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Synthesis of new linear poly(phenylpyridyl) chains

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ABSTRACT

This paper describes for the first time an efficient approach of Suzuki Miyaura cross-coupling reaction leading to new mixed linear unsymmetric phenylpyridyl chains (garlands). We have studied the synthesis of new phenylpyridyl boronic species and their reactivity with a dihalogenated bipyridine to obtain four and six unit phenylpyridines.

1. Introduction

Conjugated systems, such as oligopyridines are widely described in literature for their applications, including use as organic light-emitting materials, liquid crystalline materials, effective drug delivery agents, and highly efficient catalysts.[1–3] This property has been featured in several applications not only in organic chemistry but also in biology. Quite recently, Hamilton et al. synthesize, as protein–protein interaction inhibitor, a terphenyl scaffold, which is able to induce of apoptosis in human cancer cells.[4]

Even though symmetric conjugated systems have been extensively studied and documented in literature, only few methods are available for the synthesis of unsymmetric systems. A simple strategy, efficient, and green is the Suzuki–Miyaura cross-coupling reaction (SMC).[5] However the preparation of such systems requires the implementation of highly regioselective reactions. In our laboratory, we have already described a potent iterative '1+1' synthesis of oligopyridines,[6] phenylpyridines,[7] and oligothienylpyridines.[8] This method, named Garlanding,[9] which uses bifunctional haloboronic species and halides takes advantage of the nature and the position of the halogen atom on the aromatic ring.[10]

Now, in this paper we describe the synthesis of new boronic species and the study of their reactivity in the SMC reaction using for the first time a '2+2' regiocontrolled approach. Preparation of these bi(het)aryl boronic species as building blocks allows to consider quick access to four or six unit phenylpyridines and this strategy could be of great interest because of its possible applicability to automated synthesis.

The chemical challenge will be, first, to synthesize new boronic species, and second, to prepare new four/six unit phenylpyridyl derivatives in order to explore the reactivity of these species. The general '2+2' mechanism of the explored reaction is reported in Scheme 1.

2. Results

During our ongoing investigation, we first examined the reactivity of the coupling partners with the preparation of dihalophenylpyridines **3a** and **3b**[7] obtained by the SMC reaction[11] between 6-bromopyridin-3-yl boronic acid **1a**[10a] and 6-bromo-5-methylpyridin-3-yl boronic acid **1b**[6a] and bromoiodotoluene **2a** as illustrated in Scheme 2.

The first results of these couplings were disappointing. The presence of a bromine atom on the alpha position of pyridylboronic acids **1a** and **1b** can explain the relative low yields for compounds **3a** and **3b**, because this alpha bromine atom can be the source of a third SMC reaction leading to the formation of small amounts of terphenylpyridines (10–15%). Modifications of the reaction conditions, particularly, the use of 1,2-dimethoxyethane in place of 1,4-dioxane allowed us to increase the yield, in the case of **3b** (68%).

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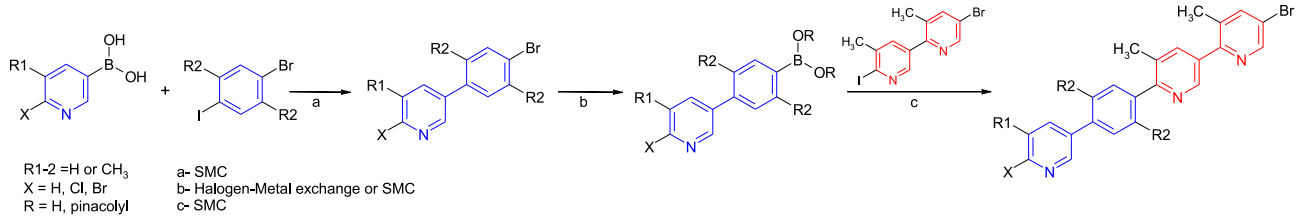
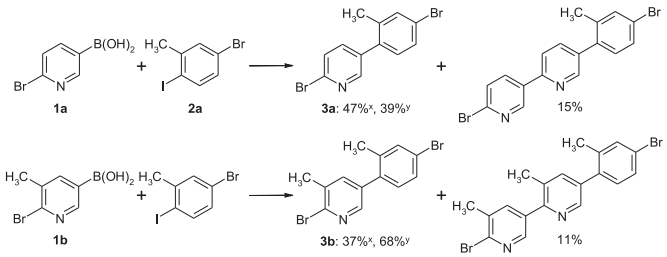
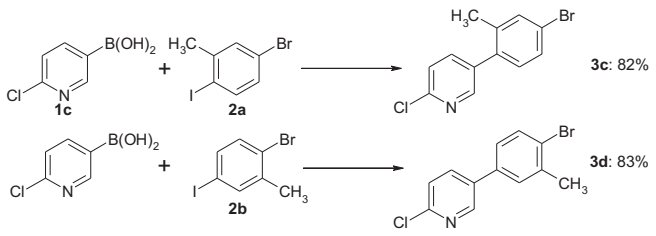


Scheme 1. The '2+2' approach.



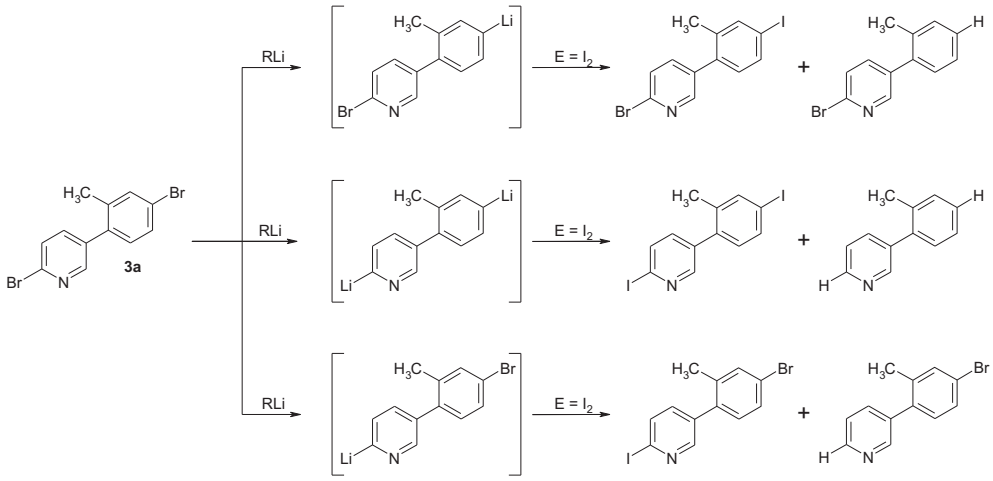
Scheme 2. Preparation of 2-bromo-5-(4-bromo-2-methylphenyl)pyridine **3a** and 2-bromo-5-(4-bromo-2-methylphenyl)-3-methylpyridine **3b**. Reagents and conditions: boronic acids **1a**,**b** 1.25 equiv, $Pd(PPh_3)_4$ 0.05 equiv, Na_2CO_3 aq 2.5 equiv, 1,4-dioxane[x] or DME[y], reflux, 24 h.

Then we studied the synthesis of corresponding boronic acids **4a**,**b** starting from phenylpyridines **3a**,**b** by using the halogen–metal exchange methodology experimented in our laboratory[10] as illustrated in Scheme 3. Unfortunately, and after numerous trials (^{n}BuLi, ^{n}BuLi/TMEDA, ^{t}BuLi) we did not succeed to obtain boronic acid, these reactions leading always to the formation of mono and di-dehalogenated compounds. Due to this potential instability of boronic acids, we chose to replace the triisopropylborate by iodine in order to try to trap lithiated species. In this case LCMS analyses revealed the formation of a mixture of six compounds as showed in Scheme 3.



Scheme 4. Preparation of 2-chloro-5-(4-bromo-2-methylphenyl)pyridine **3c** and 2-bromo-5-(4-bromo-3-methylphenyl)pyridine **3d**. Reagents and conditions: boronic acid **1c** 1.25 equiv, $Pd(PPh_3)_4$ 0.05 equiv, Na_2CO_3 aq 2.5 equiv, DME, reflux, 24 h.

With these two new chlorinated species the results of halogen–metal exchange have not been better than the previous ones. It is the reason why we decided to turn our efforts toward the use of bis(pinacolato)diboron as a coupling partner with **3a** and **3b** in the presence of palladium.[2] We carefully followed this reaction by TLC and ^{1}H NMR. After 1 h of stirring at room temperature no reaction took place. The increase of the temperature to 50 °C then to reflux of 1,4-dioxane with stirring for additional 30 min allowed for the first time, the formation of an ester in the C(2) position, but its reactivity was such that it reacted very quickly with the starting material to give, as a byproduct, a dimer accompanied with a great amount of degradation products (Scheme 5).



Scheme 3. Halogen–metal exchange reaction of compound **3a**. Reagents and conditions: (1) ^{n}BuLi, or ^{n}BuLi/TMEDA, or ^{t}BuLi 1.25 equiv, THF anhyd, −78 °C, 45 min; (2) I_2 1.25 equiv, THF anhyd, −78 °C, 1 h; (3) hydrolysis.

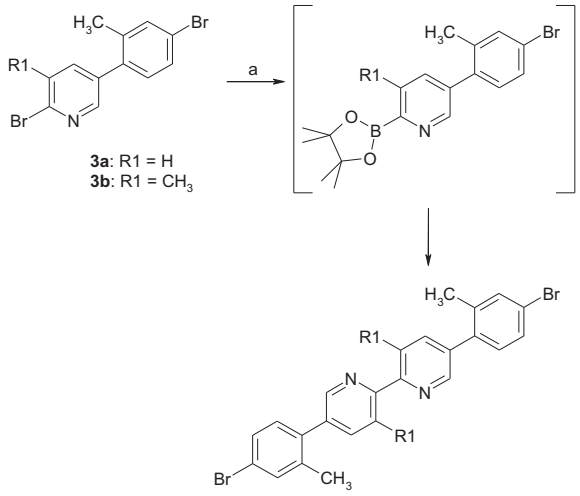
The formation of such a mixture illustrates the poor stability of lithiated intermediate and the lack of regioselectivity of the halogen–metal exchange.

To gain in selectivity we replaced bromine on alpha position of pyridine by chlorine, this latter being reputed of a very less reactivity. We prepared two new mixed phenylpyridines **3c**,**d** by SMC reaction between 6-chloro-3-pyridyl boronic acid **1c**[10] and 2-iodo-5-bromotoluene **2a** or 2-bromo-5-iodotoluene **2b** (Scheme 4).

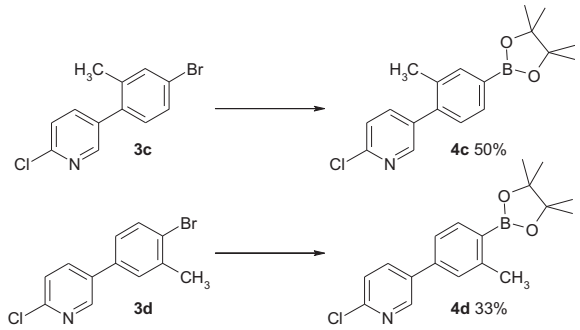
Encouraged by this new result, we also tried the same reaction with the two chlorinated species **3c**,**d** and this time, we isolated boronic esters **4c**,**d** with moderate yields (Scheme 6).

We finally prepared mono halophenylpyridines **3e** and **3f** with excellent yields (80–85%) from pyridin-3-yl boronic acid **1d**[12] and 2-iodo-5-bromotoluene **2a** or 2-bromo-5-iodotoluene **2b** (Scheme 7).

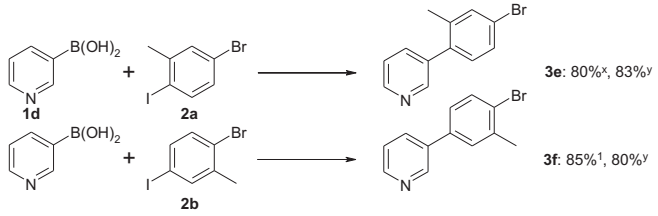
With these more simple reactants we succeeded to prepare 3-methyl-4-pyridin-3-yl phenyl boronic acid **4e** and 2-methyl-4-



Scheme 5. Preparation of phenylpyridyl boronic esters. Reagents and conditions: bis(pinacolato)diboron 1.1 equiv, KOAC 3 equiv, $PdCl_2$(dppf) 0.08 equiv, 1,4-dioxane, reflux, 24 h.

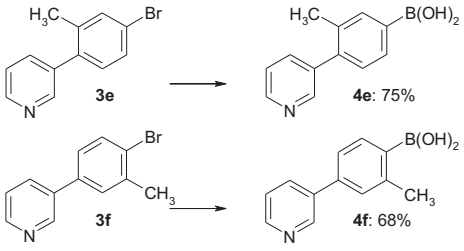


Scheme 6. Preparation of phenylpyridyl boronic esters. Reagents and conditions: bis(pinacolato)diboron 1.1 equiv, NaOAC 3 equiv, $PdCl_2$(dppf) 8%, 1,4-dioxane, reflux, TLC.



Scheme 7. Preparation of 3-(4-bromo-2-methylphenyl)pyridine **3e**, 3-(4-bromo-3-methylphenyl)pyridine **3f**. Reagents and conditions: boronic acids **1d** 1.25 equiv, $Pd(PPh_3)_4$ 0.05 equiv, Na_2CO_3 aq 2.5 equiv, 1,4-dioxane[x] or DME[y], reflux, 24 h.

pyridin-3-yl phenyl boronic acid **4f** with good yields using the classical halogen–metal exchange methodology (Scheme 8).



Scheme 8. Preparation of 3-methyl-4-pyridin-3-yl phenyl boronic acid **4e** and 2-methyl-4-pyridin-3-yl phenyl boronic acid **4f**. Reagents and conditions: (1) ^{n}BuLi, 1.25 equiv, THF anhyd, −78 °C, 1 h; (2) B(O^{i}Pr)$_3$, 1.25 equiv, THF anhyd, −78 °C, 45 min; (3) hydrolysis.

So, we have carefully studied the synthesis of new phenylpyridyl boronic species. On one hand we have succeeded the synthesis of halogenated phenylpyridyl boronic esters without being bothered by the presence of the halogen and we have overcome in this case the lack of selectivity of the halogen–metal exchange.

On the other hand, we succeeded the synthesis of phenylpyridyl boronic acids by the implementation of the halogen–metal exchange without using of director functional groups and/or stabilizator of the lithiated intermediate.

In the second part of this study, we explored the reactivity of boronic species **4c**–**f** by engaging them in an SMC reaction with the 5-bromo-6′-iodo-3,5′-dimethyl-[2,3′]bipyridine **6**.

This bipyridine **6** was obtained from the 5-bromo-6′-iodo-3,5′-dimethyl-[2,3′]bipyridine **5** as we previously described[7] by applying a Br–I exchange that occurs exclusively at the C(2) position with excellent yield (93%, Scheme 9). In the Garlanding concept, we remind of the interest of using an iodinated bipyridine compared to a brominated one: even if the alpha position of the pyridine ring is more sensitive to a cross-coupling reaction than the beta one, the formation of byproducts is limited by using an iodinated bipyridine because of a better regioselectivity of the SCM reaction.

Then, the implementation of the SMC reaction in the same conditions as described in Scheme 2 did not allow us to obtain four unit phenylpyridines **7c**–**f**.

The modifications of conditions we have made are the choice of different bases. The role of base is to facilitate the slow transmetalation of the boronic acids in cross-coupling reaction by forming a more reactive boronate species. In general, inorganic bases work better, and the reactivity is in the order Cs_2CO_3>CsF>K_2CO_3>KOAc>Na_2CO_3.[13] Therefore, we chose to use K_3PO_4 rather than Na_2CO_3. In these conditions, with 1.25 equiv of boronic species **4**, all desired four unit compounds **7** were obtained predominantly (**7c**: 71%, **7d**: 64%, **7e**: 65%, **7f**: 77%). The low excess of boronic species also leads to produce a little amount of six unit phenylpyridines **8** (**8c**: 19%, **8d**: 21%, **8e**: 17%, **8f**: 8%), which has been isolated after chromatography (Scheme 9, Table 1).

The ^{1}H and ^{13}C NMR signals of **7e**,**f** and **8e**,**f** were precisely assigned using one and two-dimensional (COSY, HSQC, and HMBC) spectra.

Furthermore, the suitable crystals for X-ray diffraction studies were obtained for the two four unit phenylpyridines **7e** and **7f** by slow evaporation of a mixture of dichloromethane/cyclohexane (1/5). The ORTEP diagrams of the **7e** and **7f** crystal structures are shown in Fig. 1. They confirm the expected structures.

3. Conclusion

We have successfully synthesized four unit phenylpyridines and four sexi unit phenylpyridines through a '2+2' approach of the SMC reaction between new phenylpyridyl boronic species and dihalogenated bipyridine. These new compounds were characterized by all the spectroscopic data and confirmed by single-crystal X-ray diffraction studies for two four unit phenylpyridines.

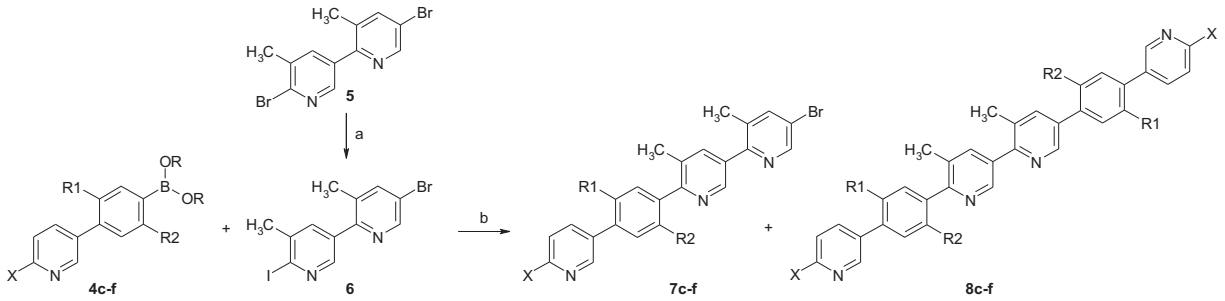
These linear garlands are being explored as alpha-helical mimics for the disruption of protein–protein interactions; our efforts in this direction will be reported subsequently.

Then, on the basis of the results presented in this work, further applications and investigations of the Garlanding approach in the field of mechanistic and synthetic organic chemistry as well as in biological area are currently ongoing in our laboratory.

4. Experimental section

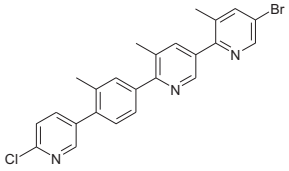
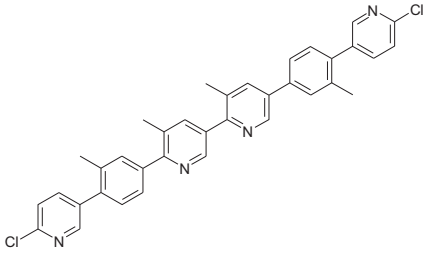
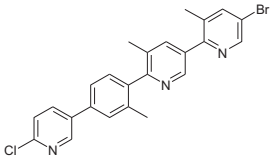
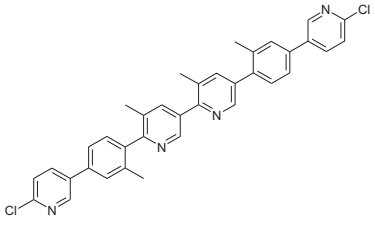
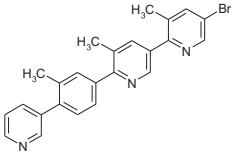
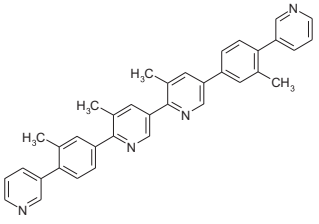
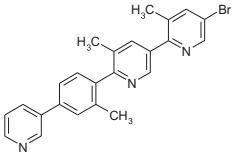
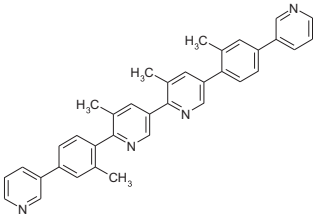
4.1. General procedure

Commercial reagents were used as received without additional purification. Melting points were determined on a Kofler heating bench.



Scheme 9. Preparation of phenylpyridyl bipyridines **7c**–**f**. Reagents and conditions: (a) AcCl (2×1.5 equiv), NaI (2×2.5 equiv), CH_3CN, reflux, 2×4 h; (b) K_3PO_4 aq 2.5 equiv, $Pd(PPh_3)_4$ 5%, DME, reflux, 20 h.

Table 1
Cross coupling reactions between boronic species **4c**–**f** and 5-bromo-6′-iodo-3,5′-dimethyl-[2,3′]bipyridine **6**

Phenylpyridine	R1	R2	X	Four unit phenylpyridine	Six unit phenylpyridine	Yield (%)	Conversion rate
4c	CH_3	H	Cl	 **7c**	 **8c**	65/17	8/2
4d	H	CH_3	Cl	 **7d**	 **8d**	77/8	9/1
4e	CH_3	H	H	 **7e**	 **8e**	71/19	8/2
4f	H	CH_3	H	 **7f**	 **8f**	64/21	7/3

IR spectra were recorded on a Perkin–Elmer BX FT-IR spectrophotometer. The band positions are given in reciprocal centimeters (cm^{-1}).

^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a JEOL Lambda 400 spectrometer. Four units **7e**,**f** and six units **8e**,**f** oligophenylpyridine ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) data were recorded on a Bruker 500 Avance III spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard and coupling constants in hertz. Chemical shift are reported in part per million (ppm) relative to the solvent resonance.

Chromatography was carried out on a column using flash silica gel 60 Merck (0.063–0.200 mm) as the stationary phase. The eluting solvent indicated for each purification was determined by

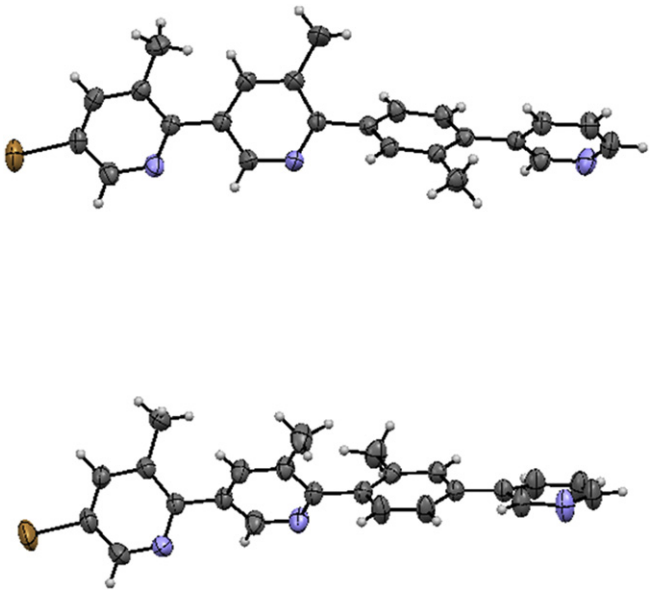


Fig. 1. ORTEP diagrams of **7e** and major conformation of **7f**.

thin layer chromatography (TLC) performed on 0.2 mm precoated plates of silica gel 60F-264 (Merck) and spots were visualized using an ultraviolet-light lamp.

Elemental analyses for new compounds were performed at the 'Institut de Recherche en Chimie Organique Fine' (Rouen). The data for C, H, and N were within ±0.4 of the theoretical values for all final compounds.

6-Bromo-3-pyridyl boronic acid **1a**,[10a] 6-bromo-5-methyl-3-pyridyl boronic acid **1b**,[6a] 6-chloro-3-pyridyl boronic acid **1c**,[10] and 3-pyridyl boronic acid **1d**[12] are prepared according to literature.

*4.1.1. 2-Bromo-5-(4-bromo-2-methylphenyl)pyridine **3a**.* To a stirred solution of 6-bromo-3-pyridyl boronic acid (1.25 equiv, 847 mg, 4.20 mmol) in 1,4-dioxane (30 mL) under nitrogen were added 5-bromo-2-iodotoluene (1 g, 3.36 mmol) and tetrakis-(triphenylphosphine)palladium(0) (0.05 equiv, 195 mg, 0.17 mmol). After 5 min of stirring, aqueous Na_2CO_3 (2.5 equiv, 892 mg, 8.42 mmol) in 5 mL of water was added. Then the mixture was heated to 80 °C until the starting material was consumed (TLC). After cooling down to room temperature, the mixture was filtered on Celite and washed with CH_2Cl_2. The aqueous layer was extracted with EtOAc (2×50 mL). Combined organic layers were washed with saturated aqueous solution of NaCl (50 mL), and dried over $MgSO_4$. Solvent was removed in vacuo and crude product was purified by column chromatography, with 99:1 cyclohexane/EtOAc affording **3c** as a white solid (520 mg, 47%). Mp 103 °C. IR (KBr): 3044, 2952, 1573, 1451, 1347, 1088, 992, 8047, 805, 740, 671, 555 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, *J*=2.9, 1H, *H*6), 7.54 (d, *J*=8.8, 1H, *H*3), 7.48 (dd, *J*=8.8, 2.9, 1H, *H*4), 7.46 (d, *J*=3.9, 1H, *H*3′), 7.40 (dd, *J*=7.8, 2.0, 1H, *H*5′), 7.05 (d, *J*=7.8, 1H, *H*6′), 2.23 (s, 3H, *CH*$_3$*–ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0 (C6), 141.0 (C2), 138.9 (C4), 137.7 (C2′), 135.6 (C5, C1′), 133.5 (C3′), 131.2 (C6′), 129.4 (C5′), 127.7 (C3), 122.6 (C4′), 20.2 (CH_3). Anal. Calcd for $C_{12}H_9NBr_2$: C, 44.07; H, 2.77; N, 4.28. Found: C, 43.91; H, 3.97; N, 4.12.

*4.1.2. 2-Bromo-3-methyl-5-(4-bromo-2-methylphenyl)pyridine **3b**.* Following the procedure for phenylpyridine **3a** synthesis, 5 g of 5-bromo-2-iodotoluene (16.84 mmol) was reacted with 4.54 g of 6-bromo-5-methyl-3-pyridyl boronic acid (21.05 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (973 mg, 0.84 mmol), aqueous Na_2CO_3 (4.46 g, 42.10 mmol), and (100 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with 99:1 cyclohexane/EtOAc affording **3d** as a white solid (3.92 g, 68%). Mp 120 °C. Same experimental data described in the literature.[7]

*4.1.3. 2-Chloro-5-(4-bromo-2-methylphenyl)pyridine **3c**.* Following the procedure for phenylpyridine **3a** synthesis, 2 g of 5-bromo-2-iodotoluene (6.73 mmol) was reacted with 1.325 g of 6-chloro-3-pyridyl boronic acid (8.42 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (389 mg, 0.34 mmol), aqueous Na_2CO_3 (1.785 g, 16.84 mmol), and (50 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with 99:1 cyclohexane/EtOAc affording **3c** as a yellow solid (1.55 g, 82%). Mp 88 °C. IR (KBr): 3062, 2959, 2917, 2863, 1928, 1581, 1562, 1547, 1452, 1349, 1140, 1104, 995, 878, 849, 827, 743, 677, 560, 540 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, *J*=2.4, 1H, *H*6), 7.59 (dd, *J*=8.3, 2.4, 1H, *H*4), 7.46 (d, *J*=1.7, 1H, *H*3′), 7.40 (dd, *J*=8.0, 2.2, 1H, *H*5′), 7.39 (d, *J*=8.0, 1H, *H*3), 7.05 (d, *J*=8.0, 1H, *H*6′), 2.24 (s, 3H, *CH*$_3$*–ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3 (C2), 149.4 (C6), 139.1 (C4), 137.7 (C2′), 135.6 (C1′), 135.2 (C5′), 133.4 (C3′), 131.2 (C6′), 129.3 (C5′), 123.8 (C3), 122.4 (C4′), 20.1 (CH_3). Anal. Calcd for $C_{12}H_9NBrCl$: C, 51.01; H, 3.21; N, 4.96. Found: C, 51.14; H, 3.17; N4.91.

*4.1.4. 2-Chloro-5-(4-bromo-3-methylphenyl)pyridine **3d**.* Following the procedure for phenylpyridine **3a** synthesis, 2 g of 2-bromo-5-iodotoluene (6.73 mmol) was reacted with 1.325 g of 6-chloro-3-pyridyl boronic acid (8.42 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (389 mg, 0.34 mmol), aqueous Na_2CO_3 (1.785 g, 16.84 mmol), and (50 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with 99:1 cyclohexane/EtOAc affording **3c** as a yellow solid (1.58 g, 83%). Mp 98 °C. IR (KBr): 3036, 2981, 2917, 1975, 1584, 1552, 1454, 1399, 1379, 1346, 1264, 1153, 1111, 1028, 1017, 877, 843, 813, 759, 681, 634, 525 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J*=2.7, 1H, *H*6), 7.80 (dd, *J*=8.3, 2.4, 1H, *H*4), 7.63 (d, *J*=8.3, 1H, *H*5′), 7.40 (s, 1H, *H*2′), 7.39 (d, *J*=8.3, 1H, *H*5), 7.22 (dd, *J*=8.3, 2.2, 1H, *H*6′), 2.47 (s, 3H, *CH*$_3$*–ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5 (C1), 147.7 (C6), 138.9 (C3′), 136.9 (C4), 135.6 (C1′), 134.6 (C5), 133.1 (C5′), 129.3 (C2′), 125.8 (C6′), 125.4 (C4′), 124.2 (C3), 23.1 (CH_3). $C_{12}H_9NBrCl$: C, 51.01; H, 3.21; N, 4.96. Found: C, 50.88; H, 3.23; N, 4.91.

*4.1.5. 3-(4-Bromo-2-methylphenyl)pyridine **3e**.* Following the procedure for phenylpyridine **3a** synthesis, 1 g of 2-bromo-5-iodotoluene (3.36 mmol) was reacted with 517 mg of 3-pyridyl boronic acid (4.21 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (195 mg, 0.17 mmol), aqueous Na_2CO_3 (892 mg, 8.42 mmol), and (30 mL) of 1,4-dioxane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 9:1 to 5:5 cyclohexane/EtOAc, affording **3e** as yellow oil (690 mg, 83%). IR (KBr): 3026, 2958, 2923, 1586, 1569, 1469, 1412, 1385, 1196, 1090, 998, 852, 805, 717, 558 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J*=4.0, 1H, *H6*), 8.37 (s, 1H, *H2*), 7.42 (d, *J*=7.5, 1H, *H4*), 7.26 (s, 1H, *H3′*), 7.20 (d, *J*=8.0, 1H, *H5′*), 7.16 (t, *J*=6.0, 1H, *H5*), 6.88 (d, *J*=8.0, 1H, *H6′*), 2.05 (s, 3H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6 (C2), 148.4 (C6), 137.8 (C2′), 137.0 (C1′), 136.3 (C4, C3), 133.3 (C3′), 131.3 (C6′), 129.1 (C5′), 123.0 (C5), 122.0 (C4′), 20.2 (CH_3). Anal. Calcd for $C_{12}H_{10}NBr$: C, 58.09; H, 4.06; N, 5.65. Found: C, 57.89; H, 4.03; N, 5.48.

*4.1.6. 3-(4-Bromo-3-methylphenyl)pyridine **3f**.* Following the procedure for phenylpyridine **3a** synthesis, 1 g of 2-bromo-5-iodotoluene (3.36 mmol) was reacted with 517 mg of 3-pyridyl

boronic acid (4.21 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (195 mg, 0.17 mmol), aqueous Na_2CO_3 (892 mg, 8.42 mmol), and (30 mL) of 1,4-dioxane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 9:1 to 5:5 cyclohexane/EtOAc, affording **3f** as yellow oil (710 mg, 85%). IR (KBr): 3030, 2979, 2922, 2851, 1588, 1575, 1469, 1419, 1379, 1187, 1067, 1025, 882, 825, 801, 710, 620, 588 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, J=2.9, 1H, *H2*), 8.60 (d, J=4.9, 1H, *H6*), 7.83 (dt, J=7.8, 2.0, 1H, *H4*), 7.62 (d, J=8.8, 1H, *H5′*), 7.43 (d, J=2.0, 1H, *H2′*), 7.35 (dd, J=7.8, 4.9, 1H, *H5*), 7.25 (dd, J=8.8, 2.0, 1H, *H6′*), 2.47 (s, 3H, *CH₃—ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7 (C6), 148.1 (C2), 138.7 (C3′), 137.0 (C1′), 135.7 (C3), 134.2 (C4), 133.0 (C5′), 129.5 (C2′), 126.0 (C6′), 125.0 (C4′), 123.6 (C5), 23.1 (CH_3). Anal. Calcd for $C_{12}H_{10}NBr$: C, 58.09; H, 4.06; N, 5.65. Found: C, 57.87; H, 4.01; N, 5.44.

4.1.7. 2-[3-Methyl-4-(4-chloro-pyridin-3-yl)phenyl]-4,4,5,5-tetramethyl-1,3-dioxaborolane ***4c****.* To a stirred solution of 2-chloro-5-(4-bromo-2-methylphenyl)pyridine **3c** (1 equiv, 1 g, 3.54 mmol) in 1,4-dioxane (50 mL) under nitrogen were added bispinacolatodiboron (918 mg, 3.89 mmol), [1,1′-bis(diphenylphosphino)ferrocene]palladium(II) chloride (0.08 equiv, 215 mg, 0.26 mmol) and sodium acetate (3 equiv, 809 mg, 9.86 mmol). Then the mixture was heated to reflux for 16 h. After cooling down to room temperature, the mixture was filtered on Celite and washed with CH_2Cl_2. Solvent were removed in vacuo and crude product was purified by chromatography (cyclohexane/EtOAc 98:2) affording product **4c** as white solid (580 mg, 50%). Mp 130 °C. IR (KBr): 3436, 3035, 2974, 2926, 1610, 1560, 1503, 1458, 1412, 1362, 1314, 1267, 1145, 1106, 999, 855, 839, 760, 751, 676, 633, 492 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J=2.4, 1H, *H2′*), 8.75 (s, 1H, *H2*), 7.71 (d, J=7.6, 1H, *H6*), 7.62 (dd, J=8.3, 2.4, 1H, *H6′*), 7.39 (d, J=8.0, 1H, *H5′*), 7.21 (d, J=7.6, 1H, *H5*), 2.27 (s, 3H, *CH₃—ph*), 1.37 (s, 12H, *CH₃pinacol*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 149.5, 139.5, 139.2, 137.0, 136.2, 134.8, 132.5, 129.2, 123.7, 83.9, 26.9, 24.8, 20.0. Anal. Calcd for $C_{18}H_{21}NBClO_2$: C, 65.59; H, 6.42; N, 4.25. Found: C, 65.73; H, 6.37; N, 4.12.

4.1.8. 2-[2-Methyl-4-(4-chloro-pyridin-3-yl)phenyl]-4,4,5,5-tetramethyl-1,3-dioxaborolane ***4d****.* To a stirred solution of 2-chloro-5-(4-bromo-3-methylphenyl)pyridine **3d** (1 equiv, 1 g, 3.54 mmol) in 1,4-dioxane (50 mL) under nitrogen were added bispinacolatodiboron (918 mg, 3.89 mmol), [1,1′-bis(diphenylphosphino)ferrocene]palladium(II) chloride (0.08 equiv, 215 mg, 0.26 mmol) and sodium acetate (3 equiv, 809 mg, 9.86 mmol). Then the mixture was heated to reflux for 16 h. After cooling down to room temperature, the mixture was filtered on Celite and washed with CH_2Cl_2. Solvent were removed in vacuo and crude product was purified by chromatography (cyclohexane/EtOAc 98:2) affording product **4d** as white solid (390 mg, 33%). Mp 101 °C. IR (KBr): 3469, 3414, 2977, 2925, 1608, 1584, 1567, 1508, 1458, 1380, 1358, 1347, 1271, 1139, 1108, 1074, 1048, 962, 856, 820, 754, 661, 499 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, J=2.7, 1H, *H2′*), 7.86 (d, J=7.8, 1H, *H6*), 7.84 (dd, J=8.5, 2.7, 1H, *H6′*), 7.38 (d, J=8.3, 1H, *H5′*), 7.35–7.33 (m, 2H, *H3*, *H5*), 2.61 (s, 3H, *CH₃—ph*), 1.36 (s, 12H, *CH₃pinacol*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 148.0, 145.9, 138.5, 137.2, 136.8, 135.5, 128.3, 124.1, 123.2, 83.6, 25.0, 24.9, 22.3. Anal. Calcd for $C_{18}H_{21}NBClO_2$: C, 65.59; H, 6.42; N, 4.25. Found: C, 65.63; H, 6.51; N, 4.27.

4.1.9. 3-Methyl-4-(pyridin-3-yl)phenyl boronic acid ***4e****.* To a slurry of 2.5M of ^{n}BuLi (1.25 equiv, 2.01 mL, 5.04 mmol) in anhydrous THF (100 mL), cooled at −78 °C, was added a solution 3-(4-bromo-2-methylphenyl)pyridine (1 g, 4.03 mmol) in THF (25 mL). The mixture was allowed to react at this temperature for over 60 min. A solution of triisopropylborate (1.25 equiv, 1.16 mL, 5.04 mmol) was then added and left to react for 45 min. The mixture was allowed to warm to room temperature and was quenched by slow addition of 4% aqueous NaOH solution (50 mL). The resulting aqueous layer was collected and acidified to pH 7 by dropwise addition of 3 N HCl. Extraction with ethyl acetate, evaporation of the organic layer and recrystallization from ether gave product **4e** as a white solid (640 mg, 75%). Mp 211 °C. IR (KBr): 3413, 3022, 2975, 1735, 1609, 1409, 1370, 1324, 1263, 1191, 1164, 1112, 1047, 767, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, J=4.2, 1H, *H6*), 8.52 (s, 1H, *H2*), 7.85 (dt, J=7.9, 1.7, 1H, *H4*), 7.61 (br s, 2H, *H2′*, *H6′*), 7.54 (dd, J=7.8, 4.9, 1H, *H5*), 7.22 (d, J=7.5, 1H, *H5′*), 2.28 (s, 3H, *CH₃—ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9 (C2), 148.5 (C6), 146.0 (C3), 139.7 (C1′), 138.8 (C4), 137.1 (C6′), 135.6 (C4′), 132.5 (C2′), 134.0 (C3′), 130.0 (C5′), 125.0 (C5), 20.4 (CH_3). Anal. Calcd for $C_{12}H_{12}BNO_2$: C, 67.65; H, 5.68; N, 6.57. Found: C, 67.28; H, 5.42; N, 6.21.

4.1.10. 2-Methyl-4-(pyridin-3-yl)phenyl boronic acid ***4f****.* Following the procedure for boronic acid **4e** synthesis, 2 g of 3-(4-bromo-3-methylphenyl)pyridine (8.06 mmol) was reacted with 4.03 mL of ^{n}BuLi (10.07 mmol) and 2.32 mL of triisopropylborate (10.07 mmol) in presence of THF (100 mL). The mixture was then treated as described in representative procedure giving **4f** as a white solid (1.17 g, 68%). Mp 184 °C. IR (KBr): 3406, 2956, 2922, 1607, 1431, 1400, 1312, 1276, 1240, 1187, 803, 771, 709 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, J=2.0, 1H, *H2*), 8.50 (dd, J=5.0, 1.5, 1H, *H6*), 8.09 (dt, J=7.5, 1.5, 1H, *H4*), 7.51 (dd, J=8.0, 5.0, 1H, *H5*), 7.49 (s, 1H, *H3′*), 7.46 (d, J=8.0, 1H, *H5′*), 7.40 (d, J=8.0, 1H, *H6′*), 2.42 (s, 3H, *CH₃—ph*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7 (C6), 148.3 (C2), 142.3 (C2′), 138.8 (C4′), 138.7 (C3), 136.5 (C4), 135.4 (C1′), 133.3 (C6′), 128.8 (C3′), 125.5 (C5), 124.6 (C5′), 22.1 (CH_3). Anal. Calcd for $C_{12}H_{12}BNO_2$: C, 67.65; H, 5.68; N, 6.57. Found: C, 67.31; H, 5.39; N, 6.31.

4.1.11. 5′-Bromo-3′,5-dimethyl-6-[3-methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3,2′-bipyridine ***7c****.* Following the procedure for phenylpyridine **3a** synthesis, 500 mg of 5′-bromo-3′,5-dimethyl-6-iodo-3,2′-bipyridine (1.28 mmol) was reacted with 486 mg of boronic ester **4e** (1.47 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (74 mg, 0.06 mmol), aqueous K_3PO_4 (738 mg, 3.2 mmol), and (30 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 9:1 to 5:5 cyclohexane/EtOAc affording **7c** as a yellow solid (390 mg, 65%), mp 178 °C and a byproduct **8c** as a yellow solid (130 mg, 17%). IR (KBr): 3045, 2960, 2917, 2849, 1705, 1597, 1579, 1545, 1450, 1416, 1382, 1295, 1156, 1113, 995, 923, 886, 772, 654 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, J=2.0, 1H), 8.63 (d, J=2.2, 1H), 8.43 (d, J=2.4, 1H, *H2‴*), 7.81 (s, 2H, *H6*, *H4′*), 7.68 (dd, J=8.1, 2.4, 1H, *H6‴*), 7.55 (s, 1H, *H2″*), 7.48 (dd, J=7.8, 1.2, 1H, *H6″*), 7.42 (d, J=8.3, 1H, *H5‴*), 7.30 (d, J=7.8, 1H, *H5″*), 2.49 (s, 3H), 2.46 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 153.9, 150.1, 149.7, 148.4, 146.8, 141.0, 140.3, 139.3, 139.1, 136.5, 136.0, 135.7, 133.3, 133.1, 131.3, 130.7, 129.5, 126.8, 123.7, 119.6, 20.4, 20.1, 19.9. Anal. Calcd for $C_{24}H_{19}N_3BrCl$: C, 62.02; H, 4.12; N, 9.04. Found: C, 61.94; H, 4.08; N, 8.96.

4.1.12. 5′-Bromo-3′,5-dimethyl-6-[2-methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3,2′-bipyridine ***7d****.* Following the procedure for phenylpyridine **3a** synthesis, 250 mg of 5′-bromo-3′,5-dimethyl-6-iodo-3,2′-bipyridine (0.64 mmol) was reacted with 264 mg of boronic ester **4e** (0.80 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (37 mg, 0.03 mmol), aqueous K_3PO_4 (369 mg, 1.6 mmol), and (15 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 9:1 to 5:5 cyclohexane/EtOAc affording **7d** as a yellow solid (230 mg, 77%), mp 190 °C and a byproduct **8d** as a yellow solid (30 mg, 8%). IR (KBr): 3038, 2963, 2921, 1953, 1638, 1612, 1600, 1555, 1451, 1416, 1383, 1353, 1108, 1021, 901, 838, 763, 735, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J=2.2, 1H), 8.66 (d, J=2.7, 1H), 8.64 (d,

J=2.2, 1H), 7.89 (dd, *J*=8.3, 2.4, 1H, *H6‴*), 7.82 (s, 2H, *H4*, *H4′*), 7.49 (s, 1H, *H3″*), 7.47 (d, *J*=7.8, 1H, *H5″*), 7.42 (d, *J*=8.3, 1H, *H5‴*), 7.33 (d, *J*=7.8, 1H, *H6″*), 2.47 (s, 3H), 2.23 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 154.0, 150.3, 148.3, 148.0, 146.6, 141.0, 140.1, 138.3, 137.2, 136.9, 136.2, 135.4, 134.0, 133.1, 131.4, 129.5, 128.9, 124.4, 124.2, 119.7, 19.9, 19.6, 19.1 Anal. Calcd for $C_{24}H_{19}N_3BrCl$: C, 62.02; H, 4.12; N, 9.04. Found: C, 61.97; H, 4.15; N, 8.93.

4.1.13. 5′-Bromo-3′,5-dimethyl-6-(3-methyl-4-pyridin-3-ylphenyl)-3,2′-bipyridine ***7e***. Following the procedure for phenylpyridine **3a** synthesis, 1 g of 5′-bromo-3′,5-dimethyl-6-iodo-3,2′-bipyridine (2.56 mmol) was reacted with 683 mg of boronic acid **4e** (3.20 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (148 mg, 0.13 mmol), aqueous K_3PO_4 (1.476 g, 6.41 mmol), and (30 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 8:2 to 5:5 cyclohexane/EtOAc affording **7e** as a yellow solid (790 mg, 71%), mp 147 °C and a byproduct **8e** as a beige solid (253 mg, 19%). IR (KBr): 3024, 3006, 2924, 2857, 1592, 1554, 1451, 1437, 1414, 1381, 1311, 1190, 1136, 1117, 1072, 997, 922, 909, 888, 851, 806, 776, 715, 695, 616, 539, 500 cm^{-1} ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (d, *J*=2.0, 1H, *H2*), 8.65 (d, *J*=2.0, 1H, *H2‴*), 8.62 (d, *J*=2.0, 1H, *H6′*), 8.61 (dd, *J*=7.8, 3.0, 1H, *H6‴*), 7.81 (d, *J*=2.0, 1H, *H4*), 7.80 (d, *J*=2.0, 1H, *H4′*), 7.70 (dt, *J*=7.8, 2.0, 1H, *H4‴*), 7.54 (s, 1H, *H2″*), 7.47 (d, *J*=7.0, 1H, *H6″*), 7.37 (dd, *J*=7.8, 4.8, 1H, *H5‴*), 7.31 (d, *J*=7.8, 1H, *H5″*), 2.49 (s, 3H, *CH*$_3$), 2.45 (s, 3H, *CH*$_3$′), 2.35 (s, 3H, *CH*$_3$″). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0 (C6), 154.0 (C2′), 149.9 (C2‴), 148.4 (C6′), 148.2 (C6‴), 146.8 (C2), 141.0 (C4′), 140.0 (C1″), 139.1 (C4), 138.0 (C4″), 137.2 (C3‴), 136.6 (C4‴), 135.7 (C3″), 133.7 (C3), 133.2 (C3′), 131.2 (C2″), 130.8 (C5), 129.7 (C5″), 126.7 (C6″), 123.1 (C5‴), 119.7 (C5′), 20.5 (CH_3″), 20.2 (CH_3), 20.0 (CH_3″). Anal. Calcd for $C_{24}H_{20}N_3Br$: C, 66.98; H, 4.68; N, 9.76. Found: C, 66.62; H, 4.24; N, 9.35.

4.1.14. 5′-Bromo-3′,5-dimethyl-6-(2-methyl-4-pyridin-3-ylphenyl)-3,2′-bipyridine ***7f***. Following the procedure for phenylpyridine **3a** synthesis, 1 g of 5′-bromo-3′,5-dimethyl-6-iodo-3,2′-bipyridine (2.56 mmol) was reacted with 683 mg of boronic acid **4f** (3.20 mmol) in presence of tetrakis-(triphenylphosphine)palladium(0) (148 mg, 0.13 mmol), aqueous K_3PO_4 (1.476 g, 6.41 mmol), and (30 mL) of dimethoxyethane. The mixture was then refluxed and treated as described in representative procedure. The crude product was purified by column chromatography, with a gradient of solvent from 8:2 to 5:5 cyclohexane/EtOAc affording **7f** as a pale yellow solid (710 mg, 64%), mp 164 °C and a byproduct **8f** as a white solid (270 mg, 20%). IR (KBr): 3022, 2980, 2958, 2923, 2858, 1598, 1574, 1553, 1451, 1417, 1382, 1188, 1137, 1115, 1065, 1021, 999, 907, 874, 802, 763, 706, 678, 619, 565 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.90 (d, *J*=2.0, 1H, *H2‴*), 8.68 (d, *J*=2.0, 1H, *H2*), 8.64 (d, *J*=2.0, 1H, *H6′*), 8.61 (d, *J*=4.9, 1H, *H6‴*), 7.93 (dt, *J*=7.8, 2.0, 1H, *H4‴*), 7.82 (s, 2H, *H4*, *H4′*), 7.53 (s, 1H, *H3″*), 7.50 (d, *J*=7.8, 1H, *H5″*), 7.39 (dd, *J*=7.8, 4.9, 1H, *H5‴*), 7.33 (d, *J*=6.8, 1H, *H6″*), 2.47 (s, 3H, *CH*$_3$′), 2.24 (s, 3H, *CH*$_3$), 2.22 (s, 3H, *CH*$_3$–*ph*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0 (C6), 154.2 (C2′), 148.7 (C6‴), 148.5 (C6′, C2‴), 146.8 (C2), 141.2 (C4′), 139.9 (C1″), 138.4 (C4), 137.8 (C4″), 136.8 (C2″), 136.6 (C3‴), 134.5 (C4‴), 134.1 (C3), 133.3 (C3′), 131.6 (C5), 129.5 (C6″), 129.3 (C3″), 124.7 (C5″), 123.7 (C5‴), 119.8 (C5′), 20.1 (CH_3′), 19.8 (CH_3″), 19.3 (CH_3). Anal. Calcd for $C_{24}H_{20}N_3Br$: C, 66.98; H, 4.68; N, 9.76. Found: C, 66.68; H, 4.31; N, 9.43.

4.1.15. 5′-[3-Methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3′,5-dimethyl-6-[3-methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3,2′-bipyridine ***8c***. Yellow solid mp 206 °C. IR (KBr): 3030, 2963, 2923, 2850, 1618, 1582, 1555, 1456, 1423, 1357, 1103, 1032, 998, 896, 828, 779, 763, 749, 699, 510 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (d, *J*=1.7, 1H), 8.78 (d, *J*=1.7, 1H), 8.44–8.43 (m, 2H), 7.91 (d, *J*=1.7, 1H), 7.87 (d, *J*=1.4, 1H), 7.68 (dd, *J*=8.0, 2.4, 2H), 7.59–7.56 (m, 3H), 7.51 (d, *J*=7.8, 1H), 7.45–7.41 (m, 2H), 7.35 (d, *J*=7.5, 1H), 7.31 (d, *J*=7.8 1H), 2.56 (s, 3H), 2.52 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 154.4, 150.3, 150.1, 149.7, 149.6, 147.0, 145.8, 140.5, 139.3, 139.2, 137.5, 137.1, 136.7, 136.5, 136.1, 135.7, 135.0, 134.9, 134.4, 131.4, 131.3, 130.7, 130.6, 130.1, 129.6, 129.4, 127.9, 126.8, 124.9, 123.8, 123.7, 20.6, 20.4, 20.2, 20.1. Anal. Calcd for $C_{36}H_{28}N_4Cl_2$: C, 73.59; H, 4.80; N, 9.54. Found: C, 73.28; H, 4.88; N, 9.43.

4.1.16. 5′-[2-Methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3′,5-dimethyl-6-[2-methyl-4-(4-chloro-pyridin-3-yl)phenyl]-3,2′-bipyridine ***8d***. Yellow solid mp 218 °C. IR (KBr): 3041, 2972, 2919, 2855, 1623, 1590, 1564, 1442, 1412, 1360, 1099, 1029, 1001, 888, 827, 783, 755, 678, 517 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, *J*=1.7, 1H), 8.67 (d, *J*=2.0, 2H), 8.61 (d, *J*=2.0, 1H), 7.93 (d, *J*=2.0, 1H), 7.92 (d, *J*=2.4, 1H), 7.89 (d, *J*=2.7, 1H), 7.70 (s, 1H), 7.52–7.47 (m, 4H), 7.45–7.36 (m, 4H), 2.56 (s, 3H), 2.45 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 154.1, 150.5, 150.2, 148.0, 147.9, 147.3, 146.8, 140.2, 139.2, 138.4, 137.9, 137.1, 137.0, 136.9, 136.7, 136.3, 136.1, 135.7, 135.4, 135.0, 134.7, 131.3, 130.8, 130.7, 129.5, 129.2, 128.9, 124.7, 124.4, 124.2, 124.1, 20.6, 20.1, 19.6, 19.1. Anal. Calcd for $C_{36}H_{28}N_4Cl_2$: C, 73.59; H, 4.80; N, 9.54. Found: C, 73.76; H, 4.84; N, 9.38.

4.1.17. 5′-(3-Methyl-4-pyridin-3-ylphenyl)-3′,5-dimethyl-6-(3-methyl-4-pyridin-3-ylphenyl)-3,2′-bipyridine ***8e***. Beige solid mp 150 °C. IR (KBr): 3024, 2955, 2921, 2856, 1592, 1562, 1455, 1408, 1382, 1144, 1027, 1000, 909, 835, 808, 777, 716, 541 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (d, *J*=2.0, 1H, *H6′*), 8.78 (d, *J*=2.0, 1H, *H2*), 8.66 (s, 2H, *H2″*, *H2‴′*), 8.63 (dt, *J*=5.2, 1.6, 2H, *H4″*, *H4‴′*), 7.91 (d, *J*=1.6, 1H, *H4*), 7.87 (d, *J*=1.6, 1H, *H4′*), 7.73 (s, 1H, *H6″*), 7.71 (s, 1H, *H6‴′*), 7.59 (s, 1H, *H2‴*), 7.57 (s, 1H, *H2‴′*), 7.57–7.55 (m, 1H, *H6‴*), 7.50 (d, *J*=8.0, 1H, *H6‴′*), 7.42–7.38 (m, 2H, *H5″*, *H5‴′*), 7.37 (d, *J*=7.6, 1H, *H5‴*), 7.33 (d, *J*=7.6, 1H, *H5‴′*), 2.59 (s, 3H, *CH*$_3$′), 2.55 (s, 3H, *CH*$_3$), 2.42 (s, 3H, *CH*$_3$‴), 2.39 (s, 3H, *CH*$_3$‴′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5 (C6), 154.2 (C2′), 149.8 (C2‴′), 149.7 (C2″), 148.2 (C4‴′), 148.1 (C4″), 146.9 (C2), 145.7 (C6′), 140.0 (C1‴′), 139.1 (C4), 137.9 (C4‴), 137.7 (C4‴′), 137.1 (C1‴, C1‴′), 137.0 (C4′), 136.7 (C1″), 136.4 (C6‴′, C6″, C3‴), 135.6 (C3‴′), 134.9 (C5'), 134.3 (C3), 131.1 (C2‴′, C3′), 130.6 (C5‴, C5), 129.5 (C5‴′), 129.2 (C2‴), 126.6 (C6‴′), 124.7 (C6‴), 123.0 (C5″, C5‴′), 20.5 (CH_3′), 20.5 (CH_3‴′), 20.5 (CH_3′), 20.5 (CH_3). Anal. Calcd for $C_{36}H_{30}N_4$: C, 83.37; H, 5.83; N, 10.80. Found: C, 83.02; H, 5.55; N, 10.66.

4.1.18. 5′-(2-Methyl-4-pyridin-3-ylphenyl)-3′,5-dimethyl-6-(2-methyl-4-pyridin-3-ylphenyl)-3,2′-bipyridine ***8f***. White solid. Mp 177 °C. IR (KBr): 3022, 2956, 2920, 2858, 1588, 1571, 1456, 1419, 1379, 1184, 1129, 1071, 1021, 995, 882, 841, 805, 710, 616, 531 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.91 (s, 2H, *H2″*, *H2‴′*), 8.79 (s, 1H, *H2*), 8.61 (s, 3H, *H6'*, *H4″*, *H4‴′*), 7.94 (d, *J*=8.0, 2H, *H6″*, *H6‴′*), 7.93 (s, 1H, *H4*), 7.67 (s, 1H, *H4'*), 7.56–7.51 (m, 4H, *H4‴*, *H5‴*, *H3‴′*, *H5‴′*), 7.41 (d, *J*=8.0, 1H, *H6‴*), 7.41–7.40 (m, 2H, *H5″*, *H5‴′*), 7.38 (d, *J*=8.0, 1H, *H6‴′*), 2.55 (s, 3H, *CH*$_3$′), 2.45 (s, 3H, *CH*$_3$‴), 2.27 (s, 3H, *CH*$_3$), 2.24 (s, 3H, *CH*$_3$‴′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.5 (C6), 154.1 (C2′), 148.6 (C4‴′), 148.4 (C4″), 148.3 (C2‴′, C2″), 147.5 (C6′), 146.8 (C2), 139.9 (C1‴′), 139.3 (C4'), 138.5 (C4), 137.7 (C1″), 137.6 (C1‴), 137.5 (C4‴′), 136.8 (C2‴′), 136.6 (C2‴, C1‴′), 136.1 (C4‴), 135.9 (C5'), 134.7 (C3), 134.4 (C6‴′, C6″), 131.4 (C5), 130.8 (C3′), 130.7 (C6‴), 129.4 (C6‴′, C3‴), 129.1 (C3‴′), 124.9 (C5‴), 124.6 (C5‴′), 123.6 (C5‴′, C5″), 20.7 (CH_3‴), 20.2 (CH_3′), 19.7 (CH_3‴′), 19.1 (CH_3). Anal. Calcd for $C_{36}H_{30}N_4$: C, 83.37; H, 5.83; N, 10.80. Found: C, 83.12; H, 5.45; N, 10.54.

Supplementary data

Crystallographic data (excluding structure factors) for the structures of compounds **7e** and **7f** in this paper have been

deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 814118 and 814119. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.Uk).

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