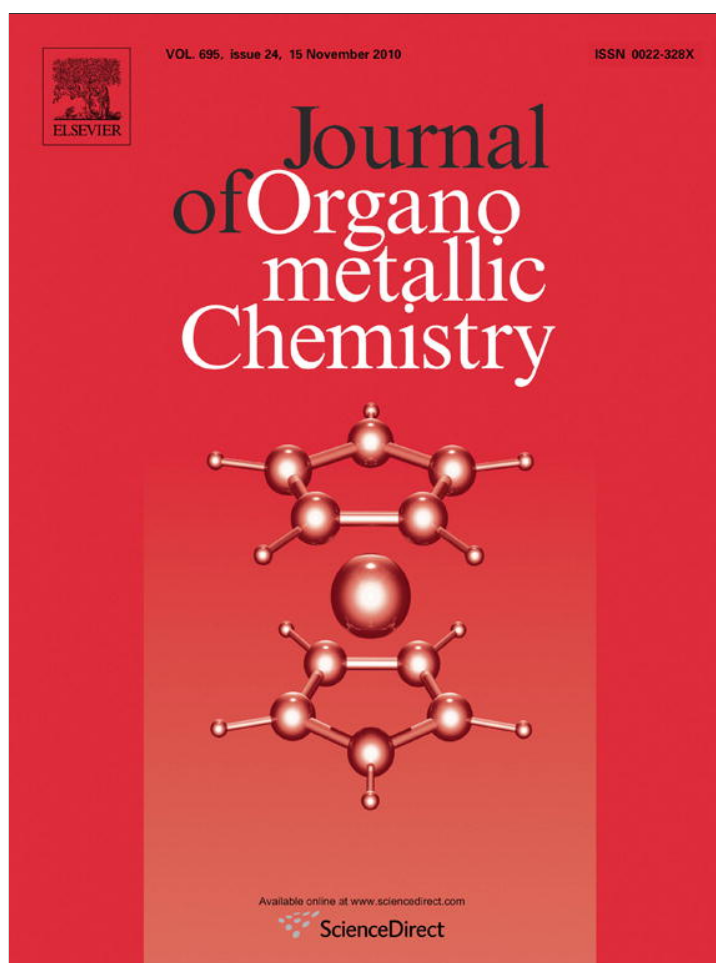


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# Selective synthesis of mono- and distannylpyridines from chloropyridinols via an $S_{RN}1$ mechanism

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## ABSTRACT

A selective two-step synthesis of either mono- or distannylated pyridines from commercially available pyridinols, involving its conversion to the corresponding diethyl pyridyl phosphates (pyDEP) followed by the reaction with  $\text{Me}_3\text{SnNa}$  in liquid ammonia, is described.

The results obtained clearly indicate that the reactions proceed through an unimolecular radical nucleophilic substitution mechanism ( $S_{RN}1$ ) with intermediacy of a monosubstitution product.

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## 1. Introduction

Heterocyclic compounds are of great interest because of their role as versatile building blocks in the synthesis of more complex structures. Among them, pyridine is the most common heterocyclic ring found in natural products [1] as well as in biologically active compounds [2], and plays an extraordinary diverse role as chelating ligand in transition metal chemistry [3]. These facts have made functionalized pyridines attractive goals for synthesis over more than three decades and justify continuous interest in the development of new synthetic routes [4].

Over the past two decades the synthesis and application of organotin intermediates has become a significant aspect in organic heterocyclic chemistry. For example, much supramolecular architectures are based on ligands synthesized through a Stille-type carbon–carbon bond-forming reaction [5]. This reaction has been widely employed owing to its versatile nature, great functional group toleration and better yields.

In connection with the synthetic importance of organotin compounds, we are involved in searching new routes for their synthesis starting from cheap commercially available materials [6]. For example, we have demonstrated that arylstannanes could be synthesized in excellent yields from phenols *via* the reaction of the corresponding aryl diethyl phosphate (ArDEP) with organostannides in liquid ammonia [6a,6d]. Taking into account this background and the importance of finding new ways to synthesize pyridylstannanes we started our study. We report here on the significant results obtained as well as important mechanistic aspects of the reaction of diverse diethyl pyridyl phosphates towards trimethyltin sodium ( $\text{Me}_3\text{SnNa}$ , **1**) in liquid ammonia, which open up a very efficient route to selective mono- and distannylated pyridine rings, versatile starting materials for the tailor-made synthesis of more complex functionalized pyridine structures.

## 2. Results and discussion

We chose inexpensive and commercially available pyridinols and we synthesized the corresponding diethyl pyridyl phosphates (pyDEP) used as starting materials (Chart 1).

The results obtained are summarized in Table 1

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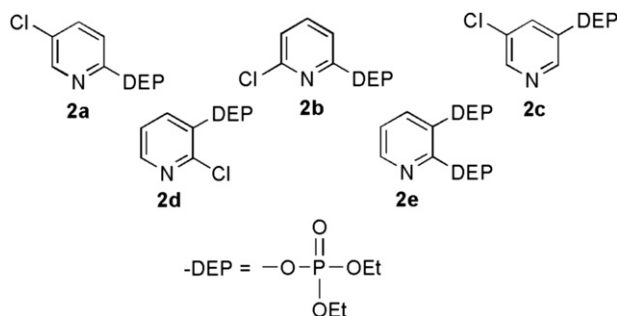


Chart 1.

It should be emphasized that we employed a special reaction work-up in order to avoid the generation of undesired proto-distannylation products during this step (see Experimental Section).

Photostimulated reaction of **1** and **2a** (**1/2a**, 2.2:1) proceeded smoothly (30 min) rendering 2,5-bis(trimethylstannyl)pyridine (**3a**) in 96% yield, together with tiny amounts of 2-(**5a**) and 3-trimethylstannylpyridine (**5b**)<sup>2</sup> (4% and traces, respectively) (entry 1). When this reaction was carried out in the dark (60 min), we found that there was a spontaneous reaction between **1** and **2a** giving, as the only product, the monostannylated compound diethyl 5-(trimethylstannyl)pyridin-2-yl phosphate (**4a**) in a 98% yield of pure compound (entry 2). It should be noted that no starting material was detected and that this reaction was totally inhibited by the addition of *p*-dinitrobenzene (*p*-DNB) (20 mol %), a well-known inhibitor of radical anions [7], recovering starting substrate almost quantitatively (entry 3). Taking into account that **4a** could be really useful as starting material in selective substitution reactions [8], and with the aim of finding out if its synthesis was possible using only one equivalent of **1** (in order to minimize waste material) we carried out a dark reaction with a defect of **1** (**4a/1**, 1:1). Unfortunately, the reaction rendered, even after 2 h, **4a** in 63% yield together with a considerable amount of remaining unreacted starting material (21%) (GC/MS) (entry 4).

The fact that the reaction between **1** and **2a** is stimulated by irradiation and that the reaction in the dark is suppressed by *p*-DNB, shows the radical-chain character of the substitution process. Two extra reactions between **2a** and **1** (1:2.2 ratio), quenched at shorter times, showed that the yield of **3a** progressively increased with time at the expense of **4a**, being **3a** the main product after 30 min (entries 1, 5 and 6).

Upon these results we are able to say that **4a** is an intermediate in the synthesis of **3a**, chlorine is the first nucleofuge replaced in the reaction<sup>3</sup> and the reaction occurs by the  $\text{S}_{\text{RN}}1$  mechanism, through two propagation cycles, as sketched in Scheme 1. The positive dark reaction supports a spontaneous electron transfer (ET) from the anion **1** to the substrate.

The radical anion **4a**<sup>•−</sup> may go through two competitive reactions: electron transfer to **2a** rendering the monosubstituted product **4a** (step 1) or the expulsion of diethyl phosphate anion, generating the C6 radical of **5b** (step 2) which at the end leads to the distannylated pyridine **3a**. As compound **4a** is an intermediate, step 1 must be faster than step 2 under the reaction conditions. In a second cycle, compound **4a** reacts with **1** leading at last to **3a**.

Taking into account that step 1 is bimolecular and step 2 is unimolecular, the products ratio should depend on the substrate

concentration, so, we carried out a series of reactions with different substrate concentrations using an insufficient amount of **1** (1:1 ratio, 30 min). The results obtained showed that even at lower substrate concentration (3.12 mM) step 1 competes very efficiently over step 2; thus, in all the experiments, compound **4a** was obtained as the main reaction product (69–74%) together with minor amounts of **6a** (5–9%) and no distannylated product **3a** was detected (entries 7–9). In order to confirm that **4a** is an intermediate in the generation of **3a** we carried out a reaction between **4a** and **1** (1:1 ratio). After 1 h under irradiation, the GC/MS showed that **3a** was the only reaction product.

The presence of **6a** in both reactions carried out at short times (entries 5 and 6) and in the reactions carried out with a defect of **1** (entries 4, 7–9) could be due to the hydrogen abstraction by C5 radical of **6a** from ammonia. On the other hand, the presence of 2- and 3-(trimethylstannyl)pyridine (**5a** and **5b**) in experiment 1 is probable due to the photostimulated reaction of **6a** with **1**, and to the hydrogen abstraction of radical C6 of **5b** from ammonia, respectively. Nevertheless, these competitive reactions could be considered worthless.

In general, similar results were obtained in the reactions carried out between **2b** and **1**. Thus, under irradiation (**2b/1**, 1:2.2, 120 min) the reaction rendered 2,6-bis(trimethylstannyl)pyridine (**3b**) as the only product (96% of isolated product). While the analysis (GC/MS) of the dark reaction of **2b** with **1** (1:2.2) showed the presence of diethyl 6-(trimethylstannyl)pyridin-2-yl phosphate (**4b**, 82%), a similar reaction was totally inhibited by the addition of *p*-DNB (20 mol %) (entries 11 and 12). These results enable us to say that, as occurs with **2a**, there is a spontaneous ET from **1** to **2b**. Moreover, when the irradiated reaction between **2b** and **1** was quenched at shorter times (30 min), a mixture of monostannylated pyridine **4b** and distannylated pyridine **3b** was obtained in a 1:2.2 ratio, demonstrating that **4b** is an intermediate in the formation of **3b** (entry 13).

In order to analyze the effect of substrate concentration on the competition between steps 1 and 2, we carried out experiments 14 and 15. The results obtained showed that meanwhile at higher substrate concentration (12.50 mM) compound **4b** was the only product (100%) (step 1 prevailed effectively over step 2), at general substrate concentration (6.25 mM) step 2 competes with step 1 and a mixture of **3b/4b** (0.8:1) was obtained.

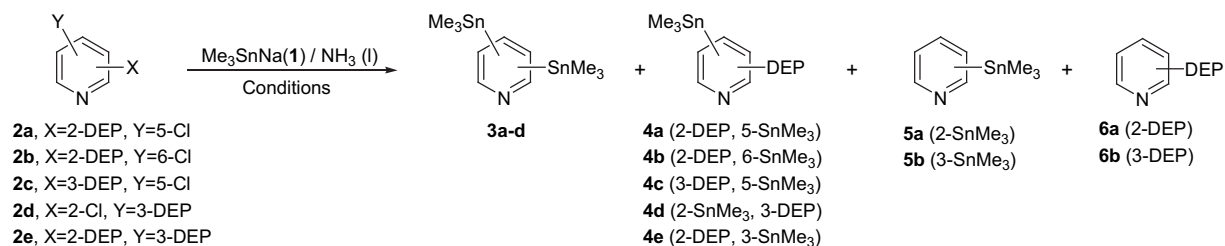
With the main goal of finding optimal reaction conditions for the synthesis of **4b** using only one equivalent of **1**, we also carried out the dark experiment 16. With pleasure we found that the reaction rendered **4b** in very high yield (94% of isolated product).

The reactions carried out between compound **2c** and **1** also support an  $\text{S}_{\text{RN}}1$  mechanism with intermediacy of a mono-substitution product. The presence of a considerable amount of **5b** (11%) in the product mixture obtained in the photostimulated reaction (entry 17) could be due either to the photostimulated reaction of **6b** with **1**, or to the hydrogen abstraction of C5 radical of **5b** from ammonia. In order to minimize the formation of compound **5b**, which difficult the purification of **3c** diminishing its isolated yield, we carried out a reaction employing an excess of **1** (**2c/1**, 1:5) (entry 18). We found that under these reaction conditions the yield of **3c** was improved (90%) and the amount of **5b** diminished. These results would be probably due to the fact that an excess of **1** increased the rate of the bimolecular reaction between the C5 radical of **6b** and/or the C6 radical of **5b** with **1** leading at last to the disubstitution product **3c**. It should be mentioned that in the dark, although there was a slow reaction which was inhibited by *p*-DNB, it was not possible to obtain significant amounts of monostannylated compound **4c**, rendering large amounts of **6b** (entries 20 and 21). On the other hand, the photostimulated reaction of **2c** and **1** (1:1 ratio), at higher substrate concentration, led to

<sup>2</sup> Identified by their retention times (GC/MS).

<sup>3</sup> This is in accord with the fact that chlorobenzene is more reactive than diethyl phenyl phosphate towards **1** in liquid ammonia. Unpublished results.

**Table 1**  
Reactions of **2a–e** towards Me<sub>3</sub>SnNa (**1**) in liquid ammonia.



| Entry <sup>a</sup> | Substrate <sup>b</sup> | Conditions, time (min)  | Products (%) <sup>c</sup>            |                                   |   |                                      |
|--------------------|------------------------|-------------------------|--------------------------------------|-----------------------------------|---|--------------------------------------|
|                    |                        |                         | (Me <sub>3</sub> Sn) <sub>2</sub> py | (Me <sub>3</sub> Sn)pyDEP         | pySnMe <sub>3</sub>                       | pyDEP                                |
| 1                  | <b>2a</b>              | hv, 30                  | <b>3a</b> , 96 (87)                  | —                                 | <b>5a</b> , <b>4</b> , <b>5b</b> , traces | —                                    |
| 2                  | <b>2a</b>              | Dark, 60                | —                                    | <b>4a</b> , 100 (98)              | —   | —                                    |
| 3 <sup>d</sup>     | <b>2a</b>              | Dark, <i>p</i> -DNB, 60 | —                                    | —                                 | —   | —                                    |
| 4 <sup>e</sup>     | <b>2a</b>              | Dark, 120               | —                                    | <b>4a</b> , 63                    | —   | <b>6a</b> , 2                        |
| 5                  | <b>2a</b>              | hv, 5                   | —                                    | <b>4a</b> , 92                    | —   | <b>6a</b> , traces                   |
| 6                  | <b>2a</b>              | hv, 15                  | <b>3a</b> , 72                       | <b>4a</b> , 24                    | —   | <b>6a</b> , 4                        |
| 7 <sup>e</sup>     | <b>2a</b>              | hv, 30                  | —                                    | <b>4a</b> , 70                    | —   | <b>6a</b> , 6                        |
| 8 <sup>e,f</sup>   | <b>2a</b>              | hv, 30                  | —                                    | <b>4a</b> , 74                    | —   | <b>6a</b> , 9                        |
| 9 <sup>e,g</sup>   | <b>2a</b>              | hv, 30                  | —                                    | <b>4a</b> , 69                    | —   | <b>6a</b> , 5                        |
| 10                 | <b>2b</b>              | hv, 120                 | <b>3b</b> , 100 (96)                 | —                                 | —   | —                                    |
| 11                 | <b>2b</b>              | Dark, 10                | —                                    | <b>4b</b> , 82 (74)               | —   | —                                    |
| 12 <sup>d</sup>    | <b>2b</b>              | Dark, <i>p</i> -DNB, 10 | —                                    | —                                 | —   | —                                    |
| 13                 | <b>2b</b>              | hv, 30                  | <b>3b</b> , 31                       | <b>4b</b> , 69                    | —   | —                                    |
| 14 <sup>e</sup>    | <b>2b</b>              | hv, 60                  | <b>3b</b> , 45                       | <b>4b</b> , 55                    | —   | —                                    |
| 15 <sup>e,g</sup>  | <b>2b</b>              | hv, 60                  | —                                    | <b>4b</b> , 100 (94)              | —   | —                                    |
| 16 <sup>e</sup>    | <b>2b</b>              | Dark, 10                | —                                    | <b>4b</b> , 100 (94)              | —   | —                                    |
| 17                 | <b>2c</b>              | hv, 60                  | <b>3c</b> , 79 (69)                  | —                                 | <b>5b</b> , 11                            | —                                    |
| 18 <sup>h</sup>    | <b>2c</b>              | hv, 60                  | <b>3c</b> , 90 (84)                  | —                                 | <b>5b</b> , 7                             | —                                    |
| 19                 | <b>2c</b>              | hv, 10                  | <b>3c</b> , 16                       | <b>4c</b> , 72                    | <b>5b</b> , 5                             | <b>6b</b> , 6                        |
| 20                 | <b>2c</b>              | Dark, 60                | —                                    | <b>4c</b> , 34                    | —   | <b>6b</b> , 44                       |
| 21 <sup>d</sup>    | <b>2c</b>              | Dark, <i>p</i> -DNB, 60 | —                                    | —                                 | —   | —                                    |
| 22 <sup>e</sup>    | <b>2c</b>              | hv, 60                  | <b>3c</b> , 53                       | <b>4c</b> , 38                    | <b>5b</b> , 9                             | <b>6b</b> , traces                   |
| 23 <sup>e,g</sup>  | <b>2c</b>              | hv, 60                  | —                                    | <b>4c</b> , 89 (80)               | —   | <b>6b</b> , 8                        |
| 24                 | <b>2d</b>              | hv, 20                  | <b>3d</b> , 90 (84)                  | —                                 | <b>5a</b> , <b>3</b> ; <b>5b</b> , traces | —                                    |
| 25 <sup>e</sup>    | <b>2d</b>              | Dark, 30                | —                                    | <b>4d</b> , 90 (86)               | —   | <b>6b</b> , traces                   |
| 26 <sup>d</sup>    | <b>2d</b>              | Dark, <i>p</i> -DNB, 30 | —                                    | —                                 | —   | —                                    |
| 27 <sup>e</sup>    | <b>2d</b>              | hv, 30                  | <b>3d</b> , 23                       | <b>4d</b> , 62                    | <b>5a</b> , 5                             | —                                    |
| 28 <sup>e,g</sup>  | <b>2d</b>              | hv, 30                  | —                                    | <b>4d</b> , 94 (89)               | —   | <b>6b</b> , 3                        |
| 29                 | <b>2e</b>              | hv, 180                 | <b>3d</b> , 65                       | —                                 | <b>5a</b> , 16; <b>5b</b> , 10            | —                                    |
| 30                 | <b>2e</b>              | hv, 15                  | —                                    | <b>4d</b> , traces; <b>4e</b> , 7 | —   | <b>6a</b> , <b>3</b> ; <b>6b</b> , 2 |
| 31 <sup>h</sup>    | <b>2e</b>              | hv, 180                 | <b>3d</b> , 62                       | —                                 | <b>5a</b> , 19; <b>5b</b> , 10            | —                                    |
| 32 <sup>i</sup>    | <b>2e</b>              | Dark, 180               | —                                    | —                                 | —   | —                                    |
| 33 <sup>e,g</sup>  | <b>2e</b>              | hv, 180                 | <b>3d</b> , 6                        | <b>4d</b> , 17; <b>4e</b> , 39    | <b>5a</b> , 7; <b>5b</b> , traces         | <b>6a</b> , 18; <b>6b</b> , 6        |

<sup>a</sup> All reactions were conducted at molar ratio of substrate/**1** = 1:2.2 unless otherwise stated.

<sup>b</sup> [substrate] = 6.25 mM unless otherwise stated.

<sup>c</sup> Determined by GC/MS; isolated yields between parentheses as an average of at least three independent runs.

<sup>d</sup> *p*-DNB added, 20 mol %. Starting substrate was recovered.

<sup>e</sup> Molar ratio of substrate/**1** = 1:1.

<sup>f</sup> [substrate] = 3.12 mM.

<sup>g</sup> [substrate] = 12.50 mM.

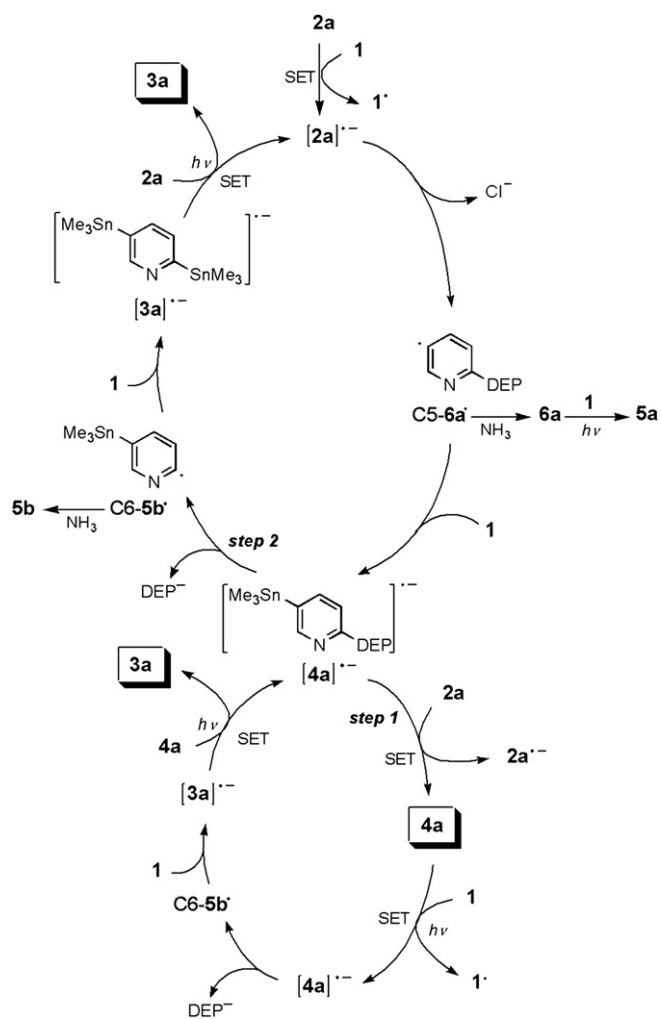
<sup>h</sup> Molar ratio of **2c**/**1** = 1:5.

<sup>i</sup> **2e** was recovered.

compound **4c** (89%) accompanied with an 8% of **6b** (entry 23) confirming, once more, the prevalence of step 1 over step 2 under these reaction conditions. On the other hand, at lower concentration, the reaction of **2c** and **1** (1:1 ratio) rendered a mixture of **3c**/**4c** in a 1.4:1 ratio, confirming the competition between steps 1 and 2 (entry 22).

The results summarized in experiments 24–33 point out that the reactions of either **2d** or **2e** with **1** also go through an S<sub>RN</sub>1 mechanism with intermediacy of monosubstituted products. Nevertheless, there are some divergences. The reactions carried out between **2d** and **1** rendered either distannylated pyridine **3d** (entry 24) or monostannylated pyridine **4d** (entries 25 and 28) in high yields (90%, 90% and 94%, respectively), being detected insignificant

amounts of the secondary products **5a**, **5b** and **6b**. On the other hand, the photostimulated reaction of **2e** with **1** (1:2.2, 180 min) rendered product **3d** in 65% yield, together with significant amounts of the undesired products **5a** (16%) and **5b** (10%) (entry 29). The use of an excess of **1** (**2e**/**1**, 1:5) did not produced an increment on **3d** yield (entry 31). It should be mentioned that when the reaction was quenched at shorter reaction time (15 min) there was detected diethyl 3-(trimethylstannyl)pyridin-2-yl phosphate (**4e**) as the main monostannylated product supporting the preferential expulsion of the DEP anion from position 3 rather than position 2 (entry 30). These results are sustained by the different reactivity previously shown by 2-, 3- and 4-pyridinyl phosphates towards **1** [6d]. Keeping in mind the results obtained in the



**Scheme 1.** Proposed mechanistic pathways in the  $S_{RN}1$  reaction of **2a** towards **1** in liquid ammonia.

reactions performed at large substrate concentrations and with the main goal of finding optimal reaction conditions for the synthesis of **4e**, we carried out experiment 33. Unfortunately, the expulsion of the DEP anion from carbon 3 did not compete efficiently with its expulsion from carbon 2 and we obtained a mixture of isomeric monosubstituted pyridines **4d** and **4e** in a 1/2.3 ratio, together with considerable amounts of **6a** (18%) and **6b** (6%). It should be mentioned that, as we expected [9], the dark reaction of substrate **2e** with **1** was negative and starting substrate was completely recovered (entry 32).

A comparison of the results obtained in experiments 24 and 29 suggests that **2d** is more reactive than **2e** toward **1** under those reaction conditions. Probably, the different reactivity is due to the fact that chloride is a better leaving group compared with diethyl phosphate anion, affecting the rate of formation of the first pyridinyl radical.

It is known that the success of a chain reaction depends on the competition between the chain propagation steps and the termination steps. This competition depends on the rates of the different propagation steps [7].

An analysis of Scheme 1 shows that the C5 radical of **6a**, formed by elimination of the first nucleofuge, may go through two competitive reactions, that is, hydrogen abstraction from the solvent, rendering **6a**, or coupling reaction with nucleophile **1**, continuing with the propagation cycle. Thus, the generation of

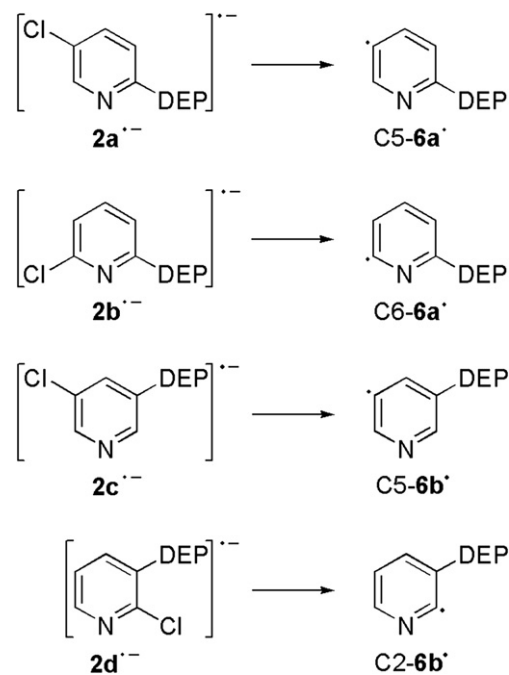
undesired secondary product **6a** is a consequence of the lower reactivity of the C5 radical of **6a** towards anion **1** which can be attributed to its lower electrophilicity [7].

The evaluation of the products distribution obtained in the dark reactions of the different substrates could allow us to link the reactivity of the diverse radicals towards **1** with this distribution and, in particular, the effect exerted by the DEP substituent at different positions of the ring. For this purpose we compare those reactions that generate radicals on C3 or on C2 of the pyridine ring (Scheme 2).

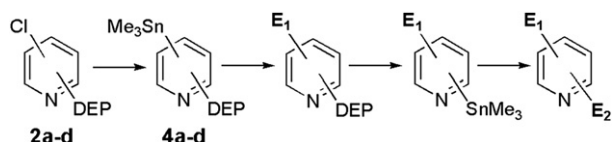
For example, the results obtained in experiments 2 and 20 (Table 1) show that the C5 radical of **6b** has a lower reactivity towards **1** comparing with that of the C5 radical of **6a**, i.e., larger amounts of **6b** were obtained in experiment 20 confirming that the relative position of the DEP substituent affect the electrophilicity of these pyridin-3-yl radicals. On the other hand, a comparison of experiments 16 and 25 (Table 1) shows that there is not an appreciable difference between the reactivity of both C6 radical of **6a** and C2 radical of **6b** and the coupling reaction with **1** competes efficiently with the proton abstraction.

Also, the  $S_{RN}1$  reaction of nucleophiles with substrates supporting two nucleofugal substituents afford either mono-substitution or disubstitution product depending on the structure of the substrate, the nature of the nucleofugal group or the nucleophile [7]. Moreover, the product ratio must be controlled by the rate of fragmentation. Córscico and Rossi have reported the reaction of 2,5-, 2,6- and 3,5-dichloropyridines towards **1** in liquid ammonia [10], and they did not mention the existence of monosubstitution products as intermediates. Therefore, the different reactivity shown by chloropyridyl phosphates **2a**, **2b** and **2c** with that shown by the equivalent dichloropyridines is a consequence of the nature of the nucleofugal groups and may be due to the different rate of fragmentation of a C–Cl bond comparing with a C–DEP bond. The intermediate radical anion expels the halide faster than it transfers an electron to the substrate rendering the disubstitution product (step 2 is faster than step 1 in Scheme 1).

In previous works we have found that meanwhile the reaction of diethyl 2-chlorophenyl phosphate with **1** afforded the



**Scheme 2.** pyDEP radicals.



**Scheme 3.** Synthetic strategy for aromatic bifunctionalization by sequential  $S_{RN}1$ -SEA reactions.

corresponding disubstitution product with intermediacy of a mono-substitution product [6c], isomers 1,3- and 1,4-rendered the disubstitution product without intermediates [6d]. We considered that the different reactivity was governed by the rate of fragmentation of the intermediate radical anions and that these different rates of fragmentation were probably due to different spin densities at the 2-, 3-, and 4-carbon atoms. The results reported now with analogous pyridine derivatives are an interesting example of the influence of the nature of the aromatic core. All the reactions go through two propagation cycles independently of the relative positions of the nucleofugal groups, indicating the preferential ET to the substrate rather than the expulsion of the nucleofuge.

### 3. Conclusions

The overall results obtained are important not only from a mechanistic but also from a synthetic point of view.

First, experimental results strongly suggest that the reactions go through an  $S_{RN}1$  mechanism with intermediacy of a mono-substitution product whatever the relative positions of both nucleofuges, which is not a common process in  $S_{RN}1$  mechanism. Moreover, there are fewer reports related to this special mechanism involved with heteroaromatic systems [7].

Second, we have developed an efficient and simple two-step approach for the selective synthesis of bistannylated pyridines from inexpensive and commercially available pyridinols, being this a practical alternative to the existing methodologies of synthesis: reaction of **1** with dihalopyridines, in dimethoxyethane without irradiation [11], or in liquid ammonia under irradiation [10]. It should be emphasized that the side products formed by reduction of the radicals were kept at a minimum (with one exception) and, as a consequence, the yields of isolated distannylpyridines were increased.<sup>4</sup>

Moreover, the special reactivity shown by the different starting substrates towards **1** allows us to find optimal reaction conditions for the chemoselective monostannylation of the pyridine ring. Thus, we synthesized a series of new isomeric stannylpyridyl phosphate esters (**4a–d**) in excellent yields (80–98%), which should prove to be valuable intermediates for the unsymmetrical substitution of the pyridine ring as is resumed in Scheme 3.

It is known that a heteroaryl–tin bond is highly reactive towards diverse electrophiles [12]. For instance, these compounds would be suitable intermediates for Stille cross-coupling reactions leading to a broad range of asymmetric functionalized pyridines [13]. The organic synthetic strategy resumed in Scheme 3 is based on the successive selective substitution of a leaving group with a trimethyltin group followed by a Pd-catalyzed cross-coupling reaction or a simple electrophilic substitution, avoiding protection and deprotection steps [8]. All the reactions involved are chemoselective; therefore, it would be possible to synthesize tailored bi-, tri- and polyheteroaryl materials by choosing the appropriate starting

<sup>4</sup> The separation of distannylated products (**3a–d**) from monostannylated pyridines (**5a** and **5b**) is hard because of their similar chromatographic behavior. This fact diminishes the yield of purified distannylated pyridines.

substrates. In addition, it is important to mention that many substituents are compatible with the  $S_{RN}1$  mechanism [7], hence, the range of functionality would be constrained to the availability of the coupling partners.

We can affirm that all the pyridylstannanes obtained are potential synthetic intermediates for a vast number of changes through organotin chemistry.

## 4. Experimental

### 4.1. General considerations

All manipulations were performed under nitrogen or argon. The solvents used were dried and distilled in accordance with standard procedures. Irradiation was conducted in a reactor made of Pyrex, equipped with four 250 W UV lamps emitting maximally at 350 nm (water-refrigerated). Compounds described in the literature were characterized by comparing their  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, and melting points (mp) to the previously reported data. Unknown compounds were purified and analyzed from a single run and, then, were repeated to determine an average yield. They were characterized by  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS, mp and elemental analysis. Flash chromatography was performed over silica gel 60, 40–63  $\mu\text{m}$ . Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. NMR spectra were recorded in  $\text{CDCl}_3$  on a 300 MHz spectrometer (300.1 MHz for  $^1\text{H}$ , 75.5 MHz for  $^{13}\text{C}$ , 121.5 MHz for  $^{31}\text{P}$  and 111.9 MHz for  $^{119}\text{Sn}$ ) at 23 °C. Chemical shifts ( $\delta$ ) are given in ppm downfield relative to TMS ( $^1\text{H}$  and  $^{13}\text{C}$ ),  $\text{Me}_4\text{Sn}$  ( $^{119}\text{Sn}$ ) or  $\text{PPh}_3$  ( $^{31}\text{P}$ ) and coupling constants ( $J$ ) are in Hz. Mass spectra were obtained with a GC/MS instrument (HP5-MS capillary column, 30 m  $\times$  0.25 mm  $\times$  0.25  $\mu\text{m}$ ) equipped with 5972 mass selective detector operating at 70 eV (EI). Program: 50 °C for 2 min with increase 10 °C/min to 280 °C. Most of the reagents and catalyst were commercially available. Diethyl pyridinyl phosphates were prepared by the method of Kenner and Williams [14] and characterized by IR<sup>5</sup> and NMR spectroscopy, and used without further purification.

To carry out the reactions in dark, the reaction flask was wrapped with aluminium foil.

### 4.2. Synthesis of starting diethyl pyridinyl phosphates

#### 4.2.1. Diethyl 5-chloropyridin-2-yl phosphate (**2a**)

Kenner's method was employed for the reaction of 5-chloropyridin-2-ol (5.0 mmol, 0.645 g) with diethyl hydrogen phosphite (5.2 mmol, 0.670 mL) and triethylamine (5.2 mmol, 0.785 mL) in  $\text{CCl}_4$  (3 mL) as solvent. The title compound was obtained as a pale yellow liquid (0.795 g, 3.0 mmol, 60%);  $^1\text{H}$  NMR:  $\delta$  8.20–8.13 (m, 1H); 7.70–7.62 (m, 1H); 6.96 (m, 1H); 4.33–4.17 (m, 4H); 1.38–1.28 (m, 6H).  $^{13}\text{C}$  NMR:  $\delta$  155.5 ( $^2J_{\text{CP}} = 5.9$  Hz, C); 145.8 (CH); 139.2 (CH); 127.8 (C); 113.9 ( $^3J_{\text{CP}} = 6.4$  Hz, CH); 64.3 ( $^2J_{\text{CP}} = 5.3$  Hz,  $\text{CH}_2$ ); 15.5 ( $^3J_{\text{CP}} = 6.7$  Hz,  $\text{CH}_3$ ).  $^{31}\text{P}$  NMR:  $\delta$  43.23. MS ( $m/z$ , relative intensity): 265 (6,  $\text{M}^+$ ), 237 [2, ( $\text{M} - 28$ )<sup>+</sup>] 210 (7), 192 (20), 156 (21), 139 (39), 129 (100), 112 (17), 101 (34), 81 (29). Anal. Calcd. for  $\text{C}_9\text{H}_{13}\text{ClNO}_4\text{P}$  (265.63): C 40.69; H 4.93; N 5.27. Found: C 40.80; H 4.95; N 5.25.

#### 4.2.2. Diethyl 6-chloropyridin-2-yl phosphate (**2b**)

Kenner's method was employed for the reaction of 6-chloropyridin-2-ol (5.0 mmol, 0.645 g) with diethyl hydrogen phosphite (5.2 mmol, 0.670 mL) and triethylamine (5.2 mmol, 0.785 mL) in  $\text{CCl}_4$  (3 mL) as solvent. The title compound was obtained as a pale

<sup>5</sup> The IR spectra of the esters present characteristic absorptions at 1030, 1155–1164, 1183–1214, and 1265–1274  $\text{cm}^{-1}$ .

yellow liquid (0.861 g, 3.25 mmol, 65%);  $^1\text{H}$  NMR:  $\delta$  7.77 (dt,  $^3J_{\text{HH}} = 7.8$  Hz,  $^5J_{\text{HP}} = 1.0$  Hz, 1H); 7.23 (dd,  $^3J_{\text{HH}} = 7.8$  Hz,  $^4J_{\text{HP}} = 1.8$  Hz, 1H); 7.05 (dd,  $^3J_{\text{HH}} = 8.0$  Hz,  $^4J_{\text{HP}} = 1.5$  Hz, 1H); 4.46–4.34 (m, 4H); 1.45 (dt,  $^3J_{\text{HH}} = 7.0$  Hz,  $^4J_{\text{HP}} = 1.0$  Hz, 6H).  $^{13}\text{C}$  NMR:  $\delta$  156.4 ( $^2J_{\text{CP}} = 5.9$  Hz, C); 148.6 (C); 141.8 (CH); 120.7 (CH); 111.3 ( $^3J_{\text{CP}} = 5.9$  Hz, CH); 64.8 ( $^2J_{\text{CP}} = 5.9$  Hz,  $\text{CH}_2$ ); 15.7 ( $^3J_{\text{CP}} = 6.4$  Hz,  $\text{CH}_3$ ).  $^{31}\text{P}$  NMR:  $\delta$  43.23. MS ( $m/z$ , relative intensity): 265 (5,  $\text{M}^+$ ), 237 [2, ( $\text{M} - 28$ ) $^+$ ], 210 (6), 192 (19), 156 (20), 139 (49), 129 (100), 101 (34), 81 (28). Anal. Calcd. for  $\text{C}_9\text{H}_{13}\text{ClNO}_4\text{P}$  (265.63): C 40.69; H 4.93; N 5.27. Found: C 40.59; H 4.94; N 5.29.

#### 4.2.3. Diethyl 5-chloropyridin-3-yl phosphate (2c)

Kenner's method was employed for the reaction of 5-chloropyridin-3-ol (5.0 mmol, 0.645 g) with diethyl hydrogen phosphite (5.2 mmol, 0.670 mL) and triethylamine (5.2 mmol, 0.785 mL) in  $\text{CCl}_4$  (3 mL) as solvent. The title compound was obtained as a brown liquid (0.928 g, 3.5 mmol, 70%);  $^1\text{H}$  NMR:  $\delta$  8.63–8.58 (m, 1H); 7.83 (dt,  $^3J_{\text{HH}} = 2.3$  Hz,  $^4J_{\text{HP}} = 1.0$  Hz, 1H); 7.49 (s, 1H); 4.48–4.36 (m, 4H); 1.54 (dt,  $^3J_{\text{HH}} = 7.1$  Hz,  $^4J_{\text{HP}} = 1.0$  Hz, 6H).  $^{13}\text{C}$  NMR:  $\delta$  147.4 ( $^2J_{\text{CP}} = 6.4$  Hz, C); 145.0 (CH); 139.9 ( $^2J_{\text{CP}} = 5.9$  Hz, CH); 131.4 (C); 127.3 ( $^3J_{\text{CP}} = 4.1$  Hz, CH); 65.1 ( $^2J_{\text{CP}} = 5.9$  Hz,  $\text{CH}_2$ ); 16.0 ( $^3J_{\text{CP}} = 6.4$  Hz,  $\text{CH}_3$ ).  $^{31}\text{P}$  NMR:  $\delta$  44.67. MS ( $m/z$ , relative intensity): 265 (39,  $\text{M}^+$ ), 236 [36, ( $\text{M} - 29$ ) $^+$ ], 209 (34), 157 (23), 139 (45), 129 (100), 109 (22), 81 (68). Anal. Calcd. for  $\text{C}_9\text{H}_{13}\text{ClNO}_4\text{P}$  (265.63): C 40.69; H 4.93; N 5.27. Found: C 40.55; H 4.95; N 5.26.

#### 4.2.4. Diethyl 2-chloropyridin-3-yl phosphate (2d)

Kenner's method was employed for the reaction of 2-chloropyridin-3-ol (5.0 mmol, 0.645 g) with diethyl hydrogen phosphite (5.2 mmol, 0.670 mL) and triethylamine (5.2 mmol, 0.785 mL) in  $\text{CCl}_4$  (3 mL) as solvent. The title compound was obtained as a pale yellow liquid (0.835 g, 3.15 mmol, 63%);  $^1\text{H}$  NMR:  $\delta$  8.34 (dd,  $^3J_{\text{HH}} = 4.6$  Hz,  $^4J_{\text{HP}} = 0.8$  Hz, 1H); 7.95 (dd,  $^3J_{\text{HH}} = 8.0$  Hz,  $^4J_{\text{HP}} = 1.1$  Hz, 1H); 7.39 (dd,  $^3J_{\text{HH}} = 8.1$  Hz,  $^3J_{\text{HH}} = 4.7$  Hz, 1H); 4.48–4.36 (m, 4H); 1.52 (dt,  $^3J_{\text{HH}} = 7.0$  Hz,  $^4J_{\text{HP}} = 1.0$  Hz, 6H).  $^{13}\text{C}$  NMR:  $\delta$  145.0 (CH); 143.8 ( $^2J_{\text{CP}} = 5.9$  Hz, C); 142.7 ( $^2J_{\text{CP}} = 8.2$  Hz, C); 129.0 ( $^3J_{\text{CP}} = 2.3$  Hz, CH); 123.1 (CH); 65.1 ( $^2J_{\text{CP}} = 6.4$  Hz,  $\text{CH}_2$ ); 15.8 ( $^3J_{\text{CP}} = 7.0$  Hz,  $\text{CH}_3$ ).  $^{31}\text{P}$  NMR:  $\delta$  44.23. MS ( $m/z$ , relative intensity): 265 (1,  $\text{M}^+$ ), 230 [30, ( $\text{M} - 35$ ) $^+$ ], 202 (21), 174 (100), 156 (2), 129 (11), 109 (21), 81 (33). Anal. Calcd. for  $\text{C}_9\text{H}_{13}\text{ClNO}_4\text{P}$  (265.63): C 40.69; H 4.93; N 5.27. Found: C 40.77; H 4.95; N 5.29.

#### 4.2.5. 2,3-Bis[(diethoxyphosphoryl)oxy]pyridine (2e)

Kenner's method was employed for the reaction of pyridine-2,3-diol (5.0 mmol, 0.555 g) with diethyl hydrogen phosphite (10.4 mmol, 1.340 mL) and triethylamine (10.4 mmol, 1.570 mL) in  $\text{CCl}_4$  (3 mL) as solvent. The title compound was obtained as a pale yellow liquid (0.670 g, 1.75 mmol, 35%);  $^1\text{H}$  NMR:  $\delta$  8.09 (d,  $^3J_{\text{HH}} = 4.4$  Hz, 1H); 7.79 (dd,  $^3J_{\text{HH}} = 8.0$  Hz,  $^4J_{\text{HP}} = 1.1$  Hz, 1H); 7.2 (dd,  $^3J_{\text{HH}} = 8.0$  Hz,  $^3J_{\text{HH}} = 4.8$  Hz, 1H); 4.43–4.34 (m, 4H); 4.33–4.21 (m, 4H); 1.44–1.36 (m, 6H).  $^{13}\text{C}$  NMR:  $\delta$  149.0 (t,  $^2J_{\text{CP}} = 6.4$  Hz, C); 142.7 (CH); 135.9 (dd,  $^2J_{\text{CP}} = 7.8$  Hz,  $^3J_{\text{CP}} = 6.8$  Hz, C); 130.0 ( $^3J_{\text{CP}} = 2.3$  Hz, CH); 121.0 (CH); 64.7 ( $^2J_{\text{CP}} = 6.2$  Hz,  $\text{CH}_2$ ); 64.5 ( $^2J_{\text{CP}} = 6.0$  Hz,  $\text{CH}_2$ ); 15.6 ( $^3J_{\text{CP}} = 6.8$  Hz,  $\text{CH}_3$ ).  $^{31}\text{P}$  NMR:  $\delta$  44.67; 43.43. MS ( $m/z$ , relative intensity): 383 (3,  $\text{M}^+$ ), 355 [1, ( $\text{M} - 28$ ) $^+$ ], 310 (3), 275 (8), 248 (9), 229 (88), 201 (92), 174 (100), 111 (91), 81 (78). Anal. Calcd. for  $\text{C}_{13}\text{H}_{23}\text{NO}_8\text{P}_2$  (383.27): C 40.74; H 6.05; N 3.65. Found: C 40.62; H 6.07; N 3.66.

### 4.3. Reactions in liquid ammonia

#### 4.3.1. Synthesis of 2,5-bis(trimethylstannyl)pyridine (3a)

##### Representative procedure

In a 100 mL two-necked round-bottomed flask, equipped with a cold finger condenser charged with acetone-liquid nitrogen,

a nitrogen inlet and magnetic stirrer, were condensed 80 mL of N-dried ammonia.  $\text{Me}_3\text{SnCl}$  (0.220 g, 1.1 mmol) was dissolved and sodium metal (0.051 g, 2.2 mmol) was added until the blue colour persisted for at least 5 min. When the blue colour disappeared, diethyl 5-chloropyridin-2-yl phosphate (**2a**, 0.5 mmol, 0.132 g) was added drop wise and the solution was irradiated with stirring for 30 min. The reaction was quenched with IMe (32  $\mu\text{L}$ , 1.1 mmol); 10 mL of  $\text{Et}_2\text{O}$  was added and then liquid ammonia was allowed to evaporate.<sup>6</sup> The resultant solution was treated with water and extracted with  $\text{Et}_2\text{O}$  ( $3 \times 10$  mL). The organic phase was successively washed with water and brine, dried over  $\text{MgSO}_4$ , filtered, and concentrated *in vacuo*. Purification by crystallization<sup>7</sup> from EtOH gave 2,5-bis(trimethylstannyl)pyridine (**3a**) as a white solid (0.177 g, 0.43 mmol, 87%); mp: 112–113 °C (Lit [11]: 115–116 °C);  $^1\text{H}$  NMR:  $\delta$  8.54 (s,  $^3J_{\text{HSn}} = 23.6$  Hz, 1H); 7.38 (d,  $^3J_{\text{HH}} = 7.2$  Hz, 1H); 7.17 (d,  $^3J_{\text{HH}} = 7.2$  Hz, 1H); 0.11 (s,  $^2J_{\text{HSn}} = 55.5/53.2$  Hz, 18H,  $\text{SnCH}_3$ ); 0.09 (s,  $^2J_{\text{HSn}} = 56.1/53.6$  Hz, 3H,  $\text{SnCH}_3$ ).  $^{13}\text{C}$  NMR:  $\delta$  172.7 (C); 156.2 ( $^2J_{\text{CSn}} = 61.4/38.1$  Hz, CH); 141.1 ( $^2J_{\text{CSn}} = 32.3/25.8$  Hz, CH); 135.4 (C); 131.9 ( $^2J_{\text{CSn}} = 84.8/27.2$  Hz, CH); -9.6 ( $^1J_{\text{CSn}} = 346.4/331.8$  Hz,  $\text{SnCH}_3$ ); -9.8 ( $^1J_{\text{CSn}} = 356.2/339.0$  Hz,  $\text{SnCH}_3$ ).  $^{119}\text{Sn}$  NMR:  $\delta$  -25.01; -48.07. MS ( $m/z$ , relative intensity): 407 (7,  $\text{M}^+$ ), 392 [34, ( $\text{M} - 15$ ) $^+$ ], 377 (2), 362 (22), 328 (13), 309 (7), 257 (32), 238 (29), 212 (27), 165 (87), 135 (100), 116 (30).

#### 4.3.2. 2,6-Bis(trimethylstannyl)pyridine (3b)

The representative procedure was followed using  $\text{Me}_3\text{SnCl}$  (1.1 mmol, 0.220 g), sodium metal (2.2 mmol, 0.051 g) and diethyl 6-chloropyridin-2-yl phosphate (**2b**, 0.5 mmol, 0.132 g) as starting material. The mixture was irradiated under stirring for 120 min. Purification by distillation (Kügelrohr) gave **3b** as a colorless liquid (0.195 g, 0.48 mmol, 96%); b.p.: 100 °C/5 Torr (Lit [11]: 132–134 °C/10 Torr);  $^1\text{H}$  NMR:  $\delta$  7.35–6.90 (m, 3H); 0.13 (s,  $^2J_{\text{HSn}} = 55.5/53.2$  Hz, 18H,  $\text{SnCH}_3$ ).  $^{13}\text{C}$  NMR:  $\delta$  174.0 (C); 133.5 ( $^2J_{\text{CSn}} = 41.1$  Hz, CH); 131.1 ( $^2J_{\text{CSn}} = 92.1$  Hz, CH); -9.40 ( $^1J_{\text{CSn}} = 346.9/331.0$  Hz,  $\text{SnCH}_3$ ).  $^{119}\text{Sn}$  NMR:  $\delta$  -50.46. MS ( $m/z$ , relative intensity): 407 (1,  $\text{M}^+$ ), 392 [99, ( $\text{M} - 15$ ) $^+$ ], 377 (3), 362 (30), 345 (6), 328 (20), 242 (23), 212 (42), 165 (59), 150 (22), 135 (100), 120 (26).

#### 4.3.3. 3,5-Bis(trimethylstannyl)pyridine (3c)

The representative procedure was followed using  $\text{Me}_3\text{SnCl}$  (1.1 mmol, 0.220 g), sodium metal (2.2 mmol, 0.051 g) and diethyl 5-chloropyridin-3-yl phosphate (**2c**, 0.5 mmol, 0.132 g) as starting material. The mixture was irradiated under stirring for 60 min. Purification by crystallization from EtOH gave **3c** as a white solid<sup>8</sup> (0.138 g, 0.34 mmol, 69%); mp: 107–109 °C (Lit [11]: 118–119 °C/3.5 Torr);  $^1\text{H}$  NMR:  $\delta$  8.42 (s,  $^3J_{\text{HSn}} = 22.5$  Hz, 2H); 7.69 (s,  $^3J_{\text{HSn}} = 40.2$  Hz, 1H); 0.22 (s,  $^2J_{\text{HSn}} = 55.3/53.0$  Hz, 18 H,  $\text{SnCH}_3$ ).  $^{13}\text{C}$  NMR:  $\delta$  155.1 ( $^2J_{\text{CSn}} = 42.3$  Hz, CH); 150.8 ( $^2J_{\text{CSn}} = 24.6$  Hz, CH); 137.2 (C); -9.6 ( $^1J_{\text{CSn}} = 356.2/340.9$  Hz,  $\text{SnCH}_3$ ).  $^{119}\text{Sn}$  NMR:  $\delta$  -25.18. MS ( $m/z$ , relative intensity): 407 (11,  $\text{M}^+$ ), 392 [100, ( $\text{M} - 15$ ) $^+$ ], 377 (1), 362 (21), 345 (6), 330 (13), 315 (15), 165 (22), 150 (12), 135 (28), 120 (9).

#### 4.3.4. 2,3-Bis(trimethylstannyl)pyridine (3d)

The representative procedure was followed using  $\text{Me}_3\text{SnCl}$  (1.1 mmol, 0.220 g), sodium metal (2.2 mmol, 0.051 g) and diethyl 2-chloropyridin-3-yl phosphate (**2d**, 0.5 mmol, 0.132 g). The mixture

<sup>6</sup> We observed that the usual work-up procedure for reactions with organostannides, i.e.,  $\text{NH}_4\text{Cl}$  as quencher and evaporation of liquid ammonia to dryness, prompted proto-destannylation process.

<sup>7</sup> Proto-destannylation products were formed by purification on silica gel column chromatography.

<sup>8</sup> Spectroscopic data of **3c** are in accord with those reported in reference [11]. Nevertheless, we found a divergence in physical characteristics.

was irradiated under stirring for 20 min. Purification by distillation (Kügelrohr) gave **3d** as a pale orange liquid (171 g, 0.42 mmol, 84%); b.p.: 139–141 °C/5 Torr (Lit [11]: 125–127 °C/3 Torr); <sup>1</sup>H NMR: δ 8.60–8.43 (m, 1H); 7.55 (dd, *J*<sub>HH</sub> = 1.9 Hz, *J*<sub>HH</sub> = 7.3 Hz, 1H); 7.03–6.90 (m, 1H); 0.27 (s, <sup>2</sup>*J*<sub>H<sub>Sn</sub></sub> = 53.0 Hz, 18H). <sup>13</sup>C NMR: δ 181.6 (C); 150.0 (<sup>3</sup>*J*<sub>CSn</sub> = 41.6 Hz, CH); 148.1 (C); 141.8 (<sup>2</sup>*J*<sub>CSn</sub> = 59.2 Hz, CH); 121.6 (<sup>3</sup>*J*<sub>CSn</sub> = 42.4 Hz, CH); –7.1 (<sup>1</sup>*J*<sub>CSn</sub> = 346.2/332.9 Hz, SnCH<sub>3</sub>); –7.5 (<sup>1</sup>*J*<sub>CSn</sub> = 345.4/330.9 Hz, SnCH<sub>3</sub>). MS (*m/z*, relative intensity): 407 (7, M<sup>+</sup>), 390 [40, (M – 15)<sup>+</sup>], 360 (13), 330 (8), 313 (5), 256 (32), 242 (37), 212 (63), 186 (16), 165 (100), 135 (69), 120 (25).

#### 4.3.5. Diethyl 5-(trimethylstannyl)pyridin-2-yl phosphate (**4a**)

The representative procedure was followed using Me<sub>3</sub>SnCl (1.1 mmol, 0.220 g), sodium metal (2.2 mmol, 0.051 g) and diethyl 5-chloropyridin-3-yl phosphate (**2c**, 0.5 mmol, 0.132 g) as starting material. The flask was wrapped with aluminium foil and the mixture was stirred for 60 min. Elimination of the solvent rendered **4a** as a pale yellow liquid (0.387 g, 0.98 mmol, 98%); <sup>1</sup>H NMR: δ 7.33 (dt, <sup>4</sup>*J*<sub>HP</sub> = 0.9 Hz, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, 1H); 7.04 (d, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, 1H); 6.63 (d, <sup>3</sup>*J*<sub>HH</sub> = 8.2 Hz, 1H); 4.14–4.04 (m, 4H); 1.14 (dt, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, <sup>4</sup>*J*<sub>HP</sub> = 0.9 Hz, 6H); 0.09 (s, <sup>2</sup>*J*<sub>H<sub>Sn</sub></sub> = 56.1/53.8 Hz, 9H, SnCH<sub>3</sub>). <sup>13</sup>C NMR: δ 172.0 (C); 157.4 (<sup>2</sup>*J*<sub>CP</sub> = 5.9 Hz, C); 137.4 (<sup>2</sup>*J*<sub>CSn</sub> = 37.6 Hz, CH); 128.9 (<sup>2</sup>*J*<sub>CSn</sub> = 82.7/79.8 Hz, CH); 111.9 (<sup>3</sup>*J*<sub>CP</sub> = 7.0 Hz, CH); 64.3 (<sup>2</sup>*J*<sub>CP</sub> = 5.9 Hz, CH<sub>2</sub>); 15.9 (<sup>3</sup>*J*<sub>CP</sub> = 7.0 Hz, CH<sub>3</sub>); –9.5 (<sup>1</sup>*J*<sub>CSn</sub> = 354.5/338.6 Hz, SnCH<sub>3</sub>). <sup>31</sup>P NMR: δ 43.75. <sup>119</sup>Sn NMR: δ –25.16. MS (*m/z*, relative intensity): 395 (1, M<sup>+</sup>), 380 [10, (M – 15)<sup>+</sup>], 365 (1), 350 (20), 322 (69), 304 (21), 290 (19), 275 (26), 258 (7), 244 (100), 228 (28), 214 (41), 199 (10), 183 (23), 165 (62), 150 (17), 135 (66), 123 (17), 109 (45), 94 (26), 81 (74), 65 (14). Anal. Calcd. for C<sub>12</sub>H<sub>22</sub>NO<sub>4</sub>PSn (393.99): C 36.58; H 5.63; N 3.56. Found: C 36.72; H 5.62; N 3.57.

#### 4.3.6. Diethyl 6-(trimethylstannyl)pyridin-2-yl phosphate (**4b**)

The representative procedure was followed using Me<sub>3</sub>SnCl (0.5 mmol, 0.100 g), sodium metal (1.1 mmol, 0.025 g) and diethyl 6-chloropyridin-2-yl phosphate (**2b**, 0.5 mmol, 0.132 g) as starting material. The flask was wrapped with aluminium foil and the mixture was stirred for 10 min. Purification by column chromatography on silica gel (hexane:EtOAc = 60:40) gave **4b** as a beige syrup (0.186 g, 0.47 mmol, 94%); <sup>1</sup>H NMR: δ 7.59–7.23 (m, 1H); 6.79 (d, <sup>3</sup>*J*<sub>HH</sub> = 8.2 Hz, 1H); 6.32 (d, <sup>3</sup>*J*<sub>HH</sub> = 8.6 Hz, 1H); 3.95 (m, 4H); 1.15 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, 6H); 0.33 (s, <sup>2</sup>*J*<sub>H<sub>Sn</sub></sub> = 59.9 Hz, 9H, SnCH<sub>3</sub>). <sup>13</sup>C NMR: δ 165.3 (C); 155.9 (<sup>2</sup>*J*<sub>CP</sub> = 5.7 Hz, C); 142.8 (CH); 128.4 (CH); 114.3 (<sup>3</sup>*J*<sub>CP</sub> = 7.0 Hz, CH); 64.9 (<sup>2</sup>*J*<sub>CP</sub> = 6.4 Hz, CH<sub>2</sub>); 15.9 (<sup>3</sup>*J*<sub>CP</sub> = 6.7 Hz, CH<sub>3</sub>); –9.6 (<sup>1</sup>*J*<sub>CSn</sub> = 363.3/346.4 Hz, SnCH<sub>3</sub>). <sup>31</sup>P NMR: δ 43.70. <sup>119</sup>Sn NMR: δ –50.44. MS (*m/z*, relative intensity): 395 (13, M<sup>+</sup>), 380 [100, (M – 15)<sup>+</sup>], 365 (4), 350 (3), 322 (15), 244 (41), 228 (11), 214 (25), 165 (20), 150 (11), 135 (32), 109 (15), 81 (43), 65 (7). Anal. Calcd. for C<sub>12</sub>H<sub>22</sub>NO<sub>4</sub>PSn (393.99): C 36.58; H 5.63; N 3.56. Found: C 36.68; H 5.61; N 3.55.

#### 4.3.7. Diethyl 5-(trimethylstannyl)pyridin-3-yl phosphate (**4c**)

The representative procedure was followed using 40 mL of sodium-dried ammonia as solvent and Me<sub>3</sub>SnCl (0.5 mmol, 0.100 g), sodium metal (1.1 mmol, 0.025 g) and diethyl 5-chloropyridin-3-yl phosphate (**2c**, 0.5 mmol, 0.132 g) as starting material. The mixture was irradiated under stirring for 60 min. Purification by column chromatography on silica gel (hexane:EtOAc = 60:40) gave **4c** as a pale yellow liquid (0.158 g, 0.40 mmol, 80%); <sup>1</sup>H NMR: δ 8.38–8.29 (s, 2H); 7.60–7.58 (m, 1H); 4.23–4.11 (m, 4H); 1.30 (dt, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, <sup>4</sup>*J*<sub>HP</sub> = 1.1 Hz, 6H); 0.28 (s, <sup>2</sup>*J*<sub>H<sub>Sn</sub></sub> = 56.4/54.2 Hz, 9H, SnCH<sub>3</sub>). <sup>13</sup>C NMR: δ 151.7 (<sup>2</sup>*J*<sub>CSn</sub> = 36.4, CH); 147.8 (<sup>2</sup>*J*<sub>CP</sub> = 7.0 Hz, C); 141.5 (<sup>3</sup>*J*<sub>CP</sub> = 5.3 Hz, CH); 138.4 (C); 134.2 (<sup>3</sup>*J*<sub>CP</sub> = 4.1 Hz, <sup>2</sup>*J*<sub>CSn</sub> = 34.6/25.8 Hz CH); 64.8 (<sup>2</sup>*J*<sub>CP</sub> = 5.9 Hz, CH<sub>2</sub>); 16.1 (<sup>3</sup>*J*<sub>CP</sub> = 6.4 Hz, CH<sub>3</sub>); –9.5 (<sup>1</sup>*J*<sub>CSn</sub> = 362.7/346.2 Hz, SnCH<sub>3</sub>). <sup>31</sup>P NMR: δ 44.65. <sup>119</sup>Sn NMR: δ –25.20. MS (*m/z*, relative

intensity): 395 (15, M<sup>+</sup>), 380 [100, (M – 15)<sup>+</sup>], 365 (2), 350 (25), 322 (5), 304 (4), 290 (4), 265 (5), 243 (5), 217 (10), 165 (9), 135 (8), 120 (5). Anal. Calcd. for C<sub>12</sub>H<sub>22</sub>NO<sub>4</sub>PSn (393.99): C 36.58; H 5.63; N 3.56. Found: C 36.68; H 5.61; N 3.54.

#### 4.3.8. Diethyl 2-(trimethylstannyl)pyridin-3-yl phosphate (**4d**)

The representative procedure was followed using 40 mL of sodium-dried ammonia as solvent and Me<sub>3</sub>SnCl (0.5 mmol, 0.100 g), sodium metal (1.1 mmol, 0.025 g) and diethyl 2-chloropyridin-3-yl phosphate (**2d**, 0.5 mmol, 0.132 g) as starting material. The mixture was irradiated under stirring for 30 min. Purification by column chromatography on silica gel (hexane:EtOAc = 60:40) gave **4d** as a beige syrup (0.176 g, 0.45 mmol, 89%); <sup>1</sup>H NMR: δ 8.56 (d, <sup>3</sup>*J*<sub>HH</sub> = 4.5 Hz, 1H); 7.77–7.58 (m, 1H); 7.15 (m, 1H); 4.27–4.15 (m, 4H); 1.35 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.0 Hz, 6H); 0.39 (s, <sup>2</sup>*J*<sub>H<sub>Sn</sub></sub> = 55.7 Hz, 9H, SnCH<sub>3</sub>). <sup>13</sup>C NMR: δ 164.8 (C); 153.7 (<sup>2</sup>*J*<sub>CP</sub> = 6.0 Hz, C); 147.1 (CH); 123.5 (CH); 122.4 (<sup>3</sup>*J*<sub>CP</sub> = 7.8, CH); 64.6 (<sup>2</sup>*J*<sub>CP</sub> = 5.9 Hz, CH<sub>2</sub>); 15.9 (<sup>3</sup>*J*<sub>CP</sub> = 7.6 Hz, CH<sub>3</sub>); –8.9 (<sup>1</sup>*J*<sub>CSn</sub> = 342.7/326.2 Hz, SnCH<sub>3</sub>). <sup>31</sup>P NMR: δ 44.59. <sup>119</sup>Sn NMR: δ –50.41. MS (*m/z*, relative intensity): 395 (3, M<sup>+</sup>), 380 [100, (M – 15)<sup>+</sup>], 352 (20), 324 (78), 308 (25), 292 (48), 276 (18), 259 (3), 244 (15), 229 (21), 214 (33), 199 (21), 183 (21), 165 (39), 150 (9), 135 (58), 120 (12), 107 (10), 81 (32), 65 (10). Anal. Calcd. for C<sub>12</sub>H<sub>22</sub>NO<sub>4</sub>PSn (393.99): C 36.58; H 5.63; N 3.56. Found: C 36.48; H 5.65; N 3.57.

#### 4.3.9. Diethyl 3-(trimethylstannyl)pyridin-2-yl phosphate (**4e**)

The representative procedure was followed using Me<sub>3</sub>SnCl (0.5 mmol, 0.100 g), sodium metal (1.1 mmol, 0.025 g) and 2,3-bis[(diethoxyphosphoryl)oxy]pyridine (**2e**, 0.5 mmol, 0.191 g) as starting material. The mixture was irradiated under stirring for 180 min. We were not able to isolate compound **4e** from the reaction mixture. MS (*m/z*, relative intensity): 380 [54, (M – 15)<sup>+</sup>], 350 (6), 324 (7), 294 (7), 244 (100), 214 (42), 183 (14), 165 (8), 135 (20), 120 (10), 81 (30), 65 (4).

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## Appendix A. Supplementary data

Copies of <sup>1</sup>H, <sup>13</sup>C and <sup>31</sup>P NMR spectra of compounds **4a–d**.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2010.08.032.

## References

- [1] M. Balabrubramanian, J.G. Keay, in: A.R. Katritzky, C.W. Rees, E.V.F. Scriven (Eds.), *Comprehensive Heterocyclic Chemistry II*, vol. 5, Pergamon Press, London, 1996 (Chapter 6, and references cited therein).
- [2] A.A.-M. Abdel-Aziz, *Tetrahedron Lett.* 48 (2007) 2861; (b) F. Hoffmann-Emery, H. Hilpert, M. Scalone, P. Waldmeier, *J. Org. Chem.* 71 (2006) 2000; (c) J.-C. Fernández, L. Solé-Feu, D. Fernández-Former, N. de la Figuera, P. Fornis, F. Albericio, *Tetrahedron Lett.* 46 (2005) 581.
- [3] E.C. Constable, *Coord. Chem. Rev.* 252 (2008) 842; (b) I. Eryazici, C.N. Moorefield, G.R. Newkome, *Chem. Rev.* 108 (2008) 1834; (c) J. Vicente, J. Gil-Rubio, N. Barquero, P.G. Jones, D. Bautista, *Organometallics* 27 (2008) 646.
- [4] G. Burzicki, A.S. Voisin-Chiret, J. Sopková-de Oliveira Santos, S. Rault, *Tetrahedron* 65 (2009) 5413; (b) C. Corinne Gosmini, C. Bassene-Ernst, M. Durandetti, *Tetrahedron* 65 (2009) 6141; (c) H. S.-Kim, R.D. Rieke, *Tetrahedron Lett.* 50 (2009) 5329; (d) J. Barluenga, A. Jimenez-Aquino, M.A. Fernández, F. Aznar, C. Valdés, *Tetrahedron* 64 (2008) 778; (e) S.J. Teague, *J. Org. Chem.* 73 (2008) 9765; (f) Y. Liu, Q. Ding, X. Wu, *J. Org. Chem.* 73 (2008) 6025; (g) S. Diring, P. Retailleau, R.J. Ziessel, *Org. Chem.* 72 (2007) 10181;



- (h) B.C. Ranu, R. Jana, S. Sowniah, *J. Org. Chem.* 72 (2007) 3152 and further references cited therein.
- [5] F. Havas, N. Leygue, M. Danel, B. Mestre, Ch. Galaup, C. Picard, *Tetrahedron* 65 (2009) 7673;  
(b) Y.A. Getmanenko, R.J. Twieg, *J. Org. Chem.* 73 (2008) 830;  
(c) D. Alberico, M.E. Scott, M. Lautens, *Chem. Rev.* 107 (2007) 174;  
(d) N. Giuseppone, J.-L. Schmitt, J.-M. Lehn, *J. Am. Chem. Soc.* 128 (2006) 16748;  
(e) M. Ghirotti, P.F.H. Schwab, M.T. Indelli, C. Chiorboli, F. Scandola, *Inorg. Chem.* 45 (2006) 4331;  
(f) Y.D.M. Champouret, R.K. Chaggar, I. Dadhiwala, J. Fawcett, G.A. Solan, *Tetrahedron* 62 (2006) 79.
- [6] A.B. Chopa, M.T. Lockhart, G.F. Silbestri, *Organometallics* 19 (2000) 2249;  
(b) A.B. Chopa, M.T. Lockhart, G.F. Silbestri, *Organometallics* 20 (2001) 3358;  
(c) A.B. Chopa, M.T. Lockhart, G.F. Silbestri, *Organometallics* 21 (2002) 5874;  
(d) A.B. Chopa, M.T. Lockhart, V.B. Dorn, *Organometallics* 21 (2002) 1425;  
(e) A.B. Chopa, V.B. Dorn, M.A. Badajoz, M.T. Lockhart, *J. Org. Chem.* 69 (2004) 3801;
- (f) V.B. Dorn, M.A. Badajoz, M.T. Lockhart, A.B. Chopa, A.B. Pierini, *J. Organometal. Chem.* 693 (2008) 2458.
- [7] For reviews see: (a) R.A. Rossi, R.H. de Rossi, *Aromatic substitution by the S<sub>RN</sub>1 mechanism*, In: ACS Monograph 178. American Chemical Society, Washington, DC, 1983;  
(b) R.A. Rossi, A.B. Pierini, A.N. Santiago, in: L.A. Paquette, R. Bittman (Eds.), *Organic Reactions*, vol. 54, Wiley & Sons, 1999 (Chapter 1);  
(c) R.A. Rossi, A.B. Pierini, A.B. Peñeñory, *Chem. Rev.* 103 (2003) 71.
- [8] A.B. Chopa, G.F. Silbestri, M.T. Lockhart, *J. Organometal. Chem.* 690 (2005) 3865.
- [9] Previous results showed that different aryl DEP's did not react with organotin anions without photostimulation. See Ref. 6d.
- [10] E.F. Córscico, R.A. Rossi, *Synlett* (2000) 227.
- [11] Y. Yamamoto, A. Yanagi, *Chem. Pharm. Bull.* 30 (1982) 1731.
- [12] M. Gielen, A. Davies, K. Pannell, E. Tiekink, *Tin Chemistry: Fundamentals, Frontiers and Applications*. Wiley & Sons, Chichester, 2008;  
(b) T. Sato, *Comprehensive Organometallic Chemistry II*, vol. 8, Pergamon, New York, 1995.
- [13] L.-C. Campeau, K. Fagnou, *Chem. Soc. Rev.* 36 (2007) 1058.
- [14] G.W. Kenner, N.R. Williams, *J. Chem. Soc.* (1955) 522.