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Synthesis of novel halopyridinylboronic acids and esters. Part 4: Halopyridin-2-yl-boronic acids and esters are stable, crystalline partners for classical Suzuki cross-coupling☆

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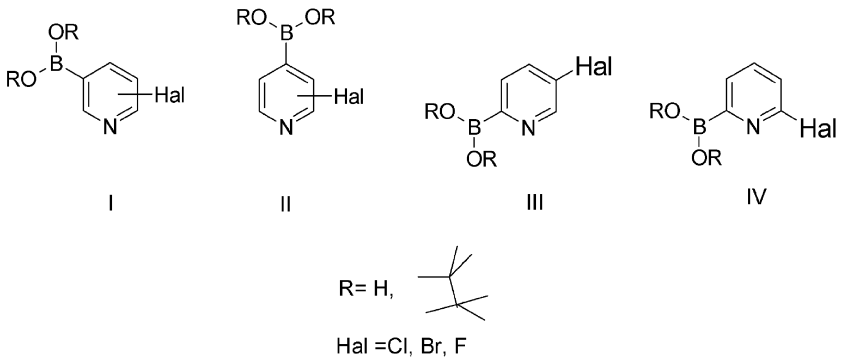
Abstract—This paper describes some methods for the synthesis and the isolation of novel 5 or 6-halopyridin-2-yl-boronic acids and esters **3**, **4**, **7**. These compounds are prepared via a regioselective halogen–metal exchange using *n*-butyllithium and subsequent quenching with triisopropylborate starting from appropriate dihalopyridines. All substrates studied to date provided a single regioisomeric boronic acid or ester product. Additionally, these compounds have been found to undergo Pd-catalysed coupling with arylhalides and authorise a strategy to produce new pyridines libraries.

1. Introduction

In order to complete our first three studies concerning mild and flexible strategies to design new pyridines libraries, we wish to describe herein the last series of halopyridinylboronic acids and esters. This work is by far the most difficult since these compounds have been proved to exhibit really poor stability. Focusing on a general method for the synthesis of halopyridin-3-ylboronic acids and esters **I**[1,2] and halopyridin-4-yl-boronic acids and esters **II**,[3] we found that such boron building-blocks are more stable than their dehalogenated homologues. Keeping in mind that the pyridin-2-yl-boronic moiety is increasingly needed by synthetic chemists to design new pyridin-based libraries, we want to turn our experience in the field of pyridinylboron derivatives to account. It is also a great challenge to prepare derivatives exhibiting such a difficult background. Thus, in the fourth part of this work, we report the synthesis, the isolation, some X-ray crystallography data and the reactivity of new 5, or 6-halopyridin-2-yl-boronic acids and esters **III** and **IV**.



☆ For Parts 1, 2, 3 see Refs. 1–3.

Keywords: boronic acids; lithiation; cross-coupling reaction; pyridine.
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2. Results and discussion

We have now proved that halopyridin-3-yl-boronic acids and esters **I** and halopyridin-4-yl-boronic acids and esters **II** can be relatively easy to prepare, following adapted procedures.[1,2,3] Such a good stability can be referred to a decreased in nitrogen basicity when the pyridine ring is substituted by an halogen atom. Yet, preparing halopyridin-2-yl-boronic acids and esters **III** appear to be a hard task since Fisher[4] has shown the unstability of the boronic moiety in α position of pyridine ring. Moreover, a brominated pyridine ring has been shown to be weakened by the introduction of an alkylborane moiety[5] so that it can be cleaved to give unsaturated nitriles. As a matter of fact, attempts to isolate the requisite pyridin-2-ylborane adducts have always been problematic.[6] For instance, attempted formation and isolation of a boronic acid from reaction of 2-lithio-6-methoxypyridine with triisopropylborate was similarly problematic. The only alternative was the method of Keay which consists of the formation of a presumed boron 'ate' complex[7,8] that is used without purification in modified Suzuki coupling.[9] But such compounds cannot be used in combinatorial approaches, boron ate complexes being difficult to quantify.

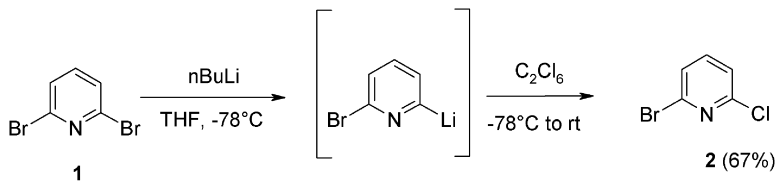
2.1. 6-Halopyridin-2-yl-boronic acids and esters

Since 2,6-dibromopyridine possesses two potential sites for bromine-lithium exchange, the first difficulty is to control the extend of lithiation. It has been reported that only monolithiation is observed with excess *n*-BuLi in ether.[10,11] But Cai et al. were unable to reproduce this result and found that clean monolithiation in THF is accomplished by reverse addition of 2,6-dibromopyridine to 1 equiv. of *n*-BuLi at −78°C.[12]

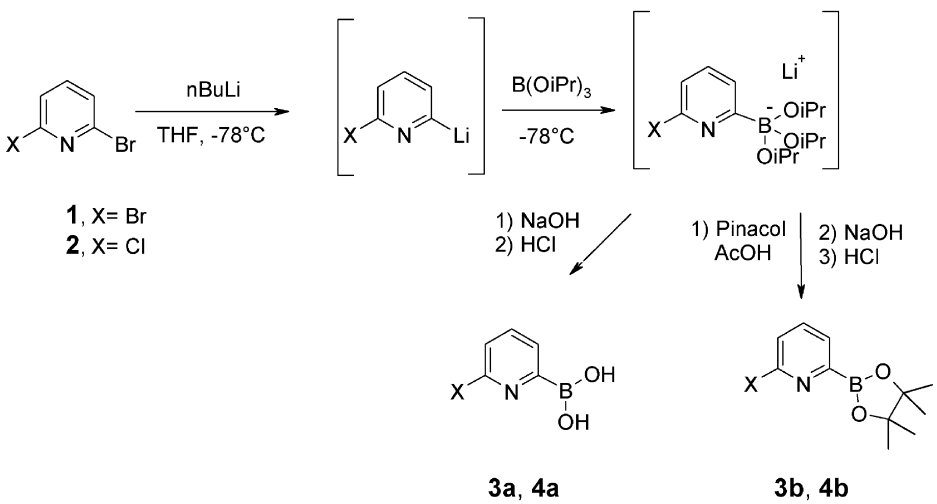
Our first concern was to prepare 2-bromo-6-chloropyridine from 2,6-dibromopyridine, using this method for desymmetrization. As expected, only one bromine was exchanged, giving the monolithiopyridine. Halogenation of organolithium compounds can usually be accomplished with a number of halogenating agents,[13] we used hexachloroethane as an electrophile, because it has been found to give optimal results[14] (Scheme 1).

Holding an efficient method for lithiation and two potential starting materials, we were able to prepare pyridin-2-yl boronic derivatives. Thus, in our case, bromine–lithium exchange was carried out in THF at −78°C by reverse addition of 2,6-dibromopyridine to 1 equiv. of *n*-BuLi followed by the reaction with triisopropylborate as an electrophile, known to form more stable intermediates than other borates[15] (Scheme 2).

Both boronic acid and corresponding pinacol ester were prepared using the method already described for halopyridin-3-yl-boronic acids and esters.[1,2] Namely, the boronic acids **3a**, **4a** were obtained within 45–55% yield after the now classical work-up avoiding the formation of pyridinium salts and the deboronation. In an ice bath, the mixture was quenched by slow addition of 3% aqueous NaOH solution and the resulting aqueous layer neutralised by careful addition of diluted aqueous HCl (3N). The boronic acids **3a** and **4a** are easy to purify and stable when they are stored below 5°C.



Scheme 1. Preparation of 2-bromo-6-chloropyridine via selective monolithiation of 2,6-dibromopyridine.

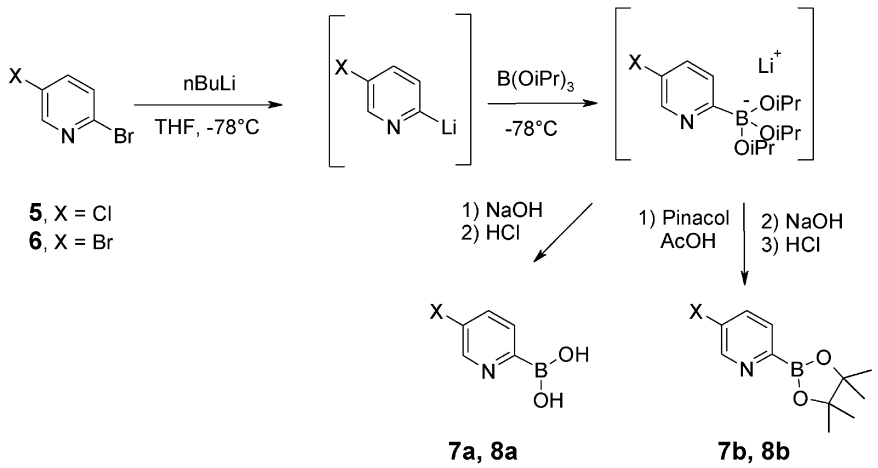


Scheme 2. Obtention of boronic acids **3a**, **4a** and esters **3b**, **4b**.

Table 1.

Compounds	X	Boronic acid	Yield (%)	Boronic ester	Yield (%)
1	Br	**3a**	55	**3b**	56
2	Cl	**4a**	45	**4b**	38

THF at −78°C seeing that chlorine will not be exchanged in such conditions.[21] Bromine–lithium exchange was carried out in THF at −78°C. Trapping the intermediate lithiopyridine with triisopropylborate and further aqueous treatments gave the expected boronic acid **7a** and ester **7b** in moderate yields (Scheme 3, Table 2).



Scheme 3. Obtention of boronic acid **7a** and ester **7b**.

Table 2.

Compounds	X	Boronic acid	Yield (%)	Boronic ester	Yield (%)
5	Cl	**7a**	36	**7b**	47
6	Br	**8a**	–	**8b**	–

Concerning the pinacol-protected boronic acids, transesterification was achieved following Coudret's one-pot procedure.[16] These conditions, applied to **1** and **2** and followed by a similar work-up to the one we used for boronic acids, yielded 38–56% of the corresponding pinacol esters **3b** and **4b** which crystallised quite easily (Scheme 2, Table 1).

In order to compare the structure of 6-bromopyridin-2-yl boronic ester to that of 6-bromopyridin-3-yl boronic ester,[17] X-ray crystallography studies were conducted, seeking for C–B bond length and Nitrogen effect in particular.

First results showed a slight deformation of the boronic ester moiety which undergoes the effect of nitrogen. As a consequence, C–B bond is quite longer (1.578 vs 1.557) and may be more fragile than pyridin-3-yl derivatives. Nevertheless, we found that crystal structure of 6-bromopyridin-2-yl boronic ester is not very different from the pyridin-3-yl isomer's, showing that strong interactions between boron and nitrogen are not encountered in this case. More details, and a comparison between the ester **3b** and some others have been published.[18]

These X-ray crystallography data are ones of the few solved structure containing the N–C–B chain.[19,20] Moreover this is the first pyridin-2-yl boron moiety ever solved.

2.2. 5-Halopyridin-2-yl-boronic acids and esters

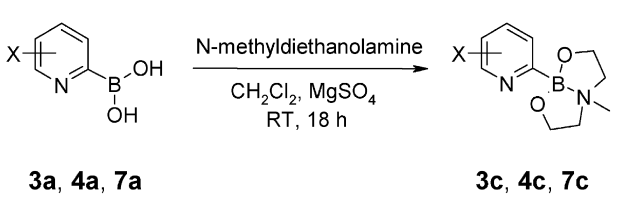
In the case of 2-bromo-5-chloropyridine, we used the fact that bromine can be exchanged selectively, using *n*-BuLi in

The case of 2,5-dibromopyridine was much more problematic. It has been shown that bromine–lithium exchange can be selectively driven either at the 2-position or the 5-position.[22] In our laboratory, we were able to prepare selectively the 6-bromopyridin-3-ylboronic derivatives in ether. Modifying the solvent, the temperature, the reaction time or the concentration could be a great solution to totally change the regioselectivity of the lithiation.[23] Unfortunately, all the assays we attempted resulted in isolation of very poor yields of 6-bromopyridin-3-ylboronic derivatives and no 6-bromopyridin-2-ylboronic derivatives were detected.

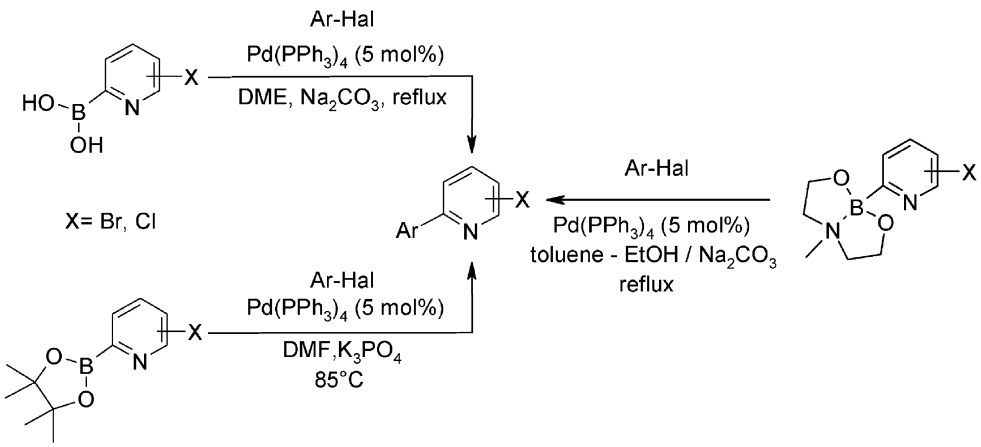
2.3. Synthesis of dioxazaborocanes

Another way to obtain more stable and usable boron derivatives stands in the formation of particular esters.[4,24] These dioxazaborocanes possess a tetracoordinated boron[25] which can no more interact with pyridine nitrogen. Their synthesis is quite easy and can even be realised starting from crude boronic acid (Scheme 4). Yields are quantitative and these particular esters are much more stable than every other boron derivative.

A special general study concerning these pyridinyl dioxazaborocanes, their stability and special reactivity will be published as soon as possible.



Scheme 4. Obtention of dioxazaborocanes **3c**, **4c**, and **7c**.



Scheme 5. Suzuki cross-couplings of pyridin-2-ylboronic acids a or esters b.

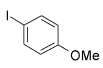
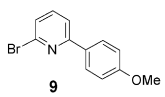
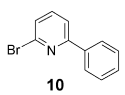
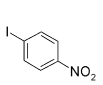
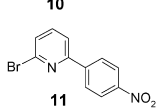
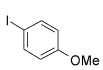
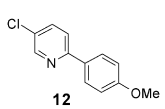
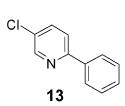
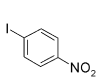
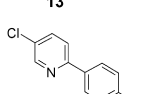
2.4. Suzuki couplings

As illustrated in Scheme 5, the boronic acids **a**, the esters **b** and dioxazaborocane **c** were efficiently coupled with aryl halides under standard Suzuki-type conditions,[26,27] furnishing a range of unknown (**11**, **12**, **14**) or not easily accessible (**9**,[28,29] **10**,[30] **13**)[31,32] arylpyridines, as exemplified in Table 3.

These cross-couplings gave moderate yields of pure arylpyridines **9**–**14** which were isolated following column chromatography.

Interestingly, **3a**, **3b** or **3c** do not react as both the aryl boronic and aryl bromide fragments since no 'homo-coupled' products were observed.[33]

Table 3.

Compounds	Ar-X	Arylpyridine	Yield (%)
3a		 **9**	58
3b			54
3c			47
3a		 **10**	53
3a		 **11**	45
3b			42
7a		 **12**	65
7b			58
7a		 **13**	55
7b		 **14**	78

It is very important to recognise the dual role of halogens in such compounds. On the one hand, they stabilise the boron derivative, on the second hand, they can be involved in other chemical transformations. Further experiments concerning the double reactivity of these compounds are currently under investigation in order to use these new starting materials in the production of new pyridine libraries. These results will be published elsewhere.

3. Experimental

3.1. General procedures

Commercial reagents were used as received without additional purification. Melting points were determined on a Köfler melting point apparatus and are uncorrected. IR spectra were taken with a Perkin–Elmer Spectrum BX FT-IR System spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a JEOL Lambda 400 Spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. The mass spectra (MS) were taken on a JEOL JMS GCMate spectrometer at a ionizing potential of 70 eV. Thin-layer chromatographies (TLC) were performed on 0.2 mm precoated plates of silica gel 60F-264 (Merck). Visualization was made with ultraviolet light (254 nm). Column chromatographies were carried out using silica gel 60 (0.063–0.2 mm) (Merck). Elemental analyses for new compounds were performed at the 'Institut de Recherche en Chimie Organique Fine' (Rouen).

2,6-Dibromopyridine, 2-amino-5-chloropyridine, were purchased from Acros Organics and were used without further purification.

3.2. General procedure for the synthesis of halopyridin-2-ylboronic acids (3a, 4a, 7a)

To a slurry of 2.5 M solution of *n*-BuLi (9.4 mL, 24 mmol, 1.2 equiv.) in freshly distilled tetrahydrofuran, cooled to −78°C, was added a solution of appropriate 2-bromohalopyridine (1 equiv.) in THF. The resulting dark colored mixture was allowed to react at this temperature over

45 min. A solution of triisopropylborate (4.42 g, 24 mmol, 1.2 equiv.) was then added and the mixture was abandoned at −78°C for 2 h, and then allowed to warm to room temperature and stirred for an additional hour. The mixture was quenched by slow addition of 3% aqueous NaOH solution (200 mL). The resulting aqueous layer was collected and acidified down to pH 5–6 by dropwise addition of 3N HCl (≈90 mL), keeping the internal temperature below 5°C. Extraction with ethyl acetate, evaporation of the organic layer and crystallisation from ether gave **3a**; **4a**; **7a**.

3.2.1. 6-Bromopyridin-2-yl-boronic acid (3a). White solid, dec 210°C. IR (KBr): 3391, 1573, 1543, 1447, 1415, 1385, 1303, 1171, 1108, 987, 789, 681 cm^{-1}. ^1H NMR (d6-DMSO) δ 7.95 (s, 2H), 7.84 (d, J=7.2 Hz, 1H), 7.76 (dd, J=7.2, 7.9 Hz, 1H), 7.68 (d, J=7.9 Hz, 1H). Anal. calcd for $C_5H_5BBrNO_2$: C, 29.76; H, 2.50; N, 6.94. Found: C, 29.81; H, 2.39; N, 6.77.

3.2.2. 6-Chloropyridin-2-yl-boronic acid (4a). White solid, dec 200°C. IR (KBr): 2989, 1452, 1396, 1345, 1318, 1144, 1129, 860, 805 cm^{-1}. ^1H NMR (d6-DMSO) δ 8.15 (s, 2H), 7.69–7.55 (m, 3H). Anal. calcd for $C_5H_5BClNO_2$: C, 38.16; H, 3.20; N, 8.90. Found: C, 38.34; H, 3.42; N, 8.65.

3.2.3. 5-Chloropyridin-2-yl-boronic acid (7a). Yellowish solid, mp>250°C. IR (KBr): 3388, 3105, 1613, 1410, 1184, 1072, 774 cm^{-1}. ^1H NMR (d6-DMSO) δ 8.66 (s, 2H), 8.52 (s, 1H), 8.43 (d, J=4.1 Hz, 1H), 7.39 (d, J=4.1 Hz, 1H). Anal. calcd for $C_5H_5BClNO_2$: C, 38.16; H, 3.20; N, 8.90. Found: C, 38.39; H, 3.40; N, 8.64.

3.3. General procedure for the synthesis of halopyridin-2-yl boronic esters (3b, 4b, 7b)

To a slurry of 2.5 M solution of *n*-BuLi (17 mL, 43 mmol, 1.2 equiv.) in dried tetrahydrofuran, cooled to −78°C, was added a solution of 2-bromohalopyridine (1 equiv.) in THF. The resulting dark coloured mixture was allowed to react at this temperature over 45 min. A solution of triisopropylborate (8.0 g, 43 mmol, 1.2 equiv.) was then added dropwise and the mixture allowed to warm to room temperature and stirred for an additional hour. A solution of anhydrous pinacol (5.65 g, 48 mmol, 1.35 equiv.) in THF was added and, after 5 min, a solution of glacial acetic acid (2.3 g, 40 mmol, 1.05 equiv.). The mixture was filtered through Celite, and extracted by 2.5% aqueous NaOH solution (200 mL). The resulting aqueous layer was collected and acidified down to pH 6–7 by dropwise addition of 3N HCl, keeping the internal temperature below 5°C. Extraction with ether, evaporation of the ethereal layer and washing with acetonitrile gave **3b**; **4b**; **7b**.

3.3.1. 2-[2-(6-Bromo)pyridine]-4,4,5,5-tetramethyl-1,3-dioxaborolane (3b). White solid, mp 128°C. IR (KBr): 2976, 2934, 1545, 1450, 1391, 1343, 1318, 1126, 858, 801, 710 cm^{-1}. ^1H NMR (d6-DMSO) δ 7.72–7.65 (m, 3H), 1.28 (s, 12H). ^{13}C NMR (d6-DMSO) δ 142.4, 138.6, 130.1, 129.8, 84.4, 24.7. MS [m/z] 283–284–285–286, [m/z-Br] 202–204. Anal. calcd for $C_{11}H_{15}BBrNO_2$: C, 46.53; H, 5.32; N, 4.93. Found: C, 46.60; H, 5.45; N, 4.87.

3.3.2. 2-[2-(6-Chloro)pyridine]-4,4,5,5-tetramethyl-1,3-dioxaborolane (4b). White solid, mp 108°C. IR (KBr): 2989, 1452, 1396, 1345, 1318, 1144, 1129, 860, 805 cm^{-1}. ^1H NMR (d6-DMSO) δ 7.83 (dd, J=7.0, 8.0 Hz, 1H), 7.69 (d, J=7.0 Hz, 1H), 7.55 (d, J=8.0 Hz, 1H), 1.29 (s, 12H). ^{13}C NMR (d6-DMSO) δ 151.0, 138.8, 129.7, 126.1, 84.4, 24.6. MS [m/z] 238–239–240–241, [m/z-Cl] 203–204. Anal. calcd for $C_{11}H_{15}BClNO_2$: C, 55.16; H, 6.31; N, 5.85. Found: C, 55.28; H, 6.40; N, 5.92.

3.3.3. 2-[2-(5-Chloro)pyridine]-4,4,5,5-tetramethyl-1,3-dioxaborolane (7b). White solid, mp 107°C. IR (KBr): 2974, 1460, 1405, 1382, 1191, 1167, 1146, 1043, 880, 821, 762, 700 cm^{-1}. ^1H NMR (d6-DMSO) δ 8.62 (s, 1H), 8.52 (d, J=4.4 Hz, 1H), 7.55 (d, J=4.4 Hz, 1H), 1.31 (s, 12H). ^{13}C NMR (d6-DMSO) δ 148.7, 147.2, 135.3, 129.6, 84.7, 24.5. MS [m/z] 238–239–240–241, [m/z-Cl] 203–204. Anal. calcd for $C_{11}H_{15}BClNO_2$: C, 55.16; H, 6.31; N, 5.85. Found: C, 55.29; H, 6.41; N, 5.93.

3.4. General procedure for the synthesis of dioxazaborocanes

To a solution of pyridin-2ylboronic acid and $MgSO_4$ (ca. 1 g per mmol) in freshly distilled CH_2Cl_2 (15 mL) is added dropwise a solution of *N*-methyldiethanolamine (1.05 equiv.) in CH_2Cl_2, The mixture is allowed to react under strong stirring for 18 h. The mixture is then filtered under reduced pressure. The filtrate is dried over $MgSO_4$ and concentrated to dryness. The residue was pure enough for further purpose but analytical samples could be prepared by crystallisation from acetonitrile.

3.4.1. 2-[2-(6-Bromo)pyridine]-1,3,6-dioxazaborocane (3c). Cream solid (98%), mp 160°C. IR (KBr): 3076, 3053, 2966, 2878, 2848, 1572, 1535, 1468, 1424, 1380, 1224, 1151, 1106, 1085, 965, 852, 802, 737, 708 cm^{-1}. ^1H NMR (d6-DMSO) δ 7.51 (m, 2H), 7.34 (dd, J=8.6, 1.8 Hz, 1H), 3.88 (m, 4H), 3.25 (m, 2H), 2.99 (m, 2H), 2.34 (s, 3H). Anal. calcd for $C_{10}H_{14}BBrN_2O_2$: C, 42.15; H, 4.95; N, 9.83. Found: C, 42.10; H, 4.99; N, 9.88.

3.4.2. 2-[2-(5-Chloro)pyridine]-1,3,6-dioxazaborocane (7c). Beige solid, mp 135°C. IR (KBr): 3070, 3050, 2963, 1570, 1532, 1470, 1422, 1376, 1220, 1152, 1085, 965 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.39 (s, 1H), 8.31 (d, J=4.7 Hz, 1H), 7.61 (d, J=4.7 Hz, 1H), 4.10 (m, 4H), 3.19 (m, 4H), 2.52 (s, 3H). Anal. calcd for $C_{10}H_{14}BClN_2O_2$: C, 49.94; H, 5.87; N, 11.65. Found: C, 49.82; H, 5.79; N, 11.74.

3.5. General procedure for the palladium-assisted coupling of pyridylboronic acid with halo compounds

A mixture of halopyridylboronic acid (1.2 equiv.), halocompound (bromobenzene, 2-iodo-4-nitrobenzene or 4-iodoanisole) (1 equiv.), tetrakis-(triphenylphosphine)palladium (0) (4% mol) and aqueous Na_2CO_3 (2.3 equiv.) in DME was heated to reflux for 3–12 h (total consumption of halocompound seen on TLC). Ethyl acetate and water were then added to the mixture. The organic layer was separated, dried over $MgSO_4$ and concentrated to dryness. The residue was chromatographied on silica gel (cyclohexane 80–ethyl acetate 20).

3.6. General procedure for the palladium-assisted coupling of pyridylboronic ester with halo compounds

A mixture of halopyridylboronic ester (1.1 equiv.), halo-compound (bromobenzene, 2-iodo-4-nitrobenzene or 4-iodoanisole) (1 equiv.), tetrakis-(triphenylphosphine) palladium (0) (4% mol) and 2N aqueous K_3PO_4 (2 equiv.) solution in DMF was heated at 85°C for 3–12 h. (consumption of halocompound seen on TLC). Ethyl acetate and an excess of water were then added to the mixture. The organic layer was separated, dried over $MgSO_4$ and concentrated to dryness. The residue was chromatographied on silica gel (cyclohexane 80–ethyl acetate 20).

3.7. General procedure for the palladium-assisted coupling of pyridyldioxazaborocane with halo compounds

A mixture of halopyridyldioxazaborocane (1.1 equiv.), halo-compound (bromobenzene, 2-iodo-4-nitrobenzene or 4-iodoanisole) (1 equiv.), tetrakis-(triphenylphosphine) palladium(0) (4% mol) and aqueous Na_2CO_3 solution in a mixture of 80% of toluene with 20% of ethanol was heated to reflux for 3–12 h (disappearance of halocompound seen on TLC). Ethyl acetate and water were then added to the mixture. The organic layer was separated, dried over $MgSO_4$ and concentrated to dryness. The residue was chromatographied on silica gel (cyclohexane 80–ethyl acetate 20).

3.7.1. 2-Bromo-6-(4-methoxyphenyl)pyridine (9). White solid, mp 110°C. IR (KBr): 2961, 2840, 1609, 1576, 1550, 1513, 1432, 1252, 1180, 1126, 1025, 841, 793 cm^{-1}. ^1H NMR (d6-DMSO) δ 7.99 (d, J=8.8 Hz, 2H), 7.93 (d, J=8.0 Hz, 1H), 7.77 (t, J=8.0 Hz, 1H), 7.50 (d, J=7.9 Hz, 1H), 7.04 (d, J=8.8 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR (d6-DMSO) δ 160.7, 157.1, 141.2, 140.4, 129.3, 128.1, 125.6, 118.6, 114.3, 55.2.

3.7.2. 2-Bromo-6-phenylpyridine (10). White solid, mp <60°C. IR (KBr): 2961, 2840, 1609, 1576, 1550, 1513, 1432, 1252, 1180, 1126, 1025, 841, 793 cm^{-1}. ^1H NMR ($CDCl_3$) 7.29 (d, 1H, J=6.0 Hz), 7.38 (m, 3H), 7.50 (t, 1H, J=6.0 Hz), 7.59 (d, 1H, J=6.0 Hz), 7.98 (m, 2H). ^{13}C NMR ($CDCl_3$) 119.0, 127.4, 129.1, 129.4, 137.9, 139.9, 140.5, 141.3, 157.2.

3.7.3. 2-Bromo-6-(4-nitrophenyl)pyridine (11). Cream solid, mp 134°C. IR (KBr): 1674, 1576, 1554, 1508, 1426, 1337, 1162, 1125, 1047, 858, 796, 786, 754, 690 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.32 (d, J=8.6 Hz, 2H), 8.18 (d, J=8.6 Hz, 2H), 7.78 (d, J=7.7 Hz, 1H), 7.68 (t, J=7.7 Hz, 1H), 7.53 (d, J=7.8 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 155.8, 142.6, 139.3, 134.7, 130.2, 127.9, 127.8, 124.0, 119.8. Anal. calcd for $C_{12}H_{11}BrN_2O_2$: C, 48.84; H, 3.76; N, 9.49. Found: C, 48.86; H, 3.83; N, 9.61.

3.7.4. 5-Chloro-2-(4-methoxyphenyl)-pyridine (12). Orange solid, mp 84°C. IR (KBr): 2959, 2836, 1601, 1575, 1432, 1260, 1176, 1122, 1022, 837, 788 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.50 (d, J=8.9 Hz, 2H), 7.41 (s, 1H), 7.22 (d, J=8.7 Hz, 1H), 6.95 (d, J=8.7 Hz, 1H), 6.63 (d, J=8.9 Hz, 2H), 3.72 (s, 3H). Anal. calcd for $C_{12}H_{10}ClNO$: C, 65.61; H, 4.59; N, 6.38. Found: C, 65.70; H, 4.63; N, 6.43.

3.7.5. 5-Chloro-2-(4-nitrophenyl)-pyridine (14). Yellow solid, mp 158°C. IR (KBr): 1601, 1577, 1531, 1513, 1464, 1393, 1349, 1104, 836, 774, 734, 716, 696 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.74 (s, 1H), 8.61 (d, J=4.8 Hz, 1H), 8.36 (d, J=8.5 Hz, 2H), 7.66 (d, J=8.4 Hz, 2H), 7.30 (d, J=4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 150.4, 148.2, 148.0, 145.4, 142.7, 130.1, 129.8, 124.8, 123.7. Anal. calcd for $C_{12}H_{11}ClN_2O_2$: C, 57.50; H, 4.42; N, 11.17. Found: C, 57.38; H, 4.29; N, 11.33.

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