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Functional polypyridine ligands from copper-mediated room temperature coupling of 4-chloro-2-trimethylsilylpyridine

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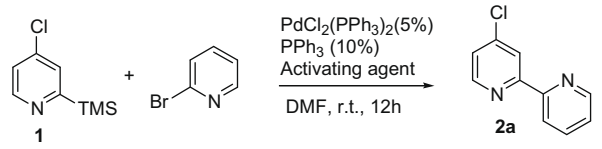
ABSTRACT

A range of functional polypyridine ligands (bipyridines and terpyridine) has been synthesized by copper-mediated oxidative homocoupling of 4-chloro-2-trimethylsilylpyridine or cross-coupling with functional bromopyridines. The reaction proceeded smoothly at room temperature.

Bipyridines (bpy) are highly popular transition metal ligands known since at least one century. Exciting research fields have emerged and were developed, thanks to their unique properties such as supramolecular chemistry,[1–3] NLO,[4,5] and solar cells sensitization.[6–8] All these applications have generated a strong demand for new bpy bearing specific functionalities. This urged the chemists to develop straightforward and chemoselective synthetic routes to these ligands. Since the Krönke synthesis,[9] a ring-building method with low degree of substituent tolerance, several metal-catalyzed approaches have been developed to couple pyridine units. The homocoupling of halogenopyridines has been reported using stoichiometric amount of nickel[10,11] or one-pot Stille reaction using dialkylditins in the presence of catalytic palladium.[12,13] Dissymmetrical bpy were obtained by coupling pyridylzinc (Negishi-type coupling) with pyridyl triflates[14] or chlorides.[15] The most extensively used methodology remains the Stille coupling between pyridylstannanes and pyridyl halides.[16] Good yields have been obtained even on large-scale synthesis.[17–19] However, this methodology suffers from drawbacks such as the purification of starting stannanes, the release of highly toxic tin halides during the transmetallation step, and the often-extended refluxing times favoring side reactions. For example, the preparation of bpy bearing the synthetically useful but sensitive 4-chloro moiety has not been reported by this method.

The Hiyama cross-coupling[20–22] of pyridyltrialkylsilanes is an attractive alternative to this methodology. Indeed the synthesis and purification of the starting silanes is generally easy[23–25] and silicon-containing compounds have a weak environmental impact. Efficient Ag_2O-mediated couplings of 2-allyldimethylsilylpyridines or 2-trimethylsilylpyridine have been reported by the groups of Yoshida[26] and Whittaker,[27] respectively, but only aromatic halides

Table 1
Cross-coupling of 1 with 2-bromopyridine[a]



Entry	BrPy (equiv)	Activating agent (equiv)	**2a**[b] (%)
1	0.5	Ag_2O (1)-TBAF (0.1)[c]	0[d]
2	0.5 or 1	TBAF (2)	0[d]
3	1	CuBr (1)-TBAF (2)	30[e]
4	0.75	CuBr (1)-TBAF (2)	67
5	0.5	CuBr (1)-TBAF (2)	75
6	0.5	CuI (1)-TBAF (2)	90

[a] Reaction performed on 1 mmol of **1**.
[b] Isolated yield from 2-BrPy after column chromatography.
[c] Reaction performed at rt and 90 °C.
[d] Desilylation of **1** and reduction of 2-BrPy.
[e] Compound **1** was recovered (60%).

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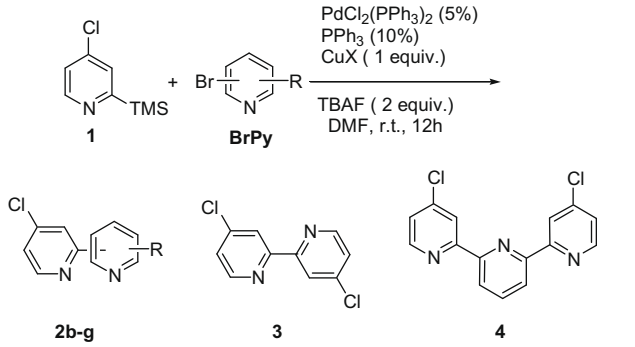
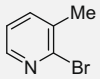
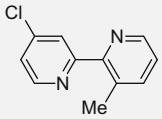
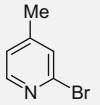
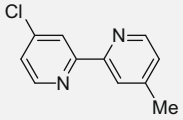
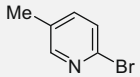
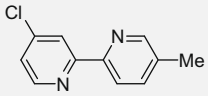
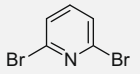
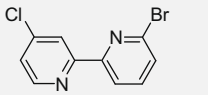
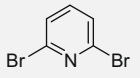
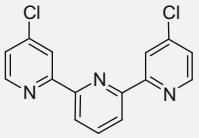
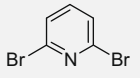
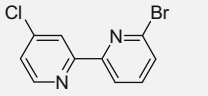
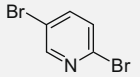
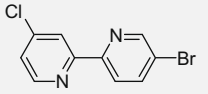
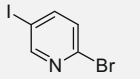
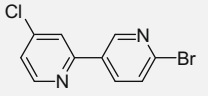
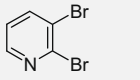
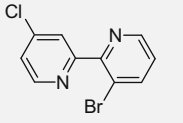
Table 2
Cross-coupling of **1** with functional bromopyridines[a]



BrPy (equiv)		CuX	Conv%[b]	Product	Yield[c] (%)
	0.5	CuI	>98		**2b**, 59
	0.5	CuI	>98		**2c**, 66
	0.5	CuI	>98		**2d**, 73
	0.5	CuI	50		**2e**, 20[d] **4**, 20[d]
	0.25	CuI	>98		**4**, 68
	0.5	CuBr	92		**2e**, 62
	0.5	CuI	96		**2f**, 73
	0.5	CuI	97		**2g**, 40
	0.5	CuI	94		**2h**, 0[e]

[a] Reaction performed on 1 mmol of **1**.
[b] Conversion of BrPy.
[c] Isolated yield after column chromatography except when otherwise stated.
[d] GC yields.
[e] 3-Bromopyridine (40%) and **3** (35%) were formed.

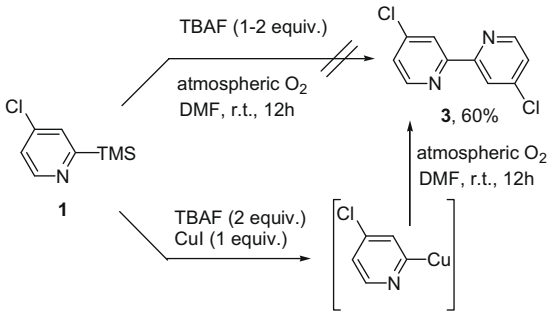
were reacted. Our group has disclosed another approach involving the copper-mediated coupling of trimethylsilyl halogenopyridines.[25] As part of a program on the modular synthesis of bpy-based dyes for solar cells, we needed efficient methods for the preparation of ligands bearing chlorine at C-4 for further tuning the electronic properties. Since no general synthesis of functional bpy was available using the Hiyama reaction, we decided to investigate the cross-coupling of 4-chloro-2-trimethylsilylpyridine **1**[24,28] that can be prepared in high yield on the gram scale. We focused on reactions with various halogenopyridines partners bearing moieties of synthetic interest.

The reaction of **1** with 2-bromopyridine was chosen as the model reaction and investigated using various activating agents (Table 1). The Ag_2O-mediated coupling was first attempted using the conditions of Whittaker and co-workers, reported to give excellent yields with aromatic halides. Unfortunately, no bipyridine **2a** was formed even after extended reaction time and only desilylation of **1** was observed (entry 1). The copper-mediated coupling was then examined using DMF as the solvent and TBAF as the fluoride source.

The control experiments clearly showed the influence of copper salts on the reaction pathway. Indeed the cross-coupling occurred exclusively in their presence. The coupling performed in the presence of TBAF alone only gave desilylation of **1** (entry 2). The amount of bromopyridine was also a key factor; the best yields being obtained with 0.5 equiv. A significant copper halide effect was observed under these conditions. Indeed the yield of the target product **2a** was raised from 75% to 90% using CuBr and CuI, respectively (entries 5 and 6). Attempts with lower amounts of CuI (0.5 equiv) gave lower yields and concomitant desilylation. Thus a methodology of high interest for the preparation of chlorinated bipyridines was in our hands.

The scope of the cross-coupling was next examined by reacting various substituted pyridines focusing on those bearing reactive groups (Table 2). Bromopicolines are highly useful substrates since functionalities can be introduced on the methyl substituent such as halogens,[29,30] sulfanyl groups.[31] It can be also oxidized or turned into styryl group to give conjugated systems.[32,33] Applying the above-determined coupling conditions to a set of 2-bromopicolines, the new bipyridines **2b–d** bearing both donor and acceptor moieties were obtained in good yields. To our knowledge, despite their attractiveness for coordination chemistry, the preparation of such ligands has not been reported yet probably due to lack of efficient methodologies. The cross-coupling with dibromopyridines, another class of important partners, was next examined.

Several isomers were reacted with **1**. 2,6-Dibromopyridine was first studied with the aim to obtain the brominated bpy **2e** or terpyridine **4**. A first run, applying the above-mentioned conditions with CuI, gave a 1:1 mixture of **2e** and **4** in low yield. This meant that it was possible to obtain **4** in a one-pot route. The dibromopyridine amount was then decreased to 0.25 equiv and we were pleased to obtain the expected terpyridine **4** exclusively in good 68% yield. To our knowledge this important ligand has not been reported and very mild conditions have been found here to access it. Since CuI or in situ formed TBAI probably favored the second coupling via bromine–iodine exchange, the control of mono-coupling was then attempted by switching from CuI to CuBr. Under these conditions, the brominated bpy **2e** was isolated in 62% yield. 2,5-Dibromopyridine was also gently coupled giving **2f** in very good yield (73%). No terpyridine was formed in this case due to the lower polarization of the C–Br bond at C-5 and consequent low propensity to give oxidative addition of palladium at room temperature. An increase of reaction temperature up to 90 °C did not promote the subsequent coupling but only degradation of starting **1**. The mild conditions used here also had a consequence on the stability of **2f** by preventing reduction of the C–Br bond in contrast with reported refluxing processes.[34] The use of 2-bromo-3-iodopyridine allowed to introduce the chloropyridyl group at the C-3 position leading to **2g** in 40% yield. 2,3-Dibromopyridine was converted (94%) but only into 3-bromopyridine as a result of reduction at C-2. Compound **3** was also obtained (35%). In this case



Scheme 1. Preparation of **3** by oxidative coupling of **1**.

steric effects due to bromine at C-3 were held responsible for the absence of cross-coupling. Dichlorobipyridine **3** is a useful ligand,[35] and its preparation usually requires the use of toxic hexamethylditin[12] or multistep synthesis from 4,4′-dinitro-2,2′-bipyridine *N*-dioxide.[35] It was thus of interest to optimize our procedure. The formation of **3** strongly suggested the involvement of a pyridylcopper intermediate resulting from silicon–copper transmetallation in the pyridylfluorosilicate first generated by reaction of **1** with TBAF. Such a silicate–copper transmetallation was reported by Mori and co-workers with aryldifluorosilanes.[36] This process has been found to be highly favored by polar solvents like DMF (the solvent used here). Organocuprates are known to release homocoupling products upon contact with oxygen of air.[36,37] Thus, **1** was reacted with TBAF (2 equiv) and CuI (1 equiv) in DMF in the presence of atmospheric oxygen. Bipyridine **3** was obtained in 60% yield (Scheme 1). As shown, the homocoupling did not occur from the pyridylsilicate in the absence of copper iodide and only degradation of **1** was observed.

In summary, we have developed an efficient room temperature synthesis of polypyridine ligands from the easily accessible 4-chloro-2-trimethylsilylpyridine. The cross-coupling and oxidative homocoupling proceeded under mild conditions allowing the retention of reactive moieties such as methyl groups and halogens. Additionally, an access was also opened to a new dichlorinated terpyridine in good yield by one-pot double cross-coupling. This methodology is of high interest for the design of tunable ligands for coordination chemistry. Works are in progress in this field.

Acknowledgments

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Supplementary data

Supplementary data (experimental procedures and characterization data for all compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.133.

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