JOC The Journal of Organic Chemistry

Article

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Synthesis of Heteroaryl Compounds through Cross-Coupling Reaction of Aryl Bromides or Benzyl Halides with Thienyl and Pyridyl Aluminum Reagents

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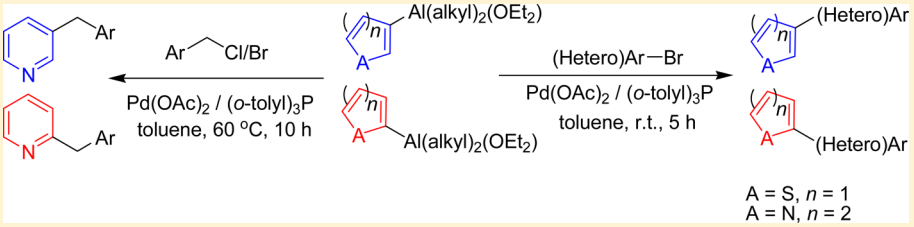
Supporting Information



ABSTRACT: An efficient method for synthesis of useful biaryl building blocks containing 2-thienyl, 3-thienyl, 2-pyridyl, and 3-pyridyl moieties was provided through cross-coupling reactions of aryl bromides or benzyl halides with heteroaryl aluminum reagents in the presence of $Pd(OAc)_2$ and $(o\text{-tolyl})_3P$. The coupling reaction also worked efficiently with heteroaryl bromides affording series of heterobiaryl compounds. The reaction of phenylbromide with in situ prepared 3-pyridyl aluminum was demonstrated to afford the product **8a** in high yield. Additionally, the catalytic system was also suited well for the coupling reaction of benzyl halides with pyridyl aluminum reagents to afford series of pyridyl-arylmethane.

INTRODUCTION

The aryl−aryl couping reactions have been known for several decades, and advances in recent years have greatly extended their scope and practicality.[1,2] Despite the tremendous progress in this area, the remaining challenge is to develop a compatible method for a variety of heterobiaryl compounds, mainly due to the unique reactivity of each heteroaryl compound, which usually makes ineffective the simple extension of a coupling method developed for a particular type of heterocycle when applied to others. Moreover, many catalytic systems are successful for simple aryl halides and aryl boronic acids, but reactions involving their heteroaryl analogues often lead to low reactivity and selectivity in coupling reactions due to binding of heteroatoms in the substrates and products to the catalysts. Efforts to circumvent these problem have focused on the developments of highly efficient catalytic systems or utilizing alternate heteroaryl organometallics. Fu and co-workers have championed an unusual versatile catalyst for Suzuki reactions of nitrogen-containing cross-coupling partners including nitrogen-containing boronic acids, boronate esters, and trifluoroborates.[3] Buchwald have successfully developed highly active and efficient palladium catalyst systems based on monophosphine ligands S-Phos and X-Phos for the Suzuki−Miyaura cross-coupling reaction of nitrogen-containing boronic acids and aryl halides.[4] Since these pioneering works, some types of heteroaryl organometallic reagents, such as heteroaryl stannanes,[5] heteroaryl boronic acids or esters,[6] heteroaryl lithium or magnesium borates,[7] heteroaryl zinc reagents,[8] heteroaryl magnesium reagents,[9] heteroaryl trimethylsilanes,[10] and heteroaryl indium reagents,[11] were synthesized and applied in the cross-coupling reaction. Notably, Knochel and co-workers have also successfully realized the coupling reaction of functionalized heteroaryl copper reagents using iron catalysts.[12]

In sharp contrast to the aryl−aryl coupling reactions, the coupling of benzylic halides with organometallic reagents has been less reported. Moreover, the motifs of diarylmethane and heteroaryl-arylmethane are key intermediates leading to bioactive compounds.[13] The common synthetic method for obtaining diarylmethanes includes the Friedel−Crafts alkylation of aromatic compounds with benzylic halides,[14] which are usually unsuccessful for heteroaryl compounds such as pyridines, because of poor eletrophilicity. The transition metal-catalyzed cross-coupling reactions of benzyl derivatives with aryl- or heteroaryl-metallic reagents provide powerful tools for the formation of diarylmethane and heteroaryl-aryl-methane.[15]

Organoaluminiums are more reactive than organoboron, organosilicon, and organozinc reagents; therefore, organoalanes are widely applied in the addition to carbonyl compounds[16] and cross-coupling reactions.[17] Recently, arylalanes have been demonstrated to be highly efficient coupling reagents with aryl bromide and chlorides without use of a base.[18] More recently, Knochel and his co-workers reported Pd-catalyzed cross-coupling of functionalized organoaluminum halides or amides with aryl and heteroaryl iodides, bromides, and

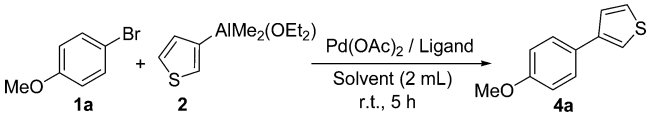
Received: October 29, 2013
Published: December 5, 2013

nonaflates without the need for a transmetalation.[19] Despite the success in this area, the development of the heteroaryl aluminum reagents as nucleophiles for the challenging cross-coupling reactions is scare.[19] In this paper, we will report an efficient method for the synthesis of heteroaryl compounds through Pd-catalyzed cross-coupling reactions of (hetero)aryl bromides or benzyl halides with heteroaryl aluminum reagents. Noteworthy is that the simple and commercially available $Pd(OAc)_2$/(*o*-tolyl)$_3$P was demonstrated to be an efficient catalytic system, and the catalytic system could suit well for different heteroaryl aluminiums affording heterobiaryl compounds containing 2-thienyl, 3-thienyl, 2-pyridyl, and 3-pyridyl moieties, which would provide more alternatives to the existing Pd-catalyzed cross-coupling reactions for the synthesis of heteroaryl compounds.

RESULTS AND DISCUSSION

Palladium-Catalyzed Cross-Coupling Reaction of Aryl Bromides with Thienyl Aluminum Reagents. The reactions of 4-bromoanisole with 3-thienyl aluminum reagent as template were first optimized, and the results are summarized in Table 1. The investigations for the choice of

Table 1. Optimizations of Cross-Coupling Reaction[a]



entry	$Pd(OAc)_2$ (mol %)	ligand (mol %)[b]	(3-thieny)Al (equiv)	solvent	yield (%)
1	2	MePhos (4)	1.7	toluene	80
2	2	MePhos (4)	1.7	THF	54
3	2	MePhos (4)	1.7	*n*-hexane	52
4	2	MePhos (4)	1.7	Et_2O	58
5	2	MePhos (4)	1.7	CH_2Cl_2	44
6	2	MePhos (4)	1.5	toluene	84
7	2	MePhos (4)	1.3	toluene	89
8	2	MePhos (4)	1.1	toluene	42
9	2	Cy_3P (4)	1.3	toluene	75
10	2	Ph_3P (4)	1.3	toluene	48
11	2	(*o*-tolyl)$_3$P (4)	1.3	toluene	96
12	2	(*p*-tolyl)$_3$P (4)	1.3	toluene	59
13	2	dppm (4)	1.3	toluene	trace
14	2	(*o*-tolyl)$_3$P (0)	1.3	toluene	NR
15	2	(*o*-tolyl)$_3$P (2)	1.3	toluene	63
16	2	(*o*-tolyl)$_3$P (6)	1.3	toluene	53
17	1	(*o*-tolyl)$_3$P (2)	1.3	toluene	60

[a]Equivalent of (3-thienyl)Al is relative to **1a**. [b]MePhos: 2-dicyclohexylphosphino-2′-methylbiphenyl; dppm: bis-(diphenylphosphinyl)methane.

the solvent showed that toluene is the best one (entry 1). Tuning amounts of 3-thienyl aluminum reagent from 1.7 to 1.1 equiv (entries 1, 6–8), it is found that the yield of **4a** were the highest when 4-bromoanisole was treated with 1.3 equiv 3-thienyl aluminum reagent (entry 7). For palladium/phosphine catalytic systems, the choice of phosphine ligands was crucial for coupling reactions (entries 9–13). In this case, the commercially available and relatively cheap phosphine ligand, (*o*-tolyl)$_3$P, was the most active one among the selected ligands affording the coupling product **4a** in yield of 96% (entry 11). To examine the efficiency of the catalytic system, catalyst loading was decreased to 1 mol % providing the product **4a** in a lower yield of 60% (entry 17).

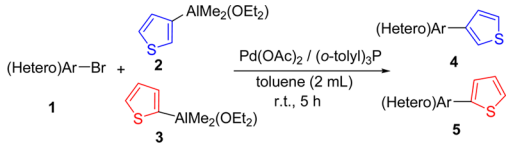
With the optimized conditions in hand, namely 2 mol % of $Pd(OAc)_2$ and 4 mol % of (*o*-tolyl)$_3$P in toluene at room temperature, the coupling reactions of substituted aromatic bromides with 3-thienyl aluminum reagent were then studied (Table 2). The catalytic system was compatible with a wide range of aryl bromides; even those with highly sterically hindered substituents on the aryl groups were well tolerated. For example, the coupling reaction between 2,4,6-trimethylphenyl bromide with corresponding thienyl aluminum reagents afforded products **4e** and **5e** in 80 and 85% yields, respectively (entries 9 and 10). However, for aryl bromides bearing cyano and nitro groups, the corresponding coupling products **4g–4j** were obtained in low yields under the same conditions. The reaction yields of bromobenzonitrile with 3-thienyl aluminum reagents could be remarkably improved (to >90%) by employing 4 mol % of $Pd(OAc)_2$ and 8 mol % of (*o*-tolyl)$_3$P. However, improvements of catalyst have little influence on the corresponding yields of 4-nitrobromobenzene with 3-thienyl aluminum reagents, probably because of a strong affinity of the nitro group toward the metal center.[18a,20] Furthermore, heteroaryl bromides such as 2-bromopyrimidine, 5-bromopyrimidine, 2-bromothiazole, and 3-bromoquinoline were successfully coupled with the corresponding aluminum reagents affording the biheteroaryl compounds **4k–4n** in high yields.

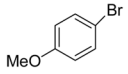
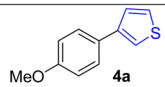
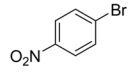
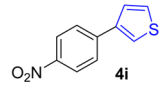
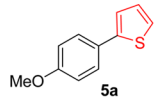
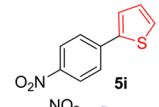
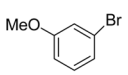
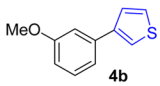
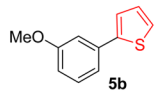
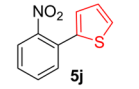
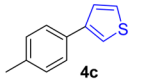
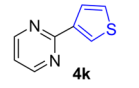
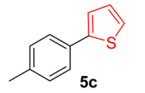
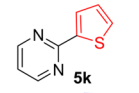
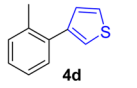
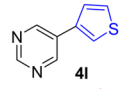
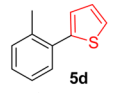
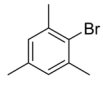
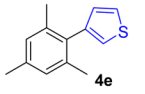
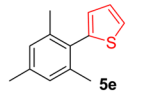
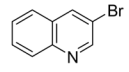
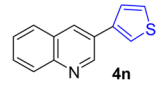
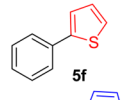
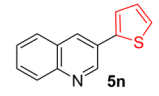
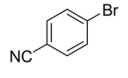
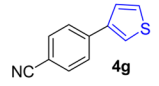
The satisfactory results obtained for the construction of 3-thienylaryl compounds encouraged an effort to expand the scope of this catalytic system to 2-thienyl aluminum reagent, which is more challenging as a coupling partner because of the easier binding of the heteroatom in the substrates and the products to the metal catalyst (Table 2). It was also found that the catalytic system suited well for coupling reactions of aromatic bromides with 2-thienyl aluminum reagent. For electron-rich aryl bromides, coupling products **5a–5e** were obtained in good to high yields regardless of the steric effect of the substituents on the aryl groups. For aryl bromides bearing cyano group, an increased catalyst loading amount was also required to obtain high yields **5g** and **5h**. Heteroaryl bromides such as 2-bromopyrimidine, 5-bromopyrimidine, 2-bromothiazole, and 3-bromoquinoline were also successfully coupled with corresponding aluminum reagents affording biheteroaryl compounds **5k–5n** in good yields (85–89%). Furthermore, the catalytic system also suited for the coupling reaction of aryl bromide bearing ester with 2-thieny aluminum affording the corresponding compound **5p** in moderate yield (Table 2, entry 30). However, the coupling reaction of 2-thieny aluminum with aryl bromide bearing carbonyl group such as ketone and the catalytic system was complexed probably because of strong nucleophilicity of aluminums.

Palladium-Catalyzed Cross-Coupling Reaction of Aryl Bromides with Pyridyl Aluminum Reagents. The biaryl compounds containing pyridyl group are a ubiquitous common heterocyclic motif in biologically active molecules.[21] Thus, preparative methods of pyridine-containing heterobiaryl derivatives remain an attractive research topic in organic syntheses. The pyridine-containing organoaluminium reagents were prepared from transmetalation of $AlMe_2Cl$ with pyridyl lithium (generated in situ from lithium-halogen exchange of 3-

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230–239

Table 2. Cross-Coupling of 2- or 3-Thienyl Aluminium Reagents with Aryl Bromides[a]



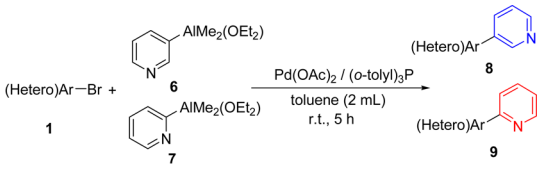
Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1		 **4a**	96	17		 **4i**	37 (40)[b]
2		 **5a**	92	18		 **5i**	50
3		 **4b**	85	19		 **4j**	42
4		 **5b**	74	20		 **5j**	39
5		 **4c**	95	21		 **4k**	90
6		 **5c**	94	22		 **5k**	85
7		 **4d**	75	23		 **4l**	83
8		 **5d**	80	24		 **5l**	85
9		 **4e**	80	25		 **4m**	89
10		 **5e**	85	26		 **5m**	87
11		 **4f**	95	27		 **4n**	91
12		 **5f**	94	28		 **5n**	89
13		 **4g**	50 (92)[b]	29		**5o**	63
14		**5g**	47 (91)[b]				
15		**4h**	95[b]	30		**5p**	58
16		**5h**	94[b]	31		-	(-)[c]

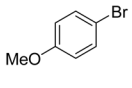
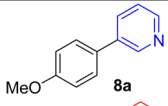
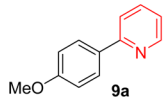
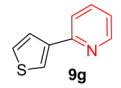
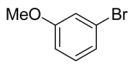
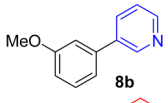
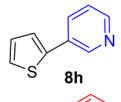
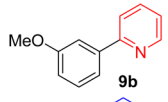
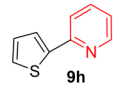
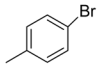
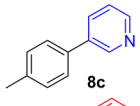
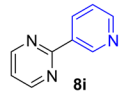
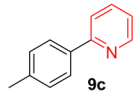
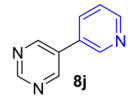
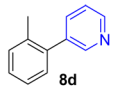
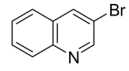
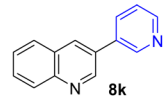
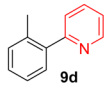
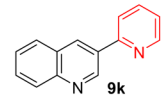
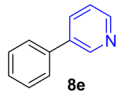
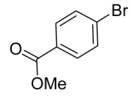
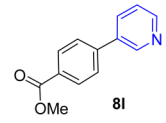
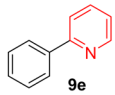
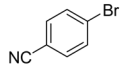
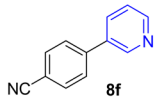
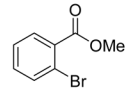
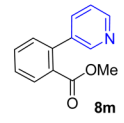
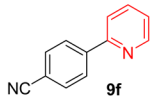
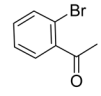
[a]Aryl bromide/Al reagent = 1/1.3 mmol, 2 mol % of $Pd(OAc)_2$ and 4 mol % of $(o\text{-tolyl})_3P$. [b]4 mol % of $Pd(OAc)_2$ and 8 mol % of $(o\text{-tolyl})_3P$. [c]The catalytic system was complexed.

bromopyridine or 2-bromopyridine with of *n*-BuLi at −78 °C).[22] Compared to pyridyl lithium, the pyridyl aluminum reagents were stable for a few months at room temperature. Next, coupling reactions of substituted aromatic bromides with

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230−239

Table 3. Cross-Coupling of 2- or 3-Pyridyl Aluminium Reagents with Aryl Bromides[a]



Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1		 **8a**	96	13		 **8g**	91
2		 **9a**	95	14		 **9g**	83
3		 **8b**	95	15		 **8h**	93
4		 **9b**	88	16		 **9h**	80
5		 **8c**	95	17		 **8i**	83
6		 **9c**	91	18		 **8j**	86
7		 **8d**	92	19		 **8k**	83
8		 **9d**	83	20		 **9k**	81
9		 **8e**	91 (90)[b]	21		 **8l**	56
10		 **9e**	92				
11		 **8f**	85[c]	22		 **8m**	50
12		 **9f**	89[c]	23		-	(-)[d]

[a]Aryl bromide/Al reagent = 1/1.3 mmol, 2 mol % of $Pd(OAc)_2$ and 4 mol % of $(o\text{-tolyl})_3P$. [b]Yield from reaction of phenylbromide with in situ prepared 3-pyridine aluminum reagent. [c]4 mol % of $Pd(OAc)_2$ and 8 mol % of $(o\text{-tolyl})_3P$. [d]The catalytic system was complexed.

pyridine-containing organoaluminium reagents such as 2- or 3-pyridyl aluminum reagents were examined, and results were listed in Table 3. Under the same standard conditions as thienyl-containing organoaluminium, 2- or 3-pyridyl aluminum reagents reacted with a variety of aryl bromides affording biaryl compounds containing pyridyl groups in good yields. The catalytic system was a little affected by electronic effect of substituents. For example, substituted aryl bromides containing electron-donating substituents on the aromatic ring could effectively couple with the corresponding 2- or 3-pyridyl aluminum reagents to produce the coupling products **8a**−**8d** and **9a**−**9d** in good yields. However, coupling of substituted aryl bromides containing electron-withdrawing substituents on the aromatic ring with 2- or 3-pyridyl aluminum reagents required a 4 mol % of catalyst and 8 mol % of $(o\text{-tolyl})_3P$ loading affording the coupling product **8f** and **9f** in good yields. The catalytic system worked well for 3-pyridyl aluminum with heteroaryl bromides such as 3-bromothiophene, 2-bromothiophene, 2-bromopyrimidine, 5-bromopyrimidine, and 3-bromoquinoline affording biheteroaryl compounds **8g**−**8k** in good yields (≥83%). For the reaction of 2-pyridyl aluminum reagent with heteroaryl bromides such as 2-bromopyrimidine and 5-

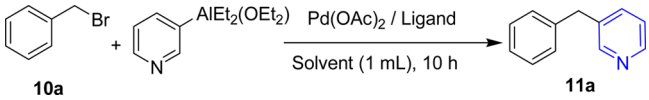
dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230−239

bromopyrimidine, we did not isolate corresponding biheteroaryl compounds probably because of strong binding ability of products. The catalytic system also suited for the coupling reaction of aryl bromides bearing ester and 3-pyridyl aluminum affording the corresponding compounds **8l** and **8m** in moderate yields (Table 2, entries 21 and 22).

To demonstrate the practicality of the coupling reactions, phenylbromide was reacted with in situ prepared 3-pyridyl aluminum reagent in 5 mmol scale. The in situ reaction afforded the product in a desired 90% yield (Table 3, entry 9).

Palladium-Catalyzed Cross-Coupling Reaction of Benzyl Halides with Pyridyl Aluminum Reagents. In order to further explore the heteroaryl aluminum compounds as efficient coupling reagents, we studied the cross-coupling reaction of benzyl halides with pyridyl aluminum reagents. It was also found that (heteroaryl)$AlEt_2(OEt_2)$ was superior to (heteroaryl)$AlMe(OEt_2)$ in the beginning test of benzyl bromide with 3-pyridyl aluminum reagents, indicating that the alkyl group of pyridyl aluminum reagents has effects for the coupling reaction. Then, the coupling reaction of benzyl bromide and (3-pyridyl)$AlEt_2(OEt_2)$ was first screened for palladium catalysts with a variety of phosphine ligands in different temperatures, and the results were summarized in Table 4. The desired yield of 91% was obtained under optimal conditions of $Pd(OAc)_2$ and $(o\text{-tolyl})_3P$ in a ratio of 1 to 2 in toluene at 60 °C (entry 3, Table 4).

Table 4. Optimizations of Cross-Coupling Reaction of 3-Pyridyl Aluminium with Benzyl Bromides



10a 11a

entry	$Pd(OAc)_2$ (mol %)	ligand (mol %)	(3-thieny) Al (equiv)	T (°C)	solvent	yield (%)
1	1	$(o\text{-tolyl})_3P$ (2)	1.5	rt	toluene	66
2	1	$(o\text{-tolyl})_3P$ (2)	1.5	40	toluene	75
3	1	$(o\text{-tolyl})_3P$ (2)	1.5	60	toluene	91
4	1	$(o\text{-tolyl})_3P$ (2)	1.5	80	toluene	91
5	1	0	1.5	60	toluene	NR
6	1	PPh_3 (2)	1.5	60	toluene	51
7	1	PCy_3 (2)	1.5	60	toluene	63
8	1	$(p\text{-tolyl})_3P$ (2)	1.5	60	toluene	58
9	1	$(o\text{-MeOPh})_3P$ (2)	1.5	60	toluene	67
10	1	MePhos (2)[a]	1.5	60	toluene	45
11	1	$(o\text{-tolyl})_3P$ (2)	1.3	60	toluene	72
12	1	$(o\text{-tolyl})_3P$ (2)	1.7	60	toluene	90

[a]MePhos: 2-dicyclohexylphosphino-2′-methylbiphenyl.

Under the optimized conditions, we examined the cross-coupling reaction of benzyl chloride with 3-pyridyl or 2-pyridyl aluminums, and we were delighted to find that the catalytic system also exhibited similar reactivity toward benzylic chloride compared to benzylic bromide to afford **11a** and **12a** in the excellent yields (Table 5, entries 1−4). So, studies on the scope of the catalytic system were performed on substituted benzyl chlorides, and results were listed in Table 5. The catalytic system was compatible with a wide range of benzyl chlorides, regardless of the electronic nature or the steric effect of the substituents on the aryl groups. In general, the cross-coupling reaction reactivity of benzyl chloride with 3-pyridyl was slightly higher than that of benzyl chloride with 2-pyridyl aluminums. It was also found that the substituent position had a little influence on yields as revealed in the case of methyl benzylchloride (Table 5, entries 5−10), methoxy benzylchloride (Table 5, entries 11−14) and trifluoromethyl benzylchloride (Table 5, entries 15−19). For substituted benzyl chlorides containing electron-withdrawing substituents on the aromatic ring such as trifluoromethyl benzylchloride and nitrile benzylchloride, the coupling products were obtained in a moderate yield of 73 to 83% yields (Table 5, entries 15−19).

CONCLUSION

In summary, we have developed an efficient method for the challenging cross-coupling reactions of pyridyl or thienyl aluminum reagents with various aryl bromides using commercially available $Pd(OAc)_2$ and $(o\text{-tolyl})_3P$. The reactions proceeded effectively at room temperature without a base affording the coupling products in good to excellent yields. Furthermore, the coupling reaction also worked efficiently with heteroaryl bromides affording a series of heterobiaryl compounds. The in situ reaction of phenylbromide with 3-pyridyl aluminum reagent was demonstrated to give the product in high yield. Moreover, the catalytic system was also suited well for the coupling reaction of benzyl halides with pyridyl aluminum reagents to afford series of pyridyl-arylmethane.

EXPERIMENTAL SECTION

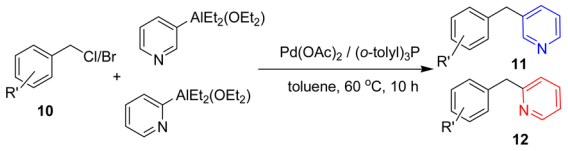
General Methods. All syntheses and manipulations of air- and moisture-sensitive materials were performed under a dry argon atmosphere using standard Schlenk techniques or in a glovebox. Solvents were refluxed and distilled over sodium/benzophenone (THF, Et_2O, *n*-hexane and toluene) or P_2O_5 (CH_2Cl_2) under argon prior to use. ^1H and ^{13}C NMR spectra in $CDCl_3$ were recorded on a 300 NMR (^1H, 300 MHz; ^{13}C, 75 MHz) spectrometer with chemical shifts given in ppm from the internal TMS. High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI and a TOF analyzer.

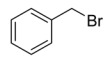
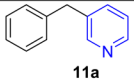
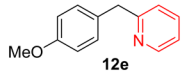
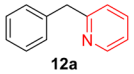
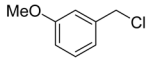
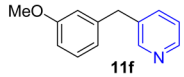
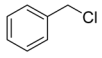
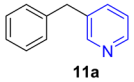
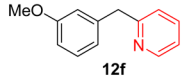
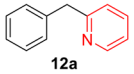
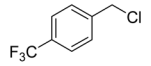
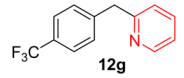
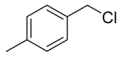
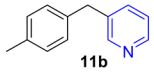
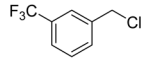
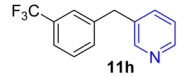
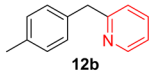
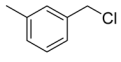
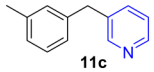
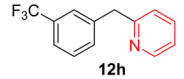
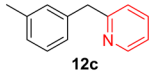
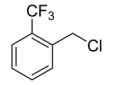
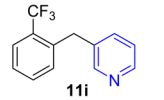
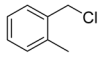
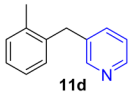
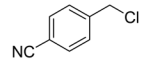
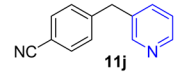
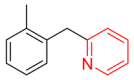
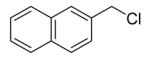
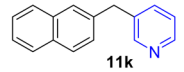
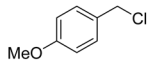
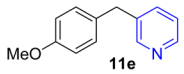
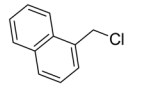
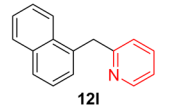
General Procedures for the Synthesis of (Heteroaryl)Al(alkyl)$_2$(OEt$_2$). To a Et_2O (50 mL) solution of a heteroaryl bromide (40 mmol) was added *n*-BuLi (40 mmol, 2.5 M in hexane, 16 mL), and the mixture was stirred for 1 min, followed by an addition of $AlMe_2Cl$ (40 mmol, 2 M in hexane, 20 mL) at −78 °C. The mixture was stirred at the same temperature for 3 h. The resulted solution was filtered, followed by an evaporation of the solvent under reduced pressures to afford a heteroarylaluminum reagent (heteroaryl)$AlMe_2(OEt_2)$ in a quantative yield, which was directly used in the coupling reactions. Heteroarylaluminum reagent (heteroaryl)$AlEt_2(OEt_2)$ was prepared in the similar procedures for the preparation of (heteroaryl)$AlMe_2(OEt_2)$ using $AlEt_2Cl$. ^1H NMR of heteroarylaluminum reagents showed that compounds in $CDCl_3$ solution contained a mixture of four species, which were assigned as (heteroaryl)$_x$Al(alkyl)$_{3-x}$(OEt_2) (alkyl = Me or Et; x = 0, 1, 2, or 3). Though heteroarylaluminum reagents exist as a mixture of four species in solution, they are represented as a general formula of (heteroaryl)$Al(alkyl)_2(OEt_2)$ for simplification. These results were similar with our previously reported $AlArEt_2$(THF) (Ar = Ph, 4-MePh, 4-MeOPh, 4-Me_3SiPh, 2-naphthyl, and 2-furanyl).[16i,j]

General Procedures for the Coupling Reaction of Aryl Bromides with Thienylaluminums Catalyzed by Pd(OAc)$_2$ and (*o*-Tolyl)$_3$P. Under a dry argon atmosphere, $Pd(OAc)_2$ (0.02 mmol)

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230−239

Table 5. Cross-Coupling of 2- or 3-Pyridyl Aluminium Reagents with Benzyl Halides[a]



Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1		 **11a**	91	12		 **12e**	91
2		 **12a**	87	13		 **11f**	91
3		 **11a**	90	14		 **12f**	89
4		 **12a**	85	15		 **12g**	77
5		 **11b**	91	16		 **11h**	83
6		 **12b**	86				
7		 **11c**	87	17		 **12h**	73
8		 **12c**	84	18		 **11i**	79
9		 **11d**	82	19		 **11j**	75
10		 **12d**	80	20		 **11k**	86
11		 **11e**	93	21		 **12l**	70

[a]Benzyl bromide/Al reagent = 1/1.5 mmol, 1 mol % of $Pd(OAc)_2$ and 2 mol % of $(o\text{-tolyl})_3P$.

and $(o\text{-tolyl})_3P$ (0.04 mmol) were mixed in 2 mL of toluene at room temperature, and the mixture was stirred for 10 min, followed by an addition of aryl bromide (1.00 mmol) and thienylaluminum reagent (1.3 mmol). After stirring for 5 h, the mixture was diluted with dichloromethane, passed through a filter, and concentrated. The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 100/1) to give the corresponding products **4** or **5**.

*3-(4-Methoxyphenyl)-thiophene (**4a**).*[8a] White solid (182 mg, 96% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J = 8.7 Hz, 2H), 7.36–7.34 (m, 3H), 6.94 (d, J = 8.7 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 142.0, 128.7, 127.5, 126.2, 126.0, 118.9, 114.2, 55.3.

*3-(3-Methoxyphenyl)-thiophene (**4b**).* Colorless oil (161 mg, 85% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.38–7.36 (m, 2H), 7.34–7.29 (m, 2H), 7.21–7.17 (m, 1H), 7.13 (s, 1H), 6.86–6.83 (m, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 142.1, 137.2, 129.8, 126.4, 126.1, 120.5, 119.0, 112.4, 112.2, 55.2; HRMS (ESI) calcd. for $C_{11}H_{10}SO$ [M + H$^+$] 191.0531, found 191.0533.

*3-(4-Tolyl)thiophene (**4c**).*[8a] White solid (166 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 6.9 Hz, 2H), 7.40–7.33 (m, 3H), 7.20 (d, J = 6.9 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 136.8, 133.0, 129.5, 126.3, 126.0, 119.7, 119.6, 21.1.

*3-(2-Tolyl)thiophene (**4d**).*[2a] Colorless oil (131 mg, 75% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.15 (m, 7H), 2.34 (s, 3H); HRMS (ESI) calcd. for $C_{11}H_{10}S$ [M + H$^+$] 175.0582, found 175.0580.

*3-Mesitylthiophene (**4e**).*[9a] Colorless oil (162 mg, 80% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.33 (m, 1H), 7.02–7.00 (m, 1H), 6.93–6.90 (m, 3H), 2.31 (s, 3H), 2.05 (s, 6H).

*3-Phenyl-thiophene (**4f**).*[8a] White solid (152 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62–7.59 (m, 2H), 7.46–7.39 (m, 4H), 7.32–7.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 135.8, 128.8, 127.1, 125.4, 125.3, 125.2, 120.2.

*4-(Thiophen-3-yl)benzonitrile (**4g**).*[6h] White solid (170 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71–7.67 (m, 4H), 7.58 (s, 1H), 7.45–7.41 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 140.0, 132.6, 127.1, 126.8, 125.9, 122.6, 118.9, 110.4; HRMS (ESI) calcd. for $C_{11}H_7NS$ [M + H$^+$] 186.0378, found 186.0376.

*2-(Thiophen-3-yl)benzonitrile (**4h**).* Yellow oil (175 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.56 (m, 4H), 7.44–7.34 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 138.5, 133.8, 132.8, 129.3, 127.4, 127.3, 126.3, 124.5, 118.9, 110.3; HRMS (ESI) calcd. for $C_{11}H_7NS$ [M + H$^+$] 186.0378, found 186.0379.

*3-(4-Nitrophenyl)thiophene (**4i**).*[8a] Yellow solid (70 mg, 37% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28–8.25 (m, 2H), 7.75–7.72

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230–239

(m, 2H), 7.65−7.63 (m, 1H), 7.48−7.43 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 141.9, 139.9, 127.3, 126.8, 126.0, 124.3, 123.2.

*3-(2-Nitrophenyl)thiophene (**4j**).* Yellow oil (86 mg, 42% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.8 Hz, 1H), 7.61−7.55 (m, 1H), 7.51−7.42 (m, 2H), 7.38−7.33 (m, 2H), 7.08 (d, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.0, 132.1, 131.7, 130.7, 128.1, 127.4, 126.2, 123.9, 123.5; HRMS (ESI) calcd. for $C_{10}H_7NO_2S$ [M + H^+] 206.0276, found 206.0277.

*2-(Thiophen-3-yl)pyrimidine (**4k**).*[6a] White solid (146 mg, 90% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, J = 5.1 Hz, 2H), 8.30−8.28 (m, 1H), 7.90−7.87 (m, 1H), 7.40−7.36 (m, 1H), 7.14−7.10 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 157.2, 141.5, 127.9, 127.3, 126.1, 118.6.

*5-(Thiophen-3-yl)pyrimidine (**4l**).*[6j] White solid (135 mg, 83% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.96 (s, 2H), 7.61 (s, 1H), 7.53−7.50 (m, 1H), 7.42−7.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 154.0, 134.9, 129.3, 127.7, 125.2, 122.4.

*2-(Thiophen-3-yl)thiazole (**4m**).*[6b] Light yellow oil (148 mg, 89% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.82 (s, 1H), 7.59−7.57 (m, 1H), 7.41−7.39 (m, 1H), 7.28−7.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 143.2, 135.6, 126.7, 126.1, 123.7, 118.0; HRMS (ESI) calcd. for $C_7H_5NS_2$ [M + H^+] 167.9942, found 167.9943.

*3-(Thiophen-3-yl)quinoline (**4n**).*[6i] Brown solid (192 mg, 91% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.21 (d, J = 2.4 Hz, 1H), 8.29 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.73−7.66 (m, 2H), 7.59−7.48 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.4, 147.1, 138.8, 132.0, 130.9, 129.2, 128.8, 128.7, 128.1, 127.8, 127.1, 126.1, 121.7.

*2-(4-Methoxyphenyl)thiophene (**5a**).*[23] White solid (175 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, J = 8.1 Hz, 2H), 7.25−7.20 (m, 2H), 7.06−7.03 (m, 1H), 6.92 (d, J = 8.1 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 143.9, 127.9, 127.3, 127.2, 123.8, 122.0, 114.2, 55.3.

*2-(3-Methoxyphenyl)thiophene (**5b**).*[24] Yellow oil (140 mg, 74% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.26 (m, 4H), 7.23−7.21 (m, 1H), 7.15 (s, 1H), 7.06 (s, 1H), 6.86−6.83 (m, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 144.2, 135.7, 129.9, 127.9, 124.9, 123.3, 118.6, 112.9, 111.7, 55.3; HRMS (ESI) calcd. for $C_{11}H_{10}SO$ [M + H^+] 191.0531, found 191.0530

*2-(4-Tolyl)thiophene (**5c**).*[24] White solid (163 mg, 94% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.8 Hz, 2 H), 7.26−7.23 (m, 2H), 7.20 (d, J = 7.8 Hz, 2H), 7.07−7.05 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 137.2, 131.6, 129.5, 127.9, 125.8, 124.2, 122.5, 21.1.

*2-(2-Tolyl)thiophene (**5d**).*[23] Colorless oil (139 mg, 80% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.39 (m, 1H), 7.35−7.32 (m, 1H), 7.26−7.22 (m, 3H), 7.10−7.06 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 136.0, 134.1, 130.7, 130.4, 127.7, 127.0, 126.3, 125.9, 125.1, 21.1; HRMS (ESI) calcd. for $C_{11}H_{10}S$ [M + H^+] 175.0582, found 175.0580.

*2-Mesitylthiophene (**5e**).*[24] Colorless oil (172 mg, 85% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 6.8, 1.6 Hz, 1H), 7.10−7.08 (m, 1H), 6.93−6.83 (m, 2 H), 6.79 (d, J = 3.3, 1.6 Hz, 1H), 2.32 (s, 3 H), 2.11 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.4, 138.3, 137.8, 131.0, 128.0, 127.0, 126.4, 125.2, 21.1, 20.7.

*2-Phenylthiophene (**5f**).*[9a] Colorless oil (152 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J = 7.2 Hz, 2H), 7.41−7.34 (m, 2H), 7.31−7.25 (m, 3H), 7.11−7.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.3, 134.3, 128.8, 128.0, 127.4, 125.9, 124.8, 123.0.

*4-Thiophen-2-yl-benzonitrile (**5g**).*[20] White solid (170 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.64 (m, 4H), 7.43−7.38 (m, 2H), 7.14−7.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 132.7, 128.5, 127.0, 126.0, 125.1, 118.8, 110.5; HRMS (ESI) calcd. for $C_{11}H_7NS$ [M + H^+] 186.0378, found 186.0379.

*2-Thiophen-2-yl-benzonitrile (**5h**).*[25] Yellow oil (174 mg, 94% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73−7.58 (m, 4H), 7.42−7.34 (m, 2H), 7.16−7.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 137.2, 134.0, 133.7, 132.8, 129.4, 128.0, 127.3, 127.1, 118.7, 109.6.

*2-(4-Nitrophenyl)thiophene (**5i**).*[26] White solid (102 mg, 50% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.49−7.42 (m, 3H), 7.17−7.15 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 141.6, 140.6, 128.7, 127.7, 126.0, 125.7, 124.4.

*2-(2-Nitrophenyl)thiophene (**5j**).* Yellow oil (80 mg, 39% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76−7.72 (m, 2H), 7.60−7.54 (m, 2H), 7.49−7.40 (m, 2H), 7.09−7.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 141.7, 137.1, 132.3, 131.9, 128.6, 128.4, 127.7, 127.1, 123.5; HRMS (ESI) calcd. for $C_{10}H_7NO_2S$ [M + H^+] 206.0276, found 206.0274.

*2-(Thiophen-2-yl)pyrimidine (**5k**).*[6a] White solid (138 mg, 90% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71 (d, J = 4.5 Hz, 2H), 8.03−8.01 (m, 1H), 7.49 (d, J = 4.5 Hz, 1H), 7.16−7.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 157.1, 143.0, 129.8, 128.9, 128.3, 118.4.

*5-(Thiophen-2-yl)pyrimidine (**5l**).*[6j] White solid (138 mg, 85% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.96 (s, 2H), 7.46−7.42 (m, 2H), 7.19−7.16 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 153.4, 143.4, 136.1, 128.5, 127.2, 125.2.

*2-(Thiophen-2-yl)thiazole (**5m**).*[27] White solid (145 mg, 87% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.53 (s, 1H), 7.40 (d, J = 4.5 Hz, 1H), 7.27−7.25 (m, 1H), 7.10−7.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 143.2, 137.2, 127.8, 127.6, 126.5, 118.0; HRMS (ESI) calcd. for $C_7H_5NS_2$ [M + H^+] 167.9942, found 167.9944.

*3-(Thiophen-2-yl)quinoline (**5n**).*[6j] White solid (188 mg, 89% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.29 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.59−7.51 (m, 2H), 7.41 (d, J = 4.5 Hz, 1H), 7.18−7.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 147.0, 140.4, 131.0, 129.1, 129.0, 128.2, 127.6, 127.3, 127.0, 125.9, 124.2.

*2-(4-Dimethylamino-phenyl)thiophene (**5o**).* Blue liquid (128 mg, 63% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.40 (m, 1H), 7.31−7.28 (m, 1H), 7.19−7.11 (m, 2H), 7.07−7.00 (m, 1H), 6.96−6.90 (m, 2H), 2.52 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 141.5, 129.5, 128.9, 128.0, 126.1, 126.0, 124.8, 122.9, 119.6, 44.0; HRMS (ESI) calcd. for $C_{12}H_{13}NS$ [M + H^+] 203.0769, found 203.0765.

*Methyl 2-(thiophen-2-yl)benzoate (**5p**).*[5a] Yellow oil (126 mg, 58% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 7.5 Hz, 1H), 7.37 (d, J = 3.6 Hz, 2H), 7.29−7.22 (m, 2H), 6.96−6.93 (m, 2H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 141.9, 134.0, 131.5, 131.0, 130.9, 129.3, 127.6, 127.1, 126.1, 125.8, 52.1.

General Procedures for the Coupling Reaction of Aryl Bromides with Pyridylaluminums Catalyzed by $Pd(OAc)_2$ and (*o*-Tolyl)$_3$P. Under a dry argon atmosphere, $Pd(OAc)_2$ (0.02 mmol) and (*o*-tolyl)$_3$P (0.04 mmol) were mixed in 2 mL of toluene at room temperature, and the mixture was stirred for 10 min, followed by an addition of aryl bromide (1.00 mmol) and heteroarylaluminum reagent (1.3 mmol). After stirring for 5 h, the mixture was diluted with dichloromethane, passed through a filter, and concentrated. The crude product was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to give the corresponding products **8** or **9**.

*3-(4-Methoxyphenyl)pyridine (**8a**).*[2m] White solid (177 mg, 96% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.54 (d, J = 3.0 Hz, 1H), 7.83 (d, J = 7.5 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.35−7.31 (m, 1H), 7.02 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ. 159.8, 148.0, 147.8, 136.4, 133.9, 128.2, 123.5, 114.5, 55.4.

*3-(3-Methoxyphenyl)pyridine (**8b**).*[28] Yellow oil (175 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85−8.84 (m, 1 H), 8.61−8.58 (m, 1 H), 7.89−7.84 (m, 1H), 7.43−7.33 (m, 2H), 7.19−7.15 (m, 1 H), 7.12−7.10 (m, 1H), 6.93−6.98 (m, 1H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ. 159.8, 148.3, 148.0, 138.9, 136.1, 134.0, 129.8, 123.2, 119.2, 113.0, 112.6, 55.0.

*3-(4-Methylphenyl)-pyridine (**8c**).*[2m] Yellow solid (160 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78−8.76 (m, 1 H), 8.51−8.48 (m, 1 H), 7.85−7.80 (m, 1 H), 7.47−7.44 (m, 2 H), 7.37−7.25 (m, 3 H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 138.0, 136.4 134.9, 134.1, 129.8, 126.9, 123.5, 21.1.

*3-(2-Methylphenyl)-pyridine (**8d**).*[3] Colorless oil (155 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 2H), 7.61 (d, J = 6.0

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230−239

Hz, 1 H), 7.27−7.19 (m, 5H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 147.9, 137.8, 137.2, 136.1, 135.3, 130.3, 129.6, 127.8, 125.8, 122.7, 20.1.

*3-Phenyl-pyridine (**8e**).*[3] Colorless oil (141 mg, 91% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86−8.85 (m, 1H), 8.59−8.57 (m, 1H), 7.88−7.84 (m, 1H), 7.59−7.57 (m, 2H), 7.50−7.34 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ. 148.4, 148.3, 137.7, 136.5, 134.3, 129.0, 128.0, 127.1, 123.5.

*4-(Pyridin-3-yl)benzonitrile (**8f**).*[2m] White solid (153 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87−8.86 (m, 1H), 8.69−8.66 (m, 1H), 7.92−7.87 (m, 1H), 7.81−7.74 (m, 2H), 7.72−7.68 (m, 2H), 7.45−7.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 148.2, 142.3, 134.7, 134.5, 132.8, 127.8, 123.8, 118.5, 111.9; HRMS (ESI) calcd. for $C_{12}H_8N_2$ [M + H$^+$] 181.0766, found 181.0766.

*3-(Thien-3-yl)pyridine (**8g**).*[6a] White solid (146 mg, 91% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1 H), 8.53−8.51 (m, 1H), 7.85−7.83 (m, 1H), 7.52−7.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 147.5, 138.6, 133.3, 131.3, 126.9, 125.7, 123.5, 121.3.

*3-(Thien-2-yl)pyridine (**8h**).*[8d] Yellow oil (150 mg, 93% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.89−8.87 (m, 1H), 8.52−8.50 (m, 1H), 7.86−7.84 (m, 1H), 7.36−7.21 (m, 3H), 7.13−7.09 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 146.8, 140.2, 132.9, 130.2, 128.2, 126.0, 124.1, 123.5.

*2-(Pyridin-3-yl)pyrimidine (**8i**).*[29] White solid (130 mg, 83% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.65 (s, 1H), 8.86−8.84 (m, 2H), 8.72−8.68 (m, 2H), 7.45−7.43 (m, 1H), 7.28−7.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 157.3, 151.3, 149.7, 135.4, 133.0, 132.3, 119.7; HRMS (ESI) calcd. for $C_9H_7N_3$ [M + H$^+$] 158.0718, found 158.0716.

*5-(Pyridin-3-yl)pyrimidine (**8j**).*[6b] White solid (175 mg, 86% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.35−9.28 (m, 1H), 8.99 (m, 2H), 8.87 (s, 1H), 8.75−8.73 (m, 1H), 7.93−7.90 (m, 1H), 7.51−7.46 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 158.1, 154.84, 154.75, 150.1, 147.8, 134.3, 134.0; HRMS (ESI) calcd. for $C_9H_7N_3$ [M + H$^+$] 158.0718, found 158.0717.

*3-(Pyridin-3-yl)quinoline (**8k**).*[3] White solid (171 mg, 83% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (d, J = 2.4 Hz, 1H), 8.97 (s, 1H), 8.68 (d, J = 4.2 Hz, 1H), 8.34 (d, J = 1.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.1, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.78−7.72 (m, 1H), 7.63−7.57 (m, 1H), 7.48−7.44 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 148.9, 148.2, 147.3, 134.8, 133.9, 133.5, 130.5, 130.1, 129.0, 128.0, 127.7, 127.4, 123.9; HRMS (ESI) calcd. for $C_{14}H_{10}N_2$ [M + H$^+$] 207.0922, found 207.0921.

*Methyl 4-(pyridin-3-yl)benzoate (**8l**).*[5e] White solid (119 mg, 56% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.63 (s, 1H), 8.15−8.11 (m, 2H), 7.94−7.90 (m, 2H), 7.67−7.62 (m, 2H), 7.42−7.38 (m, 1H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 148.9, 148.40, 142.0, 134.7, 130.3, 129.7, 127.0, 125.5, 123.7, 52.3.

*Methyl 2-(pyridin-3-yl)benzoate (**8m**).*[30] Yellow oil (107 mg, 50% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61−8.56 (m, 2H), 7.98−7.95 (m, 1H), 7.70−7.68 (m, 1H), 7.59−7.56 (m, 1H), 7.52−7.48 (m, 1H), 7.41−7.33 (m, 2H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 148.1, 147.4, 138.8, 136.6, 131.9, 131.0, 130.6, 130.1, 128.2, 123.0, 52.1.

*2-(4-Methoxyphenyl)pyridine (**9a**).*[2n] White solid (175 mg, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (m, 1H), 7.95 (d, J = 8.7 Hz, 2H), 7.72−7.65 (m, 2H), 7.19−7.17 (m, 1H), 7.00 (d, J = 8.1 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ. 160.5, 157.1, 149.5, 136.6, 132.2, 128.2, 121.4, 119.8, 114.1, 55.3.

*2-(3-Methoxyphenyl)pyridine (**9b**).*[31] Yellow oil (163 mg, 88% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71−8.68 (m, 1H), 7.76−7.72 (m, 2H), 7.60−7.52 (m, 2H), 7.39−7.37 (m, 1H), 7.26−7.21 (m, 1H), 6.99−6.95 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ. 160.1, 149.6, 140.9, 136.7, 129.7, 122.2, 120.7, 119.3, 115.1, 112.0, 55.4.

*2-(4-Methylphenyl)pyridine (**9c**).*[2n] Yellow oil (154 mg, 91% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57−8.55 (m, 1H), 7.80−7.79 (m, 2H), 7.57−7.56 (m, 2H), 7.18−7.15 (m, 2H), 7.07−7.02 (m, 1H) 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 149.4, 138.8, 136.5, 129.3, 126.6, 121.6, 120.1, 21.1.

*2-(2-Methylphenyl)pyridine (**9d**).*[32] Yellow oil (140 mg, 83% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71−8.68 (m, 1H), 7.70−7.12 (m, 1H), 7.42−7.38 (m, 2H), 7.20−7.22 (m, 4H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 149.2, 140.4, 136.1, 135.7, 130.7, 129.6, 128.2, 125.8, 124.1, 121.6, 20.3

*2-Phenyl-pyridine (**9e**).*[2m] Colorless oil (142 mg, 92% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.99 (d, J = 6.9 Hz, 2H), 7.74 (s, 2H), 7.51−7.42 (m, 3H), 7.27−7.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 149.5, 139.3, 136.7, 128.9, 128.6, 126.8, 122.0, 120.5.

*4-(Pyridin-2-yl)benzonitrile (**9f**).*[2m] Yellow solid (160 mg, 89% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75−8.73 (m, 1H), 8.13−8.11 (mz, 2H), 7.85−7.68 (m, 4H), 7.34−7.30 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 143.5, 137.1, 132.8, 132.5, 127.9, 127.4, 123.3, 120.9, 112.4; HRMS (ESI) calcd. for $C_{12}H_8N_2$ [M + H$^+$] 181.0766, found 181.0766.

*2-(Thien-3-yl)pyridine (**9g**).*[8d] Light yellow oil (133 mg, 83% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62−8.60 (m, 1H), 7.90−7.88 (m, 1H), 7.67−7.60 (m, 3H), 7.41−7.37 (m, 1H), 7.18−7.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 142.1, 136.7, 126.3, 126.1, 123.5, 121.8, 120.3.

*2-(Thien-2-yl)pyridine (**9h**).*[8d] Yellow solid (129 mg, 80% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58−7.56 (m, 1H), 7.68−7.65 (m, 2H), 7.59−7.57 (m, 1H), 7.40−7.38 (m, 1H), 7.17−7.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 149.5, 144.8, 136.6, 128.0, 127.5, 124.5, 121.9, 118.8.

*3-(Pyridin-2-yl)quinoline (**9k**).*[8e] White solid (167 mg, 81% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.79 (s, 2H), 8.18−8.16 (m, 1H), 7.96−7.83 (m, 3H), 7.77−7.75 (m, 1H), 7.61−7.59 (m, 1H), 7.35−7.33 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 150.2, 149.3, 148.2, 137.1, 133.9, 131.9, 130.0, 129.2, 128.5, 127.8, 127.0, 122.8, 120.8; HRMS (ESI) calcd. for $C_{14}H_{10}N_2$ [M + H$^+$] 207.0922, found 207.0919.

General Procedures for the Coupling Reaction of Benzyl Halides with Pyridylaluminums Catalyzed by Pd(OAc)$_2$ and (*o*-Tolyl)$_3$P. Under a dry argon atmosphere, Pd(OAc)$_2$ (0.01 mmol) and (*o*-tolyl)$_3$P (0.02 mmol) were mixed in 2 mL of toluene at room temperature, and the mixture was stirred for 10 min, followed by an addition of benzyl halide (1.00 mmol) and pyridylaluminum reagent (1.5 mmol). After stirring for 10 h at 60 °C, the mixture was diluted with dichloromethane, passed through a filter, and concentrated. The crude product was purified by column chromatography (petroleum ether/EtOAc = 5/1) to give the corresponding products **11** or **12**.

*3-Benzylpyridine (**11a**).*[15e] Yellow oil (152 mg, 90% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.50 (s, 1H), 8.45−8.43 (m, 2H), 7.45−7.42 (m, 1H), 7.31−7.14 (m, 6H), 3.95 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.0, 147.5, 139.6, 136.3, 136.1, 128.7, 128.5, 126.3, 123.3, 38.9.

*3-(4-Methylbenzyl)pyridine (**11b**).*[33] Yellow oil (166 mg, 91% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (s, 1H), 8.45−8.43 (m, 1H), 7.45−7.42 (m, 1H), 7.19−7.04 (m, 5H), 3.92 (s, 2H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.0, 147.5, 136.6, 136.1, 135.9, 129.2, 128.6, 123.3, 38.5, 20.9.

*3-(3-Methylbenzyl)pyridine (**11c**).*[33] Yellow oil (159 mg, 87% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.41 (s, 1H), 8.36−8.34 (m, 1H), 7.37−7.34 (m, 1H), 7.11−7.06 (m, 2H), 6.95−6.86 (m, 3H), 3.82 (s, 2H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9, 147.4, 139.5, 138.1, 136.4, 136.1, 129.4, 128.4, 127.0, 125.7, 123.2, 38.8, 21.2.

*3-(2-Methylbenzyl)pyridine (**11d**).*[33] Yellow oil (151 mg, 82% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.46−8.43 (m, 2H), 7.39−7.35 (m, 1H), 7.18−7.08 (m, 5H), 3.97 (s, 2H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.2, 147.5, 137.6, 136.4, 136.0, 135.7, 130.5, 129.8, 126.8, 126.2, 123.3, 36.6, 19.6.

*3-(4-Methoxybenzyl)pyridine (**11e**).*[34] Yellow oil (185 mg, 93% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.39−8.35 (s, 1H), 7.35−7.33 (m, 1H), 7.09−6.98 (m, 3H), 6.76−6.73 (m, 2H), 3.81 (s, 2H), 3.67

dx.doi.org/10.1021/jo4024123 | J. Org. Chem. 2014, 79, 230−239

(s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.1, 149.9, 147.4, 136.8, 136.1, 131.7, 129.7, 123.3, 113.9, 65.1, 38.0.

*3-(3-Methoxybenzyl)pyridine (**11f**).* Yellow oil (181 mg, 91% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42−8.37 (m, 2H), 7.39−7.36 (m, 1H), 7.16−7.10 (m, 2H), 6.69−6.62 (m, 3H), 3.85 (s, 2H), 3.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.7, 150.1, 147.6, 141.3, 136.2, 129.6, 123.4, 121.2, 114.6, 111.6, 55.1, 39.0; HRMS (ESI) calcd. for $C_{13}H_{14}NO$ [M + H$^+$] 200.1075, found 200.1071.

*3-(3-(Trifluoromethyl)benzyl)pyridine (**11h**).* Yellow oil (173 mg, 73% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (s, 1H), 7.64−7.41 (m, 5H), 7.15−7.11 (m, 2H), 4.21 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.8, 149.5, 140.3, 136.7, 132.5, 131.1, 128.9, 125.7, 125.6, 123.30, 123.25, 123.1, 121.6, 44.3; HRMS (ESI) calcd. for $C_{13}H_{10}F_3N$ [M + H$^+$] 238.0838, found 238.0843.

*3-(2-(Trifluoromethyl)benzyl)pyridine (**11i**).* Yellow oil (187 mg, 79% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.48 (s, 1H), 7.71−7.66 (m, 1H), 7.49−7.32 (m, 3H), 7.22−7.16 (m, 2H), 4.19 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.2, 147.8, 137.9, 136.3, 135.3, 132.0, 131.6, 126.7, 126.1, 123.4, 35.0; HRMS (ESI) calcd. for $C_{13}H_{10}F_3N$ [M + H$^+$] 238.0838, found 238.0843.

*4-(Pyridin-3-ylmethyl)benzonitrile (**11j**).*[34] Yellow oil (146 mg, 75% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.50 (s, 2H), 7.61−7.58 (m, 2H), 7.48−7.45 (m, 1H), 7.31−7.22 (m, 3H), 4.05 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.7, 147.8, 145.1, 136.0, 134.6, 132.1, 129.3, 123.3, 118.4, 110.0, 38.6.

*3-(Naphthalen-2-ylmethyl)pyridine (**11k**).* Yellow oil (188 mg, 86% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.41 (s, 1H), 8.27 (s, 1H), 7.74−7.57 (m, 3H), 7.28−7.06 (m, 5H), 6.70−6.88 (s, 1H), 4.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.8, 147.3, 135.7, 135.0, 133.7, 131.5, 128.5, 127.3, 127.1, 126.0, 125.5, 125.3, 123.6, 123.1, 35.9; HRMS (ESI) calcd. for $C_{16}H_{14}N$ [M + H$^+$] 220.1121, found 220.1126.

*2-Benzylpyridine (**12a**).*[15i] Yellow oil (144 mg, 85% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.54−8.52 (m, 1H), 7.56−7.50 (m, 1H), 7.32−7.18 (m, 5H), 7.09−7.05 (m, 2H), 4.15 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.9, 149.2, 139.4, 136.4, 129.0, 128.5, 126.2, 123.0, 121.31, 44.6.

*2-(4-Methylbenzyl)pyridine (**12b**).*[15i] Yellow oil (157 mg, 87% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.53 (s, 1H), 7.56−7.53 (m, 1H), 7.13−7.09 (m, 6H), 4.11 (s, 2H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 149.3, 136.4, 135.8, 129.2, 128.9, 122.9, 121.1, 44.2, 20.9.

*2-(3-Methylbenzyl)pyridine (**12c**).*[35] Yellow oil (153 mg, 84% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.54−8.52 (m, 1H), 7.57−7.51 (m, 1H), 7.21−7.00 (m, 6H), 4.11 (s, 2H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 149.3, 139.3, 138.1, 136.5, 129.8, 128.4, 127.1, 126.1, 123.1, 121.2, 44.6, 21.3.

*2-(2-Methylbenzyl)pyridine (**12d**).*[36] Yellow oil (147 mg, 80% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56−8.54 (m, 1H), 7.55−7.50 (m, 1H), 7.17−7.07 (m, 5H), 6.96−6.93 (m, 1H), 4.18 (s, 2H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.7, 149.3, 137.5, 136.9, 136.5, 130.4, 130.2, 126.8, 126.2, 122.7, 121.1, 42.4, 19.8.

*2-(4-Methoxybenzyl)pyridine (**12e**).*[15i] Yellow oil (181 mg, 91% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55−8.52 (m, 1H), 7.59−7.54 (m, 1H), 7.23−7.18 (m, 2H), 7.12−7.07 (m, 2H), 6.88−6.83 (m, 2H), 4.09 (s, 2H), 3.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 158.1, 149.3, 136.5, 131.6, 130.0, 122.9, 121.1, 114.0, 55.2, 43.8.

*2-(3-Methoxybenzyl)pyridine (**12f**).*[37] Yellow oil (177 mg, 89% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55−8.53 (m, 1H), 7.60−7.55 (m, 1H), 7.22−7.10 (m, 3H), 6.87−6.75 (m, 3H), 4.13 (s, 2H), 3.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.8, 159.7, 149.3, 141.0, 136.6, 129.6, 123.1, 121.4, 121.3, 114.8, 111.8, 55.1, 44.7.

*2-(4-(Trifluoromethyl)benzyl)pyridine (**12g**).*[15i] Yellow oil (182 mg, 77% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56−8.55 (m, 1H), 7.62−7.54 (m, 3H), 7.39−7.36 (m, 2H), 7.17−7.11 (m, 2H), 4.21 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.8, 149.6, 143.5, 137.0, 136.8, 129.4, 126.8, 125.5, 125.4, 123.2, 121.6, 44.4.

*2-(3-(Trifluoromethyl)benzyl)pyridine (**12h**).*[15i] Yellow oil (173 mg, 73% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.57 (s, 1H), 7.64−7.41 (m, 5H), 7.14−7.11 (m, 2H), 4.21 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.8, 149.6, 140.4, 136.8, 132.5, 128.9, 125.8, 125.7, 123.4, 123.3, 123.2, 121.6, 44.3.

*2-(Naphthalen-1-ylmethyl)pyridine (**12l**).*[15i] Yellow oil (153 mg, 70% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59−8.58 (m, 1H), 8.02−8.00 (m, 1H), 7.86−7.77 (m, 2H), 7.46−7.43 (m, 5H), 7.10−7.08 (m, 1H), 6.97−6.94 (m, 1H), 4.63 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.8, 149.2, 136.5, 135.2, 133.9, 132.1, 128.6, 127.7, 127.5, 126.1, 125.6, 124.5, 122.9, 121.2, 42.3.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectra of heterobiaryl compounds containing 2-thienyl, 3-thienyl, 2-pyridyl, and 3-pyridyl moieties. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors are thankful for the financial support of this work from the National Natural Science Foundation of China (21172003, 21372009) and the Natural Science Foundation of Anhui Province (11040606M36).

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