knowledge, only one example has been reported by Zoltewicz[7] from *N*-functionalized pyridylstannanes. More recently we described the first example[8] of Stille reaction[9] involving quinolizinium cations. In the present paper, we wish to report our results using the Stille reaction for the successful substitution of pyridinium salts (Scheme 1) as a model for the preparation of the novel systems **2**.



3a, X= 3-Br
3b, X= 2-Br
3c, X= 4-Br

4 - 6

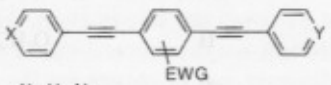
Y^- = I, TsO

Scheme 1

3-Bromo-*N*-methylpyridinium iodide **3a** was treated with tributylvinylstannane in the presence of 5 mmol% $Pd(PPh_3)_4$ in DMF at room temperature with 10 mmol% copper(I) iodide as co-catalyst (Method A).[10] In this case, however, only traces of the desired derivative were obtained. Repeated attempts at 80 °C gave the 3-vinyl derivative **4a** in only 20% yield. In contrast, coupling of **3a** with donor[11] units such as phenylethynyl-, phenyl-, 2-thienyl-, 2-furanyl- and *N*-methyl-2-pyrrolyl tributylstannane gave moderate yields, even after heating (80 °C) in some cases.

After considering alternatives to prepare the desired vinyl derivative **4a**, coupling of **3a** with tributylvinyltin was tested in the presence of tri-*ortho*-tolylphosphine (5 mmol%) and tris(dibenzylideneacetone)dipalladium (5 mmol%) [$P(o\text{-Tol})_3/Pd_2(dba)_3$] at 80 °C for 1.5 hours in DMF. This reaction gave **4a** in 63% yield. These new reaction conditions (Method B)[12] were successfully applied to the coupling of **3a** with phenyl- and 2-furanyl tributylstannane as representative examples. The results summarized in Table 1 show the most satisfactory yields under the conditions used for **3a**.

On the basis of these results, we focused our attention on coupling with π-deficient stannanes, which would produce units with linkers for subsequent coordination (Table 1, entries 7–9). Initially, 2- and 4-pyridinylstannanes were tested, yielding the coupled products as a com-



X= Y= N
X= CH; Y= N
X= N, Y =CH

1

2

Figure 1

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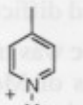
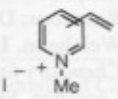
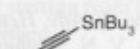
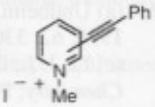
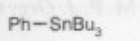
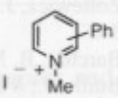
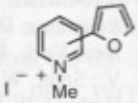
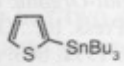
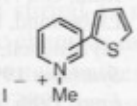
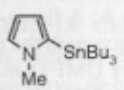
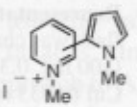
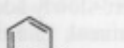
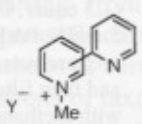
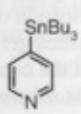
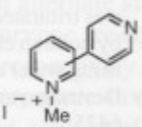
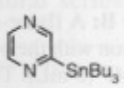
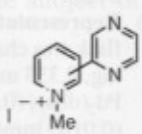
Table 1 Palladium-Catalyzed Cross-Coupling Reaction between **3** and Stannanes

Entry	Stannane	Coupling product	Yield (%)		
					
1			**4a** (63)[b]	–	–
2			**4b** (80)[a]	**5b** (79)[a,b]	**6b** (69)[b]
3			**4c** (79)[b]	**5c** (54)[b]	**6c** (64)[b]
4			**4d** (91)[b]	**5d** (75)[b]	**6d** (65)[b]
5			**4e** (78)[a]	**5e** (68)[b]	**6e** (86)[b]
6			**4f** (51)[a]	**5f** (59)[b]	**6f** (66)[b]
7			**4g** (44)[c]	**5g**[c] (59)[a]	
8			**4h** (44)[c]		
9			**4e** (20)[c]		

[a] Method A: Bu_3Sn-R, $Pd(PPh_3)_4$ (5 mmol%) CuI (10 mmol%), DMF, r.t. or heating at 80 °C.
[b] Method B: Bu_3Sn-R, $Pd_2(dba)_3/P(o\text{-}Tol)_3$ (5 mmol%), DMF. r.t. or heating at 80 °C.
[c] Method C: Bu_3Sn-R, $Pd_2(dba)_3/P(o\text{-}Tol)_3$ (5 mmol%), KF (1.3 equiv), DMF, 80 °C.
[d] **4g** Isolated as iodide.
[e] **5g** Isolated as tosylate.

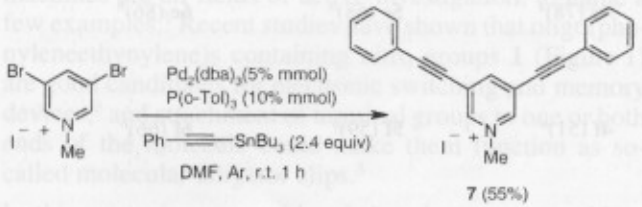
plex mixture. However, the use of KF[13] (Method C)[14] to avoid homocoupling, gave compounds **4g** and **4h** in 44% yield. The reaction of **3a** with 2-pyrazinylstannane afforded **4i** (20%) along with the homocoupled product (38%).

Application of the Methods A and B, to the preparation of 2-vinyl derivative **5a** from **3b** and tributylvinylstannane proved unsuccessful, giving only the dehalogenated *N*-methylpyridinium iodide. Similarly, coupling with furanyl- and thienylstannane by method A failed to produce the heteroaryl derivatives. However, the same reaction with phenylethynylstannane was complete in 15 hours at room temperature (Table 1, entry 2). Alternatively, the reaction of **3b** with stannanes by Method B produced the corresponding derivatives **5** (Table 1, entries 2–6) in good yields, either at room temperature or by heating at 80 °C. By contrast, the same procedure with **3b** in the presence of 2-tributyl stannylpyridine, by either Methods A or B, gave the dehalogenated pyridinium salt as the main product. In an attempt to overcome the competing dehalogenation process, the counterion was changed from iodide to tosylate.[7] Thus, *N*-methylpyridinium **3b**, as the tosylate, was coupled with 2-tributylstannylpyridine to give **5g** in 59% yield (Table 1, entry 7). Under identical conditions,

the reaction of **3b** with 2-tributylstannylpyrazine also gave the coupled compound, as evidenced by NMR spectroscopy. In this case, however, isolation of the product has proved difficult so far.

Finally, **3c** was treated with different stannanes under the conditions of Method B. Table 1 shows the results obtained in the coupling of **3c** with representative alkenyl, alkynyl and heteroaryl organotin compounds. Unfortunately, coupling with tributylvinylstannane led to extensive decomposition (Table 1, entry 1) either on using Method A or B. A number of modifications such as changes in solvents, amount of alkene, or use of cosolvents were tried but the coupling was unsuccessful. An explanation for this result with **3b** and **3c** could be related with the activation of pyridinium α- and γ-positions, which bear a partial positive charge that favours nucleophilic attack and even polymerization of the final product.[15]

It is anticipated that the methodology described here will be useful for the preparation of highly conjugated systems such as **7** (Scheme 2) by a double Stille reaction.



Scheme 2

In summary, we have developed an efficient and mild protocol for the synthesis of substituted azinium cations using vinyl-, alkynyl-, aryl-, and heteroaryl stannanes and bromopyridinium salts. Further work is currently underway, aimed at the preparation of more complex systems from other dihaloheteroaromatic cations and the construction of systems with alternating donor/acceptor repeated units.

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(10) **Representative Procedure A:** A flame-dried two-necked flask was charged under argon with the pyridinium salt (100 mg, 0.333 mmol) in dry DMF (5 mL). Then, 10 mol% CuI (0.033 mmol, 6.3 mg) and the corresponding stannane (1.3 equiv, 0.429 mmol) were slowly added followed by 5 mol% $Pd(PPh_3)_4$ (0.0165 mmol, 15.1 mg). The reaction mixture was heated at 80 °C or stirred at r.t. (as indicated) and then filtered through a small pad of celite and washed with methanol. The solvent was removed and the residue was triturated with EtOAc. Purification of the crude product by column chromatography on silica gel (reverse phase), using water as the eluent yielded the coupling product.

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(12) **Representative Procedure B:** A flame-dried two-necked flask was charged under argon with the pyridinium salt (100 mg, 0.333 mmol) in dry DMF (5 mL). Then, 5 mol% $Pd_2(dba)_3$ (0.0165 mmol, 15.1 mg) and 5 mol% P(*o*-Tol)$_3$ (0.0165 mmol, 5 mg) were slowly added followed by the corresponding stannane (1.3 equiv, 0.429 mmol). The mixture was stirred at r.t. and the work-up procedure, which was similar to Method A, yielded the coupling product.

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(14) **Representative Procedure C:** A flame-dried two-necked flask was charged under argon with the pyridinium salt (100 mg, 0.333 mmol) in dry DMF (5 mL). Then, 5 mol% $Pd_2(dba)_3$ (0.0165 mmol, 15.1 mg), 5 mol% P(*o*-Tol)$_3$ (0.0165 mmol, 5 mg) and 1.3 equiv KF (0.429 mmol, 24.9 mg) were slowly added followed by 1.3 equiv of the corresponding stannane (0.429 mmol). The reaction mixture was heated at 80 °C (as indicated), the residue was triturated with acetonitrile and the liquid was purified by column chromatography on silica gel (reverse phase) using water as the eluent.

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