

## Synthesis of new polyaza heterocycles. Part 42: Diazines

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**Abstract**—Using Pd-catalyzed Stille cross-coupling reactions, we report here the synthesis of various mono- or bis(tri-*n*-butylstannyl)diazines which were reacted with various halogenated diazines to access to various polyaza heterocyclic derivatives.  
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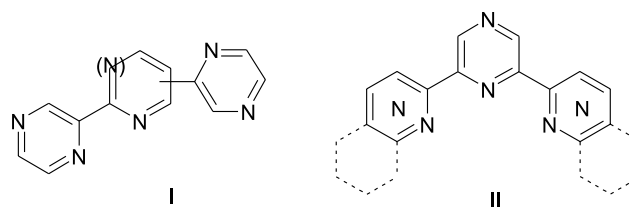
Polyaromatic compounds containing N-heterocyclic sub-units have received considerable attention due to their wide use in various fields such as molecular recognition, metal cryptates, supramolecular devices and self-assembly. Among them, oligopyridines have been extensively studied during the last two decades and many well-defined supramolecular architectures with 2,2'-bipyridines (bpy) and 2,2',6',2''-terpyridines (tpy) units as building blocks have found applications in catalysis,<sup>1</sup> electrochemistry,<sup>2</sup> photochemistry<sup>3</sup> or new materials.<sup>4</sup>

More recently, synthesis of polydentate nitrogen ligands based on pyridine and 1,3-pyrimidine<sup>5</sup> or 3,6 pyridazine<sup>6</sup> units have been reported. Interest in this class of molecules incorporating several coordination sites is mostly due to their use in supramolecular chemistry, and as building blocks for self-assembled polynuclear coordination arrays.<sup>7</sup>

We report here the synthesis of a new family of polyaromatic compounds containing a pyridine or pyrimidine ring as central unit substituted by two pyrazinyl groups (type I) and symmetrical structures with a pyrazine central unit substituted at the 2 and 6 positions by  $\pi$ -deficient heterocycles such as pyridine, quinoline, diazine or benzodiazine (type II) (Scheme 1).

Synthetic approaches to such polyaza heterocyclic compounds are based either on palladium-catalyzed cross-coupling procedures: Suzuki,<sup>8</sup> Negishi<sup>9</sup> and Stille<sup>10</sup> coupling reactions or by generation of the aza-heterocyclic rings with the help of ring-closure reactions.

**Keywords:** Stille cross-coupling reaction; Diazines; Polyaza heterocycles.  
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**Scheme 1.**

The Suzuki reaction involves the palladium-catalyzed cross-coupling of heteroarylboronic acids with heteroaryl halides (or triflates). It is remarkable that whereas halopyridines have often been employed in Suzuki reactions there are only few examples in the literature of use of pyridylboronic acids or esters.<sup>11</sup> In diazine series only the 5-pyrimidylboronic acids or esters have been described<sup>12</sup> while to our knowledge, they are unknown with pyrazine or pyridazine rings probably because of their instability.

Some Negishi reactions have been achieved with organozinc derivatives of diazines to give cross-coupling reactions with iodo or bromo aromatics leading to diazine-aryl or (heteroaryl) bound.<sup>13</sup>

Stille-type coupling provides another efficient way for the formation of aryl-aryl bonds in particular between  $\pi$ -deficient N-heterocycles. This process has been used to prepare a wide variety of functionalized 2,2'-bipyridines and 2,2',6',2''-terpyridines.<sup>14</sup>

Using a synthetic strategy based on Stille coupling reaction, we report here the synthesis of mono- or bis(tri-*n*-butylstannyl) diazines which were reacted with various halogenated diazines to obtain polyaza heterocyclic derivatives.

## 1. Results

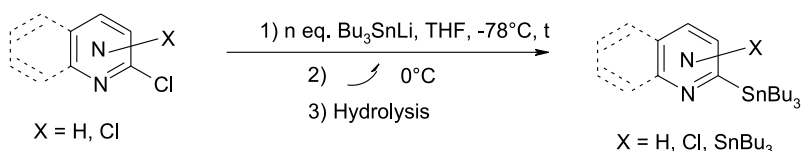
The synthesis of diazinylstannanes could be performed either using the lithiation reaction of diazine followed by a transmetalation step with tributyltin chloride<sup>15</sup> or by use of the nucleophilic substitution of a chlorine atom by the stannyl anion.<sup>16</sup>

We have investigated this last procedure to synthesize the tri-*n*-butylorganostannanes (**1–9**) with a diazine moiety (Scheme 2) the results of which are given in Table 1.

One can observe a monosubstitution with very low yields for dichloro-pyridazine and pyrimidine (entries 1 and 3). These low yields could be explained by competitive radical reactions, since some dimers and dibutyltin were observed besides the expected compounds. Good results

were obtained for chloropyrazine (entry 5) and 2,6-dichloropyrazine (entry 6). For this last compound, mono or distannylation has been achieved in good and moderate yield (entries 6 and 7). The nucleophilic substitution was performed successfully with good yield with 2-chloro-4-methoxypyrimidine (entry 4) whereas the yield was low with 2,4-dichloropyrimidine (entry 3). Such a result could suggest that the presence of a methoxy group makes the substitution reaction more easy, however, it can be noticed that stannylation failed with 3-chloro-6-methoxypyridazine (entry 2). In benzodiazine series good yields with monochloro-quinazoline (entry 8) or quinoxaline (entry 9) were observed. With 2,3-dichloroquinoxaline, a disubstitution can be obtained with a very good yield (entry 10) despite the steric hindrance of the tri-*n*-butylstannyl group.

Coupling reactions of the stannyl derivatives **3, 7–9** were



Scheme 2.

Table 1. Synthesis of tri-*n*-butyl-*N*-heteroarylstannanes

Entry	Het-Cl	Product	<i>n</i> (equiv)	<i>t</i> (h)	Compound	Yield (%)
1			1.1	5	<b>1</b>	9
2			1.1	5	—	—
3			1.1	6	<b>2</b>	4
4			1.1	1	<b>3</b>	70
5			1.1	8	<b>4</b>	85 <sup>a</sup>
6			1.1	21	<b>5</b>	95
7			2.1	24	<b>6</b>	56
8			1.1	1	<b>7</b>	97
9			1.1	1	<b>8</b>	54
10			2.1	1	<b>9</b>	98

<sup>a</sup> Hydrolysis was performed at  $-40^\circ\text{C}$ .

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