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Synthesis of Trisubstituted Pyridines *via* Chemoselective Suzuki–Miyaura Coupling of 3,5- and 4,6-Dibromo-2-tosyloxypyridines

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Abstract: Chemoselective Suzuki–Miyaura reactions on 3,5- and 4,6-dibromo-2-tosyloxypyridines have been studied for the preparation of trisubstituted pyridines. The optimized conditions allow for a facile access to 3,5- and 4,6-diaryl-2-tosyloxypyridines in yields of 8 to 99%. Further functionalization such as palladium-catalyzed amination and copper-free Sonogashira reaction of the tosylate group in the diarylpyridine derivatives obtained was accomplished for the synthesis of novel and biologically relevant trisubstituted pyridines. The formal synthesis of ficuseptine, a bioactive alkaloid, has also been achieved *via* the palladium-catalyzed cross-coupling reaction of 3,5-dibromo-2-tosyloxypyridine in 5 steps from 3,5-dibromo-2-hydroxypyridine with 50% overall yield.

Keywords: chemoselective Suzuki–Miyaura reaction; copper-free Sonogashira reaction; ficuseptine; palladium-catalyzed amination; trisubstituted pyridines

Introduction

Pyridines are a common moiety found in biologically active natural products and are important building blocks in pharmaceuticals and agrochemicals.[1] They are also integral to synthetic chemistry fields such as catalysis, supramolecular chemistry and coordination chemistry.[2] Among the pyridine derivatives, 2,3,5- and 2,4,6-trisubstituted pyridines serve as synthons for compounds with antibacterial and anticancer activity (Figure 1).[3]

Thus, several methods for the synthesis of 2,3,5- and 2,4,6-trisubsituted pyridines employing transition metal catalysis or organocatalysts have been investigated.[4] Nervertheless, due to their usefulness in the aforementioned areas, new and efficient synthetic methods are still necessary for the preparation of trisubstituted pyridines. Today, Suzuki–Miyaura cross-coupling reactions have become the most widely used method to form carbon-carbon bonds due to the mild reaction conditions, low toxicity, and high stability afforded by boronic acids compared to other cross-coupling substrates.[5] Particularly, interest in chemoselective cross-coupling reactions has increased in recent years.[6] These reactions generally take advantage of the different reactivities of the electrophilic sites or boron sites. Thus, we hypothesized that the use of orthogonal functionalization of dibromo-2-tosyloxypyridines through Suzuki–Miyaura cross-coupling reactions, followed by further functionalization of the tosyl group would allow for the facile preparation of 2,3,5- and 2,4,6-trisubstituted pyridines (Scheme 1).

In general, the selectivity of palladium-catalyzed cross-coupling for Br over OTs on an aryl moiety is well established.[7] Even though excess amounts of ar-

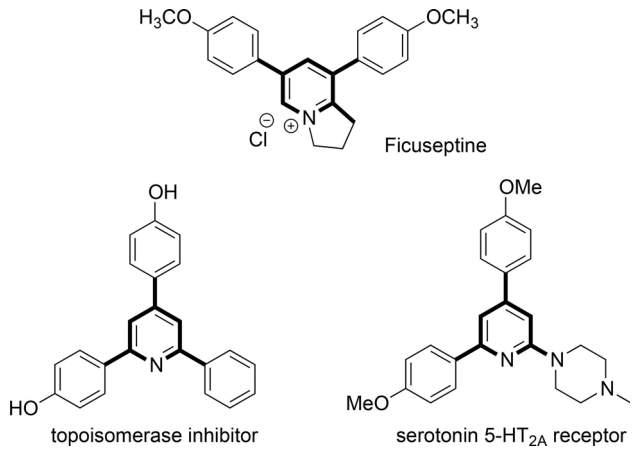
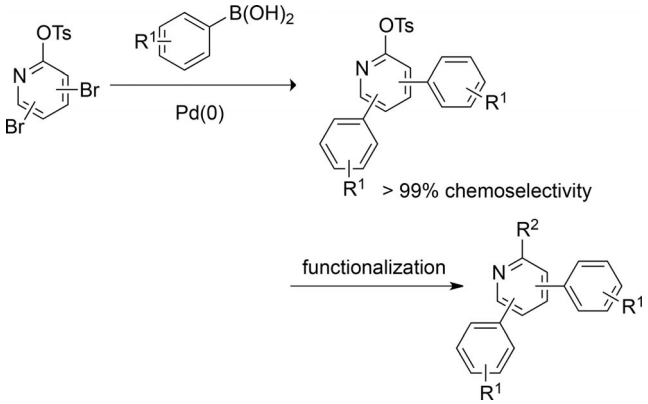
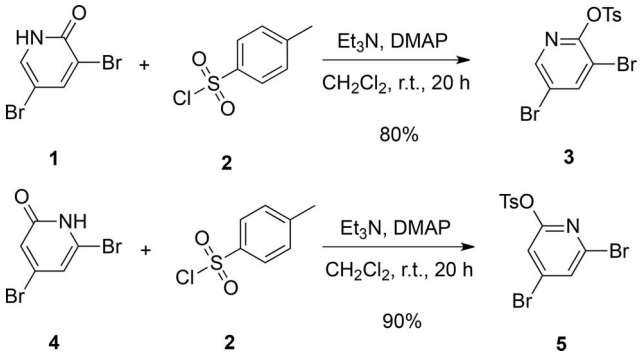


Figure 1. Bioactive compounds containing a pyridine moiety.



Scheme 1. Synthesis of 2,3,5- and 2,4,6-trisubstituted pyridines via chemoselective Suzuki reactions.



Scheme 2. Preparation of 3,5- and 4,6-dibromo-2-tosyloxypyridines.

ylboronic acids are employed, the monoarylated product is obtained as major product in excellent yield due to the low reactivity of aryl tosylates.[7a,b,e] However, fewer studies have been conducted on the selectivity for Br over OTs on the pyridine moiety.[8] Recently, Wang and co-workers reported the palladium-catalyzed Suzuki–Miyaura cross-coupling reactions employing 2-tosyloxypyridines.[8b] While they demonstrated that the Br group on the pyridine ring can be selectively arylated over the OTs group in coupling with arylboronic acid, this reaction provided significant amounts of diarylated product. For example, when 5-bromo-2-tosyloxypyridine was employed in the presence of $Pd(OAc)_2$, PPh_3 and K_3PO_4 in 1,4-dioxane at 110 °C, 5-phenyl-2-tosyloxypyridine and 2,5-diphenylpyridine were obtained in 30% and 48% yields in 7 h. These results indicate that the tosylate group attached to the C-2 position of the pyridine moiety is a quite reactive group. Thus, to achieve our goals, we need to suppress the reactivity of the tosylate group at the C-2 position of pyridine by employing an efficient catalyst system.

With these considerations in mind, we report herein the chemoselective Suzuki–Miyaura cross-coupling reactions of 3,5- and 4,6-dibromo-2-tosyloxypyridnes with boronic acids and the subsequent functionalization of the remaining tosyl group for the synthesis of 2,3,5- and 2,4,6-trisubsituted pyridines.

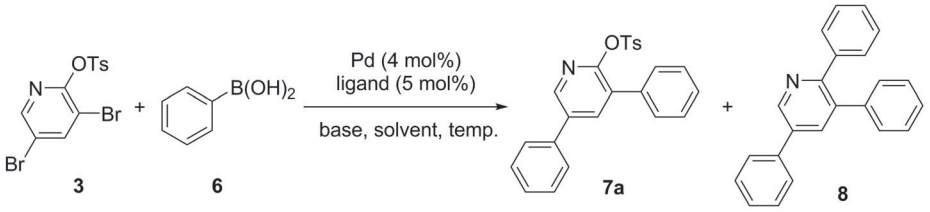
Results and Discussion

The 3,5- and 4,6-dibromo-2-tosyloxypyridines were prepared from 3,5-dibromo-2-hydroxypyridine **1** and 4,6-dibromo-2-hydroxypyridine **4**[9] *via* tosylation (Scheme 2).

Subsequently, optimization of the chemoselective Suzuki–Miyaura cross-coupling reaction was initially attempted using 3,5-dibromo-2-tosyloxypyridine **3** and phenylboronic acid **6**. As shown in Table 1, the use of 2.7 equivalents of phenylboronic acid, $Pd(OAc)_2$, and K_2CO_3 with a ligand in toluene furnished the cross-coupled product **7a** in good-to-excellent yields within 20 h. When $Pd(OAc)_2$ and a ligand such as Xphos, Sphos, Ruphos, and Brettphos were employed, the desired product **7a** was obtained in good yields along with significant amounts of triarylated product **8** (Table 1, entries 1–5). However, utilizing either $P(Cy)_3$ or Ad_2BnP as the ligand provided only the desired product **7a** without loss of the tosyl group. When the reactions were performed at either 100 °C or 80 °C in the presence of Ad_2BnP, the reactions did not go to completion due to competitive homocoupling of the phenylboronic acid (Table 1, entries 6 and 7). Next, we extensively screened bases, solvents, and temperature. As a result, the use of Ad_2BnP in the presence of $Pd(OAc)_2$ and K_2CO_3 in toluene at 50 °C led to the highest isolated yields (Table 1, entries 8 and 19). Surprisingly, when the reaction was performed at room temperature, product **7a** was also obtained in 99% yield in 20 h (Table 1, entry 9). Furthermore, when less than 2.7 equivalents of phenylboronic acid were used, product **7a** was isolated in a lower yield in 15 h (entries 17 and 18). However, utilizing 4.0 equivalents of phenylboronic acid **6** resulted in a shortened reaction time providing the desired product **7a** in 99% isolated yield (Table 1, entry 19). In addition, when 4.0 equivalents of phenylboronic acid were used in the presence of Xphos in toluene at 100 °C, triarylated product **8** was obtained as major product (Table 1, entry 20).

With the optimized conditions (*cf.*, Table 1, entry 8) in hand, we first examined the scope of the Pd-catalyzed chemoselective Suzuki–Miyaura cross-coupling reaction with various boronic acids (Table 2). Inexplicably, the use of 2.7 equivalents of boronic acid under the optimized conditions was not optimal for all substrates. However, in most cases, the use of 4.0 equivalents of boronic acid under the optimized conditions provided the corresponding products in a short time without reacting with the tosyl group. As illustrated in Table 2, utilizing arylboronic acids containing elec-

Table 1. Optimization of the chemoselective Suzuki–Miyaura reaction employing **3** and **6**.[a]



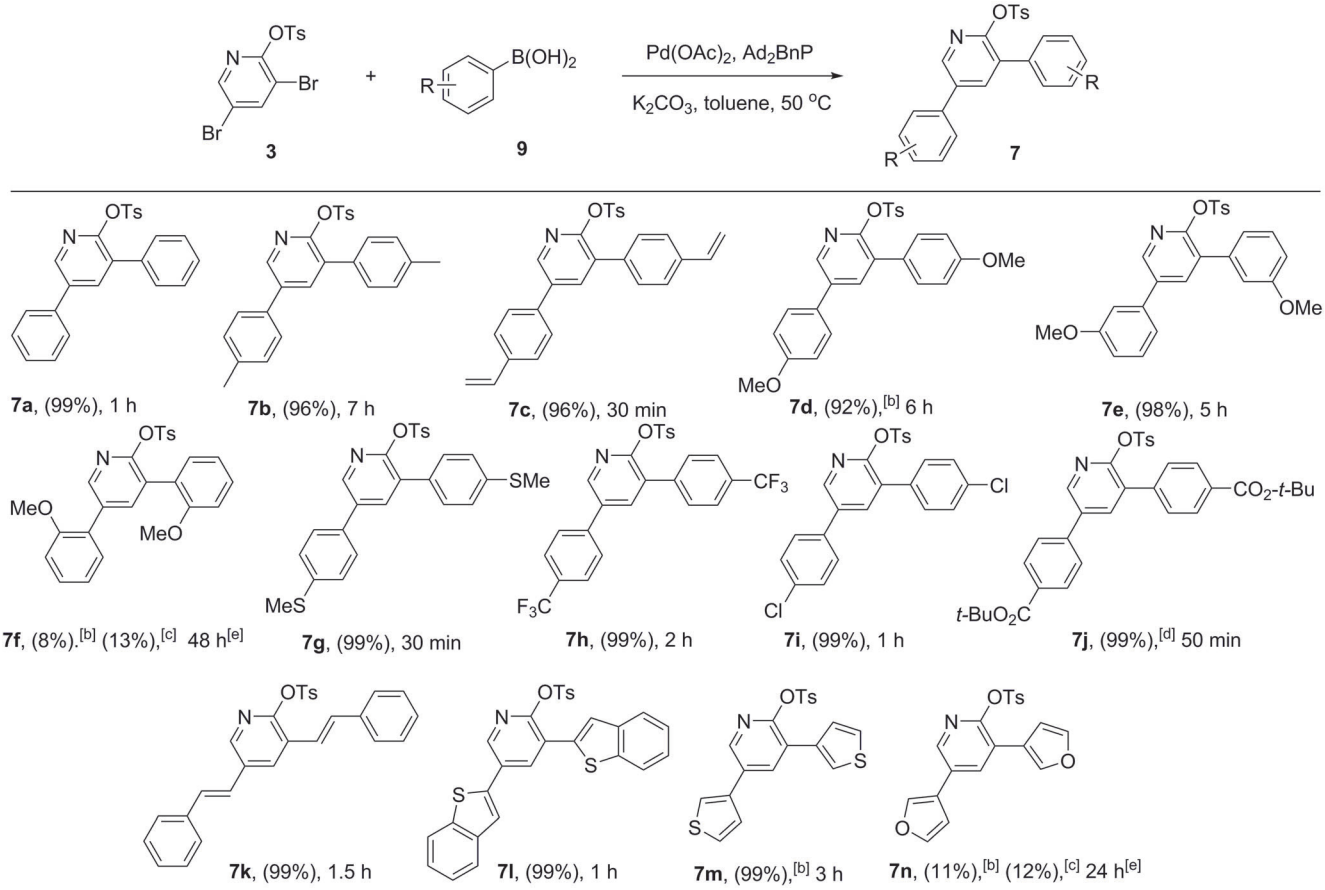
Entry	Equiv. of **6**	Pd catalyst	Ligand	Base	Solvent	Temp. [°C]	Time [h]	Yield **7a** [%][b]	Yield **8** [%][b]
1	2.7	$Pd(OAc)_2$	XPhos	K_2CO_3	toluene	100	6	75	20
2	2.7	$Pd(OAc)_2$	SPhos	K_2CO_3	toluene	100	7	80	18
3	2.7	$Pd(OAc)_2$	RuPhos	K_2CO_3	toluene	100	7	74	21
4	2.7	$Pd(OAc)_2$	BrettPhos	K_2CO_3	toluene	100	1	85	10
5	2.7	$Pd(OAc)_2$	$P(Cy)_3$	K_2CO_3	toluene	100	7	87	-
6	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	100	15[c]	69	-
7	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	80	15[c]	65	-
8	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	50	6	99	-
9	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	25	20	99	-
10	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2PO_4	toluene	50	20	83	-
11	2.7	$Pd(OAc)_2$	Ad_2BnP	Cs_2CO_3	toluene	50	5[c]	80	-
12	2.7	$Pd(OAc)_2$	Ad_2BnP	Na_2CO_3	toluene	50	20	69	-
13	2.7	$PdCl_2(MeCN)$	Ad_2BnP	K_2CO_3	toluene	50	4	88	-
14	2.7	$Pd(PPh_3)_4$	-	K_2CO_3	toluene	50	20	13	-
15	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	DMF	50	20	4	-
16	2.7	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	THF	50	20	43	-
17	2.2	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	50	15[c]	84	-
18	2.5	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	50	15[c]	90	-
19	4.0	$Pd(OAc)_2$	Ad_2BnP	K_2CO_3	toluene	50	1	99	-
20	4.0	$Pd(OAc)_2$	XPhos	K_2CO_3	toluene	100	6[c]	29	68

[a] *Reaction conditions:* 1.0 equiv. of **3**, phenylboronic acid **6**, 2.2 equiv. of base, 4 mol% of catalyst, 5 mol% of ligand, toluene (0.1 M).
[b] Isolated yield.
[c] Reaction time based on complete consumption of boronic acid as determined by TLC analysis.

tron-neutral, electron-donating, and electron-withdrawing groups furnished the coupled products in good-to-excellent yields. When sterically hindered 2-methoxyphenylboronic acid was used, however, the reaction was sluggish and gave the desired product **7f** in 8% yield with 13% conversion after 48 h. When a 4-*tert*-butoxycarbonyl-substituted arylboronic acid was employed, the reaction did not go to completion in 24 h. However, increasing the reaction temperature from 50 °C to 100 °C, provided full conversion and furnished the coupled product **7j** in 99% yield in 50 min. Furthermore, the non-aryl boronic acid (*E*)-styrylboronic acid also proved effective as a coupling partner, giving the desired product **7k** in 99% yield. Heteroarylboronic acids such as benzothiophen-2-ylboronic acid and 3-thienylboronic acid reacted with 3,5-dibromo-2-tosyloxypyridine **3** to form the corresponding coupled products **7l** and **7m** in 99% yield, respectively, while 3-furanylboronic acid furnished the desired product **7n** in 11% yield with 12% conversion after 24 h due to competitive homocoupling of the boronic acid.

Next, we turned our attention towards 4,6-dibromo-2-tosyloxypyridine **5** as the electrophile. Pleasingly, the reaction conditions [*cf.*, $Pd(OAc)_2$, Ad_2BnP, K_2CO_3, toluene, 50 °C] that proved effective with 3,5-

Table 2. Chemoselective Suzuki–Miyaura reaction employing **3** and various boronic acids **9**.[a]



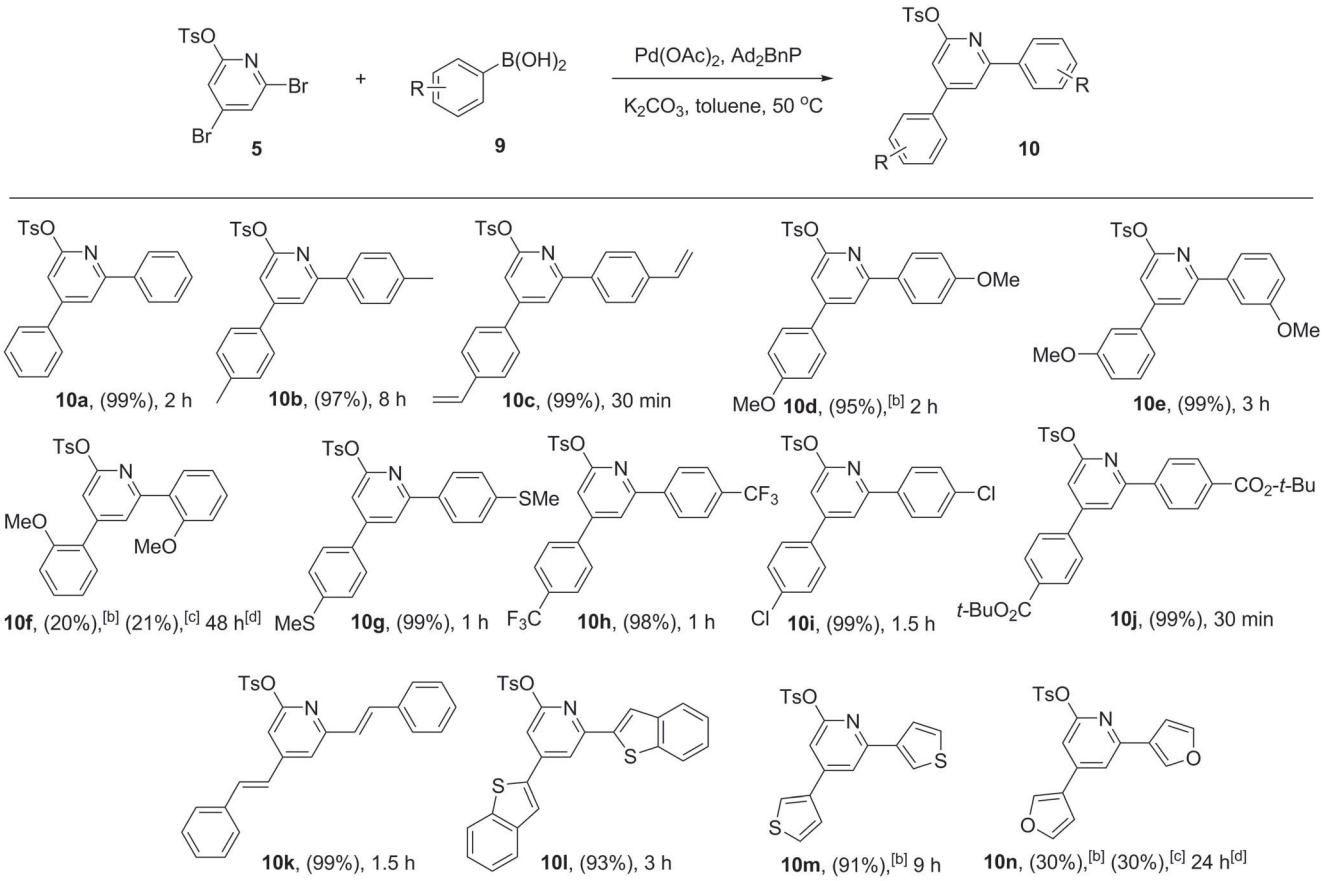
[a] *Reaction conditions:* 1.0 equiv. of **3**, 4.0 equiv. of boronic acid, 2.2 equiv. of K_2CO_3, 4 mol% of $Pd(OAc)_2$, 5 mol% of Ad_2BnP, toluene (0.1 M), 50 °C.
[b] 5.0 equiv. of boronic acid.
[c] Conversion.
[d] The reaction was conducted at 100 °C.
[e] Reaction time based on complete consumption of boronic acid as determined by TLC analysis.

dibromo-2-tosyloxypyridine **3** were also optimal for the Pd-catalyzed chemoselective Suzuki–Miyaura cross-coupling reaction with **5**. As shown in Table 3, a variety of heteroaryl- and arylboronic acids with electron neutral, electron-donating, and electron-withdrawing groups were transformed into diarylpyridine derivatives **10a**–**10n** in 20% to 99% yields.

Encouraged by the viability of this chemoselective Suzuki–Miyaura reaction for the synthesis of 3,5- and 4,6-diaryl-2-tosyloxypyridines, we next turned our attention to the preparation of the 2,3,5- and 2,4,6-trisubstituted pyridines found in many biologically active compounds. A tosylate group attached to the C-2 position of pyridine is a reactive group in coupling reactions such as Suzuki coupling,[8b,10] Sonogashira coupling,[8b] Kumada coupling,[11] amination[12] and reduction.[13] We, therefore, began to modify the aforementioned methods for the preparation of trisubstituted pyridines employing 3,5- and 4,6-diphenyl-2-tosyloxypyridine (Scheme 3). Pleasingly, **7a** underwent reduction to furnish **11** in 92% yield, Suzuki reaction to afford **12** in 95% yield, and detosylation to give **13** in 99% yield. In particular, Pd-catalyzed amination and Cu-free Sonogashira reaction, which to date have not yet been investigated, employing diaryl-substituted pyridine furnished the coupled products **14** and **15** in 99% and 85% yields, respectively. In addition, iron-catalyzed sp^2–sp^3 coupling of **10a** with isopropylmagnesium bromide provided product **16** in 53% yield.

Finally, to demonstrate the feasibility of the regioselective Pd-catalyzed Suzuki–Miyaura coupling reaction of 3,5- and 4,6-dibromo-2-tosyloxypyridines, we applied our method to a formal synthesis of ficuseptine [4,6-bis(4-methoxyphenyl)-1,2,3-trihydroindolizidinium chloride] **20**, an indolizidinium alkaloid isolated from the leaves of *Ficus septica* in 1990.[3a,14] As shown in Scheme 4, treatment of alkyne **17** with **7d**

Table 3. Chemoselective Suzuki–Miyaura reaction employing **5** and various boronic acid **9**.[a]



[a] *Reaction conditions:* 1.0 equiv. of **5**, 4.0 equiv. of boronic acid, 2.2 equiv. of K_2CO_3, 4 mol% of $Pd(OAc)_2$, 5 mol% of Ad_2BnP, toluene (0.1 M), 50 °C.
[b] 5.0 equiv. of boronic acid.
[c] Conversion.
[d] Reaction time based on complete consumption of boronic acid as determined by TLC analysis.

prepared from **3** *via* chemoselective Suzuki–Miyaura coupling under Cu-free Sonogashira conditions furnished pyridine **18** in 90% yield. Pd/C-catalyzed hydrogenation, followed by desilylation of pyridine **18** in MeOH provided pyridylpropanol **19** in 95% yield.[15] Finally, employing MsCl and Et_3N to cyclize **19** and form the indolizidinium ring furnished the antibacterial ficuseptine **20** in 79% yield.[16]

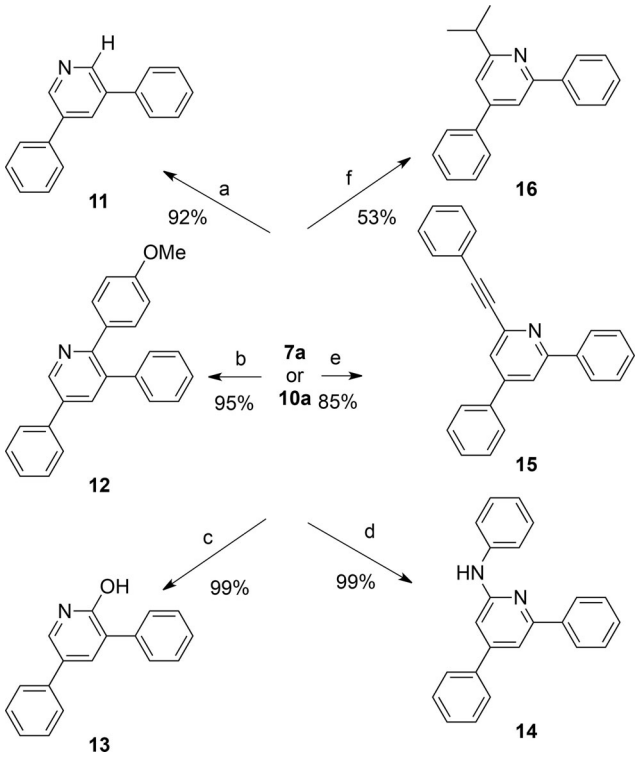
Conclusions

In conclusion, we have described the chemoselective Suzuki–Miyaura reactions employing 3,5- and 4,6-dibromo-2-tosyloxypyridines. Most reactions proceeded well without reacting with the tosyl group under the optimized conditions of 4 mol% of $Pd(OAc)_2$, 5 mol% of Ad_2BnP and 2.2 equivalents of K_2CO_3 in toluene at 50 °C. The scope of this methodology has been explored employing aryl-, vinyl- and heteroarylboronic acids. Moreover, it was found that diarylpyridine derivatives prepared in this manner can be further transformed into trisubstituted pyridines by functionalization of the tosyl group. Particularly, Pd-catalyzed amination and Cu-free Sonogashira reactions employing diarylpyridines provided the coupled products in good-to-excellent yields. Finally, the formal synthesis of ficuseptine **20** was achieved in five steps and 50% overall yield from 3,5-dibormo-2-hydroxypyridine **1** employing chemoselective Suzuki and Cu-free Sonogashira couplings as the key steps.

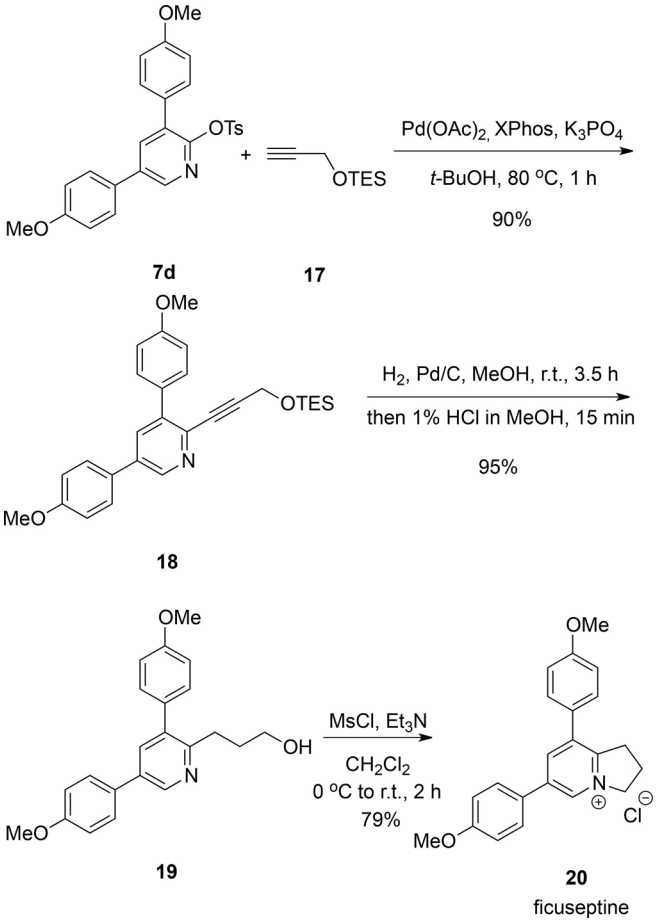
Experimental Section

General Considerations

Unless otherwise indicated, all chemical reagents were purchased from commercial suppliers and were used without further purification. All reactions were carried out in oven-



Scheme 3. Various functionalization of 3,5- and 4,6-diphenyl-2-tosyloxypyridines. a: HCOOH, 5 mol% of $Pd(OAc)_2$, 5 mol% of dppp, Et_3N, DMF, 60 °C, 1 h. b: 4-methoxyphenylboronic acid, 4 mol% of $Pd(OAc)_2$, 5 mol% of Sphos, K_2CO_3, toluene, 50 °C, 2.5 h. c: NaOH, THF/MeOH (1/1), 50 °C, 1 h. d: Aniline, 5 mol% of $Pd(OAc)_2$, 60 mol% of dppf, K_2CO_3, toluene, 110 °C, 6 h. e: Phenylacetylene, 3 mol% of $Pd(OAc)_2$, 7 mol% of Xphos, K_3PO_4, *t*-BuOH, 85 °C, 1 h. f: Isopropylmagnesium bromide, 20 mol% of $FeCl_3$, THF/NMP (1/5), −30 °C, 1 h.



Scheme 4. Synthesis of ficuseptine **20**.

dried glassware equipped with a magnetic stir bar. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm pre-coated silica gel plates (Kieselgel $60F_{254}$). Products were detected by viewing under a UV light, by staining with an anisaldehyde solution composed of acetic acid, sulfuric acid, and MeOH, or by staining with a $KMnO_4$ solution composed of potassium carbonate, sodium hydroxide, and water. Flash column chromatography was performed on silica gel (70–230 mesh). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz NMR spectrometer. Chemical shifts are reported as δ values relative to internal $SiMe_4$ or chloroform ($\delta = 0.00$ for ^1H and $\delta = 77.0$ for ^{13}C) or DMSO-d_6 ($\delta = 2.50$ for ^1H and $\delta = 39.5$ for ^{13}C). IR spectra were measured as neat oils and solids on an FT-IR spectrometer. HR-MS data were obtained by electron ionization and fast atom bombardment with a double-focusing high-resolution magnetic sector mass analyzer.

3,5-Dibromo-2-tosyloxypyridine (3)

A solution of 3,5-dibromo-2-hydroxypyridine (2.0 mmol), TsCl (2.4 mmol), Et_3N (4.0 mmol) and DMAP (10 mol%) in anhydrous CH_2Cl_2 (6 mL) was stirred at room temperature for 20 h. The reaction mixture was quenched with H_2O and extracted with diethyl ether (3 × 10 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 20:1) to obtain the pyridine **3** as a white solid; yield: 655.2 mg (1.61 mmol, 80%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.23$ (d, $J = 2.3$ Hz, 1H), 8.08 (d, $J = 2.3$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 2H), 7.37 (d, $J = 8.0$ Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 153.1$, 147.2, 145.7, 145.2, 133.6, 129.7, 128.8, 117.9, 112.0, 21.7; Data are consistent with those reported in the literature.[8a]

Preparation of 4,6-Dibromo-2-hydroxypyridine (4)

4,6-Dibromo-2-hydroxypyridine was prepared as according to the cited literature procedure.[9]

4,6-Dibromo-2-tosyloxypyridine (5)

A solution of 4,6-dibromo-2-hydroxypyridine (2.0 mmol), TsCl (2.4 mmol), Et_3N (4.0 mmol) and DMAP (10 mol%) in anhydrous CH_2Cl_2 (6 mL) was stirred at room temperature for 20 h. The reaction mixture was quenched with H_2O and extracted with diethyl ether (3 × 10 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and

concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 20:1) to obtain the pyridine **5** as a white solid; yield: 732.8 mg (1.80 mmol, 90%); mp 86–88 °C; R_f 0.32 (hexane/ethyl acetate = 5:1). IR (neat): ν = 3450, 3110, 2534, 2144, 1559, 1376, 1179, 796, 724, 554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 1.3 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 1.3 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0, 146.0, 139.5, 136.0, 132.9, 129.7, 129.2, 129.1, 117.3, 21.8; HR-MS-FAB: m/z = 405.8748 $[M+H]^+$, calcd. for $C_{12}H_{10}Br_2NO_3S^+$: 405.8751.

General Procedure I for Synthesis of Diaryl-2-pyridyl 4-Methylbenzenesulfonates

A round bottom flask was charged with dibromo-2-tosyloxypyridine (1.0 equiv), boronic acid (4.0 equiv), K_2CO_3 (2.2 equiv), Ad_2BnP (5 mol%) and $Pd(OAc)_2$ (4 mol%). Toluene (2.5 mL) was then added to the flask. The reaction mixture was stirred at 50 °C under argon purged flask. After completion of the reaction as monitored by TLC analysis, the reaction solution was extracted by ethyl acetate (3× 10 mL). The combined organic layer was then concentrated, and the residue was purified by flash column chromatography on silica gel to obtain the desired product.

3,5-Diphenyl-2-pyridyl 4-methylbenzenesulfonate (7a): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and phenylboronic acid (0.984 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7a** as a white solid; yield: 98.2 mg (0.245 mmol, 99%); mp 176–180 °C; R_f 0.21 (hexane/ethyl acetate = 5:1). IR (neat): ν = 3034, 2923, 1591, 1377, 1175, 1090, 889, 819, 695, 545 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 2.5 Hz, 1H), 7.95 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.59–7.56 (m, 2H), 7.51–7.40 (m, 8H), 7.23 (d, J = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.3, 144.9, 144.87, 139.1, 136.5, 136.3, 134.8, 134.2, 129.4, 129.2, 129.17, 129.0, 128.5,128.47, 128.4, 128.3, 127.1, 21.7; HRMS-EI: m/z = 401.1083 $[M^+]$, calcd. for $C_{24}H_{19}NO_3S^+$: 401.1086.

2,3,5-Triphenylpyridine (8): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol), phenylboronic acid (0.984 mmol) and RuPhos (5 mol%), and the reaction was completed in 7 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **7a**; yield: 72.8 mg (0.181 mmol, 74%) and **8**; yield: 16.0 mg (0.052 mmol, 21%) as a white solid; R_f 0.28 (hexane/ethyl acetate = 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.93 (d, J = 2.3 Hz, 1H), 7.91 (d, J = 2.3 Hz, 1H), 7.68–7.7.65 (m, 2H), 7.51–7.46 (m, 2H), 7.43–7.38 (m, 3H), 7.30–7.22 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.8, 146.6, 139.8, 139.76, 137.3, 136.8, 135.9, 134.9, 129.8, 129.5, 129.1, 128.3, 128.1, 127.9, 127.8, 127.3, 127.1; Data are consistent with those reported in the literature.[17]

3,5-Di-*p*-tolyl-2-pyridyl 4-methylbenzenesulfonate (7b): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.247 mmol) and *p*-tolylboronic acid (0.988 mmol), and the reaction was completed in 7 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7b** as a white solid; yield: 102.0 mg (0.237 mmol, 96%); mp 170–174 °C; R_f 0.27 (hexane/ethyl acetate = 5:1). IR (neat): ν = 3446, 2073, 1638, 1376, 1176, 1085, 884, 698, 552 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.42 (d, J = 2.5 Hz, 1H), 7.88 (d, J = 2.5 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 7.19 (dd, J = 2.4 Hz and 5.9 Hz, 4H), 2.40 (s, 3H), 2.38 (d, J = 2.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1, 144.7, 144.3, 138.7, 138.3, 138.1, 136.1, 134.3, 133.5, 131.8, 129.8, 129.3, 129.1, 129.0, 128.9, 128.4, 126.8, 21.6, 21.2, 21.1; HR-MS-EI: m/z = 429.1401 $[M^+]$, calcd. for $C_{26}H_{23}NO_3S^+$: 429.1399.

3,5-Bis(4-vinylphenyl)pyridin-2-yl 4-methylbenzenesulfonate (7c): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.247 mmol) and (4-vinylphenyl)-boronic acid (0.988 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7c** as a white solid; yield: 107.0 mg (0.236 mmol, 96%); mp 54–60 °C; R_f 0.6 (hexane/ethyl acetate = 2:1). IR (neat): ν = 3046, 1698, 1600, 1377, 1089, 895, 828, 695, 552, 481 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.49 (d, J = 2.5 Hz, 1H), 7.94 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 2.3 Hz, 4H), 7.44 (s, 4H), 7.21 (d, J = 8.2 Hz, 2H), 6.76 (dd, J = 10.9 Hz and 17.6 Hz, 2H), 5.82 (d, J = 17.6 Hz, 2H), 5.33 (dd, J = 4.1 Hz and 11.2 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1, 144.8, 144.6, 138.5, 137.6, 137.5, 136.1, 135.9, 135.7, 135.5, 134.1, 133.9, 129.3, 129.28, 128.6, 128.3, 127.1, 126.9, 126.2, 114.7, 114.68, 21.6; HR-MS-EI: m/z = 453.1398 $[M^+]$, calcd. for $C_{28}H_{23}NO_3S^+$: 453.1399.

3,5-Bis(4-methoxyphenyl)-2-pyridyl 4-methylbenzenesulfonate (7d): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and (4-methoxyphenyl)boronic acid (1.230 mmol), and the reaction was completed in 6 h. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **7d** as a white solid; yield: 104.6 mg (0.227 mmol, 92%); mp 48–50 °C; R_f 0.34 (hexane/ethyl acetate = 2:1). IR (neat): ν = 3439, 3054, 2051, 1608, 1513, 1436, 1377, 1249, 1177, 1033, 826 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.40 (d, J = 2.5 Hz, 1H), 7.86 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.41 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.85 (d, J = 1.3 Hz, 6H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9, 159.7, 152.9, 144.8, 143.9, 138.3, 135.9, 134.3, 130.4, 129.3, 128.9, 128.6, 128.4, 128.2, 127.1, 114.6, 113.9, 55.3, 55.28, 21.6; HR-MS-EI: m/z = 461.1299 $[M^+]$, calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

3,5-Bis(3-methoxyphenyl)-2-pyridyl 4-methylbenzenesulfonate (7e): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and (3-methoxyphenyl)boronic acid (0.984 mmol), and the reaction was completed in 5 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7e** as a white solid; yield: 111.7 mg (0.242 mmol, 98%); mp 102–104 °C; R_f 0.3 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3442, 2950, 2841, 1596, 1378, 1173, 1042, 858, 773, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.49 (d, J = 2.5 Hz, 1H), 7.94 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.39 (t, J = 8.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.16–7.13 (m, 1H), 7.09–7.05 (m, 2H), 7.00–6.91 (m, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 159.5, 153.2, 144.9, 144.87, 139.0, 137.7, 136.1,

135.9, 134.1, 130.2, 129.5, 129.4, 128.8, 128.4, 121.5, 119.4, 114.5, 114.2, 113.7, 112.8, 55.3, 55.2, 21.6; HR-MS-EI: m/z = 461.1295 [M^+], calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

3,5-Bis(2-methoxyphenyl)-2-pyridyl 4-methylbenzenesulfonate (7f): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.245 mmol) and (2-methoxyphenyl)boronic acid (1.225 mmol), and the reaction was completed in 48 h. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **7f** as a white solid; yield: 8.9 mg (0.019 mmol, 8%); mp 134–136 °C; R_f 0.38 (hexane/ethyl acetate = 2:1). IR (neat): ν = 3442, 2065, 1636, 1497, 1421, 1374, 1254, 1172, 1026, 754, 550 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.42 (d, J = 2.4 Hz, 1H), 7.91 (d, J = 2.4 Hz, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.40–7.30 (m, 3H), 7.25–7.21 (m, 3H), 7.06–6.92 (m, 4H), 3.79 (d, J = 8.5 Hz, 6H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.7, 156.5, 153.5, 146.8, 144.4, 142.5, 134.9, 133.0, 131.3, 130.6, 129.8, 129.6, 129.3, 128.4, 125.8, 125.0, 124.1, 121.0, 120.4, 111.2, 111.0, 55.5, 55.4, 21.6; HR-MS-EI: m/z = 461.1298 [M^+], calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

3,5-Bis(4-(methylthio)phenyl)pyridin-2-yl 4-methylbenzenesulfonate (7g): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.245 mmol) and (4-(methylthio)phenyl)boronic acid (0.980 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7g** as a white solid; yield: 120.0 mg (0.243 mmol, 99%); mp 62–66 °C; R_f 0.37 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3441, 2071, 1639, 1430, 1375, 1174, 999, 874, 808, 661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.43 (d, J = 2.5 Hz, 1H), 7.87 (d, J = 2.5 Hz, 1H), 7.73 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.35 (q, J = 8.5 Hz, 4H), 7.25–7.22 (m, 4H), 2.51 (d, J = 1.7 Hz, 6H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 144.9, 144.4, 139.4, 139.3, 138.3, 135.6, 134.2, 132.8, 131.1, 129.4, 129.36, 128.4, 128.35, 127.3, 126.7, 125.9, 21.6, 15.4, 15.3; HR-MS-EI: m/z = 493.0843 [M^+], calcd. for $C_{26}H_{23}NO_3S_3^+$: 493.0840.

3,5-Bis(4-(trifluoromethyl)phenyl)pyridin-2-yl 4-methylbenzenesulfonate (7h): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.247 mmol) and (4-(trifluoromethyl)phenyl)boronic acid (0.988 mmol), and the reaction was completed in 2 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **7h** as a white solid; yield: 131.0 mg (0.244 mmol, 99); mp 180–182 °C; R_f 0.6 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3442, 2074, 1637, 1373, 1176, 1093, 963, 844, 725, 547 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.56 (d, J = 2.5 Hz, 1H), 7.96 (d, J = 2.5 Hz, 1H), 7.77–7.57 (m, 10H), 7.24 (d, J = 8.3 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 145.9, 145.4, 139.7, 139.1, 138.1, 135.0, 134.0, 131.1 (q, J = 12.0 Hz), 130.4 (q, J = 12.0 Hz), 129.6, 129.5, 128.4, 127.9, 127.5, 126.3, 126.23, 126.18, 126.1, 125.7, 125.55, 125.50, 125.45, 125.40, 122.1, 21.6; HR-MS-EI: m/z = 537.0831 [M^+], calcd. for $C_{26}H_{17}F_6NO_3S^+$: 537.0833.

3,5-Bis(4-chlorophenyl)-2-pyridyl 4-methylbenzenesulfonate (7i): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.245 mmol) and (4-chlorophenyl)boronic acid (1.225 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7i** as a white solid; yield: 114.5 mg (0.243 mmol, 99%); m.p 190–194 °C; R_f 0.63 (hexane/ethyl acetate = 2:1). IR (neat): ν = 3455, 1641, 1494, 1435, 1370, 1170, 1091, 1014, 886, 718, 548 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.46 (d, J = 2.4 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.47 (dd, J = 8.6 Hz and 11.4 Hz, 4H), 7.38 (dd, J = 8.9 Hz and 10.9 Hz, 4H), 7.26 (d, J = 8.3 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.4, 145.2, 145.1, 138.7, 137.0, 135.2, 134.9, 134.7, 134.69, 134.1, 133.0, 130.5, 129.5, 129.4, 128.8, 128.4, 128.3, 21.7; HR-MS-EI: m/z = 469.0303 [M^+], calcd. for $C_{24}H_{17}Cl_2NO_3S^+$: 469.0306.

Di-*tert*-butyl 4,4′-[2-(tosyloxy)pyridine-3,5-diyl]dibenzoate (7j): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and (4-(*tert*-butoxycarbonyl)phenyl)boronic acid (0.984 mmol), and the reaction was completed in 50 min. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7j** as a white solid; yield: 146.0 mg (0.243 mmol, 99%); mp 84–90 °C; R_f 0.59 (hexane/ethyl acetate = 2:1). IR (neat): ν = 3436, 2981, 1707, 1634, 1378, 1295, 1171, 1112, 1017, 811, 708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.52 (d, J = 2.5 Hz, 1H), 8.09 (d, J = 8.6 Hz, 2H), 8.02 (d, J = 8.6 Hz, 2H), 7.97 (d, J = 2.5 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H), 1.63 (s, 9H), 1.61 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 165.1, 153.6, 145.5, 145.1, 140.0, 139.0, 138.5, 135.3, 134.0, 131.9, 131.8, 130.2, 129.5, 129.4, 129.0, 128.4, 128.3, 126.8, 81.3, 81.2, 28.13, 28.10, 21.6; HR-MS-EI: m/z = 601.2130 [M^+], calcd. for $C_{34}H_{35}NO_7S^+$: 601.2134.

3,5-Di[(*E*)-styryl]pyridin-2-yl 4-methylbenzenesulfonate (7k): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and (*E*)-styrylboronic acid (0.984 mmol), and the reaction was completed in 1.5 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7k** as a yellow solid; yield: 111.0 mg (0.245 mmol, 99%); mp 58–65 °C; R_f 0.47 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3442, 2345, 2074, 1637, 1373, 1176, 1094, 963, 844, 725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, J = 2.3 Hz, 1H), 8.08 (d, J = 2.3 Hz, 1H), 7.97 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 7.1 Hz, 2H), 7.48 (d, J = 6.8 Hz, 2H), 7.41–7.29 (m, 8H), 7.18–7.00 (m, 4H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.2, 145.2, 144.6, 136.3, 136.2, 134.1, 133.1, 132.5, 132.3, 131.4, 129.6, 128.7, 128.6, 128.5, 128.47, 128.3, 126.9, 126.6, 124.9, 123.4, 119.9, 21.6; HR-MS-EI: m/z = 453.1397 [M^+], calcd. for $C_{28}H_{23}NO_3S^+$: 453.1399.

3,5-Bis(benzo[*b*]thiophen-2-yl)pyridin-2-yl 4-methylbenzenesulfonate (7l): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.245 mmol) and benzo[*b*]-thiophen-2-ylboronic acid (0.980 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7l** as a white solid; yield: 124.5 mg (0.243 mmol, 99%); mp 168–170 °C; R_f 0.53 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3455, 1636, 1419, 1373, 1170, 1091, 887, 822, 755, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.52 (d, J = 2.4 Hz, 1H), 8.23 (d, J = 2.5 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.87–7.78 (m, 5H), 7.59 (s, 1H), 7.40–7.37 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.8, 145.3, 143.8, 140.2, 140.0, 139.99, 139.7, 138.3, 136.6, 135.2, 134.2, 139.7, 129.5, 128.8, 125.4, 125.3, 125.2, 125.0, 124.7, 124.3, 124.0, 122.3, 122.0, 121.9, 121.4, 21.7; HR-MS-EI: m/z = 513.0526 [M^+], calcd. for $C_{28}H_{19}NO_3S_3^+$: 513.0526.

3,5-Di(thiophen-3-yl)pyridin-2-yl 4-methylbenzenesulfonate (7m): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.245 mmol) and thiophen-3-ylboronic acid (1.225 mmol), and the reaction was completed in 3 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7m** as a white solid; yield: 100.5 mg (0.243 mmol, 99%); mp 128–130 °C; R_f 0.4 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3442, 2347, 2079, 1636, 1440, 1370, 1173, 1089, 741, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.41 (d, J = 2.4 Hz, 1H), 8.0 (d, J = 2.4 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.62 (t, J = 2.2 Hz, 1H), 7.50 (dd, J = 1.3 Hz and 3.0 Hz, 1H), 7.43–7.40 (m, 1H), 7.35 (d, J = 2.2 Hz, 2H), 7.33 (dd, J = 1.4 Hz and 5.0 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.5, 145.0, 143.5, 137.2, 136.9, 134.4, 134.1, 131.0, 129.4, 128.5, 127.6, 127.2, 125.9, 125.7, 125.1, 123.4, 121.8, 21.6; HR-MS-EI: m/z = 413.0216 [M^+], calcd. for $C_{20}H_{15}NO_3S_3^+$: 413.0214.

3,5-Di(furan-3-yl)pyridin-2-yl 4-methylbenzenesulfonate (7n): General procedure **I** was used employing 3,5-dibromo-2-tosyloxypyridine (0.246 mmol) and furan-3-ylboronic acid (1.230 mmol), and the reaction was completed in 24 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7n** as a white solid; yield: 10.4 mg (0.0273 mmol, 11%); mp 96–100 °C; R_f 0.21 (hexane/ethyl acetate = 5:1). IR (neat): ν = 3450, 2925, 1637, 1508, 1440, 1372, 1174, 875, 762, 597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, J = 2.3 Hz, 1H), 7.99 (d, J = 3.6 Hz, 2H), 7.95 (s, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.75 (s, 1H), 7.51 (dt, J = 1.7 Hz and 5.2 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 6.77 (d, J = 1.1 Hz, 1H), 6.67 (d, J = 1.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.7, 145.2, 144.3, 143.4, 142.4, 142.3, 139.1, 134.8, 134.5, 129.5, 128.8, 127.7, 122.2, 119.9, 118.9, 109.1, 108.5, 21.7; HR-MS-EI: m/z = 381.0674 [M^+], calcd. for $C_{20}H_{15}NO_5S^+$: 381.0671.

4,6-Diphenylpyridin-2-yl 4-methylbenzenesulfonate (10a): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.247 mmol) and phenylboronic acid (0.988 mmol), and the reaction was completed in 2 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10a** as a white solid; yield: 98.1 mg (0.244 mmol, 99%); mp 118–120 °C; R_f 0.53 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3438, 2348, 1612, 1368, 1174, 1083, 962, 795, 666, 560 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 1.2 Hz, 1H), 7.80–7.76 (m, 2H), 7.67–7.64 (m, 2H), 7.53–7.48 (m, 3H), 7.42 (t, J = 3.3 Hz, 3H), 7.38 (d, J = 8.4 Hz, 2H), 7.25 (s, 1H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 156.5, 153.7, 145.0, 137.4, 137.2, 134.4, 129.6, 129.5, 129.1, 128.7, 128.5, 127.0, 126.9, 116.9, 111.5, 30.8, 21.6; HR-MS-FAB: m/z = 402.1160 [$(M+H)^+$], calcd. for $C_{24}H_{20}NO_3S^+$: 402.1164.

4,6-Di-*p*-tolylpyridin-2-yl 4-methylbenzenesulfonate (10b): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.248 mmol) and *p*-tolylboronic acid (0.992 mmol), and the reaction was completed in 8 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10b** as a white solid; yield: 103.8 mg (0.242 mmol, 97%); mp 148–150 °C; R_f 0.58 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3445, 2347, 2102, 1616, 1372, 1177, 1083, 925, 808, 758, 662 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.3 Hz, 2H), 7.80 (d, J = 1.2 Hz, 1H), 7.67 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.23 (s, 1H), 7.21 (d, J = 1.1 Hz, 2H), 2.48 (s, 3H), 2.42 (d, J = 6.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 156.4, 153.5, 144.9, 139.8, 139.6, 134.8, 134.4, 134.39, 129.8, 129.5, 129.2, 128.8, 126.9, 126.8, 116.3, 110.8, 21.6, 21.2, 21.19; HR-MS-EI: m/z = 429.1398 [M^+], calcd. for $C_{26}H_{23}NO_3S^+$: 429.1399.

4,6-Bis(4-vinylphenyl)pyridin-2-yl 4-methylbenzenesulfonate (10c): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.245 mmol) and (4-vinylphenyl)-boronic acid (0.980 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10c** as a white solid; yield: 110.5 mg (0.244 mmol, 99%); m.p: 142–146 °C; R_f 0.56 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3439, 2341, 2070, 1637, 1371, 1174, 1082, 646, 552, 482 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 1.2 Hz, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 1.2 Hz, 1H), 6.82–6.71 (m, 2H), 5.85 (dd, J = 7.0 Hz and 17.6 Hz, 2H), 5.34 (dd, J = 3.1 Hz and 11.0 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 156.0, 153.1, 145.0, 138.9, 138.7, 136.7, 136.3, 136.1, 135.8, 134.4, 129.5, 128.7, 127.2, 127.0, 126.9, 126.4, 116.4, 115.3, 114.9, 111.1, 21.7; HR-MS-EI: m/z = 453.1397 [M^+], calcd. for $C_{28}H_{23}NO_3S^+$: 453.1399.

4,6-Bis(4-methoxyphenyl)pyridin-2-yl 4-methylbenzenesulfonate (10d): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.244 mmol) and (4-methoxyphenyl)boronic acid (1.220 mmol), and the reaction was completed in 2 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10d** as a white solid; yield: 107.0 mg 0.232 mmol, 95%); mp 122–126 °C; R_f 0.26 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3446, 2843, 2054, 1607, 1521, 1371, 1249, 1180, 1084, 925, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.3 Hz, 2H), 7.73–7.58 (m, 3H), 7.58 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 1.2 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 3.85 (d, J = 1.7 Hz, 6H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.8, 160.7, 157.6, 156.0, 153.0, 144.9, 134.4, 130.1, 129.5, 129.47, 128.7, 128.2, 115.4, 114.5, 113.8, 109.9, 55.3, 55.2, 21.6; HR-MS-EI: m/z = 461.1296 [M^+], calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

4,6-Bis(3-methoxyphenyl)pyridin-2-yl 4-methylbenzenesulfonate (10e): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.247 mmol) and (3-methoxyphenyl)boronic acid (0.988 mmol), and the reaction was completed in 3 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10e** as a white solid; yield: 112.8 mg (0.244 mmol, 99%); mp 80–82 °C; R_f 0.34 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3464, 3003, 2837, 1602, 1549, 1373, 1288, 1178, 1088, 956, 769 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 1.1 Hz, 1H), 7.43–7.20 (m, 6H), 7.25–7.20 (m, 2H), 7.14 (t, J = 2.0 Hz, 1H), 7.01 (dd, J = 2.0 Hz and 8.0 Hz, 1H), 6.96–6.92 (m, 1H), 3.85 (d, J = 11.4 Hz, 6H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 159.9, 157.5, 156.3, 153.6, 145.1, 138.9, 138.7, 134.3, 130.3, 129.6, 129.56, 128.7, 119.5, 119.2, 117.2, 114.9, 114.89, 112.8, 112.7, 111.9, 55.4, 55.3, 21.6; HR-MS-EI: m/z = 461.1296 [M^+], calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

4,6-Bis(2-methoxyphenyl)pyridin-2-yl 4-methylbenzenesulfonate (10f): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.246 mmol) and (2-methoxyphenyl)boronic acid (1.230 mmol), and the reaction was completed in 48 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10f** as a white solid; yield: 22.8 mg (0.049 mmol, 20%); mp 102–104 °C; R_f 0.24 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3447, 2838, 1605, 1496, 1373, 1248, 1169, 1126, 927, 804, 754, 551 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, J = 1.2 Hz, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.42–7.31 (m, 6H), 7.25 (d, J = 5.6 Hz, 1H), 7.08–6.93 (m, 4H), 3.83 (d, J = 5.0 Hz, 6H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.1, 156.6, 153.8, 150.3, 144.7, 134.5, 131.4, 130.5, 130.4, 130.2, 129.5, 128.9, 127.2, 127.1, 124.4, 121.0, 120.6, 113.8, 111.4, 111.36, 55.54, 55.5, 21.6; HR-MS-EI: m/z = 461.1296 [(M + H)$^+$], calcd. for $C_{26}H_{23}NO_5S^+$: 461.1297.

4,6-Bis[4-(methylthio)phenyl]pyridin-2-yl 4-methylbenzenesulfonate (10g): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.246 mmol) and (4-(methylthio)phenyl)boronic acid (165.3 mg, 0.984 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10g** as a white solid; yield: 120.5 mg, (0.244 mmol, 99%); mp 98–102 °C; R_f 0.41 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3452, 2924, 2348, 1602, 1371, 1177, 1084, 926, 816, 664 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 1.1 Hz, 1H), 7.67 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.372–7.311 (m, 4H), 7.23 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 1.1 Hz, 1H), 2.50 (d, J = 2.1 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 155.9, 152.9, 145.0, 141.1, 140.7, 134.3, 133.96, 133.4, 129.5, 128.7, 127.2, 127.1, 126.3, 125.8, 115.8, 110.6, 21.7, 15.2, 15.18; HR-MS-EI: m/z = 493.0843 [M$^+$], calcd. for $C_{26}H_{23}NO_3S_3^+$: 493.0840.

4,6-Bis[4-(trifluoromethyl)phenyl]pyridin-2-yl 4-methylbenzenesulfonate (10h): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.243 mmol) and (4-(trifluoromethyl)phenyl)boronic acid (0.972 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10h** as a white solid; yield: 128.0 mg (0.238 mmol, 98%); mp 148–150 °C; R_f 0.73 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3437, 2943, 2078, 1637, 1327, 1170, 1119, 1069, 924, 647 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.1 Hz, 2H), 7.86 (d, J = 1.2 Hz, 1H), 7.77 (s, 4H), 7.66 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 1.2 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 155.3, 152.6, 145.4, 140.5, 134.2, 131.8 (q, J = 32.6 Hz), 131.5 (q, J = 32.6 Hz), 129.7, 128.7, 127.6, 127.3, 126.34, 126.29, 126.24, 126.19, 125.74, 125.68, 125.63, 125.59, 125.5, 122.1, 122.0, 117.4, 112.7, 21.7; HR-MS-FAB: m/z = 538.0913 [(M + H)$^+$], calcd. for $C_{26}H_{17}F_6NO_3S^+$: 538.0912.

4,6-Bis(4-chlorophenyl)pyridin-2-yl 4-methylbenzenesulfonate (10i): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.245 mmol) and (4-chlorophenyl)boronic acid (1.225 mmol), and the reaction was completed in 1.5 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10i** as a white solid; yield: 114.5 mg (0.243 mmol, 99%); mp 160–164 °C; R_f 0.62 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3447, 2361, 1636, 1542, 1375, 1171, 1089, 927, 825, 666 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 1.2 Hz, 1H), 7.70 (d, J = 8.7 Hz, 2H), 7.57 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.38–7.33 (m, 4H), 7.19 (d, J = 1.2 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 155.4, 152.6, 145.2, 136.0, 135.8, 135.7, 135.5, 134.3, 129.6, 129.5, 128.8, 128.7, 128.3, 128.2, 116.4, 111.6, 21.7; HR-MS-FAB: m/z = 470.0386 [M + H]$^+$; calcd. for $C_{24}H_{18}Cl_2NO_3S^+$: 470.0384.

Di-*tert*-butyl 4,4′-[6-(tosyloxy)pyridine-2,4-diyl] dibenzoate (10j): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.247 mmol) and [4-(*tert*-butoxycarbonyl)phenyl]boronic acid (0.988 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) provided pure **10j** as a white solid; yield: 147.2 mg (0.245 mmol, 99%): mp 70–72 °C; R_f 0.53 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3447, 2978, 1714, 1604, 1369, 1297, 1170, 930, 774, 665, 568 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.12 (d, J = 8.4 Hz, 2H), 7.99 (dd, J = 8.4 Hz and 13.7 Hz, 4H), 7.88 (d, J = 1.0 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 1.1 Hz, 1H), 2.48 (s, 3H), 1.63 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 164.9, 157.7, 155.5, 152.9, 145.2, 140.8, 140.7, 134.3, 133.0, 132.8, 131.5, 130.2, 129.6, 129.57, 128.7, 126.9, 126.7, 117.4, 112.3, 81.5, 81.3, 28.1, 21.6; HR-MS-FAB: m/z = 602.2215 [M + H]$^+$; calcd. for $C_{34}H_{36}NO_7S^+$: 602.2212.

4,6-Di[(*E*)-styryl]pyridin-2-yl 4-methylbenzenesulfonate (10k): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.246 mmol) and (*E*)-styrylboronic acid (0.984 mmol), and the reaction was completed in 1.5 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10k** as a yellow solid; yield: 110.7 mg (0.244 mmol, 99%); mp 148–150 °C; R_f 0.49 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3441, 2083, 1633, 1599, 1541, 1371, 1175, 973, 784, 692, 549 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 6.9 Hz, 2H), 7.44 (d, J = 6.9 Hz, 2H), 7.46–7.28 (m, 9H), 7.24 (d, J = 4.1 Hz, 1H), 7.20 (s, 1H), 7.00 (s, 1H), 6.96 (d, J = 4.1 Hz, 1H), 6.91 (d, J = 3.6 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 154.7, 149.7, 144.9, 136.2, 135.7, 134.5, 134.3, 134.2, 129.5, 129.0, 128.8, 128.74, 128.7, 128.6, 127.14, 127.1, 126.0, 124.8, 118.7, 110.4, 21.7; HR-MS-EI: m/z = 453.1400 [M$^+$], calcd. for $C_{28}H_{23}NO_3S^+$: 453.1399.

4,6-Bis(benzo[*b*]thiophen-2-yl)pyridin-2-yl 4-methylbenzenesulfonate (10l): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.246 mmol) and benzo[*b*]thiophen-2-ylboronic acid (0.984 mmol), and the reaction was completed in 3 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10l** as a pale yellow solid; yield: 117.0 mg (0.228 mmol, 93%); mp 192–096 °C; R_f 0.32 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3433, 2348, 1612, 1368, 1174, 1082, 962, 794, 666, 560 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.3 Hz, 2H), 7.86–7.77 (m, 7H), 7.42–7.36 (m, 6H), 7.25 (d, J = 0.4 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 152.0, 146.5, 145.2, 142.5, 140.8, 140.1, 140.0, 139.9, 139.3, 134.1, 129.7, 129.0, 126.0, 125.5, 125.1, 124.7, 124.5, 124.4, 123.3, 122.7, 122.5, 122.49, 115.1, 110.6, 21.8; HR-MS-EI: m/z = 513.0526 [M$^+$], calcd. for $C_{28}H_{19}NO_3S_3^+$: 513.0527.

4,6-Di(thiophen-3-yl)pyridin-2-yl 4-methylbenzenesulfonate (10m): General procedure **I** was used employing 4,6-di-

bromo-2-tosyloxypyridine (0.244 mmol) and thiophen-3-ylboronic acid (1.220 mmol), and the reaction was completed in 9 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10m** as a brown solid; yield: 92.0 mg (0.222 mmol, 91%); mp 98–112 °C; R_f 0.44 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3441, 2070, 1609, 1556, 1368, 1305, 1162, 1090, 965, 787, 665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 8.3 Hz, 2H), 7.68 (dd, J = 1.5 Hz and 2.8 Hz, 1H), 7.65 (dd, J = 1.2 Hz and 4.1 Hz, 2H), 7.45 (dd, J = 2.9 Hz and 5.0 Hz, 1H), 7.42 (m, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.32 (dd, J = 2.9 Hz and 5.0 Hz, 1H), 7.14 (d, J = 1.2 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 152.6, 147.7, 145.0, 140.5, 138.5, 134.3, 129.5, 128.7, 127.3, 126.2, 125.9, 125.6, 124.6, 124.0, 115.8, 110.3, 21.6; HR-MS-EI: m/z = 413.0214 [M^+], calcd. for $C_{20}H_{15}NO_3S_3^+$:413.0214.

4,6-Di(furan-3-yl)pyridin-2-yl 4-methylbenzenesulfonate (10n): General procedure **I** was used employing 4,6-dibromo-2-tosyloxypyridine (0.248 mmol) and furan-3-ylboronic acid (1.240 mmol), and the reaction was completed in 24 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **10n** as a brown solid; yield: 28.2 mg (0.074 mmol, 30%); mp 128–130 °C; R_f 0.41 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3441, 2070, 1620, 1370, 1175, 1019, 871, 772, 665, 564 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.3 Hz, 2H), 7.89 (s, 1H), 7.73 (s, 1H) 7.52 (t, J = 1.6 Hz, 1H), 7.43 (t, J = 1.7 Hz, 1H), 7.37 (d, J = 8.2 Hz, 3H), 7.01 (d, J = 1.0 Hz, 1H), 6.72 (d, J = 1.0 Hz, 1H), 6.66 (d, J = 1.1 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 151.1, 145.1, 145.0, 144.5, 143.8, 142.0, 140.9, 134.4, 129.5, 128.7, 125.8, 123.6, 115.0, 109.7, 108.3, 108.2, 21.7; HR-MS-EI: m/z = 381.0668 [M^+], calcd. for $C_{20}H_{15}NO_5S^+$: 381.0671.

3,5-Diphenylpyridine (11)

A 10-mL round-bottom flask was charged with pyridine **7a** (0.250 mmol), Et_3N (1.250 mmol), 1,3-bis(diphenylphosphino)propane (5 mol%), $Pd(OAc)_2$ (5 mol%) and formic acid (0.750 mmol). DMF(1.7 mL) was then added to the flask. The reaction mixture was stirred at 60 °C for 1 h in under argon purging. Once cooled, the reaction mixture was quenched with H_2O and extracted with ethyl acetate (3 × 5 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 10:1) to obtain the pyridine **11** as a white solid; yield: 53.0 mg (0.229 mmol, 92%). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.84 (d, J = 1.7 Hz, 2H), 8.05 (s, 1H), 7.65 (d, J = 7.1 Hz, 4H), 7.54–7.7.41 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.9, 137.7, 136.5, 132.8, 129.0, 128.1, 127.2; the data are consistent with those reported in the literature.[4d]

2-(4-Methoxyphenyl)-3,5-diphenylpyridine (12)

A round-bottom flask was charged with pyridine **7a** (0.250 mmol), (4-methoxyphenyl)boronic acid (0.500 mmol), K_2CO_3 (0.550 mmol), SPhos (5 mol%) and $Pd(OAc)_2$ (4 mol%). Toluene (1.7 mL) was then added to the flask. The reaction mixture was stirred at 50 °C for 2.5 h under argon purging. Once cooled, the reaction mixture was quenched with H_2O and extracted with ethyl acetate (3 × 5 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (Hexane/Ethyl acetate = 20:1) to obtain the pyridine **12** as a white solid; yield: 80.0 mg (0.237 mmol, 95%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.65 (d, J = 7.32, 2H), 7.47 (t, J = 7.3 Hz, 2H), 7.41–7.26 (m, 8H), 6.77 (d, J = 8.44 Hz, 2H), 3.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 155.4, 146.5, 140.1, 137.4, 136.9, 135.5, 134.4, 132.1, 131.1, 129.4, 129.0, 128.4, 128.0, 127.2, 127.0, 113.3, 55.1; the data are consistent with those reported in the literature.[4c]

3,5-Diphenylpyridin-2(1*H*)-one (13)

To a solution of pyridine **7a** (0.249 mmol) in THF (5.0 mL) and methanol (5.0 mL) was added 1N NaOH solution (2.5 mL). The reaction mixture stirred at 50 °C for 1 h. The mixture was diluted with ethyl acetate (10 mL), washed with H_2O and extracted with ethyl acetate (3 × 10 mL). The organic phase was collected, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to obtain the pyridine **13** as a white solid; yield: 61.0 mg (0.247 mmol, 99%). ^1H NMR (300 MHz, DMSO-d_6): δ = 12.10 (br s, 1H), 7.96 (d, J = 2.6 Hz, 1H), 7.82 (d, J = 7.1 Hz, 2H), 7.73 (d, J = 2.6 Hz, 1H), 7.65 (d, J = 7.3 Hz, 2H), 7.44–7.29 (m, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.7, 137.6, 136.7, 136.3, 131.8, 130.0, 128.9, 128.4, 127.9, 127.4, 126.8, 125.5, 118.3; the data are consistent with those reported in the literature.[4d]

2-Phenylamino-4,6-diphenylpyridine (14)

A round-bottom flask was charged with pyridine **10a** (0.249 mmol), aniline (375 mmol), K_2CO_3 (0.500 mmol), DPPF (0.150 mmol) and $Pd(OAc)_2$ (5 mol%). Toluene (1.9 mL) was then added to the flask. The reaction mixture was stirred at 110 °C for 6 h in under argon purging. Once cooled, the reaction mixture was quenched with H_2O and extracted with ethyl acetate (3 × 5 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 10:1) to obtain the pyridine **14** as a pale green solid; yield: 80.0 mg (0.248 mmol, 99%). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, J = 1.2 Hz, 2H), 8.11 (m, 2H), 7.68–7.65 (m, 2H), 7.55–7.40 (m, 9H), 7.39–7.26 (m, 2H), 7.09 (t, J = 7.2 Hz, 1H), 7.04 (d, J = 1.2 Hz, 1H), 6.82 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.8, 156.2, 151.1, 140.6, 139.6, 139.2, 129.3, 128.9, 128.81, 128.76, 128.6, 127.0, 126.9, 122.6, 120.2, 110.8, 104.8; the data are consistent with those reported in the literature.[18]

2,4-Diphenyl-6-(phenylethynyl)pyridine (15)

A round-bottom flask was charged with pyridine **10a** (0.252 mmol), phenylacetylene (0.428 mmol), K_3PO_4 (0.353 mmol), XPhos (5 mol%) and $Pd(OAc)_2$ (3 mol%). *t*-BuOH (1.9 mL) was then added to the flask. The reaction mixture was stirred at 85 °C for 1 h under argon purging. Once cooled, the reaction mixture was filtered with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatog-

raphy over silica gel (hexane/ethyl acetate = 60:1) to obtain the pyridine **15** as a yellow oil; yield: 70.6 mg (0.213 mmol, 85%); R_f 0.32 (hexane/ethyl acetate = 20:1). IR (neat): ν = 3450, 3056, 2352, 2218, 1592, 1245, 1169, 1024, 756, 538 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 2H), 7.88 (d, J = 1.5 Hz, 1H), 7.74–7.65 (m, 5H), 7.55–7.45 (m, 6H), 7.41–7.38 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.6, 149.5, 143.8, 139.0, 137.9, 132.1, 129.3, 129.2, 129.1, 128.9, 128.7, 128.4, 127.3, 127.1, 123.9, 122.4, 118.1, 89.2, 89.0; HR-MS-EI: m/z = 331.1360 [M^+], calcd. for $C_{25}H_{17}N^+$: 331.1361.

2-Isopropyl-4,6-diphenylpyridine (16)

Pyridine **10a** (0.249 mmol) and $FeCl_3$ (0.050 mmol) were dissolved in THF (1.0 mL) and NMP (0.2 mL). Isopropylmagnesium bromide (0.87 mL, 2.0 M, 1.743 mmol) was added dropwise and the reaction mixture was stirred for 1 h at −30 °C. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 20:1) to obtain the pyridine **16** as a yellow oil; yield: 36.1 mg (0.132 mmol, 53%); R_f 0.68 (hexane/ethyl acetate = 5:1); IR (neat): ν = 3451, 3057, 2961, 2352, 1600, 1453, 1160, 1065, 761, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.15–8.11 (m, 2H), 7.77 (d, J = 1.47 Hz, 1H), 7.73–7.70 (m, 2H), 7.55–7.43 (m, 6H), 7.35 (d, J = 1.45 Hz, 1H), 3.241 (m, 1H), 1.45 (d, J = 6.87 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 157.0, 149.5, 140.0, 139.3, 129.0, 128.7, 128.6, 127.1, 127.07, 117.2, 116.2, 36.6, 22.7; HR-MS-EI: m/z = 273.1519 [M^+], calcd. for $C_{20}H_{19}N^+$: 273.1517.

3,5-Bis(4-methoxyphenyl)-2-{3-[(triethylsilyl)oxy]-prop-1-yn-1-yl}pyridine (18)

A round-bottom flask was charged with pyridine **7d** (0.500 mmol), triethyl(prop-2-yn-1-yloxy)silane (0.650 mmol), K_3PO_4 (0.700 mmol), XPhos (7 mol%) and $Pd(OAc)_2$ (3 mol%). *t*-BuOH (4 mL) was then added to the flask. The reaction mixture was stirred at 80 °C for 1 h under argon purging. Once cooled, the reaction mixture was filtered with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (hexane/ethyl acetate = 10:1) to obtain the pyridine **18** as a pale brown solid; yield: 207.8 mg (0.452 mmol, 90%); mp 55–60 °C; R_f 0.36 (hexane/ethyl acetate = 3:1). IR (neat): ν = 3445, 2956, 2059, 1629, 1515, 1250, 1086, 1023, 736, 538, 465 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.73 (d, J = 2.2 Hz, 1H), 7.79 (d, J = 2.2 Hz, 1H), 7.59–7.54 (m, 4H), 7.02–6.97 (m, 4H), 4.48 (s, 2H), 3.86 (d, J = 2.6 Hz, 6H), 0.92 (t, J = 7.6 Hz, 9H), 0.58 (q, J = 7.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0, 159.6, 146.2, 139.2, 138.7, 135.3, 134.4, 130.4, 130.3, 129.4, 128.2, 114.6, 113.7, 90.3, 83.8, 55.3, 55.2, 51.8, 6.6, 4.4; HR-MS-EI: m/z = 459.2230 [M^+], calcd. for $C_{28}H_{33}NO_3Si^+$: 459.2228.

3-[3,5-Bis(4-methoxyphenyl)-pyridin-2-yl]propan-1-ol (19)

A solution of pyridine **18** (0.435 mmol) in methanol (4.0 mL) and palladium on charcoal (10 mol%) was hydrogenated under ambient pressure (balloon) at room temperature for 3.5 h. Then a 1% HCl in methanol solution (1.2 mL) was added dropwise to the mixture. The reaction was completed in 15 min. The reaction mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (DCM/MeOH = 20:1) to obtain the alcohol **19** as a light brown oil; yield: 145.0 mg (0.415 mmol, 95%). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.68 (d, J = 2.3 Hz, 1H), 7.69 (d, J = 2.3 Hz, 1H), 7.53 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.00 (dd, J = 1.7 Hz and J = 8.8 Hz, 4H), 3.86 (d, J = 4.8 Hz, 6H), 3.71 (t, J = 5.7 Hz, 2H), 2.99 (t, J = 6.5 Hz, 2H), 1.98–1.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7, 159.2, 156.9, 145.1, 136.7, 135.9, 133.8, 131.8, 130.2, 129.8, 128.0, 114.5, 113.9, 62.7, 55.4, 55.3, 32.5, 31.2; the data are consistent with those reported in the literature.[14a]

2,3-Dihydro-6,8-bis(4-methoxyphenyl)-1*H*-indolizinium Chloride (Ficuseptine, 20)

Mesyl chloride (0.572 mmol) was added to alcohol **19** (0.286 mmol) and trimethylamine (0.858 mmol) in anhydrous CH_2Cl_2 (13 mL) with stirring at 0 °C and the mixture was allowed to warm up to room temperature over 2 h. The mixture was poured into saturated NaCl solution (30 mL). The aqueous layer was washed with diethyl ether (3 × 10 mL), followed by extraction with $CHCl_3$ (3 × 20 mL). The organic phase was collected and dried over anhydrous $CaCl_2$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (DCM/MeOH = 30:1) to obtain the pyridine **20** as light brown solid; yield: 83.0 mg (0.226 mmol, 79%). ^1H NMR (300 MHz, $CDCl_3$): δ = 10.14 (s, 1H), 8.24 (d, J = 1.27 Hz, 1H), 7.85 (d, J = 8.80 Hz, 2H), 7.44 (d, J = 8.77 Hz, 2H), 7.05 (dd, J = 8.8 Hz and 11.4 Hz, 4H), 5.05 (t, J = 7.6 Hz, 2H), 3.87 (d, J = 16.83 Hz, 6H), 3.55 (t, J = 7.6 Hz, 2H), 2.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5, 161.1, 152.6, 140.4, 139.4, 138.8, 138.2, 129.9, 126.7, 125.3, 115.3, 115.0, 60.4, 55.7, 55.6, 32.4, 22.4; the data are consistent with those reported in the literature.[14a]

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14 Synthesis of Trisubstituted Pyridines *via* Chemoselective Suzuki–Miyaura Coupling of 3,5- and 4,6-Dibromo-2-tosyloxypyridines

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